ENDOTHELIAL DYSFUNCTION AND VASOREACTIVITY IMPAIRMENT MEASUREMENT IN NON-DIABETIC HYPERGLYCEMIC PATIENTS USING THE ENDOPAT DEVICE

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O-1

7TH FRAMEWORK PROGRAM – FUNDED EHEALTH SYSTEMS FOR DIABETES

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Diabetes is a condition of rising prevalence in Europe, which treatment is not only costly, but also very laborious. Thus, it creates major problems to European public health. In the era of limited resources in healthcare – both in terms of workforce and budget – there is an urgent need to redesign approaches to diabetes treatment. This might be possible with employment of novel eHealth technologies to both prevention and treatment of diabetes.

European Commission, being fully aware of this situation, decided to facilitate research and technological development in the field of diabetes. Thus, several RTD projects were funded under the 7th Framework Program. Of these, five complementary projects will be presented during this workshop:

- AP@home (Artificial Pancreas at home) – project aiming at developing a functional artificial pancreas
- REACTION Project – project aiming at developing an integrated ICT platform that supports improved long-term management of diabetes
- COMMODITY12 – project aiming at developing a system providing COntinuous Multi-parametric and Multi-layered analysis Of DIabetes TYpe 1 & 2
- EMPOWER – project aiming at supporting the self-management of diabetes patients through a modular and standards-based Patient Empowerment Framework
- GoCarb – project aiming at designing a computational system which will support individuals with type 1 diabetes in automatically estimating the grams of carbohydrate in a meal in near real-time

Due to its large spectrum, the workshop will be a perfect forum to learn latest European eHealth initiatives for diabetes, and get in touch with newest eHealth technologies. Both academia and business are cordially invited to take part in this event.

O-2

DO WE NEED A REMOTE MONITORING SYSTEM IN THE PRODUCT? REMOTE MONITORING - PRO

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During the initial outpatient pilot-trials of the DREAM project the sessions are performed under the supervision of a diabetes research team consisting of an onsite physician specialized in diabetes treatment and technical supporter engineer. The patients glucose levels (glucose sensor and SMBG), and technical alarms were transferred from patient's home via the internet and the Remote safety and control diabetes management system (MDRS) to the command and control center within the clinic and externally to the other team members at other remote sites. Optionally, the study team can provide the patient's caregivers with a PC which will be connected to the MDRS system and will show only the information and alarms relating to that specific patient. This allows the patient's caregiver to view glucose levels and insulin delivery from the own bedside. If required, support will be provided over the phone by the study team. The MDRS system is composed from two modules, the Remote diabetes monitoring (RDM) module and the Safety Module for patient alerts. This software is based on the ZONTM Control Software Package of Galooli Ltd. It is designed to transfer all the data from the patient to a remote control & command center which is capable of controlling tens of patients simultaneously.

Thus, the remote monitoring enables the supervising personnel to alert the patient and intervene in cases of impending hypoglycemia, long standing hyperglycemia and technical faults of any component of the AP system and provides an added benefit of the whole closed loop system.

O-3

KEYNOTE SPEAKER: GLUCOSE MONITORING - AND BEYOND?

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Back in the 1980s when first programmes for patient education were established and validated monitoring glucose control became recognized as being a valuable part of diabetes care. Technical improvement in BG monitoring like the development of more accurate, small und fast acting devices led to a broad use of SMBG. Besides technical improvement SMBG was focused to structured measurements providing information on daily glucose variability. This challenge got support by the development of CGMS. New systems became a treatment complement predominantly used in patients on intensive insulin treatment regimens. Glucose sensor augmented insulin pump treatment meanwhile approaches the long aimed-for closed-loop system. Additional steps like the low glucose suspend to prevent hypoglycaemic reactions as well as the development of self-learning algorithms will probably further enhance glycaemic control. Beyond these technical device oriented steps into the future measures to improve patient empowerment and compliance need to be enforced. According to ongoing research the near future will probably provide each diabetic patient with some kind of a CGMS replacing currently used conventional structured SMBG. The use of smart phones or related e-health technology providing easy and time-sparing measures for physical activity (e.g. kind of, duration, intensity), nutrition (e.g. carbohydrate content/counting, fat content) and stress (illness, accident, psychological stress) combined with SMBG/CGM as well as information on blood pressure, lipids, body weight, smoking habits, etc. could help to improve treatment quality when embedded into a continuous feedback loop between patients and caring medical personal.

O-4

A RANDOMIZED TRIAL OF A HOME SYSTEM TO REDUCE NOCTURNAL HYPOGLYCEMIA IN TYPE 1 DIABETES

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Background: Overnight hypoglycemia is common in individuals with type 1 diabetes (T1D) and has many ramifications, including being a major barrier for optimal glycemic control. It is likely the predicted low-glucose suspend (PLGS) feature will be the second component of the artificial pancreas (AP).

Methods: Following in-hospital safety studies, we have participated in an in-home randomized trial to determine whether nocturnal hypoglycemia could be safely reduced by temporarily suspending insulin pump delivery when hypoglycemia was predicted by an algorithm based on continuous glucose monitor (CGM) glucose levels. Following an initial run-in phase, 45 individuals with T1D (age 15–45 years) participated in a 42-night trial (total 1,912 nights) of randomized PLGS vs. control nights.

Results: Overnight hypoglycemia with at least one CGM value ≤ 60 mg/dl occurred in 196 of 942 (21%) intervention nights versus 322 of 970 (33%) control nights (odds ratio 0.52, 95% confidence interval 0.43 to 0.64, $P < 0.001$). Median hypoglycemia area under the curve was reduced by 81% and hypoglycemia lasting >2 hours was reduced by 78%. Median morning blood glucose was 129 mg/dl after control nights and 144 mg/dl after intervention nights ($P < 0.001$). In each arm, 6% of nights had morning blood glucose >250 mg/dl and morning ketosis was present $<1\%$ of the time.

Conclusion: Use of a nocturnal PLGS system can substantially reduce overnight hypoglycemia, with only a slight increase in morning hyperglycemia and no increase in ketosis.

O-5

PREDICTIVE LOW GLUCOSE MANAGEMENT WITH SENSOR AUGMENTED CSII IN RESPONSE TO EXERCISE

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Background: Predictive Low Glucose Management (PLGM) may help prevent hypoglycemia by stopping insulin pump delivery based on predicted sensor glucose (SG) values.

Methods: Hypoglycemic challenges were simulated using the FDA-accepted glucose simulator with 100 virtual patients. PLGM was then tested with a system composed of a Paradigm insulin pump, an Enlite glucose sensor, and a Blackberry-based controller. Subjects (n = 22) on CSII [5f, 17m; age 15 (14–20) years, diabetes duration 7 (2–14) years; HbA1c 8.0 (6.7–10.4)%, (median(range)) exercised until the PLGM system suspended insulin delivery or until the reference blood glucose value (HemoCue®) reached the predictive suspension threshold setting.

Results: PLGM reduced hypoglycemia (<70 mg/dL) *in silico* by 26.7% compared to no insulin suspension, as opposed to a 5.3% reduction in hypoglycemia with use of LGS. The median duration of hypoglycemia (time spent <70 mg/dL) with PLGM was significantly less than with LGS (58 min vs 101 min, respectively, $p < 0.001$). In the clinical trial the hypoglycemic threshold during exercise was reached in 73% of the patients and hypoglycemia was prevented in 80% of the successful experiments. The mean ($\pm$SD) sensor glucose at predictive suspension was 92 ± 7 mg/dL resulting in a post suspension nadir (HemoCue®) of 77 ± 22 mg/dL. The suspension lasted for 90 ± 35 (range: 30 to 120) min resulting in a sensor glucose at insulin resumption of 97 ± 19 mg/dL.

Conclusions: *In silico* modeling and early feasibility data demonstrate that PLGM may further reduce the severity of hypoglycemia beyond that already established for algorithms that use a threshold-based suspension.

O-6

SAFE CONTROL ALGORITHMS TO PERSONALIZE THE OUTPATIENT ARTIFICIAL PANCREAS

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Model-based control algorithms for the artificial pancreas have been demonstrated in numerous clinical trials as effective

methods to manage overnight periods, postprandial excursions, and even some forms of physical exertion (mild to moderate exercise). However, the requirements for patient safety are somewhat reduced in the in-clinic setting where medical professionals (and often engineers) are hovering over the patient for the duration of the trial.

As we move to the outpatient testing for the artificial pancreas, patient safety is a paramount concern. Our experience points strongly to personalization as a key component of an algorithm for effective and safe feedback control. The overall approach in our studies includes three main elements: MPC with time-varying zones, a Health Monitoring System (HMS) overlay, and customization in the form of subject specific attributes (e.g., insulin sensitivity). Our zone MPC has been extended to deal with (personalized) varying safety concerns over diurnal cycles, and allows the design of safe strategies for the overnight window. Our Health Monitoring System (HMS) incorporates hypoglycemic alarming as well as meal detection, signaling to the subject for possible interventions (snack ingestion, missed bolus, etc.). Finally, we have explored a number of approaches for personalization, from the model parameters used in MPC to adaptation that takes place over hours or days to ''learn'' patient attributes. All of these elements enhance the safety of a closed-loop artificial pancreas. Clinical data from pilot outpatient studies will be discussed along with algorithmic details.

O-7

21ST CENTURY TECHNOLOGY AND ITS USE IN DIABETIC FOOT CARE

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As Auguste Comte said two centuries ago, ''Demography is destiny''. Even he, however, couldn't foresee the massive changes occurring at breakneck speed in our world.

Over the past generation, significant advances in care have led to incremental improvements in healing worldwide. However, it may be argued that the most potent advances in healing have been in organization of care. Technologies are now emerging that may allow further enhancements of organization and integration of care while also bringing in much needed bedside, chairside, and in-home diagnostics to identify key points in healing and potential early warning signs for recurrence. This symposium reviews what are believed to be several key areas of change over the next generation all yielding specific advances in wound diagnostics. The authors believe that devices will be organized into personal health servers in cloud-synchronized devices already existing in the home (eg, a scale), the clinic, and on (or in) the patient. This talk will explore the intersection of consumer technology with medical devices and their collision– or perhaps synergy – with our aging species.

O-8

THE ROLE OF THE INTERVENTIONAL RADIOLOGIST IN DIABETIC FOOT MANAGEMENT

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The role of the radiologist in diabetic foot management.

Diabetic foot (DF) is recognized as one of the most serious complications of diabetic disease. About 5% off all patients with diabetes type II will develop an arterial diabetic foot problem. Up to 70% of all lower-leg amputations are performed in patients with diabetes and up to 85% of all amputations are preceded by an ulcer. Ulcer prevention is therefore recognized to be the best way to prevent amputation. However when an ulcer is present, the primary need is to achieve fast ulcer healing. If there is also concomitant infection the ulcer healing is often more difficult. Optimal wound care, antibiotics, off loading and other techniques should all be applied in daily practise to achieve ulcer healing. Active revascularisation plays a crucial role in achieving ulcer healing. Non-surgical revascularisation options for DF have expanded over the last decade and have become a prominent tool to prevent amputation

The radiologist plays in important role in the management of the diabetic foot. Both imaging and treatment are closely related. The definition and diagnosis of diabetic foot syndrome is not the same as CLI, and new diagnostic parameters can play an important role.

Traditional imaging with duplex, CTA or MRA will guide the endovascular treatment options. Both open and endo treatment have the same outcome regarding limb salvage. Decision on all available treatment options is best done in a Multidisciplinary team.

O-9

CURRENT STRATEGIES FOR THE TREATMENT OF THE SEVERELY INSULIN RESISTANT PATIENT

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Historically, the most severely insulin resistant patients had high levels of insulin antibodies from animal insulins. This resulted in the development of U-500 regular insulin in the early 1950s. Over time, this was also used for the more insulin resistant patients with type 2 diabetes. More recently, the use of U500 insulin has become extremely common due to the explosion of the severely insulin resistant patient. Many don't appreciate that our currently available U100 insulin glargine has minimal effect with doses greater than 1 u/kg. As a way to improve absorption, we are learning that splitting the large depot into more than one site can improve glycemia, but robust trials examining this strategy are lacking. Since the main rationale for using insulin analogues is to reduce hypoglycemia risk, it is reasonable and perhaps preferable to use NPH as the basal insulin for these patients. As for mealtime insulins, there are few studies comparing human insulin to a rapid-acting analogue for these patients, but the fast-acting insulins will have a prolonged activity with higher doses. The other strategy that often helps is adding a GLP-1 agonist to these patients. Small trials have shown improvements in glycemia and weight.

For patients who still require high-doses of insulin, we currently utilize U-500 regular insulin that has a longer duration of action than U-100 regular insulin, and thus we use it both as a basal and a prandial insulin. Indeed, many use it in an insulin pump with good success.

O-10

PATIENT NARRATIVES ON THEIR EXPERIENCES OF CGM

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Relatively little is known about the patient experience of real-time continuous glucose monitoring (CGM) in type 1 diabetes when used in everyday practice and when described in patients' own words. We therefore conducted an online survey of patient narratives about continuous CGM, with analysis of the first 100 responses by qualitative framework analysis. There were 50 adults and 50 children, median CGM use 1.9 years, with 87% using it in conjunction with CSII. We identified 6 themes, with various subthemes: metabolic control, life on CGM, GGM procedures, technical issues, financial issues and attitudes to CGM. Most patients had an overwhelmingly positive experience with reduced HbA1c and hypoglycaemia and improved quality of life. Patients tended to recognize and accept limitations such as sensor inaccuracies. Some healthcare professionals were reported to have a very negative attitude to the technology. Many patients said that CGM was life-changing.

O-11

PROMOTING DIABETES SELF CARE: WHAT WORKS AND WHAT DOESN'T

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Living with diabetes can be very challenging. We ask patients to perform multiple tasks day after day including monitoring blood glucose at frequent intervals, planning meals, calculating insulin doses based on current blood glucose and carbohydrate intake and balancing meals and medication with physical activity to achieve and maintain glycemic targets. It is no wonder that many patients have difficulty doing all that they are asked to do on a daily basis.

Research has shown that knowledge is not enough to promote diabetes self-care and behavior change. A number of behavioral change theories offer the clinician guidance in preparing, motivating and supporting patients in diabetes self-care. These include patient empowerment, health belief model, transtheoretical model and motivational interviewing. The patient empowerment model puts the patient in control of their self-care and promotes informed decision-making. In the health belief model, benefits and barriers to performing self-care behaviors are identified and potential strategies to reduce barriers are generated. The transtheoretical model views behavior change as an ongoing process of stages ranging from precontemplation where the patient is unaware of a problem to maintenance where the patient has the ability to perform self-care over time. Motivational interviewing is an approach where the clinician uses active listening and encourages and supports self-efficacy. With the availability of more and more technological tools to manage diabetes, it is more important than ever to provide comprehensive education and support to our patients in order for them to succeed in controlling their diabetes without compromising quality of life.

O-12

HOW TO SAFELY AND EFFECTIVELY TRAIN PATIENTS TO USE INSULIN PUMPS AND STAY ON THE DEVICE

H. Rogers[1]

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How to Assist Patients to use an Insulin Pump Safely and Effectively and to Stay on the Device

People with diabetes wish to be able to **self-manage** their diabetes in order to **achieve biomedical outcomes** within target **and they also** desire to have the **burden** of self-management reduced to the extent that their quality of life is improved. Insulin Pump therapy can assist, but this is not always the case. A certain approach needs to be in place in order to ensure that Insulin Pump therapy is not just another treatment given to patients with an expectation that they will both master it and achieve improved outcomes. Education is the key to ensuring improvements in biomedical outcomes, in self-management and in burden reduction. And not just any education programme - structured education that is underpinned by facets that lead to mastery and maintenance is required. Health Care Professionals (HCPs) are accustomed to providing education that includes knowledge and self-management skills, however HCPs are beginning to recognise that these alone are not enough. If the twin goals of self-management and reduced burden are to be achieved then the structured education also needs to incorporate ways to improve confidence, participation in goal setting and decision making, coping skills, and self-efficacy.

Insulin pump pathway
Choice of pump
Trial using saline
Education - bite-sized chunks
Availability of HCPs and Pump Expertise

We will examine the attributes above to establish how the knowledge and skills needed for Insulin Pump therapy can be best presented by HCPs.

O-13

HOW TO SAFELY AND EFFECTIVELY TRAIN PATIENTS TO USE CGM AND STAY ON THE DEVICE

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Education and the use of continous glucose monitoring
Ana Gianini

Modern technology entered diabetes treatment with continuous subcutaneous insulin infusion (CSII) and was frequently leading to improved matabolic control. In the last 10 years next to CSII, systems for continuous glucose monitoring (CGM) gave new information about glucose excursions in different situations. According to different databases such as Type 1 Diabetes Exchange more than 10% of adults are using CGM routinely, next to them 3% in pediatric cohorts.

In Slovenia children and adolescents use CSII in more than 80% (530 from 660). The use of sensors was reimbursed for children in February 2010 and since then the number of young patients that continuously use CGM is increasing steadily, reaching 10% of pump users in 2013.

Structured education for patients, families and often professional caregivers about the sensor use is of extreme importance at the CGM introduction. In the first month patients can be confused by the number of informations and alarms from CGMS leading frequently to disappointment and discontinuation of CGM use.

Topics discussed at CGM introduction are

- Proper insertion of the sensor
- Importance of good calibration
- Alarms, troubleshooting

- ISIG signal
- Practical use of CGM (profiles, correction boluses, food boluses, sport activity, sick days, school or kindergarten regimen …)

Sometimes parents are advised to shut down the alarms for the first sensor or even for the first month of sensor use. In this case they simply follow CGM curve and values on the screen.

24/7 telephone support can help to support the patient.

O-14

THE SWEET-PROJECT - USE OF TECHNOLOGY FOR LONGITUDINAL BENCHMARKING OF INTERNATIONAL PEDIATRIC DIABETES CENTRES 2006 TO 2013: DATA ANALYSIS FROM 122.853 VISITS FROM 10.767 PATIENTS

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Objectives: ''SWEET'' is an acronym derived from ''Better control in Pediatric and Adolescent diabeteS: Working to crEate cEnTers of Reference'' and is based on a partnership of established national and European diabetes organizations (www.sweet-project.eu) led by ISPAD. Data in participating centres were directly extracted from 2006 ongoing from local electronic health records.

Methods: The SWEET Online platform allows presently nineteen centres from fifteen countries to connect to one unified anonymized diabetes database. Aggregate data are de-identified and exported for longitudinal health and economic data analysis.

Results: The number of patients and patient visits increased from 2006 (n = 921) to 2012 (n = 7633), currently including 10,767 patients and 122,853 patient-visits overall. For example, patients with a valid HbA1c in the database rose from 744 (mean HbA1c: 8,1%) in 2006, to 1161 (8,1%) in 2007, 1412 (8,2%) in 2008, 1972 (8,2%) in 2009, 3320 (8,0%) in 2010, 5952 (7,9%) in 2011 and 6372 (7,9%) in 2012. The percent of patients within the target HbA1c range <7.5% increased steadily: 33% (2010), 35% (2011), 40% (2012). Over time the completeness of data increased from 82% to 98% (HbA1c), 78% to 83% (height), 78% to 84% (weight), 50% to 60% (blood pressure), 12% to 22% (microalbuminuria screening) and 30% to 45% (hyperlipidemia screening).

Conclusions: Ongoing collection of benchmarking data motivates centres to improve data collection and reflects improving glycemic control in most participating European pediatric diabetes centres. While the degree of completeness is close to 90% or above for HbA1c, weight and height, the assessment of diabetes-associated co-morbidities leaves much room for improvement. Thus, information technology allows transparent analysis of real life diabetes treatment data as a basis for local center improvement, scientific studies and health economic analyses.

O-15

INTERNATIONAL ASSESSMENT OF DIABETES MANAGEMENT, GLYCEMIC CONTROL AND DIABETES-RELATED BURDEN IN YOUTH WITH TYPE 1 DIABETES (T1D): THE TEENS STUDY

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Background: TEENS, a cross-sectional study in 21 countries, collected data on management, HbA_{1c}, acute complications, and burden from ~6200 youth with T1D of ≥1 year and onset <18 y/o. Results from 1000 participants from 2 countries completing the study provide direction for future post-hoc analyses.

Objectives: To examine treatments and HbA_{1c} in T1D youth from USA/Russia in three predefined age groups and relate HbA_{1c} to acute complications and diabetes burden.

Methods: 25 US/20 Russian centers uniformly collected data by interview, record review and survey. A recruitment ratio of 25%/50%/25% was implemented in 3 age groups (8–12/13–18/19–25 y/o). Participants were sampled sequentially to avoid bias.

(n=USA/RUS)	8-12y/o (n=260) (n=130/130)	13-18y/o (n=493) (n=247/246)	19-25y/o (n=247) (n =122/125)
Diabetes Management			
Daily BG Monitoring (median)	7 / 5	4 / 4	3 / 3
Pump %	72 / 21	62 / 24	56 / 8
Syringes/Pens %	26 / 79	38 / 76	43 / 91
Insulin total daily dose U/kg (median)	0.85 / 0.90	0.96 / 0.91	0.81 / 0.89
Insulin dose never missed (%)	45 / 77	39 / 63	33 / 70
Using Carb counting (%)	95 / 66	86/ 52	80 / 66
Daily exercise ≥30 min/day every day (%)	41 / 15	24 / 13	16 / 24
HbA1c (%) median	7.9 / 8.8	8.4 / 9.0	8.2 / 8.0
Acute complications* (% patients)			
DKA	3.1 / 7.7	5.7 / 8.5	1.6 / 3.2
Severe hypoglycemia (Seizure/loss of consciousness)	1.5 / 3.1	0.4 / 0.8	3.3 / 0
Diabetes burden total score (0 – 100) (100=highest burden, median score shown)			
PAID (patient)	-	14 / 23	16 / 28
PAID-PR (parent)	45 / 56	46 / 53	-

*During past 3 months

HbA_{1c} was measured uniformly; targets: < 7.5% (58 mmol/mol) < 18 y/o (ISPAD); < 7% (53 mmol/mol) ≥ 18 y/o (ADA). Burden was assessed with the PAID (20-item) for patients (≥ 13 y/o) and PAID-PR (18-item) for parents of youth (≤ 18 y/o). Acute complications were assessed (% with DKA, severe hypoglycemia [seizure/coma]).

Results: Median T1D duration was similar: 7.0 years (0.6–22.1) in US; 6.3 years (0.8–23.5) in Russia. Both syringes/pens were used by 36%/80% of US/Russian patients; pumps were used by 63%/19%, respectively. In both countries, only a small minority of participants achieved HbA_{1c} targets (24%/16% in USA/Russia). Parents from both countries perceived greater diabetes burden than patients across all ages. Outcomes (DKA/hypoglycemia) are shown by age group (table).

Conclusion: Diabetes burden appears to be universal; patients experience suboptimal HbA_{1c} and acute complications. In both countries, despite differences in management, there are opportunities to implement management programs to improve HbA_{1c} and outcomes.

Study sponsored by Sanofi.

O-16

GLYCEMIC VARIABILITY DOES NOT PREDICT POSTOPERATIVE OUTCOMES IN ELECTIVE CARDIAC SURGERY PATIENTS ON TIGHT GLUCOSE CONTROL

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Objective: The aim of our study was to assess the relationship between glycemic variability and postoperative complications in elective cardiac surgery patients with either perioperatively (PERI) or postoperatively (POST) initiated protocols for tight glucose control (TGC).

Material and methods: 2383 patients undergoing elective cardiac surgery were randomized into either PERI (1134 subjects) or POST (1151 subjects) group according to the time of initiation of intravenous insulin infusion therapy. Glycemic variability was calculated using selected formulas including SD (standard deviation) and MAGE (mean amplitude of glycemic excursions). Adverse events from any cause were collected during the postsurgical hospital stay.

Results: In the whole cohort, perioperatively initiated TGC markedly reduced the number of patients with postoperative complications (23.8 vs. 31.4%, $p < 0.001$) in spite of only modest improvement of glucose control (blood glucose 6.6 ± 0.7 vs. 6.7 ± 0.7 mmol/l, $p < 0.001$). The positive effect of TGC on postoperative complications was driven by non-diabetic patients (20.3 vs. 31.7%, $p < 0.001$) while no significant effect was seen in the diabetic subgroup (33.2 vs. 30.5%, n.s.). No clinically significant difference in glycemic variability could be seen between any of the study groups (SD 3.33 ± 0.73 vs. 3.34 ± 0.71, n.s. for PERI vs. POST group). No correlation between the number of postoperative complications and various glycemic variability indices was observed in the study.

Conclusion: Perioperative initiation of intensive insulin therapy during elective cardiac surgery reduces postoperative morbidity only in non-diabetic subjects. Glycemic variability does not seem to play an important role in postoperative outcomes of elective cardiac surgery patients.

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O-17

LUDIDIAB TRIAL: IMPACT OF A SERIOUS GAME ON KNOWLEDGE AND SKILLS OF YOUNG PATIENTS ABOUT THEIR TYPE 1 DIABETES

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We hypothesized that the use of a serious game designed for education of young T1D subjects could improve their knowledge and skills, as an alternative to usual education. In this before-after pilot study, we used the game ''L'affaire Birman'', designed on a problem-solving concept, focusing on diet, flexible insulin therapy and emergency situations. The game was used in an unstructured program at home: patients were asked to play at least one complete game then were evaluated before (T0), a few days after (T1), and 6 months after (T2) this experiment with PedCarbQuiz (PCQ) and Diabetes Self Monitoring Profile (DSMP), two validated questionnaires. 47 patients were included in 5 French hospitals: age 13.9 ± 2.1 years; M/F 22/25; diabetes duration 5.9 ± 3.7 years; treatment: MDI 51.1%, CSII 49.9%; baseline HbA1c 8.4 ± 1.3%; baseline PCQ and DSMP scores 31.9 ± 6.7 and 59.1 ± 9.9, respectively. 20% patient did not play any complete game and 47% only one game. PCQ improved at T1 and T2: 33,8 ± 5,0 and 36,1 ± 3,9 ($p < 0.001$), respectively. A greater PCQ improvement was found in patients with higher baseline HbA1c. DSMP score was not significantly improved. HbA1c was not different from baseline at T1 and T2: 8,4 ± 1,2 and 8,0 ± 0,8% (ns). This slight efficiency highlights weaknesses of such educational tool: methods of use, game design and/or methods of assessment must be questioned. This result suggests

to include such game in a complete and structured education program supervised by health professionals, with initial objectives and regular debriefing.

O-18

ARE WE MISSING SOMETHING? CONTINUOUS GLUCOSE MONITORING COMPARED WITH POCT AMONG HOSPITALIZED TYPE 2 DIABETES PATIENTS ON BASAL-BOLUS INSULIN THERAPY

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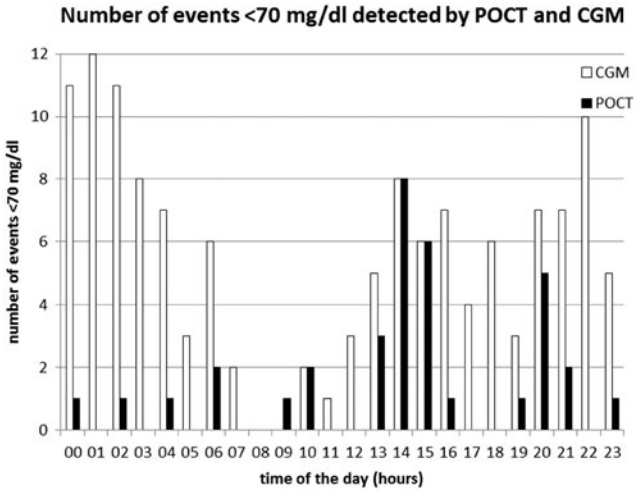
Background: Glycaemic management in the hospital is based on glucose point-of-care testing (POCT) which lacks continuous information particularly in detecting hypoglycaemic events. The aim of this study was to analyse and compare the capability to detect hypoglycaemic events.

Methods: A total of 59 patients with type 2 diabetes (age: 68.9 ± 9.5 yr, DM duration 14.3 ± 10.3 yr, A1C: 8.5 ± 3%, BMI: 29.9 ± 6 kg · m^{-2}, length of stay 8 ± 4.5 days (mean ± SD)) were treated with basal-bolus insulin therapy. Glucose POCT was performed at least 4 times per day (premeal, before bedtime), CGM was performed with the iPro2 system (MiniMed Medtronic) which was calibrated with the blood glucose measurements retrospectively.

Results: 8,578 hours were recorded with 1,480 paired blood glucose-sensor readings. After adjusting the offset of sensor data 35 hypoglycaemic events.

Conclusion: Although the sensitivity of the CGM sensor signal system was low the data indicate a high number of hypoglycaemic events.

Acknowledgement: The study is supported by the European Commission, Project REACTION (FP7-248590).



O-19

INPATIENT GLYCEMIC CONTROL BY CONTINUOUS GLUCOSE MONITORING (CGM) VERSUS CAPILLARY POINT-OF-CARE (POC) TESTING IN TYPE 2 DIABETICS

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Background: Capillary glucose finger-stick tests are the accepted method of glucose monitoring in hospitals. No previous studies compared the efficacy of CGM in the management of hyperglycemia in general medicine type 2 diabetics. This prospective randomized study compared glycemic control (CGM vs bedside POC testing) in non-ICU patients treated with insulin for ≥ 3 days. Patients and hospital staff were blinded to CGM data. POC testing measurements were performed before and 2-h after meals, at bedtime and 3 AM. Primary outcomes were differences in daily BG, hypoglycemia (180 mg/dl) events between groups.

Methods: 40 insulin-naïve patients (age: 65.8 ± 8 yr, DM duration 14.7 ± 9 yr, admission BG: 251 ± 9 mg/dl, A1C: 9.7 ± 2.4%, ± SD) were treated with glargine and glulisine at a starting total dose of 0.4 U/kg/day if BG was 140–200 mg/dl and 0.5 U/kg/day if BG was 200–400 mg/dl.

Results: We observed no difference in daily BG after the 1st day of treatment between groups (176,2 ± 33,9 vs 176,6 ± 33,7 mg/dl, p:0.828). 10 patients with BG180 mg/dl was 36.8% by CGM and 42.1% by POC, p = 0.828.

Conclusion: The use of CGM recognized more hypoglycemic events compared to POC testing. It could be beneficial to use real-time CGM in the hospital to detect hypoglycemia more timely.

O-20

PEDOMETER USE TO EVALUATE PHYSICAL ACTIVITY, AND MOTIVATE TYPE 2 DIABETIC PATIENTS, FOR BETTER METABOLIC CONTROL AND WEIGHT REDUCTION

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Background and aims: Physical activity (PA) is at the cornerstone of diabetes prevention and care. It helps to improve metabolic control, lipid profile, and to reduce weight. The aim of our study was to demonstrate the positive effect of a single session of PA to the glycaemic profile, and to use the technology for increasing daily physical activity, with a positive impact on metabolic, weight and lipid profile.

Patients and method: 50 patients with type 2 diabetes, were recruited for an 8-week training session. Every PA session lasted 30 minutes of brisk walking. The number of daily steps was measured through a pedometer, and the participants were encouraged to complete at least 10000 steps/day. All the patients had completed anthropometric measures, fat body composition and lipid profile at the beginning and the end of the study period.

Results: 30 (60%) of the patients completed the 8-week training session, 17 (56.6%) males. Mean age 52.07 ± 11.3 yrs,

mean diabetes duration 4.37 ± 2.9 yrs. Mean HbA1c decreased from 8.43 ± 1.09% to 8.17 ± 1.07% (p = 0.07), mean weight 81.74 ± 20.8 kg vs 79.47 ± 20.11 kg (p < 0.05), mean of daily steps 4535 ± 2590 vs 11315 ± 2013.6 (p < 0.01). Body fat composition decreased from 33.04 ± 11.8% to 31.09 ± 11.2% (p < 0.05). The patients had a slight increase in HDL cholesterol 54.7 ± 7.65 mg/dl to 59.05 ± 7.29 mg/dl.

Conclusions: Physical activity, even in simple everyday actions, should be an integrated part of diabetes treatment and weight control. Technology, assuring measurable results, could help diabetic patients to implement and increase PA in their daily life.

O-21

EVALUATION OF GLYCEMIC CONTROL USING AN ALGORITHM FOR BASAL BOLUS INSULIN THERAPY IN HOSPITALISED PATIENTS WITH DIABETES MELLITUS TYPE 2

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Background and aims: Current guidelines recommend fasting/pre-meal blood glucose (BG) levels of <140 mg/dl in hospitalized patients. The aim of this study was to evaluate glycemic control and usability of a workflow-integrated algorithm for basal-bolus insulin therapy (REACTION algorithm) for glycemic management in patients with diabetes mellitus type 2 (T2D) hospitalized at the general ward.

Methods: In this feasibility study in 30 T2D patients (11 female, age 71 ± 10 years, HbA1c 69 ± 25 mmol/mol, BMI 30 ± 6) blood glucose management was performed using the REACTION algorithm running on a tablet PC. BG measurements were performed four times per day (pre-breakfast, pre-lunch, pre-dinner, at bedtime) and insulin injections were given according to the advice of the algorithm. A basal-bolus regimen with advice for total daily dose (TDD) (50% basal insulin, 50% pre-meal bolus insulin with additional corrective dose if necessary) was generated once daily. In case of safety concerns nursing staff could overrule the advice.

Results: Mean BG was 155 ± 32 mg/dl. 15/913 measurements (1.6%) were in the hypoglycemic range (< 70 mg/dl). Mean TDD was 47 ± 27 IU (basal: 21 ± 12 IU, bolus: 26 ± 15 IU). Adherence to the insulin advices by the algorithm was 223/226 [98.7%] for TDD, 205/213 [96.2%] for basal insulin and 643/672 [95.7%] for bolus insulin.

Conclusion: The REACTION algorithm could safely establish glycemic control without increased risk of hypoglycemia. Adherence to insulin dosing advices generated by the REACTION algorithm was high both for basal and bolus insulin. The REACTION algorithm has the potential to improve glycemic management in the hospital setting.

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O-22

EEG BASED PREDICTION OF HYPOGLYCAEMIA IN CHILDREN WITH T1D

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Background and Aim: The fear of hypoglycaemia is a major obstacle of obtaining near-normal blood glucose levels (BGL) in children. Hypoglycaemia avoidance behaviour might adversely affect glycaemic control in T1D children thereby increasing the risk for long-term diabetic complications. Here, we test an automated EEG algorithm initially developed in adults in predicting hypoglycaemia in children.

Subjects and Methods: 8 pre-pubertal children (4 males), aged 9.6 ± 2.3 yrs, T1D duration of 3.0 ± 1.4 yrs, HbA1c 55 ± 3,4 mmol/mol and 7/8 on CSII treatment underwent hyperinsulinimic hypoglycaemic clamp in awake state during daytime. The hypoglycemia was terminated at nadir either by significant hypoglycemic symptoms (evaluated by either the patient, parents or physician) or by a BGL level at 2.2 mmol/l. EEG was recorded and analysed using an automated EEG algorithm.

Results: The automated algorithm detected the induced hypoglycaemia in all children on average at a BGL of 2,5 ± 0.5 mmol/l and 18,4 ± 20,3 minutes (range 0–55 minutes) prior to BGL nadir on average 2.3 ± 0.5 mmol/l. No false positive alarms were recorded.

Conclusions: This automated EEG algorithm identified hypoglycaemia in 8/8 pre-pubertal children in awake state before severe hypoglycaemia developed. The potential of this new automated algorithm should be evaluated in children during sleep for predicting nocturnal hypoglycaemia.

O-23

HYPOGLYCEMIA REDUCTION IN ASPIRE IN HOME STUDY

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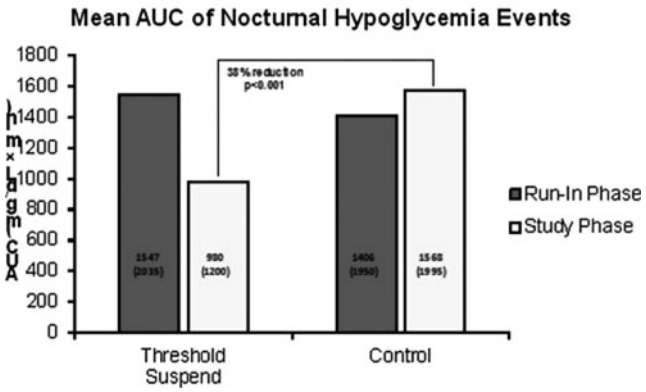
Introduction: Prevalence and cost of diabetes (both type 1 and type 2) is increasing globally, and according to the International Diabetes Federation (2011) it is predicted to reach 550 million individuals by 2030. (1) Diabetes continues to be associated with a high mortality rate–mainly due to cardiovascular disease, with approximately 5% of all deaths worldwide being attributable to diabetes. (2) Intensive diabetes management with multiple daily injections (MDI) and or continuous subcutaneous insulin infusion (CSII) in type 1 diabetes (T1D) lowers A1c values effectively which reduces both micro- and macrovascular complications of diabetes. (3) However, intensive diabetes treatment results in >3 fold increase in severe hypoglycemia. (3) Despite all the advances in diabetes treatment (new insulin analogs, glucose meters and continuous glucose monitors [CGM]), recent data from T1D exchange confirms only small improvements in glucose control with with A1c values ranging

Table 1- Baseline Demographics

	Threshold Suspend	Control
Age	41.6 ± 12.8	44.8 ± 13.8
% Male	38	39.7
Diabetes Duration	27.1 ± 12.5	26.7 ± 12.7
BMI, kg/m^2	27.6 ± 4.7	27.1 ± 4.3

Figure-1
Nocturnal Hypoglycemia (AUC) in ASPIRE at home study.



from 7.7–8.7% in >50% of patients. In addition severe hypoglycemia continues to be a hurdle in better implementation of intensive diabetes management.

Using a closed loop system is one way to reduce severe hypoglycemic events. The low glucose suspend (LGS) feature on the paradigm Veo sensor-augmented insulin pump system (Medtronic MiniMed, Inc., Northridge, CA) is a closed loop system for insulin delivery. (6–9) The use of LGS feature automatically stops insulin delivery for 2 hours when a pre-programmed glucose threshold is reached with manual intervention option at any time. The Automation to Simulate Pancreatic Insulin REsponse (ASPIRE) study was done to see if duration and severity of hypoglycemia could be reduced in subjects with T1D during an in-clinic exercise induced hypoglycemia. (10, 11)

Subjects and Methods: ASPIRE at home study randomized 247 subjects with T1D (demographics provided below) in to a Control arm using SAP and a Threshold Suspend (TS) arm using SAP + TS.

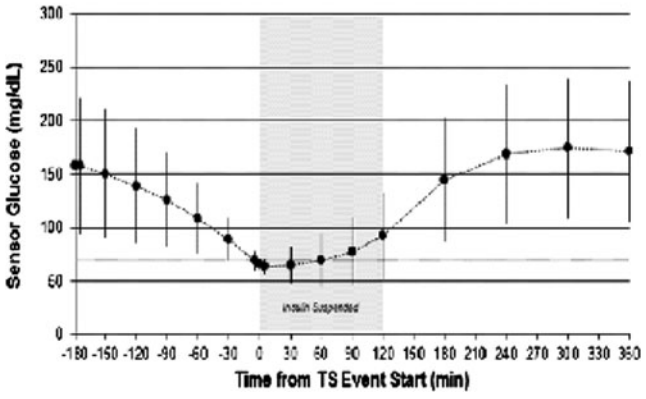
Results: Similar to the studies with ASPIRE in-Clinic (exercise-induced hypoglycemia), ASPIRE at home study (12) documented a 37% reduction of nocturnal hypoglycemia Figure-1. The results were similar in different age groups without any change in glucose control.

There were total of 1438 2 hour suspensions in ASPIRE study and the data confirms reduction of hypoglycemia without any significant hyperglycemia (Figure-2).

Discussion: The LGS feature is designed (recently approved by the FDA) to imitate the pancreatic beta cells and regulate glucose levels by stopping insulin delivery when blood glucose reaches a pre-defined threshold. The 2 hr suspension time was designed to decrease rebound hyperglycemia.

Future developments in closed loop systems will include (a) the use of predictive alarms/ glucose threshold to suspend insulin delivery (LGS) before hypoglycemia occurs, (b) insulin delivery when hyperglycemia is detected (>180 mg/dL), and (c) and/or a hybrid system where subjects will deliver part of their bolus before meals to imitate normal physiologic function, as currently available rapid acting insulins are not rapid enough in onset of action. Newer insulin formulations with more rapid onset of action are in development. Furthermore, there is development of dual compartment pumps that may incorporate glucagon to prevent and treat hypoglycemia or use pramlintide (Symlin®) to limit post-prandial hyperglycemia. Other than developing better basal insulins e.g. deguldec (approved in Japan and Europe) and pegylated lispro (phase-3 studies ongoing), more accurate CGMs are needed to create a true closed loop system.

Figure-2: ASPIRE-In Home Study: Mean SG values from 1438 nocturnal 2-hour TS events. Time 0 is the time of pump suspension and 120 minutes is when insulin delivery resume



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O-24

NOVEL STRATEGIES TO LIMIT HYPOGLYCEMIA DURING EXERCISE

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Balancing blood glucose concentrations during exercise in patients with type 1 diabetes has always been a major challenge. Hypoglycemia can be induced within minutes after the start of exercise and may also occur in both early and late recovery. Aerobic exercise increases insulin sensitivity and increases blood glucose disposal into skeletal muscle more than 6-fold compared to rest. This increase in glucose disposal must be matched with either increased glucose production by the liver (glycogenolysis, gluconeogenesis), typically by lowering circulating insulin levels and by increasing the levels of glucagon, or by the consumption of ''extra'' carbohydrates (Ex Carbs) during the activity. A number of novel strategies are being developed to assist with the prevention of exercise-induced hypoglycemia including the use of nutritional agents (e.g. caffeine, maltodextrins), pharmacotherapies (e.g. low dose glucagon, somatostatin receptor antagonism, SGL2 inhibitors) and modifications to the exercise itself (resistance type exercise, sprinting). This session will highlight some of these newer approaches for hypoglycemia prevention that are at various stages of research from early conceptual work to later proof of concept studies in rodents to small clinical trials.

O-25

MEANINGFUL SUPPORT OF BASAL INSULIN TREATED TYPE 2 PATIENTS BEYOND SMBG RESULTS - WHAT DOES IT TAKE?

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Use of self-monitoring of blood glucose (SMBG) in basal insulin-treated Type 2 diabetes patients is very well accepted in both the clinical and economic world. In contrast, there is still some ongoing debate as to whether this is an effective tool for insulin naïve Type 2 patients; however, there is now increasing evidence that this population would also benefit clinically and psychologically from the use of SMBG.

Despite the increasing use of SMBG, it is clear that many patients are still not reaching their treatment goals. Even in RCTs, in which patients have frequent contact with the treating centers and free access to SMBG supplies, the blood glucose goals set in these trials are rarely met.

This raises the question as to whether patients actually receive and fully understand the messages and information that are provided to them by the treating Healthcare Professional (HCP). Several patient attributed factors, such as motivation, literacy and social environment may contribute to prevent treatment success with regard to metabolic control, despite all necessary information being at hand.

This suggests that there is a need for an improvement in the communications between HCP and patient. Whilst several attempts have been made to evaluate the impact of this, unfortunately many of these proved to be time consuming for the HCP or patient's site, which might prevent the success of this type of approach in real life.

Use of new technology, both in development or already on the market, provides an opportunity to develop a new approach to SMBG. Above all, it will be essential to use a variety of tools which provide meaningful support to HCP and patients, to truly improve the treatment success.

Abstract supported by Sanofi.

O-26

CHALLENGES IN IMPLEMENTING SAP IN REAL LIFE

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Insulin pumps have been integrated with glucose meters, continuous glucose monitoring sensors (CGM), data analytic systems, and now closed-loop algorithms that allow for automation of insulin delivery. The use of an integrated insulin pump and CGM in the STAR 3 study showed an early and persistent reduction in A1C and severe hypoglycemia rates of 13 per 100-patient years, some of the lowest hypoglycemia rates reported. The recent ASPIRE In-Home trial revealed that automating insulin shut-off at a pre-set threshold significantly reduced nocturnal hypoglycemia without increasing A1C. Automatic insulin shut-offs occurred frequently and those lasting the full 2-hour duration occurred mainly at night. Recently, predicted low glucose management systems have shown that shutting off insulin when it is predicted that within 30 minutes a low glucose threshold will be reached have further reduced hypoglycemia. There have been many reports of the use of fully closed-loop systems at nighttime only, from studies occurring in both the hospital and home settings.

To benefit from sensor augmented pump therapy, patients, caregivers and diabetes healthcare providers need to work collaboratively, and be adequately trained and motivated. However, despite many advances and the promise of diabetes technology in the future, barriers persist to the use of these integrated systems. These include issues such as body image, cost, meeting criteria for pump approval, pump/human tissue interface, fear of technology, diabetes burn-out and being overwhelmed by diabetes management. Success with sensor augmented pump therapy relies on education and support by a proactive health care team.

O-27

CLINICAL RESULTS FROM TRANSITIONAL AND HOME TRIALS OF OUTPATIENT CLOSED-LOOP CONTROL

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The introduction of the Diabetes Assistant (DiAs) – a portable outpatient closed-loop control platform based on a smart phone – opened new possibilities to the transition of the artificial pancreas to outpatient use. In October 2011, DiAs was tested in pilot trials done simultaneously in Padova (Italy) and Montpellier (France). A subsequent multi-site feasibility study was completed in 2012 at the University of Virginia (UVA), Padova, Montpellier, UC Santa

Barbara, and the Sansum Diabetes Research institute. A second multi-site randomized cross-over trial testing the efficacy of DiAs in outpatient setting was completed in June 2013: compared to open loop, DiAs reduced significantly the frequency of hypoglycemia (BG < 70 mg/dl) from 2.4 to 1.2 episodes/subject requiring carbohydrate treatment, p = 0.02. The effect size of this risk reduction was 0.64 (p = 0.003) as assessed by the Low BG Index - a risk marker for hypoglycemia. In the summer of 2013, DiAs was deployed at Stanford University camp studies for children with diabetes, which resulted in very good overnight glucose control and only one mild hypoglycemic episode during ~50 nights of closed loop use. Outpatient clinical trials of new adaptive advisory/automated control strategies are ongoing at UVA, Padova, and the Mayo clinic. In this presentation we summarize the results from these studies and place them in the context of the worldwide transition of the artificial pancreas to ambulatory use. We conclude that technology has evolved to bring elements of closed-loop control to patient's homes, initially in controlled trials, and then into the clinical practice of diabetes.

O-28

CONTINUOUS GLUCOSE SENSORS AND AP SYSTEMS

T. Peyser[1], A. Garcia[1], A.L. Rack-Gomer[1], N. Bhavaraju[1], H. Hampapuram[1], A. Kamath[1], A. Facchinetti[2], C. Zecchin[2], G. Sparacino[2], C. Cobelli[2]

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The viability of artificial pancreas systems depends heavily on the accuracy and reliability of the continuous glucose monitor (CGM) providing input data to the closed loop algorithms. The Dexcom G4 PLATINUM was approved in Europe and the United States in 2012 and represents a significant improvement in accuracy and reliability compared with the previous generation Dexcom CGM device, the SevenPlus.

The G4 PLATINUM has been widely adopted by patients for routine clinical use, but also by artificial pancreas groups around the world.

Dexcom has developed an advanced CGM, called the G4AP, in collaboration with the University of Padova that utilizes the same sensor and transmitter as the G4 PLATINUM, but contains new denoising and calibration algorithms in the receiver. These algorithms were applied to raw data from an existing G4 PLATINUM clinical study using a simulated prospective procedure. The results show that the mean absolute relative difference (MARD) compared with venous plasma glucose was reduced by 1.5%. In addition, there was further improvement in sensor performance in hypoglycemia.

Parameter	SevenPlus	G4 PLATINUM	G4AP
MARD (40 – 400 mg/dL)	15.9%	13.2%	11.7%
%20/20 mg/dL	76%	82%	86%
MAD (YSI < 70 mg/dL)	16 mg/dL	11 mg/dL	8.8 mg/dL
MARD (YSI < 70 mg/dL)	27%	18%	14.8%

The G4AP also performed better than G4 PLATINUM on several recently proposed metrics for assessing CGM performance in AP applications. The improved accuracy of the G4AP algorithm is expected to benefit patients routinely using CGM for management of their diabetes as well as research groups seeking to develop improved artificial pancreas prototypes.

O-29

CONTINUOUS GLUCOSE SENSORS AND AP SYSTEMS

H. Eikmeier[1]

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Recent discussions on key performance parameters for CGM-sensors and their potential usage for Artificial Pancreas (AP) systems mainly focused on accuracy, often expressed by mean absolute relative difference (MARD).

This presentation aims to challenge MARD being handled as exclusive parameter for the assessment of CGM sensors as part of an AP system. We also see other features of CGM systems as essential elements of such solutions:

- Accuracy of CGM signals in critical situations (e.g. hypoglycemic levels / fast changing glucose values)
- Reliability of CGM signals and built-in features for signal and operational safety
- Holistic AP system architecture to enhance patients' confidence of having everything they need to effectively manage their diabetes

Roche's current sensor system under development will address the 3 aspects mentioned above. Moreover, clinical study data involving prototypes of this technology already confirm the effectiveness of the sensor design in patients tested:

- Excellent overall MARD (40–400 mg/dl) of 9.4% and performance during hypoglycemic episodes (<70 mg/dl) with MARDs of 13.0%, as well as during induced glucose swings with MARDs of 11%
- High precision between 2 simultaneously operating sensors with overall percent absolute relative deviation (PARD) of 7.8% guarantees a highly reliable signal quality
- CGM-data storage on patch and safe transmission of missed data (if receiver was out of communication range) safeguards availability of the complete data. Bluetooth low energy (BLE)-enabled transmission of calibrated CGM values from the patch at an enhanced frequency of 1/min is combined with an easy-to-read visualization and user-friendly User Interface (UI) on the controller

O-30

INSULIN PUMPS IN AP SYSTEMS

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Insulin pumps have evolved into technologically precise medical devices and the value they bring to patients has been widely demonstrated. CGM integration into insulin pumps has provided access to trending glucose data and alarms, thereby facilitating

better glycemic management. Titrating insulin pump dose using CGM data is a natural next step and can mitigate the severity of glycemic excursions, particularly hypoglycemic events [1].

Reactive, threshold-based systems represent the first generation of AP systems, but their benefits are limited due to the simplistic nature of the controller. More sophisticated predictive controllers that account for CGM trending information can be used to not just mitigate, but potentially avoid glycemic excursions [2]. The challenges associated with delivering such products to the market lie not only with developing the algorithm technology, but more broadly with ensuring a rigorous holism among all components of such a hybrid solution, including critical human factors aspects.

Lessons learned from real-world use of reactive systems with simple decision trees will lead to more complex, robust predictive systems to reduce hypoglycemia first, then hyperglycemia. Continued collaboration across the community (academia, industry, advocacy and government/regulators) is fundamental to the acceleration of such innovation to patients in need.

[1] TT Ly et al. Effect of sensor-augmented insulin pump therapy and automated insulin suspension vs standard insulin pump therapy on hypoglycemia in patients with type 1 diabetes: a randomized clinical trial. JAMA 2013.
[2] DA Finan et al. Hypoglycemia safeguard capabilities of the predictive Hypoglycemia-Hyperglycemia Minimizer (HHM) System. ATTD 2013.

O-31

REPETITIVE HBA1C MEASUREMENTS DURING PREGNANCY

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During gestational diabetes mellitus (GDM), the current recommendations are to achieve glucose control as near to normal as possible. We conducted a retrospective chart review of all GDM patients seen in the Diabetes-Pregnancy Clinic between December 2005 and December 2007 during which the goal of glucose control was an A1C of 5%. We evaluated the maternal characteristics and neonatal outcomes of 123 GDM pregnancies. Maternal A1C (DCA 2000, Bayer) between 35–41 weeks gestation were averaged, and gestational age at delivery, neonatal weight and neonatal complications were recorded. Data was available for 120 neonates of which 114 charts had A1C and birthweight records, with 100 charts also having recorded neonatal mode of delivery, gender and gestational age.

Weight increased 35.8 Gm with each 0.1 increase in A1C. Macrosomia (birthweight $\geq$4000 Gm) was significantly associated with A1C (O.R. = 5.1, CI = 1.2–21.0). There was no significant difference in frequency of caesarian section relative to birthweight and mode of delivery. Of 8 macrosomic infants (7?, 1?) 4 were delivered by C-section and four by vaginal delivery.

O-32

DOES THE PLACENTA PLAY A ROLE FOR THE OUTCOME OF DIABETIC PREGNANCIES

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The hallmark of the neonate born to T2DM and gestational diabetic (GDM) pregnancies is its excessive deposition of fat, which also contributes to the offspring risk for impaired glucose tolerance and obesity later in life. Fetal fat accumulation is mainly driven by fetal insulin as a result of fetal hyperglycemia. Transplacental glucose flux, at least at the end of gestation, is dictated by the glucose concentration gradient between the maternal and fetal circulation and, thus, is not much under placental control. The insulin-stimulated enhanced aerobic metabolism in the fetus increases the oxygen demand. If not adequately covered at least transient fetal hypoxia can ensue. In such a situation the placenta responds by upregulating angiogenesis. This leads to longer placental vessels with increased branching, ultimately resulting in more capillaries available for oxygen supply to the fetus.

Poor maternal glycemic control prior to or during the first weeks of pregnancy may lead to defects in the initial steps of placental development such as implantation and placental, ie. trophoblast, invasion. Combined with potentially pre-existing vascular defects in the maternal circulatory systems, uteroplacental blood flow may be impaired. Whether this contributes to the increased risk for maternal pregnancy complications associated with T1D (and likely also T2D), such as pre-eclampsia, is a current speculation.

O-33

FERTILITY IN T1DM AND T2DM PATIENTS

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Patients with diabetes mellitus often have reproductive disturbances. For women these include delayed menarche, menstrual irregularities, subfertility, early onset of menopause, and increased incidence of spontaneous abortions, and for men impotence, hypospermia, and impaired spermatogenesis.

The exact mechanisms underlying diabetes-related infertility remain unknown. Studies have implicated a central defect on the pituitary-gonadal axis, abnormal antral follicle development, as in polycystic ovary syndrome (PCOS), and microangiopathy or other tissue-damaging factors.

This presentation reviews the known data on the association between diabetes and infertility, including the cumulative information on the pivotal role of insulin resistance in the pathogenesis of prediabetic states such as PCOS.

O-34

TREATMENT WITH AN ULTRARAPID INHALED INSULIN - WHAT DO WE KNOW NOW?

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Prandial insulin regimens strive to mimic the physiological relationship between glucose absorption and insulin release. Current regimens are challenged by the inadequate synchronization of insulin action to postprandial plasma glucose excursions, leading to post prandial hyperglycemia as well as a significant risk of late post prandial hypoglycemia and weight gain. Technosphere® Insulin (TI) is an inhaled ultra-rapid acting human insulin that is quickly absorbed in the alveoli. With a

Tmax of about 14 min and a Emax of 35–40 min, TI more closely match the postprandial insulin concentrations seen in non-diabetic individuals. Studies have shown that long-term administration of prandial TI in combination with long-acting basal insulin results in reductions in hemoglobin A1c comparable to conventional subcutaneously injected prandial insulins, but with improved control of early postprandial blood glucose, a lower incidence of hypoglycemia and less weight gain. However, the different action profile require that the ultra rapid acting insulin is used differently from current prandial insulins. Dose timing, the time of measurement and blood glucose target levels used for dose adjustments all need to be evaluated. In addition, the shorter duration of action may permit a post prandial dosing, either as the only dose or as a second dose when a large meal is consumed.

O-35

NOVEL FORMULATIONS TO MODIFY MEALTIME INSULIN KINETICS

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Insulin absorption can be accelerated by formulating recombinant human insulin (RHI) or insulin analogs with ethylenediaminetetracetic acid (EDTA) and citrate. These excipients have been shown to speed the dissociation of insulin hexamers into dimers/monomers upon dilution in extracellular fluid. Such formulations at standard 100 U/ml (U-100) insulin concentrations exhibit distinct pharmacokinetic (PK) profiles dependent on whether the active ingredient is RHI or lispro. Both RHI and lispro formulations have been demonstrated in humans to exhibit accelerated absorption relative to commercial insulin lispro (Humalog®). However declines from peak are slightly longer for RHI/EDTA/citrate formulations relative to Humalog®, whereas lispro/EDTA/citrate formulations decline from peak faster than Humalog®. The clinical significance of these distinct PK profiles is unknown, however safety and efficacy of RHI formulation BIOD-123 has recently been demonstrated in a multi-center phase 2 trial evaluating patients with type 1 diabetes. BIOD-531 is a concentrated (400 IU/ml, U-400) RHI/EDTA/citrate formulation that has been shown in a diabetic swine model to exhibit yet a third distinct PK profile characterized by more rapid absorption compared to concentrated regular insulin (Humulin® R U-500) and lispro/protamine prandial/basal mixes but with basal duration of action comparable to that seen with Humulin® R U-500. BIOD-531 has entered clinical development and may prove to be attractive for patients with type 2 diabetes who use either concentrated insulin or pre-mixed prandial/basal insulins. Understanding the influence of insulin type and concentration on the PK properties of EDTA/citrate formulations has yielded clinical development candidates for multiple patient populations.

O-36

RECOMBINANT HUMAN HYALURONIDASE FACILITATES A CONSISTENTLY ULTRAFAST INSULIN PROFILE ACROSS INFUSION SET LIFE IN T1DM PUMP PATIENTS

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Rapid acting insulins (RAI) represent improvement over regular insulin, with advantages in post prandial glucose excursions, hypoglycemia, A1C and patient convenience. However, RAI is still too slow in onset and too long in duration to mimic endogenous insulin response. We have studied the impact of recombinant human hyaluronidase (rHuPH20) to increase the dispersion and accelerate the absorption of RAI in both basal/bolus treatment and insulin pumps. In pumps we have explored the use of a formulation of RAI + rHuPH20 in the pump reservoir as well as using a pretreatment of the infusion site with rHuPH20 at each infusion set change. rHuPH20 results in acceleration of insulin absorption and action, rendering an ''ultrafast'' insulin profile. Typically, the fraction of total insulin absorption that occurs in the first hour ($fAUC_{0–60}$) is doubled from ~15% to ~30%, and onset of insulin action (early $t_{GIR50\%}$), during euglycemic clamp studies is shortened by about 1/3 or about 10–20 minutes. Duration of insulin action in the clamp, measured using the same calculation employed in pharmacokinetics to assess Mean Residence Time, is typically reduced by about 45 minutes. These changes in insulin absorption and action are accompanied by significant reductions of ~30 mg/dL in postprandial glycemic excursions in response to mixed test meals. Importantly, rHuPH20 preadministration also eliminates the systematic acceleration of insulin absorption and action (the ''Tamborlane Phenomenon'') that occurs as infusion sets age; this provides consistent, predictable insulin absorption and action over infusion set life and may thus improve diabetes control by reducing unanticipated variability.

O-37

IMPACT OF STANDARDIZED INJECTION SITE WARMING ON GLYCEMIC CONTROL

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Temperature changes on the skin surface result in changes of the (sub)cutaneous microcirculation. This well-known phenomenon was used to develop the InsuPad device for improvement of prandial insulin absorption. Standardized warming cycles applied after insulin injection result in a more rapid increase in insulin plasma concentrations and faster action. In standardized meal studies, use of a similar dose of short-acting insulin analogs resulted in significantly better postprandial control when using InsuPad. To achieve the same level of control, InsuPad use allows for a mean dose reduction by 20%. Injection of insulin after the meal still results in a better glycemic control than injecting the same dose without the device prior to food uptake. Use of InsuPad under real-world conditions was tested in a controlled randomized parallel study for three months in 145 patients with type 1 and type 2 diabetes. Target HbA1c levels (HbA1c: 6.3 ± 0.5%) were reached in both treatment groups (with and without the device). However, InsuPad patients needed 28% less prandial insulin as compared to the control group ($p < 0.001$), 12% less total insulin ($p < 0.001$), and had 46% less hypoglycemic events ($p < 0.05$). Treatment satisfaction remained unchanged despite the additional treatment procedure and the overall vast majority continued with the use of the device after study termination. HbA1c treatment targets were achieved with InsuPad with substantially less insulin and less hypoglycemic events.

O-38

JET ADMINISTRATION OF SHORT ACTING INSULIN

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The pharmacokinetic and pharmacodynamic profile of rapid-acting insulin analogs, although better than that of regular insulin, is still far from resembling the profile of endogenous insulin secretion, in large part due to protracted absorption from the subcutaneous space. Indeed, the firm extracellular matrix of the subcutaneous tissue impedes drug transport and hence its absorption into the circulation. As a consequence, patients with type 1 or insulin-requiring type 2 diabetes still face the risk of immediate postprandial hyperglycemia and late postprandial hypoglycemia, despite using rapid-acting insulin analogs. Jet-injectors, originally introduced for patients with persistent fear of needles or true needle-phobia, provide a needle-free alternative for insulin administration. After injection, insulin injected by jet stream displays a spray-like dispersion pattern in the subcutaneous tissue, which may promote absorption due to a relatively large surface area. Studies dating back to the 1980s and before already indicated faster absorption of regular insulin and more direct glucose lowering effect, when injected by a jet injector rather than by a syringe. Recently, we showed that insulin analogs are absorbed up to twice as fast when administered by jet stream compared to injection by conventional insulin pen, both in healthy subjects and in patients with type 1 or type 2 diabetes. Jet injection similarly advances the glucose-lowering effect of insulin analogs, and consequently reduces the hyperglycemic burden immediately after a meal. Studies on the reproducibility of the jet injector for insulin administration and its effect on normalizing hyperglycemia are currently underway.

O-39

THE CONTRIBUTION OF POOR METABOLIC CONTROL DURING ADOLESCENCE ON MICROVASCULAR COMPLICATIONS

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Attaining glycaemic targets often is more difficult during adolescence compared to adulthood and earlier childhood. In the DCCT for example using the same treatment protocols the mean HbA1c achieved was significantly higher in the intensively treated group (8.1 vs 7.2%). Nevertheless adolescents in the intensive compared to the conventional treatment arm had significantly reduced complications, an effect that persisted for four years after randomization.

In our noninterventional study investigating the effect of prepubertal diabetes duration to microvascular complications in young adulthood, the HbA1c achieved in puberty was an independent contributor to retinopathy and microalbuminuria[1]. 12 yr follow-up of adolescents into adulthood showed a 1 unit increase in HbA1c increased risk by 72% for retinopathy and microalbuminuria[2].

Other modifiable risk factors for diabetes microvascular disease in adolescence are higher blood pressure, higher insulin dose per kilogram and higher body mass index. It is likely that insulin resistance is therefore another key factor. It is pleasing that there has been a documented decline in microvascular disease in line with a reduction in HbA1c but the associated increase in body mass in our clinic is of concern[3].

Other biological markers measured during adolescence show associations prospectively for microvascular complications (retinovascular geometry, plantar fascia thickness, heart rate variation, small pupil size and health care utilisation). Higher HbA1c as a measure of poor metabolic control remains in all risk models.

1. *Diabetes Care* **26,** 1224–1229 (2003).
2. *Diabetes Care* **30,** 77–82 (2007).
3. *Diabetes Care* **34,** 2368–2373 (2011).

O-40

ROUTINE USE OF CGM IN PRESCHOOL CHILDREN

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Continuous glucose monitoring (CGM) provides real-time information on glucose patterns and trends, thus allowing better management of diabetes. Many studies have shown that it can improve glycemic control, especially if used frequently. Next to it CGM reduces occurrence of severe hypoglycaemic events and improves the quality of life in adults and children with T1D. But the evidence for CGM to be as effective in preschool children are limited and controversial. In current recommendations for young patients, CGM should be considered when patients:

- do frequent blood glucose testing,
- have severe hypoglycaemic episodes,
- have hypoglycaemic unawareness or nocturnal hypoglycaemia,
- have wide glucose excursions or large blood glucose variability,
- have difficulties in identifying hypoglycaemic episodes,
- have suboptimal glycemic control,
- want to mantain good glycemic control with the aim to limit the risk of hypoglycaemia.

In the consensus statement on CGM for paediatric population overall it is concluded that CGM can be used safely and effectively for lowering HbA1c, reaching target HbA1c, reducing the MAGE without increasing the risk of severe hypoglycaemia; it can be used effectively for reducing severe hypoglycaemia and shortening the time in hypoglycaemia. The effectiveness of CGM is significantly related to the frequency of sensor use. Education on the use of CGM is crucial for success.

Currently, the use of CGM in preschool children is still not a routine practice. Further studies are needed to evaluate the effectiveness of CGM in this age group.

O-41

IMPROVEMENT OF METABOLIC CONTROL AFTER THREE MONTHS OF RT-CGM IN TYPE 1 DIABETICS WITH CSII. THE GREEK MULTICENTER STUDY DIAMOND

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Aim: To evaluate the efficacy of adding continuous glucose monitoring (CGM) for three months to insulin pump therapy (CSII) in patients with Diabetes Mellitus Type 1 (DMT1) in a multicenter Greek study (THE DIAMOND STUDY).

Patients-methods: Eleven Diabetes Centers in Greece participated to the study. Forty-three patients (24 female) treated with CSII were enrolled prospectively. All patients were on CSII for three months before the use of CGM. Then all participants were instructed to wear the MiniMed Paradigm REAL-Time System, which integrates both CSII and RT-CGM functionalities for the next three months. At the end of the study we evaluated the following parameters: HbA1c, BMI, hypoglycemic episodes (HYPO), total daily insulin requirement (TDI), total daily insulin for boluses (TDIBOL), number of daily boluses (NOBOL), total daily insulin basal (TDIBASAL) and percentage of total time use of sensor (PTTU).

Results: The mean PTTU was 74 ± 17.0%. The results of the other examined variables were as follows in patients before and after the use of CGM: HbA1c 8.3 ± 1.2% vs 7.5 ± 1.0% ($p < 0.001$), TDI 45.7 ± 15.3 vs 50.8 ± 23.9 ($p = 0.018$), TDIBOL 24.1 ± 10.4 vs 28.3 ± 19.0 ($p = 0.033$) and NOBOL 4.7 ± 1.5 vs 6.3 ± 2.4 ($p < 0.001$). No significant change observed in BMI, HYPO and TDIBASAL before and after the use of CGM.

Conclusions: In the present study CGM was associated significantly with improvement of glycemic control without BMI and HYPO change, in patients with type 1 diabetes using CSII. Better self-management and increase of the doses and units of insulin may have contributed to these beneficial effects.

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SENSOR AND SOFTWARE USE FOR IMPROVED GLUCOSE CONTROL IN PEOPLE WITH DIABETES MANAGED BY MULTIPLE DAILY INJECTIONS OF INSULIN

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Aim: To assess whether subjects with type 1 diabetes (T1DM) or T2DM managed by multiple daily injections (MDI) of insulin could improve glycaemic control by; 1) using and understanding continuous glucose monitoring (CGM) data, 2) utilising glucose trend arrows and 3) reviewing ambulatory glucose profiles (AGP) with their clinician.

Methods: A UK, multicentre (n = 9) 100 day study recruited 105 MDI-treated diabetes subjects aged 18–82 years with HbA1c of 58–108 mmol/mol. Control group subjects used standard self-monitoring of blood glucose (FreeStyle Freedom Lite), whereas the intervention group employed a FreeStyle Navigator and were asked to turn the alarms off. At days 30 and 45, subjects reviewed their AGP and summary statistics with their clinician and agreed therapy adjustments.

Results: In T1DM (n = 25) intervention subjects, a within subject analysis showed significant reduction in hypoglycaemia (<3.9 mmol/L) of 0.6 ± 1.4 hrs/day ($p = 0.0474$) and 0.4 ± 1.0 hrs/day for time spent <3.1 mmol/L ($p = 0.0644$), with no significant change in HbA1c.

In T2DM (n = 28) intervention subjects, within subject analysis showed a significant increased time within 3.9–10.0 mmol/L of 1.4 ± 3.5 hrs/day ($p = 0.0427$) without a change in hypoglycaemia and a reduction in HbA1c of 9.5 ± 11.8 mmol/mol ($p = 0.0002$).

For subjects with T1DM, frequency of blood glucose tests per day (including calibration) reduced from 4.6 ± 1.9 at baseline to 2.2 ± 1.2 ($p < 0.0001$) and in T2DM from 4.0 ± 1.4 to 2.1 ± 1.2 ($p < 0.0001$).

Conclusion: T1DM subjects showed reduced time in hypoglycaemia when managed with FreeStyle Navigator CGM (no alarms). The same intervention in T2DM subjects showed a reduction in HbA1c and significantly increased time in 3.9–10.0 mmol/L.

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DECISION ANALYTIC MODEL: COST IMPLICATIONS OF RT-CGM USE IN INSULIN REQUIRING PATIENTS WITH HYPOGLYCEMIC UNAWARENESS

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Introduction: RT-CGM use lowers A1C and reduces hypoglycemia for people with diabetes. However, the economic impact of A1C reduction is not seen for many years; we evaluated costs of RT-CGM use in patients with severe hypoglycemia (SH). Patients with long standing diabetes and those with hypoglycemia often lose their ability to detect hypoglycemia developing, 'hypoglycemia unawareness' (HUA), which results in significant decrements in health, quality of life, and economics. This analysis estimates the economic consequences of RT-CGM in the insulin requiring adult population with HUA.

Methods: Using a simple decision tree model, costs of severe hypoglycemia resulting in hospitalizations in T1D and T2D adults with HUA using RT-CGM is analyzed. The hypothetical population consists of 10 million people. Assumptions: Diabetes prevalence of 7%; T1D prevalence of 5%; T2D treated with

insulin is 27.3%. Percentage of patients with T1D HUA is 20%, and T2 with HUA is 9.8%; annual number of SH events per pt./yr. are, 2.6 and 5.9 respectively; percentage of SH events requiring hospitalization is 21%; the reduction in annual SH events in patients with T1D with HUA using RT-CGM is 45%. All assumptions are referenced from the published literature.

Results: Using a time horizon of 1 year, for people with HUA that use RT-CGM, there is an expected net savings of $60,829M USD when assuming the annual cost of RT-CGM is $5800/yr.

Conclusion: For insulin taking patients with HUA, RT-CGM can be a cost saving tool. Sensitivity analysis shows flexibility in pricing of RT-CGM to achieve cost savings.

O-44

COMPARISON OF DIFFERENT CALIBRATION STRATEGIES FOR CONTINUOUS GLUCOSE MONITORING SENSORS

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Objective: Calibration of continuous glucose monitoring (CGM) sensors is the process that transforms the raw current value, proportional to the interstitial glucose (IG) concentration, into a glycemic value exploiting few blood glucose (BG) references. Due to the presence of many critical factors, e.g. signal distortion due to BG-IG kinetics, instability and uncertainty of measured signals, etc., the accuracy of the CGM profile could be suboptimal. The aim of this contribution is to understand if and how much a smart compensation of BG-IG kinetics and the exploitation of a-priori knowledge on the parameters of the calibration law can improve calibration effectiveness.

Methods: We compared three calibration strategies of increasing complexity: i) a 2-point linear regression; ii) the calibration algorithm of Guerra et al. (IEEE-TBME 2012), which applies nonparametric deconvolution before matching BG and raw current data; and iii) the algorithm of ii) further developed to exploit a Bayesian prior available on calibration regression parameters. Algorithms efficacy was tested on 15 CGM traces collected by the Dexcom G4 Platinum (DG4P) device for 7 days. BG references on days 1, 4, and 7 were used to assess performance via Mean Absolute Relative Deviation (MARD).

Results: The 2-point algorithm achieves a MARD of 18.6%. Deconvolution decreases MARD to 16.5%. Exploitation of the Bayesian prior on calibration parameters further reduces MARD to 14.7%. Average MARD of original DG4P dataset was 14.3%.

Conclusion: Compensation of BG-IG kinetics distortion via nonparametric deconvolution and exploitation of a-priori knowledge on calibration parameters via Bayesian estimation improve calibration effectiveness.

O-45

FIRST EVALUATION OF AN ORTHOGONALLY REDUNDANT GLUCOSE SENSOR SYSTEM IN PEOPLE WITH TYPE 1 DIABETES

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Aim: To evaluate the performance of a progressively refined series of orthogonally redundant sensor (ORS) prototypes employing electrochemical and optical fluorescence-based glucose sensing in type 1 diabetes (T1D) participants.

Background: The ORS under development integrates two distinct sensing technologies with independent failure modes potentially improving continuous glucose monitoring accuracy and reliability.

Method: Eight T1D adults wore an investigational ORS and non-redundant comparator sensor (NCS) concurrently for 48–168 hours. Following sensor insertion, and later with a standardised meal, venous samples were collected over 4 hours at 30 and 15 minute intervals respectively for YSI plasma glucose. Between these study visits, subjects wore both sensors in an ambulatory real-world setting for 48–168 hours and undertook capillary blood glucose testing. Sensor glucose values were displayed only when trace characterisation algorithms deemed values to be sufficiently accurate. Sensor glucose readings from both sensors were compared to plasma and capillary glucose levels.

Results: The ORS configuration was iteratively evolved resulting in incremental improvements in optical sensors over the course of the study. After 8 subjects, average sensor display time was higher for ORS than NCS (97% versus 93%). Mean absolute relative difference (MARD) and compliance with ISO 15197:2013 accuracy metrics were similar. There was no irritation or infection at any sensor insertion sites after removal.

Conclusion: Increasing sensor display time without compromising accuracy results in improved sensor reliability. Combining optical and electrochemical sensing technologies is feasible, and potentially increases glucose sensing reliability which may facilitate artificial pancreas development.

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PARENTAL SLEEP QUALITY AND CONTINUOUS GLUCOSE MONITORING SYSTEM USE IN CHILDREN WITH TYPE 1 DIABETES

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Objective: To compare sleep quality and sleep-wake patterns in parents of children with type 1 diabetes (T1D) before routine use of continuous glucose monitoring system (CGMS) and while using it.

Methods: Thirteen parents completed the Pittsburg Sleep Quality Index (PSQI), a 7-day sleep diary, and wore an actigraph (a wristwatch sized motion detector) during the nights for 1 week before pediatric use of CGMS and 4–8 weeks after initiating routine use of the CGMS.

Results: The parents mean age was 39 (range: 32–47) years, with 10 mothers and 3 fathers. The children mean age was 9.3 years (range: 5.5–16.5) years and mean disease duration was 3.4 (range: 0.6 – 11.2) years. PSQI total score demonstrated similar quality of sleep with and without using the CGM (4.6 and 4.9 respectively, p = 0.45). PSQI score of 6 out of 13 parents was equal or greater than 5, with and without the CGMS, identified as having severe sleep problems. The sleep diary indicated more awakening episodes while using the CGMS vs. without the CGMS (1.6 and 1 respectively, p = 0.03), and actigraphy documented increase in wake bouts number (22.9 and 19.7, p = 0.03) and increase in total wake time (48.3 and 42.2 minutes p = 0.03) while using the CGMS compared to the period prior to CGMS use.

Conclusions: CGMS use seems to have negative effect on parental objective sleep continuity measures, while self-perception of sleep quality remains unchanged. Drawing realistic expectations of the parents regarding the relations between CGMS use and quality of sleep is desirable.

O-47

PARSIMONIOUS DESCRIPTION OF GLUCOSE VARIABILITY IN TYPE 2 DIABETES BY SPARSE PRINCIPAL COMPONENT ANALYSIS

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Background: Increased glucose variability (GV) is considered a risk factor for the development of diabetes complications. To quantify GV, dozens of indices have been developed. In order to limit redundancy, the use of Sparse Principal Component Analysis (SPCA) has been recently assessed in Type 1 Diabetes (T1D), obtaining a parsimonious set of up to 10 indices for describing GV. In this work, we extend the assessment of SPCA to Type 2 Diabetes (T2D) and compare results with those of T1D.

Methods: N = 27 established GV indices, including SD, MAGE, ADRR and others, are computed on 13 CGM time-series collected by the Guardian RT in T2D subjects and on 16 collected by the SEVEN Plus in T1D subjects. SPCA is used first to determine a reduced data dimension P and, then, to decrease the number of variables from N = 27 to M via LASSO estimation of sparse loadings.

Results: For both datasets, SPCA selected P = 2 principal components (PCs) and M = 5 indices for each PC. The subset of indices selected for T2D allowed preserving the 87% of the variance originally explained by all GV metrics, compared to the 67% preserved for T1D. The selected indices are reported in the table. Seven out of the 10 selected GV indices are the same for both datasets.

T1D DATASET (67%)	
PC #1	**PC #2**
range	CV
%values in target	50th percentile
MAGE of descending excursions	%values below target
J-index	MAGE of ascending excursions
GRADE eu%	ADRR
T2D DATASET (87%)	
PC #1	**PC #2**
range	CV
MAGE of descending excursions	range
MAGE	50th percentile
J-index	MAGE of ascending excursions
GRADE eu%	Hyperglycemic Index

Conclusion: SPCA can be used to extract a parsimonious set of indices describing GV from a large dataset. Some of them seem to be independent on the diabetes type 1 vs 2.

O-48

CGM SENSOR DESIGN PRINCIPLES FOR RELIABLE AND ACCURATE GLUCOSE MONITORING IN THE SUBCUTANEOUS TISSUE

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The core element of a continuous glucose monitoring (CGM) system is the glucose sensor, which should enable reliable CGM readings in the interstitial fluid in subcutaneous tissue for a period of several days. To achieve accurate CGM readings, special attention must be paid to the sensor-to-tissue interface and to physiological processes around the sensor insertion site.

Various sensor architectures and materials were investigated in clinical studies in order to better understand some of the processes that occur after sensor insertion and during the sensor usage period. Design principles were derived out of these studies for the development of a prototype CGM sensor with markedly improved precision and accuracy. Some of these design principles and their impact on sensor performance will be discussed in the presentation.

Results of a clinical study involving 40 people with type 1 diabetes show markedly improved accuracy and stability of the novel prototype sensor design. Each subject used 2 to 4 concurrent CGM systems for 7 days. Accuracy (MeanARD ± SD) and sensor-to-sensor precision (PARD ± SD) in the overall glucose concentration range were found to be 9.4% ± 2.3% and 7.8% ± 2.4%, respectively. When glucose was at or below 70 mg/dl, accuracy (MeanARD ± SD) and precision (PARD ± SD) were 13.0% ± 5.7% and 11.9% ± 5.2%, respectively. In the overall glucose concentration range 91.1% of all paired data points fell into the clinical accurate zone A of the Clarke Error Grid. When glucose was at or below 70 mg/dl, 90.7% of all paired data fell in zone A.

O-49

GLYCEMIC PATTERNS RELATED TO EXERCISE IN TYPE 1 DIABETES

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Background: Although regular physical activity is recommended as part of the treatment of diabetes, it remains to be a challenge in type 1 diabetics (T1D) as exercise has been related to hypoglycemia and the actions taken to prevent or reduce it (lowering insulin dose and carbohydrate consumption) frequently result in hyperglycemia. Moreover, no data exist concerning better exercise and timing for this population. The focus of this study was to determine the impact of two different exercise schedules on glycemic behavior.

Methodology: This randomized crossover study enrolled 35 T1D (table 1), age >15 years who used sensor-augmented insulin pumps (SAP). After standardization of meals prior to exercise, each subject underwent 2 moderate-intensity exercise sessions on different days, one in the morning and one in the afternoon. Sessions were separated by 7–14 days. Continuous glucose monitoring (CGM) data were collected during the 24 hours before and 36 hours after each session.

Results: Rate of hypoglycemia was significantly lower following morning versus afternoon exercise (5.6 vs. 10.7 events/patient, $p < 0.001$). Most events occurred 15–24 hours after exercise completion (figure 1). No severe hypoglycemic events were reported. On days following morning exercise, there were 20% more CGM readings in the near-euglycemic range (70–200 mg/dL) as compared to days prior to exercise ($p = 0.003$).

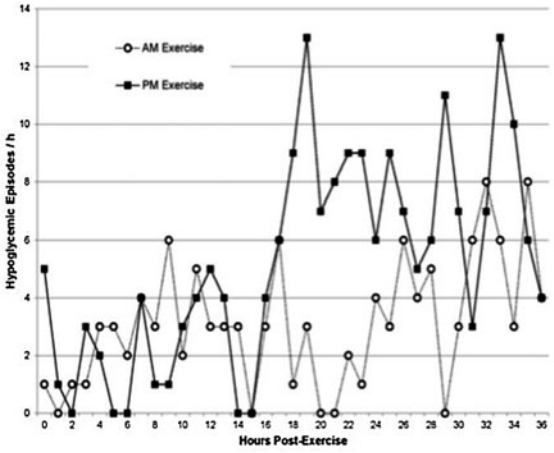
Conclusions: Among T1D on SAP therapy, physical activity in the morning resulted in a lower risk of post-exercise hypoglycemia than afternoon exercise and improved metabolic control on the subsequent day maintaining euglycemia for a longer period of time.

Table 1. Baseline characteristics of subjects

Ordenar

Age, years (mean ± SD)	30.31 ± 12.66
Male (N, %)	17 (48.5)
Time since diagnosis of diabetes in years (mean ± SD)	13.67 ± 9.15
Weight, kg (mean ± SD)	62.47 ± 12.21
Height, cm (mean ± SD)	164 ± 9
BMI, kg/m2 (mean ± SD)	23.2 ± 3.4
A1c level (mean± SD)	7,28 ± 1,03
Time on SAP therapy (months)	9,58 ± 9,77
SAP Therapy Indication (N,%)	
Inadequate metabolic control	20 (57.14)
Hypoglycemia	6 (17.14)
Variability	9 (25.71)
Sensor Use (81-100 %of time) (N,%)	35 (100)
Use of Bolus Wizard (100% of Boluses)	35 (100)
Easy Bolus	0 (0)
Insulin Total Daily Dose (U/kg/day)	0.75 ± 0.34

Figure. 1. Hypoglycemic episodes following morning exercise is represented by (open circles) and afternoon exercise (solid squares).



O-50

SENSOR-AUGMENTED PUMP THERAPY FOR THE TREATMENT OF PATIENTS WITH TYPE 2 DIABETES AND ITS IMPACT ON HYPOGLYCEMIC EVENTS

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Background: Insulin pumps have been used in type 1 diabetics (T1D) however, the experience in type 2 diabetics (T2D) is limited and the few studies that have evaluated this population have shown contradictory results. We describe our experience with SAP therapy in T2D with high risk of severe hypoglycemia that were previously treated with multiple daily injections (MDI).

Patients And Methods: 28 T2D with hypoglycemia who were initially treated with MDI and then switched to SAP therapy, with at least three months of treatment, receiving care at a teaching hospital were analyzed. Data included total daily dose of insulin (TDD), A1C, severe hypoglycemic events, weight, and diabetic complications before and after the therapy.

Results: 28 T2D with hypoglycemia were included (see table 1). All patients had an A1C over 8.5% prior to SAP therapy,

Table 1. Baseline demographic characteristics	
	n=28
Age, years	60.0 ± 12.6
Age at diagnosis, years	41.9 ± 14.8
Sex, male	17 (60.7)
Weight, kg	72.2 ± 14.6
BMI, kg/m²	26.7 ± 4.1
Duration of Diabetes, years	18.1 ± 10.8
Hba1c, %	8.5 ± 1.7
DTID, U/kg	1.0 ± 0.5
Severe hipoglycemia episodes, patients	15 (53.6)
Microvasculares complications	14 (50)
Macrovascular complications	5 (17.8)

Data are means ± SD or n (%). DTID, daily total insulin dose.

Table 2. MDII vs SAP results

Parameter	MDII	SAP	P
Weight (kg)	72.2 ± 14.6	73.76 ± 13.81	0.6842
HbA1c (%)	8.6 ± 1.6	7.7 ± 1.6	0.0351
DTID (U/kg)	1.02 ± 0.51	0.69 ± 0.21	0.0024
Severe hypoglycemia episodes	1.21 ± 1.87	0.11 ± 0.31	0.0032

MDII, multiple daily insulin injections. SAP, sensor augmented pump therapy. DTID, daily total insulin dose.

53% have had at least one event of severe hypoglycemia. Patients wore the sensor more than 80% of the time, used the Bolus Wizard for all boluses, 53% of the patients had less than 5 basal rates. Comparing results before and after the pump use, there was no difference of body weight but there was a significant reduction on HbA1C levels (8.6% vs. 7.7%, p = 0.03), and severe hypoglycemic events (1.21 vs. 0.11 p = 0.0032).

Conclusions: In T2D, SAP therapy is efficacious in glycemic control. It reduces insulin requirements and makes severe hypoglycemia less likely in those people who have failed MDI therapy.

O-51

USE OF PAQ®, A SIMPLE 3-DAY BASAL/BOLUS INSULIN DELIVERING DEVICE, REDUCES BARRIERS TO INSULIN THERAPY IN PATIENTS WITH TYPE 2 DIABETES

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Background: PaQ® (CeQur SA) is a simple to use patch-on device which provides set basal rates and bolus insulin on demand. In addition to feasibility of use, safety and efficacy this study analyzed the impact of the PAQ use on barriers against insulin treatment, diabetes related distress and negative appraisal towards insulin therapy in type 2 diabetes patients on a multiple daily injections insulin regimen.

Methods: This was a mono-center, open label, single arm study. Three validated questionnaires were completed before and two weeks after PaQ treatment; Barriers to Insulin Treatment – (BIT), Problem Areas In Diabetes (PAID) and Insulin Treatment Appraisal Scale (ITAS).

Results: Nineteen patients (age 59 ± 5 y, diabetes duration 15 ± 7 y, 21% female, A1C 7.7 ± 0.7%) completed the questionnaires. There was a large and significant effect of PaQ on the mean BIT total score (difference (Δ) = 0.4 ± 0.6; p = .01, effect size (d) = 0.70). Patients perceived less hardship from insulin therapy (d = 0.35), less stigmatization by insulin injection (d = 0.28) and less fear of hypoglycemia (d = 0.29). Diabetes related distress was reduced (Δ = 0.7 ± 6.7, p = 0.79, d = 10). A reduction was also seen in the ITAS score (Δ = 2.0 ± 6.5, p = .20, d = 31).

Conclusion: The study is limited by the uncontrolled design and small sample size. However, the results and the moderate to large effects sizes suggest that the use of PAQ® has clinically relevant effects to overcome barriers to insulin treatment, without increasing diabetes related distress.

O-52

SEVERE HYPOGLYCAEMIA IN PATIENTS WITH TYPE 1 DIABETES TREATED WITH INSULIN PUMPS IN A REAL LIFE SETTING

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Background and aims: Insulin pumps deliver insulin in a more physiologic manner compared with conventional insulin treatment and may thereby reduce the risk of severe hypoglycaemia (SH). The aim of this study was to evaluate the impact of insulin pump therapy (CSII) on the frequency of SH compared with conventional insulin treatment (CIT).

Material and Methods: A questionnaire on hypoglycaemia and related topics posted from six Danish diabetes clinics to 6112 unselected adult patients with type 1 diabetes was filled in by 3861 patients (63%). In a subpopulation of 1728 patients (45%) supplementary clinical and laboratory data were available.

Results: 3813 patients with type 1 diabetes ((CSII vs. CIT): 211 vs. 3602 patients, men 37% vs. 54%, age 45 ± 14 vs. 48 ± 15 years (mean ± SD), duration of diabetes 25 ± 13 vs. 23 ± 14 years, awareness status (aware/impaired/unaware) 38/47/15 vs. 46/42/12 %) were eligible. The number of episodes of SH was 1.3 ± 4.3 and 1.2 ± 5.0 per patient-year in the CSII and CIT groups, respectively (p = 0.8). This result was confirmed in a multiple regression analysis.

In the subpopulation ((CSII vs. CIT): 112 vs. 1616 patients, awareness status (aware/impaired/unaware) 38/46/16 vs. 44/42/14%, HbA1c 7.6 ± 0.9 vs. 8.0 ± 1.0% (p < 0.001)), frequency of SH was 1.2 ± 4.1 and 1.2 ± 5.0 episodes per patient-year (p = 0.2). This finding was confirmed in the adjusted regression analysis.

Conclusion: Occurrence of SH was similar in patients treated with CSII and CIT regimens. Results should be viewed in the context of indications for starting CSII. Attention toward SH should be maintained after commencing pump therapy.

O-53

BETTER THAN INTERNATIONAL AVERAGE HBA1C REDUCTIONS IN AUSTRALIAN INSULIN PUMP SERVICE FOR ADULTS WITH TYPE-1 DIABETES

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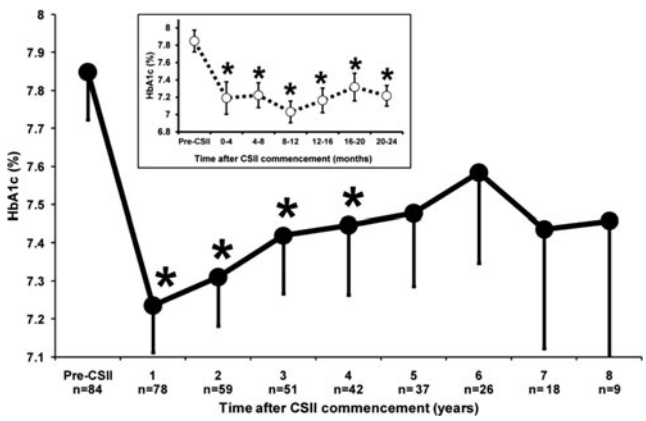
Aim: To follow clinical measures in Type-1 diabetes (T1D) adults starting insulin pump (CSII) therapy.

Methods: A retrospective review of data of T1D adults commencing CSII therapy in diabetes clinics. Data collected included: age, T1D duration, blood pressure (BP), BMI, HbA1c, lipids, and urinary albumin to creatinine ratio (ACR). Results are mean ± SD.

Results: Data were available from before to up to eight years after CSII initiation for 88 (34% males) of 103 subjects who commenced CSII in or after 2003. Age and diabetes duration at CSII-initiation was 37.5 ± 11.5 and 16.0 ± 9.3 years respectively. Eleven % of subjects were <25 years old, 39% were 25–35 years, 25% were 35–45 and 25% were >45 years. BMI was 28.2 ± 4.6 kg/m^2. BP 123 ± 12/75 ± 5 mmHg. Follow-up was 3.9 ± 2.4 (range 0.33–8) years. Pre CSII HbA1c (Fig. 1) was 7.8%, with 19% of subjects with HbA1c <7% at baseline and 38% at year 1 post-CSII. Lipids (mmol/L) were: total cholesterol 4.6 ± 0.9, HDL-C 1.6 ± 0.4, LDL-C 2.5 ± 0.8 and (median(Q1-Q3)) triglycerides 1.0(0.6–1.4). Urine ACR (median(Q1-Q3)) was 0.1(0.1–0.5) mg/mmol. Annual mean ± SEM HbA1c are shown in the Figure, with the inset showing HbA1c in the first 2 years.

Conclusions: In T1D adults commencing CSII in our clinics, mean HbA1c fell from 7.8% to 7.2% at one year, and remained significantly lower for up to 4 years. In the few patients with longer follow-up, HbA1c returned towards baseline. Internationally, mean HbA1c reduction in CSII-using T1D adults is 0.25%, substantially less than locally. Weight, BP, lipids and ACR did not change after CSII initiation.



O-54

ACCURACY OF A NEW PATCH PUMP, THE JEWEL PUMP (DEBIOTECH) COMPARED TO THAT OF TRADITIONAL PUMPS

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For patients with insulin-treated diabetes, patch pumps should soon replace conventional pumps. The Jewel patch pump (JP) is a smart pump equipped with an electromagnetic motor and no tubing. We aimed to compare the *in vitro* JP accuracy to that of conventional pumps (AccuChek/Combo (AC), Medtronic/MiniMed (MN), AnimasVibe (AV) and OmniPod (OP)).

The evaluation consisted in a continuous weighing of the infused liquid with a Sartorius MC5 high precision balance. Data were recorded in the infuscale and processed, in accordance with the IEC/EN601-2-24 standard.

For a rate of 1U/h, the average flow error tested with three samples for each pump model was +1.2% with the JP vs −1.5 and −0.7% respectively with the MN and OP pumps, the absolute difference between the three pump models being not significant. At least, for a flow rate of 1U/h and considering short periods of time (15 and 30 minutes), the accuracy measured with the method of the trumpet curves, was significantly better with the JP than with the MN and OP pumps ($p < 0.01$); similar results were obtained for the infusion repeatability study.

In conclusion, for a basal rate of 1U/h and for a 24-hour period, the Jewel pump shows similar accuracy of infusion as conventional pumps *in vitro*; regarding the infusion repeatability for short periods, the JP did significantly better. The clinical impact of these results has to be tested in sensitive systems such as closed loop systems.

O-55

CONTINUOUS INTRAPERITONEAL INSULIN INFUSION IN TYPE 1 DIABETES: A 6 YEAR POST TRIAL FOLLOW-UP

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Continuous intraperitoneal insulin infusion (CIPII) with an implantable pump is a last resort treatment option for patients with brittle diabetes. Aim was to describe long-term metabolic control, quality of life (QoL) and treatment satisfaction among T1DM patients treated with CIPII, and compare this with their previous subcutaneous (SC) mode of therapy.

Retrospective, longitudinal analysis of patients with T1DM treated with CIPII. Data from a previous randomized cross-over trial using CIPII and SC therapy were compared with 2012 data. QoL was measured using the SF-36 and WHO-5 questionnaires and treatment satisfaction using the DTSQ.

Nineteen patients (52.6% male, mean age 45.8 ± 9.9 years, diabetes duration 24.9 ± 17.3 years) were included. Duration of follow-up was 6.4 ± 0.4 years. Mean HbA1c in 2012 (65.3 ± 23.2 mmol/mol) did not differ from HbA1c at the end of the CIPII (7.1 mmol/mol (95% CI −3.3, 17.5) and SC treatment phase (-0.1 (95%CI −10.5, 10.3)). The number of severe hypoglycaemic events in 2012 was lower compared to the SC treatment in 2006 and more time was spent in hyperglycaemia. QoL remained stable using CIPII and treatment satisfaction was better than with SC therapy. Seven CIPII related complications necessitated re-operation with a hospital admission duration of 0.6 (IQR 0.3, 0.8) days.

Among patients with T1DM treated with CIPII, long-term metabolic control and QoL remains stable over time. Treatment satisfaction with CIPII is superior to SC insulin and complications are scarce. CIPII is a safe and effective treatment option for selected patients with T1DM.

O-56

EXTENDED INSULIN BOLUSES CANNOT CONTROL THE POSTPRANDIAL GLUCOSE RISE AS WELL AS STANDARD BOLUS FOR PERSONS USING INSULIN PUMP THERAPY

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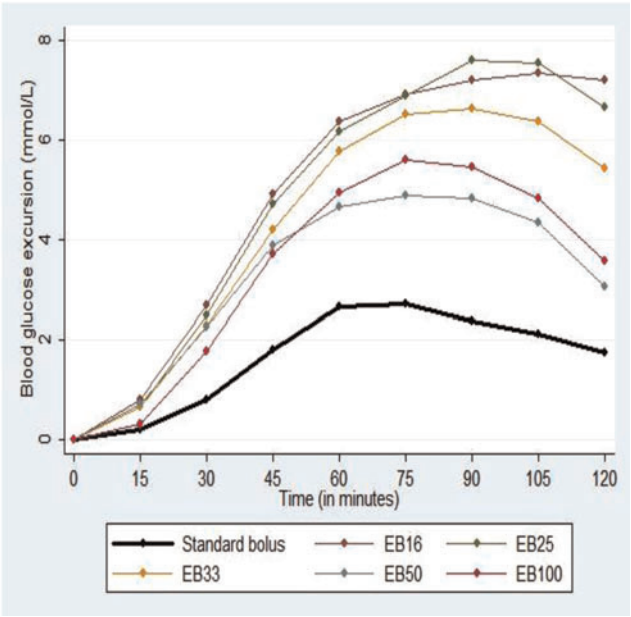
Background: Extended insulin pump boluses (EBs) have been recommended for high fat and protein meals and banquets, however early postprandial hyperglycaemia has been shown. We aimed to determine if an EB could control the postprandial glucose rise as well as a standard bolus (SB) after a standardised meal.



Methods: Twenty children and adults participated in a randomised, repeated-measures trial comparing the glycaemic excursions following five different EBs of insulin with a SB as control. The insulin dose was determined according to the participants' insulin: carbohydrate ratio. The EB was delivered over 2 hours. EB100 = 100% of the insulin dose per hour (i.e. 200% normal insulin dose), EB50 = 50% insulin dose per hour, EB33 = 33% insulin dose per hour, EB25 = 25% insulin dose per hour and EB16 = 16% insulin dose per hour. Continuous glucose monitoring assessed glucose levels for 2 hours following the test meal.

Results: Figure 1 shows the postprandial glycaemic excursions following the test meal. The postprandial glycaemic excursion at 60 min was lower for SB compared to all EBs ($p < 0.05$). The area under the curve was lower for SB compared to all EBs ($p < 0.05$). The peak postprandial glycaemic excursion was lower for SB compared to all EBs.

Conclusions: The EB results in higher postprandial glycaemic excursions at 1 hour than a SB, regardless of the total bolus insulin dose. The EB was unable to adequately control the postprandial glucose rise.

O-57

OPT2MISE: RANDOMIZED CONTROLLED TRIAL COMPARING INSULIN PUMP THERAPY WITH MULTIPLE DAILY INJECTIONS IN TYPE 2 DIABETES — RESEARCH DESIGN AND METHODS

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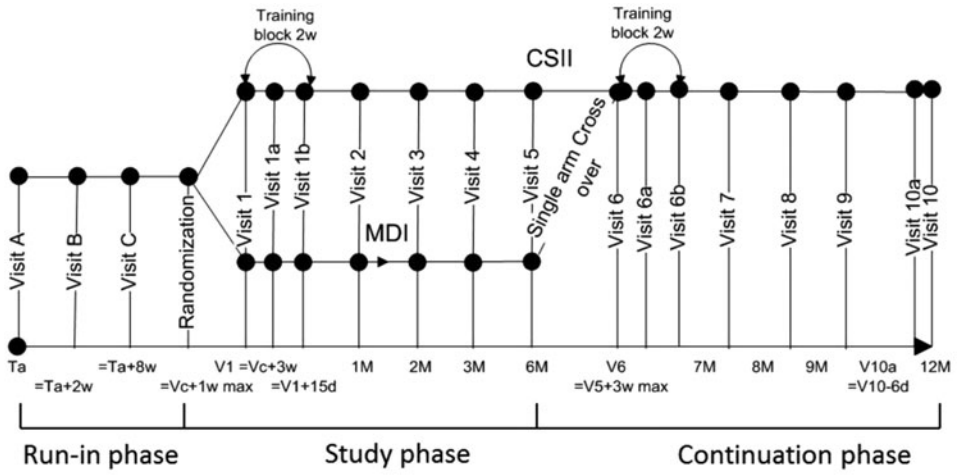
Background: In type 2 diabetes (T2D), current insulin therapy approaches have not consistently achieved optimal glycemic control. Previous studies have suggested benefit to continuous subcutaneous insulin infusion (CSII) in these patients. The OPT2MISE study is a multicenter, randomized, trial comparing CSII to multiple daily injection (MDI) of insulin in a large cohort of T2D subjects with persistent hyperglycemia.

Methods: Subjects were enrolled into a run-in period to optimize their MDI regimen. Subjects with persistent hyperglycemia (HbA1c ≥8%) were randomly assigned to CSII or continuing an MDI regimen. The primary endpoint was the between-group difference in mean HbA1c change from baseline to 6 months. Secondary endpoints included change in mean 24-hour glucose values; area under the curve, time spent in hypoglycemia and hyperglycemia; measures of glycemic excursions; change in postprandial hyperglycemia; and treatment satisfaction and safety endpoints including hospitalizations and emergency room visits.

Results: Subject enrollment was completed in May 2013. 590 patients were screened and 495 were enrolled into the run-in phase. 164 patients (33.1%) benefited from the run-in phase titration and were not randomized. A total of 331 patients, from



35 investigative sites from Europe, Canada, Israel, USA and South Africa, were successfully randomized.

Study completion for the Primary endpoint is expected in January 2014.

Conclusions: OPT2MISE represents the largest comparison of CSII to MDI in a cohort of T2D patients with persistent hyperglycemia despite optimized MDI therapy. OPT2MISE will help define the role of CSII in insulin intensification including safety, hypoglycemia, patient adherence and treatment satisfaction.

O-58

DEVELOPING PAQ®: A SAFE AND EASY TO USE INSULIN DELIVERY DEVICE

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Aim: To develop an insulin delivery device for people with type 2 diabetes mellitus (T2DM) that is safe and easy to use. Usability testing was utilized throughout PaQ development to assess prospective users' ability to assemble, fill, prime, and apply PaQ, as well as deliver boluses doses and interpret communication signals, without committing use errors that could lead to user harm.

Methods: Usability tests, simulating PaQ use, involved 93 untrained and trained people with T2DM and/or diabetes educators. Participants performed hands-on tasks using PaQ and its user documentation. Use errors were documented and participants' ratings of each task's ease of completion (1 = difficult, 7 = easy) and use-safety (1 = low, 7 = high) were collected.

Results: Use errors were identified with assembly and bolus dosing, as well as interpreting user documentation. Improvements to PaQ and user documentation were implemented and assessed with follow-up usability testing resulting in reduced use error rates. Ease of task completion averaged 5.9 for PaQ assembly, 6.9 with bolus dosing, with and without distraction, and 6.8 for interpreting communication signals. Use-safety ratings associated with preparing the device for use and interpreting communications signals averaged 6.7 and 6.8, respectively. Ratings for delivering bolus doses with and without distraction averaged 6.4.

Conclusions: Usability testing provided valuable input in the iterative development of PaQ and its user documentation. Iterative testing and redesign mitigated safety-related use errors prior to clinical testing, and resulted in a product that the intended users reported was easy and safe to use.

O-59

MODULAR ARCHITECTURE OF CLOSED-LOOP CONTROL – THE BLUEPRINT FOR SEQUENTIAL PRODUCT DEVELOPMENT OF THE ARTIFICIAL PANCREAS

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The next logical step in artificial pancreas (AP) development is the gradual transition of the AP into product development and mainstream ambulatory use. A critical element of this transition would be wide availability of outpatient Modular AP Systems (MAPS) capable of running closed-loop algorithms and communicating with CGMs and insulin pumps. Running MAPS on consumer electronics (e.g. smart phone, Google Glass) will drive a paradigm shift in the technology-based treatment of diabetes by allowing any sufficiently capable mobile device to become inherently a medical system running closed-loop control.

The key characteristics of MAPS are:

- Informed by a Body Sensor Network;
- Modular – layered architecture that distributes data processing tasks across various application modules; individual modules are easily replaceable;
- Scalable – naturally supports new and expanded functionality and multiple data sources;
- Local and Global modes of operation – certain processes and patient interaction are available through the portable device; other services and analytics are available via telecommunication.

In this presentation, we introduce a multi-module architecture of MAPS consisting of system level (e.g. medical OS), sensor/pump interface, safety modules (e.g. prevention of hypoglycemia), real-time control modules, and Cloud interface.

We conclude that the artificial pancreas *is* a mobile medical network which coordinates multiple devices and multiple control modules. Such a modular structure allows the sequential deployment of treatment modalities in the field, beginning with mitigation of hypoglycemia and progressing with control-to-range and fully-automated closed loop. Regulatory environment and clinical preferences favor the concept of MAPS as a vehicle towards AP product development.

O-60

ARTIFICIAL PANCREAS USING INTRA-PERITONEAL INSULIN DELIVERY: WHY SHOULD IT BE DEVELOPED AND HOW TO MOVE TOWARD MARKET APPROVAL

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The pharmaco-kinetics and –dynamics of subcutaneous (SC) insulin represent a true challenge for closed-loop delivery. The prevention of post-meal hyperglycemia and hypoglycemia following physical exercise leads to very sophisticated algorithms aiming at the modulation of insulin delivery following mandatory announcements of carbohydrate intakes or exercise practice. Some models include glucagon infusion to counteract excess of insulin action in late post-meal or post-exercise periods. The usefulness of a quicker and shorter insulin action is consensually admitted. Intra-peritoneal (IP) insulin infusion route has shown quicker insulin action and return to baseline thanks to a more direct insulin absorption combined with a liver-oriented distribution. Lower peripheral plasma insulin level and restored glucagon response to hypoglycemia and to exercise are other characteristics. IP delivery systems have remained confidential at the market level although still very useful for patients with disorders of SC insulin absorption or high blood glucose variability resulting in recurrent severe hypoglycemia. Integration of IP delivery in closed-loop trials has shown effectiveness in reducing post-meal hyperglycemia and reaching very stable overnight basal control. These results match well with the wish of a quicker and very reproducible insulin action. The patients who present high variability in insulin action would be the first candidates for closed-loop delivery with IP route but indications could extend to a wider population who expect further reduction of the device burden associated with current closed-loop systems. Evolution toward market approval will need both a wider experience with IP insulin delivery systems and further trials documenting the benefits for closed-loop.

O-61

MONOGENIC DIABETES: UPDATE IN DIAGNOSIS AND TREATMENT

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Here I will describe our web-based registry for monogenic diabetes (MDM) (http://monogenicdiabetes.uchicago.edu/neonatal-registry/). Low-cost web-based tools, including surveys, discussion groups and electronic data capturing has facilitated enrollment and support for patients with MDM. For diabetes presenting in the first year of life (neonatal diabetes mellitus, NDM), the registry has helped identify mutations in >140 patients. The most common mutations are in the genes encoding the two subunits of the ATP-sensitive potassium channel, *KCNJ11* (n = 78) and *ABCC8* (n = 20). Over 90% have been transitioned from insulin to oral sulfonylurea therapy. Those with abnormalities in chromosome 6q24 (n = 20) may have early transient diabetes with recurrence of hyperglycemia in early adulthood. Through longitudinal follow-up and recruitment for dynamic studies we have seen benefit from non-insulin based therapies. These are dramatic example of personalized genetic medicine leading to improved glucose regulation and quality of life with decreased costs. Maturity-onset diabetes of the young (MODY) is a clinically heterogeneous group of monogenic disorders characterized by autosomal dominant inheritance of young-onset, non-insulin-dependent diabetes. A correct genetic diagnosis can yield appropriate treatment, identifies associated syndromes, and help at-risk family members and future generations. Recent identification of >200 individuals with MODY through our registry shows genetic testing in a population with increased prevalence of MODY can be cost-effective. Our results make a compelling argument for routine coverage of genetic testing costs in patients with a high clinical suspicion of MODY, confirming the importance of a diagnosis of MDM and the utility of web-based technologies for attracting subjects.

O-62

CURRENT THINKING FOR THE DIAGNOSIS AND TREATMENT OF CYSTIC-FIBROSIS-RELATED-DIABETES

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Since CF impacts pancreatic endocrine function, cystic-fibrosis-related-diabetes (CFRD) is common. After the age of 30 years about 40–50% of individuals have CFRD. While microvascular disease is starting to be seen more often, cardiovascular disease has never been reported.

One of the greatest controversies is how often individuals with CF should be screened for diabetes. Current guidelines state this should be done yearly after the age of 10 years, yet the only way to diagnose this population is with an oral glucose tolerance test which is burdensome and often not done. Furthermore, hypoglycemia is not uncommon at the end of this test, mostly likely related to a delayed glucagon response.

The other major controversy is the impact of glycemic control on pulmonary function. The one intervention study showed a statistically significant (but clinically insignificant) improvement of BMI but no change in pulmonary function.

Given these individuals are living much longer due to improved treatments, including lung transplants, it seems that since we have definitive proof about the impact of tight control on microvascular complications in both type 1 and type 2 diabetes, the same is extremely likely to be the case with CFRD.

The other practical issues are the many issues that impact the diabetes treatments on a regular basis. Frequent infections, steroid therapy, advanced liver disease, and pregnancy can all complicate the diabetes management, thus a team expert in the care of this population should ideally manage these patients.

O-63

ALTERATION IN GLUCOSE DYNAMICS FOLLOWING WITHDRAWAL OF USUAL THERAPY AND CLOSED-LOOP INSULIN DELIVERY IN INSULIN-NAIVE TYPE 2 DIABETES SUBJECTS

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Discontinuation of antihyperglycemic oral agents and initiation of insulin is recommended in certain clinical situations for inpatients with type 2 diabetes (T2D). We studied alterations in glucose turnover following withdrawal of non-insulin therapy.

Twelve subjects with insulin-naive T2D were studied during two 24-hour visits. During control visit, subject's usual antihyperglycaemic therapy was continued. At another visit, usual therapy was discontinued and replaced by closed loop insulin delivery. Subjects consumed 50–80 g carbohydrate at each meal, matched for both visits. Stable-label [6,6-$^2H_2$]glucose was infused intravenously to measure the systemic glucose appearance and glucose disposal.

Plasma glucose during both visits were comparable (p = 0.57). Glucose appearance (R_a) significantly increased during the day [21.4 (19.5, 23.5) vs. 18.6 (17.0, 21.6) μmol/kg/min, p = 0.019] and decreased overnight [9.7 (8.5, 11.4) vs. 11.6 (10.3, 12.9) μmol/kg/min, p = 0.004] when usual therapy was discontinued but no difference over 24-hours was observed (p = 0.79). Similarly, increased glucose disposal (R_d) was observed during the day [21.2 (19.4, 23.9) vs. 18.8 (18.3, 21.7) μmol/kg/min, p = 0.002] and decreased overnight [10.4 (9.1, 12.0) vs. 11.8 (10.7, 13.7) μmol/kg/min, p = 0.005] when closed loop replaced usual therapy. There was increased hepatic insulin resistance [1.4 (0.8, 2.5) vs. 1.3 (0.6, 2.2) mmol/kg/min × pmol/l, p = 0.023] and decreased peripheral insulin sensitivity [0.05 (0.03, 0.07) vs. 0.06 (0.04, 0.08) μmol/kg/min per pmol/l, p = 0.034] when usual therapy was discontinued.

Discontinuation of non-insulin therapy affects glucose turnover by altering R_a and insulin sensitivity, highlighting the need of appropriate insulin dose adjustments to compensate for these changes.

O-64

SAFETY OF AN OVERNIGHT CLOSED LOOP SYSTEM WITH INDUCED CALIBRATION ERROR

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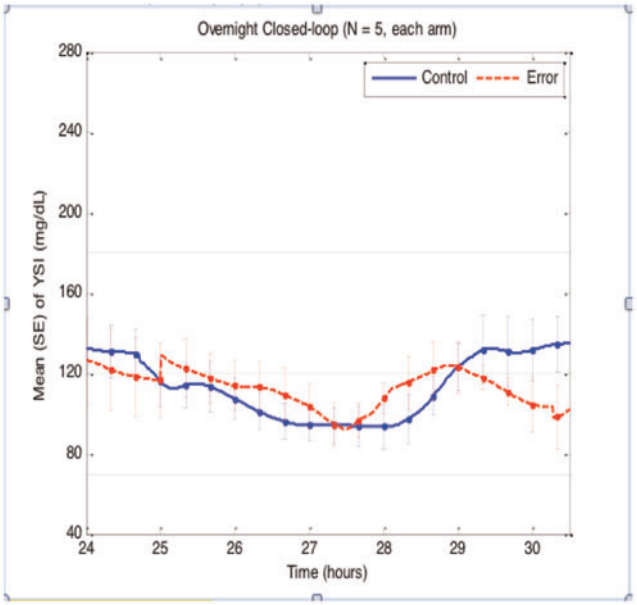
Introduction: Closed loop systems rely on sensor glucose values to determine insulin dosing which in turn are reliant on calibration by capillary glucose readings. Capillary and interstitial glucose concentrations may differ during rapid glucose fluctuations such as in the post-meal phase prior to starting overnight closed loop. We tested the safety of overnight operation of a closed loop system, using a proportional-integral-derivative (PID) algorithm, with the maximum permissible calibration error prior to starting.



Methods: 8 subjects with type 1 diabetes were recruited. They underwent overnight closed loop control in a clinical research facility on two occasions. A calibration error of 30% was deliberately induced on one of the experiments in random sequence. YSI glucose was measured every 30 minutes through the night [11pm–6am]. We present preliminary analysis of the first 5 paired experiments

Results: 5 subjects [2 male and 3 female] with type 1 diabetes treated with insulin pump therapy have been studied till date. The mean absolute error on calibration was 23.3%. Mean YSI glucose was 115 mg/dl vs 108 mg/dl between the two arms and there was no difference in time <70 mg/dl [5.5 vs 6.2% control vs error; p = NS]. There was a reduction in time >180 mg/dl [4.3% vs 0.0%; p = 0.34].

Summary: The PID based overnight closed loop system can accommodate at least a 30% error in initial calibration without detriment to the patient. Given the likelihood of patients starting closed loop on a rapidly changing glucose, this information enhances the safety of the system.

O-65

CLINICAL TRIAL OF AN ARTIFICIAL PANCREAS WITH LARGE UNANNOUNCED MEALS

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Closed-loop control of blood glucose (BG) levels in people with type 1 diabetes can reduce patient burden and the incidence of complications. We tested a multiple model probabilistic predictive controller (MMPPC) on six patients. Each admission

lasted for 32 hours with five unannounced meals each containing 1 g/kg of carbohydrate (CHO).

The controller used an Abbott Navigator CGM and Insulet Omnipod insulin pump implemented through the UCSB artificial pancreas system. Therapy began at 9 AM with unannounced meals at 9 AM, 1 PM, 5:30 PM, and 9 AM and 1 PM the next day. The patients had a mean (±SD) HbA1C of 7.3 ± 0.6%, age of 28 ± 5 years, total daily dose of 43 ± 13 U, and weight of 74 ± 13 kg.

The algorithm predicts the BG value with explicit uncertainty estimates. Insulin boluses are calculated to maintain a roughly 3% risk of BG levels below 80 mg/dl. At night, a target of 100 mg/dl was used, with attenuated control providing smooth corrections.

On a 24-hour basis, the mean reference/CGM values of 161/142 mg/dl, with 63/78% of time spent between 70 and 180 mg/dl. One CHO intervention was given for a nocturnal glucose of 66 mg/dl with a rate of change of −0.25 mg/dl per min. Three CHO interventions occurred due to system failures. For the 30 unannounced meals the mean pre-meal, post-meal maximum, and 3-hour post-meal values were 139/132, 223/208, and 168/156 mg/dl respectively.

The MMPPC was tested in-clinic against repeated, large, unannounced meals and maintained good control overnight and during meals.

O-66

OVERNIGHT CLOSED-LOOP CONTROL WITH A PROPORTIONAL-INTEGRAL-DERIVATIVE BASED ALGORITHM IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES AT DIABETES CAMP

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The Medtronic Android-based proportional-integral-derivative with insulin feedback (PID-IFB) system is designed for overnight closed-loop (OCL) control in patients with type 1 diabetes. The automated system consists of a Revel 2.0 insulin pump and Enlite glucose sensor, PID-IFB algorithm based on an Android phone, Bluetooth-RF translator and remote monitoring capabilities.

The objective was to evaluate the efficacy and safety of this OCL controller in participants (10–35 years) with type 1 diabetes on insulin pump therapy, in a camp setting.

Participants were randomized to either OCL (n = 50) or sensor-augmented pump (control) (n = 52) on alternate nights in up to 6 consecutive nights at camp. There were 21 subjects with mean ± SD age 14.7 ± 3.9 y, duration of diabetes 7.9 ± 5.3 y and A1C 7.9 ± 1.4%. OCL was commenced in 50 of 55 potential nights (91%). Full OCL lasting a minimum 6 hours was achieved in 37 (67%) nights. OCL was stopped in 18% of nights due to sensor error being >20%, 4% due to a sensor failing to pass a performance evaluation upon restarting OCL and 2% due to loss of communication between devices.

The median (IQR) percent time spent between 70–150 mg/dL was 46% (32,76) for controls vs. 86% (58,98) for full OCL (n = 37), $P < 0.001$. There was less time spent in the hypoglycemic range <70 mg/dL with a median 9% (0,39) in the control period vs. 0% (0,0) in full OCL, $P < 0.001$.

Overnight closed-loop control with the Android-based PID-IFB controller resulted in a significant reduction in nocturnal hypoglycemia and increased time spent in range compared to sensor-augmented pump therapy.

O-67

CLINICAL ASSESSMENT OF A RETROFITTING ALGORITHM FOR A POSTERIORI ENHANCEMENT OF CGM TRACES

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Objective: When assessing new diabetes therapies in outpatient trials, only a few blood glucose (BG) references can be collected and the sole use of unprocessed Continuous Glucose Monitoring (CGM) may lead to under/overestimation of the indicators quantifying treatment efficacy.

Recently, we proposed a 'retrofitting' algorithm (Del Favero et al., ATTD 2013) that produces accurate continuous-time BG profile by simultaneously exploiting the accuracy of the few BG references available and the high temporal-resolution of CGM.

Here we assess the method on a large clinical dataset, showing that it reduces the error in outcome-metrics computation with respect to the use of unprocessed CGM.

Method: The retrofitting algorithm was tested on data of 47 subjects studied within a trial of the AP@home project (Luijf et al., Diabetes Care, in press). Each patient underwent three 20 h-admissions. Frequent YSI measurements were available: about 12 references/day were given to the algorithm to enhance CGM and the remaining (about 80% of the collected ones) were used for testing the reconstructed profile.

Result: The retrofitted profile were more accurate than unprocessed CGM: MAD was reduced by 48.5% (almost halved) and MARD was reduced by 47.86%. Error in the evaluation of time below 70 mg/dl and time in target [70–180]mg/dl reduced by 45.7% and 64.8%, respectively, when compared to the unprocessed CGM.

Conclusion: The use of the retrofitted profile rather than unprocessed CGM reduces errors in assessing treatment-efficacy.

O-68

UTILIZING PHYSICAL ACTIVITY TRACKERS IN MOBILE DIABETES SELF-MANAGEMENT

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For people with diabetes, continuous feedback about their physical activity can be of importance for maintaining a healthy blood glucose level. A variety of activity trackers are available on the market today. Their step-counting functionality is frequently accompanied by an estimation of energy expenditure. Unfortunately, these sensors' automatic data interpretation does not provide additional information about physical activity and are hard to integrate in digital diabetes diaries. Their unprocessed data itself do not shape particular activities, but holds a potential

FIG. 1. Overview of multiple Fitbit devices in the context of activity data import into the Diabetes Diary application through the associated Web-service.

to render such information in connection with mobile-phone-based applications.

The solution we present provides a compact and specific overview of the user's daily physical activity. This is achieved through the use of preprocessed records of steps and calories and can easily be applied onto existing application architectures. In our Diabetes Diary application [1] we access this data from a Fitbit Flex activity tracker [2] and its Web-service [3] that records steps and calories values captured in 1-minute intervals. The built-in algorithm identifies basic activity types and corresponding intensity levels for significant segments of the logged data series.

This approach represents a promising way of helping patients with managing physical activity as part of their diabetes self-management. Its simplicity and straightforwardness shows a potential for future usage, which could cover a wide selection of activity tracking devices.

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O-69

PERFORMANCE, USER SATISFACTION AND SAFETY EVALUATION OF CONNECTED CARE DEVICE IN PATIENTS WITH DIABETES MELLITUS

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Objective: To evaluate the performance, patient satisfaction, and safety of the Connected Care device. The Connected Care device transfers CGM and pump data to CareLink online every 5th minute, thereby making it available to patients and/or care partners on their individual web connected devices such as smartphones, tablets and PCs.

Methods: This was a multi-center, non-randomized pre-market study of the Connected Care device. Forty subjects with Diabetes Mellitus being treated with a Sensor-Augmented Pump (SAP) participated for 15 days. Connectivity and usability of Connected Care was evaluated and device related safety was assessed. Subject and care partner acceptance of the Connected Care device and training materials were measured by questionnaires using 7-point likert scale.

Results: Preliminary analysis on 19 T1DM subjects (12–26 years) shows overall average system connectivity of 22 ± 2.45 hr/d. On average, the mobile displays were viewed 11.08 times/d with the highest frequency in evenings (6 PM-12 AM; 36.2% of all views). The most frequent text message sent was regarding the high glucose alarm (692 SMS sent). Questionnaire results indicated overall device feature satisfaction, with care partners being more aware of the patient's BG levels post-study (daytime: 77.8%; nighttime: 57.9% agreement).

Conclusion: Incorporating the Connected Care device into everyday use for patients with Diabetes Mellitus that use SAP, increases accessibility of CGM and pump data via web connected devices. It is projected to improve satisfaction, safety and convenience for patients on SAP and their care partners. The full dataset of 40 subjects will be discussed to support this conclusion.

O-70

LONG-TERM TELEMONITORING OF PATIENTS WITH DMT2: PRELIMINARY RESULTS OF THE GREEK PILOT OF THE RENEWING HEALTH MULTICENTER RANDOMIZED TRIAL

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Objective: To study the impact of a long-term telemonitoring program for patients with type 2 diabetes mellitus (DMT2) on

glycemic control and health-related quality of life (QoL) compared to usual care.

Participants: 154 patients with DMT2 capable to use the telemonitoring device, with an HbA1c >53 mmol/mol (7.0% according to NGSP), were randomly assigned in the telemonitoring (I), (N = 74) and the control (C), (N = 80) group after having signed the informed consent.

Methods: In the (I) group patients' blood glucose profiles were collected weekly using a mobile phone health platform, for a period of one year. Allocated health professionals provided by phone the appropriate counseling on lifestyle and medication changes when required. Patients in (C) group received usual care with face-to-face consultations. QoL was assessed using a generic (SF36v2) questionnaire and a disease-specific questionnaire, the Problem Areas in Diabetes (PAID) scale. (Local Trial Registration NCT01498367.)

Results: A greater reduction in HBA1C was observed in the telemonitoring group [(I) −1.27, (C) −0.85, p = 0.001]. There was a statistically significant improvement in the generic QoL, both in the mental component summary [MSC: (I) +3.46, (C) −3.24, p = 0.000] and in the physical component summary [PSC: (I) +1.17, (C) −1.26, p = 0.00] in the telemonitoring group. Disease specific QoL was also significantly improved in the intervention group compared to control (11.25 PAID score units, 95% CI, p = 0.000).

Conclusion: Our preliminary results indicate that home telemonitoring is more effective in improving glycemic control and QoL in DMT2 patients compared with the usual care.

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NOVEL MENDOR BALANCE GLUCOSE PROFILING TOOL SHOWS SIGNIFICANT POST-MEAL BLOOD GLUCOSE EXCURSIONS IN INSULIN-TREATED TYPE 2 DIABETIC PATIENTS

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Background: Majority of patients with type 2 diabetes on basal insulin are uncontrolled but real-life glucose excursions in this population are unknown.

Methods: 70 uncontrolled (HbA1c >7%) type 2 diabetes patients on stable dose of basal insulin ± oral medications were recruited in Finland. Any other injectables (meal insulin, premixed insulin or GLP-1 agonists) were not allowed. Mendor Balance™ was used as a novel tool for glucose profiling to investigate post-meal blood glucose excursions.

Patients were introduced the Mendor Balance™, which analyses blood glucose profile automatically from three daily routines (sleep, breakfast and main meal). Subjects performed carefully-timed measurements before bedtime and at wake-up (overnight pairs) and before and 1.5–2.5 h after each meal (breakfast pairs and main meal pairs). Over 2 mmol/L average post-meal excursion was considered clinically significant.

Results: 90% of subjects completed profiling successfully. Interim analysis showed that 79% of subjects showed at least +2 mmol/L average breakfast excursions, whereas excursions on main meal were not as frequent (56%). Overnight negative excursions more than −4 mmol/L occurred in 48% of the subjects.

Conclusions: Glucose profiling using Mendor Balance™, is a simple, high-compliance tool to evaluate blood glucose profiles in real-life setting. Vast majority of uncontrolled patients with type 2 diabetes on basal insulin have significant post-meal excursions.

O-72

INTRADERMAL INSULIN INFUSION ACHIEVES FASTER INSULIN ACTION THAN SUBCUTANEOUS INFUSION FOR THREE DAY WEAR

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Aims: This study investigated the ability of intradermal (ID) basal/bolus delivery of a fast-acting insulin analog to maintain an advantage of faster insulin action (Tmax) compared to subcutaneous (SC) delivery over the course of a three day infusion period. Pharmacodynamics (PD) and other measures of device performance and patient experience were also assessed.

Design: This was a single center, open-label, 2-period crossover study in 28 type 1 diabetes patients on continuous subcutaneous insulin infusion (CSII). Each subject was administered a three-day infusion for each route across two in-clinic visits in a randomized order. Insulin aspart (NovoRapid®) was administered via an Animas® Vibe™ insulin infusion pump connected to a Medtronic Quick-Set® (SC) or investigational intradermal microneedle infusion set (1.5 mm, 34 gauge). Individual bolus doses were determined based on the subjects' insulin sensitivity. At each visit bolus insulin infusions were given prior to a standardized breakfast and lunch test meal on each of the three

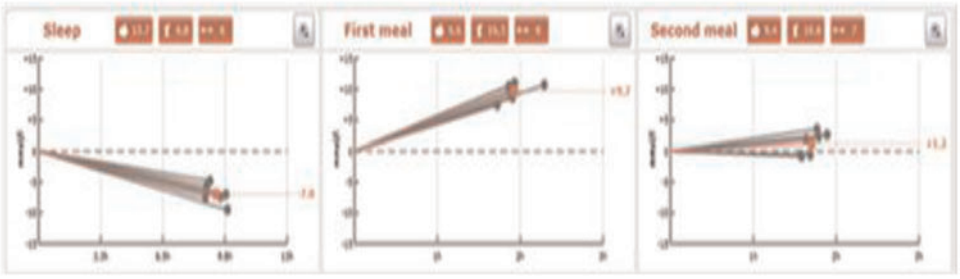

FIG. 1. Illustration of a typical excursion analysis in the study (variation and average excursion)

treatment days. Before and after each bolus, blood was drawn to measure insulin aspart and blood glucose in serum.

Results: ID bolus infusion had a significantly shorter Tmax than SC infusion (Δ 20 minutes), and this difference was maintained over three days. Intra-subject variability of Tmax was significantly smaller for ID delivery, but inter-subject variability was not. For 0–2 hours post-prandially, the insulin and glucose ΔAUC values were significantly larger and smaller, respectively, with ID delivery.

Conclusion: The faster insulin action that ID delivery provides over SC can be maintained over a three-day basal/bolus infusion period.

O-73

EFFECTIVENESS OF TITRATION ALGORITHMS WITH INSULIN GLARGINE IN PATIENTS WITH TYPE-2 DIABETES MELLITUS

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In this study, we collect data regarding the effectiveness of different dose titration algorithms (TA) for optimization or initiation of basal insulin supported oral therapy (BOT) in type 2 patients.

Methods: A total of 50 patients were enrolled in this trial (33 men, age: 63 ± 8 yrs., 7.9 ± 0.8%). The investigator decided on an individual basis for one of four standard titration algorithms (TA): standard (S: fasting glucose target 90–130 mg/dL, n = 39), standard-fast titration (S-FT: 90–130 mg/dL, larger dose increments at FBG).

Investigator-initiated trial supported in part by Sanofi.

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METABOLISM OF INSULIN GLARGINE IN HUMANS IS THE SAME AFTER ADMINISTRATION OF GLA-100 AND GLA-300

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Aims: Investigational new insulin glargine U300 (Gla-300; 300 U/mL) has improved PK and PD profiles compared with Gla-100 (100 U/mL). Insulin glargine (M0) is a 21^{A}-Gly-modified mimic of a human insulin intermediate with low solubility at tissue pH, which is processed *in vivo* into soluble M1 (predominantly responsible for metabolic effects). This sub-study compared metabolism of Gla-300 with Gla-100 in people with T1DM.

Methods: Blood samples were collected during a double-blind, 2-treatment, 2-period, 2-sequence cross-over study. Participants received 0.4 (n = 18) or 0.6 U/kg Gla-300 (n = 12), and 0.4 U/kg Gla-100 once daily in randomised order. Trough values of M0, M1 and M2 were determined for 7 days; a 36-h euglycaemic clamp was conducted on Day 8. M0, M2 and M1 were quantified by LC-MS/MS (LLOQ 0.2 ng/mL).

Results: M1 was the principal active moiety circulating in blood after administration of both Gla-100 and Gla-300. Trough values of M1 were quantifiable after 2–3 injections regardless of treatment. Steady state concentrations of M1 were achieved after 2 days for Gla-100, and 3–4 days for Gla-300. Trough concentrations of M0 and M2 were low and only detected in a few samples in a few participants.

In steady state, M1 defined concentration time profiles which were dose dependent and even flatter after Gla-300 administration than Gla-100 administration. Steady state M1 PK profiles were consistent with those from unspecific radioimmunoassay measurements.

Conclusion: Insulin glargine metabolism is the same after administration of Gla-100 and Gla-300, and M1 is the main circulating active component.

Study sponsored by Sanofi (NCT01349855).

O-75

INVESTIGATIONAL NEW INSULIN U300: GLUCOSE CONTROL AND HYPOGLYCAEMIA IN TYPE 2 DIABETES PEOPLE ON BASAL INSULIN AND OADS (EDITION II)

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Aims: Investigational new insulin glargine U300 (Gla-300) has even flatter and more prolonged PK and PD profiles than insulin glargine 100 U/mL (Gla-100). EDITION II compared the efficacy and safety of Gla-300 vs Gla-100 in people with T2DM using basal insulin and OADs.

Methods: In this multicentre, open-label, 6-month study, participants were randomised to Gla-300 or Gla-100 once daily in the evening. Primary endpoint was change in HbA_{1c} (baseline to month 6). First main secondary efficacy endpoint was participants (%) with ≥1 severe or confirmed (≤3.9 mmol/L) nocturnal hypoglycaemia (month 3–6).

Results: Gla-300 was non-inferior to Gla-100 for change in HbA_{1c} at month 6 (LS mean change −0.57 [0.09] % and −0.56 [0.09] %; difference −0.01 [95% CI: −0.14–0.12] %). Significantly fewer participants had ≥1 severe or confirmed nocturnal hypoglycaemia (month 3–6) with Gla-300 vs Gla-100 (87 [21.6%] vs 113 [27.9%]; RR 0.77 [95% CI: 0.61–0.99]; p = 0.038). A similar, consistent reduction in severe or confirmed nocturnal hypoglycaemia was observed during the first 8 weeks (13.2% vs 24.6%; RR 0.53 [95% CI: 0.38–0.75]) and over the 6-month treatment period (28.3 vs 39.9%; RR 0.71 [0.58–0.87]).

Over the 6-month period, fewer participants experienced ≥ 1 nocturnal hypoglycaemic event with Gla-300 vs Gla-100 (30.5% vs 41.6%; RR 0.73 [95% CI: 0.60–0.89]), and any hypoglycaemia at any time of day (71.5% vs 79.3%; RR 0.90 [95% CI: 0.84–0.97]).

Conclusion: Gla-300 provides similar effective glycaemic control, with less confirmed or severe nocturnal hypoglycaemia, compared with Gla-100.

Study sponsored by Sanofi (NCT01499095).

O-76

BRAIN RESPONSES TO FOOD INGESTION AFTER ROUX-EN-Y GASTRIC BYPASS (RYGB): A [18F]-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY (FDG-PET) NEUROIMAGING STUDY

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Background: Mechanisms of weight loss post-RYGB are unclear. Modulation of appetite may contribute.

Aim: To investigate whether brain responses to food ingestion are different post-RYGB compared to non-operated obese and normal-weight subjects.

Materials and Methods: Twelve normal-weight (NW, age 32.3 ± 9.3 years, BMI 22.3 ± 1.4 kg/m^2), nine obese (Ob, age 32.7 ± 10.1 years, BMI 33.8 ± 2.6 kg/m^2) and nine post-RYGB (age 45.1 ± 10.7 years, BMI 33.9 ± 3.7 kg/m^2) subjects underwent FDG-PET neuroimaging twice: once FED, once FASTED. Brain FDG uptake, a marker of neuronal activation, was compared using Statistical Parametric Mapping. Satiety was assessed using visual analogue scales and post-scan *ad-libitum* meal.

Results: The FED state was associated with increased fullness ($p < 0.001$) and reduced *ad-libitum* food consumption ($p = 0.006$). Post-RYGB had higher fullness scores ($p = 0.009$) and lower *ad-libitum* consumption ($p = 0.021$).

The FED state was associated with increased (voxelwise $p < 0.001$, cluster-level-corrected $p < 0.05$) FDG uptake (neuronal activation) in interoceptive and reward regions (insula, globus pallidus, ventral striatum, amygdala, hippocampus, ventral cingulate) and decreased uptake (deactivation) in inhibitory control regions (dorsolateral frontal cortex (DLFC)) and default mode network (DMN) (posterior cingulate, precuneus, angular gyrus).

There were differences between groups in brain responses to food ingestion (rmANOVA $p < 0.01$, cluster-size >50 voxels) in: medial orbital cortex (reward salience) with activation post-RYGB versus deactivation in NW; inhibitory-control regions (DLFC) with deactivation in NW and post-RYGB attenuated in Ob; and DMN, with exaggerated deactivation post-RYGB.

Conclusions: Increased fullness and decreased food consumption post-RYGB are associated with differences in brain responses to food ingestion. These differences may represent negative rather than positive experiences of eating and improved inhibitory control and may contribute to weight loss.

O-77

NEW INSIGHTS INTO OXIDATIVE MODIFICATION OF PROTEINS IN DIABETES. GLYCATED ALBUMIN AS A RELEVANT BIOMARKER

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Oxidative stress and protein modifications are frequently observed in numerous disease states. Albumin, the major circulating protein in blood, can undergo increased glycoxidation in diabetes. Protein glycoxidation can lead to the formation of advanced glycoxidation end products, which induce various deleterious effects on cells.

Works in our group, revealed structural damages induced by the glycoxidation of blood-purified Human Serum albumin (HSA) and of albumin purified from diabetic patients.

Oxidative modifications was found to be enhanced in *in vitro* or *in vivo* glycated albumin, after determination of their free thiol group content, relative electrophoretic migration, carbonyl content. Impaired antioxidant and drug-binding capacities (warfarin and ketoprofen) of glycated albumins were evidenced.

Also we identified deleterious pathophysiological effects of glycated albumin on human adipose and monocyte cell lines as well. We observed an overgeneration of intracellular reactive oxygen species, impairments in proteasomal activities and an accumulation of carbonylated proteins in glycated-albumins treated cells. We established links between HSA modifications with the oxidative impact on the protein structures and on cells pathophysiology.

Involvement of glycated albumin in diabetes pathology was evidenced *in vivo* in a model of isolated perfuse rat heart and in Db/Db transgenic mice.

All our recent data provide new information supporting albumin as an important biomarker to be considered for monitoring diabetic pathophysiology.

O-78

TECHNICAL FEASABILITY AND SAFETY OF ILEAL INTERPOSITION FOR TYPE-2 DIABETES–MULTI-CENTER DATA

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Introduction: In morbidly obese patients with type 2 diabetes (T2DM), bariatric surgery offers effective treatment with low mortality (<0.5%). Ileal Interposition with sleeve gastrectomy (IISG) is a novel procedure, shown to be safe and effective in the treatment of T2DM in morbidly obese as well as low weight patients. We present our morbidity and mortality data and technical feasibility with IISG surgery in poorly controlled type II diabetic patients.

Methods: A total of 411 patients treated at 2 centers – Kirloskar Hospital, Hyderabad, India & Alman Hastanesi, Istanbul, Turkey, between Feb 2008 to May 2013. Mean Age = 45.5; Sex Ratio = 270 males and 141 Females; Mean BMI = 30.5. 65.7% of the patients had BMI <35 and 34.3% had BMI >35 kg/m2. Most patients had long standing diabetes (mean 10.3 years);

with a mean preoperative HbA1c of 9.41%. Follow-up from 5-65 months.

Results: Remission of T2DM (HbA1c < 6.5% without medication) in 81.2%; hypertension in 96.1% and dyslipidemia in 92.2%. Mean reduction in BMI was 6.27 kg/m^2, 7.91 kg/m^2, 10.41 kg/m^2, 13 kg/m^2 where preoperative BMI was < 30, 30–35, 35–40 and > 40, respectively.

Total complication rate: 7,5%.

Mortality rate from procedure: 0.25%; Other Cause Mortality – 1.7%

Conclusion: With this 2 center and 2 surgical teams study, IISG is seen to be technically feasible with safety and sequelae that are comparable with other Bariatric and Metabolic procedures, with a high remission rate for diabetes and other co-morbidities, even in lower BMI patients.

O-79

INCREASED INSULIN CLEARANCE AND NORMALIZATION OF C-PEPTIDE SECRETION IN DIABETIC PATIENTS AFTER ROUX EN Y GASTRIC BYPASS

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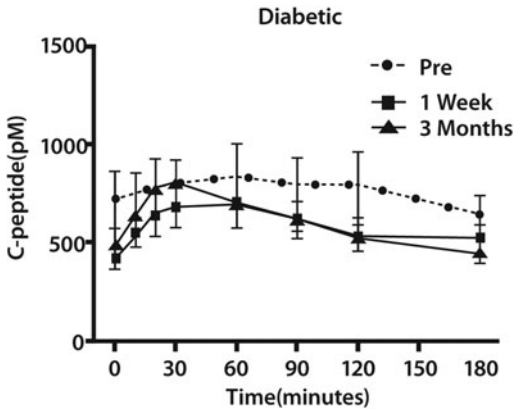
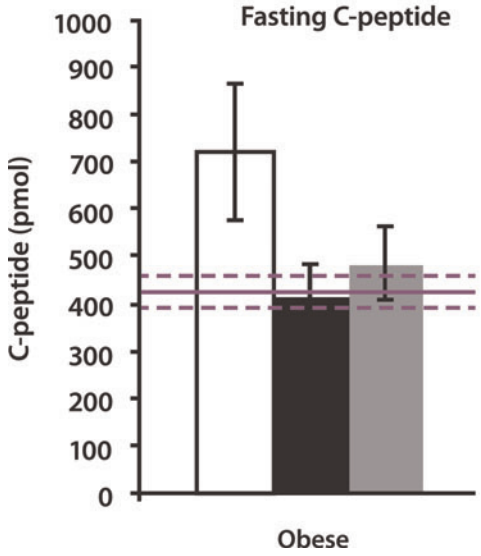
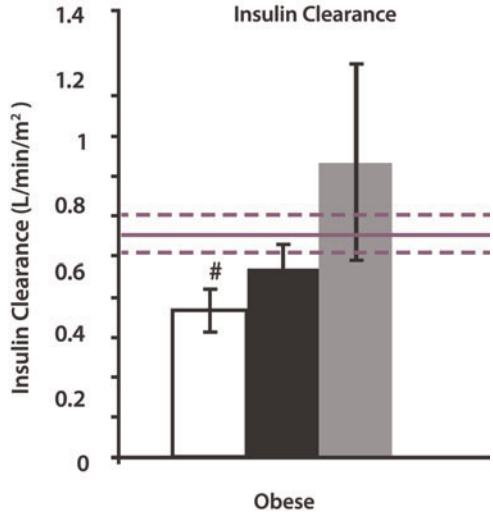
Introduction: We previously reported that Roux En Y gastric bypass normalized fasting insulin and insulin response to a mixed meal in diabetic patients. In this study we investigated whether this was a result of changes in insulin secretion and/or insulin clearance.

Methods: In nine obese-diabetic patients a standardized liquid meal was given after an overnight fast. Blood samples were drawn at several intervals relative to the start of the meal. C-peptide and insulin, were measured. AUC for insulin secretion (in pmol/min/m^2) divided by the AUC of plasma insulin (in pmol/L) was used to determine insulin clearance. Incremental area under the curve (AUC) was calculated using the pre-meal values as baseline. The subjects were tested again at 1 week and 3 months post surgery.

Results: Compared to 1 week and 3 months post surgery, pre-surgery fasting c-peptide was higher ($P < 0.05$) in the diabetic group. C-peptide area under the curve after surgery was unchanged in the patients with type 2 diabetes. In the type 2 diabetic patients, insulin clearance doubled from pre-surgery to 3 months post-surgery (0.46 ± 0.07 L/min/m^2 pre-surgery vs. 0.93 ± 0.31 L/min/m^2 3 months post-surgery).







Conclusions: Fasting insulin and insulin response to a meal are normalized in diabetic patients through changes in both insulin secretion and insulin clearance.

O-80

TOWARDS GDM SCREENING AND CARE IN LOW RESOURCE SETTINGS WITH A NEW GENERATION OF ALTERNATIVE BIOMARKER ASSAYS

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Gestational diabetes is a global epidemic where many urban areas in Southeast Asia exceed the highest prevalence rates in the developed world. In addition to the serious risk GDM poses during birth, GDM leads to increased risk to both mother and child of developing T2DM later in life and its related complications. While the Oral Glucose Tolerance Tests (OGTT) is an acceptable and accurate screening method for GDM in developed countries, few women in developing countries are screened for GDM primarily

due to the complexity and fasting requirement of the OGTT requiring additional visits and added cost. To increase awareness of the disease, and cost-effective prevention and treatment, a low-cost, easy to use, and convenient screening approach is needed.

Several biomarkers have been identified that may allow the development of low cost, fasting-free, easy to use rapid GDM screening assays, including glycated albumin, CD59, glycated fibronectin, and other glycated and glycosylated proteins such as Glycosylated Alpha-1 acid glycoprotein (A1AG) and glycosylated alpha-1 antitrypsin (A1AT).

In this presentation, we will give an overview over current assay development efforts for these markers, and present progress towards a new, simple, low-cost semiquantitative rapid diagnostic strip test for glycated albumin, which determines the ratio of glycated albumin to total albumin as a marker for gestational diabetes without the use of a reader instrument. We will also discuss how the new test could be integrated into health systems with an emphasis on antenatal care in rural and periurban low resource settings.

O-81

METABOLIC SURGERY IS NO LONGER JUST BARIATRIC SURGERY

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Six decades mark the maturation of the specialty of metabolic surgery. Originally intended as a treatment for severe obesity, it has proven to be the most effective therapy not only for the obesity but also for type 2 diabetes, hypertension, hyperlipidemias and even non-alcoholic steatotic hepatitis (NASH), polycystic ovary syndrome (PCOS).

The observation that these disparate diseases, often referred to as the ''metabolic syndrome'', are usually associated with elevated insulin levels and that the hyperinsulinemia is corrected by the gastric bypass operation has stimulated the development of a new understanding of these illnesses and a new skepticism about the current insulinocentric therapies of type 2 diabetes.

This presentation will review 1) the development of metabolic surgery, 2) the outcomes of the four accepted operations, i.e. gastric banding, gastric sleeve, gastric bypass and biliopancreatic bypass with a duodenal switch and 3) early explanations of the effects of surgery on the pathologic metabolic pathways of the TCA and Cori cycles.

O-82

PHYSICAL ACTIVITY AND EXERCISE

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Exercise has been prescribed for diabetes treatment since at least 600 B.C. The early East Indian text, the Shushruta, described a reduction in the sweetness of urine from diabetic patients after exercise. One might think that very little could be left to discover in the field of exercise and diabetes, yet surprisingly this is far from the truth. Ongoing research is refining the exercise prescription for patients of all ages, with the main types of diabetes (gestational, type 1 and type 2) and discovering new ways in which exercise has benefits. Alterations in metabolism caused by diabetes and new types of exercise modalities are also actively being researched. A search, of several hundred articles on exercise published between July 1st 2012 to June 30th 2013, uncovered the following 10 articles we felt had the most relevance to patients with diabetes or pre diabetes.

O-83

EXPLOITING INFORMATION TECHNOLOGY, GUIDED BY EVIDENCE-BASED MODELS OF HEALTH BEHAVIOR CHANGE, TO STRENGTHEN SELF-MONITORING OF BLOOD GLUCOSE AND SELF-MANAGEMENT ACTION

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The current approach involves texploitation of information technology guided by evidence-based models of health behavior change, to strengthen self-monitoring of blood glucose and self-managment action, in efforts to achieve and maintain glycemic control. We review the Information–Motivaiton–Behavioral Skills (IMB) model of health behavior change (Fisher & Fisher, *Psychological Bulletin*, 1992), and applications of this model aimed at understanding and promoting self-monitoring of blood glucose and maintainence of glycemic control. According to the IMB model, *information* that is relevant to self-monitoring of blood glucose and appropriate self-management action, and which is easy to translate into action, is an essential prerequisite of optimal diabetes self-management. *Motivation* to act on what one knowns with respect to adherene to self-monitoring of blood glucose and self-management action is a second, critical determinant of whether well-informed indivudals with diabetes will be inclined to act on what they know with respect to self-monitoring and self-management. *Behavioral skills* for acting effectively are a third, essential determinant of whether or not even well-informed and well-motivated indivduals will be capable of acting effectively with respect to self-monitoring and self-managment. Discussion will consider studies which have linked diabetes information, motivaiton, and behavioral skills to self-monitoring adherence and glycemic control among indivdiuals with type 1 and type 2 diabetes, and review research that has employed technology to target the information, motivaiton, and behavioral skills demands of diabetes self-management and resulted in improved adherence to self-monitoring. The leveraging of information technology, guided by evidence-based models of health behavior, is advocated in efforts to advance diabetes self-managment.

O-84

OBESITY IS NOW A DISEASE IN ADDITION TO IMPACTING DIABETES: CAN INTERNET-BASED BEHAVIOR CHANGE INTERVENTIONS HELP?

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Obesity is a known driver of a variety of poor health outcomes and high healthcare cost. It is the main driver for increasing the rate of progression from pre-diabetes/metabolic syndrome to full-blown type 2 diabetes.

Until a person with obesity develops complications of associated diseases with an increase in hospitalization and emergency department visits, their increased healthcare cost is usually associated with increased outpatient, pharmacy and durable medical equipment claims. This makes strategies for cost savings different than traditional disease management approaches which focus on avoiding hospitalization. These individuals also don't respond to traditional wellness approaches which are often not intensive enough to improve outcomes and lower costs.

Given the marked increase in the prevalence of overweight and obesity, healthcare providers must implement effective approaches to support patients' weight loss. To do this it is essential individuals are given the knowledge and skills to adopt and sustain healthy habits that lead to sustained weight loss. The challenge for healthcare providers is to be able to provide successful, affordable, and scalable approaches. There is increasing evidence that technology-enabled self-management support interventions can be approaches that work and which can show a positive return on investment (ROI).

This presentation provides information about unique aspects of the overweight/obese population that need to be taken into account when implementing a program and the qualities of interventions that make a difference. It also provides a demonstration of a research-proven online approach to weight loss in adults and provides information about associated outcomes and ROI.

O-85

MOBILE HEALTH: PATIENT ENGAGEMENT IN DIABETES CARE

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Increased access to mobile devices and applications offer great promise for assisting adults with diabetes to self-manage health behaviors. A main concern is whether levels of patient engagement are adequate to promote and sustain behaviors to improve diabetes outcomes.

Engagement is a popular term in mobile and wireless health. Methods for defining and measuring patient engagement are challenging to link patient characteristics, usage, retention, self-care behaviors, and health outcome change over time. Evaluating engagement spans multiple research methods and scientific disciplines including behavior, communication, social, and clinical sciences. Two themes emerge in current research explorations (1) identifying active psychosocial and communication components of mobile interventions and (2) examining the impact of increasing tailoring on health behavior change. Understanding these points is important to developers and researchers.

The primary purpose of this paper is to first, discuss recent study methods and results for evaluating patient engagement in diabetes type 2 interventions. Second, based on results in a randomized clinical trial (RCT), we report on overall engagement communications between study patients and providers, components of the mobile health and website portal usage, which patient characteristics were associated with usage and correlations between different measures of patient engagement and diabetes outcomes over a one year treatment period.

Rapidly changing interfaces, software, and capabilities of mobile/wireless health require dynamic approaches to evaluating patient engagement.

O-86

USE OF INSULIN PUMPS IN T2D IN INDIA: MERITS AND DEMERITS LEARNT OVER A DECADE

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Use of Insulin pumps in T2D in India: Merits and Demerits learnt over a decade.

Though insulin pumps are primarily meant for T1D, in India 80% of users are patients with T2D. Insulin can be delivered with a syringe, pen or pump. Hence, pumps are an alternative delivery device for any patient either with T1D or T2D requiring insulin. Studies have shown clinically and statistically significant improvement in numbness and pain of peripheral neuropathy and improvement in erectile dysfunction in >85% affected individuals switched over to Insulin Pump Therapy (IPT) from MDI. For those T2D with significant glucose excursions, nocturnal hypoglycemia, frequent traveling, recurrent hypoglycemia, IPT offer significant improvement in their quality of life. Though insulin pumps are an absolute indication in majority of patients with T1D, only a minority of patients can afford pump and consumables since in India there exists no reimbursement or government run policies for CSII based therapies. When pumps were introduced in India in early 2000, majority of the users were rich T2D insulin requiring subjects. Failure to follow up, adhere to instructions etc led to necessity for country specific document and resulted in publication of suggested guidelines for IPT in India. The guidelines clearly state that affordability should never be the criteria to deploy insulin pump. Willingness to attend pump training, motivation to use technology and gadgets and a track record of regular self monitoring were incorporated into the guidelines. Considering multiple benefits of IPT in T2D, eligible and affordable candidates should never be denied of this technology.

O-87

A report from labs: the NIDDK PROJECT "LONGITUDINAL ASSESSMENT OF BARIATRIC SURGERY"

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The Longitudinal Assessment of Bariatric Surgery (LABS) is a National Institutes of Health (NIH)-funded consortium of six clinical centers (Columbia/Cornell, East Carolina University, and the Universities of North Dakota, Oregon, Pittsburgh and Washington) at ten clinical sites and a data coordinating center (the University of Pittsburg) working in cooperation with NIH scientific staff to plan, develop, and conduct coordinated clinical, epidemiological, and behavioral research in bariatric surgery.

The initial study[i], funded in 2003 with 6,118 patients, documented the safety of bariatric surgery with a 30 day

mortality of 0.3%, identical to the risk of routine cholecystectomy. Of these, 2,458 were continued into the current long-term study[ii].

At baseline, participants were 18 – 78 years old, 79% were women, median BMI was 45.9 (IQR, 41.7–51.5), and median weight was 129 kg (IQR, 115–147). For their first bariatric surgical procedure, 1738 participants underwent RYGB, 610 LAGB, and 110 other procedures. At baseline, 774 (33%) had diabetes, 1252 (63%) dyslipidemia, and 1601 (68%) hypertension. Three years after surgery, median actual weight loss for RYGB participants was 41 kg (IQR, 31–52), corresponding to a percentage of baseline weight lost of 31.5% (IQR, 24.6%-38.4%). For LAGB participants, actual weight loss was 20 kg (IQR, 10–29), corresponding to 15.9% (IQR, 7.9%-23.0%). The majority of weight loss was evident 1 year after surgery for both procedures. Five distinct weight change trajectory groups were identified for each procedure. Among participants who had diabetes at baseline, 216 RYGB participants (67.5%) and 28 LAGB participants (28.6%) experienced partial remission at 3 years. The incidence of diabetes was 0.9% after RYGB and 3.2% after LAGB. Dyslipidemia resolved in 237 RYGB participants (61.9%) and 39 LAGB participants (27.1%); remission of hypertension occurred in 269 RYGB participants (38.2%) and 43 LAGB participants (17.4%).

Conclusions and Relevance.

Among participants with severe obesity, there was substantial weight loss 3 years after bariatric surgery, with the majority experiencing maximum weight change during the first year. However, there was variability in the amount and trajectories of weight loss and in diabetes, blood pressure, and lipid outcomes.

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[ii]. Courcoulas AP, Christian NJ, Belle SH, Berk PD, Flum DR, Garcia L, Horlick M, Kalarchian MA, King WC, Mitchell JE, Patterson EJ, Pender JR, Pomp A, Pories WJ, Thirlby RC, Yanovski SZ, Wolfe BM; for the Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. Weight Change and Health Outcomes at 3 Years After Bariatric Surgery Among Individuals With Severe Obesity. JAMA. 2013 Nov 4. doi: 10.1001/jama.2013.280928. [Epub ahead of print] PubMed PMID: 24189773.

O-88

TYPE 2 DIABETES IN THE PEDIATRIC AGE GROUP: INSULIN RESISTANCE, INSULIN DEFICIENCY, BOTH, MODY?

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TYPE 2 DM IN THE PEDIATRIC AGE GROUP:INSULIN RESISTANCE? INSULIN DEFICIENCY? BOTH? MODY?

The incidence and prevalence of T2DM is increasing in the pediatric population, in parallel with the pandemic of obesity and the Metabolic Syndrome, particularly in specific ethnic groups. In the USA, the incidence of T2DM in those diagnosed with diabetes between the ages of 10–20 years varies from approximately 2/100,000/yr in Caucasians, to 15/100,000/yr in African in Americans, and 30/100,000/yr in Native American Indians. Although ''Insulin Resistance'' is commonly ascribed to be the link between obesity and the development of T2DM, accumulating data implicate genetic defects in the ability to compensate for resistance to insulin by increasing it's secretion as the ultimate cause of T2DM. In addition to known genetic defects in insulin secretion associated with MODY (Monogenic Diabetes of Youth) or Neonatal Diabetes (NDM), newly identified factors include the hormones Betatropin, which mediates the sensing of resistance to augment secretion of insuIin, including beta cell hypertrophy, Irisin, which mediates beneficial effects of exercise by augmenting catabolism of fat, and the role of the zinc transporter ZnT8 in hepatic insulin clearance. Together, these discoveries point to new mechanisms responsible for T2DM, it's diagnosis and it's treatment.

ATTD 2014 Poster Presentations

P-89

OUR EXPERIENCE WITH REAL TIME CGMS IN NEWBORNS OF MOTHERS SUFFERING FROM TYPE 1 DIABETES

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In babies of diabetic mothers perinatal complications including hypoglycaemia are still seen more frequently than in newborns of healthy mothers.

We analysed by real time continuous glucose monitoring (RT-CGMS) newborns of mothers suffering from type 1 diabetes (T1D group; n = 20) in comparison with controls (6 newborns born in term to healthy women).

Median of gestation age in T1D group was 264 days (range 221–271 days), 9/20 of these newborn required intensive care during their first days of life. The first Enlite sensor was placed immediately after the birth (connected to Guardian real time device, Medtronic, Minneapolis, MN, USA). The median of monitoring in T1D group was 6 days (range 3–8 days) and 4 days in controls (range 4–6 days).

RT-CGMS revealed higher frequency of later hypoglycaemia (≤ 2.5 mmol/l) after 3rd monitoring day in T1D group ($p = 0.01$). In control newborns hypoglycaemia episodes were present too but during the first 4 days of life only and were less frequent and shorter.

In T1D group the occurrence and severity of hypoglycaemia were influenced by: the presence of macrosomia ($p = 0.024$), length of the newborn ($p = 0.003$), maternal HbA1c in 3rd trimester ($p = 0.001$), maternal weight gain ($p = 0.022$), maternal total insulin dose ($p = 0.021$) and by maternal age ($p = 0.042$).

Hypoglycaemia events were always confirmed and in general sensor readings correlated well with laboratory findings ($r = 0.817$, $p = 0.004$).

RT-CGMS was useful in revealing late postnatal hypoglycaemia which together with an adequate treatment can improve adaptation of these newborns.

Supported by the Project of MHCR for conceptual dev. of research org.00064203.

P-90

REAL-TIME CONTINUOUS GLUCOSE MONITORING IN PREGNANT WOMEN WITH TYPE 1 DIABETES: PATIENT EXPERIENCES AND OPINIONS

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Background: Real-time-continuous glucose monitoring (RT-CGM) improves glycaemic control in non-pregnant patients. Less is known about RT-CGM in pregnant diabetic women. Analysis of personal experiences provides information to optimally implement RT-CGM during pregnancy.

Patients and Methods: Women delivering in 2012 using RT-CGM were interviewed using a structured questionnaire on user preferences, technical problems, effects on daily life and care received.

Results: Twenty women with type 1 diabetes delivered in 2012; 12 (60%) chose RT-CGM, all on CSII, 10 (83%) started during the first trimester. Most (11 women, 92%) pregnancies were planned. Education: university in 4, higher vocational in 5, middle vocational in 3. Two-thirds used RT-CGM continuously; others allowed themselves a few days off. Two-thirds needed 1–4 weeks to learn to use RT-CGM; blood glucose was measured on average 3–5 times a day. Social and working activities did generally not suffer from RT-CGM. Technical problems were minimal; delay between changes in plasma and interstitial glucose values were frequent mentioned practical problem, especially in the lower range. Most women continued RT-CGM during lactation and all would use RT-CGM a next pregnancy. All women expressed that care was best given by a small team well-attuned to their condition.

Conclusion: RT-CGM in pregnancy in well-educated women with type 1 diabetes is associated with high maternal compliance, minimal effect on daily life and greatly appreciated with about half of the pregnant women wanting to use it. Delay in timely detecting hypoglycaemia is a major issue and optimal use of RT-CGM requires care by a small, local team.

P-91

STANDARDIZED PROCEDURE FOR THE ASSESSMENT OF NEW-TO-MARKET CONTINUOUS GLUCOSE MONITORING (CGM) SYSTEMS (SPACE2)

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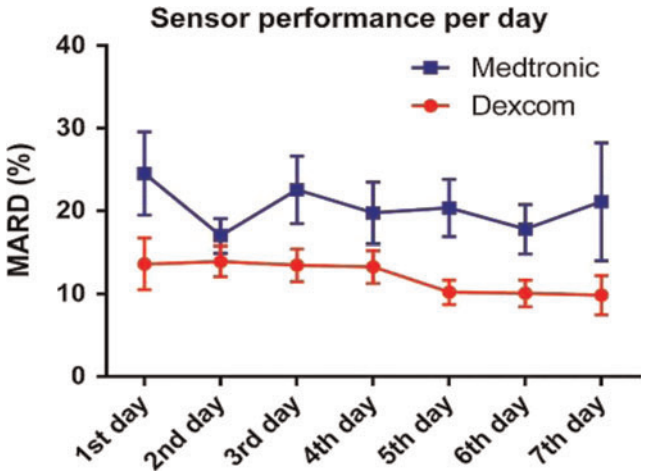
Aims: To assess accuracy and reliability of the two most widely used CGM systems.

Methods: We studied the Dexcom G4 Platinum and Medtronic Enlite, in 24 patients with type 1 diabetes. Sensors were tested during a six days home study and a nested 6 hours Clinical Research Centre (CRC) visit. During the CRC visit frequent venous blood glucose samples were taken while patients received a meal with an increased insulin bolus to induce an aggravated postprandial glucose nadir. At home, patients performed at least 6 reference fingersticks per day. Wilcoxon signed-rank test was performed on all data points ≥15 min apart.

Results: System uptime was 99.2% for Dexcom and 97.9% for Medtronic. Overall Mean Absolute Relative Difference (MARD) (SD) measured at the CRC was 13.6 (11.0)% for Dexcom and 16.6 (13.5)% for Medtronic ($P<0.001$ n=532). Overall MARD assessed at home was 12.2 (12.0)% for Dexcom and 19.9 (20.5)% for Medtronic ($P<0.001$ n=843). During the CRC visit, MARD in the hypoglycaemic range (≤70 mgdL), was 17.6 (12.5)% and 24.6 (18.8)% for Dexcom and Medtronic respectively ($P<0.0001$ n=117). Both sensors showed lower accuracy during hypoglycaemia as compared to euglycaemia (70–180 mgdL) (Dexcom 17.6% vs. 13.0% and Medtronic 24.6 vs. 14.2%).

Conclusions: During circumstances of intended use, including both a CRC and home-phase the Medtronic sensor was noticeably less accurate than the Dexcom sensor. Both sensors showed lower accuracy in the hypoglycaemic range.

This study was funded by Dexcom, San Diego, USA



P-92

CONTINUOUS GLUCOSE MONITORING CAN UNCOVER MISTAKES IN SELF-TRETMENT OF HYPOGLYCEMIA IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

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Background and aims: Hypoglycemia is an uncomfortable episode which besides another problems may also swing glycemic curve and cause an improper diabetes control. We analysed CGM records to see how successful are our patients in selftreatment of hypoglycemia.

Material and methods: We analyzed CGM records of patients with type I diabetes mellitus treated with CSII and MDI. Each patient used CGMS for 3–6 days and was asked to record all improtant events such as insulin injection, meal, exercise, hypoglycemic episodes. We reviewed glycemic profiles to identify glycemic excursions after hypoglycemic episodes. We evaluated the number of recurent hypoglycemias within next two hours after every episode. We considered self-treatment as successful if glycemic curve after hypoglycemia kept between 5 and 12 mmol/l.

Results: We evaluated 3763 hoursof CGM records in 32 patients with type I diabetes mellitus (21 men, 11 woman). We found 98 hypoglycemic episodes (0,6 per day), 18 of all the episodes were followed by reccurent hypoglycemie within 2 hours (18,4%). We found glycemic curve during next 2 hours after hypoglycemia in target limits (5–12 mmol/l) in 44 cases (44,9%). In the rest of the cases (36) glycemic values exceeded 12 mmol/l (36,7%). Precise amount of sacharides used in self-treatment were able to control only 18 patients.

Conclusion: We found that in more than half of hypoglycemic episodes another hypogycemia follows or hyperglycemia occures. Self-treatment of hypoglycemia should be matter of repeted education. Automatic analysing of posthypoglycemic curve could possibly become another part of CGMS software.

P-93

HEMATOCRIT INTERFERENCE IN MODERN BLOOD GLUCOSE METERS FOR PATIENT SELF-TESTING

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Background: Dynamic electrochemistry (DE), has been shown to correct for hematocrit (HCT) interference. This laboratory investigation assessed the HCT stability of a new DE-based device (MyStar Extra, Sanofi) in comparison to seven competitive devices (AccuChek Aviva Nano & AccuChek Performa, Roche Diagnostics; Contour XT and Contour Link, Bayer; FreeStyle Freedom Lite, Abbott; MyLife Pura, Ypsomed; OneTouch Verio Pro, LifeScan).

Method: Venous heparinized blood was immediately aliquoted and manipulated to contain 3 different blood glucose concentrations (50–80 mg/dL, 150–180 mg/dL, and 350–400 mg/dL) and 5 different HCT levels (20–25%, 30–35%, 40–45%, 50–55%, and 60–65%). After careful oxygenation to normal blood oxygen pressure, each of the 15 different samples was measured 8x with two devices and two strip lots of each meter (=32 measurements/meter/sample). YSI Stat 2300 served as laboratory reference method. Stability to HCT influence was

assumed, when less than 10% difference occurred between the highest and lowest mean glucose deviations in relation to HCT (HIF: Hematocrit Interference Factor).

Results: Four of the devices showed stable performance: Contour XT (HIF: 6.09%), MyStar Extra (7.07%), OneTouch Verio Pro (7.30%), and Contour Link (9.32%). The four other meters were influenced by HCT (AccuChek Performa: 20.92%, AccuChek Aviva Nano: 22.40%, FreeStyle Freedom Lite: 24.49%; MyLife Pura: 28.74%).

Conclusions: In this study, 50% of the tested meters, including MyStar Extra, were shown to reliably correct for potential hematocrit influence on the meter results.

Investigator-initiated trial supported in part by Sanofi.

P-94

PERFORMANCE OF THE EA1C ALGORITHM IN T1DM: SMBG BASED A1C TRACKING

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Introduction: Hemoglobin A1c (HbA1c) has become an established clinical marker for average glycemic control. While methods to link HbA1c to average glycemia have been developed, their application to estimate HbA1c from episodic SMBG readings has proven more challenging. A novel algorithm, using SMBG data to track HbA1c daily, was presented at EASD 2013[1,2], showing significantly improved accuracy over previous methods in Type 2 diabetic subjects. The presented work validates this method is T1DM.

Method: Previously reported data from 120 type 1 diabetic subjects [3] was used to assess accuracy of the estimation procedure. The data contained 188,219 SMBG measurements that were randomly distributed in time, on average 4–5 readings per subject per day. Fasting, pre- and post-meal tags were assigned based on daytime.

The eA1c algorithm was applied retrospectively and reference HbA1c was used to assess accuracy; reporting mean absolute deviation, mean relative absolute deviation, and correlation. An established glycemic average method [4] provided a point of comparison with previous research.

Results: eA1c was computable for 457 of the 478 reference HbA1c (15 without enough fasting BG, 3 without current profiles, and 3 references before eA1c initialization. Results are presented in Table 1.

Conclusion: Performances of the eA1c algorithm in T1DM were comparable to previously reported performance in T2DM, and confirmed improved accuracy when compared to established average methods.

Acknowledgments: Study supported by Sanofi.

1. Kovatchev et al. EASD 2013;
2. Breton et al. EASD 2013;
3. Kovatchev et al. Diabetes Care 2011;34:302–307;
4. Nathan et al. Diabetes Care 2008;31:1473–1478.

Table 1: Accuracy of eA1c and glycemic average methods in T1DM and T2DM

	T1DM		T2DM from Kovatchev et al.[Error! Reference source not found.]	
	eA1c	Average method	eA1c	Average method
MAD	0.64	0.87	0.51	0.98
MARD	7.98%	11.4%	6.8%	13.1%
correlation	0.75	0.76	0.76	0.73

P-95

ROLE OF NON-INVASIVE SCREENING METHODS IN ESTIMATING PREVALENCE OF DYSGLYCAEMIA IN PATIENTS ADMITTED TO HOSPITAL WITH ACUTE CORONARY SYNDROME

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Aims: To determine the prevalence of undiagnosed diabetes and impaired glycaemic state (IGS) and compare WHO 1998 and IEC criteria in patients admitted to hospital with acute coronary syndrome. In addition we also looked at using novel screening algorithms to determine glycaemic status.

Methods: A prospective 3 year study carried out in two large inner city hospitals in United Kingdom.

Results: 118 Patients were included in the analysis. The prevalence of diabetes mellitus was 20% and 16% respectively according to the W.H.O and IEC criteria at baseline. The prevalence remained similar at 3 months. However two thirds of participants with IGS and a third of those with DM changed their glycaemic status at 3 months. This could be due to stress hyperglycaemia as urinary cortisol creatinine ratio was elevated in patients who had T2DM at baseline compared to other groups. Our screening algorithm had sensitivity of over 85% at baseline in comparison with W.H.O criteria. We also designed diabetes predictor score based on age, fasting plasma glucose and HbA1c and it had excellent sensitivity of over 80% and negative predictive value of over 90%. By contrast the sensitivity of IEC criteria was only 57%.

Conclusion: The W.H.O and IEC diagnostic criteria identify different populations with diabetes at baseline as well as 3 months. This is clinically relevant as we are basing screening in high risk population on these criteria. The IEC criteria do not identify patients with IGS which is known to be associated with increased cardiovascular morbidity and mortality.

P-96

TRANSITION OF CSII SYSTEMS IN A VERY SHORT TIMEFRAME AS A CONSEQUENCE OF A PUBLIC TENDER PROCESS. FEASIBILITY AND SAFETY ISSUES

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Background: CSII is widely reimbursed by National Health Systems. The procurement of pumps/supplies through a tender process is common practice of public services. We describe the feasibility and safety of the transition from a CSII system to another in a very short timeframe as a consequence of a public tender.

Methods: The CSII replacement process in a large population for a very short time frame (< 1 month) was designed. The most remarkable aspects were an intensive structured training program and 24-h technical/clinical support availability. Training was performed in groups of 4 patients. Educational contents were organized in modules and adapted to the necessities of each

group. The program was composed of 3 sessions: (i) system start-up training and a patient satisfaction questionnaire; (ii) 72-h later, a telephone call from the technical-education staff; and (iii) a session of training after 3 months.

Results: 219 subjects were included (62% women, 45.1 ± 11.2 yr-old, duration of diabetes 25.2 ± 9.7 yrs, on CSII 7.3 ± 3.4 yrs). 30 calls were performed to reinforce training. 7 technical incidences occurred and rapidly sorted out. 24 out of 31 clinical events were considered mild, 6 moderate needing medical assistance (5 hyperglycemia/1 ketosis) and 1 severe requiring hospitalization (ketoacidosis). All were related to infusion sets issues and were satisfactorily solved. Overall satisfaction of the patients with the training process scored 9.4 out of 10.0.

Conclusions: The transition of CSII systems in large populations in the context of a public tender could be performed safely and in a very short time using a specific training program.

P-97

HOW DO PRE-GESTATIONAL BMI AND WEIGHT GAIN INFLUENCE PREGNANCY OUTCOME IN WOMEN WITH GESTATIONAL DIABETES?

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Table 1: BMI class and pregnancy outcomes. Univariate Analysis

	393 Singleton Pregnancies			
	GROUP A: BMI <25 (N=199)	GROUP B: 25<BMI<30 (N=109)	GROUP C: BMI>30 (N=85)	p
Birthweight (g)	3009±571	3135±538	3157±682	0.056
Birth Weight Percentile	46.44±26,2	53,93±26,7*	55,4±28,8*	**0.007**
Week of delivery	38,3±2,0	38,5±2,1	38,2±2,0	0.589

**Significative compared to GROUP A*

Table 2. Multiple linear regression (Reduced model). Covariable: Clinical and laboratoristic parameters

Dipendent variable	Covariate	Correlation coefficients	Standard Error	p
Birth weight Percentile	BMI groups	32.364	4.403	**<0.001**
	Weight gain	0.826	0.234	**<0.001**
Birth weight	BMI groups	114.522	35.601	**0.001**
	Weight gain	22.614	4.924	**<0.001**

TABLE 3. Multiple logistic regression (Reduced model). Dipendent variable: **Macrosomia presence**. Covariable: Clinical and laboratoristic parameters

Variable	β ± S.E.	P	OR
BMI classes		**0.007**	
Group B vs Group A	-0.066 ± 0.620	0.916	0.936
Group C vs Group A	1.447 ± 0.509	**0.004**	4.252
Weight gain (Kg)	+0.095 ± 0.035	**0.007**	1.099

TABLE 4. Multiple logistic regression ((Reduced model). Dipendent variable: **Congenital Malformation (CM) presence**. Covariable: Clinical and laboratoristic parameters

Variable	β ± S.E.	P	OR
BMI classes		**0.044**	
Group B vs Group A	2.658 ± 1.0760	**0.013**	14.3
Group C vs Group A	2.538 ± 1.103	**0.021**	12.7

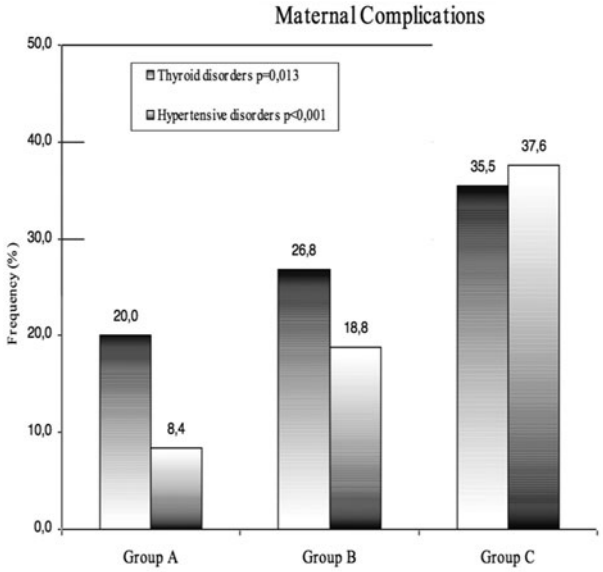

Figure 1: Frequency of Thyroid and Hypertensive disorders according to the three BMI groups.
Group A : BMI< 25
Group B: 25 ≤BMI> 30
Group C· BMI> 30

Introduction: The maternal obesity could be an additional risk factor for complications, regardless of diabetes. The aim of this study was to evaluate the pregnancy outcome among women affected by GDM, according to pre-pregnant BMI and GWG.

Materials and Methods: Four hundred-twelve patients with 393 singleton pregnancies (17 twin pregnancies and 2 triple

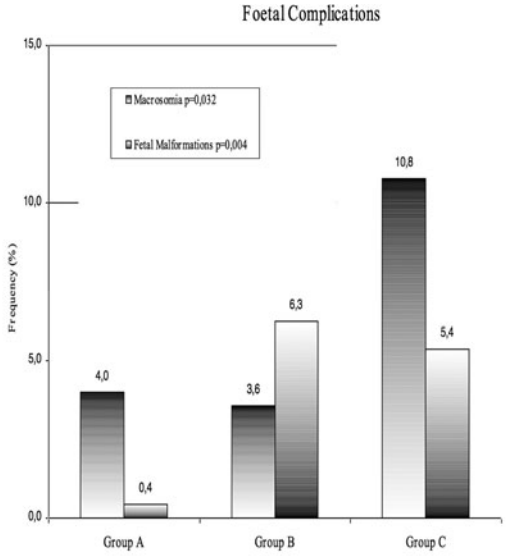

Figure 2: Frequency of Macrosomia and Congenital Malformations (CM) according to the three BMI groups.

pregnancies) complicated by GDM were considered. According to HAPO study, the diagnosis of GDM was made. After the diagnosis, all women started a diet therapeutic regimen and the capillary blood glucose self-monitoring; in patients in which the glicemic control did not result optimal, we convert the diet therapeutic regimen to a pharmacological management. All women were monthly assisted by both the physicians and glycaemic values and maternal weight were controlled.

Results: Seventy-six (18.4%) women were affected by hypertensive and 108 (26.2%) were affected by thyroid disorders and this complications were correlated with the increasing of BMI classes. The incidence of macrosomia was 5.3%. Even the foetal complications were correlated with the pre-pregnant maternal BMI. Women who delivered a macrosomia had a significantly greater pregnancy weight gain and a major fasting glucose levels at OGTT. Thirteen newborns (3.0%) presented malformations at delivery closely correlated to a maternal BMI ≥ 30.

Conclusions: A patients training to lifestyle modifications is recommended. Obese and diabetic pregnant women need of a multidisciplinary team management that, according to our study, can give very good results even if closely outpatient.

P-98

EQUIVALENT WEIGHT LOSS BUT DIFFERENT DIABETES BENEFITS WITH METABOLIC SYNDROME IN NON-MORBID OBESITY T2DM PATIENTS AFTER GASTRIC BYPASS

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Background: Metabolic syndrome (MS), a constellation of metabolic abnormalities, has an intertwined link with morbid obesity and type 2 diabetes (T2DM). Gastric bypass (GBP) is considered an effective option for the management of these patients. However, most of the diabetes patients in China have distinguishing abdominal obesity rather than severe obesity, while some patients may have MS and some may not. Otherwise, data concerning non-morbid obesity patients with MS has rarely been reported. It is important to investigate if the same principles of GBP that improve diabetes with MS could be applied to the diabetes without MS in non-obesity patients.

Objective: We sought to determine effects of laparoscopic gastric bypass on weight loss and diabetic remission in patients with MS compared with appropriately matched cohort without MS.

Methods: Retrospective analysis of 42 T2DM patients with BMI 28–35 kg/m2, stratified by MS into two groups (group 1, MS group, group 2, non-MS group). Anthropometric, biochemical, and clinical evaluations were performed preoperatively and then at 1,3,6 and 12 months postoperatively.

Results: During the one year follow-up, all groups showed a significant reduction in BMI, waist circumference, LDL-C and HOMA-IR. However, remission of T2DM is different, higher in MS group (18/20, 90%) and lower in non-MS group (14/22, 64%), which total remission is 86% (32/42).

Conclusions: Laparoscopic gastric bypass has an independent mechanism with weight loss on non-obesity T2DM, which is associated with resolution of insulin resistance. Furthermore, BMI is not the only main inclusion criteria for gastric bypass on diabetes while metabolic disorders maybe the next important one.

P-99

INSULIN: TOO MUCH OF A GOOD THING

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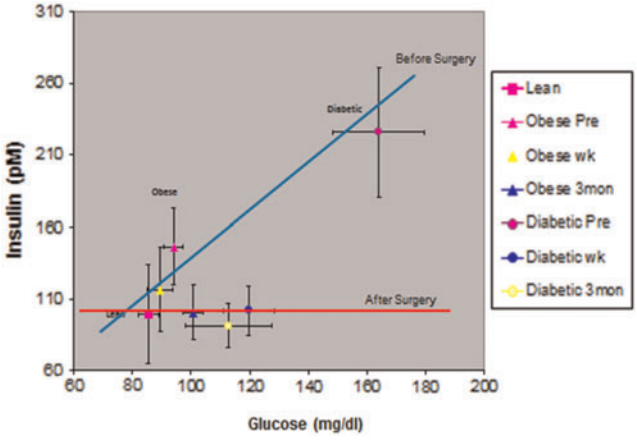
Introduction: In 1984 we first documented that the Roux-en-Y gastric bypass achieved full and durable remission of type 2 diabetes (T2DM) in a matter of days (*Ann Surg*) and in 1992, we reported that the basal insulin levels in patients with advanced type 2 diabetes mellitus was 900% higher than those found in euglycemic individuals (*Am. J. Clin. Nutr*). We have documented that these elevated basal levels of insulin are corrected in a matter of days, long before there are significant improvements in insulin resistance (*J. Endocrin & Metabol* 2011).

Methods: Nine obese non-diabetic and nine obese diabetic women were studied before surgery, one week and 3 months after RYGB. Nine lean females not undergoing surgery were



used as controls. Fasting blood samples were drawn before a mixed meal test. Sequential blood draws were then performed over a 3 hour period, measuring changes in insulin and glucose. An intravenous glucose tolerance test was also performed after an overnight fast. Changes in insulin and glucose concentrations were measured.

Results: Recalculated data from the previously reported studies document (figure below) the remarkable finding that the RYGB uncouples the insulin/glucose, i.e. after the operation, the normal direct relationship between insulin vs. glucose is abolished. Thus, even though glucose levels rise in these patients, the expected rise in insulin is abolished.

Conclusion: These results contradict the current understanding of the hyperinsulinemia of T2DM. We should re-direct our search for anti-diabetic medications into these pathways rather than the pursuing medications which increase insulin levels in patients.

P-100

METABOLIC SYNDROME – NEUROTROPHIC THEORY EFFECTS OF METFORMIN AND NON-STEROIDAL ANTIINFLAMMATORY DRUG TREATMENT

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Metabolic syndrome (MS) presents with central obesity, impaired glucose metabolism, dyslipidaemia and hypertension. Our aim was to examine the effect of metformin treatment alone and in combination with non-steroidal antiinflammatory drugs (NSAID) on plasma levels of nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) in patients with early stage MS (MS-es) and generalized MS (MS-ge).

Materials/methods: The study covered 35 female patients with MS-es (at mean age of 43.39 ± 1.54 years) and 40 ones with MS-ge (at mean age of 45.69 ± 2.18 years) compared to 10 age-matched controls each. Patients with MS-es were administered metformin in a dose of 850 mg twice daily. The patients with MS-ge were divided in two groups of 20 patients each. They received metformin either alone, or in combination with aspirin in a dose of 500 mg daily and Diclac in a dose of 150 mg daily. Plasma NGF and BDNF levels were measured by ELISA. Statistical data processing was done by ANOVA method.

Results: Plasma NGF and BDNF levels were significantly higher in MS-es patients and lower in MS-ge ones than in controls. NGF levels were decreased after treatment with metformin in both groups. NGF levels were significantly higher in MS-ge patients on combined therapy than in those on metformin only.

Conclusions: The combination of metformin and NSAID exerts a better effect than metformin alone on NGF and BDNF production, metabolism-related anthropometric and laboratory features as well. It represents a pathogenetic therapeutic mechanism in MS because of its strong antiinflammatory effect and improves MS-ge manifestations.

P-101

GROUP EDUCATION IN TYPE 1 DIABETES PATIENTS ON INSULIN PUMP THERAPY

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Aim: To assess the effectiveness of group education on glycemic control and Quality of Life (QoL) among users of continuous subcutaneous insulin infusions (CSII).

Methods: Cross-sectional study included 43 subjects (18 male, mean age 28 years [24; 36]) with type 1 diabetes (duration of diabetes 14 years [8; 19]). All patients were transferred from multiple daily injection regimen to insulin pump therapy using special structured program for group education for CSII which included basic information about general diabetes self-management and technical aspects of pump therapy for 9 days. QoL was assessed using questionnaire ADDQoL, WB12, SF-36. We estimated metabolic and QoL parameters in 16 weeks after education.

Results: After 16 weeks HbA_{1c} significantly decreased from 8,9% [7,9; 9,5] to 7,4% [6,6;7,9] ($p = 0{,}0001$) without increasing the frequency of hypoglycemia; absolute decrease of HbA_{1c} was 1,2% [0,5; 1,8]. There were significantly improvements in all aspects of QoL accordingly ADDQoL, SF36 and WB12 compared to baseline data.

Conclusion: Our study showed that using CSII after special structured program for group education improved glycemic control and QoL. So it recommended to educate patients about basic principles of general diabetes self-management in group transferring to CSII.

P-102

PATIENTS PROFILE EVALUATION WITH TYPE 1 DIABETES IN INSULIN PUMP IN BRAZIL

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To date, there is no data about features of patients using insulin pump in Brazil. Our goal was to describe these patients and evaluate how they are using their pump. This is a cross sectional study, using patients with type 1 diabetes in insulin pump in different states in Brazil. A questionnaire was applied; simple frequency was used and Mann-Whitney test.

Results: 415 patients, 59% female and 41% male. The indications to use pump were: quality of life (74%), unsatisfying glycemic control (55,2%), to decrease injections (41,4%) and severe hypoglycemia (30,1%). Approximately 47,9% patients said the main advantage is the improvement of glycemic control and 19,7% flexibility. As main disadvantage: cost (40,5%) and skin spots (27,8%). Insulin pump therapy decreased fear of hypoglycemia in 60,3% and 49% improved the perception of hypoglycemia. An increase number of patients has some difficulty to use important resources of the pump (86,4%): 60,8% never use temporary basal and 53,5% never use different bolus. Severe hypoglycemia was less frequent after pump. They showed a decrease in A1c after 6 months using pump (8,69 ± 1,82 vs.7,62 ± 1,18%).

Conclusion: There was an improvement in A1C and a decrease in severe hypoglycemia after insulin pump. Patients didn't know how to use some important resources of the pump. These show as the needs to improve education after beginning insulin pump therapy.

P-103

IDENTIFICATION OF VARIABILITY IN POSTPRANDIAL BEHAVIOR OF PATIENTS WITH TYPE 1 DIABETES FROM INSULIN PUMP DATA

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Individual model identification in diabetic patients is considered a challenge mainly due to uncertainty in glucose measurements and glycemic variability, especially in the postprandial period. Previous work showed that identifying patients' interval models characterizing intra-patient variability from blood glucose and insulin concentration data is feasible. Good model predictions were achieved for a 5-hour prediction horizon in a cross-validation study, especially when the identification data was fully representative of the patient's variability.

In this work, the existing patient model is extended to include a SC route of insulin absorption. Data from twelve type 1 diabetic patients who underwent four mixed meal studies registering blood glucose reference data. Three postprandial periods were used for identification and one for validation following a one-day-leave-out cross-validation study. From the subcutaneous insulin infusion model two parameters were identified: subcutaneous insulin absorption and plasma insulin elimination rates.

Despite the use of less information as compared to the previous study fed with plasma insulin data, prediction capability of the resulting model was satisfactory. MARD for the validation days was 4.3% in median, with respect to the predicted glucose envelope containing all possible patient responses (median glucose band width of 72.7 mg/dL) and 56.8% of the data predicted within the glucose envelope. Data prediction was much better for the best case permutation fully representing variability, with a 94.5% of samples predicted with a width of 99.1 mg/dL in median. No further overestimation was registered in the fitting of the best cases when compared with the cross-validation fitting performance.

P-104

RISKS OF HYPOGLYCEMIA AND HYPERGLYCEMIA ARE LINKED TO MENSTRUAL CYCLE PHASES IN WOMEN WITH T1D

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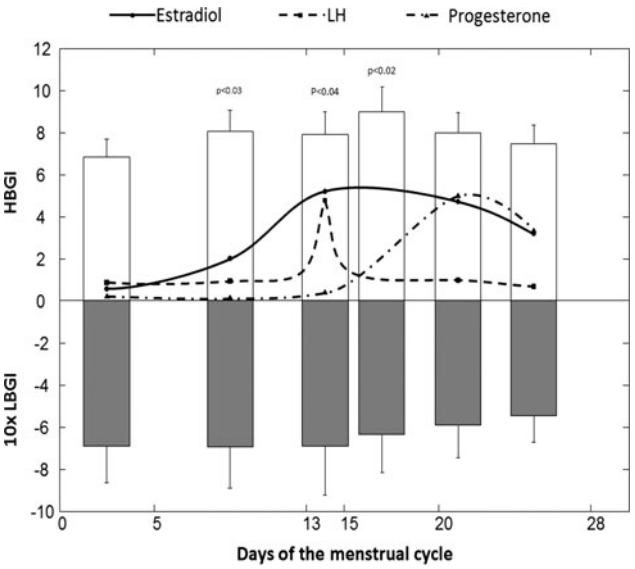
Background/aims: A challenge in management of Type 1 Diabetes (T1D) and development of an artificial pancreas is defining and predicting factors that affect daily glycemic variability. Our aim is to define glycemic variability over several menstrual cycles, an important inadequately studied area.

Methods: Women with T1D using CSII were studied for 3 consecutive menstrual cycles. Glycemia was assessed using CGM (Dexcom Platinum) and cycle phases determined using ovulation prediction kits and repeated serum hormone measures. Cycle



Phases are defined as early follicular, mid-late follicular, periovulatory (ovulation ± 1 day), and early-mid-late-luteal phase. Glycemic risks and variability are reported (LBGI, HBGI, ADRR). Overall change significance was assessed by repeated measure ANOVA, specific phases were then emphasized using contrasts.

Results: 12 subjects were studied (Age 34.8 ± 6.2 yrs, BMI 26.6 ± 2.9 kg/m^2, A1c 6.9 ± 0.6%) with ovulation confirmed in 33 of 36 cycles. Risk for Hyperglycemia changed significantly during the cycle ($p = 0.023$), with HBGI increasing until early luteal phase and returning to initial levels thereafter (see figure). LBGI was steady in follicular phase, decreasing thereafter (ns). ADRR increased significantly after ovulation ($p = 0.02$) to slowly return to initial levels during the luteal phase. Total daily insulin, as well as total daily carbohydrates or calories did not show any significant fluctuations.

Conclusions: Women with T1D have glycemic variability changes that are specific to the individual and are linked to phase of cycle. Higher glucoses were observed during the periovulatory period and early luteal phases compared to the early follicular phase, greater glucose variability was present in the early luteal phase.

P-105

IMPACT OF A REDUCED ERROR RANGE OF SMBG IN INSULIN-TREATED PATIENTS IN GERMANY

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Background: Modelling approaches demonstrate that improvement of accuracy of blood glucose (BG) meters may lead to cost savings. An improvement of accuracy of BG meters on the basis of a reduction in error range from 20 to 5% has been reported to be associated with substantial cost savings in Germany. The aim of this study is to analyse potential cost savings related to a reduction in error range from 20% to 15% and 10% of glucose meters in Germany.

Methods: The health economic analysis included the number of type 1 diabetic and the number of insulin-treated patients in Germany, the costs for glucose monitoring, a model on the effects of the improvement of accuracy on the impact of severe hypoglycemic episodes, HbA1c, and

subsequently myocardial infarctions and the costs of diabetes-related complications in Germany. In the model, a reduction of 1% and 3.5% reduction in severe hypoglycemic episodes, and a 0.14% and 0.28% reduction in HbA1c were included.

Results: In type 1 diabetes the savings could be equal to a reduction in health care expenditures of more than €1.0 million (20% vs. 15% error range) and €3.4 million (20% vs. 10% error range). Respectively, potential savings of more than €6.0 million and €20.1 million were calculated for the group of insulin-treated patients.

Conclusions: The model demonstrates that a reduction of error range of blood glucose meters from 20% to 15 and 10% may translate into substantial savings for the German health care system.

P-106

CLINICAL UTILITY OF CGM IN PRE-DIABETES AND ITS IMPACT ON MODIFYING LIFESTYLES

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Glycemic excursions in pre-diabetes are seldom evaluated in clinical practice.

We assessed clinical utility of CGM in pre-diabetes and its impact on modifying lifestyles to prevent diabetes.

6 patients were enrolled in 3 month study via convenience sampling based on ability and willingness to follow instructions. Mean age 48.5 yrs, mean BMI 26.73 kg/m2. Measured blood glucose were < 126 mg/dl during fasting and < 150 mg/dl post breakfast. CGM was performed using iPro2 recorder at 0 and 3 months (5–7 days). Advice on lifestyle modifications were repeated once in 2 weeks by a multi-disciplinary team of doctors, dietitians, pharmacist, nurse educators, device technician, psychologist etc. who made detailed analyses of CGM recordings.

Trends observed in CGM at month 0 included hyperglycemic spikes 30–90 mins after breakfast and dinner and glycemic variability missed in usual SMBG. At 3 months, CGM revealed smooth curves with average weight reduction of 2.35 kgs (Table).

CGM may prove an excellent tool to unravel glycemic excursions most often missed in SMBG in pre-diabetes patients. CGM could evolve as motivational tool in pre-diabetes patients to prevent progression to overt diabetes.

CGM Parameters (n = 6)	Mean (mg/dl) (0 month)	Standard deviation (0 month)	Mean (mg/dl) (3 months)	Standard deviation (3 months)
FBS	110.8	20.77	91	6.42
HbA1c	5.9%	0.38	5.4%	0.28
No: of High Excursion	7.2	5.23	2.2	2.14
No: of Low Excursion	2.8	3.82	1.5	1.52
Highest Sensor Value	178.2	28.99	151.5	6.44
Lowest Sensor Value	66	12.33	73.8	3.06
Duration within 70-40 mg/dl	89.7	9.27	96.3	2.73

P-107

SOCIAL MEDIA AND DIABETES: A TOOL TO IMPROVE GLUCOSE CONTROL IN TYPE 1 DIABETIC ADOLESCENTS ON INSULIN PUMP: CROSS-OVER STUDY

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Background and aims: To evaluate results from Facebook as tool to improve glucose control in adolescents with type 1 diabetes.

Materials and methods: A total of 114 adolescents with type 1 diabetes on insulin pump, ages 13–23, were randomized in two groups: **Regular visits** (Group 1)- 55 type 1 diabetes patients were treated using standard medical protocol with regular visits at clinic (evaluation glycemic control and education) were given to the patient and **Internet visits** (Group 2)- 59 type 1 diabetes patients were treated using Facebook, Skype and Carelink personal program (Medtronic Diabetes), where the data was downloaded by the patient at home and interventions (same as group 1) were given via Facebook. After a period of 6 months with washout period of 8 weeks, a crossover study was performed for next 6 months, where patients from regular group switched to internet group and patients from internet group switched to regular group. A1C was obtained before and every three months during the study in one year period.

Results: Regular visits were 0.4. ± 0.8 per patient/month in group 1 and Internet visits were 0.5 ± 0.9 per patient/month retrospectively. There was significantly improvement in both groups (group 1 and 2 retrospectively, 7.8 ± 0.7% and 7.9 ± 1.0% on beginning with 6.4 ± 0.8% and 6.3 ± 1.2%, $p < 0.05$) in the first six months. After the crossover (the next 6 months), A1c in both groups (regular 6.5 ± 0.7% and internet 6.4 ± 0.6%) stays on satisfactory level without significant difference.

Conclusion: We can conclude that social media such as Facebook and Skype with special glucose software can be used as treatment option for type 1 diabetics on insulin pump.

P-108

EFFECT OF GLYCEMIC VARIABILITY ON QUALITY OF LIFE IN TYPE 1 DIABETES

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Background and aims: Poor glycemic control impacts quality of life (QL). The aim of the study is to evaluate the influence of glycemic variability (GV) on QL in type 1 diabetes.

Material and Methods: We performed a CGM (Ipro2, Medtronic Minimed) for 4.3 ± 1.8 days in 32 type 1 diabetes patients, 19 women, aged 34 ± 10 years old, duration of diabetes

15 ± 7 years, HbA1c 8.2 ± 1.1%. GV parameters were calculated by EasyGV© program. A validated QL questionnaire was used.

Results: Health scores correlated negatively with CONGA ($r = -0.446$), J-index ($r = -0.352$) and HBGI ($r = -0.376$), ($p < 0.05$). Patients with lower health scores had higher CONGA (8.7 ± 1.7 vs 7.4 ± 1.4), J-index (55.6 ± 16.2 vs 42.3 ± 14.7) and HBGI values (12.4 ± 5.1 vs 8.4 ± 3.7) ($p < 0.05$) than patients with higher health scores. CONGA was significantly higher in patients with lower psychological scores (8.8 ± 1.9 vs 7.3 ± 1.3; $p = 0.020$).

In women and patients older than 32 years old, GV parameters correlated with different QL indexes (Table 1), while in men and patients younger than 32 years old, no correlation was found.

Table 1. Correlation Coefficient Between GV Parameters and QL Indexes

	Women		Age ≥32	
	Overall QL	Health	Health	Socio-economic
CONGA	−0.504	−0.629	−0.636	NS
J	−0.486	−0.538	−0.634	NS
HBGI	−0.483	−0.549	−0.611	NS
M	−0.469	−0.575	−0.524	NS
DS	NS	NS	NS	−0.505
MAGE	NS	NS	NS	−0.640

All $p < 0.05$

Conclusions: QL indexes reflecting overall QL, health, psychological and socio-economic aspects are affected by GV, mainly in women and older patients.

P-109

OVERNIGHT GLUCOSE CONTROL WITH MODULAR CONTROL TO RANGE ALGORITHM IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES AT DIABETES CAMP

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The objective of this study was to determine the efficacy of an automated insulin delivery system in overnight closed-loop (OCL) control in participants with type 1 diabetes aged 10–35 years in a camp setting.

The system was informed by a G4 Platinum continuous glucose sensor (DexCom, Inc.) and controlled a modified t:slim insulin pump (Tandem Diabetes Care, Inc.). Insulin doses were computed to avoid hypoglycemia and prolonged hyperglycemia, whilst slowly achieving glycemic control overnight. The system was implemented on the DiAs mobile platform (University of Virginia).

Twenty participants were randomized to either OCL (n = 54) or sensor-augmented pump (control) (n = 52) on alternate nights in up to 6 consecutive nights at camp. The mean ± SD age was 15.1 ± 3.2 y, diabetes duration was 5.6 ± 3.5 y and A1C of 8.1 ± 1.1%. OCL was started in all 54 potential nights. Full OCL lasting a minimum 6 hours was achieved in 41 nights (76%). OCL was stopped on 13 nights, mainly due to sensor error > 20% or loss of sensor reading (12%) and pump or infusion set failure (9%).

The median percent time spent between 70–150 mg/dL was 55% (25, 80) on control nights (n = 52) vs. 73% (50, 91) with OCL (n = 41), $p = 0.012$. Time spent in the hypoglycemia (< 70 mg/dL) was reduced with median of 0% (0,11) during control vs. 0% (0,0) in full OCL period, $p < 0.001$.

Overnight automated insulin delivery in children and adolescents with type 1 diabetes resulted in a significant reduction of nocturnal hypoglycemia and increased time spent in range compared to sensor-augmented pump therapy.

P-110

"STRESS TESTING" A FUZZY LOGIC ARTIFICIAL PANCREAS CONTROLLER

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Background: We have developed an Artificial Pancreas (AP) dosing controller, the FLC, using Fuzzy Logic methodology.

Methods: To assess the robustness of the ver 2.0 FLC in the clinical environment we 'stress tested' it under two different protocols, one involving exercise and another involving consumption of 120 gm CHO pizza meal involving a sixteen subjects. We used repeat studies on the same subjects increasing or decreasing the dosing intensity by varying the personalization factor (PF) for a total of 27 studies. After completing nine 'pizza' and four exercise studies, we used a dosing analysis tool to evaluate the v.2.0 FLC dosing matrix rules. Changes in the FLC dosing rules matrix in v.2.1 FLC that were validated through regression testing with clinical datasets. 7 studies were then conducted on 6 subjects in the exercise protocol and 7 studies on 3 subjects in the pizza protocol using v.2.1 FLC.

Results: V. 2.1 FLC showed dramatic improvements over version 2.0. For the 19-hour exercise studies, mean glucose dropped 27% to 146 mg/dL ($^{+}$/-13), % time in 70–180 mg/dL range increased 50% to 80% ($^{+}$/-9.4), %time > 180 mg/dL decreased 59% to 19% ($^{+}$/-1.9). Midnight to 8 am %time in 70–180 mg/dL increased 58% to 96% ($^{+}$/-4.1). For the six hours following the pizza meal the mean %time > 250 mg/dL decreased from 62% to 32%. %time < 70 mg/dL for both FLC versions was less than 1% for the pizza and exercise studies.

Conclusion: Stress testing an AP Controller can lead to improved glucose control.

P-111

NO EFFECT OF AGE OF INSULIN CATHETER ON OVERNIGHT CLOSED-LOOP GLUCOSE CONTROL IN HOME SETTINGS

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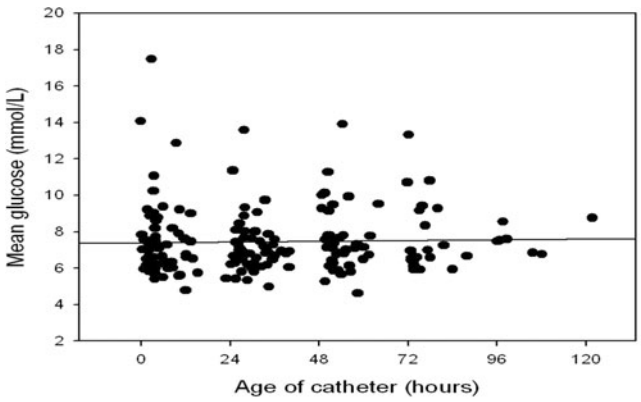
Objective: Insulin catheter wear-time can influence insulin absorption and may affect glucose control. We investigated the relationship between the age of the insulin catheter and overnight glucose control in adolescents with type 1 diabetes during home use of automated closed-loop insulin delivery.

Method: 16 adolescents [M 4; age 15.5 ± 2.1 yrs; A1C 7.9 ± 0.8%; BMI 23.3 ± 2.2 kg/m^2, duration of diabetes 6.1(3.8) yrs; total daily dose 0.9(0.2) U/kg/day; mean ± SD] participated in a study evaluating overnight closed-loop in home settings. During a three-week period, overnight insulin delivery was modulated by a model predictive control algorithm. Mean overnight glucose was computed from continuous glucose sensor data between 23:00 and 07:00. Instances of infusion catheter replacements were obtained from pump logs.

Result: Closed-loop was operational for at least 4 hours and catheter age information available on 184 nights. Mean overnight glucose was 7.0 (6.3,7.9) mmol/L, median (IQR). A repeated measures regression model with an autoregressive first-order covariance structure adjusted for catheter replacements found no effect of catheter age on overnight mean glucose ($p = 0.78$).

Conclusion: Overnight glucose control by a model predictive control algorithm is not affected by the wear-time of the insulin catheter in adolescents with type 1 diabetes.



P-112

PREVENTION OF HYPOGLYCAEMIA WITH PREDICTIVE LOW GLUCOSE MANAGEMENT SYSTEM: COMPARISON OF HYPOGLYCLAEMIA INDUCTION WITH EXERCISE AND SUBCUTANEOUS BOLUS

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The aim of the study was to determine the effectiveness of Predictive Low Glucose Management (PLGM) system in preventing hypoglycaemia in individuals with type 1 diabetes (T1DM). The primary outcome was the glucose nadir in participants following moderate-intensity exercise and increased subcutaneous insulin bolus with and without PLGM.

PLGM system consists of a Medtronic Veo pump, Enlite sensor, MiniLink REAL-Time transmitter, Bluetooth-RF translator and PLGM algorithm operating from a Blackberry smartphone. PLGM suspends basal insulin delivery when the preset hypoglycaemic threshold is predicted to be reached in 30 minutes.

Participants with T1DM performed 30–60 minutes of moderate-intensity exercise or were administered a subcutaneous bolus of insulin following a glucose stabilisation period on basal CSII on 2 separate days; randomised to a control day with PLGM off and an intervention day with PLGM on. On both days, participants were observed until plasma glucose dropped to 50 mg/dL or were symptomatic.

21 participants were studied with exercise. PLGM suspended basal insulin in 17 and did not suspend in 4 as hypoglycaemia did not occur. Plasma glucose nadir with PLGM on was higher than with PLGM off in 7 of the 17 participants. 8 participants were studied with insulin bolus. PLGM suspended in 7 and prevented hypoglycaemia in 6 participants.

PLGM system appears to be more effective when hypoglycaemia is induced by insulin bolus than exercise. This difference, if confirmed may be due to different rate and trajectory of plasma glucose decline with exercise as compared with insulin bolus.

P-113

VIRTUAL TRIAL PREDICTS CLINICAL TRIAL OUTCOMES – ACCELERATING DEVELOPMENT AND REDUCING RISK THROUGH MODEL-BASED DESIGN

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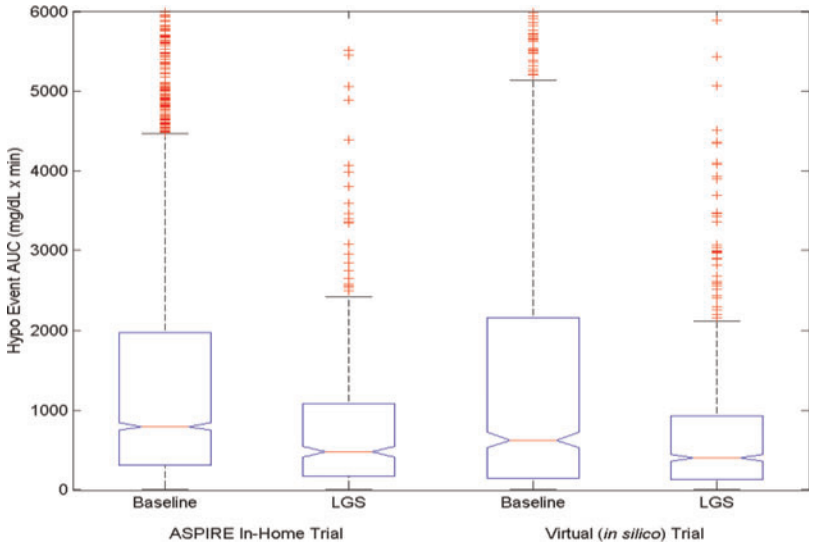
Bringing new technologies to market can be expensive and the process fraught with technical risk. Clinical trials are expensive and take time to complete; therefore, the desire is to maximize confidence that the final design meets expectations.

We used model-based design in the development of a predictive low glucose management (PLGM) algorithm. The goal was to improve on the performance of the current low glucose suspend (LGS) algorithm. To this end, we created a model to run virtual clinical trials. In this virtual trial there were multiple 'study arms' with different algorithms and parameter settings. Among these was a baseline case of a pump without automatic suspend, as well as the LGS algorithm already in the market.

Recently, the ASPIRE In-Home clinical trial evaluated the efficacy and safety of the LGS algorithm. This provided an



opportunity to validate the modeling platform used for the virtual clinical trials.

The primary effectiveness outcome metric was the area under the curve (AUC) for hypoglycemic events (< 65 mg/dL). The virtual trial showed a statistically significant ($p < 0.001$) reduction in hypoglycemic AUC, with a reduction in the median AUC of 35.4%. In the ASPIRE In-Home study the LGS group showed a reduction in the median AUC of 39.5%, also statistically significant ($p < 0.001$). The safety outcome was also consistent between the two trials.

The consistency of the outcomes predicted by the virtual trials with those observed in the ASPIRE In-Home study increase our confidence that the performance improvements of PLGM will be realized in a clinical setting.

P-114

EFFECTS OF HAWTHORN (CRATAEGUS) ON HBA1C AND LIPIDS LEVELS IN DIABETIC PATIENTS (TYPE 2)

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The present study was designed to investigate the effects of supplementation of Hawthorn on HbA1C and lipids levels among type 2 diabetics. The samples consisted of 55 subjects with type 2 diabetes and the doses of Hawthorn were equally administered orally in the form of capsules each capsules contain (500 mg), with breakfast, lunch and dinner. The doses were given for 12 weeks. Blood samples were taken on the starting day of the experiment and at the end of 12 weeks. The fasting blood glucose and lipids levels of types 2 were determined, from the results obtained the mean value of fasting blood glucose levels for Hawthorn doses on the starting day, was found to be 223.6 mg/dl and the mean values of HbA1C was 8.5% and for lipids were triglyceride (235.5 mg/dl), total cholesterol (310 mg/dl), low-density lipoprotein (LDL) (155.2 mg/dl) and high density lipoprotein (HDL) (52.4 mg/dl). When the diabetic individuals used the doses of Hawthorn for 12 weeks, their mean fasting blood glucose level dropped to 186.34 mg/dl, HbA1C 7.2, triglycerides (160 mg/dl), total cholesterol (187.6 mg/dl), LDL (115.5 mg/dl) and increase HDL (69.2. mg/dl) The reduction in the blood glucose and lipids levels were significant at $P < 0.05$ $P < 0.001$ and respectively.

Key words: Hawthorn, HbA1C, blood glucose, lipids level, type 2 diabetes.

P-115

INSULIN VERSUS ORAL HYPOGLYCEMIC AGENT AS INITIAL THERAPY FOR NEWLY DIAGNOSED DIABETES MELLITUS TYPE 2: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Initial benefits of OHA are caused by increasing insulin secretion from deteriorating pancreatic beta cells to the point of total failure. Initial insulin therapy can rapidly address the glucose toxicity and improve beta cell function in newly diagnosed type 2 diabetics.

Objectives: This study aims to evaluate the effectiveness of initial insulin therapy versus oral hypoglycemic agents in terms of glucose control, pancreatic beta-cell function and adverse effects.

Search Strategy: PubMed, EMBASE, Cochrane Library, Science Direct, Clinical Trials.gov were searched using the medical subject headings (MeSH): diabetes mellitus type 2, insulin, oral hypoglycemic agent.

Selection Criteria: RCTs with adults newly diagnosed with type 2 DM as subjects and given insulin (± metformin) vs. OHA (multiple or monotherapy) with outcomes of glycemic control, measures of insulin resistance and beta-cell function, weight and hypoglycemia were included.

Data Collection and Analysis: RCTs with quality grade of B were included and results summarized as graphs and forest plots using the random effects due to foreseen sources of heterogeneity.

Results: Presence of substantial heterogeneity prevents us from making a conclusion. All four studies showed lower post treatment BMI among participants in the insulin treatment arm. An opposite finding was expected as insulin is known to cause weight gain. Main adverse effects where hypoglycemic episodes and diarrhea.

Conclusion: Among newly diagnosed type 2 DM patients, there is inconclusive evidence that use of insulin compared to OHA as initial management resulted in improvement glycemic control, decrease in insulin resistance, and improvement in beta cell function.

P-116

ASSOCIATION OF INSULIN ANTAGONIST ADIPOKINES GENE POLYMORPHISM WITH METABOLIC RISK FACTORS IN POSTMENOPAUSAL WOMEN

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Introduction: Insulin antagonist adipokines such as TNF-α, IL-6 and Resistin impart an essential role in lipid metabolism insulin sensitivity and energy expenditure. Disturbance of these peptides level could lead to metabolic diseases.

Aim & Objective: The present study was design to investigate insulin antagonist adipokines (TNF-α, IL-6 and Resistin) gene polymorphism and their correlation with metabolic risk factors, insulin resistance in postmenopausal women.

Method: This is a case control study. Total 230 postmenopausal with & without metabolic syndrome were recruited for the study. Fasting blood samples were collected. Anthropometrical parameters and metabolic risk factors were measured. Circulating adipokines, insulin was estimated by ELISA and adipokines gene polymorphism was done by PCR-RFLP.

Result: Homozygous mutant genotype (GG v/s GA + AA) ($p = < 0.042$: OR = 1.84: 95% CI = 1.02–3.31) and mutant allele (A) ($p = 0.032$: OR = 1.78: 95% CI = 1.04–3.05) of TNF- α and (CC v/s CG + GG) ($p = < 0.005$: OR = 2.22: 95% CI = 1.29–3.80) and mutant allele (G) ($p = 0.004$: OR = 1.79: 95% CI = 1.21–2.64) of Resistin gene polymorphism were observed higher in postmenopausal women with metabolic syndrome as compare postmenopausal women without metabolic syndrome. Plasma glucose, serum TG and serum cholesterol, insulin and circulating TNF- α, IL-6 and resistin were found significantly high in postmenopausal women with metabolic syndrome.

Conclusion: Our results suggest that the adipokines gene (TNF- α 308 G/A & Resistin 420 C/G) polymorphism is likely to play an important role in the development of metabolic syndrome and metabolic abnormalities.

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THE EFFECT OF NUTRITIONAL EDUCATIONAL PROGRAM ON GLYCEMIC CONTROL OF ELDERLY PATIENTS WITH TYPE 2 DIABETES

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Background: The objective of this study was to determine the effects of nutritional educational program on glycemic control of elderly patients with type 2 diabetes.

Methods: In this parallel randomized controlled educational trial, 100 diabetic elderly patients (≥ 60 years) were chosen (50 in control and 50 in test group). Nutrition education based on beliefs, attitudes, subjective norms and enabling factors (BASNEF model) was conducted. Dietary intake and glycemic indices as well as the components of the BASNEF model were assessed. The four 70-minute educational sessions were conducted in one month. Three months after training intervention, questionnaire was completed again and blood tests were performed.

Results: Increased intake in the mean daily servings of fruits (0.91 ± 0.82 vs. 0.17 ± 0.79; $p < 0.001$), vegetables (0.87 ± 0.86 vs. 0.03 ± 1; $p < 0.001$) and dairy (0.35 ± 0.52 vs. and 0.12 ± 0.76; $p < 0.001$) were reported in the intervention group compared to the control group ($p < 0.001$). The amount of fruits, vegetables and dairy increased in the intervention group at the end of the study ($p < 0.001$). However, it was not significantly changed in the control group. HbA1c and fasting blood sugar (FBS) levels decreased significantly in the interventional group compared to the control group ($p < 0.001$). Comparing the amount of FBS and HbA1c at the end of the study with the baseline measurements showed significant reduction in interventional group ($p < 0.001$).

Conclusions: BASNEF–based nutritional educational intervention improved dietary intakes as well as glycemic control, 3 months after intervention.

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EFFECTS OF CAPTOPRIL AND ENALAPRIL ON ADVANCED GLYCATION END PRODUCTS-INHIBITED NITRIC OXIDE SIGNALING IN HUMAN RENAL TUBULAR CELLS

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To explore whether angiotensin-converting enzyme inhibitors captopril and enalapril were linked to altered advanced glycation end products (AGE)-mediated renal tubulopathy in diabetic nephropathy, the molecular mechanisms of captopril and enalapril responsible for inhibition of AGE-reduced nitric oxide (NO) bioactivity in human renal proximal tubular cells were examined. We found that raising the ambient AGE concentration causes a dose-dependent decrease in NO generation when compared with control or non-glycated BSA. Captopril and enalapril significantly reverse AGE-inhibited NO generation and induces high levels of cGMP synthesis and cGMP-dependent protein kinase (PKG) activation in these cells. Interestingly, treatments with captopril and enalapril, the NO donor S-nitroso-N-acetylpenicillamine, and the nuclear factor-kappa B (NF-κB) inhibitor pyrrolidine dithiocarbamate markedly attenuated AGE-inhibited inducible nitric oxide synthase (iNOS) protein synthesis and NO generation. Moreover, AGE-induced synthesis of fibronectin and collagen IV and cellular hypertrophy were reversed by captopril and enalapril. The ability of captopril and enalapril to suppress AGE-induced NF-κB activation was also verified by the observation that it significantly reduced IκBα kinase (IKK) activity. These findings indicate for the first time that captopril and enalapril attenuates AGE-inhibited the iNOS/NO/PKG pathway at least partly by decreasing IKK/NF-κB signaling in human renal tubular cells.

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ASSOCIATION OF ESBL GENE (CTX-M, TEM, SHV) POSITIVITY IN ISOLATES OF DIABETIC FOOT INFECTION FROM NORTH INDIA: A 3-YEAR HOSPITAL BASED STUDY

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Aim: Aim of this study was to evaluate the incidence and factors responsible for plasmid mediated ESBL infection among patients with diabetic foot ulcer (DFU).

Methods: A prospective study on 162 DFU inpatients treated in a multidisciplinary based diabetes and endocrinology centre of J. N Medical College of Aligarh Muslim University, Aligarh, India during the period of 2008–2012. Detailed history and patient's profile, grade of DFU, co-morbidities and complications, laboratory data and final outcome were collected. Standard methods were used for culture identification, sensitivity testing and ESBL detection. PCR for bla genes was performed and the risk factors for bla gene positivity were determined by univariate analysis with 95% of CI.

Result: A total of 127(78.3%) Enterobacteriaceae members were isolated. The bla_{CTX-M} gene was positive in 81.8% isolates followed by bla_{TEM} (50%) and bla_{SHV} (46.9%). The significant predictive factors which were more likely to be associated with $bla_{(CTX-M,\ TEM,\ SHV)}$ gene have an association was LDL-C (>100 mg/dl) [OR 13.4, RR 8.65], triglycerides (>200 mg/dl) [OR 6.5, RR 4.11], duration of infection >1 month [OR 1.25, RR 1.21], nature of ulcer (necrotic) [OR 5.33, RR 4.54], T2DM [OR 2.15, RR 1.92], history of previous antibiotic use [OR 6.75, RR 5.60], Smoking history [OR 1.098, RR 1.08], HDL-C(<40 mg/dl) [OR 3.29, RR 2.80], and total cholesterol (>150 mg/dl) [OR 3.52, RR 2.9] for bla gene positivity.

Conclusions: ESBL constitutes a major threat to currently available β-lactam therapy leading to complications in DFUs. Aminoglycosides, cephalosporin & beta lactam inhibitor drugs would probably be more appropriate empirical agent often establishing the patient's history of previous antibiotic use and the detection ESBL shall be done on routine basis.

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SHORT-TERM RESVERATROL SUPPLEMENTATION IMPROVES METABOLIC PROFILE IN TYPE 2 DIABETES

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Table: 1 Anthropometric, clinical and biochemical parameters for the placebo and resveratrol group at baseline and after supplementation for 45 days.

	Control/placebo group			Intervention/resveratrol group		
	Baseline	After 45 days	P value	Baseline treatment	After treatment	P value
Body weight (kg)	76.60±14.27	76.60±14.16	0.809	74.26±11.39	74.48±11.34	0.712
BMI (kg/m2)	27.83±4.21	27.69±4.15	0.332	27.05±3.13	27.16±3.13	0.395
Systolic blood pressure (mmHg)	129.31±15.16	130.68±13.21	0.147	129.03±14.91	121.45±10.26	<0.0001*
Diastolic blood pressure (mmHg)	78.58±15.39	81.55±5.84	0.279	76.93±19.54	78.54±6.35	0.169
Fasting glucose (mg/dl)	151.24±51.52	161.13±53.16	0.002*	175.74±49.63	140.80±39.74	<0.0001*
Insulin (μIU/ml)	9.04±5.35	8.77±4.16	0.642	10.20±4.33	5.37±2.62	<0.0001*
HbA1c	8.30 ±1.43	8.50±2.46	0.764	8.6±1.390	7.60±1.32	<0.0001*
HOMA-IR	3.20±2.37	3.43±1.83	0.423	4.61±2.77	1.91±1.17	<0.0001*
HOMA-β	36.13±8.45	35.68±7.95	0.039	32.15±5.32	25.80±4.43	0.009*
Triglyceride (mg/dl)	134.69±45.61	123.13±43.27	0.145	160.1±58.96	142.28±52.61	0.051
Total cholesterol (mg/dl)	168±41.97	175.34±41.31	0.424	203.61±52.70	192.28±53.13	0.156
HDL-cholesterol (mg/dl)	41.73±9.52	39.69±10.83	0.133	41.40±8.35	46.15±8.40	0.001*
LDL-cholesterol (mg/dl)	107.95±31.67	117.18±29.88	0.003*	134.04±36.18	122.71±38.19	0.106
SGOT (IU/l)	24.0±5.47	25.0±6.71	0.212	26.0±5.87.	26.0±7.56	0.837
SGPT (IU/L)	19.44±8.79	21.65±8.67	0.202	21.45±7.91	22.61±9.74	0.365
GGT (IU/L)	30.82±17.79	29.93±17.01	0.545	32.12±15.32	33.38±17.92	0.441
ALP (IU/L)	169.37±52.63	189.41±48.38	0.001*	185.29±59.35	190.64±47.55	0.372
Creatinine (mg/dl)	0.92±0.24	0.97±0.25	0.281	0.96±0.24	0.90±0.21	0.098

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Few earlier studies have tested resveratrol as an anti-diabetic supplement in humans. However, the results to date on the efficacy of resveratrol to significantly reduce blood glucose have been inconclusive. Accordingly, the main objective of this study was to examine the effectiveness of resveratrol in lowering blood glucose in presence of standard anti-diabetic treatment in patients with type 2 diabetes, in a randomized placebo-controlled double-blinded parallel clinical trial. A total of 66 subjects were enrolled to this study, and randomly assigned to intervention group (n = 32) which was supplemented with resveratrol at a dose 1 g/day for 45 days, and control group (n = 34) which received placebo tablets. All patients were asked to continue their anti-diabetic medications while in the study. Body weight, blood pressure, fasting blood glucose, haemoglobin A1c, insulin, triglycerides, total cholesterol, low density lipoprotein, high density lipoprotein, and markers of liver and kidney damage were measured at baseline, and after the treatment period. Insulin resistance and beta cell function was calculated using homeostasis model of assessments, HOMA-IR and HOMA-β respectively. Our results show that resveratrol treatment significantly decreased systolic blood pressure, fasting blood glucose, haemoglobin A1c, insulin and insulin resistance, while HDL was significantly increased, when compared to their baseline levels. Liver and kidney function markers were unchanged in the intervention group while alkaline phosphatase was significantly increased in the placebo group. Overall, this study showed that resveratrol supplementation exerted strong anti-diabetic effects in patients with type 2 diabetes.

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PRODUCTION OF ANTI-DIABETIC MILK BIOACTIVE PEPTIDES BY USING LACTOBACILLUS SPP

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Purpose: Diabetes is a metabolic disorder and is characterized by high blood glucose level (Hyperglycemia). Antidiabetic property of bioactive peptide is related to inhibition of Alpha-glucosidase and Dipeptidyl Peptidase-IV (DPP-IV) enzymes, which cause Type 2 diabetes. Therefore, inhibition of Alpha-glucosidase and DPP-IV is an effective strategy for controlling/managing of Type 2 diabetes. Bioactive peptide fragments are formed during degradation of the milk proteins by digestive enzymes in the gastrointestinal tract or by proteolytic lactic acid bacteria (LAB) during fermentation of milk. Hence, the present study has been designed to exploit the proteolytic activity of *Lactobacillus spp*. for the production of anti-diabetic milk peptides having Alpha-glucosidase and DPP-IV inhibitory activity

Methods used: In present study, 22 *Lactobacillus* strains were procured from National Collection of Dairy Cultures, NDRI, Karnal. Milk was fermented with *Lactobacillus* strains and Evaluated for Proteolysis by estimating peptide content by OPA method and Alpha-glucosidase and DPP-IV inhibitory activity by spectrophotometeric method. The process was optimized for the production of these bioactive peptides in milk during fermentation.

Summary of results: Based on results, all 22 isolates were observed to possess different proteolytic activity and Alpha-glucosidase and DPP-IV inhibitory activity.

Conclusion: The results from this study showed that peptides with Alpha-glucosidase and DPP-IV inhibitory activity can be generated by using *Lactobacillus* spp. from milk proteins. Therefore, these anti-diabetic peptides can be produced in fermented dairy product by selected proteolytic strains of Lactic Acid Bacteria or peptides rich formulation can be incorporated into functional foods or administered via nutraceuticals.

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METFORMIN REDUCES GLYCEMIC FLUCTUATIONS IN TYPE 2 DIABETIC PATIENTS WITH CHRONIC HEART FAILURE

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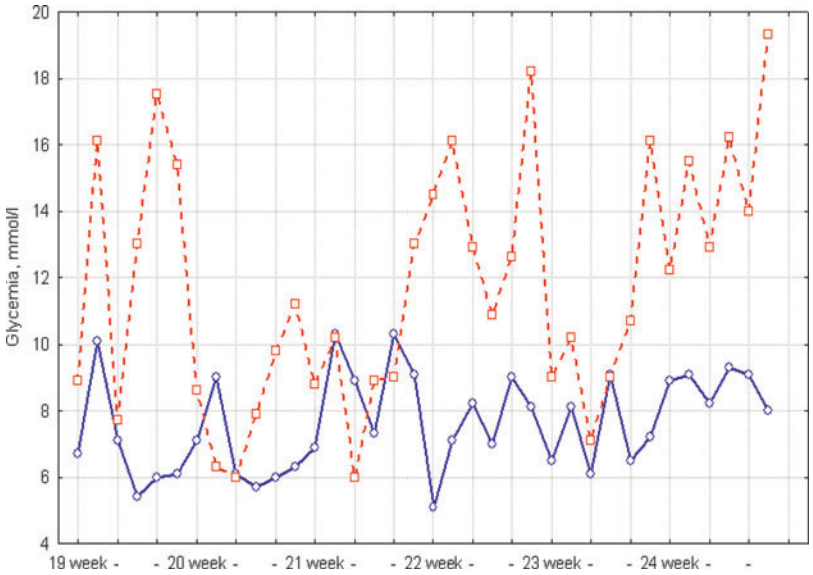

Background: The increased risk of lactic acidosis may be considered an argument against metformin in type 2 diabetes (T2DM) in the presence of chronic heart failure (CHF). Meanwhile, the register data indicate widespread use of metformin in CHF patients. The purpose of the study is evaluation the efficacy and safety of metformin in these patients.

Material and Methods: 30 T2DM patients with CHF and HbA1c >7.5% were randomized into a main group (16 subjects, metformin in the dose up to 2000 mg was administrated) and control group (14 subjects). The efficacy was assessed by HbA1c, glycemia and MAGE. The influence on CHF was assessed by BNP, echo and results of 6-minute walk test (6MWT). Safety was assessed by pH, BE, lactic acid, ALT and eGFR. Follow-up was 6 months.

Results: Significant changes of HbA1c, lactic acid, pH, BE, ALT, eGFR, BNP, echo parameters and 6MWT were not detected during the study in both groups. Significant effect of metformin on the glycemic fluctuations was identified. The median of MAGE during 6 months (MAGE was evaluated weekly) in the metformin group was 2.4 [1.7, 3.4] mmol/l vs 4.0 [3.0, 5.4] mmol/l in the control ($p = 0.02$, Mann-Whitney). The figure shows examples of glycemic curves of 2 patients with equal doses of insulin (red - control, blue - metformin).

Conclusion: Application of metformin in T2DM patients with CHF reduces glycemic fluctuation without increasing the risk of lactic acidosis and an unfavorable course of heart failure.

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INCREASED INFLAMMATORY ACTIVITY AND CHRONIC MICROVASCULAR COMPLICATIONS IN TYPE 1 DIABETES

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Background and aim: Chronic hyperglycemia causes exceeded Advanced Glycation End-products (AGEs) synthesis. This leads to increased macrophage activation, oxidative stress and production of inflammatory cytokines. Chronic inflammation causes endothelial dysfunction. The aim of our study is analysis of C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) levels in relation to existence of chronic microvascular complications in type 1 diabetes patients.

Methods: Retrospective study included 76 type 1 diabetes patients. Blood was sampled for glucose metabolism and lipid parameters, CRP, IL-6 and TNF-α. Classical fundoscopy, neurological examination and 24 hour albuminuria measurement were performed and 46 patients were diagnosed with at least one of the chronic microvascular complications. For statistical analysis we used χ^2, Mann Whitney and Kruskal Wallis test.

Results: Patients with chronic microvascular complications were older and had longer duration of disease ($p = 0.015$; $p < 0.0001$). They had higher total ($p = 0.021$), LDL cholesterol ($p = 0.048$) and triglycerides ($p = 0.002$). CRP and TNF-α were higher in patients with chronic microvascular complications ($p = 0.004$; $p = 0.048$). Diabetic retinopathy patients had higher CRP ($p = 0.039$), IL-6 ($p = 0.039$) and TNF-α ($p = 0.045$) than patients without retinopathy. Patients with diabetic polyneuropathy had higher CRP ($p = 0.009$) than patients without this complications. Diabetic nephropathy patients didn't have higher values of inflammatory markers than patients with normoalbuminuria.

Conclusion: Chronic microvascular complications are associated with increased inflammatory activity reflected through higher values of inflammatory markers. This requires investigation of specific anti-inflammatory drugs and their possible favorable effects on prevention of development of chronic microvascular complications, especially in patients with long duration of disease.

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EFFECTIVENESS OF SESAME AND RICE BRAN OILS BLEND IN TYPE 2 DIABETIC PATIENTS-AN OPEN LABEL, RANDOMIZED STUDY

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Recently there is substantial interest in the potential health benefits of sesame and rice bran oils, especially in relation to cardiovascular health. The objective of the current study was to examine the extent to which the daily incorporation of the blend of unrefined sesame (20%) and physically refined oryzanol rich rice bran oils (80%) as cooking oil in type 2 diabetic patients. This open label study comprised of three hundred, men ($n = 162$) and women ($n = 138$) with type 2 diabetes mellitus and they were randomly assigned to three groups, receiving Vivo™, a blend of sesame and rice bran oils ($n = 100$), 5 mg/d (single dose) of glibenclamide ($n = 100$), or their combination ($n = 100$). Blend of sesame and rice bran oils was supplied to the respective groups and instructed to use it as sole cooking oil for 60 days. Blood glucose was measured at 0, 15, 30, 45 and 60th days. HbA_1C and lipid profile were measured at 0 and 60th days. Blood glucose and HbA_1C were significantly lowered in oil alone treated and/or glibenclamide groups. Total, low-density lipoprotein cholesterols and triglycerides were significantly reduced by oils blend or combination with glibenclamide while HDL-C was significantly improved respectively. Replacement of cooking oils with the blend of sesame and rice bran oils articulates rapid and clinically vital improvements in blood glucose, HbA_1C and lipids, providing the evidence that this oils blend could be effective edible oil with potentially important anti-diabetic and cardio protective efficacies.

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ALPHA-LIPOIC ACID AND ANTI-OXIDANT DIET HELPS TO IMPROVE ENDOTHELIAL DYSFUNCTION IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES

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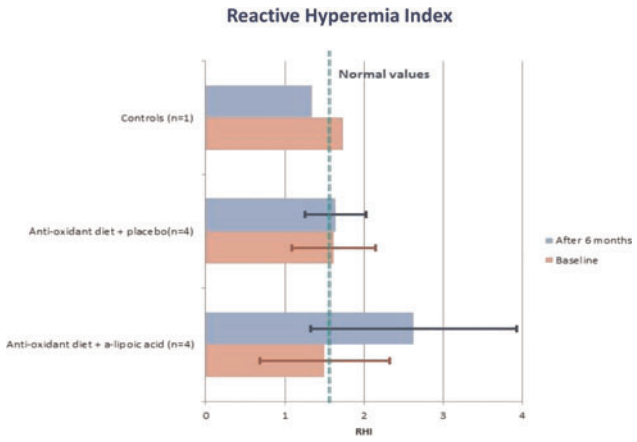

After evaluating the prevalence of early endothelial dysfunction, as measured by mean of reactive hyperemia in adolescents with type 1 diabetes (T1D), at baseline and after 1-year follow-up, we started a 6-month, double-blind, randomized trial to test the efficacy of an anti-oxidant diet (±a-lipoic acid) in improving endothelial dysfunction. Sixty-one children and adolescents, ages 16±3.5 yrs., with T1D since 8.9±4.3 yrs., using either MDI or CSII, were randomized into 3 arms: a) anti-oxidant diet 10.000 ORAC + a-lipoic acid; b) anti-oxidant diet 10.000 ORAC + placebo; c) controls. BMI, blood pressure, fasting lipid profile, HbA1c, insulin requirement, dietary habits and body composition were determined in each child. After 3 months BMI, blood pressure, lipid profiles, HbA1c, and body composition did not change, while insulin requirement significantly decreased only in patients in arm with anti-oxidant diet and a-lipoic acid (0.74±0.18 U/kg/day vs. 0.83±0.26 U/kg/day, $p < 0.05$), as well as bolus insulin (22.0±9.4 U/day vs. 26.3±10.8 U/day, $p < 0.05$), but not basal insulin (25.9±9.4 U/day vs. 25.5±8.6 U/day, P NS). After 6 month we evaluated till now only 24 patients (study ended on September 30th). These very first data are very encouraging (Figure) with a significant improvement of endothelial function in group treated with a-lipoic acid. Insulin requirement and bolus insulin keep to be decreased. Adolescent with T1D displayed evidence of endothelial improvement after a-lipoic acid and anti-oxidant diet, but not in controls. Moreover, to our knowledge these data demonstrate for the first time and effect in sparing insulin in T1D in pediatrics.

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SILYMARIN INDUCES EXPRESSION OF PANCREATIC GLP-1 AND β-CELLS NEOGENESIS IN A PANCREATECTOMY MODEL

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An important physio-pathological feature of diabetes mellitus is a significant reduction of β-pancreatic cells. Glucagon-like peptide-1 is an incretin produced in gut L-cells of intestine that accounts for approximately 70% of total insulin secreted upon oral administration of glucose, whereas it is reduced in type 2 diabetes mellitus. It has been reported that GLP-1 induces β pancreatic cells proliferation and differentiation and inhibits its apoptosis. Previously, we reported that Silymarin recovers normal morphology and endocrine function of damaged pancreatic tissue after alloxan-induced diabetes mellitus in rats. The aim of this study was to analyze the effect of Silymarin on pancreatic GLP-1 expression and its consequence in β cells neogenesis. 60 male Wistar rats were partially pancreatectomized and divided into twelve groups. Six groups were treated with Silymarin (200 mg/Kg p.o) for 3, 7, 14, 21, 42 and 63 days. Additionally, an unpancreatectomized control group was performed. GLP-1 and insulin gene expression were assessed by RT-PCR assay in total pancreatic RNA. β-cell neogenesis was determined by immunoperoxidase assay (double tinction). Silymarin treated group showed an increase in GLP-1 and insulin genic expression. Also in this group, there was an increment of β-cell neogenesis in comparison to pancreatectomized untreated group. Silymarin treatment produced a rise in serum insulin and serum glucose normalization. These results suggest that Silymarin may improve the reduction of β pancreatic cells observed in diabetes mellitus type 1 or 2.

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DEVELOPMENT AND EVALUATION OF BI-LAYERED GASTRO-RETENTIVE TABLET CONTAINING METFORMIN HCL SR AND PIOGLITAZONE HCL IR

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To get advantage of novel drug delivery in treatment of diabetes mellitus is centered aim of this work. Bi-layered gastro-retentive tablet containing Metformin HCl and Pioglitazone HCl for treatment of type-II diabetes mellitus has been formulated. To make the system more effective, combination of immediate layer, Pioglitazone HCl 15 mg and sustained release layer of Metformin HCl 500 mg were prepared. The core tablet of Metformin HCl was prepared by using different swellable polymers like HPMC E15, HPMC K100 and carbopol by wet granulation method and evaluated for swelling index, total floating time and floating lag time. *In vitro* release studies were carried out with 0.1N HCl using USP dissolution apparatus 2 (paddle). Tablet thus formulated using HPMC K100M and E15 provided sustained release of Metformin HCl over a period of 10 hours. The immediate release layer of Pioglitazone HCl was prepared by using crosspovidone, a super disintegrant by direct compression method and evaluated for disintegration time and dissolution also. Then bilayered tablet was prepared with the selected core tablet batch of Metformin HCl followed by compression coating with the selected immediate release layer of Pioglitazone HCl. The present study concluded that bilayered tablet can be a good way to treat diabetic patients with combination therapy.

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PREDIABETES AND TYPE 2 DIABETES SIMULATOR: *IN SILICO* TESTING OF NEW DRUGS

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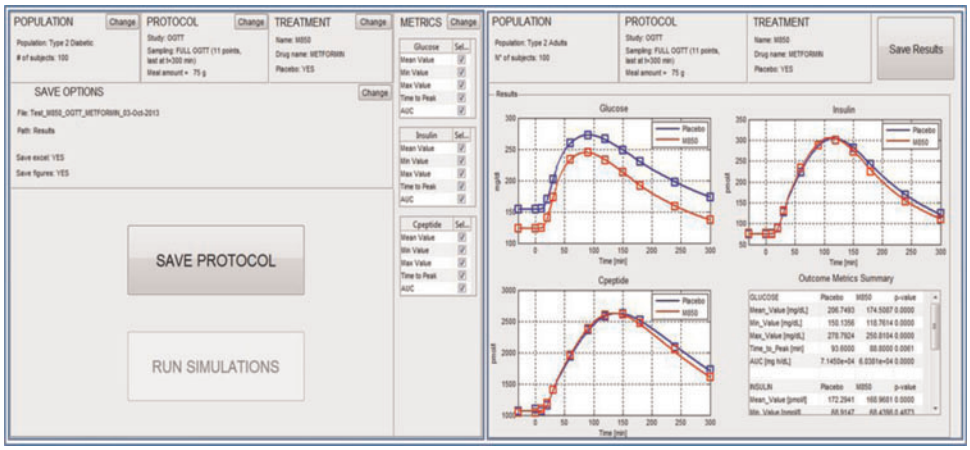

FIG. 1. Screenshots of *in silico* experiment configuration (left) and simulation results (right panel).

The increasing incidence of diabetes stimulates research on new drugs. However, their development is complex, costly and time consuming. Computer simulation can allow relevant time- and cost-saving, alleviating the need of *animal* trials and providing useful information for optimal experiment design and drug dosing. In this contribution, we present a prediabetes and type 2 diabetes simulator for *in silico* testing of new molecules.

The simulator is based on a large-scale model of glucose-insulin system (Dalla Man et al., TBME 2007), which can be extended to incorporate pharmacokinetics-pharmacodynamics (PK-PD) of a new test drug. The simulator has been equipped with a user-friendly graphical interface, which allows an easy design of new *in silico* experiments. Specifically, it is possible to select the *in silico* population (Type 2 Diabetic, Prediabetic, Nondiabetic), configure protocol attributes (duration of the experiment, sampling schedule, glucose doses, etc.) and define treatment details (drug dose and PK-PD). Moreover, the user can choose the outcome metric variables to be computed and the results to be displayed.

The simulator has been successfully validated using metformin as a case study: metformin PK-PD model has been incorporated in the simulator, and the simulation results are in agreement with those observed in *in vivo* clinical experiments.

In conclusion, the proposed prediabetes and type 2 diabetes simulator is a valuable tool for the design and *in silico* testing of new antidiabetic drugs.

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NO DIFFUSE HEPATIC STEATOSIS IN TYPE 1 DIABETIC PATIENTS RECEIVING INTRAPERITONEAL INSULINOTHERAPY

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Background: Recent studies published conflicting data about whether steatosis could be associated with diabetes mellitus type 1 or not. One of the criteria is a moderate elevation of alanine transaminase (ALAT). Furthermore, rare cases reported focal hepatic steatosis in type 1 diabetes treated with implantable pumps.

Aim: We investigated whether treatment with an implantable pump was more likely than treatment with a subcutaneous pump to induce biological profile for diffuse steatosis in type 1 diabetes.

Patients and methods: Seventeen patients receiving intraperitoneal insulin (group 1) were matched with 17 subjects receiving subcutaneous insulin (group 2) for sex, age, duration of diabetes and pump. We compared transaminases before internal or external pump at one year and at the end of the study.

Results: Initially, the 2 groups were comparable in term of age, BMI, transaminases, duration of diabetes and pump (11 ± 5.3 versus 9.1 ± 7.2 years); there was a trend toward better metabolic control in group 1 than in group 2 ($p = 0.058$). In 2013, mean ALAT were similar in the 2 groups (26.1 ± 11.8 versus 28.3 ± 18.1 UI/L); HbA1c was lower in patients treated with implantable pumps than in those with external pumps ($p = 0.02$), in spite of similar BMI and increased weight in each group (NS).

Conclusions: ALAT in patients long-term treated with an implantable pump was no higher than that in patients treated with an external pump, which argues against an increased risk of diffuse hepatic steatosis in such patients.

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DOES THE PUMP SPECIFIC DOSE ADJUSTMENT FOR NORMAL EATING (PUMP DAFNE) PROGRAMME PROVIDE ADDED GLYCAEMIC OUTCOMES IN ESTABLISHED PUMP USERS?

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Aim: To establish if there are added glycaemic benefits for CSII established adults attending the pump specific structured education programme: Pump DAFNE.

Methods: Improvement in glycaemic outcomes following MDI DAFNE is well documented in adults with T1DM; of which attendance is usually compulsory before CSII eligibility is considered in the UK. However, there is a cohort of DAFNE naive, CSII managed patients attending King's College Hospital.

Twenty-nine of these patients attended Pump DAFNE between 2009 and 2011. Retrospective case note analysis extracted glycaemic outcomes and self-management behaviours (SMB) data at baseline, 2, 6 and 12 months.

Results: Completed records of 28 patients (age 35.1 ± 10.8; 19 female) with type 1 diabetes (duration 16.7 ± 9.0 years) were retrieved. Mean A1c was 8.1% (± 1.2) at baseline; 7.5 ± 0.7% ($p = 0.004$) at 2 months; 7.6% (± 0.8) at 6 months and 7.9% (± 1.2) ($p = 0.392$) at 12 months follow-up. Severe hypoglycaemia rates fell from 0.8 to 0.2 episodes/patient/year from baseline to 12 months ($p < 0.05$). DKA episodes fell from 0.15 to 0.00 episodes/patient/year from baseline to 12 months ($p < 0.0001$). Effective diabetes/pump SMB were absent at baseline, but were widely adopted post-intervention.

Conclusions: Pump DAFNE provides significant improvements in glycaemic outcomes and SMB in pump established adults. Clinicians and policy makers need to consider resourcing in order to deliver quality structured follow-up to maintain these effects long-term.

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FUNCTIONAL INTENSIFIED INSULIN THERAPY AND BOLUS CALCULATOR USE IN PAEDIATRICS PRACTICE: 2012 SITUATION IN THE "AIDE AUX JEUNES DIABETIQUES" CAMPS

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Introduction: Functional Intensified insulin Therapy (FIT) practice is very complex, due to many calculations. The use of a bolus calculator (BC) could help children to manage FIT. Our study evaluated FIT practice and real life experience in children attending an ''Aide Aux Jeunes Diabétiques'' French 2012 summer camp.

Methods: We compared data between 167 children who practiced FIT (FIT +) and 636 who did not (FIT-), and between children who used a BC in FIT practice (BC + ; n = 27) and those who did not (BC-; n = 73). Statistical analyses were performed using T-test, and Chi2 test.

Results: FIT + were predominantly girls (sex ratio 0.84 vs 1.21 $p = 0.04$), and more aged (13.7 years [11.9–15.4] vs 12.83 [10.9–14.6]) than FIT-. Diabetes or FIT duration, sex ratio, age, BMI z-score, HbA1c and QoL were similar between BC + and BC- except a lower insulin daily dose (0,84 U/kg vs 0,94, $p = 0,04$). The use of the BC wasn't associated with a better assiduity, neither accuracy in the carbohydrates counting.

Conclusion: In our study, the use of a BC in children practicing FIT did not change HbA1c, QoL or other parameters except insulin daily dose. So it could improve adequacy between insulin dose and what the children really need.

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MONITORING DIFFERENT PARAMETERS DURING 3 WEEKS WALKING IN A TYPE 1 DIABETIC PATIENT WITH INSULIN PUMP AND CMGS

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The purpose of this project is monitoring different parameters in a T1DM patient using an insulin pump with a Continuous Glucose Monitoring System (CGMS) performing a 3 weeks walking exercise (700 km). In a 40 years old T1DM patient we evaluated body composition by bioelectrical impedance analysis, continuously monitored the glycemic profile for 3 weeks via CGMS, and evaluated the energy expenditure 3 days each week during the walking. We registered a decrease in total body weight (PRE = 83.5 to POST = 81.1 kg) and fat mass (PRE = 12.2 to POST = 8.9 kg), and an increase in fat free mass plus water (PRE = 71.3 to POST = 72.9 kg). The CGMS data showed a 9% decrease in the average glucose concentration comparing the first week (W1 = 133 mg/dl) to the third week (W3 = 121 mg/dl). The average daily insulin decrease by 12% was (W1 = 38, to W3 = 33.5 IU), resulted from the sum of average daily basal insulin (W1 = 16.2 to W3 = 12.6 IU) and average daily insulin bolus (W1 = 21.8 to W3 = 20.9 IU). The % in which glucose level stayed on target [between 80 – 160 mg/dl] increase by 7% (W1 = 57 to W3 = 64%) and decrease by 8% during hyperglycemia (W1 = 26 to W3 18%). Data showed that an aerobic exercise performed for 3 weeks can improve the glucose profile and the other metabolic parameters in a T1DM patient. A simple walking exercise without engaging in any risky high intensity - physical activity can have overall beneficial effects on health in a T1DM patients.

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GLYCEMIC CONTROL AND PREGNANCY OUTCOME IN WOMEN WITH TYPE 1 DIABETES ON CONTINUOUS SUBCUTANEOUS INSULIN INFUSION (CSII)

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Aim: Insulin pump with continuous subcutaneous insulin infusion (CSII) is nowadays the most modern method of type 1 diabetes treatment. We evaluate metabolic control, maternal and fetal outcomes in our group of pregnant type 1 diabetic (DM1) patients treated with CSII. Patients and methods: In the last 5 years we treated 17 pregnant women with DM1 on insulin pump and we evaluate metabolic control, maternal and fetal outcomes.

Results: HbA1c in the first trimester was 6,1% (4,6–7,3%), in the third trimester 6,4% (5,0–7,8%), in the postnatal period was 7,1% (5,7–8,0%). The average age at childbirth was 27,7 years (22–31). 41% of the children were born by Caesarean section, of which 59% boys, on average at 37 (35–40) week of pregnancy. The average newborn weight was 3460 g (2260–4500 g), length 49,56 cm (46–54 cm), only 2 (11%) were weighing more than 4000 g (4500 and 4400 g), of which one mother was less metabolically regulated (HbA1c 7,5%), while the other not (HbA1c 5,8%).

Conclusion: All pregnancies ended successfully. Only 11% of newborns were overweight, without other complications, deliveries were at 37 week. Women with diabetes are more likely to have a large baby, which can cause problems around birth. Early elective

delivery (labour induction or Caesarean section) aims to avoid these complications, so 41% were completed by Caesarean section. Metabolic arrangement during pregnancy was good, after giving birth the loss of motivation was apparent. Insulin pump is a safe treatment in pregnant women with DM1.

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BOTH NIGHTTIME AND DAYTIME GLUCOSE VARIABILITIES ARE REDUCED AFTER SWITCHING TYPE 1 DIABETIC PATIENTS TO CSII

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Background: We used Poincaré plot (PCP) derived metrics for studying glucose variability (GV) in type 1 diabetic patients switching to CSII.

Methods: PCP metrics ($\Delta t = 30$ and 120 minutes) including daytime (08-22) and nighttime (22-08) partial indices and classical GV measures were computed from CGMs of 13 patients, before and six months after CSII. PCP-derived SD1 and SD2 represent short- and long-term GV (panel A). Area of the fitting ellipse (AFE = πxSD1xSD2) is a marker of diabetes instability.

Results: CV (49.1 ± 8.7 vs 42.5 ± 5.0 on CSII; $p < 0.030$) and other classical indices were reduced but number of hypoglycemic events did not change significantly on CSII. SD1-30, SD2-30, SD1-120 and SD2-120 decreased significantly as AFE-30 ($p < 0.005$) and AFE-120 ($p < 0.004$). The daytime reductions of AFE-30 and AFE-120 were of 29.3% ($p < 0.01$) and 36.3% ($p < 0.008$). Nighttime AFE-30 and AFE-120 decreased from 42.3% ($p < 0.006$) and 43.2% ($p < 0.004$). See figure for absolute numbers.

Conclusions: CSII reduced both nighttime and daytime GVs. The absolute value of night GV and its reduction was as impressive when measured by both AFE-30 and AFE-120. The apparent GV degradation when Δt increases from 30 to 120 minutes is thus due to not only daytime post-meal peaks but is also linked to intrinsic variability.

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TECHNICAL DETERMINANTS OF DIABETES CONTROL IN INSULIN PUMP THERAPY IN CHILDREN AND ADOLESCENTS

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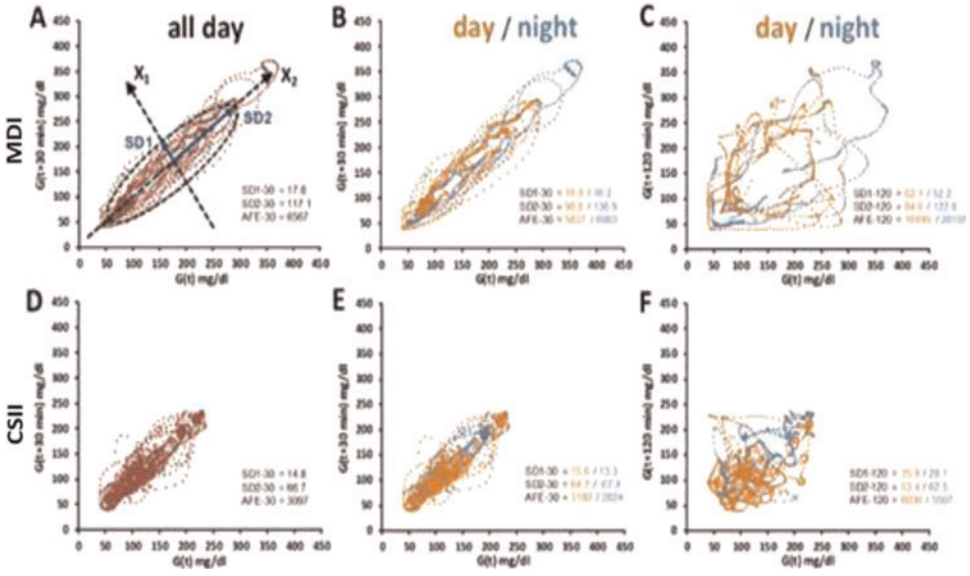
Insulin pumps (IPs) are equipped with advanced functions. However, intensive training and adherence are required for optimum use of the technology. We aim to assess the association of various key elements in IP functions on blood glucose (BG) control. Patients with T1DM on IP therapy were enrolled. IPs were downloaded (Care-link 3) and data over 8–12 weeks were collected. Patients were grouped, based on HbA1c of ≤8% and >8% into controlled (G1) and uncontrolled (G2) respectively. Variables studied are; use of sensors and duration, frequency of BG monitoring, bolus wizard (BW) use, frequency of correction boluses and frequency of cannula changing. 60 patients were enrolled. Age range was 2.3–17.1 with a median of 12 years. 25 patients were in G1 and 35 in G2. Median BG checks were 4.4 (2–11.4) and 3.2 (0.5–7.9) for G1 and G2 respectively ($P < 0.021$). Frequency of BW use showed a median of 6 (3.9–12.9) and 4.15 (0.6–9) for G1 and G2 respectively ($P < 0.001$). 8 (30%) of G1 and 14 (40%) of G2 used sensors. G1 used sensors for longer (5 vs 2.9 days/week). G1 did more corrections than G2 (3.9 vs 2.5). There was no difference in the frequency of changing the infusion cannula in both groups (3.5 days). We conclude that the frequency of BG monitoring and bolus wizard use have a favorable correlation with glycemic control. Our data shows that patients with better control tend to bolus more for correction and wear sensors for longer.



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RELATIONSHIP BETWEEN BASAL INSULIN REQUIREMENT AND BODY MASS INDEX IN CHILDREN AND ADULTS WITH TYPE 1 DIABETES USING INSULIN PUMP THERAPY

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It is recommended that basal insulin (BI) for children and adolescents to be between 30–50% of the insulin total daily dose (TDD) which is lower than the adults' basal requirement. As patients with higher body mass index (BMI) are more insulin resistant, we hypothesize that they might require higher BI compared to those with normal BMI. We aim to examine the correlation between BMI and BI requirement in paediatric and adult patients.

Patients with type 1 diabetes on insulin pump (IP) therapy were enrolled. Subjects were categorized to normal weight (NWt) and overweight (OvWt) based on BMI. IP were downloaded and data over 8–12 weeks' period were collected. BI requirement is considered high if it exceeded 50% of TDD. Selected variables included; HbA1c, insulin TDD, and daily carbohydrate consumption.

72 patients were enrolled (50 children). Median (range) was 12 (2.5–17.2) and 30 (20–48) for children and adults. 14 children and 9 adults were NWt while 36 and 13 were OvWt. There was no difference in the number of NWt and OvWt with BI over 50% in the children or the adult groups ($P = 0.86$, 0.80). However, a positive correlation was seen between BMI and BI in older children ($P < 0.03$).

We found no correlation with BMI and BI requirement in young children and adults regardless of the insulin TDD, HbA1c or carbohydrate consumption. Nonetheless, older children showed a higher requirement for BI. We hypothesize that pubertal factor has an impact on BI requirement regardless of the BMI.

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IMPACT OF INSULIN PUMP THERAPY IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES ON LONG-TERM METABOLIC CONTROL

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Objectives: This study was designed to assess the impact of CSII in children with type 1 diabetes (T1DM) on long-term metabolic control and acute diabetic complications at initiation of pump therapy and after one year of follow-up.

Methods: A total of 21 patients (12M/9F) with T1DM mean age 12.78 ± 2.31 years (4–18 years) and disease duration of 5.2 ± 1.9 (3 months–14 years) participated in the study. Insulin pumps (Minimed 722 Paradigm Real time and Minimed 712) were used administering short–acting insulin analogue.

Results: After 1 year CSII, a significant reduction in HbA1c levels was observed ($8.9 \pm 1.6\%$ to $7.6 \pm 0.9\%$, $P = 0.01$) from CSII initiation. Total insulin dose required decreased in all patient from 1.2 ± 0.4 to 0.8 ± 0.26 U/kg/day, $p = 0.00$). The frequency of significant hypoglycemia during CSII were less than initiation (4.8 ± 3.5 to 1.6 ± 1.9, $P = 0.007$), hyperglycemic attacks was lower especially episodes exceeding 300 mg/dl ($P = 0.00$). One patient had an attack of DKA due to catheter trouble, non had mechanical troubles or skin problems. Rate of post-prandial hyperglycemia decreased ($P = 0.09$) as a result of adequate insulin bolus on each food intake using Bolus Wizard calculator. The rate of hospitalization due to acute events was less ($P = 0.03$). Patients were satisfied with decreasing the frequency of injections (one per three to four days).

Conclusion: This study revealed the importance of CSII therapy in sustaining good metabolic control and blood glucose stability for one year follow-up.

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COMPARISON DAILY DOSE INSULIN BETWEEN CONTINUOUS SUBCUTANEOUS INSULIN INFUSION AND MULTIPLE DAILY INJECTIONS IN CHILDREN WITH ONSET TYPE 1 DIABETES MELLITUS

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Background: The purpose of this study was to investigate potential benefit of using continuous subcutaneous insulin infusion from onset diabetes type 1 in children.

Methods: In the study were included 72 children with first diagnosed type 1 diabetes during 4 weeks after diagnosis. All patients were with good glycemic control. The patients were divided in two groups. The children from the first group ($n = 54$, mean age 9.85 ± 3.12, diabetic ketoacidosis 51.8%) were treated by multiple daily injections. The patients from the second group ($n = 18$, mean age 9.89 ± 3.29, diabetic ketoacidosis 44.4%) were treated by subcutaneous insulin infusion.

Results: In the first group the mean daily dose of insulin was 0.4 ± 0.2 U/kg, the rate of basal insulin - $43.64 \pm 10.3\%$. In the second group the mean daily dose of insulin was 0.36 ± 0.16 U/kg ($p = 0.4$), the rate of basal insulin - $38.99 \pm 10.42\%$ ($p = 0.1$).

Conclusion: The mean daily dose of insulin and rate of basal insulin is similarly in two groups. The result highlights the potential benefit of subcutaneous infusion in diabetes care in children at the beginning of treatment.

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INSULIN PUMPS AND CONTINUOUS GLUCOSE MONITORING IN CHILDREN WITH TYPE 1 DIABETES: A LONG-TERM FOLLOW-UP OF PATIENTS AND THEIR DEVICES

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The aim was to perform a long-term retrospective evaluation of type 1 diabetes (T1DM) pediatric patients treated with insulin pumps (CSII) and continuous glucose monitoring (CGM) at our clinic. Patients ($n = 156$) were included if treated with CSII for at least 12 months from year 2007, were interviewed and their

medical records reviewed. Mean age: 12.9 yrs ± 4.29. Mean age at diabetes onset: 5.71 yrs ± 3.65. Mean diabetes follow-up: 3.16 yrs ± 2.04. All commercially available CSII and CGM devices in Italy were used. HbA1c was measured with DCA2000. Control group: 500 patients in multidrug injection therapy (MDI) matched for age, sex and follow-up. CSII use was 48.7%, 30.7% and 20.6% in patient ages 7–12 yrs, 0–6 yrs, and 13–18 yrs respectively. Mean age of CSII initiation: 8.9 yrs ± 4,12 (range: 9 months to 18 years). Of our study cohort only 4.5% suspended CSII. Mean HbA1c: 7.27% ± 0,47 and 7.3% ± 1.4 in CSII and MDI groups respectively. Mean HbA1c reduction: 0.1% and 0.2% in the 7–12 years and 13–18 years respectively when comparing CSII vs MDI. Diabetic ketoacidosis in the CSII group was 1.28/100 patients/year (no significant difference vs MDI group). Pumps were replaced in 50% of cases (55% for malfunction). Of the patients using CGM, 72.7% suspended its use for invasiveness (28.4%) or imprecise readings (8%). Our data confirms that CSII enables to achieve adequate glucose control in all ages during an average follow-up period of 3 years. Furthermore, this is accomplished safely and without increasing the risk of acute complications compared to MDI.

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THE MANDATORY REQUIREMENT FOR SENSOR AUGMENTED INSULIN PUMP THERAPY IN INFANTS WITH ILLUSTRATION OF THE PITFALLS WITHIN THIS AGE GROUP

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Background: Diabetes in an infant (< 12 months) is rare most cases are monogenic either transient or permanent. Diabetes management is complex due to patients size, insulin sensitivity and feeding patterns.

Case series: We report 2 infants, one 11 days old female term (IUGR) with permanent neonatal diabetes and a pre-term 11 month male with type 1A diabetes. The female presented with failure to thrive whereas the male had polyuria and poydypsia, neither were in Diabetic Ketoacidosis(DKA) but had glycosuria. Diagnosis was confirmed via random laboratory glucose of 19 mmol/l/342 mg/d]l and 26.7 mmol/l/481 mg/dl respectively. Both required Intravenous rehydration and IVI insulin infusion to stabilise glycaemic control. Transition onto CSII(continuous subcutaneous insulin infusion) via a sensor augmented pump occurred between day 18 and 7 respectively. Glycaemic control proved extremely difficult with marked glucose variability/ protracted hypoglycaemia with emergency management. which occurred secondary to insulin sensitivity, demand feeding via breast, bottle and solids. We used a modified insulin regime which required. No boluses, Suspension of the basal rate with cannula reinsertion and prolonged hypoglycaemia, delivered via the glucose sensor as well as manual suspension. Use of the temporary basal rates, higher than recommended (ADA) glycaemic ranges (6–14 mmol/l) for the first month from diagnosis. We identified and addressed issues with cannula insertion due to lack of subcutaneous fat with Sensor malfunction/calibration; Training of parents, ward staff and the parental psychological fear of hypoglycaemia and its treatment.

Conclusion: The patients demonstrated extreme insulin sensitivity, unpredictable hypoglycaemia with need for accurate insulin titration. It is our experience that this was only achieved with a sensor augmented insulin pump despite its pitfalls.

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EXAMINING GLYCAEMIC CONTROL AND VARIABILITY UTILISING THE MEDTRONIC CONTINUOUS GLUCOSE MONITORING SYSTEM (CGMS) IN PRE AND POST CSII THERAPY

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Introduction: Currently measures of glycaemic variability (Standard Deviation, Mean and MAGE) all fail to fully highlight the extent of blood glucose variability so there is a need for improved measures of glycaemic variability.

Aim: To utilise clinical data produced using CGMS to develop and validate a clinically-relevant novel measure of glycaemic variability and to use it to compare CSII with MDI.

Methods: 20 participants (6 months pre and post CSII) with 24 hr CGM data sets were analysed. Glucose variability Rating (GVR) was calculated in three steps including change in sensor reading at 5 minute intervals which were then squared and averaged to obtain GVR (mmol/L) ^{2}/hr. GVR was plotted, area under curve (AUC) calculated and pre vs. post-CSII GVR compared. Time series analysis was also investigated to try and identify specific periods with increased variability. A comparison of the percentage change in GVR vs the change in HbA_{1c} value in pre vs post-CSII was also analysed to identify correlation between these two measures.

Results: GVR was applied to pre and post-CSII CGM data; 75% of participants showed < 20% reduction of GVR post-CSII vs. MDI. The group also showed a significant reduction in GVR ($p < 0.003$) post-CSII (vs MDI).

Conclusions: Results indicate a reduction in glucose variability with CSII and highlight the limitations of HbA1c, as well as the useful potential of GVR to highlight specific time periods where intervention is required to control blood glucose variability.

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HBA1C AND WEIGHT DEVELOPMENT ONE YEAR AFTER INITIANTION OF CONTINUOUS SUBCUTANEOUS INSULIN INJECTION THERAPY IN ADULT SUBJECT

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Aims: We performed a retrospective analysis in Type 1 diabetes patients initiating continuous subcutaneous insulin injection (CSII to evaluate the effect on hba1c and weight).

Materials and methods: All subjects initiating CSII after year 2002 were analyzed for age, HbA1c, weight, total insulin dose prior to and one year after pump initiation.

Results: 505 (184 males/ 321 females) entered into the analysis; at CSII initiation age: 40 ± 0.6 years, weight: 82.9 ± 1.1 and 70.0 ± 0.8 kg for males and females, respectively (p 312 ± 2.5

days) HbA1c (mmol/mol) 62.6 ± 0.9 in males vs 60.6 ± 0.6 in females ($p < 0.01$).

Conclusion: From MDI to CSII in type 1 diabetes patients the HbA1c decrease is relatively greater in females with a marginal increase in weight.

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TO DISCUSS OUTCOMES AND CONTROL IN 21 PREGNANCY EPISODES IN TWO GROUPS OF WOMEN WITH TYPE 1 DM, USING CSII

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Methods: In 9 pregnancies, CSII was started during pregnancy (first group), while in 12 CSII was started before pregnancy (second group).

HbA1c, DR, ACR data were reviewed in the pregnancies that went through the 3 trimesters.

Results: In the first group, 8 pregnancies had successful outcome compared to 11 on the second group.

In the first group mean HbA1c was 53 mmol/l, first trimester, 45, second trimester & 44 mmol/mol, third trimester. Change from 57 to 51 at the upper bound, 49 to 37 at the lower bound.

In the second group mean HbA1c was 50 mmol/l first trimester & 47 mmol/mol second & third trimesters. Change from 54 to 53 at the upper bound, 46 to 41 at the lower bound.

In first group; 4 (50%) patients progressed to STDR compared to 3 (30%) the second group, while 5 (62%) patients progressed to maculopathy compared to 4 (40%) the second group.

Any DR progression; 7 (87.5%) patients first group, compared to 7 (70%) the second group.

ACR values were normal in all patients in both groups.

Conclusions: When CSII was started during pregnancy, HbA1c values started higher & ended lower compared to pregnant women who had CSII before pregnancy. Both groups had DR progression, but progression was worde in the patients who started pump during pregnancy.

CSII appears to provide a safe method of glycaemic control in pregnant women with Type 1 diabetes.

Starting CSII before pregnancy would allow enough time to acclimatise to the insulin pump suggesting clear importance of preconception care in women with Type 1 DM.

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ESTIMATED GLOMERULAR FILTRATION RATE IS THE DETERMINANT OF EXTENDED BOLUS INSULIN DURATION TIME OF INSULIN PUMP

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Backgrounds: Extended insulin bolus time of insulin pump (square-wave bolus insulin) might be a beneficial option for patients who have postprandial hypoglycemia followed by hyperglycemia. It has not been investigated the clinical characteristics of the patients who use square-wave bolus insulin. The objective is to investigate the clinical characteristics and extended bolus insulin time of the patients who use square-wave bolus insulin.

Methods: Fifty-three patients with type 1 diabetes, who use insulin pump, were investigated during 2–3 weeks of hospitalization. Each meal omission was done to confirm basal insulin rate. The amount and duration time of each bolus insulin was adjusted to set blood glucose to 100 and 150 mg/dL before and 2 hours after meal, respectively. Insulin pump setting and clinical characteristics, which contributed the average duration time of bolus insulin was investigated.

Results: Total daily insulin dose (TDD) ($p < 0.001$), the percent of daily basal insulin rate to TDD ($p < 0.05$), average carbohydrate-to-insulin ratio ($p < 0.001$), retinopathy score ($p < 0.01$), and estimated glomerular filtration rate (eGFR) ($p < 0.001$) were significantly correlated with average bolus insulin duration time. According to multiple regression analysis, eGFR ($F = 10.10$) was the independent determinant for bolus insulin duration time.

Conclusions: Extended bolus insulin time should be considered in patients who have kidney dysfunction.

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LESSONS LEARNED FROM SUCCESSFUL RECRUITMENT TO A PUMP/CGM TRIAL

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[7]Canada

Background: Recruitment failures and delays threaten the success and resources of clinical trials, with more than 80% of trials failing to reach recruitment targets.

Objective: To determine whether lessons learned from a pilot study improved recruitment in the multicenter trial.

Method: Pilot study recruitment rates and strategies were compared to those of the multicenter CGM TIME Trial.

Results: The pilot study and TIME Trial had the same eligibility criteria and design other than longer trial duration for the TIME Trial (12 vs. 4 months). The pilot study required 24 months to recruit 20 patients through 2 sites, whereas the TIME Trial exceeded its required sample size, recruiting 144 patients through 5 sites within the 21 months. In the pilot study, 25% of patients met eligibility criteria vs. 43% in the TIME Trial. 20/41 (48.7%) patients eligible for the pilot study consented to participation vs. 144/152 (94.7%) for the TIME Trial. 25% of pilot study subjects terminated the study prematurely vs. 5.6% of the TIME Trial. The TIME Trial incorporated a research recruitment tool, modeled after patient decision aids, comparing the pros and cons of participating vs. not participating in the Trial which was provided to eligible families along with the consent

form in 3/5 sites. Six of 8 refusals to the TIME Trial and 5/8 early terminations came from the 2 sites not using the recruitment tool.

Conclusion: Use of a research recruitment decision tool which addresses family preferences and perceptions of trial participation may improve trial recruitment and retention.

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HEALTH RISKS OF YOUNG ADULT TRAVELERS WITH TYPE 1 DIABETES

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Objective: International travel has become a popular mode of travel among young adults. We evaluated the rate and characteristics of travel-associated health risks among young adults with type 1 diabetes mellitus (T1DM) compared to healthy same-aged individuals.

Methods: A retrospective study of 47 young adults with T1DM and 48 without (controls). Structured questionnaires accessed information regarding 154 international trips that occurred during the preceding 5 years and that lasted 7 days and longer.

Results: Mean ± SD ages of the diabetic and control groups were 26.6 ± 5.0 and 26.9 ± 2.6 years respectively. Mean trip durations were 80.0 (range 7.0–390.0) and 87.6 days (range 7.0–395.0) respectively. The number of trips per person was 1.5 ± 0.6 and 1.7 ± 0.8, and the proportion of trips to developing countries 64% and 61%, respectively. There was no difference in travel-related diseases that required medical consultation between the groups (11% vs. 15% for all trips, $p = 0.25$). No patient sought medical attention due to acute diabetes complications. Prior to 71% of the trips to developing countries, respondents with diabetes consulted their diabetes physician; Prior to 26% of the trips they switched from an insulin pump to injections; during 41% they increased glucose monitoring; and for the period of 11% they defined their metabolic control as poor. Mean reported HbA1c levels before and after trips were 7.65 ± 1.45% and 7.81 ± 1.23 respectively ($p = 0.42$, paired T test).

Conclusions: Young adults with diabetes did not report more travel-related diseases than did healthy individuals. Glycemic regulation during the trip was manageable, without severe consequences.

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CSII AND SAP VALUABLE TOOLS IN THE TREATMENT OF DIABETES; A SWEDISH HEALTH TECHNOLOGY ASSESMENT

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Continuous subcutaneous insulin infusion (CSII) is used by approximately 20% of adults and 50% of children with Type 1 diabetes in Sweden.

This report aims to present a systematic review to establish available evidence on effects of CSII and SAP (sensor-augmented pump) in adults (A), Children (C) and Pregnant women (P) compared to MDI (multiple daily injections) with mealtime insulin analogs and SMBG (self-monitored blood glucose).

Methods: The literature search included PubMed, Cochrane Library, Cinahl and PsychINFO until November 2012. Two reviewers independently assessed each included study for quality by using the SBU checklists. The quality of evidence was rated by using the GRADE system.

Results: Of 1130 identified abstracts, 11 studies on CSII were included for quality assessment; 8 had low quality (5C + 3P), 2 moderate (1C + 1P) and 1 high (C). On SAP, 10 studies were included; 3 had low quality (1C + 2A), 6 moderate (2C + 4A) and 1 high (C). For adults, 1 systematic review on CSII of high quality was included.

There was a lack of high quality research in both areas. Short-term HbA_1 was slightly improved by CSII, more so by SAP. Patients with SAP reported higher treatment satisfaction. Limited information was available on the frequency of severe hypoglycemia and ketoacidosis. Calculations of intervention costs demonstrated an increased cost of 1189 EUR for CSII and 3026 EUR for SAP.

Conclusion: Compared with MDI, CSII and SAP demonstrate short-term benefits including a reduced Hb1c level, which if sustained will reduce the risk of long-term diabetes complications.

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EVALUATION OF PATIENT ACCEPTANCE OF THE CELLNOVO INSULIN INFUSION PUMP

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Introduction: 'Patch pumps' have a pump controller which communicates with an infusion component attached to the skin directly instead of via a catheter. The Cellnovo System is a CE marked insulin delivery system, comprising of mobile connected Handset, Pump and online web-based Management System.

Aim: This was a single-site pilot study designed for investigation of the acceptance of end-users' of the study devices.

Methods: Subjects (n = 3) aged >18 years with Type 1 diabetes and already on insulin pump therapy for at least 12 months and compliant with their therapy were recruited. After a screening visit, subjects stayed within a clinical research facility over a period of 3 (24 h) days for training and use of the Cellnovo System. Following this they used the system at home for 7 days. At the end of the study visit, subjects returned to complete a questionnaire and return to their previous insulin pump.

Results: All subjects successfully completed the study. Subjects were successfully trained to use the pumps during the 3 in-patient days and managed with minimal support during the 7 days at home. Insulin requirements were reduced in two of the subjects and in the third subjects the rates were adjusted more appropriately throughout the day. User feedback recorded by questionnaire was very positive for all subjects. There were no adverse events that resulted in professional medical intervention.

Discussion: User feedback was very positive and all three subjects expressed a preference to continue using the Cellnovo System in preference to their previous pumps.

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THE ASSOCIATION BETWEEN THE FREQUENCY OF SMBG ASSESSED BY DATA MANAGEMENT SOFTWARE AND THE GLYCAEMIC CONTROL IN T1DM PATIENTS

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We investigated the association between the frequency of self-monitoring of blood glucose (SMBG) and the glycaemic control in type 1 diabetes mellitus (T1DM) patients at NHO Kyoto Medical Center.

Method: We recruited 148 adult T1DM patients (48.5 ± 17.0 years old, male 43%, mean BMI 21.6 ± 2.6 kg/m2, mean diabetes duration 12.6 ± 11.3 years, mean HbA1c 8.1 ± 1.4%, continuous subcutaneous insulin infusion [CSII] 28%), of whom SMBG records were uploaded to MEQNET™ SMBG Viewer software (Arkray, Inc., Kyoto, Japan). Subjects younger than 20 years old were excluded. The mean SMBG frequency for 30 days was calculated from uploaded data, and the HbA1c was compared between those ≥3.5 times/day vs. <3.5 times/day using Fisher's exact test. SMBG frequency, mean blood glucose (BG) and HbA1c were examined by Pearson correlation coefficient analysis.

Results: The mean SMBG frequency was 3.5 ± 1.7 times/day (range: 0.0–7.1 times/day). The mean HbA1c was significantly lower in those ≥3.5 times/day compared to <3.5 times/day (7.7% vs. 8.4%, $P = 0.006$). Subjects on CSII demonstrated similar results (7.3% vs. 8.2%, $P = 0.002$), however subjects on multiple daily injections (MDI) did not (8.0% vs. 8.4%, $P = 0.172$). There was significant negative correlation between mean SMBG frequency and mean BG ($r = -0.222$, $P = 0.007$), and between mean SMBG frequency and HbA1c ($r = -0.219$, $P = 0.008$).

Conclusion: In this cohort, the higher SMBG frequency was associated with better glycaemic control.

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DIFFERENT TYPES OF BOLUSES IN CSII THERAPY FROM PATIENTS' AND PHYSICIANS' POINTS OF VIEW

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Background: Using variable boluses can be a great opportunity for better postprandial replacement and can make control of diabetes tighter. However precise recommendations about situations when patient should use variable boluses still not exist.

Subjects and methods: We gave for 30 endocrinologists (mean age 37 ± 9 years) and for 30 CSII patients with type 1 diabetes (T1DM) (mean age 27 ± 11 years, mean diabetes duration 12 ± 6 years, CSII duration 3 ± 1,5 years) questionnaire about situations when variable boluses should be used. It was an open test with several answer options of using variable boluses and also responders could propose their answers.

Results: 100% of patients and 90% of doctors answered that using of variable boluses influenced on glycaemic control. Using variable boluses helps to manage diabetes better and makes feel more confident about not getting high glucose blood level (70% vs. 60%), allows to make diet more wide. 20% of patients and 10% of doctors answered that they still don't understand when variable boluses should be used. Furthermore younger doctors revealed more knowledge about using insulin pump. Among patients whose with close to target HbA1c level (<7,0%) gave more full answers and showed more optimistic attitude to variable boluses.

Conclusions: Our results show that there is still no clear understanding of the variable boluses using among patients and doctors. Repeated theoretical and practical educational courses about prandial replacement in CSII therapy is essence not only for patients but also for doctors.

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COPING STYLES AND DIABETES OUTCOME IN PATIENTS ON CONTINUOUS SUBCUTANEOUS INSULIN INFUSION THERAPY

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Introduction: Coping strategies are key components in the management of chronic diseases like diabetes. The way that patients cope in several demanding treatment situations severely influenciates their psychological balance and therefore could affect quality of life outcomes.

Aims: To analyse the differences in coping styles and other psychological aspects in diabetic patients on Continuous Subcutaneous Insulin Infusion treatment (CSII).

Patients: We gathered a sample of 21 type 1 diabetic subjects, 66.7% females, with a mean age of 30.4 ± 7.1 (18–46) years.

Methods: We applied the following instruments 9 months after the CSII placement: A general biographical questionnaire, the Diabetes Health Profile (DHP), the Problem Areas in Diabetes Scale (PAIDS), and the Problem Solving Inventory (PSI).

Results: We noticed that the coping styles more often used by these patients were: problem confrontation and active resolution followed by strategy planification. The least used were: internal/external agressivity and emotion control strategies. We found a correlation between the total health profile and problem areas in diabetes ($r = 0.84$; $p \leq 0.001$). We also found that people who don't let problems interfere with daily activities have less psychological distress ($r = -0.56$; $p = 0.01$).

Conclusion: In this sample, we found that patients adopt confrontation strategies more often, in order to solve their diabetes related problems. On the other hand, patients demonstrate less emotional control skills that studies shown to be a major factor in diabetes outcome. These results attest that it is important to investigate coping styles to be able to help the diabetes outcome in patients on CSII.

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SUCCESSFUL DESENSITIZATION IN TYPE 2 DIABETIC PATIENT WITH AN INSULIN ALLERGY WITH GLARGINE AND INSULIN PUMP: A CASE REPORT

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Introduction: Insulin allergy are rare but they can occur occur in patients starting insulin therapy. There are different insulin desensitization protocols where insulin is diluted and given to the patient in small doses in a period of couple of days. We are presenting case report in type 2 diabetic patient with insulin allergy, where desensitization was performed using insulin pump (Medtronic Minimed Veo) with glargine.

Case presentation: A 54-year-old man with 8 year history of type 2 diabetes, BMI 27.8 kg/m2 was used metformin (2 gr) and glymepiride (4 gr). His average Hba1c was 9.2 ± 0.3% in the last year. In a period of 1 month, different insulin preparation (NPH insulin, glargine, detemir and biphasic insulin aspart/NPH) were used, but patient developed pruritic plaques (3–8 cm) at the injection sites that persisted for several days. Allergologic testing revealed positive reactions against every insulin preparation, with smaller reaction on insulin glargine. Insulin desensitization with glargine was performed using insulin pump (Medtronic Minimed Veo), where insulin was given as basal dose of 4 hour every day in the next 2 weeks, starting with daily dose of 0.1 units and slight increase up to 16 units at day 14th. During the two weeks, there was no reaction at the infusion site. After 2 weeks, the patient continued with insulin glargine using insulin pen (Sanofi Solostar) with titration algorithm (2–4 units increase) for fasting glycaemia of 5.6 mmol. Hba1c decreased to 6.2% in the next 6 months with insulin dose 36 units of glargine and 2 gr of metformin.

Conclusion: As reported in this case, desensitization for long acting insulin (such as glargine) can be successfully performed using insulin pump and may present an easy form of therapy that is successful within a few days.

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PILOT STUDY FOR THE ASSESSMENT OF TOLERABILITY OF PROLONGED CATHETER USE IN INSULIN PUMP THERAPY

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Use of insulin infusion sets in insulin pump therapy is recommended for two to three days. However, many patients use the catheters even longer for economical reasons risking adverse events and skin reactions. This study was performed to investigate the tolerability of regular catheter use (two days) with extended use (four days) in a real world setting. Here we report on an interim analysis which was performed with 12 patients (4 men, 8 women, age 47 ± 11 years, BMI: 27.4 ± 3.2 kg/m^2), who participated in a prospective open randomized cross-over study with 2 × 3 month observation periods using the infusion sets for 2 days and 4 days, respectively. The number of treatment related adverse events was 189 with 2 day use vs. 201 with 4 day use (n.s.). The number of catheter related events was 42 with 2 day use vs. 130 with 4 day use ($p < 0.001$). The combination of catheter related and treatment related was significantly favorizing 2 day use (231 vs. 331, $p < 0.001$). Several patients reported a major increase in infusion site problems when extending the usage time to 4 days. Glycemic variabiity was also less favorable with extended use (e.g. hypoglycemic events: 238 vs. 341 events, $p < 0.001$). In conclusion, using the infusion sets for a longer than recommended usage period of 2 days resulted in a clinically relevant increase in treatment-related tolerability problems and impaired glycemic control. Patients should be encourage to not use insulin pump infusion sets for a longer then recommended time period.

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CARBOHYDRATE COUNTING AND INSULIN PUMP THERAPY HELP CHILDREN WITH TYPE 1 DIABETES TO BETTER COPE WITH DIETARY REGIMEN

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To investigate the effect of carbohydrate counting (carbsC) on metabolic control and dietary habits in type 1 diabetes children treated using multiple daily injections (MDI) or continuous subcutaneous insulin infusion (CSII). We enrolled 50 children (mean age 9.2 ± 4.3 yrs) with type 1 diabetes for more than 6 months, using MDI (n = 31) or CSII (n = 19). Patients using MDI were trained in carbsC (n = 8) or not (n = 23), while CSII patients were all trained in carbsC. Each subject filled a 7-day dietary recall, subsequently evaluated by a skilled registered dietitian. BMI, HbA1c, insulin requirement, self-monitoring blood glucose/day were recorded in each patient. No difference has been observed in BMI, HbA1c, insulin requirement and number of glucose testing in patients using carbsC vs patients not using it. However, number of insulin boluses in carbsC patients was higher than in patients not using carbsC ($p < 0.01$). Moreover, stratifying carbsC users according therapy, Hba1c was significantly higher in MDI than in CSII patients ($p < 0.05$), while number of boluses was significantly less ($p < 0.01$). Patients not using carbsC were more likely to be less flexible regarding dietary regimen (OR 2.333, IC 0.721–7.547) than patients using it, and were more worried when they had to eat outside the home (OR 2.619, IC 0.799–8.588).

CarbsC increases flexibility in dietary regimen, improving dietary habits and CSII seems to favor a even better metabolic control.

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THE IMPACT OF INSULIN INFUSION RATE VARIABILITY ON GLYCAEMIC VARIABILITY IN ADULTS WITH TYPE 1 DIABETES

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Objective: Improving glycaemic variability (GV) may reduce long-term diabetes related complications and quality of life. Continuous subcutaneous insulin infusion (CSII) and long-acting basal analogue insulins improve HbA1c and reduce the frequency of hypoglycaemia. CSII does this with variable basal rates and analogues by providing stable basal insulin concentrations. We aimed to assess the impact variable insulin infusion rates have on GV, and in particular hypoglycaemia and risk of hypoglycaemia.

Method: Subjects wore a Medtronic iPro2 retrospective continuous glucose monitor (CGM) for 5 days. GV measures including LBGI, LI, ADDR and % time in hypoglycaemia were calculated using the EasyGV version 9.0 software. We then performed a linear regression analysis to evaluate the relationship between GV and insulin infusion rate variability (measured as standard deviation of insulin/hour).

Results: 20 adult subjects with type 1 diabetes (T1DM) were included in the study (55% male, mean (SD) age 44 (10) years, duration of diabetes 22 (12) years, duration of CSII 3.4 (4) years, HbA1c 7.4 (0.7) %, body mass index 25 (4) kg/m^2). There were no significant associations between insulin infusion rate variability and GV or hypoglycaemia: LBGI ($R^2 = 0.02$, $p = 0.55$), LI ($R^2 = 0.06$, $p = 0.32$), ADDR ($R^2 = 0.03$, $p = 0.45$) and % time in hypoglycaemia ($R^2 = 0.04$, $p = 0.41$).

Conclusion: The results suggest, surprisingly, that insulin infusion rate variability has no impact on hypoglycaemia risk or % time spent in hypoglycaemia in adults with T1DM on pump therapy. Further work is needed to understand how CSII and multiple daily injections affect glycaemic quality.

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GLYCAEMIC VARIABILITY AND QUALITY OF LIFE IN SUBJECTS WITH TYPE 1 DIABETES MELLITUS – IS THERE A CORRELATION?

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Objective: Hypo- and hyperglycaemic excursions have been associated with oxidative stress and vascular risk. Glycaemic variability has been associated with reduced quality of life in subjects with type 2 diabetes. We aimed to evaluate if there is a correlation between glycaemic variability and quality of life in subjects with type 1 diabetes (T1DM) on insulin pump therapy.

Method: Subjects wore a Medtronic iPro2 retrospective continuous glucose monitor (CGM) for 5 days and completed the diabetes quality of life questionnaire (DQOL) and diabetes treatment satisfaction questionnaire (DTSQ). Glycaemic variability measures (SD, CONGA, LI, JINDEX, LBGI, HBGI, GRADE, MODD, MAGE, ADDR, MVALUE, MAG) were calculated using the EasyGV version 9.0 software. We then calculated Pearson's correlation coefficient and linear regression to assess whether there was a correlation between glycaemic variability, diabetes treatment satisfaction and quality of life.

Results: 20 adult subjects with T1DM (55% male, mean (SD) age 44 (10) years, duration of diabetes 22 (12) years, duration of insulin pump therapy 3.4 (4) years, HbA1c 7.4 (0.7) %, body mass index 25 (4) kg/m^2) participated in the study. None of the glycaemic variability metrics showed significant correlation with diabetes treatment satisfaction or quality of life outcome measures (p-values > 0.05).

Conclusion: Contrary to findings in type 2 diabetes, our study suggests that increased glycaemic variability does not impact overall or subscale quality of life in adults with T1DM. A larger scale study is needed to validate these findings.

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IN TYPE 1 DIABETES INSULIN PUMP TREATMENT IS ASSOCIATED WITH REDUCED ARTERIAL STIFFNESS

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Aim: Insulin pump (CSII) treatment is associated with reduced glucose variability and in small improvements in glycaemic control. This might reduce development of vascular complications. We investigated the relationship between arterial stiffness, evaluated by pulse wave velocity (PWV), and CSII treatment, and examined if this association was dependent of glucose control.

Methods: Cross-sectional study, from 2009–2011, including 639 patients with type 1 diabetes. PWV measurements (SphygmoCor, AtCorMedical, Australia) were available in 58 patients with CSII (35 with albuminuria) and 542 (274 with albuminuria) treated with multiple daily injections (MDI). ANCOVA compared groups and adjusted linear regression examined the association between PWV, HbA_{1c} and treatment groups.

Results: CSII *vs.* MDI treated patients were 48% *vs.* 57% men, 51 ± 11 *vs.* 54 ± 13 years old, 33 ± 11 *vs.* 32 ± 16 years diabetes duration and HbA_{1c} 62 ± 10 *vs.* 64 ± 13 mmol/mol ($p > 0.08$ for all). PWV was lower in CSII *vs.* MDI (9.3 ± 2.8 *vs.* 10.4 ± 3.4 m/s; $p = 0.02$). This difference remained significant ($p = 0.003$) after adjustment for gender, diabetes duration, eGFR, urine albumin excretion rate, HbA_{1c}, total-cholesterol, smoking, mean arterial pressure, heart rate and BMI.

In patients with albuminuria, PWV was lower in CSII *vs.* MDI (9.3 ± 2.5 *vs.* 11.3 ± 3.4 m/s; adjusted $p = 0.002$).

In adjusted regression analysis, treatment with CSII was significantly ($p = 0.003$) associated with lower PWV, while HbA_{1c} was not ($p = 0.95$).

Conclusion: CSII treatment was independently associated with reduced arterial stiffness, while HbA_{1c} was not. Although glucose variability was not assessed, our results suggest that glucose variability and not HbA_{1c}-level affects arterial stiffness. This needs confirmation in randomised prospective studies.

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A RETROSPECTIVE COMPARISON: PREGNANCY OUTCOME AND GLYCEMIC CONTROL WITH CSII OR MDI TREATMENT

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Aim: Aim of present study was to assess glycemic control and maternal-fetal outcome in pregnant type 1 diabetic patient treated with continuous subcutaneous insulin infusion (CSII) or multiple daily injections of insulin (MDI).

Patients and Methods: A retrospective observational study included thirty-four pregnant type 1 diabetic patients. Patients were divided into two groups, CSII treated group (n = 24) and MDI treated group (n = 35). The HbA1c level and maternal-fetal outcome were evaluated in both the treatment group. Outcome parameters such as glycemic control (HbA1c), hypoglycemic events, time and mode of delivery and labour results (Abortion, premature labour, perinatal mortality, neonatal weight, Apgar score, neonatal hypoglycaemia, presence of congenital abnormalities) were analyzed.

Results: Pregnancy outcome and glycemic control in pregnant type 1 diabetic patients treated with CSII and MDI were evaluated and compared. Two groups were compared for their epidemiological parameters, although patients on CSII treatment had longer duration of diabetes compared to MDI treated group. Reduction in HbA1c level was higher in CSII treated patients at first (CSII: 1.2% Vs MDI: 0.58%), second (CSII: 1.81% Vs MDI: 0.99%) and third trimester (CSII: 1.82% Vs MDI: 1.31%) of pregnancy compared to MDI treated patients. Duration of pregnancy and new born baby weight were founded similar in both group. Moreover, the rate of abortion, preterm labour, caesarean section and hypoglycemia in new born were founded less in CSII treated group compared to MDI treated group and apgar score was significantly ($p < 0.05$) higher in CSII treated group compared to MDI treated group.

Conclusion: Results of present study revealed that the CSII gives better glycemic control and pregnancy outcome in pregnant type 1 diabetic patients compared to MDI treatment. CSII also decreases the daily insulin requirement compared MDI.

Keywords: Abortion, CSII, HbA1c, MDI, Type 1 Diabetes

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CORRECTION BOLUS FOR PREPRANDIAL HYPERGLYCEMIA IN CHILDREN WITH TYPE 1 DIABETES USING INSULIN PUMP THERAPY: TO SEPARATE OR NOT TO SEPARATE?

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Objective: Type 1 diabetes (T1D) is often characterized by high glycemic variability. When it happens before meals, especially for a hyperglycaemic value, may be challenging to inject the right insulin dose at the right time to gain postprandial euglycaemia. The aim of the present study was to evaluate the best correction strategy for each value > 160 mg/dl in children and adolescents with T1D, using insulin pump therapy (CSII).

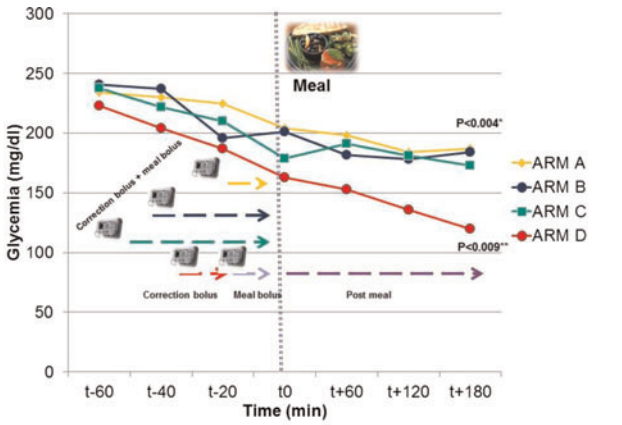

Figure 1 – Glycemic values after correction bolus given together meal bolus 20 min before (arm A), 40 min before (arm B), 60 min before meal (arm C), or given separated as correction bolus and meal bolus (arm D). * among arms by ANOVA; ** intra arm D by paired *t*-test

Methods: One-hundred-sixty-three young patients (87 males), aged 13.7 ± 3.4 years, with T1D since 9.1 ± 4.8 years (BMI 21.6 ± 4.9 kg/m2, insulin requirement 0.84 ± 0.24 U/kg/day; HbA1c 7.6 ± 1.6%), using CSII therapy, were randomly allocated to one or more of the following experimental arms: simultaneous injection of correction and pre-prandial bolus given 20 min (arm A), 40 min (arm B), or 60 min (arm C) before meal; arm D provided a correction bolus injected 20 min before a pre-prandial bolus, given 15 min before meal.

Results: Results are summarized in Figure 1. The best strategy seems to be when correction bolus and pre-prandial bolus are injected separately. Arm D (n = 83): −60 min: 223 ± 32 mg/dl, −40 min: 204 ± 44 mg/dl, −20 min: 187 ± 32 mg/dl, 0 min: 163 ± 43 mg/dl, +60 min: 153 ± 52 mg/dl, +120 min: 136 ± 47 mg/dl, +180 min: 120 ± 40 mg/dl ($p = 0.004$ among arms by ANOVA; $p = 0.009$ intra arm D by paired *t*-test).

Conclusions: To separate the correction bolus, injecting it 20 min before the pre-prandial bolus, seems the best strategy to quickly recover from a hyperglycaemia and to maintain a postprandial euglycaemic state in children with T1D using CSII.

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NEONATAL HYPOGLYCEMIA IN SIBLINGS OF WOMEN WITH TYPE 1 DIABETES ON CONTINUOUS SUBCUTANEOUS INSULIN INFUSION VERSUS MULTIPLE DAILY INJECTION THERAPY

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Introduction: An uneventful pregnancy with an optimal outcome in women with type I diabetes (DM) is strictly dependent on tight glycemic control during pregnancy.

Objective: Two treatments, multiple daily insulin injections (MDI) and continuous subcutaneous infusion insulin therapy (CSII) were implemented in women with type 1 DM during pregnancy with the aim to compare glycemic control.

Material and Methods: Twenty-six (26) women with type 1 DM, eleven (11) on MDI and fifteen (15) on CSII were studied. Body Mass Index (BMI), HbA1c before pregnancy and before delivery, rate and severity of hypoglycemia, duration of pregnancy, newborn birth weight and neonatal hypoglycemia were recorded.

Results: For women on MDI, mean age was 35 ± 4.8 years, BMI 23.75 ± 2.34 before pregnancy and 27.08 ± 2.1 before delivery ($p = 0.005$). For women on CSII, mean age was 32 ± 4.84 years, BMI 23.78 ± 2.85 and 26.12 ± 3.07 before pregnancy and before delivery respectively ($p = 0.001$). There was also no difference regarding the duration of pregnancy, the weight of the newborn and the incidence of hypoglycemia of the mother between the two study groups. A higher rate of neonatal hypoglycemia was observed in the MDI group compared to the CSII group; the difference was statistically significant ($p = 0.02$).

Conclusion: CSII seems to be more effective than MDI in achieving a lower incidence of neonatal hypoglycemia although there was no statistically significant difference between the two study groups regarding glycemic control during the pregnancy, the duration of the pregnancy and the weight of the newborn.

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BODY WEIGHT CHANGES DURING THE CONTINUOUS SUBCUTANEOUS INSULIN INFUSION (CSII) THERAPY IN ADULT TYPE 1 DIABETES PATIENTS

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Clinical observation suggests that CSII therapy in adult type 1 diabetes patients leads to a significant weight loss in some of them. We conducted an observational study aiming at assessing body weight changes during first 6 months of CSII therapy at our centre. Non-pregnant subjects with at least 1 year duration of diabetes, normal thyroid function, not participating in any weight loss programmes were enrolled into the study. The group comprised 27 subjects (21 women, mean age 27.4 ± 9.5 years, diabetes duration 9.5 ± 8.2 years, CSII duration 3.1 ± 3.4 years, body weight 71.1 ± 13.9 kg, BMI 24.6 ± 3.7 kg/m^2, HbA_{1c} 8.3 ± 1.7%, blood glucose 161 ± 68 mg/dl), who were followed for 6 months. The patients were seen at least every 6 weeks; all necessary adjustments to basal rate, normal and dual-wave bolus instructions were made during this period. After the follow-up 14 subjects (52%) lost (mean ± SD) 2.6 ± 1.7 kg (3.7 ± 2.4%) (weight reduction group, WR), whilst the others gained 0.7 ± 1.0 kg ($p < 0.01$) (comparator group, C). WR patients were older (30.4 ± 7.6 vs. 24.2 ± 5.4 years, $p < 0.05$) and had longer duration of diabetes (5.4 ± 9.7 vs. 2.8 ± 3.2 years, $p < 0.01$). No change in hypoglycaemia rates was noted in any of the subgroups. No major differences in CSII parameters were found between the groups, however WR subjects showed tendency of decreasing insulin basal rate and increasing use of prandial boluses. Detailed changes in metabolic and CSII parameters are presented in the table. In conclusion, CSII therapy may lead to body weight reduction in adult type 1 diabetes subjects, particularly those with longer diabetes duration.

	WR		C	
	Baseline	After 6 months	Baseline	After 6 months
Body Weight (kg)	69.5±13.6	66.9±12.2*	72.88±14.6	73.5±14.5**
Body Mass Index (kg/m²)	24.3±3.1	23.4±2.7*	24.9±4.5	25.1±4.5**
HbA1c (%)	7.86±1.78	7.74±2.54	8.4±1.5	8±1.4
Time of Wearing the Infusion Set (days)	3.9±1.6	3.9±1.4	4±1.1	3.8±1.7
Blood Glucose (mg/dl)	151±37	157±73	174±93	152±42
SD Blood Glucose (mg/dl)	58±27	67±42	73±36	66±32
Blood Glucose Readings/day	4.2±3	4.9±3.5	3.6±2	4.7±2.1**
Total Daily Insulin (IU)	37±14	39±14	37±14	39±21
Total Daily Insulin/Body Weight (IU/kg)	0.53±0.16	0.57±0.16	0.51±0.18	0.53±0.25
Daily Basal (%)	48±11	47±11	44±9	45±12
Bolus Events/day	5.9±2.2	5.5±2.6	5.7±1.3	4.9±1.7
Manual Boluses (MB)/day	3.1±3.5	3.4±4.6	3.2±3.2	2.1±2.2
Bolus Wizard (BW) Events/day	2.9±2.2	3±2.5	2.4±1.9	2.8±2.4
% BW with Food	86±16	84±25	84±24	82±21
% BW with Correction	56±24	63±31	54±29	70±27
% BW Overriden	56±25	55±20	48±31	44±32
Dual-Wave Bolus (DWB)/day	1,66±0,98	1,56±0,96	2,1±1	2±1
DWB as % of all Daily Boluses (MB+BW) (%)	30±16	28±14	42±23	47±28
Daily Carbs Intake (g)	216±120	248±106	251±137	219±144

Data are means±SD *p<0.001 **p<0.05

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AN OBSERVATIONAL STUDY OF PEDIATRIC INSULIN PUMP THERAPY IN KAZAKHSTAN: PRELIMINARY RESULTS

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Background: Large-scale introduction of advanced diabetes technologies to improve glycemic control may be facilitated by partnerships between national health services and industry. Such a partnership was used to introduce insulin pump therapy (CSII) to children in Kazakhstan.

Methods: Pediatric endocrinologists from all 17 regions of Kazakhstan were identified and trained by experts in CSII from Medtronic Diabetes. Children age 5–15 with type 1 diabetes and their families received pumps and training beginning in February 2012. Baseline A1C measurements were obtained. Clinic visits at 3-month intervals included A1C measurements, pump data uploads to CareLink, review of CareLink reports, and therapy adjustments as needed.

Results: As of 8/19/2013, 635 children had enrolled with per-site enrollments ranging from 11 to 135. Most children (N = 442, 69.6%) had baseline A1C values ≥ 7.5. In a subgroup of 313 children who had completed baseline and 12-month visits, the A1C range at 12 months was 4.3% to 14.0%, and for those with baseline A1C ≥ 7.5% (N = 221, 70.6%), mean A1C decreased by 0.85 ± 3.07%. Mean daily blood glucose values (averaged over 4 weeks) for this group fell from 12.28 ± 3.99 to 10.45 ± 2.47 mmol/L, a mean 1.83 ± 4.52 (14.9%) mmol/L decrease. A report from the Kazakhstan Ministry of Health documented decreases in both severe hypoglycemic events and DKA during calendar year 2012.

Conclusions: Children adopting CSII in the context of government-industry collaborations, particularly those with baseline A1C ≥ 7.5%, may realize significant glycemic benefits. The Kazakhstan/Medtronic collaboration provides a model for other initiatives that require rapid deployment and/or massive enrollment for introduction of CSII.

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CONTINUES GLUCOSE MONITORING SYSTEM AS A TOOL FOR MANAGEMENT IN TYPE 2 DIABETES ON BIPHASIC INSULIN DURING RAMADAN: CASE REPORT

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Introduction: Fasting during the holy month of Ramadan is an important spiritual practice in Muslims. The Quran states that groups of people who do not have to fast like children, pregnant or breastfeeding women. Diabetic patients using insulin have to discuss with their health care professionals about insulin titration and possibility risks.

Case presentation: A 57-year-old woman with 5 year history of type 2 diabetes, BMI 28.4 kg/m2 was used biphasic insulin analogue with Hba1c 7.1%. Her insulin dose was 38 units in the morning and 30 units at evening (0.9 U/kg). During the first week of Ramadan, blinded continuous glucose monitoring (CGM) for 7 days was performed with Medtronic Ipro2. CGM revealed hypoglycemic episodes during the day and hyperglycemic periods during the nights. According the CGM, insulin was given as 20 units in the morning and 34 units at evening (0.72 U/kg). Another blinded CGM was performed which confirmed the switch of the morning and evening dose with satisfactory glucose profile.

Conclusion: CGM can be used as a tool for management of insulin regime in type 2 diabetic patients during Ramadan to decrease potential glucose variations.

Key words: Ramadan, CGM, glucose variations, switching dose

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ACCURACY, PRECISION, AND USER PERFORMANCE EVALUATION OF THE CONTOUR® NEXT LINK 2.4 BLOOD GLUCOSE MONITORING SYSTEM

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Objective: Two studies were conducted, in the laboratory and in the clinical setting, to evaluate the accuracy of the CONTOUR® NEXT LINK 2.4 blood glucose monitoring system (BGMS).

Methods: In the laboratory study, fingerstick samples from 100 subjects were tested in duplicate using 3 test strip lots and assessed per ISO 15197:2003 section 7 and ISO 15197:2013 section 6.3 accuracy criteria. In the clinical study, 219 subjects with diabetes enrolled at 2 clinical sites. Subjects naive to the BGMS tested capillary blood from their fingertips and palms; BGMS glucose results were compared with YSI reference method. Subjects in the clinical setting completed questionnaires on ease of use and diabetes management.

Results: In the laboratory study, 100% of results met ISO 15197:2003 section 7 and ISO 15197:2013 section 6.3 accuracy criteria. Also, 99% (594/600) of results were within ±10 mg/dL (0.6 mmol/L) or ± 10% of the YSI reference method. Regression analysis demonstrated a high degree of agreement between BGMS and reference ($R^2 = 0.9926$). In the section 8 clinical study, 100% of subject fingerstick and 99.1% of palm results met ISO 15197:2003 accuracy criteria; 98.6% of subject fingerstick and 97.2% of palm results met ISO 15197:2013 section 8 accuracy criteria. Questionnaire results showed most subjects found the BGMS easy to use.

Conclusion: The CONTOUR® NEXT LINK 2.4 BGMS, which wirelessly communicates with Medtronic devices, exceeded ISO 15197:2003 sections 7 and 8 and ISO 15197:2013 sections 6.3 and 8 accuracy criteria in analytical accuracy evaluations and in the hands of untrained lay users.

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COMPARATIVE EVALUATION OF CONTOUR NEXT USB BLOOD GLUCOSE MONITORING SYSTEM USING ISO 15197:2013 ACCURACY CRITERIA AND MARD

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Objectives: Study purpose was to test primarily the performance of a Bayer Blood Glucose meter (BGM) and secondly in comparison with two additional BGMs versus hexokinase method.

Method: Accuracies of Contour® NEXT USB (Bayer), FreeStyle InsuLinx® (Abbott), One Touch Verio IQ® (Lifescan) were evaluated with two test strip lots each. Left-over venous blood samples of 204 subjects were measured. Results were compared to Dimension EXL (Siemens) hexokinase method data to determine whether results are within either ±15 mg/dL of the corresponding Dimension result, when Dimension result < 100 mg/dL, or within ± 15% of corresponding Dimension result when it is ≥100 mg/dL.

Furthermore, Mean Absolute Relative Differences (MARD) from hexokinase reference results were compared for each of the three BGMs.

Parkes Error Grid and BGM precision were analyzed.

Results: Overall, 99,75% of CONTOUR® NEXT USB BGMS results met the more stringent ISO 15197:2013 accuracy criteria, compared with 97,55% of FreeStyle InsuLinx® results and 97,55% of OneTouch Verio IQ®results. ANOVA indicated that differences in MARD between meters were statistically significant. MARD (%): Contour NEXT USB (3,44%); Freestyle Insulinx (4,23%) and One-Touch Verio IQ (5,17%). For Contour NEXT USB all results were in Parkers Error Grid zone A and in zones A or B for the other BGMs.

Conclusion: Analyses showed that all three meters exceeded the more stringent ISO 15197: 2013 accuracy requirements, but Contour Next USB had a significantly lower MARD than either Freestyle Insulinx or One-Touch Verio IQ.

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COMPARISON OF CONTOUR NEXT STRIPS USED WITH THREE DIFFERENT BAYER BLOOD GLUCOSE METERS

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Introduction: In the recent years Bayer has developed three different blood glucose meters (BGM), Contour XT, Contour Next and Contour Next USB that uses the same strip, Contour NEXT, for glucose measurement. Each of these three BGM presents different characteristics and specifications and are intended to be used by different types of patients.

Objective: To evaluate BGM precision. To compare the results obtained with these three BGM and to determine if they are exchangeable. To determine if results obtained with the three BGM fulfil ISO 15197:2013 criteria.

Methods: 100 venous blood samples were measured with each of the three meters as well as by a Dimension EXL chemistry analyzer (Siemens) that uses hexokinase method for serum glucose measurement.

Results: Imprecision for the three meters, measured at three different glucose concentration levels, is below 2%. Comparison, using Passing-Bablok method, demonstrated that results are totally exchangeable between the three meters, since in all the linear equations 95% confidence interval always include 1 for the slope and 0 for the intercept. All three meters fulfil the ISO 15197:2013 criteria with percentage of measurements with accuracy compliance close to 100%.

Discussion: For each of the BGM, operating and technical specifications are different, making each of them more recommendable for certain types of situations and patients. Despite these differences, all the meters use the same strips and provide the same results, allowing doctors to choose the best BGM for each patient, situation and clinical condition without putting quality at risk.

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A CHIP-BASED NEAR INFRARED SENSOR FOR CONTINUOUS GLUCOSE MONITORING

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In this work we present the concept and *in vivo* results of a minimally invasive, chip-based near infrared (NIR) sensor, combined with microdialysis, for continuous glucose monitoring. The sensor principle is based on difference absorption spectroscopy in the 1st overtone band of the near infrared spectrum, using a multi-emitter near infrared LED at wavelengths of 1300, 1450 and 1550 nm. The LED's together with two InGaAs-Photodiodes are located on a single electronic board (non-disposable part) which is connected to a personal computer via Bluetooth. The disposable part consists of a chip containing the fluidic connections for microdialysis, two fluidic channels acting as optical transmission cells and total internally reflecting mirrors for in- and out-coupling of the LED light to the chip and to the detectors. The sensor is combined with an intravascular microdialysis to separate the glucose from the cells and proteins in the blood and operates without any chemical consumption.

In vivo measurements on 10 patients showed that the NIR-CGM sensor data reflects the blood reference values adequately, if a proper calibration and signal drift compensation is applied. The MARE (mean absolute relative error) value taken over all patient data is 13.8%. The best achieved MARE value is at 4.8%, whereas the worst is 25.8%, with a standard deviation of 5.5%.

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COMPARISON OF CROSS-CALIBRATED SENSORS AND STANDARD FINGERSTICK-CALIBRATED SENSORS: FEASIBILITY OF UNIVERSAL CALIBRATION

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Background: Subcutaneously inserted glucose monitoring systems require sensor specific calibration. Ideally, universal calibration allows for any calibration factor valid for one sensor to be valid for other sensors, without subject specific information. This analysis compares a hypothetical cross-calibration method to a standard fingerstick-calibration method.

Methods: A total of 33 subjects with diabetes were enrolled to wear four sensors simultaneously. Sensors from a lot with low *in vitro* sensitivity CV (=2.9%) were used in the study. A constant calibration factor is determined on three randomly selected sensors from the study data. The median is used to cross-calibrate the other sensors. To evaluate the potential variability introduced by the random cross-calibrator sensor selection, this virtual study is repeated 1000 times. Per-sensor MARD distribution of the cross-calibrated sensors is compared against the same sensors under standard fingerstick-calibration schedule of five fingersticks over the 5 day wear duration.

Results: Within the 1000 virtual studies, the mean of the per-sensor MARD in the cross-calibrated system averages at 13.6% with a standard deviation of 0.9%. The standard method achieves a similar 13.1% mean (of per-sensor MARD). The mean of the 90th percentile MARD in the cross calibration averages at 18.1%, with a standard deviation of 1.7%. The 90th percentile MARD in the standard method is 19.2%.

Conclusions: Mean and 90th percentile per-sensor MARD comparisons of cross-calibrated sensors against standard fingerstick-calibrated sensors, in subjects with diabetes using sensors with low *in vitro* sensitivity CV, suggest the feasibility of non-subject-specific universal calibration.

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OFFLINE CONTINUOUS GLUCOSE MONITORING: DOES IT MATTER?

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Background: Offline continuous glucose monitoring (OCGM) offers the possibility to improve glycaemic control by comparing nutrition and activities with glucose profiles registered blindly. Little is known about the effect of using OCGM in daily practice on glycaemic control. We assessed retrospectively the effect of OCGM on HbA1c as measure of glycaemic control.

Patients and Methods Patients with type 1 diabetes (DM1) and insulin-requiring type 2 diabetes mellitus (DM2) who were assessed with OCGM during 2009–2011 were identified. OCGM were re-analysed blindly and divided in those with mainly hyperglycaemia and those with mainly hypoglycaemia. HbA1c before and maximally 4 months after OCGM were recorded.

Results 100 patients were identified: 79 with hyperglycaemia-related indication (46% male, age 48.4 ± 15.5 years, DM1 61.5%, HbA1c 71.8 ± 16.1 mmol/l) and 21 with hypoglycaemia-related indication with comparable baseline characteristics (62% male, age 42.3 ± 10.8, DM1 76%) with HbA1c being significantly lower (52.8 ± 12.4 mmol/mol, $p < 0.001$). After OCGM decreased with 4.8 ± 11.7 mmol/mol ($p < 0.001$) in the hyperglycaemia-group with no significant change (+1.4 ± 6.2 mmol/mol) in the hypoglycaemia-group ($p = 0.32$).

Conclusion OCGM improved glycaemic control as assessed by HbA1c in patients in the mainly hyperglycaemia-group with no change in the mainly hypoglycaemia-group. Assessing the effect of OCGM depends on the reason to do OCGM.

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NATIONAL REGISTRATION PROGRAMME REAL TIME CONTINUOUS GLUCOSE MONITORING IN THE NETHERLANDS: THE "TRACING"-STUDY (REGISTRATION CONTINUOUS GLUCOSE MONITORING IN THE NETHERLANDS)

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Background: Real-time-continuous glucose monitoring (RT-CGM) may to improve glycaemic control in patients with type 1 diabetes. Patient selection is an important issue taking into account self-management, compliance and use of sensors >70–75% of the time. Prediction of success is important in view of costs of RT-CGM. In the Netherlands, RT-CGM is nationally reimbursed for children, pregnant women and adults on CSII with HbA1c ≥ 64 mmol/mol, with locally other indications. A national registration programme has started to assess nationwide use and results of RT-CGM. We report preliminary results on the adult groups.

Patients and Methods: Hospitals in the Netherlands were approached to participate. Participation required providing baseline data of patients starting RT-CGM including quality of life assessment (EQ5D, 0-100) and follow-up data such as HbA1c, severe hypoglycaemia, hospital admissions and use of sensors during the first year. Data were sent to the coordinating centre (University Medical Centre Utrecht). Here we report preliminary results.

Results: 50 major hospitals already participate with inclusion of 302 patients. Indications: adults HbA1c ≥ 64 mmol/mol 55%, pregnancy 12%, other indications 33%, mainly hypoglycaemia-related or unstable glucose profiles; 88% on CSII. Mean age 42.5 ± 13.9 years, 67% female, mean EQ5D 65 ± 15; mean HbA1c 59 ± 11 mmol/molmol. Study is on-going with growing number of participants.

Conclusion: A national registry on RT-CGM has been set up in the Netherlands. Initial results suggest use also outside nationally set indications, especially hypoglycaemia. Results will help to optimise use of RT-CGM. Such a registry can be used as template in the implementation of other innovations.

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THE DEADLY MOTHER INSTINCT

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Background: Realtime-continuous glucose monitoring (RT-CGM) has shown in non-pregnant patients to be associated with improved glycaemic control. Less experience is available in pregnant women with type 1 diabetes. These women differ from non-pregnant women in that glycaemic control is often already quite good and hypoglycaemia an important problem. Analysis of individual patients may provide important clinical findings and guidance. We would like to present a case analyse illustrating a particular behavioural pattern in pregnancy.

Case description: She is a 35-year-old well-educated woman with type 1 diabetes for 31 years without organ complications. Preconceptional HbA1c level was 34 mmol/mol. She used RT-CGMS from the moment of positive testing. During the first 12 weeks she experienced very frequent severe hypoglycaemias, several times requiring ambulance assistance with also her first ever epileptic fit. RT-CGM clearly could not protect her from

severe hypoglycaemia but even possibly contributed to them because direct questioning and analysis of glucose profiles and insulin administration, showed that she so much focused on her glucose values that she impatiently administered insulin for each elevated glucose value, not taking insulin accumulation into account and even gave insulin bolus when glucose levels were already falling. This fetus-protecting mother instinct, with care for herself coming second after that for her child, can be very dangerous and potentially lethal.

Conclusion: The many and accurate glucose data can be associated with unrestrained insulin administration in pregnant women with type 1 diabetes and aggravate severe hypoglycaemia. We have coined this the ''deadly mother instinct''.

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A NEAR FIELD COMMUNICATION (NFC) SMARTPHONE INTERFACE TO A FULLY IMPLANTABLE GLUCOSE SENSOR

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This abstract presents the development of a convenient interface to the Senseonics subcutaneous fluorescent based glucose sensor which enables users to have an on demand glucose reading without a body worn transmitter. The fully implantable sensor is targeted at 180 day insertion duration. The project utilizes an application running on an NFC capable smartphone, which provides the hardware and system level support, for remote powering of an otherwise dormant sensor using the extended command set of ISO 15693. The antenna used for NFC communication is embedded inside currently available, off-the-shelf smartphones. The phone used for this development work is the Samsung Galaxy SIII. Figure 1 shows the NFC Sensor Interface App running on the NFC enabled Smartphone with capability for on-demand readings of the fully implanted sensor. Current clinical testing of the sensor is targeted at upper arm and abdomen insertion sites. Visual, audible, or haptic feedback can be used for alignment on upper arm, which is shown in Figure 1, or abdomen insertion sites. Further testing of the long-term implantable sensor is targeted to include both sites as this use case continues to be developed.

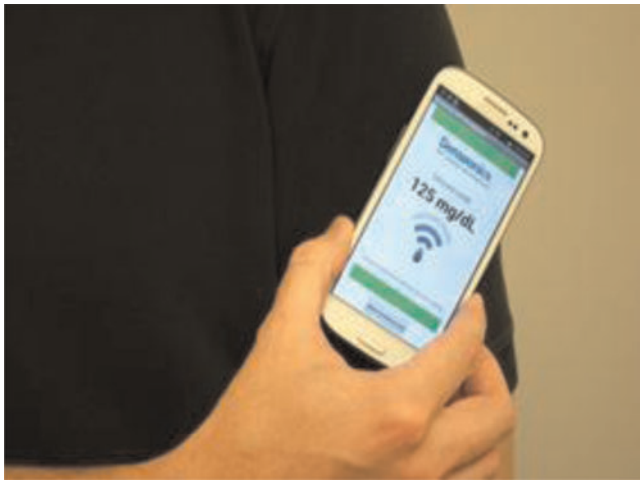

FIG. 1.

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A WEARABLE CONTINUOUS GLUCOSE MONITORING SYSTEM WITH BUILT-IN ACTIVITY TRACKING

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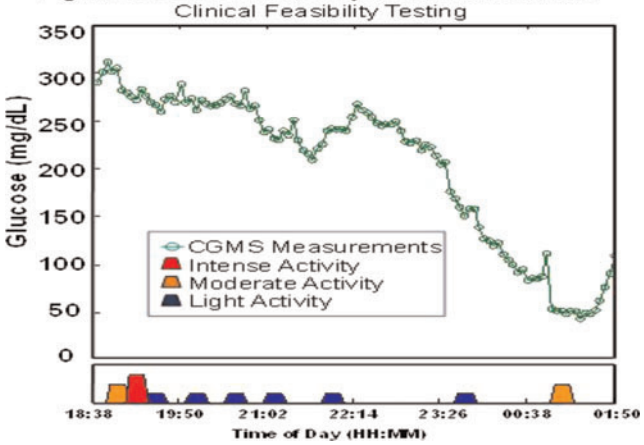
This abstract presents the development of a single, wearable device that enables both continuous glucose monitoring (CGM) and activity tracking. The Transmitter for the Senseonics' CGM System, when paired with the Mobile Medical Application, can facilitate individuals with diabetes to extend the measured physiologic parameters with user-entered information, such as insulin and meal boluses, caloric consumption, and exercise regimen. The Transmitter hardware incorporates a low-power, tri-axial accelerometer enabling near-continuous activity tracking. This system is currently being used in feasibility study clinical testing. The data from this study, which is 4 subjects for 180 days duration, has been analyzed to segment four activity levels; sedentary, light, moderate and intense. Further, the activity monitoring information was fused with the continuous glucose measurements to assess correlation between the two sets. Figure 1 shows a nighttime hypoglycemic episode that was preceded by extended durations of activity, which is similar to approximately 8% of the hypoglycemic sessions in the total data set. In these cases, subjects could show benefit from the real time feedback of the cumulative day activity levels. Overall, incorporation of activity tracking technology into our base CGM system can enable more information to the subject in managing their therapeutic regimens.

Figure 1: CGMS and Activity Measurements from Clinical Feasibility Testing



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DEVELOPMENT OF A NOVEL MICROPROBE ARRAY CONTINUOUS GLUCOSE SENSOR FOR TYPE 1 DIABETES: INTERFERENCE STUDIES

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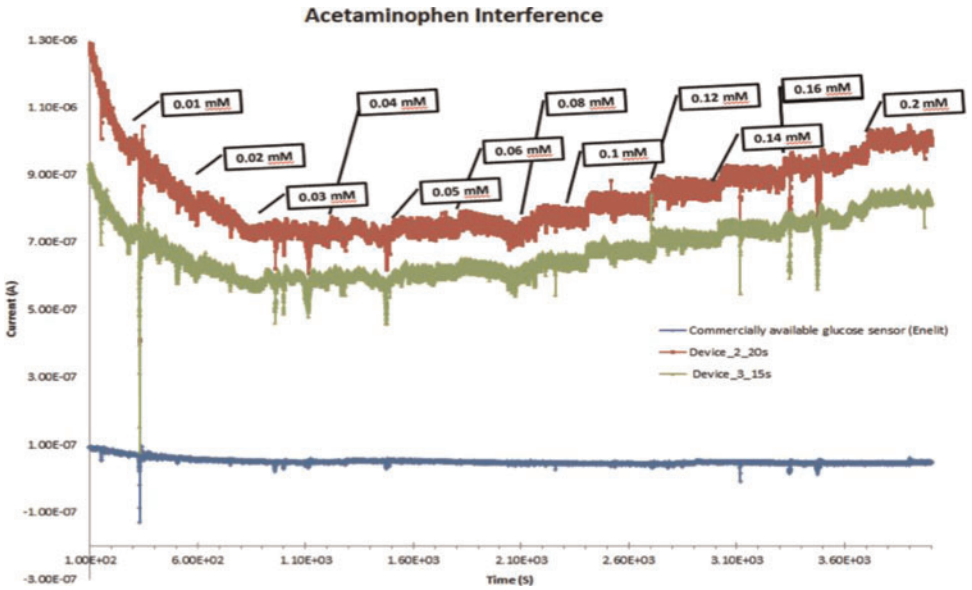

Background: Invasiveness, pain and reduced accuracy limit the use and effectiveness of continuous glucose monitors (CGM). We have developed an electrochemical microprobe biosensor for painless, accurate continuous monitoring of interstitial fluid (ISF) glucose. The solid microprobes are 1000 μm in length and 15 μm tip and are fabricated from SU8 epoxy metalized with gold and functionalized with glucose oxidase. They are finally coated with a PU (polyurethane) membrane, limiting interference and reducing glucose diffusion to enhance selectivity and maintain enzyme activity.

Aim: To optimize the PU membrane thickness and assess its ability to resist interference from ascorbic acid, uric acid or acetaminophen.

Method: Metalized microprobes were conformally covered with PU membrane of variable thickness by adjusting the duration of dip coating (5,10,20 seconds). They were then assessed using chronoamperometry. Interference studies were performed by polarizing the metal electrode at 0.7 V or 0.53 V in the presence of uric acid, ascorbic acid and acetaminophen.

Results: From chronoamperometry the optimum PU membrane thickness was obtained by dip coating for 15 s. For microprobes dip coated for more than 10 seconds, interference was seen only at 0.7 V with acetaminophen concentrations higher than 0.1 mM (therapeutic concentration 0.03–0.13 mM). However at 0.53 V no interference was seen from any of the three interferents.

Conclusion: *In vitro* sensor optimization showed the optimum PU membrane thickness to resist interferents was obtained by dip coating for 15 seconds with no interference from ascorbic acid, uric acid or acetaminophen at 0.53 V. Further *In vitro* tests to assess glucose sensitivity at these parameters are planned.

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HYPOGLYCEMIA-INDUCED EEG CHANGES IN TYPE 1 DIABETIC SUBJECTS

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Background: Hypoglycemic events have been proven to be associated with EEG changes, especially in the low frequency bands, suggesting the possible role of the brain as a biosensor to detect hypoglycemia in real-time. Many indices can be extracted from the EEG, in particular in time, frequency, and time-frequency domains, but the set of the most sensitive to hypoglycemia is not completely established.

Methods: EEG recordings and sparse blood glucose (BG) concentrations were collected in parallel in 18 T1D subjects during an insulin-induced hypoglycemia experiment. P3-C3 (P4-C4) and P3-T3 (P4-T4) EEG recordings were assessed by linear spectral analysis (in canonical as well as in individualized bands), variability of EEG power modulation, and nonlinear complexity indices. Statistical significance of the changes of EEG indices during the transition from eu- to hypo-glycemic conditions has been evaluated.

Results: In all the domains of analysis, statically significant differences in the EEG signal by passing from eu- to hypoglycemia have been observed. For instance, an increase of the power spectral density in both theta and alpha bands (in particular in the left brain channels), a significant decrease in EEG complexity measured by Approximate Entropy, and an increase of the variability of the reactivity index in theta band were noted.

Conclusion: Remarkable changes of some EEG indicators measurable in real-time in time, frequency, and time-frequency domains have been shown to occur during insulin-induced hypoglycemia. Possible use of these indicators in the real-time detection of hypo-events will be a matter of future investigations.

P-176

LONG-TERM OUTCOMES OF CONTINUOUS GLUCOSE MONITORING IN YOUNG CHILDREN WITH TYPE 1 DIABETES UNDERGOING INSULIN PUMP THERAPY: A RETROSPECTIVE EVALUATION

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To evaluate the long-term outcomes of continuous glucose monitoring (CGM) use in young children with type 1 diabetes mellitus (T1DM). We retrospectively evaluated 36 (19 males, 17 females) young children (mean age: 5.9 ± 1.5 years) who had undergone insulin pump therapy for at least 5 months (mean treatment time: 2.2 years). Average HbA1c before CGM placement: 7.6%. Height, weight, BMI, and HbA1c were evaluated at 5 ± 4 and 17 ± 8 months of CGM follow-up. CGM was worn daily in 85% of patients for an average 17 ± 8 months. CGMS use was interrupted only in 10 cases due to poor child compliance (n = 7), skin reactions (n = 2), sensor malfunction (n = 1). HbA1c and BMI after CGM use were analogous at the end of follow-up (HbA1c −0.2%) However, a statistically significant difference was found in those with HbA1c > 7.5% at the beginning of follow-up: −0.7% at 6 months ($p < 0.05$). Furthermore this reduction in HbA1c was maintained at a mean follow-up period of 15 ± 6 months ($p < 0.05$). In the population with HbA1c < 7.5%, metabolic control did not differ at the end of follow-up. No severe hypoglycemic events were documented. Our data confirm that long-term daily use of CGM is feasible in preschool children with T1DM. A significant reduction can be achieved in those who start CGM with HbA1c above target and HbA1c may be maintained stable in those who start CGM with adequate HbA1c. Further studies involving larger cohorts are necessary to eventually establish age-specific behavioral algorithms, which may aid in reducing glycemic excursions associated to preschool age.

P-177

CLINICAL IMPACT OF SENSOR-AUGMENTED INSULIN PUMP (SAP) THERAPY IN TYPE 1 DIABETES LONG-TERM RELATED COMPLICATIONS IN COLOMBIA

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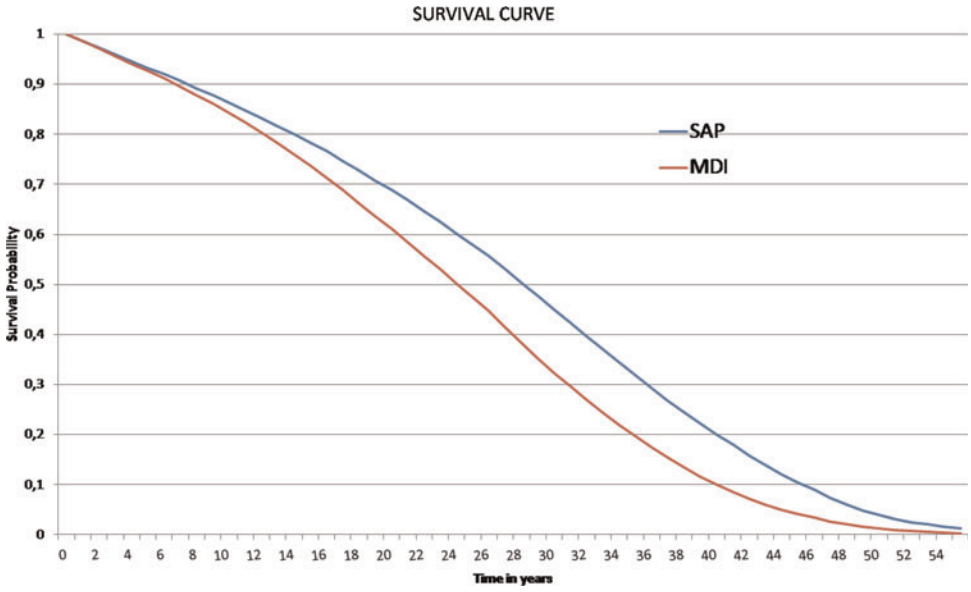
Background: Sensor Augmented Pump Therapy (SAP) is more effective than multiple daily injections (MDI) achieving a good metabolic control in patients with Type 1 Diabetes (T1D) and has a positive clinical impact.

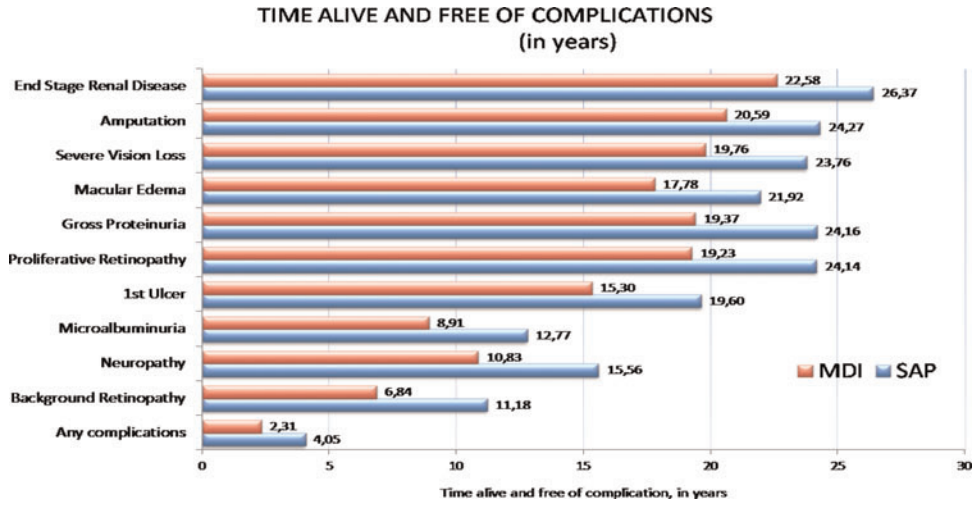
Objective: To show the impact of SAP Therapy in life expectancy and long-term complications related to Type 1 Diabetes in comparison to multiple daily injections (MDI), in Colombia.

Methods: In order to project the incidence and associated costs of diabetes-related complications over a lifetime, a Core Diabetes Model was adapted to Colombian population. It is an internet-based, validated, simulation model developed to determine the long-term health outcomes and economic consequences of diabetes interventions(1). The inputs were taken from a Colombian real life clinical study(2) of 217 T1D on SAP therapy, which reported −1.47% reduction in HbA1c levels and a significant reduction in severe hypoglycemic events (5.22 events/year vs. 0.37 with SAP; $p = 0.0009$).

Results: Life expectancy of patients with SAP was increased by 3.51 years and diabetes complications were delayed on average by 1.74 years. The relative reduction in long-term complications including, proliferative diabetic retinopathy (PDR) 42%, Severe Vision Loss (SVL) 20%, End Stage Renal Disease (ESRD) 46% and Amputations (AMP) 12%, as well as the average delay in their onset (4.9 years, 4.0 years, 3.8 years, 3.7 years, respectively).

Conclusions: SAP therapy, in comparison to MDI, increased the life expectancy by 3.51 years, delayed the related complications by 1.74 years on average and had a relative risk reduction in T1D related long-term complications.





P-178

POSTPRANDIAL GLYCEMIC PROFILES IN NON DIABETIC SUBJECTS: PRELIMINAR RESULTS FROM A POPULATION-BASED STUDY

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Objectives: The present study aimed to depict postmeal glucose profiles and to assess the effects of macronutrient intake on postprandial glycemic responses in non diabetic subjects who consumed their foods without any restrictions.

Methods: 22 males and 20 females, non previously diagnosed of diabetes. Participants wore a continuous glucose monitor and simultaneously kept a food diary for 6 days. We calculated postprandial glycemic profiles for each dinner (from starting the meal up to 8 hours), glucose AUCs and glucose concentrations.

Results: Median total energy taken per dinner was 691 (interquartile range, 460, 902) kcal, carbohydrates 67 (46, 96) g, proteins 30 (19, 46) g, and lipids 25 (13, 37) g. Mean age was 47 years; BMI, 29.0 kg/m^2; fasting glucose, 89 mg/dL; HbA1c, 5.4%

Postprandial glucose profiles are shown for the 156 dinners corresponding to the 42 subjects (Figure 1).

When the subjects were divided into three groups according to calories intake levels (1000 Kcal), the average glucose level, postprandial peak glucose level, and AUCs increased steadily (Figure 2). Multivariate analysis showed that carbohydrates intake was the only significant variable at predicting higher glucose levels ($p < 0.05$).

Conclusions: There is a great variability in postprandial glucose profiles between subjects. Postprandial glycemic responses are related to the total amount of calories intake. As regards the macronutrients intake, only the absolute amount of carbohydrates intake seems to have effect on postmeal glycemic response.

Acknowledgements: Grants by Spanish Ministry of Health (FIS PI11/02219, RD12/0005/0007) and Medtronic Inc.

Figure 1

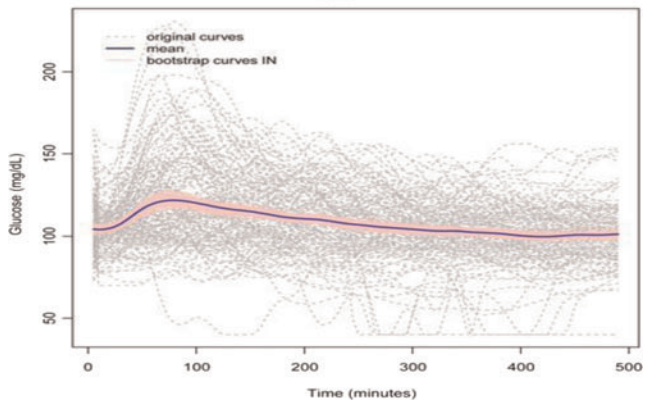
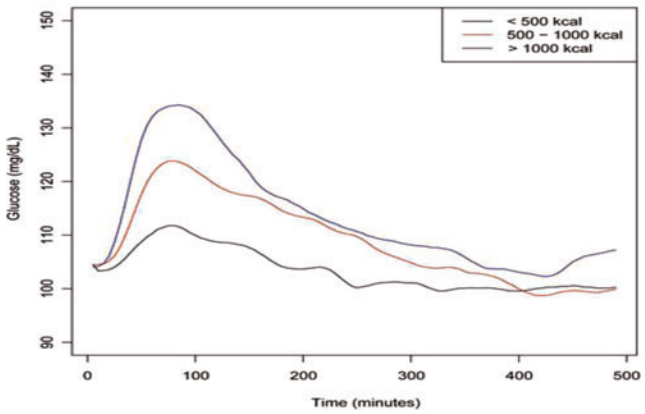


Figure 2



P-179

INFLUENCE OF GLUCOSE VARIABILITY IN A1C INTERPRETATION

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Introduction: While A1C remains the standard reference to assess mean glycaemia, the variations of glucose at cellular level only are evaluated by direct measuring of interstitial glucose. Under physiological conditions there is a strong correlation between glycaemia and interstitial glucose; however, in periods of rapid glucose fluctuations the reliability of this correlation could be affected. This study aimed to evaluate whether glucose variability (GV) influences the A1c interpretation.

Methods: Continuous glucose monitoring, using CGMS® system, was performed in 130 T1D patients with diabetes duration of 17,1 ± 8,6 years, in intensive insulin therapy (49.8 ± 17.9 UI). Mean interstitial glucose (in mg/dL) and GV measured by SD of mean interstitial glucose (in mg/dL) were assessed. HbA1c was simultaneous measured. Statistical analysis was performed using SPSS, version 21.0®.

Results: Mean ± SD for A1C was 8,2 ± 1,4% and for mean interstitial glucose (MG) was 161 ± 34,8 mg/dl. GV was correlated with mean interstitial glucose and A1C (r = 0,58 and r = 0,29, p = 0,05).

Conclusions: T1D patients with poor glycemic control had higher GV, and this, per se, impairs the correlation of A1C with mean interstitial glucose. The combination of GV with A1C may be a more reliable indicator of blood glucose control than A1C alone.

P-180

COMPARATIVE PERFORMANCE BETWEEN THE FORMER GLUCOWATCH® AND AN IMPROVED NON-INVASIVE CONTINUOUS GLUCOSE MONITORING WATCH (CGM WATCH™)

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Background: The original FDA approved GlucoWatch presented a number of difficulties including skipped readings due to movement and perspiration, and skin irritation due to proximity with the skin of hydrogen peroxide generating sensors.

Method: The CGM Watch is a device that has been developed by Nemaura Pharma Limited, currently undergoing clinical studies for CE approval.

Results: During bench trials 12 healthy volunteers (56 paired data points) were tested over 6 hr duration. 92.86% of the data points were in Clark Error Grid A zone, i.e. clinical accurate (Fig.1). Skipped readings were not observed during the study, and only one subject showed slight redness on the skin after the study, which disappeared within 2 hours after removal of the patch.

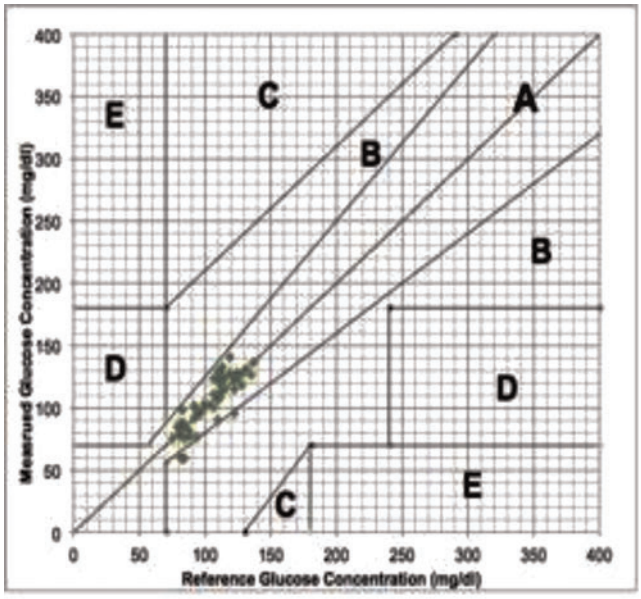

Fig.1 Clark Error Grid Analysis of CGM Watch™ Device

TABLE 1. CGM WATCH™ IMPROVEMENTS OVER GLUCOWATCH

Feature	*Glucowatch Biographer*	*Nemaura CGM-Watch™*	*Benefit*
Skin Contact Material	Hydrogel with Phosphate buffer (20 ul), impregnated with Glucose Oxidase	Phosphate Buffer Solution (pH = 7, 300 ul)	- Eliminate the swelling effect of Hydrogel - Reduced oxygen deficiency problem due to the increase of buffer volume - Reduction in H2O2 concentration more than 10 fold, leading to reduced/absent skin irritation
Electro-Chemistry	GOx immobilised in Hydrogel	Cross-linked GOx covered with Zirconia/Nafion membrane	Increased GOx stability by cross-linking, increased sensor shelf life
User Interface Screen	Character LCD	Graphic LCD	Permits viewing of trends on device
Iontophoresis Drive	DC	Higher Frequency DC	Reduces Parasthesia (tingling)
Control Sensor for Interference reduction	No	Yes	Reduces interfering effect of extraneous substances such as uric acid and drugs

P-181

CALIBRATION SCHEMES OF A TRULY NON-INVASIVE GLUCOSE MONITOR FOR VARIETY OF DIABETICS

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Calibration is an essential process in Non-Invasive (NI) blood glucose (BG) monitors. This process minimizes the impact of individual quasi-stable factors and sets a baseline for individual detection of physiological change. Previous publications about GlucoTrack®, a NI glucose monitoring device (CE-mark approved), proposed a calibration process that increases BG level, in order to track physiological changes. However, in order to have a utilizable process available to all users, an additional scheme of glucose level decrease was evaluated.

Calibration of GlucoTrack requires an overnight fasting beforehand. During calibration, BG is changed, so that user's upper and lower BG levels are reached (with some degree of flexibility at the edges). However, in some cases, fasting values do not always represent the user's lower BG values. Therefore, two calibration schemes are applied: depending on the user's fasting BG value, the calibration is performed at either glucose increase or decrease mode.

The calibration schemes' robustness was evaluated in clinical trials. 87 out of 139 participants were calibrated in glucose increase mode, the rest, mostly insulin treated subjects, were calibrated by BG decrease mode.

Clarke Error Grid analysis for BG increase and decrease modes shows that 96.9% and 94.6% of the points are in the clinically acceptable A + B zones, respectively. Mean Absolute Relative Differences are 30.0% and 31.6%, correspondingly.

The two calibration schemes yield similar GlucoTrack accuracy. The new calibration scheme can therefore be used when BG fasting level deviates from subject's lower level. The two calibration modes create an approachable process, which overcomes inappropriate user's initial BG level, thus enables more flexibility in the calibration process.

P-182

USABILITY OF A TRULY NON-INVASIVE GLUCOSE MONITOR IN HOME USE

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Glucose monitoring adherence is considered essential for achieving tight glycemic control in diabetic patients. Non-invasive (NI) glucose monitoring is expected to encourage frequent self-monitoring by overcoming pain and complexity involved in invasive measurements. To motivate contributive utilization, a NI device should be user friendly and simple-to-manage at home and home-alike environment.

GlucoTrack® is a NI, CE Marked glucose monitoring device. GlucoTrack suitability for home use was tested by 50 educated subjects (high-school and higher) based on device accuracy and user feedback analyses. First trial day included individual calibration and brief training by a proficient team. 42 subjects conducted the measurements by themselves for three more days. 8 more participants used the device at home for 5–7 days after calibration.

Clarke Error Grid analysis shows 96.2% of the points in the clinically accepted A + B zones. Mean Absolute Relative Difference of 30.5% was observed. 82% of all subjects expressed willingness to use the device regularly. 78% were generally pleased with the device. GlucoTrack display appeared clear and understandable to 89% of the participants. The operating instructions were clear to 81% of the high-school-educated and to 84% of the higher-educated participants. 64% and 61% claimed the device is easy to use among high-school and higher-educated, respectively.

GlucoTrack yields fair accuracy and is user friendly regardless of education level. These advantages, along with its painless nature of measuring and competitive long-term cost of use, suggest GlucoTrack as utilizable device for enhanced blood glucose monitoring and tighter glycemic control.

P-183

THE STATSTRIP GLUCOSE MONITOR IS SUITABLE FOR USE DURING HYPERINSULINEMIC EUGLYCEMIC CLAMPS IN A PEDIATRIC POPULATION

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The hyperinsulinemic euglycemic clamp is the gold standard for assessment of insulin resistance, and requires frequent, accurate measurements of blood glucose concentrations, typically utilizing the YSI 2300 STAT Glucose Analyzer (YSI Incorporated, Yellow Springs, OH). Despite its accuracy, the YSI has several limitations, including: cost, lengthy run time, need for trained personnel, frequent maintenance, and large blood volumes. Simpler hospital-grade handheld glucose meters are now available, but have not been validated for use in pediatric clamp settings. This study evaluated the accuracy, precision, and reliability of the StatStrip (SS) Hospital Glucose Meter (Nova Biomedical, Waltham, MA) relative to the YSI 2300 STAT Glucose Analyzer in a pediatric hyperinsulinemic euglycemic clamp setting. 460 blood specimens were drawn from 11 pediatric patients undergoing hyperinsulinemic euglycemic clamps and were simultaneously analyzed by SS and YSI. The imprecision of SS and YSI were measured and the bias of SS relative to YSI was calculated. The SS showed a slight mean positive bias of 0.75 mg/dl ± 2.83 mg/dl vs. the YSI. Coefficients of variance for SS and YSI were 9.53% and 9.25%, respectively. Using a Bland-Altman plot, the limits of agreement were ± 5.7 mg/dl. The coefficient of repeatability for SS was 6.63; the coefficient of individual agreement between the YSI and SS was 0.995. The SS is a

suitable replacement for the YSI in pediatric hyperinsulinemic euglycemic clamp studies and is more cost effective, faster, requires less blood and is easier to use. Future euglycemic clamp studies can consider utilizing this methodology.

P-184

THE BENEFIT OF CONTINUOUS GLUCOSE MONITORING SYSTEM(CGMS-IPRO2) IN REDUCING A1C IN SUBOPTIMALLY CONTROLLED TYPE 2 DIABETES

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Aim: To study the benefit of short-term blinded continuous glucose monitoring (CGM) studies in conjunction with therapy intensification with respect to A1C reduction.

Materials and Methods: Fifty-five patients with type 2 diabetes were selected from the outpatient diabetes service at Lakeshore Hospital & Research Centre Ltd, Kochi. Initial A1C values ranged from 7.5% to 12.6%. A blinded 3-day CGM study (iPro2, Medtronic) was conducted in each patient and data were retrospectively analyzed by physicians; results were shared with patients and areas for therapy intensification and behavioral/dietary adjustments were discussed. Therapy intensification options included addition of oral hypoglycemic agents (OHA), multiple daily injections (MDI), OHA + MDI, adjustments to insulin dose, OHA + adjustments to insulin dose, and addition of an insulin pump. After 3–6 months, patients returned to the clinic for A1C determination.

Results: All 55 patients experienced an A1C reduction. The average A1C reduction was 2.12% (range, 5.2% to 0.1%). The number of patients with A1C < 7.5% increased from 0 (0%) to 36 (65.45%). The number of hypoglycemic events decreased during the post-iPro2 interval.

Conclusion: Results of iPro2 studies can provide clinicians with insights to guide effective therapy intensification efforts in patients with type 2 diabetes with suboptimal control. With iPro2 as a tool in the management of diabetes mellitus, most patients can achieve A1C reductions and reach the goal of A1C < 7.5% without any severe hypoglycemic events. Further studies of the effects of iPro2 studies on patient motivation and adherence to treatment regimens are warranted.

P-185

MODY3 IN CHILDHOOD: DIAGNOSIS AND TREATMENT WITH CONTINUOS GLUCOSE MONITORING

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Background and aims: MODY3 (also known as HNF1A-MODY) is caused by mutation of the HNF1alfa, a homeobox gen on chromosme 12. Beside MODY2 this is the most common type of MODY in pupolations with Europena ancestry, accounting for about 70% of all cases in Europe. HNF1alfa is a transcriptional faktor (TCF1) that is thought to controll a regulatory network important for differentiation of beta-cells. In mature beta-cells takes part in the transcriptional process of insulin gen. Mutations of this gene lead to reduced beta-cell mass as well as impaired beta-cell function, reduced insulin releasing capacity. About 70% of people develope MODY3 diabetes by age 25 years.

Materials and methods: Our patient had the genetic diagnosis of MODY3 by age 6 years (following her mother's genetic diagnosis). During her follow-up (beside OGT) we peformed CGM to monitor her beta-cell function, when developing diabetes. Even the first OGT result proved to be diabetic, according to diagnostic criteria. HbA1c was in normal range. She was treated with life-style modification and diet. Her metabolic dysfunction was worsening, repeated OGT result showed deterioriation. She was started on sulfonilurea: glibenclamid 7,5 mg daily. The treatment was followed by CGM- as to prevent hypoglycemia and to titrate the dose.

Results: Our patients blood-glucose returned within normal limits despite unsatisfactory life-style and diet.

Conclusion: CGM is a useful tool to help decision making: initiation of treatment, to adjust dose of medication: to achive normal BG without hypoglycemia in this special sulfonilurea sensitiv and limited number patients.

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EFFECT OF CGM SENSOR TIME DELAY ON MARD AND PARD PERFORMANCE MEASURE

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The clinical and laboratory standards institute document POCT05-A, performance metrics for continuous glucose monitoring (CGM) suggests to report theinherent lag times of the sensors. In this study, the effect of two approachesfor lag time estimation on the MARD and PARD (mean and precision absoluterelative deviation) between continuous and reference glucose measurements isanalyzed.

Methods: Data from 12 patients wearing 6 CGM sensors (two FreeStyle Navigator™, two MiniMedGuardian® REAL-Time with Enlite sensor and two DexCom™ Seven®Plus) inparallel (Freckman et al., J. of Diabetes Science and Technology 7(4), pp. 842–853) were analyzed. Sensor lag was estimated by cross-correlationanalysis using CGM data and interpolated reference measurements and by choosinga time delay between paired CGM data and reference measurements which resultsin the minimum MARD.

Results: Estimated timedelays by the cross-correlation method are (mean ± SD): SevenPlus 9.24 min ± 2.66, Navigator 14.23 min ± 6.96 and Guardian 13.83 min ± 4.87. Time delays found byminimizing the MARD are: SevenPlus 9.05 min ± 3.26, Navigator 12.23 min ± 3.37 and Guardian 14.33 min ± 1.94. Both methods give comparable results consistent with previouslypublished ones.

On average (12 patients), MARD is reduced relatively by 9.7% (SevenPlus), 17.7% (Navigator) and 20.9% (Guardian) when taking the time delay into account. Minimum/maximum reductions are 1%/19% (SevenPlus), 3%/37% (Navigator) and1%/40% (Guardian). PARD is not substantially affected, even if the delaybetween two sensors of same type is not identical.

Conclusions: Both methods give accurate results for lag time. Time delay has asignificant effect on the MARD and should be considered in performanceassessments. Effect on PARD is insignificant.

P-187

INFLUENCE OF LONG DISTANCE RUNNING ON CGMS VALUES CORRELATION WITH CAPILLARY GLUCOSE IN PATIENTS WITH DIABETES

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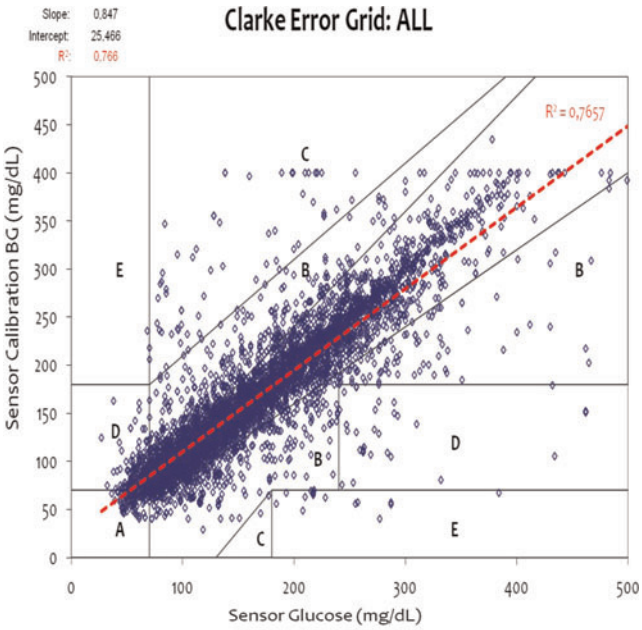
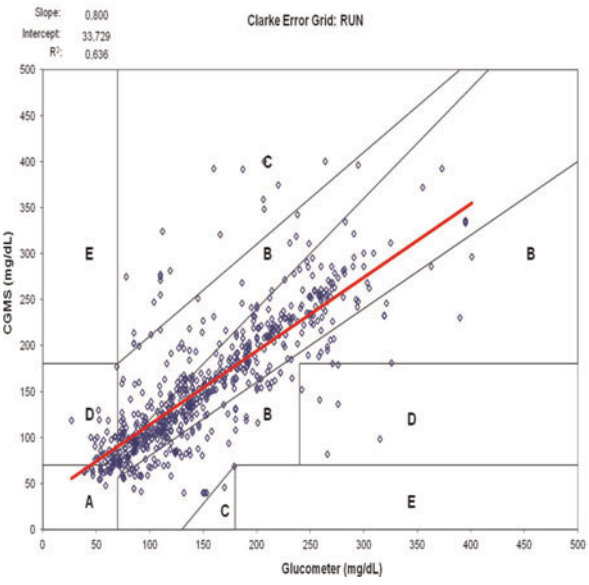
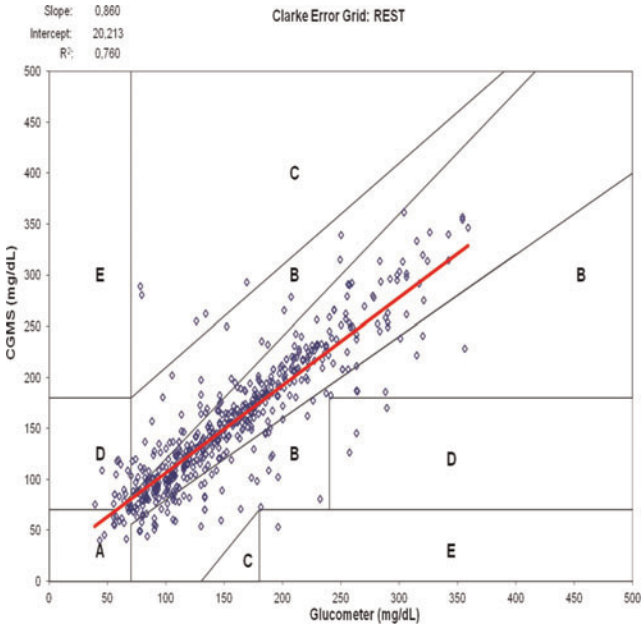
Aim: To evaluate the correlation of sensor (SG) and capillary glucose (CG) and the impact of long distance running on this correlation.







Methods: 301 CGMS procedures were analyzed, 80 done in Type 1 Diabetes runners. Overall SG and CG correlation was obtained and compared with the correlation within 36 h around running long distance (RUN), and during resting time (REST). Clark's Errors Grid Analysis (EGA) was performed.

Results: The whole sample (ALL) included 5946 paired points, with 688 points in RUN and 558 in REST periods respectively. Average SG and CG were $163^{*\#} \pm 73$ mg/dL, 164 ± 70 mg/dL (ALL); $153^{*} \pm 72$ mg/dL, 156 ± 72 mg/dL (RUN) and $155^{\#} \pm 66$ mg/dL, 154 ± 66 mg/dL (REST), respectively. There was no difference within each group. ALL had higher average SG than both RUN ($^{*}p = 0.001$) and REST ($^{\#}p = 0.007$). SG and CG correlation were $R^2 = 0.77$; $R^2 = 0.76$; and $R^2 = 0.64$ for ALL, REST and RUN, respectively. ($p = 0.005$, for RUN *versus* both ALL and REST). EGA showed 95.5%, 96% and 92% of paired points in A and B zones, for groups ALL, REST and RUN respectively. While 1.1%, 3.2% and 0.3% in C, D and E zones in group ALL, 0.9%, 3% and 0.2% in group REST and 3%, 5% and 0%, in group RUN. None of the 80 distance runs were interrupted by hypoglycemia.

Conclusion: In this sample, SG showed good correlation with CG. This correlation was modified by exercise, but this difference did not affect error chance.

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CGMS IN 67 TYPE 1 DIABETES ATHLETES DURING AN 18 KM DISTANCE RUN

R.N. Lamounier[1], G.L.C. Mendes[2], A.S. Silva[1], E.S. Oliveira[3], A.H. Silva[3], T.M. Ferreira[1], D. Giannella-Neto[4]

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Aims: The project ''Volta Monitorada'' prepares and empowers T1DM subjects to participate in long distance run events in Brazil. We evaluated their glucose profile during an 18 km run.

Methods: 67 T1DM athletes and 10 controls completed the 18 km run with CGMS. According to their previous treatment, they were divided in three groups: CSII, n = 17; Basal analogs (BA), n = 34; NPH, n = 16.

Results: Average age was 28.8 ± 8.3 years and time for completing 18 km was 139.9 ± 33.6 min. HbA1c was 7.6 ± 1.32%, and similar among the three groups. C peptide was higher in NPH vs CSII (0.5 vs 0.1; p = 0.02). CGM time was 4431.6 ± 108.3 min, with 886.32 ± 357.06 readings. Average sensor glucose was 152.09 ± 23.6 mg/dL, similar between groups and different from CT, 96.7 ± 7.8 mg/dL; p < 0.0001. Hypo and Hyperglycemia exposition was similar between groups with 5% of values below 70 mg/dL. Run speed inversely correlated with HbA1c (RR: −0.32; P < 0.001) and sensor AUC (RR −0.31; P < 0.002). Glucose variability (GV) was similar among diabetes groups. CT had maximum glucose value of 138 mg/dL vs 342 mg/dL in T1DM runners (p < 0.0001). Glucose decrease correlated positively with glucose value at start (RR −0.49; P < 0.0001). After run Lactate correlated positively with maximum glucose value and GV.

Conclusion: In this study GV was similar among different treatments, but NPH group had higher C peptide values than CSII. Better fitness was related to better glycemic control, while higher glucose values related to higher post run lactate.

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DEVELOPMENT OF A STANDARDIZED APPROACH TO INITIATING CONTINUOUS GLUCOSE MONITORING IN A MULTICENTRE PEDIATRIC STUDY

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Objective: To evaluate a standardized approach to education and device setting options for continuous glucose monitoring (CGM) in children and adolescents with type 1 diabetes (T1D) starting pump therapy with simultaneous or delayed CGM initiation.

Method: All participants are part of the CGM TIME Trial, a multicentre 5-site RCT of pump naïve 5–18 year olds with T1D > 1 year who were randomized to simultaneous initiation of pump (Medtronic Veo) and CGM (Enlite) or to standard pump therapy with delayed CGM introduction 6 months later. Prior to the trial, diabetes educators at the 5 participating centers critically reviewed published and unpublished education materials and approaches to initiating CGM.

Results: A standardized approach to CGM education and settings was developed and implemented study-wide along with a novel study-specific algorithm for trend arrow adjustments. All sites utilized the standardized CGM settings and education materials, resulting in a consistent and step-wise approach to initiating CGM amongst the 144 subjects participating in the trial. Analysis of CGM adherence and effectiveness, and their relationship to participants' use and frequency of alarms will begin in July 2014.

Conclusion: The CGM TIME Trial successfully developed and standardized a step-wise approach to CGM education and settings. Its conclusions will enhance our understanding of optimal CGM settings for simultaneous and delayed CGM initiation, and offer guidelines to support other centers in best practices to improve CGM adherence and effectiveness.

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TIMING OF INITIATION OF CONTINUOUS GLUCOSE MONITORING IN ESTABLISHED PEDIATRIC DIABETES: RECRUITMENT AND BASELINE CHARACTERISTICS IN THE CGM TIME TRIAL

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Objective: To determine if initiating continuous glucose monitoring (CGM) at the same time as starting pump therapy in pump naïve children and adolescents results in greater CGM adherence and effectiveness compared to delaying CGM introduction by 6 months, and whether this is related to greater readiness for making behavior change at the time of pump initiation.

Method: Multicentre 5-site RCT of 5–18 year olds with T1D > 1 year who are starting pump therapy and willing to be randomized to simultaneous initiation of pump (Medtronic Veo) and CGM (Enlite) or to standard pump therapy with delayed CGM introduction 6 months later. Primary outcomes are CGM adherence and A1C at 6 and 12 months post pump initiation. Secondary outcomes include glycemic variability and patient reported outcomes.

Results: Recruitment was completed in 21 months, during which 353 children started pump therapy. 144 (95%) of the 152 eligible patients were enrolled and randomized (73 simultaneous, 71 delayed; mean age 12.0 +/− 3.3 (SD) years; T1D duration 3.3 +/− 3.0 years; baseline A1C 8.0 +/− 1.0%). Reasons for exclusions (n = 201) included: not willing to use CGM (20.9%), < 5 years old (9.0%), < 1 year T1D (7.0%), unwilling to be randomized to delayed CGM (1.5%), chose non Medtronic pump [but met other inclusion criteria] (53.2%).

Conclusion: The CGM TIME Trial is the first study to examine the relationship between readiness for behavior change, timing of

CGM initiation, and subsequent CGM adherence in pump naïve children and adolescents. Analysis of 12 month primary outcomes will begin in July 2014.

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EFFICACY OF BLINDED, 3 DAY CONTINUOUS GLUCOSE MONITORING IN THE REGULATION OF POORLY CONTROLLED DIABETES

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As the application of continuous glucose monitoring (CGMS) evolves, most studies have focused on the long-term placement of CGMS on individual patients (single-user). The effectiveness of short term, multi-user professional CGMS has been studied less extensively with conflicting results. To evaluate short-term CGMS effectiveness in our Center, we carried out a retrospective review of 113 consecutive patients. We used a three day, blinded, multi-user CGMS protocol supplemented by food and activity diaries. Hemoglobin A1c (Hgb A1c) was measured 6–12 weeks before the study and 6–12 week after changes in treatment were implemented, based on the results of the CGMS assessment. Baseline Hgb A1c in the entire group was $8.81 \pm 0.14\%$, and fell to $8.26 \pm 0.14\%$ following the testing ($p < 0.000002$). Hgb A1c in patients with type 1 diabetes was $8.78 \pm 0.18\%$ at baseline and $8.36 \pm 0.17\%$ at follow-up ($p < 0.01$). Hgb A1c also significantly declined in patients with type 2 diabetes ($8.88 \pm 0.23\%$ vs $8.07 \pm 0.24\%$) ($p = 0.000003$). Hgb A1c declined significantly in patients on insulin therapy alone ($p = 0.004$), and insulin plus oral hypoglycemics ($p = 0.0035$). The change in Hgb A1c was not significant in patients on oral hypoglycemic agents; however, the number of subjects in this group was small ($n = 10$). We conclude that use of blinded, short-term, multi-user CGMS is an effective tool for improving glycemic control in diabetic patients on insulin therapy, when implemented with supplemental lifestyle data.

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CGM AND SAP ARE VALUABLE TOOLS IN THE TREATMENT OF DIABETES; A SWEDISH HEALTH TECHNOLOGY ASSESSMENT

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Long-term use of CGM (continuous glucose monitoring) is used by a few percent of adults and 3–16% of children with Type 1 diabetes in Sweden.

Aim: to present a systematic review to establish available evidence on effects of CGM and SAP (sensor-augmented pump) in adults (A), children (C) and pregnant women (P) compared to SMBG (self-monitored blood-glucose).

Methods: Literature search included PubMed, Cochrane Library, Cinahl and PsychINFO until November 2012. Two reviewers independently assessed the quality of each included study by using the SBU checklists. Quality of evidence was rated by the GRADE system.

Results: Of 1130 identified abstracts, 24 CGM studies were quality assessed; 11 had low quality (6C,1P,4A), 8 moderate (5C,3A) and 5 high (4C,1A). For SAP, 10 studies were assessed; 3 had low quality (1C,2A), 6 moderate (2C,4A) and 1 high (C). For adults, 1 systematic review of high quality was included.

There was a lack of high quality research. Short-term HbA_{1c} was improved by CGM if used ≥ 6 days/week, more so by SAP. Patients with CGM reported higher treatment satisfaction, especially when using SAP. Limited information was available on frequency of severe hypoglycemia and ketoacidosis.

Calculations of costs demonstrated an increased cost of 3026 EUR for CGM vs. SMBG and 4216 EUR for SAP vs. MDI and SMBG.

Conclusion: CGM and SAP demonstrate short-term benefits including a reduced HbA_{1c} level, which if sustained may reduce the risk of long-term diabetes complications.

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PERFORMANCE EVALUATION OF FOUR BLOOD GLUCOSE MONITORING SYSTEMS

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Objective: Self monitoring of blood glucose (SMBG) is used for therapy adjustment by patients. Therefore, high quality SMBG systems are required. In this study, system accuracy of four SMBG systems was evaluated following ISO 15197:2003 and the recently published ISO 15197:2013 criteria. In addition, measurement performance on 100 native samples with BG concentration < 70 mg/dl was assessed.

Methods: Four systems were evaluated with three test strip lots each: Contour® XT (Bayer Consumer Care AG), GlucoCheck XL (aktivmed GmbH), Accu-Chek® Aviva (Roche Diagnostics GmbH), GlucoMen® LX Plus+ (A. Menarini Diagnostics S.r.l). System accuracy evaluation was performed following the standard ISO 15197:2003/2013. In addition, 100 capillary blood samples of 40 subjects with BG concentrations < 70 mg/dl (mean 60.1 mg/dl, range 38.5 mg/dl–69.6 mg/dl) were collected to analyze mean absolute relative differences (MARD) between system and comparison method results (hexokinase, cobas c111).

Results: All systems met the ISO 15197:2003 criteria with 95.5% to 100% of measurement results within the respective limits. When applying the ISO 15197:2013 criteria, three systems met these criteria (95.5% to 100% of results within the limits). For native samples < 70 mg/dl SMBG systems showed MARD of 2.7%, 5.1%, 6.8% and 15.2%, respectively.

Conclusion: All investigated SMBG systems fulfilled system accuracy criteria of the standard ISO 15197:2003, whereas only three of them fulfilled the requirements of ISO 15197:2013. These showed only small deviations from the comparison method in the low glycemic range which is important to detect hypoglycemic events.

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PERFORMANCE ASSESSMENT OF A CONTINUOUS GLUCOSE MONITORING CALIBRATION ALGORITHM IN HYPOGLYCEMIA

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Background: The aim of this study was to assess the performance of a new continuous glucose monitoring (CGM) calibration algorithm.

Method: CGM data from 10 type 1 diabetes patients undergoing insulin-induced hypoglycemia were collected in two sessions using Guardian® REAL-Time (RT) (Medtronic Diabetes). Data from the same CGM sensor were calibrated by two calibration methods: the Guardian RT algorithm, and a new algorithm.

Results: For the new calibration algorithm, the median (mean) absolute relative deviation of the sensor glucose (SG) readings from the hypoglycemic plasma glucose (PG) values ($PG \leq 70$ mg/dl) were 35.9% (44.8%), and for the Guardian RT calibration, they were 60.9% (62.8%). Friedman's analysis of variance, with algorithm and patient as the two factors and the sessions of the data collection as the replication indicated that the sample-based hypoglycemia sensitivity of the new algorithm was significantly higher than that of the Guardian RT algorithm (median sensitivity was 82% for the new calibration and 23% for the Guardian RT calibration, Friedman's test, $X^2(2) = 5.7$, $P = 0.0169$). The sample-based specificity of the new algorithm was lower; however the difference was not significant (median specificity of 95% for the new calibration vs. 100% for the Guardian RT calibration, Friedman's test, $P > 0.05$).

Conclusions: The results suggest that the new calibration algorithm may reduce the inaccuracy of Guardian RT CGM in hypoglycemia; however, thorough evaluation by using a more varied set of performance metrics and larger datasets is required to compare the clinical reliability of the two algorithms.

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INITIATION STUDY: A MODEL OF CARE FOR COMMENCING BASAL/PRANDIAL INSULIN IN T2D IN PRIMARY CARE WITH ADJUNCT RETROSPECTIVE-CONTINUOUS GLUCOSE MONITORING

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Objective: To evaluate a model of care for T2D insulin initiation in Australian primary care and compare retrospective-continuous glucose monitoring (r-CGM) with self-monitoring of blood glucose (SMBG).

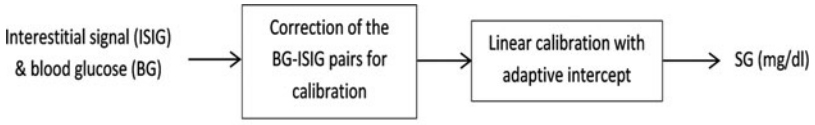

Figure 1. The new calibration algorithm

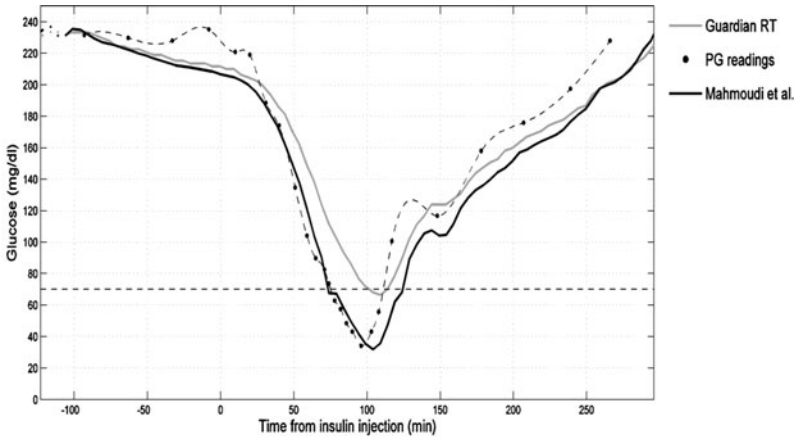

Figure 2. The CGM calibrated by Guardian RT algorithm and the algorithm presented by *Mahmoudi et al.*, and the reference plasma glucose measurements for one of the patients.

Methods: Primary care patients commenced glargine with glulisine added if deemed necessary. Outcomes were benchmarked against ambulatory T2D specialist data. An embedded randomised-controlled trial compared r-CGM and SMBG. *Primary Outcome:* Initiation vs benchmark DHbA1c (baseline vs 24 week). *Secondary Outcomes:* DHbA1c; CGM time in target range; proportion of patients with glulisine added to glargine in r-CGM (n = 48) vs SMBG (n = 44).

Results: 92 T2D participants with HbA1c Mean (SD) 10.1 (1.6)%; 55 M/37F; Age (range) 59 (28–77) Y from 20 general practices commenced insulin. Mean (95%CI) DHbA1c reduction was −2.6% (−2.9, −2.2); $p < 0.0001$ for 88 attending at 24 weeks. 82 T2D patients HbA1c Mean (SD) 9.6 (1.8)%; 51 M/31 F; Age (range) 60 (25–86) Y in specialist care commenced insulin. DHbA1c for 66 patients attending at 24 weeks was −1.7% (−2.1, −1.3); $p < 0.001$. HbA1c reduction in Initiation vs Benhmark Groups: $p = 0.0017$. Comparing r-CGM with SMBG there were no differences in major hypoglycaemia ($p = 0.17$) and no significant difference in HbA1c reduction (Mean [SD]) r-CGM vs SMBG (−2.7 [1.8] vs −2.4 [1.4] %; $p = 0.31$) or any r-CGM parameters. More r-CGM participants commenced glulisine (26/48 vs 7/44; $p = 0.0001$)

Conclusions: Reduced loss to follow-up and outcomes comparable to specialists were obtained in primary care. R-CGM use in primary care was feasible, enhanced post-prandial hyperglycaemia recognition, and has potential to improve T2D health-care delivery.

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CONTINUOUS GLUCOSE MONITORING SYSTEM (CGMS): A USEFUL DEVICE IN METABOLIC DISEASES AFFECTING CARBOHYDRATES METABOLISM AS WELL AS IN TYPE 1 DIABETES

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Background: CGMS is commonly used for detecting hypoglycaemic events in type 1 diabetic patients. In the last years, the development of more technological CGMS devices has suggested their potential application in the study of carbohydrates metabolic disorders as well as in Type 1 Diabetes.

Aim: To examine the efficacy of CGMS Medtronic in 20 patients with documented/suspect metabolic disorders: one type 1A glycogen storage disease (A), one suspect hyperinsulinism (B), one phospho-fructose isomerase deficit (C), one congenital hyperinsulinism (D), one Wolfram syndrome (E), 15 patients in follow-up for symptomatic/asymptomatic hypoglycaemic events.

Results: In (A) CGMS demonstrated the importance of small frequent meals and overnight enteral nutrition in order to avoid severe hypoglycaemia. In (B) it recorded recurrent asymptomatic hypoglycaemic events, especially at night, and post-prandial hyperglycaemic spikes, thus excluding hyperinsulinism. Similar pattern was noticed in (C). (D) presented a constant hypoglycemic trend without post-prandial spikes and an improvement after therapy with diazoxide. In (E) we observed post-prandial hyperglycemic spikes. 6 patients presented asymptomatic nocturnal hypoglycaemic events, 2 tendency to hyperglycaemia, 7 did not record any significative hypo/hyperglycaemic events. Our results could allow a correct prophylaxis for avoiding nocturnal hypoglicaemia and identifying a glucose metabolism alteration which is not caused by a peculiar deficit.

Conclusions: Experimental preliminary evidences suggest that CGMS could be applied in diagnosis/follow-up process of patients with suspect/documented carbohydrates metabolic disorders, in order to evaluate glucose excursions, to identify nocturnal hypoglicaemic events and treat them with more adequate therapy.

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TRANSITORY BENEFICIAL EFFECTS OF PROFESSIONAL CONTINUOUS GLUCOSE MONITORING ON THE METABOLIC CONTROL OF PATIENTS WITH TYPE 1 DIABETES

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Background: The benefit of professional continuous glucose monitoring (PCGM) in the metabolic control of patients with type 1 diabetes mellitus (T1D) is uncertain.

Methods: This was a retrospective study of all consecutive T1D patients who underwent a 6 day PCGM in our Diabetes Unit over the course of 17 months. According to the indication, two groups were arbitrarily defined: a ''hyperglycemic'' and a ''hypoglycemic'' one. Data from medical files and sensor reports were reviewed. HbA_{1c} was evaluated 2–4 weeks prior to PCGM, as well as 3–5 and 12 months after PCGM. In the hypoglycemic group, the number of self-reported mild hypoglycemic episodes (as defined by the American Diabetes Association) was collected.

Results: Of the 67 patients reviewed, 43 belonged to the hyperglycemic group and 24 to the hypoglycemic one. In the hyperglycemic group, the HbA_{1c} dropped at 3–5 months post-intervention from 8.45 ± 0.72% to 8.04 ± 0.9%, the decline being statistically significant (−0.4%, $p = 0.001$) and positively correlated with the initial HbA_{1c} value (0.366, $p = 0.016$). One year after the PCGM study, the HbA_{1c} tended to return to the initial values: 8.20 ± 1.05% (−0.24%, $p = 0.081$). In the hypoglycemic group, HbA_{1c} did not change neither 3–5, nor 12 months after PCGM, while the percentage of patients in whom the number of mild hypoglycemic episodes was significantly reduced was 86% ($p = 0.001$).

Conclusions: Although transiently, PCGM can be useful at the short term in improving metabolic and clinical profile of T1D subjects suboptimally controlled including those with repeated hypoglycemia.

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HOW PEOPLE USE DIRECTION AND RATE OF CHANGE INFORMATION PROVIDED BY REAL-TIME CONTINUOUS GLUCOSE MONITORING (RT-CGM) TO ADJUST INSULIN DOSING

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There is no published data on how CGM users utilize rate of change (ROC) arrows for glycemic management. Accordingly, practitioners are limited in guidance they provide patients regarding insulin dosage adjustments based on ROC. To address this issue, 222 adult successful CGM users with T1DM in the US completed 70 multiple-choice, scenario-based questions in an on-line survey which probed their use of RT-CGM data. Study population: age 46 ± 14; A1C 6.9% ± 0.8%; 75% CSII, 25% multiple daily injections.

In response to rising glucose levels (at 12 mmol/L) showing either one arrow up (glucose increasing 0.11 to 0.17 mmol/L/min) or two arrows up (increasing > 0.17 mmol/L/ min) subjects reported increasing their typical correctional insulin dose by 111% and 140%, respectively. In response to two arrows up prior to a 50 g carbohydrate meal, subjects would increase their mealtime dose by 81%. In response to dropping glucose levels, subjects would decrease correctional insulin by 41% and 47% with one arrow down (decreasing 0.11 to 0.17 mmol/L/min) or two arrows down (decreasing > 0.17 mmol/L/min), respectively. Mealtime insulin doses were reduced by 53% in response to two arrows down. With decreasing glucose at euglycemia (6.7 mmol/L), 70% of subjects would prophylactically consume carbohydrates to avoid hypoglycemia. Finally, most subjects would alter not only the dose of insulin, but also the timing of their premeal doses based on ROC.

Successful RT-CGM patients use ROC arrows to make major modifications to multiple aspects of insulin therapy including correctional doses, mealtime doses, and dose timing.

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ACCURACY EVALUATION OF THE CONTOUR® PLUS LINK 2.4 BLOOD GLUCOSE MONITORING SYSTEM

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Objective: This study evaluated the accuracy of the CONTOUR® PLUS LINK 2.4 blood glucose monitoring system (BGMS) as assessed per ISO 15197:2003 section 7 and ISO 15197:2013 section 6.3 accuracy criteria.

Methods: Fingerstick capillary blood samples from 100 subjects were evaluated using 3 CONTOUR® PLUS test strip lots and each sample was tested in duplicate utilizing 6 CONTOUR® PLUS LINK 2.4 meters (N = 600). Samples were also tested in parallel on a YSI 2300 STAT Plus™ reference analyzer to obtain reference values for comparison. Accuracy was assessed based on ISO 15197:2003 section 7 (≥ 95% of results within ± 15 mg/dL [0.8 mmol/L] or ± 20% of reference at glucose concentrations.

Results: Overall, 100% (600/600) of results using the CONTOUR® PLUS LINK 2.4 BGMS met ISO 15197:2003 section 7 and ISO 15197:2013 section 6.3 accuracy criteria. Also, 99.3% (596/600) of results were within ± 10 mg/dL (0.6 mmol/L) or ± 10% of the YSI reference. Regression analysis demonstrated a high degree of agreement between CONTOUR® PLUS LINK 2.4 BGMS and reference results ($R^2 = 0.9936$). Parkes-Consensus Error Grid analysis showed that 100% of results were within Zone A.

Conclusion: Study findings showed that the accuracy of the CONTOUR® PLUS LINK 2.4 BGMS met ISO 15197:2003 section 7 and ISO 15197:2013 section 6.3 accuracy criteria.

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GLUCOSE SENSING BY COMBINING TWO DIFFERENT SENSING TECHNOLOGIES. PRECLINICAL CGM TESTING IN DIET INDUCED OBESE RATS

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Objective: Together with the JDRF and Helmsley Charity Foundation, Medtronic Diabetes is exploring the potential benefits of combining two fundamentally different glucose sensing technologies in a single device to improve CGM accuracy and reliability for a closed loop application. The Orthogonally Redundant Sensor device (ORS) employs an electrochemical glucose sensor and an optical glucose sensor. For the preclinical animal testing of the sensor part of the future closed loop system a test protocol using Diet Induced Obese (DIO) rats has been developed.

Methods: Preclinical testing of the ORS is conducted in DIO rats. The DIO rats typically have a weight of 600 g to 1100 g. The rats are exposed to three glucose excursions over a period of six days of CGM. Insertion of devices is done under anesthesia whereas the rats are awake and allowed to move around freely in their cages during the entire trial period.

Results: Results obtained in earlier *in vivo* short term rat studies under anesthesia are very different to the *in vivo* long term trial using the current protocol. Examples will be given.

Conclusion: The use of DIO rats for *in vivo* testing offers several advantages in the development of a robust device. The DIO rats can carry two to four CGM devices each. Combined with the relatively small size of the animal and the high acceptance of carrying devices this makes the rat model cost effective. A high level of animal well-being during the trial is obtained by avoiding handling of the animal during the trial.

P-201

INTERFERENCE EVALUATION OF THE CONTOUR® NEXT TEST STRIP

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Objective: A new platform of blood glucose monitoring systems (BGMSs) utilizes the CONTOUR® NEXT test strip containing the FAD-GDH enzyme and a proprietary electron mediator and algorithm. Common endogenous and exogenous substances were evaluated for interference effect in accordance with ISO 15197:2013.

Methods: Interfering substances were tested in pooled venous blood at glucose concentrations of 80 mg/dL (4.4 mmol/L) and 300 mg/dL (16.7 mmol/L) with guidance from the Interference Testing in Clinical Chemistry EP7-A2 guidelines. A series of test samples containing a range of concentrations of each interfering substance was prepared. Results were analyzed according to ISO 15197:2013 Section 6.4.4 guidelines (interference effects shall be described in the instructions for use if the average difference between test and control samples exceeds 10 mg/dL [0.55 mmol/L] or 10% at glucose concentrations < 100 mg/dL [5.55 mmol/L] and ≥ 100 mg/dL [5.55 mmol/L], respectively).

Results: More than 20 common interfering substances (including acetaminophen, ascorbic acid, bilirubin, galactose, maltose, uric acid) showed ≤1 mg/dL (0.055 mmol/L) or ≤1% bias at maximum therapeutic concentration (MTC) or upper reference value. Only 1 substance tested, xylose, had a limiting concentration (13.7 mg/dL [0.91 mmol/L]) considerably lower than its MTC (57 mg/dL [3.8 mmol/L]).

Conclusion: Study findings showed that, with the exception of xylose, common endogenous reducing substances in blood or exogenous substances from therapeutic treatments did not significantly affect performance of the CONTOUR® NEXT test strip. Thus, results obtained with this new BGMS platform can be expected to be accurate in the presence of these interfering substances.

P-202

ACCURACY EVALUATION OF FOUR BLOOD GLUCOSE MONITORING SYSTEMS THAT CAN COMMUNICATE WITH AN INSULIN PUMP

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Objective: To assess the accuracy of 4 blood glucose monitoring systems (BGMSs) that can communicate wirelessly with an insulin pump: the CONTOUR® NEXT LINK, CONTOUR® NEXT LINK (Europe and Canada), CONTOUR® NEXT LINK 2.4, and CONTOUR® PLUS LINK 2.4.

Methods: Data from separate studies of each individual BGMS were used to compute estimates of mean absolute relative difference (MARD) between meter and YSI reference results. In each study, study staff tested fingerstick capillary blood samples from 100 subjects in duplicate using 3 lots of test strips (N = 600 results per BGMS). BGMS results were compared to YSI results from the same sample source. It is important to note that since each study was performed with different groups of subjects and the variation in blood glucose levels differs greatly between individuals, it is not possible with these data to determine the statistical significance of differences in MARD estimates among BGMSs.

Results: The MARD (standard deviation [SD]; 95% confidence interval [CI]) for CONTOUR® NEXT LINK was 3.167% (2.3907%; 2.975–3.359), and for CONTOUR® NEXT LINK (Europe and Canada) was 3.676% (2.9623%; 3.439–3.914). The MARD (SD; 95% CI) for CONTOUR® NEXT LINK 2.4 was 3.705% (3.3912%; 3.433–3.976), and for CONTOUR® PLUS LINK 2.4 was 3.448% (2.9822%; 3.208–3.687).

Conclusion: The 4 BGMSs that can communicate wirelessly with an insulin pump demonstrated accuracy as assessed by MARD. Average deviations from the reference method were small, as evidenced by the MARD estimate of each BGMS falling within the range of 3%–4%.

P-203

REAL-TIME CONTINUOUS GLUCOSE MONITORING AS A TOOL TO PREVENT SEVERE HYPOGLYCAEMIA IN SELECTED PREGNANT WOMEN WITH TYPE 1 DIABETES – AN OBSERVATIONAL STUDY

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Aims: Given severe hypoglycaemia the year before pregnancy, 70% of the women with type 1 diabetes also experience this complication in pregnancy. We evaluated whether real-time continuous glucose monitoring (CGM) in the first half of pregnancy could prevent severe hypoglycaemia in these women.

Methods: Among 140 consecutive women with type 1 diabetes, real-time CGM was initiated early in pregnancy and continued until mid-pregnancy in 11 (8%) women with a history of severe hypoglycaemia the year before pregnancy or before first antenatal visit in pregnancy. Severe hypoglycaemia was defined as hypoglycaemia requiring assistance from others to treat the condition and was recorded prospectively in pregnancy. A questionnaire on real-time CGM alarms was collected during the intervention.

Results: Eight (73%) women experienced in total 33 (range 1–11) severe hypoglycaemic events in the year before pregnancy, and 7 (64%) experienced 19 (1–10) events early in pregnancy before initiation of real-time CGM. From initiation of real-time CGM until delivery, two (18%) women experienced one severe hypoglycaemic event each. The incidence rate of severe hypoglycaemia was 3.0 events/patient-year in the year before pregnancy and declined in pregnancy from 12.3 before to 0.4 after real-time CGM initiation. HbA1c at first pregnancy visit was median 6.7% (5.8–11.5) (50 (40–102) mmol/mol) and diabetes duration was 13 (6–21) years. Real-time CGM was used from 9 (7–18) gestational weeks for 11 (2–32) weeks and for 90% (34–100) of the time.

Conclusions: In selected pregnant women with type 1 diabetes, continuous real-time CGM may reduce the risk of severe hypoglycaemia.

P-204

THE 3RD GENERATION CGM SENSOR UTILIZING DIRECT ELECTRON TRANSFER PRINCIPLE

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Objective: Current sensors for CGM employ either the 1st generation (oxygen/hydrogen peroxide electrochemistry) or the 2nd generation (artificial electron acceptor electrochemistry) principle of enzyme electrochemical glucose measurements. Here, we introduce the challenge in the development of the 3rd generation of CGM sensor based on the Direct Electron Transfer (*Di*ET) technology. We employed a unique glucose dehydrogenase (GDH) capable of direct electron transfer from enzyme redox-center to electrode. This study reports the features and performances of the novel CGM sensor.

Method: Bacterial Flavin Adenine Dinucleotide Glucose Dehydrogenase (FAD-GDH) was recombinantly prepared and characterized its electrochemical performances. A micro enzyme electrode was constructed and the correlation between glucose concentration and sensor responses was investigated in phosphate buffer containing glucose. Influence of dissolved oxygen was measured. A healthy person wore the sensor and capillary blood glucose values were obtained at the same time.

Result: FAD-GDH is a thermostable enzyme made up of a catalytic subunit having FAD in its redox center and a multiheme cytochrome-complex electron-transfer subunit. The electron-transfer subunit confers the ability to transfer electrons directly to an electrode. The linearity was shown at glucose range of 20 to 500 mg/dl, and little change was observed in the sensitivity after seven-day continuous measurement. *In vivo* study revealed that the sensor correlated very well with the low and high blood glucose values ($R^2 = 0.93$, 86 pairs).

Conclusion: We have developed the 3rd generation CGM sensor. Consequently, it has made the sensor composition simple, which means no mediator is needed.

P-205

DETECTION OF GLUCOSE-SENSOR AND INSULIN-PUMPS FAILURES: FROM OVERNIGHT TO NIGHT & DAY

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Objective: Failures of continuous glucose monitoring (CGM) sensor and insulin pump represent a critical issue for the safety of Type-1 diabetic patients, especially under closed-loop control. Recently, Facchinetti et al. (IEEE TBME 2013) proposed a failure detection method (FDM) for their detection overnight, exploiting simultaneously information of insulin pump and CGM sensor. The aim of this work is to assess the usability of FDM to night & day, in which meals presence makes failures detection more challenging.

Methods: Transient CGM failures such as spikes and compression artifacts of different amplitudes were simulated for 100 virtual subjects with the UVA/Padova Type-1 Diabetes Simulator 2013 release (Dalla Man et al, JSDT 2013). FDM was assessed on night & day scenarios and the classifier threshold was optimized on the basis of sensitivity/specificity trade-off through the receiver operating characteristic (ROC) analysis.

Results: Simulations showed satisfactory results in terms of sensitivity and specificity, both overnight and whole-day. Even with spike amplitudes of only 10 mg/dl, FDM exhibits a sensitivity of 95% and a specificity of 99.3% with failure occurrences all day, a performance similar to that achieved overnight. Similar results were obtained in the case of pump failures

Conclusion: In *silico*, the proposed FDM exhibits a good performance, even in presence of meals. In particular, both pump and CGM failures can be detected with high sensitivity and specificity. Future work will focus on assessment on real data.

P-206

MINIMALLY INVASIVE INTERSTITIAL FLUID EXTRACTION TECHNOLOGY TO MEASURE 8-H AVERAGE GLUCOSE LEVELS DURING THE NIGHT

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Objective: We developed a glucose area under the curve (AUC) monitoring system using minimally invasive interstitial fluid extraction technology (MIET) with which we could easily obtain glucose AUC without blood sampling and calculate average glucose level by dividing AUC by the measurement time. This system is easy to handle and does not require blood sampling; thus, it helps in the measurement of glucose levels over long hours, particularly during the night. In this study, we compared MIET and continuous glucose monitoring (CGM) measurements of nocturnal 8-h average glucose levels in diabetes patients.

Methods: We evaluated 28 inpatients with diabetes who underwent CGM. MIET comprises a pretreatment step that uses a plastic microneedle array to enhance transdermal interstitial fluid glucose (IG) extraction and an accumulation step with a hydrogel patch placed on the pretreated area for 8 h. Hydrogel patches were affixed at two sites from 10 pm to 6 am. After IG extraction, accumulated glucose and sodium ion levels in the hydrogel patches were measured to calculate average glucose levels.

Results: The predicted average glucose levels by MIET correlated well with those by CGM ($r = 0.83$), which is equivalent to those during daytime ($r = 0.83$, previously reported). Mean CV of the two simultaneous measurements at different sites was 6.4%. The patient questionnaires confirmed the minimal discomfort of MIET procedure.

Conclusion: Nocturnal 8-h average glucose levels could be precisely estimated using MIET, which may contribute to wider settings of glucose management in diabetes patients, such as estimation of nocturnal hypoglycemia.

P-207

CGM SYSTEM WITH IMPROVED ACCURACY AND RELIABILITY DURING A 10-DAY WEAR

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Objective: In existing CGM systems, a continuous sensor glucose (SG) output is calculated from a single sensing signal often affected by periods of sensor instability. System accuracy and reliability can be improved by calculating this continuous SG output from redundant sensing signals with Electrochemical Impedance Spectroscopy (EIS) assisted diagnostic algorithms and calibration that evaluate individual signal performance. Redundant outputs can then be combined to deliver one superior SG output. Additional accuracy advancements can be made by incorporating sensor design improvements that favorably influence sensor hydration, localized compression effects and performance variability. Data from an ongoing Human Feasibility Clinical Trial in California were analyzed to demonstrate this advantage.

Method: Data were obtained from a clinical trial where subjects with Type 1 and Type 2 diabetes wore four sensors for 10 days. Frequent sampling testing (multi-hour time periods when blood glucose reference values were collected every 15 minutes) took place on days 1, 3 and 7. Each sensor provided multiple

glucose sensing signals within one insertion site. Data were retrospectively processed to deliver one superior SG output per sensor.

Results: Sensor design, diagnostics and algorithm improvements have positively impacted clinical results. A total of 47 sensors were analyzed. Results yielded MARD of 11.7% for the entire wear, Day 1 MARD of 12.6%, and no sensors above 20%. Study is ongoing.

Conclusion: A prototype sensor consisting of redundant sensing signals, sensor design improvements and diagnostic algorithms was developed to deliver one SG output with improvements in reliability and accuracy.

P-208

INFLUENCE OF THE STRATUM CORNEUM THICKNESS ON NON-INVASIVE GLUCOSE MEASUREMENT BY MIDDLE INFRARED PHOTOACOUSTIC SPECTROSCOPY

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The epidermal thickness of the *Stratum corneum* (Sc) theoretically is of critical influence in non-invasive glucose monitoring (NIGM) systems based on middle infrared photoacoustic spectroscopy (Mid-IR PAS).

Recently, we have developed a new photoacoustic (PA) sensor with improved properties such as low dependence on temperature, low influence of ambient noise and improved signal to noise ratio. We study the question if, while using this sensor, differences between skin regions with literature reported different thicknesses of the Sc can be found, as well as their influence on NIGM. We compared different skin regions where we performed an oral glucose test applying mid-IR PAS for NIGM.

There were remarkable differences in the spectrum which might be due to the differences in the thickness of the Sc. In a region with a Sc. thickness of around 100 μm the changes of PA measured glucose only correlated with an prediction error of up to >30 mg/dl in partial least squares (PLS) correlation. This is in contrast to a region with a thickness of around 15 μm. Here the prediction error was <12 mg/dl.

This sensor made it possible to find different MIR spectra in different skin regions with high and with low thickness of the Sc. Our data support the idea that the prediction of glucose based on the mid-IR PAS spectroscopy is influenced by the thickness of the Sc.

The new PA sensor allows to identify locations of the skin which seem to be suitable for the NIGM.

P-209

USE OF A FLUORESCENCE-BASED GLUCOSE BINDING PROTEIN (GBP) SENSOR TO TRACK GLYCEMIC EXCURSIONS IN A CANINE MODEL

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Objective: Continuous glucose monitoring has the potential to improve glycemic control in patients with diabetes. We assessed the short term performance of a subcutaneously inserted GBP sensor.

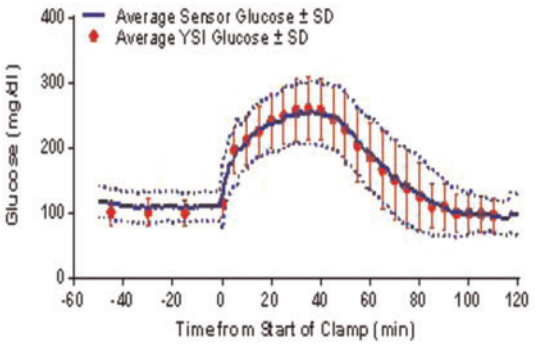
Methods: Thirty-six fluorescence based GBP sensors were used to estimate run-in time and to track hyperglycemic excursions in a non-diabetic canine model. The interstitially measured sensor signal estimates plasma glucose using the following equations:

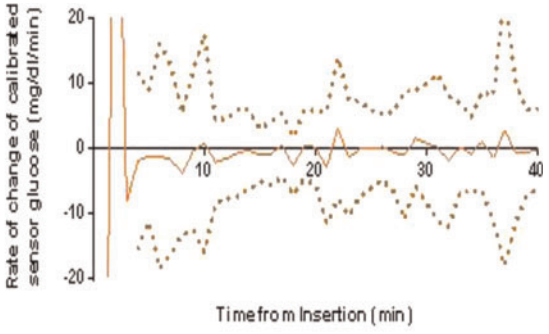
$$G_{ISF} = \frac{K_d(R_0 - R)}{R - R_{inf}} \quad , \quad G_P = \alpha\left(\tau\frac{dG_{ISF}}{dt} + G_{ISF}\right)$$

K_d is the dissociation constant of the GBP, R_0 and R_{inf} are the ratio metric signal at 0 and saturated glucose, respectively. R is the sensor ratio at the interstitial glucose concentration, G_{ISF}. α is the ratio of the steady state plasma glucose, G_P to G_{ISF}. is the first order time constant delay between G_P and G_{ISF}. Parameters $\alpha * K_d$, R_0, R_{inf} and were retrospectively identified by fitting the sensor signal to approximately twenty-six sampled plasma glucose measurements (YSI). Run-in times were estimated by the time it took for the rate of change of the calibrated glucose signal to stabilize prior to the hyperglycemic excursion.

Results: Sensors were shown to track plasma glucose well ($R^2 = 0.92 \pm 0.065$) with a time constant of $= 5.2 \pm 5.1$ min. The average run-in time following sensor insertion was less than 10 minutes.

Conclusions: Using optimal calibration, the GBP sensor follows the hyperglycemic excursions accurately with short run-in time.





P-210

USER PERFORMANCE EVALUATION OF THE CONTOUR® PLUS LINK 2.4 BLOOD GLUCOSE MONITORING SYSTEM

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Objective: To evaluate performance and ease of use of the CONTOUR® PLUS LINK 2.4 blood glucose monitoring system (BGMS) in the hands of untrained lay users with diabetes and of healthcare professionals (HCPs).

Methods: 113 lay users (mean age, 59 years) with type 1 (n = 22) or type 2 (n = 91) diabetes were enrolled. Subjects' fingertip capillary glucose was tested by subjects naive to the BGMS, and by HCPs. BGMS results were compared with YSI reference results. Accuracy was assessed using ISO 15197:2003 (≥ 95% of results within ± 15 mg/dL [0.8 mmol/L] or ± 20% of reference at glucose concentrations.

Results: 99.1% of subject fingerstick and 100% of HCP fingerstick results met ISO 15197:2003 accuracy criteria. 97.3% of subject fingerstick and 100% of HCP fingerstick results met ISO 15197:2013 Section 8 accuracy criteria. Questionnaire results showed the majority of subjects responded 'strongly agree,' 'agree,' or 'neutral' that the BGMS was easy to use (97%) and it was easy to understand the CONTOUR® PLUS LINK 2.4 results (99%).

Conclusion: The CONTOUR® PLUS LINK 2.4 BGMS, which can wirelessly communicate with new Medtronic devices, exceeded both ISO 15197:2003 and ISO 15197:2013 Section 8 accuracy criteria and demonstrated ease of use in a lay population.

P-211

DIFFERENCES BETWEEN PATIENTS WITH AND WITHOUT NOCTURNAL HYPOGLYCAEMIA DETECTED ON CONTINUOUS GLUCOSE MONITORING (CGM)

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Introduction: Hypoglycaemia remains a major barrier in the intensification of glycaemic control in people with diabetes. Nocturnal hypoglycaemia (NH) is difficult to identify on usual parameters such as HbA1c and self-monitoring of blood glucose (SMBG).

Methods: CGM (Medtronic iPro™) data from 50 subjects with diabetes mellitus (56% type 1 diabetes) with hypoglycaemia was retrospectively analysed. NH was defined as any CGM reading of < 4 mmol/L between midnight and 8 am.

Results: Duration of CGM (mean ± SD) was 82.0 ± 16.3 hours. Average glucose was 9.3 ± 1.9 mmol/L. Thirty subjects (60%) experienced NH. Fifty percent of these subjects had > 1 episode of NH and 26.7% had > 1 episode of hypoglycaemia per night. A total of 50 hypoglycaemia nights and 126 nights without hypoglycaemia were analysed.

Nadir glucose during NH was 2.9 ± 0.6 mmol/L, duration of NH was 2.9 ± 1.9 hours with NH occurring most commonly between 2–4 am (40%), followed by 4–6 am (30%). Capillary fasting following and bedtime glucose preceding NH was significantly lower compared to nights without NH [Median (IQR): 5.7 (4.5–8.6) mmol/L vs. 9.0 (7.2–13.1) mmol/L, p < 0.001; 8.2 (5.6–11.7) mmol/L vs. 9.9 (6.7–14.3) mmol/L, p = 0.032 respectively]. There was a greater rate change of glucose [(Fasting–bedtime SMBG)/hours in between] in those with NH compared to those without (− 0.33 ± 0.64 vs − 0.08 ± 0.75 mmol/L/hour, p = 0.045). No differences in HbA_{1c}, duration of diabetes and bedtime snack were found between NH and non-NH nights.

Conclusion: A lower fasting and bedtime glucose on SMBG may indicate the presence of NH. Real-time CGM sensors with improved accuracy and alarm systems are vital in alerting the patient to the presence of NH.

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INSULIN AND MEAL INFORMATION IMPROVEMENT OF GLUCOSE PREDICTION BY A NEURAL NETWORK

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Objective: Exploiting information on insulin and meal may improve accuracy of on-line short-term glucose prediction based on CGM data. A quantification of this potential improvement is missing in the literature. In this work we compare the performance of four neural network (NN) predictors exploiting different input combinations (NN_I + M using CGM, insulin and meal; NN_I using CGM and insulin; NN_M using CGM and meal; and NN_CGM using CGM) for prediction horizons (PH) ranging from 15 to 60 min.

Method: The NN were optimized and tested on data of 15 type 1 diabetic subjects (3-day monitoring, Dexcom Seven Plus sensor). Meal and insulin information was recorded manually and pre-processed before entering the NN algorithm using the physiological model of (Dalla Man et al, Trans Biomed Eng, 2006). Accuracy is assessed by Mean Absolute Error (MAE).

Result: For PHs longer than 15 min, NN_I + M and NN_M perform significantly better (statistical sign-test), in terms of MAE, than the other models during the 2 h following meals and relative insulin injections (see Table 1).

The benefit of using insulin and meal information is no longer visible if MAE is computed globally, on the entire recording of days.

Conclusion: When PHs of at least 30 min are considered, adding insulin and meal information to CGM history improves prediction accuracy, but only during the 2 h following insulin injections and meals.

PH	NN_I+M	NN_I	NN_M	NN_CGM
15min	14.1±7.7	14.4±6.6	13.5±7.0	14.3±7.2
30min	27.6±13.9	29.9±12.3	28.6±14.1	30.7±14.5
45min	40.2±18.8	45.8±18.6	44.2±20.3	45.9±19.3
60min	51.3±24.4	60.8±25.2	55.9±25.0	60.5±25.4

Table 1. MAE [mg/dl] during the 2h following meal and relative insulin injection.

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SHORT-TERM INTERVAL PREDICTION OF GLUCOSE WITH PROBABILISTIC MODELS

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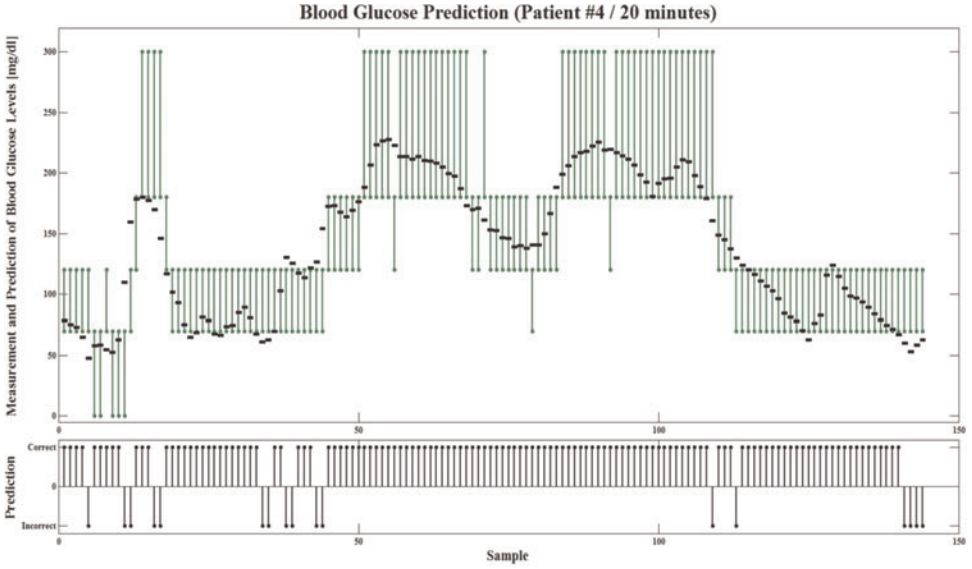

Fig 1: Predicted intervals (green) in top panel, correct/incorrect predictions after evaluation algorithm in bottom panel

Prediction of future glucose using continuous glucose monitoring (CGM) data is an active area of research and many predictors have been proposed. An inherent difficulty is the high variability associated with unknown or immeasurable influence factors. The approach proposed here utilizes Gaussian mixture models to predict a range of future glucose levels, taking into consideration their specific probability distribution.

Method: 7 days of CGM data from 12 patients (Freckman et al., Journal of Diabetes Science and Technology 7(4), pp.842–853) were analyzed. First 6 days were used for model training and the remaining one for validation. The predicted range depended on the preceeding glucose value and the glucose values measured 12 and 24 hours ago (ascertained through periodicity analysis). The prediction ranges were < 70 mg/dl, 70—120 mg/dl, 120—180 mg/dl, 180—300 mg/dl and > 300 mg/dl.

Results: 10, 20 and 30-minute predictions were calculated. Exemplary, for the patient #4 93% of the 10-minute, 88% of the 20-minute and 76.4% of the 30-minute predictions were correct (Fig. 1 shows the 20-minute prediction).

Conclusion: The high percentage of correct predictions shows the efficiency of the proposed algorithm. Prediction of ranges rather than specific values might reduce the risk of patients being hastily or inadequately medicated with insulin.

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BLOOD GLUCOSE REGULATION IN DIABETIC GÖTTINGEN MINIPIGS BASED ON A NEW SWITCHING HYBRID CONTROL METHOD

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Objective: The focus of the project is the development of an automatic insulin therapy system which can be applied to type 1 diabetes patients. Here, a new control method is evolved and individualised controller are tested under realistic conditions by means of closed-loop animal trials with diabetic Göttingen minipigs.

Methods: The new hybrid control method switches between two operation modes. Insulin boli are injected during the day, and at night, the insulin basal rate is re-adjusted. As a basic control law, a robust PI-controller is used. The required control performance is to stabilise the blood glucose concentration at 130 mg/dl while avoiding critical blood glucose drops and reducing meal-induced blood glucose rises as fast as possible. In the absence of a continuously measuring blood glucose sensor, blood samples have to be drawn manually for glucose measurements by means of a blood gas analyser. Individualised controller were applied to the minipigs for 48 h including two feeding times per day.

Results: In total, seven closed-loop trials could be successfully performed with two diabetic Göttingen minipigs. During the trials, two critical blood glucose drops occurred which were counteracted by 'emergency' food, and the meal-induced blood glucose peaks could be rapidly antagonised by the controller. For comparison, one critical blood glucose drop occurred during two manually performed therapy trials with the same minipigs according to a standard protocol.

Conclusion: The experimentally evaluated switching hybrid controller stabilised the blood glucose concentration in a diabetic acceptable range of 70–180 mg/dl despite several physiological and technical limitations.

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HYPOGLYCEMIA PREDICTION BASED ON EXTENDED KALMAN FILTER USING A PHYSIOLOGICAL MODEL OF GLUCOSE REGULATION

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Objective: Real-time continuous glucose monitoring (CGM) is a valuable tool for hypoglycemia detection and prevention. However, the high inaccuracy of commercially available CGM sensors diminished its potential. This work proposes a novel hypoglycemia prediction algorithm and validates it in an *in silico* environment.

Method: An Extended Kalman Filter (EKF) using a validated metabolic model of the glucose regulation was employed for filtering noisy CGM measurements and estimating the model states. Glucose levels were then forecasted using the aforementioned model. The UVa-Padova simulator (adult population) was used to evaluate the performance of the proposed algorithm. A 60-minute prediction window, a hypoglycemic threshold of 60 mg/dl and a 1-week scenario were selected for this purpose. A robustness analysis was performed to test the influence of insulin sensitivity (IS) variability (±20%) and uncertainty on carbohydrate (CHO intake (±30%).

Result: The EKF significantly improved the mean absolute relative difference of the CGM measurement with respect to reference plasma glucose (12.8% vs. 8.3%). The results corresponding to the hypoglycemia prediction algorithm are summarized below.

Conclusion: EKF using a validated metabolic model of the glucose regulation is a valid approach for denoising CGM measurements. The proposed EKF-based hypoglycaemia prediction algorithm showed good sensitivity, precision and robustness in a simulation environment.

	TP	FP	FN	Sensitivity (%)	Precision (%)	Lead-Time (min)
No Uncertainty	82	0	14	85.4	100	48.5
+20% IS	95	0	1	98.9	100	48.5
−20% IS	65	5	31	67.7	92.8	38.1
+30% CHO	74	1	22	77.1	98.6	43.4
−30% CHO	89	2	7	92.7	97.8	60

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EFFECT OF THE INSUPAD DEVICE ON POST MEAL GLUCOSE AND INSULIN LEVELS WITH DELAYED INSULIN INJECTIONS

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The InsuPad device is intended for use by diabetic subjects using rapid acting insulin analogs for meal time bolus injections. The device applies local controlled heat to the skin in the vicinity of the injection site which promotes local blood perfusion and enables faster absorption of the injected insulin. In this study we tested the effect of the InsuPad on post meal glucose and Insulin levels when insulin was injected 30 minutes post meal compared to pre-meal insulin bolus injection.

Type 2 diabetic subjects on basal bolus insulin therapy were admitted after overnight fast for a meal tolerance test. Subjects consumed standardized liquid meals. The study was conducted twice: with the InsuPad device (0.2 IU/kg injected 30 min post meal; Test) and without the InsuPad device (0.2 IU/kg injected before meal; Control). The aim of the study was to show non-inferiority of post meal glucose levels of Test compared to Control.

15 type 2 diabetic subjects participated in the study (4 females), aged 58.4±6.8 years, HbA1c of 8.6±1.1, BMI of 28.2±4.7 kg/m^2.

Mean maximum glucose excursion was lower when the InsuPad device was used (129±15 mg/dl vs. 142±15 mg/dl $p=0.013$) as was the Area under the curve of the glucose excursion during five hours post meal (54±9 mg/dl vs. 70±9 mg/dl $p=0.017$). The Insulin time profiles showed compatible pattern to the glucose profiles.

Using the InsuPad device can enable more flexiblity of injection time which can have benefit in subjects with unpredictable eating patterns.

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TRIGGER MATTERS: AN ERGONOMY ANALYSIS OF THE CURRENTLY AVAILABLE INSULIN PENS

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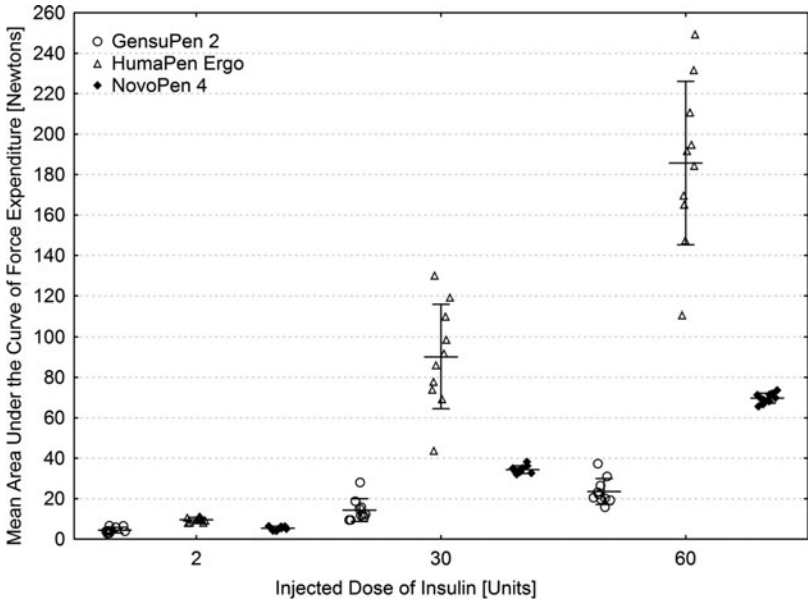
Excessive force required deliver a set dose of insulin may result in bending/breakage of the injector's needle. The GensuPen2 (Copernicus/Bioton, Warsaw, Poland) pen has a unique spring-assisted delivery system and a lateral trigger device for injection of insulin to improve its ergonomy.

Aim: We tested the force required to administer insulin using three most frequently used pen injectors in Poland: GensuPen2, NovoPen4 (Novo Nordisk, Bagsværd, Denmark) and HumaPen-Ergo (Eli Lilly, Indianapolis, USA).

Methods: Using a certified dynamometer DMP1 (JBA Zb. Staniak, Poland) we tested injection force at three doses of insulin: 2, 30 and 60 IU, using each of the three injectors (N=10) in triplicate. Area under the curve (AUC) and maximum force used were calculated for each series of injections.

Results: When administering doses of 2, 30 and 60 units of insulin the GensuPen2 (6.55±1.09,6.52±1.92 and 6.89±1.15 N respectively) required significantly lower maximum force than NovoPen4 (9.04±0.61, 12.96±1.45, 15.42±0.99 N) and HumaPen Ergo (17.66±1.88, 32.14±6.08, 40.39±7.64 N; all $p<0.0001$). The maximum force used for insulin injection with GensuPen2 did not differ significantly depending on the administered dose ($p=0.82$). In all cases, GensuPen2 required significantly lower values than the other two injectors (figure 1). Moreover, the mode of holding of Gensupen2 was more similar to the natural arrangement of the hand while gripping a cylindric item in comparison to NovoPen and HumaPen.

Conclusions: Usage of the GensuPen2 injector with a lateral trigger location and spring-assisted delivery system vastly reduces the force required for drug administration especially considering high doses of insulin.



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LOWER SHORT-TERM HEALTHCARE COST WITH AN AUTOMATED BOLUS ADVISOR IN MDI TREATED DIABETES PATIENTS: LEARNINGS FROM THE ABACUS STUDY

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Objectives: The Automated Bolus Advisor Control and Usability Study (ABACUS) assessed the impact of using the automated insulin bolus advisor within the Accu-Chek Aviva Expert system in combination with intensive diabetes therapy on glycemic control in patients treated with Multiple Daily Insulin Injection (MDI) therapy. We assessed the potential incremental economic impact of using this device on the short-term healthcare costs (SHC).

Methods: The economic analysis was performed with a spreadsheet-model from a UK (£) and Germany (€) payer's direct cost perspective and based on ABACUS outcomes. Correlations between HbA1c change and expected cost are based on published literature. Model outputs include expected impact on SHC and sensitivity analysis.

Results: 56% of intervention (EXP) patients and 34% of control (CNL) patients achieved the goal, which led to an average 1.2% HbA1c reduction among all achievers. There was no clinically relevant HbA1c effect in non-achievers. Goal achievement correlates with an expected reduction in SHC of £189/€265 per person/per year (PPY). The expected SHC reduction is £104/€146 PPY in the EXP and £74/€104 PPY in the CNL. The goal-achievement-rate increased by 63%, driving a comparative economic benefit of £30/€42 PPY for automated bolus advisor use. No significant differences in complications or intervention cost were observed.

Conclusions: Use of the Accu-Chek Aviva Expert system leads to a 63% higher rate of goal achievement in MDI-treated diabetes patients tested, leading to an expected incremental reduction in SHC of £30/€42 PPY, thereby improving the cost-effectiveness of self-monitoring of blood glucose in this study population.

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PHARMACOKINETIC ANALYSIS OF 3 DAY INTRADERMAL VERSUS SUBCUTANEOUS INSULIN INFUSION: A COMPARISON OF ONE ROUTE VERSUS TWO ROUTE TRANSPORT MODELS

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Objective: Intradermal (ID) insulin delivery results in faster pharmacokinetics (PK) than subcutaneous (SC) delivery. This study looked to characterize and compare PK using plasma insulin profiles obtained during routine pump therapy.

Methods: Four different PK models were fit to ID and SC insulin-aspart profiles obtained in 24 adults with type 1 diabetes studied over 3 consecutive days (SC and ID delivery; random order). Model A assumed insulin appeared in plasma via 2 parallel 2-compartment paths (hypothesized as lymph and capillary). Model B assumed a single path consisting of 3 compartments (including plasma); Model C was identical to B but with first two rate constants constrained equal; Model D

Model	#Unique Params.	ID		SC	
		SSE (uU/ml)²	p	SSE (uU/ml)²	p
A	5	89	**0.0057**	196	0.20
B	4	168	N/A	221	**0.03**
C	3	353	N/A	309	N/A
D	3	267		516	

P value refers to significance v next row using the F-test. Once a p value of less than 0.05 is found, the model on that row is assigned as the most appropriate eliminating the need for subsequent tests.

consisted of 2 compartments. The optimal model was selected using F-Tests comparing Sum Squared Error (SSE) of two models to determine the significance of higher order model. Time to maximum (T_{MAX}) and maximum concentration (C_{MAX}) were obtained from the optimal model simulating a single bolus.

Results: With ID delivery, Model A was significantly better at describing plasma insulin kinetics than Model B (table), with 30 ± 15% of insulin estimated to appear in plasma via the faster path. The two path model was not necessary to describe SC delivery with Model B being optimal. ID delivery had a faster kinetics with a lower T_{MAX} (29 ± 11 v. 47 ± 16 min) and higher C_{MAX} (57 ± 48 v 48 ± 40 uU/ml) as compared to ID delivery.

Conclusions: Different models are needed to adequately describe ID and SC delivery. ID delivery requires a two path model and has more rapid appearance.

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APPLES VERSUS ORANGES? COMPARISON OF PEOPLE WITH TYPE 1 AND TYPE 2 DIABETES ON MDI THERAPY: RESULTS FROM ABACUS

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Aims: Intensive glycemic management is recommended for type 1 and type 2 diabetes, however, confusion abounds regarding the differences between these patient groups, particularly among those using multiple daily insulin injections (MDI). We compared characteristics of people with type 1 and type 2 diabetes.

Methods: We used baseline data from people with type 1 and type 2 diabetes from the Automated Bolus Advisor Control and Usability Study (ABACUS), a large, 26-week, prospective, randomized, controlled, multi-national study that enrolled 218 suboptimally controlled MDI-treated people with diabetes (202 type 1, 16 type 2). People with type 2 were matched with those

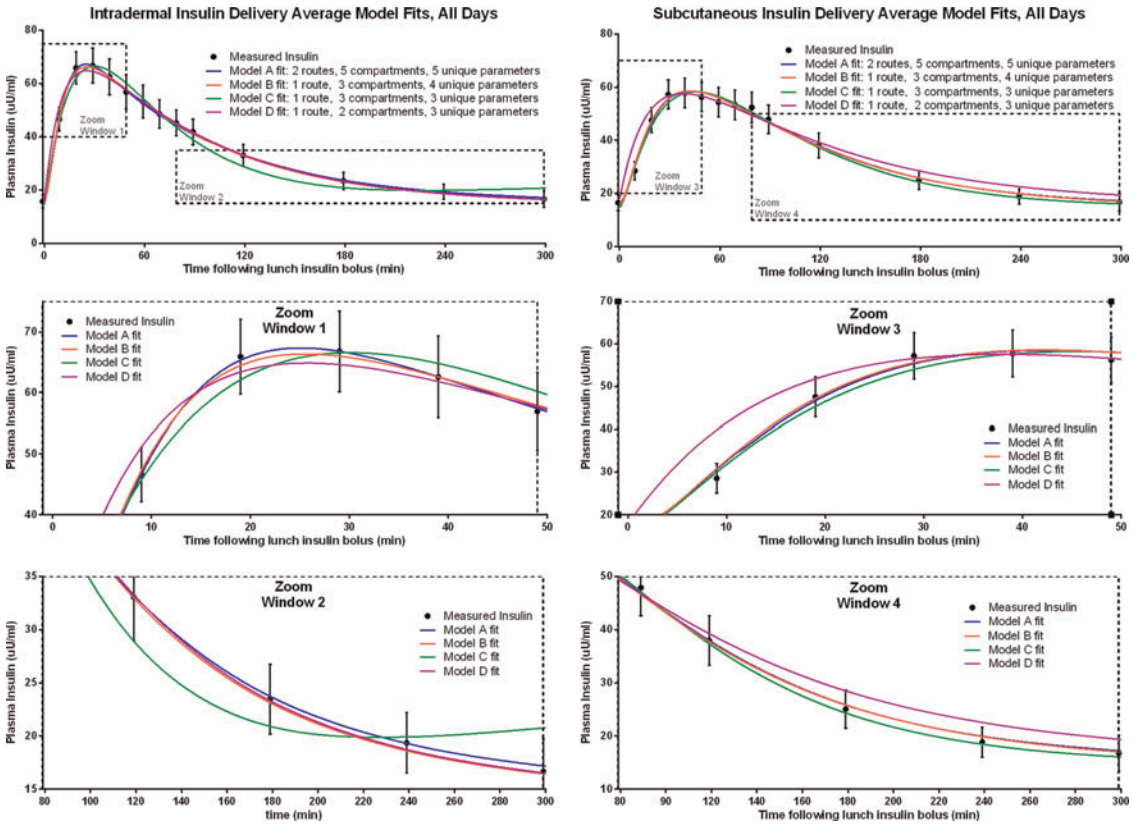

Table. Characteristics of people with type 1 and 2 diabetes in the ABACUS Study

Characteristic	Type 1 (n=16)	Type 2 (n=16)	p value
Male	13	13	NS
Age (yrs)	55.2 (9.9)	59.1 (10.2)	p<0.01
BMI	26.8 (3.8)	29.8 (3.8)	NS
HbA1c %	8.69 (0.63)	8.67 (0.66)	NS
Duration of Diabetes (yrs)	21.7 (10.0)	17.9 (8.1)	p<0.05
Time from MDI start (yrs)	16.9 (10.4)	8.28 (5.82)	p<0.01
Total daily basal dose [IU]	30.6 (16.4)	37.0 (22.6)	NS
Total daily bolus dose [IU]	31.1 (13.6)	41.8 (21.3)	NS
Average # of boluses/day	3.75 (0.93)	3.31 (0.60)	NS
Average # of SMBG/day	4.75 (1.18)	3.75 (1.39)	NS

with type 1 diabetes for this analysis. Ranked scores for gender, age, HbA1c, diabetes duration, and PHQ severity score were used.

Results: People with type 2 diabetes were older, with a shorter duration of diagnosed diabetes, and significantly shorter duration of MDI than their type 1 pairs, however, MDI knowledge and behaviors were similar in both groups. **(Table)** Psychosocial assessment revealed a trend towards higher PHQ severity scores but no differences in problem areas in diabetes (PAID) or EQ-5D, a general health measure.

Conclusions: Healthcare providers and payers should provide similar healthcare benefits and education to both patient groups.

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QUALITY OF CARE AND HEALTH ATTITUDES IN MDI-TREATED PEOPLE WITH DIABETES CAN VARY BY COUNTRY: RESULTS FROM ABACUS

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Aims: We examined differences in diabetes care and patient perceptions between the UK and Germany in a sub-analysis of the Automated Bolus Advisor Control and Usability Study (ABACUS).

Methods: ABACUS, a large prospective, randomized study of 218 MDI-treated people with type 1 (n = 202) and type 2 (n = 16) diabetes with suboptimal diabetes control, assessed the impact of using the Accu-Chek® Aviva Expert blood glucose meter, which provides an integrated automated bolus advisor to calculate insulin dosages, compared with standard meter use. Patients from the UK (n = 124) and Germany (n = 94) participated in the study. Changes in glycemic and psychosocial status were assessed. Measures included the Diabetes Treatment Satisfaction Questionnaire (DTSQ) and EuroQoL Health Status Index (EQ-5D-5L).

Table. Mean (SD) between-country differences at baseline

	UK (n=124)	Germany (n=94)	P-Value
HbA1c			
Baseline HbA1c (%)	9.1 (1.3)	8.6 (1.0)	<0.01
HbA1c Change at Study End (%)	-0.6 (0.7)	-0.5 (0.7)	NS
Diabetes Management			
Diabetes Duration (yrs)	19.2 (11.6)	15.7 (10.0)	<0.05
Duration of MDI Therapy (yrs)	9.8 (8.3)	13.0 (9.0)	<0.01
Insulin Boluses (per day)	3.2 (0.7)	3.9 (1.0)	<0.01
SMBG Frequency (per day)	3.9 (1.5)	4.9 (1.3)	<0.01
Parameters Changed			
Lower Target Range (%/pts)	19.8	5.3	<0.05
Upper Target Range (%/pts)	15.4	1.3	<0.01
I:CHO (%/pts)	39.0	13.0	<0.01
Psychosocial Measures			
Mean total DTSQ status score	29.1 (5.9)	26.5 (6.2)	<0.01
Mean EQ-5D-5L index value	0.82 (0.21)	0.93 (0.10)	<0.01

Results: Between-country differences were seen in diabetes management and patient perceptions. (**Table**) UK patients were significantly more satisfied with their treatment than German patients at baseline. However, UK patients perceived themselves to be in poorer health.

Conclusions: Despite the geographic proximity and cultural similarities, our findings suggest that country differences may influence key aspects of clinical care, which can potentially impact outcomes. Although UK patients perceived their health to be worse than German patients, they were more satisfied with their diabetes treatment.

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LESSONS LEARNED FROM ABACUS: HEALTHCARE PROFESSIONAL PERSPECTIVES

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Aims: We explored the experiences of investigators in the Automated Bolus Advisor Control and Usability Study (ABACUS) who used the Accu-Chek® Aviva Expert blood glucose meter with study patients.

Methods: Two focus groups were conducted by a health psychologist and diabetes clinician, using guided questions and open discussion.

Results: 15 UK and 10 German investigators participated: 13 diabetes specialist nurses and educators; 7 research nurses; and 5

Table. Summary of key findings from investigator focus groups*

		Yes	No
Used the Accu-Chek Aviva Expert system prior to the study.	UK	8	7
	Germany	6	3
	TOTAL	**14**	**10**
Routinely use the Accu-Chek Aviva Expert system after study completion	UK	9	6
	Germany	8	1
	TOTAL	**17**	**7**
MDI/CHO assessment process was different than assessment used prior to study.	UK	7	8
	Germany	8	2
	TOTAL	**15**	**10**
Structured MDI/CHO knowledge assessments were helpful.	UK	14	1
	Germany	7	3
	TOTAL	**21**	**4**
More likely to make a parameter change in patients using the Accu-Chek Aviva Expert system than those using manual calculations.	UK	8	7
	Germany	5	5
	TOTAL	**13**	**12**
Routinely used downloaded SMBG** data for MDI patients prior to the study.	UK	3	12
	Germany	10	0
	TOTAL	**13**	**12**
Currently use downloaded SMBG** data in MDI patient consultations.	UK	10	5
	Germany	10	1
	TOTAL	**20**	**6**
The Accu-Chek Aviva Expert system data was more useful than SMBG** data, alone.	UK	11	4
	Germany	5	5
	TOTAL	**16**	**9**

*Some questions were answered only by clinicians who directly provide patient care.
**SMBG=self-monitoring of blood glucose

diabetologists. Most clinicians continue bolus advisor use. (Table) Reasons for continued use include: helps achieve better blood glucose control during pregnancy; facilitates transition to insulin pump therapy; addresses problems with hypoglycemia and carbohydrate/bolus calculation; downloaded data facilitates easy interpretation of glycemic control; greater patient motivation; more personal consultations, enhanced communication; and provides greater precision, and facilitating better data analysis to support clinical practice. UK clinicians reported that all intervention patients who completed the study continue to use the bolus advisor; all control patients are now using the bolus advisor (German data not captured).

Conclusions: Clinicians reported that participation in the ABACUS trial was a positive experience and identified several benefits of the Accu-Chek Aviva Expert blood glucose meter use, all of which can enhance both clinical outcomes and patient quality of life.

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AUTOMATED BOLUS ADVISOR USE BESTOWS GLYCEMIC BENEFITS TO MDI-TREATED PEOPLE WITH DIABETES IN REAL-WORLD SETTINGS: FOLLOW-UP RESULTS FROM ABACUS

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Aims: The Automated Bolus Advisor Control and Usability Study (ABACUS), a randomized, multi-center, 26-week trial, assessed the use of a blood glucose meter with an integrated automated bolus advisor (EXP) compared with standard meter use (CNL) on glycemic status in sub-optimally controlled subjects treated with multiple daily insulin injections (MDI). More EXP than CNL subjects achieved >0.5% HbA1c reductions: 56.0% vs. 34.4%, $p<0.01$. CNL subjects were offered the bolus advisor at study end. We assessed changes in HbA1c levels among CNL and EXP subjects who used the bolus advisor for 6 months following the ABACUS trial.

Methods: 193 subjects (CNL, n=93; EXP, n=100) completed the ABACUS trial. Data from 147 (76.1%) subjects were available for this analysis: CNL, 69(74.2%); EXP, 78(78.0%). Of these, 43(62.3%) CNL subjects initiated use and 64(82.0%) EXP subjects continued bolus advisor use for 6 months. Changes in HbA1c at the 6-month follow-up were assessed.

Results: At 6 months, mean (SD) HbA1c increased in both CNL and EXP subjects: 0.35(0.59)% vs. 0.47(0.71)%, $p<0.01$, respectively, with no between-group differences. However, EXP bolus advisor users experienced smaller increases in HbA1c than EXP non-users: 0.46(0.69)% vs. 0.60(0.90)%, $p=0.04$. There was a trend toward smaller HbA1c increases among CNL users than CNL non-users: 0.27(0.64)% vs. 0.57(0.58)%, p=NS, respectively.

Conclusions: Automated bolus advisor use bestows glycemic benefits in MDI-treated diabetes patients. The smaller increases seen in HbA1c for bolus advisor users compared to non-users, suggests that automated bolus advisor use may help MDI-treated patients with diabetes management under real world conditions.

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IMPACT OF AUTOMATED BOLUS ADVISOR USE ON TIMING/FREQUENCY OF INSULIN PARAMETER CHANGES IN MDI THERAPY: RESULTS FROM ABACUS

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Aims: Because calculating insulin dosages is challenging for most people with diabetes on multiple daily insulin injection

(MDI) therapy, clinicians may be reluctant to change therapy parameters when needed. We assessed the frequency of insulin parameter adjustments made during the Automated Bolus Advisor Control and Usability Study (ABACUS).

Methods: ABACUS was a large prospective, 26-week, randomized, multi-national study of 218 MDI-treated people with type 1 and type 2 diabetes with suboptimal diabetes control. Patients randomized to the control group (CNL) used a standard blood glucose meter and manual bolus calculation; patients randomized to the intervention group (EXP) used the Accu-Chek® Aviva Expert blood glucose meter, which provides an integrated automated bolus advisor to calculate insulin dosages.

Results: More EXP than CNL patients achieved the study goal of >0.5% HbA1c reduction (56 vs. 34%, $p<0.01$). Clinicians changed insulin sensitivity factor (ISF) settings in more EXP than CNL patients at Week 4 (24.5% vs. 10.8%, $p<0.05$) and Week 12 (29.3% vs. 8,6%, $p<0.01$). More EXP than CNL patients received additional ISF settings per day at all visits ($p<0.05$). The number of ISF and insulin-to-carbohydrate (I:CHO) settings increased longitudinally from baseline to study end in EXP but not CNL patients (both $p<0.05$).

Conclusions: Use of the automated bolus advisor led to earlier, more frequent therapy parameter changes in EXP patients. These changes may have contributed to the enhanced ability of EXP patients to achieve the study goal by reducing patient burden and improving HCP confidence in the patients' ability to implement change.

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CONTROLLED WARMING OF THE INJECION SITE ENHANCES INSULIN ABSORPTION - RESULTS FROM A REAL WORLD STUDY WITH THE INSUPAD DEVICE

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The InsuPad device enhances insulin absorption by standardized warming of the injection site. Primary study objective was to investigate the impact of InsuPad on prandial insulin analog dose and glycemic control.

Material and Methods: This study was performed with 145 patients (51 female, 94 male, 13 type 1 and 132 type 2 patients, age: 61.6±8.4 yrs., body weight: 105.7±18.6 kg) on multiple daily injections with insulin glargine and a short acting insulin analog. Patients were randomized to continue therapy for three months without (Control, n=72) or with InsuPad (n=73 patients). Observation parameters included HbA1c, insulin dose, and frequency of hypoglycemia.

Results: HbA1c decreased from 6.8±0.5% in both arms to 6.3±0.5% until study end (both $p<0.001$ vs. baseline). Patients in the control group needed 8% more prandial insulin (from 66±32 U to 71±38 U, $p<0.05$). Patients in the InsuPad group required less prandial insulin (−19%, 70±43 U to 55±34 U, $p<0.001$). No difference was seen in basal insulin dose. The number of hypoglycemic events (blood glucose readings <63 mg/dL) during the observation period was significantly higher in the control group (6.2±9.9/patient) than in the InsuPad group (3.4±4.9/patient, $p<0.05$).

Conclusion: When treating patients to target with intensified insulin therapy, InsuPad reduced the frequency of hypoglycemic events and prandial insulin dose as compared to a control group. InsuPad may allow to achieve treatment targets with a safer and more efficient insulin therapy in insulin-treated patients with type 1 and type 2 diabetes.

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IMPACT OF USING OF THE INSUPAD DEVICE ON TREATMENT SATISFACTION AND DIABETES RELATED DISTRESS

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The InsuPad is intended for accelerating insulin absorbtion after administration by standardized skin warming. Here we report on the impact of InsuPad use on treatment satisfaction and diabetes related distress during three month of device daily use.

A total of 145 insulin-resistant diabetic patients (91% type 2) on an intensive insulin regimen (51 female, 94 male, age: 61.6±8.4 yrs., disease duration: 16.6±7.2 yrs., HbA1c: 6.8±0.5%, daily insulin dose:1.2±0.6 U/kg) were randomized either to use the InsuPad or a control group (no InsuPad use). At endpoint, the Diabetes Treatment Satisfaction Questionnaire (DTSQ) and the Problem Areas in Diabetes (PAID) questionnaire were completed.

The InsuPad group reduced prandial insulin demand by 28% compared to the control group while achieving an equivalent glycaemic control with 46% less hypoglycemic episodes. Overall diabetes treatment satisfaction was highly comparable between intervention (29.1±6.7) and control group (29.6±6.6; $p=.720$; post-hoc power 1-ß=0.82). Diabetes related distress was highly comparable in the intervention and the control group (19.3±14.5 vs. 18.8±18.9, $p=0.85$, power 1-ß=0.85). One third of the intervention group (34.3%) reported less injection related pain while using the InsuPad.

The use of InsuPad requires an additional effort for patients (overnight recharging of the InsuPad, adhering the device to the body, switching on the InsuPad prior to injection). The analysis of patient reported outcomes, however, did not indicate any negative impact of the InsuPad use on treatment satisfaction nor on diabetes related distress.

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CLINICAL EVALUATION OF DUO, A COMBINED INSULIN INFUSION/GLUCOSE SENSING DEVICE

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Background: Sensor-augmented pump (SAP) therapy typically requires separate procedures and anatomic locations for insertion of the sensor and insulin infusion catheter. Duo is a combined infusion set and glucose sensor intended to simplify device insertion and site management.

Design and Methods: This was a multi-center, non-randomized, interventional study of Duo used with the Veo insulin pump. Forty-five subjects with type 1 diabetes and previous use of SAP (mean ± SD age, 45.5 ± 10.9 years, 48% female) participated for 15 days. Each subject was to wear 5 devices over 15 days and test capillary blood glucose 7 times per day. The primary endpoint was the percentage of sensor-SMBG paired points within 20%. Investigator and subject experiences were assessed via questionnaires.

Results: Overall, 74.81% of the sensor-SMBG paired points were within 20% of one another, meeting the primary endpoint. Consensus and Clarke error grid analysis showed that >90% of points were within the A + B zones, exceeding the clinical accuracy threshold. The mean ARD was 15.5 ± 17.1%. The functional survival of the device entering day 3 was 90.5%. There were no device complaints/deficiencies assessed to potentially result in a serious adverse device effect-related event. There were no reported deaths, serious adverse events, or unanticipated adverse device effects during the study. Questionnaire results indicated overall satisfaction with the device.

Conclusion: Duo provides CGM sensing and insulin infusion in a single device, which is safe to wear, acceptable to patients, and provides accurate glucose readings. It is projected to improve satisfaction and convenience for patients on SAP therapy.

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INVESTIGATIONAL NEW INSULIN GLARGINE U300 HAS A FLAT AND PROLONGED STEADY STATE PROFILE

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Aims: Investigational new insulin glargine U300 (Gla-300; 300 $U.mL^{-1}$) has a prolonged duration of action and even flatter PK/PD profiles vs insulin glargine 100 $U.mL^{-1}$ (Gla-100) at single subcutaneous doses. We investigated how these characteristics transfer into steady state.

Methods: This randomised, double-blind, 2x2 crossover study in participants with T1DM compared PK/PD properties and safety of once-daily Gla-300 (0.4 $U.kg^{-1}$ [n = 18] and 0.6 $U.kg^{-1}$ [n = 12]) with 0.4 $U.kg^{-1}$ Gla-100. The 8-day treatment regimen was administered with an automated euglycaemic clamp over 36 h after the last injection.

Results: At steady state, mean, smoothed, body weight standardised glucose infusion rate (GIR) of Gla-300 0.4 $U.kg^{-1}$ showed a stable, plateau-like profile over 24 h post-dosing, and a slow decline beyond, with activity until clamp end. Maximum GIR and individual fluctuations were lower, and euglycaemia (blood glucose [BG] ≤ 105 $mg.dL^{-1}$) maintained for longer with Gla-300 0.4 $U.kg^{-1}$ vs Gla-100 (mean end of activity ~32 h and 29 h after last dosing). Gla-300 0.6 $U.kg^{-1}$ showed greater and longer activity (~34 h) with a higher GIR than the lower dose while maintaining the flat GIR profile. Serum insulin glargine concentrations showed an even flatter, more stable profile with Gla-300 vs Gla-100. Gla-300 exposure increased with dose, and was quantifiable until 32 h and 36 h with 0.4 and 0.6 $U.kg^{-1}$ Gla-300, and 28 h with Gla-100. Treatments were well tolerated.

Conclusion: In participants with T1DM, at steady state, Gla-300 confers even flatter and more stable PK and PD profiles with longer and tighter BG control than Gla-100.

Study sponsored by Sanofi (NCT01349855).

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INVESTIGATIONAL NEW INSULIN GLARGINE U300: GLYCAEMIC CONTROL AND HYPOGLYCAEMIA IN TYPE 2 DIABETES USING A MEALTIME+BASAL INSULIN REGIMEN (EDITION I)

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Aims: Investigational new insulin glargine U300 (Gla-300, 300 U/mL) has even flatter and more prolonged PK and PD profiles than insulin glargine 100 U/mL (Gla-100). EDITION I compared efficacy and safety of Gla-300 vs Gla-100 in T2DM using mealtime + basal insulin.

Methods: In this multicentre, open-label, phase 3a, 6-month study, 807 participants were randomised (1:1) to Gla-300 or Gla-100 once daily in the evening. Primary endpoint was change in HbA_{1c}, baseline to 6 months; first main secondary efficacy endpoint was participants (%) with ≥ 1 severe or confirmed (≤ 3.9 mmol/l) nocturnal (0000–0559 h) hypoglycaemia (months 3–6).

Results: Gla-300 was non-inferior to Gla-100 for change in HbA_{1c} (LS mean change −0.83 [SE 0.06] % in both groups at 6 months; difference −0.00 [95% CI: −0.11–0.11] %). Significantly fewer participants experienced severe or confirmed nocturnal hypoglycaemia (months 3–6) with Gla-300 compared with Gla-100 (146 [36.1%] vs 184 [46.0%]; RR 0.79 [95% CI: 0.67–0.93]; p = 0.0045). A similar and consistent reduction was observed during the first 8 weeks (26.2% vs 33.3%; RR 0.79 [95%CI: 0.64–0.98]) and over the 6-month treatment period (44.6% vs 57.5%; RR 0.78 [95%CI: 0.68–0.89]). Over the 6-month treatment period the rate of severe or confirmed nocturnal events was lower with Gla-300 than with Gla-100 (3.13 vs 4.20 events/person-yr), and the rates of daytime (0600–2359 h) events were similar (22.4 vs 22.6 events/person-yr).

Conclusion: Gla-300 provides similar effective glycaemic control with less confirmed or severe nocturnal hypoglycaemia, compared with Gla-100.

Study sponsored by Sanofi (NCT01499082).

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EFFECTS OF METFORMIN AND SULFONYLUREA ON EFFICACY AND HYPOGLYCAEMIA WHEN ADDED TO GLARGINE OR NPH INSULIN IN TYPE 2 DIABETES

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Aim: To compare efficacy and safety outcomes with glargine or NPH in insulin-naive patients with type 2 diabetes (T2D) receiving metformin +/− sulfonylurea.

Methods: Pooled analysis of harmonised patient-level data from 3 treat-to-target (FPG < 100 mg/dL) RCTs, ≥ 24 weeks duration, evaluating glargine (at bedtime) or NPH with background sulfonylurea or metformin + sulfonylurea. HbA1c, FPG, insulin dose, weight at endpoint, and hypoglycaemia (plasma glucose < 70 mg/dL overall and nocturnal [00:01 – 05:59 AM], and severe [3rd party assistance]) were assessed.

Results: 1419 patients were analysed (Table); 51% male. Endpoint HbA1c and FPG were similar for glargine and NPH, but patients treated with metformin + sulfonylurea were more obese and more likely to achieve HbA1c < 7.0% without hypoglycaemia. Nocturnal hypoglycaemia rates were significantly lower in glargine-treated patients, irrespective of background OAD.

Conclusions: Patients with T2D on metformin + sulfonylurea had better outcomes than those on sulfonylurea alone when glargine or NPH was added, at the price of higher overall and nocturnal hypoglycaemia rates. Glargine significantly reduced nocturnal hypoglycaemia compared with NPH irrespective of concomitant OAD therapy.

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BIPHASIC INSULIN ASPART 30 VS. NPH PLUS REGULAR HUMAN INSULIN IN TYPE 2 DIABETIC PATIENTS: A COST-EFFECTIVENESS STUDY

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Objective: To compare the efficacy, safety, costs, and cost-effectiveness of biphasic insulin aspart 30 (BIAsp 30) with NPH plus regular human insulin (NPH/Reg) in patients with type 2 diabetes mellitus (T2DM).

Design: Single-center, parallel-group, randomized, clinical trial (Registration no. NCT01889095).

Participants: One hundred and seventy four T2DM patients with poorly controlled diabetes with oral medicationswere randomly assigned to trial arms and were followed up for 48 weeks. A total of 164 patients (n = 82 in BIAsp 30 arm, n = 82 in NPH/Reg) completed the trial.

Intervention: BIAsp 30 was started at an initial dose of 0.2–0.6 IU/Kgin two divided doses and was titrated according to the glycemic status of the patient. Similarly, NPH/Reg insulin was initiated at a dose of 0.2–0.6 IU/Kg with a 2:1 ratio and was subsequently titrated.

Main outcome measures: Level of glycemic control, hypoglycemic events, direct and indirect costs, cost-effectiveness, and utility scores.

Results: Forty-eight week glycemic control was comparable between the two arms (HbA1c, FPG, and PPG ANCOVA p value). 39% and 28% of BIAsp 30 and NPH/Reg arms

	Sulfonylurea		Metformin + Sulfonylurea	
	Glargine n = 426	NPH n = 455	Glargine n = 257	NPH n = 281
Age, years	58.3 (9.8)	59.4 (9.4)	55.6 (9.0)	56.7 (8.8)
BMI, kg/m^2	27.9 (3.9)	28.0 (4.0)	32.5 (4.5)	31.9 (4.8)
Diabetes duration, years	9.7 (6.7)	10.3 (6.2)	9.0 (5.8)	9.6 (5.8)
Baseline				
HbA1c, %	9.1 (1.0)	9.1 (1.0)	8.5 (0.9)	8.5 (0.9)
FPG, mg/dL	210.9 (60.1)	209.1 (59.2)	198.1 (50.5)	194.0 (47.0)
Endpoint				
HbA1c, %	7.9 (1.3)	8.0 (1.3)	7.0 (0.8)	7.0 (0.7)
FPG, mg/dL	119.3 (39.5)	120.2 (43.4)	119.1 (38.5)	117.8 (34.7)
Insulin dose, U/kg	0.4 (0.2)	0.4 (0.2)	0.5 (0.2)*	0.4 (0.2)
HbA1c < 7.0% (FPG ≤ 100 mg/dL), %				
Overall	20.0 (35.3)	20.7 (37.1)	55.0 (32.9)	52.4 (28.1)
Without overall hypoglycaemia < 70 mg/dL	8.7 (15.0)	8.8 (13.6)	11.2 (6.9)	8.8 (3.8)
Without nocturnal hypoglycaemia < 70 mg/dL	16.7 (26.5)	14.8 (24.6)	28.1* (18.7*)	20.5 (8.4)
Hypoglycaemia, adjusted event rate/patient year[a] (SE)				
Overall < 70 mg/dL[b]	5.5 (0.5)	6.4 (0.5)	9.9 (0.8)	11.7 (0.9)
Nocturnal < 70 mg/dL	0.8 (0.1)*	1.7 (0.2)	2.8 (0.3)*	4.6 (0.5)
Severe	0.06 (0.02)	0.11 (0.03)	0.08 (0.03)	0.05 (0.02)
Weight change from baseline, kg	+3.8 (3.5)*	+3.1 (3.7)	+3.0 (3.2)	+2.8 (2.9)

Data are mean (SD) unless stated.

*P < 0.05 vs. NPH. [a]Modelled considering baseline characteristics; [b]Including severe events.

attained target Hb1Ac values <7.0%. Lower frequencies of minor, major, and nocturnal hypoglycemic episodes were observed with BIAsp 30 ($p<0.05$ for all analyses). Additionally, BIAsp 30 was associated with less weight gain (ANCOVA p value), and also higher quality adjusted life years ($+0.12\pm0.05$ versus $+0.04\pm0.02$, ANCOVA p value). Total medical and non-medical costs wassignificantly lower with BIAsp 30 as compared with NPH/Reg (XXX USD vs. XXX USD, ANCOVA p value).

Conclusions: Despite being more expensive, BIAsp 30 offers comparable glycemic control as to NPH/Reg, but appears to be more cost-effectiveinIranian patients with type 2 diabetes.

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TWICE DAILY VERSUS ONCE DAILY BASAL INSULIN DOES NOT RESULT IN BETTER GLYCEMIC OUTCOMES AMONG MDI PATIENTS WITH T1D

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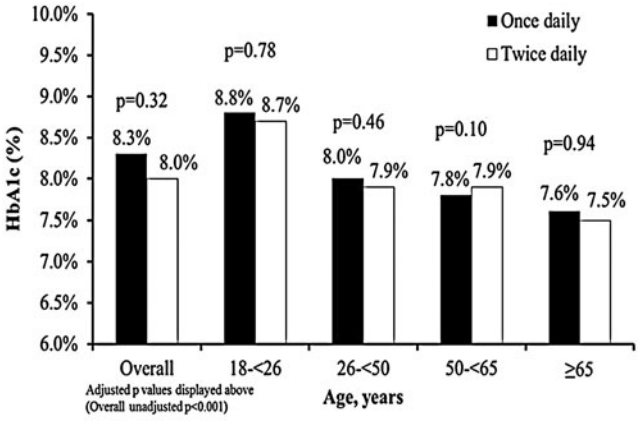
Prevailing wisdom is that twice daily basal insulin results in better glycemic outcomes than once daily. To assess this, data were analyzed from 3,925 adults with T1D duration ≥1 year enrolled in the T1D Exchange clinic registry (median age 32 yrs; T1D duration 14 yrs; 46% female, 83% white) taking either insulin glargine or detemir once daily (n = 2,819) or twice daily (n = 1,106), indicated by self-report.

Regression analyses assessed differences in HbA1c and severe hypoglycemia (SH), adjusted for age, T1D duration, race/ethnicity, education, income, and daily self-monitoring blood glucose measurements. No difference was found in most recent HbA1c (Figure). Further, there was no difference in proportion who had a SH event resulting in seizure/loss of consciousness in the past year (11% for once vs 13% for twice daily, $p=0.92$). The proportion with SH was also similar among those with HbA1c < 7% (11% for once vs 12% for twice daily, $p=0.40$). Results were similar for glargine and detemir.



Glycemic outcomes do not appear to be associated with whether basal insulin is given once or twice a day in adults with T1D. However, bias related to the decision to treat with once vs twice daily basal insulin may exist in these observational data.

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PHARMACOKINETICS OF INSULIN ASPART IN PREGNANT WOMEN WITH TYPE 1 DIABETES: EVERY DAY IS DIFFERENT

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Aim/Objective: To evaluate clinical/demographic factors affecting pharmacokinetics of insulin Aspart in type 1 diabetes (T1D) pregnancy.

Research Design and Methods: 22 pregnant women with T1D [age 32.4 years, diabetes duration 17.7 years, BMI 27.0 kg/m^2, booking HbA1c 7.1% (54 mmol/mol)], were studied over a breakfast and dinner meal on two occasions between 12–33 weeks gestation. 88 profiles (time series) of insulin concentration over a breakfast or dinner were included. Insulin Aspart was delivered by continuous subcutaneous insulin infusion (CSII). Time-to-peak plasma concentration (t_{max}), metabolic clearance rate (*MCR*), rate of accumulation (I_a) and post-prandial concentration (I_b) were calculated using a two-compartment model. The relationship between Aspart pharmacokinetics and 15 clinical/demographic factors was examined using Bayesian averaging of linear regression models. Reproducibility is measured by variance component analysis of each pharmacokinetic parameter.

Results: There was strong evidence of associations between Aspart t_{max} with physical activity, diabetes duration and pregnancy gestation. Physical activity is associated with faster post-prandial accumulation and faster t_{max}. We estimated that time-to-peak t_{max} increases with gestation by 1.6% per week, and decreases 1.1% per year of diabetes. Inter-occasion variation is high for all four pharmacokinetic parameters (t_{max} 88%; *MCR* 92%; I_a 100%; I_b 76%) and persists even after adjustment for associations with clinical and demographic factors (t_{max} 86%; MCR 85%, I_a 100%; I_b 84%).

Conclusion: CSII facilitates stable basal insulin concentration but post-prandial variability is high and changes with diabetes duration, physical activity and pregnancy gestation. Reproducibility of post-prandial pharmacokinetics within and between pregnant women is low.

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BENEFITS OF A MEDITERRANEAN-STYLE DIET ON INSULIN RESISTANCE, PLASMA LIPIDS, INFLAMMATION AND OXIDATIVE STRESS IN ALGERIAN METABOLIC SYNDROME PATIENTS

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Objectives: This study was to explore the effects of Mediterranean diet (MD) adoption on insulin resistance, oxidative and inflammatory status in metabolic syndrome (MS) patients.

Subjects and methods: Eighty-four patients with MS were randomly recruited in the medical centers of Oran. Eighteen healthy participants were selected as a control group. Among these 84 patients, only 36 patients have followed-up the nutritional advices for 3 months. Patients were instructed to follow a Mediterranean-style diet and received some other selected nutritional and physical activity instructions. Anthropometric measurements were performed and a questionnaire was used to assess dietary intake. Blood samples were drawn at baseline and after 3 months of nutritional intervention and in healthy subjects.

Results: At baseline, the MS patients were obese and had altered anthropometric parameters, higher systolic and diastolic blood pressure, plasma lipids, glucose, insulin, HOMA-IR, HbA_1C, urea, creatinine, uric acid and lower albumin compared to healthy subjects. A decrease in plasma and erythrocytes antioxidant enzymes and a rise in lipid and protein oxidation, plasma CRP and fibrinogen were noted in the MS patients. Moreover, they had an unbalanced dietary pattern when compared to Mediterranean recommendations. Patients following the Mediterranean-style diet had significantly reduced weight, BMI, waist circumference, waist/hip circumference ratio, decreased systolic and diastolic blood pressure, plasma glucose, insulin, HOMA-IR, HbA_1C, cholesterol, triacylglycerols, CRP, urea, creatinine, creatinine clearance, lipid and protein oxidation and higher plasma and erythrocytes antioxidant enzymes.

Conclusion: A lifestyle intervention based mainly on nutritional advices improves metabolic, oxidative and inflammatory abnormalities of metabolic syndrome.

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EFFICACY OF NOVEL IADPSG CRITERIA IN THE DIAGNOSIS OF GESTATIONAL DIABETES MELLITUS: A RETROSPECTIVE ANALYSIS

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Objective: In 2011, the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) proposed new criteria for the diagnosis of gestational diabetes mellitus (GDM) based on the results of the multicentric Hyperglycemia and Adverse Pregnancy Outcome (HAPO) trial. The aim of our study was to compare the prevalence of GDM using the new IADPSG criteria versus the currently used WHO recommendations in a tertiary hospital in Czech Republic.

Research design and methods: Data from a standard 75 g 2-hour oral glucose tolerance test (oGTT) of 2567 pregnant females were analyzed using the novel IADPSG criteria for GDM (plasma glucose ≥ 5.1 mmol/l at baseline, ≥ 10.0 mmol/l at 1 hour and ≥ 8.5 mmol/l at 2 hours of oGTT) and compared with the currently recommended WHO criteria (plasma glucose ≥ 5.5, 8.8 and 7.6 mmol/l at baseline, 1 and 2 hours of oGTT).

Results: When using the novel IADPSG criteria GDM was diagnosed in 818 (31.94%) females as compared to 628 (24.46%) cases according to WHO criteria. 13.72% of females met the IADPSG but not the WHO criteria and thus were not treated for GDM. In contrast, 6.31% of tested women who accomplished the WHO but not the IADPSG criteria received unnecessary treatment.

Conclusion: GDM prevalence is higher with the novel IADPSG criteria as compared with the currently used WHO recommendations. Switching to IADPSG criteria might help unravel hitherto unidentified cases of GDM and thus improve outcomes for females with GDM and their offsprings.

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BENEFITS OF AN INTERVENTION CONCEPT FOR WEIGHT REDUCTION IN NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN OVERWEIGHT ADULTS

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As obesity is combined with FLD, weight reduction may be advantageous for FLD patients. Therefore, results of a weight reduction concept are presented with references to FLD in overweight adults.

In 66 patients (49.2 ± 13.8 yrs, 33.6 ± 4.5 m/kg^2 BMI) anthropometric, metabolic and FLD markers including FLI were evaluated before and after six weeks of intervention. The patients performed a defined program which consists of life style instructions, the use of a low-glycemic soy-yoghurt-honey product (Almased®, 2x p.d. standardized per body weight), and the facility for guidance by phone.

44 of the 66 participants showed a FLI > 70 (90.8 ± 7.4) indicating a FLD specificity greater than 90%. Comparing with the 22 participants showing a FLI < 70 (39.6 ± 17.3), the FLI > 70-group were of older age (51.5 ± 13.0 vs. 44.7 ± 14.5 yrs) and had a higher BMI (35.7 ± 5.0 vs. 29.5 ± 2.9 kg/m^2). All patients of the FLI > 70-group were successful in losing weight (106.9 ± 17.1 to 102.0 ± 20.8 kg; $p < 0.001$); the weight reduction was accompanied by improvements in FLD markers. FLI decreased to 78.2 ± 18.6 ($p < 0.001$), and GPT was reduced from 45 ± 24.1 to 36 ± 15.7 U/l ($p < 0.01$).

The results confirm that even patients with high FLD specificity and risk for T2DM showed health benefits after short-time intervention not only in metabolic, but in FLD markers also. Nevertheless, subsequent controls of the patients have to be performed in order to continue the initially success in weight reduction and FLD improvement. In conclusion, the soy-milk protein formula selected in this concept may play a significant role in the achievement of benefits in the obesity-associated FLD phenotype.

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HIGH TONE ELECTRICAL STIMULATION THERAPY FOR PREVENTION OF DIABETIC DISTAL POLYNEUROPATHY IN CHILDREN AND ADOLESCENTS WITH DIABETES TYPE 1

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Objective: Diabetic neuropathy is a common complication of diabetes type 1. Non-pharmacological strategies such as

electrotherapy is a potential recourse. High tone electrical stimulation therapy (HTEST) is a promising alternative treatment for diabetic distal polyneuropathy (DDP) in children and adolescents with diabetes type 1, as demonstrated in short-term study.

Methods: A total of 80 patients with diabetes type 1, aged 8–17 years and diagnosed DDP, underwent bilateral nerve conduction studies of median, tibial and plantar nerves using electroneuromyography before and after treatment by HTEST with use of high tone frequency unit. As shown in our studies, DDP diagnosed in the first year of the disease in 70% of patients. This shows the high incidence of DDP irrespective of the duration diabetes. Also was invastigated hormonal and metabolic parameters before and after treatment. Patients were divided into two groups with regard to degree of violation of the peripheral nerve conduction. Conducted five or ten procedures course of treatment.

Results: All patients hormonal and metabolic parameters before and after treatment remaind in the normal range. According to the results of electroneuromyography, conduction velocity of nervus medianus and plantaris improved 300% independently of the number of procedures. What concerns conduction velocity of nervus plantaris was improved only after ten procedure course.

Conclusions: This pilot study shows the high incidence of DDP irrespective of the duration of diabetes type 1 without any clinical symptoms and that the HTEST is safe and effective treatment of DDP. Its proved tha the optimal is to use the course of ten procedures.

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A CONTINUOUS REAL TIME MONITORING AND RECORDING OF GLYCAEMIA DURING SCUBA DIVING: CASE REPORT

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Introduction: A frequent complication of diabetic type 1 mellitus (DM) is sudden hypoglycaemia. This is why (DM) was considered a contraindication to scuba diving.

The position is currently being reconsidered.

To prevent worsening of hypoglycaemia and to correctly interpret hypoglycaemia-like symptoms whilst diving, diabetic divers could benefit from real-time Blood Glucose (BG) monitoring during their dives.

The scope of this work is developing a continuous BG monitoring system using a dedicate real time monitor during diving.

Material and Method: A Female diver with Diabetes, N.B. (Female, 29 yo, weight 53 Kg, height 1.57 mt) was monitored every 5 minutes on every dive, by a dedicate Continuous Glucose Monitor & Subcutaneous Glucose Sensor (Dexcom G4). The CGM Monitor was hosted in a waterproof case (Dive system Furyo diving computer) and the BG level was shown on the Furyo's display, allowing the diver to continuously check her BG. Data were recorded every 5 minutes for 1 hour before and 1 hour after the dive.

Result: 26 dives were recorded; no statistical difference between the BG recorded every 5 minutes pre, during and post dives could be found (P Value = 0,2113).

However occasional borderline hypoglycaemia value was observed (< 70 mg/d).

Discussion: Our data showed that even if scuba diving does not imply significant risks of hypoglycaemia the possibility of occasional hypoglycaemia exists. A real time Continuous Glucose Monitoring (CGM) system that Divers with Diabetes can use while diving can significantly their diving safety.

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DIETARY OMEGA-3 FATTY ACIDS PREVENT ERYTHROCYTE MEMBRANE ATPASE REDUCTION IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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Background and aim: Diabetes mellitus is a metabolic disease induces changes in lipid composition and alters the cellular structure of membrane bound enzymes by changing phospholipids and fatty acids composition. The aim of this study was to compare the effect of flaxseed oil and fish oil administration on erythrocyte membrane phospholipids fractions and their role on the activities of membrane bound enzymes in experimental diabetic rats.

Methods: Sixty male albino rats were used in this study and classified into six groups including control, flaxseed oil, fish oil, diabetic, treated flaxseed oil and treated fish oil groups. Fasting blood sugar, urinary isoprostane, erythrocyte membrane ATPase were determined. Fractionation of erythrocyte membrane phospholipids was carried out by HPLC using stainless steel phenomenx bond with 250x 4.60 mm, 5 μl silica. Photodiode array UV-visible detector was used and set at 203 nm.

Results: Fasting blood glucose was elevated in diabetic group concomitant with the elevation of urinary isoprostane and phospholipids fractions, in addition to a reduction of erythrocyte membrane ATPase. However, supplemented oils improved these complications.

Conclusion: Flaxseed and fish oils have an important effects on improving cell membrane phospholipids and decreasing oxidative stress in addition to the prevention of ATPase reduction during diabetes, although our results observed that, fish oil is more potent than flaxseed oil in attenuating diabetic complications.

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MULTICENTER, OBSERVATIONAL STUDY OF THE USE OF A SMART GLUCOSE MONITORING SYSTEM TO GUIDE INSULIN DOSING IN PATIENTS WITH DIABETES

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Background: Insulin dosing accuracy can contribute to glycemic control. It is therefore appropriate to assess the utility of devices that may overcome patient difficulties in calculating correct insulin doses.

Method: A multicenter observational study was conducted in patients with diabetes receiving multiple daily injections (MDI) of rapid/short-acting insulin ($n = 203$). Patients received the

FreeStyle InsuLinx Blood Glucose Monitoring system, set-up according to each patient's insulin dose calculation method: Easy mode for fixed doses of mealtime insulin plus correction doses based on pre-meal blood glucose levels, and Advanced mode for carbohydrate counting. Glycated hemoglobin (HbA1c) levels were determined at baseline, and at 3 and 6 months. Patients also completed opinion surveys.

Results: Average HbA1c levels declined from 8.28% at baseline to 8.08% at 6 months ($p = .0333$). In patients with baseline HbA1c ≥ 7.5%, the HbA1c reduction was −0.19% ($p = .0049$) at 3 months and −0.36% ($p = .0003$) at 6 months. Patients expressed greater confidence in their ability to correct blood glucose levels after 3 months ($p < .0001$).

Conclusions: Improved glycemic control and self-management, especially confidence in calculating accurate insulin doses was demonstrated in a population of insulin-using patients after introduction of the FreeStyle InsuLinx Blood Glucose Monitoring System. This may increase adherence and aid accurate calculation of mealtime correction doses.

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EXPERT STUDY: A BOLUS CALCULATOR IMPROVES GLYCEMIC CONTROL AND QUALITY OF LIFE OF TYPE 1 DIABETIC PATIENTS (T1DM) (PRELIMINARY RESULTS)

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Aims: To evaluate the impact on glycemic control and quality of life of a bolus calculator.

Methods: Multicentre randomized prospective cross-sectional study. Patients were randomized to control phase (3 months; calculation of prandial insulin according to insulin-to-carbohydrate ratio and insulin sensitivity factor using a single strip meter) or intervention phase (3 months; calculation of prandial insulin with a bolus advisor), with a washout period (3 months). Patients wore a continuous glucosensor (7 days) and answered a quality of life questionnaire at the beginning and at the end of each phase. A questionnaire of satisfaction was obtained at the end of both phases. Inclusion criteria: Adults; T1DM > 1 year, $HbA_{1c} > 7.5\%$, basal-bolus therapy with insulin analogs, experience with carbohydrate counting.

Results: Data from the first 32 subjects with at least 1 ended phase (27 females, age 38 ± 11 years, diabetes duration 16.8 ± 7.5 years).

Basal characteristics were comparable independently of the starting phase. No differences were found between phases in terms of mean blood glucose, standard deviation (from meter neither from sensor) and satisfaction.

Conclusions: The use of a bolus calculator improves glycemic control and quality of life of T1DM subjects.

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HEMORRHEOLOGICAL APPROACH FOR EARLY DETECTION OF DIABETIC MICROANGIOPATHY

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Hemorheological parameters, such as erythrocyte deformability, erythrocyte aggregation are altered in patients with diabetes. These changes of erythrocyte make whole blood more viscous and play a role on the pathogenesis of vascular complications of diabetes. So in this study, we intended to discover the comprehensive hemorrheological parameters which can early detect diabetic microangiopathic complications.

190 subjects were enrolled and their blood and urine samples were obtained. Also, they had a carotid IMT test and their eye's examination. Erythrocyte deformability, Aggregation index, Critical shear stress were measured. All subjects were divided by five groups according to their past history and test results as follows: Healthy control (n = 28), prediabetes (n = 14), diabetes without vascular complications (n = 89), diabetes with microvascular complications (n = 43) and diabetes with macrovascular complications (n = 15).

A significant reduction of erythrocyte deformability was observed in DM-no Cx and DM-microCx group compared with healthy control ($p < 0.05$). Whereas, AI does not show significant tendency ($p < 0.05$). And critical shear stress shows significant difference between DM-no Cx and DM-microCx group ($p < 0.05$). $SS_{1/2}$/EImax that means the value of half shear stress devided by maximal Elongation Index shows significant reduction in DM-no Cx and DM-microCx group compared with healthy control ($p < 0.05$).

EI is a sensitive parameter to detect impairment of erythrocyte in diabetic process. And critical shear stress is also a

	Control phase			*Intervention phase*		
	Basal	*End*	*p*	*Basal*	*End*	*p*
HbA_{1c} (%)	8.15 ± 0.4	7.93 ± 0.7	NS	8.06 ± 0.6	7.35 ± 0.47	< 0.001
N of glucose measurements	3.9 ± 1.2	4.2 ± 1.2	NS	5.1 ± 0.9	4.3 ± 1.6	NS
Insulin(UI/kg/day)	0.40 ± 0.14	0.41 ± 0.12	NS	0.37 ± 0.12	0.36 ± 0.11	NS
Basal	0.31 ± 0.09	0.27 ± 0.09	0.014	0.29 ± 0.08	0.28 ± 0.12	NS
Prandial	0.71 ± 0.13	0.68 ± 0.14	0.049	0.66 ± 0.13	0.66 ± 0.19	NS
Total						
Weight(kg)	72.5 ± 17	69.8 ± 19	NS	67.3 ± 11	67.5 ± 11	NS
Quality of life	95.7 ± 20	89.7 ± 16	NS	101.6 ± 23	93.1 ± 18	0.019

useful parameter to detect diabetic microangiopathic complications early. Through analyzing tendency of these hemorrheologic factors, discovering the new hemorrheologic paramteter and making the equation or scoring system to detect diabetic microcomplications is a very important task.

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IS THERE A DIALLING TORQUE COMFORT ZONE FOR INSULIN PENS? STUDY ON TORQUE AND COMFORT FOR 4 DISPOSABLE INSULIN PENS

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Background: When setting doses, ergonomic dialling torque may enhance safety and comfort when using insulin pens. Limited data are available on the correlation of dialling torque and dialling comfort. We investigated dialling comfort of 4 disposable insulin pens, as perceived by patients.

Material and Methods: 16 pen-experienced patients with diabetes participated. Subjective dialling comfort rankings and ratings (using Likert scale) were investigated for SoloSTAR (SS), FlexPen (FP), KwikPen (KP), and FlexTouch (FT1) at 0–20 U each and for FlexTouch (FT2) at 60–80 U. Dialling torque was measured in a previous laboratory study (Friedrichs A, et al. ATTD 2013).

Results: SS was ranked most comfortable for up- and down-dialling by 8 and 6 of all participants, respectively; FP, 5 and 8; FT1, 2 and 1; and KP, 1 and 1. Dialling up and down with FT2 was ranked least comfortable by the majority (12 and 10) of patients. Using the Likert scale, comfort for up- and down-dialling was rated very comfortable for SS by 15 participants each, followed by FP (12 and 14), KP (10 each), and FT1 (9 and 7); FT2 was rated less or not comfortable by 10 and 11 patients, respectively, in line with previous ranking.

Conclusion: Subjective ratings of dialling comfort for different insulin pens by patients concur with previous laboratory dialling torque study results. There appears to be a 'torque comfort zone.' Lowest torques do not imply best comfort, while torques above 50 Nmm (maximum ISO 894–3:2010-recommended torque) reduce subjective handling comfort.

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CLINICAL USEFULNESS OF STATIN THERAPY FOR PREVENTION OF CARDIOVASCULAR DISEASES IN DIABETES AND PRE-DIABETES

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Background: There is no sufficient evidence to recommend the use of statins for prevention of cardiovascular diseases in all diabetic and pre-diabetic individuals.

Objective: we aimed to determine the potential advantages of statin therapy in all diabetic and pre-diabetic subjects vs. treatment based on American Diabetes Association (ADA) guideline, applying different harm-to-benefit ratios for this treatment.

Methods: A population-based cohort of 1075 (473 males) diabetic and 1515 (674 males) pre-diabetic subjects was followed 9.2 years for cardiovascular events. Expected Net Benefit (NB) was calculated for statin therapy. It is a sum of necessary treatments minus a weight of unnecessary treatments; necessary if it is given to subjects for whom events occur during follow-up (a treatment that would prevent the event), and unnecessary if given to subjects without any event during follow-up (a treatment that would just bring the cost and probable side effects). Weight is defined by the harm-to-benefit ratio of treatment. A Decision Curve was drawn by plotting expected NB against a wide range of harm-to-benefit ratios.

Results: Expected NB of preventive therapy for diabetes was valuable in a wide range of harm-to-benefit ratios of treatment. It was negative in males and females with impaired fasting glucose and females with impaired glucose tolerance, for harm-to-benefit ratios >0.1. It was negative in males with impaired glucose tolerance, for harm-to-benefit ratios >0.2. Expected NB was not so different based on the ADA guideline or treating all subjects.

Conclusions: All diabetic, but not pre-diabetic subjects would most likely benefit from statin therapy.

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M-HEALTH INTERVENTION FOR TYPE II DIABETES MELLITUS PATIENTS IN INDIAN RURAL AREAS

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Background: India is known as the 'Diabetes capital of the world' and has an urgent need to implement effective preventive and management strategies to reduce its high prevalence. Evidence for acceptability of the m-Health technology among Indian rural population is lacking. This study is an attempt to evaluate the acceptability and behavioural outcomes of e-Health Technology to Type II Diabetes Mellitus patients.

Methods: An experimental mixed-method study design was employed with a main focus on qualitative data and quantitative data to support the study. 3 rounds of interviews were conducted at an interval of one week using a structured questionnaire. Focus group discussion was also conducted which included both participants and stakeholders to reveal their opinion and suggestions on the designed tool to help in further revision of the tool for its implementation in a future large study.

Results: The results from the qualitative and quantitative data aided in identifying the strengths and weaknesses of the tool in terms of acceptability, suitability and feasibility in the specified setting and population. Strengths of the study were found to co-exist with many weaknesses; the latter suggesting changes to future study protocols.

Conclusion: The identified strengths and weaknesses of the tool were analysed to generate recommendations for improvement and revision of the tool. A revised tool tailored to the local setting could be used in the intended future trials.

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INJECTION FORCE OF REUSABLE INSULIN PENS AVAILABLE IN INDIA: ALLSTAR, GLARITUS PEN ROYALE, HUMAPEN ERGO, INSUPEN, NOVOPEN 3, NOVOPEN 4

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Insulin pen injection force (IF) is an important practical aspect of therapy for patients with diabetes (especially those with limited dexterity) and a key element in the design and characteristics of insulin pens. We compared IF of 6 reusable insulin pens available in India: NovoPen® (NP) 4, NP3, HumaPen® Ergo (HPE), Glaritus® Pen Royale, InsuPen® (IP) and AllStar® (AS). There were 20 measurements per pen type per test series. Mean IF was measured by dispensing a dose of 60 U insulin. The IF was tested with two dispense rates (6 and 10 U/s; constant volume flow rate). Pens were fitted with different needles as recommended by manufacturers (Micro-Fine® 31G × 5 mm for HPE, WR, IP, AS and NovoFine® 31G 6 mm for NP4 and NP3) and tested with different insulins: Lantus® (AS, Glaritus® (WR), Humulin® 30/70 (HPE), Basalog® (IP), NovoMix® 30 (NP3), and NovoRapid® (NP4).

At 6 and 10 U/s, AS required significantly lower mean IF vs NP3, HPE and IP (Table). Mean IF for NP4 and WR is similar to AS. Mean IF was 56%, 49% and 21% higher with NP3, HPE, IP vs AS, respectively (p

In conclusion, AS, NP4, and WR require lower IF at different dispense rates vs other reusable insulin pens. This may enable patients, especially those with dexterity problems, to administer insulin more easily and improve diabetes management.

Table 1. Injection forces with various reusable pen types, doses and injection speed combinations

	Dose (U)	Injection speed (U/s)	Mean plateau injection force ± SD (N)
NOVOPEN 3®	60	6	11.06 ± 0.87
	60	10	16.74 ± 1.15
HUMAPEN® ERGO	60	6	10.54 ± 0.73
	60	10	15.70 ± 0.96
INSUPEN®	60	6	8.59 ± 0.36
	60	10	13.25 ± 0.79
GLARITUS® PEN ROYALE	60	6	7.59 ± 1.13
	60	10	11.10 ± 1.36
NOVOPEN 4®	60	6	6.85 ± 0.28
	60	10	10.54 ± 0.38
ALLSTAR®	60	6	7.10 ± 0.87
	60	10	11.11 ± 0.75

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EASE OF USE OF A NEW REUSABLE INSULIN DEVICE ALLSTAR: RESULTS OF A PILOT STUDY

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Objectives: AllStar® (Sanofi, Paris), a new reusable insulin pen, can be used for injecting either insulin glargine (LANTUS®) or glulisine (APIDRA®) or human insulin (INSUMAN®). Study objectives included assessment of device usability (primary) and patient ratings for specific features of a fully functional AllStar prototype (equivalent to intended commercial product) (secondary).

Methods: Patients with T1DM/T2DM for ≥ 1 year were trained in correct usage of the pen and provided an instruction manual. They returned 24 hours later for a face-to-face interview and carried out simulated use (prepare pens, set dose, and inject into receptacle) under observation. Usability (ability to carry out tasks with predefined training, % use errors and their causes) and ease of use (11-point questionnaire; overall rating) were assessed. Results of patient ratings associated with device usage are reported.

Results: Eighteen patients (3 T1DM + 15 T2DM; 10 injection-naïve/non-users of pens, 5 current disposable pen users, 3 current reusable pen users) participated from India. Overall, patients found the pen either 'very easy' (n = 15) or 'easy' (n = 3) to use. A high proportion of the patient-evaluated specific tasks like dispensing, dialing and reading doses, needle attachment, and cartridge change as either 'very easy' or 'easy' to perform.

Conclusions: These preliminary data suggest that AllStar is a user-friendly pen. This study is limited by inherent biases. To confirm findings and determine the impact of AllStar in diabetes management, a larger user study conducted with the commercially available pen would be relevant.

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OPTIMIZATION AND EVALUATION OF A BREATH ACETONE ANALYZER FOR DIABETES DIAGNOSIS USING CAVITY RINGDOWN SPECTROSCOPY (CRDS) AT 266NM

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To date, breath analysis as a noninvasive diagnostic method has gained rapid development and will play a significant role in early disease diagnosis. More and more biomarkers in human breath have been recognized and applied to clinical research, including acetone for type-1 diabetes (T1D). Laser spectroscopy, as one of the highly accurate analytical techniques, has been applied to breath analysis for over 30 years. We have constructed an instrument using cavity ringdown spectroscopy (CRDS) for trace breath acetone detection. Using a signal mode ultraviolet laser at 266 nm as a light source, along with all other components of the instrument such as a pair of high reflectance mirrors (R = 99.84%), a 50 cm-length stainless steel cavity, a mini photomultiplier (PMT), an oscilloscope, and a laptop, we constructed a portable (90 cm × 20 cm) system that is being used for clinical study. Concentration of acetone is determined by the background subtraction method.. The newly developed software of this

instrument is optimized to offer faster performance and more accurate results. Detection limit of this system is estimated to be 0.22 ppmv based on the 3-σ criteria. Three health human breath samples were tested preliminarily and the ringdown measurements were compared with those from GC-MS. The results revealed a consistent tendency of breath acetone with blood glucose level. Several critical steps in future efforts are discussed in details.

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LIFESTYLE MODIFICATION OF TYPE 2 DIABETES MELLITUS AMONG ADULT WOMEN

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Background: Diabetes Mellitus (DM) has emerged as an epidemic problem in Egypt. The global increase in the prevalence of DM is attributed to many risk factors, as inactive lifestyles. Many risk factors have been identified as modifiable or non modifiable risk factors. Lifestyle modification interventions are a top priority for prevention and control many of chronic diseases. Thus, the purpose: of the current study was to examine the effect of lifestyle modification intervention on reducing some of modifiable risk factors among adult diabetic women.

Methods: A quasi experimental design was used to test research hypothesis. A convenience Sample of 104 adult women who diagnosed as type ''2'' diabetes was selected.

Setting: this study was conducted in the out-patient clinic of Teaching Hospital, at Shebin El-Kom City.

Tools for data collection: A) Interviewing questionnaire, B) Medication Adherence Rating Scale (MARS), C) 24 hours dietary recall, D) Exercise questionnaire and E) Biophysiological Measurements.

Results: There was statistical significant improvement in medication adherences post intervention compared to pre intervention. Also, there was statistical significant decrease in calories intake post intervention than before intervention. The implementation of lifestyle modification interventions is more effective in redacting random blood sugar in pre than post intervention (227.8 ± 128.9 to 157.5 ± 37.9 respectively).

Conclusions: lifestyle modification intervention can favorably decrease some of modifiable risk factors among adult diabetic women.

Recommendation: Encourage nurses to provide health education about lifestyle modification intervention to enhance patient care, and adoption of healthy behavior.

KeyWords: Type 2 Diabetes, adult Women, Lifestyle modification

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PATIENT REPORTED CHALLENGES OF SELF-MONITORING OF BLOOD GLUCOSE REQUIRE PATIENT-SUPPORTIVE TECHNOLOGY: LESSONS FROM THE EXACT STUDY

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Objectives: Recent research has established that the information, motivation, and skills demands of self-monitoring of blood glucose (SMBG) represent significant challenges to patient adherence and achievement of glycemic control. Improved self-monitoring technology could be employed to lessen the demands of self-monitoring and achieve optimal patient—technology 'fit.'

Methods: Insulin using individuals with type 1 ($n = 139$) and type 2 ($n = 326$) diabetes who were non-adherent to recommended frequency of SMBG were enrolled in the ExAct study and completed assessments of the challenges of self-monitoring at study baseline.

Results: In this sample, testing frequency averaged 2.38 times per day, and HbA1c 8.56%. Participants frequently reported forgetting to test (55.18%), lack of motivation for self-management (24.45%), lack of understanding of the risks of not testing (18.80%), lack of understanding the benefits of testing (10.12%), and lack of confidence for self-management on a daily basis (4.34%), as well as feeling that results are discouraging (13.22%), and that testing is a waste of time (4.84%). Lack of motivation, lack of confidence, and feeling discouraged were associated with higher HbA1c at baseline ($p < .05$).

Conclusions: In this study, insulin using individuals with type 1 and type 2 diabetes who were non-adherent to SMBG reported multiple challenges to self-monitoring that may be addressed via the development of supportive technologies that minimize the demands of self-monitoring and optimize 'patient-technology' fit.

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BETTER ADHERENCE AND GLYCEMIC CONTROL WITH THE INTEGRATED STRIP-FREE ACCU-CHEK MOBILE SYSTEM AT MARGINAL EXTRA COST - LEARNINGS FROM THE EXACT-STUDY

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Objectives: The randomized controlled ExAct study assessed the impact of using integrated strip-free self-monitoring of blood glucose (SMBG) technology (Accu-Chek® Mobile)

on testing frequency and glycemic control in patients treated with multiple daily injection therapy who were non-adherent to recommended SMBG test frequencies. This analysis assessed the potential economic impact on short-term healthcare costs (SHC).

Methods: Study outcomes were HbA1c and SMBG test frequency. The economic analysis was performed with a spreadsheet-model from a Dutch payer's direct cost perspective, based on ExAct study outcomes. Data on correlation between HbA1c change and expected cost are based on published literature. Model outputs include expected impact on SHC and sensitivity analysis.

Results: Testing frequency in patients using integrated strip-free technology increased by 0.37 measurements/day ($p = 0.007$) compared to standard single strip systems. HbA1c improved by 0.22% ($p = 0.044$). The 17.2% increase in test frequency creates extra cost of €60.8 per person per year (PPY). Reduced HbA1c decreases expected SHC cost by €56.7 PPY. Net incremental cost for a decrease of 0.22% HbA1c are €4.1 PPY or €0.16 per month per 0.1% HbA1c reduction from a population perspective.

Conclusions: In this study integrated strip-free SMBG technology was effective in reducing non-adherence to recommended SMBG test-frequencies. The increase in test frequency resulted in better glycemic control – fully in line with other studies. While higher test frequencies for improved adherence will increase cost for SMBG, expected cost reduction from better HbA1c will absorb 93.2% of extra cost. Therefore integrated strip-free SMBG technology (Accu-Chek® Mobile) is highly cost-effective.

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METABONOMICS BASED ASSESSMENT OF TYPE 2 DIABETES WITH 1H NMR SPECTROSCOPY AND ARTIFICIAL NEURAL NETWORK MODELING

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Introduction: Type 2 diabetes is a metabolic disorder caused by an increase in blood glucose as the result of insulin resistance, a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency. Its incidence is increasing rapidly, and by 2030, this number is estimated to almost double. The disease is characterized by chronic hyperglycemia with disorder in carbohydrate, fat, and protein metabolism. Although there are many studies, the pathogenesis of the disease still remains unclear. Metabonomics and NMR spectroscopy is an emerging complementary post-genomic technology used in clinical research. 1H NMR spectroscopy of human serum with the help of artificial neural network (ANN) modeling is widely used in medical studies nowadays. In the present study we used the ANN modeling to differentiate between type 2 diabetes patients and healthy individuals, which can be used as a diagnostic method.

Materials and methods: In this study sixty people were participated, they were divided into two groups, 30 in each. The first group was patients with type 2 diabetes, and the second group was healthy subjects. They were matched for age. Serum samples were taken from patients and the normal individuals. 1H NMR spectroscopy was carried out using Carr – Purcell-Meiboom – Gill protocol in Bruker 500 MHZ. ProMetab software which is the metabolomics data processing cod was used. PCA was applied to reduce the dimension of our data and subsequently feed forward neural networks were used for classification and modeling. Insulin, glucose, LDL, HDL, Cholesterol and TG were also assayed.

Result and discussion: The present study showed significant changes in amino and nucleotide sugar metabolic pathways in the case group compared with the control. Also significant changes were observed in the patterns of metabolic pathways of galactose, Starch, Sucrose, glycolysis and gluconeogenesis in the serum samples of the case group as compared with the controls. 10 PCA loading were taken in to feed forward ANN along with other biochemical parameters. ANN output was shown that our model successfully classified the samples with the type I error rate of 0.00 and type II error rate of 0.16 respectively.

Conclusion: Our study suggests that Metabonomics and HNMR spectroscopy techniques along with (ANN) modeling can be used as a diagnostic method to differentiate between type 2 diabetes patients and healthy individuals.

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EVERYDAY USE OF AN AUTOMATED BOLUS CALCULATOR

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Aim: To investigate usage patterns and perceived usability of an automated bolus calculator (ABC) (Accu-Chek Aviva Expert) in the everyday life of adults with diabetes treated with multiple daily injections.

Methods: In June 2013, an online survey was sent via email to all Danish patients who had received an ABC and accepted inclusion in the Roche Diagnostics patient register ($N = 614$). The response rate was 23.9%. Here we present the results of the 140 questionnaires returned by adult users of the ABC.

Results: Demographics: female sex 58%, age 45 ± 12 years, diabetes duration 20 ± 13 years, ABC use 9 ± 6 months.

90% of respondents used the ABC for blood glucose monitoring ≥ 4 times/day. 93% used the ABC daily for bolus calculation in relation to meals. 51% used the device for daily between-meal correction bolus calculations. The ABC functions that adjust bolus size according to health status, activity level etc., were activated more than once weekly by 57%.

On a 5-point Likert scale, respondents agreed or strongly agreed that bolus calculation had become easier with the ABC (83%), that bolus calculations were more reliable with than without the ABC (78%), and with feeling comfortable using the ABC (74%).

88% of respondents were dismissive of the thought of changing to another blood glucose meter without an ABC-function.

Conclusions: This cross-sectional study in a group of current users of an ABC showed that the device widely served the intended purpose and that perceived ease of use was high.

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DISTRIBUTION OF DEGREE OF GLUTATHIONE SYSTEM ENZYMES ACTIVITY IN PATIENTS WITH PREDIABETES AND TYPE 2 DIABETES

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Glutathione reductase (GR) and glutathione peroxidase (GP) prevent oxidative stress secondary to hyperglycemia by glutathione reduction.

Purpose: Study activity of glutathione system enzymes in patients with prediabetes (impaired glucose tolerance ant impaired fasting glucose) and type 2 diabetes (T2D).

Materials and methods: Group 1 – 39 patients with prediabetes, group 2 – 35 patients with T2D, group 3 – 36 almost healthy people. We measured activity of GP and GR by biochemical methods.

Results: Value range of GR activity was 0,69 – 1,29 mmol/min. According to different limits each study group was divided into 5 subgroups. Results are included in Table 1.

GR activity over 1 mmol/min was revealed in 56,4% patients with prediabetes, but $<0,7$ mmol/min was not registered, that can be caused by intracellular activation of antioxidant defense. In T2D 42,8% GR activity was $<0,8$ mmol/min compared to 5,1% in prediabetes and 88,9% in almost healthy person that probably results from deterioration of antioxidant system. We didn't reveal significant differences in GP activity, further analyses of activity distribution was not conducted.

Conclusion: Activation of endoglobular antioxidant defense was mainly caused by GR and had maximal activity in patients with prediabetes. In patients with T2D GR activity was decreased probably because of deterioration of enzyme activity in the setting of longstanding hyperglycemia.

Table 1 Comparative Distribution of GR Activity

GR, mmol/min	*Group 1 (n/%)*	*Group 2 (n/%)*	*Group 3 (n/%)*
$<0,7$	0/0	9/25,7	27/75
0,7–0,8	2/5,1	6/17,1	5/13,9
0,8–0,9	6/10,3	8/20	4/11,1
0,9–1,0	9/23,1	2/5,7	0/0
$>1,0$	22/56,4	10/31,4	0/0

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ACTIVITY OF ANTIOXIDANT ENZYMES IN PREDIABETES AND TYPE 2 DIABETES

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Hyperglycemia causes oxidative stress (OS), the last one activates intracellular pathologic signaling pathways and stimulates genetic production of proteins that factors into DNA, proteins and lipids damage and results in apoptosis.

Purpose: Study activity of antioxidant enzymes in patients with prediabetes and T2D.

Materials and methods: We included 74 patients. Group 1 – 39 patients with newly diagnosed prediabetes (impaired fasting glucose, impaired glucose tolerance), group 2 – 35 patients with T2D treated with blood glucose lowering drug and 36 almost healthy people (group 3). We measured activity of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GP) and glutathione reductase (GR) by biochemical methods.

Results and discussion: SOD activity was higher in prediabetes (95,10 RU/ml [76,88;113,7]), compared to control group (82,03 RU/ml [64,98;103,46]). CAT activity in group 1 was 13,17 mcat/l [9,86; 22,91], that is almost 2 times less than in group 3 (15,98 mcat/l [14,65; 17,11]), and 2,81 less than in group 2 (13,17 mcat/l [9,86; 22,91]) compared to group 3. CAT activity was 5,31 greater in group 2 than in group 1. We didn't reveal changes in GP activity in patients with prediabetes and T2D compared to control group. GR activity was greater in patients with prediabetes (1,06 mmol/min [0,95; 1,29]) compared to patients with T2D (0,82 mmol/min [0,69; 1,10]) and control group (0,92 mmol/min [0,74 1,11]).

Conclusions: In patients with prediabetes activity of antioxidant enzymes (SOD, GR) is increased. In T2D patients CAT activity was greater. Decreased activity of GR in group 2 suggests depletion of endoglobular antioxidant enzyme.

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ENDOTHELIAL DYSFUNCTION AND VASOREACTIVITY IMPAIRMENT MEASUREMENT IN NON-DIABETIC HYPERGLYCEMIC PATIENTS USING THE ENDOPAT DEVICE

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Introduction: Endothelial dysfunction (ED) has been shown to be a major pathophysiological mechanism in Metabolic Syndrome. It leads to changes in vasoreactivity. This ED could be the result of both higher insulin serum levels and/or high serum glucose levels. So far, published studies are focused in established Diabetes Mellitus and not in dysglcemic non-diabetic patients.

Objectives: To present a series of 17 patients who aren't diabetic and with significant alterations in vasoreactivity, measured through the ENDOPAT device.

Methods: Non-diabetic patients having hyperglycemia and underwent a routine medical check-up were included.

Anthropometric parameters were recorded, requested laboratory tests were serum glucose levels, serum lipid profile and hypersensitive C reactive protein levels (HS CRP). All patients were tested with the ENDOPAT Device.

Results: Yet all 17 patients were shown to have changes in vasoreactivity. However, HS CRP levels, a well known marker of ED, were not elevated as expected.

Conclusions: These results clearly suggest that vasoreactivity changes are earlier alterations rather than increases in HS CRP of ED. As a matter of fact these observations imply that a more extensive study is further required to confirm these findings.

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DUAL-CHAMBER PEN DESIGN AND TESTING FOR INJECTION OF EXENATIDE DISPERSED IN POLY-(D,L-LACTIDE-CO-GLYCOLIDE) MICROSPHERES FOR ONCE-WEEKLY TREATMENT OF TYPE 2 DIABETES

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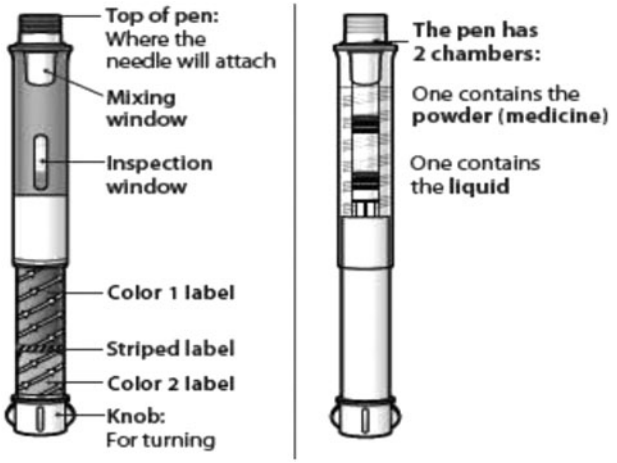
Exenatide, a glucagon-like peptide-1 receptor agonist, lowers blood glucose in patients with type 2 diabetes and has been formulated for consistent, sustained release by dispersion within medical grade poly-(D,L-lactide-co-glycolide) polymer microspheres. Creation of an injection pen for self-administration of a fixed-dose subcutaneously was challenging due to the need for separate containment of diluent and microspheres until suspension and mixing shortly before delivery. Design requirements included the transfer of diluent into the microsphere chamber, mixing to create a homogeneous suspension, purging air before injection, and consistent, straightforward delivery of the specified dose with minimal error. A pen-injector delivery system was developed, consistent with FDA guidance, that housed an aseptically prefilled dual-chamber cartridge containing exenatide microsphere powder and diluent, and a Becton Dickinson needle designed to inject the suspension uniformly (Figure). Dose preparation requires attachment of the provided needle to the needle-specific hub, transfer of diluent to microsphere chamber, suspension of microspheres within diluent by mixing, and priming to purge air from cartridge. Human factors engineering principles were leveraged to optimize usability and reduce errors with use. The dual-chamber pen design improves delivery system ergonomics for dose preparation and self-injection of exenatide once-weekly, as verified by subjective evaluation and functional/performance testing.



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INVESTIGATE AND SUMMARIZE RETINOPATHY RISK FACTORS IN TYPE II DIABETIC PATIENTS USING FACTOR ANALYSIS AND DISCRIMINANT ANALYSIS

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Introduction: Diabetes is one of the most common chronic diseases in the world. Incidence and prevalence of diabetes is increasing in developing countries as well as in Iran. Retinopathy is the most common chronic disorder in diabetic patients.

Method: In this study we used the information of diabetic patients' reports which refer to endocrine and metabolism research center of Isfahan University of medical sciences, to determine diabetic retinopathy risk factors. We used factor analysis to extract retinopathy's factors. Factor analysis is using to analyze multivariate data, in which a large number of dependent variables summarize in to the fewer independent factors. Factor analysis is applied, in both diabetic and non-diabetic patients, separately. To investigate the efficacy of factor analysis, we used discriminant analysis.

Results: We investigated 3535 diabetic patients whose prevalence of retinopathy was 53.4%. Six factors were extracted in each group (i.e. diabetic and non-diabetic groups). These six factors were explained 69.5% and 69.6% of total variance in diabetic and non-diabetic groups respectively. Using original variables such as sex, weight, blood sugar control method and some laboratory variables, correct classification rate of discriminant analysis was 67.4%. But it decreased to 49.5% by using factors extracted.

Discussion: Retinopathy is one of the important disorders in diabetic patients that involves a large number of variables and can affect its incidence. By the method of factor analysis we summarize diabetic retinopathy risk factors. In this way, 10 variables were summarized into the six factors.

Keywords: type II diabetic, retinopathy, factor analysis

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GUSTAVO IN GNAM'S PLANET: A SERIOUS GAME TO PROMOTE HEALTHY BEHAVIOURAL CHANGES. A PILOT STUDY

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Introduction: Obesity and Type 2 Diabetes are diseases of great social relief, whose incidence and prevalence are increasing. Serious games have been used as a tool allowing the players to interact with games in order to acquire knowledge and skills on healthy topics.

Aim of study: Within a project supported by the Italian Ministry of Health, a Video Game called 'GUSTAVO IN GNAM'S PLANET' has been developed with the scope to promote healthy choices and awareness in young people. Aim of our pilot study was to assess the efficacy of this innovative tool.

Material and Methods: A multidisciplinary team consisting of experts in nutrition and metabolic diseases, psychologist, dietitian, musician, and games designers was assembled. Behavioral change theories were adopted to guide the design of the health messages. A sample of 48 subjects aged 15–18 years were included in the study. On-line validated questionnaires on knowledge of healthy food (scoring from 0 to 88) and on eating habits were administered at baseline. Participants were asked to play the game for at least half an hour per day during the following week. After that, the same questionnaires were re-administered.

Results: After playing the video game, subjects showed significant higher scores (i.e. much more knowledge) in the questionnaire on knowledge of healthy food ($70.0 +/- 1.3$ vs. $71.3 +/- 1.4$; $p < 0.05$) and much more healthy eating habits.

Conclusion: Our pilot study demonstrates that the video game 'GUSTAVO' is an effective tool for teaching nutrition knowledge and promoting healthy lifestyle.

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THE SMART SOCK FOR DIABETICS: A FEASIBILITY STUDY

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Pressure reduction inside the shoe is an important procedure to prevent the diabetic foot syndrome (DFS). Until now only the plantar pressure distribution can be measured. However, many recurrent defects are located at other regions of the foot, such as toes or dorsum of the foot.

We developed a pressure measuring system based on a pressure sensitive filament we invented. We established an appropriate hard- and software which enable an online presentation of the pressure on a textile. The system can cover any pressure range of interest, can have a local resolution as required and a good local (VC of $< 7\%$) and pressure/area (VC $< 13\%$) reproducibility. A long-term use over at least 3 months is possible.

To construct a sock we applied the filament on a sock, developed a new software giving 3D presentations of the pressure distribution and a suitable connection to a portable part of the hard ware – producible on an industrial basis. A model of this product will be presented.

As a result it will be possible to evaluate the fit of the shoe by looking at a recorded video of the changes of the pressure during waking tunable to the region of interest.

This ''smart sock'' is an instrument which will predict if a shoe exerts too much pressure to the foot of the diabetic and to control the correction of such a finding. This will reduce the incidence of new defects at the feet of patients at risk for DFS.

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PERSONALIZED RULE-BASED CLOSED-LOOP CONTROL ALGORITHM FOR TYPE 1 DIABETES

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Background: Type 1 diabetes-mellitus implies a life-threatening absolute insulin deficiency. Artificial pancreas (CGM sensor, insulin pump and control algorithm) is promising to outperform current open-loop therapies.

Methods: We designed a predictive rule-based algorithm (pRBA) that uses current and past CGM glucose measurements, a predicted rate-of-change (pROC) for glucose and patient's optimal basal therapy (OBT). It requests information about prandial boluses administered manually in accordance to the amount of carbohydrate intake. Prior to its use, pRBA demands patient-based individual adjustment.

Controller's performance was tested ''*in silico*'' using the Virginia/Padova simulator in two scenarios of suboptimal basal insulin regimes ($\pm 20\%$ deviation with respect to OBT). We measured time spent on target BG range (70–180 mg/dl) during pRBA control and compared it against CSII therapy for the period between 10:00 pm and 2:00 pm of the next day. We distinguished two stages: night/basal (10:00 pm-08:00 am) and breakfast/post-prandial (08:00 am-02:00 pm).

Results: The pRBA provided a superior metabolic control for the 120%-OBT scenario by decreasing hypoglycemia time from 12% to 3%. In the 80%-OBT scenario, time in target was augmented from 77% to 97% for the night/basal period, whereas the increase in post-prandial stage was from 66% to 99% time.

		Open-Loop(CSII)			Closed-Loop(pRBA)		
OBTratio	Period	< 70 mg/dl	70–180 mg/dl	> 180 mg/dl	< 70 mg/dl	70–180 mg/dl	> 180 mg/dl
120%	Night/Basal	12%	88%	0%	3%	97%	0%
	Postprandial	0%	100%	0%	0%	100%	0%
80%	Night/Basal	0%	77%	23%	0%	97%	3%
	Postprandial	0%	66%	34%	0%	99%	1%

Conclusions: The pRBA improved metabolic control by increasing time in target with respect to reference suboptimal basal-insulin regimes.

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PSYCHOSOCIAL IMPACT OF CLOSED LOOP THERAPY ON ADOLESCENTS WITH TYPE 1 DIABETES: OVERNIGHT CLOSED LOOP AT HOME STUDY

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The burden of diabetes is relentless and can be particularly challenging during adolescence. Nocturnal hypoglycaemia is common and a serious complication of insulin treatment in people with type 1 diabetes (T1DM) representing represents a critical problem in disease management.

The development of the artificial pancreas, a system combining glucose monitoring with computer-based algorithm dictated insulin delivery, may provide a solution and represent an additional realistic treatment option for people with T1DM.

Semi-structured, qualitative interviews were conducted to explore participants' perceptions of the impact of the three-week home overnight closed loop use on their lived experience. Content and thematic analyses were conducted to explore positive and negative experiences of the closed loop technology.

Participants: 15 adolescents (11–19 years)

Key positive themes:

Improved sleep (n = 8); Stable blood glucose levels (n = 14); Safety (n = 14)

'The perfect sugar control overnight' (015)

'I felt I could completely trust it at night and I felt completely relaxed about it being there' (004)

'At night I didn't have to worry about being diabetic' (006)

Key negative themes:

Calibration difficulties (n = 4); Alarms beeping (n = 5); Discomfort/size of device (n = 8)

'The implants for the pump, they were annoying…. the needle was sore' (008)

'Just having this little brick on my arm really…. Just the size of it' (002)

All participants reported a positive experience taking part in the trial. 'Perfect' blood glucose control and 'time off' from diabetes were key benefits. Technological and practical difficulties should be addressed before people with diabetes are entirely comfortable with the device.

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PSYCHOSOCIAL IMPACT OF CLOSED LOOP THERAPY - ADULTS WITH TYPE 1 DIABETES: OVERNIGHT CLOSED LOOP AT HOME STUDY

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The burden of diabetes management presents sustained challenges for people living with the condition. Nocturnal hypoglycaemia is common and a serious complication of insulin treatment in people with type 1 diabetes (T1DM) representing a critical problem in disease management.

The closed loop (CL), combining glucose monitoring with computer-based algorithm modulating insulin delivery, may provide a solution and represent an additional realistic treatment option.

Participants in the Angela03 study (cross-over comparison of overnight open vs CL) were interviewed within 2 weeks of completion of CL arm to explore perceptions of the impact of the four-week home overnight CL use on their lived experience. Content and thematic analyses were conducted.

Participants: 8 adults with T1DM aged > 18 years

Key positive themes:

Better control (n = 7); Reassurance (n = 5); Improved sleep leading to improved daily functioning and diabetes control (n = 5)

'The best control I have had for several years'

'You've got more reassurance with the closed loop'

'Anything suffers in comparison to the closed loop and I felt a real sense of loss when I came off that'

Key negative themes:

Alarms beeping (n = 7); Technical issues/calibration (n = 5); Device/equipment size (n = 4)

'The pump had quite a lot of pump alarms'

'Making it smaller would be the biggest thing'

'One inadvertent press of the power button….. shut the thing down'

Participation in the trial was reported as positive by all. Increased reassurance, security and confidence were key benefits. Technical issues and human-factor aspects should be addressed before people with diabetes are entirely comfortable with the device.

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PSYCHOSOCIAL IMPACT OF CLOSED LOOP THERAPY ON PARENTS OF ADOLESCENTS WITH TYPE 1 DIABETES: OVERNIGHT CLOSED LOOP AT HOME STUDY

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Caring for a child with type 1 diabetes is demanding and associated with increased rates of stress/depression among parents. Fear of nocturnal hypoglycaemia is common causing heightened anxiety and leading to maladaptive coping strategies.

The development of the artificial pancreas, a system combining glucose monitoring with computer-based algorithm dictated insulin delivery, may represent an additional realistic treatment option for people with T1DM.

Semi-structured, qualitative interviews were conducted to explore perceptions of the impact of the three-week home overnight closed loop use. Content and thematic analyses were conducted exploring positive/negative experiences of closed loop technology.

Participants: 13 parents of participating adolescents

Key positive themes:

Felt safe/reduced anxiety (n = 13); Stable blood glucose levels (n = 8); Improved sleep (n = 6)

'Knowing that they're going to be OK in the night…that's a safety thing' (004)

'Not having the worry…not having to drag yourself out of bed testing at 2 or 3 o'clock in the morning…. It was reliable' (002)

'Improved HbA1c was probably best' (001)

Key negative themes:

Calibration difficulties (n = 5); Size of device (n = 4); Alarms beeping (n = 2)

'It sometimes wouldn't connect which took quite a long time to sort out'(013)

'Probably the alarm because they were just really loud' (010)

'It was quite big and I'd quite like to have a slightly littler one' (012)

All participants reported a positive experience taking part in the trial. Reduced anxiety and feeling their child was safe were key benefits. Alarms and calibration difficulties were noted as downsides to the technology.

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AN INTEGRATED HYPOGLYCEMIA EARLY ALARM AND ADAPTIVE CONTROL SYSTEM FOR ARTIFICIAL PANCREAS

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Preventing hypoglycemia and reducing the fear of hypoglycemia of patients with type 1 diabetes (T1D) are important issues in the development of AP systems. Patient-specific multivariable recursive models are developed to predict hypoglycemia and construct adaptive automatic control systems. Glucose concentrations from a CGM and physical activity information such as energy expenditure and galvanic skin response from a sports armband are used in the model to predict glucose concentrations 30 minutes into the future. Closed-loop studies without any meal or activity announcement were conducted to assess the performance of the integrated alarm and control system. The single variable version of the model (with CGM data) and the alarm and control system were tested with 30 virtual subjects (10 adults, 10 adolescents, and 10 children) from the UVa-Padova simulator. The multivariable alarm and control system was tested in a clinical study with three adult subjects without any meal or activity announcement. Glucose concentration values and physical activity information were measured and transmitted to the alarm and control system every 10 minutes. The daily exercise consisted of running on a treadmill at medium intensity for 20 minutes before or after a meal. The alarm system suggested additional snacks if hypoglycemia were predicted.

Integration of a hypoglycemia early alarm and an adaptive control system was seen to be successful for glucose regulation in patients with type 1 diabetes. Postprandial or exercise-induced hyperinsulinemia and hypoglycemia did not occur when this system was used.

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PERSONALIZED INSULIN INFUSION IN TYPE 1 DIABETES BASED ON REINFORCEMENT LEARNING

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The design of control algorithms for an artificial pancreas (AP) faces the challenges of inter- and intra-patient variability, system uncertainties and strict safety constraints. These facts direct research towards personalized insulin treatment. In this study, a control algorithm inspired by the field of reinforcement learning (RL) is employed able to optimize insulin infusion through learning of patient-specific characteristics. The control algorithm optimizes the daily basal insulin rate and insulin:carbohydrate ratio for each patient based on his/her measured glucose profile. In order to improve performance and accelerate convergence, the patient-sensitive parameters of the controller are automatically and individually tuned based on the estimation of transfer entropy (TE) from insulin to glucose signals. The controller was evaluated *in silico* using the FDA-accepted 100 adult population of the UVa-Padova simulator, under a complex meal protocol, meal uncertainty in the order of ±50% and diurnal insulin sensitivity (SI) variation. The controller achieved 95.66% of time spent in normoglycemia under meal uncertainty and 93.02% under combined meal uncertainty and SI variation. The time spent in hypoglycemia was 0.27% in both cases. The TE-based tuning method reduced the risk of severe hypoglycemia especially in patients with low SI. The results suggest that the RL class of algorithms might offer a significant boost in the development of an AP towards personalized and optimized glucose regulation in T1D.

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REAL-TIME ESTIMATION OF THE INSULIN-ON-BOARD USING THE EXTENDED KALMAN FILTER FOR GLUCOSE CONTROL IN ARTIFICIAL PANCREAS

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Continuous glucose monitors play a key role in the development of the artificial pancreas, as they can measure interstitial glucose concentrations in real-time. Insulin-on-board (IOB) constraints are included in control algorithms and safety modules to mitigate hypoglycemic events, especially during postprandial control. They are based on IOB estimations using static active insulin remaining curves of different duration and/or pharmacokinetic models. However, intra-patient variability may be a limitation for the estimation accuracy compromising performance and patient's safety.

In this work, individualized real-time estimations of IOB from continuous glucose monitoring and pump infusion data is addressed. Hovorka's insulin pharmacokinetic model was incorporated in an Extended Kalman Filter (EKF) in which selected time-variant model parameters were considered as extended states. The observability of the extended models was evaluated by their Lie derivatives. We evaluated this methodology using clinical data from 12 insulin pump patients with Type 1 diabetes who underwent four mixed meal studies. Since IOB is non-measurable, to assess performance real-time insulin concentration estimations were compared to real plasma insulin measurements.

The best results with the EKF were obtained when the parameters k_e (plasma insulin elimination rate) and $t_{max,I}$ (time to maximum insulin absorption) were considered as time-variant. Consequently, time variations in both parameters may be responsible, at least in part, of intra-patient variability in insulin stacking leading to inaccurate IOB estimations.

From these results, we consider that the proposed approach may be beneficial for increasing the efficiency and safety of control algorithms for the artificial pancreas.

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QUANTITATIVE ESTIMATES OF INTER/INTRA DAY VARIABILITY IN PHARMACOKINETIC/ PHARMACODYNAMIC PARAMETERS – HOW MUCH VARIABILITY DOES ARTIFICIAL PANCREAS ALGORITHM NEED TO CONTEND WITH?

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Objective: AP algorithms need to adapt or be robust to changes in PK/PD parameters. The objective of the present study was to quantify within and between day variability in the PK/PD response to subcutaneous (SC) and intradermal (ID) insulin delivery.

Methods: 28 type 1 diabetes adults were studied for 3 consecutive days on 2 occasions, once with SC and once with ID delivery. Breakfast (B) and lunch (L) meal size and content was fixed. Intraday variability was assessed by correlating area under the curve (AUC) of the B and L PK and PD curves. Interday variability was assessed by correlating the AUC on day 1 with day 3. Previously validated minimal models (PVMM) were used to fit B and predict L.

	PK	*PD*
R^2 B v L AUC		
SC	0.923	0.123
ID	0.896	0.027
R^2 Day 1 v 3 AUC		
SC	0.976	0.730
ID	0.947	0.380

Results: B AUC_{PK} was highly correlated with L AUC_{PK} (Table) and day 1 was well correlated with day 3. B AUC_{PD} was a poor predictor of L, and day 1 AUC_{PD} was a poor predictor of day 3. PVMM fit the B PD curve well (RMSE = 1.89 mg/dL; $R^2 = 0.988$) but did not accurately predict L PD (RMSE = 38.62 mg/dL).

Conclusions: AP systems relying on adaptive control algorithms will need to rapidly identify changes in PD parameters within and between days. Systems relying on fixed parameter control algorithms will need to be robust to these changes. PK parameters are more stable.

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PERSONALIZED RULE-BASED CLOSED-LOOP CONTROL ALGORITHM FOR TYPE 1 DIABETES

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[3]*Endocrinology and Nutrition Dept. CSPT, Hospital de Sabadell, Sabadell, Spain*

Background: T1DM implies a life-threatening absolute insulin deficiency. Artificial pancreas (CGM sensor, insulin pump and control algorithm) is promising to outperform current open-loop therapies.

Methods: We designed a predictive rule-based algorithm (pRBA) that uses current and past CGM measurements, a predicted rate-of-change (pROC) for glucose and patient's optimal basal therapy (OBT). It requests information about pre-prandial boluses administered manually according to the amount of carbohydrate intake. Prior to its use, pRBA demands patient-based individual adjustment.

Controller's performance was tested '*in silico*' using the Virginia/Padova simulator in two scenarios of suboptimal basal insulin regimes (±20% deviation with respect to OBT). We measured time spent on target BG range (70–180 mg/dl) during pRBA control and compared it against CSII therapy for the period between 10:00 pm and 2:00 pm of the next day. We

	Open-Loop (CSII) < 70 mg/dl	*Open-Loop (CSII) 70–180 mg/dl*	*Open-Loop (CSII) > 180 mg/dl*	*Closed-Loop (pRBA) < 70 mg/dl*	*Closed-Loop (pRBA) 70–180 mg/dl*	*Closed-Loop (pRBA) > 180 mg/dl*
Night/Basal OBT-120%	12%	88%	0%	3%	97%	0%
Postprandial OBT-120%	0%	100%	0%	0%	100%	0%
Night/Basal OBT-80%	0%	77%	23%	0%	97%	3%
Postprandial OBT-80%	0%	66%	34%	0%	99%	1%

distinguished two stages: night/basal (10:00 pm-08:00 am) and breakfast/post-prandial (08:00 am-02:00 pm).

Results: The pRBA provided better metabolic control (see results).

Conclusions: The pRBA improved metabolic control by increasing time in target with respect to reference suboptimal basal-insulin regimes.

P-270

PROCEDURE FOR CREATING BASELINE DYNAMIC BAYESIAN NETWORK GLUCOREGULATORY SYSTEM STATISTICAL MODEL FOR ARTIFICIAL PANCREAS SAFETY MONITOR

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Objective: Develop a robust procedure for initializing the glucoregulatory system statistical model component of the Dose Safety Artificial Pancreas (AP) controller safety monitor for a new user.

Method: The procedure used 100-subject UVA data simulating our 2011 JDRF-funded, 18-hour two-meal AP clinical protocol. The Fuzzy Logic controller commanded 100% of the insulin used in the study. Active insulin (AI) was calculated for each of the *in silico* subjects using a 3-hour period of action, with peak action after 1 hour. Glucose predictions, based on CGM and AI dynamics, were calculated every 15 minutes.

A 1x15000 real-valued vector lambda represents the statistical model combining glucose and insulin dynamics. The vector was initialized to zero. The perceptron-learning algorithm, utilizing 15000 CGM and AI 1-hour feature vectors, then processed ten (10) CGM and AI datasets to produce the baseline lambda. A second and different set of 20 test subjects used that baseline lambda, with learning turned off, to predict CGM values 30, 45 and 60 minutes into the future.

Prediction error (percent) was calculated as $|B_T - B_P| / B_T$ over the entire 18-hour data sequences, where B_T is the True glucose value and B_P is the Predicted value.

Result: The mean prediction errors (SD) for the 20 test subjects were 6.6% (3.6), 10.3% (5.9), and 13.6% (4.4) for 30, 45 and 60-minute predictions respectively.

Conclusion: The procedure for initializing the statistical glucoregulatory system statistical model produced good results. The next step is to validate the procedure using Dose Safety artificial pancreas clinical data.

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CONSTRAINED MODEL PREDICTIVE CONTROL FOR ARTIFICIAL PANCREAS: DESIGN BASED ON CLINICAL DATA

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One of the most promising control technique adopted for the development of an Artificial Pancreas is Model Predictive Control (MPC). In the first clinical experiences Unconstrained MPC (UMPC) was the most used in order to avoid the implementation of an optimization problem in a clinical device. UMPC implementation is simple but in some cases it may bring the patient to dangerous situations that could be avoided by taking into consideration constraints like pump limitation, limits on the maximum insulin variation, on the maximum insulin on board and on the minimum insulin on board (when glycaemia is relatively high). Thus, a set of constraints, designed from the experience gained during past clinical trials, are introduced in the MPC formulation. The constrained optimization problem has been solved in an exact way (Constrained MPC (CMPC)) and in a suboptimal way by adding ad hoc saturations to the UMPC (SCMPC). UMPC, CMPC and SCMPC have been compared on the 100 virtual patients of the UVA/PADOVA simulator. The time below 70 mg/dl is reduced from 5.64% (UMPC) to 0.04% (CMPC) and 0.05% (SCMPC), the time below 50 mg/dl is reduced from 2.12% (UMPC) to 0% (CMPC and SCMPC), while the time in target [70–180] mg/dl is virtually the same: 87.89% (UMPC), 89.14% (CMPC) and 87.64% (SCMPC). Hence, the introduction of constraints is very effective to reduce the hypoglycemic events while maintaining almost the same time in target. The suboptimal solution results a good approximation of the optimal one.

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PK/PD STUDY IN A DIABETIC PIG MODEL USING MICRO-DOSES OF STABLE, PUMPABLE GLUCAGON

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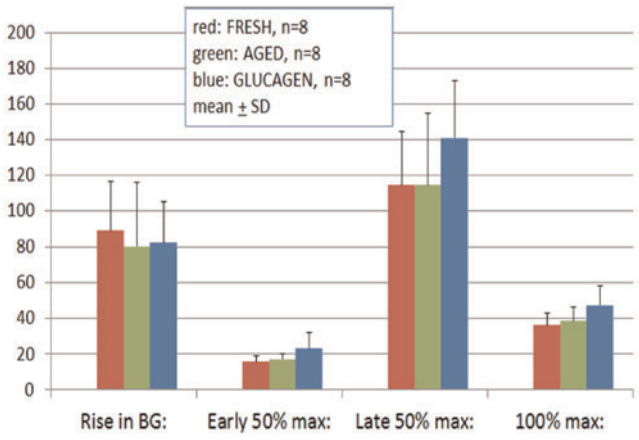

Maintenance of blood glucose levels within a narrow range remains an ongoing treatment challenge for diabetic patients, and a potential solution to this problem is a closed-loop bihormonal insulin-glucagon pump. As such, a bioactive, pumpable glucagon formulation is needed and would require a minimum stability of three days at body temperatures. The present study utilized the Insulet Omnipod® placed on the abdominal skin to measure glucose response of micro-dosed glucagon into the subcutaneous tissue of fasted, octreotide-treated Yorkshire pigs. Twenty-four experiments were conducted in 4 anesthetized pigs that received the following: fresh non-aqueous glucagon (5 mg/mL; Xeris Pharmaceuticals); Xeris glucagon aged 7 days in an Omnipod®; or freshly reconstituted GlucaGen® (Novo Nordisk) as a comparator (N = 8 experiments per formulation). Each pig received 2 μg/kg of each formulation (20–40 μl) SC via Omnipod®. Blood was obtained for determination of glucose and glucagon levels (glucagon analysis ongoing) for 240 minutes. Within 5 minutes of pump initiation, glucose levels rose substantially and were above baseline by an average of 89, 81, and 83 mg/dL respectively. The rise to 50% of the maximum response and the time to a decrease to 50% of the maximum response was not significantly different among the three formulations. By 240 minutes, glucose levels returned to baseline. Erythema and edema were absent at all pump sites. We conclude that subcutaneous infusion of very low doses of Xeris' fresh or aged non-aqueous liquid glucagon provides a rapid, substantial rise in glucagon levels comparable to reconstituted GlucaGen®.

P-273

DAILY PATTERN OF INSULIN SENSITIVITY ENABLES OPTIMIZATION OF INSULIN TO CARBOHYDRATE RATIO: FIRST RESULTS FROM THE STAR 3 STUDY

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Recently, the existence of patient-specific insulin sensitivity (S_I) daily pattern, in type 1 diabetes (T1D) patients (Hinshaw et al., Diabetes 2013), has been demonstrated using a 3-day triple tracer protocol and minimal model analysis. This has been confirmed in (Schiavon et al., DTM 2013), using a recently validated index of insulin sensitivity (S_I^{SP}) based on glucose sensor (CGM) and subcutaneous insulin delivery (CSII) data (Schiavon et al., Diabetes Care 2013).

Here, we tested if the knowledge of the patient-specific S_I pattern may help in optimizing the insulin to carbohydrate ratio (CR), a fundamental parameter for the calculation of the pre-meal insulin bolus.

To do that, we used a subset of the STAR 3 data base (Davis et al., DTT 2010) consisting of 20 (among 244) type 1 diabetic subjects wearing a sensor augmented insulin pump for one month.

The optimal CR is calculated for each recorded meal from S_I^{SP}, area under the CGM and CSII curves and the position of the subject in the Control Variability Grid (CVGA) (Magni et al., JDST 2008).

Results show the existence of a patient-specific trend of CR, in spite of nonnegligible intra-subject variability. It is worth noting that the estimated CR significantly correlated with those reported in bolus wizard for each patient.

If results are confirmed in a larger cohort of subjects, the method could be used for optimizing both standard insulin therapy and closed-loop control algorithms for patients with T1D.

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OPTIMIZATION OF INSULIN TO CARBOHYDRATE RATIO IN TYPE 1 DIABETES THERAPY USING CGM AND INSULIN PUMP DATA

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The insulin to carbohydrate ratio (CR) is a parameter used by type 1 diabetic (T1DM) patients to optimally calculate the pre-meal insulin bolus. Usually, it is calculated based on patient diary but CGM and subcutaneous insulin delivery (CSII) data can provide information for its optimization.

Here we propose a method for CR optimization based on an insulin sensitivity index calculated from sensor (S) and pump (P) data (S_I^{SP}) (Schiavon et al., 2013), area under CGM and CSII curves and the position of the subject in the Control Variability Grid (CVGA) (Magni et al., 2008).

The method was tested *in silico* using the UVA/Padova T1DM simulator (Dalla Man et al., 2014), by simulating a single-meal scenario (75 g of CHO) with optimal patient-specific CR, CR reduced by 20% and CR increased by 20%. In addition, the effect of systematic overestimation/underestimation of meal size (CHO amount) was considered.

In all simulations, the use of the optimal CR, calculated with the proposed method, improves the overall glycemic control in a significant percentage of the simulated subjects and worsens it in a negligible percentage. As an example, Figure 1 shows the CVGA for the 20% reduction of optimal CR (left) and the optimized CR (right).

A novel method for the optimization of CR based on CGM and CSII data is proposed. This can be used both for optimizing standard insulin therapy and initializing closed-loop control algorithms.

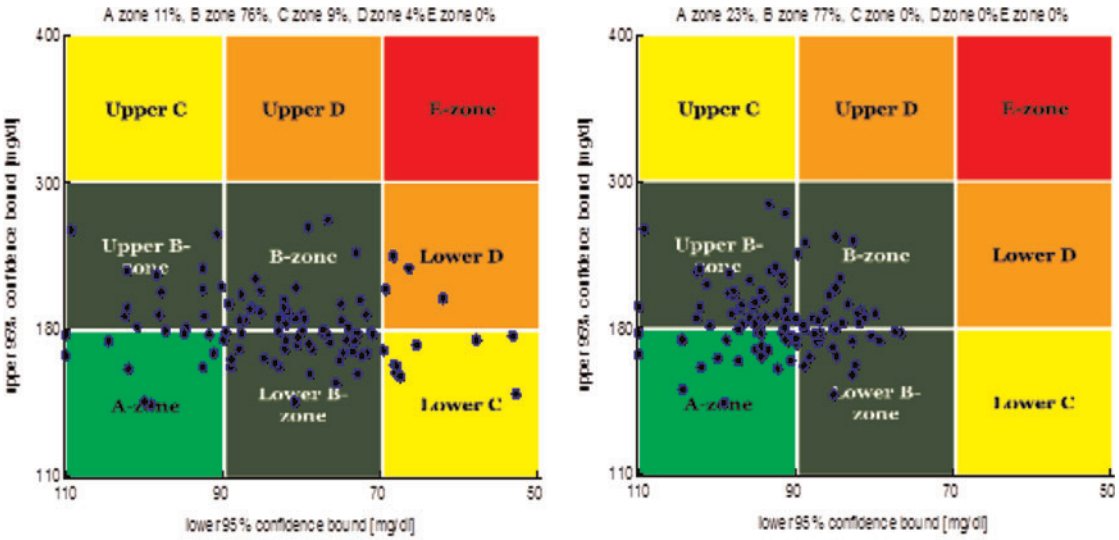

Figure 1: CVGA for the 20% reduction of optimal CR (left) and the optimized CR (right).

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PREVENTION OF HYPOGLYCEMIA IN THE ASPIRE IN-HOME STUDY

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Background: In the ASPIRE In-Home Study, subjects with type 1 diabetes were randomized to receive sensor-augmented pump therapy with or without use of the Threshold Suspend (TS) feature, which interrupts insulin delivery when a low sensor glucose value is detected. Lower rates of nocturnal hypoglycemic (NH) events (defined as sensor glucose values ≤65 mg/dL for >20 minutes starting between 10:00 PM and 8:00 AM) were noted in the TS group than in the control group. The AUC of the NH events was also significantly lower in the TS group ($p < 0.001$ for each).

Methods: We tested whether the value of the TS feature lies more in preventing second and subsequent NH events in a given night, or in preventing NH events entirely, by enumerating nights with single and multiple NH episodes.

Results: In the TS group, 18.4% of the patient-nights (1662 of 9052) featured exactly one hypoglycemic event, and 1.9% had ≥2. This is in contrast to the control group, where 22.1% of the patient-nights (2044 of 9247) featured exactly one event, and 4.8% featured ≥2. Therefore, patients in the TS group had a 24.6% reduction in the number of nights with any hypoglycemic event and a 60.1% reduction in nights with multiple events compared to patients in the control group. In the TS group, all NH events were associated with pump suspensions.

Conclusion: The TS feature appears to significantly decrease not just the rate of second and subsequent hypoglycemic events, but the rate of initial hypoglycemic events as well.

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CHANGE IN A1C AND REDUCTION IN HYPOGLYCEMIA WITH THRESHOLD SUSPEND IN THE ASPIRE IN-HOME STUDY

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Background: The ASPIRE In-Home Study randomized 247 subjects with type 1 diabetes to receive sensor-augmented pump therapy with Threshold Suspend (TS), that automatically stops insulin delivery at a pre-set sensor glucose value, or to sensor-augmented pump therapy alone (Control).

Methods: Nocturnal hypoglycemia (NH) events were defined as SG ≤65 mg/dL for >20 min from 10 PM and 8 AM. The mean rate of NH events, mean AUC of NH (AUC_{hypo}), and effects of change in A1C values ($\Delta A1C < -0.3\%$, ≥ -0.3 to $\leq 0.3\%$, $> 0.3\%$) from baseline to study end were compared in TS vs Control groups.

Results: Twenty-five TS subjects and 28 Controls reduced their baseline A1C by >0.3%. Among participants who improved their A1C, those in TS group had lower rates of NH (1.5 vs. 2.4 events/week for TS vs Controls, p_{hypo} (p_{hypo} (p0.3% during the study (26 TS and 19 Controls), NH rate was comparable (1.5 and 1.6 events/week, respectively), but AUC_{hypo} was lower in the TS group (p

Conclusions: Lower and stable A1C values were associated with decreased hypoglycemia with the TS feature. Regardless of TS feature use, increasing A1C values were associated with similar hypoglycemic events, but AUC_{hypo} was lower in the TS group. The Threshold Suspend feature in ASPIRE In-Home study improved glucose control along with a decrease in hypoglycemia.

P-277

RAPID MODEL IDENTIFICATION FOR ONLINE GLUCOSE PREDICTION OF NEW SUBJECTS WITH TYPE 1 DIABETES USING MODEL MIGRATION METHOD

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Table 1. Model prediction accuracy for thirty *in silico* subjects and 30 minute predictions (mean ± standard deviation)

Type of Model	RMSE (mg/dL)	R-EGA (% in zone A)	Time Lag for hyper event (samples)	Sensitivity for hyper event (%)	Time Lag for hypo event (samples)	Sensitivity for hypo event (%)
Model migration with two-hour modeling data	17.95±11.50	88.00±3.11	2.47±1.22	0.72	1.90±1.45	0.79
Subject-dependent model with three-day modeling data	14.52±8.58	77.08±9.92	2.10±0.93	0.77	4.00±0	0.89
p value based on paired-t test (α=0.05)	9.1625e-007	2.3701e-008	------	------	------	------

The base model is developed based on subject #10; similar results are obtained for base models based on other subjects.

For online glucose prediction, model identification has to be repeated with sufficient data collected for each subject because different subjects may give different responses to the excitation of meal, insulin and other exogenous inputs, which causes burden of patients and clinician.

Here, model migration algorithm is proposed for rapid model development for new subjects with small amount of new subject data where parameters of a base model are properly adjusted with adjusting step and direction. Two autoregressive with exogenous inputs (ARX) modeling methods are considered with meal and insulin as inputs: (i) model migration with limited data; (ii) subject-dependent model with sufficient data. Online short-term (0–60 min) glucose predictions are made for thirty *in silico* subjects using UVa/Padova metabolic simulator with 5 mins as sampling interval. Prediction accuracy is evaluated by comparing glucose predictions with actual measurement, which is summarized in Table 1.

The results indicate that the accuracy of model migration is comparable to that for subject-dependent model with adequate data as evaluated by Time Lag. Besides, both models produce 30 mins ahead glucose predictions that are primarily located in zone A of R-EGA. The proposed model migration strategy can be regarded as an effective and economic modeling method instead of subject-dependent modeling method.

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PRANDIAL INSULIN DOSAGE CALCULATORS: ONE YEAR EXPERIENCE

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Month	*N*	*Weight (kg)*	*HbA1c*	*Basal dose*	*Bolus dose**
0	45	73.1	8.29	28.9	17.8
1	43	−0.24	–	−0.9	+0.8
3	42	−0.44	−0.28	+0.8	−2.3**
6	20	+1**	−0.64	+2	−0.5
12	13	+0.7**	−0.77**	+1.1	−2.4**

* Correction bolus not included. Several patients used advanced mode.
** $p < 0.05$

Introduction: Within the conventional insulin therapy, ''basal-bolus'' is considered the most physiological and effective method. However it requires frequent dose changes to adapt to the different needs over the time. Diabetes education seeks to enable patients to carry out these changes for themselves, but in practice many do not do this or do so in an incorrect way.

Recently, systems that recommend rapid-acting insulin dose to be administered, based on current blood glucose and insulin sensitivity, have been developed. Initially, they were set out for diabetics treated with continuous insulin infusion, but nowadays these systems have been adapted for patients with basal-bolus regimen.

Patients and methods: 45 patients (17 men and 28 women), 40 with type 1 diabetes, 3 with type 2 and 2 post-pancreatectomy, with an average age of 39.8 years and 14.4 years of evolution. They were given a glucometer with prandial dose. Two patients gave up the device for handling disability. Table shows initial variables and their evolution.

Conclusions: Prandial insulin dosage calculators may be an useful tool for monitoring patients with diabetes on treatment with basal-bolus pattern, by facilitating dosage decisions, reducing glycemic variability and improving the diabetes education level, which it is likely to result in better metabolic control.

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A PROTOTYPE SYSTEM FOR CARBOHYDRATE CONTENT ESTIMATION BASED ON COMPUTER VISION METHODS

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A prototype for the automatic computer vision-based estimation of meals' carbohydrate (CHO) content is presented. The system is designed for diabetic patients and aims at CHO estimation with an error less than ±20 grams/meal. The user places a reference object (e.g. credit card) next to the meal and acquires two images using a smart phone's camera. Then, the different food items on the plate are segmented and recognized while their 3D shape is reconstructed. Based on the shape, the segmentation results and the reference object, the volume of each item is estimated. Finally, the CHO content is calculated by combining the food type with its volume, and using nutritional databases.

For developing and testing the system, a database containing almost 3000 images was created with foods belonging to 8 different major classes. Individual experiments on segmentation, recognition and volume estimation resulted in accuracies of 88.5%, 90% and 90%, respectively. The various computational steps were integrated into a prototype system designed for Android devices with the computer vision parts running on the server side. The prototype was evaluated using a validation dataset of 10 meal image pairs of known CHO content. The system was able to estimate the CHO content with an average error of ±9 grams/meal and an average execution time below 15 seconds. Future work includes the algorithms' optimization to succeed a near real-time execution, which will run entirely on the phone. Additional experiments regarding the stability of the system on real-life conditions will be carried out.

P-280

ALCOHOL HEALTH LITERACY IN YOUNG ADULTS WITH TYPE 1 DIABETES: A WEB-BASED STUDY HIGHLIGHTS THE EXTENT OF THE PROBLEM

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Background: Alcohol-specific health literacy is poor in the general population. Alcohol directly affects glycaemic control, and accurate estimation of alcohol intake can support effective diabetes management. Little is known about the accuracy of alcohol knowledge and management strategies of young adults with type 1 diabetes when consuming alcohol.

Aims: To investigate knowledge of alcohol and carbohydrate content of commonly consumed beverages among young adults with Type 1 diabetes;

To explore alcohol consumption and;

To identify diabetes self-management strategies for minimising alcohol-associated risk.

Method: An open-access, multiple-choice web-survey investigating knowledge of alcohol and carbohydrate content of 10 typical alcoholic drinks using images. Participants also recorded current alcohol consumption and diabetes self-management strategies when drinking.

Results: 547 participants aged 18–30 years participated (341 women, 192 men; mean age 24.5 SD 3.7 years), of whom 365 (66.7%) drank alcohol. 142 (41.6%) female and 83 (43.2%) of male respondents score ≥ to the AUDIT3 cut-off for potentially problem drinking. Knowledge accuracy of alcohol units was poor: only 7.3% ($n=40$) scored ≥5 correct answers out of ten. Carbohydrate content was also poor: no participants scored ≥5 correct answers out of ten. Strategies to minimise alcohol-associated risk were reported, however, these were variable and inconsistent.

Conclusions: Alcohol consumption was common amongst participants; however, alcohol and carbohydrate health literacy are poor. Further research is required to develop effective strategies to improve health literacy and support safe drinking for young adults with T1DM. Electronic social media may be appropriate to host such resources.

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MOBILE TECHNOLOGY AS A TOOL FOR PATIENT EDUCATION AND SELF-MANAGEMENT IN THE DIABETIC POPULATION

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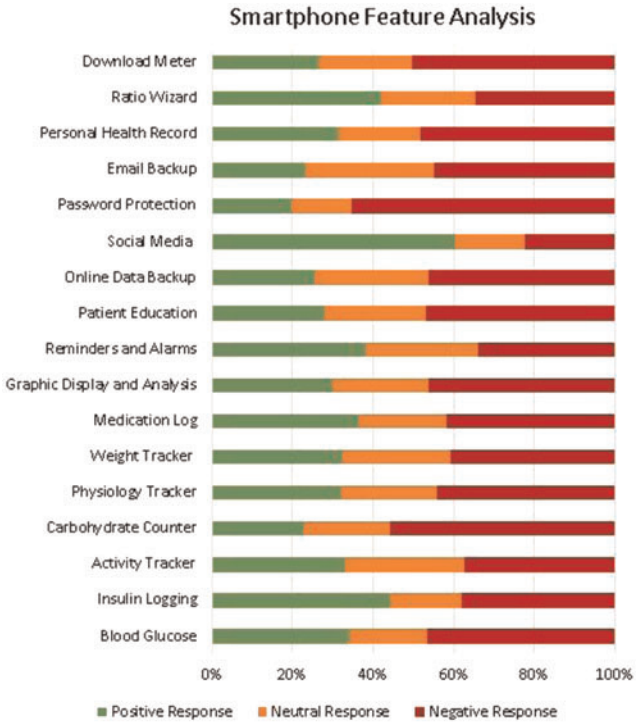
Objectives: This study aims to ascertain the desire for mobile technology, namely Smartphone apps (SA), which can support patient education, self-management and data sharing with the health-care team.

Methods: This prospective questionnaire study sampled 200 Patients from My Diabetes My Way (MDMW), an interactive database for patients in Scotland allowing access to personal online clinical information. The anonymous questionnaire explored areas of current management techniques, technology literacy, patient education, self-management and desirable features for a future SA. Prior consent for patient contact had been agreed.

Results: 200 patients from MDMW were contacted via email. 122/200 participants responded. Results below highlight response 1 or 2 versus response 4 or 5 on a likert scale (1 = strongly agree and 5 = strongly disagree). There is a strong desire for SA development (48/68, 71%, 95%CI 59–80). Half of the participants would use SA for education (60/119, 50%, 95%CI 42–59) and a similar number (54%) would prefer SA to current methods of self-management (37/68, 54%, 95%CI:42–66). Desirable features are detailed in the chart below. Desirable features included social media integration (70/116, 6%,



95%CI:51–69). Carbohydrate tracking was undesirable (58/119, 52%, 95%CI:42–61).

Conclusions and Discussions: Preliminary results from the study suggest that there is a desire for SA. In particular offering integration with health-care systems. Providing patients with contemporary methods to support their care will enable better health outcomes to be achieved and maintained.

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IS IT POSSIBLE TO IMPROVE ADHERENCE TO TREATMENT IN PATIENTS WITH TYPE 1 DIABETES IN MULTIPLE-DOSE INSULIN THERAPY AND BOLUS CALCULATOR?

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[1]Department of Personality Assessment and Psychological Treatment, Faculty of Psychology University of Malaga, Instituto de Investigación Biomédica de Malaga (IBIMA), Málaga, Spain [2]Unidad de Gestión Clínica Intercentros de Endocrinología y Nutrición, Hospitales Universitarios Regional y Virgen de la Victoria Malaga, Instituto de Investigación Biomédica de Malaga (IBIMA), CIBERDEM Instituto de Salud Carlos III, Málaga, Spain

Aims: 1) To study the variables related to adherence to treatment in patients with type 1 diabetes (T1DM) treated with multiple-dose insulin (MDI) and bolus-calculator at 4 months of study. 2) Determine an explanatory model of adherence at 4 months of study. 3) Compare these results with a control group treated with MDI.

Methods: 37 patients with T1DM and initial poor glycemic control were randomized to receive MDI and bolus-calculator (CBMDI group) (n = 19) and MDI alone (control group) (n = 18). At baseline and at 4 months were analyzed sociodemographic, clinical and psychological variables: treatment satisfaction (DTSQ), depression (BDI-II), anxiety (STAI), fear of hypoglycemia (FH-15), distress associated with diabetes (DDS) and treatment adherence (SCI-R). Statistical Analysis: Pearson correlation coefficient and multiple regression model with forward selection procedure.

Results: At 4 months follow-up, in the CBMDI group we found a positive association between adherence, years of evolution with diabetes and treatment satisfaction, and a negative association with overall distress and distress associated with treatment compliance. In the control group, adherence was positively associated with number of self-monitoring, and negatively correlated with state anxiety and distress associated with treatment compliance. CBMDI group: distress associated with treatment compliance, treatment satisfaction and state anxiety were predictors of adherence to treatment (60.8% of the total variance). Control group: the predictors of adherence to treatment were distress associated with treatment compliance and satisfaction with treatment (49.7% of the total variance).

Conclusions: It has been found a profile predictive of adherent patients to treatment with CBMDI. These data could be clinically useful to improve adherence to CBMDI.

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A NEW RISK MARKER FOR HYPOGLYCEMIA DERIVED FROM QUANTIFICATION OF POINCARÉ PLOTS OF CGM DATA IN TYPE 1 DIABETIC PATIENTS

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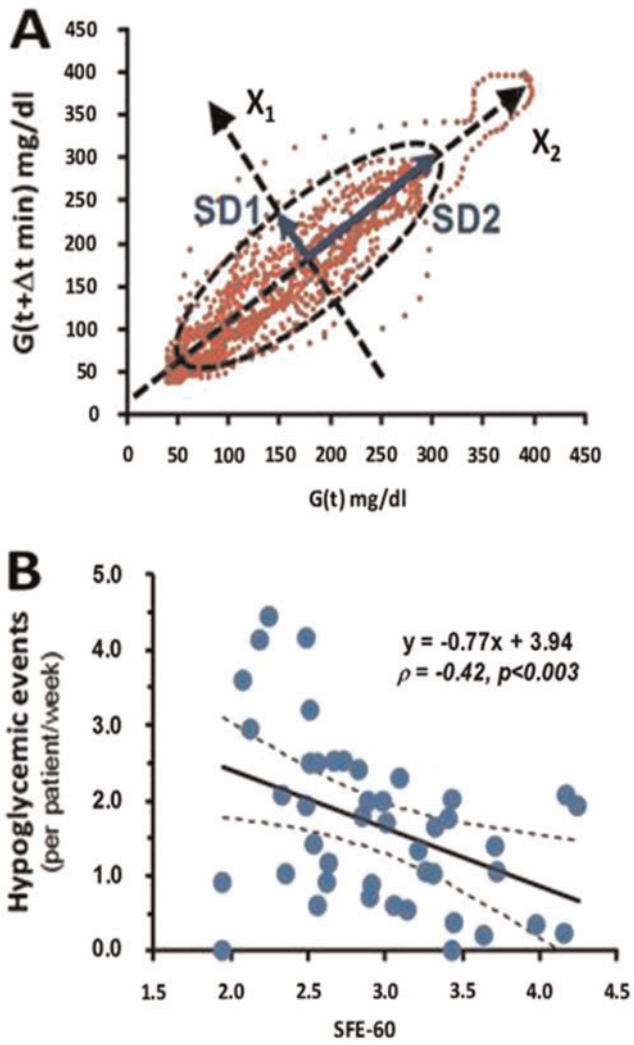
Background: The Poincaré plot (PCP) is a tool for describing glucose variability (GV) of which each point represents a pair (Gt, Gt + Δt), where Gt and Gt + Δt are glucose values at time t and t + Δt. The aim of this work was to validate metrics for the PCP geometry.

Methods: We reviewed CGM recordings of 44 patients with type 1 diabetes. The new metrics were computed from PCPs with Δts of 30, 60 and 120 minutes and correlated with classical GV indices and hypoglycemia.

Results: SD related to the PCP fitting ellipse (SD1, SD2), its area (AFE = πxSD1xSD2) and shape (SFE = SD2/SD1) are shown on panel A. SD1 represents short-term GV and is equivalent to CONGA. SD2 represents long-term GV and correlates with glucose SD ($r \geq 0.98$), MODD ($r \geq 0.91$) and MAGE ($r \geq 0.88$). SFE-60 did not correlate with main GV indices but was inversely correlated with hypoglycemic events < 70 mg/dl (panel B, Spearman's $\rho = -0.42$; $p < 0.003$). In a multivariate analysis, both LBGI (partial $r = 0.72$) and SFE-60 (partial $r = -0.34$; $p < 0.00001$ for both) maintained significance for predicting hypoglycemia, demonstrating complementary properties of SFE and LBGI (multiple $r = 0.76$; $p < 0.00001$).



Conclusions: PCP-derived metrics are correlated with known GV indices and may be used for the study of CGM series in type 1 diabetes. SFE-60 is a new risk marker for hypoglycemia independent of LBGI.

P-284

RETROSPECTIVE AUDIT OBSERVING EFFECT BOLUS CALCULATOR USE AND CARBOHYDRATE COUNTING HAS ON GLYCAEMIC CONTROL IN CHILDREN WITH TYPE 1 DIABETES

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Automated Bolus Calculators (ABC) were introduced into two inner city hospitals with a high deprivation index in August 2010.

Objective: To observe the change in Hba1C for 3–6 months after the introduction of ABC and carbohydrate counting (CC). To explore the effects of age, gender, psycho-social circumstances on HbA1c as well as the uptake of insulin pump therapy after implementation.

Method: ABC were offered to families who were CC or required a method of calculating a correction bolus. Two ABC were used: Accuchek Expert, Roche and Insulinx, Abbott. Hba1C was recorded at time of obtaining the meter and on average 167 days after implementation. Data was collected retrospectively. Patients using the meter within the year of diagnosis were excluded. Results were statistically analysed.

Results: Sample size 105. Mean Hba1C decreased by a small statistically significant amount (0.41%) (2.54 mmol/l) $P < 0.001$. 80% of the sample size carbohydrate counted all their meals whereas 15% counted only evening meals. Those reported to have no known psycho-social problems had an improved mean difference in the Hba1C.

Conclusion: ABC used for corrective dosages or CC shows a statistically significant change in Hba1C over time. There were reductions in Hba1C when stratified by age, gender, difficulties, or CC. These were not statistically significant however the sample size was underpowered to detect significance in the different subgroups. This evidence supports the belief that regular usage of ABC alongside CC has a positive effect on HBa1C. Accurate advice is best obtained when using ABC alongside CC.

P-285

TREC DIABETES: A NEW TELEMEDICINE SYSTEM

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Background: Telemedicine systems for diabetes are often evaluated by healthcare professionals following questions raised from patients. However the physician can not be contacted by the patient in situation of metabolic risk.

Aim: To test a new telemedicine system that allows healthcare professionals to access the dashboard only following a previously decided alarm.

Materials and method: TreC Diabetes was produced by FBK and was given on smartphone to 10 paediatric patients with type 1 diabetes. The application allows the patient to enter blood glucose, food and insulin data that are stored in real time in the centralized database.

From the analysis of these data, the platform generates some previously decided alarms of repeated hypo and/or hyperglycaemia and some predictive alarms for these condition on the basis of LBGI and HBGI. These alarms are sent to the Paediatric Endocrinologist by e-mail

A simulation for 9 months was undertaken to test the platform and the paediatric diabetologist responded to the alarms by choosing among a few options

Results: During the 9 months, the Paediatric diabetologist received 180 alarms.

The most frequent alarm was LBGI > 2.5 (n = 89). In response to the alarm LBGI > 5 (n = 15) the physician would want to contact the patient by phone.

Conclusion: This is a new telemedicine system for diabetes that allows healthcare professional to access the dashboard only following a previously decided alarm. The platform is now complete, and we will begin a new study to assess the acceptability and satisfaction of patients enrolled.

P-286

HELPING GENERAL PRATICTIONER TO MANAGE DIABETIC KETOACIDOSIS REDUCING RISK OF COMPLICATIONS: OUR SIMPLE TREATMENT SOFTWARE

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In the Department of Pediatrics of Brindisi Hospital we don't treat exclusively diabetes mellitus, but every pediatric disease, including emergencies and first aid accesses. In each shift there are at least one medical doctor and two nurses. The diabetic ketoacidosis is demanding but it cannot stop the other department activities and urgencies. It is therefore necessary to optimize human resources, allowing medical staff to treat the diabetic emergency with pertinence and accuracy. We made a specific Excel© software, based on ISPAD Clinical Practice Consensus Guidelines 2009: child age, weight, blood pH, glycaemia, base excess, potassium dose, are required; the physician also decides if needs to correct hypernatremia or to use bicarbonate. The program gives rehydrating fluids composition (saline solution, glucose, KCl and potassium phosphate), and suggests hydration and insulin rate (in ml/h and ml/Kg/h) for the first 18 hours of therapy - there are five periods of timing treatment (1^{st} hour, from 2^{nd} to 4^{th} hour, from 5^{th} to 7^{th} hour, from 8^{th} to 13^{th} hour, from 14^{th} to 18^{th} hour). The software adapts fluids and insulin therapy every time the doctor changes the basic parameters as above indicated. We hadn't any ketoacidosis complication during treatment.

Now any department physician can manage ketoacidosis, while pediatric diabetologist can concentrate his attention to teach proper diabetes education and self-management.

example	Name				
age	11				
weight	31				
Correct hypernatremia	0	0=No 1= yes	Best after 1st hour		
Base Excess	22				
Glycemia	229				
Bicarbonate	0	0=No 1=Yes	If pH < 7 and HCO3 < 6 mmol/l. Stop when ph > 7,1		
K dose (mEq/Kg/h)	0,3	Insert value from 0,1 to 0,5			
Therapy	Fluid	Quantity (ml)	ml/Kg	Infusion rate	Regular insulin infusion rate (25 U in 250 ml of NaCl 0,9 % solution) - ml/h
1st hour	NaCl 0.9%	310	10	310	-
	Acqua Distillata	0			
	NaHCO3	0			
2nd to 4th	NaCl 0.9%	164	8	248	27
	glucose 5%	82			
	KCL	4,65			
	K2HPO4	4,65			
	Acqua Distillata	0			
	NaHCO3	0			
5th to 7th	NaCl 0,9%	150	7	217	35
	Glucose 10%	150			
	KCl	4,65			
	K2HPO4	4,65			
8th to 13th	NaCl 0,9%	115	5	155	38
	Glucose 10%	335			
	K2HPO4	4,65			
	KCL	4,65			
14th to 18th	Nacl 0,9%	50	3	93	23
	Glucose 10%	160			
	KCL	4,65			
	K2HPO4	4,65			

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DESIGN EVALUATION OF A PROTOTYPE USER INTERFACE TO SUPPORT A GUIDELINE-BASED DECISION SUPPORT SYSTEM IN GESTATIONAL DIABETES

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Background: Gestational Diabetes (GD) has increased over the last 20 years, affecting up to 15% of pregnant women worldwide. The complications associated can be reduced with the appropriate glycemic control during the pregnancy.

Methods: The EU FP7 project 'MobiGuide: Guiding patients anytime everywhere', focuses on GD patients to provide guidance based on clinical guidelines supported by an intelligent decision-support system integrated in a mobile application. The application for GD patients consists of a software implemented on a Smartphone running Android from 2.x. The evaluation was performed with a prototype version with self-explanatory messages to access each of the scenarios: a) Patients logbook (including glycemia, diet compliance and exercise); b) Recommendations; c) Settings; and d) Automatic physical activity monitoring.

We collected feedback on the design and functionality of the mobile application after the patients interacted with the system, in order to support subsequent iterations of the application development. The system was tested with 8 patients with GD, who answered a questionnaire about the design, perceived ease of use and perceived usefulness of the mobile application.

Results: Most patients have shown positive comments. 75.0% strongly agree that the system will help them to be more confident with the disease. 87.5% consider that the terminology is clear and the information is logically shown. And, 75.0% stated that it will be easy to use and easy to learn the application.

Conclusions: Including patient feedback in design-concept development is essential to identify critical factors to fulfill usability, ease of use and usefulness requirements.

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IMPROVING DIABETES CARE BY USING MOBILE TECHNOLOGY IN ADULTS WITH TYPE 1 DIABETES

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Objectives: The role of mobile technology to improve diabetes care in adults with type 1 diabetes (**REMOTE-T1D**) study was aimed to evaluate the use of mobile technology (iBGStar® [iPhone plus the BGStar®]) in improving Patient Reported Outcomes (PRO).

Methods: This single-center, prospective, randomized, open-label, investigator initiated pilot study enrolled 100 adult patients with T1D. Patients were randomized in a 1:1 fashion to an intervention group using self-monitoring of blood glucose (SMBG) with BG Star® and mobile technology (iBG Star) vs. SMBG with Accu-Chek Nano® (Control). All subjects had similar clinic and phone visits for 3 months with a 3 month extension period and wore a blinded DexCom Gen4 Platinum® continuous glucose monitor (CGM) for 4 separate 7-day periods.

Change in A1c and Hypoglycemia Fear at 3 Months

	Control (n=43)	iBG Star (n=45)	P-value comparing change in control vs. change in iBG Star
Change in A1c (%)	-0. 0.21 ± 0.65*	-0.38 ± 0.72**	0.24
Change in Hypoglycemia Fear Scale	-2.9 ± 11.2	-4.48 ± 9.4	0.90
Change in Hypoglycemia Behavior Scale	-1.2 ± 5.9	2.5 ± 6.1	0.32
Change in Hypoglycemia Worry Scale	-3.0 ± 9.2	-2.0 ± 6.3**	0.55

*p=0.05; **p=0.001

This was an Investigator Initiated study supported by Sanofi

The PRO included a hypoglycemia fear questionnaire and the secondary outcomes included improvement in glycemic variability indices and reduction in A1c values.

Results: Baseline characteristics included age (39 ± 12 years old), gender distribution (~52% male), diabetes duration (23 ± 12 years), glycemic control (A1c 7.9%) and body mass index (~27 kg/m^2) were similar between the two groups. There was a significant improvement in Hypoglycemia Behavior Scale (HBS) and A1c at three months compared to baseline in each arm (Table), with a difference which may be more meaningful for iBGStar group. Both groups significantly improved in Hypoglycemia Fear Scale and Hypoglycemia Worry Scales. SMBG and CGM data analysis is pending.

Conclusions: Glucose control and HBS improved similarly in both groups with a tendency for meaningful improvement in the iBGStar group.

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DIABETES MANAGEMENT ON SMARTPHONES

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Type 1 diabetic patients require a very strict control of their disease. This implies registering glucose levels, carbohydrate intake, insulin, exercise and other factors that influence glycaemic values. This allows patients to review their decisions and evaluate results. These records are also important to discuss the treatment with their doctors. As such, the records should contain the greatest amount of information and be as accurate as possible. Usually, records are kept on paper, making it difficult for patient and doctor to review, interpret and correlate the data. To assist them, we developed a smartphone application with a simple design to overcome the stated goals for patient records. This resulted in a process oriented application instead of just focusing on registering data, which emphasises the activity (ex.: a meal), guiding the patient to register the appropriate measurements. All information is recorded for further analysis and manipulation. The presentation of measurements, both in the application itself as in generated reports, is simple and easy to interpret, relating the records to each other for better interpretation. In addition to the most important records for glycaemic control, the application also stores other patient's health information, from weight, blood pressure, cholesterol to other diseases. This development led to an intuitive mobile healthcare application for diabetics that can improve their disease control. As future work, we plan to implement intelligent warnings based on medical guidelines that apply to the context inferred by the records kept and to undertake clinical trials to assess its possible gains.

P-290

VALIDATION OF IPRA© (DECISION SUPPORT SOFTWARE FOR PATIENTS USING RT CONTINUOUS GLUCOSE MONITORING) BY A PANEL OF EXPERT PATIENTS

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Introduction: Insulin Pump-RT Advisor© (IPRA©), presented last year at the ATTD meeting, is a smartphone application designed to help insulin pump treated patients in making decisions based on real time continuous glucose monitoring (RT-CGM) data. A prospective study was conducted to validate this tool by RT-CGM users in real-life.

Methods: 6 type 1 diabetic patients treated by insulin pump for more than 2 years and RT-CGM for more than 6 months used IPRA© for 2 weeks. They completed an online questionnaire at each connection. Patients were asked about their intention before IPRA© advice delivery. They were then asked to assess IPRA© advice and to propose alternative action in case of disagreement. The rate of agreement and the kappa coefficient to assess concordance between IPRA© advices and expert decisions were calculated. At the end of the study a satisfaction questionnaire was completed.

Results: 304 connections were analyzed. Experts agree with IPRA© advices in 93% of cases. Rate of agreement was lower at bedtime (84%) compared to pre-meal (96%) or post-meal time (90%, p = 0,011, Fisher's exact test). The kappa coefficient was 69%. Satisfaction score assessing IPRA© usefulness, ergonomics and impact on behavior was 4.2/5.

Conclusion: IPRA© is validated by a panel of expert patients. A new version of IPRA© taking evolutions proposed by these experts into account is currently being developed. The effects of IPRA© on patient behavior when using RT-CGM, quality of life and glycemic parameters will be studied.

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USING GOOGLE GLASS AS A NOVEL PLATFORM FOR INTERACTION WITH AND ANALYSIS OF THE DIABETES DATA ECOSYSTEM

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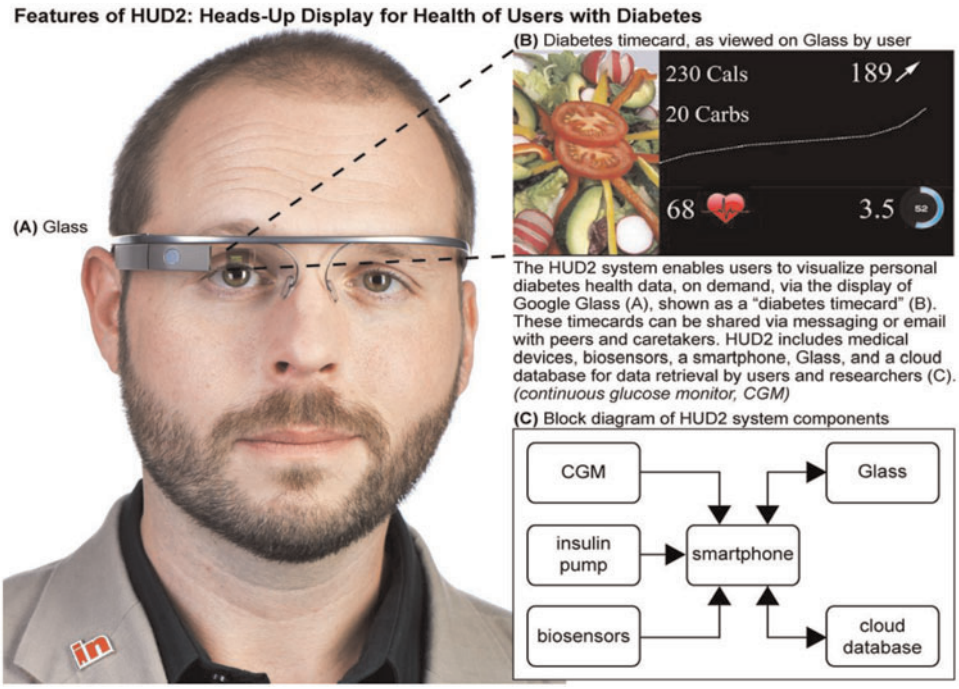
Patients with diabetes currently struggle to view and share their personal health data. Recent advances in wearable computing can enable meaningful interactions with the diabetes data ecosystem. Our objective is to leverage the new wearable computing platform, Google Glass, in a system to collect, visualize, and share multimodal diabetes data for use in patient decision-making and diabetes informatics research.



Glass, a lightweight wearable computing device, features a heads-up display, camera, microphone, memory, various sensors, WiFi and Bluetooth. Users interact with Glass via built-in touchpad or hands-free voice commands.

Our system, Heads-Up Display for Health of Users with Diabetes (HUD2), integrates Glass, a smartphone, body-worn medical devices (continuous glucose monitor, insulin pump), biosensors (flexible, disposable sensors for heart rate, temperature, etc), and a cloud database. The smartphone passively collects data from the biosensors, Glass, and the user's medical devices, and transmits data to the database. Users photographically document meals with Glass's camera; these time-stamped images are integrated into the database. All data are retrievable for processing by the investigators' analytics engine.

Via Glass's display, users may view all of their data (CGM readings/trends, insulin on board, meal photos, other physiologic/activity measures) in one integrated, simplified visualization, the 'diabetes timecard', on-demand or according to configurable notifications, per user preferences. Timecards are shareable (via messaging/email) with family, peers, and caretakers, for real-time decision-making support.

HUD2 captures a substantial portion of an individual's diabetes data ecosystem without undue user burden, providing new data-driven resources for patients, their peers and caretakers, and researchers.

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GLUCOTAB – AUTOMATIC DECISION SUPPORT FOR TREATMENT OF PATIENTS WITH DIABETES TYPE 2 IN HOSPITAL

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Objective: GlucoTab is a mobile system for healthcare professionals supporting blood glucose management of hospitalized patients with type 2 diabetes mellitus, by (1) workflow management, and (2) insulin dose recommendations. We present the path from an idea to the CE-labeled medical device.

Methods: A team of nurses, physicians and engineers gathered requirements to improve the inpatient glucose management. In an iterative approach, involving end users in all design decisions, increasingly detailed prototypes were developed. The development process complied with the regulatory requirements for medical device software which apply to decision support systems. After an intensive state of the art survey, the algorithm behind the decision support was evaluated paper-based. Subsequently the GlucoTab was tested at a clinical ward; thereby a strict observation to detect problems and deviations took place. Finally, after some technical innovations and algorithm adjustments a study on 4 different wards followed, to demonstrate efficacy and safety of the GlucoTab as a basis for the upcoming CE certification.

Results: The GlucoTab was well accepted during the clinical studies, especially nurses, who are the main users of the GlucoTab, perceive the system as a relief and felt safe in using it. Also the clinical outcome shows that the blood glucose level could be clearly decreased without the appearance of critical hypoglycemic events.

Outlook: At the moment the CE certification of the GlucoTab is in progress and is expected to be finished in November 2013. With the CE labeled product a multicenter clinical trial is planned.

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A VIRTUAL EHEALTH INTERVENTION FOR DIABETES SELF-MANAGEMENT AND SUPPORT

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Innovative interventions that utilize the benefits of Web 2.0 to empower patients in diabetes self-management (DSM) are needed to provide accessible, sustainable, cost-effective patient education and support. Studies suggest that skills acquired in virtual environments (VEs) transfer to real-world behaviors. A VE is a real-time 3D representation of a setting running over the Internet. We developed and pilot tested a VE that facilitated DSM through synchronous DSM classes, resources and social networking in a community where participants practiced skills such as grocery shopping and dining out. We evaluated the feasibility and preliminary efficacy of participation using a one group, pre-mid-post measure design. At baseline, 3 and 6 months we assessed perceived usability and usefulness; self-efficacy; self-management behaviors; social support and diabetes knowledge using validated survey measures; and metabolic indicators (HbA1c, BP, BMI). We enrolled 20 participants with a mean age of 54 years (range 39–72). Overall participants rated perceived usefulness and ease of use as high. They logged into the site a mean of 2.5 hours/week over 6 months. High DSM class attendance was reflected by the largest percentage of time spent in the classroom (48%). Self-efficacy, social support, and foot care showed significant improvement ($p < 0.05$). Clinical outcomes showed trends toward improvement. These preliminary data suggest that VEs provide a feasible platform for patients and educators. Access to diabetes education, skill building, and support from a home computer removed barriers to traditional DSM support. This program has potential for improving DSM in an easily disseminated alternative model.

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SWEET-O-BIKE TM - A COMPUTER-BASED NOVEL INTERACTIVE DIABETES EDUCATIONAL TOOL

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Aim: In this pilot study feasibility of recruitment, validity and acceptability of the Sweet-o-Bike (S-o-B) intervention in a small group of type 2 diabetes patients was explored.

Methods: Patients were asked to participate in a consecutive way until 30 agreed to participate. Random selection of 6 OAD-only and 6 insulin/OAD-treated patients attended 2 sessions during 1 month in small groups. Selected questions of the AD-Knowl questionnaire were verbally administered by the dietician. Each had 3 cycling tours. A print-out of their cycling served as a discussion tool for the patients to understand what happened during cycling. After cycling, the ADKnowl was applied again. Finally, patients were interviewed about acceptability of the S-o-B. After 1 month the intervention was repeated in the same manner. Paired t-tests were applied to calculate the mean differences in scores before and after the intervention.

Results: For the OAD-groups 27 patients were asked of which 17 patients agreed to participate. For the Insulin groups, 29 patients were asked of which 16 patients agreed to participate. The mean ADKnowl score of both groups was 16.6 at baseline (maximum score = 22). The scores improved at follow-up. Mean difference between the first and second measurement was 2.9 ($p < 0.01$); between the first and third measurement 2.9 ($p < 0.05$); and between the first and fourth (last) measurement 3.8 ($p < 0.05$).

Conclusion: Sweet-o-Bike™ appears to be a feasible and promising educational tool, which type 2 diabetic patients, both on OAD-only and on insulin/OAD treatment, highly benefit from.

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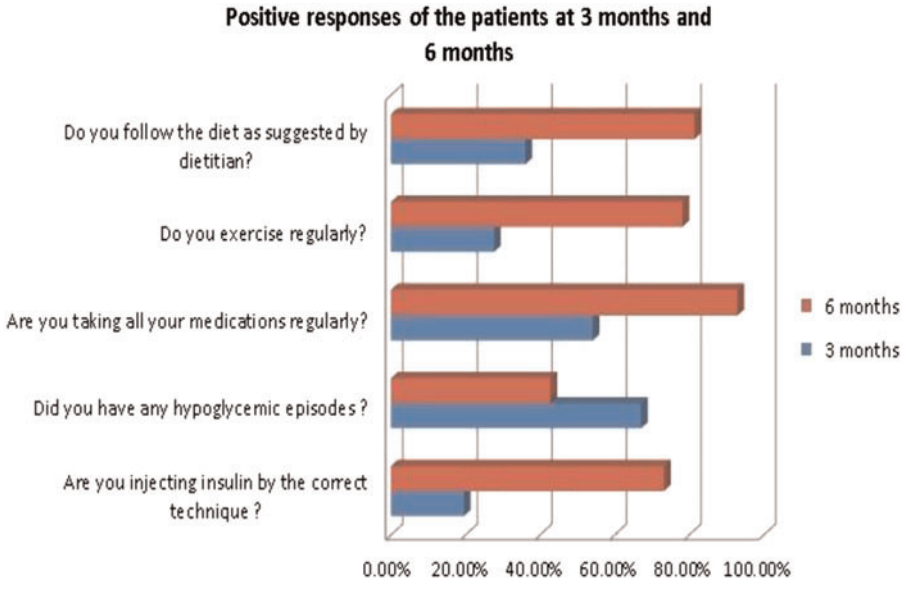
LIVE BRIEF WEEKLY EDUCATIONAL QUESTIONNAIRE VIA DTMS® AS A TOOL TO IMPROVE THE ACCEPTABILITY AND OUTCOME IN TYPE 2 DIABETES

J. Kesavadev[1], A. Shankar[1], G. Sanal[1], J. Lally[1], G. Krishnan[1], S. Jothydev[1]



[1]*Diabetes, Jothydev's Diabetes Research Centre, Thiruvanathapuram, India*

Effective patient education strategies translate to better outcomes in diabetes care. In India, there exists no uniform or structured diabetes education program for patients with diabetes. We analyzed the acceptability and outcomes of a structured, customized, live, interactive, brief and frequent educational program via Diabetes Tele Management System (DTMS®) in our center. DTMS® involves a unique software & trained multidisciplinary diabetes team of physicians, dietitians, pharmacists, nurses, diabetes educators and psychologist communicating with patients through phone/email for slow, steady titration of drugs combined with frequent tele counselling precluding physical visits to the hospital. Each tele consultation offers an opportunity for education, interactive communication and troubleshooting. The contents of educational modules via telephone/internet are decided based on individual requirements addressing technique of glucose monitoring and injections, diet advises, type and duration of physical activity etc. A validated 5 item questionnaire addressing the key themes in diabetes care was administered to 9463 patients on DTMS® follow-up and the acceptability and outcome measures were graded and compared at 3 months of first visit to the center and after 6 months via telephone when patients contacted the DTMS® team for routine follow-up. The positive responses are as follows (Fig.) Diabetes education utilizing tele medicine technology and communication devices are easy to deliver, customize, is patient friendly and cost effective resulting in better outcomes. Individualized education and trouble shooting in management of diabetes, at specified frequent intervals via DTMS® is highly acceptable with profound benefits in achieving targets overcoming usual treatment barriers.

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INCORPORATING THE INTAKE OF MEALS IN THE EINDHOVEN DIABETES EDUCATION SIMULATOR (E-DES)

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Background: Most glucose metabolism models are developed on oral glucose tolerance test (OGTT) data. Therefore, these models cannot simulate meals. However, incorporating meals is crucial for an educational simulator to mimic real life. We hypothesize that we can include various meals in the physiology-based mathematical model of the Eindhoven Diabetes Education Simulator (E-DES) by only adjusting the four food-related parameters. We validate this method on data from healthy subjects, as an intermediate step towards patients with diabetes type 1 and 2.

Methods: We adapted the food ingestion part of the model to simulate meals with both a fast and slower ingestion component. Glucose and insulin data of healthy subjects were obtained from literature. 57 different meals were included, e.g., cereal, milk, fruit, bread, pasta with tomato sauce and chicken with rice. We fitted our model to the data using a non-linear weighted least squares algorithm, adjusting only the four food-related parameters.

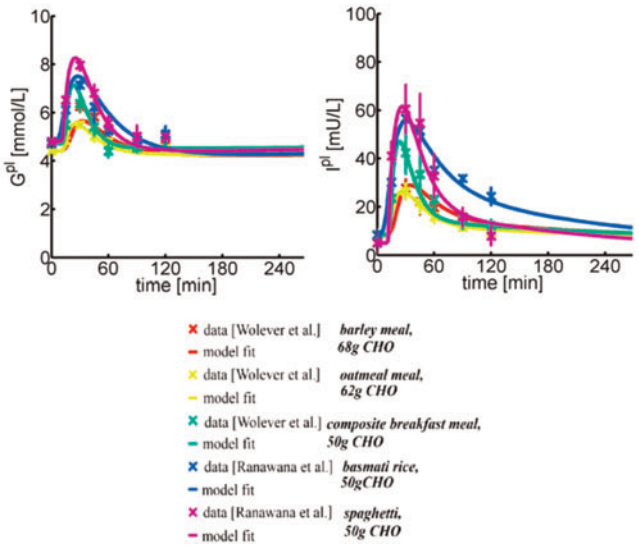

FIG. 1. Glucose (left) and insulin (right) data and model fit for five meals.

Results: We accurately fitted the data of 35 meals, of which five are shown in Figure 1. If a meal could not be fitted, it usually had few data points. Clearly, our model is flexible enough to simulate the response to different meals.

Conclusion: By adjusting only the four food-related parameters, we successfully simulated glucose and insulin responses to 35 different meals in healthy subjects. This method is incorporated in the E-DES, and will be validated for patients with diabetes type 1 and 2.

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USE OF PATIENT-RECORDED DATA IN SMARTPHONE-BASED GAME FOR CHILDREN WITH DIABETES

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Background: Games represent an unobtrusive and ubiquitous way of learning for children. An educational smartphone-based game for children with diabetes, DiaSpill, has been developed and integrated with a mobile-phone-based self-help platform for people with type 1 and type 2 diabetes, the Few Touch Application (FTA).

Methods: User-specific parameters including the user's blood glucose measurements (BGM) data are embedded into the gameplay. A small-scale game test by children with diabetes has been performed and got positive feedback.

Results: For a child playing DiaSpill, insulin sensitivity- and carbohydrate compensation factors are calculated using the user's input of age and height at the first time the game is played.

These parameters influence the effects of game enemies and useful items to the game character's BG level.

DiaSpill accesses the FTA database in the mobile phone's internal storage. At each game level, the game character's BG level corresponds to the user's last BGM value. The child's success in regularity, periodicity and frequency of BGMs is encouraged in the game. The better BGM management - the more Superpoints (which are used for purchasing useful items in the game) and Goldpoints (which can be spent for real-life bonuses) the player gets.

Game test feedback from the children has been collected both using semi-structured interviews and test monitoring of real-life gameplay.

Conclusion: Since the blood glucose control when having diabetes is one of the main cornerstones in good self-management, encouraging this behavior based on patient-gathered data is considered promising as motivator for educational games for children with diabetes.

P-298

ONLINE CONSULTING AS THE ELEMENT OF THE TRAINING SKILLS IN PREGNANT WOMEN WITH TYPE 1 DIABETES MELLITUS ON PUMP THERAPY

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Aim: Evaluate the effectiveness of the distant online consulting system in pregnant women with type 1 diabetes mellitus (DM1).

Subjects and methods: Control group (group 1) consists of 11 pregnant women with DM1 on insulin pump therapy consulted in the clinic. In the other group (group 2) 16 pregnant women with DM1 have been consulted via online consulting. The duration of the disease was 9,8 ± 4,1 yrs, comparable in both groups. Glycaemia, HbA1c, glucose variability index (MAGE) and frequency of hypoglycaemia (< 3,5 mmol/l) per week were studied.

Results: Initially both groups were similar in HbA1c (7,46 ± 1,09% vs. 7,19 ± 0,95%), mean glycaemia level (7,4 vs. 7,6 mmol/l), MAGE (4,214 vs. 4,396) and hypoglycaemic episodes (29 vs. 39). After 3 months of the study HbA1c decreased in both groups: group 1 6,54 ± 0,69% (p = 0,03) vs. group 2 6,38 ± 0,44% (p < 0,045); the mean glycaemia level significantly decrease in group 2 (6,4 ± 2,21 mmol/l) vs. group 1 (7,6 ± 3,14 mmol/l, t = 8,031 p < 0,001). Glycaemia variability by MAGE was significantly lower in group 2 (4,18 [range 2,3–6,0]) vs. group 1 (5,10 [range 3,2–7,0]), p < 0,001. Frequency of hypoglycaemia at the end of the study in group 2 was lower (1,25 episodes per week) in comparison with control group (3,18 episodes per week) (p = 0,731).

Conclusion: Online consulting tends to improve training skills in pump insulin therapy. Also it helps to optimize glycaemic control and decrease glycaemic variability without any increase in hypoglycaemic episodes in pregnant women with DM1.

P-299

TYPE 1 DIABETES MORTALITY ON THE BASIS OF THE REGISTER OF MOSCOW REGION

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Aim of study was to analyze mortality rate, standardization mortality ratio (SMR), life expectancy (LE), survival rate and causes of death in patients with type 1 diabetes mellitus (T1DM) of Moscow region.

Materials and methods: It was retrospective study of 11451 T1DM patients, who live in Moscow Region and registered in National Diabetes Register of RF. Register contains information on age at diabetes onset, date of death, causes of death of patients. LE and causes of death were examined by dividing cohort by age at onset of T1DM. Age adjusted SMR was calculated as ratio of observed and expected deaths. 95% confidence interval is calculated by exact Poisson method of Owen.

Results: During 2003–2012 yrs 1518 deaths were observed. In 2008–2012 yrs mean LE was 49,08 ± 1,16 yrs (males-47,27 ± 1,3, females-52,61 ± 2,2). Compared with previous five years, it has slightly increased in women and decreased in men. Patient with onset of T1DM method indicated cumulative survival rates of 95,3% at 5 years after diagnosis. At onset T1DM ≤ 25 yrs major causes of death was renal failure-12,8%, et onset > 25 yrs – heart failure (16,8%).

Conclusion: Age-adjusted mortality rate remains to be high compared with general population. Mean life duration depends on age at onset of T1DM and it is longer if T1DM was diagnosed at age 21–25 than at age < 10 yrs.

P-300

UTILITY OF BLOOD GLUCOSE METERS CALCULATING INSULIN DOSE IN THE MANAGEMENT OF TYPE 1 DIABETIC PATIENTS.

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Objectives: Describe the impact of blood glucose meters (BGM) with dosing suggestion for rapid-acting insulin in care of type 1 diabetes patients.

Patients and Methods: A descriptive study of 334 DM1 patients introduced in January 2012 in our on-line medical history as part of Diraya platform for Andalucia with integrated BGM download on.

Results: Mean age was 33.95 ± 11.71 years, 53.6% were men, 46.4% women. 24% smokers. 21.3% had high blood pressure (SBP 124.7 ± 18.4 mmHg and DBP 75.7 ± 11.7.). 42.8% had dyslipidemia. 20.4% had diabetic retinopathy, 13.2% diabetic nephropathy. Weight 73.5 ± 14.7 kg. BMI 25.7 ± 4.2. Total dose of insulin 55.8 ± 25.5 IU, basal insulin 32.7 ± 15.8 IU, fast acting insulin 23.1 ± 14.6 IU and sensitivity factor 38.8 ± 21.1. Glucose 154 ± 74 mg/dl, HbA1c 7.95 ± 1.38%, cholesterol 171 ± 30.8 mg/dl, LDL-C 96.2 ± 26.4 8 mg/dl, HDL-C 15.5 58 ± 8 mg/dl, triglycerides 87.1 48 ± 8 mg/dl.

We analyzed a subgroup of 70 patients (they received BGM with suggestion for insulin dose); mean HbA1c at baseline (8 ± 1.1%) and two months later (7.79 ± 1.4%). Mean difference 0.27 ± 1.2 (p = 0.15).

Conclusions:

- The inclusion of these patients in a specific on-line medical history, represents a breakthrough in their management.
- We reported slightly improvement in metabolic control, despite the short time between appointments.
- Insulin dose suggestions with these BGM modify adherence and increase glucose testing.

P-301

INITIATION OF THE ACCU-CHEK CONNECT REPORTS UTILITY AND EFFICIENCY STUDY (ACCRUES) TO ASSESS NOVEL DIABETES DECISION SUPPORT SOFTWARE

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Objectives: Use of diabetes management software to display the results of SMBG testing and other diabetes related data facilitates data interpretation and diabetes management decision-making. We initiated a study to assess the ability of healthcare providers (HCPs), MDI-treated patients with diabetes (PwDs), CSII-treated PwDs and caregivers to obtain and interpret data from self-monitored blood glucose (SMBG), insulin administration and carbohydrate intake using Accu-Chek® CONNECT software compared with standard logbook use. Hinnen.

Methods: This multicentric, prospective, self-controlled, randomized study will enroll approximately 30 HCPs, 20 MDI-treated PwDs, 20 CSII-treated PwDs, 20 caregivers of pediatric (≤ 18 years) MDI-treated PwDs and 20 caregivers of pediatric (≤ 18 years) CSII-treated PwDs. An expert panel of diabetes specialists will create 8 clinical cases based on actual data from diabetes patient histories (4 MDI, 4 CSII) and determine the correct multiple choice responses regarding identification of meaningful diabetes information, recognition of glycemic patterns and appropriate diabetes management decisions. Data will be presented in software views and standard logbook for analysis and interpretation by 5 study groups: MDI-treated PwD; CSII-treated PwD; and caregivers for MDI-treated and CSII-treated PwDs; and HCPs.

Results: Results will show and compare each study group's proficiency in identifying key data and ability to make management decisions using the software views compared with standard logbook views.

Conclusions: Results will provide essential information regarding the accuracy and speed of PwDs, caregivers and HCPs ability to obtain and act on information relevant to diabetes management from the software versus the standard logbook.

P-302

AP-REPORTING: A COLLABORATIVE TOOL TO ANALYSE ARTIFICIAL PANCREAS TRIAL DATA

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Several artificial pancreas (AP) systems are being tested worldwide in various clinical studies. Numerous data are thus collected and need to be analysed to assess levels of safety and efficiency of each system. Proper statistical analysis is time consuming and requires specialized skills and equipment. A collaborative data analysis tool could therefore simplify this step and empower researchers.

AP-Reporting is a new protected application, which aims at quickly producing high quality charts and detailed statistics of AP trial data. Users can define protocols, visits and subjects; then upload experiments data files generated by devices (glucose meters, pumps, continuous glucose monitors, AP platforms, e.g. DiAs) or provided manually (datasheets). Once uploaded, individual and global reports are automatically generated and can be shared online seamlessly with other users. Reports include charts with glucose curve and insulin delivery, as well as various metrics such as glucose mean, standard deviation, time spent in range, amount of insulin delivered, low blood glucose index, etc. Time periods, based on study events, can be defined (e.g. meal + 3 hours) and contrasted. Calculations were validated against results from three clinical studies were both AP-Reporting and conventional data processing (Matlab, SAS) were performed. The application was developed with Django python framework. Data are securely and anonymously stored in a central MySQL database. AP-Reporting may help research teams working in AP field. It could limit calculation errors and reduce time spent in data analysis while providing comprehensive reports. The application is available at www.ap-reporting.com.

P-303

WHAT DO PATIENTS NEED? ICT-BASED EMPOWERMENT MEETING THE INDIVIDUAL NEEDS OF DIABETES PATIENTS

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One of the main challenges faced by diabetes patients is to be compliant to their treatment plan, since this may have a deep impact into their daily lives and behavioural patterns. This paper presents a multi-dimensional approach for designing self-management functions of a web based diabetes portal used in the European research project EMPOWER (http://www.empower-fp7.eu/).

The concept of empowerment relies fundamentally on the understanding and meeting of patient's needs. In order to assess those needs and to understand how they may foster patients 'empowerment three focus groups with diabetes patients and doctors were conducted, followed by a 'cross-sectional survey with patients only.

The results led to a better understanding of how to cluster potential EMPOWER users to their stage of diabetes self-management learning processes and competences. Based on that and on the Access-Competence-Motivation model, which explains different learning paths in adopting a new eHealth solution, the EMPOWER maturity levels were defined. Those are described as a nine-dimensional matrix covering a spectrum from low to high and refer to a patient's attained level of how to manage his/her diabetes by him/herself. Paper-based prototypes were specified in order to illustrate how different maturity levels can be addressed and realised in the EMPOWER software solution.

This study made clear that it is essential to design an IT-supported empowerment service which is tailored to individual patient needs and skills. The EMPOWER model is useful to target individual proficiency levels in diabetes self-management.

P-304

EFFICIENCY NORMASUGAR TELEMEDICINE SYSTEM FOR REMOTE MONITORING AND MANAGEMENT OF PATIENTS WITH DIABETES

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Objective: To evaluate the effectiveness of the system in NormaSugar to compensation of diabetes type 1 and type 2.

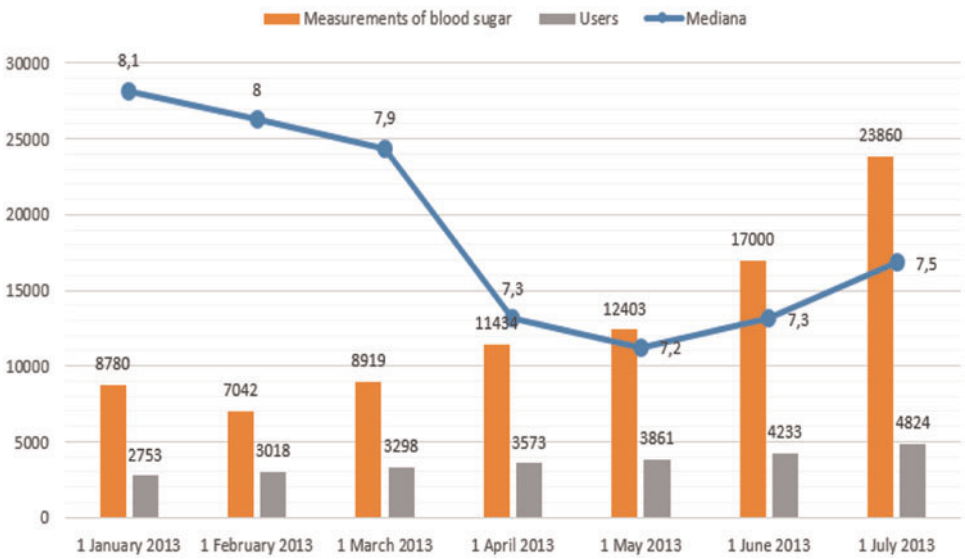
Methods: NormaSugar - a system consisting of a mobile application for patients and their physicians, with insulin dose calculator, 10000 base foods, automatic control system and the mechanism of control hypoglycemia, and consultation with a physician in real time. For the study was analyzed array of data accumulated from January to August 2013.

Results: More than 53% percent of the time, patients using NormaSugar, were within the target level of glucose (3.5–7.5 mmol/l, including post-prandial blood glucose levels). In this case, the frequency of hypoglycemia (blood glucose less than 3.5 mmol/l) was only 4% of the time of observation observation. Estimated average glycated hemoglobin (the formula research ADAG) NormaSugar's members was 6,65% HbA1c.

If you follow the dynamics of the frequency of self-control, the NormaSugar shows a threefold increase in the frequency of self-control among the users of the system since the beginning of 2013.

It is natural that with the increase in frequency of self-control blood sugar in people, they have also improved and the compensation of diabetes. Despite the continued registration of users in the system (number of users doubling in six months), the median blood sugar has reached the target values ??- up to 7.5 mmol / L, including postprandial glycemia.

Thus, mobile applications NormaSugar stimulate an increase in the frequency of self-control, improves patient compliance to therapy and contributes to the normalization of blood glucose levels.



P-305

TELEMEDICAL OUTPATIENT MONITORING AND MANAGEMENT OF GESTATIONAL DIABETES MELLITUS BY THE G-DEMANDE SYSTEM: A RANDOMIZED CONTROLLED FEASIBILITY STUDY (TELE-GDM)

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Background: Gestational Diabetes Mellitus (GDM) is the most frequent metabolic complication during pregnancy affecting up to 9% of all pregnant women. Its prevalence is expected to further increase. A telemedicine technology compared to classical follow-up could be of interest in this setting. We aimed at assessing the feasibility of outpatient monitoring and management by utilizing a pervasive health care system (PHS) for GDM.

Methods: Single-center, parallel group, open randomized controlled trial conducted in Lausanne University Hospital. Patients were assigned to 2 different groups: Standard protocol group (SP) and telemedicine group (TM). SP patients were managed by regular clinic visits. TM patients were managed the G-DEMANDE PHS system (Figure 1). The targeted feasibility outcome was whole trial feasibility, functioning of the PHS and its apropriatness for patient use.

Results: Mean age was 32 ± 5 years and patients were pregnant for 29.1 ± 1.9 weeks at study inclusion. Patients came from 16 different countries. The follow-up rate was 100%. Acceptability in the TM-group was high, as 100% were satisfied with the care provided and equally 100% were at ease with the technology. Overall median[IQR] glucose control was 5.4 mmol/l [4.7–6.4] in the TM-group and 5.7 mmol/l [4.9–6.7] in the SP-group ($p < 0.001$). Four out of 6 daily plasma glucose values were significantly better controlled with telemedicine compared to standard care.

Conclusion: Telemedical outpatient monitoring and management of GDM by the G-DEMANDE system is feasible and peformant. This study suggests that telemedicine care improves glycemic control in GDM, but a main trial is needed to corroborate these findings.

P-306

STANDARDIZED METRIC FOR AUTOMATED EVALUATION OF 24-H GLUCOSE PROFILES: THE Q-SCORE

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Background and aims: Structured glucose monitoring has high potential to improve significantly diabetes care. However, an objective and practicable tool to evaluate measured glucose profiles is missing. It was the aim of our study to develop and to verify an automatically to calculate evaluation score (Q-Score) that considers all important aspects of measured glucose profiles.

Materials and methods: 1495 registered glucose profiles provided the database for this study. First, a factor analysis was performed to identify factors with major impact on the measured

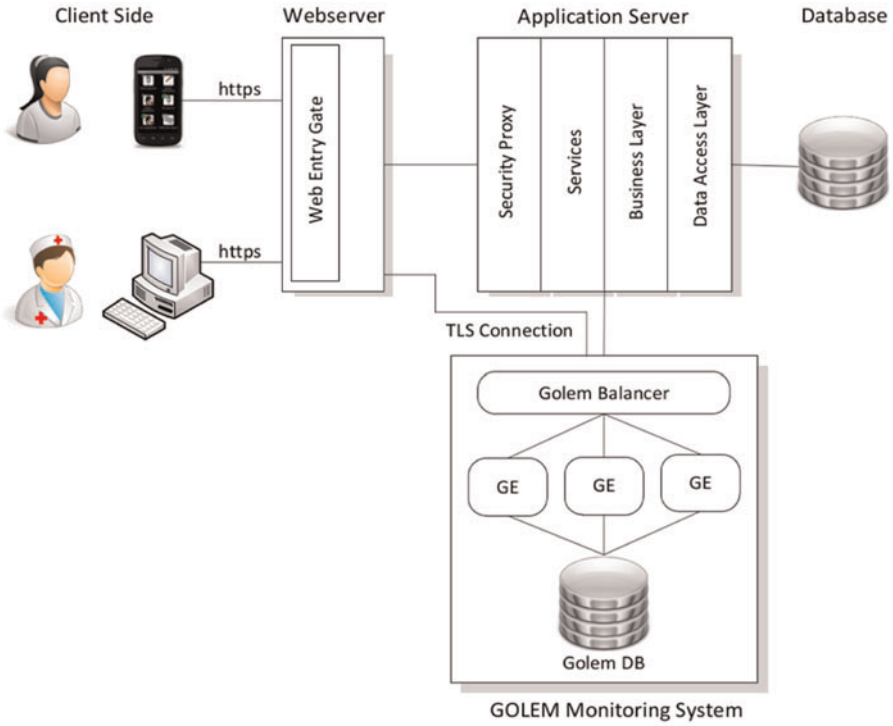

FIG. 1.

profiles. For each factor one parameter was selected and used for the development of the Q-Score.

Results: This study resulted in a Q-Score for objective evaluation of glucose profiles. To verify the Q-Score two diabetes specialists (DS) diagnosed independently 729 glucose profiles. The results were analysed for the inter-individual variation. There was a high correlation between the Q-Score and the results of both DS. The Q-Score was then tested for categorisation of glucose profiles. 729 profiles were categorised by one DS in very good, good, satisfactory, borderline, and not satisfactory and compared with the result obtained from the evaluation by applying the Q-Score. The Q-Score was significantly correlated with the results obtained from the evaluation of the DS.

Conclusions: The Q-Score combines all essential quality parameters to describe glucose profiles in only one parameter. The Q-Score is independent of subjective opinions and can be used therefore for automated evaluation of glucose profiles. The Q-Score has the potential to become a practical tool in diabetes diagnosis and therapy.

P-307

EFFECTIVENESS OF A WEB-BASED DIABETES INFORMATION SYSTEM ON GLYCEMIC CONTROL AND QOL OF PEDIATRIC PATIENTS WITH TYPE 1 DIABETES IN CSII TREATMENT

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Background and aim: SMBG and insulin pump data are the main source of information for changes in diabetes treatment. However, these decisions, often use a limited sample of the potential data available. DIASEND is a web-based diabetes management system that collects, stores and analyzes SMBG/CGM and insulin pump data. The aim of this study was to evaluate the impact of this diabetes information solution on glycemic control and QoL of pediatric patients with type 1 diabetes in insulin pump treatment.

Methods: 45 patients (aged 12,1–16,7 years; 21 males) in CSII treatment for at least 1 year (mean time 3,1 ± 0,6 years) were randomized to ''usual care'' group (using SMBG/pump data stored in the devices or recorded in a monitoring book, during the contacts with the diabetologist) or experimental group (using, during the contacts with the diabetologist, the data uploaded weekly in the Diasend System) and followed for 6 months. There were not differences between groups in age, CSII time of use, HbA1c and BG levels at the start of the study.

Results: HbA1c and postprandial BG decreased significantly over the 6 months in the experimental group but not in the control group. There were no differences over the follow-up period in fasting BG and BMI z-score in both groups. Diabetes-Specific QoL for Youth score increased significantly in the experimental group.

Conclusion: The use of this web based diabetes solution was effective in improving glycemic control and QoL of pediatric patients with type 1 diabetes in CSII treatment.

P-308

UTILIZING DATA GATHERED THROUGH MOBILE APPS FOR SELF-MANAGEMENT OF TYPE 1 DIABETES

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	"Usual" care group (22 patients)			Experimental group (23 patients)		
	0 month	6 months	p	0 month	6 months	p
HbA1c (%)	8,3±1,1	8,1±1,6	0,08	8,4±1,2	7,9±1,4	0,02*
Mean daily preprandial BG values (mmol/l)	11,2±3,1	10,3±2,3	0,23	11,7±2,4	10,1±1,9	0,07
Mean daily 2h postprandial BG values (mmol/l)	11,8±3,5	10,7±1,6	0,11	11,7±2,8	9,9±2,1	0,01*
BMI z-score	0,18±0,84	0,14±0,8	0,14	0,16±0,81	0,12±0,79	0,12
Diabetes-Specific QoL for Youth score 23,5±6,8 25,6±7,2 0,09 24,4±7,9 29,8±,7,9 0,03*						

Introduction: The computing power of current smartphones means that these devices can be used for complex data management and analysis purposes. Data for patients on self-monitored blood glucose (SMBG) regimes can be utilized through assembling and processing of relevant data using digital diabetes diary (DDD) apps.[1]

Methods: We developed a DDD for the Android platform including a data processing and visualization component known as *Diastat*, consisting of three analytics components[2]. In a six-month study the diary was given to 30 patients with Type 1 Diabetes. Diastat was deployed to half of the cohort at times one and three months after study start-up. In addition to the self-registered data using the DDD, HbA1c was measured at intervention points.

Results: The patients reported back on the components of Diastat, and which components were used and perceived as useful. In particular, the periodicity and situation matching components were considered useful features. The participants' HbA1c decreased by 0.6 pp over the first three months ($p = 0.0004$). The participants with Diastat had a larger drop in HbA1c, though not significantly (0.76 pp vs 0.47 pp, $p = 0.29$).

Discussion: The study demonstrates the potential of advanced functionalities built into digital diabetes diaries using feedback based on data-processing of local DDD data. The observed short-term decrease in HbA1c needs to be validated to conclude on long-term benefit.

1. Skrøvseth SO, Årsand E, Godtliebsen F, Hartvigsen G. *Diabetes Technol Ther*. 2012;14:1098–1104.
2. Skrøvseth SO, Årsand E, Godtliebsen F, Joakimsen RM. *Trials*. 2013;14:139.

P-309

ASSESSMENT OF THE USEFULNESS OF THE BOLUS CALCULATOR IN TYPE 1 DIABETIC PATIENTS TREATED WITH MULTIPLE DAILY INJECTIONS. PRELIMINARY RESULTS

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Introduction: Bolus calculator (CB) is a device that measure glucose level and recommend an appropriate insulin dose for type 1 diabetic patients (DM1) on multiple daily injections.

Aim: To show that DM1 patients can improve glycemic control when treated with CB as compared to intensive treatment including carbohydrate counting.

Design: Randomized, controlled, two-arms parallel, crossover clinical trial. Inclusion criteria: 18–65 years, HbA1c >7%, on basal bolus therapy. Sample size estimate: 82 patients. For the first phase (4 months) they were assigned either to CB group (CB; using Accu chek Expert® for prandial and correction boluses), or control group (Co; calculating insulin boluses mentally, according to algorithms and their own experience). In a second phase, all patients were allocated to CB. We present the results from the first phase for a subsample, regarding glycemic control.

Results: 41 patients, 23 women (56,1%); mean age 34,07 (SD 12,18) years, evolution of diabetes 16,9 (SD 9,36) years. CB $n = 23$ patients (56,1%), Co $n = 18$ (43,9%). Both groups had similar characteristics at baseline. There were six dropouts, 4 in CB group. Results are presented for baseline and 4 months (Tables 1 and 2). HbA1c decreased in both groups, being the decrease significantly larger for the CB group. Mean glycemia did not show significant changes as a whole.

Conclusion: Our preliminary results confirm that the use of CB can reach a decrease in HbA1c greater than in control group, not associated with an increase in hypoglycemic episodes.

	HbA1c (%)			Decrease in HbA1c (%)	Number of hypoglycemic events (<70 mg/dL)/2 weeks			Frecuency of glucose testing/ 2 weeks		
	basal	4 m	p	4 m	basal	4 m	p	basal	4 m	p
CB	8,71 (SD 0,87)	7,66 (SD 0,69)	<0,000	-1,05* (SD 0,79)	9,47 (SD 4.8)	7,79 (SD 3,68)	NS	5,15 (SD 1,15)	4,61 (SD 0,99)	NS
Control	8,56 (SD 0,88)	8,06 (SD 1,05)	0,01	-0,5 (SD 0,68)	7,69 (SD 5,3)	5,94 (SD 4,82)	NS	5,36 (SD 1,35)	4,86 (SD 1,46)	NS

Table 1:Results.
*p<0,05 between CB and Co, no other differences between groups.

	Glycemia (mg/dL)			Preprandial glycemia (mg/dL)			Postprandial glycemia (mg/dL)		
	basal	4 m	p	basal	4 m	p	basal	4 m	p
CB	165,93 (SD 22,37)	157,02 (SD 19,02)	NS	164,91 (SD 25,13)	160,44 (SD 22,47)	NS	184,19 (SD 34,18)	167,11 (SD 37,79)	0,08 (NS)
Control	156,54 (SD 23,74)	168,21 (SD 34,35)	NS	149,5 (SD 25,18)	166,78 (SD 31,19)	0,03	165,37 (SD 22,6)	168, 46 (SD 44,36)	NS

Table 2:Results.
No differences between CB and Co groups.

P-310

THE KUWAIT HEALTH NETWORK: AN INTEGRATED APPROACH TO SUPPORTING QUALITY IMPROVEMENT OF DIABETES CARE IN KUWAIT

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[2]IT dept, Dasman Diabetes Institute, Kuwait City, Kuwait
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Aims: The Kuwait Health Network (KHN) informatics system supports management of patients with diabetes in Kuwait – approximately 24% of the population. KHN is an outcome-focused analytical application that integrates multiple source data providing an instant epidemiological snapshot regarding current provisions of care

Methods: KHN v1.0 was implemented in Feb 2013 in 4 primary health centres (Kuwait capital region). A secure network with both role and domain based access links laboratory data with a disease registry (defined dataset of coded clinical terms). Additional data entry is completed during episodes of care. KHN assesses adherence to Quality Performance Indicators (QPIs) based on Kuwait national clinical standards. In addition to viewing results via an online analytics module, HCPs can access QPI summaries in a print/tablet-friendly format (automated report generator). A similar approach will provide patients with individually tailored summaries.

Results: As of April 2013, 4390 registered patients, 4305 (98.1%) with T2DM

Conclusion: Despite best efforts of HCPs, large numbers of patients with diabetes in Kuwait are not meeting national clinical standards. If representative, the Kuwaiti diabetic population is at significant risk of developing disease complications. KHN can provide instantly accessible and robust population level data to enable the effective targeting of quality improvement interventions.

Recorded (last 15 months)

HbA1C	*Lipids*	*BMI*	*BP*
68.4% (3006)	**37.5%** (1645)	**46.1%** (2026)	**62.0%** (2721)

P-311

USE OF IPRO2 IN REAL-LIFE MANAGEMENT OF TYPE 2 DIABETES PATIENTS IN INDIA

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Background: Retrospective CGM studies (iPro2, Medtronic) may provide healthcare professionals (HCPs) with better understanding of glycemic patterns in patients with type 2 diabetes and thereby support appropriate therapeutic interventions.

Design and Methods: The study is a 3-month, interventional, post-market, prospective study of up to 250 adults age 19–70 years with baseline A1C values >8–10.0% across India. Patients were to complete baseline and month-2 iPro evaluations, followed by therapy adjustments and A1C determinations. Questionnaires for HCPs (to evaluate the utility of iPro2 results) and patients (to evaluate understanding of the importance of compliance with HCP recommendations) were collected. Glycemic control and variability were to be estimated from iPro2 data.

Results: In an interim analysis of the first 30 completers, iPro2 was found to be safe and was not associated with any serious adverse device effects. Most subjects (93.3%) had ≥1 therapy change after the iPro2 data review. Mean A1C decreased from 8.7% (baseline) to 7.7% (month-3). All HCP and patient questionnaires were consistent with the acceptability and utility of iPro2 studies and results (mean responses ≥5 on a 7-point Likert scale). The average SMBG value decreased (168 to 155 mg/dL) and there were consistent decreases of SG-based glycemic variability metrics (CV(%):0.29 to 0.28, SD:49.1 to 44.6, MAGE: 109.2 to 97.9) between the two iPro2 studies.

Conclusion: iPro2 studies provided HCPs with insights and opportunities for therapy adjustment, resulting in favorable reductions of A1C and glycemic variability metrics. Patients showed improved knowledge of the importance of therapy compliance.

Targets

HbA1C < 53 mmol/mol	*HbA1C > 75 mmol/mol*	*Cholesterol < 5.2 mmol/mol*	*BMI 18–24.9 kg/m²*	*BMI ≥ 30 kg/m²*	*BP < 130/80 mmHg*
25.8% (95%CI 24.3–27.4)	**29.9%** (95%CI 28.3–31.6)	**81.2%** (95%CI 79.2–83.1)	**25.7%** (95%CI 23.8–27.7)	**33.3%** (95%CI 31.2–35.4)	**37.0%** (95%CI 35.2–38.8)

P-312

A NOVEL COMPUTER-BASED MODEL TO SIMULATE DIABETIC GASTROPARESIS AND TO ASSESS THE EFFECTIVENESS OF THERAPEUTICAL MANAGEMENT

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Diabetic gastroparesis is a disorder that produces symptoms of gastric retention in the absence of physical obstruction. Although the clinical profile of this condition is well described, the understanding of pathophysiological mechanisms involved is still lacking. As a result, there is a therapeutic deficiency in the management of diabetic gastroparesis which includes prokinetic, antiemetic, antidepressant drugs and gastric electrical stimulators. The focus of current investigation is a mathematical modelling and quantitative assessment of gastric motility in the diabetics. A three-dimensional mathematical model of the stomach has been developed. It is based on actual experimental - anatomical, histomorphological, physiological, biochemical, pharmaco-logical and mechanical data - obtained from *in vivo* and *in vitro*. The model accurately reproduces the dynamics of electromechanical processes in the myenteric nervous plexi, afferent and efferent neural circuits; the chemical mechanisms of nerve-pulse transmission including multiple neurotransmitters; the variety of electromechanical patterns, i.e., slow wave and bursting type myoelectrical activity; the dynamics of active force generation. Results of numerical simulations of electrical, mechanical and conjoint electromechanical stimulations of the gastroparetic stomach have revealed different electrical and mechanical responses, i.e., with increased frequency and intensity of excitation there is a shift from phasic to tonic bursting and the development of long-lasting non-propagating contractions. Application of prokinetic drugs, e.g., metoclo-pramide, domperidone, did not produce a significant improvement of motility. Comparison of theoretical and experimental results has revealed good qualitative and quantitative agreement.

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METFORMIN IN COMBINATION WITH VILDAGLIPTIN, BUT NOT METFORMIN ALONE, ATTENUATES STREPTOZOTOCIN-INDUCED DIABETIC NEPHROPATHY IN UNINEPHRECTOMIZED RATS

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Currently, a great attention is being paid to investigation of antihyperglycaemic agent's pleiotropic effects. Several recent studies have established that use of metformin and vildagliptin could result in some positive effects on kidney function in diabetes. however, whether metformin in combination with vildagliptin can possess renoprotective properties, hasn't been reported before. This pilot study, concerned with uninephrectomized streptozotocin (STZ)-induced diabetic rats, aimed to evaluate the effects of antidiabetic drugs metformin, vildagliptin and their combination on kidney histopathology and routine renal function markers. Diabetes in male Wistar rats was induced by intraperitoneal administration of STZ (60 mg/kg) three weeks following unilateral nephrectomy. 8 weeks later, rats were classified into five groups: control (non-diabetic (ND)) and diabetic groups treated for 8 weeks with metformin (300 mg/kg/day in drinking water (M)), vildagliptin (8 mg/kg/day (M)), combination (metformin 150 mg/kg/day + vildagliptin 4 mg/kg/day (M + V)), or placebo (P), n = 5 each. Glycated haemoglobin(%) didn't differ between diabetic treated groups ($M = 10,7 \pm 0,26$; $V = 11,1 \pm 0,28$; $M + V = 10,7 \pm 0,26$; $p \geq 0,05$ each), and was markedly higher compared with ND ($4,7 \pm 0,15$, $p < 0,01$ each). Although all antidiabetic compounds ameliorated serum creatinine (umol /L) level (ND = $76,5 \pm 3,1$; $M = 93,8 \pm 6,7$; $B = 84,7 \pm 2,9$; $M + B = 79,4 \pm 5,8$, $p \geq 0,05$ each; $P = 103,1 \pm 3,7$, $p < 0,01$), and vildagliptin significantly decrease serum urea level (mmol/l) ($V = 10,6 \pm 2,5$; $ND = 5,8 \pm 0,2$, $p = 0,14$), but only combined treatment was able to considerably improve creatinine clearance ($M + V = 3,4 \pm 0,4$ ml/min/kg, $ND = 3,6 \pm 0,3$, $p = 0,51$), and reduce urinary albumin excretion ratio ($M + V = 6,7 \pm 1,1$ mg/24 h, $ND = 4,2 \pm 2,5$, $p = 0,08$). Moreover, nephroprotection in M + Vgroup was also associated with restoring morphological changes in kidney tissue. Our study suggested that this combination might ameliorate diabetic nephropathy, in addition to hypoglycemic action.

P-314

SURGICAL TREATMENT OF TYPE II DIABETES AND OTHER CO-MOBIDITIES WITH ILEAL INTERPOSITION SURGERY

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Aim: Metabolic Syndrome and its related co-morbidities, particularly type 2 diabetes (T2DM) recently became a global problem. In obese patients with type 2 diabetes (i.e., with a body mass index [BMI] ≥ 35 kg/m2), bariatric surgery offers a treatment modality that is effective and has a low procedure related mortality (< 0.5%). Ileal Interposition with sleeve gastrectomy (IISG) is a novel procedure that has been shown to be safe and effective in the treatment of T2DM in obese and overweight patients. We hereby declare our initial results on IISG surgery in poorly controlled type II diabetic patients.

Material & Method: A total number of 465 patients were surgically treated at our dedicated institute. Of those 311 underwent IISG operation, while other surgical options were applied to the remaining. Our patients consisted of 209 males and 102 females with a mean age of 42.2 (min 24, max 79). All patients had a long standing (mean 10.3 years) diabetes with a mean preoperative HbA1c of 9.41%. Two third of the patients (65.7%) had a BMI < 35 and one third (34.3%) had a BMI >35 kg/m2. A total of 192 patients also had hypertension and 168 had dyslipidemia.

Results: Complete remission (HbA1c < 6%) occurred in 61.1% (190 patients) and partial remission in 20.1% (65 cases). Glycemic control (HbA1c < 7) was noted in 31 patients (9.9%). The remaining 25 patients (8.1%) had an HbA1c level above 7%. In total 91.1% of patients experienced a glycemic control. Remission of hypertension (blood pressure < 130/80 mmHg) was noted in 299 patients (96.1%) and remission of dyslipidemia was observed in 287 patients (92.2%). Mean change in BMI according to preoperative levels were 6.27 kg/m2, 7.91 kg/m2,

10.41 kg/m2, 13 kg/m2 in preoperative BMI < 30, 30–35, 35–40 and > 40, respectively.

Conclusion: IISG operation may provide effective control in all components of metabolic syndrome in subjects who failed to obtain metabolic control under medical treatment. More clinical investigation is warranted to define the exact mechanism of action and pathophysiology.

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ESTIMATION RISK MODEL OF INSULIN INDUCED LIPOHYPERTROPHY IN DIABETIC PATIENTS

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Objectives: To develop the estimation risk model of insulin induced lipohypertrophy (LH) in diabetic patients.

Material and methods: This study was done on 140 diabetic patients (89 females and 51 males) with insulin treatment a mean 8 years. Observation and palpation techniques, ultrasonography of subcutaneous fat were used in assessing LH in these diabetics. All patients were divided into two groups. First group included 117 patients with LH, second – 23 diabetics without pathologic areas of subcutaneous fat. Further, all known, as well as additional LH risk factors were statistically processed using Spearman's, Kendall tau, Gamma rank correlation coefficients and binary logistic regression. Results were statistically significant when $p < 0{,}05$. Also measure AUC was determined.

Results: All risk factors were analyzed using rank correlation coefficients on first stage. Statistically insignificant parameters were eliminated ($p > 0{,}05$). 10 factors from 23 were remained after first stage. Further, 10 parameters were subjected to ROC-analysis. All risk factors had high predictive value (AUC > 0,5). They were used to development the estimation risk model. On the basis of binary logistic regression the estimation risk model was created. Predictive value of model was 86% taking into account threshold cut-off 0,3 and confidence interval 95%. Efficacy of estimation risk model were tested on 34 diabetic patients.

Conclusions: Nowadays, LH remains severe insulinotherapy complication. Primary prevention is necessary for diabetic patients with pathologic areas of subcutaneous fat. Therefore, we developed the estimation risk model with good quality and high predictive value (86%) for diabetic patients with reatment with insulin.

P-316

HBA1C IN IDENTIFYING PREDIABETES IN HYPERTENSIVE PATIENTS

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Introduction: Identifying individuals at risk for diabetes is important for preventing both diabetes and cardiovascular diseases, which is strongly associated with prediabetes. The American Diabetes Association has incorporated the use of glycated haemoglobin (HbA1c) as an additional test in the criteria for the identification of prediabetes (5,7%–6,4%). Because HbA1c testing is simple and can be performed regardless of prandial status, it is tempting to rely on HbA1c alone in finding such patients. But this has not been introduced into Europe.

We aim to evaluate the performance of HbA1c compared to an oral glucose tolerance test (OGTT) in a primary care population.

Materials and methods: Seventy-three patients ($57{,}6 \pm 7{,}6$ years, females 41 (55%) males 32 (44%)) with hypertension were examined. They were further investigated by OGTT with HbA1c taken simultaneously, HbA1c $6{,}30 \pm 1{,}91\%$, fasting glucose $5{,}42 \pm 1{,}34$ mmol/L, 2-hour glucose $6{,}41 \pm 1{,}17$ mmol/L.

Results: OGTT identified 34 (46,58%) with prediabetes (12 with impaired glucose tolerance, 22 with isolated impaired fasting glycaemia) and 39 (53,42%) with normoglycaemia. Using HbA1c values to classify these categories would identify 47,05% (16/34) of those with diabetes, 5,90% (2/34) with prediabetes and 47,05% (16/34) with normoglycaemia and 46,16% (18/39) of those with prediabetes and 53,84% (21/39) with normoglycaemia. HbA1c provides a sensitivity and specificity 52,95% for identifying prediabetes. 16 subjects were misclassified as not having prediabetes and 18 as prediabetes although they were either normoglycaemic.

Conclusion: HbA1c alone is not accurate enough to screen individuals for prediabetes. Many at risk for diabetes will be missed by HbA1c values in the ADA-specified range. Screening should include fasting glucose and OGTT.

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THE USE OF HIGH-DEFINITION VIDEO TECHNOLOGY ON IMPROVING DIABETES MANAGEMENT

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Background: Diabetes, a metabolic disorder, has reached epidemic proportions in developed and developing countries. So, The Use of High-Definition Video Technology has gained acceptance as a tool for improving diabetes management. **The Aim** of this study was to determine the effect of using High-definition video technology on improving diabetes management.

Methods: Subjects: All ''120'' diabetic children, in the Diabetic center in The EL Mogamaa EL Teby AL Shamal, Menoufia Governorate, Egypt.

Instruments: It consisted of three tools; 1) questionnaire for socio demographic data. 2) Questionnaire for nutritional practices and practicing of exercise. 3) Observational checklists; urine analysis for acetone or sugar, care for feet and nails and blood glucose monitoring by using the home device. All tools were used for pre-post intervention.

Results: The study showed a statistical significant reduction in fasting blood sugar, Post prandial blood sugar and glycosylated hemoglobin level of cases group after intervention ($120.57 + 29.13$, $165.57 + 29.13$ and $7.08 + 1.56$, respectively) compared with cases group before intervention ($166.37 + 27.66$, $232.80 + 57.02$ and $9.61 + 1.94$, respectively). Also, there was statistical significant improvement in care of feet and nails, blood glucose monitoring and nutritional practices of cases group after intervention ($64.25 + 2.81$, $36.35 + 2.44$, and $10.88 + 1.45$, respectively) compared with control group ($23.21 + 1.37$, $17.63 + 2.11$, and $5.28 + 1.37$, respectively).

Conclusion: the implementation teaching-assisted High-Definition Video Technology has succeeded in achieving significant improvement in diabetic children' diabetes management practices skills.

Recommendations: implementation of teaching-assisted High-definition video technology for all patients' health education fields.

Keywords: Diabetes, health education, nursing, High-Definition Video Technology

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MANAGEMENT OF NOCTURNAL HYPOGLYCEMIA IN HOSPITAL SETTINGS IN CHILDREN AND ADOLESCENTS WITH T1DM USING REAL-TIME CONTINUOUS GLUCOSE MONITORING

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Objective: To reduce risk of nocturnal hypoglycemia and increase time in target using real-time continuous glucose monitoring (RT-CGM) in children and adolescents with type 1 diabetes mellitus (T1DM) during hospital stay.

Research design and methods: In this study, 190 children and adolescents on intensive therapy for type 1 diabetes and age of 1–18 years were assigned to two different groups according to the type of glucose monitoring system (''Blinded'' or ''Real-Time'' technology). ''Group 1'' - masked continuous glucose monitor (CGM); ''Group 2'' – RT-CGM. The study was conducted during participants hospital stay under regular self-monitoring of blood glucose (SMBG) at least nine times a day. All participants underwent 72-hour continuous glucose monitoring. The primary outcomes were the time spent in hypo- (interstitial glucose concentration $\leq 3{,}9$ mmol/l) and hyperglycemia ($> 10{,}0$ mmol/l), frequency of hypoglycemia during the night (23.00-7.00).

Results: Frequency of hypoglycemia was higher in group 1 and 2 (Group 1 vs. 2, participants with at least one nighttime hypoglycemia: 48,9 vs. 20,8%, respectively; $p < 0{,}05$). In group 2 numbers of nighttime hypoglycemic episodes were significantly lower than in group 1 (70,2 vs. 29,8%, respectively; $p < 0{,}05$). The time per night spent in hypoglycemia was significantly shorter in the groups wearing RT-CGM (Group 1 vs. 2, mean ± SD: 23 ± 44, 6 ± 14 min/night, respectively; $p < 0{,}05$). The time per night spent in hyperglycemia was significantly longer in the group wearing a masked continuous glucose monitor (Group 1 vs., mean ± SD: 440 ± 120, 220 ± 138 min/night, respectively; $p < 0{,}05$). In the RT-CGM group the duration of nighttime hypoglycemia was shorter (mean ± SD: 88 ± 83 vs. 58 ± 38 min/episode; $p < 0{,}05$).

Conclusions: Nocturnal hypoglycemia is common in children and adolescents with T1DM even in hospital settings under regular SMBG. Real-time continuous glucose monitoring was associated with reduced time spent in hypo- and hyperglycemia and frequency of hypoglycemia during the night.

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NEONATAL PERMANENT DIABETES CAUSED BY MUTATION INS/Y50C: COMBINED USE OF CGMS AND INSULIN PUMP

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Case description: first born female, SGA (2500 g), non consanguineous parents. No gestational diabetes, no familiarity for type 2 diabetes. Breastfed, normal weight gain in the first two weeks. Hospitalysed at 24 days for irritability and mild jaundice: blood glucose 509 mg/dl, normal venous hemogasanalysis.

Diagnosis and therapy: Since the beginning of rehydration and parenteral insulin therapy (regular insulin, starting dose 0,02 IU/kg/h), we positioned continuous glucose monitoring system (CGMS Medtronic), glycaemic range 80–200 mg/dl. After 6 days, we positioned insulin pump (Paradigm Veo) and started therapy with Lispro (basal dose: 0,025 UI/h - 0,1 UI/h, pre-prandial bolus 0,025–0,1 UI with automatic suspension of basal insulin delivery for glycaemia < 80 mg/dl). Exclusive breastfeeding was continued, CHO calculation could never be performed and insulin dose was always very variable. Laboratory exams: negative IAA, GAD e IA2; C-peptide: 1,4–0,73 ng/ml; normal thyroid function, cholesterol and triglycerides, slight increase of AST/ALT. Normal abdominal ultrasonography. Molecular analysis underlined a *de novo* heterozygous mutation c.A149->G TAC (Tyrosin)>TGC (Cysteine), (p.Tyr50Cys; position 50 of proinsulin), described as INS/Y50C. Discharged, after 38 days of hospitalization, with CGMS and insulin pump (total basal insulin: 2,1 UI/day; 0,7 UI/kg/day) with lower night basal dose and pre-prandial bolus (0,025 UI before every meal when glycaemia > 150 mg/dl). After 6 months, normal weight gain and neuropsychological development (Q.I. 141/100).

Conclusions: Combined use of CGMS and insulin pump, together with the automatic suspension of insulin delivery for glycaemia < 80 mg/dl, allowed to personalize insulin therapy, reducing glycaemic variability and avoiding psychological burden correlated to hypoglycaemia.

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LOW POWER LASER ACCELERATES WOUND HEALING IN DIABETIC RATS

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Introduction: Diabetic wounds have been the area of challenge since many years with different approaches to improve the problem. Nitric Oxide (NO) has been shown to play a crucial role in wound healing. In addition, application of laser on wound healing has already been examined. Thus, this study was designed to investigate the efficacy of low power laser irradiation for possible immune-stimulation of macrophage-derived NO for dermal wound healing of diabetic rats.

Materials And Methods: 36 male SD rats were used in this study. Diabetes was induced by IP injection of streptozotocin. A full-thickness circular wound was made on the back of all rats.

Rats were selected to be irradiated directly upon their wound with a combination of 670 nm (100 mw, 2 J/cm^2) and 810 nm (50 mw, 1 J/cm^2) every other day. Wound imaging was performed on days 0, 7, 12, 16, 20 and 22. The wounds margin and context were scored pathologically. NO was measured by NO analyzer.

Results: Percent open wound area (POWA) was significantly lower in the Diabetic Laser group in comparison to the Diabetic Non-Laser group in all measurement days. Also the POWA decrease in DML group was quicker than DMNL group (P = 0.021; mean difference = 19.7%). Total pathologic scores of wound margin were higher in DML group compared to DMNL group both on days 12 and 22 (P = 0.049 and P = 0.013, respectively). NO production was increased in DML group as compared to DMNL group.

Conclusion: Our study showed that the irradiation of diabetic wounds with a combination of low dose 670 nm and 810 nm lasers accelerates wound healing process possibly by stimulation of macrophage-derived NO which would be new approach to wound healing.

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DELAYED PUPILLARY CONSTRICTION VELOCITY AS A MARKER OF AUTONOMIC NEUROPATHY IN ADOLESCENTS WITH TYPE 1 DIABETES

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Objective: To evaluate pupillary function as a simple and non-invasive screening tool for detection of subclinical diabetic autonomic neuropathy (DAN) in adolescents with type 1 diabetes.

Methods: 65 type 1 diabetic adolescents (female/male (29/36), median age 14.8, range 12.0–19.0 years, median diabetes duration 7.5, range 0.1–15.1 years, mean HbA1C 8.7% ± 1.5) and 219 healthy controls (female/male (132/87), median age 14.6, range 12.0–19.0 years) were exposed to a light flash (180 μW for 800 ms) with a handheld infrared pupillometer (NeurOptics PLR-200 Pupillometer) under consistent indoor light conditions. Latency (LAT), average constriction velocity (ACV), maximum constriction velocity (MCV), minimum pupil diameter (MIN) and average dilatation velocity (ADV) were determined. Statistic tests: Pearson's (r), Student's t-test (p), $p < 0{,}05$ was regarded as significant.

Results: Significant differences were found for **MCV** (patients $-3.96 \pm 0.86\,mms^{-1}$ versus controls $-5.1 \pm 0.71\,mms^{-1}$, $p < 0.001$) (Fig.), **ACV** (patients $-3.12 \pm 0.67\,mms^{-1}$ versus controls $-4.00 \pm 1.26\,mms^{-1}$, P = 0.002), the **MIN** diameter (patients 3.68 ± 0.86 mm versus controls 4.39 ± 0.64 mm, $p < 0.001$) and **latency** (patients 0.24 ± 0.04 s versus controls 0.22 ± 0.03 s, p = 0.012). **MCV**, **ACV**, **MIN** diameter and **latency** didn't correlate with duration of diabetes and recent HbA1C respectively. In controls **MCV** was slightly age related (r = 0.150, p = 0.03) as was **ACV** (r = 0.174, p = 0.01) and **latency** (r = 0.150, p = 0.03), but not **MIN** diameter.

Conclusion: In type 1 diabetic adolescents pupillometry showed significant alterations mainly in constriction velocity and minimum constriction diameter. However, in our patient group these parameters didn't correlate with duration of diabetes and recent HbA1C. Thus other factors seem to contribute to the development of diabetic autonomic neuropathy.

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EFFECTS OF SOY FLOUR ENRICHED BREAD ON SERUM LIPIDS PROFILE IN OVERWEIGHT AND OBESE WOMEN. ISFAHAN- IRAN

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Background: Recent studies suggest that inclusion of soy product in the diet may have favorable effects on cardiovascular diseases risk factors in overweight and obese individuals. Our aim of this study was to evaluate the effects of consumption of

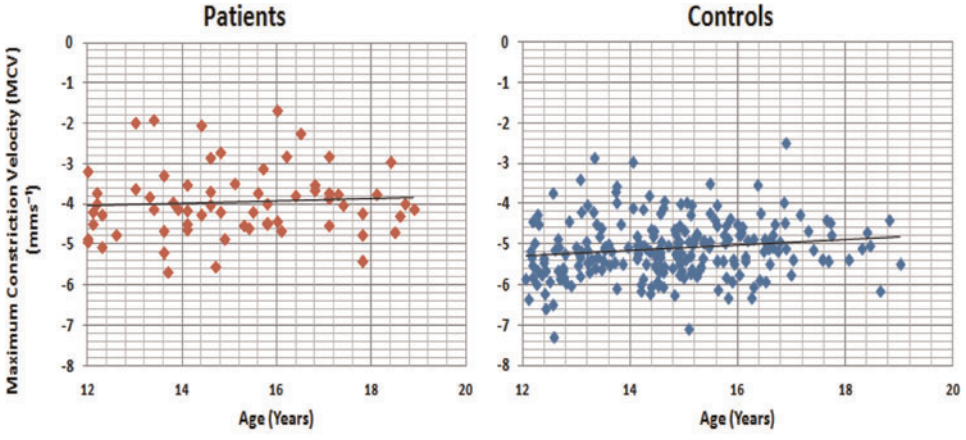

Figure: Maximum Constriction Velocity in Patients and Controls

soy flour enriched bread on blood lipid profile in overweight and obese women.

Methods: This study was a randomized cross-over clinical trial performed among overweight and obese women. All participants received a mild weight loss diet. Individuals were randomized to a regular diet and a soy bread diet, each for 6 weeks and a washout period for 20-d. Subjects in the soy bread diet were asked to replace 120 gr of soy bread with equal amount of their daily usual bread intake and if necessary other cereal products.

Results: The results of the study showed no significant effects of soy bread on serum lipid profile. Comparing the mean differences of variable showed that soy bread could decrease low density lipoprotein (LDL) by 2.2 ± 10.8, total cholesterol (TC) by 3.09 ± 13.8 and triglyceride (TG) by 5.26 ± 16.76 but these reductions were not significant ($P = 0.05$). Comparing with the regular diet soy bread diet also decreased high density lipoprotein cholesterol (HDL-C) by 0.0017 ± 2.56, $P = 0.9$ but this effect also was not significant.

Conclusion: Our results indicate that soy bread consumption had no significant effects on blood lipid profiles in overweight and obese female.

Keywords: Soy, obese women, lipids profile, Isfahan

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LEPTIN MRNA EXPRESSION, METABOLIC RISK FACTORS AND INSULIN RESISTANCE IN POSTMENOPAUSAL WOMEN

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Introduction: Leptin, the product of the *ob* gene produced in the adipocytes, has a key role in the regulation of metabolism energy expenditure and body weight.

Objective: The present study was design to investigate Leptin mRNA expression and its correlation with biochemical parameters, insulin resistance in postmenopausal women.

Method: This is a case control study. A total of 160 postmenopausal women were recruited for the study (80 with metabolic syndrome and 80 without metabolic syndrome). Fasting blood samples were collected at admission and abdominal visceral adipose tissue (VAT) were obtained during surgery for gall bladder stones or hysterectomy. Physical parameters (height, weight and BMI) were measured. Biochemical parameters were estimated by enzymatic methods. Serum leptin level and Insulin was estimated by ELISA. The VAT leptin mRNA expression was estimated by real-time PCR.

Result: In VAT, leptin mRNA expression was significantly lower in postmenopausal women with metabolic syndrome as compare to premenopausal women without metabolic syndrome (0.06 ± 0.04 vs. 1.71 ± 0.72), plasma glucose (113.91 ± 14.72 vs. 95.88 ± 13.61), serum TG (141.12 ± 24.30 vs. 123.89 ± 25.12) and serum cholesterol (186.69 ± 23.03 vs. 152.53 ± 22.31) were found highly significant except serum HDL (33.50 ± 9.50 vs. 42.53 ± 10.56). Serum leptin levels (13.01 ± 6.25 vs. 9.55 ± 3.79) were directly correlated with insulin resistance and metabolic syndrome

Conclusion: These results indicate that leptin mRNA expression play a anti protective role in the development of metabolic syndrome and insulin resistance.

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OVERWEIGHT AND OBESITY AMONGST CHILDREN AND ADOLESCENTS IN GULF COOPERATION COUNCIL STATES: A SYSTEMATIC REVIEW

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The Gulf Cooperation Council (GCC) States are facing considerable health challenges related to obesity. This systematic review examined prevalence of overweight and obesity amongst children and adolescents in GCC states over the last 40 years. Study quality was determined by means of a 23-item checklist. Thirty-six studies met the inclusion criteria. The main findings were: (1) considerable variability (14.9–46.2%) in combined prevalence of overweight and obesity reported within States; but with evidence that prevalence had reached a plateau amongst males and females in Saudi Arabia by 2006; by contrast the rate continued to increase amongst both sexes in the United Arab Emirates up to 2010; (2) females were more overweight and obese than males in 60% of studies; (3) a general trend for prevalence of overweight and obesity to increase with age in 70% and 76% of studies in males and females respectively. The main quality limitations of studies were: explanation of how missing data were addressed (87% of studies); discussion of study design limitations (72%); eligibility criteria and selection of participants (50%). This review has highlighted consistency of findings as regards obesity in the GCC States.

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EFFECTS OF INTERLEUKIN-4 ON PROTEIN EXPRESSION PROFILES IN ADIPOCYTES

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Obesity, characterized by excess intra-abdominal adipose tissue, is closely associated with a cluster of metabolic disorders such as type 2 diabetes mellitus (T2DM). Our previous study revealed significant associations between *interleukin-4 (IL-4)* genotypes and T2DM, as well as *IL-4* genotypes and high density lipoprotein-cholesterol levels, which suggest that IL-4 is involved in lipid metabolism. Our most recent animal study uncovers that IL-4 regulates glucose and lipid metabolism by promoting glucose tolerance and inhibiting lipid deposits. We aimed identifying differentially expressed proteins in 3T3-L1 adipocytes under IL-4 treatment for further elucidating regulation of IL-4 to lipid metabolism. Differentially expressed proteins in mature 3T3-L1 adipocytes under IL-4 treatment were identified by proteomic strategy. Levels of ATP synthase δ chain, cytochrome *c* reductase, pyrophsphatase and vimentin are increased, whereas levels of alpha-enolase, gelsolin, vinculin and valosin are down-regulated in the presence of IL-4 stimulus. IL-4 tends to potentiate the elevation of intracellular ATP levels and promote metabolism in adipocytes by up-regulating expression levels of proteins accelerating ATP synthesis. Our results suggest that lipid metabolism in adipocytes is deviated to catabolism with

an unfavorable condition for lipid storage by IL-4. The lipids in adipocytes might either be released into periphery or metabolized intracellularlly, which in turn influence the systemic energy metabolism of other insulin-targeted organs.

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EFFECT OF DIABETES EDUCATION PROGRAM ON TYPE 2 DIABETIC PATIENTS IN PALESTINE

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Background: In the Palestinian community, lifestyle changes, rapid urbanization, stress, and smoking, may increase the risk of non-communicable diseases especially type 2 diabetes mellitus. Diabetic complications can be prevented if the glycemic status is maintained within a nearly normal range. Therefore, patient education is critical in controlling glucose levels within the normal range. The aim of the study was to measure the effect of diabetes educational program on type 2 diabetic patients.

Methods: In total, a convenient sample of 215 patients were attended a group-based educational intervention sessions about diabetes. Knowledge evaluation questionnaires were administered before and after the implementation of the intervention program. Anthropometric measurements and lab tests were also measured before and after the intervention.

Significance of the results was assessed by paired t-test at 95% confidence interval using SPSS version 16.

Results: A significant increase in knowledge evaluation test scores (Mean ± SD) were shown after the educational intervention program (60.6 ± 20.7 to 78.1 ± 13.4) ($p < 0.001$). BMI (Mean ± SD) was decreased significantly after conducting the educational intervention program (32.1 ± 5.76 to 31.23 ± 5.8) ($p < 0.001$). Moreover, a significant decrease was reported in glycosylated hemoglobin (Mean ± SD) after the intervention program (8.57 ± 1.21 to 7.95 ± 1.42) ($p < 0.001$).

Conclusion: Diabetes education is a cornerstone in the management and care of diabetes and should be an integral part of health planning involving patient's family, diabetes care team, community and decision makers in the education process.

KeyWords: Diabetes, Educational Program, Intervention.

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A MATHEMATICAL MODEL OF BETA-CELL MASS, GLUCOSE, INSULIN, FREE FATTY ACIDS AND INSULIN RECEPTORS DYNAMICS

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As indicated in a paper published by Poitout and Robertson in Endocrine reviews (2008, 29: 351–356) on glucolipotoxicity: fuel excess and β-cell dysfunction, many studies are being carried out in order to understand the mechanisms leading to the β-cell dysfunction and hence to diabetes. Although some studies have provided evidence (*in vitro* and *in vivo*) on the fact that lipotoxicity occurs in the presence of concomitantly high glucose levels, more research is needed to understand the β-cells dynamics (apoptosis vs replication) according to glucose, free fatty acids and other factors.

Following a mathematical model published by Topp et al (2000) on β-cell mass, insulin, and glucose kinetics: pathways to diabetes, and an extension of the previous model published by Hernandez et al (2001) in which they added the surface insulin receptor dynamics, we propose an extended mathematical model by adding the free fatty acids dynamics.

The mathematical model is given by:

$$\frac{dG}{dt} = a - bG(t) - cR(t)\frac{G(t)I(t)}{(\alpha G(t)+1)} + m_1F(t)G(t)$$

$$\frac{dI}{dt} = \frac{d\beta(t)}{(1+R(t))}\frac{G(t)^2}{(e+G(t)^2)} - fI(t) - fR(t)I(t)$$

$$\frac{d\beta}{dt} = (-g + hG(t) - iG(t)^2)\beta(t)$$

$$\frac{dR}{dt} = j(1-R(t)) - kI(t)R(t) - l(t)R(t) + h_1F(t)R(t)$$

$$\frac{dF}{dt} = -m_2(F(t)-F_b) + m_3(G(t)F(t) - F_bG_b) - m_4F(t)I(t)$$

where G(t) (in g/l), I(t) (in μU/ml), β(t) (in mg), R(t) and F(t) (in μmol/l) represent respectively the blood glucose concentration, blood insulin concentration, Beta-cell mass, fraction of insulin receptors on the surface and Free Fatty Acids level at time t.

The mathematical model has three equilibrium points: a stable pathological point P1 (6, 0, 0, 0.91, 436), an unstable saddle point P2 (1.45, 6.19, 213, 0.87, 475) and a stable physiological point P3 (0.82,12.8, 863, 0.84, 327).

We discuss and compare the results yielded by our model to the results previously published by other authors.

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ASSOCIATION OF CTLA-4 GENE POLYMORPHISMS IN TAIWANESE PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Type 2 diabetes mellitus (T2DM) is characterized by abnormally high blood glucose resulting mainly from insulin resistance and/or a relative deficiency of insulin. Recent finding suggest that T2DM is an acute-phase disease in which increased concentrations of cytokines contribute to the regulation of balance between T_H1 and T_H2 cells. The present study investigated the single nucleotide polymorphisms (SNPs) of T cell response negative regulator, cytotoxic T lymphocyte-associated antigen-4 (*CTLA-4*), among Taiwanese T2DM patients. One hundred and fifty-six Taiwanese T2DM patients and 77 healthy controls were recruited, with their peripheral blood sample collected, genomic

DNA extracted, and 2 CTLA-4 SNPs (+49 A/G and −318 C/T) analyzed by PCR and RFLP. The prevalence of CTLA-4 +49 A/A, G/G and A/G genotype in T2DM patients was 8.3%, 43.0% and 48.7%, respectively, as compared to 15.5%, 23.4% and 59.1% in control subjects, respectively. The frequency of CTLA-4 −318 C/C, T/T and C/T genotype in T2DM patients was 85.0%, 0.7% and 14.3%, respectively, while that in control individuals was 67.5%, 0% and 32.5%, respectively. Interestingly, no CTLA-4 −318 T/T genotype was found in our control subjects. Significant differences in the distribution of CTLA-4 +49 A/G ($p=0.024$) and −318 C/T SNPs ($p=0.005$) between T2DM patients and healthy controls were observed. Our findings suggest that the CTLA-4 +49 A/G and −318 C/T gene polymorphisms are associated with T2DM.

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VALIDITY OF LIFESTYLE MEDICINE PROGRAM IN CHRONIC DISEASE CENTOR

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Objective: We are going to check the validity of lifestyle medicine intervention composed of nutrition and exercise in the field of chronic disease center for the 10 yr cv risk, body composition, physical fitness and disease control.

Method: From 2013 January to June 270 chronic disease patients were recruited. They got 13 weeks lifesytle medicine program including exercise and nutrition test, prescription and regular exercises. We checked WHO physical activity questionnaire, Beck's Depression scale, QOL, laboratory test (systolic and diastolic BP, Total cholesterol, TG, HDL, LDL), Body composition test using InBody720 body composition analysis (body weight, BMI, fat%, LBM, BMR) and physical fitness (grip strength, back strength, trunk flexion/extension, vertical jump). Also we calculated 10 yr CV risk and the achievement of the program at point 70% attendance.

Results: Total 148 patients completed 13 weeks lifestyle program including exercise and they showed significant improvement in physical activity, QOL, body weight, BMI, fat%, grip strength, trunk flexion/extension after the program but not significant in depression score, LBM, BMR and 10 year CV risk score. In the lab data, systolic BP and HDL showed significant improvement but not the others. In the hypertension group (n = 79), systolic BP decreased by 3.43 mmHg. In the dyslipidemia group (n = 20), all lipid profile data deteriorated except HDL. In the obese group (n = 49), body weight, BMI, fat% showed significant improvement but LBM, BMR seemed to be decreased.

Conclusion: Lifestyle medicine program showed some benefit in disease control including body composition, physical fitness. But still medical intervention and more intensive muscle strengthening program might be required.

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SAFETY AND EFFICACY OF LIRAGLUTIDE IN PATIENTS WITH TYPE 2 DIABETES AND OBESITY IN CLINICAL PRACTICE

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Aim: To evaluate the safety and efficacy of Liraglutide as second or third step of treatment of T2DM and obese patients under clinical practice conditions.

Materials and methods: A prospective, single center study was performed in an Endocrinology Unit in Gijón, Spain from July 2011 to September 2012. Obese (BMI ≥ 30 Kg/m2), inadequately controlled (HbA1c > 6.5%) T2DM patients on OADs-therapy were included. Clinical and analytical data were collected at 12 and 24 weeks.

Results: A total of 37 patients were included, 60% males and 40% females. Liraglutide 1.2 mg/day (after 0.6 mg/day for 1 week) was prescribed. Baseline characteristics (mean ± SD) were age 57 ± 10 years, diabetes duration 6 ± 4 years, HbA1c 8.2 ± 1.2%, FPG 192 ± 47 mg/dl, C-Peptide 5 ± 1.7 ng/ml, HOMA-IR index 9.8 ± 3.6, weight 110.5 ± 23 Kg, waist circumference 123.5 ± 14 cm and BMI 40.9 ± 8 Kg/m2. Hypertension (73%) and dyslipidemia (76%) were commonly reported with a low rate of vascular complications (19%).

After 24 weeks of treatment HbA1c was reduced (mean ± SD) 1.5 ± 1.3% (p < 0.001), FPG 70 ± 50 mg/dl (p < 0.001), weight 5.2 ± 6.5 Kg (p 0.001), waist circumference 7.6 ± 7.2 cm (p 0.001) and BMI 1.9 ± 2.5 Kg/m2 (p 0.002) form baseline (paired t-test applied). Improvement in blood pressure and lipid profile was also noticed (p > 0.05).

16 subjects (40%) reported adverse events, mainly mild, transitory, gastrointestinal ones. No serious adverse event was noted. Minor hypoglycaemia was registered in only 3 subjects, all of them on concomitant sulfonylurea treatment.

Conclusions: Liraglutide has shown efficacy and tolerability, achieving a great HbA1c reduction associated with a significant weight lost after 6 months of treatment.

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THE ROLE OF OBESITY IN CHANGING OF CIRCULATING ANDROGENS AND THEIR PRECURSORS

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Introduction: The association of obesity with a lower circulating testosterone level in men is well documented. However, reports on possible changes in the androgen spectrum in obesity are rare. Understanding of these changes could help in the searching of new possibilities in treatment of obesity.

Methods: To investigate this phenomenon, serum sex hormone–binding globulin (SHBG), testosterone, dihydrotestosterone, androstenedione, dehydroepiandrosterone and its sulphate, 17α-hydroxypregnenolone, 17α-hydroxyprogesterone and gonadotrophins LH and FSH concentrations were measured in fasting blood samples of 224 men divided into three groups – normal (BMI = 18–25, n = 109, overweight (BMI 25.10–30, n = 78) and obese (BMI 30.1–39, n = 37). The study was authorized by local Ethical committee.

Results: A significant decrease in testosterone, dihydrotestosterone, 17α-hydroxypregnenolone, 17α-hydroxyprogesterone and SHBG with increasing body mass index was observed, whereas insignificant changes for dehydroepiandrosterone and its sulphate, androstenedione and gonadotrophins LH and FSH, were found. The

ratios of corresponding pairs of steroids were in agreement with the concept that in obesity splitting of the side chain of C_{21}-steroids, and 17β-hydroxysteroid dehydrogenase-reducing activity are decreased. No changes for steroid 5α-reductase or 3β-hydroxysteroid dehydrogenase (HSD3B2) were found.

Conclusion: The findings demonstrate that, in men with increasing body mass index, the formation of C_{19} steroids decreases from their C_{21} precursors and lower 17β-hydroxysteroid dehydrogenase further confines the production of testosterone and dihydrotestosterone.

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METABOLIC EFFECTS OF FLAXSEED OIL SUPPLEMENTATION (W3/ALA) IN MICE

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Liver plays a key role in pathological conditions of insulin resistance, such as diabetes mellitus and metabolic syndrome. The anti-inflammatory effects of polyunsaturated fatty acid ω3 EPA and DHA have been studied. The α-linoleic acid (ALA) found in seeds oil, little is known about its effect on liver. The aim of this study was to evaluate the effects of supplementation of ω3/ALA in mice.

Methods: 40 mice (C57/BL6) were divided into 4 groups: control (C), control + ω3 (CW), obese (O) and obese + ω3 (OW). For a period of eight weeks, the groups O and OW received a high-fat diet with 60% fat, while the C and CW received regular chow. After, the groups CW and OW received supplementation of ω3 10% of flaxseed extract, daily, for another 8 weeks.

Results: After 8 weeks, CW had greater weight gain in relation to C. The same result was founded between O and OW. Serum total cholesterol and HDL was significantly higher in CW, while groups O and OW the values were similar; Triglycerides values were similar between all groups. Area under the curve of glucose by GTT test showed a significant decrease compared O to the OW, and was similar between C and CW. Moreover, total liver fat levels were significantly lower in CW and OW, comparing to C and O.

Conclusion: ALA supplementation changed the animals weight between the groups. However, supplementation of ω3/ALA showed to be effective in preventing hepatic steatosis, elevated serum levels of HDL and the reduction of insulin resistance.

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INTERLEUKINS 33 AND 1B, LEFT VENTRICULAR REMODELING AND DIASTOLIC DYSFUNCTION IN HYPERTENSIVE PATIENTS WITH OBESITY

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Objective: To investigate interrelations between interleukin 33 (IL-33) and 1β (IL-1β) serum levels, left ventricular (LV) remodeling and diastolic dysfunction (DD) in hypertensive patients with obesity.

Method: 80 hypertensive patients (51 obese) underwent transthoracic echocardiography. IL-33 and IL-1β serum levels were estimated using ELISA.

Results: IL-33 and IL-1β were higher in hypertensive patients ($p < 0{,}001$), independently of BMI. Increase of IL-33 > 73 pg/ml, IL-1β > 25 pg/ml was associated with highest LV myocardial mass index (MMI) (160,5 (142,8;185,8) g/m^2, $p < 0{,}05$), E′ of (9,95 (8,32;10,60) cm/sec), PWP of (9,23 (8,83;13,03) mm Hg) and 70,0% LVDD. IL-1β > 20 pg/ml with IL-33 < 71 pg/ml was characterized by LVMMI of (116,9 (104,4;163,1) g/m^2), lowest E′ (7,68 (6,50;9,67) cm/sec, $p < 0{,}01$), highest PWP (12,26 (10,72;13,12) mm Hg, $p < 0{,}05$) and highest rate of DD (85,0%). IL-33 > 71 pg/ml with IL-1β < 25 pg/ml was associated with MMI of 121,4 (111,7;140,5) g/m^2, highest E′ (11,04 (9,49;12,00) cm/sec), lowest PWP (9,07 (7,04;11,51) mm Hg) and lowest prevalence of LVDD (66,7%). IL-33 < 71 pg/ml with IL-1β < 20 pg/ml had intermediate characteristics: LV MMI of 137,4 (121,3;157,8) g/m^2, E′ of 9,95 (8,30;12,20) cm/sec, PWP of 11,20 (9,55;12,33) mm Hg, and 71,1% rate of DD.

Conclusion: Significant increase in IL-33 and IL-1β levels in hypertensive patients independently of BMI was revealed. Increase in both cytokines' levels was associated with highest rates of LVH and DD. Prevalent increase in IL-1β was connected to the worst state of diastolic function despite low rates of hypertrophy. Prevalent increase in IL-33 had the most favorable influence on the severity of LVH as well as diastolic filling.

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ASSOCIATION BETWEEN APOLIPOPROTEIN AI-CIII-AIV GENE CLUSTER POLYMORPHISMS AND METABOLIC SYNDROME PATIENTS

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The Apolipoprotein (APO) AI-CIII-AIV gene cluster presents high relevance in lipid metabolism. Thus, it has important epidemiological implications in diabetes, metabolic syndrome (MS) and thrombotic conditions. In light of these, we studied for the variation patterns of seven polymorphisms (APOAI *Xmn*I, *Msp*I, *Pst*I; APOCIII *Msp*I, *Fok*I, *Sst*I; APOAIV *Hinc*II) in cross-sectional cohort population to examine associations with MS patients. Five hundred and fifteen healthy controls and 320 MS patients were participated in this study. APOAI-CIII-AIV gene cluster polymorphisms were analyzed by polymerase chain reaction-restriction fragment length polymorphism assay. The adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were used to evaluate the strength of genetic associations. The genotype frequencies of the APOAI-CIII-AIV gene cluster polymorphisms showed significant differences between the MS and control groups. Haplotype frequencies were also significantly different between the two groups. In stratified analysis by metabolic syndrome risk factors, the strong associations were found. Therefore, the APOAI-CIII-AIV gene cluster polymorphisms may predispose to susceptibility of MS by interacting MS risk factors. Further studies are needed to improve understanding of the effect of APO gene polymorphisms and genes in related pathways using a larger and more heterogeneous cohort.

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CHANGES OF GHRELIN AND MELATONIN BASED ON FOOD INTAKE

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Introduction: Melatonin plays a key role in the circadian timing system. Researchers have found an independent association between decreased secretion of melatonin and an increased risk for the development of type 2 diabetes. The question remains whether changes in endogenous melatonin may be associated with food intake. Ghrelin is involved in the regulation of energetic homeostasis. Therefore, we decided to obtain more detailed data on the circadian changes of ghrelin and melatonin for identification of the changes in these hormones to food intake and day-time, together with glycemic and C-peptide levels.

Methods: Five women (mean age 31.6 ± 2.8 years, mean BMI 23.2 ± 2.3 kg/m^2) in follicular phase of menstrual cycle were examined. The levels of ghrelin, melatonin, C-peptide and glucose were studied during a daily regimen (16 hours) including standardized food intake. The study was approved by local Ethical Committe.

Results: The levels of blood glucose and C-peptide reflected periodic food intake being in a physiological range. A significant negative correlation between melatonin and C-peptide was found (Pearson's correlation, $r = -0.5525$, $p < 0.0001$, $n = 50$, partial correlation $r = -0.3532$, $p < 0.02$, $n = 50$). A borderline significant relationship between melatonin and blood glucose was detected (Pearson's correlation, $r = -0.4679$, $p < 0.0006$, $n = 50$). Ghrelin negatively correlated with C-peptide ($r = -0.356$, $p < 0.02$). We found positive correlation between melatonin and ghrelin ($r = 0.453$, $p < 0.003$).

Conclusions: The negative relationship between melatonin and C-peptide as well as relatively rapid changes in melatonin levels permits speculation about food as one of the factors influencing daytime melatonin production.

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THE STUDY OF RS9939609 POLYMORPHISM OF FTO GENE IN PATIENTS WITH OBESITY AND TYPE 2 DIABETES

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The most significant association with obesity and type 2 diabetes is shown for gene polymorphisms FTO. The European populations revealed significant association rs9939609 variant of the FTO gene with obesity and type 2 diabetes. It was found that the A allele of this variant can be viewed as the risk factor in the development of obesity and type 2 diabetes.

Objective: To determine frequency of the A allele of the FTO gene in patients with obesity and type 2 diabetes.

Materials and Methods: The study included 50 patients with obesity I- III degree and type 2 diabetes aged 40 to 60 years. Genotyping of polymorphism rs9939609 of the FTO gene using a multiplex allele-specific polymerase chain reaction. DNA was extracted from blood by standard method using a sorbent and a set of reactants ''DNA-sorb-C'' produced by FSISTSNIIE Epidemiology, Moscow. For the conduct of amplification using a thermalcycler ''RotorGene-6000'', Germany.

Results: The study of the gene FTO rs9939609 polymorphism inpatients with obesity and type 2 diabetes showed that 12% of them are carriers of a mutant allele (A) in the homozygous state, and 64% - in the heterozygous state. In population studies, the frequency of detection of allele A was 35%.

Conclusions: The results showed an association of the FTO geners 9939609 polymorphism with the risk of obesity and type 2 diabetes.

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CERTIFICATE COURSE IN EVIDENCE BASED DIABETES MANAGEMENT: AN APPROACH TOWARD BUILDING CAPACITY OF PRIMARY CARE PHYSICIANS IN DIABETES CARE, INDIA

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Objective: This article/paper is aimed to assess the impact and effectiveness of PAN INDIA Certificate Course in Evidence Based Diabetes Management (CCEBDM).

Methods: Improvement in knowledge of physicians was assessed by quantitative and qualitative methods. For quantitative analysis pre and post test scores were used and for qualitative analysis, end-line evaluation as a cross-sectional survey was conducted with 100 and 125 randomly selected physicians from CCEBDM Cycle-I and cycle-II respectively using pre tested scheduled questionnaires two months after completion of cycles.

Results: Pre-post test score of 2776 physicians were assessed for the knowledge improvement and it was found that there is significant improvement (*P value < 0.05)*. Frequency of physicians who confident to manage diabetic complication like hypoglycaemia (73%), peripheral neuropathy (94%), skin complication (82%), sexual dysfunction (78%), diabetic foot (74%) and nephropathy (71%) increased. 90% were confident about managing patients on insulin independently.

While assessing the clinic structure it was found that 66% of physicians had provision for laboratory facilities routine blood screenings, 53% had on-site dieticians who helps the diabetic patients, 35% had a counsellor to guide the patients, 49% were using DBMS, 79% had full time nurses on duty, 76% used various forms of Patient Education Resources to elicit awareness about diabetes.

Conclusion: CCEBDM is evidence based course and uses recent clinical findings in developing clinical guidelines for better management of diabetic patients is very effective in knowledge improvement of physicians and ultimately improvement of clinical practices in diabetes management.

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TREATMENT OF DIABETES MELLITUS USING A NEW PLANT (PHYLLANTUS AMARUS)

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Introduction: The purpose of this study was to determine the effect of a new plant (Phyllantus Amarus) in the treatment of diabetes mellitus.

Methods: Two hundred and fifty adults of ages 45–65 years, comprising one hundred males and one hundred and fifty females, that were known diabetic patients, were randomly recruited into the study. Their consent was received verbally and were assured of strict confidentiality. Moreover, the ethics committee approval of College of Medical Services University of Benin, ethnics committee was received before commencement of study. The patients fasting blood glucose levels before treatment commenced were between 180 mg/100 mls – 250 mg/100 mls.

The patients were given a cupful of the extracts at least 30 minutes, before breakfast and daily for a period of six months and their fasting blood glucose was equally monitored during the period of study.

Results: Satisfactory clinical response was achieved at the end of the six month period as their fasting blood glucose level dropped to 80 mg/100 mls – 110 mg/100 mls.

Conclusion: This study presents the treatment of diabetes patients using a new plant (Phyllantus amarus)

Keywords: Diabetes, Mellitus, Treatment, Phyllantus, Amarus

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THE ROLE OF A LIFESTYLE MODIFICATION IN PREVENTING TYPE 2 DIABETES MELLITUS AND INFLUENCE IT ON CHANGES SERUM LEPTIN LEVELS

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The aim of our study is to assess the efficacy of a lifestyle modification including altered diet composition and physical activity in preventing diabetes mellitus type 2 (DM 2) in individuals with impaired glucose tolerance and impaired fasting glucose (IGT/IFG) and influence it on changes serum leptin levels.

Materials and methods: The study included 327 patients with IGT/IFG (68 m 258 f) 25–65 years. Patients were divided into 2 groups matched by sex, age, weight, body mass index (BMI). Research group included 183 patients (32 m, 150 f) who received and carried out individual recommendations of a balanced diet and physical activity. Control group included 144 patients (36 m 108 f) who did not lifestyle modification. Related to fasting leptin (FL) concentrations by sensitive ELISA.

Results: Patients of the research group demonstrated reduction of body weight ($p < 0.01$). They had positive dynamics of FPG and 2-h PG concentrations also ($p < 0.001$). Persons of the control group had significant increase in weight and BMI and FPG and 2-h PG concentrations elevated ($p < 0.05$). The main novel finding was that median serum leptin in research group decreased on −23.9% ($p < 0.01$) and increased in control group on +27.6% ($p < 0.01$) among subjects with IGT Among patients of the research group was a reduction of new care DM 2 by 11.9% and an increase in the control group by 35.1%.

Conclusion: Thereby, lifestyle modifications lead to reduction not only fasting plasma glucose, postprandial glucose concentrations but and fasting leptin concentrations in individuals with IGT/IFG.

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PREDICTORS SELF-CARE BEHAVIORS OF PATIENT WITH TYPE 2 DIABETES, QOM CITY IRAN

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Background: Diabetes has no definite treatment. The most important treatment strategy employed to control diabetes is adherence to Self-care behaviors such as special diet, physical activity, blood glucose monitoring, daily foot care and taking the prescribed medicine. This study aimed to assess rates of adherence to different dimensions of self-care behaviors and evaluate the predicting value of each dimension on glycemic control among type 2 diabetic patients under coverage of Diabetic Clinic of Qom University of Medical Sciences (Qom, Iran).

Methods: This cross-sectional, descriptive, analysis study was conducted on 275 Randomized patients. Data was collected using the Summary of Diabetes Self-Care Activities (SDSCA) measure, a ccognitive health questionnaire, and Beck Depression Questionnaire. Glycated hemoglobin (HbA1c) test was also performed. Data was analyzed through bivariate correlations and multivariate linear regression in $SPSS_{17}$.

Findings: The final regression model introduced education level, medicine taking behavior, nutrition, physical activity and blood glucose monitoring as the main predictors. This model accounted for 66% of the variance of the HbA1c level as a glycemic control indicator ($p < .0.001$).

Conclusion: Various dimensions of self-care behaviors of patients with type 2 diabetes have different impacts on metabolic control. Medicine taking the medicine and nutritional dimensions of self-care behaviors has the greatest effect on glycemic control.

Keywords: Type 2 diabetes, Adherence, Self-care behaviors, Glycemic control.

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RESOLUTION OF DIABETIC NEPHROPATHY FOLLOWING LAPAROSCOPIC ILEAL INTERPOSITION WITH SLEEVE GASTRECTOMY IN PTS WITH TYPE-2 DIABETES – MULTI-CENTER STUDY

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Introduction: Diabetic nephropathy is the leading cause of chronic kidney disease, and associated with increased cardiovascular mortality. 30–40% of diabetics develop nephropathy. The aim of this study was to evaluate the regression of nephropathy in poorly controlled type-2 diabetics, by laparoscopic ileal interposition with sleeve gastrectomy, through better glycemic control, even in non-obese patients.

Methods: This was a retrospective, 2-center study in 60 patients treated at Kirloskar Hospital, Hyderabad, India and at Alman Hastanesi, Istanbul, Turkey. 51 were men and 21 women. Mean age was 50.7 years (22–70). Mean BMI was 33.8 kg/m^2 (23.5–51). Insulin therapy was been used by 41% of the patients. Mean duration of T2DM was 11.5 years (3–32). Mean HbA1c was 9.2% (6.1—15.8). Microalbuminuria (30–299 μg/min) was diagnosed in 47% of the patients and macroalbuminuria (>300 μg/min) in 53%. The mean clearance of creatinine was 62.2 mL/min (33–128). 48% of the patients had creatinine clearance ≤ 60 mL/min. Arterial hypertension present in 66%.

Results: Mean post-operative follow-up was 14 months (8–60). Mean postoperative BMI was 25.2 kg/m^2 (19.8 – 34.5). Mean HbA1c was 6.9% (5.2–9.6). Overall, 52.4% of the patients achieved remission of T2DM. Microalbuminuria was normalized in 89%. Macro-albuminuria persisted in 8.6%. The mean clearance of creatinine was 98 mL/min (48 – 120). Arterial hypertension was controlled in 90% of the patients

Conclusion: Laparoscopic IISG seems to be a promising procedure to control diabetic nephropathy, possibly through remission of micro-albuminuria and T2DM.

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POTENTIAL BENEFITS OF CONTINUOUS GLUCOSE MONITORING IN PREDICTING FETAL OUTCOMES IN PREGNANT DIABETIC WOMEN

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Background: Infants born to mothers with diabetes mellitus are more likely to be macrosomic and are at greater risk of birth-related injury, foetal anomalies and metabolic sequelae. Poor glycaemic control contributes and transient hyperglycaemia may exacerbate. The impact of glycaemic variability on macrosomia has not been investigated in women with diabetes.

Methods: 19 pregnant diabetic women attending a multidisciplinary antenatal clinic underwent 72 hours of blinded continuous glucose monitoring (CGM) in the 2nd-3rd trimesters. Glycaemic variability markers (mean glucose, SD, CONGA, LI, JINDEX, LBGI, HBGI, GRADE, MVALUE and MAG) were calculated using EasyGV software (v9.0).

Results: Maternal age mean(SD) was 33.3(6.3) yrs, BMI 30.7(6.4) kg/m^2, and booking HbA1c 54 mmol/mol(15.4). 63.2% were non-caucasian. 26.3% had Type 1 diabetes (T1DM); 73.7% type 2 diabetes (T2DM). 31.6% of infants were macrosomic. There were no differences in glycaemic variability between women with T1DM and T2DM. Women who delivered macrosomic infants and those who did not were compared. Differences in booking BMI and HbA1c were non-significant. LI, J INDEX and HBGI were significantly higher in the macrosomic group: LI and J INDEX correlated significantly with birthweight ($r^2 = 0.49$ and 0.21 respectively). Differences in mean glucose, CONGA, LBGI, GRADE, M Value, and MAG were non-significant. SD values were lower in the macrosomic group (3.76 vs 8.22:$p < 0.005$).

Conclusions: Markers of glycaemic variability (LI, J INDEX, and HBGI) were significantly associated with fetal macrosomia and LI and J Index correlate with fetal birthweight, suggesting a potential role for CGM in pregnancy and implicating glucose excursions in the pathogenesis of macrosomia.

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BODY COMPOSITION IN ADULTS WITH NEWLY DIAGNOSED TYPE 2 DIABETES: EFFECTS OF METFORMIN

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Aims: To measure the body composition in adults with newly diagnosed type 2 diabetes mellitus and to explore the effect of metformin therapy on various components of body composition, insulin sensitivity, and glucose homeostasis.

Materials and Methods: This study consisted of 51 newly diagnosed type 2 diabetic people on 1000 mg metformin twice daily for 6 months. The body composition of each subject was measured by dual energy X-ray absorptiometry at enrollment and

	Female			*Male*		
	Week 0 (n = 30)	*Week 24 (n = 27)*	*P-value*	*Week 0 (n = 21)*	*Week 24 (n = 14)*	*P-value*
Android fat mass (kg)	2.80 ± 0.77	2.63 ± 0.78	0.03	2.35 ± 0.79	2.04 ± 0.78	0.001
Gynoid fat mass (kg)	4.60 ± 1.02	4.42 ± 1.02	0.02	3.37 ± 0.83	3.11 ± 0.90	0.004
Android Fat Mass/Gynoid Fat Mass	0.61 ± 0.12	0.60 ± 0.13	0.45	0.70 ± 0.16	0.65 ± 0.12	0.015
Trunk/ limb fat	1.02 ± 0.15	1.01 ± 0.15	0.47	1.21 ± 0.27	1.18 ± 0.24	0.25
Fat mass/h^2 (kg/m^2)	12.45 ± 3.1	11.88 ± 2.98	0.027	7.68 ± 2.1	7.11 ± 2.03	0.022
Appendicular lean mass/h^2 (kg/m^2)	7.49 ± 0.91	7.18 ± 1.03	0.006	8.75 ± 0.74	8.70 ± 0.92	0.38
Appendicular lean mass/W	0.24 ± 0.02	0.24 ± 0.02	0.29	0.31 ± 0.02	0.32 ± 0.02	0.69
SMI	0.03 ± 0.01	0.03 ± 0.01	0.6	0.038 ± 0.001	0.039 ± 0.001	0.005
Total fat mass (kg)	29.91 ± 6.91	28.68 ± 6.58	0.015	21.88 ± 5.87	20.12 ± 6.00	0.003
Percentage of Fat (%)	43.03 ± 5.35	41.54 ± 5.77	0.000	27.11 ± 3.61	25.82 ± 4.90	0.08
Total lean mass (kg)	41.95 ± 4.86	40.79 ± 5.12	0.014	53.6 ± 6.59	52.67 ± 7.60	0.17
Lean/Fat ratio	1.45 ± 0.31	1.48 ± 0.33	0.65	2.60 ± 0.69	2.8 ± 0.71	0.041

h^2: Height Squared; W: Weight; SMI: Skeletal Muscle Index

24 weeks after metformin mono-therapy. Sarcopenia was defined and compared based on the ratio of appendicular skeletal muscle and height squared, skeletal muscle index and residual methods.

Homeostasis model assessment-insulin resistance and Quantitative Insulin Sensitivity Check Index were used for estimating insulin sensitivity. The level of physical activity was assessed using self-administered International physical Activity questionnaire.

Results: Forty-one subjects (80.4%) completed the study. The mean age of the participants was 52.67 ± 10.43 years. Metformin treatment was associated with a significant decrease in total fat mass (-1.6 kg, $P = 0.000$). By week 24, the lean to fat ratio increased ($P = 0.04$) as well as skeletal muscle index ($P = 0.02$) with men showing greater significant changes. Twenty percent of the female participants were detected to have sarcopenia. In addition, there was a significant improvement of glucose homeostasis and insulin sensitivity.

Conclusions: Metformin therapy results in significant improvement in body composition and insulin sensitivity of adults with newly diagnosed type 2 diabetes. Furthermore, sarcopenia begins in diabetic women much earlier than expected as an age related phenomenon.

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CLINICAL VALUE OF CYTOKINES IN DIABETIC NEPROPATHY

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Objectives: To study the role of inflammatory chemokine; monocyte chemoattractant protein-1 (MCP-1), and fibrogenic markers [transforming growth factor beta-1 (TGF-β(1)), connective tissue growth factor (CTGF) and fibronectin (FN)] in diabetic nephropathy (DN).

Design and Methods: This study included 17 control and 65 type 2 diabetic subjects (18 normoalbuminuric, 22 microalbuminuric and 25 macroalbuminuric). Demographic characteristics, diabetic index and kidney function tests were monitored. Serum TGF-β(1), plasma CTGF, MCP-1 and FN levels were assayed.

Results: Microalbuminuric and macroalbuminuric subjects showed a significant elevation in TGF-β(1), CTGF, MCP-1 and FN levels as compared with control and normoalbuminuric subjects. There was positive correlation between these markers and fasting plasma glucose, albumin excretion rate and with each other.

Conclusion: This study revealed the importance of these markers in DN pathogenesis which is powered by their association and thus the possibility of their use as biochemical markers in DN was suggested.

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THE PREVALENCE, AUTOIMMUNE AND GENETIC MARKERS OF LATENT AUTOIMMUNE DIABETES OF ADULTS IN THE COASTAL AREA /SYRIA

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Objectives: This study aims to assess the perevalence, clinical characteristics, the frequency of islet β-cell autoimmune markers (ICA, GADA, IA-2, and IAA), and HLA-DQB1 genotypes association with latent autoimmune diabetes of adults (LADA) in the city of Latakia/ Syria.

Materials and Methods: Based on glutamic acid decarboxylase autoantibodies positivity, a population of 254 type 2 diabetics, males and females aged 35 to 75 years, were subdivided into $GADA^+$(positive) and $GADA^-$ (negative) subgroups. Both subgroups ($GADA^+$ and $GADA^-$) were studied in terms of the clinical and laboratory characteristics. Also, a subgroup of type 2 diabetics ($n = 70$) with c-peptide ≤ 1.2 ng/ml were studied in terms of the frequency of islet β-cell autoimmune markers (ICA, GADA, IA-2, and IAA). Moreover, LADA and type 1 diabetics (4–33 years) were evaluated in terms of susceptible and protective DQB1 genotypes in comparison with normal control.

Conclusion: Overall, in the city of Latakia, the prevalence of LADA was 17.7% in the studied type 2 diabetics. LADA patients showed similar laboratory and clinical features as type 2 diabetics with the exception of low BMI levels and poor glycemic control. Diagnostically, both ICA and IAA almost have 100% diagnostic value in identifying LADA in type 2 diabetics with c-peptide ≤ 1.2 ng/ml. The significance of HLA-DQB1 genotypes associated with susceptible alleles (*0201 and *0302) and protective one (*0601) was confirmed in classic type 1 diabetes group. Only *0302 susceptible allele was significantly increased in LADA.

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THE PROCESS OF CARING FOR DIABETIC FOOT ULCER

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The Purpose of this study is the clarification of the caring process in the diabetic foot ulcer among Iranian diabetic patients. The main question of this research was ''How is the caring process for the diabetic foot ulcer and how do patients experience it?'' This study was within the Grounded Theory method. Data collection was carried out up to reaching saturation. Saturation was attained after interviewing 11 patients, 4 physicians, one head nurse and one nurse. Three main themes emerged out of this study which included of: ''disease management, disease experience and the continuity of care.'' Each of these cases comprised of different sub-themes. Knowing the patients' experiences and the manner of dealing with them once faced with foot ulcer could facilitate the comprehensive decision making by therapists and the better recuperation of diabetic patients.

Keywords: care, education, diabetics, qualitative study, wound care

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DEFINING A SINGLE TIME POINT FOR BLOOD GLUCOSE MEASUREMENT THAT WOULD PREDICT FOR GLYCEMIC FLUCTUATIONS IN TYPE 2 DIABETIC PATIENTS

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The objective of this study is to investigate whether a single-point glucose measurement may predict for glycemic fluctuations in drug-naïve type 2 diabetic patients by using parameters derived from continuous glucose monitoring (CGM).

This study included a total of 31 drug-naïve type 2 diabetic patients, and their 24-hour CGM data were analyzed. As potential predictors of HbA1c values, 1-hour and 2-hour postprandial glucose levels, the range of glucose increase from premeal to 1-h and 2-h postprandial glucose levels were analyzed. Finally, the indices for glycemic control and variability and the potential predictors of glycemic fluctuations were examined for correlation and regression.

The median age of the patients was 57 (43–65) years of age, their median HbA1c value was 7.8% (6.8–8.9%). Their HbA1c values had the strongest correlation with their 2-hour postprandial glucose levels after breakfast ($r = 0.607$; $P < 0.001$). Likewise, their SD showed the strongest correlation with their 2-hour postprandial glucose levels after lunch ($r = 0.917$; $P < 0.0001$).

In drug-naïve type 2 diabetic patients, the higher their 2-h postprandial glucose levels after breakfast, the higher their HbA1c values. Again, the higher their 2-h postprandial glucose levels after lunch, the higher the SD. CGM-derived SD of their glucose levels were shown to be predicted by the following equations: their 2-h post-lunch glucose levels $\times 0.25 - 13$.

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PROGNOSTIC VALUE OF GLYCEMIC VARIABILITY IN SURGICAL PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Purpose to investigate the prognostic value of glucose variability.

Materials: 88 patients, were randomized to 4 groups: in 1 (n = 25) and 2 (n = 20) the target glucose level was 6,5 – 8,5 mmol/l; in 3 (n = 21) and 4 (n = 22) - 8,6–11,0. In group 1,3 we used continuous intravenous insulin infusion, in group 2, 4 - subcutaneous injections Acute Physiology and Chronic Health Evaluation (APACHE) score was calculated. We used the mean amplitude of glycemic excursions (MAGE) as a marker of variability.

Results: Hypoglycemic events were common for subcutaneous injection groups (? = 0,001). Parameters of APACHE II score decreased in group 1 on 10,0 (5,9–11,5) points, in group 2 - on 6,3 (5,2–11,3), 3 - on 8,1 (5,9–9,6), 4 - on 6,9 (6,0–9,3), p = 0,04. 90 - day survival rate was: 96,0%, 50%, 97,6% and 54,5% in groups 1, 2, 3 and 4, accordingly (? = 0,03). MAGE level: in group 1 - 1,1 ± 0,48; 2 – 3,4 ± 0,92; 3–0,9 ± 0,4; 4- 2,9 ± 0,9, p = 0,01. A higher MAGE level was associated with the higher rate of hypoglycemia (r = 0,6, p = 0,0001), mean glycemic level (r = 0,0017, p = 0,14), the amount of insulin (r = 0,58, p = 0,01). The level of MAGE > 3 was associated with the worst dynamic according to APACHE II scoring (p = 0,004), increased the risk of hypoglycemia in 2,4 times, p = 0,03, the risk of mortality in 1,8 times = 0,0003.

Conclusions: The level of MAGE ≥ 3 increased the rate of hypoglycemia, have a deleterious effect on dynamic of APACHE score and may be a predictor of mortality.

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REPEATIBILITY OF PLASMA GLUCOSE CONCENTRATIONS ESTIMATED ON GLUCOMETER CALLA UNDER VARIOUS CLINICAL CONDITIONS

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Introduction: Measurement repeatability is defined as measurement precision under a set of conditions of measurement that includes the same measurement procedure, same operators, same operating conditions and same location and replicate measurements on the same or similar glucometer-strips system over a short period of time.

Aim of this trial was to assess the repeatability (precision) of glucometer CALLA premium (Wellion, Austria) using the glucoseoxidase strips under routine conditions of monitoring in clinical practice.

Method: A total of 28 ten-point sets of PG estimations were performed in 6 persons with Type 1 or Type 2 diabetes mellitus. Each person used his/her personal glucometer CALLA premium. In each set the strips from one box were used. Capillary blood was obtained from one to ten fingerpricks either by the tested person or by a nurse using autolancet. The time period from the first to the last PG-estimation ranged from 2 to 10 min. In each set the mean value of PG concentration and Coefficient of variation (CV) were counted. The mean, median, mimimum and maximum value of CV was estimated for the whole group of 28 sets.

Results: The mean value of PG concentration in individual 28 sets ranged from 2.93 mmol/l to 19.01 mmol/l. CV ranged from 4.3% to 19.5% (mean 7.7%, median 7,4%). Pearsons correlation coefficient r = 0.026 revealed no significant correlation between mean absolute PG concentration and repeatability of results.

Conclusion: The estimated repeatability (precision) of PG measurements on glucometer CALLA corresponds to international standard ISO 15197:2013.

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ESTIMATION OF THE COST OF COMPLICATIONS RELATED TO GLYCATED HEMOGLOBIN IN THE ITALIAN DIABETES TYPE 1 POPULATION

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Objectives: In Type 1 diabetes (T1D) high values of glycated-hemoglobin (HbA1c) have been shown to be associated with a higher risk of complications leading to high costs to the National

Health System (NHS). The aim of this analysis is to evaluate the economic impact of poor glycaemic control, and the potential savings associated with better glycemic control in the Italian T1D population.

Methods: A probabilistic model using published risk-curves was developed to project incidence and progression of diabetes-related complications associated with different HbA1c levels over 1-year and 5-year time-horizons in T1D. Associated costs of diabetic ketoacidosis, severe hypoglycemia, micro-vascular and cardiovascular complications, were used to estimate the economic impact of complications in each HbA1c interval from the Italian NHS perspective.

Results: Estimated costs per patient of diabetes-related complications in the first year of occurrence, stratified by HbA1c interval, ranged from 4,463€ for HbA1c ≥ 10% to 2,006€ for HbA1c between 7%–8%. A 5 year analysis was also conducted. A treatment strategy able to reduce HbA1c level from ≥ 10% to 9% could lead to potential savings of 1,342€ per-patient in the first year of treatment. Considering the total T1D Italian population, improving HbA1c to < 8% in the first year would result in potential savings of about 17 million euros.

Conclusions: The economic impact of diabetes-related complications is significant. Consequently the potential savings for the NHS derived from the implementation of strategies aimed at improving HbA1c in T1D should be considered. The greater the reduction in Hba1c, the greater the associated savings.

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ASSESSEMENT OF THE QUALITY OF GLYCEMIC CONTROL IN INTENSIVE CARE PATIENTS TREATED WITH AN INSULIN INFUSION IN AN ACADEMIC CENTER

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Introduction: Glycemic control is an important aspect of care of ICU patients. The use of a reliable and safe insulin protocol is recommended. In the paper protocol used in our center, the rate of infusion is determined by the actual blood glucose (BG).

Objective: Describe the quality of glycemic control in ICU patients treated with an IV insulin infusion in our academic center.

Method: This retrospective study was realized in patients admitted to ICU and treated with an IV insulin infusion for at least 12 hours between August 1st and November 30, 2011. Medical charts were reviewed. The primary quality indicator of glycemic control was the mean % of BG in the 6,1–8 mmol/L target by patient.

Results: A total of 351 patients were included. 61,5% of them had no known diabetes. Admissions were mainly surgical (57%). Mean APACHE II score was 16,8 ± 7,3. The mean % of BG values in the 6,1–8 mmol/L range was 35% for all subjects and 26,2% for diabetics. If a target of 6,1–10 mmol/L was considered, those values become 63% and 54,6%. At least one episode of hyperglycemia (>10 mmol/L), hypoglycemia (< 4 mmol/L) and severe hypoglycemia (< 2,2 mmol/L) was seen in 68%, 9% and 1% of subjects, respectively. Glycemic variability (SD) was 1,9 mmol/L and the median hyperglycemic index was 0,8 (IQ: 0,2–1,6).

Conclusion: Quality of glycemic control of ICU patients in our center needs to be improved. A new computerized IV insulin protocol will be implemented.

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SPECIFICITY ASSESSMENT OF CURRENTLY AVAILABLE GLUCOSE METERS

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Background and aim: The accuracy of glucose meters can be adversely affected by a range of endogenous/exogenous substances in patient whole blood and as such many current generation meters have been modified to address this. The aim of this study was to assess the accuracy of current generation hospital meters (HBG, StatStrip Connectivity and Xpress Menarini, Accu-Chek Inform II Roche) and self-monitoring blood glucose meter (SMBG, Breeze®2 Bayer).

Methods: Specificity studies were performed according to CLSI EP7. The effects of various concentrations of substances such as non-glucose sugars or reducing agents were assessed in three whole blood specimens with different glucose concentrations (~70, ~240, ~330 mg/dL). The influence of varying haematocrit levels (~25%, ~46%, ~60%) on glucose results was also detected. A range of currently used HBG and SMBG glucose meters was assessed and results were compared to a Roche modular hexokinase reference laboratory method.

Results: The specificity of the meters assessed varied. Ascorbic acid and galactose influenced the performance of Accu-Chek Inform II, while xylose affected StatStrip glucose readings. Fluctuating haematocrit didn't affect the HBG meters tested, even though Breeze®2 SMBG meter presented glucose results varying by up to −47% at high haematocrit levels to −30% at low haematocrit levels.

Conclusion: This analytical study shows that there is a continuing specificity differential between the HBG and SMBG meters tested and that the effect of haematocrit as an interfering factor is still an issue for some SMBG meters.

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THE RELATIONSHIPS BETWEEN SHORT-TERM GLYCEMIC FLUCTUATION AND OXIDATIVE STRESS MARKERS IN PATIENTS WITH DIABETES

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The hyper- and hypoglycemic excursion may cause the oxidative stress, which is one of the pathogenic factors of diabetic complications. This study aimed at investigating surrogate markers in relation to short-term fluctuations in blood glucose detected by continuous glucose monitoring (CGM). Methods:T2DM (n = 30), T1DM (n = 13), and controls (n = 17) were subjected to the CGM. The oxidative stress markers such as total free radicals derived from reactive oxygen species (ROS), urinary output of 8-hydroxy-2'-deoxyguanosine, and 15-isoprostane F2t (isopro), and glycated products such as HbA1c, glycated albumin, and pentosidine were simultaneously measured. The lipid profiles, and high-sensitivity (hs)-CRP,

adiponectin, and L-fatty acid binding protein (FABP) were also measured. Results: The mean values of total ROS, LDL, small dense LDL, oxidative LDL, and RLP were higher in T2DM, while that of adiponectin was lower than those in control. The values of total ROS were correlated with those of average glucose ($r^2 = 0.242$), average glucose plus SD ($r^2 = 0.254$), total percentages of hyper- and hypoglycemia, or hsCRP, and negatively correlated with adiponectin in T2DM. The urinary output of isopro was correlated with the values of average glucose. Discussion and conclusion: Hyperglycemia and fluctuation of blood glucose increased the production of oxidative stress detected by total ROS and urinary output of isopro. These hyperglycemic excursions resulted in increased risk factor, hsCRP in T2DM. Other biomarkers for oxidative stress were not correlated with short-term glycemic excursion in T1DM.

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GLUCOMETABOLIC ABNORMALITIES AND THEIR ASSOCIATION WITH NOVEL BIOMARKERS IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Aims: To explore the potential of a panel of biomarkers to enhance to predict power of our screening tests to detect diabetes in patients with acute coronary syndrome.

Methods: A prospective 3 year study carried out in two large inner city hospitals in United Kingdom.

Results: Patients (n = 118) were included in the analysis. At baseline we noticed a clear positive association between fasting plasma glucose and C-peptide, pro-insulin, HOMA I.R and HOMA β. In contrast HOMA I.S was negatively associated with baseline FPG. The post-load glucose concentrations were positively associated with most variables including C-peptide, pro-insulin, glucagon, leptin, leptin adiponectin ratio, HOMA I.R, TIMP-1 and IL-Ira. HOMA I.S was negatively associated with post-load glucose. The HbA1c was positively associated with C-peptide, pro-insulin, HOMA I.R, HOMA β and IL-Ira.

At baseline mean C-peptide, glucagon, intact pro-insulin and HOMA IR were higher in the diabetic group compared to normal and IGS groups. HOMA IS was lower in the diabetic and IGS groups compared to normal cohort At 3 months mean C-peptide, IL 1 RA, TIMP 2 and intact pro-insulin were higher in the diabetic group compared to NGT and IGS groups.

Conclusion: These findings suggest we can in future potentially look at utilizing some of the markers on insulin production and function as helpful in predicting glycaemic status. One of our future aspirations is to look at comparing this with long-term cardiovascular morbidity and mortality data in those with normal as well as impaired glycaemic status or T2DM.

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IMPACT OF GENDER AND BODY WEIGHT ON POSTPRANDIAL GLUCOSE AND LIPID METABOLISM IN ADULTS WITH TYPE 2 DIABETES

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Background: Massive health problem is caused by the increasing worldwide prevalence of type 2 diabetes both in developed and developing countries. The magnitude of the healthcare problem of type 2 diabetes is the result of the disease itself and also its association with several risk factors for cardiovascular diseases such as obesity and postprandial dyslipidemia.

Objective and Methods: This study took place in two cities from the north-western region of Algeria (Sidi-Bel-Abbès and Mascara). The main goal was to assess the impacts of body weight and gender difference on postprandial lipid and glucose responses in type 2 diabetes patients. Ninety-three adult patients with type 2 diabetes (age 55.65 ± 13.81 years) were studied. Weight, height, waist girth and body mass index (BMI) were measured. Fasting and postprandial glucose and lipid (total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, apo A-I and apo B) profiles were studied.

Results: Our results indicated positive correlation between postprandial glucose and BMI in women ($r^2 = 0.041$). Negative correlation with BMI was noticed for PP TG in both males ($r^2 = 0.011$) and females ($r^2 = 0.021$). A significant difference ($p = 0.019$) was observed for PP HDL-c in women (0.39 ± 0.10 g/L *vs.* men 0.33 ± 0.12 g/L) and also for PP apo A-I (women: 1.33 ± 0.27 g/L *vs.* men: 1.09 ± 0.34 g/L; $p = 0.0003$). According to gender and weight groups (normal weight, overweight and obese), our results indicated that female gender and overweight are associated with elevated PP HDL-c and PP apo A-I levels. However, obesity in women is related to high concentration of PP TG.

Conclusion: Results of the present study suggest that gender difference and weight classes are important factors that contribute to determining the postprandial responses, both for glucose and lipids, in type 2 diabetic patients.

Keywords: Type 2 diabetes; Gender difference; Weight groups; Postprandial dyslipidemia

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NON-GLUCOSE CARBOHYDRATES CAN INTERFERE WITH THE MEASUREMENT OF GLUCOSE ON BLOOD GAS ANALYZERS

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Blood gas analyzers with glucose electrodes are increasingly used at the point of care to monitor a patient's glucose concentration. It is commonly assumed that non-glucose carbohydrates will not affect the measurement of glucose with blood gas analyzer technology. However, upon review of blood gas analyzer reference manuals, it appeared that the potential for cross reaction could exist. This study examined the extent of non-glucose carbohydrate interference on three blood gas analyzers from two manufacturers.

Glucose was measured using left over patient whole blood specimens spiked with increasing concentrations of either maltose, xylose, galactose or glucosamine. Glucose concentration was measured using the following blood gas analyzers: GEM3500 (Instrumentation Laboratory, Boston, MA),

ABL90 and ABL800 (Radiometer, Copenhagen, Denmark). The concentration of interferents tested were: maltose (2, 5 and 10 mmol/L); galactose (2, 5 and 10 mmol/L); xylose (1, 2, and 3 mmol/L); glucosamine (1, 3 and 5 mmol/L). Linear regression analysis was conducted to determine the extent to which interferent concentration and initial glucose concentrations influence the blood gas glucose electrode performance. (model below):

$$Glucose_{BGA} = \beta_0 + \beta_1 \quad Glucose_{initial} + \beta_2 \quad Inft + \beta_3 \quad Inft\ Glucose_{initial}$$

The GEM3500 demonstrated large biases with galactose, xylose and glucosamine. A lessor bias was observed on the ABL800 in the presence of maltose, galactose and glucosamine. The ABL90 demonstrated minimal interference with any of the interferents tested.

In conclusion, different blood gas analyzers demonstrated varying degrees of susceptibility to interference by non-glucose carbohydrates. The clinical significant of this interference is under investigation.

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THE IMPACT OF LOW CONCENTRATIONS OF GALACTOSE ON THE PERFORMANCE OF MODIFIED PQQ-GDH GLUCOSE METERS TO DETECT HYPOGLYCEMIA

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It have been established that concentrations of galactose ($\geq$3.33 mmol/L) can introduce a positive bias in the performance of PQQ- glucose dehydrogenase (GDH) glucose meters. A newborn reference range for galactose has been reported as $<$1.11 mmol/L and metabolic screen positive cutoffs for galactose range from 1.11 to 1.67 mmol/L. The objective of this study was to measure the effect of low concentrations of galactose ($\leq$2 mmol/L) on the ability of modified PQQ-GDH glucose meters to detect hypoglycemia.

Galactose (0, 0.5, 1.0, 1.5 and 2.0 mmol/L) was added to aliquots of left over patient specimens (N = 50). Glucose concentrations were measured using the Nova StatStrip glucose meter (Waltham, MA, USA) and the Roche Inform II glucose meter (modified PQQ-GDH) (Mannheim, Germany). A mathematical model was applied to determine the extent to which galactose concentration and unspiked glucose concentration influence the performance of the respective glucose meters (see model below):

$$Glucose_{meter} = \beta_0 + \beta_1\ Glucose + \beta_2\ Galactose + \beta_3\ Galactose * Glucose$$

Clinically and statistically significant positive biases (up to 0.7 mmol/L) were predicted with low galactose concentrations ($<$2 mmol/L) at low glucose concentrations ($<$3 mmol/L) when using the Roche Inform II glucose meter, (β_3 and $\beta_2 \neq 0$). No biases were apparent with the Nova StatStrip glucose meter, ($\beta_3 = \beta_2 = 0$).

In conclusion, the Roche Inform II glucose meter system appears to be susceptible to interference by low concentrations of galactose which could potentially influence the ability to detect hypoglycemia.

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IMPACT OF THE COMPARATIVE METHOD ON THE OUTCOME OF A GLUCOSE METER EVALUATION

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Consensus documents (CLSI, ISO) outlining method comparison protocols have been reported, debated and refined for decades. The lack of consistency in protocol design has contributed to a diversity of results. In general, studies evaluate precision and bias relative to ''a'' comparative method. This study was conducted to determine the effect of different comparative methods on the outcome of a glucose meter evaluation.

Patient correlation data sets (N = 23) (Nova StatStrip versus routine clinical laboratory plasma glucose method) were analyzed with a Passing Bablok regression to determine the line of best fit for each experiment and its associated slope and intercept values. Experiments that used the Roche plasma glucose - hexokinse method showed slopes remarkably close to 1.0, [95% CI: 0.924 – 1.088] while other comparative methods (plasma glucose methods and blood gas analyzers) showed a wider range of slope values, [95% CI: 0.871–1.215]. Analysis of Y-intercepts demonstrated a mean intercept of 0.71 mg/dL [95% CI: 5.34–9.97 mg/dL] for studies that used the Roche method as the comparator. The average intercept value for the other methods was $-$2.65 mg/dL [95% CI: $-$20.81–15.51 mg/dL].

The inherent variation between plasma glucose comparative methods makes it problematic to unequivocally evaluate the bias of glucose meters using hopsital patient correlation data. Very little fixed or proportional bias was observed when the Nova StatStrip meter results were compared with an ID-GCMS traceable routine Roche plasma hexokinase method. We propose that all published method comparison evaluations describe their traceability to the highest standard.

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INTRAVENOUS INSULIN VARIABILITY PREDICTS GLYCAEMIC VARIABILITY IN INSULIN-TREATED ACUTE RESPIRATORY PATIENTS WITH DIABETES, BUT NOT THOSE WITH NORMAL GLUCOSE TOLERANCE

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Glycaemic variability (GV) may contribute to oxidative stress and long-term vascular risk. Stress hyperglycaemia is commonly seen in acute illness in individuals with diabetes (DM) and normal glucose tolerance (NGT). Intensification of glucose

control during acute illness has been advocated, however the impact of variability of intravenous insulin delivery and diabetes status on GV has not been investigated.

Methods: Continuous glucose monitoring was undertaken in DM and NGT patients admitted with acute exacerbations of chronic obstructive pulmonary disease. Glycaemia was managed with intravenous insulin. Standard deviation (SD) of hourly insulin units delivered (HI) were correlated to established measures of GV (mean, SD, CONGA-1, LI, J index, LBGI, HBGI, GRADE, M-value, MAG), using linear regression, sub-analysed by diabetes status.

Results: 19 patients (4DM) were studied. HI-SD was higher in DM subjects (2.82 units/hr) than NGT (1.58 units/hr), $p = 0.006$. Except for mean glucose, GV indices were not different between DM and NGT. HI-SD significantly correlated with mean glucose, CONGA, J-Index, GRADE and MAGE in DM subjects, but showed no correlation in NGT subjects except with LBGI.

Conclusions: Results from this small study suggest variability in intravenous insulin delivery rates, predict indices of GV in people with diabetes. The DM subjects had higher mean glucoses and required more insulin but similar GV to NGT patients, suggesting that GV in NGT subjects with stress hyperglycaemia is driven by factors other than insulin variability. Further work is needed to investigate these factors, and whether variability of insulin should be considered when interpreting GV in subjects with DM.

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PREDICTION OF MORTALITY BY ADMISSION BLOOD GLUCOSE LEVELS IN CRITICALLY ILL PATIENTS

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Aim: The aim of this study is to observe the outcome of critically ill patients in relation to admission blood glucose levels, and to determine the optimal range of admission blood glucose predicting lower hospital mortality among critically ill patients.

Methods: We conducted a retrospective cohort study of total 1,224 subjects (male: 798, female: 426) admitted to the ICU, from 1 January 2009 to 31 December 2010. Admission blood glucose levels were categorized into 4 groups (group 1: < 100 mg/dl, group 2: 100 ~ 199 mg/dl, group 3: 200 ~ 299 mg/dl, group 4: ≥ 300 mg/dl).

Results: Among 1,224 patients, 319 patients were already known diabetics and 296 patients were dead in ICU. 557 subjects received insulin therapy and 118 received oral hypoglycemic agents. Total mortality rate was 24.2% (296 patients). The causes of death and mortality rates of diabetic patients were not different from non-diabetic subjects. The mortality curve showed J shape, and there showed significant differences in mortality between groups of admission blood glucose level. Especially, group 2 had the lowest mortality rate ($p < 0.05$).

Conclusions: These results could suggest that serum glucose levels on ICU admission were associated with clinical outcomes in patients in the ICU. Blood glucose levels of 100 ~ 199 mg/dl on ICU admission could predict the lower hospital mortality in critically ill patients.

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TABLET-BASED WORKFLOW AND DECISION SUPPORT OF IN-HOSPITAL GLYCAEMIC MANAGEMENT—PERCEPTIONS OF NURSES AND PHYSICIANS

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Background: Hyperglycaemia is very often inadequately treated in hospitalized patients with T2D. Electronic decision support systems can improve the quality of inpatient glycaemic management. The aim of the study was to assess the usability of a tablet-based system for workflow and decision support with integrated software algorithm for a basal-bolus-insulin therapy for hospitalized patients with T2D (GlucoTab-System) in clinical practice.

Method: We investigated the GlucoTab-System in 30 patients with T2D at the general ward. After completion of the study, clinical staff was invited to fill out the anonymous questionnaire.

Results: Twelve nurses and six physicians (16 female, mean age 32 ± 11 years, work experience 0.1–32 years) participated in the questionnaire. 17 users felt safe by using the GlucoTab-System. 98% of suggested total daily dose were accepted by the physicians. The nurses accepted the suggested basal- and bolus-insulin dose to 98% and 95% respectively. 17 users stated that the GlucoTab-System supported achieving blood glucose in the recommended glycaemic target range. All users ($n = 18$) reported that the GlucoTab-System prevents insulin dosage errors and that glycaemic management is efficient. The GlucoTab-System supports the daily work process of in-hospital glycaemic management ($n = 16$) as well as the independent clinical decisions of the nurses ($n = 17$). The work effort by using the GlucoTab-System is rated as follows: increased ($n = 10$), unchanged ($n = 5$), decreased ($n = 3$).

Conclusion: The implementation of the GlucoTab-System is well accepted by the users and it supports the workflow of an effective inpatient glycaemic management.

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GLYCAEMIC PROFILE OF HIV+PATIENTS ON HAART IN KIGALI UNIVERSITY TEACHING HOSPITAL: A REVIEW OF 117 CASES

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HAART has been reported to be associated with new-onset diabetes mellitus. However the data available in Rwanda is scarce. This study aimed to determine the prevalence of diabetes mellitus in HIV-infected patients receiving ART.

In this prospective study, HIV-infected patients on HAART who attained the clinic of Kigali University Teaching Hospital from May to November 2010 were studied. Fasting plasma glucose was performed in each patient.

There were 117 patients with a mean age of 43.5 (range, 15 to 65) years and male were 46.2%. The most common risk factor was an habitual physical inactivity, retrieved in 42 patients, followed by an overweight status (BMI $\geq$ 25 kg/m^2) for 36 patients (30.8%). The waist-to-hip ratio was abnormal in 16.7% of male patients and 70.3% of female patients of this study. 29 patients (24.8%) presented a lipodystrophy syndrome.

Changes of glucose homeostasis have been observed in 48 patients (41%), 18 of them having diabetes mellitus (15.4%).

No factor (either traditional risk factors or HAART regimen characteristics) appeared to have influenced the occurrence of impaired fasting glucose among the patients of this study.

Glucose impairments are fairly high among HIV-infected patients receiving HAART, especially in those presenting a lipodistrophy syndrome. Therefore, those patients should be submitted to a regular Fasting Plasma Glucoses. However, a large-scale study is undoubtedly required to confirm our results.

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COMPARISON OF INSULIN GLULISINE VERSUS HUMAN REGULAR INSULIN IN PATIENTS RECEIVING PREDNISOLONE WITH DIABETES USING CONTINUOUS GLUCOSE MONITORING

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There is a report that prednisolone predominantly causes hyperglycemia in the afternoon and evening, using continuous glucose monitoring. It is uncertain that there is a difference between insulin glulisine and human regular insulin in patients receiving prednisolone with diabetes. The purpose of this study is to compare insulin glulisine with regular insulin in patients receiving prednisolone with diabetes using continuous glucose monitoring.

The subjects were seven hospitalized patients receiving prednisolone with diabetes. The subjects were on either insulin glulisine followed by regular insulin, or vice versa, with no change of insulin dose, and continuous glucose monitoring data obtained continuous two days.

There were no significant difference between insulin glulisine and regular insulin with 24 hours mean glucose (150.6 mg/dl versus 148.7 mg/dl), their SD values were 45.8 versus 47.1. There were also no significant difference between insulin glulisine and regular insulin with 12–24 h mean glucose (175.0 mg/dl versus 170.4 mg/dl), their SD values were 41.4 versus 39.5.

24 hours mean glucose and SD of insulin glulisine were not different from those of regular insulin in patients receiving prednisolone with diabetes.

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GLUCOSE METER WITH BOLUS CALCULATOR: RESULTS AFTER SIX MONTHS OF EXPERIENCE

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TABLE 1

	0	*6M*
BMI (Kg/m^2)	26,6 ± 3,9	26,1 ± 3,9
MG(mg/dL)	183,6 ± 62,8	179,5 ± 48
SD	66,6 ± 29,6	59,6 ± 21,4
HYP(%)	9,49 ± 8,2	9,4 ± 5,7
HbA1C	9,1 ± 1,4	8,2 ± 1,7

Objectives: The present study aim to evaluate the usefulness of the new systems capillary blood glucose meter with bolus calculator and its effect on the metabolic control.

Methods: 9 patients followed over six months after starting therapy with glucose meter with built-in automated bolus calculator.

All patients performed a structured therapeutic educational program in which included concepts related to the prandial insulin bolus calculation, (ratio, insulin sensitivity factor and counting carbohydrates), as well as the management of devices.

We evaluated the metabolic control evolution and the hypoglycemia perception during this period.

Results: 9 DM1 patients (7 women, 2 men), age between 18 and 64 (mean: 33 years old).

They were included in the educational program because of the tendency to hypoglycemia, poor glycemic control and loss of compliance to insulin pump therapy.

We studied the changes in relation with HbA1c, body mass index (BMI) percentage of glycaemia values.

All the values decreased, although there were not significant differences. HbA1c and SD had the largest reduction. The majority of patients had a subjective improvement in the threshold of the perception of hypoglycemia.

Conclusions: The use of this system of self-monitoring along with structural education programs are an useful tool that helps to improve metabolic control and glycemic variability decrease.

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INCIDENCE OF PERIOPERATIVE HYPERGLYCEMIA EVALUATED BY CGM METHOD IN PATIENTS WITH DM/IGT UNDERGOING AMPUTATION OR BYPASS SURGERY

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Aims of study: To compare the perioperative insulin resistance in patients with DM/IGT after amputation and bypass surgery for lower extremity vascular complications.

Methods: We monitored two groups of patients during their surgery for lower extremity vascular complications. Group No. I (5 adult males, median age 54 years, average admission HbA_{1C} 7.4%) had an amputation surgery, group No. II (5 adult males, median age 64 years, average admission HbA_{1c} 7,72%) had a bypass surgery. None of the patients was in septic or critical condition. CGM (Guardian® REAL-Time CGMS, Medtronic, Nortridge, USA) was introduced on the day before surgery and

continued for the period of postoperative metabolic instability - in average for 3.2 days. We compared the incidence of perioperative hyperglycemia exceeding 15 mmol/l in both groups.

Results: We obtained 4836 CGM glycemia values in the first group, 1075 (22.2%) of them exceeding 15,0 mmol/l, and 4100 CGM glycemia values for the second group with 348 (8.5%) of them exceeding 15,0 mmol/l.

Conclusion: The group of patients undergoing bypass operations had a lower incidence of perioperative hyperglycemia despite of higher age, higher HbA_{1c} and substantionally longer time of surgery. Results of our pilot study suggest that a more pronounced insulin resistance is expectable after amputations than after clean bypass surgery. Guidelines for multimodal prevention of postoperative metabolic instability (by medicaments, nutrition, pain control and all possible means) could decrease the incidence of postoperative ongoing infection and prevent the need of higher amputations. Our results should be validated by a larger study.

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EVALUATION OF QUALITY OF LIFE IN DIABETIC AND NON DIABETIC PATIENTS ON HEMODIALYSIS THERAPY

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Background: Chronic Kidney Disease is a worldwide public health problem and being a chronic disease deteriorates quality of life. Diabetes is recognized as co-morbidity in patients of end stage renal disease. This study evaluated quality of life in diabetic and nondiabetic patients on maintenance dialysis therapy.

Study Design: Cross-sectional

Setting and Participants: End stage renal disease patients with or without diabetes on hemodialysis therapy for at least three months or more were enrolled at kidney center, Sheikh Zayed Medical Complex, Lahore Pakistan.

Predictor: End stage renal disease (ESRD)

Outcome: Quality of life

Covariates: Diabetes mellitus

Measures: WHOQOL-BREF questionnaire by World Health Organization

Results: One hundred and thirty seven ($n = 137$) hemodialysis patients were observed. 59(41.8%) were with diabetes (DM) and 78 (55.3%) were without diabetes (DM). 81 (54.4%) were on hemodialysis (HD) for more than 2 years. There was no statistically significant ($p \geq 0.066$) difference in QOL scores of hemodialysis patients with or without diabetes; however a significant ($p \leq 0.025$) difference was observed in responses of 'meaningfulness' and ''ability to concentrate'' by patients of both groups. The scores were divided in two categories of ''≤ 50'' and ''> 50''; a significant ($p \leq 0.047$) difference between two groups in physical domain only.

Limitations: Observational study, patients had limited access to regular dialysis

Conclusion: The current study on diabetic and non-diabetic hemodialysis patients showed no statistical difference in their quality of life except in ''meaningfulness of life'' and ''ability to concentrate''.

Index Words: End stage renal disease, diabetes mellitus, quality of life, hemodialysis.

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THE EFFECTIVENESS, TOLERABILITY, AND SAFETY OF LOW CARBOHYDRATE DIETS IN WOMEN WITH GESTATIONAL DIABETES

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Background and aims: According to the revised criteria released in 2010, it is estimated that the diagnosis rate of gestational diabetes mellitus (GDM) will increase four-fold in Japan by 2014. Nutrition therapy is an integral part of GDM management. The purpose of this study was to evaluate the effectiveness, tolerability, and safety of low carbohydrate diets in women with GDM.

Methods: The study group comprised 189 Japanese women who had been newly diagnosed with GDM via a 75-g oral glucose tolerance test. The women chose either a low carbohydrate diet with 40–50% of energy supply coming from carbohydrates ($n = 110$) or balanced diet ($n = 79$). In all subjects we measured their HbA1c, and fasting levels of glucose, free fatty acids, 3-hydroxybutyrate, and acetoacetate.

Results: The median of the percentage of kilocalories from carbohydrate was significantly lower in the low carbohydrate diet group compared to that of the balanced diet group ($p < 0.01$). Pre-pregnancy BMI and glucose concentrations before implementation of the diet regimen did not differ between the groups. Blood ketone and HbA1c levels after dietary intervention did not differ between the groups. No differences were found in the obstetric and perinatal outcomes between the two groups.

Conclusion: The low-carbohydrate diet was well tolerated and achieved optimal blood glucose concentrations in women with GDM. Low carbohydrate diets are effective and safe. A diet with a carbohydrate limitation may be recommended as part of the nutritional management of pregnant women with GDM.

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COMBINED USE OF HBA1C AND FRUCTOSAMINE IN CHILDHOOD DIABETES

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Aims: HbA1c is usually used as an indicator of glucose control. It usually reflects the average glucose levels of 2–3 months and correlates with the development of long-term diabetic complications. But it can be variable in the situation of hemoglobinopathy or the conditions of altered RBC lifespan. Serum fructosamine levels reflect the mean glucose levels of 2–3 weeks. This study was designed to see the clinical usefulness of the combined measurement of serum fructosamine and HbA1c in the management of childhood diabetes and to see the correlation between the HbA1c and fructosamine levels.

Methods: Clinical data were evaluated for the seventy-four Korean patients who are on the management of diabetes in the department of Pediatrics, Dankook University Hospital. Fructosamine and HbA1c levels were also reviewed on the basis of clinical information and analyzed using IBM SPSS Statistics version 20.

Results: HbA1c levels showed strong correlation with the fructosamine levels ($r = 0.865$, $p < 0.001$). Because fructosamine level indicated the average glucose concentration over the previous 2–3 weeks better than HbA1c, it was useful for the prompt evaluation of the recent therapeutic efficacy after the change of the therapeutic modality as well as for the decision of the initial therapeutic modality. It was also useful for the estimation of the disease onset such as fulminant diabetes.

Conclusion: The measurement of both fructosamine and HbA1c levels was useful in the management of childhood diabetes especially, if there is some discrepancy between the clinical information and HbA1 levels.

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EFFECTS OF SELF-MONITORING OF BLOOD GLUCOSE ON GLUCOSE CONTROL IN NON INSULIN-TREATED TYPE 2 DIABETES. META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: The use of self-monitoring of blood glucose (SMBG) in non-insulin-treated patients with type 2 diabetes is debated. Available meta-analyses of randomized clinical trials (RCTs) document a small reduction of HbA1c among patients using SMBG.

Methods: A meta-analysis was performed including all RCTs in non-insulin-treated patients, featuring an intervention of at least six months, and comparing patients using SMBG and patients not using SMBG, or patients using structured SMBG and patients using non-structured SMBG, and with HbA1c as the primary endpoint.

Results: In the $N = 8$ RCTs comparing SMBG with no SMBG (1,277 and 1,072 patients, respectively), SMBG reduced HbA1c by -0.2% [95% CI -0.3 to -0.1%], $p < 0.001$. The reduction in HbA1c was greater in RCTs in which SMBG data were used for adjusting diabetes treatment ($N = 3$ RCTs, HbA1c -0.3% [-0.4 to -0.1%], $p = 0.005$ for RCTs using SMBG data for adjusting diabetes treatment, versus $N = 6$ RCTs, HbA1c -0.1% [-0.2 to 0.0%], $p = 0.01$, for RCTs not using SMBG data for adjusting diabetes therapy). In the two RCTs comparing structured and non-structured SMBG (692 and 677 patients, respectively), in which structured SMBG was also used for adjusting diabetes treatment, HbA1c was reduced by -0.2% [-0.3 to -0.1%], $p < 0.001$. Conclusions. In RCTs conducted in non-insulin-treated patients with type 2 diabetes, the use of SMBG was associated with a significant, although small, reduction in HbA1c. The reduction in HbA1c was greater when SMBG data were used for adjusting diabetes treatment.

P-370

HYPERGLYCEMIA AMONG NON-DIABETICA POST-SURGICAL PATIENTS IN AN INTENSIVE CARE UNIT

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Introduction: A surgical procedure implies an acute inflammatory subsequent state. As a part of this physiological response hyperglycemia has been observed. It is expected that this acute inflammatory post-surgical phase relapses after 72 hours. Thus, hyperglicemia must not exceed this lapse. Inflammation may trigger a metabolic imbalance leading to Insulin resistance.

Objective: To present a series of 26 patients who weren't diabetic and underwent a surgical procedure and afterwards developed high serum glucose levels beyond 72 hours after surgery.

Methods: This is a prospective and longitudinal Clinical Study. Patients admitted to the ICU were included, who underwent a surgical procedure. Clinical laboratory test comprises serum glucose levels detemination, arterial gases measurements and a record of administered insulin units.

Results: 19 patients developed persistent hypreglycemi after 72 hours, which persisted for the next 7 days in 16 of them. In this later group it was noticed that Insulin requirements surpassed 20 UI per day after day 4.

Conclusions: This results suggest that an acute inflammatory state may trigger a permanent Insulin resistance. The set of patience and the nature of the study cannot allow to establish an statiscal significant evidence, therefore a subsequent study is required.

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THIAMINE ADMINISTRATION IN CRITICALLY ILL PATIENTS TO OPTIMIZE CARBOHYDRATE METABOLISM AND REDUCE INSULIN REQUIREMENTS

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Introduction: Thiamin is an essential cofactor in the oxidative decarboxylation, glycolysis and energy production. Studies have shown that the illness is characterized by the depletion of thiamine, and that this is associated with an increase of almost 50% mortality. Currently published studies are inconclusive as to whether there may be certain population subgroups in which it is really beneficial supplement use.

Objective: To demonstrate that supplementation with intramuscular and intravenous thiamine in critically ill patients during the first 3 days of stay, optimizes carbohydrate metabolism and reduces insulin requirements.

Methods: This is a prospective and longitudinal Clinical Study. Patients admitted to the ICU were included. They were randomly selected whether for 300 mg intravenous thiamine or Placebo. Clinical Lab tests were a blood glucose, lactate and insulin determination.

Results: After comnparing the relative risk of huperglycemia in both groups protective factor to 50% in thiamine was found. Thus thiamine administration reduces the risk of patients in critical condition to present episodes of hyperglycemia.

Conclusions: While it has been found that alterations in glucose concentrations were lower in whom it was supplemented Thiamine, the results did not reach statistical significance, it has also observed that the insulin requirements were lower in this group. This analysis is necessary to supplement a study involving a larger number of patients.

P-372

EVALUATION OF A REAL-TIME INTRAVENOUS BLOOD GLUCOSE MONITORING SYSTEM IN VOLUNTEERS DURING EXERCISE AND MEALS

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Background: The FDA 510K reviewed GlucoScout (International Biomedical) was designed to automatically measure the concentration of BG every 5 minutes for 72 hours in hosptialized patients using blood sampled from a peripheral vein/artery or a central vein.

Method: GlucoScout was evaluated in 8 normal and 5 T1DM. Subjects consumed two meals and exercised on a bicycle (8.2 hour protocol). GlucoScout automatically sampled blood from a peripheral vein and measured plasma glucose (PG) every 5 minutes. Blood samples were assayed using a Hemocue Analyzer (HC) as reference.

Results: Mean PG was 90 ± 14 mg/dl using HC and 96 ± 12 mg/dl using GlucoScout (N subjects) and 194 ± 64 mg/dl using HC and 173 ± 49 mg/dl using GlucoScout (T1DM subjects). MARD was 17.4% in < 80 mg/dl range, 7.7% in 80–130 mg/dl range, 8.2% in 131–180 mg/dl range, 13.2% in 181–240 mg/dl range, and 15.0% in > 240 mg/dl range. Linear regression analysis was $r^2 = 0.954$, with the regression line equation: GlucoScout = 0.732, HC + 30.5. CEG analysis revealed 86% points in zone A, 11% zone B, and 2% in zone D. GlucoScout data was transformed using linear regression equation to correct for bias. After correction, MARD was $< 10\%$ and the mean absolute bias < 3 mg/dl in all glucose ranges.

Conclusions: GlucoScout reliably sampled blood for 8.2 hours in the majority of volunteers. GlucoScout correlated closely with HC for all glucose ranges after correcting for a glucose-dependent bias.

P-373

REDUCTION OF BLOOD GLUCOSE VARIABILITY AND FREQUENCY OF HYPOGLYCEMIA USING CGMS AND INSULIN PUMPS IN CHILDREN

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The difficulty of compensation of T1D in children to the high blood glucose variability, possible asymptomatic hypoglycaemia.

Objective: To compare the frequency and severity of hipoglycaemia and glycemic variability in children using the CGMS and CSII.

Methods: 40 children with T1D who use CSII /, 20 of them are CGMS. The average age of 10.2 years. Average duration of T1D 3.7. Control of postprandial hyperglycemia, hypoglycemia, estimation of the severity of hypoglycemia, HbA1C.

Results: Comparative analysis of postprandial hyperglcemia in children of group1 (using CGMS) in children 2 group revealed no significant differences. 1 group 9.2 +/− 2.7 mmol/l, 2 group 8.9 +/−2.5 mmol/l. The frequensy of hypoglycaemia in the group using CGMS was 2.9 +/−0.8 per day, compared with a 2 group 0.9 +/−0.7 per day/ What could say skip asymptomatic hypoglycemia in children not usung CGMS. Severity of hypoglycaemia in both groups was the same, severe hypoglycemia was not. The average amplitude of glycemic excursions in children using the CGMS 7.2 mmol/l? in the second group of 9.4 mmol/l. HbA1C in first group 7.9% +/− 1.3 and in second group 8.1% +/−1.5/

Conclusions: The significant differences in the level of blood glucose and HbA1C in both groups were found. In the group of children using the CGMS detection rate of hypoglycaemia above. One reason for the significanty smaller amount of hypoglycemia in patients not using CGMS may be the presence of asymptomatic hypoglycemia. With the combination of the use of CSII and CGMS in children reduces risk of severe hypoglycemia.

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INTRA-ARTERIAL VERSUS SUBCUTANEOUS CONTINUOUS GLUCOSE MONITORING IN POST-OPERATIVE CARDIAC SURGERY PATIENTS IN THE ICU

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Background: The GluCath continuous glucose monitoring system uses a novel quenched chemical fluorescence sensing mechanism to measure blood glucose in arterial blood (IA-CGM). The aim of this study was to compare the accuracy of the

GluCath IA-CGM and the Freestyle Navigator® subcutaneous continuous glucose monitoring (SC-CGM) system.

Methods: After ICU admission, the IA-CGM was inserted via a secondary 20 gauge radial arterial study catheter and the SC-CGM was placed at the abdominal wall of post-operative cardiac surgery patients with an expected ICU length of stay of >24 hours. Each device was calibrated according to manufacturer instructions. Glucose values of the CGM systems were blinded for the clinical staff. Reference blood glucose samples were collected from the study catheter every 1–2 hours for at least 24 hours and analyzed on a Radiometer ABL Blood Gas Analyzer.

Results: The IA-CGM and SC-CGM sensors were successfully inserted in eight subjects. Accuracy assessment was performed with 183 paired points: 77.0% of the IA-CGM measurements and 82.4% of the SC-CGM measurements met ISO 15197 glucometer criteria across a 4.4–13.8 mmol/L glucose range ($P=0.66$). Overall ± SD mean absolute relative difference was 12.3 ± 3.6% for IA-CGM and 11.1 ± 3.0% for SC-CGM and was statistically not significantly different (difference −1.2%, 95% CI −3.3 to 0.8; $P=0.24$).

Conclusion: Although IA-CGM measures intra-arterially, SC-CGM gave similar accuracy compared to arterial reference blood samples.

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TRACEABILITY OF THE STATSTRIP BEDSIDE GLUCOSE MONITOR TO ID-GCMS AND CONCORDANCE TO THE CLINICAL LABORATORY ID-GCMS ALIGNED HEXOKINASE METHOD

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While publications identify many instruments and enzymatic methods as legitimate comparative methods to evaluate glucose monitoring meters, this study group, however, presents data to support the preferred use of an isotope dilution Gas Chromatograph Mass Spectrometry (ID-GCMS) aligned hexokinase method with perchloric deproteinization on a central laboratory clinical chemistry analyzer (Modular, Roche Diagnostics, Mannheim, Germany).

We have calibrated the definitive reference ID-GCMS method with varying concentrations of glucose in water (primary standards). NIST secondary protein based standards demonstrated the performance of this method; values within NIST assigned target range. We then calibrated the central laboratory chemistry reference hexokinase method with the primary standards. Subsequently, we applied perchloric acid to deproteinize patient whole blood specimens with varying glucose concentrations. An aliquot of the supernatant of each specimen obtained after centrifugation of the precipitated whole blood, was then analyzed on the reference Modular hexokinase method. This same process was also used to verify the NIST standards described above. The intra-assay repeatability was 0.65% for the ID-GCMS aligned hexokinase method. The day-to-day variance of this method was less then 2%. The routine plasma method hexokinase was aligned similarly. The reference ID-GCMS aligned hexokinase and routine plasma method were then used to evaluate the trueness and accuracy of a point-of-care bedside glucose analyzer, StatStrip (Nova Biomedical, Waltham, MA, USA),

The StatStrip glucose monitoring system data demonstrate traceability to ID-GCMS and comparability (concordance) to the ID-GCMS aligned hexokinase methods. The data presented show that StatStrip performance meets and exceeds the new CLSI POCT12-A3 and ISO15197:2013 criteria.

P-376

GLUCOSE CONTROL IN ICU: CGM OR INTERMITTENT BLOOD GLUCOSE MEASUREMENTS

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Introduction: Newly marketed CGM devices could replace intermittent BG measurements when implementing glucose control protocols in the critically ill.

Objective: The objective was to establish the level of accuracy of CGM needed to implement glucose control in ICU.

Methods: Validated virtual population of critically ill subjects created from routine clinical data collected at four European surgical and medical ICUs was used to simulate 48 h ICU stay with three established glucose control protocols: the Yale, the University of Washington and NICE-SUGAR. Each protocol was directed by either CGM or intermittent BG measurements to maintain protocol-specific glucose target range and treat hypoglycaemia at protocol-specific threshold. CGM error was classified into three categories, low (MARD 0–5%), medium (MARD 5–10%) or high (MARD 10–15%). Overall, 560 simulations were run for each CGM error category as well as for BG-directed protocol.

Results: Apart from Washington protocol, CGM with MARD up to 15% resulted in similar mean glucose as with the use of intermittent BG measurements. Glucose variability was also similar for CGM and BG-directed protocols. Frequency and duration of mild and severe hypoglycaemia was reduced or similar using CGM with MARD at or below 10%. Glucose protocol had a greater impact on clinical outcomes than the glucose measurement method.

Conclusion: The efficacy of standard CGM-directed and BG-directed protocols is similar but the risk of hypoglycaemia may be reduced using CGM with MARD at or below 10%. Protocols choice has greater influence on outcomes than the glucose measurement method.

P-377

REAL-TIME CONTINUOUS GLUCOSE MONITORING VS POINT OF CARE TESTS IN ACUTE CORONARY SYNDROME PATIENTS WITH DM TYPE 2

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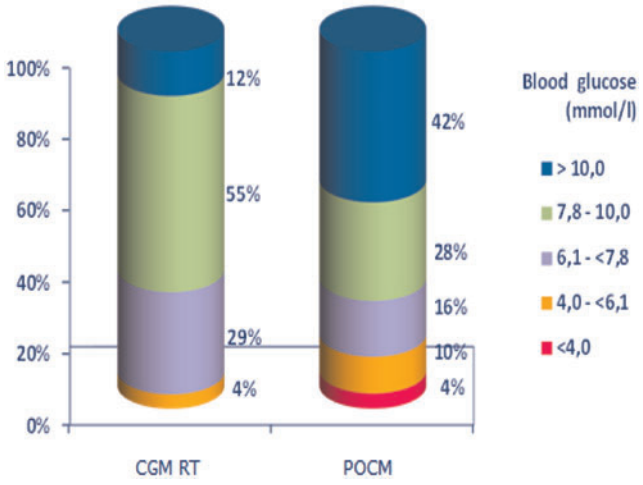
Research on the optimization of the control of carbohydrate metabolism, the definition of target glycemia, the use of new technologies in diabetic patients are the trend of recent years.

In this regard, we examined 90 patients with previously diagnosed DM2 admitted to intensive care unit with acute coronary syndrome (ACS). They were randomized to real time continuous glucose monitoring (CGM RT) - 21 patients, or to point of care measurement (POCM) - 69 patients. All patients were assigned to intravenous infusion of insulin, and the same protocol of blood glucose lowering was used in both groups.

As shown in Figure 1, patients of CGM RT group were most of the time within the glucose target range (7,8–10,0 mmol/l) compared to patients of the POCM group (55% vs 28%, $p < 0{,}001$). No one had hypoglycemia (< 4.0 mmol/l) in CGM RT group, but 4% of POCM had ($p < 0.001$). Duration of blood glucose levels above target range was also longer in the POCM group (42% vs 12%, $p < 0{,}001$).

CGM RT allow a reduction in glycemic targets for ICU patients with ASC and DM2 on the intravenous infusion of insulin to 6,1–10,0 mmol/l without raising the risk of hypoglycemia.



ATTD 2014 Read By Title

R-378 PREVENTIVE EFFECT OF OROXYLIN-A ON EXPERIMENTAL DIABETIC NEPHROPATHY IN TYPE-2 DIABETIC RATS: PLAUSIBLE ROLE OF OXIDATIVE-NITROSATIVE STRESS AND INFLAMMATION

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R-379 SELECTIVE ESTROGEN RECEPTOR MODULATORS DIFFERENTIALLY EFFECT VASCULAR ENDOTHELIAL FUNCTION IN POSTMENOPAUSAL DIABETES

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R-380 CHALLENGING IN MANAGEMENT OF THE DIABETIC PATIENT: LIRAGLUTIDE IN REAL CLINICAL PRACTISE

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R-381 EFFECT OF KRUPPEL-LIKE FACTOR3 (KLF3) ON GLUCOSE METABOLISM

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R-382 THE BLOOD GLUCOSE REGULATION OF MONASCIN AND ANKAFLAVIN IN HYPERGLYCEMIA RAT INDUCED BY HIGH FRUCTOSE AND HIGH FAT DIET

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R-383 EFFECT OF MONASCUS-FERMENTED YELLOW PIGMENT ON BLOOD GLUCOSE REGULATION IN HYPERGLYCEMIA RAT INDUCED BY HIGH FRUCTOSE AND HIGH FAT DIET

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R-384 ENERGY RESTRICTION-MIMETICS: MECHANISTIC PERSPECTIVE IN PANCREATIC CANCER

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R-385 EXPERIENCE AND EFFICACY OF GLIBENCLAMIDE IN NEONATAL DIABETES

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R-386 RETROSPECTIVE ANALYSIS OF THE EFFICIENCY OF INSULIN PUMP THERAPY IN THE TREATMENT OF TYPE 1 DIABETES IN TEENAGERS

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R-387 START OF INSULIN PUMP THERAPY IN THE THIRD TRIMESTER OF PREGNANCY

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R-388 PSYCHOLOGICAL DIFFERENCES BETWEEN TYPE 1 DIABETES PATIENTS ON CSII AND MDI THERAPIES

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R-389 CONNECTION BETWEEN DURATION OF SLEEP AND NEXT DAY PERCENTAGE OF BOLUS INSULIN

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R-390 INSULIN PUMP-RELATED PROBLEMS IN TYPE 1 DIABETES MELLITUS (T1DM) PATIENTS

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R-391 A PROPOSAL FOR ELECTRONIC MEDICAL RECORDS TO MANAGE THE SUBJECT WITH DIABETES TREATED BY CONTINUOUS SUBCUTANEOUS INSULIN INFUSION

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R-392 COMPARATIVE STUDY OF CAPILLARY BLOOD GLUCOSE VALUES OBTAINED WITH SAME SAMPLE AT VARIOUS GLUCOMETERS AND ACCURACY TO LABORATORY RESULTS

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R-393 NOVEL USE OF GLUCOCORTICOIDS FOR LONG-TERM *IN VIVO* PROTECTION OF IMPLANTABLE GLUCOSE SENSORS

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R-394 SURFACE PLASMON RESONANCE GLUCOSE SESNOR WITH MICROFLUIDIC SYSTEM OF INTERSTITIAL FLUID TRANSDERMAL EXTRACTION FOR CONTINUOUS GLUCOSE MONITORING

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R-395 CONSTRUCTION AND CHARACTERIZATION OF THE 3RD GENERATION CGM SENSORS EMPLOYING DIRECT ELECTRON TRANSFER TECHNOLOGY

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R-396 CGM REDUNDANCY FOR ENABLING CLOSED LOOP THERAPY – ONE YEAR LATER

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R-397 TECHNOLOGY ASSISTED AUTONOMOUS RECORDING OF DIABETIC INDICES AS A TOOL TO ENFORCE TREATMENT COMPLIANCE

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R-398 STRESS TESTING BLOOD PRESSURE AND HEART RATE RESPONSES IN NON-DIABETIC PATIENTS HAVING HYPERGLICEMIA AND MEMORY RECALL DEFICITS

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R-399 INSULIN GLARGINE VS. NPH INSULIN IN TYPE 2 DIABETES; A COST EFFECTIVENESS STUDY

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R-400 COMPARING EFFICACY OF ANALOG VS HUMAN INSULIN IN TYPE 2 DIABETES PATIENTS, PREVIOUSLY INSULIN TREATED

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R-401 FLAXSEED OIL AFFECTS INSULIN SENSITIVITY IN STREPTOZOTOCINE INDUCED DIABETIC RATS

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R-402 QUALITY OF LIFE AMONG TYPE II DIABETIC PATIENTS

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R-403 MEASURING PHYSICAL ACTIVITY LEVEL, AND SEDENTARY BEHAVIOURS AMONG STUDENTS AT THE UNIVERSITY OF MEDICINE, ALBANIA

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R-404 THE DIABETES ASSISTANT (DIAS) VERSION 2: A SMARTPHONE BASED ARTIFICIAL PANCREAS PLATFORM DESIGNED FOR LONG-TERM STUDIES AT HOME

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R-405 A NOVEL BIOELECTRONIC SENSOR OF DISTINCT ELECTRICAL ACTIVITIES OF ISLET-CELLS FOR DRUG RESEARCH, TISSUE ENGINEERING AND PRE-TRANSPLANTATION QUALITY CONTROL

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R-406 NEWEST RESULTS OF THE HUNGARIAN ARTIFICIAL PANCREAS PROJECT

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R-407 AUTOMATIC ADAPTATION OF BASAL/BOLUS THERAPY FOR TYPE 1 DIABETIC PATIENT WEARING A GLUCOSE SENSOR: *IN SILICO* TRIAL RESULTS

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R-408 OPTIMIZATION OF INSULIN DOSING IN PATIENTS WITH TYPE I DIABETES MELLITUS

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R-409 MOBILE AND WEB INTERFACE FOR DIABETICS AND BLOOD PLEASURE SERVICES

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R-410 A NOVEL SMART APPROACH FOR SOCIAL BEHAVIOURAL CHANGE INTERVENTION AND MANAGEMENT FOR SAUDI DIABETIC PATIENTS

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R-411 MOBILE DIABETES MANAGEMENT SYSTEM EMBEDDING SOCIAL NETWORKING IN THE GULF COUNTRIES: THE CURRENT STATUS AND POTENTIAL IMPACT

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R-412 A POTENTIAL INTELLIGENT MOBILE DIABETES MANAGEMENT AND EDUCATIONAL SYSTEM FOR SAUDI ARABIA (SAED)

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R-413 A REVIEW OF MATHEMATICAL MODELS FOR DIABETES AND ENERGY HOMEOSTASIS

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R-414 TELEDIABETI: A DIARY/BLOG SOLUTION THAT FACILITATES DOCTORS-PATIENTS COMMUNICATION IN ALBANIA

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R-415 DESIGNING A DASHBOARD FROM THE ANALYSIS OF SELF-MADE DIARIES FOR TYPE 1 DIABETES

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R-416 EFFECTIVE TELEMEDICINE PROJECT IN BANGLADESH: SPECIAL FOCUS ON DIABETES HEALTH CARE DELIVERY IN A TERTIARY CARE IN BANGLADESH

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R-417 LONGITUDINAL CHANGE OF UTERINE ARTERY DOPPLER INDICES IN GESTATIONAL DIABETES

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R-418 CAUSAL INFERENCE WITH UNCERTAINTY IDENTIFIES FEATURES OF PHYSICAL ACTIVITY AS SIGNIFICANT PREDICTORS OF HYPERGLYCEMIA IN TYPE 1 DIABETES

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R-419 ONLINE CONSULTING AND ITS EFFICACY IN WOMEN WITH TYPE 1 DIABETES MELLITUS DURING PLANNING AND ACTUAL PREGNANCY

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R-420 APPLICATION FOR SMARTPHONE: MONITORING THE SHARES OF DIABETES CONTROL AND ALERTS ABOUT GLYCEMIC OSCILLATIONS

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R-421 INSULIN PEN WITH ALARM FUNCTIONS CONNECTED TO A SMARTPHONE APPLICATION AND GLUCOMETER DEVICE

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R-422 BEYOND MEDICAL USABILITY ENGINEERING: EXPLORING THE INFLUENCE OF AFFECTIVE EXPERIENCE ON THE USE OF TYPE 1 DIABETES TECHNOLOGIES

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R-423 COMPARISON OF THE PSYCHOLOGICAL STATE OF WOMEN WITH TYPE 1 DIABETES MELLITUS IN GROUP ON STANDARD ALGORITHM VS. DISTANT ONLINE CONSULTING

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R-424 SOFTWARE FOR TREATMENT ROUTINE MANAGEMENT OF TYPE 1 DIABETES THROUGH MOBILE DEVICES: CONTROL IN THE PALM OF YOUR HAND

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R-425 AN ONLINE INTELLIGENT INSULIN INJECTOR FOR BETTER MANAGEMENT OF DIABETTES MELLITUS

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R-426 CASE REPORT: ADVANCED TECHNOLOGY IN DIABETIC FOOT CARE

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R-427 MONONUCLEAR CELLS THERAPY IN THE TREATMENT OF DIABETIC FOOT

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R-428 ESSENTIAL HYPERTENSION: ADIPOKINES ACTIVITY IN THE DEVELOPMENT OF LEFT VENTRICLE REMODELING

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R-429 BONE MINERAL DENSITY AND FAT/LEAN MASS DISTRIBUTION IN TYPE 1 DIABETIC PATIENTS

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R-430 INVESTIGATION OF CIRCADIAN HEART RATE CHANGES IN DIABETES PATIENTS WITH PERMANENT ATRIAL FIBRILLATION FOR MORTALITY RISK ASSESSEMENT

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R-431 IMPACT OF THE MESODIENCEFALIC MODULATION ON SKIN MICROCIRCULATION AND HBA1C IN PATIENTS WITH DIABETES MELLITUS

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R-432 TECHNOLOGY AND DIABETIC SELF MANAGEMENT; THEIR EFFECTS ON KNOWLEDGE AND PRACTICE OF DIABETIC CHILDREN AND THEIR MOTHERS

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R-433 NEW TECHNOLOGIES FOR PROMOTING HYPOGLYCAEMIA SELF-MANAGEMENT IN TYPE 1 DIABETIC CHILDREN

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R-434 DIABETES TECHNOLOGY IN TREATMENT OF PAEDIATRIC PATIENTS IN KRASNOYARSK REGION, RUSSIA

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R-435 BIOCHEMICAL RISK FACTORS AT SURGICAL TREATMENT OF PATHOLOGIC OBESITY OF PATIENTS WITH METABOLIC SYNDROME

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R-436 THE DEFINITION OF OBESOGENIC FOOD IN OBESE CHILDREN OF DIFFERENT AGES

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R-437 THE QUALITY OF LIFE OF PATIENTS WITH DIABETES TYPE 2 IN BOSNIA AND HERZEGOVINA

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R-438 WHAT IS THE PATTERN OF YOUR HEMODIALYSIS PATIENT'S LIFESTYLE?

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R-439 FEATURES OF THE VITAMIN STATUS IN PATIENTS WITH TYPE 2 DIABETES IN A PERSONALIZED DIET

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R-440 DIABETES MELLITUS TYPE 2 (DMT2) PREVENTION

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R-441 DOSE DEPENDENT GLYCEMIC RESPONSE TO COMMONLY CONSUMED FOODS IN INDIAN DIET

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R-442 ASSESSMENT OF QUALITY OF LIFE AMONG DIABETES MELLITUS TYPE 2 PATIENTS

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R-443 "BLINDED" CONTINUOUS GLUCOSE MONITORING IN INPATIENT'S CLINIC

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R-444 PREDICTORS AND COMPLICATIONS OF DM 2 IN PATIENTS WITH GOUT IN YAKUTIA

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ATTD 2014 Late Breaking Abstracts

L-445

VIEWPOINTS OF RESIDENTS OF SHIRAZ UNIVERSITY OF MEDICAL SCIENCES (S.U.M.S) ABOUT MANAGING AND TREATING DIABETES WITH HERBAL MEDICATION

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Introduction: Many common herbs and natural ingredients are claimed to have blood sugar lowering properties that make them useful and show potential links between herbal therapies and improved blood glucose control. The aim of this study is to assess the viewpoints of residents of S.U.M.S about treating diabetes with herbal medication.

Method: 120 Resident of Shiraz universities of medical sciences (S.U.M.S) were evaluated based on their information about herbal medication influencing diabetes. Data were analyzed by spss19.

Result: 120 residents of (S.U.M.S) participated in this study. Green tea can decrease diabetes type 1 and prevent cells from death in reaction with harmful substance, 73% of residents agree with effect of green tea on diabetics. *Eucalyptus globoulus* has an effective substance that can decrease 80% of blood sugar. diabetics should use that substance intra mascular (IM), 40% residents agree with effect of Eucalyptus globoulus on diabetics. Cinnamomum zelanicum reduce blood sugar. Diabetics should steam the Cinnamomum zelanicum and then use it three times in a day, 56% of residents agree with effect of Cinnamomum zelanicum steam. Aloe vera can reduce blood sugar too, 54% of residents agree with effect of Aloe vera on diabetics.

Conclusion: Use of medical plants is a traditional way that can cure diseases and now we can use it in modern world because in some diseases herbal medication might be the best way to protect patients from some harmful side effects. so programming for more awaerness of physions and students is suggested, so get tested! Get treated! Get better!

L-446

THE NOVEL EFFECT OF HERBAL MEDICATION ON DIABETES

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Aim: Diabetes is a lifelong condition that causes a person's blood sugar level to become too high and Diabetes is a serious medical condition that requires constant care and attention and also is a chronic health problem associated with unsafe levels of sugar in blood. Some herbal medications help to control blood sugar. The aim of this study is to assess the awareness of residents of (S.U.M.S) about treating diabetes with herbal medication.

Method: In this descriptive cross-sectional study, knowledge of 455 residents of Shiraz University of medical sciences was evaluated about treating diabetes with herbal medication. Data were analyzed by spss19. ($P < 0.05$) was considered significant.

Result: 455 of residents of Shiraz University of medical sciences participated in this study. These herbal medicines can reduce blood sugar. *Hibiscus Sabdariffa*, people with diabetes should steam it for 20 minute. 48% of residents know this effect. *Nasturtium officinalis*, people with diabetes should use it crude or use extract of it, 27% of residents were aware of this effect. *Pelargonium,* people with diabetes should steam it for 20–30 minute, 12% of residents know this effect. *Glycyrrhiza glabra,* people with diabetes should steam it for 15–20 minute, 54% of residents were aware of this effect.

Conclusion: Our study confirm the effect of these herbal medicines and their properties and also some of them are remarkably effective. So people with diabetes can control diabetes and also can protect themselves from harmful side effects by these herbal medicines. And they have lower price than other medications.

L-447

METFORMIN IN COMBINATION WITH VILDAGLIPTIN, BUT NOT METFORMIN ALONE, ATTENUATES STREPTOZOTOCIN-INDUCED DIABETIC NEPHROPATHY IN UNINEPHRECTOMIZED RATS

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Currently, a great deal of attention is being paid to investigation of antihyperglycaemic agent's pleiotropic effects. Several recent studies have established that use of metformin and vildagliptin could result in some positive effects on kidney function in diabetes. However, whether metformin in combination with vildagliptin can possess renoprotective properties, hasn't been reported before.

Aim: This pilot study, concerned with uninephrectomized streptozotocin (STZ)-induced diabetic rats, aimed to evaluate the effects of antidiabetic drugs metformin, vildagliptin and their combination on kidney histopathology and routine renal function markers.

Methods: Diabetes in male Wistar rats was induced by intraperitoneal administration of STZ (60 mg/kg) three weeks following unilateral nephrectomy. 8 weeks later, rats were classified into five groups: control (non-diabetic (ND)) and diabetic groups treated for 8 weeks with metformin (300 mg/kg/day in drinking water (M)), vildagliptin (8 mg/kg/day (V)), combination (metformin 150 mg/kg/day + vildagliptin 4 mg/kg/day (M + V)), or placebo (P), n = 5 each.

Results: Glycated haemoglobin (%) didn't differ between diabetic treated groups (M = 11,1 ± 0,28; V = 10,7 ± 0,26; M + V = 10,7 ± 0,26; p ≥ 0,05 each), and was markedly higher compared with ND (4,7 ± 0,15, p < 0,01 each). Although all antidiabetic compounds ameliorated serum creatinine (umol /L) level (M = 93,8 ± 6,7; V = 84,7 ± 2,9; M + V = 79,4 ± 5,8; ND = 76,5 ± 3,1; p ≥ 0,05 each; P = 103,1 ± 3,7, p < 0,01), but only combined treatment was able to considerably improve creatinine clearance (M + V = 3,4 ± 0,18 ml/min/kg; P = 1,7 ± 0,11, p < 0,01; ND = 3, 6 ± 0,3, p = 0,51), and reduce urinary albumin excretion ratio (M + V = 6,7 ± 0,47 mg/24 h; P = 26,9 ± 2,0, p < 0,01) to ND-level (ND = 4,2 ± 1,26, p = 0,07). Moreover, nephroprotection in M + Vgroup was also associated with restoring morphological changes in kidney tissue.

Conclusion: Our study suggested that this combination might ameliorate diabetic nephropathy, in addition to hypoglycemic action.

L-448

EFFECTS OF TOPICAL AND SYSTEMIC L-ARGININE ADMINISTRATION ON WOUND HEALING IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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Purpose: The purpose of this study was to compare the topical versus systemic L-arginine treatment on NO_x and vascular endothelial growth factor (VEGF) concentrations in wound fluid and rate of wound healing in an acute incisional diabetic wound model.

Methods: Fifty-six Sprague-Dawley rats were used of which thirty-two were rendered diabetic. Animals underwent a dorsal skin incision. Dm-sys-arg group (n = 8, diabetic) and Norm-sys-arg group (n = 8, normoglycemic) were gavaged with L-arginine. Dm-sys-control group (n = 8, diabetic) and Norm-sys-control group (n = 8, normoglycemic) were gavaged with water. Dm-top-arg group (n = 8, diabetic) and norm-top-arg group (n = 8, normoglycemic) received topical L-arginine gel. Dm-top-control group (n = 8, diabetic) received gel vehicle. On the days 5, 7 and 11 the amount of NO_x in wound fluid was measured by griess reaction. VEGF level of wound fluid was also measured on day 5 using ELISA. All wound tissue specimens were fixed and stained to be evaluated for rate of healing.

Results: In diabetic systemic L-arginine group the level of NO_x on days 5, 7 and 11 were significantly more than topical L-arginine group ($p < 0.05$).

Conclusions: Systemic L-arginine is more efficient than topical L-arginine in wound healing. This process is mediated at least in part, by increasing VEGF and NO in the wound fluid

L-449

ATORVASTATIN INCREASES CIRCULATING ENDOTHELIAL PROGENITOR CELLS NUMBER AND FUNCTION IN PATIENTS WITH TYPE 2 DIABETES

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Objective: Endothelial progenitor cells (EPCs) play an important role in vascular repair and reduced in type 2 diabetes. This study therefore aimed to whether the atorvastatin modulates EPC number and function levels in type 2 diabetic patients.

Research Design And Methods: This was a controlled, nonrandomized clinical trial comparing 4-week atorvastatin (n = 58) versus no additional treatment (n = 58) in addition to metformin and/or secretagogues and/or insulin in type 2 diabetic patients. The number of EPCs was studied using flow cytometry by co-expression of CD34 and VEGFR2. The EPCs were cultured and characterized by the expression of UEA-I, CD34, VEGFR2, vWF and Dil-Ac-LDL engulfment, as well as the ability to form capillary-like structures. An *in vitro* study on the effect of atorvastatin on the proliferation and viability of the cultured EPCs was also performed.

Results: There was no difference in clinical baseline data between the atorvastatin and control arms. After 4 weeks, patients receiving atorvastatin showed a significant increase in EPCs number and function compared with those control subjects.

L-450

POST-INJECTION LIPOHYPERTROPHY IN T1DM PATIENTS USING CONTINUOUS INSULIN INFUSION (CSII) AND MULTIPLE DAILY INJECTIONS (MDI)

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Aim: To evaluate the frequency of lipohypertophy (LH) in patients with T1DM using different insulin regimens (CSII, MDI), the form of LH in these patients (ultrasound method (USM))[†] in typical places of insulin injection/infusion set location with analysis of factors, involving in LH formation.

Materials and methods: 14 patients (mean age 27 ± 4 years, diabetes duration 13.7 ± 2.1 years, HbA_{1C} 7.9 ± 0,3%) with T1DM on CSII (during period more than 6 months) (group 1) and 15 patients (age 28 ± 6 years, diabetes duration 9.8 ± 4.2 years, HbA_{1c} 6.8 ± 0 9%) on MDI regimen (group 2), all - on insulin analogs, were examined by USM after medical history and CGM performing with following glucose variability measurement.

[†]N. Volkova Saharrniy Diabet. 2011;(2):86–89.

Results: in group 1–10 patients had LH on US investigation, in group 2–12 patients.There was no correlation between duration of T1DM, HbA_{1c} level, subcutaneous tissue thickness and LH occurrence, but it was shown a strong correlation between glucose variability measurements (R = 0.8) and some violations in insulin injection technique/infusion set changing (R = 0.7). In group 2 the amount of lipohypertrophic nodules was significantly higher.

Conclusions: Patients should receive not only initial education but also periodic re-education of the correct injection/infusion technique. According to our findings insulin regimens (CSII, MDI) has no effect on frequency of lipohypertrophic skin lesions, but can influence on amount of lipohypertrophic nodules.

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GLUCOSE-LOWERING EFFECT AND GLYCEMIC VARIABILITY OF ACARBOSE ADDED TO A METFORMIN/VILDAGLIPTIN COMBINATION IN TYPE 2 DIABETIC PATIENTS

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Aims: To evaluate the effect of acarbose on glycemic variability in type 2 diabetic patients.

Material and Methods: We enrolled 53 type 2 diabetic patients, taking a stable dosage of metformin 850 mg three times a day and vildagliptin 50 mg twice a day. Patients were randomized to add placebo or acarbose 100 mg three times a day to their current therapy. To assess glycemic excursions, we used a continuous glucose monitoring system (CGMS), in particular *i*Pro Digital Recorder (Medtronic MiniMed, Northridge, CA) for one week. Glycemic control was estimated as the mean blood glucose (MBG), the area under the glucose curve above 70 mg/dl ($AUC_{>70}$) or 180 mg/dl ($AUC_{>180}$), and the percentage of time above 70 mg/dl ($t_{>70}$) or 180 mg/dl ($t_{>180}$). Intraday glycemic variability was assessed as the standard deviation (SD) and the mean amplitude of glycemic excursions (MAGE). Day-to-day glycemic variability was assessed as the mean of daily difference (MODD), that is the mean of the absolute difference between glucose values taken on 2 consecutive days at the same time.

Results: The SD resulted significantly lower in the group where acarbose was added, in particular in the post-prandial period. $AUC_{>70}$ did not differ between the two groups, while $AUC_{>180}$ was lower in the acarbose group during the daytime. Moreover, the MAGE value was lower with acarbose. The MODD value was not significantly changed in neither groups and no differences were recorded between groups.

Conclusions: Acarbose seems to reduce glycemic excursions, in particular in the post-prandial state.

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GLUCOSE-LOWERING EFFECT AND GLYCEMIC VARIABILITY OF INSULIN GLARGINE, INSULIN DETEMIR, AND INSULIN LISPRO PROTAMINE IN TYPE 1 DIABETIC PATIENTS

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Aims: To compare the effect on glycemic variability of insulin glargine, insulin detemir, and insulin lispro protamine.

Material and Methods: We enrolled 49 type 1 diabetic patients, not well controlled by three times daily insulin lispro. Patients were randomized to add insulin glargine, detemir or lispro protamine, once daily, in the evening. We used a continuous glucose monitoring system (CGMS), in particular *i*Pro Digital Recorder (Medtronic MiniMed, Northridge, CA) for one week. Glycemic control was estimated as the mean blood glucose (MBG), the area under the glucose curve above 70 mg/dl ($AUC_{>70}$) or 180 mg/dl ($AUC_{>180}$), and the percentage of time above 70 mg/dl ($t_{>70}$) or 180 mg/dl ($t_{>180}$). Intraday glycemic variability was assessed as the standard deviation (SD) and the mean amplitude of glycemic excursions (MAGE). Day-to-day glycemic variability was assessed as the mean of daily difference (MODD).

Results: The SD resulted significantly lower with insulin lispro protamine compared to insulin glargine or detemir. $AUC_{>70}$ was higher and $AUC_{>180}$ was lower with insulin lispro protamine compare to other insulin regimens. Moreover, the MAGE value was lower with insulin lispro protamine compared to insulin glargine and detemir. Also the MODD value was significantly lower with insulin lispro protamine than with insulin glargine or detemir. Fewer hypoglycemic events were recorded during the nighttime with insulin lispro protamine compared with glargine and detemir.

Conclusions: Insulin lispro protamine seems to be more effective than glargine or detemir in reducing glycemic variability and improving glycemic control in type 1 diabetic patients.

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MEDTRONIC ENLITE VS. DEXCOM G4 COMPARISON DURING A SPORT 3-DAY CAMP IN CHILDREN WITH TYPE 1 DIABETES: AN IN-FIELD STUDY

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This study assessed the accuracy and reliability of two continuous glucose monitoring systems. We studied the Dexcom(®) (San Diego, CA) G4™ sensor (G4) and the Medtronic (Northridge, CA) Enlite™ sensor (ENL) in 10 children, aged 10.3 ± 1.2 yrs, with type 1 diabetes for more than 1 year (mean: 4.3 ± 2.1 yrs). All patients were well-trained (weekly physical exercise: 12 h/wk), in good shape (BMI 19.3 ± 1.7 kg/m2) and in good metabolic control (mean HbA1C value: 7,46 ± 0,34%) All children underwent two 2-h sessions of moderate-intensity exercise for each day (6 sessions in total), wearing at the same time the two sensors (G4 vs ENL). Furthermore each child performed blood glucose monitoring (SMBG) before and after each exercise bout, every 60-min for three hours after exercise, and during the night. All patients followed the same diet regimen. Being an in-field study, in case of pre-exercise glycemia <100 mg/dl we made corrections according to guidelines, while in case of hyperglycemia (>180 mg/dl) a correction bolus according to insulin sensitivity factor of each child was performed. Overall average mean absolute relative difference (MARD) measured for each exercise session was at 16.5 ± 7.9% for G4 and at 15.9 ± 9.1% for ENL (P = 0.0862). Overall MARD when assessed at night was 13.5 ± 3.1% for G4 and 14.1 ± 6.4% for ENL

(P = 0.526). All hypglycemic episodes detected with SMBG were detected by both G4 and ENL (r = 0.76, p = 0.03). In an in-filed study during exercise both G4 and ENL give the same performances, showing (in the present study) similar accuracy when compared with SMBG.

L-454

FIRST EVALUATION OF THE PRINCIPLE OF A NOVEL GLUCOSE SENSOR BASED ON BORONIC ACID AND BIOCOMPATIBLE CMOS

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Frequent daily self-measurement of glucose (SMBG) improves diabetes management, but current technologies are perceived as painful and cumbersome. Continuous glucose monitoring (CGM) reveals details of glycemic control, but current technologies are expensive and have only short duration. The objective is to provide an easy, pain-free, minimally invasive and yet precise glucose measurement technology for SMBG and/or CGM. We propose to integrate glucose specific boronic acids with novel biocompatible CMOS integrated circuit (IC) arrays. This combination will provide a simple, low-cost glucose sensor without the need for advanced fluorescence detection currently associated with boronic acid glucose sensors.

Polymers on the boronic acids ensure glucose specificity, and the CMOS ICs are made biocompatible by anodising aluminium electrodes to form a corrosion resistant nano-porous alumina. The pores are infiltrated by the boronic acid chemosensor medium. The reversible binding of glucose to boronic acids depends on glucose concentration and alters the electrical impedance of the boronic acid alumina combination, which can be measured by the CMOS circuitry.

Initial measurements were made using ZnO–borogel films to determine the equivalent circuit for the ZnO-borogel film/electrode combination and determine how this depends on fructose concentration. The experiment used fructose concentrations of zero and 10 mmol/L. The resulting impedance data are summarised in Table 1. Significant differences in both resistance and capacitance were noted in the two fructose concentrations.

Future work will include repeating the experiments with borogel mounted directly on CMOS to determine the most effective way to use the parameter changes noted in Table 1.

Potential (V)	Resistance (Ω)	Capacitance (μF)
Absence of fructose		
0.5	1097	1.43
0	1090	2.14
-0.5	1076	47.90
10 mmol/L fructose		
0.5	1141	1.54
0	1134	2.07
-0.5	1142	27.20

L-455

TRANSDERMAL INSULIN DELIVERY WITH HIGH INTENSITY FOCUSED ULTRASOUND

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Transdermal insulin delivery, though offering a less painful and less invasive alternative to subcutaneous insulin injections, needs a viable method of ensuring precise dose delivery due to the highly variable phenomenon of skin barrier disruption, in part due to cavitation. The aim of the current work is to investigate the role and monitoring potential of cavitation in transdermal insulin delivery. Fluorescently stained insulin was placed on the surface of human skin-mimicking materials subjected to 265 kHz, 10% duty cycle focused ultrasound. A confocally aligned, 5 MHz broadband ultrasound transducer was used to detect cavitation. Two different skin models were used: a 3% agar gel, which was insonated with a range of pressures (0.25–1.4 MPa peak rarefactional focal pressure – PRFP), with and without the presence of cavitation nuclei in the form of 0.05% talc solution, and pig skin, insonated at 1.0 and 1.4 MPa PRFP. In both models, fluorescence measurements were used to determine penetration depth and concentration of delivered insulin. Results show that in agar gel, both insulin penetration depth and concentration are only increased significantly by ultrasound exposure when inertial cavitation is present. Interestingly, the presence of cavitation nuclei seems to enhance the peak transport distance but reduce average insulin concentration. In pig skin the amount of fluorescent insulin was higher in the epidermis of those samples which were exposed to ultrasound compared to the control samples, but there was no significant increase in penetration distance. The results highlight the potential of cavitation-based monitoring of transdermal insulin delivery.

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SYNERGISTIC USE OF AEROBIC EXERCISE AND ORAL CONSUMPTION OF SAFFRON EXTRACT IN THE TREATMENT OF HYPERGLYCEMIA IN DIABETIC RATS

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Introduction: The aim of the present study was to investigate the effects of oral consumption of saffron extract along with moderate aerobic exercise on glysemic and lipid profiles of diabetic rats.

Method: In an experimental trial, 42 Wistar rats were studied. Animals received single dose of streptozotocin (60 mg/kg) or citrate buffer solution (as the controls) intraperitoneally. Hyperglycemia was observed in rats after 4 days. Rats were divided into five groups: the control, diabetic, diabetic with aerobic exercise, diabetic with saffron extract and combination of saffron with exercise. Blood samples were collected before and after two weeks of treatment, and plasma levels of glucose, insulin, cholesterol, triglycerides and FFA were measured.

Results: Serum levels of glucose and cholesterol were significantly decreased in diabetic rats treated with saffron and aerobic exercise compared to the diabetic and healthy controls. However, no difference was observed in serum triglycerides, insulin, FFA, and insulin resistance.

Conclusions: The results of the present study suggest that consumption of saffron extract combined with aerobic activity may be used in controlling blood glucose and cholesterol levels.

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BIOMECHANICAL EVALUATION DEVICES FOR THE PREVENTION OF DIABETIC FOOT BY USING TELEHEALTH

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Different technologies for the evaluation of biomechanical foot alteration such as (plantar pressure distribution platforms, in shoe plantar instrumentation system and balance control), in a group of diabetic patients in the early stage of diabetic foot, were assessed. The Loran Platform and the Parollog system, those technologies used for plantar pressure measurements, were studied in order to evaluate its repeatability during barefoot standing in diabetic and non-diabetic subjects, for future diabetic foot clinical evaluation using a telehealth system. 40 subjects were evaluated (10 females, 10 males, 10 non-diabetics and 10 diabetics, age range 30–70 years) and had no musculoskeletal symptoms. Ten measurements were taken using two different techniques for feet and posture positioning, during three sessions, once a week. MANOVA analysis results established that the platform measurements are reproducible for variables body barycenter and foot barycenter through time. with coefficients of variation lower than 1.6% for body barycenter and lower than 2.06% for foot barycenter, with a 99% confidence interval. In addition, the Parollog system that obtains the in shoe plantar pressure distribution in static and dynamic conditions were also assessed and similar results were found; and wireless pressure in-shoe system for continuous dynamic remote monitoring is being developed, also will be evaluated. The integration of those biomechanical measurements devices will be used for the prevention of Diabetic Foot by using a telehealth system in order to improve treatment and monitoring of diabetic patients, for future implementation in clinical environment.

L-458

INITIAL TESTING OF THE DIABELOOP SETTINGS ALGORITHM IN T1D PATIENTS ON PUMP THERAPY FOR BOTH SCHEDULED AND UNSCHEDULED PHYSICAL ACTIVITY

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Aim: Pilot study to test the 'Diabeloop' settings algorithm (DSA) for scheduled and unscheduled physical activity (PA) regarding glycemia reduction at 1h and proposed therapeutic adjustment (modification of basal flow rate (BFR), addition of bolus and preventive carbohydrates (CH) where BFR changes are insufficient to prevent hypoglycemia).

Patients and Methods: 6 type-1 diabetes patients on insulin pump therapy wearing a masked Dexcom G4 transmitter underwent testing 3 h after a standardized lunch. Testing comprised 30 min of physical activity on a bicycle ergometer in one of three scenarios: moderate (50%VO2max), BFR-50% during PA + 2h (n = 2, test A); intense (75%VO2max), BFR-80%, PA + 2h (n = 2, test B); moderate, BFR unchanged (n = 2, test C). Each test was performed twice: once by patients without DSA and once manually using DSA through to the next morning. DSA includes therapeutic parameters (BFR, carbohydrate/insulin ratio, CH/correction factor, BFR) and proposes different adjustments (change of DB, additional prandial bolus, preventive CH).

Results: Percentage time inside the desired range [70–180 mg/dl] was similar for all tests, whether insulin levels were determined by patients or by ARD: afternoon after PA: 57 ± 20% vs. 70 ± 30% p = 0.30, dinner (75 ± 24% vs. 76 ± 30) and nighttime (66 ± 28% vs. 84 ± 16%), as was time at < 70 mg/dl (afternoon: 12 ± 21% vs. 15 ± 31%, dinner: 4 ± 6% vs. 5 ± 11%, nighttime: 17 ± 17% vs. 6 ± 11%). During test C, one patient required 5 consecutive moderate doses of CH, both with and without ARD.

Conclusion: These initial tests show that ARD provides acceptable insulin pump regulation during PA. However, for unscheduled PA, higher levels of preventive CH are necessary.

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PROPOSITION OF A NEW NONLINEAR CONTROL MODEL OF THE GLUCOSE METABOLISM FOR T1DM PATIENTS

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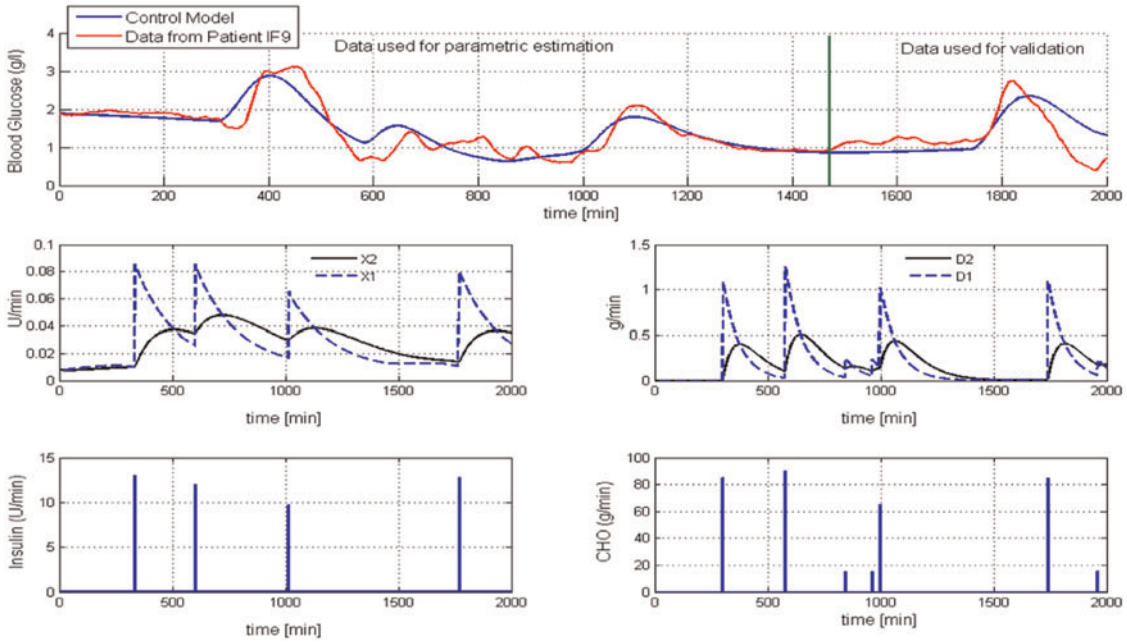
Objective: In this contribution, we present a new nonlinear control model of the glucose metabolism for T1DM patients with parameters being identifiable from easily available patients' treatment data (i.e. data from the insulin pump, CHO of the meals and CGM).

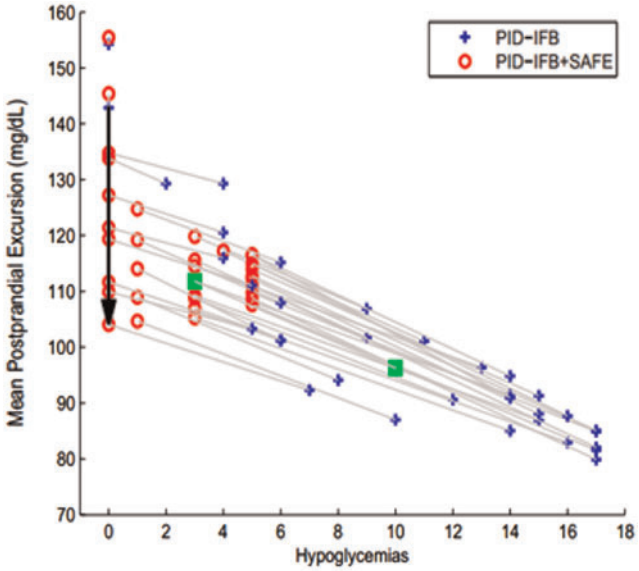
Methods: The proposed nonlinear model is composed of five continuous time state equations and seven parameters. Its design is determined in two steps. Firstly, two successive remote compartments are introduced to account for the insulin and glucose distribution in the organism. Secondly, the insulin action in



glucose disappearance is modeled through an original nonlinear form chosen so that the mathematical equilibrium relation of the control model is consistent with observed equilibrium points from virtual patients.

Results: We proved that, for fixed initial conditions and usual control (positive and bounded), the model admits a unique positive and bounded solution which is locally accessible. Therefore, it can be used as a control model. We also proved its structural and practical identifiability. Data issued from the treatment of six real T1DM patients' were used to estimate the parameters. The obtained mean fit (50.30% ± 13.29%) indicates a good approximation of the patients' glucose metabolism. Furthermore, the model accurately forecasts the glycemia during few hours after the identification of its parameters.

Conclusion: This novel T1DM control model accurately represents the glucose metabolism of real patients from their treatment data. Thus the obtained results validate the relevance of this new model as a control model to be applied in closed-loop algorithms.



Performance results on one virtual patient for the PID-IFB algorithm with (circle) and without (cross) the SAFE layer using several combinations of the control gain and the insulin feedback term. The nominal performance with and without the SAFE layer are highlighted with green squares.

L-460

SAFE TUNING AND IMPROVEMENT OF THE POSTPRANDIAL RESPONSE IN CLOSED-LOOP BLOOD GLUCOSE CONTROLLERS

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This work presents a performance evaluation of a novel safety layer for Type 1 diabetes closed-loop glucose controllers, the so-called SAFE loop [1], and shows that it can be employed to safely re-tune such controllers. Traditional therapies are prone to show poor glucose regulation especially in the postprandial period owing to both physiological and technological limitations.

Regarding this problem, a single control loop for glucose regulation has to be tuned to: 1) minimize the postprandial excursion, and 2) avoid late hypoglycemia. Due to the intrinsic limitations of the problem, a trade-off between postprandial peak and late hypoglycemia risk is implicit. The SAFE outer loop monitors the estimated amount of insulin on board, and according to a unique constraint which can be adjusted with clinical criteria, modifies the control action if the constraint is close to be violated. Here, a very challenging test scenario for the SAFE layer is implemented including mixed meals, diurnal and day-to-day time-varying metabolic changes, inherent drawbacks in sensor and actuator, and other realistic conditions.

The results show a significant reduction of hypoglycemia events when SAFE is added, regardless the closed-loop glucose controller. The SAFE approach becomes not only a safety ''net'', but it also allows re-tuning the inner controller so that a very good postprandial response can be obtained (close to the given by an aggressive controller) while maintaining safety (even better than a relaxed controller).

[1] Revert et al. Safety Auxiliary Feedback Element for the Artificial Pancreas in Type 1 Diabetes. IEEE-TBE, 60(8): 2113:22, 2013.

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A METHOD TO GENERATE A VIRTUAL COHORT REPRESENTING A REAL COHORT OF TYPE 1 DIABETES PATIENTS

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Using virtual patients helps to accelerate diabetes control systems design addressing real situations in a safe way before its practical application. A usual way of creating a virtual patient is by model identification. However, the identification process of type 1 diabetes (T1D) patients is costly as the number of virtual patients obtained with a conventional procedure of data-fitting is equivalent to the number of real patients.

The approach proposed in this work is based on the statistical data of the model parameters of Hovorka et al. (PhD Thesis Chassin, 2005), and a sampling procedure derived from the probability distributions. Quasi-monte carlo method (for univariate parameters) and the covariance matrix (for multivariate parameters) are used to generate a number of virtual patients. Then, constraints both in model parameters (parameter values beyond the allowable range, or forbidden relationships like $F_{01} > EGP_0$) and clinical outcomes (clinical outcomes beyond the target range) are used to discard unfeasible patients. Finally, the obtained virtual patient cohort is indirectly assessed using open-loop tests to calculate the clinical outcomes.

Parameter	Clinical	In silico
Basal (IU)	20.8±8	22.6±8
Bolus (IU)	20.1±10	24.2±6
TDD (IU)	40.9±15	46.7±11
I:CHO (IU/g)	0.13±.04	0.12±.02
Mean BG (mg/dL)	158±20	131±0.9
DIA (h)	4±0	6.1±1.5

In a proof-of-concept example prior to clinical trials, given 100 virtual patients initially generated by the sampling procedure, 17 have selected after the proposed discard method. The used clinical information was the total daily insulin dose, the daily basal dose, the daily bolus dose, the insulin-to-carbohydrates ratio, mean blood glucose, and the duration of insulin action.

Mean and standard deviation of clinical parameters from a real patient cohort and the virtual cohort obtained.

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NON-PARAMETRIC METHODS FOR ASSESSMENT OF GLYCAEMIC VARIATION: ITS PLACE IN LIMITED SETTINGS

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Objective: To account for a probable *between-tool* variation in glycaemic stata of individuals during opportunistic screening exercise.

Methods: A random sample of individuals whose both fasting and 2-hour postprandial glycaemia were to be taken for comparison after a verbal informed consent was obtained. Blood collection was via a finger prick under asceptic technique. Glycaemic readings were done at the same time and using the same person. A wilcoxon's signed rank test was used in deriving the probable differences of the 2 glucometers used in the exercise. Study power relative to paired t-test was determined using pitman asymptotic efficiency formula. Analysis was done using SAS version 9.2 and unless otherwise stated, probability of committing type 1 error was fixed at 5%.

Results: Screening exercise consisted of 5 different people whose both fasting and 2-hour postprandial measurements were taken. The Wilcoxon's signed rank score of 1.5 ($p = 0.75$) was found for the fasting glycaemia category and a score of -1 ($p = 0.75$) was found for the 2-hour postprandial glycaemia category. The corresponding pitman asymptotic efficiency for the Wilcoxon's signed rank test was 0.971.

Conclusion: There was no evidence of a statistically significant difference between readings of the two glucometers both for fasting as well as for 2-hour postprandial glycaemic values. The Pitman asymptotic efficiency value provided an evidence of a good approximation of the Wilcoxon's scores to the corresponding parametric tests.

Recommendations: Current findings have provided a potential solution to the challenge of handling a small sample testing/estimation in resource limited settings.

L-463

DONOR PANCREAS NETSCORE: HISTOMORPHOLOGY-SOFTWARE FOR STANDARDIZED CHARACTERIZATION AND COMPOSITE SCORING OF PANCREATA OR ISLET QUALITY ASSESSMENT FOR ISLET TRANSPLANTATION

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Aim: To develop a customized, user-friendly histomorphology software to i) facilitate optimal organ allocation for pancreas/islet transplantation and ii) record islet quality.

Methods: This software records and stores pertinent data and images regarding i) donor pancreas (organ allocation and donor points (DP) score received) and ii) native/isolated islet quality. It also automatically calculates the estimated: ''pancreas weight (gms), total islet mass in Islet Equivalents (IEQ), islet hormones and cell turnover indices, insulin-secreting viable islet mass in IEQ (composite of the IEQ, insulin index% and cell turnover%)'' and the ''DONOR PANCREAS NETSCORE'' a composite of the organ allocation and DP score and insulin-secreting viable islet mass in IEQ. We used the software to assess post-thaw human islet quality and survival in culture (24-hours, 3-days, 5-days and 7-days) comparing islets processed using the Pre-Edmonton protocol with islets processed using the Edmonton protocol (»50,000 IEQ each).

Results: Shown is a recorded image of the dye-exclusion membrane integrity viability assay carried out (fluorescein diacetate (FDA)/propidium iodide(PI)). Viability was 8.3% at 24-h for islets processed using the Pre-Edmonton protocol and 59.1% for islets processed using the Edmonton protocol ($p < 0.001$). Tissue turnover correlated negatively with culture duration for both protocols ($p < 0.001$) with the Edmonton protocol preserving islets better.

Conclusions: This software has the possibility of i) prescreening donor pancreata and ii) systematically characterizing native/isolated islet viability and functionality thus helping improve the cost-effectiveness of the clinical islet transplant programs especially in resource constrained countries.

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DEVELOPMENT OF A NEW SOFTWARE TO COMPUTE INDIAN BODY FAT PERCENT (IBF%): IN ASIAN INDIANS

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Background: Simultaneous knowledge of the body-mass-index (BMI) and the body fat percent (BF%) of an individual could potentially have tremendous applications in a clinical setting. Dual-energy X-ray absorptiometry (DXA) and computerized tomography (CT) measures of BF% are expensive and not easily available. The aim of the present study was to develop a simple, user-friendly software which will calculate BF% in Asian Indians.

Methods: We had previously developed two formula-based BF% estimators i) IBF%-Anthro (Indian BF% estimated from anthropometric measures), and ii) IBF%-CT (Indian BF% estimated from CT measures). This new IBF% Calculator incorporates the two formula-based IBF% estimators developed using multivariate linear regression (MLR) in 156 non-diabetic subjects and this was further validated in 103 diabetic subjects.

Results: Using the IBF% calculator software, the IBF%-Anthro $33.3 \pm 0.7\%$ and IBF%-CT $33.7 \pm 0.8\%$ did not significantly differ ($p > 0.900$) from the observed $BF\%_{DXA}$ $32.5 \pm 0.8\%$ value (gold standard) using the Tukey's HSD. It also showed good agreement by linear regression ($r > 0.837$, $p < 0.001$) and the Bland and Altman plot.

Conclusion: The newly developed ''IBF% Calculator software'' has the flexibility to estimate BF% in Asian Indians from either anthropometric or CT measures and will be useful both for clinical and epidemiological purposes.

L-465

TO WHATSAPP OR NOT TO WHATSAPP? WHAT COULD BE DONE WITH NEW SOCIAL MEDIA TO MANAGE TYPE 1 DIABETES IN ADOLESCENTS

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Objective: WhatsApp Messenger is a proprietary, cross-platform instant messaging subscription service for smartphones. The aim of our study has been to evaluate if using WhatsApp

Messenger could in any way influence glycemic control in children and adolescents with type 1 diabetes.

Methods: Just after our last summer camp, a group on WhatsApp Messenger has been initiated, involving 18 patients, aged 14.8 ± 3.6 years, with type 1 diabetes since 6.8 ± 4.2 years (insulin requirement 0.84 ± 0.24 U/kg/day; HbA1c 7.9 ± 1.1%). The group was named 'Disciulina alla mattina …' that is something like 'Pills to be more smart given in the morning …'. At the beginning the aim was only to maintain contact among patients and between them and the diabetes team (physicians, psychologist, dietician). After some time we had the feeling that this simple tool could help the young patients to behave themselves. That is why we compared HbA1c and insulin requirement before starting the group and after 4-month follow-up.

Results: Surprisingly, HbA1c improved (7.6 ± 0.9%, −0.3%, p = 0.048), especially in the group that at baseline had HbA1c > 8.0% (n = 10, 8.6 ± 1.7% vs 8.0 ± 0.9%, p = 0.003). Insulin requirement did not change during follow-up.

Conclusions: New social media could be useful and effective in create harmony in a group of teens, some of them with poor motivation and compliance, to food their spur and help them succeeding in gain a better glycemic control. Our are only preliminary results of an unplanned study that need to be confirmed in larger cohort, during a longer follow-up and better in a RCT study.

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ISOLATION OF CONJUGATED LINOLEIC ACID PRODUCING PROBIOTIC LACTOBACILLUS SP. FROM HUMAN ORIGIN AND ITS EFFECT ON OBESITY MARKERS IN MICE

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Obesity and type 2 diabetes mellitus is increasing globally and become stigma on society. Current, pharmacological approaches have not proven very successful due to its various side effects posed on the health of a consumer. Conjugated linoleic acids (CLA) are isomers of linoleic acid found mostly in dairy and meat based products that have proven lipid lowering and anticancerous activity. This study was aimed to isolate high CLA (Trans-10, cis-12) producing probiotic lactobacillus sp. from infant faeces that can be used as a biotherapeutic in obesity management. CLA production was carried out in skimmed milk and formulation was feed daily for 12 weeks to high fat diet induced C57Bl/6J obese mice. More than 250 lactobacilli isolates were screened for specific CLA production, amongst all, *Lactobacillus fermentum* DDHI27 was found to be the probiotic and good CLA producer (∼5.4 ug/ml). Results showed that probiotic feeding reduced plasma leptin (∼1.5 fold) and blood glucose levels (∼1.2 fold), it significantly lowers serum total cholesterol ($p < 0.05$), total triglycerides ($p < 0.05$) and serum low density lipoprotein cholesterol levels ($p < 0.05$) as compared to control animals. Moreover, probiotic formulation significantly downregulated and upregulated the mRNA expression levels of SREBP-1C (2.0 fold), C/EBP-α (3.0 fold), FAS (1.8) and UCP-2 (1.6) genes in adipose tissue compared to control animals. Results revealed that administration of CLA producing *L.fermentum* DDHI 27 has the potential to exert anti-obesity effects in mice. Further studies are required to investigate the human clinical potential of this probiotic culture in affecting the markers of obesity and type-2 diabetes.

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GLYCEMIC PROFILE OF A NEWLY DEVELOPED HIGH FIBRE WHITE RICE COMPARED TO NORMAL WHITE RICE IN ASIAN INDIANS

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Background: Polished white rice has a high glycemic response and is associated with an increased risk of type 2 diabetes in Asian Indians. A new high fibre white rice variety was developed in order to provide an easily acceptable healthy replacement to normal white rice.

Aim: To compare the 24 hr glycemic response of Bapatla Parboiled White Rice (BPWR) [commonly consumed white rice] with the newly developed parboiled High Fibre White Rice (HFWR) in obese Asian Indians.

Methods: In a randomized cross-over design, 12 obese (body mass index ≥ 25 kg/m^2) non- diabetic subjects (females, n = 7) aged 25–45 yrs, were provided iso-caloric (∼2000 kcal/day) BPWR and HFWR diets on 2 non-consecutive days. The menu was identical on both the test diet days except for the type of rice given. A Medtronic iPro2 Continuous Glucose Monitoring(CGM) was used to measure the mean change in glucose concentration over 24 hr from baseline. The incremental area under the curve (IAUC) was calculated using the trapezoid rule.

Results: The subjects' mean age and BMI were 37.5 ± 7.3 yrs and 28.4 ± 4.3 kg/m^2 respectively. The standardized 24 hr incremental area under the curve (IAUC) for HFWR (18.1 ± SE 7.7 mg*min/dl) was significantly lower ($p = 0.028$) compared to BPWR (57.2 ± SE 9.9 mg*min/dl). Overall there was a 56% reduction in the 24 hr glycemic response.

Conclusions: Replacing regular white rice with this unique high fibre white rice may help to reduce the 24 hr glycemic response among obese Asian Indians especially in those in whom rice is the staple diet.

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HPLC ANALYSIS AND BENEFICIAL EFFECT OF FICUS AMPLISSIMA SMITH. FRUIT ON STREPTOZOTOCIN INDUCED HYPOGLYCEMIA AND HYPERGLYCEMIA IN RATS

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RAPAMYCIN/GABA COMBINATION TREATMENT REVERSES DIABETES IN NOD MICE

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L-470

CHOICE – COMPARING PERCEPTION OF INSULIN THERAPIES FOR TYPE 1 DIABETES PATIENTS WITH THE AIM TO IMPROVE QUALITY OF CARE

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ALWAYS CONNECTED SWEETLY

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L-472

THE RELEVANCE OF SOCIAL NETWORKS FOR TYPE 1 DIABETES MELLITUS (T1DM) PATIENTS

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L-01

PHYSICAL ACTIVITY AND CLOSED LOOP ALGORITHMS

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The effects of physical activity/exercise on glucose homeostasis represents a significant challenge to glucose control in closed loop control algorithms currently being developed to treat type 1 diabetes. A traditional input for the algorithms include changes in glucose concentrations obtained from continuous glucose monitoring systems. However, non-glucose inputs especially during exercise are being explored to improve and refine such control algorithms. These inputs include, but are not limited to heart rate, energy expenditure, accelerometer units, cutaneous galvanic inputs as well as changes in insulin sensitivity (SI) induced by exercise. Quantifying the effect size of acute exercise on insulin sensitivity in the postprandial state has remained a limitation in humans. In a recent study applying state of the art methods in humans, we determined that moderate exercise doubles insulin sensitivity. Simulation studies incorporating these changes in SI have provided information on changes to suggested rates of insulin infusion both during and after end of exercise to prevent hypoglycemia both during and after exercise. Low grade exercise mimicking activities of daily living, has also been shown to substantially lower post prandial glucose excursions. Incorporation of changes to heart rate during exercise is being explored in closed loop algorithms while considering confounders that include non-specific changes to heart rate (meals, anxiety, stress etc) and/or autonomic neuropathy that frequently co-exists with type 1 diabetes. Significant intra and inter-individual variabilities on the effects of exercise on all such parameters need to be tackled by smart algorithms for artificial pancreas systems to meet the challenges of daily living.

L-02

TIME LAG OF GLUCOSE FROM INTRAVASCULAR TO INTERSTITIAL COMPARTMENT IN HUMANS

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The accuracy of continuous interstitial fluid glucose sensing is an essential component of current and emerging open and closed loop systems for type 1 diabetes. An important determinant of sensor accuracy is the physiological time lag of glucose transport from the vascular to the interstitial space. We have performed the first direct measurement of this phenomenon in 8 healthy subjects under overnight fasted condition. Microdialysis catheters were inserted into the abdominal subcutaneous space. After intravenous bolus administrations of glucose tracers, timed samples of plasma and interstitial fluid were collected sequentially and analyzed for tracer enrichments. After accounting for catheter dead space and assay noise, the mean time lag of appearance of tracer into the interstitial space after intravenous bolus was 5.3 to 6.2 minutes. We conclude that in the overnight fasted state in healthy adults, the physiological delay of glucose transport from the vascular to the interstitial space is 5–6 minutes. Physiological delay between blood glucose and interstitial fluid glucose should, therefore, not be an obstacle to sensor accuracy in overnight or fasting state closed loop systems of insulin delivery or open loop therapy assessment for type 1 diabetes. Ongoing studies are being conducted in subjects with type 1 diabetes to determine the effects of meals and varying plasma glucose levels on the time lag of glucose transport from the intravascular to the interstitial compartment and will be discussed.