

Incidence and predictors of suicide attempts among primary-care patients with depressive disorders: a 5-year prospective study

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Background. No previous study has prospectively investigated incidence and risk factors for suicide attempts among primary care patients with depression.

Method. In the Vantaa Primary Care Depression Study, a stratified random sample of 1119 patients was screened for depression, and Structured Clinical Interviews for DSM-IV used to diagnose Axis I and II disorders. A total of 137 patients were diagnosed with a DSM-IV depressive disorder. Altogether, 82% of patients completed the 5-year follow-up. Information on timing of suicide attempts, plus major depressive episodes (MDEs) and partial or full remission, or periods of substance abuse were examined with life charts. Incidence of suicide attempts and their stable and time-varying risk factors (phases of depression/substance abuse) were investigated using Cox proportional hazard and Poisson regression models.

Results. During the follow-up there were 22 discrete suicide attempts by 14/134 (10.4%) patients. The incidence rates were 0, 5.8 and 107 during full or partial remission or MDEs, or 22.2 and 142 per 1000 patient-years during no or active substance abuse, respectively. In Cox models, current MDE (hazard ratio 33.5, 95% confidence interval 3.6–309.7) was the only significant independent risk factor. Primary care doctors were rarely aware of the suicide attempts.

Conclusions. Of the primary care patients with depressive disorders, one-tenth attempted suicide in 5 years. However, risk of suicidal acts was almost exclusively confined to MDEs, with or without concurrent active substance abuse. Suicide prevention among primary care patients with depression should focus on active treatment of major depressive disorder and co-morbid substance use, and awareness of suicide risk.

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Introduction

Improved detection and management of depression have a central role in national suicide prevention strategies (Mann *et al.* 2005; National Institute for Health and Clinical Excellence, 2010). However, surprisingly little is known about suicidal behaviour among depressive primary care patients. To prevent suicidal acts among depressive patients, improved knowledge of risk factors for completed and attempted suicide is crucial. Current information is mostly based on psychological autopsy studies of completed suicides, and cohort studies of completed and attempted

suicides in psychiatric care settings. As one in two completed suicides (Isometsä & Lönnqvist, 1998) and suicides accompanied by major depression (Isometsä *et al.* 1994) are preceded by at least one attempt, and up to one-fifth of attempters eventually die by suicide (Suominen *et al.* 2004), the study of suicide attempts as a feasible proxy outcome would be informative with regard to completed suicide.

Medium- and long-term studies among depressive psychiatric care patients have documented risk factors such as severity of symptoms and duration of time spent in depression (Sokero *et al.* 2005; Valtonen *et al.* 2008; Holma *et al.* 2012). A 5-year prospective study found the incidence of suicide attempts during major depressive episodes (MDEs) to be 21-fold that during full remission (Holma *et al.* 2010). Current suicidal ideation is associated with both past suicide attempt (Mann *et al.* 2008) and future completed suicide

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(Brown *et al.* 2000). Other risk factors for suicide attempt include co-morbidity with personality disorders and alcohol abuse, younger age, lacking a partner, and low perceived social support (Duggan *et al.* 1991; Malone *et al.* 1995; Mann *et al.* 1999; Sokero *et al.* 2003; Oquendo *et al.* 2004; Haw *et al.* 2013). In later life, co-morbid physical illness may play an important role (Szanto *et al.* 2002).

Depressive primary care patients usually suffer from mild to moderate depression, which is often co-morbid and recurrent or chronic (Sartorius *et al.* 1993; Thompson *et al.* 2001; Vuorilehto *et al.* 2005; Riihimäki *et al.* 2011). Few studies have investigated the risk factors for suicide attempt in this patient group. In our earlier cross-sectional and retrospective study, every sixth patient had attempted suicide during their lifetime (Vuorilehto *et al.* 2006). Preceding attempts were most strongly associated with personality disorders and a history of psychiatric care; attempts during the index episode associated with current severity of depression. Due to a lack of comprehensive prospective studies in primary care, generalizability of risk factor findings from psychiatric settings to primary care remains uncertain. Furthermore, since sub-threshold depressive symptoms are common among primary care patients, elucidation of whether or not risk of suicidal behaviour is related to and predicted by severity of symptoms is warranted. A major methodological problem is difficulty in obtaining information on severity of depression at the time of suicidal acts. Similarly, a diagnosis of a co-morbid substance use disorder is in itself not informative with regard to actual concurrent substance use at the time of a suicide attempt. Use of life-chart methodology allows examining temporal relationships and the relative importance of state *versus* trait factors. However, no such primary care studies have been published.

In this prospective 5-year study of primary care patients with depressive disorders, we used semi-structured interviews to diagnose all Axis I and II disorders, investigated the role of some psychosocial and socio-economic risk factors, and used life-chart methodology to examine temporal covariation of depression, substance use and suicide attempts. We also investigated the relationship between suicidal ideation and severity of depression, and described treatment received before and after the suicide attempts. We hypothesized that incidence of suicide attempts would be high during MDEs and active substance abuse, and highest when both are present. The incidence was also expected to be high among those with previous suicide attempts, other psychiatric co-morbidity, or adverse psychosocial or socio-economic circumstances.

Method

The Vantaa Primary Care Depression Study (PC-VDS) is a naturalistic and prospective cohort study on depressive disorders. The pertinent ethics committee approved both the baseline study protocol and the 5-year follow-up. The PC-VDS is a collaborative research project between the National Institute of Health and Welfare, the University of Helsinki and the City of Vantaa, Finland. Screening for depression was based on stratified sampling within two representative catchment areas with a total population of 63400 inhabitants, served by 30 general practitioners with a population-based responsibility. The baseline methodology (Vuorilehto *et al.* 2005) and details on the 5-year follow-up (Riihimäki *et al.* 2011) have been reported elsewhere.

Screening and baseline evaluation

Altogether, 1119 patients aged 20–69 years were screened with the Primary Care Evaluation of Mental Disorders tool (Spitzer *et al.* 1994), and 373 had a positive screen. The presence of at least one core symptom of major depressive disorder (MDD) according to the Structured Clinical Interview for DSM-IV (SCID) Axis I Disorders (SCID-I/P; First *et al.* 2001) was then confirmed by telephone. All of the 175 potentially eligible patients were interviewed face to face using the SCID-I/P with psychotic screen. Inclusion criteria were current (1) MDD; (2) dysthymia; (3) subsyndromal MDD with two to four depression symptoms (minimum one core symptom) and lifetime MDD; and (4) minor depression (MinD) otherwise similar to subsyndromal MDD, but without MDD history. Distress or functional impairment was required for all. Dysthymia was regarded as subsyndromal MDD or MinD according to a positive or negative history of MDD. Patients who refused to participate (15%) did not differ significantly in age or gender from those who consented. The diagnostic reliability for current MDD and current subsyndromal diagnoses was excellent ($\kappa=1.0$) (Vuorilehto *et al.* 2005).

Current and lifetime psychiatric disorders were assessed with SCID-I/P and SCID Axis II (SCID-II; First *et al.* 1997). Observer scales included the 17-item Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960), the Scale for Suicide Ideation (SSI; Beck *et al.* 1979) and the Social and Occupational Functioning Assessment Scale for DSM-IV (Goldman *et al.* 1992). Self-report scales included the 21-item Beck Depression Inventory (BDI; Beck *et al.* 1961), the Beck Anxiety Inventory (BAI; Beck *et al.* 1988), the Beck Hopelessness Scale (HS; Beck *et al.* 1974) and the Perceived Social Support Scale – Revised (PSSS-R;

Blumenthal *et al.* 1987). A self-report questionnaire, medical records and an interview were used for chronic medical illnesses. Lifetime course of depression was reconstructed from the interview and medical and psychiatric records (Vuorilehto *et al.* 2005).

Follow-up

After baseline, patients were investigated at 3, 6 and 18 months and 5 years. BDI and other self-report scales were used at 3 months. The current state of depression was investigated by telephone at 6 months and diagnosed face to face at 18 months by SCID-I/P, and all psychiatric disorders were assessed face to face at 5 years with SCID-I/P and SCID-II (First *et al.* 1997). In addition to the interviews, the above-mentioned scales and all medical and psychiatric records were used.

Of the 137 patients initially included in the study, 127 (93%) participated in the 18-month and 112 (82%) in the 5-year follow-up evaluation. The median time for the 5-year interview was 62.9 (mean 63.3) months. Drop-outs did not differ from participants in age, gender or baseline depression severity.

Information on 134/137 patients (98%) was included in the analyses of risk of suicide attempts. Their baseline characteristics are shown in Table 1. Patients remained in the cohort until they were censored due to change of diagnosis (4%) or death (4%) (Riihimäki *et al.* 2011).

Life charts

At the 18-month and 5-year follow-up assessments, depression and possible substance use disorders (dependence or abuse) were diagnosed in face-to-face interviews with the SCID-I/P, and co-morbid Axis II disorders with the SCID-II. In addition, self-report and observer scales were used. Longitudinal course information was obtained by gathering information from medical and psychiatric records and interviewing about changes in psychopathological states by using calendars and personal important life events as probes. The data were integrated into a graphic life chart based on DSM-IV criteria. Course of depression was evaluated by dividing follow-up time into three categories: (1) state of a MDE (five or more of the nine MDE criteria symptoms); (2) state of partial remission (between one and four symptoms); or (3) state of full remission (no symptoms) (Vuorilehto *et al.* 2009; Riihimäki *et al.* 2011). The periods of active, continuous and harmful (usually daily) substance abuse were timed (approximate beginning and end of each period) and placed on the life chart.

Suicide attempts

By definition, a suicide attempt had to involve at least some degree of intent to die. We assessed episodes of depression and substance use disorder, and suicide attempts independently, by questioning the patients first about their life events, mood and possible substance use, and then about suicide attempts, to avoid automatically attributing the disorders to each other, or the acts to the episodes.

We documented the methods and classified medical severity of the attempts as mild (not necessitating treatment), moderate (necessitating emergency room) or severe (necessitating hospitalization). We also recorded preceding communication of intent, and later communication of attempts to attending health care professionals, and seeking and receiving treatment before and after the attempt.

Statistical methods

Patients who attempted suicide were compared with those who did not using the χ^2 test statistic with Yates's correction or Fisher's exact test, the two-sample *t* test and the Mann-Whitney and Kruskal-Wallis tests, when appropriate. However, univariate analyses were used for descriptive purposes only, and therefore corrections for multiple testing were not made. To evaluate consistency of findings between suicide attempts and ideation, we also compared differences in distributions of SSI scores between different levels of depression by using Spearman's correlation and the Kruskal-Wallis test.

Multivariate models constitute the main findings. Univariate and multivariate logistic regression models were used to analyse baseline predictors for a future suicide attempt. To avoid circularity, we omitted the suicidality items of the depression rating scales in the regression models. Cox's proportional hazards regression models were used to investigate association between time-varying and fixed (time-invariant) explanatory variables and hazards of suicide attempts. The association between concurrent level of depression (for small number of events, full and partial remission combined *versus* MDE), level of substance abuse (present or not) and suicide attempts in the life chart was analysed using level of depression as a time-varying covariate. For each individual, the follow-up was divided into time periods where the values of the time-varying variables were constant. Thus, the follow-up consisted of several contiguous time periods, each defined by a specific entry and exit time. Because there were several observations (time periods) for the same individual, robust sandwich variance estimator was used. We included predictor variables on the basis of our primary hypothesis. The predetermined

Table 1. Baseline differences between depressed primary care patients who did and did not attempt suicide in a 5-year prospective follow-up study

Characteristic	Not attempt (n=120)	Attempted suicide (n=14)	All patients (n=134)	p
Sociodemographic features				
Gender, n (%)				
Male	31 (25.8)	2 (14.3)	33 (24.6)	
Female	89 (74.2)	12 (85.7)	101 (75.4)	
Mean age, years (s.d.)	46.0 (13.4)	39.8 (15.1)	45.3 (13.6)	
Married or cohabiting, n (%)	67 (55.8)	5 (35.7)	72 (53.7)	
Professional education, n (%)	78 (65.0)	5 (35.7)	83 (61.9)	
Unemployed	23 (19.2)	3 (21.4)	26 (19.4)	
Employed	49 (40.8)	5 (35.7)	54 (40.3)	
Disability pension	22 (18.3)	2 (14.3)	24 (17.9)	
Welfare benefits	28 (23.3)	9 (64.3)	37 (27.6)	0.001
Co-morbidity, n (%)				
Psychiatric co-morbidity, any	87 (72.5)	12 (85.7)	99 (73.9)	
Lifetime anxiety disorder, any			74 (55.2)	
Current co-morbid Axis I diagnosis	68 (56.7)	12 (85.7)	80 (59.7)	
Anxiety disorder, any			57 (42.5)	0.036
Generalized anxiety disorder	18 (15.0)	2 (14.3)	20 (14.9)	
Panic disorder	6 (5.0)	3 (21.4)	9 (6.7)	0.020
Social phobia	18 (15.0)	4 (28.6)	22 (16.4)	
Somatoform disorder	15 (12.5)	2 (14.3)	17 (12.7)	
Any current Axis II diagnosis	61 (50.8)	9 (64.3)	70 (52.2)	
Cluster A personality disorder	6 (5.0)	1 (7.1)	7 (5.2)	
Cluster B personality disorder	31 (25.8)	7 (50.0)	38 (28.4)	0.059
Cluster C personality disorder	37 (30.8)	6 (42.9)	43 (32.1)	
Substance use disorder (any)	12 (10.0)	8 (57.1)	20 (14.9)	<0.001
Alcohol dependence	9 (7.5)	5 (35.7)	14 (10.4)	0.001
Current Axis III diagnosis				
Chronic medical illness	61 (50.8)	9 (64.3)	70 (52.2)	
Clinical features				
Suicide attempt prior to study entry, n (%)	17 (14.2)	6 (42.9)	23 (17.2)	0.007
Mean no. of previous depressive episodes (s.d.)	2.7 (4.0)	3.1 (3.5)	2.8 (3.9)	
Mean HAMD (s.d.)	16.0 (5.1)	17.9 (7.0)	16.2 (5.3)	
Mean BDI (s.d.)	18.6 (9.4)	24.7 (13.2)	19.3 (10.0)	0.031
Mean BAI (s.d.)	16.0 (11.2)	24.6 (20.3)	16.9 (12.7)	0.015
Mean SSI (s.d.)	2.4 (5.1)	6.4 (8.5)	2.8 (5.6)	0.037
Mean HS (s.d.)	8.4 (5.3)	11.9 (4.1)	8.8 (5.3)	0.018
Mean SOFAS (s.d.)	60.0 (11.1)	54.9 (15.7)	56.7 (11.6)	
Mean PSSS-R (s.d.)	43.6 (12.0)	36.7 (16.6)	42.9 (12.7)	0.054
Follow-up variables				
Mean time spent in MDE, months (s.d.)	15.9 (20.2)	33.9 (22.5)	17.8 (21.1)	0.001
Mean time spent in full remission, months (s.d.)	24.5 (25.0)	12.8 (18.0)	23.3 (24.6)	0.093
Mean time to full remission, months (s.d.)	771.7 (766.5)	1338.3 (741.8)	828.3 (779.9)	0.025

HAMD, Hamilton Depression Rating Scale; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; SSI, Scale for Suicide Ideation; HS, Beck Hopelessness Scale; SOFAS, Social and Occupational Functioning Assessment Scale for DSM-IV; PSSS-R, Perceived Social Support Scale – Revised; MDE, major depressive episode.

independent variables at baseline comprised HAMD (alternatively BDI), history of former MDE and suicide attempts, BAI, SSI, HS, psychiatric co-morbidity (substance use disorder, cluster A, B and C personality

disorders, and anxiety disorders), and marital, education, and employment status, welfare benefits, and PSSS-R. In the final models, we omitted the non-significant variables.

Table 2. Univariate logistic regression analyses of possible predictors of suicide attempt in the Vantaa Primary Care Depression Study over 5 years of follow-up (n = 134/137) adjusted for age, gender and follow-up time

Predictor at entry	OR	(95% CI)	p
Age, years	0.967	(0.928–1.008)	0.111
Gender, male	0.478	(0.101–2.258)	0.352
Follow-up time	1.001	(0.999–1.002)	0.425
HAMD	1.090	(0.978–1.215)	0.118
HAMD ^a	1.064	(0.949–1.193)	0.289
BDI	1.0955	(1.001–1.112)	0.045
BDI ^a	1.058	(1.002–1.116)	0.043
HS	1.163	(1.030–1.312)	0.014
BAI	1.046	(1.006–1.087)	0.024
SSI	1.085	(1.005–1.172)	0.038
PSSS-R	0.945	(0.902–0.990)	0.018
SOFAS	0.975	(0.928–1.025)	0.321
Lifetime suicidal behaviour	2.629	(1.319–5.241)	0.006
Lifetime suicide attempts	4.689	(1.393–15.779)	0.013
Lifetime suicidal ideation	1.438	(0.400–5.164)	0.578
Axis I co-morbidity	5.025	(1.050–23.810)	0.043
Anxiety disorder (any)	2.062	(0.652–6.494)	0.218
Generalized anxiety disorder	1.087	(0.182–4.655)	0.920
Panic disorder	4.525	(0.935–21.740)	0.061
Social phobia	2.545	(0.677–9.615)	0.167
Somatoform disorder	1.536	(0.292–8.065)	0.613
Substance use disorder (any)	22.222	(5.076–95.254)	0.001
Alcohol dependence	13.077	(2.678–63.852)	0.001
Any current Axis II diagnosis	1.681	(0.520–5.435)	0.386
Cluster A personality disorder	1.499	(0.157–14.286)	0.725
Cluster B personality disorder	2.268	(0.678–7.578)	0.184
Cluster C personality disorder	1.949	(0.610–6.25)	0.260
Chronic physical illness	2.660	(0.775–9.091)	0.120
Welfare benefits	5.286	(1.589–17.584)	0.007

OR, Odds ratio; CI, confidence interval; HAMD, Hamilton Depression Rating Scale; BDI, Beck Depression Inventory; HS, Beck Hopelessness Scale; BAI, Beck Anxiety Inventory; SSI, Scale for Suicide Ideation; PSSS-R, Perceived Social Support Scale – Revised; SOFAS, Social and Occupational Functioning Assessment Scale for DSM-IV.

^a Suicidality items omitted.

All models were adjusted for age and gender, the logistic models also for follow-up time. PASW, version 19.0, was used; Cox and Poisson models were constructed with R language (1 R Development Core Team; R: A Language and Environment for Statistical Computing, Vienna, Austria: 2011. <http://www.R-project.org/>).

Results

There were no completed suicides. During the 5-year follow-up 10.4% (14/134) of the depressive primary care patients attempted suicide, with altogether 22 discrete attempts. Two subjects attempted twice, and three attempted three times. Of the patients who had

attempted suicide before study entry (23/137), six attempted suicide during the follow-up. Overall, 31 patients (22.6%) attempted suicide before or after study entry, with altogether 62 attempts over lifetime.

Predictors for attempting suicide during follow-up

The characteristics of patients with and without suicide attempts during the follow-up are presented in Table 1. All the patients who had attempted suicide had a lifetime diagnosis of MDD at study entry (120/134); none of those with MinD (14/134) attempted suicide. In univariate analysis, patients who had attempted suicide differed significantly from those who had not in terms of BDI, HS, SSI, BAI and PSSS-R, history of

Table 3. Multivariate logistic regression model for suicide attempts during 5 years of follow-up (n=134/137)

Variable	OR	(95% CI)	Wald χ^2	p
Gender, male	0.409	(0.067–2.494)	0.939	0.333
Age, years	0.957	(0.910–1.006)	2.943	0.086
Follow-up time	1.001	(0.999–1.002)	1.682	0.195
Co-morbid substance use disorder	20.399	(4.571–91.026)	15.615	<0.001
Suicide attempts prior to study entry	4.386	(1.095–17.558)	4.360	0.037

OR, Odds ratio; CI, confidence interval.

Table 4. Incidence of suicide attempts during MDEs and partial and full remission, and substance abuse in the Vantaa Primary Care Depression Study over 5 years of follow-up (n=134)

Active substance abuse	Depressive phase	Time, years	Events	Incidence, 1000 person-years	(95% CI)
No	Full remission	241.41	0	0	(0–15)
Yes	Full remission	2.24	0	0	(0–164)
No	Partial remission	156.98	0	0	(0–24)
Yes	Partial remission	14.00	1	71	(2–398)
No	MDE	142.43	12	84	(44–147)
Yes	MDE	53.78	9	167	(77–318)

MDE, Major depressive episode; CI, confidence interval.

previous suicide attempts, time spent in MDEs during follow-up, Axis I co-morbidity overall, and specifically co-morbid substance use disorders and alcohol abuse or dependence, and in having received welfare benefits (Table 2). In multivariate logistic regression analyses, after removing the non-significant variables, suicide attempts were robustly predicted by previous suicide attempts and presence of a co-morbid substance use disorder, which increased the risk 20-fold (Table 3).

Incidence and time-varying predictors for suicide attempts

Nearly all of the suicide attempts during follow-up (95%, 21/22) occurred during MDEs, and one (5%, 1/22) during partial remission. More specifically, almost half of the attempts (41%, 9/22) occurred during periods of concurrent MDE and substance abuse, over half (55%, 12/22) during MDEs but without substance abuse, and one (5%, 1/22) during partial remission and substance abuse. No suicide attempts were made during full remission or during partial remission in the absence of concurrent substance abuse.

The 5-year follow-up of the 134 patients comprised altogether 610 patient-years. Of the total time, 196 patient-years were MDEs, 171 partial remission, and 244 full remission. Thus, the overall estimate of incidence of suicide attempts was 36.0 per 1000 patient-years [95% confidence interval (CI) 22.5–54.6], during MDEs 107 (95% CI 66.4–164), during partial remission 5.8 (95% CI 0.1–32.6) and during full remission 0 (95% CI 0–15.1) per 1000 patient-years. The proportion of follow-up time spent with substance abuse was 70 patient-years (11%), and without substance abuse 540 patient-years. About half (45%) of all attempts (10/22) occurred during periods of substance abuse. Thus, the incidence of suicide attempts during substance abuse was 142 (95% CI 68.4–262.7) and without substance abuse 22.2 (95% CI 11.4–38.8) per 1000 patient-years. Incidences during MDEs and substance abuse are presented in more detail in Table 4.

In the Cox proportional hazards models, after removing the non-significant variables, hazard of suicide attempts was significantly higher [hazard ratio (HR) 33.5, 95% CI 3.6–309] during MDEs. Periods of

Table 5. HAMD and SSI at study entry in the Vantaa Primary Care Depression Study (n=134)

SSI percentile ^a	HAMD 0–10 (n=23)	HAMD 11–15 (n=43)	HAMD 16–18 (n=34)	HAMD >18 (19–31) (n=34)
10	0.0	0.0	0.0	0.0
25	0.0	0.0	0.0	0.0
50	0.0	0.0	1.0	1.0
75	0.0	1.0	2.25	8.25
90	2.6	10.2	11.0	19.5

HAMD, Hamilton Depression Rating Scale; SSI, Scale for Suicide Ideation; df, degrees of freedom.

^a Kruskal–Wallis test ($\chi^2=15.702$, $df=2$, $p<0.001$).

substance abuse were not significant as independent predictors (HR 1.98, 95% CI 0.65–6.01).

Methods used and medical severity of suicide attempts

The most common methods for attempted suicide were poisoning by drugs (59%, 13/22) and cutting by knife (27%, 6/22). The degree of medical severity was mostly moderate (45%, 10/22), more seldom mild (32%, 7/22) or severe (23%, 5/22). Of the attempters, two-thirds (68%, 15/22) received immediate medical care; one-fourth (18%, 4/22) were hospitalized in psychiatric care.

Treatment received for depression and communication about suicide attempts to health care personnel

At the time of suicide attempts, most (59%, 13/22) of the patients were not receiving any treatment for their depression. Of those receiving treatment, about half received it in primary care and the other half in psychiatric care. According to the interviews and the primary care records, the patients did not communicate their suicidal thinking or intentions, or seek help before the attempt. After the attempt, altogether 41% (9/22) of attempters received psychiatric care (in- or out-patient), either immediately after the attempt or later for depression. However, only in one of the suicide attempts (5%, 1/22) did the patient talk about the attempt to her attending health care personnel in primary care, and even then long afterwards. Thus, despite suicide attempts being documented in emergency room and psychiatric records when treatment was received, attending personnel in primary care was rarely aware of these attempts.

Suicidal ideation and severity of depression

SSI scores correlated with both HAMD (at baseline: $r_s=0.395$, $p\leq 0.001$; at 18 months: $r_s=0.449$, $p\leq 0.001$; and at 5 years: $r_s=0.470$, $p\leq 0.001$) and BDI scores (at baseline: $r_s=0.477$, $p\leq 0.001$; at 18 months: $r_s=0.566$, $p\leq 0.001$; and at 5 years: $r_s=0.502$, $p\leq 0.001$), being essentially similar at different time points. Like suicide attempts, suicidal ideation was very rare in the absence of clinically significant depression and was associated strongly ($p<0.001$) with depression severity (Table 5). However, the distribution of SSI scores was highly skewed at all levels, and even in the highest severity group a significant minority had no suicidal ideation.

Discussion

In this long-term, prospective study of suicidal behaviour in a regionally representative cohort in primary care, every tenth patient with depressive disorders attempted suicide within 5 years. These suicidal acts took place almost exclusively (in 95%) during MDEs, often with concurrent active substance abuse. The attending primary care doctors were rarely aware of the attempts.

To our knowledge, this is the first prospective long-term study investigating suicide attempts among primary care patients with depressive disorders, and the first using a life chart to identify variations in the incidence of attempts during different levels of depression and substance use. Major study strengths include a medium-sized cohort covering the whole spectrum of depressive disorders, effectively representing primary care patients in the fourth largest Finnish city, derived from a screened stratified sample of 1119 primary care patients (Vuorilehto *et al.* 2005). To our knowledge, no previous study has been able to integrate information on timing of suicide attempts and concurrent state of

mood and substance use. Of our patients, only 2% dropped out from all follow-ups, and 82% underwent a face-to-face interview at 5 years. The use of the Cox proportional hazards model enabled analyses of information on subjects remaining in the study for different lengths of time. We also investigated a broad range of potential risk and protective factors from several domains.

However, some methodological limitations need to be noted. First, while the cohort probably represents the Finnish urban and suburban primary health care populations with depressive disorders well, generalizability to rural or foreign populations remains unknown. Second, although we had access to all patient records, the 3.5 years between the last two interviews probably caused some degree of retrospective recall bias. However, we found the shapes of, for instance, the Kaplan–Meyer curves for attainment of remission or first recurrence, or other similar time-related outcomes to be fairly regular, suggesting no significant bias regarding depression outcomes (Riihimäki *et al.* 2011). Similarly, there is no unexplained year-to-year variation in substance abuse during the follow-up, again consistent with, but not guaranteeing, an absence of significant bias. Nevertheless, timing of periods of substance abuse is unavoidably crude, and the findings must therefore be interpreted with caution. Third, since prevalence is a product of incidence and duration of illness, cross-sectional sampling of patients always enriches chronicity, compared with sampling from the onset of illness. However, prevalence-based sampling accurately reflects the workload of a primary care physician. Fourth, effort after meaning could affect the timing of the attempts and the MDEs or substance abuse episodes, with patients attributing their attempts to these disorders and emphasizing their co-occurrence. We deliberately attempted to avoid this bias by investigating the timings separately, but good intentions are no guarantee of success. However, intensity of suicidal ideation had similar association with severity of depression at all the three cross-sectional time points as that of suicide attempts. Thus, we found a very consistent association between severity of depression and presence of suicidal behaviour. Fifth, when using life charts, we could only investigate average risk for time spent in risk states. The risk for suicide attempts probably covaries markedly with variations in levels of hopelessness, depression, and possibly anxiety, none of which we could measure on a daily basis. Crudely categorizing depression into three alternative states (MDE, partial remission, full remission) grossly underestimates the true variation. Despite this, the order of magnitude of variations in incidence between the three states is

remarkable. Sixth, the proportion of patients who attempted suicide was small, and the number of discrete attempts was low. Thus, a risk for both type II errors and spurious findings exists. However, the findings related to suicide attempts and ideation (measured from all patients) were quite consistent and in accordance with the literature on suicidal behaviour in mood disorders in general. Seventh, because of the naturalistic nature of our study, the treatment received was not controlled. However, our study represents realistic and generalizable risk estimates under usual treatment conditions.

Although the role of severity of depression in the risk for suicidal acts is known, it has not been prospectively investigated in primary care. In our earlier cross-sectional study, suicide attempts were associated with severity of depression (Vuorilehto *et al.* 2006). In this prospective study, we observed marked variations in the incidence of attempts between different levels of depressive symptoms; suicide attempts took place almost exclusively during MDEs, and never during full remission. This was concordant with our psychiatric care studies (Sokero *et al.* 2005; Holma *et al.* 2010). Moreover, we observed a similar cross-sectional pattern with suicidal ideation, which was rare without clinically significant depressive symptoms. In a prospective psychiatric care study, we reported suicidal ideation to usually vanish over time upon alleviation of depressive symptoms, when criteria for MDEs are no longer met (Sokero *et al.* 2006). The incidence of suicide attempts in primary care depressive patients during MDEs was one-third of that in psychiatric care (Holma *et al.* 2010) or psychiatric bipolar patients (Valtonen *et al.* 2008). This finding is consistent with other psychiatric care studies (Oquendo *et al.* 2002), and with generally higher severity of depression, particularly among in-patients, and higher proportion of patients with psychotic features or suicidal ideation in psychiatric settings (Vuorilehto *et al.* 2007). It is also in accord with higher suicide mortality in psychiatric than in primary care depressive patients (Bostwick & Pankratz, 2000). Overall, risk of suicidal acts among depressive patients appears lower in primary care than in psychiatric care, and is almost exclusively confined to MDEs.

No previous study has investigated variations in the incidence of suicide attempts during different levels of substance use among primary-care patients with depressive disorders. We found the incidence to be over sevenfold during periods of substance abuse compared with abuse-free periods. However, the risk was strongly intertwined with the presence of concurrent MDE, and no suicide attempts were made during substance abuse in the absence of significant depressive symptoms. Although baseline substance abuse

strongly predicted future suicide attempt, substance abuse failed to reach significance in the Cox multivariate model accounting covariation with MDEs. This may or may not represent a type II error arising from the limited number of individuals with substance abuse and suicide attempts. As well as alcohol dependence or abuse, other types of substance abuse were present in our study, including abuse of analgesics or benzodiazepines. In contrast, use of illicit drugs, such as opioids or stimulants, was very rare in this largely middle-aged cohort. These findings are consistent with psychological autopsy studies of completed suicides (Cheng, 1995; Foster *et al.* 1997; Henriksson *et al.* 1993; Isometsä *et al.* 1994; Seguin *et al.* 2006). Overall, a reasonable hypothesis to be verified in future prospective studies is that concurrent presence of MDE and substance abuse is related to a markedly higher incidence of suicidal acts than either disorder alone.

We investigated a wide variety of credible risk factors for suicide attempt from multiple domains. As expected, in univariate analyses, several clinical, psychosocial or socio-economic factors were associated with future suicide attempts. However, in multivariate models, only current substance abuse and previous attempts significantly predicted future attempts, and only concurrent MDEs in models accounting for time-varying risk factors persisted as a significant independent risk factor. This is likely to be due to multiple factors, including independent risk factors probably mediating the influence of other risk factors, and, in part, limited statistical power. In our earlier retrospective study of primary care patients, the risk for an attempt was associated with personality disorders (Vuorilehto *et al.* 2006), and in psychiatric care, previous suicide attempt and sociodemographic characteristics, such as younger age, living alone, and low perceived social support, increased the risk for an attempt (Sokero *et al.* 2005; Holma *et al.* 2010). These factors predispose to depression and substance abuse. Depressive mood appears to be a necessary precondition for the occurrence of suicidal ideation (Hintikka *et al.* 2009). While our findings of co-occurrence of depression and substance abuse are consistent with studies suggesting that impaired control of impulses markedly contributes to risk for suicidal acts when depressed (Nock *et al.* 2009), the very high hazard in the Cox multivariate analyses and coherence of the findings between suicidal ideation and attempted suicide are noteworthy. While numerous factors influence risk of suicidal acts to some extent, it is unlikely that their effect exceeds that of the presence of MDEs or substance abuse. Thus, the obvious implication is that both maintenance treatment of depression and treatment of co-morbid substance use disorders in

primary care settings must be improved to advance prevention of suicidal acts.

Our prospective study highlights many important aspects about treatment and communication of suicide attempts in primary health care. We, like others (Goldney *et al.* 2001), found most patients not receiving any treatment for their depression at the time of the suicide attempts, or afterwards. Even if receiving treatment for depression, patients only rarely communicated their suicide attempts to attending health care personnel. Health care personnel should ensure that information about suicide attempts is mediated from the emergency units to the facilities treating patients' depression. The finding here of suicide attempt being unknown to the attending physicians is similar to our earlier findings among psychiatric patients with bipolar disorder (Valtonen *et al.* 2006). It is also consistent with our previous finding that suicidal ideation may often go unnoticed in primary care, even if depression is recognized (Vuorilehto *et al.* 2006). Moreover, psychological autopsy studies have documented lack of communication of suicide intent to be more the rule than the exception in the last appointments preceding suicide, and particularly so in primary health care (Isometsä *et al.* 1995). Thus, it appears that in primary care settings there is an urgent need not only to improve treatment of depression, but also recognition of patients' suicidal thoughts and attempts, and awareness of suicide risk.

Primary health care provides treatment for most patients with depressive disorders. Because depression is present in up to two-thirds of suicides, identifying and treating depression and suicidal behaviour is essential. Practical suicide risk management in primary health care includes continuation and maintenance treatments of depression (Angst *et al.* 2005; Mann *et al.* 2005). Special attention should be paid to identifying and treating co-morbid substance abuse (Szanto *et al.* 2007). Suicidal thoughts, plans and previous attempts should be systematically evaluated in routine clinical practice in primary care (Rihmer, 2001; Friedman *et al.* 2005). In primary care intervention studies, some success in reducing suicide ideation (Gilbody, 2007; Alexopoulos *et al.* 2009; van Spijker *et al.* 2012), suicide attempts (Hübner-Liebermann *et al.* 2010) and completed suicides (Rutz *et al.* 1989; Thompson *et al.* 2000; Szanto *et al.* 2007) has been documented. Overall, as suicidal behaviour seems confined to MDEs, targeting preventive efforts to these is warranted.

Conclusions

A significant minority of depressive patients in primary care will attempt suicide; one in every 10 in

this 5-year prospective study. However, risk of suicidal acts is likely to be almost exclusively confined to MDEs, with or without concurrent active substance abuse. In the absence of these factors, significant suicidal ideation or attempts rarely occur. Primary care physicians or other attending professionals are usually unaware of the suicidal ideation or attempts of their patients. In primary care patients with depression, the focus should be on active acute and maintenance treatment of MDD, treatment of comorbid substance use disorders, and increased awareness of suicidal behaviour.

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