Familial Cancer
DOI 10.1007/s10689-014-9711-x

ORIGINAL ARTICLE

A family history questionnaire improves detection of women at risk for hereditary gynecologic cancer: a pilot study

Margot M. Koeneman · Arnold-Jan Kruse · Simone J. S. Sep · Cynthia S. Gubbels · Brigitte F. M. Slangen · Toon van Gorp · Alberto Lopes · Encarna Gomez-Garcia · Roy F. P. M. Kruitwagen

Abstract Pilot study to evaluate whether the use of a standardized questionnaire to document family history of cancer improves identification of women who warrant referral to cancer genetic services (CGS) for increased risk of hereditary cancer, compared to their identification in usual care. Prospective intervention study with historic control group. Gynecology outpatient clinic, Maastricht University Medical Centre, the Netherlands. The prospective intervention group consisted of new outpatients between June 1 and August 1, 2011. The historic control group consisted of new outpatients between May 1, 2009 and April 30, 2010. A standardized questionnaire based on established referral criteria for hereditary breast/ovarian cancer and Lynch syndrome was completed for the intervention group. The referral rate in routine consultation, based on non-standardized family history recording, was determined retrospectively for the control group. The difference in referral rate between intervention and control group, tested by Chi square test. In the control group, 8 of 3,036 women (0.26 %) were referred to CGS. In the intervention group, 209 (42 %) of 500 screening questionnaires were completed. Nineteen women (9, 1 %) met the referral guidelines, of which 5 were newly referred to CGS (2, 4 %). Referral rates differed significantly ($p < 0.001$) between the two groups. This pilot study shows that the routine use of a screening questionnaire may improve detection and referral rate to CGS of individuals at risk for hereditary cancer. Improving genetic literacy of physicians and use of web-site questionnaires deserve attention in future studies.

Keywords Gynae-oncology · BRCA 1 genes · BRCA 2 genes · Hereditary nonpolyposis colorectal neoplasms · Pedigree · Questionnaires

Abbreviation
CGS Cancer genetic services

Introduction

Approximately 10 % of ovarian cancers occur as a manifestation of breast cancer susceptibility mutations in BRCA1/2, and 2–5 % of endometrial cancers are due to Lynch syndrome mutations. Lynch syndrome is an

M. M. Koeneman (✉) · A.-J. Kruse · B. F. M. Slangen · T. van Gorp · R. F. P. M. Kruitwagen
Department of Obstetrics and Gynecology, Maastricht University Medical Center, Postbus 5800, 6202 AZ Maastricht, The Netherlands
e-mail: m.koeneman@alumni.maastrichtuniversity.nl

M. M. Koeneman · A.-J. Kruse · B. F. M. Slangen · T. van Gorp · E. Gomez-Garcia · R. F. P. M. Kruitwagen
GROW, School for Oncology and Developmental Biology, Maastricht University Medical Center, Postbus 5800, 6202 AZ Maastricht, The Netherlands

S. J. S. Sep
Internal Medicine, Maastricht University Medical Center, Postbus 5800, 6202 AZ Maastricht, The Netherlands

S. J. S. Sep
Epidemiology, Maastricht University Medical Center, Postbus 5800, 6202 AZ Maastricht, The Netherlands

C. S. Gubbels · E. Gomez-Garcia
Clinical Genetics, Maastricht University Medical Center, Postbus 5800, 6202 AZ Maastricht, The Netherlands

A. Lopes
Department of Gynecologic Oncology, Royal Cornwall Hospital Truro, Truro, Cornwall TR1 3LJ, UK

Published online: 15 March 2014

autosomal, dominantly inherited predisposition to cancer resulting from germ-line mutations in the genes that regulate DNA mismatch repair [1, 2]. The syndrome is further characterized by malignancies at other sites including the gastrointestinal tract, the hepatobiliary system, and the urinary tract. BRCA1/2 mutations confer a breast cancer risk of 45–85 % and an ovarian cancer risk of 10–46 % by the age of 70 [3]. Women with Lynch syndrome have a 42–60 % risk of developing endometrial cancer and a 9–12 % risk of developing ovarian cancer by the age of 70 [3].

Identification of women with BRCA1/2 and/or DNA mismatch repair gene mutations is important because, in many cases, validated screening and risk reduction modalities are available. An appropriate implementation of primary screening for BRCA1/2 and/or mismatch repair gene mutations in individuals would involve two steps: (1) assessment of an individual's risk of carrying a mutation based on personal and family history of cancer, and (2) genetic testing of individuals whose risks exceed a certain threshold [4]. National and international guidelines exist for appropriate referral of patients to cancer genetic services (CGS) [3].

A recent publication in this journal has shown that nearly all doctors believe that it is their duty to inform individuals at risk for hereditary cancer about the availability of genetic counselling [5]. Their knowledge on the subject, however, seems to be suboptimal. Indeed, the majority of patients do not receive adequate familial cancer risk assessment. Family history of cancer is often incompletely and inadequately recorded, or is not recorded at all, and referral indications are not recognized [6–11]. Consequently, patients at high risk for hereditary cancer syndromes are often not identified. The use of a standardized screening questionnaire in hospital care may improve detection and referral rates of patients at risk for hereditary cancer syndromes. Although several studies have shown the value of questionnaires for identification of patients at high risk, standardized screening questionnaires are lacking [12].

The objective of this pilot study was to assess whether the use of a standardized screening questionnaire improves referral rates to CGS for individuals at high risk for BRCA1/2 and/or mismatch repair gene mutations in the gynecology outpatient clinic.

Materials and methods

Study overview

This combined retrospective and prospective observational study was performed at the gynecology outpatient clinic of Maastricht University Medical Center in The Netherlands. We examined referral rates to CGS among individuals visiting the gynecology outpatient clinic. As detailed herein, we assessed referral rates recommended by the patients' physician over two periods: (1) retrospectively, before the introduction of a standard screening questionnaire, from May 1, 2009 until April 30, 2010, and (2) prospectively, after the introduction of a standardized screening questionnaire, from June 1 to August 1, 2011. As the recording of personal and family history is a fundamental part of the medical history, the study was exempt from Institutional Review Board approval.

Retrospective analysis

The overall number of outpatients was determined from outpatient clinical records. The referral rate to CGS from the gynecology outpatient clinic from May 1, 2009 until April 30, 2010 was determined from CGS records at the Department of Clinical Genetics.

Prospective analysis

A two-stage screening design was used. For the first stage, health care providers at the clinic were asked to record a family history of cancer for 500 new gynecologic outpatients by the use of a standardized screening questionnaire, which can be found in Fig. 1. In this questionnaire, Lynch syndrome associated malignancies include carcinomas of the colon, endometrium, ovaria, stomach, biliary tract, small intestine, pancreas, ureter, pyelum of the kidney, carcinomas and adenomas of sebaceous glands and brain tumors. The screening questionnaire is based on national guidelines for individual assessment of hereditary cancer risk and the corresponding referral indications to CGS. The applied guidelines can be found in Tables 1, 2 and can be found online at http://www.stoet.nl/uploads/richtlijnenboekje.pdf and http://www.oncoline.nl/richtlijn/doc/index.php?type=pda&richtlijn_id=545. We aimed for the questionnaire to be compact and easy to use. For this reason, the questionnaire was designed to provide a first global assessment of a patient's risk of carrying a BRCA1/2 or DNA mismatch repair mutation. The questionnaire is fully sensitive (all patients that meet referral guidelines are identified), but additional information on family history can be required in certain cases. The questionnaire indicates when additional information is necessary. For the second phase, all individuals who—according to the questionnaire—met the referral criteria or needed additional family history recording, were scheduled for a telephone consultation. Physicians were also instructed to schedule a telephone appointment in cases of uncertainty about a cancer type or the age of onset during the patient's first visit. Patients who were scheduled for a telephone consultation were given a written document stating the types of cancer relevant to our study prior to the actual consultation. These

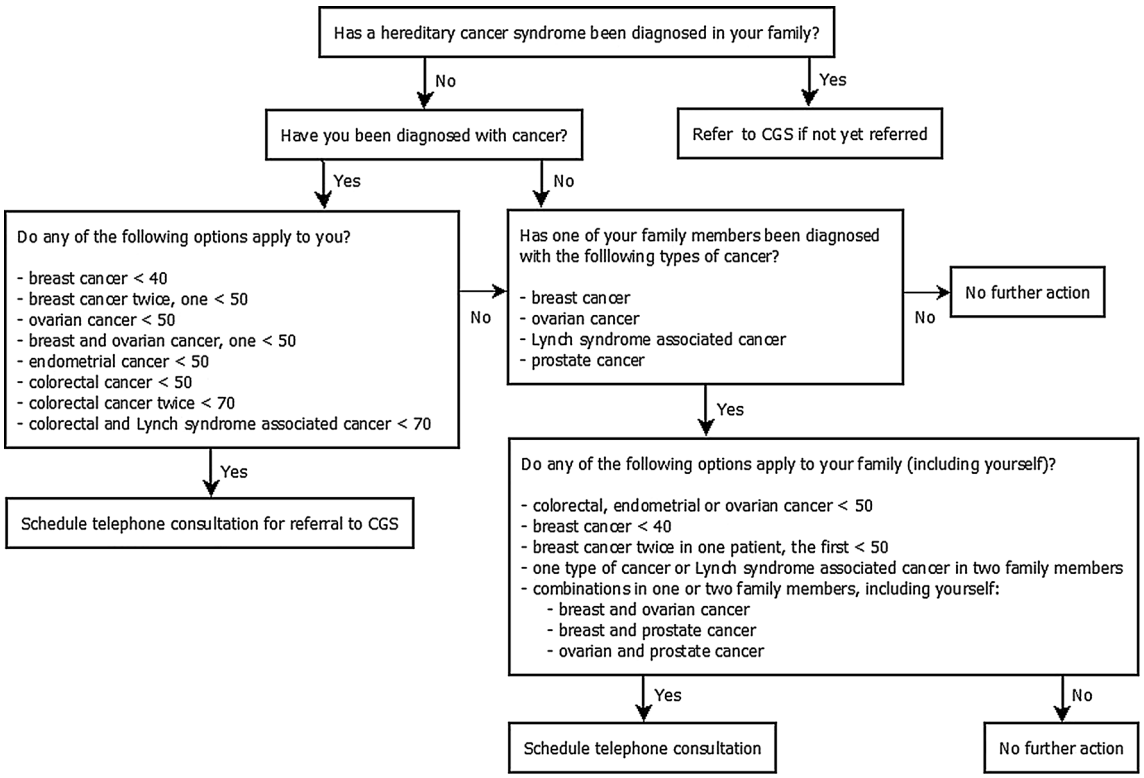

Fig. 1 Screening questionnaire

Table 1 Criteria for referral to CGS for breast and ovarian cancer, based on national referral criteria

Breast cancer	Ovarian cancer
Breast cancer <35 years	Ovarian/tubal cancer <50 years (epithelial tumor)
Bilateral breast cancer, first tumor <50 years	Ovarian/tubal cancer in two first degree or one first degree and one second degree family members
Breast cancer <40 years, hormone receptor triple negative	
Breast cancer <50 years in two or more first degree family members	
Breast cancer in three or more first and second degree family members, at least one tumor <50 years	
Breast cancer and ovarian/tubal cancer in one or two family members, at least one <50 years	
Breast cancer in brother or father and breast or ovarian cancer in female family member	
Breast or ovarian cancer <50 years and prostate cancer <60 years in another family member	

patients were asked to retrieve a complete family history of these types of cancer. The purpose of this telephone consultation was to verify the provided family history and to obtain a more detailed personal and family history of cancer if necessary, based on which the individual's risk of carrying BRCA1/2 and/or mismatch repair gene mutations was estimated. Individuals who fulfilled referral criteria were referred to CGS. Telephone consultations were conducted by one of the authors (MK).

After the completion of the inclusion, the participating physicians received an evaluation questionnaire, in which they were asked for the most important reason for not completing the screening questionnaire and whether or not they were confident about their personal knowledge on CGS referral criteria before the introduction of the screening questionnaire.

The primary outcome measure was the difference in referral rates to CGS before and after the introduction of the screening questionnaire.

Statistical analysis

SPSS, version 16.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Differences in proportions between groups were calculated using standard Chi square tests.

Table 2 Criteria for referral to CGS for Lynch syndrome associated cancer, based on revised Bethesda and MIPA referral criteria

Healthy patient or patient with MSI negative colorectal cancer and
Colorectal cancer or endometrial cancer <50 years in first degree family member
Colorectal cancer or other Lynch syndrome associated cancer in three or more first or second degree family members, all <70 years
Mismatch repair gene mutation in family
Patient with colorectal cancer and
<50 years
Colorectal cancer or other Lynch syndrome associated cancer in a first degree family member, at least one <50 years
A second colorectal cancer in the same patient <70 years
Another Lynch syndrome associated cancer <70 years
Colorectal cancer or another Lynch syndrome associated cancer in two or more first or second degree family members, all <70 years
Patient with a colonic adenoma with high grade dysplasia <40 years
Patient with endometrial cancer <50 years

Results

Between May 1, 2009 and April 30, 2010, 3,036 women visited the outpatient clinic and were retrospectively included in the study. A review of the CGS records revealed that eight (0.26 %) of 3,036 outpatients had been referred to CGS for evaluation of a potential hereditary gynecological cancer syndrome, based on the non-standardized family history of cancer that was taken by their physician. Referral indications included a family history of breast cancer in five women, a personal and family history of breast cancer in one woman, a family history of breast and ovarian cancer in one woman and a personal history of ovarian cancer in one woman.

Between June 1 and August 1, 2011, a total of 500 screening questionnaires were handed out to the physicians at the gynecology outpatient clinic. Of these, 209 (42 %) questionnaires were completed by the physicians, and these women were included in the prospective part of the study. Table 3 shows the characteristics of the women for whom the questionnaire was completed ($n = 209$), and those for whom the questionnaire was not completed ($n = 291$). The group of patients for whom the questionnaire was completed was characterized by higher mean age and higher frequency of ovarian extirpation, breast cancer, cardiovascular disease, and previous pregnancy. A history of gastrointestinal disease was more common in women for whom the questionnaire was not completed, as compared with their counterparts.

Table 3 Characteristics of the patients for whom the questionnaire was completed ($n = 209$) and of patients for whom the questionnaire was not completed ($n = 291$)

	Questionnaire completed ($n = 209$)	Questionnaire not completed ($n = 291$)	*P* value
Age (years)	48.1 ± 18.6	42.3 ± 15.2	<0.01
BMI (kg/m^2)	25.6 ± 5.4	27.1 ± 6.8	0.21
Obesity (BMI >30 kg/m^2)	26 (20 %)	7 (24 %)	0.65
Smoking	40 (29 %)	17 (35 %)	0.42
Previous pregnancy	105 (71 %)	133 (58 %)	0.01
Reason for consultation			
Suspected malignancy, including postmenopausal bleeding	16 (8 %)	13 (5 %)	0.13
Proven malignancy	10 (5 %)	7 (2 %)	0.15
Abnormal cervical cytology	5 (2 %)	9 (3 %)	0.64
Benign gynecological disorders	145 (69 %)	207 (71 %)	0.67
Gynecological history			
Premalignant gynecological disorders	19 (9 %)	17 (6 %)	0.17
Uterus extirpation	20 (10 %)	15 (5 %)	0.06
Adnex extirpation	9 (4 %)	4 (1 %)	0.04
Benign gynecological disorders	34 (16 %)	61 (21 %)	0.19
Oncological history			
Breast cancer	15 (7 %)	6 (2 %)	<0.01
Ovarian cancer	3 (1 %)	1 (< 1 %)	0.18
Endometrial cancer	4 (2 %)	1 (< 1 %)	0.08
Other	15 (7 %)	11 (4 %)	0.09
General history			
Cardiovascular disease	42 (20 %)	36 (12 %)	0.02
Diabetes	7 (3 %)	8 (3 %)	0.70
Endocrinological disease	16 (8 %)	15 (5 %)	0.25
Auto-immune disease	10 (5 %)	12 (4 %)	0.72
Renal disease	4 (2 %)	8 (3 %)	0.55
Pulmonary disease	12 (6 %)	9 (3 %)	0.15
Gastro-enterological disease	2 (1 %)	19 (7 %)	<0.01
Contraception			
Hormonal	54 (26 %)	70 (24 %)	0.65
Nonhormonal	13 (6 %)	8 (3 %)	0.06
Systemic hormonal therapy	7 (4 %)	6 (2 %)	0.32
Systemic immunosuppressant therapy	6 (3 %)	5 (2 %)	0.36

Additional telephone consultation was indicated for 24 of the 209 screened patients (11.5 %). A total of nineteen (9, 1 %) women met the criteria for referral to CGS. Of these, 14 had already undergone previous referral. Five women (2.4 % of screened patients) were referred to CGS as a result of this study. These five referrals were appropriate according to the established referral guidelines. Referral indications for these patients included a family history of breast cancer in two women, a personal history of bilateral breast cancer in one woman, a family history of colorectal carcinoma in one woman and a family history of colorectal and ovarian carcinoma in one woman. The referral rate was statistically different from the 0.26 % referral rate that occurred during usual care ($p < 0.001$).

Based on the evaluation questionnaires completed by the participating physicians, the most important reason for not completing the screening questionnaire was a lack of time (67 % of responders). 14 % of the respondents was confident about his or her knowledge on its content.

Discussion

One of the most effective tools to identify individuals at increased risk of cancer is to ascertain their personal and family history of cancer. The importance of a careful recording of family history of cancer for this purpose has been stressed by both the Society of Gynecologic Oncologists and the American Medical Association [3, 13]. Individuals with increased familial risk should be referred to CGS for genetic counseling and testing and should be offered appropriate screening, as well as preventive and therapeutic strategies. Unfortunately, recognition and uptake of individuals at increased familial risk of cancer is low, which may be due to suboptimal collection and interpretation of family and personal history of cancer by the patients' health care providers. Our pilot study has shown that the identification and referral of patients at risk for hereditary cancer syndromes may be improved by the use of a screening questionnaire for the personal and family history of cancer.

Several studies have shown that a significant proportion of the general and primary practice population meets the family history referral criteria for BRCA1/2 or Lynch syndrome mutations, with estimates ranging from 1.1 % up to 6 % [14–16]. However, there is evidence that the majority of patients do not receive adequate familial cancer risk assessment in the primary practice setting, and patients at risk are missed [9, 11]. Although primary care clinicians are often the first (or the only) providers to initiate collection of family medical history and are an important source of referral for cancer screening, other physicians have the same responsibility. However, cancer risk assessment appears to be suboptimal in many fields of hospital care [6–8, 10].

For this pilot study, we concentrated on risk assessment for BRCA1/2 and/or DNA mismatch repair gene mutations in a hospital setting. Our results indicate that the majority of patients visiting a gynecology outpatient clinic may not receive adequate familial cancer risk assessment for BRCA1/2 and/or mismatch repair gene mutations, supporting the suggestion that familial cancer risk assessment is suboptimal. The use of a standardized screening questionnaire for personal and family history of cancer improved the detection of individuals at high risk of BRCA1/2 and/or mismatch repair gene mutations in our study population. The referral rate to CGS among screened patients after introduction of the standardized questionnaire (2.4 %) proved to be comparable to the prevalence of a family history that meets CGS referral criteria reported in the literature (1.1–6 %). However, a significant proportion of the distributed questionnaires were not completed. A lack of time to complete the questionnaires was the main reason reported by physicians participating in this study (67 % of responders). This important impediment to an adequate evaluation of an individual's familial cancer risk could possibly be countered by offering patients a standardized questionnaire to fill in themselves before the initial and/or routine visits. Another solution could be found in a web-based medical record system designed for this purpose, which would alert physicians when patients meet the criteria for referral to CGS. An advantage of this strategy is that these systems can be updated periodically. This is important, as family history of cancer may change over time, thereby also changing the indication for referral to CGS [17]. Another important barrier to the recording of family history reported by the participating physicians is a lack of knowledge of CGS referral criteria: although all physicians were aware of the existing CGS referral guidelines, only 14 % of the respondents was completely confident about his or her knowledge on its content. These results are consistent with reports by other authors, and indicate that a greater awareness of the importance of family history recording and increased knowledge of CGS referral guidelines among physicians are also necessary to improve the identification of patients at risk [18–20]. This study aims to contribute to this awareness of family history recording and provides a tool for the identification of patients at risk.

The subject of population screening for hereditary cancer syndromes has raised significant debate, in which the emotional burden for patients is often addressed. However, previous studies show that genetic counseling and testing does not lead to an increase in psychological distress in most patients [21–23]. Furthermore, Ackermann et al. [24] have shown that the majority of the female population with

a positive family history for breast and gynecological cancers accepts genetic testing: 85 % would consider testing for breast cancer and 77.8 % for gynecological cancer. Durfy et al. [25] found that 79–94 % of women with a positive family history of breast cancer would want to know if they had a gene mutation that increases their risk of developing breast cancer. None of the patients in our study refused cooperation or referral and none expressed a negative opinion about the proceedings.

One might argue that the scope of family history-based screening for hereditary cancer syndromes should be wider than the percentage of the population that visits a physician. After all, women visiting a gynecology outpatient clinic account for only a small proportion of all individuals at risk for BRCA1/2 and mismatch repair gene syndromes. Furthermore, there are other hereditary cancer syndromes for which screening could be applied. The general public appears to be developing an increasing interest in a variety of health-related subjects, including cancer. This is reflected in the emergence of health information on the internet, in social media, as described by the US Department of Health and Human Services (http://www.health.gov/communication/ehealth/ehealthtools/pdf/ehealthreport.pdf) and the Change Foundation (http://www.changefoundation.ca/docs/socialmediatoolkit.pdf), and in applications on smartphones [26]. Web-based risk calculators have already been developed to make hereditary cancer screening tools more widely available to the public. The 'new media' could enhance usage of these applications by increasing the public's awareness of their existence and importance. As such, social networking sites like Facebook and Twitter could play an important role in the identification of individuals at increased risk for cancer. Future research and debate is needed to establish the desirability and benefits of this application of hereditary cancer screening.

In this analysis, the referral rate after standardized risk assessment may have been overestimated due to indication bias. Although the main reason reported by physicians for not completing the questionnaire was lack of time (67 % of responders), the physicians' a priori estimate of hereditary cancer risk, based on medical history or other characteristics, may have influenced the likelihood of completing the questionnaire for their patient. This is supported by some differences listed in Table 3. However, in the most extreme scenario, the referral rate after standardized screening approximates 1 % (five of 500 prospectively included patients). This is still a four-fold increase in referral rate and, potentially, detection rate when compared to common practice with non-standardized risk assessment ($p < 0.01$).

Another limitation of this study may be its partially retrospective design. However, we believe that retrospective evaluation was the best approach to study common practice, because we assume that prospective data collection would have increased awareness for the recording of a family history of cancer among participating physicians. This would have resulted in a biased estimate of the referral rate in care as usual.

In summary, this pilot study found that detection of patients at high risk for hereditary cancer syndromes based on their personal and family history of cancer is suboptimal in a secondary care setting and can be improved by using a standardized questionnaire. The application of such screening tools in a web-based medical system in hospital settings and in social networking sites may further improve the detection of individuals at high risk for hereditary cancer syndromes. Although some previous studies have shown satisfying results, the desirability, cost-effectiveness, and practicalities of this type of screening need further investigation.

With this study, we wish to stress the importance of adequate family history recording. We wish to encourage further research on this subject and contribute to the discussion on how and by whom family history recording should take place.

Acknowledgments None.

Conflict of interest None declares by all authors.

Ethical standard As the recording of personal and family history is a fundamental part of the medical history, the study was exempt from Institutional Review Board approval.

References

1. Lu KH (2008) Hereditary gynecologic cancers: differential diagnosis, surveillance, management and surgical prophylaxis. Fam Cancer 7(1):53–58
2. Meyer LA, Broaddus RR, Lu KH (2009) Endometrial cancer and lynch syndrome: clinical and pathologic considerations. Cancer Control 16(1):14–22
3. Lancaster JM, Powell CB, Kauff ND, Cass I, Chen LM, Lu KH, Mutch DG, Berchuck A, Karlan BY, Herzog TJ (2007) Society of Gynecologic Oncologists Education Committee statement on risk assessment for inherited gynecologic cancer predispositions. Gynecol Oncol 107(2):159–162
4. Dinh TA, Rosner BI, Atwood JC, Boland CR, Syngal S, Vasen HF, Gruber SB, Burt RW (2011) Health benefits and cost-effectiveness of primary genetic screening for lynch syndrome in the general population. Cancer Prev Res (Phila) 4(1):9–22
5. Teng I, Spigelman A (2013) Attitudes and knowledge of medical practitioners to hereditary cancer clinics and cancer genetic testing. Fam Cancer. doi:10.1007/s10689-013-9695-y
6. Marquez-Rodas I, Lopez-Trabada D, Ruperez Blanco AB, Custodio Cabello S, Peligros Gomez MI, Orera Clemente M, Calvo FA, Martin M (2012) Family history record and hereditary cancer risk perception according to national cancer institute criteria in a Spanish medical oncology service: a retrospective study. Oncology 82(1):30–34
7. Lanceley A, Eagle Z, Ogden G, Gessler S, Razvi K, Ledermann JA, Side L (2012) Family history and women with ovarian

cancer: is it asked and does it matter?: an observational study. Int J Gynecol Cancer 22(2):254–259
8. Grover S, Stoffel EM, Bussone L, Tschoegl E, Syngal S (2004) Physician assessment of family cancer history and referral for genetic evaluation in colorectal cancer patients. Clin Gastroenterol Hepatol 2(9):813–819
9. Murff HJ, Byrne D, Syngal S (2004) Cancer risk assessment: quality and impact of the family history interview. Am J Prev Med 27(3):239–245
10. Meyer LA, Anderson ME, Lacour RA, Suri A, Daniels MS, Urbauer DL, Nogueras-Gonzalez GM, Schmeler KM, Gershenson DM, Lu KH (2010) Evaluating women with ovarian cancer for BRCA1 and BRCA2 mutations: missed opportunities. Obstet Gynecol 115(5):945–952
11. Bellcross CA, Kolor K, Goddard KA, Coates RJ, Reyes M, Khoury MJ (2011) Awareness and utilization of BRCA1/2 testing among U.S. primary care physicians. Am J Prev Med 40(1):61–66
12. Reid GT, Walter FM, Brisbane JM, Emery JD (2009) Family history questionnaires designed for clinical use: a systematic review. Public Health Genomics 12(2):73–83
13. Family Medical History in Disease Prevention (2004) American Medical Association. http://www.ama-assn.org/resources/doc/genetics/family_history02.pdf
14. Scheuner MT, McNeel TS, Freedman AN (2010) Population prevalence of familial cancer and common hereditary cancer syndromes. The 2005 California health interview survey. Genet Med 12(11):726–735
15. Wallace E, Hinds A, Campbell H, Mackay J, Cetnarskyj R, Porteous ME (2004) A cross-sectional survey to estimate the prevalence of family history of colorectal, breast and ovarian cancer in a Scottish general practice population. Br J Cancer 91(8):1575–1579
16. Hughes KS, Roche C, Campbell CT, Siegel N, Salisbury L, Chekos A, Katz MS, Edell E (2003) Prevalence of family history of breast and ovarian cancer in a single primary care practice using a self-administered questionnaire. Breast J 9(1):19–25
17. Ziogas A, Horick NK, Kinney AY, Lowery JT, Domchek SM, Isaacs C, Griffin CA, Moorman PG, Edwards KL, Hill DA, Berg JS, Tomlinson GE, Anton-Culver H, Strong LC, Kasten CH, Finkelstein DM, Plon SE (2011) Clinically relevant changes in family history of cancer over time. JAMA 306(2):172–178
18. Suther S, Goodson P (2003) Barriers to the provision of genetic services by primary care physicians: a systematic review of the literature. Genet Med 5(2):70–76
19. Mehnert A, Bergelt C, Koch U (2003) Knowledge and attitudes of gynecologists regarding genetic counseling for hereditary breast and ovarian cancer. Patient Educ Couns 49(2):183–188
20. Acton RT, Burst NM, Casebeer L, Ferguson SM, Greene P, Laird BL, Leviton L (2000) Knowledge, attitudes, and behaviors of Alabama's primary care physicians regarding cancer genetics. Acad Med 75(8):850–852
21. Schlich-Bakker KJ, ten Kroode HF, Ausems MG (2006) A literature review of the psychological impact of genetic testing on breast cancer patients. Patient Educ Couns 62(1):13–20
22. Vadaparampil ST, Miree CA, Wilson C, Jacobsen PB (2006) Psychosocial and behavioral impact of genetic counseling and testing. Breast Dis 27:97–108
23. Hopwood P (2005) Psychosocial aspects of risk communication and mutation testing in familial breast-ovarian cancer. Curr Opin Oncol 17(4):340–344
24. Ackermann S, Lux MP, Fasching PA, Strissl P, Renner SP, Poehls U, Bender HG, Beckmann MW (2006) Acceptance for preventive genetic testing and prophylactic surgery in women with a family history of breast and gynaecological cancers. Eur J Cancer Prev 15(6):474–479
25. Durfy SJ, Bowen DJ, McTiernan A, Sporleder J, Burke W (1999) Attitudes and interest in genetic testing for breast and ovarian cancer susceptibility in diverse groups of women in western Washington. Cancer Epidemiol Biomarkers Prev 8(4 Pt 2):369–375
26. Boulos MN, Wheeler S, Tavares C, Jones R (2011) How smartphones are changing the face of mobile and participatory healthcare: an overview, with example from eCAALYX. Biomed Eng Online 10:24