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Collection and Use of Cancer Family History in Primary Care

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The Centers for Disease Control and Prevention (CDC) requested and provided funding for this report. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome comments on this evidence report. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to **epc@ahrq.gov.**

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Structured Abstract

Objectives: This systematic review was undertaken to: (1) evaluate the accuracy of patient reporting of cancer family history, (2) identify and evaluate tools designed to capture cancer family history that are applicable to the primary care setting, and (3) identify and evaluate risk assessment tools (RATs) in promoting appropriate management of familial cancer risk in primary care settings.

Data Sources: MEDLINE®, EMBASE®, CINAHL® and Cochrane Central® from 1990 to July 2007.

Review Methods: Standard systematic review methodology was employed. Eligibility criteria included English studies evaluating breast, colorectal, ovarian, or prostate cancers. All primary study designs were included. For family history tools (FHxTs) and RATs, studies were limited to those applicable to primary care settings. RATs were excluded if they calculated the risk of mutation only, required specialist genetics knowledge, or were stand-alone guidelines.

Results: *Reporting Accuracy*: Of 19 eligible studies, 16 evaluated the accuracy of reporting family history and three on reliability. Reporting accuracy was better for relatives free of cancer (specificity) than those with cancer (sensitivity). Accuracy was better for breast and colorectal than for ovarian and prostate cancers.

Family History Tools: Of 40 eligible studies, 18 FHxTs were applicable to primary care. Most collected information on more than one cancer, employed self-administered questionnaires, and favored paper-based formats to collate family information. Details collected were often focused on specific conditions and affected relatives. Eleven tools were evaluated relative to current practice and seven were not. Irrespective of study design, compared to best current practice (genetic interviews) and standard primary care practice (family history in medical records) the FHxTs performed well.

Risk Assessment Tools: Of 15 eligible studies, three RATs were identified for patient use and eight for use by professionals. They were presented in a range of computer-based and paper-based formats, and preliminary evidence indicated potential efficacy, but not definitive effectiveness in practice.

Conclusions: Although limited in generalizability, informants reporting their cancer family history have greater accuracy for relatives free of cancer than those with cancer. Reporting accuracy may vary among different cancer types.

FHxTs varied in the extent of family enquiry depending on the tool's purpose. These tools were primarily developed as an integral part of risk assessment. The few tools that were evaluated performed well against both best and standard clinical practice.

A number of RATs designed for primary care settings exist, but evidence is lacking of their effectiveness in promoting recommended clinical actions.

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Appendixes and Evidence Tables for this report are provided electronically at http://www.ahrq.gov/clinic/downloads/pub/evidence/pdf/famhistory/famhist.pdf

Executive Summary

Introduction

The systematic collection and assessment of family history information is a potentially valuable tool in preventive medicine, and is crucial in the identification of genetic risk.[1] In some situations, family history information alone can form the basis for offering patients appropriately tailored preventive interventions.[2,3] In addition, the clinical predictive value of even the most accurate DNA test is strongly influenced by prior probability—such as a positive family history.[4] Family history is an important risk factor for many of the more common cancers.

Primary care providers (PCPs) have always used family history information as a core tool for their practice.[5] However, the increasing emphasis on identifying and managing genetic susceptibility, and the question of what might now be considered an "adequate" family history for this purpose, presents real challenges for PCPs.[6] There is no single agreed upon approach to guide PCPs in taking a genetic family history within office consultations (which are often brief). In practical terms, the systematic collection of family history as it pertains to cancer history is linked with the interpretation of that information which in turn is linked to whether PCPs take appropriate clinical action on the basis of the information collected.

The aim of this review is to provide a partial contribution to the evidence base underlying analytic validity (the ability of a tool to capture accurate family history data) and clinical validity (the ability of a tool to correctly assess or predict disease risk) of tools for capturing and interpreting family history.

Scope and Purposes of the Systematic Review

This systematic review addresses three research questions relating to the clinical utility of ascertaining family history as follows:

1. What is the evidence that patients or members of the public accurately know and report their family history of each one of, or a combination of, the following cancers: breast, ovarian, prostate, and colorectal?

2. How well do the different systematic family history collection forms and tools, such as take home tools, web based tools, etc., improve non-systematic approaches to family history collection by PCPs?
   a. Identify tools intended to improve family history collection by PCPs.
   b. Compare these tools against current practice.

3. What tools exist to enable PCPs to calculate, interpret, and act upon family history based risk information, and how well do these tools perform? For each cancer of interest,
   a. Identify tools designed to facilitate calculation and/or interpretation of family history based risk information, with the purpose of promoting recommended clinical actions.
   b. Assess the evidence for effectiveness of these tools in facilitating calculating and/or interpretation of family history based information.

c. Assess the evidence for effectiveness of these tools in promoting recommended clinical actions.
d. For each tool, identify the evidence base for each recommendation.

Methods

Standard systematic review methodology was employed. MEDLINE®, EMBASE®, CINAHL® and Cochrane Central® from 1990 to July 2007 were searched for primary studies. Eligibility criteria included English-only studies evaluating breast, colorectal, ovarian, or prostate cancers in adults. All primary study designs were included and reviews excluded. For family history tools (FHxTs) and risk assessment tools (RATs) studies were limited to those applicable to primary care settings. Primary care practitioners included family physicians/general practitioners, general internists, obstetricians, gynecologists (obstetrics and gynecology practitioners are PCPs for some women), nurses, nurse practitioners, physician assistants, nutritionists, and behavior counselors. All studies that described or evaluated a tool or standardized method to systematically capture/collect/collate information related to family history for the relevant cancers or history of illness in other family members by any method whether self-report or collected by a professional were eligible. FHxTs were eligible if developed specifically for primary care or developed in other settings but also applicable to primary care. RATs were excluded if they calculated the risk of mutation only or required specialist genetics knowledge.

Results

A total of 15,390 unique citations were identified in the search for all three research questions combined. During two levels of title and abstract screening, 14,840 articles were excluded. A total of 338 citations proceeded to full text screening. From these, a total of 56 studies were eligible for the three research questions.

Question 1: Accuracy of Family History Reporting

A total of 19 unique studies (20 publications) evaluated the accuracy of reporting family history. From these, 16 studies evaluated accuracy by attempting to verify the cancer status of relatives (i.e., accuracy compared with a gold standard), and three evaluated the repeatability or reliability of the informant's knowledge of family history rather than the true status of the relatives (i.e., no external gold standard). For the purposes of this review we use the terms "affected" and "unaffected" to refer to those relatives who have had cancer, and those who have not, respectively.

All but three of the 19 studies recruited participants who had cancer; two studies involved individuals at high risk for colorectal[7] or breast cancer,[8] and one involved women undergoing mammography.[9] There were four case control studies (five publications),[10-14] with controls derived from the general population matched for age,[10,11] spouses of the informants or regional general practice lists,[14] and from a linkage with license registration and health care

administration database.[13] In general, family history informant characteristics such as mean age, ethnicity, or education were infrequently evaluated.

Sixteen studies (17 papers)[7,8,10-24] evaluated the accuracy of family history reports by attempting to confirm the true cancer status of the relatives about whom informants provided information. Eight studies [13,14,19-24] verified the cancer status in relatives reported to be affected and those reported to be unaffected. The other eight studies (nine publications)[7,8,10-12,15-18] only confirmed the cancer status of relatives reported to be affected. We considered the former studies to be of higher methodological rigor and therefore evaluated these two groups of studies separately.

For the studies verifying affected and unaffected relatives, specificity across all cancers types and with varying modes of collection was consistently high (range 91 to 99 percent), suggesting that patients were very accurate in identifying relatives without cancer. These varied as follows for the different cancers: breast 95 to 98 percent; colorectal 91 to 92 percent; ovarian 96 to 99 percent; prostate 93 to 99 percent. The sensitivity values showed greater variability, with breast cancer having the highest values. The percent varied as follows: breast 85 to 90: colorectal 57 to 90; ovarian 67 to 83; prostate 69 to 79. The extent to which the verification method or the manner of family history collection affected the sensitivity estimates has not been well evaluated.

Fifteen factors were identified within the studies which could influence accuracy of family history reporting. The most frequently reported factors were age (no clear effect), gender (some effect depending on type of cancer and family line), education level (mixed effects) and degree of relatives (consistent trend towards increased accuracy of reporting for first degree compared to second or third).

Question 2: Family History Tools Designed To Improve Collection by Primary Care Professionals

A total of 39 different tools, implemented in 40 unique studies, and reported in 45 publications passed full text criteria. Our initial focus was on identifying studies that described FHxTs developed or used in a primary care setting; however, after careful review, we noted that many studies described tools used in other settings that appeared potentially relevant to primary care (criteria included length, ease of use, complexity of information, need for specialized training). We also sent e-mail queries to all authors of eligible studies that did not provide sufficient detail of the FHxT or a copy of the tool. Fifteen authors (of 16 publications) [8,10,11,16,17,21,23,25-33] did not respond and therefore we were unable to determine whether the FHxT was applicable for use within primary care. For those studies for which we evaluated the FHxT, six tools from seven publications[13,18-20,24,34,35] were assessed as inappropriate for primary care; all of these had been developed and used in research settings. Of the remaining 22 publications, four [36-39] described the prototype and final versions of the same FHxT (RAGS/GRAIDS), which we counted as a single tool; and two [40,41] were companion publications. Thus 18 distinct tools, from 22 publications, were identified as being applicable to primary care settings.

Fourteen tools [42-55] were designed for completion by patients, and four tools (eight papers) [36-41,56,57] were designed for use by health professionals. The majority of tools (n = 15) were designed to collect data on family history of breast or breast/ovarian cancer and only two tools captured data on prostate cancer. The published reports indicated that eight of the tools[46,48,49,51,52,54,55,57] were used in a proactive way (intended for general or targeted population

coming into contact with PCP, irrespective of a known cancer risk or concern), eight (12 papers)[36,38-41,43-45,47,53,56] in a reactive manner (intended for individuals with perceived or recognized familial risk of cancer, including individuals concerned about cancer risk), and two in a mixed approach.[42,50] The majority used a paper-based format to collect family history.

The tools were evaluated using a range of study designs. Eleven tools were evaluated relative to "ideal", best estimate genetic interview, or current ("standard") practice and seven tools were not evaluated relative to a comparator. Of the five tools evaluated against genetic interview, in three there was no control arm to the study, with interview being completed after FHxT.[43,45,49] Similarly, when compared to current practice, in three studies, patients completed the FHxT followed by capturing information in medical records.[47,50,52] Despite these different study designs the findings were consistent, with FHxTs performing well against "ideal" interviews and significantly better than standard practice.

Question 3: Risk Assessment Tools Designed To Improve Management of Patients

For the purposes of this review we have defined a RAT in primary care as: An active knowledge resource that uses family history data, with or without other relevant evidence to generate case specific advice [knowledge component], designed to support decision making relating to management of cancer risk in individual patients [target decision component, timing component], by health professionals, the patients themselves, or others concerned about them [user component].

Sixteen publications, representing 10 unique studies, were included. All 10 tools were designed to stratify individuals into risk categories, and all had a component which indicated some form of clinical or personal action. Six tools, reported in seven papers,[43-45,58-61] were designed to assess risk of breast or breast/ovarian cancer only, four tools (seven papers)[31,36-39,62,63] were designed to assess risk of breast/ovarian and colorectal cancer, and one tool (two papers) [40,41] focused on breast/ovarian, colorectal and prostate cancer. No tool was identified that focused solely on ovarian, colorectal, or prostate cancer risk.

Of the seven tools intended for use by professionals, five were developed explicitly for use by PCPs, either family physicians (four tools)[36-39,58,60-63] or physicians working in ambulatory care settings (one tool, two papers).[40,41] Two appeared to have been developed in settings other than primary care, but intended for eventual use in that setting.[43,59] One patient tool[31] was developed in a primary care setting, and the other two[44,45] were considered potentially applicable to use in primary care settings.

Three tools (five publications) were robustly evaluated in controlled trials.[36,60-63] The development of one tool was described over four papers from evaluation in "laboratory- type" conditions[38,39] to controlled trials in routine practice.[36,37] The success of two of these RATs was confirmed by compliance to referral criteria in two studies (three papers), [36,60,61] however in one study there was no subsequent significant difference in patients identified at increased risk by genetic specialist.[36] The final tool (two papers) did not demonstrate any statistical difference in physician confidence and patients' risk perception.[62,63]

Discussion and Conclusions

This review explored both the accuracy of family history reporting by patients and the effectiveness of tools for collecting and using familial cancer history in a primary care setting. Ideally, patients are able to report accurate information on their family history, assisted by effective tools, and health care providers are able to use the information to make beneficial preventive and clinical management decisions.

The accuracy of self reported family history has implications for the correct risk assessment and management of patients. Accuracy of cancer family history reporting appears to be dependent on cancer type and method of collection, and accurate reporting of absence of cancer (specificity) appears to be greater than accurate reporting of presence of cancer (sensitivity). Accuracy of recall and reporting may be influenced by both patient factors and by the method used to capture the data (the tool). No studies appear to have examined both of these together, so it is impossible to comment definitively on their relative contributions to any lack of accuracy.

Very few FHxTs have been developed for, and evaluated in, primary care settings. Further, few tools have been compared with either "best practice" (genetic interview) or current primary care practice (family history as recorded in charts). Although the evidence is very limited, and depends on extrapolation of studies of tools in settings other than primary care, it suggests that systematic FHxTs may add significant genetic family history information compared to current primary care practice.

A number of RATs, of varying format and complexity, have been developed for primary care settings, and a few of these have been evaluated in controlled trials. These studies provide tentative evidence for the effectiveness of such tools, but their utility in routine practice has not been established.

Recommendations

1. Family history is a fundamental element of health information, and the ability to take an adequate and accurate family history should be recognized as a core skill for all PCPs, irrespective of the availability of tools.

2. Consensus should be reached on the extent of family history enquiry necessary for different clinical purposes and circumstances, taking into account the likelihood of accuracy of self reported information for different relatives, and the use to which the information will be put (e.g., overall or specific risk assessment). Until the evidence base is clear, it is suggested that a minimum adequate cancer family history should include information on siblings, parents and grandparents (and the paternal and maternal lineage of the latter), specific enquiry about whether other relatives had the cancers of interest, and the ethnicity of the respondent. When cancer is identified, the age of diagnosis should also be noted, and other relatives with similar or related conditions identified.

3. The benefits, costs and harms of using patient-completed tools for systematic family history collection and risk assessment, as a substitute for, or complement to, professional tools should be further examined. As well as assessing technical outcomes such as accuracy and completeness of data captured, evaluations should consider outcomes which relate to patient "empowerment" and the use of practitioner and health care resources.

4. Further research is required to identify the specific strategies and tool features which promote the most accurate reporting of family history information.

5. The optimum interval for updating a patient's family history information in primary care should be formally evaluated.

6. Further evaluation of FHxTs and RATs in routine clinical settings and practice is required. Studies should: adopt appropriate comparators (generally current practice); ensure that tools are optimized (in terms of, for example, face and content validity) before evaluation; measure outcomes that relate to utility in routine practice; measure outcomes that provide information on potential costs or harms as well as benefits; and address or explore contextual factors which may modify utility in practice (e.g., practice infrastructure, time available).

Evidence Report

Chapter 1. Introduction

Importance of Family History Collection for Cancer Risk Evaluation

A positive family history is a risk factor for many chronic diseases, reflecting "the consequences of genetic susceptibilities, shared environment, and common behaviors".[2] The systematic collection and assessment of family history information is a potentially valuable tool in preventive medicine, and is crucial in the identification of genetic risk.[1] In some situations, family history information alone can form the basis for offering patients appropriately tailored preventive interventions.[2,3] In addition, the clinical predictive value of even the most accurate DNA test is strongly influenced by prior probability—such as a positive family history.[4] For example, Rich and colleagues[3] illustrated how the positive predictive value of the same DNA-based test for familial adenomatous polyposis (FAP) could rise from about 11 percent in a patient where no family history information was available to over 99 percent if the patient accurately reported FAP in just one sibling or parent. Thus, family history information is potentially useful both as a clinical tool in its own right, and also as an important adjunct to DNA-based testing.

Cancers are a group of relatively common conditions in which, for at least some, family history appears to be an important risk factor. A British study suggested that a typical UK family physician with 2,000 patients would expect up to 50 of those aged 35 to 64 to have a history of familial cancer, and 30 to 40 patients meriting some form of active preventive surveillance.[64] Cancer family histories can broadly be divided into three categories: hereditary, familial, and sporadic.[65] Hereditary cancers are predominantly single gene disorders with Mendelian patterns of inherited risk. Familial cancers describe other less obvious clusters of cancer within families, thought to be due to combinations of multiple low penetrance gene mutations with or without contributions from shared environmental and/or behavioral risk factors. Sporadic cancers are those which occur without an apparent hereditary or familial pattern.

This report focuses on four cancer types: breast, ovarian, prostate, and colorectal. These are some of the most common cancers where the role of family history is widely recognized as a risk factor.[66-70] For each of them, the contribution of familial risk is reflected in evidence-based consensus statements[71-73] (e.g., http://www.ahrq.gov/clinic/uspstfix.htm). In some families, these cancers form part of recognized hereditary syndromes; for example, BRCA1 mutations increase familial risk of breast, ovarian and prostate cancer while MLH1, MSH2, and other DNA mismatch repair genes increase the familial risk of colorectal, endometrial, ovary, small bowel, and pancreatic cancers, among others.[65] In some cases, ethnic ancestry is also associated with risk of cancer-associated genetic mutation, such as breast cancer in the Ashkenazi Jewish community.[74-77]

Primary Care Physicians and Cancer Risk Assessment and Management

Primary care providers (PCPs) have always used family history information as a core tool for their practice,[5] well before the arrival of the "genomics age". However, the increasing emphasis

on identifying and managing genetic susceptibility, and the question of what might now be considered an "adequate" family history for this purpose, presents real challenges for PCPs.[6] While a genetics specialist may be able, indeed advised, to devote substantial time to eliciting and confirming family history data (on the order of several hours)[65,78,79] family physicians, internists, and other non-genetics providers may have only minutes. Other barriers to more than a "minimal" approach include unfavorable reimbursement policies, pressure from colleagues and patients to focus on other aspects of care, perceived lack of skills, and lack of confidence.[3,80] Conversely, family physicians and other PCPs may be able to capture family history data over time, and are well placed to keep such information up to date.

The use of family history information to make preventive and clinical management decisions also depends on the adequacy of providers' knowledge, skills and confidence; this is extremely challenging in a field where the knowledge base is rapidly evolving. To complement more general educational interventions, there is a strong case for the development of effective tools, designed for use in primary care settings, which permit providers to translate an individual's family history data into meaningful risk stratification, with linkage to evidence-based guidance on appropriate preventive and clinical management interventions. Thus, the translation of family history information into improved health outcomes depends on the availability and integrated use of effective interventions for data capture, risk assessment, and clinical intervention.

Accuracy of Family History Reporting

In order for family history to be of value in clinical decision making, patients must possess, and PCPs must be able to ascertain, accurate family health information. Assessing accuracy requires a clear idea of an appropriate gold standard—what patients "should" know, and what clinicians "should" be able to obtain. In simple terms, an "accurate" family history could be considered to be one which is sensitive (disease in relatives is correctly identified) and specific (lack of disease in relatives is correctly identified). Work in the field of psychiatry has suggested three gold standards for studies of family history taking: an "ideal" standard, based on comprehensive data obtained from the relatives, hospital and physician records and/or disease registers;[81-83] a "best estimate diagnosis" (BED) standard,[84] based on best available data from death certificates and medical records;[65,85,86] and a "pragmatic BED", based on the family history obtainable in a detailed interview conducted by a trained clinical genetics professional. Our consultation with the key stakeholders in this review has indicated that an appropriate practical gold standard for evaluating accuracy would be information obtained directly from relatives' medical records, cancer registries, and/or death certificates. Such information should be used both to confirm reported cases of cancer in the family, and to confirm absence of a cancer diagnosis in relatives who were reported not to have cancer.[87]

Collection of Family History in Primary Care

There is no single agreed-upon approach to guide primary care practitioners in taking a genetic family history within office consultations (which are often brief). Family history taking can be conducted as part of a disease specific approach which aims to identify risk of selected single gene disorders (e.g., hereditary breast or colon cancer) for the purpose of ensuring appropriate specialist intervention.[88,89] Alternatively, it can be directed more broadly towards

identifying possible risk of a number of common multi-factorial disorders such as cancer, diabetes, and coronary heart disease.[46,49]

Family history data may be recorded as notes or lists within patient charts, represented as family trees or genetic pedigrees, or stored within computer databases which can be linked to decision support systems. In the last few years several computer-based pedigree drawing packages have been developed, such as genogram software.[38,90] It is not clear whether such approaches translate well from specialist use to application in primary care.

There is also no consensus on the extent or detail of family history information which needs to be recorded in primary care, compared with specialist genetics settings. The extent of cancer family history collection has to be adequate to enable PCPs to make appropriate clinical and prevention decisions, but it is not clear whether this necessarily requires the same approach as that used by a genetics specialist.[3]

Risk Assessment in Primary Care

There are several issues which may influence the translation of family history information into meaningful risk assessment for patients. These include the level of complexity of family history information which is actually required for risk assessment for any given disorder, the validity of risk stratification guidelines or algorithms, the kind of tools that exist to facilitate risk stratification, (and their effectiveness in practice), and the actual predictive value of risk assessment tools (RATs).

At its most simple, assessing familial risks associated with common adult-onset diseases requires setting a threshold where the family history indicates a cause for suspicion (i.e., dichotomizing risk into reassuring the patient or recommending further action). A more complex approach is to separate risk into three or more strata (e.g., "high", "moderate" and "average").[91,92] In general terms, individuals at "average" risk (the risk level of the general population) would be offered standard preventive advice, those at "moderate" risk would be offered a higher level of intervention, such as more extensive or more frequent surveillance, and those at "high" risk would usually be referred for specialist assessment and possibly considered for mutation testing.[2]

Risk assessment tools need to be valid, in terms of their clinical predictive value, but they must also be feasible for use in the intended settings, and generate benefits in the process or outcome of care when compared with current practice. Feasibility and effectiveness in practice may be influenced by the actual implementation format; for example, a risk stratification protocol could be presented in paper-and-pencil format, on a personal digital assistant, or on the desktop in a web-based format. Such tools may be passively disseminated, or accompanied by educational interventions and/or ongoing support from genetics professionals. Recent examples of web-based tools include Harvard's "Your Disease Risk"[93] and the Centers for Disease Control's (CDC) Family HealthWare.[94]

The ACCE Framework

Tools for family history collection and risk assessment lend themselves to evaluation using the framework developed for genetic predictive testing by the Secretary's Advisory Committee on Genetic Testing.[95] This framework (see Table 1, derived from Yoon 2003), widely referred to

as the "ACCE" framework, comprises four evaluative elements: analytic validity, clinical validity, clinical utility, and ethical legal and social issues.[2,96]

Table 1. Application of the ACCE framework[96] to family history as a screening tool

Element	Definition	Components
Analytic validity	An indicator of how well a family history tool measures the characteristic ("family history") that it is intended to measure	Analytical sensitivity and specificity
Clinical validity	A measurement of the accuracy with which a RAT based on family history information predicts disease risk	Clinical sensitivity and specificity Positive and negative predictive values
Clinical utility	The degree to which benefits are provided by using a clinically valid RAT based on family history information	Availability of effective preventive and clinical interventions Health risks and benefits of preventive and clinical interventions Health risks and benefits of family history and RATs Economic assessment
Ethical, legal, and social implications	Issues affecting data collection and interpretation that might negatively impact individuals, families and societies	Stigmatization Discrimination Psychological harm Risks to privacy and confidentiality

Yoon P.W., Scheuner M.T., Khoury M.J. Research priorities for evaluating family history in the prevention of common chronic diseases. Am J Prev Med 2003;23 (2):128-135.

Thus, in terms of family history, analytic validity describes the ability of a family history tool to correctly identify the pertinent information on disease in relatives. This is dependent on the effectiveness of a tool in promoting acquisition of appropriate family history data, and also on the ability of an informant to provide accurate information. Clinical validity describes the ability of a RAT to use valid family history data to correctly predict or stratify cancer risk in the informant. Risk assessment tools may vary in their complexity, from simply identifying an elevated cancer risk in the family, to more detailed risk prediction scores—but all are dependent on valid risk stratification criteria. An effective risk prediction tool therefore depends on a valid family history tool, and may or may not also take account of non-genetic factors which modify disease risk. Clinical utility considers the evidence that family history assessment, risk stratification, and subsequent preventive or clinical interventions actually bring overall health benefit to the individual patient. The ethical, legal, and social issues component of the framework considers the impact and consequences of using a family history based approach from a broader societal perspective.

The aim of this review is provide a partial contribution to the evidence base underlying analytic validity (the ability of a tool to capture accurate family history data) and clinical validity (the ability of a RAT to correctly predict disease risk). The main focus is on describing the availability and format of available family history and RATs, and the evidence that these are more effective than current practice in promoting accurate family history collection and assessment in primary care and population settings. It is not within the scope of the review to assess either the evidence underlying risk stratification systems (i.e., the predictive value of guidelines or criteria), or the evidence that preventive or clinical interventions based on such stratification provide overall benefit to patients (i.e., clinical utility). However, the evidence assembled in this review is a crucial element of determining how best to capture and use family history information in primary care to promote the anticipated population health benefits.

Scope and Purpose of the Systematic Review

This systematic review addresses three research questions relating to the clinical utility of ascertaining family history as follows:

1. What is the evidence that patients or members of the public accurately know and report their family history of each one of, or a combination of, the following cancers: breast, ovarian, prostate, and colorectal?

2. How well do the different systematic family history collection forms and tools, such as take home tools, web based tools, etc., improve non-systematic approaches to family history collection by PCPs?
   a. Identify tools intended to improve family history collection by PCPs.
   b. Compare these tools against current practice.

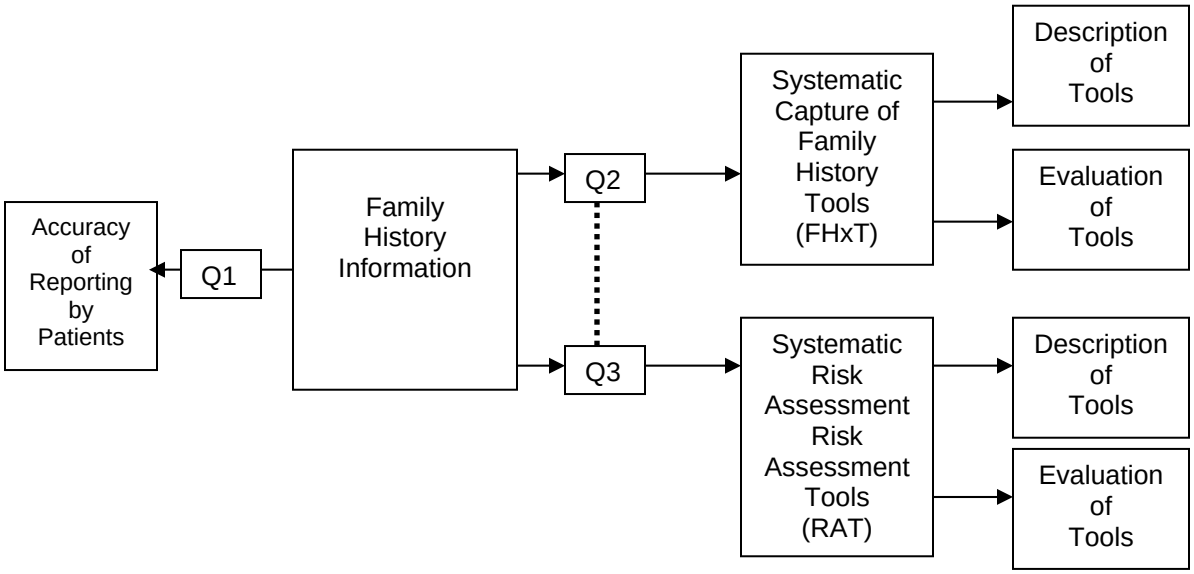
3. What tools exist to enable PCPs to calculate, interpret, and act upon family history based risk information, and how well do these tools perform? For each cancer of interest:
   a. Identify tools designed to facilitate calculation and/or interpretation of family history based risk information, with the purpose of promoting recommended clinical actions.
   b. Assess the evidence for effectiveness of these tools in facilitating calculating and/or interpretation of family history based information.
   c. Assess the evidence for effectiveness of these tools in promoting recommended clinical actions.
   d. For each tool, identify the evidence base for each recommendation.

Chapter 2. Methods

Analytic Framework

An analytic framework is a schematic representation of the strategy for organizing topics for review and for guiding literature searches. Figure 1 illustrates the inter-relationships among the three research questions being addressed in this systematic review. As shown in Figure 1, the collection of family history data, a central focus of this systematic review, connects with the three questions. First, the validity of reporting of family history data (in general) by patients (Q1), second, characteristics of the systematic family history collection tools, designed to be used to capture such data in the primary health care settings (Q2), and, third, the characteristics and effectiveness of risk assessment tools (RATs) designed to allow practitioners and patients to make use of family history information to improve health outcomes (Q3). Other important questions are the format of various tools, strategies underlying family history collection and risk assessment, the settings in which tools are intended for use, the settings in which tools are evaluated, and the comparisons against which both family history tools (FHxTs) and RATs are actually evaluated.

Figure 1. Analytic framework for the research questions evaluated in this review



While there is some overlap between FHxTs and RATs, some FHxTs do not contain a decision support element, while some RATs collect family history data which is so targeted that it is unlikely to be sufficient for a complete or generic FHxT, and others have no FHxT component at all. The evaluative framework for both FHxTs and RATs is described in further detail in the topic refinement section.

Note on Terminology. In the published literature, a number of terms have been used to indicate the individuals from whom family history information is collected, including "patient", "consultant", "subject", "participant", and "proband", but there is no single standard, accepted term in general use. Within this report, we wish to promote consistency of terminology, and

reduce potential ambiguity and confusion. Therefore, although it is used with a particular meaning in some clinical contexts, we have adopted the use of the term "informant" in the rest of the report to indicate the individual who provides the family history information.

Accuracy of Family History Reporting

Accuracy of a test (in this case reporting of family history) represents the proportion of all test results that are true (both positive and negative outcomes). If individuals reporting family history were 100 percent accurate they would correctly identify all relatives with cancer and all those without cancer. A number of metrics may be used to convey accuracy. Of these, sensitivity and specificity are not influenced by the underlying prevalence of the characteristic of interest in the population (in this case, positive family history). We therefore report sensitivity and specificity, where this is reported in (or can be calculated from) eligible papers. Consider the situation where "reporting of family history by the informant" is considered the "test", and is compared to a "gold standard" (the real situation). In this context, sensitivity indicates how accurate informants are at identifying relatives who truly have cancer. If reporting is highly sensitive, only a few relatives with cancer will be reported as cancer-free. Conversely, if reporting is highly specific, only few relatives who are truly cancer-free are misreported as having cancer.

It is likely that accuracy of reporting will be influenced by both informant factors and factors relating to the method of capturing the family history data. As much as possible, we captured information on such attributes and considered how the results appeared to be influenced by them, although we did not attempt a formal regression analysis to examine their independent effects(s). We also examined reliability (repeatability and reproducibility) where this was possible, recognizing that this is also a product of accuracy of recall and consistency of reporting (informant factors) and performance of the instrument used to capture the data (tool factors). There are several measures of test-retest reliability such as intra-class correlation co-efficient and Cohen's kappa statistic. We note that there is no consensus on the ideal interval for assessing reliability of family history information, bearing in mind that the medical status of relatives inevitably changes over time.

As discussed in Chapter 1, three gold standards have been suggested for studies of family history taking: an "ideal" standard, a "best estimate diagnosis" (BED) standard and a "pragmatic BED" standard. We accepted the following gold standards for the presence or absence of cancer in the first and second degree relatives of the informant: (1) the relative's medical record, (2) confirmation of status by the relative's physician, (3) death certificate, (4) cancer registration, (5) direct confirmation by the relative in question. Ideally, accuracy studies should demonstrate verification of health status (presence or absence of cancer) both in relatives who are reported to have had cancer, and relatives reported not to have had cancer; however, in order to evaluate as wide a range as possible of the available literature, we did not exclude review studies which verified only the status of relatives reported to have had cancer.

We defined a priori what we meant by the degree of the relative. First degree relatives were defined as those who share one-half of their genetic information with the individual reporting family history—their full siblings, parents and children. Similarly, second degree relatives were those who shared one-quarter of their genetic information with the informant—their grandparents, grandchildren, uncles, aunts, and half-siblings.

Family History Collection Tools

We defined a FHxT as:

> "A systematic and coherent approach used to capture and document family history, appropriate for the clinical setting, with the potential to lead to decision making by a clinician."

This review focused on FHxTs which could be applied in the clinical setting, but we also included studies that described tools developed for research purposes, and for settings other than primary care, where we judged they appeared potentially applicable within primary care settings. We captured data on the following tool characteristics that may influence the clinical utility of the tool in current primary care practice.

1. Patient targeting—"reactive" or "proactive".
   - Reactive—the tool was intended to be used only to collect family history information from individuals with perceived or recognized familial risk of cancer, including individuals concerned about cancer risk.
   - Proactive—the tool was intended to be used to collect family history information from a general or targeted population coming into contact with primary care, irrespective of a known cancer risk or concern.

2. Study setting in which the FHxT is being administered—"clinical" or "research".
   - Clinical—the primary objective of the study was to assess the use of the FHxT in routine clinical practice.
   - Research—the primary objective of the study was to use the FHxT for purposes other than routine clinical practice, for example designed for data capture in epidemiological studies.

3. Type of comparator—"best estimate" or "current practice".
   - Best estimate—the comparator was information collected by a clinical genetic specialist interview or equivalent.
   - Current practice—the comparator was information collected in a way that was "standard" for the primary care setting, e.g., family history information recorded in patient charts.

Where a tool was not described as designed for or evaluated in a primary care setting, applicability was assessed by two independent reviewers against five criteria: length of tool, ease of completion, need for specialist knowledge, whether it was designed to capture data on at least all first degree relatives, and clarity of layout (including appropriate structure and logical sequence).

Risk Assessment Tools

While there is no one commonly accepted definition of a RAT, for the purposes of this study, we have followed the approach of Liu et al. who define a decision tool as:

"…an active knowledge resource that uses patient data to generate case specific advice, which supports decision making about individual patients by health professionals, the patients themselves or others concerned about them."[97] (p90)

Defined thus, RATs have four essential characteristics:

1. The tool is designed to aid a clinical decision by a health professional and/or patient ("user");

2. The tool focuses on decisions concerning individual patients ("target decision");

3. The tool uses patient data and knowledge from family history to generate an interpretation that aids clinical decision making ("knowledge component");

4. The tool is designed to be used before the health professional or patient takes the relevant decision ("timing").

This definition encompasses a wide range of potential tool "technologies", including computer-based decision support systems, reminder cards, guidelines, predictive scores, checklists, etc. Drawing on this definition, we have developed the following working definition of a "family history based cancer risk assessment/decision tool", for use in this review:

"An active knowledge resource that uses family history data and other relevant evidence to generate case specific advice [knowledge component], designed to support decision making relating to management of cancer risk in individual patients [target decision component, timing component], by health professionals, the patients themselves, or others concerned about them [user component]."

We translated the four "essential characteristics" into this specific form for the context of this review:

1. Users—health professionals, patients, members of the general population

2. Target decision—clinical management (e.g., referral for genetic counseling), or individualized preventive management strategies (e.g., disease screening or surveillance)

3. Knowledge component—a defined model or set of criteria which transform family history data into information which serves the target decision making process

4. Timing—designed to be used before the health professional or patient takes the relevant decision.

The breadth of this definition potentially allows for the inclusion of a large number of guidelines, algorithms, statistical models, etc. In order to maintain the focus of this review on tools most likely to be feasible for use in primary care, we included only those which were explicitly developed for primary care, or where specialist genetics knowledge did not appear necessary to use the tool. We excluded tools where the *only* output was risk of carrying a cancer-associate mutation (e.g., BRCAPRO[98] or BOADICEA[99]), rather than risk of disease, as we judged this required genetics specialist knowledge for interpretation. Noting also that there

are many hundreds, possibly thousands, of guidelines which have been developed over the past few years around familial cancer risk, we included them only if they were part of a package, system, or intervention designed to foster their effective implementation in practice. Thus, widely used guidelines such as the modified Amsterdam criteria,[100] the Manchester scoring system,[101] the UK NICE guidelines on familial breast cancer[72] were not included unless they were part of such a system. For each tool which met the inclusion criteria, we collected data on the guideline(s) or evidence cited which appeared to form its knowledge component.

Topic Refinement

The first step during the topic assessment and refinement process was a teleconference with partner organizations. The Task Order Officer (TOO) invited topic experts and the McMaster multidisciplinary research team to define the scope of the topic to be addressed and to refine/clarify the preliminary research questions for this evidence report. An international Technical Expert Panel (TEP) was assembled to provide high level content expertise on this topic (Appendix E*) and to participate in conference calls on an as-needed basis throughout the data refinement and extraction phase. The TEP assisted in refining the research questions and raising methodological issues of relevance to this review.

The initial work order specified that the systematic review should be limited to adult populations and should examine the family history of at least one of the following cancers: (1) breast, (2) ovarian, (3) prostate, and (4) colorectal. The second and third questions of the review were limited to primary care settings or practitioners.

The first research question in this systematic review focuses on the accuracy of family history knowledge and reporting. The investigative team considered, but ultimately rejected, addressing this question by updating a previous systematic review.[102] This review included original articles describing the accuracy of self-reported family history for breast, colon, ovarian, prostate, endometrial, and uterine cancers using verification from identified relatives' medical records, physician, death certificate, and/or verification within a population cancer registry. The limitations of this review included: lack of a delineated search strategy, overly specific search terms, non-reporting of agreement between reviewers, non-reporting of data collection forms used, and lack of clarity of reasons for excluding reports.

A number of issues relevant to the identification and evaluation of FHxTs were identified and discussed with the TEP, including: (1) the most important attributes that should be considered within each of these tools; (2) which of these elements were most relevant for primary care; and (3) the incremental value of the tool relative to current practice. The TEP recognized that the selection of gold standards for family history reporting and collection is arbitrary and that an "adequate" family history (for the purposes of making decisions relating to familial cancer risk) requires not only identifying relatives with and without the cancer, but also the relationship of the affected relative, the age of onset of cancer in those affected, and identification of several cancer types beyond the "target" cancer in question (e.g., family history of endometrial and kidney cancer is relevant in considering risk for hereditary nonpolyposis colorectal cancer).

For the purposes of the review, a definition of primary care was established with the participation of the partner at the CDC and the TEP. Primary care practitioners included family physicians/general practitioners, general internists, obstetricians, gynecologists (obstetrics and

* Appendixes cited in this report are provided electronically at http://ahrq.gov/clinic/tp/famhisttp.htm

gynecology practitioners are PCPs for some women), nurses, nurse practitioners, physician assistants, nutritionists, behavior counselors.

Family history information is of clinical value only if it can be used for some form of meaningful risk stratification. Issues around risk assessment and stratification were explored with the TEP, particularly whether the various risk stratification algorithms or guidelines on which tools are based are themselves evidence-based—i.e., whether such algorithms or guidelines have adequate predictive value (i.e., clinical validity) and their use has been shown to improve patient or clinical outcomes (i.e., clinical utility). It was recognized that exploration of this would broaden the scope of the review to such an extent that it would become unmanageable. Therefore, it was determined that the validity of underlying algorithms or guidelines should be taken at face value. Thus, the focus of the review should be confined to evaluating whether tools were effective in facilitating the translation of a patient's family history information into a specific risk stratum, compared with current primary care practice, on the assumption that such stratification was worthwhile.

Methods

Search Strategy

The systematic review protocol search included the electronic databases MEDLINE®, EMBASE®, CINAHL® and Cochrane Controlled Trials Register (CCTR)® from 1990 to July 2007. In addition we retrieved and evaluated references from eligible articles. Hand searching was not undertaken for this review. However, we did review the publication types "letters" (normally excluded from reviews); the investigators suggested that, within the content area of cancer genetics, primary data information might be published as letters in some journals. We also undertook a search of relevant grey literature sources. Detailed search strategies and websites explored are listed in Appendix A.*

Eligibility Criteria

A list of eligibility criteria was determined and standardized forms were developed in Systematic Review Software (SRS) for the purposes of this systematic review. The forms and help guides detailing the eligibility criteria can be found in Appendix B.*

Publication Year, Type and Language

Inclusion:

Language: Only English language studies were eligible.

Publication Date: 1990 to July 2007.

Exclusion:

Publication type: Narrative and systematic reviews (except for Q2b), editorials, letters (with no primary data), comments, opinions, abstracts and unpublished studies.

* Appendixes cited in this report are provided electronically at http://ahrq.gov/clinic/tp/famhisttp.htm

Study Design

Inclusion:

There was no restriction of primary study designs for both quantitative and qualitative types.

Exclusion:

Narrative and systematic reviews.

Population

Inclusion:

Any subject 18 years of age or older.

Intervention Cancer Type

Inclusion:

Examination of family history of breast, ovarian, prostate, or colorectal cancer.

Exclusion:

Tools that do not include at least one of the four specified cancers or cancer data presented in aggregated form that includes non-eligible cancers.

Intervention Practitioner Type (Applicable Only to Q2 and Q3)

Inclusion:

Studies with practitioners from primary care settings; the definition of primary care for this review was established as follows:

family physicians/general practitioners
general internists
obstetricians
gynecologists (obstetrics and gynecology practitioners are primary care providers for some women)
nurses
nurse practitioners
physician assistants
nutritionists
behavior counselors.

Exclusion:

All other health/medical professional groups.

Intervention Tool

Inclusion Question 2:

Tool or standardized method to systematically capture/collect/collate information related to family history for the relevant cancers or history of illness in other family members by any method whether self report or collected by a professional.

Exclusion Q2:

Any ad hoc approach that is not systematic, or uses open questions, when collecting family history for the relevant cancers or a personal medical history taking only with no components dealing with family history.

Inclusion Q3:

A standardized method or tool designed to stratify, or interpret level of familial cancer risk, in order to support decisions made by PCPs relating to management of risk of familial

cancer. The cancer risk calculation method or stratification method must be based primarily on family history information. The tool meets the definition of RAT (defined as one that specifies a user, target decision, knowledge, and timing), and, at a minimum, stratifies individuals into categories on the basis of risk of disease.

Exclusion Q3:

Family history tools without a risk calculation, stratification or patient-specific decision support component tool which calculate risk of mutation only, tools which require specialist genetics knowledge, and stand-alone guidelines.

Also explicitly excluded from Question 2 and Question 3:

- Articles with a primary focus on genealogy (non-medical family history)
- Articles which include mention of family history in some form but do not describe a tool or measure for use in clinical settings.

Applicability of Tools

Inclusion:

Tools designed specifically for use by PCPs, or tools developed for other practitioners with the potential to be used in primary care.

Exclusion:

Tools depending on specialist expertise in genetics for their use or interpretation.

Study Selection

A team of study assistants was trained to apply the eligibility criteria in preparation for screening the title and abstract lists and the full text papers. All levels of screening were done in web-based Systematic Review Software (SRS) (TrialStat Corporation, Ottawa, Ontario Canada). Standardized forms and a training manual explaining the criteria were developed and reviewed with the screeners (Appendix B[*]). For the title and abstract phase, two reviewers evaluated each citation for eligibility. Articles were retrieved if either one of the reviewers judged it as meeting eligibility criteria or if there was insufficient information to determine eligibility. For screening of full text articles, two screeners came to consensus on the identification, selection, and abstraction of information. Disagreements that could not be resolved by consensus were resolved by one of our McMaster research team members. The level of agreement for inclusion of studies was measured using kappa statistics.

Data Extraction

Appropriate data collection forms were developed for use in the systematic review (Appendix B[*]). All eligible studies from the selection phase (full text screening) were abstracted onto a data form according to predetermined criteria. One data extractor transferred the data onto these forms, and another checked the answers for accuracy before they were entered into SRS. Data entries were verified by the investigators responsible for summarizing the different report results sections.

Quality Assessment of Included Studies. To assess the quality of primary studies, we utilized standardized rating scales with acceptable reliability and validity. The specific scale

[*] Appendixes cited in this report are provided electronically at http://ahrq.gov/clinic/tp/famhisttp.htm

used was dependent on the study design and the research question. The Quality Assessment of Diagnostic Accuracy Studies (QUADAS)[103] was selected to evaluate studies primarily focused on accuracy (i.e., included in Q1). The Jadad scale was used for studies that were randomized controlled trials (RCTs).[104] For true observational study designs, the Down's and Black quality assessment scale was used.[105] Studies that were neither of these study designs were evaluated qualitatively without the use of formal checklists. The instruments used to evaluate quality are shown in Appendix B.*

Summarizing Our Findings: Descriptive and Analytic Approaches

A qualitative descriptive approach was used to summarize study characteristics and outcomes. Multiple publications on the same study cohort were grouped together and treated as a single study with the most current data reported for presentation of summary results. Standardized summary tables explaining important study population and population characteristics, as well as study results, were created. Meta-analysis was not undertaken for eligible studies within this review as the clinical heterogeneity between studies was considerable.

For those papers evaluated for research Q1, where the actual numbers of true and false positive and negative results (TP, FP, TN, FN) were presented, or where enough information was given to allow us to calculate and estimate these numbers, we recalculated the sensitivities and specificities with the accompanying 95 percent confidence intervals (CI) where possible.

For those papers evaluated for research Q2, descriptive data on the attributes of FHxTs were presented. For those FHxTs that had been formally evaluated, we reported outcome data separately for those tools compared with best estimate, and those compared with current practice comparators.

For those papers evaluated for research Q3, we presented descriptive data on the attributes of RATs, including the evidence base, if any, underlying each tool. For those RATs that had been formally evaluated, we reported data on outcomes relevant to the use of the tool in supporting decisions by users in practice (e.g., the pattern of referrals from primary to specialist care, patient perceptions of their cancer risk, health professional confidence in counseling patients concerned about their risk, etc.). Data regarding the validity of the knowledge component of each RAT (e.g., the scientific basis for guidelines, the predictive value of a stratification system, etc.) were captured where possible, but it is not within the scope of this review to consider the quality of such evidence (see "Topic Refinement", above).

Peer Review Process

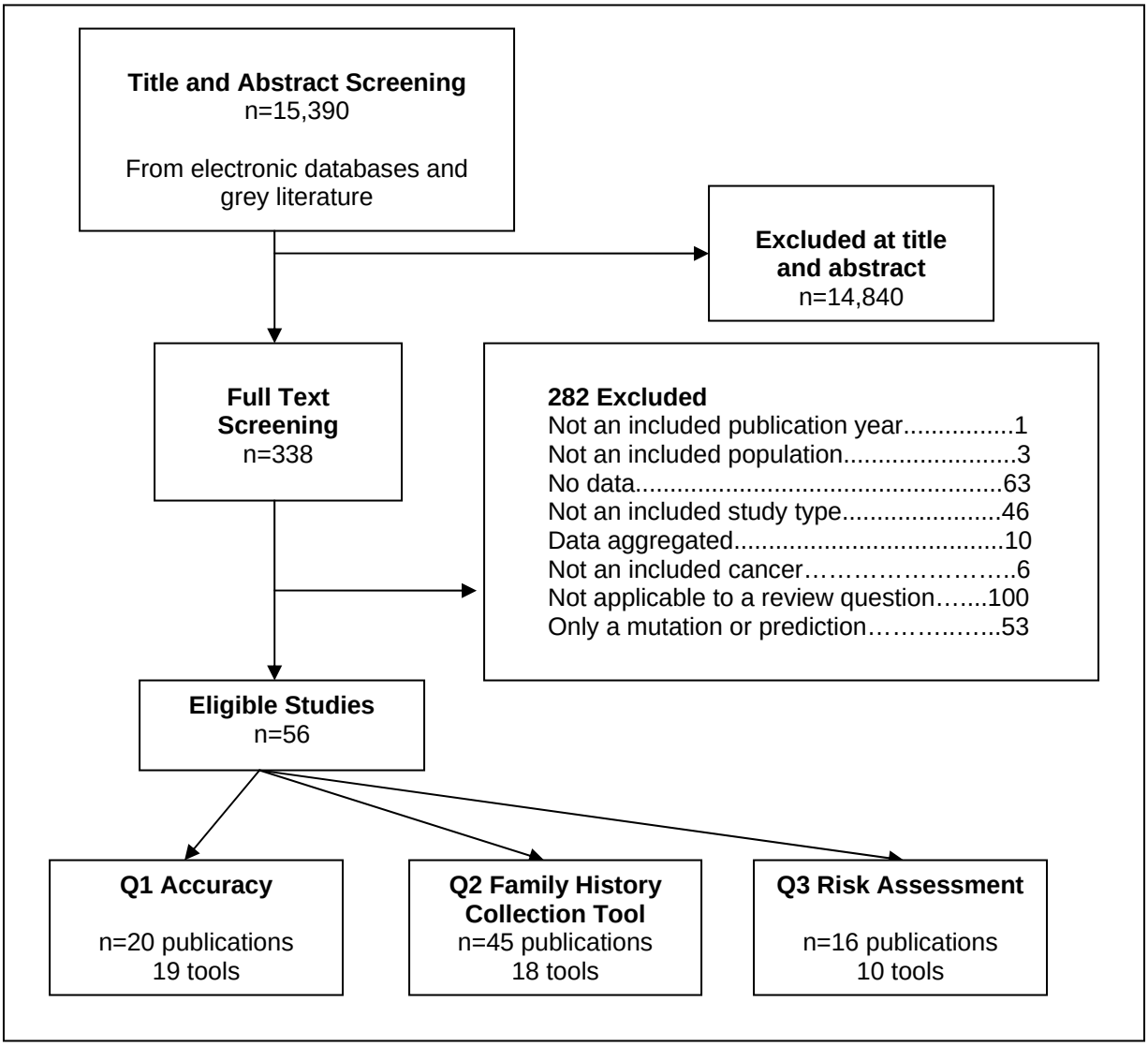
A list of potential peer reviewers was assembled at the outset of the study from a number of sources including our TEP, our partners, the McMaster research team, and the AHRQ. During the course of the project, additional names were added to this list by the McMaster Center and AHRQ. The content experts were asked to review the draft report and their comments and suggestions have been incorporated where possible for the final report (see Appendix E*).

* Appendixes cited in this report are provided electronically at http://ahrq.gov/clinic/tp/famhisttp.htm

Chapter 3. Results

The original search yielded 15,390 unique citations for all three research questions combined. During two levels of title and abstract screening, 14,840 articles were excluded. A total of 338 citations proceeded to full text screening. After the final eligibility screening a total of 56 studies were abstracted for data for the three research questions. Figure 2 details the number of eligible studies for each research question. The results of the systematic review are presented in this chapter according to the three main areas of investigation: accuracy, family history collection, and risk stratification.

Figure 2. Flow of studies to final number of eligible studies. Q1: Accuracy of family history reporting



Question 1: What is the Evidence That Patients or Members of the Public Accurately Know and Report Their Family History?

General Approach

We undertook a broad approach to identifying studies evaluating accuracy of reporting family history. We did not limit studies to those presenting specific diagnostic accuracy metrics and included studies whose primary aim was to ascertain repeatability (variation observed when conditions are kept constant by using the same instrument and individual and repeating within a short time interval).

Studies Reviewed

A total of 20 publications evaluated the accuracy of reporting family history and were eligible for data extraction. One study was based on two publications[10,11] leaving a total of 19 unique studies. Study and patient characteristics (such as study design, setting recruited, cancer type, relatives evaluated and criterion standard evaluated) are detailed in Appendix C* evidence tables.

We further classified studies by the type of accuracy that was evaluated as follows: 1) those studies (16 studies in 17 publications) which evaluated accuracy of family history reporting by attempting to verify the cancer status of relatives (i.e., accuracy compared with a gold standard), and 2) those (three) which evaluated the repeatability or reliability of the informant's knowledge of family history rather than the true status of the relatives (i.e., no external gold standard).

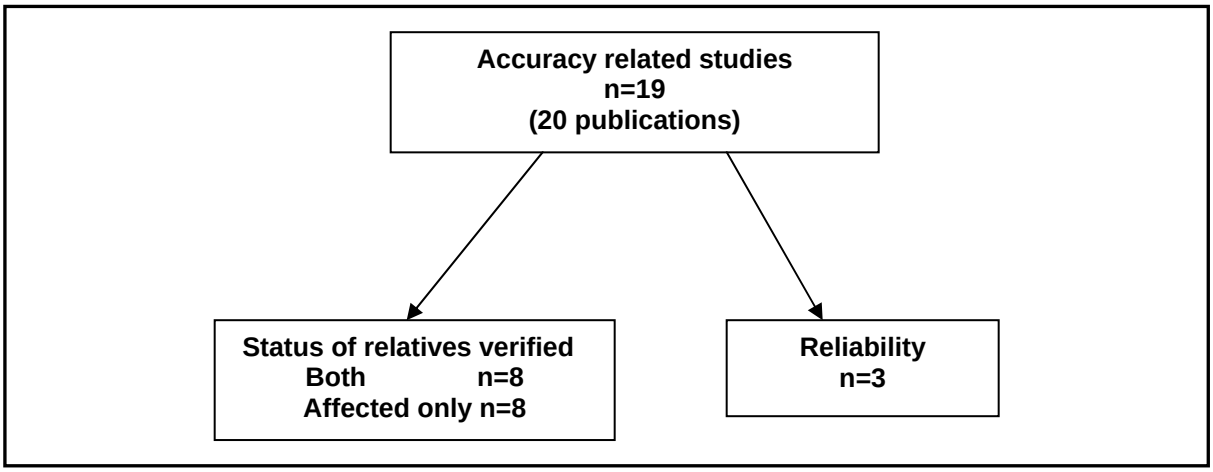
For the purposes of this review we use the terms "affected" and "unaffected" to refer to those relatives who have had cancer, and those who have not, respectively. We present the results for accuracy according to these groupings, and with regard to specific participant characteristics, type of accuracy evaluated (gold standard or reliability), method of verification, and potential predictors or confounders of accuracy of reporting family history (Figure 3).

In general we can summarize the accuracy studies as predominantly having recruited participants who had cancer. Within the 19 studies (20 publications), there were three that recruited an entire sample of patients who were free of cancer; two studies involving individuals at high risk for colorectal[7] or breast cancer,[8] and one involving women undergoing mammography.[9] In the four case control studies (five publications),[10-14] the controls were derived from the general population matched for age,[10,11] spouses of the informants or regional general practice lists,[14] and from a linkage from license registration and health care administration database.[13]

All studies were classified as case series except four which were case control studies. Several important factors restrict comparisons across accuracy studies, such as the cancer diagnosis of the informants and the cancer information collected about the relatives. There were more studies evaluating informants with breast cancer than other types of cancers; there was a single study evaluating ovarian cancer syndromes within the informants. Some studies probed only specific cancers within relatives while others reported on all cancers within their family

* Appendixes cited in this report are provided electronically at http://ahrq.gov/clinic/tp/famhisttp.htm

Figure 3: Flow of accuracy studies



histories. While there were only three studies with fewer than 100 informants, the number of relatives reported varied greatly between studies.

Studies Evaluating the Accuracy of Reporting by Verifying no Presence or Absence of Cancer in Relatives. Sixteen studies[7,8,10-17,19-24] evaluated the accuracy of family history reports by attempting to confirm the true cancer status of the relatives about whom informants provided information. Eight studies [13,14,19-24] verified the cancer status in relatives reported to be affected and those reported to be unaffected. The other eight studies (nine publications)[7,8,10-12,15-18] only confirmed the cancer status of relatives reported to be affected. We considered the former studies to be of higher methodological rigor and therefore evaluated these two groups of studies separately.

Studies With Verification in Both Affected and Unaffected Relatives. Table 2 shows the eight studies that verified the cancer status both of relatives reported to be affected and unaffected. Three were case control studies[13,14,19] that recruited participants with colon or colorectal cancer. The remaining five studies evaluated breast cancer patients and a single study evaluated patients with breast, ovarian or colorectal.[24] A single study[22] evaluated the accuracy of relatives' perception of "awareness of cancer" rather than informants' accuracy in reporting family members with cancer. Three studies[13,14,23] recorded the informant's recollection of any type of cancer in relatives, and the remaining studies examined reporting of relatives' colorectal cancer,[19,22] breast cancer,[20] breast or ovarian cancer,[21] or one syndromic group of cancers[24] (breast, ovarian or colorectal). In general, family history informant characteristics such as mean age, ethnicity, or education were poorly reported (Table 2). Similarly, characteristics of the relatives were also poorly reported within these studies.

The methods of family history collection varied with face-to-face interviews in two studies,[13,14] mailed survey in four studies,[19,21-23] and two with telephone interviews.[20,24] The methods of verification of relatives' cancer status varied between studies; also, within some studies different methods were used for checking the status of relatives reported to be affected and those reported to be unaffected. The methods used were: (1) personal interview (reportedly affected) and cancer registry; (reportedly unaffected[23]) (2) face-to-face interview, survey, and death registry;[24] (3) self report from mail-in survey of relatives;[22] (4) relatives' medical chart records and survey; (type not specified)[19] (5) cancer registry alone;[13,14,20] and (6) combined strategy (medical record or cancer registry or death certificate).[21]

Table 2. Study and patient characteristics of studies evaluating accuracy of reporting and verified in both affected and unaffected relatives

Author Year Country	Study Design	Informant n	Setting	Informant Cancer Status	Informant Male (%)	Informant Mean Age (yr)	Informant Ethnicity or Other	Method of Family History Collection	Cancers Types in Relatives	Method of Verification	Accuracy Metric Reported
Mitchell[14] 2004 UK	Case control	Ca 199 Co 133	Clinic	Cr	Ca 56 Co 55	Ca 64 Co 64	Ethnicity: NR Education: NR	F to F personal interview by genetics nurse	All cancers	**Affected relatives:** Scottish Cancer Registry **Unaffected relatives:** Scottish Cancer Registry	% agreement sensitivity specificity PPV NPV
Kerber[13] 1997 USA	Case control	Ca 537 Co 910	Ca clinic Co Population based	Colon (excluding appendix, rectosig-moid function and rectal cancers)	NR	30-79	Ethnicity: White Black and Hispanic proportion NR Education: NR	Computer assisted F to F personal interview computer assisted	All cancers but reported on Cr, uterine, Br, Ov, and prostate	**Affected relatives:** Cancer registry (a subset of data from the Utah Cancer Registry). Other: Utah Population Database **Unaffected relatives:** Utah Population Database (genealogic database)	Sensitivity Kappa OR for type of cancer

Abbreviations: Ca=cases; Co=controls; Br=breast; Ov=ovarian; Cr=colorectal; 1DR=first degree relative; 2DR=second degree relative; F to F=Face to face; NPV=negative predictive values; NR=not reported; OR=odds ratio; PPV=positive predictive values

* not specified but likely all female subjects due to the type of disease

Table 2. Study and patient characteristics of studies evaluating accuracy of reporting and verified in both affected and unaffected relatives (continued)

Author Year Country	Study Design	Informant n	Setting	Informant Cancer Status	Informant Male (%)	Informant Mean Age (yr)	Informant Ethnicity or Other	Method of Family History Collection	Cancers Types in Relatives	Method of Verification	Accuracy Metric Reported
Aitken[19] 1995 Australia	Case control Cross-sectional	Ca 341 Co 903 positive history: 419	Clinic following colon-oscopy	Cr	NR	NR	NR	Self-completed mail survey	Cr and any cancers or bowel polyp obstruction	**Affected relatives:** Medical records; medical history questionnaires were mailed to living relatives and surviving spouses asking whether the relative had colorectal or other cancer, if so, the age at diagnosis **Unaffected relatives:** Medical record; confirmation only on a random sample (n=231) of non affected relatives (n=6994)	Statistical differences between Ca and Co sensitivity and specificity extrapola-ted to entire sample

Table 2. Study and patient characteristics of studies evaluating accuracy of reporting and verified in both affected and unaffected relatives (continued)

Author Year Country	Study Design	Informant n	Setting	Informant Cancer Status	Informant Male (%)	Informant Mean Age (yr)	Informant Ethnicity or Other	Method of Family History Collection	Cancers Types in Relatives	Method of Verification	Accuracy Metric Reported
Glanz[22] 1999 USA	Case series	160	Population based	Cr	NR	50 19-84	Ethnicity: Japanese Hawaiian descent 78.9, White 9.4	Self-completed mail survey	Awareness of Cr	**Affected relatives:** Self-completed survey (postal): an epidemiological survey (see ref #7) and a psychosocial survey both **Unaffected relatives:** Self-completed survey (postal)	Data presented on accuracy of the relatives (not informants) in awareness of cancer, worry about getting and general knowledge of colon cancer
Eerola[21] 2000 Finland	Case series	NR	Clinic	Br	0*	NR	NR	Self-completed mail survey: Series 1&2 mailed	Br and Ov	**Affected relatives:** Medical records, cancer registry and parish registry **Unaffected relatives:** Medical records, cancer registry and parish registry	% incorrectly reported
Anton-Culver[20] 1996 USA	Case series	359	Population based registry	Br	0*	NR	Ethnicity: White 89% Hispanic 8% Asian 4% Education: NR	Telephone interview using structured questionnaire	Br	**Affected relatives:** Cancer registry **Unaffected relatives** Cancer registry	sensitivity specificity

Table 2. Study and patient characteristics of studies evaluating accuracy of reporting and verified in both affected and unaffected relatives (continued)

Author Year Country	Study Design	Informant n	Setting	Informant Cancer Status	Informant Male (%)	Informant Mean Age (yr)	Informant Ethnicity or Other	Method of Family History Collection	Cancers Types in Relatives	Method of Verification	Accuracy Metric Reported
Theis[23] 1994 Canada	Case series	165	Clinic	Br	0*	median 52 31-70	Ethnicity: NR Education: University degree 22% College or vocational training 38%	Self-completed mail questionnaire	Any cancer	**Affected relatives:** Personal interview **Unaffected relatives:** Cancer registry: A random sample of 1DRs reported as unaffected by cancer submitted to Ontario Cancer Registry	% agreement
Ziogas[24] 2003 USA	Case series	Br=670 Ov=123 Cr=318	Population based & clinic based: included if relative had cancer	Br 60% Ov 11% Cr 29%	15.5	NR	Ethnicity: Non-Hispanic Whites 92%	Telephone interview using structured questionnaire	One syndrome cancers (any cancer): focus on Br, Ov, and colon	**Affected relatives:** Personal interview, Self-completed survey (site completed), medical record, death certificate **Unaffected relatives:** Personal interview, self-completed survey (site-completed), death certificate	Probability of agreement in relative (yes cancer, no cancer) sensitivity specificity PPV NPV

Table 3 shows the sensitivities and specificities in studies that evaluated the status of both reportedly affected and reportedly unaffected relatives, where sufficient data were presented to compute these. One study[22] was excluded from Table 3 as it evaluated accuracy only in terms of "awareness" of parent or sibling's colorectal cancer. The sensitivity varied by the cancer of interest; for ascertainment of relatives with breast cancer, the range was 85 to 95 percent based on three studies; for colon cancer, 57 to 65 percent (studies using personal interview) and 86 to 90 percent (studies using telephone interview and self report) based on four studies; for ovarian cancer, 67 to 83 percent based on two studies; and for prostate cancer, 69 to 79 percent based on two studies. It is not clear to what extent the verification method of cancer registry versus medical records/death certificates contributed to the ranges observed within a cancer type and between the different cancer types. Similarly, it is difficult to establish how the various methods of collecting family history may have influenced the estimates of sensitivity.

In general, specificity across all cancer types and with varying modes of collection was consistently high, (Table 3). For ascertainment of relatives with breast cancer, the specificities were 95 to 98 percent; for colon cancer, 91 to 92 percent; for ovarian cancer, 96 to 99 percent; and for prostate cancer, 93 to 99 percent.

Table 3. Accuracy for studies evaluating patients who report cancer in first degree relatives in studies that verified the status of both affected and unaffected relatives

Study	Study Population/ Recruitment Site	Method of Collection	Criterion Standard	Sensitivity(95%) a/a+c; value[ ]	Specificity(95%) d/ b+d; value [ ]
Breast Cancer in Relatives					
Anton-Culver[20] 1996 USA Case series [cohort] (n=359)	Consecutive cancer patients from either a population based or cancer registry	Telephone interview trained interviewers (interviewers' background NR) Paper and electronic collection Format: Structured interview organized in tables to collect status of 1DRs and 2DRs	Cancer registry	54/60; [0.90] (0.79-0.96)	364/369; [0.98] (0.97-1.00)
Kerber[13] 1997 USA Case-control (cases =125, controls=206)	Population based cases with diagnosed colon cancer, controls from Diet, Activity, and Reproduction in Colon Cancer study (DARCC)	Personal interview (interviewers' background NR) Electronic medium collection Format: Structured interview with tables and codes to access information	Utah population database; Cancer registry	11/13; [0.85] (0.55-0.98)	107/112; [0.95] (0.90-0.98)

Abbreviations: Br=breast; Ov=ovarian; Cr=colorectal; 1DR=first degree relative; 2DR=second degree relative; NR=not reported; PCP=primary care provider

Table 3. Accuracy for studies evaluating patients who report cancer in first degree relatives in studies that verified the status of both affected and unaffected relatives (continued)

Study	Study Population/ Recruitment Site	Method of Collection	Criterion Standard	Sensitivity(95%) a/a+c; value[ ]	Specificity(95%) d/ b+d; value [ ]
Ziogas[24] 2003 USA Case series (n=1111)	Recruited from population based and clinic based family registries of Br, Ov and Cr cancer patients from Orange County	Telephone interview (interviewers' background NR) Electronic collection entered into Genetics Registry System (GRIS) Format: pedigree produced by GRIS	Confirmation in at least one of the following: (1) Medical records (pathology reports, tumour tissue samples, or clinical record), or (2) self report from affected and unaffected relatives of informants, or (3) death certificates of deceased relatives	188/197; [0.95] (0.91-0.98)	850/873; [0.97] (0.96-0.98)
Colorectal Cancer in Relatives					
Kerber[13] 1997 USA	As above	Personal interview (interviewers' background NR)	Cancer registry	11/17; [0.65] (0.38-0.86)	98/108; [0.91] (0.84-0.95)
Ziogas[24] 2003 USA	As above	Telephone interview (interviewers' background NR)	Medical records, death certificate	174/194; [0.90] (0.84-0.93)	1454/1498; [0.97] (0.96-0.98)

Table 3. Accuracy for studies evaluating patients who report cancer in first degree relatives in studies that verified the status of both affected and unaffected relatives (continued)

Study	Study Population/ Recruitment Site	Method of Collection	Criterion Standard	Sensitivity(95%) a/a+c; value[ ]	Specificity(95%) d/ b+d; value [ ]
Mitchell[14] 2004 UK Case control study n=199 cases, 133 controls	Cancer patients and community controls (from general practice lists in the same county and some spouses of affected cancer patients)	Personal interview by genetics nurse Paper collection; family history recorded in a structured proforma Format: Pedigree	Cancer registry (record linkage with discharge data, cancer registry, and cause of death)	30/53; [0.57] (0.43-0.69)	1256/1269; [0.99] (0.98-0.99)
Aitken[19] 1995 Australia Case control study (cases=74, controls=163)	Patients from PCP setting who had undergone colonoscopy	Self report (mail survey) Paper collection Format: self report questionnaire with tables for information on 1DRs only	Medical record, death certificates	70/81; [0.86] (0.77-0.93)	219/239; [0.92] (0.87-0.95)
Ovarian Cancer in Relatives					
Kerber[13] 1997 USA	As above	Personal interview (interviewers' background NR	Cancer registry	2/3; [0.67] (0.09-0.99)	117/122; [0.96] (0.91-0.99)
Ziogas[24] 2003 USA	As above	Telephone interview (interviewers' background NR)	Medical records, death certificate	35/42; [0.83] (0.69-0.93)	1017/1028; [0.99] (0.98-0.99)

Table 3. Accuracy for studies evaluating patients who report cancer in first degree relatives in studies that verified the status of both affected and unaffected relatives (continued)

Study	Study Population/ Recruitment Site	Method of Collection	Criterion Standard	Sensitivity(95%) a/a+c; value[ ]	Specificity(95%) d/ b+d; value [ ]
Prostate Cancer in Relatives					
Kerber[13] 1997 USA	As above	Personal interview (interviewers' background NR)	Cancer registry	11/16; [0.69] (0.41-0.89)	101/109; [0.93] (0.86-0.97)
Ziogas[24] 2003 USA	As above	Telephone interview (interviewers' background NR)	Medical records, death certificate	46/58; [0.79] (0.67-089)	557/564; [0.99] (0.98-0.99)

There were three case control studies that therefore allowed for comparison of reporting accuracy between cases and controls. They all involved cases who were patients with colorectal cancer, and controls who did not have cancer. The first study[19] suggested that cases were slightly more accurate than controls (82 percent vs. 76 percent) in reporting history of colorectal cancer in relatives. The second[14] indicated a sensitivity of 57 percent (95 percent CI 43-69) in cases compared with 53 percent (95 percent CI 31-74) in controls in reporting relatives with colorectal cancer. Within this study, the corresponding specificities were 99 percent (95 percent CI 98-99) in both cases and controls. The third study[13] compared cases and controls with respect to accuracy of reporting several cancer types in their relatives: (1) sensitivity of reporting relatives' breast cancer – cases 85 percent (95 percent CI 55-98), controls 82 percent (CI NR); (2) sensitivity of reporting relatives' colorectal cancer – cases 65 percent (95 percent CI, 38-86), controls 81 percent (CI NR); (3) sensitivity of reporting relatives' ovarian cancer – cases 67 percent (95 percent CI, 9-99), controls 50 percent (CI NR); and (4) sensitivity for reporting relatives' prostate cancer – cases 69 percent (95 percent CI, 41-89), controls 70 percent (CI NR). The corresponding specificities were: 1) relatives' breast cancer status - cases 98 percent, controls 91 percent; 2) relatives' colorectal cancer status – cases 91 percent, controls 94 percent; 3) relatives' ovarian cancer status – cases 96 percent, controls 98 percent; and 4) relatives' prostate cancer status – cases 93 percent, controls 94 percent. Taken together, these data suggest broadly similar specificities across the reporting of cancer types and between cases and controls – i.e., generally, the participants with and without cancer themselves were fairly good at correctly identifying relatives without a history of cancer, irrespective of the specific cancer family history being enquired about. In contrast, the sensitivities were generally lower, meaning that informants appeared to miss some cancers in affected relatives; the highest sensitivities were seen for reporting relatives' history of breast cancer. The results also suggested some differences in sensitivities of reporting between cases and controls – controls being more likely than cases to miss colorectal and ovarian cancers in relatives. In addition, the data from this study would suggest differences in sensitivities such that controls are more accurate for colorectal cancer but less accurate for ovarian cancers. In contrast, the specificities were similar for the cancers evaluated, suggesting no difference between cases and controls with respect to their accuracy in identifying who of their relatives does not have specific cancers. These observations are based on a single study and therefore should be interpreted cautiously.

Studies With Verification in the Affected Relatives Only. Table 4 shows the eight studies (nine publications)[7,8,10-12,15-18] that verified the cancer status only of relatives reported to be affected by cancer. A single study (two publications) was a case control design[10,11] and the remaining were case series. Two studies involved participants who did not have cancer but who were at high risk for breast[8] or colorectal cancer.[7] Two studies[15,17] involved patients who had prostate cancer, and one study involved colorectal cancer patients;[16] one study combined Li-Fraumeni Syndrome (LFS) and Hereditary Breast-Ovarian Syndrome (HBOCS)[12] (both women at genetic high risk and some with cancer) and one study (two papers)[10,11] involved women with breast cancer. A single study involved a range of participants with and without cancer.[18]

Five studies[7,12,16-18] assessed the informant's ability to report any cancer within relatives, and the remaining studies appeared to assess reporting of relative's breast cancer [8,10,11] or prostate cancer[15] history. In general, informant characteristics such as mean age, ethnicity, or education were poorly reported. Similarly, characteristics of the relatives were also poorly reported (Table 4).

Table 4. Study and patient characteristics of studies evaluating the accuracy of reporting verified in the affected relatives only

Author Year Country	Study Design	Informant n	Setting	Informant Cancer Status	Informant Male (%)	Informant Mean Age (yr)	Informant Ethnicity or Other	Method of Family History Collection	Cancers types in relatives	Method of Verification	Accuracy Metric Reported
Parent[10,11] 1995, 1997 Canada	Case Control	Sampled Ca 414 Co 429 Positive history Ca 68 Co 37	Clinic	Br	Ca 0 Co 0	Age for those reporting positive history 59 (30-79)	Ethnicity: NR except French speaking 100% and, born in Canada 97%. Education: Post high school 68%	F to F structured interview for 1DRs only	Br	**Affected relatives:** Medical record of 1DR	OR Mean difference in errors
Schneider[12] 2004 USA	Case Series	Family history of LFS 32 HBOCS 52	Clinic	LFS group are cancer free HBOCS both with and without Br or Ov cancer	LFS 47 HBOCS 28	LFS 72<40 HBOCS 40<40	Ethnicity: White:84.5% Education: LFS some college education 59%, HBOCS some college education 91%	Self-completed survey; interview type NR	All cancers	**Affected relatives:** Medical record; death certificate documented cancer histories often comprised four generations. Efforts were made to confirm all cancers in the extended pedigrees.	% agreement overall and as a function of cancer site. OR to predict accuracy

Abbreviations: Ca=cases; Co=controls; Br=breast; Ov=ovarian; Cr=colorectal; 1DR=first degree relative; F to F=face to face; LFS = Li-Fraumeni Syndrome; HBOCS=hereditary breast-ovarian cancer syndrome; NR=not reported; NPV=negative predictive values; PPV=positive predictive values; OR=odds ratio.
* not specified but likely all female subjects due to the type of disease

Table 4. Study and patient characteristics of studies evaluating the accuracy of reporting verified in the affected relatives only (continued)

Author Year Country	Study Design	Informant n	Setting	Informant Cancer Status	Informant Male (%)	Informant Mean Age (yr)	Informant Ethnicity or Other	Method of Family History Collection	Cancers Types in Relatives	Method of Verification	Accuracy Metric Reported
Breuer[8] 1993 USA	Case series	166	Clinic	Cancer free but high risk for Br	0	Median 40	Ethnicity: White 86-95% Education: no difference between those reporting and not reporting history	Self-completed questionnaire administered prior to 1st breast exam at cancer prevention centre	Br	**Affected relatives:** Personal interview; Medical record	Kappa for laterality of Br cancer (one versus both breasts) % agreement
Katballe[16] 2001 Denmark	Case series	87 had relatives with cancer from 1,200 surveyed	Clinic	Cr	NR	NR	NR	Interview by surgeons	All cancers (Amsterdam criteria)	**Affected relatives:** Medical record; cancer registry; death certificate.	Proportions True positive rates

Table 4. Study and patient characteristics of studies evaluating the accuracy of reporting verified in the affected relatives only (continued)

Author Year Country	Study Design	Informant n	Setting	Informant Cancer Status	Informant Male (%)	Informant Mean Age (yr)	Informant Ethnicity or Other	Method of Family History Collection	Cancers Types in Relatives	Method of Verification	Accuracy Metric Reported
Kupfer[7] 2006 USA	Case series	139	Clinic	Cancer free but high risk for Cr	32	NR	Ethnicity: White 66%, Black 27%, Hispanic 6% Asian < 1%	Telephone interview	All cancer (significant cancers)	**Affected relatives:** Medical record: verification of cancer histories was done by reviewing pathology and operative reports,hospital admissiona nd discharge summaries. Death certificate: death certificate and autopsy reports when available.	Chi Square testing differences between groups
Gaff[15] 2004 Australia	Case series	141 husbands from 301 68 wives from 85	Population based	Prostate	100 husbands 0 wives	58	Ethnicity: NR except only 8% were born in Australia Education: Diploma or degree 21%	F to F personal interview. Self-completed survey (mail)	Prostate	**Affected relatives:** Relatives' medical record.	OR for accuracy and completeness
King[17] 2002 USA	Case series	143 from 422	Clinic	Prostate	100	80% older than 60 yr	Ethnicity: White 98% Education: Post high school education 71%	Personal structured interview: (not reported if done F to F or by telephone)	All cancers	**Affected relatives:** Relatives' medical record.	% agreement

Table 4. Study and patient characteristics of studies evaluating the accuracy of reporting verified in the affected relatives only (continued)

Author Year Country	Study Design	Informant n	Setting	Informant Cancer Status	Informant Male (%)	Informant Mean Age (yr)	Informant Ethnicity or Other	Method of Family History Collection	Cancers Types in Relatives	Method of Verification	Accuracy Metric Reported
Sijmons[18] 2000 Netherlands	Case series	129 120 families	Clinic	Br, Ov, or Cr.	NR	NR	Ethnicity: NR Education: NR	Pedigree	All cancers	**Affected relatives:** Contact with living relatives', medical records (including pathology reports).	% agreement

The methods of family history collection varied with face-to-face interviews used in three studies (four papers),[10,11,15,16] telephone interviews in one study,[7] interview with mode not reported in one study,[17]survey completed in the clinic in one study,[8] and mailed survey in two studies.[12,18] The methods of verification of the relatives actual cancer status included: (1) personal or telephone interview with relatives and medical records,[8] (2) relatives' medical chart records alone,[10,11,15,17,18] and (3) a combined strategy (medical record or cancer registry or death certificate).[7,12,16]

From five studies[7,12,16-18] that reported on the informant's ability to report any cancer within relatives, only two studies provided information on the percent agreement as a function of the cancer reported. One study[18] indicated that breast and colorectal cancers had 93 percent and 89 percent agreement and lower rates of agreement for other cancers (42 percent for extra-colorectal alimentary tract and 37 percent uterine cancer). Another study[17] showed similar results with higher percent agreements for breast, colon, and prostate cancer (95, 92, and 86 percent respectively) in patients with prostate cancer. One study [12] who evaluated subjects with LFS and HBOCS found differences in the accuracy of reporting, with 85 percent agreement and 92 percent agreement with the reported cancers within their relatives.

Two studies reported on the accuracy of breast cancer within relatives and the percent agreement varied from 89 percent in one study[8] (with greater accuracy in living relatives with unilateral disease 94 percent) to a sensitivity of 90 percent (CI 95 percent 81-96) in a second study.[10,11] The specificity for this latter study[10,11] was estimated at 3 percent suggesting errors in reporting of unaffected relatives. One study[15] reported 90 percent agreement for relatives with prostate cancer. Another study[16] reported on the accuracy of colorectal cancer in relatives, with a sensitivity of 61 percent (CI 95 percent 36 – 83) and a specificity of 96 percent (CI 95 percent 88-99). Although, the magnitude of the agreements are generally high for reporting on some cancers, caution should be used when interpreting the results from studies that evaluate accuracy by confirming the status of the affected relatives only, as these contain errors and bias.

Other Factors That May Affect Reporting Accuracy. A variety of factors which could potentially influence accuracy of family history reporting were considered in some studies. Table 5 shows the factors that have been evaluated within some of these studies and, indirectly, the degree of evidence for each of these. We examined 15 characteristics, although some were only evaluated in a small number of studies. Those characteristics infrequently evaluated were: (1) type of first degree relative (1DR), (2) vital status of the relative, (3) number of relatives, (4) cancer history of interest, (5) cancer type of the informant, (6) race of the informant, (7) marital status, (8) laterality within breast cancer, (9) population versus clinic setting recruitment, (10) health insurance status, and (11) gender or age of diagnosis of the relative. It is difficult to generalize for these factors from this heterogeneous series of studies evaluating informants with different cancers and reporting on different cancers within their relatives. Moreover, some of the studies did not actually statistically evaluate differences between the factors of interest; thus, these findings should be regarded as indicating attributes that could be further evaluated in the future research.

Eight studies (nine publications)[8,10,11,13-15,18,19,24] evaluated the effect of age of the informant on accuracy; no clear trend was observed, and it was not possible to separate any effect of informant age from the possible effects of their own cancer type, gender, or differences in how age was categorized.

Table 5. Factors that can influence accuracy of reporting cancer family history

Factors	Main Findings
Infrequently evaluated factors	
Type of 1DR (n=2)	1) Anton-Culver 1996[20]: Slightly lower sensitivity identifying breast cancer for sisters than mothers when evaluating individuals versus families in informants with breast cancer. 2) King 2002[17]: Most accurate for identifying any cancer within brothers, then mothers; accuracy was lowest for fathers and sisters in informants with prostate cancer.
Deceased versus living relative (n=1)	1) Breuer 1993[8]: In informants who were free but high risk for breast cancer, reporting accuracy for laterality was better for living than deceased relatives (higher percent) with breast cancer.
Number of relatives within a family of the Informant (n=1)	1) Breuer 1993[8]: In informants who were free but high risk for breast cancer, there was no statistical difference as a function of the number of affected relatives (p=0.6) with respect to accuracy of reporting laterality of breast cancer.
Cancer type/site in relative as identified by the Informant (n=3)	1) King 2002[17]: In prostate cancer informants, the greatest inaccuracies occurred with reporting of bone, liver, and uterus was the most inaccurate. 2) Mitchell 2004 [14]: In informants with and without colorectal cancer, accuracy was greatest for breast and colorectal and least accurate for bronchus, lung, and stomach. 3) Ziogas 2003[24]: In informants with cancer (breast, ovarian, or colorectal) the negative predictive values and the probability of not having cancer did not differ as a function of the type of cancer in the relative. This was not the case for the positive predictive value and probability of having cancer, where the type of cancer did affect accuracy.
Type of cancer within the Informant (n=1)	1) Schneider 2004[12]: Age at diagnosis was less accurately reported than cancer sites by LFS relative to HBOCS. Overall, those with HBOCS cancer, were shown to be more accurate in reporting than those with LFS in a multivariate analysis (OR=3.3 p<0.01).

Abbreviations: 1DR=first degree relative; 2DR=second degree relative; 3DR=third degree relative; HBOCS=hereditary breast-ovarian cancer syndrome; LFS=Li-Fraumeni Syndrome; OR=odds ratio

Table 5. Factors that can influence accuracy of reporting cancer family history (continued)

Factors	Main findings
Race of the Informant (n=2)	1) Kupfer 2006[7]: In cancer free but high risk patients for colorectal cancer, Blacks were more likely to lack knowledge compared to Whites with regards to paternal family history ($p<0.05$). However, there were no differences with accuracy of maternal history ($p<0.9$). 2) Ziogas 2003[24]: White informants with cancer (breast, colorectal or ovarian) were more accurate for all cancer sites but not statistically significant for false positive rates relative to other races.
Marital Status (n=2)	1) Aitken 1995[19]: In informants with and without colorectal cancer, marital status had no effect on accuracy or reporting colorectal cancers in relatives. 2) Gaff 2004[15]: In men with prostate cancer, the relationship status (yes or no relationship) made no difference ($p=0.32$) to reporting prostate cancer within the relatives.
Reporting of laterality in Breast cancer (n=2)	1) Breuer 1993[8]: In informants who are free but at high risk for breast cancer, women reported more accurately relatives with single rather than bilateral cancer (statistically significant, $p<0.0005$); this was likely confounded by the status of living versus dead relatives. That is unilateral living relatives showed best accuracy and bilateral deceased showed worst for percent correct. 2) Theis 1994[23]: Informants with breast cancer were more accurate in reporting laterality for first degree than second degree relatives; however, the authors noted that some medical records did not actually provide information on laterality.
Setting from which Informant was recruited (n=1)	Ziogas 2003[24]: Although majority of sample with cancer (either breast, ovarian, or colorectal) was population based, they showed that clinic based informants were more accurate (less false negatives) than population based sample when reporting on one syndrome cancer within relatives.
Health Insurance Status (n=1)	Aitken 1995[19]: In informants with and without colorectal cancer, there was higher accuracy for those with private insurance ($p=0.01$).
Attributes of the Relatives (n=1)	Ziogas 2003[24]: In informants with cancer (breast, ovarian, or colorectal) the gender of the relative or age of diagnosis of the relative were not significant predictors of accuracy; the exception was for prostate cancer where younger age (60-69) of relative did affect accuracy.
More frequently evaluated factors	
Age of the Informant (n=8)	1) Aitken 1995[19]: In informants with and without colorectal cancer, accuracy increased with age ($p=0.03$) 2) Kerber 1997[13]: In informants with and without colon cancer, younger subjects (<66) generally reported family histories of cancer with greater accuracy than older (>67) patients with the exception of female reproductive tact cancers. 3) Mitchell 2004[14]: In informants with and without colon cancer, no differences in accuracy were found due to age. 4) Sijmons 2000[18]: Age did not affect accuracy of reporting both organ and type of disease. 5) Breuer 1993[8]: In informants without but at high risk for breast cancer, older women were shown to be more accurate reporting laterality. 6) Parent 1995, 1997[10,11]: Age of the informant with and without breast cancer had no effect on the accuracy of the age of diagnosis of the relative (no differences between cases and controls with regards to accuracy +/- 5 yrs); similarly, age was not a factor with the exception of informant over the age of 70, who made more mistakes than those younger. 7) Gaff 2004[15]: Men with prostate cancer and younger than 55 years were more accurate (OR=4.0 (95% CI 1.1-8.1, $p=0.03$) and more complete in their reporting (OR=3.6 (95% CI 1.6 – 8.4, $p=0.03$).

Table 5. Factors that can influence accuracy of reporting cancer family history (continued)

Factors	Main findings
	8) Ziogas 2003[24]: Younger informants were more likely to have lower false negative rates, particularly for breast (p=0.0008), colon (p=0.027) and prostate (p=0.02).
1DRs versus 2DRs or 3DRs (n=6)	1) Gaff 2004[15]: Informants with prostate cancer were more accurate reporting prostate cancer in 1DRs (OR 4.0 (95% CI 1.2-10.7, p < 0.0006) and more complete in their reporting (OR = 12.7 (95% CI 6.0-27.1, p< 0.001) compared to reporting for 2DRs or 3DRs). 2) Mitchell 2004[14]: Better sensitivity to detecting any cancer for 1DRs of informants with colorectal cancer; however, there were fewer 2DRs identified overall. 3) Schneider 2004[12]: Multivariate analysis showed more accurate for reporting any cancer within 1DRs (OR = 0.2, p < 0.01) in informants with LFS or HBOCS. 4) Theis 1994[23]: The reporting of the age of diagnosis for any cancer within relatives was more accurate for 1DRs than 2DRs in informants with breast cancer; this improved if age categories were dichotomized to above or below 50 yrs. Informants with breast cancer were more accurate for laterality for 1DRs than 2DRs. The authors did note that it was more difficult to obtain records for 2DRs overall. 5) Ziogas 2003[24]: Informants with cancer (breast, ovarian or colorectal) showed better positive predictive, negative predictive and % agreement was for 1DRs versus 2DRs. Conversely, there was greater risk of over-reporting in 1DRs rather than 2DRs. 6) Sijmons 2000[18]: The degree of kinship (closer relatives) improved the accuracy of reporting accuracy of age at diagnosis.
Gender of the Informant (n=6)	1) Aitken 1995[19]: Informants with or without colorectal cancer showed no statistically significant differences with regards to gender. 2) Mitchell 2004[14] Informants with and without colorectal cancer showed no difference in accuracy due to gender. 3) Kerber 1997[13]: In informants with or without colorectal cancer there was some evidence that women reported more accurately for ovarian cancer, but not much difference for other types of cancers. 4) Kupfer 2006[7]: Men who are free of colorectal cancer (but at high risk) were more likely to lack knowledge of family history relative to women. Of those that lacked family history, men were more likely to lack paternal history compared to women (p<0.01). No difference in the maternal family history between men and women. 5) Ziogas 2003[24] Male informants with cancer (type not specified) were more likely to over-report cases that were not true for all cancers compared to females. 6) Sijmons 2000[18]: There was no evidence that gender affected accuracy of reporting organ and type of cancer.
Education Level of the Informant (n=5)	1) Aitken 1995[19]: Informants with or without colorectal cancer showed no statistically significant differences with regards to education level. 2) Gaff 2004[15]: Education level not significant for accuracy or completeness in informants with prostate cancer. 3) Kerber 1997[13]: Education level had no influence on sensitivities or level of agreement in informants with or without colorectal cancer; however, those with college education were more likely to report breast and prostate cancer more accurately. 4) Parent 1995, 997[10,11]: Women with or without breast cancer showed no difference in accuracy due to education level. 5) Schneider 2004[12]: Higher education level OR=2.2, p<0.01 increased accuracy in women with LFS or HBOCS.

Six studies[7,13,14,18,19,24] evaluated the effect of the informant's gender on accuracy, and suggested no general effect. One study[13] suggested that women might be more accurate in correctly identifying relatives who had ovarian cancer. Another[7] suggested that there were gender differences in knowledge of paternal versus maternal family history. A third[24] suggested that men may over-report cancers compared to women.

Six studies[12,14,15,18,23,24] evaluated whether accuracy varied with the degree of relative whose status was being reported; there was a consistent trend towards increased accuracy of reporting for 1DRs compared to second degree relatives (2DR) or third degree relatives (3DRs) (Table 5). Several studies[14,23] noted challenges in confirming the true status of 2DRs and also that fewer 2DR and 3DRs were identified overall, suggesting the potential for reporting and confirmation biases.

Five studies (six publications)[10-13,15,19] evaluated the effect of education level using a variety of categorizations; all but one study[12] showed an effect on accuracy of reporting.

Quality Assessment of Studies

We evaluated quality of the accuracy studies at several different levels. At one level, we considered that the method by which the cancer status of the relatives was evaluated was of great importance in determining accuracy of reporting. At another level, we applied traditional internal validity criteria for study designs that included a comparison group or were considered diagnostic in their design. Since so few of the studies were of traditional study design with control groups, the majority of standardized assessment scales could therefore only be applied to a subset of papers. If we considered all the studies as "diagnostic" in their design, the QUADAS (a quality assessment scale for diagnostic studies) could be applied to most studies. However, not all 14 criteria (or biases) applied to the "diagnostic test" of "family history collection" were relevant in the context of accuracy of reporting; we selected three criteria from the QUADAS to compare the different studies.

Methodological Issues in the Verification of the Cancer Status of the Relatives. For accuracy of family history reporting, we considered verification of the status of both the affected and unaffected relatives to be of the highest quality. Studies that verified the status of the affected relatives only were considered to be of lesser quality or more susceptible to bias with respect to accuracy of reporting.

A number of difficulties were identified by authors with regards to ascertaining the cancer status of the relatives. The range of estimates of difficulties in obtaining some type of confirmation varied from 31 percent[19] to 9 percent.[21] Some of the difficulties with verification of cancer status of the relative included: (1) errors in medical records or pathology reports,[8,21] (2) death of relative prior to registry formation or other form of record keeping,[21] (3) relative emigrated to another geographic region, for which medical records were not available to the researchers,[8,21] (4) informants provided incorrect address or contact information for hospitals where relatives were treated,[8] (5) retrieval of death certificate information was impossible due to peculiar national laws affecting access by researchers or it was certain the files had been destroyed,[18] (6) some difficulty obtaining medical records of fathers compared to brothers, mothers, and sisters,[17] (7) reports concerned relatives for a branch of the family not of interest to the genetic investigation,[18] (8) the reported cases were late onset common type tumors in distant relatives not likely of interest in the referral,[18] and (9) informants were not in touch with the relatives concerned, so consent could not be obtained.[18] Some studies found it difficult to obtain

medical records of deceased relatives when recruitment of relatives for consent depended upon the informants contact.[9] There was some suggestion that verification rates were lower among negative relatives[19] as these tended to have less physician visits. Studies undertaken in countries with longstanding national cancer and death registries linked with service provision databases, tended to report very high rates of retrieval (97-98 percent) of verification of diagnoses on relatives.[16]

Although there were a variety of possible factors that impeded verification of the cancer status of the relative, not all studies excluded from the analysis those informants or relatives for which there were some difficulties in complete confirmation. Note that many studies did not compare the characteristics of the informants who did not wish to contact relatives for their medical records relative to those that did; similarly, comparisons between those relatives that provided consent to medical records and those that did not were not consistently undertaken.

QUADAS Assessment of Methodological Quality for Diagnostic Studies. We applied the QUADAS to those studies that verified the status within their relatives. The QUADAS, a 14 item quality assessment scale for diagnostic studies, was used to evaluate all studies eligible for accuracy of reporting. From these items, three were considered to be of greatest relevance to identifying potential biases within these studies that considered the collection of family history as the "diagnostic test" of interest and the method of verification as the "reference test". The first challenge was to assume that the "diagnostic test" was the same method of family history collection, in order to compare ratings across studies; clearly, the tools or methods used to collect family history varied significantly amongst studies. The second assumption, we made was that the reference standards specified within each study were equivalent across studies; that is that cancer registry verification and death certificate verification were equivalent.

Three items from the QUADAS were selected to evaluate spectrum bias, verification bias (both differential and partial), and blinding of those who verified the cancer status of the relatives. If present within the studies, each of these biases will result in overestimation of accuracy.

Spectrum Bias. The first question within the QUADAS asks: Was the spectrum of patients' representative of the patients who will receive the test in practice? Theoretically, being asked to take the "test" of cancer family history collection may be received by any person (with or without cancer) in clinical practice. Thus, it was challenging to define which informants are not "typical" of those likely to be tested in practice.

We would indicate the presence of spectrum bias, when the study population did not reflect the spectrum of informants likely to be seen within the clinical setting. For example, patients recruited due to their high risk for familial cancer syndromes would not reflect the spectrum of patients who would report cancer "family history", albeit they are an important group to evaluate. Similarly, in those studies with informants with cancer of differing severity or who were differentially assigned to study groups, the likelihood of spectrum bias is evaluated as high. We considered a sufficient spectrum of disease should include participants who reflect a complete range of staging (severity) of their cancer if the informant had cancer when the family history was collected. Additionally we believe that an adequate spectrum should reflect informants that included both genders in those studies that did not affect sex-specific organs, such as ovaries or prostate.

When considering the eight studies that verified the status of both the affected and unaffected relatives, the potential for spectrum bias was evident. In general, these studies did not report information on the informants with respect to the severity of disease. One case control study[13]

specified that the cases were "first primary cases" while the others of the same study design did not specify; however, there is still potential for spectrum bias in these studies. One of the studies evaluating breast cancer informants included women of restricted age (< 40 yrs), one third of subjects with bilateral breast cancer, referred to university hospital oncology centre.[21] Another[23] included informants that were English speaking, North American born, without brain metastases and had a least one 1DR with breast cancer. Both these studies, although they reflect patients likely to be seen in cancer clinics, do not represent the spectrum of breast cancer patients and therefore these studies have spectrum bias.

When considering those studies that evaluated the status of the affected relatives alone, the potential for spectrum bias was also evident. Two studies[7,8] recruited cancer free informants who were at very high risk for familial cancers due to a history of 1DRs already diagnosed with the cancer of interest. For the remaining studies, the severity of cancer within the informants was not detailed. This suggests the potential for spectrum bias.

Verification Bias. The fifth question within the QUADAS asks: Did the whole sample or a random selection of the sample, receive verification using a reference standard? Partial verification bias occurs when not all members of the study group receive confirmation of the diagnosis by the reference standard. Similarly, differential verification bias can occur if a subgroup of patients is given a different reference standard test. Partial verification bias can occur if some of the relatives identified by the informant did not have their cancer status verified. Even in studies where both affected and unaffected relatives were evaluated, we did observe that some studies were not able to verify the status of some of the relatives for many of the reasons stated above. One study,[19] (which employed very rigorous ascertainment methods of reportedly affected relatives, even sending notes to hospitals overseas for determining the status of deceased relatives), indicated that they did not attempt to check the medical record of all relatives who were cancer free (the overwhelming majority). Other studies[7,13,19,20,22] limited their evaluation or reporting to 1DR only; this in itself may reflect a type of differential verification bias in that not all relatives reported by the informants were verified. In those studies that evaluated only the affected relatives, clearly partial verification bias was present. The presence of partial or differential biases may lead to overestimation of accuracy.[106]

Blinding of Those Verifying Cancer Status in Relatives to the Status of the Informant. The eleventh question of the QUADAS states: Were the reference standard results interpreted without knowledge of the results of the index test? In the context of family history collection, our interest was in having those who verified the status of the relatives blinded to the cancer status of the relative and possibly the informant. It is possible that the research assistant extracting the cancer status of the relative, having knowledge of their cancer status, might interpret information (for example, from medical charts) differently than if they were not aware of the cancer status of the relative. Problems with lack of blinding may be less likely to occur in studies that use linkages with cancer or hospital registries; presumably the criteria for verification are not dependent on interpretation by a research assistant. However, there are errors associated with linking databases.

Of the eight studies that evaluated the status of both affected and unaffected relatives, three[13,14,20] relied solely on linkages with cancer or population health registries, and one[7] on patient report or health records alone; the remaining four studies used a combination of interview, health records and death registries. For those studies that evaluated the affected relatives alone, a single study[18] used computerized linkage alone with patient records to ascertain

the status of the relative. Overall, blinding of the status of the relative or the informant was not undertaken in the majority of studies.

Methodological Quality Assessment for Case Control Studies. We applied traditional internal validity criteria to the four case control studies (five publications),[10,11,13,14,19] using the Down's and Black standardized quality assessment scale.[105] One study[19] originated as a case control study but undertook a sample from the original to perform a validation study on accuracy of reporting; informants were selected on the basis of having relatives with cancer rather than their cancer status. We did not evaluate the quality of this study using the Down's and Black scale. The range of composite quality scores varied between 14 and 17 (from a possible score of 23), indicating a moderate level of quality for the three case control studies. One of the main methodological flaws was the omission of descriptions of the distribution of principal confounders in two of the studies (three publications).[10,11,13] In addition, only one study[13] enrolled subjects who appeared to be representative of the general population from which they were recruited and only one study (two publications)[10,11] indicated that cases and controls were recruited over the same time period. It was impossible to tell, based on the information contained in the studies, whether cases and controls were recruited from the same source population. There was insufficient information in all four studies to assess blinding, but all studies had reports of losses to follow up. The authors of one study[12] adjusted for potential confounders in the analysis.

The potential for selection or information bias in these four case control studies is difficult to assess. The lack of reporting on recruitment and blinding does not necessarily mean that the authors ignored these issues. It is possible that all subjects were recruited from the same source population and all subjects and investigators were blinded. The authors may simply not have reported this information in the published manuscripts.

Table 6. Study and patient characteristics of studies evaluating reliability

Author Year Country	Study Design	Informant n	Setting	Informant Cancer Status	Informant Male (%)	Informant Mean Age (yr)	Informant Ethnicity or Other	Method of Family History Collection	Cancers Types in Relatives	Method of Verification	Accuracy Metric Reported	Comments
Acheson[42] 2006 USA	Case series	151 from 755 61 for reliability testing	Clinic	Mixed cancers	7	41	Ethnicity: White 85%, Black 6% Native American 10% Hispanic 4% Ashkenazi Jewish 16% Education: Some college 51 %, Advanced degree 26%, High school 23%	Genetic Risk Assessment Tool (GREAT) and genetic consultation	Not specified	Not applicable: evaluated on test-retest reliability in sub-sample of 61 participants	% agreement Correlation	Some completed the questionnaire after genetic consultation
Geller[9] 2001 USA	Case series	33 from 50	Popula-tion based	Cancer free	0	48% (34-64)	Ethnicity: White 100% Education: Some college or greater 82%	Telephone interview	Breast and Ovarian	**Affected relatives:** Personal interview (telephone), Cancer registry: Vermont Breast cancer surveillance system. **Unaffected relatives:** As for affected relatives	Test-retest reliability co-efficient.	Only 27 % of relatives agreed to release information.

Abbreviations: Ca=Cases; Co=controls; 1DR=first degree relative; 2DR=second degree relative; F to F=Face to face; LFS=Li-Fraumeni Syndrome; HBOCS=hereditary breast-ovarian cancer syndrome; NR=not reported; OR=odds ratio

* not specified but likely all female subjects due to the type of disease

Table 6. Study and patient characteristics of studies evaluating reliability (continued)

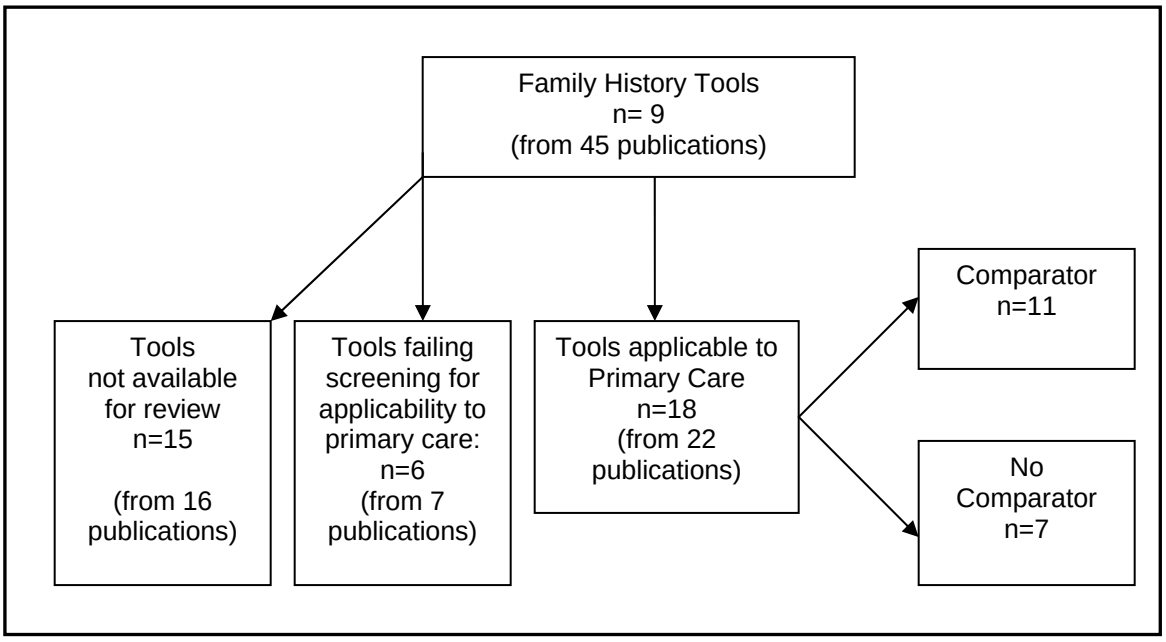
Author Year Country	Study Design	Informant n	Setting	Informant Cancer Status	Informant Male (%)	Informant Mean Age (yr)	Informant Ethnicity or Other	Method of Family History Collection	Cancers Types in Relatives	Method of Verification	Accuracy Metric Reported	Comments
Weinrich[33] 2002 USA	Case series	159 time 1, 100 time 2	Population	Prostate	100	50.4	Ethnicity: African American 100% Education: Some college or above 47%	Interview F to F time 1 and telephone time 2	Prostate	**Affected relatives:** Medical record **Unaffected relatives:** NR	% agreement OR for predicting change	59/159 could not be reached for second re-interview

Question 2: Improvement of Family History Collection by Primary Care Professionals Through the Use of Forms and Tools

Studies Reviewed

A total of 39 different tools, implemented in 40 unique studies, and reported in 45 publications passed full text criteria. Our initial focus was on identifying studies that described FHxTs developed or used in a primary care setting; however, after careful review, we noted that many studies described tools used in other settings that appeared potentially relevant to primary care (criteria for "primary care applicability" is outlined in Chapter 2). We also sent email queries to all authors of eligible studies that did not provide sufficient detail of the FHxT or a copy of the tool. Fifteen authors (of 16 publications) [8,10,11,16,17,21,23,25-33] did not respond in time for the publication of this review and therefore we were unable to determine whether the reported FHxT was applicable for use within primary care. For those studies for which we evaluated the FHxT, six tools from seven publications[13,18-20,24,34,35] were assessed as inappropriate for primary care; all of these had been developed and used in research settings. The scoring system and scoring of actual FHxTs is displayed in Appendix B.* Of the remaining 22 publications, four [36-39] described the prototype and final versions of the same FHxT (RAGS/GRAIDS), which we counted as a single tool; and two[40,41] were companion publications. Thus, 18 distinct tools, from 22 publications, were identified as being applicable to primary care settings (Figure 4). Full study details are summarized in the evidence table (Appendix C,* Table 2).

Figure 4. Flow of accuracy studies



* Appendixes cited in this report are provided electronically at http://ahrq.gov/clinic/tp/famhisttp.htm

Description of Tools

Target User. Fourteen tools[42-55] were designed for completion by patients, and four tools (eight publications)[36-41,56,57] were designed for use by health professionals.

Format. Eleven tools[43,45-49,51-55] were paper-based, generally in some form of questionnaire or structured questions. Four tools (eight publications)[36-41,44,50] were presented in a form for use on a desktop or laptop computer, including web-based and touch screen applications, and one on a personal digital assistant.[57] One tool[42] was an automatic telephone interview, and one was a structured interview schedule.[56]

Cancer Type. Fifteen tools, reported in nineteen articles,[36-43,45-50,52,53,55-57] were designed to collect data on family history of breast or breast/ovarian cancer. Nine tools (ten publications) [40-42,46-50,52,57] captured data on colorectal cancer and two[40,41] tools (three publications)[40-42] on prostate cancer. Five tools (six papers)[36,37,42,47,48,57] also captured data on one or more additional cancer types. For two,[51,54] the tool appeared to invite information on any cancer type.

Clinical Setting. Four tools (seven publications)[36-39,48,49,56] described tools which were implemented in family practice settings, and four tools[46,52,54,57] in internal medicine clinics. One tool[47] was implemented in a gastrointestinal clinic, and another[45] in a screening mammography setting. Three tools[46,54,55] were designed for use in cancer centers or clinics and three[42-44] were implemented in genetic clinics. One tool (two publications)[40,41] was web-based and designed for use by any health professional, and the remaining tool[53] was used in a large population-based research study. The published reports indicated that eight of the tools were used in a proactive way,[46,48,49,51,52,54,55,57] eight (12 papers) in a reactive manner,[36,38-41,43-45,47,53,56] and two in a mixed approach.[42,50]

Links to Risk Assessment Tools. The output of five tools (nine publications)[36-41,44,45,57] was linked directly to some form of defined risk assessment tool (RAT) (i.e., the family history data were converted directly into a risk categorization), although several of the publications describing other tools also described companion RATs.

Content of FHxTs. Fourteen tools[36-39,42-45,47-52,54-56] reported in seventeen publications, were designed to capture data on all, or selected, 1DRs. Eleven tools (fourteen papers)[36-39,42,44,45,47,49,50,52,54-56] were designed to capture data on all or some 2DRs, and one[49] on grandparents only. Five tools[42,44,45,47,50] explicitly went beyond 2DRs, although not necessarily to capture all 3DRs. For the remaining tools, the extent of family history enquiry was not explicitly described. For all tools except five[48,51,53,55,57] there were explicit instructions for users to capture data on relatives on both sides of the family. Two tools[49,54] were designed to explicitly capture ethnicity data. Further details of the data captured are presented in Summary Table 7.

Other Family History Tools. Eleven web-based FHxTs were also identified during the grey literature search. Nine tools were actually available from the web, and these are listed with relevance scores in Appendix B.* For all except one, (JamesLink)[50] which was included in the main review, no information was provided on their development or evaluation, which precluded their inclusion in the main review. The highest scoring of these tools for applicability to primary care were the Family History Tool developed by American Academy of Family Practice[107] and the U.S. Surgeon General's Family History Initiative.[108]

* Appendixes cited in this report are provided electronically at http://ahrq.gov/clinic/tp/famhisttp.htm

Table 7. Characteristics of family history tools

Paper	Tool	Cancer(s)	Target User	Medium, Form of Questions	Direct/ Automated Pedigree Output	Degree of Relatives Covered	Side of Family Covered	Data on Unaffected Relatives	Automatic/ Direct Risk Assessment Output
Hurt[55]	Family history questionnaire	Breast	Patient	Paper, Form NS	NR	1DR, 2DR	NR	NR	No
Yang[53]	Family history questions within larger questionnaire	Breast	Patient	Paper, Form NS	NR	NR	NR	NR	No
House[48]	Family history questionnaire	Breast Colorectal Ovarian Prostate Uterine	Patient	Paper, structured questions	NR	Selected 1DR	NR	No	No
Hughes[54]	Family history questionnaire	Breast Ovarian	Patient	Paper, structured questions	No	1DR, 2DR	Both	NR	No
Colombet[40,41]	Personalised estimate of risks (EsPeR)	Breast Colorectal Prostate	Professional	Web-based, Dynamic data input	Yes	NR	Both	NR	Yes
Braithwaite[44]	Genetic Risk Assessment in the Clinical Environment (GRACE)	Breast	Patient	Interactive software, structured pedigree production	Yes	1DR, selected 2DR, 3DR	Both	NR	Yes
DeBock[56]	Structured interview	Breast	Professional	In-person interview schedule, structured questions	NR	1DR, 2DR	Both	No	No

Abbreviations: 1DR=first degree relative; 2DR=second degree relative; 3DR=third degree relative; EsPeR= Personalized Estimate of Risks; NR=not reported; NS=not specified;
[1]Separate companion risk assessment tool (FCAT) described in Q3 results
[2]Includes prototype tool, Risk Assessment in Genetics (RAGS)

Table 7. Characteristics of family history tools (continued)

Paper	Tool	Cancer(s)	Target User	Medium, Form of Questions	Direct/ Automated Pedigree Output	Degree of Relatives Covered	Side of Family Covered	Data on Unaffected Relatives	Automatic/ Direct Risk Assessment Output
Benjamin[43]	Family history questionnaire	Breast Others	Patient	Paper, structured questions	No	1DR, further extent unclear	Both	NR	No[1]
Fisher[45]	Family history questionnaire	Breast Ovarian	Patient	Paper, question flow chart	No	Selected 1DR, 2DR, 3DR	Both	No	Yes
Kelly[51]	Family history questionnaire	All	Patient	Paper, Form NS	No	1DR	NR	NR	No
Qureshi[49]	Family history questionnaire	Breast Colorectal Ovarian	Patient	Paper, tabular questions	No	1DR Selected 2DR	Both	Yes	No
Acheson[42]	Genetic Risk Easy Assessment Tool (GREAT)	Breast Colorectal Ovarian Prostate Other	Patient	Automated structured telephone interview	Yes	1DR, 2DR, first cousins	Both	Yes	No
Frezzo[46]	Family history questionnaire	Breast Colorectal Ovarian	Patient	Paper, Form NS	No	NR	Both	No	No
Emery[36-39]	Genetic Risk Assessment in an Intranet and Decision Support (GRAIDS)[2]	Breast Ovarian Colorectal	Professional	Web-based tool, form NS	Yes	1DR, 2DR	Both	NR	Yes
Schroy[57]	Personal digital assistant application	Colorectal	Professional	Personal digital assistant, question prompts	No	NR	NR	No	Yes
Grover[47]	Family history questionnaire	Colorectal Other	Patient	Paper, structured questions	No	1DR, 2DR, 3DR	Both	NR	No

Table 7. Characteristics of family history tools (continued)

Paper	Tool	Cancer(s)	Target User	Medium, Form of Questions	Direct/ Automated Pedigree Output	Degree of Relatives Covered	Side of Family Covered	Data on Unaffected Relatives	Automatic/ Direct Risk Assessment Output
Murff[52]	Family history questionnaire	Breast Ovarian Colorectal	Patient	Paper, tabular questions	No	Selected 1DR, 2DR	Both	No	No
Sweet[50]	JamesLink	Breast Colorectal Ovarian Prostate Others	Patient	Touch-screen computer application, branched-point screens	NR	1DR, 2DR, Selected 3DR	Both	No	No

Evaluating the Family History Tools

The tools were evaluated using a range of study designs. In order to avoid ambiguity in terminology, we drew a distinction between the concepts of "comparator" and "control" (or "controlled"). In keeping with the methods described in Chapter 2, we use the term "comparator" to refer to the use of a reference method to assess the extent, nature and/or accuracy of the family history data captured by the tool in question, the comparators being either "ideal", best estimate interview, or current ("standard") practice. We use the term "controlled" to indicate a study design where there are at least two arms, one of which is the tool in question and the other an alternative method of capturing family history data. Thus, in a controlled design, participants are assigned (randomly or otherwise) to either the "tool" group or the control group. We considered crossover studies, where the order of data capture (tool or comparator method) was reversed for some participants, to be controlled studies. Table 8 describes the distribution of studies, in which tools were used, between the four possible categories of study design. We noted that one tool [44] was evaluated in a controlled study, but that no comparator for family history data capture was used, and no outcomes were reported which were relevant to the tool performance as a method of family history data collection (although outcomes relevant to performance as a RAT are presented under Question 3).

Using this approach, for the purposes of this review, we considered those studies which were uncontrolled studies with no comparator as descriptive, and those which either had a comparator or were controlled to be evaluative, so long as outcomes were reported which were directly relevant to the use of the tool as a method of capturing family history data.

Table 8. Classification of study types

		Controlled	Not controlled
Comparator	Genetics interview	Kelly[51*]	Acheson[42*] Benjamin[43] Fisher[45] Qureshi[49]
	Current practice	Emery[36-39] Frezzo[46] Schroy[57]	Grover[47] Murff[52] Sweet[50]
No comparator		Braithwaite[44]	Columbet[40,41] Hughes[54] Hurt[55] Yang[53] De Bock[56] House[48]

*Crossover design

Validity and Reliability

Six tools (nine publications) were described as having undergone a development or piloting phase[36-39,42,45,48,49,51] including one tool (two publications) (Risk Assessment in Genetics, RAGS)[38,39] which was the prototype for the Genetic Risk Assessment and Decision Support (GRAIDS) tool,[36,37] and a self-completion tool which was developed from a previously validated interview schedule.[51] Five studies assessed acceptability and ease of completion of the tool.[36,37,42-44] Qualitative techniques were also described in studies of four tools, including semi-

structured interviews with practitioners[38,39] and patients,[49] and focus groups with practitioners.[40,41,49] Three studies,[42,44,45] reported how long it took to complete the tool, ranging from 8 to 30 minutes. One study[42] reported test-retest reliability of 97 percent for 1DR, and 93 percent for 2DR respectively, and 98 percent for cancers identified.

Six tools were presented in seven descriptive papers,[40,41,48,53-56] without a comparator group or control arm. One study of a family history tool embedded in a RAT[44] presented no outcome data pertaining specifically to performance in capturing family history data.

The performance of the 11 remaining tools was assessed in some way against a defined comparator. For five tools,[42,43,45,49,51] this was a genetics interview. For one tool,[51] the self-completion questionnaire was assessed against the parent interview schedule administered by non-genetics investigators. Six tools (eight publications)[36-39,47,50,52,57] were compared with current practice in some form. This included the family history as recorded in patient charts, and accuracy or completeness of pedigrees derived from simulated patient histories drawn without access to a tool.

Outcomes

Evaluated Against Genetics Interview. Acheson and colleagues[42] described an automated telephone interview tool which was evaluated in a sample of genetics patients. Pedigrees obtained by the tool were blindly compared with those obtained from their clinic interview with a genetic counselor. There was an overlap between the data captured by the tool and the interview. The tool was statistically significantly better than genetics interview at identifying 2DRs and first cousins, and identified more cancers in 2DR and distant relatives. When the risk stratification based on the tool and interview pedigrees was compared, there was good agreement (kappa=0.70) for the breast cancer risk assessment, and moderate agreement for colorectal cancers and all cancers combined. Three families classified as high risk by the tool would be classified low risk on the basis of the interview, and one family classified as low risk by the tool would be classified high risk by the interview pedigree. The tool showed high test-retest reliability.

Qureshi and colleagues[49] described a paper-based, self-completion family history questionnaire, which was compared with a genetics interview conducted by trained researchers. On the basis of the family history captured, 24 percent of tool histories, and 36 percent of interview pedigrees, suggested possibly elevated disease risk which would warrant further investigation. The interview identified 15 percent more 1DRs, and 51 percent more 2DRs, than the tool. The validity of the risk assessments was not determined by a full genetics assessment, so it is not possible to conclude whether the tool was less sensitive or more specific than the interview comparator.

Benjamin and colleagues[43] assessed a standard paper-based, mailed, self-completion family history questionnaire with a clinical genetics interview, as part of a study whose primary aim was to evaluate a companion RAT. Using the interview as the gold standard, the tool had 95 percent sensitivity and 96 percent specificity for family breast cancer risk assessment. On the basis of the tool data alone (before the interview), 51 percent of patients would be assessed as having an elevated risk of familial breast cancer; following the genetics interview, this figure was 62 percent.

Fisher and colleagues[45] assessed a paper-based, patient-completed family history questionnaire in a study whose primary aim was to assess its embedded risk categorization

scheme. The participants were women attending for routine breast screening, and the history obtained by the tool was confirmed by follow up telephone interview by a genetic counselor. The authors report that this was to check that the tool data reflected the women's current knowledge of their family history, not to verify it. Of 45 women classified at population risk by the tool, none were reassigned a higher risk on the basis of the genetics interview. Of 45 women classified at elevated risk, none were reclassified as population risk. Further validation of the risk status of the participants through full genetic assessment was not reported.

Kelly and colleagues[51] describe a paper-based, patient-completed tool which was assessed in a sample of cancer patients. In a study whose primary aim was to explore psychosocial outcomes related to accuracy of family history reporting, they compared the questionnaire with an interview-based version of the same tool, using a randomized crossover trial design. The authors report around 77 percent concordance for reporting relatives' age, 81 percent concordance for reporting of relatives' diagnoses, and 82 percent concordance for reporting of age of diagnosis. There were no discrepant data on whether or not a relative had cancer. The order of completion of tools was not associated with differences in these outcomes.

Evaluated Against Current Practice. Emery and colleagues describe the development of a family history tool and RAT (GRAIDS), the prototype for which was RAGS.[36-39] GRAIDS was evaluated using a pragmatic cluster randomized controlled trial,[36,37] but no outcomes relating to performance as a FHxT were specifically reported. However, data were reported from a evaluation of the RAGS prototype,[39] in which 36 family physicians used three different methods to draw pedigrees and assess the risk of simulated patients. Pedigrees produced using the RAGS tool were statistically significant and more likely to be accurate than those prepared by a genetics software package (Cyrillic) or by traditional pen and paper methods (median correct pedigrees, 5.0/6 for RAGS, 3.5/6 for Cyrillic, 2.0/6 for pen and paper). Participating physicians also preferred RAGS (75 percent) over the other methods (8 percent preferring Cyrillic and 17 percent preferring pen and paper).

Frezzo and colleagues[46] compared a paper-based, patient-completed family history questionnaire with a genetics interview in a quasi-randomized parallel group study. Of the 39 internal medicine patients who completed the tool, two were identified at elevated risk of breast/ovarian cancer, three at risk of colorectal cancer, and one at risk of prostate cancer. Review of these patients' charts revealed only one patient at elevated risk, of colorectal cancer. In the group whose risk was assessed by interview, the corresponding figures are five at risk for breast/ovarian, and four at risk of colorectal cancer, on the basis of the interview, compared with two and two, respectively, on the basis of chart audit. No data were presented regarding the outcome of eventual genetic risk assessment, if any, of the participants.

Schroy and colleagues[57] developed an educational intervention for internal medicine residents and assessed the effect of a software tool designed for use on a personal digital assistant. Patients' family history relevant to colorectal cancer risk was assessed by a structured interview with a research assistant. Patients' charts were then audited to assess whether positive and negative colorectal cancer family histories were correctly documented. Of 33 residents to whom the software was sent, 29 acknowledged receipt, two acknowledged downloading it, and one indicated that they had used it clinically. Residents supplied with the tool were no more likely than control residents to document a positive cancer family history in patients' charts (41 percent versus 48 percent), but they were statistically significantly more likely to document a negative family history (89 percent versus 48 percent). The study had low statistical power to

detect small to medium effects, and the residents supplied with the tool also received extra educational intervention compared with controls.

Sweet and colleagues[50] describe the JamesLink system, which is a touch screen, patient-completed tool for capturing family history data. In a study of 362 ambulatory cancer patients, data for 165 indicated moderate or high risk status when reviewed by a geneticist; of these, 16 percent were consistent with a family cancer syndrome. Of 101 patients in the high risk category on the basis of tool data, the chart records suggested family cancer history for 69; seven of the latter had received a full genetics assessment. It was noted that the charts of only 69 percent of patients using JamesLink had family history information available.

Grover and colleagues[47] prospectively assessed concordance between family history information captured by a paper-based, patient-completed family history questionnaire and then subsequently (and independently) recorded in their cancer clinic charts. They noted discordance between data recorded by the two methods. For 127 (41 percent) of the cases in which there was discordant data, 37 charts (29 percent) had reported a negative cancer history, or not documented a cancer history, which was captured by the tool. For 69 patients (54 percent), only some cancers captured by the tool were documented in the notes, and in 21 patients (17 percent), the tool and the notes were completely discordant. Charts did not document 32 percent of cancers reported by patients in the tool, and a third of notes missed cancers in 1DRs captured by the tool.

Murff and colleagues[52] compared a paper-based, self-completion family history questionnaire with the charts of 310 internal medicine patients. They noted that the tool identified more 1DRs and 2DRs with colorectal, breast, or ovarian cancer than the charts and were more likely to capture the age of diagnosis for affected relatives, as well as more likely to identify relatives who were diagnosed before the age of 50. For all cancers together, the age of diagnosis was recorded in the chart for about 62 percent of affected 1DRs compared with 95 percent of those captured in the tool. The corresponding figures for 2DRs were 27 percent and 76 percent, respectively. These differences were highly statistically significant. Out of 48 patients who were identified as being at increased risk, the tool identified 29 who would have been missed by charts alone.

In summary, compared to genetic interviews as a gold standard, many FHxTs performed well. However, the studies reported here are limited because the genetic interviews were not supplemented with confirmation of relatives' reported medical histories. Compared with current practice, generally the family history documented in patient charts, FHxTs appeared to identify more relatives, more relatives with cancer, and more details about these relatives. In some cases, this would lead to reassignment of risk category and altered prevention plans. Again, validation of the "true" status of relatives was not performed.

Quality Assessment of Studies

Quality assessment using standardized checklists was undertaken on seven observational studies, five parallel RCTs, and one study[51] that was a crossover trial in which cancer patients were randomized to the order of either a personal interview or a survey and a second study. The quality scores for the seven observational studies[10,11,13,34,46,48,53] ranged from 14 to 21, thereby indicating a moderate to high level of quality. Initial reporting of hypotheses, interventions, outcomes, and sample characteristics was transparent and complete. However, the authors of only three of the studies[34,46,53] listed important confounders (two adjusted for confounding in the analysis[46,53]) and one author[53] reported on blinding. Reporting of subject recruitment was also lacking. Confirmation that subjects were representative of the entire population from which they

were drawn was provided in two studies;[11,46] recruitment of cases and controls from the same source population was mentioned in three studies.[19,48,53]

The five parallel RCTs scored either a 4[36,44,55] or 5[39,57] on the extended Jadad quality scale.[109] Major quality issues centered around a failure to describe randomization,[44,55] non-reporting of blinding,[36,39,44,55,57] and non-reporting of withdrawals,[44,55] or methods used to assess adverse effects.[36,39,57]

The absence of information on issues such as recruitment, randomization, and blinding suggests potentially biased results. Since it is not possible to assess whether the absence of information is linked to poor methods or poor reporting, the actual impact of any biases cannot be ascertained.

Other Methodological Aspects. Few studies described a sample size calculation.[23,36,37,39,42,49] Further, for comparative studies where concealment was necessary in qualitative assessment of the FHxT, only a few studies provided evidence that this had been performed.[43,49]

The participants of most studies would have had a better recall of their family history than the general public due to the fact that very few studies used an unselected general population.[46,48,49,54] Special populations included, for example, respondents with the cancers of interest,[47,51] or on a cancer registry,[25] and patients seen in specialist clinics.[42-45,50] Also, the sequence of FHxT evaluation against comparator may have affected patient recall. The FHxT was given first followed by the best estimate in six studies.[23,43-45,47,49] In one study, interpretation would have been affected by the paper family history questionnaire and structured "best estimate" interview having identical formats, with both approaches being delivered immediately after each other.[51] Other study designs affecting interpretation included non-randomized allocations[46,49,52] and variable response rate to FHxT. When reported, this varied from 40 percent[49] to 98 percent.[47] Non-completion of items accounted for about half the errors in an in-office self-completed FHxT.[45]

Research Q3: Risk Assessment Tools

General Approach

For the purposes of this review we followed the definition of RAT as described in Chapter 2. Some papers were identified which described tools consistent with this definition but which were not developed for use by PCPs, or were evaluated in settings other than primary care. We included some where we considered them to be "potentially applicable to primary care", in that they did not appear to require specialist genetics knowledge to be applied as intended.

Studies Reviewed

Sixteen publications, representing ten distinct tools, were included in this section of the review. Full study details are summarized in evidence tables (Appendix C*), which include information on the evidence cited in support of risk stratification and/or recommended clinical actions. Table 9 presents a description of the tools, assessed against the defined tool

* Appendixes cited in this report are provided electronically at http://ahrq.gov/clinic/tp/famhisttp.htm

Table 9. Assessment of risk assessment tool characteristics

Paper	Tool	Characteristics		
		User	Target Dcision	Knowledge Cmponent
Benjamin[43]	Familial Cancer Assessment Tool (FCAT)	health professional	clinical management	risk stratification algorithm
Braithwaite[44]	Genetic Risk Assessment in the Clinical Environment (GRACE)	patient	risk perception, preventive behavior	risk calculation, risk stratification, clinical guidelines
Colombet[40,41]	EsPeR computerized decision support system	health professional	clinical management	epidemiological data, risk calculation, clinical guidelines
Emery[36-39]	Genetic Risk Assessment in an Intranet and Decision Support (GRAIDS), and its prototype Risk Assessment in Genetics (RAGs) Computerized decision support system	health professional	clinical management	risk stratification, clinical guidelines
Fisher[45]	Family history questionnaire	patient	risk categorization	risk stratification algorithm
Gilpin[59]	Family History Assessment Tool (FHAT)	health professional	disease risk prediction	risk scoring system
Gramling[58]	Pocket laminated card	health professional	clinical management	risk stratification criteria, benchmark ranges, clinical guidelines
Skinner[31]	Cancer Risk Intake System (CRIS)	patient	preventive behavior	clinical guidelines
Watson[60,61]	Information pack	health professional	clinical management	clinical guidelines
Wilson[62,63]	Multifaceted computerized decision support system	health professional	clinical management	risk stratification criteria, clinical guidelines

Abbreviations: EsPeR=Personalized Estimate of Risks

characteristics. All tools fulfilled the criterion of timing of use (designed to be used before the health professional or patient takes the relevant decision).

Description of Tools

Cancer Type. Six tools, reported in seven papers,[43-45,58-61] were designed to assess risk of breast or breast/ovarian cancer only, four tools (seven papers) were designed to assess risk of breast/ovarian and colorectal cancer,[31,36-39,62,63] and one tool (two papers) focused on breast/ovarian, colorectal and prostate cancer.[40,41] No tool was identified that focused solely on ovarian cancer risk, colorectal cancer risk, or prostate cancer risk.

Clinical Purpose of Tool. All ten tools (16 papers) were designed to, in simple or complex ways, stratify individuals into risk categories, and all had a component which indicated some form of clinical or personal action.

Target User. Three of the tools[31,44,45] were designed for use by patients or the general population, the remainder having been designed for health professionals.

Knowledge Component. Each of the ten tools indicated at least one basis for the knowledge component. These components included: the Claus model;[36-39,43,44] the Gail model;[31,40,41] national recommendations (e.g., French National Agency for Health Evaluation,[40,41] the Australian National Breast Cancer Centre,[45] the U.S. Preventive Services Task Force,[58] and the Scottish Executive Health Department;[62,63] guidelines developed by professional groups (e.g., the UK Cancer Family Study Group[43,60,61] and the American Medical Association;[31,58]) and guidelines developed by local groups.[36,37,58,59] For one tool (four papers),[36-39] it was indicated that it was designed to facilitate the implementation of appropriate knowledge components in general, not any specific guideline or risk calculation program.

Implementation Format. Five of the tools (nine papers)[36-41,44,62,63] were presented in a computer or web-based format and the other five (six papers)[43,45,58-61] were presented in document-based format (Table 10). The five computer-based tools incorporated some form of family history data capture with risk calculation and guideline-based recommended actions.[31,36-41,44,62] Of the document-based tools, one was a paper-based form with checklist for each relative and an embedded scoring system,[59] two were paper questionnaires incorporating suggested actions;[43,45] one was a pocket laminated card;[58] and one was an information pack with a laminated card and other components.[60,61]

Applicability to Primary Care. Of the seven tools intended for use by professionals, five were developed explicitly for use by PCPs—either family physicians (four tools, 9 papers)[36-39,58,60-63] or physicians working in ambulatory care settings (one tool, two papers).[40,41] Two appeared to have been developed in settings other than primary care, or without involving primary care practitioners, but intended for eventual use in that setting.[43,59] One patient tool[31] was developed in a primary care setting, and the other two [44,45] were considered potentially applicable to use in primary care settings.

Evidence of Effectiveness. Findings related to the development of one distinct tool (RAGS/GRAIDS)[36-39] is presented across a number of publications. In general, we report findings for this as one distinct tool, but, where appropriate, we present (and clearly indicate) separate data relating to the evaluation of the prototype version (RAGS)[38,39] and the current version (GRAIDS).[36,37] For four tools (nine papers)[36-39,44,60-63] data were presented relating to effectiveness against a defined comparator, in achieving outcomes relevant to supporting decisions by users in practice. One tool[31] was evaluated in an uncontrolled before-after study.

Table 10. Tools presented in format designed to facilitate implementation

Target group	Implementation format	Study and details
Patients	Computer-based	Braithwaite 2005[44] GRACE - Structured family history collection with risk stratification and management advice. Skinner 2005[31] CRIS – stand-alone, touch screen system, capture of family history and other risk factor data, with production of printable, tailored messages designed to facilitate discussions with physician regarding preventive interventions.
Patients	Not computer-based	Fisher 2003[45] Structured family history questionnaire with binary risk stratification and advice to see doctor if high risk
Professionals	Computer-based	Colombet 2003[40,41] EsPeR - web-based, directed clinical and family history questions with risk calculation and individualized patient guidelines; also risks of avoidable causes of death according to demographic characteristics and printable summaries. Emery[36-39] RAGs - computer-based, pedigree drawing, risk calculation, guideline-based recommendations. GRAIDS, developed from RAGs - web-based, pedigree drawing, risk calculation, guideline-based risk reports and recommendations, patient information. Wilson 2006[62,63] Computer-based, directed family history questions, guideline-based recommendations, background information, web links, printable patient information leaflets, contact email, automatic draft referral letter
Professionals	Not computer-based	Watson 2000 Information pack, laminated card with referral guidelines, booklet with background information, patient leaflets. Benjamin 2003[43] Paper-based, directed family history questions, algorithm, suggested onward management. Gramling 2004[58] Pocket laminated card, risk stratification criteria, benchmark risk ranges for breast cancer, screening recommendations, contact numbers.

Abbreviations: CRIS=Cancer Risk Intake System; EsPeR=Personalized Estimate of Risks; GRACE=Genetics Risk Assessment in the Clinical Environment; GRAIDS=Genetic Risk Assessment in an Intranet and Decision Support; RAGs=Risk Assessment in Genetics

Data are reported to the evaluation of four tools (seven papers)[31,36,37,60-63] implemented in routine practice settings, including the GRAIDS tool, and three studies of two tools[38,39,44] where evaluations were conducted under "laboratory-type" conditions, including the RAGS prototype tool.[38,39] Table 11 summarizes the key points of these studies, including the range of outcomes measured. The remaining studies were tool development or descriptive studies, or the outcomes presented related to the validity or evidence base underlying the stratification system used rather than practice related outcomes.

Quality Assessment of Studies

Standardized quality assessment checklists were employed on the five studies that used randomized trial design. The Jadad scores ranged from 4 to 6.[36,39,44,60-63] Major problem areas were a failure to report whether the studies were blinded[39,44,60,62] and a failure to report numbers of withdrawals.[44,60,61]

The potential for bias in these studies appears quite low. Concerns about non-differential misclassification are always relevant when there is no blinding, but it is impossible to say whether subjects and investigators were not blinded or whether the authors of the manuscripts simply omitted mention of blinding in their published articles.

Table 11. Summary of evaluative studies

Study	Tool	Users	Design	Comparator	Outcomes
Braithwaite[44]	"GRACE" Computerized family history and risk assessment tool	Patients	RCT	Consultation with clinical nurse specialist	1. Acceptability 2. Risk perception 3. Anxiety, cancer worry
Emery[38,39]	"RAGs" prototype Computer-based decision support system	Practitioners	RCT	1. Pen and paper with available guidelines 2. Cyrillic risk calculation package	Number of appropriate management decisions
Emery[36,37]	"GRAIDS" Computer-based decision support system	Practitioners	Cluster RCT	Education session	1. Appropriateness of referrals 2. Patient risk perception 3. Patient knowledge 4. Patient cancer worry
Skinner[31]	"CRIS" Computerized cancer risk assessment tool	Patients	Uncontrolled before-after	None	Discussion of preventive action with physician
Watson[60,61]	Hereditary breast cancer information pack	Practitioners	Cluster RCT	1. No intervention 2. Tool plus education session	Rate of correct referral decisions
Wilson[62,63]	Multifaceted computer-based decision support system	Practitioners	Cluster RCT	Guidelines document disseminated by mail	1. Physician confidence 2. Patient understanding of cancer risk and risk factors 3. Proportion of referred patients at low and elevated risk

Abbreviations: CRIS=Cancer Risk Intake System; GRACE=Genetic Risk Assessment in the Clinical Environment; GRAIDS=Genetic Risk Assessment in an Intranet and Decision Support; RAGs=Risk Assessment in Genetics; RCT=Randomized Controlled Trial

Outcomes

Of the evaluative studies of tools directed towards professionals, one (two papers) (the RAGS prototype) was conducted under "laboratory-type" conditions[38,39] and three (five papers) were implemented in routine practice settings,[36,60-63] including the GRAIDS tool.[36,37] In the first of these, the computer-based RAGS prototype application[38,39] was compared with pen and paper risk calculation and a specialist risk calculation software package, Cyrillic. The evaluation showed a statistically significant effect of the tool on clinical management decision making for hypothetical cases presented in vignette form. In the study by Watson and colleagues,[60,61] a hereditary breast cancer information pack (presented with or without an active educational co-intervention) was compared with no intervention. An analysis of referral letters subsequently received by the relevant genetics centers and breast clinics indicated a statistically significant trend across the three groups in terms of compliance with referral criteria. In the study by Emery and colleagues,[36] a randomized controlled cluster trial was used to evaluate a complex intervention which comprised a web-based decision support system (the GRAIDS software, for which RAGS was the prototype) and a nominated "lead clinician" within the practice who received extra training in use of the software and was expected to manage all patients expressing concerns about family history of colorectal or breast cancer. All physicians and nurses in intervention practices also received a short educational session on cancer genetics and an introduction to the GRAIDS software. The control intervention was a mailed paper copy of the relevant regional guidelines, along with a short educational session on cancer genetics. The intervention arm contained an "adaptive" sub-group, in which extra training or software adjustment was used to increase actual use of the intervention. The primary outcome was appropriateness of referrals made to the regional genetics clinic, as assessed by comparison of each referral letter with the regional guidelines. For both cancer groups combined, 95 percent of referrals made by physicians in the intervention group met the guideline criteria, compared with 79 percent in the control group, a statistically significant result. For breast/ovarian cancer referrals, the proportions were 93 percent and 73 percent, respectively (statistically significant) and for colorectal cancer referrals, the proportions were 99 percent and 92 percent (not statistically significant). Overall, there were no statistically significant differences in proportions of patients who were subsequently assessed as being at increased cancer risk by genetics specialists. At the patient level, cancer worry scores were lower in those referred from intervention practices than from control practices, but no statistically significant differences were observed in knowledge or risk perception scores. The fourth study[62,63] compared a stand-alone computer based decision support tool with a control intervention of national guidelines disseminated by mail to family physicians. All practices within the health care administrative region were included in the trial, and all intervention practices received the intervention in some form. The primary outcome was physician confidence in four domains related to assessing risk, making clinical management decisions, and counseling patients, and no statistically significant differences were detected between intervention and control groups for any of the four domains. No statistically significant differences between groups were observed in secondary outcomes related to patients' risk perceptions, beliefs about breast cancer causation, or the risk of referred patients as assessed by genetics specialists.

Of the evaluation of tools directed towards patients, one was conducted under laboratory-type conditions,[44] and one was evaluated under conditions approaching routine practice.[31] The former[44] was an evaluation of the patient oriented "GRACE" tool. It was framed as an

equivalence or non-inferiority trial, but was not statistically powered for testing of *a priori* hypotheses. The comparator was a consultation with a nurse specialist who used the same evidence base to assess risk and offer advice. Outcomes related to patient acceptability, risk perception, anxiety and cancer worry, were all either statistically non-significant, or favored the control arm. In the second study;[31] the Cancer Risk Intake System (CRIS), a touch screen system for patients, was implemented in three primary care clinics. On the basis of family and other history, patients received tailored printouts including up to three messages regarding cancer prevention, to be used as an aid for discussions with their physician. A before-after evaluation suggested that the proportion of patients reporting a physician discussion about tamoxifen use increased from 4.8 percent at baseline to 27.7 percent after using CRIS; the corresponding pre- and post-figures for cancer genetic counseling were 2.8 percent and 28.2 percent, and for colonoscopy were 16.1 percent and 45.2 percent. The lack of a control intervention makes it difficult to assess the extent to which completing the baseline survey acted as a co-intervention.

Chapter 4. Discussion

This review explored both the accuracy of family history reporting by patients and the effectiveness of tools for collecting and using familial cancer history in a primary care setting. Ideally, patients are able to report accurate information on their family history, assisted by effective tools, and health care providers are able to use the information to make beneficial preventive and clinical management decisions.

Accuracy of Family History

In order to fully interrogate this question, evidence of accuracy had to be explored beyond the primary care setting. Although this encompassed broader clinical settings than the most comprehensive published review,[102] the results were fairly similar. Most eligible studies examining accuracy of reporting of cancer family history focused on breast or colorectal cancer, with fewer examining accuracy for ovarian and prostate cancers. In contrast to a previous review, [102] we did not limit studies to those verifying the status of unaffected relatives. This strategy yielded a broader set of studies that evaluated aspects of reliability but there were no significant gains in the number or quality of studies evaluating the primary question of accuracy. Overall, the few rigorous studies which fully evaluated accuracy (i.e., accuracy of reported absence and accuracy of reported presence of cancer in relatives) appeared to suggest that informants are more accurate in identifying which relatives are free of cancer (specificity) than in identifying relatives who have been affected by cancer (sensitivity). Our results indicate that family history reporting may be more accurate for first degree relatives than second degree or beyond, although few studies examined accuracy in the latter. Our findings also suggest that accuracy may be different for different cancer types, and influenced by the method of ascertainment of family history.

Future efforts to improve accuracy of reporting would be improved by explicit consideration of whether sensitivity or specificity is the primary goal, which is dependent on the clinical context and purpose of a family history oriented strategy. For example, maximizing sensitivity prioritizes the goal of missing as few "at risk" family histories as possible, and is consistent with a policy in which the potential benefits from finding potential cases carry more weight than the potential costs and harms of investigating individuals or families with false positive histories. In contrast, maximizing specificity prioritizes avoiding the potential costs and harms of false positives, and is consistent with a policy which directs limited resources towards only identifying individuals or families with the greatest likelihood of being at significant disease risk, at the cost of missing some true positives.

The studies reviewed focused on accuracy as a binary concept (presence or absence of cancer); we do not have evidence relating to the accuracy of other information which is relevant in cancer risk assessment such as information on age of onset. We are unable to comment on which gold standard is "best" for judging accuracy, nor on the effect of clinical setting or tool format. The accuracy of reporting by patients or members of the population cannot be completely separated from the performance of tools to gather such data,[51] but we had limited information on the latter and it was not always evident whether a structured Family History Tool (FHxT) was utilized in data collection.

We also have little insight into which informant characteristics are associated with more accurate reporting; future evaluations could consider formally examining factors such sex, age, and cultural background. It is possible that informants affected by cancer may seek out more complete information on their family history after their initial diagnosis, but we were unable to confirm this speculation.

Future research should also consider the issue of reliability of patient recall, including the issue of what is an "adequate" interval for studies of repeatability. We suggest that it would be helpful to try to separate the reliability of reporting as a psychometric property in an individual from the reliability of reporting as a function of extra knowledge sought by an individual from other family members in the period between first and second data collections.

In general, we might expect that the accuracy of family history reporting will improve in future, as current initiatives lead to more awareness on the part of the general public. It is not clear whether this will be countered by the effect that increased population mobility has on people's abilities to keep up to date with the health of more distant family members.

Family History Tools

The review identified a number of FHxTs developed for use in a primary care setting, most of which had not been evaluated against either best estimate gold standard or current primary care practice. Because of the limited number of studies, the evaluation of FHxTs was extended to relevant tools in non-primary care settings. Taken together, there was reasonable agreement between FHxTs and accepted best estimate gold standard, and, when compared to current primary care standard practice, FHxTs identified significantly more genetically relevant family history information. The clinical significance and added benefit of this added information still needs to be explored.

The tools identified in this review varied considerably, from those which took a comprehensive approach, emulating the geneticist's pedigree drawing interview to those which focused on identifying selected cancers in specific relatives. Many were designed to be used in the physician's office, in paper-based or electronic format. It has been suggested that other formats, such as web-based or mailed surveys, allow patients and consumers to (potentially) take "ownership" of their family history, offer them the opportunity to gather information from relatives,[37,43,45,49,52] and may make for better use of primary care provider (PCP) time. Some electronic tools require patients to assemble family history information in advance of the office visit, which may also promote accuracy and ownership. Some studies have shown high response rates to mailed FHxTs from PCPs[48,54] and "consumer empowerment" was the basis of the previous U.S. Surgeon General's Thanksgiving "Family History Day." [110,111] Several organizations have set up similar web-based FHxTs for public use[50,112] (http://www.norwichunion.com/healthtree/index.htm[113]; http://www.ama-assn.org/ama/pub/category/13333.html[114]).

The acceptability and ease of completion of FHxTs were assessed in only a few studies. These aspects of the tools' content and face validity should be an integral part of any evaluation of future primary care FHxTs.

While some authors[3] have identified elements that could be included in an "appropriate" family history (see Figure 5), there is no explicit consensus on a minimum data set covering the extent and the nature of family history data appropriate to primary care practice. Until the evidence base is clear, it is suggested that a minimum adequate cancer family history should include information on siblings, parents and grandparents (and the paternal and maternal lineage of the latter), specific enquiry about whether other relatives had the cancers of interest, and the ethnicity of the respondent. When cancer is identified, the age of diagnosis should also be noted, and other relatives with similar or related conditions identified.

Figure 5. Typical information obtained in Three-Generation Pedigree

Age or year of birth
Age and cause of death (for those deceased)
Ethnic background of each grandparent
Relevant health information (e.g., height and weight)
Illnesses and age at diagnosis
Information regarding prior genetic testing
Information regarding pregnancies, including infertility, spontaneous abortions, stillbirths, and pregnancy complications
Information also obtained for half-siblings
Consanguinity issues directly addressed

Rich EC, Burke W, Heaton CJ, et al. Reconsidering the family history in primary care. J. Gen Intern Med 2004 Mar;19(3):273-80.

In assessing individual tools, it is important to consider the notion of "appropriateness" in relation to individual patient factors (e.g., age) and in terms of patient population characteristics.[6] For instance, for a 40-year old patient it may be appropriate to enquire about all siblings, parents and grandparents, but children's health may not be as relevant for eventually determining cancer risk. Where there is concern about risk of familial breast cancer, information on aunts and uncles may be more informative than that on grandparents. Also, while some authors have suggested that a minimum family history should cover three generations[3,115,116] the reliability of information beyond first degree relatives and grandparents is unclear (see comments on accuracy, above). On the other hand, some genetic RATs require a count of the number of unaffected relatives, as well as those with a cancer of interest (e.g., Yang 1998[53]). Accurate risk assessment generally requires information on the side of the family (maternal or paternal) to which relatives with cancer belong, and most FHxTs identified this. Finally, ethnicity (an indication of ancestry [117]) may be associated with increased risk of particular disorders, including some cancers, but few tools were designed to capture such data on ethnicity.

We suggest that, in future FHxT development studies, it would be useful to distinguish between two different purposes for FHxTs – assembly and updating of "complete" family history information in a generic approach, and ascertainment of targeted information for specific disease risk assessment. For the latter, it may be logical to evaluate the performance of a FHxT as part of a disease-specific RAT, rather than as a stand-alone tool. For more generic tools, approaches to their rational development and evaluation would benefit from agreement on the "minimum family history dataset" for primary care purposes, bearing in mind that the goal in this setting is usually to stratify or triage risk rather than ascertain or diagnose a genetic condition. An evidence-based minimum dataset would take into account evidence on accuracy of patient

reporting of family history under primary care office conditions and might not necessarily have to replicate the extent or type of data captured in a clinical genetics setting. Table 12 lists some of the elements which could be considered for inclusion in a minimum dataset. It is presented to foster discussion and evaluation only as it is not within the scope of this review to formally assess its utility or feasibility.

Family histories are not static;[45,49] however, practical issues of updating family history have not been explored. On the one hand, PCPs may be able to assemble a patient's family history information over time, but on the other, necessary updates consume time and resources. Acheson[1] has reported that most family histories were completed on the first visit. It would be worth considering formally whether a staged approach over several visits leads to more accurate or extensive information, and clarifying the optimum interval for updates.

It seems logical that FHxTs are likely to produce most benefit if they are accompanied by management plans for patients at familial cancer risk; otherwise "proactive" family history collection by PCPs and/or consumers may be wasteful of time, energy, health care resources, and may even be harmful. While some guidelines[118] recommend that family history information should only be collected in response to patient enquiry about familial breast cancer risk or if the provider suspects increased cancer risk, others argue that family history collection is an integral part of good clinical practice in primary care and that failure to do so should be considered negligence.[51,119]

Risk Assessment Tools

An inclusive definition of RAT was used to capture the widest range of interventions potentially applicable to primary care. Their formats varied from fairly simple tools designed solely to stratify risk to those in which the capture of family history data was closely linked with management recommendations within a format designed to promote implementation in practice. We chose to focus on only those guidelines that had been formally evaluated in their own right, or embedded in some form of tool designed to promote use in practice. This decision recognized the very large number of familial cancer stratification guidelines which had been published over the time period of the review. We judged that an exhaustive approach to describing such guidelines would have provided little insight into the review questions and would likely be quickly out of date. However, for information, we listed the guidelines developed by national agencies or professional organizations in an Appendix B.*

Similarly, we focused only on those RATs which produced as output a risk of cancer, and excluded those for which the only output was risk of a given mutation. Our rationale was that family history reflects an integration of risk generated by genetic factors (including gene variants which may confer only modest increase in risk), shared environments, and common behaviors[2] and is an important predictor, in its own right, of disease risk. We suggest that this approach is consistent with the overall primary care perspective of the review, and increases the likelihood that the tools included would be accepted as relevant and usable by the target professional groups, outside the specialist genetics setting. In addition, clinically valid RATs which generate disease risk strata should, by definition, allocate families with high risk of mutation into the highest risk category, therefore alerting practitioners to their need for specialist assessment.

* Appendixes cited in this report are provided electronically at http://ahrq.gov/clinic/tp/famhisttp.htm

Table 12: Potential items for inclusion in minimum family history dataset

(a) Relatives on whom data may be captured	
Degree of relatedness	**Relationship**
	Informant [1]
	Spouse/partner[2]
First degree Blood relatives	Mother, father Brothers, sisters Sons, daughters
Second degree Blood relatives	Grandparents (both sides) Aunts and uncles (both sides) Half-brothers and half-sisters Grandchildren
Third degree Blood relatives	Cousins (both sides) Nephews and nieces (both sides)
(b) Items of information that may be captured	
Individual	**Item**
Informant/patient	Age or date of birth
	History of cancer, for each • age at diagnosis • specific information (e.g., bilaterality)
	History of other relevant medical conditions (depending on cancer)
	Results of relevant investigations, including genetic tests
	Ethnicity or ancestry • Self-identified ethnic group • Ethnic group of grandparents
Relatives	History of cancer, for each • age at diagnosis • specific information (e.g., bilaterality) • source/certainty of information
	History of other relevant medical conditions (depending on cancer)
	History of relevant investigations, including genetic tests
Living relatives	Current age/date of birth
Deceased relatives	Age at death • Source of information • Certainty of information
	Cause of death • Source of information • Certainty of information

[1] Personal medical history important in risk assessment

[2] May be relevant in respect of environmental and lifestyle/behavioral aspects of risk assessment

A large number of studies reported outcomes in terms of the distribution of patients across risk strata compared with an independent standard (e.g., an accepted guideline or an assessment by a specialist geneticist). This is an approach to assessing clinical validity (i.e., predictive value) and is of course dependent on the validity of the gold standard comparator. This review was not designed to assess this component of clinical validity, which ultimately requires studies that rigorously evaluate how well risk categorization predicts eventual disease outcome. We found that very few studies examined effectiveness in terms relevant to the questions posed in this review—either professional practice outcomes (e.g., improved confidence in clinical decision making) or patient outcomes (e.g., more accurate risk perception). Taken together, the evidence is not sufficient to make definitive recommendations, but it does tentatively indicate that RATs may improve the appropriateness of referral of patients for genetic counseling. Whether this is clinically or administratively worthwhile depends on the local clinical context. The extra benefit from a RAT must be set against the costs of implementation, particularly if there is already high compliance with referral guidelines. There is insufficient evidence to determine whether RATs, by themselves, are likely to improve physician confidence or skills in broader aspects of patient care related to familial cancer.

Just as with FHxTs, the potential effectiveness of RATs may be confounded by the strategy used to implement them in practice. Decision tools are complex interventions, and thus present challenges in their development, application, and evaluation.[36,120] Recent analyses have begun to identify the characteristics of decision tools that appear most likely to promote effectiveness in practice but few studies have evaluated patient outcomes. One of the most significant predictors of decision tool effectiveness appears to be the automatic provision of decision support as part of a practitioner's workflow.[121] This should become increasingly straightforward to achieve as electronic medical records become more widely implemented and linked with computer-based RATs. Other predictors of tool effectiveness include the provision of actionable recommendations (rather than just assessments); the provision of decision support at the time and location of decision making; the periodic feedback on performance to users; built-in features that promote the sharing of recommendations with patients; and systems that request documentation of reasons for not following recommended actions.[121] It is plausible that this emerging evidence on desirable characteristics of decision tools, while still preliminary, is applicable to family history based RATs. It should be noted that many tools have been evaluated by the same investigators who developed them, and that such studies seem to report higher levels of practitioner performance than studies where tools are evaluated by independent observers.

The barriers to the use of FHxTs and RATS tools in practice include lack of time,[122] lack of PCPs' confidence in their knowledge and skills in genetics,[80,123,124] and reimbursement policies.[3] Finally, even though a typical PCP may provide care to a significant number of patients with a history of familial cancer,[64] they may make up only a very small part of his or her daily practice. Hyland et al.[125] suggested that the rate of physician contact with women with a family history of breast cancer was about 0.6 consultations per month per family physician. Systems to implement apparently efficacious tools therefore need to take account of these barriers, and broader consideration could be given to the cost-effectiveness of developing tools which assess familial risk across a range of common chronic disorders.

All of these factors taken together suggest that effective RATS require a coherent, evidence-informed approach to their design, consideration of their integration with other clinical and office systems, and attention to contextual factors which might moderate their effect, and their marginal benefit in practice.

Limitations

The studies reviewed in this report were limited to those published in English; however, the impact of any language bias is offset by the optimal applicability to English speaking countries for which this report was prepared. Our peer review process allowed content experts in this area to identify any additional studies (both published and unpublished) of relevance for this review thereby minimizing the likelihood of publication bias. In addition to using several web-based search engines, our search of relevant grey literature was limited to sites specified by the investigators, our technical expert panel (TEP), and peer reviewers. We contacted the authors of eligible studies to request copies of the tools or methods used to ascertain eligibility of family history method for this review. The majority of authors contacted did respond, but some did not. Language bias also limited the ability to interpret non-English FHxT, however this had a minimal impact on the studies described and evaluated. The budget and timelines available, however, were limiting factors in pursuing complete retrieval of all the instruments used to collect family history in the eligible studies.

Our criteria for defining a systematic FHxT or RAT resulted in the exclusion of guidelines, recommendations or mutation risk calculators (see above). These are all "decision tools" and, even though a rationale was provided, their exclusion was arbitrary. The result may be that the review has underplayed the value of guidelines (however published) in promoting effective clinical practice, and overlooked "specialist" tools which might actually be useful in primary care without further modification. Similarly, the definition used for applicability to family practice was based on criteria developed within our investigative team and has not been subject to external scrutiny. In the context of accuracy of family history reporting, eligible studies did not use the same method to ascertain family history or verify status within all relatives. As such, interpretation of the metrics of accuracy was limited to the methods of family history ascertainment and verification used in these studies.

Conclusion

The accuracy of self reported family history has implications for the correct risk assessment and management of patients. Accuracy of cancer family history reporting appears to be dependent on cancer type and method of collection, and accurate reporting of absence of cancer (specificity) appears to be greater than accurate reporting of presence of cancer (sensitivity). Accuracy of recall and reporting may be influenced by both patient factors and by the method used to capture the data (the tool). No studies appear to have examined both of these together, so it is impossible to comment definitively on their relative contributions to any lack of accuracy.

Family history is a fundamental element of health information, and the ability to take an adequate and accurate family history should be recognized as a core skill for all PCPs, irrespective of the availability of tools. Very few FHxTs have been developed for, and evaluated in, primary care settings. Further, few tools have been compared with either "best practice" (genetic interview) or current primary care practice (family history as recorded in charts). Although the evidence is very limited, and depends on extrapolation of studies of tools in settings other than primary care, it suggests that systematic FHxTs may add significant genetic family history information compared to current primary care practice.

A number of RATs, of varying format and complexity, have been developed for primary care settings, and a few of these have been evaluated in controlled trials. These studies provide tentative evidence for the effectiveness of such tools, but their utility in routine practice has not been established.

Recommendations

1. Consensus should be reached on the extent of family history enquiry necessary for different clinical purposes and circumstances, taking into account the likelihood of accuracy of self reported information for different relatives, and the use to which the information will be put (e.g., overall or specific risk assessment).

2. The benefits, costs and harms of using patient-completed tools for systematic family history collection and risk assessment, as a substitute for, or complement to, professional tools should be further examined. As well as assessing technical outcomes such as accuracy and completeness of data captured, evaluations should consider outcomes which relate to patient "empowerment" and the use of practitioner and health care resources.

3. Further research is required to identify the specific strategies (e.g., sending tools home with patients) and tool features which promote the most accurate reporting of family history information.

4. The optimum interval for updating a patient's family history information in primary care should be formally evaluated.

5. Further evaluation of FHxTs and RATs in routine clinical settings and practice is required. Studies should: adopt appropriate comparators (generally current practice); ensure that tools are optimized (in terms of, for example, face and content validity) before evaluation; measure outcomes that relate to utility in routine practice; measure outcomes that provide information on potential costs or harms as well as benefits; and address or explore contextual factors which may modify utility in practice (e.g., practice infrastructure, time available).

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Acronyms/Abbreviations

1DR	First Degree Relatives
2DR	Second Degree Relatives
3DR	Third Degree Relative
BED	Best Estimate Diagnosis
BRCAPRO	Breast Cancer Program
BOADICEA	Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm
CDC	Centers for Disease Control and Prevention
CFHF	Comprehensive FH Form
CI	Confidence Interval
CR	Cancer Registry
CRC	Colorectal Cancer
CRIS	Cancer Risk Intake System
CVD	Cardio Vascular Disease
Cyr	Cyrillic
DOB	Date of Birth
DOR	Diagnostic Odds Ratio
DQ	Direct Question
EsPeR	Personalized Estimate of Risk
FAP	Familial Adenomatous Polyposis
FCAT	Familial Cancer Assessment Tool
FHAT	Family History Assessment Tool
FHQ	Family History Questionnaire
FHS	Family History Score
FHxT	Family History Tool
GCI	Genetic Counsellor interview
GI	Genetic Interview
GNI	Genetic Nurse Interview
GP	General Practitioner
GRACE	Genetic Risk Assessment in the Clinical Environment
GRAIDS	Genetic Risk Assessment in an Intranet and Decision Support trial
HBOCS	Hereditary Breast-Ovarian Cancer Syndrome
HNPCC	Hereditary Nonpolyposis Colorectal Cancer
IM	Internal Medicine
LFS	Li-Fraumeni Syndrome
LR-	Negative Likelihood Ratio
LR+	Positive Likelihood Ratio

MR	Medical Records
N/A	Not Applicable.
NICE	National Institute for Clinical Excellence
NIDDM	Non-Insulin Dependent Diabetes Mellitus
NPV	Negative Predictive Value
NR	Not Reported
NSW	New South Wales
PAC	Probability of Agreement of Cancer
PANC	Probability of Agreement of No Cancer
PC	Primary Care
PCP	Primary Care Provider
PDA	Personal Digital Assistant
PMH	Past Medical History
PPV	Positive Predictive Values
PSI	Physician Structured Interview
Q	Question
QOL	Quality Of Life
RAGS	Risk Assessment in Genetics
RAT	Risk Assessment Tool
RCT	Randomized Controlled Trial
SD	Standard Deviation
SE	Standard Error
SRS	Systematic Review Software
TED	Thrombo-Embolic Disease
VS	Versus

APPENDIXES

Appendix A. Exact Search Strings and Web Sites Searched

All searches updated to July 22, 2007

Ovid MEDLINE(R)

1 Breast Neoplasms/
2 exp Colorectal Neoplasms/
3 exp Ovarian Neoplasms/
4 exp Prostatic Neoplasms/
5 ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
6 or/1-5
7 (note or comment or editorial or letter).pt.
8 exp Medical History Taking/
9 exp Family/ or exp Family Health/
10 exp Pedigree/
11 limit 10 to humans
12 ((family or familial) adj3 (histor$ or history-taking or risk$)).ti,ab.
13 anamnesis.ti,ab.
14 (human adj2 pedigree).ti,ab.
15 (genetic adj2 (risk adj3 (assessment or evaluation))).ti,ab.
16 genogram$.mp.
17 ((famil$ or heredi$ or inherit$) adj3 (cancer$ or carcinom$ or neoplasm$)).ti,ab.
18 or/8-9,11-17
19 6 and 18
20 limit 19 to yr="1990 - 2007"
21 20 not 7
22 exp Neoplasms/
23 cancer$.ti,ab.
24 or/22-23
25 (method$ or tool$ or form$).ti,ab.
26 ((genetic or famil$ or heredit$ or inherit$) adj2 (risk adj3 (assessment or evaluation))).ti,ab.
27 26 and 25
28 (famil$ histor$ adj3 (method$ or tool$ or form$)).ti,ab.
29 27 or 28
30 29 and 24
31 limit 30 to yr="1990 - 2007"
32 31 not 7
33 32 or 21

EMBASE

1 exp Neoplasms/
2 cancer$.ti,ab.
3 or/1-2
4 (method$ or tool$ or form$).ti,ab.
5 ((genetic or famil$ or heredit$ or inherit$) adj2 (risk adj3 (assessment or evaluation))).ti,ab.
6 4 and 5
7 (famil$ histor$ adj3 (method$ or tool$ or form$)).ti,ab.
8 or/6-7
9 3 and 8
10 limit 9 to yr="1990 - 2007"
11 exp Breast Cancer/
12 exp Colon Cancer/
13 exp Ovary Cancer/
14 exp Prostate Cancer/
15 ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
16 or/11-15
17 (note or comment or editorial or letter).pt.
18 exp anamnesis/
19 ((family or familial) adj3 (histor$ or history-taking or risk$)).ti,ab.
20 anamnesis.ti,ab.
21 (human adj2 pedigree).ti,ab.
22 (genetic adj2 (risk adj3 (assessment or evaluation))).ti,ab.
23 ((famil$ or heredi$ or inherit$) adj3 (cancer$ or carcinom$ or neoplasm$)).ti,ab.
24 genogram$.mp.
25 or/18-24
26 16 and 25
27 limit 26 to yr="1990 - 2007"
28 27 not 17
29 10 not 17
30 or/28-29

CINAHL - Cumulative Index to Nursing & Allied Health Literature

1 (note or comment or editorial or letter).pt.
2 exp Medical History Taking/
3 exp Family/ or exp Family Health/
4 exp Pedigree/
5 limit 4 to humans [Limit not valid in: CINAHL; records were retained]
6 ((family or familial) adj3 (histor$ or history-taking or risk$)).ti,ab.
7 anamnesis.ti,ab.
8 (human adj2 pedigree).ti,ab.
9 (genetic adj2 (risk adj3 (assessment or evaluation))).ti,ab.

10 ((famil$ or heredi$ or inherit$) adj3 (cancer$ or carcinom$ or neoplasm$)).ti,ab.
11 or/2-3,5-9,10
12 exp Breast Neoplasms/
13 exp Colorectal Neoplasms/
14 exp Ovarian Neoplasms/
15 exp Prostatic Neoplasms/
16 ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
17 or/12-16
18 11 and 17
19 limit 18 to yr="1990 - 2007"
20 19 not 1
21 exp Neoplasms/
22 cancer$.ti,ab.
23 or/21-22
24 (method$ or tool$ or form$).ti,ab.
25 ((genetic or famil$ or heredit$ or inherit$) adj2 (risk adj3 (assessment or evaluation))).ti,ab.
26 24 and 25
27 (famil$ histor$ adj3 (method$ or tool$ or form$)).ti,ab.
28 or/26-27
29 23 and 28
30 limit 29 to yr="1990 - 2007"
31 30 not 1
32 20 or 31

EBM Reviews - Cochrane Central Register of Controlled Trials

1 Breast Neoplasms/
2 exp Colorectal Neoplasms/
3 exp Ovarian Neoplasms/
4 exp Prostatic Neoplasms/
5 ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
6 or/1-5
7 (note or comment or editorial or letter).pt.
8 exp Medical History Taking/
9 exp Family/ or exp Family Health/
10 exp Pedigree/
11 limit 10 to humans [Limit not valid; records were retained]
12 ((family or familial) adj3 (histor$ or history-taking or risk$)).ti,ab.
13 anamnesis.ti,ab.
14 (human adj2 pedigree).ti,ab.
15 (genetic adj2 (risk adj3 (assessment or evaluation))).ti,ab.
16 genogram$.mp.
17 ((famil$ or heredi$ or inherit$) adj3 (cancer$ or carcinom$ or neoplasm$)).ti,ab.

18 or/8-9,11-17
19 6 and 18
20 limit 19 to yr="1990 - 2007"
21 20 not 7
22 exp Neoplasms/
23 cancer$.ti,ab.
24 or/22-23
25 (method$ or tool$ or form$).ti,ab.
26 ((genetic or famil$ or heredit$ or inherit$) adj2 (risk adj3 (assessment or evaluation))).ti,ab.
27 26 and 25
28 (famil$ histor$ adj3 (method$ or tool$ or form$)).ti,ab.
29 27 or 28
30 29 and 24
31 limit 30 to yr="1990 - 2007"
32 31 not 7
33 32 or 21

Internet Sites Searched

Title	Website address	Type
The Genetic Family History In Practice Newsletter - Spring 2005	http://www.nchpeg.org/newsletter/inpracticespr05.pdf	NCHPEG Newsletter for Health Care Professionals
The Genetic Family History In Practice Newsletter - Winter 2005	http://www.nchpeg.org/newsletter/inpracticewinter05.pdf	NCHPEG Newsletter for Health Care Professionals
The Genetic Family History In Practice Newsletter - Spring 2004	http://www.nchpeg.org/newsletter/inpracticespr04.pdf	NCHPEG Newsletter for Health Care Professionals
The Genetic Family History In Practice Newsletter - Spring 2003	http://www.nchpeg.org/newsletter/inpracticespr03.pdf	NCHPEG Newsletter for Health Care Professionals
Family Disease Checklist	http://www.genetests.org/servlet/access?id=8888892&key=TkUzWfsXb38xZ&fcn=y&fw=61uz&filename=/tools/concepts/checklist.html	Genetic Tools Website– Genetics Through a Primary Care Lens
Your Family Medical History	http://www.genetests.org/servlet/access?id=8888892&key=xdmgIBahsKytS&fcn=y&fw=qgJE&filename=/tools/concepts/medHist.html	Genetic Tools Website – Genetics Through a Primary Care Lens
BRCA and Breast/Ovarian Cancer -- Disorder Setting	http://www.cdc.gov/genomics/gtesting/file/print/FBR/BCDisSet.pdf	Draft Genetic Test Review
American Medical Association Adult Family History Form	http://www.ama-assn.org/ama/pub/category/13333.html	Electronic Family History Form
Decision aid for the introduction of population-based genetic screening programs (work in progress).	www.aetmis.gouv.qc.ca	Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS) Report
Contribution of BRCA1/2 Mutation Testing to Risk Assessment for Suceptibility to Breast and Ovarian Cancer	http://www.aetmis.gouv.qc.ca/site/download.php?f=b14cef3dbf7ba791b4bdf9557f9d4e6d	Summary Report from Agence D'Évaluation des Technologies et des Modes D'Intervention en Santé Summary Report
Predictive Genetic Testing for Breast and Prostate Cancer	www.ccohta.ca	Canadian Coordinating Office for Health Technology Assessment (CCOHTA) Technology Report
Molecular Diagnosis for Hereditary Cancer Predisposing Syndromes: Genetic Testing and Clinical Impact	www.ccohta.ca	Canadian Coordinating Office for Health Technology Assessment (CCOHTA) Technology Report
BRCA1 and BRCA2 Predictive Genetic Testing for Breast and Ovarian Cancers: Asystematic Review of Clinical Evidence	www.ccohta.ca	Canadian Coordinating Office for Health Technology Assessment (CCOHTA) Technology Report

Title	Website address	Type
The U.S. Surgeon General's Family History Initiative	http://www.hhs.gov/familyhistory/downloads/portraitEng.pdf	Family Health Portrait – Paper Version

Appendix B. Forms/Guides and Internet Family History Tools

Title and Abstract Screening Level 1

Reviewer Comments (Add a Comment) _____

1. Does this article focus on providers' attitudes (views, opinions) towards collecting or using family history in clinical practice?

- □Yes
- □No (neutral)

2. Does this citation focus on either: capturing/collecting/collating information related to family history of disease or history of illness in other family members by any method whether self-reported or by a professional. (exclude if it is personal medical history taking only with no components dealing with family history) *OR* a method/approach/tool/guidelines to assist a health professional use family history information in clinical decision making (e.g. genetic/familial risk assessment)

- □Yes
- □No (exclude)

3. Does the citation include the following cancers? (Check all that apply)

- □Breast, Colorectal/Colon, Ovarian, Prostate
- □Cancer Unspecified
- □None of the Above (exclude)

4. Is this a primary study, conference proceedings, thesis, technical report or letter with primary study data? OR GUIDELINES

- □Yes
- □None of the above (exclude)
- □This a review (exclude)

5. Is this article in English?

- □Yes
- □No (please specify)

Screening Instructions for Family History (Fam_Hx)

General: The first two questions are mandatory and the rest optional. Your answers to question 1 should not effect how you answer the rest of the form. Once you mark your first "exclude" answer, you do not need to fill out the rest of the form.

1. Does this article focus on providers' attitudes (views, opinions) towards collecting or using family history in clinical practice?

- Yes
- No (neutral)

Mandatory—Most of the articles that would fit the "yes" criteria for this question will use surveys, opinion polls or focus groups to determine how providers feel about collecting or using family history in their practice.

2. Does this citation focus on either: capturing/collecting/collating information related to family history of disease or history of illness in other family members by any method whether self-reported or by a professional. (exclude if it is personal medical history taking only with no components dealing with family history) *OR* a method/approach/tool/guidelines to assist a health professional use family history information in clinical decision making (e.g. genetic/familial risk assessment)

- Yes
- No (exclude)

We are interested in both how family medical history is gathered and how it is used in clinical practice. This would include such things as online tools, questions asked in the doctor's office etc. (we are interested in ANY means). Personal medical histories are a bit tricky. If it is only about the individual's medical history (e.g. what childhood illness did you have?) exclude, but if there is even one question about the medical history of other family members, then answer "yes". We are also interested in tools, methods, approaches or guidelines that help practitioners use the family history that they have collected. Genetic/familial risk assessment or risk management are common terms in these types of articles.

Exclude:

- Articles that focus on genealogy (non-medical family history)
- Articles that purely focus on molecular genetics (terms such as methylate/methylation" "micro satellite" "polymorphisms" are unlikely to be in the title of articles we want to include)
- Study collects family history and describes aspects of patients with and without positive FHx but does not emphasize attributes (including accuracy) of the tool or measure (we know some measure was used to establish family history…but it appears the focus is not on the measure)
- If a study focuses on the patient and their risk evaluation (their feelings about own family history or perception of the magnitude of risk)…the study does not focus on the providers understanding of risk.

3. Does the citation include the following cancers?

- □ Breast, Colorectal/Colon, Ovarian, Prostate
- □ Cancer Unspecified
- □ None of the Above (exclude)

Mandatory—mark the answer that applies. We are interested in articles on the specific cancers listed or those that refer to cancer generally without specifying types. If you answer "none of the above" you do not need to answer any more questions

4. Is this a primary study, conference proceedings, thesis, technical report or letter with primary study data?

- □ Yes
- □ None of the above (exclude)
- □ This a review (exclude)

Look carefully at any letters and include them if they contain primary study data (they will normally be more than 1 page long)

5. Is this article in English?

- □ Yes
- □ No (please specify) _____

Title and Abstract Screening Level 2

Reviewer Comments (Add a Comment) _____

Family History:

1. Does this citation FOCUS on the accuracy of family histories?
   - □Yes
   - □No

2. Is this citation about the capturing/collecting/collating or use of family history or in the PRIMARY CARE setting?
   - □Yes
   - □No => Exclude
   - □Can't Tell

Primary Care:

Include: family physicians, general internists, obstetricians, gynecologists, nurses, nurse practitioners, physicians assistants, nutritionists, behaviouralists, etc.

Exclude: Surgeons, oncologists, geneticists or genetics counselors.

Screening Instructions Level 2

Question 1: Answer yes if the paper describes any method of validation of the family histories (e.g. medical records, death certificate, histology report, etc.).

1. Does this citation FOCUS on the accuracy of family histories?
   - Yes
   - No

Question 2: Answer yes if the paper describes a tool for capturing/collecting/collating or assessing risk of cancer used in a primary care setting or applicable to primary care.

2. Is this citation about the capturing/collecting/collating or use of family history or in the PRIMARY CARE setting OR is it applicable to PRIMARY CARE?
   - Yes
   - No => Exclude
   - Can't Tell

Primary Care:

Include: family physicians, general internists, obstetricians, gynecologists, nurses, nurse practitioners, physicians assistants, nutritionists, behaviouralists, etc.
Exclude: Surgeons, oncologists, geneticists or genetics counselors.

Full Text Screening 1

Reviewer Comments (Add a Comment) _____

1. Year of publication 1990-2007:
   - □Yes
   - □No => Exclude

2. Is the population comprised of:
   - □Adults 18+
   - □Other => Exclude

3. Is the article in English?
   - □Yes
   - □No (Specify) => Exclude

4. Does the study report data?
   - □Yes (Any data, Quantitative data and also Qualitative description of tool development data)
   - □No (narrative description of a tool) => Exclude
   - □No (any other) => Exclude

5. Study type:
   - □Primary study
   - □Tool development and testing (reports data)
   - □Review => Exclude
   - □Other => Exclude

6. Does this article include the following cancers: (check all that apply)
   - □Breast cancer
   - □Ovarian cancer
   - □Prostate cancer
   - □Colo-rectal cancer
   - □Presents aggregate data for breast and ovarian cancers only => Include
   - □Presents aggregate date for two or more of the above cancers other than breast and ovarian cancer => Include
   - □Presents aggregate data for the above cancers and for other types of cancer => Exclude
   - □None of the above (specify) _____ => Exclude

7. Does this article examine the accuracy of patients or members of the public in knowing and reporting their family history AND is the accuracy verified by a method such as relative's medical record, physician, death certificate, a population cancer registry?
   - □Yes => Include
   - □No => Include

8. If you answered yes to question 7, was the verification done for: (Check all that apply)

- □Positive family history only: please specify method of verification
- □Negative family history: please specify method of verification

9. Where did the probands/participants came from? (Check all that apply)

- □General population (e.g. from a population survey database)
- □Specialty clinic (including cancer centers, genetic counseling clinics etc.)
- □Primary care (as defined for this study)
- □Other (Specify) _____

10. Does this original article contain a standardized method, approach or tool to collect, capture, collate information related to family history of disease or history of illness in other family members either self-reported or by any primary care practitioners

- □Yes => Include
- □No => Include

11. Does this original article contain a standardized method, tool or measure to help primary care health practitioners to identify, calculate, interpret, make clinical management decisions, promote the uptake of risk stratification and assessment for cancers of interest

- □Yes => Include
- □No => Include

12. Did you answer NO to questions 7, 10 and 11?

- □Yes => Exclude
- □No

13. Reviewer's comments: _____

Full Text Screening 1: Guide

Please complete all of the questions in the form. Stop completing the form if you choose an exclusion answer.

Questions 1-3: We are only interested in studies that were published in English from 1990 to 2007, and that examine adult population.

1. Year of publication 1990-2007:
   - □Yes
   - □No => Exclude

2. Is the population comprised of:
   - □Adults 18+
   - □Other => Exclude

3. Is the article in English?
   - □Yes
   - □No (Specify) _____ => Exclude

Question 4: We are interested in articles that report quantitative or qualitative (highly unlikely) data. Studies that present opinions or recommendations should be excluded.

4. Does the study report data?
   - □Yes
   - □No (narrative description of a tool) => Exclude
   - □No (any other)=> Exclude

Question 5. The study must be a primary study or describe the development of a tool or standardized approach for collecting/capturing/collating family history or for risk assessment

5. Study type:
   - □Primary study
   - □Tool development and testing (reports data)
   - □Review => Exclude
   - □Other => Exclude

Question 6: We are only interested in studies about Breast, Ovarian, Prostate and Colorectal Cancers. If the study examines more than 1 cancer type and the results are given separately for each cancer of interest, it should be included. If the study examines breast and ovarian cancer and the results are presented in aggregated form it should be included. If the study examines the cancers of interest with or without other cancers and the results for all the cancers are presented together, it should be excluded."

6. Does this article include the following cancers: (check all that apply)

- □Breast cancer
- □Ovarian cancer
- □Prostate cancer
- □Colo-rectal cancer
- □Presents aggregate data for breast and ovarian cancers only => Include
- □Presents aggregate date for two or more of the above cancers other than breast and ovarian cancer => Include
- □Presents aggregate data for the above cancers for other types of cancers =>Exclude
- □None of the above (specify) _____ =>Exclude

Questions 7 and 8: If the family history is not verified by any method (i.e. medical record) answer NO to question 7 and go to question 9.

7. Does this article examine the accuracy, completeness, adequacy of patients or members of the public in knowing and reporting their family history AND is the accuracy verified by a method such as relative's medical record, physician, death certificate, a population cancer registry?

- □Yes
- □No

8. If you answered yes to question 7, was the verification done for: (Check all that apply)

- □positive family history only: please specify method of verification
- □negative family history: please specify method of verification

Question 9: We are interested in unselected general population and primary care clinics population. If the paper is about accuracy, then we are interested in primary care and specialty clinics population.

9. Where did the probands/participants came from?

- □General population (e.g. from a population survey database)
- □Specialty clinic (including cancer centers, genetic counseling clinics etc.)
- □Primary care (as defined for this study)
- □Other (Specify) _____

Question 10: We are interested in collecting/collating/capturing/reporting family history in a systematic way (tool).

10. Does this original article contain a standardized method, approach or tool to collect, capture, collate information related to family history of disease or history of illness in other family members either self-reported or by any primary care practitioners.

- □Yes
- □No

Question 11: We are interested in a family history tool that helps primary care providers to identify/calculate/interpret/make management decisions/promote risk stratification and assessment for cancers of interest

11. Does this original article contain a standardized method, tool or measure to help primary care health practitioners to identify, calculate, interpret, make clinical management decisions, promote risk stratification and assessment for cancers of interest.

- Yes
- No

Question 12: We are interested in papers that examine the accuracy of family history or that analyze a tool for collecting/capturing/collating family history or a tool to interpret family history or evaluate risks for specific cancers. If the paper doesn't examine/analyze any of these then exclude it.

12. Did you answer NO to questions 7, 10 and 11?

- Yes => Exclude
- No

13. Reviewer's comments: _____

Full Text Screening 2

Reviewer Comments (Add a Comment) _____

1. To what research question does this article apply? (Check all that apply)
   - Question 1: Accuracy
   - Question 2: Tool
   - Question 3: Risk
   - A mutation or prediction model or a guideline or consensus statement

Guideline to Full Text Screening 2

1) To what research question does this article apply?

A) Question 1: Accuracy

Please check this if the article fulfills the question:

1) What is the evidence that patients or members of the public, accurately know and report their family history of each one of, or a combination of, the following cancers: breast cancer, ovarian cancer, prostate cancer, and colorectal cancer?

B) Question 2: Tool

Please check this if the article fulfills the question:

2) How well do the different systematic family history collection forms and tools, such as take-home tools, web-based tools, etc., improve non-systematic approaches to family history collection by primary care providers?

a. Identify tools intended to improve family history collection by primary care providers.
b. Compare these tools against current practice.

C) Question 3: Risk

Please check this if the article fulfills the question:

3) What tools exist to enable primary care providers to calculate, interpret, and act upon family history-based risk information, and how well do they perform?

For each cancer of interest,

a. Identify tools designed to facilitate calculation and/or interpretation of family history-based risk information, with the purpose of promoting recommended clinical actions.
b. Assess the evidence for effectiveness of these tools in facilitating calculating and/or interpretation of family history-based information.
c. Assess the evidence for effectiveness of these tools in promoting recommended clinical actions.
d. For each tool, identify the evidence base for each recommendation.

D) None of these

Articles for example using record reviews where a tool is not used to ask patients about their family history will fall into this category as well as articles where the focus is surveying opinions of practitioners about collecting family history.

2) Was the focus of this article about:

Mutation models and guidelines are very often used as the backbone to build tools to collect family history.

A) A mutation prediction model (specify)

Examples of well known mutation models that you might encounter are: Frank,
_____

B) A guideline/consensus statement (specify)

For example the Bethesda Guidelines for Hereditary Nonpolyposis Colorectal Cancer.

C) A hypothetical mutation model => Exclude

For example the authors hypothesize that along BRCA1 and BRCA2 there could be a BRCAu mutation. This does not correspond to real practice, therefore should be excluded.

3) If this article is about a tool, for what setting was it created?

A) Primary care

Please check if a setting where family physicians, general internists, obstetricians, gynecologists, nurses, nurse practitioners, physicians assistants, nutritionists, behaviouralists operate.

B) Specialist genetic clinic

Please check if a setting where geneticists or genetics counselors operate

C) Other specialist clinic

Please check if a setting where surgeons, oncologists or other specialists operate

D) Research

Please check if it was a research setting

4) If the tool was created for a specialist or research setting, is it transferable to primary care?
If the tool is not applicable or usable in primary care it should be excluded. Please explain why in the space provided.

Generic Data Abstraction Form

Generic

1. Country of research:
- □US
- □Canada
- □UK
- □Australia
- □Switzerland
- □Germany
- □Italy
- □Netherlands
- □Sweden
- □Norway
- □Denmark
- □Finland
- □China
- □Spain
- □Other

2. If you answered "other" to question 1 please specify: _____

3. Type of article. (Check all that apply)
- □Journal article reporting a primary study
- □Conference proceedings
- □Thesis
- □Technical report
- □Letter with primary study data
- □Guideline
- □Other _____

4. Study design. (Check only 1)
- □Randomized trial - experiment
- □Non-randomized trial
- □Prospective cohort
- □Other design with concurrent comparison group
- □Retrospective cohort study
- □Case control study
- □Time series study
- □Before-after study
- □Cross-sectional study
- □Non-comparative study
- □Tool development study
- □Other (specify) _____
- □Not reported

5. Other inclusion criteria: _____

6. Participants. (Check all that apply)

- □General population
- □Patients from a Primary Care Provider Setting
- □Cancer patients
- □First degree relatives of a cancer patient
- □Primary care provider
- □Hospitalized patients
- □Patients from a cancer registry
- □Other (specify) _____

7. Who was the provider who collected family history/used family history/risk assessment tool? (Check all that apply)

- □Family physician
- □General Internist
- □Obstetrician/Gynecologist
- □Nurse
- □Nurse practitioner
- □Physician's assistant
- □Nutritionist/Dietician
- □Psychologist
- □None (self-administered by patient)
- □Geneticist
- □Other (specify) _____
- □Not reported

8. Does the paper describe the provider's attitudes towards collecting or using family history in clinical practice?

- □Yes
- □No

9. What was the method used to collect family history? (Check all that apply)

- □Face-to-face personal interview
- □Telephone interview
- □Self-completed survey
- □Mail
- □Other (specify) _____
- □Not reported

10. How were data collected? (Check all that apply)

- □On paper medium
- □On electronic medium
- □Other (Specify) _____
- □Not reported

11. Was the information collected using a: (Check all that apply)
- □ Pedigree format
- □ Non-pedigree format
- □ Other information format
- □ Not reported

12. Family history included: (Check all that apply)
- □ Parents
- □ Siblings
- □ Children
- □ Second degree relatives (uncles and aunts, nieces and nephews, grandparents) Specify:
- □ 3rd degree relatives and beyond (cousins, great aunts and great uncles) Specify:
- □ Other (specify) _____
- □ Not reported

13. Reviewer's comments _____

Accuracy Data Abstraction Form

1. Age was reported for: (Check all that apply)
   - □Patients or probands (please specify age data as provided in the study)
   - □Providers (please specify age data as provided in the study)
   - □Relatives (please specify age data as provided in the study)
   - □Other (Specify) _____
   - □Not reported

2. Method used to validate family history for AFFECTED relatives. (Check all that apply)
   - □Personal interview with relatives
   - □Self completed survey (site completed) with relatives
   - □Self-completed survey (postal) with relatives
   - □Relatives' medical record
   - □Cancer registry
   - □Death certificate
   - □Physician's report
   - □Other (specify) _____
   - □Not reported

3. If applicable: method used to validate family history of NON AFFECTED relatives. (Check all that apply)
   - □Personal interview with relatives
   - □Self-completed survey (site completed) with relatives
   - □Self-completed survey (postal) with relatives
   - □Relatives" medical record
   - □Cancer registry
   - □Death certificate
   - □Physician's report
   - □Other (specify) _____
   - □Not reported

4. Setting where family history was collected. (Check all that apply)
   - □Patient's home/Community setting
   - □Primary care setting
   - □Specialty clinic
   - □Hospital
   - □Genetic counseling clinic
   - □Other _____
   - □Not reported

	Group 1	Group 2	Group 3	Group 4	Group 5
5. Participants' distribution					
6. Number recruited at onset of study					

7. Included in analysis					
8. Lost to follow-up (provide reason if available)					
9. # of participants with POSITIVE family history for cancer in first degree relatives					
10. # of participants with NEGATIVE family history for cancer in first degree relatives					

11. What was the metric used to evaluate accuracy? (Check all that apply)
- □Sensitivity (#, %)
- □Specificity (#,%)
- □+ Likelihood ratio (#, CI)
- □- Likelihood ratio (#, CI)
- □Diagnostic Odds Ratio (#, CI)
- □Summary ROC curves
- □Proportions
- □Other (specify) _____

12. Were there outcomes measured other than accuracy (please specify)?
- □1 _____
- □2 _____
- □3 _____
- □4 _____
- □5 _____
- □6 _____

13. Reviewers' comments _____

QUADAS Data Abstraction Form

	Yes	No	Unclear
1. Was the spectrum of patients representative of the patients who will receive the test in practice?			
2. Were selection criteria clearly described?			
3. Is the reference standard likely to correctly classify the target condition?			
4. Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the tests?			
5. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?			
6. Did patients receive the same reference standard independent of the index test results?			
7. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?			
8. Was the execution of the index test described in sufficient detail to permit replication of the test?			
9. Was the execution of the reference standard described in sufficient detail to permit its replication?			
10. Were the index test results interpreted without knowledge of the results of the reference standard?			
11. Were the reference standard results interpreted without knowledge of the results of the index test?			
12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?			
13. Were uninterpretable/ intermediate test results reported?			
14. Were withdrawals from the study explained?			

15. Comments: _____

Common Q2 & Q3 Data Abstraction Form

1. Was the tool developed: (Check all that apply)
   - □ In Primary Care:
   - □ In settings other than Primary Care, but it is applicable to Primary Care

2. If the tool was developed in settings other than Primary Care where was it developed? (Check all that apply)
   - □ Specialist genetic clinic
   - □ Other specialist clinic
   - □ Research

3. What was the purpose of the tool? (Check all that apply)
   - □ Clinical use
   - □ Research

4. How was the tool being used? (Check all that apply)
   - □ Proactively (everybody receives it)
   - □ Reactively (received under patient query)
   - □ As a method of data collection (i.e. not other purposes after data collection)

5. How are data presented after collection? (Check all that apply)
   - □ Table
   - □ Pedigree
   - □ Other (Specify) _____
   - □ Not reported

6. Is the information collected integrated with an electronic record?
   - □ Yes
   - □ No

7. Age was reported for: (Check all that apply)
   - □ Patients or probands (please specify age data as provided in the study)
   - □ Providers (please specify age data as provided in the study)
   - □ Relatives (please specify age data as provided in the study)
   - □ Other (Specify) _____
   - □ Not reported

8. Setting where family history tool was used: (Check all that apply)
   - □ Patient's home/Community setting
   - □ Primary care general setting
   - □ Primary care-specific clinic (e.g. good health clinic, preconceptual clinic, hormone replacement therapy clinic)
   - □ Specialty clinic
   - □ Hospital
   - □ Genetic counseling clinic

□Other (specify) _____
□Not reported

9. Tool Format A. Was the tool designed to prompt information about: (Check all that apply)
□Parents
□Siblings
□Children
□Second degree relatives (aunts and uncles, nieces and nephews, grand parents)
□3rd degree relatives and BEYOND (cousins, grand aunts and uncles)
□2 generations
□3 generations
□Not reported
□Other (specify) _____

10. Tool Format B. Was the tool designed to collect information on relatives with: (Check all that apply)
□One specified cancer
□One syndrome cancer
□Any cancers
□Cancer and other conditions
□Other (specify) _____
□Not reported

11. Tool Format C. Does the tool collect information about patient's affected relatives in order to: (Check all that apply)
□Identify exact relationship to proband
□Determine the age of diagnosis
□Determine the cause of death
□Determine the age of death
□Determine exact diagnosis
□Determine the site of cancer
□Other (specify) _____
□Not reported

12. Tool Format C (a): Does the tool collect information about unaffected relatives in order to: (Check all that apply)
□Identify exact relationship to proband
□Determine the age of the diagnosis
□Identify ethnicity
□Determine the cause of death
□Determine the age of death
□Other _____
□Not reported

13. Does the tool collect information on: (Check all that apply)

□Mother's side relatives
□Father's side relatives
□Not specified
□Participant's relevant past medical history
□Other (specify) _____
□Not reported

14. Did the tool collect information about relatives' ethnic background?
□Yes
□No

15. Reviewers' comments _____

Q2 Data Abstraction Tool

1. What are the tools/ approaches for family history collection being compared?
   - □1 _____
   - □2 _____
   - □3 _____
   - □4 _____
   - □5 _____

	Tool 1	Tool 2	Tool 3	Tool 4	Tool 5
2. Participants' distribution					
3. If applicable: Number of practices recruited					
4. Number of participants recruited at onset of study					
5. Included in analysis					
6. Number or percentage of first degree relatives recorded					
7. Number of percentage of second degree relatives recorded					

8. What was the metric used to evaluate accuracy? (Check all that apply)
   - □Sensitivity (#, %)
   - □Specificity (#,%)
   - □+ Likelihood ratio (#, CI)
   - □- Likelihood ratio (#, CI)
   - □Diagnostic Odds Ratio (#, CI)
   - □Summary ROC curves
   - □Other (specify) _____
   - □Not reported

9. Were there outcomes measured other than accuracy (please specify)?
   - □1 _____
   - □2 _____
   - □3 _____
   - □4 _____
   - □5 _____
   - □6 _____
   - □Not reported

10. Reviewers' comments _____

Q3 Risk Tool Data Abstraction Form

1. Tool purposes: (Check all that apply)
- □Stratify risk
- □Calculate risk
- □Communicate risk to the patient
- □Define/suggest a clinical management strategy
- □Other (specify) _____
- □Not reported

2. Was a consensus/ guideline/ model/ decision aid used for this tool to measure risk?
- □Yes
- □No
- □Not applicable
- □Not reported

3. If you answered Yes to Question 2: What was the consensus/ guideline/ model/ decision aid used for this family history tool to measure risk? (Check all that apply)
- □BRCAPRO
- □Claus
- □Gail
- □Ottman
- □Anderson
- □Taplin
- □Amsterdam
- □Bethesda
- □Ramsey
- □Other (specify)

4. Does the tool collect information on: (Check all that apply)
- □Mother's side relatives
- □Father's side relatives
- □Not specified
- □Participant's relevant past medical history
- □Other (specify) _____
- □Not reported

5. What comparison interventions non/current practice, other tool were evaluated?
- □1 _____
- □2 _____
- □3 _____
- □4 _____
- □5 _____
- □None
- □Not reported

	1	2	3	4	5
6. What were the outcomes used to assess the effectiveness of the tool?					
7. Sensitivity (#, %)					
8. Specificity (#, %)					
9. Positive Likelihood ratio (#, CI)					
10. - Likelihood ratio (#, CI)					
11. Diagnostic Odds Ratio (#, CI)					
12. Summary ROC curves					
13. Other (specify)					
14. Not reported					

	Group 1	Group 2	Group 3	Group 4	Group 5
15. Participants' distribution					
16. Included in analysis					
17. If applicable: Number of practices recruited					
18. Number of participants recruited at onset of study					
19. Lost to follow-up (provide reason if available)					
20. Number or percentage of first degree relatives recorded					
21. Number of percentage of second degree relatives recorded					

22. What was the timing used to measure the outcomes?

□1 _____
□2 _____
□3 _____
□4 _____
□5 _____

23. Reviewers' comments _____

Internet Sites Accessed

Family History Tools Available on the Internet

Title	Website address	Type
The U.S. Surgeon General's Family History Initiative Department of Health and Human Services (HHS)	http://www.hhs.gov/familyhistory/downloads/portraitEng.pdf Website accessed on June 28th, 2007.	Family Health Portrait – Paper Version Agencies involved in this project: Human Genome Research Institute (NHGRI), the Centers for Disease Control and Prevention (CDC), the Agency for Healthcare Research and Quality (AHRQ), the American Society of Human Genetics (ASHG) the Health Resources and Services Administration (HRSA), the National Society of Genetic Counselors and the Genetic Alliance
Family Disease Checklist	http://www.genetests.org/servlet/access?id=8888892&key=TkUzWfsXb38xZ&fcn=y&fw=61uz&filename=/tools/concepts/checklist.html Website accessed on June 28th, 2007.	Genetic Tools Website– Genetics Through a Primary Care Lens
Your Family Medical History	http://www.genetests.org/servlet/access?id=8888892&key=xdmgIBahsKytS&fcn=y&fw=qgJE&filename=/tools/concepts/medHist.html Website accessed on June 28th, 2007.	Genetic Tools Website – Genetics Through a Primary Care Lens
American Medical Association Adult Family History Form	http://www.ama-assn.org/ama/pub/category/13333.html Website accessed on June 28th, 2007.	Electronic Family History Form
Myriad Tests Family History Questionnaire	http://www.myriadtests.com/doc/cancerhistory_fhq.pdf Website accessed on June 28th, 2007.	Family History Questionnaire for Hereditary Cancers paper version
Utah Department of Health	http://health.utah.gov/genomics/familyhistory/documents/Toolkit/new%20entire%20toolkit.pdf Website accessed on June 28th, 2007.	Family History Tool Kit – paper version
Norwich Union Health Tree	http://www.norwichunion.com/healthtree/index.htm Website accessed on June 28th, 2007.	Electronic Family History Builder (pedigree)

Title	Website address	Type
James*Link*: Personalized Cancer Risk Assessment Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute	http://www.jamesline.com/patientsandvisitors/prevention/cancergenetics/#Start%20Session Website accessed on June 28th, 2007.	Interactive tool that estimates cancer risk by reviewing patterns of cancer in a
The Munroe-Meyer Institute for Genetics and Rehabilitation and the Eppley Cancer Center of the University of Nebraska Medical Center	*http://app1.unmc.edu/gencancer/* *Website accessed on June 28th, 2007.*	Interactive Cancer Family Tree
Evanston Northwestern Center for Medical Genetics	http://enh.org/clinicalservices/medicalgenetics/mygenerations/ Website accessed on June 28th, 2007.	Interactive Family History Tools
Genetic Susceptibility to Breast and Ovarian Cancer: Assessment, Counseling and Testing Guidelines American College of Medical Genetics Foundation	*http://www.health.state.ny.us/nysdoh/cancer/obcancer/append11.htm* *Website accessed on June 29th, 2007.*	Sample Cancer Family History Questionnaire

Scoring Criteria for the Family History Tools (FHT)		
Attribute	***Original scoring range***	***Corrected scoring*** 1 = lowest score; 5 =highest score
Length of tool	1= too short 3 = adequate size 5 = too long	Score 1 = 1 Score 2 = 3 Score 3 = 5 Score 4 = 3 Score 5 = 1
Ease of completion	1= very difficult 5 = very easy	No change
Need specialist knowledge to complete FHT	1= need specialist knowledge 5 = complete without knowledge input	No change
Minimum collect details on ALL 1st degree relatives	1 = no details collected 5 = details collected on all 1st degree relatives	No change
Clarity of family history collection including appropriate structure, layout & logical sequence	1 = poor clarity 5 = excellent clarity	No change

Scoring of Available Family History Tool							
Title	**Length**	**Ease**	**Specialist knowledge**	**1st Degree relatives**	**Clarity**	**TOTAL Score**	**Comments**
The U.S. Surgeon General's Family History Initiative	3	4	5	5	3	20	
AAFP Family Disease Checklist	5	3	3	3	2	16	
AAFP Your Family Medical History	3	4	5	5	3	20	Ethnicity reported
American Medical Association Adult Family History Form	3	2	3	5	2	15	Ethnicity reported
Myriad Tests Family History Questionnaire	3	4	3	1	2	13	
Utah Department of Health	NE	NE	NE	NE	NE	NE	NOT enough information on tool to evaluate
Norwich Union Health Tree	3	4	5	3	2	17	
James*Link*: Personalized Cancer Risk Assessment							Assessed as part of article by Sweet et al.*
The Munroe-Meyer Institute	3	4	3	4	2	16	
Evanston Northwestern Center for Medical Genetics	NE	NE	NE	NE	NE	NE	NOT enough information on tool to evaluate
Guidelines American College of Medical Genetics Foundation	3	4	5	4	3	19	

FHTs were independently scored by 2 assessors & any discrepancy resolved through planned consensus discussion using the criteria above

*****Sweet KM, Bradley TL, Westman JA. Identification and referral of families at high risk for cancer susceptibility. Journal of Clinical Oncology 2002 Jan 2;20(2):528-37.

Abbreviations: NE=not evaluated

Reviews Available on the Internet describing Family History Tools

Title	Website address	Type
The Genetic Family History In Practice Newsletter - Spring 2005	http://www.nchpeg.org/newsletter/inpracticespr05.pdf Website accessed on June 28th, 2007.	NCHPEG Newsletter for Health Care Professionals
The Genetic Family History In Practice Newsletter - Winter 2005	http://www.nchpeg.org/newsletter/inpracticewinter05.pdf Website accessed on June 28th, 2007.	NCHPEG Newsletter for Health Care Professionals
The Genetic Family History In Practice Newsletter - Spring 2004	http://www.nchpeg.org/newsletter/inpracticespr04.pdf Website accessed on June 28th, 2007.	NCHPEG Newsletter for Health Care Professionals
The Genetic Family History In Practice Newsletter - Spring 2003	http://www.nchpeg.org/newsletter/inpracticespr03.pdf Website accessed on June 28th, 2007.	NCHPEG Newsletter for Health Care Professionals

Summary Reports/Reviews/Health Technology Assessments Available on the Internet

Title	Website address	Type
BRCA and Breast/Ovarian Cancer -- Disorder Setting	http://www.cdc.gov/genomics/gtesting/file/print/FBR/BCDisSet.pdf Website accessed on June 28th, 2007.	Draft Genetic Test Review
Decision aid for the introduction of population-based genetic screening programs (work in progress).	www.aetmis.gouv.qc.ca Website accessed on June 28th, 2007.	Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS) Report
Contribution of BRCA1/2 Mutation Testing to Risk Assessment for Suceptibility to Breast and Ovarian Cancer	http://www.aetmis.gouv.qc.ca/site/download.php?f=b14cef3dbf7ba791b4bdf9557f9d4e6d Website accessed on June 28th, 2007.	Summary Report from Agence D'Évaluation des Technologies et des Modes D'Intervention en Santé Summary Report
Predictive Genetic Testing for Breast and Prostate Cancer	www.ccohta.ca Website accessed on June 28th, 2007.	Canadian Coordinating Office for Health Technology Assessment (CCOHTA) Technology Report
Molecular Diagnosis for Hereditary Cancer Predisposing Syndromes: Genetic Testing and Clinical Impact	www.ccohta.ca Website accessed on June 28th, 2007.	Canadian Coordinating Office for Health Technology Assessment (CCOHTA) Technology Report
BRCA1 and BRCA2 Predictive Genetic Testing for Breast and Ovarian Cancers: Asystematic Review of Clinical Evidence	www.ccohta.ca Website accessed on June 28th, 2007.	Canadian Coordinating Office for Health Technology Assessment (CCOHTA) Technology Report

Appendix C. Evidence Tables

Evidence Table 1: Characteristics of studies focusing on the accuracy of reporting cancer family history

Author, Year, Country	Study Design and Criterion Standard	Study Population, Cancer Site and Clinical setting	Method of Family History Information Collection	Relatives Characteristics and Methods Used to Validate Family History
Acheson[1] 2006 Australia	**Study design:** Case series **Criterion standard:** Interview with geneticist	**Patients:** Patients scheduled for genetics consultation at university genetics centre **Age:** Mean 40 years (SD 12) **Cancer site:** Cancer free and cancer not specified **Setting:** Genetics counseling centre	**Method of collection:** Computerized tool "Genetic Risk Easy Assessment Tool (GREAT)" and compared to face to face interview **Medium:** Paper and electronic **Format:** Pedigree format	**Relatives characteristics:** First degree relatives **Affected relatives**: Not verified due to reliability study **Unaffected relatives**: Not verified due to reliability study
Aitken[2] 1995 Australia	**Study design:** Case control **Criterion standard:** Relatives self report; relatives doctors report; pathology reports; information from hospitals and death certificates	**Patients:** Patients undergoing colonoscopy at a teaching hospital; cases had hyperplastic or adenomatous polyp diagnosed at colonoscopy; controls were free of polyps **Age:** 20 to 75 years **Cancer site:** colorectal **Setting:** Hospital	**Method of collection:** Mail survey **Medium:** Paper **Format:** NR	**Relatives characteristics:** First degree relatives **Affected relatives:** Medical records; medical history questionnaires mailed to living relatives and surviving spouses **Unaffected relatives:** Medical records
Anton-Culver[3] 1996 USA	**Study design:** Consecutive case series **Criterion standard:** Cancer registry (although author states that personal interview is the standard relative to registry)	**Patients:** Population based cancer patients derivd from a surveillance program of Orange county registry; complete family history data available for 252 of 359 patients **Age:** 30 to 80 years **Cancer site:** Breast **Setting:** Population based surveillance program in Orange county	**Method of collection:** Telephone interview using structured family history questionnaire **Medium:** Paper and electronic **Format:** Interview (questions included types of cancer dates of diagnosis, birth and death of all informant family members)	**Relatives characteristics:** First degree relatives **Affected relatives:** Cancer registry **Unaffected relatives:** Cancer registry

Evidence Table 1: Characteristics of studies focusing on the accuracy of reporting cancer family history (continued)

Author, Year, Country	Study Design and Criterion Standard	Study Population, Cancer Site and Clinical setting	Method of Family History Information Collection	Relatives Characteristics and Methods Used to Validate Family History
Breuer[4] 1993 US	**Study design:** Non-comparative **Criterion standard:** Relatives medical/ hospital records	**Patients:** Patients attending High Risk program (patients had positive history for breast cancer in relatives) **Age:** Mean age 45 years **Cancer site:** Breast **Setting:** Specialty clinic for high risk patients	**Method of collection:** Self completed questionnaire administered to patients prior to their first breast examination **Medium:** Paper **Format:** Not reported but after collection, data presented in a flow chart	**Relatives characteristics:** First and second degree **Affected relatives:** Personal interview with relatives and relatives medical record **Unaffected relatives:** NR
Eerola[5] 2000 Finland	**Study design:** Non-comparative **Criterion standard:** Hospital records of the patients and relatives reported having cancer	**Patients:** Cancer patients diagnosed before the age of 40 and those with bilateral disease **Age:** 20 to 70 years **Cancer site:** Breast **Setting:** University hospital	**Method of collection:** Mailed questionnaires and interview **Medium:** Paper **Format:** Table	**Relatives characteristics:** First through to fifth degree Families traced back as far as the first healthy parents of the oldest known breast or ovarian cancer generation **Affected relatives:** Medical records, cancer registry and parish registry **Unaffected relatives:** Medical records, cancer registry and parish registry
Gaff[6] 2004 Australia	**Study design:** Non-comparative **Criterion standard:** Cancer registry	**Patients:** Men free from cancer with a history of two or more relatives with prostate cancer or one relative with a history of prostate cancer before the age of 55 ; patients recruited from a population based study on prostate cancer **Age:** Mean 58 years (range 39 to 87) **Cancer site:** Prostate **Setting:** Patients home, community setting (mailed survey)	**Method of collection:** Face to face interview and mailed survey **Medium:** Paper **Format:** Non-pedigree format	**Relatives characteristics:** First, second and third degree relatives and beyond if available **Affected relatives:** Relatives medical records **Unaffected relatives:** NR

Evidence Table 1: Characteristics of studies focusing on the accuracy of reporting cancer family history (continued)

Author, Year, Country	Study Design and Criterion Standard	Study Population, Cancer Site and Clinical setting	Method of Family History Information Collection	Relatives Characteristics and Methods Used to Validate Family History
Geller[7] 2001 USA	**Study design:** Cross-sectional **Criterion standard:** Medical records	**Patients:** Random sample of patients undergoing mammography (from the Vermont Breast Cancer Surveillance System) where the patients had no personal history of breast cancer, and a negative mammography **Age:** <65 years **Cancer site:** Breast **Setting:** Mammography center	**Method of collection:** Telephone interview **Medium:** NR **Format:** Pedigree	**Relatives characteristics:** First, second and third degree relatives **Affected relatives:** Personal interview with relatives, cancer registry - Vermont Breast Cancer Surveillance System **Unaffected relatives:** Same as for affected relatives
Glanz[8] 1999 USA	**Study design:** Case-control **Criterion standard:** Hawaii Tumor Registry, Medical records (histology reports confirming the colorectal cancer diagnoses)	**Patients:** Population based case control study; first degree relatives of colon cancer patients **Age:** < 60 years; mean age of relatives was 50 years (range 19 to 84 years) **Cancer site:** Colorectal **Setting:** Patients home, community setting	**Method of collection:** Mailed survey **Medium:** Paper **Format:** NR	**Relatives characteristics:** First degree relatives **Affected relatives:** Mailed survey to relatives **Unaffected relatives:** Mailed survey to relatives
Katballe[9] 2001 Denmark	**Study design:** Non-comparative **Criterion standard:** Medical file or autopsy reports; Danish Cancer Registry; death certificates	**Patients:** Cancer patients derived from a prospective population based study **Age:** NR **Cancer site:** Colorectal **Setting:** Specialty surgical clinic	**Method of collection:** Interview by surgeon **Medium:** Paper **Format:** Pedigree	**Relatives characteristics:** First and second degree relatives **Affected relatives:** Relatives medical record; cancer registry; death certificate **Unaffected relatives:** NR

Evidence Table 1: Characteristics of studies focusing on the accuracy of reporting cancer family history (continued)

Author, Year, Country	Study Design and Criterion Standard	Study Population, Cancer Site and Clinical setting	Method of Family History Information Collection	Relatives Characteristics and Methods Used to Validate Family History
Kerber[10] 1997 USA	**Study design:** Case control **Criterion standard:** Utah Population Database cancer registry	**Patients:** General population and from primary care setting **Age:** 30 to 79 years **Cancer site:** Breast, ovarian, prostate, colorectal **Setting:** Patients home in a community setting	**Method of collection:** Face to face interview and computer assisted **Medium:** Electronic **Format:** NR	**Relatives characteristics:** First degree relatives **Affected relatives:** Utah Cancer registry Utah Population Database **Unaffected relatives:** Utah Population Database
King[11] 2002 USA	**Study design:** Non-comparative **Criterion standard:** Medical records and death certificates	**Patients:** Cancer patients **Age:** NR **Cancer site:** Prostate **Setting:** Prostate clinic	**Method of collection:** Face to face interview: type of collection not specified **Medium:** Paper **Format:** NR	**Relatives characteristics:** First degree relatives **Affected relatives:** Relatives medical record **Unaffected relatives:** NR
Kupfer[12] 2006 USA	**Study design:** Non-comparative **Criterion standard:** Genetic counselor interview; pathology and operative records hospital admission and discharge summaries, death certificates and autopsy reports	**Patients:** Patients at high risk for colorectal cancer **Age:** NR **Cancer site:** Colorectal **Setting:** Patients home/community setting, and at cancer clinic	**Method of collection:** Telephone interview **Medium:** NR **Format:** Pedigree	**Relatives characteristics:** First degree relatives **Affected relatives:** Relatives medical record; pathology and operative reports,hospital admissions and discharge summaries; death certificate, autopsy reports **Unaffected relatives:** NR
Mitchell[13] 2004 UK	**Study design:** Case control **Criterion standard:** Cancer registry	**Patients:** Controls, general population and spouses of cases controls Cancer patients: colorectal cancer cases **Age:** Mean age 64 years **Cancer site:** Colorectal **Setting:** Regional hospitals	**Method of collection:** Face to face interview conducted by genetics nurse **Medium:** Paper **Format:** Pedigree	**Relatives characteristics:** First and second degree relatives **Affected relatives:** Scottish Cancer Registry **Unaffected relatives:** Scottish Cancer Registry

Evidence Table 1: Characteristics of studies focusing on the accuracy of reporting cancer family history (continued)

Author, Year, Country	Study Design and Criterion Standard	Study Population, Cancer Site and Clinical setting	Method of Family History Information Collection	Relatives Characteristics and Methods Used to Validate Family History
Parent[14] 1995 Parent[15] 1997 Canada	**Study design:** Case control **Criterion standard:** Hospital records	**Patients:** Cases: French Canadian women recently diagnosed with cancer Controls: General population **Age:** Mean age 59 years, (range 30 to 79 years) **Cancer site:** Breast cancer **Setting:** Patient's home, community setting	**Method of collection:** Face to face interview **Medium:** NR **Format:** NR	**Relatives characteristics:** First degree relatives **Affected relatives:** Relatives medical record **Unaffected relatives:** NR
Schneider[16] 2004 USA	**Study design:** Prospective cohort **Criterion standard:** Medical records or death certificates	**Patients:** First degree relatives of a Li-Fraumeni Syndrome cancer patient or an hereditaty breast ovarian cancer syndrome patient **Age:** >40 **Cancer site:** Breast and ovarian **Setting:** NR	**Method of collection:** Self completed survey **Medium:** Paper **Format:** Pedigree	**Relatives characteristics:** First and second degree relatives **Affected relatives:** Relatives medical record, death certificate **Unaffected relatives:** NR
Sijmons[17] 2000 Netherlands	**Study design:** Non-comparative **Criterion standard:** Geneticist interview	**Patients:** Referred to genetic counseling clinic with and without cancer **Age:** NR **Cancer site:** Breast, ovarian, colorectal **Setting:** Patients home and genetic clinic	**Method of collection:** Paper and interview **Medium:** Paper **Format:** Pedigree	**Relatives characteristics:** First to fourth degree relatives **Affected relatives:** Medical records **Unaffected relatives:** NR

Evidence Table 1: Characteristics of studies focusing on the accuracy of reporting cancer family history (continued)

Author, Year, Country	Study Design and Criterion Standard	Study Population, Cancer Site and Clinical setting	Method of Family History Information Collection	Relatives Characteristics and Methods Used to Validate Family History
Theis[18] 1994 Canada	**Study design:** Non-comparative **Criterion standard:** Relatives self report, medical records and Ontario Cancer Registry	**Patients:** Cancer patients **Age:** Range 31 to 70 years **Cancer site:** Breast, ovarian, prostate and colorectal **Setting:** Patients home, community and clinical	**Method of collection:** Face to face interview and self completed survey (mail) **Medium:** Paper **Format:** NR	**Relatives characteristics:** First and second degree relatives **Affected relatives:** Personal interview with relatives **Unaffected relatives:** A random sample of 100 first-degree relatives reported as unaffected by cancer submitted to the Ontario Cancer Registry in order to estimate under-reporting
Weinrich[19] 2002 USA	**Study design:** Non-comparative **Criterion standard:** Hospital records	**Patients:** Patients from a cancer registry and the African American Hereditary Cancer Study **Age:** Range 40 to70 years, mean age 50.4 years (SD=7.6) **Cancer site:** Prostate **Setting:** Patient's home, community setting	**Method of collection:** Face to face interview first time Telephone interview done one year later **Medium:** NR **Format:** One Question "Have any of your men blood relatives ever had prostate cancer?"	**Relatives characteristics:** First, second and third degree relatives and beyond **Affected relatives:** Relatives medical record **Unaffected relatives:** NR
Ziogas[20] 2003 USA	**Study design:** Non-comparative **Criterion standard:** Pathology reports, tumor tissue samples or clinical records; relatives self-reports; death certificates	**Patients:** Cancer patients recruited from population based and clinic based family registries of breast, ovarian and colorectal cancer **Age:** NR **Cancer site:** Breast, ovarian, prostate, colorectal **Setting:** Patients home, community setting	**Method of collection:** Telephone interview **Medium:** Electronic (interviewers entered data into Genetics Registry In System (GRIS)) **Format:** Pedigree produced from GRIS	**Relatives characteristics:** First degree, second degree, third degree relatives and beyond **Affected relatives:** Personal interview with relatives Self completed survey, medical records, death certificate **Unaffected relatives:** Personal interview with relatives Self completed survey, medical records, death certificate

Abbreviations: GRIS=Genetics Registry in System; NR=not reported; SD=standard deviation

Evidence Table 2a. Eligible studies evaluating family history tools applicable to primary care (18 tools from 22 publications)

Author, Year, Country	Study Population, Setting, Design	Tool Purpose, Data Collection Strategy and Format	Tool Structure: Informants, General Strategy	Tool Structure: Relatives	Tool Evaluation: Details	Tool Evaluation: Outcomes
Acheson[1] 2006 USA	**Participants:** Patients attending genetics clinic, mean age 40 yrs **Setting:** Cancer genetics clinics **Cancer type:** 24 types of cancer excluding non-melanoma skin cancer **Tool implementation:** Mixed proactive and reactive **Design:** Non-controlled comparator study	**Tool:** Genetic Risk Easy Assessment Tool (GREAT) **User:** Patient **Medium:** Automated telephone interview **Output format:** Pedigree **Integrated with e-record:** No	**PMH:** Risk factors for cancer **Strategy:** General enquiry about 1DR, 2DR and first cousins Details of cancer in affected relatives Information from more distant relatives only if they had cancer	**Side of family identified:** Both **Relatives identified:** 1DR, 2DR, 1st cousin **Information on affected relatives:** Primary site of cancer, age of diagnosis, cause of death, age of death **Information on unaffected relatives:** Age at death, exact relationship to informant	**FH comparator** Genetics interview **Sample size for analysis:** n=120 **Sample size calculation for FH outcomes:** No	**Tool vs comparator:** 1. Mean % per family of all members recognized a. 1DR - 98.5 v 97.3 ($p > 0.05$) b. 2DR - 93.9 v 74.3 ($p < 0.001$); c. First cousin - 94.5 v 48.6 ($p > 0.001$) 2. Agreement on risk categories a. kappa=0.7 b. correlation= 0.77 3. Test-retest reliability a. 1DR 97% b. 2DR 93% c. cancer 98%

*Data relating to performance as a FHxT reported here pertain only to the RAGS prototype tool [21]. For performance of GRAIDS as a RAT, please see Evidence Table Q3

Abbreviations: CI = confidence interval; DR = degree relative; FH = family history; FHxT = Family History Tool; GP = general practitioner; NR = not reported; PMH = past medical history; RAT = risk assessment tool; vs = versus; yrs = years

Evidence Table 2a. Eligible studies evaluating family history tools applicable to primary care (18 tools from 22 publications) (continued)

Author, Year, Country	Study Population, Setting, Design	Tool Purpose, Data Collection Strategy and Format	Tool Structure: Informants, General Strategy	Tool Structure: Relatives	Tool Evaluation: Details	Tool Evaluation: Outcomes
Benjamin[22] 2003 UK	**Participants:** Patients attending joint surgical/genetics breast screening clinic, median age 38 yrs **Setting:** Specialist genetic clinic **Cancer type**: Breast **Design:** Uncontrolled prospective cohort **Tool implementation:** Reactive	**Tool:** Family history questionnaire **User:** Patient **Medium**: Paper **Output format:** NR **Integrated with e-record:** No	**PMH:** NR **Strategy:** Direct questions for details of relatives with breast cancer; details of cancers; number of relatives with ovarian and colorectal cancers; note of relatives with sarcoma, leukemia or brain tumor	**Side of family identified**: Both **Relatives identified:** 1DR, 2DR, 3DR **Information on affected relatives:** Age, diagnosis and site, risk of developing breast cancer **Information on unaffected relatives:** NR	**FH comparator:** Genetics interview **Sample size for analysis:** n=152 **Sample size calculation for FH outcomes:** No	**Tool vs comparator:** 1. Sensitivity = 95% (95% CI 89 to 99%) 2. Specificity = 96% (95% CI 79 to 100%)
Braithwaite[23] 2005 UK	**Participants:** Women with family history of breast cancer, age ≥18 yrs **Setting:** Genetics clinic **Cancer type:** Breast **Tool implementation:** Reactive **Design:** Randomized controlled trial	**Tool:** Genetic Risk Assessment in the Clinical Environment (GRACE) **User:** Patient **Medium:** Electronic **Output format:** Pedigree **Integrated with e-record:** NR	**PMH:** Relevant past medical history **Strategy:** Not clear	**Side of family identified:** Both **Relatives identified:** 1DR, 2DR **Information on affected relatives:** Site of cancer **Information on unaffected relatives:** NR	**FH comparator:** Genetics interview **Sample size for analysis:** NA **Sample size calculation for FH outcomes:** NA	NA

Evidence Table 2a. Eligible studies evaluating family history tools applicable to primary care (18 tools from 22 publications) (continued)

Author, Year, Country	Study Population, Setting, Design	Tool Purpose, Data Collection Strategy and Format	Tool Structure: Informants, General Strategy	Tool Structure: Relatives	Tool Evaluation: Details	Tool Evaluation: Outcomes
Colombet[24,25] 2003 France	**Participants:** Family physicians **Setting:** Research **Cancer type:** Breast, colorectal, prostate **Tool implementation:** Reactive **Design:** Formative evaluation (qualitative)	**Tool:** Personalized Estimate of Risk (EsPeR) **User:** Professional **Medium:** Electronic **Output format:** Pedigree **Integrated with e-record:** NR	**PMH:** NR **Strategy:** 'Dynamic data input' capturing family history	**Side of family identified:** Both **Relatives identified:** NR **Information on affected relatives:** Site of cancer **Information on unaffected relatives:** NR	**FH comparator:** None **Sample size for analysis:** NA **Sample size calculation for FH outcomes:** NA	NA
De Bock[26] 1997 Netherlands	**Participants:** Family practice patients, 25 to 50 yrs **Setting:** Family practice **Cancer type:** Breast **Tool implementation:** Reactive **Design:** Cross-sectional survey	**Tool:** Structured interview **User:** Professional **Medium:** Structured interview **Output format:** NR **Integrated with e-record:** No	**PMH:** NR **Strategy:** Not clear	**Side of family identified:** Both **Relatives identified:** 1DR, 2DR **Information on affected relatives:** Exact relationship to informant; age of diagnosis; cause of death; age of death; site of cancer **Information on unaffected relatives:** NR	**FH comparator:** None **Sample size for analysis:** NA **Sample size calculation for FH outcomes:** NA	NA

Evidence Table 2a. Eligible studies evaluating family history tools applicable to primary care (18 tools from 22 publications) (continued)

Author, Year, Country	Study Population, Setting, Design	Tool Purpose, Data Collection Strategy and Format	Tool Structure: Informants, General Strategy	Tool Structure: Relatives	Tool Evaluation: Details	Tool Evaluation: Outcomes
Emery*[21] 2000 Emery[27] 1999 Emery [28] 2005 Emery[29] 2007 UK	**Participants:** Family physicians **Setting:** Family practice **Cancer type:** Breast colorectal **Tool implementation:** Reactive **Design:** Randomized cross-over trial with simulated cases[21]	**Tool:** Risk Assessment in Genetics (RAGS) (prototype) Genetic Risk Assessment in an Intranet and Decision Support (GRAIDS) **User:** Professional **Medium:** Electronic **Output format:** Pedigree **Integrated with e-record:** RAGS – no GRAIDS – potentially, software connected to NHS intranet	**PMH:** Reported **Strategy:** Not clear	**Side of family identified:** Both **Relatives identified:** NR, from presented pedigrees, likely 1DR, 2DR **Information on affected relatives:** Exact relationship to informant, age of diagnosis, age of death **Information on unaffected relatives:** NR	**From Emery[21] 2000 FH comparator:** 1. Current practice (pen & paper) 2. Modified current practice (Cyrillic pedigree tool) **Sample size for analysis:** completing pedigrees for 6 simulated patients per arm n=36 **Sample size calculation for FH outcomes:** No	**Tool vs comparator:** 1. Median # correct pedigrees. RAGS – 5.06/6 Cyrillic – 3.5/6 Pen & paper – 2.0/6 p<0.0001 2. Preferred method RAGS - 75% Cyrillic – 8% Pen & paper – 17% 3. Ease of use RAGS - 86% Cyrillic – 8% Pen & paper - 6%
Fisher[30] 2003 Australia	**Participants:** Repeat screening mammogram **Setting:** Breast screening clinic **Cancer type:** Breast, Ovarian **Tool implementation:** Reactive **Design:** Cross-sectional survey	**Tool:** Family history questionnaire **User:** Patient **Medium:** Paper **Output format:** NR **Integrated with e-record:** No	**PMH:** NR **Strategy:** Direct questions on breast cancer and age of diagnosis in specific relatives (1DR, DR) - linked with guideline recommendation	**Side of family identified:** Both **Relatives identified:** 1DR, 2DR **Information on affected relatives:** Relationship to informant, age of exact diagnosis **Information on unaffected relatives:** NR	**FH comparator:** Genetic interview **Sample size for analysis:** n=89 **Sample size calculation for FH outcomes:** No	**Tool vs comparator:** 1. Agreement on risk categorization on basis of FH data (population v elevated) - 100% agreement 2. Errors in completing FHQ risk category not identified - 5%

Evidence Table 2a. Eligible studies evaluating family history tools applicable to primary care (18 tools from 22 publications) (continued)

Author, Year, Country	Study Population, Setting, Design	Tool Purpose, Data Collection Strategy and Format	Tool Structure: Informants, General Strategy	Tool Structure: Relatives	Tool Evaluation: Details	Tool Evaluation: Outcomes
Frezzo[31] 2003 USA	**Participants:** Patients attending internal medicine clinic, age range 21 to 76 years **Setting:** Clinic **Cancer type: Breast,** Colorectal, ovarian **Tool implementation:** Proactive **Design:** Quasi-randomized controlled trial	**Tool:** Family history questionnaire **User:** Patient **Medium:** Paper **Output format:** NR **Integrated with e-record:** No	**PMH:** NR **Strategy:** Not clear - focus on specific conditions	**Side of family identified:** NR **Relatives identified:** NR **Information on affected relatives:** NR **Information on unaffected relatives:** NR	**FH comparator:** Patient charts - parallel tool group and genetics interview group validated against medical records **Sample size for analysis:** Tool group n=39 Interview group n=39 **Sample size calculation for FH outcomes:** No	**Tool vs comparator:** (parallel groups) 1. # at risk on basis of FH data, a. breast/ovarian cancer tool – 2/39, chart 0/39 interview – 5/39, chart 2/39 b. colon cancer tool – 3/39, chart – 1/39 interview – 4/39, chart 2/39
Grover[32] 2004 USA	**Participants:** Cancer patients, median 58 yrs **Setting:** Gastrointestinal cancer clinic **Cancer type:** Colorectal **Tool implementation:** Reactive **Design:** Cohort study	**Tool:** Family history questionnaire **User:** Patient **Medium:** Paper **Output format:** NR **Integrated with e-record:** No	**PMH:** Reported **Strategy:** Not clear	**Side of family identified:** Both **Relatives identified:** 1DR, 2DR, 3DR **Information on affected relatives:** Age of diagnosis; site of cancer **Information on unaffected relatives:** NR	**FH comparator:** Patient charts **Sample size for analysis:** n=387 **Sample size calculation for FH outcomes:** No	**Tool vs comparator:** 1. Concordance of relatives' diagnosis and type of cancer 258/387 = 67% 2. Of 311 with 1DR or 2DR with cancer (either method) – 184/311 = 59% concordance 3. Of 127 where data discordant, 37/127 charts did not record or recorded a negative FH where tool had

Evidence Table 2a. Eligible studies evaluating family history tools applicable to primary care (18 tools from 22 publications) (continued)

Author, Year, Country	Study Population, Setting, Design	Tool Purpose, Data Collection Strategy and Format	Tool Structure: Informants, General Strategy	Tool Structure: Relatives	Tool Evaluation: Details	Tool Evaluation: Outcomes
						reported positive FH 4. 834 cancers reported in FHxT, 265 (32%) NR in charts
House[33] 1999 UK	**Participants:** All patients on a single GP list, mean 44 yrs **Setting:** Family practice **Cancer type:** Colorectal **Tool implementation:** Proactive **Design:** Cross-sectional survey	**Tool:** Family history questionnaire **User:** Patient **Medium:** Paper **Output format:** Tabular **Integrated with e-record:** No	**PMH:** Colorectal polyp or cancer, radiotherapy or abdominal operation **Strategy:** Direct questions about PMH or FH of 1DRs with colorectal cancer or polyp; if positive FH it specifies details on affected 1DRs and FH for other specified cancers	**Side of family identified:** NR **Relatives identified:** 1DR **Information on affected relatives:** Exact relationship to informant; age of diagnosis; cause of death; age of death; exact diagnosis; site of cancer **Information on unaffected relatives:** NR	**FH comparator:** None **Sample size for analysis:** NA **Sample size calculation for FH outcomes:** NA	NA
Hughes[34] 2003 USA	**Participants:** Patients in an internal medicine practice, age 21-80 yrs **Setting:** Internal medicine **Cancer type:** Breast, ovarian **Tool implementation:**	**Tool:** Family history questionnaire **User:** Patient **Medium:** Paper **Output format:** NR	**PMH:** Breast/ovarian cancer, ethnicity **Strategy:** Not clear; set of specific questions and tick boxes	**Side of family identified:** Both **Relatives identified:** 1DR, 2DR **Information on affected relatives:** Exact relationship to informant; age of diagnosis; exact diagnosis	**FH comparator:** None **Sample size for analysis:** NA **Sample size calculation for FH outcomes:** NA	NA

Evidence Table 2a. Eligible studies evaluating family history tools applicable to primary care (18 tools from 22 publications) (continued)

Author, Year, Country	Study Population, Setting, Design	Tool Purpose, Data Collection Strategy and Format	Tool Structure: Informants, General Strategy	Tool Structure: Relatives	Tool Evaluation: Details	Tool Evaluation: Outcomes
	Proactive **Design:** Cross-sectional survey	**Integrated with e-record:** No		**Information on unaffected relatives:** Not clear		
Hurt[35] 2001 US	**Participants:** Female relatives of cancer patients, mean age 41yrs **Setting:** Comprehensive cancer centre **Cancer type:** Breast **Tool implementation:** Proactive **Design:** Cohort study	**Tool:** Family history questionnaire **User:** Patient **Medium:** Paper **Output format:** NR **Integrated with e-record:** No	**PMH:** Breast cancer risk factors, ethnicity **Strategy:** Not clear	**Side of family identified:** NR **Relatives identified:** 1DR, 2DR **Information on affected relatives:** Exact relationship to informant; age of diagnosis; age of death; exact diagnosis **Information on unaffected relatives:** NR	**FH comparator:** None **Sample size for analysis:** NA **Sample size calculation for FH outcomes:** NA	NA
Kelly[36] 2007 USA	**Participants:** Cancer patients, mean age 57.6 yrs **Setting:** Ambulatory gastrointestinal oncology clinic **Cancer type:** Any type **Tool implementation:** Proactive **Design:**	**Tool:** Family history questionnaire, based on Stemmerman structured interview **User:** Patient **Medium:** Paper **Output format:** NR **Integrated with e-record:**	**PMH:** NR **Strategy:** Direct questions on affected relatives	**Side of family identified:** Both **Relatives identified:** 1DR **Information on affected relatives:** Exact relationship to informant, age of diagnosis, site of cancer **Information on unaffected relatives:** NA	**FH comparator:** Genetics interview **Sample size for analysis:** n=96 **Sample size calculation for FH outcomes:** With 53 participants, 80% power to detect a difference in marginal proportions in the amount of unspecified data between the two	**Tool vs comparator:** No discrepant data between methods on whether or not a relative had cancer a. Missing data age – 5/53 9.4%) • diagnosis – 6/53 (11.3%) • age of diagnosis – 7/53 (13.2%)

Evidence Table 2a. Eligible studies evaluating family history tools applicable to primary care (18 tools from 22 publications) (continued)

Author, Year, Country	Study Population, Setting, Design	Tool Purpose, Data Collection Strategy and Format	Tool Structure: Informants, General Strategy	Tool Structure: Relatives	Tool Evaluation: Details	Tool Evaluation: Outcomes
	Randomized controlled crossover trial	No			methods of 0.14 at α=0.05	b. Unspecified data • age – 2/53 (3.8%) • diagnosis – 2/53 (3.8%) • age of diagnosis – 5/53 (9.4%)
Murff[37] 2007 USA	**Participants:** Internal medicine patients, mean age 38.9 yrs **Setting:** Internal medicine **Cancer type:** Breast, ovarian, colorectal **Tool implementation:** Proactive **Design:** Cross-sectional survey	**Tool:** Family history questionnaire **User:** Patient **Medium:** Paper **Output format:** Table **Integrated with e-record:** Yes	**PMH:** Personal medical history **Strategy:** Identification of specified relatives, inserted into table where diagnoses and details entered	**Side of family identified:** Both **Relatives identified:** 1DR, 2DR **Information on affected relatives:** Relationship to informant, age of diagnosis, site of cancer **Information on unaffected relatives:** NR	**FH comparator:** Patient charts **Sample size for analysis:** n=541 **Sample size calculation for FH outcomes:** No	**Tool vs comparator:** 1. # 1DR relatives reported to have cancer a. colorectal = 19 vs 11 b. breast = 64 vs 51 c. ovarian = 11 vs 6 2. # 2DR relatives reported to have cancer a. colorectal = 79 vs 31 b. breast = 184 vs 52 c. ovarian = 26 vs 5

Evidence Table 2a. Eligible studies evaluating family history tools applicable to primary care (18 tools from 22 publications) (continued)

Author, Year, Country	Study Population, Setting, Design	Tool Purpose, Data Collection Strategy and Format	Tool Structure: Informants, General Strategy	Tool Structure: Relatives	Tool Evaluation: Details	Tool Evaluation: Outcomes
Schroy[38] 2005 US	**Participants:** Internal medicine residents **Setting:** Internal medicine clinic **Cancer type:** Colorectal **Tool implementation:** Proactive **Design:** Cluster randomized trial	**Tool:** PDA program **User:** Professional **Medium:** Electronic **Output format:** NR **Integrated with e-record:** NR	**PMH:** NR **Strategy:** Prompts for information on affected relatives	**Side of family identified:** NR **Relatives identified:** NR **Information on affected relatives:** Age of diagnosis. **Information on unaffected relatives:** NR	**FH comparator:** Medical charts **Sample size for analysis:** Tool group - residents n=33, patients n=57 Control group – residents n=48, patients n=69 **Sample size calculation for FH outcomes:** No	**Tool group vs control group** 1. % patients report physician asked about family history of colorectal cancer: Tool group - 33% Control group - 25%, p=0.30, 2. % patients report physician asked about family history of colorectal adenomas: Tool group - 25% Control group - 24%, p=0.89
Sweet[39] 2002 USA	**Participants:** Patients attending oncology clinic **Setting:** Cancer centre clinic **Cancer type:** Breast, ovarian, prostate, colorectal **Tool implementation:** Mixed proactive and reactive **Design:** Cross-sectional survey	**Tool:** Jameslink **User:** Patient **Medium:** Electronic **Output format:** NR **Integrated with e-record:** NR	**PMH:** PMH of cancer and ethnicity **Strategy:** Not clear	**Side of family identified:** Both **Relatives identified:** 1DR, 2DR, some 3DR **Information on affected relatives:** Age of diagnosis; exact diagnosis. **Information on unaffected relatives:** NR	**FH comparator:** Patient charts **Sample size for analysis:** n=362 **Sample size calculation for FH outcomes:** No	**Tool vs comparator:** 1. Of 362 patients whose family histories captured by tool, only 308 (85%) had some FH recorded in medical records 2. Discrepancies were noted between family histories captured by tool and those recorded in medical records

Evidence Table 2a. Eligible studies evaluating family history tools applicable to primary care (18 tools from 22 publications) (continued)

Author, Year, Country	Study Population, Setting, Design	Tool Purpose, Data Collection Strategy and Format	Tool Structure: Informants, General Strategy	Tool Structure: Relatives	Tool Evaluation: Details	Tool Evaluation: Outcomes
Yang[40] 1998 USA	**Participants:** Women in an ongoing cancer prevention prospective mortality study, median age in 1982 56 yrs **Setting:** Epidemiological cohort study **Cancer type:** Breast **Tool implementation:** NA **Design:** Cross-sectional data from cohort study	**Tool:** Family history questions embedded in health questionnaire **User:** Patient **Medium:** Paper **Output format:** NR **Integrated with e-record:** NR	**PMH:** Recorded as part of main questionnaire **Strategy:** Direct questions on parents, siblings, details of cancers in relatives	**Side of family identified:** NR **Relatives identified:** NR **Information on affected relatives:** relationship to informant, age of diagnosis, age of death **Information on unaffected relatives:** NR	**FH comparator:** None **Sample size for analysis:** NA **Sample size calculation for FH outcomes:** NA	NA

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Aitken[2] 1995 Australia **Study purpose:** To assess the validity of self-reported family histories of colorectal cancer patients by comparing patients' reports with their first degree relatives' medical records	**Patients:** Patients referred to hospital **Practitioners:** Questionnaire was self-administered by patients **Setting where developed:** Colonoscopy department from a hospital **Applicability:** Reviewed FHxT; not applicable to primary care **Setting where used:** Community setting **Cancer type:** Colorectal **Study design:** Cohort study (prospective)	**Purpose:** Clinical use; proactive **Method used to collect FH**: Self-completed mail survey **Format:** NR **Medium:** Paper **Integrated with e-record:** N/A (validation study)	**Age of Participants:** NR **Details on Relatives: Side of family identified:** Mother's side relatives; Father's side relatives **Participant PMH:** NR **Relatives identified:** 1DR **Strategy for FH enquiry:** General enquiry about 1DR relative's age and age of death, specific enquiry about condition	**Relatives' Cancers and other conditions:** Colorectal and any cancers or bowel polyp or obstruction **Information on affected relatives:** Determine the age of diagnosis, cause and of death **Information on unaffected relatives:** NR	**Tools compared:** Family and personal medical history questionnaire was mailed to the cases and controls, compared to relatives medical records & death certificates **# of participants recruited in each group:** n=419 patients **# of participants in analysis:** n=419 patients **# of first degree relatives:** n=618 **# of second degree relatives:** NR	**Metric used to evaluate the adequacy of the tool:** Accuracy of FH: Sensitivity (#, %): Overall: 0.84 (95% CI 0.77 - 0.88); Cases: 0.87; Controls: 0.82, Specificity (#,%): Overall: 0.97 (95% CI 0.95 - 0.98); Cases: 0.97; Controls: 0.97, % overall agreement of FH (Table 1) **Other outcomes measured:** NR **Follow up:** Validation study, no clinical use

+details collected on participants and relatives; † extent of details collected on i) relatives' conditions ii) affected relatives iii) unaffected relatives; * a) comparison with clinical genetics pedigree (i.e. gold standard) b) other tool; ^other measures - accuracy, validity, reliability

Abbreviations: BE = best estimate; Br Ca= Breast Cancer; Ca=Cancer; CASH=Cancer and Steroid Hormone**;** CFHF= Comprehensive Family History Form CR = cancer registry; CRC=colorectal cancer; Cyr = cyrillic; DARCC= Diet, Activity and Reproduction in Colon Cancer; DOB=date of birth; DQ=direct question; DR=degree relative; EsPeR= Personalized Estimate of Risks; FCAT = familial cancer assessment tool; FH=family history; FHQ=family history questionnaire; FHxT = family history tool; GCI = genetic counselor interview; GI = genetic interview; GNI = genetic nurse interview; GP=general practitioner; GRACE = Genetic Risk Assessment in the Clinical Environment; GRAIDS = Genetic Risk Assessment in an Intranet and Decision Support; GRIS= Genetics Registry In System; HNPCC= Hereditary Non-polyposis Colorectal Cancer; IM=Internal Medicine; MR = Medical Record; NICE= National Institute for Clinical Excellence; NR = NR; Ov Ca= Ovarian Cancer; PAC= probability of agreement of cancer; PANC= probability of agreement of no cancer PC = primary care; PDA=Personal Digital Assistant; PMH=past medical history; PSA = Prostate-Specific Antigen; PSI = physician structured interview; RR = relative risk; RAGs = Risk Assessment in Genetics; TRACE=Trial of genetic assessment in breast cancer

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Andrieu[41] 2004 France **Study purpose:** To estimate the familial risk of colorectal cancer (CRC) and other cancers and to examine how these risks vary according to tumor site.	**Patients:** Selected primary care/ community-based population: Patients from a population cancer registry contacted via GP **Practitioners:** Trained interviewer **Setting where developed:** Research **Applicability:** FHxT not available for review **Setting where used:** Community setting **Cancer type:** Colorectal **Study design:** Other	**Purpose:** Clinical use; proactive **Method used to collect FH:** Face to face personal interview using structured FHQ **Format:** NR **Medium:** NR **Integrated with e-record:** No	**Age of participants:** NR **Details on Relatives:** **Side of family identified:** NR **Participant PMH:** NR **Relatives identified:** 1DR; 2DR **Strategy for FH enquiry:** General enquiry about all 1DR and 2DR - DOB and age of death Specific enquiry of DQ each relatives medical history of cancer, age and place of diagnosis	**Relatives' Cancers and other conditions:** Colorectal (also site specified), 21 other cancers documented: uterus-SAI, ovaries, breast, prostate, testes, stomach, pancreas, urinary bladder, kidney, thyroid, leukemia, melanoma **Information on affected relatives:** Identify exact relationship to informant, determine the age of diagnosis, determine the cause of death, determine the age of death, determine the site of cancer **Information on unaffected relatives:** NR	**Tools compared:** Family history questionnaire Compared to details on relatives in cancer registry & medical records **# of participants recruited in each group:** n=767 **# of participants in analysis:** n=766 (761 independent families) **# of first degree relatives:** Group 1: n=6160 **# of second degree relatives:** n=4352	**Metric used to evaluate the adequacy of the tool:** % Confirmed diagnosis (Table 2) **Other outcomes measured:** Familial risk of developing CRC: 1.54 (95% CI 1.26-1.86), for first degree relatives RR 1.71 (95% CI 1.35-2.13) and for second degree relatives (RR 1.22 (95% CI 0.82-1.76)

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Anton-Culver[3] 1996 USA **Study purpose:** 1) To evaluate the validity of family history information on breast cancer in mother and sisters of breast cancer patients from a population-based cancer registry (CR) 2) To characterize a consecutive series of breast cancer patients on the basis of reported FH: sporadic, familial and potentially hereditary forms	**Patients:** Selected primary care /community-based population: Patients from a cancer registry **Practitioners** Trained interviewers, (Background NR) **Setting where developed:** Research: cancer registry **Applicability:** Reviewed FHxT; not applicable to primary care **Setting where used:** Patient's home/ Community setting: telephone interview **Cancer type:** Breast **Study design:** Non-comparative study (case series)	**Purpose:** research; proactive **Method used to collect FH**: Telephone interview (From original FH-T): using structured FHQ **Format:** NR; Table **Medium:** Paper and electronic **Integrated with e-record:** Yes	**Age of participants:** Patients: 30-80 years or older **Details on Relatives: Side of family identified:** Mother's side relatives: mothers and sisters **Participant PMH:** NR **Relatives identified:** 1DR **Strategy for FH enquiry:** General enquiry about "All relatives'" DOB & age of death. Specific enquiry: DQ each relatives medical history of cancer, age of diagnosis	**Relatives' Cancers and other conditions:** Breast cancer **Information on affected relatives:** Identify exact relationship to informant, determine the age of diagnosis, determine the cause of death, determine the age of death, determine exact diagnosis **Information on unaffected relatives:** Identify exact relationship to informant, determine the age of the diagnosis, determine the cause of death, determine the age of death	**Tools compared:** (1) Population based cancer registry (2) personal interviews **# of participants recruited in each group:** Group 1: n=359 Group 2: n=359 **# of participants in analysis:** Group 1: n=359 Group 2: n=359 **# of first degree relatives:** Group 1: NR Group 2: NR **# of second degree relatives:** Group 1: NR Group 2: NR	**Metric used to evaluate the adequacy of the tool:** Sensitivity (#, %): 92% mothers and 88% for sister informants, Specificity (#,%): 99% **Other outcomes measured:** familial breast cancer phenotypes
Breuer[4] 1993 USA **Study purpose:** To validate reports on bilaterality	**Patients:** Patients who attended the Strang High Risk (for Breast Cancer) program **Practitioners:** NR **Setting where**	**Purpose:** research; proactive **Method used to collect FH**: Self-completed survey **Format:** Did not report the format of	**Age of participants:** Patients or informants: mean age 45 years **Details on Relatives: Side of family identified:**	**Relatives' Cancers and other conditions:** Breast cancer **Information on affected relatives:** Identify exact relationship to	**Tools compared:** Group 1 patients report Group 2 hospital records **# of participants recruited in each group:**	**Metric used to evaluate the adequacy of the tool:** Wilcoxon's rank sums test and fisher's exact test **Other outcomes measured:** NR

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
status in first-degree relatives of women with a strong family history of breast cancer.	**developed:** Specialist clinic **Applicability:** FHxT not available for review **Setting where used:** Patient's home/Community setting **Cancer type:** Breast **Study design:** Non-comparative study (case series)	data collection. After collection data were presented in a flow chart **Medium:** Paper **Integrated with e-record:** No	Mother's side relatives: mothers and sisters **Participant PMH:** NR **Relatives identified:** First and second degree relatives	informant and determine the age of diagnosis; determine the cause of death; determine exact diagnosis; determine the site of cancer **Information on unaffected relatives:** NR	Group 1: n=112 Group 2: n=112 # **of participants in analysis:** group 1: n=94, group 2: n=94 # **of first degree relatives:** group 1: NR, group 2: NR # **of second degree relatives:** group 1: NR, group 2: NR	

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Bruner[42] 1999 USA **Study purpose:** Describe a model that assesses the risk factors of prostate cancer	**Patients:** First degree relatives of a cancer patient. **Practitioners:** health educator and genetic counselor for expanded FH. **Setting where developed:** Specialist genetic clinic **Applicability:** FHxT not available for review **Setting where used:** Specialty clinic (Cancer Center) **Cancer type:** Prostate **Study design:** Cohort study (prospective)	**Purpose:** clinical use; proactive **Method used to collect FH:** Face to face personal interview: with health educator and genetic counselor; self-completed survey: questionnaire, mail. **Format:** It doesn't report the format of data collection; data are presented in a pedigree format once collected **Medium:** Paper **Integrated with e-record:** Yes	**Age of participants:** Patients or informants age 44 to 56 years **Details on Relatives: Side of family identified:** Mother's side relatives Father's side relatives **Participant PMH** NR **Relatives identified** 1DR	**Relatives' Cancers and other conditions:** Prostate cancer **Information on affected relatives:** determine the age of diagnosis; determine the cause of death; determine the age of death; determine exact diagnosis; determine the site of cancer **Information on unaffected relatives:** NR	**Tools compared:** **# of participants recruited in each group:** Cancer registry **# of participants in analysis:** 101 men **# of first degree relatives:** NR **# of second degree relatives:** NR	**Metric used to evaluate the adequacy of the tool:** NR **Other outcomes measured:** PSA levels of men tested. Risk of cancer in men screened

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Chalmers[43] 2001 UK **Study purpose:** To develop and pilot test a newly developed questionnaire that collects information and supports the needs of women with breast cancer	**Patients:** Patients from a Primary Care Provider Setting; First degree relatives of a cancer patient. **Practitioners:** NR. **Setting where developed:** Research: pilot test. **Applicability:** FHxT not available for review **Setting where used:** Patient's home/Community setting **Cancer type:** Breast **Study design:** Non-comparative study (case series)	**Purpose:** research; proactive **Method used to collect FH:** Telephone interview; Self-completed survey (mail) **Format:** NR **Medium:** paper and electronic **Integrated with e-record:** No	**Age of participants:** Patients or informants: 24 - 54 years; Relatives: 50 or older, **Details on Relatives:** **Side of family identified:** Mother's side relatives Father's side relatives **Participant PMH** NR **Relatives identified** 1DR, 2DR **Strategy for FH enquiry:** NR	**Relatives' Cancers and other conditions:** Breast cancer; Ovarian, endometrial, colorectal cancers or sarcoma. **Information on affected relatives:** identify exact relationship to informant; determine the age of diagnosis; determine exact diagnosis; determine the site of cancer. **Information on unaffected relatives:** NR	**Tools compared:** 1: The Information and Support Needs Questionnaire. **# of participants recruited in each group:** Group 1: 42. **# of participants in analysis:** group 1: 39. **# of first degree relatives:** group 1: NR. **# of second degree relatives:** group 1: NR.	**Metric used to evaluate the adequacy of the tool:** NR **Other outcomes measured:** NR

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
de Jong[44] 2006 Netherlands **Study purpose:** To assess the prevalence of a positive family history of colorectal cancer within a random cohort among the Dutch population	**Patients:** General population Patients from a Primary Care Provider Setting **Practitioners:** Family physician: subjects were invited to participate in the study on behalf of their general practitioner **Setting where developed:** Primary care **Applicability:** FHxT not available for review **Setting where used:** General population **Cancer type:** None **Study design:** Prospective cohort	**Purpose:** Research, Proactive **Method used to collect FH:** Mailed survey, anonymous questionnaire **Format:** Table **Medium:** Paper **Integrated with e-record:** No	**Age of participants:** Patients or informants 45-70 years relatives: < 50 and any age **Details on Relatives:** **Side of family identified:** Mother's side relatives Father's side relatives **Participant PMH:** NR **Relatives identified** 1DR **Strategy for FH enquiry:** Family history questionnaire	**Relatives' Cancers and other conditions:** Colorectal **Information on affected relatives:** To identify exact relationship to informant determine the age of diagnosis determine the site of cancer **Information on unaffected relatives:** Number of brothers and sisters	**Tools compared:** One Family history questionnaire **# of participants recruited in each group:** 5072 eligible for the study **# of participants in analysis:** 3973 questionnaires were returned **# of first degree relatives:** N/A **# of second degree relatives:** N/A	**Metric used to evaluate the adequacy of the tool:** Survey data collected anonymously, data not verified **Other outcomes measured:** NR

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Eerola[5] 2000 Finland **Study purpose:** 1) To evaluate the validity of the family history of breast cancer reported by patients 2) To evaluate the number of families and individuals at risk and potentially benefiting from surveillance.	**Patients:** Cancer patients **Practitioners:** NR. **Setting where developed:** Oncology specialist clinic **Applicability:** FHxT not available for review **Setting where used:** Patient's home/Community setting **Cancer type:** Breast **Study design:** Non-comparative study (case series)	**Purpose:** Clinical use; proactive **Method used to collect FH:** Self-completed survey: Series 1&2 mailed **Format:** Table **Medium:** paper **Integrated with e-record:** No	**Age of participants:** Patients or informants less that 40 years; Relatives 20 to 70 years **Details on Relatives:** **Side of family identified:** Not specified **Participant PMH** NR **Relatives identified** First degree relatives 3rd degree relatives and beyond: grand aunts and uncles	**Relatives' Cancers and other conditions:** Breast and ovarian cancer **Information on affected relatives:** identify exact relationship to informant; determine the age of diagnosis; determine the cause of death; determine exact diagnosis **Information on unaffected relatives:** NR	**Tools compared:** 1: Young patients< 40, 2: Bilateral patients, 3: Unselected patients were administered a family history questionnaire (NR) **# of participants recruited in each group:** 1570 (170+118+1282) **# of participants in analysis:** group 1: 170, group 2: 118, group 3: 100 families identified (272 relatives diagnosed Breast/Ovarian. **# of first degree relatives:** group 1: NR, group 2: NR, group 3: NR. **# of second degree relatives:** group 1: NR, group 2: NR, group 3: NR.	**Metric used to evaluate the adequacy of the tool:** Validation method: (1) Disease - Hospital records - Cancer registry Sensitivity (%): 87% (2) Genealogy -Church parish registers - Population register centre **Other outcomes measured:** 1: Family history of ovarian cancer (ovarian cancer) among breast cancer families, 2: Incorrectly reported or unconfirmed cases, 3: Potential female candidates for genetic counselling, diagnostic testing
Fletcher, 2006[45] USA **Study purpose:** To compare screening practices and beliefs in	**Patients:** Patients from a primary care provider **Practitioners:** General internist and gastroenterologists **Setting where developed:**	**Purpose:** Research, Proactively **Method used to collect FH:** Paper based-survey, medical records **Format:**	**Age of Participants:** 35 to 55 years **Details on Relatives:** **Side of family identified:** Mother's side relatives Father's side relative	**Relatives' Cancers and other conditions:** Colorectal **Information on affected relatives:** To identify exact relationship to informant, determine	**Tools compared:** Survey vs medical record **# of participants recruited in each group:** n=1870 patients who returned the survey	**Metric used to evaluate accuracy:** Sensitivity (#, %): 59% Specificity (#,%): 95% **Outcomes (other than accuracy):**

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
patients with and without clinically important family history	Primary Care and in settings other than Primary Care **Applicability:** FHxT not available for review **Setting where used:** Specialist genetic clinic **Cancer type:** Colorectal **Study design:** Prospective cohort	Table **Medium:** Paper **Integrated with e-record:** Yes	**Participant PMH:** NR **Relatives identified:** All blood relatives who had been diagnosed with colorectal cancer **Strategy for FH enquiry:** Survey (self-reported FH) and medical chart review	the age of diagnosis, determine the site of cancer **Information on unaffected relatives:** N/A	**# of participants in analysis:** n=1854 patients who reported adequate FH **# of first degree relatives:** 1DR with onset age ≤60 years or 2 or more 1st degree relatives at any age= 53 (2.9%); 1st degree relative with onset at ≥60 years or 2 or more 2nd degree relatives=162 (8.7%) **# of second degree relatives:** other family history of colorectal cancer= 140 (7.6%)	-Family history prevalence: 355 (19.1%) respondents reported family history of colorectal cancer -Beliefs -Identification of risk: 407 (39.1%, 95% CI 36.1%, 42%) out of 1041 respondents < 50 respondents that their clinician had asked for FH colorectal cancer; 72.2% (95% CI 70.0, 76.4) of respondents 50 years or older said they had been asked about FH. -Appropriate screening -Screening test preference
Green, 2007[46] Canada **Study purpose:** To evaluate the contribution of genetic and environmental factors to the incidence of colorectal cancer	**Patients:** Cancer patients **Practitioners:** Ontario and Newfoundland Cancer Registries **Setting where developed:** In settings other than primary care, but it is applicable to primary care	**Purpose:** Research, proactively **Method used to collect FH:** Mail-in family history questionnaire **Format:** Pedigree **Medium:** Paper **Integrated with e-**	**Age of Participants:** Patients or informants and relatives **Details on Relatives: Side of family identified:** Mother's side relatives Father's side relative **Participant PMH:** NR	**Relatives' Cancers and other conditions:** Colorectal **Information on affected relatives:** To identify exact relationship to informant, determine the age of diagnosis, determine the site of cancer **Information on**	**Tools compared:** Ontario Familial Colorectal Cancer Registry (OFCCR); Newfoundland Colorectal Cancer Registry (NFCCR) **# of participants recruited in each group:** n=730 **# of participants in analysis:**	**Metric used to evaluate the adequacy of the tool:** Confirmed diagnosis of family member through review of medical records when possible **Outcomes(other than accuracy):** Newfoundland rate of FDR affected with CRC is 1.5-fold

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
	Applicability: FHxT not available for review **Setting where used:** Patients' home/Community setting **Cancer type:** Colorectal **Study design & relevance** Prospective cohort	**record:** No	**Relatives identified:** FDR, SDR **Strategy for FH enquiry:** Mail-in family history questionnaire	**unaffected relatives:** N/A	n=702 **# of first degree relatives:** In Newfoundland 31% (n=220) and in Ontario 20.4% (n=764) of cases had at least 1 first degree relative affected with CRC **# of second degree relatives:** N/A	higher than in Ontario (p<0.0001)

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Hlavaty[47] 2005 Slovakia **Study purpose:** To evaluate the interest of first degree relatives of colorectal cancer patients to participate in colonoscopy screening and to compare the findings to controls with a negative family history	**Patients:** Cancer patients; 1DR of cancer patients. **Practitioners:** None (questionnaire was self-administered by patient) **Setting where developed:** Research **Applicability:** Reviewed FHxT; not applicable to primary care **Setting where used:** Hospital Internal Medicine **Cancer type:** Colorectal **Study design:** Cohort study (prospective)	**Purpose:** research use **Method used to collect FH:** Face to face personal interview, Self-completed mailed survey **Format:** NR. **Medium:** Paper **Integrated with e-record:** No	**Age of participants:** Patients or informants: Mean age at diagnosis 65.9 +/-12.1; Relatives: over 40 years or 10 years younger than the youngest case of CRC in the family **Details on Relatives: Side of family identified:** Mother's side relatives Father's side relatives **Participant PMH** NR **Relatives identified** First degree relatives	**Relatives' Cancers and other conditions:** Hereditary non-polyposis colorectal cancer, stomach, uterus, lungs, pancreas, pharynx, breast, lymphoma, hepatocellular, prostate. **Information on affected relatives:** determine the age of diagnosis; determine the site of cancer **Information on unaffected relatives:** NR	**Tools compared:** 1: Family history of Colorectal cancer questionnaire **# of participants recruited in each group:** Group 1: 34 patients **# of participants in analysis:** group 1: 34 patients **# of first degree relatives:** group 1: 237 **# of second degree relatives:** NR	**Metric used to evaluate the adequacy of the tool:** NR **Other outcomes measured:** 1: Presence of at least 1 first degree relative with CRC in the family history was noted in 12 patients (35.5%), 2: Mean of first degree relatives with positive family history: 6.3 + - 3.4, 3: Mean of first degree relatives with negative family history

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Katballe[9] 2001 Denmark **Study purpose:** To evaluate the accuracy of family history of hereditary non-polyposis colorectal cancer (HNPCC).	**Patients:** Specialist secondary care/tertiary care population: Cancer patients **Practitioners:** General Internist: surgeon **Setting where developed:** Surgeons interviewed the patients **Applicability:** FHxT not available for review **Setting where used:** Surgical clinic **Cancer type:** Colorectal **Study design:** Non-comparative study (case series)	**Purpose:** Clinical use; reactive **Method used to collect FH:** Interviewed by surgeon using structured FHQ (not clear if face to face or phone) **Format:** Pedigree **Medium:** Paper **Integrated with e-record:** No	**Age of participants:** NR **Details on Relatives:** **Side of family identified:** Mother's side relatives Father's side relatives **Participant PMH:** info on CRC **Relatives identified:** First degree relatives second degree relatives (2DR consider if patients were diagnosed before the age of 50 or if colorectal cancer was reported among first-degree relatives) **Strategy for FH enquiry:** not clear (specific DQ)	**Relatives' Cancers and other conditions:** Any cancers **Information on affected relatives:** determine the age of diagnosis; determine the site of cancer determine the cause of death; determine the age of death; **Information on unaffected relatives:** NR Supplementary genealogical details on relatives recorded from church registers	**Tools compared:** questionnaire used by patient's surgeon compared to relatives medical records +/- autopsy report +/- cancer registry +/- death certificates # **of participants recruited in each group:** Group 1: n=1328 eligible patients. # **of participants in analysis:** Group 1: n=1200 completed the questionnaire, reported that their families belonged to Amsterdam ii categories 1, 2 or 3 and these families were subjects of this study # **of first degree relatives:** Group 1 a total of 167 informants reported colorectal cancer among 196 first-degree relatives # **of second degree relatives:** Group 1: second degree relatives were considered if the patients were	**Metric used to evaluate the adequacy of the tool:** Correct cancer reported in relatives: 1DR correct 68.4% 1DR increase to 81.7% Other (specify): true-positive rate **Other outcomes measured:** Correct allocation into risk categories= meet Amsterdam I & II False + 21% (3/14) False - 32% (7/18)

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
					diagnosed before the age of 50 years or if colorectal cancer was reported among first-degree relatives number is NR	
Kerber[10] 1997 USA **Study purpose:** To evaluate the sensitivity of patients' reports of familial cancer and to measure agreement between patients' reports and records in the Diet, Activity and Reproduction in Colon Cancer (DARCC) study	**Patients:** General population, patients from primary care **Practitioners:** NR **Setting where developed:** Research setting 1) Kaiser Permanente Medical Care Program Northern California; 2) the Twin Cities metropolitan area; and 3) an eight-county metropolitan area Salt Lake City, Utah, **Applicability:** Reviewed FHxT; not applicable to primary care **Setting where used:**	**Purpose:** research; proactive **Method used to collect FH:** Face to face (structured) personal interview **Format:** NR **Medium:** On electronic medium **Integrated with e-record:** No	**Age of participants:** Patients 30 to 79 years **Details on Relatives:** **Side of family identified:** NR **Participant PMH** NR **Relatives identified** 1DR relatives	**Relatives' Cancers and other conditions:** Any cancers: colorectal, ovarian, uterine, breast and prostate. **Information on affected relatives:** identify exact relationship to informant; determine the age of diagnosis; determine the cause of death; determine the age of death; determine exact diagnosis **Information on unaffected relatives:** NR	**Tools compared:** 1: Computer-assisted in-person interviewing, 2: Utah Population Database **# of participants recruited in each group:** Group 1: 881, group 2: 331 **# of participants in analysis:** group 1: 881, group 2: 331 **# of first degree relatives:** group 1: 881, group 2: 331 **# of second degree relatives:** group 1: NR, group 2: NR	**Metric used to evaluate the adequacy of the tool:** Sensitivity (#, %): Colorectal 73%, Uterine 30%, Ovarian 60%, breast 83%, prostate 70% **Other outcomes measured:** 1: Risk of colon cancer associated with family histories of various cancers

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
	1) Kaiser Permanente Medical Care Program Northern California; 2) the Twin Cities metropolitan area; and 3) an eight-county metropolitan area surrounding Salt Lake City, Utah, **Cancer type:** Breast, ovarian, colorectal, prostate **Study design:** Cohort study (prospective)					

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
King[11] 2002 USA **Study purpose:** 1) To examine the accuracy of prostate cancer patients' reports on specific cancer types in their families; 2) To report on the ability of investigators to document patients' report on their FH status	**Patients:** Men with prostate cancer **Practitioners:** trained interviewer **Setting where developed:** Prostate Clinic **Applicability:** FHxT not available for review **Setting where used:** Prostate Clinic **Cancer type:** Prostate **Study design:** Non-comparative study (case series)	**Purpose: research** use; reactive **Method used to collect FH:** personal structured interview: (Not clear if face to face or telephone interview) **Format:** NR **Medium:** NR **Integrated with e-record:** No	**Age of participants:** NR **Details on Relatives:** **Side of family identified:** Mother's side relatives Father's side relatives **Participant PMH** NR **Relatives identified** First degree relatives (1DR) **Strategy for FH enquiry:** ask about all 1DR. If cancer identified in relatives, specific probes about detail	**Relatives' Cancers and other conditions:** Any cancers **Information on affected relatives: age of relatives;** determine the date of diagnosis; determine the cause of death; determine the date of death; determine the site of cancer; locality of Cancer Rx facilities, contact details **Information on unaffected relatives:** age of relatives; cause of death	**Tools compared:** Interview, compared to medical record, pathology report , death certificate # **of participants recruited in each group:** Group 1: 442, group 2: 442 # **of participants in analysis:** group 1: 143, group 2: 249 # **of first degree relatives: g**roup 1: 263, group 2: 263 # **of second degree relatives:** group 1: NR, group 2: NR	**Metric used to evaluate the adequacy of the tool:** % agreement between self-report & actual relatives medical history Vary by site: Bladder/kidney (100% x/y) Prostate (80% x/y) Ovarian (50% x/y) 1DR accuracy 62-73% except brother 84% **Other outcomes measured:** NR
Parent[15] 1997 Parent[14,14] 1995 Canada **Study purpose:** To evaluate the accuracy of	**Patients:** CONTROLS: Non-specialist secondary care/territory care population General population: women who had no history of breast cancer CASES: Specialist secondary	**Purpose:** research; proactive **Method used to collect FH**: Face to face personal structured FH interview **Format**: NR	**Age of participants**: Patients: General population no older than 79 years; Mean age of women reporting positive family history of breast cancer was 59, ages ranged from 30-79.	**Relatives' Cancers and other conditions:** Breast cancer **Information on affected relatives:** determine the age of diagnosis; determine the site of cancer,	**Tools compared:** Home FH interview compared to medical record (+/- path diagnosis) of 1DR +/- contact relatives **Number of participants recruited in each**	**Metric used to evaluate the adequacy of the tool:** NR **Other outcomes measured**: Accuracy data; 1: 68 cases and 37 controls reported a history of breast

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
affected and unaffected women's reports of breast cancer in first-degree relatives	care/tertiary care population Cancer patients: women diagnosed with cancer **Practitioners**: NR **Setting where developed**: specialist clinic: Oncology Network **Applicability**: FHxT not available for review **Setting where used**: Hospital; Patients home/Community setting **Cancer type**: Breast **Study design**: Cohort study (prospective)	**Medium**: NR **Integrated with e-record**: No	**Details on Relatives: Side of family identified**: Not specified Participant PMH NR **Relatives identified** First degree relatives Other: they were asked if they has relatives affected in general **Strategy for FH enquiry**: Not clear	DOB, date of death **Information on unaffected relatives:** NR	**group**: 843 women; 414 patients, 429 controls **Number of participants in analysis**: 68 women with breast cancer and 37 without **Number of first degree relatives:** 87, 38 by control reports of breast cancer in first-degree relatives **Number of second degree relatives:** NR	cancer in at least one first degree relative. 67 (91%) cases accurate 32 (97%) controls
Quillin[48] 2006 USA **Study purpose:** Test the hypothesis that women not pre-selected for familial risk report family history of breast cancer in fewer	**Patients:** Unselected primary care, community-based population patient's attending women's health clinic **Practitioners:** None (self-administered by patient) **Setting where developed:** Primary care women's health	**Purpose:** research; proactive **Method used to collect FH:** Self-completed survey : Questionnaire was completed in the clinic **Format:** Tabular **Medium:** paper	**Age of participants:** 40 years or older; largest proportion: 55.8% age 40-49. Relatives' age NR **Details on Relatives:** **Side of family identified:** Mother's side relatives Father's side relatives	**Relatives' Cancers and other conditions:** One syndrome cancer: focus of study on Breast Cancer, Any cancers identified **Information on affected relatives:** identify exact relationship to informant: determine	**Tools compared:** 1: Self administered paper questionnaire. **# of participants recruited in each group:** 899 **# of participants in analysis:** as above **# of first degree relatives:** NR **# of second degree**	**Metric used to evaluate the adequacy of the tool:** NR **Other outcomes measured:** 1: McNemar odds of reporting a maternal family history of breast cancer was 1.71 times greater than the odds of

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
paternal than maternal relatives	clinic **Applicability:** Reviewed FHxT; not applicable to primary care **Setting where used:** Primary care women's health clinic **Cancer type:** Breast **Study design:** Non-comparative study (case series)	**Integrated with e-record:** No	**Participants PMH:** Reported with details on ethnicity, breast cancer, previous genetic counseling **Relatives identified** Any relative (excluded mothers with Breast cancer) **Strategy for FH enquiry: DQ:** list relatives with any form of cancer, with prompts for side of family, "kind of cancer", age of diagnosis, and if died from cancer	the age of diagnosis: determine the cause of death: if died from cancer, determine exact diagnosis **Information on unaffected relatives:** not collected	**relatives:** NR # **of relatives;** 202	reporting paternal family history (p< 0.01, 95% CI 1.26 – 2.34). FH not validated

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Sijmons[17] 2000 Netherlands **Study purpose:** Examine the accuracy of the family history of cancer.	**Patients:** Specialist secondary care/tertiary care population Patient referred to Genetic clinic with FH cancer **Practitioners:** (self-administered by patient) Geneticist **Setting where developed:** Specialist genetic clinic **Applicability:** Reviewed FHxT; not applicable to primary care **Setting where used:** Genetic counseling clinic **Cancer type:** Breast, ovarian and colorectal **Study design:** Non-comparative study (case series)	**Purpose:** Clinical use - reactive and proactive **Format:** Pedigree **Medium:** Paper **Integrated with e-record:** No	**Age of participants:** Patients age NR Relatives age NR **Details on Relatives:** **Side of family identified:** Mother's side relatives Father's side relatives **Participant PMH** NR **Relatives identified** First and second degree relatives Most third degree relatives	**Relatives' Cancers and other conditions:** Any cancers (exclude metastasis) **Information on affected relatives:** DOB; date of death; determine the age of diagnosis; determine the cause of death; determine exact diagnosis; determine the site of cancer **Information on unaffected relatives:** DOB; date of death	**Tools compared:** FHQ compared to medical record,(+/- path reports) **# of participants recruited in each group:** 129 **# of participants in analysis:** 120 **# of first degree relatives:** group 1: NR, group 2: NR **# of second degree relatives:** NR	**Metric used to evaluate the adequacy of the tool: A**ccuracy of Ca by site: Br Ca (93%) CRC (89%) OvCa (71%), **Other outcomes measured:** NR
Skinner, 2005[49] USA **Study Purpose:** To evaluate the impact of the computerized	**Type of article** Journal article reporting a primary study **Study design:** Non-randomized Trial	**Purpose:** Clinical use, proactively **Method used to collect FH:** Pedigree	**Age of Participants:** Patients or informants. Relatives **Details on Relatives:** **Side of family identified:**	**Relatives' Cancers and other conditions:** Breast, colorectal **Information on affected relatives:** To identify exact	**Tools compared:** CRIS (Cancer Risk Intake System) **# of participants recruited in each group:** 227	**Metric used to evaluate accuracy:** -Cancer risk assessment: 83 (47%) had Gail-calculated breast cancer risk high enough to warrant

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
cancer risk intake system (CRIS)	**Participants:** Patients from a primary care provider, family physician and general internist **Provider:** General internist **Tool development:** Primary care **Setting:** **Cancer type:** Breast, colorectal **Study design & relevance** Prospective cohort	**Format:** Questionnaire. It displays messages for patients to discuss with clinicians **Medium:** Computerized **Integrated with e-record:** No	Mother's side relatives Father's side relative **Relatives identified:** FDR, SDR **Strategy for FH enquiry:** Computer-based questionnaire about FH	relationship to informant, determine the age of diagnosis, determine the site of cancer **Information on unaffected relatives:** N/A	**# of participants in analysis:** 215 **# of first degree relatives:** N/A **# of second degree relatives:** N/A	receipt of tailored messages on tamoxifen -Cancer risk assessment: 71 (33%) had breast, ovarian or colon cancer risk high enough to warrant receipt of tailored messages on genetic counseling -Cancer risk assessment: 31 (14%) had colon cancer risk high enough to warrant surveillance via colonoscopy and were currently non-adherent

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Theis[18] 1994 Canada **Study Purpose:** To compare FH data of women with breast cancer obtained from a newly developed questionnaire with data obtained in a subsequent interview	**Patients:** Selected Secondary/ tertiary care population: Cancer patients **Practitioners:** Tool 1 self-administered by patient Tool 2 by interviewers in clinic setting **Setting where developed:** Secondary care clinic **Applicability:** FHxT not available for review **Setting where used:** Secondary care clinic **Cancer type:** Breast/ovarian, prostate, colorectal **Study design:** Non-comparative study (case series)	**Purpose:** research: Reactive. **Method used to collect FH:** Tool 1: Self-completed FHQ FH (mail) Tool 2: follow-up Face to face personal GI **Format: Tool 1:** Tabular **Medium:** Tool 1: Paper medium: Questionnaire **Integrated with e-record:** No	**Age of participants:** Patients: 31 to 70 years. **Details on Relatives:** **Side of family identified:** Not specified **Participant PMH** NR **Relatives identified** First and second degree relatives. **Strategy for FH enquiry** Not clear	**Relatives' Cancers and other conditions:** Any cancers. **Information on affected relatives:** identify exact relationship to informant; determine the cause of death; determine the date of death; determine the age of diagnosis; determine exact diagnosis; determine the site of cancer; details of any breast surgery **Information on unaffected relatives:** identify exact relationship to informant; determine the cause of death; determine the date of death.	**Tools compared:** tool 1: questionnaire (FHQ), tool 2:followup Interview (GI),; compared to contact relatives +/- medic records +/- ca register +/- death certificates # of participants recruited in each group: 203. **# of participants in analysis:** 165. **# of first degree relatives:** 1,200 for both groups. **# of second degree relatives:** 3, 456 for both groups.	**Metric used to evaluate the adequacy of the tool:** Compare accuracy FHQ & GI (1) Quantitative First degree relatives (presence of cancer; site & age diagnosis) GI slightly better FHQ Second degree relatives GI better (age of diagnosis [11%]>presence of cancer [7%] > site diagnosis [5%]) **Other outcomes measured:** Accuracy of FH: age of diagnosis 1DR>2DR

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
Tischkowitz[50] 2000 UK **Study purpose:** To compare three methods used to estimate the risk for breast cancer in a group of high risk women	**Patients:** cancer genetic clinic **Practitioners:** Geneticist **Setting where developed:** Specialist genetic clinic **Applicability:** FHxT not available for review **Setting where used:** Genetic counselling clinic **Cancer type:** Breast **Study design:** Non-comparative study (case series/ reliability)	**Purpose:** clinical use; reactive **Method used to collect FH:** NR **Format:** Pedigree **Medium:** NR **Integrated with e-record:** Yes	**Age of participants: Patients:** NR; **relatives: y**ounger than 50 years **Details on Relatives: Side of family identified:** Mother's side relatives Father's side relatives **Participant PMH** NR **Relatives identified** First, second, third degree relatives and beyond	**Relatives' Cancers and other conditions:** Breast and ovarian cancer. **Information on affected relatives:** determine the age of diagnosis**.** **Information on unaffected relatives:** Age of all unaffected female relatives was recorded.	**Tools compared:** 1: one tool - NR asking detailed family history extending to at least 3 generations **# of participants recruited in each group:** Group 1: 200 women participating in the TRACE study. **# of participants in analysis:** group 1: 200. **# of first degree relatives:** NR **# of second degree relatives:** NR	**Metric used to evaluate the adequacy of the tool:** NR **Other outcomes measured:** 1: Risk assessment as measured with 3 methods: 1) CASH, 2) Houlston/Murday and 3) Qualitative see table 1 for results
Weinrich[19] 2002 USA **Study purpose:** To report on the stability of self-reported family history of prostate cancer over one-year	**Patients:** Selected primary care/community-based population men from a cancer registry (African American Hereditary Prostate Cancer study) **Practitioners:** NR: first interview	**Purpose:** research; reactive **Method used to collect FH:** DQ on Face to face personal interview: in-person interview first time, Identical Telephone interview: second interview one year later	**Age of participants:** Patients or informants: mean age 50.4 SD=7.6 **Details on Relatives: Side of family identified:** Mother's side relatives Father's side	**Relatives' Cancers and other conditions:** prostate cancer. **Information on affected relatives:** determine exact diagnosis; determine the site of cancer	**Tools compared:** 1: question at time 1, 2: question at time 2. **# of participants recruited in each group:** 96 **# of participants in analysis:** 96 **# of first degree relatives:** group 1:	**Metric used to evaluate the adequacy of the tool:** NR **Other outcomes measured:** 1: change between time 1 and time 1 self-report (one year later) (Precision) 48 different response

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
time	Nursing student second interview **Setting where developed:** Research **Applicability:** FHxT not available for review **Setting where used:** Face to face interview at a community-based educational program on prostate cancer screening **Cancer type:** Prostate **Study design:** Non-comparative study / reliability	**Format:** Not clear **Medium:** NR **Integrated with e-record:** No	relatives **Participant PMH** NR **Relatives identified** If positive family history for Prostate Cancer; identify First degree (Brother; Father; son) Second degree positive (Grand Parents; Grand Parents siblings) **Strategy for FH enquiry:** specific direct enquiry about FH Prostate cancer. If positive identify specific relatives	**Information on unaffected relatives:** NR	NR, group 2: NR. # **of second degree relatives:** group 1: NR, group 2: NR	on 2nd enquiry 1 year later
Ziogas[20] 2003 USA **Study purpose:** 1) to evaluate the consistency of patient-reported information on cancer in their first-, second- and third-degree relatives 2) To determine	**Patients:** Selected primary care/community-based population Cancer patients **Practitioners:** Interviewers (not specified) **Setting where developed:** Research **Applicability:** Reviewed FHxT; not	**Purpose:** research; reactive **Method used to collect FH:** Telephone interview **Format:** Pedigree **Medium: electronic medium:** interviewers entered data into Genetics Registry In System (GRIS)	**Age of participants: Informants** Age is not specified although informants are presented subdivided in 5 age groups from <40 years to 70+ **Details on Relatives: Side of family identified:** Mother's side relatives	**Relatives' Cancers and other conditions:** One syndrome cancer: focus on breast, ovarian, colon, any cancers **Information on affected relatives:** identify exact relationship to informant determine the age of diagnosis, determine the cause of and age of death	**Tools compared: 1:** Telephone interview, 2: Self report, pathology report, death certificate # **of participants recruited in each group:** n=1111 # **of participants in analysis:** n=1111 # **of first degree**	**Metric used to evaluate the adequacy of the tool:** False positive rate and false negative rate **Other outcomes measured:** 1: CI, confidence interval; NPV, negative predictive value; PAC, probability of agreement of cancer; PANC, probability of agreement of no

Evidence Table 2b. Eligible studies using family history tools but with insufficient information or tools not applicable to primary care (continued)

Author, Year, Country	Study population, setting, design	Purpose, data collection strategy and tool format	Tool structure: Participants +	Tool structure: Details on Relatives †	Tool evaluation: Comparison*	Tool evaluation: other measures ^
the positive and negative predictive values and probabilities of agreement between the patient-reported cancer status in relatives and the reference standard for various cancer sites 3) to determine the effect of the characteristics of the patient's relatives on the probability of agreement between patient-reported information and reference standard	applicable to primary care **Setting where used:** Patient's home/Community setting **Cancer type:** Breast/ovarian and colorectal **Study design:** Non-comparative study (case series)	**Integrated with e-record:** Not clear	**Participant PMH:** NR **Relatives** Age is not specified although informants are presented subdivided in 5 age groups from <50 years to 70+ **Participant's relevant past medical history:** NR **Relatives identified:** 1DR, 2DR, 3DR **Strategy for FH enquiry:** Not clear	**Information on unaffected relatives:** identify exact relationship to informant, determine the age of the diagnosis	**relatives:** not clear # **of second degree relatives:** not clear # **of relatives:** 3222	cancer

Evidence Table 3: Study characteristics for studies evaluating risk assessment tools (RATS)

Author, Year, Country	Tool, Purpose, Content and Format of tool, Underlying Guidelines/Models	Study Population, Cancer Type, Clinical Setting, Applicability	Study Design, Comparison Group(s) or Interventions, Sample Size	Key Results Relating to Clinical Utility
Benjamin[22] 2003 UK	**Tool:** Familial Cancer Assessment Tool (FCAT) **Purpose:** Stratify risk of familial breast cancer **Content**: Directed family history questions based on guideline with suggested onward management **Format**: Nurse-administered interview-based questionnaire, following patient completed advance family history questionnaire **Underlying guidelines**: Eccles DM et al. J Med Genet 2000; 37: 203-9	**Study population**: Patients referred to joint surgical/genetics family history breast screening clinic **Cancer type**: Breast **Setting**: Specialist genetic clinic **Applicability**: Potentially applicable to, but not developed or evaluated in, primary care setting	**Design**: Tool development and description **Comparison groups**: 1: Text of GP letter 2: Postal self-completion family history questionnaire alone 3: Genetic interview (gold standard) **Groups sample size for each group**: n=152	**Practice-related outcomes:** Ease of completion rated by nurse interviewer on 1-10 scale (easy-difficult) • 60/100 scales were rated 1-3 **Other outcomes reported:** Sensitivity, specificity, positive predictive value, negative predictive value; gold standard = genetic interview

Abbreviations: AMA=American Medical Association; Chi-square= χ^2; EsPeR=Personalized Estimate Risks; FCAT=Familial Cancer Assessment Tool; FHAT=Family History Assessment Tool; GP=General Practitioner; GRACE=Genetic Risk Assessment in the Clinical Environment; GRAIDS= Genetic Risk Assessment in an Intranet and Decision Support; ICC=Inter Class Correlation; NR=NR; PC=Primary Care; OR=Odds Ratio; RAGs=Risk Assessment in Genetics; SD=Standard deviation; USPSTF=United States Preventive Services Task Force;

Evidence Table 3: Study characteristics for studies evaluating risk assessment tools (RATS) (continued)

Author, Year, Country	Tool, Purpose, Content and Format of tool, Underlying Guidelines/Models	Study Population, Cancer Type, Clinical Setting, Applicability	Study Design, Comparison Group(s) or Interventions, Sample Size	Key Results Relating to Clinical Utility
Braithwaite[23] 2005 UK	**Tool:** Genetic Risk Assessment in the Clinical Environment (GRACE) **Purpose:** Cancer risk assessment and communication **Content**: Pedigree-based family history data collection with personalized risk report **Format**: Patient-completed, computer-based questionnaire **Underlying guidelines**: Claus, EB et al. Am J Human Genetics 1991; 48(2), 232-42	**Study population**: Women with family history of breast cancer recruited from general population through advertisements **Cancer type**: Breast **Setting**: Unspecified 'clinical environment' **Applicability**: Potentially applicable to, but not tested in, primary care setting	**Design**: Randomized controlled trial **Comparison group(s)**: Interview by clinical nurse specialist. Comparison and intervention arms returned self-completion postal family history questionnaire at baseline **Sample size**: GRACE: n=38 Control: n=38 **Power calculation:** No	**Practice-related outcomes:** 1. Acceptability to patients (post-clinic) (a) Attitude to interventions – six attributes, 5-point scale • 2/6 comparisons statistically significant, favored control arm (b) Perceived benefits of interventions – seven attributes, 5-point Likert scale • 7/7 comparisons statistically significant, favored control arm (c) Perceptions of risk information – five attributes, 5-point Likert scale • 5/5 comparisons statistically significant, favored control arm (d) Satisfaction and risk communication preferences – single item, 4-point Likert scale • 1/1 comparisons statistically significant, favored control arm 2. Cognitive outcomes (all baseline, post-clinic, 3 months) (a) Comparative risk perception – single item, 5-point scale • No significant difference between GRACE and control arms; statistically significant time x treatment interaction indicated reduction in elevated risk perceptions in control arm compared to GRACE arm (b) Risk accuracy – binary concordance between participant and guideline/clinical nurse specialist • No significant improvements in accuracy of risk perception observed in GRACE and control arms. Baseline differences between arms

Evidence Table 3: Study characteristics for studies evaluating risk assessment tools (RATS) (continued)

Author, Year, Country	Tool, Purpose, Content and Format of tool, Underlying Guidelines/Models	Study Population, Cancer Type, Clinical Setting, Applicability	Study Design, Comparison Group(s) or Interventions, Sample Size	Key Results Relating to Clinical Utility
				3. Affective outcomes (a) Hospital Anxiety and Depression Scale score (baseline, 3 months) • No significant difference between arms or between baseline and 3 months (b) Current anxiety - Spielberger's State-Trait Anxiety Inventory (short form) (baseline, post-clinic, 3 months) • Statistically significant increase in scores baseline-3 months in both arms; statistically significant treatment effect, favored control (c) Cancer worry (baseline, 3 months) • statistically significant decrease in cancer worry in both arms; no statistically significant difference between arms **Other outcomes reported:** N/A
Colombet[24,25] 2003 France	**Tool:** EsPeR System **Purpose:** Health professional decision-support **Content**: Family history collection, pedigree drawing, risk estimation based on published models, individualization of guidelines, printable summary of prevention messages for physicians and patients **Format**: Physician-completed, interactive web-based system. **Underlying guidelines**: Colombet I et al. Proc AMIA Symp 2002; 175-9; Gail model	**Study population**: Physicians in individual practice, teaching, health centers **Cancer type**: Breast, prostate, colorectal **Setting**: Ambulatory care **Applicability**: Some formative, but not definitive, evaluation in primary care	**Design**: Description of tool **Comparison groups**: N/A **Sample size:** N/A **Power calculation:** N/A	**Practice-related outcomes:** N/A **Other outcomes measured:** N/A

Evidence Table 3: Study characteristics for studies evaluating risk assessment tools (RATS) (continued)

Author, Year, Country	Tool, Purpose, Content and Format of tool, Underlying Guidelines/Models	Study Population, Cancer Type, Clinical Setting, Applicability	Study Design, Comparison Group(s) or Interventions, Sample Size	Key Results Relating to Clinical Utility
Emery[27] 1999 Emery[21] 2000 Emery[28] 2005 Emery[29] 2007 UK	**Tool:** Genetic Risk Assessment in an Intranet and Decision Support (GRAIDS), for which Risk Assessment in Genetics (RAGS) was the prototype **Purpose:** Management of familial cancer in primary care **Content**: Family history collection; pedigree drawing; patient-specific risk report; clinical practice guidelines/management advice; patient-specific explanations for the management advice **Format**: Web-based program designed to be used by a single lead physician in each practice. Preceded by an educational visit and a 2 hour training session; patients asked to complete family history questionnaire before attending practice **Underlying guidelines**: Claus, EB et al. Am J Human Genetics 1991; 48(2), 232-42	**Patients**: Family practice patients, family physicians **Cancer type**: Breast, ovarian, colorectal **Setting**: Family practice **Applicability:** Family practice	**Design:** Cluster randomized controlled trial with adaptive sub-group in intervention arm **Comparison groups:** 1. 45 minute educational session plus mailing of regional guidelines 2. Intervention as described, in fixed and adaptive sub-arms (adaptive received further input to promote greater software use) **Sample size:** 1. Practices n=22 Referred patients n=84 2. Practices n=23 (12 fixed, 11 adaptive) Referred patients n=162 Non-referred patients n=78 **Power calculation:** 20 practices per arm required to demonstrate 15% difference between arms (β=0.2, α=0.05)	**Practice-related outcomes:** Practices 1. Appropriateness of referrals a) consistency of family history reported in referral letter with regional guidelines • Breast cancer – intervention 99/107, control 44/60, OR (95%CI) = 4.5 (1.6-13.1) • Bowel cancer – intervention 75/76, control 23/25, OR (95%CI) = 6.5 (0.5-83.7) • Combined – intervention 174/183, control – 67/85, OR(95%CI) = 5.2 (1.7-15.8), p=0.006 b) final expert risk assessment of referred patients • Breast cancer – intervention 60/78, control 23/33, OR (95%CI) = 1.4 (0.6-3.5) • Bowel cancer – intervention 30/54, control 17/20, OR (95%CI) = 0.2 (0.1-0.8) • Combined – intervention 90/132, control – 40/53, OR(95%CI) = 0.7 (0.3-1.5), p=0.35 2. Patients a) Risk perception Mean scores (SD) – intervention (referred) 4.99 (1.14), intervention (not referred) 4.25 (0.80) control 5.04 (0.88), Intervention (referred) v control, mean difference (95% CI)= -0.09 (0.34-0.51), NS Intervention (not referred) v intervention (referred), mean difference (95%CI) = 0.74 (0.38-1.09), P<0.0001 b) Knowledge Breast cancer:

Evidence Table 3: Study characteristics for studies evaluating risk assessment tools (RATS) (continued)

Author, Year, Country	Tool, Purpose, Content and Format of tool, Underlying Guidelines/Models	Study Population, Cancer Type, Clinical Setting, Applicability	Study Design, Comparison Group(s) or Interventions, Sample Size	Key Results Relating to Clinical Utility
				Mean scores (SD) – intervention 5.77 (2.9), control 5.66 (2.78), mean difference (95% CI)= 0.11 (-1.05-1.27), NS Colorectal cancer: Mean scores (SD) – intervention 5.50 (2.46), control 4.86 (3.3), mean difference (95% CI)= 0.64 (-1.01-2.29), NS c) Cancer worry Mean scores (SD) – intervention (referred) 5.74 (3.04), intervention (not referred) 4.95 (2.99), control 7.18 (3.43) Intervention (referred) v control, mean difference (95% CI) = -1.44 (-2.64-0.23), P=0.02 Intervention (not referred) v intervention (referred), mean difference (95%CI) = 0.79 (-0.19-1.76), NS
Fisher[30] 2003 Australia	**Tool:** Triage tool embedded in family history questionnaire **Purpose:** Permit women to assess their own risk of familial breast cancer **Content**: Directed family history questions; risk triage (population or increased risk) and advice to see doctor if increased risk **Format**: Patient-completion paper-based questionnaire **Underlying guidelines**: Advice about familial aspects of breast cancer and ovarian cancer: a guide for health professionals. Kings Cross, New South Wales: National Breast Cancer Centre, 2000	**Study population**: Patients having repeat mammograms **Cancer type**: Breast **Setting**: Breast screening clinic **Applicability**: Potentially applicable to primary care	**Design**: Uncontrolled trial **Comparison groups**: None **Sample size:** Total n=559 Validation study n=89 **Power calculation:** NR	**Practice-related outcomes:** # participants making errors affecting risk categorization - 29/559 **Other outcomes measured:** Concordance between questionnaire-based category (I, II or III, population, moderate, potentially high risk, according to cited guideline) and risk based on genetic counsellor telephone interview

Evidence Table 3: Study characteristics for studies evaluating risk assessment tools (RATS) (continued)

Author, Year, Country	Tool, Purpose, Content and Format of tool, Underlying Guidelines/Models	Study Population, Cancer Type, Clinical Setting, Applicability	Study Design, Comparison Group(s) or Interventions, Sample Size	Key Results Relating to Clinical Utility
Gilpin[51] 2000 Canada	**Tool:** Family History Assessment Tool (FHAT) **Purpose:** Identify patients for referral **Content**: Directed family history questions with points specified for each affected family member **Format**: Clinician-oriented, paper-based **Underlying guidelines**: Predictive scoring system, described in same paper	**Study population**: Familial breast cancer registry plus patients referred to genetics clinic **Cancer type**: Breast, ovarian cancer **Setting**: Specialist genetic clinic **Applicability**: Designed to be applicable to, but not developed or evaluated in, primary care	**Design**: Tool development study **Comparison groups**: N/A **Sample size:** N/A **Power calculation:** N/A	**Practice-related outcomes:** N/A **Other outcomes measured:** Sensitivity, specificity, positive predictive value, negative predictive value; gold standard unclear
Gramling[52] 2004 USA	**Tool:** 'Brief tool' for physicians **Purpose:** Rapid assessment of family history **Content**: Risk stratification criteria; lifetime probability benchmark ranges; screening recommendations; genetics services contact numbers **Format**: Coat pocket laminated card for physicians, plus monograph on managing inherited breast cancer risk **Underlying guidelines**: USPSTF screening recommendations; AMA Monograph, Managing inherited breast cancer risk	**Study population**: Internal medicine, family physicians **Cancer type**: Breast **Setting**: Internal medicine, family practice **Applicability:** Developed for primary care settings	**Design**: Tool development study **Comparison groups**: None **Sample size:** n=7 **Power calculation:** NR	**Practice-related outcomes:** 1. Frequency of discussing inherited risk with patients with a family history of breast cancer (baseline, 3 months) • 5/7 reported decrease in frequency, 2/7 reported no change 2. Subjective threshold for classifying a woman as 'high risk' (baseline, 3 months) • 6/7 reported increase in subjective threshold **Other outcomes measured:** N/A
Skinner[49]2005 USA	**Tool:** Cancer Risk Intake System(CRIS) **Purpose:**	**Study population:** Clinic patients **Cancer type:**	**Design:** Uncontrolled before-after trial	**Practice-related outcomes:** 1. For those participants whose risk warranted a tailored tamoxifen

Evidence Table 3: Study characteristics for studies evaluating risk assessment tools (RATS) (continued)

Author, Year, Country	Tool, Purpose, Content and Format of tool, Underlying Guidelines/Models	Study Population, Cancer Type, Clinical Setting, Applicability	Study Design, Comparison Group(s) or Interventions, Sample Size	Key Results Relating to Clinical Utility
	Risk assessment, recommendations for discussion with provider **Content:** Risk assessment algorithm Tailored printouts **Format:** Touch-screen computer application linked to printer **Underlying guidelines:** Expert opinion based on Hampel et al, J Med Genet 2004; 41: 81-91. Burt RW, Gastroenterology 2000; 119: 837-53 Winawer S et al, Gastroenterology 2003; 124: 544-60. Smith RA et al, CA Cancer J Clin 2003; 53: 27-43	Breast/ovarian Colorectal **Setting:** Primary care **Applicability:** Primary care	**Comparison groups:** None **Sample size:** n=215 **Power calculation:** NR	message, pre-post change in proportion who reported discussing tamoxifen with clinician Pre - 4/83, Post - 23/83 P=0.00026 (McNemar's χ^2) 2. For those participants whose risk warranted a tailored cancer genetic counseling message, pre-post change in proportion who reported discussing cancer genetic counseling with clinician Pre - 2/71, Post - 20/71 P=0.00012 (McNemar's χ^2) 3. For those participants whose risk warranted a tailored colonoscopy message, pre-post change in proportion who reported discussing colonoscopy with clinician Pre - 5/31, Post - 14/31 P=0.0201 (McNemar's χ^2)
Watson[53] 2001 Watson[54] 2002 UK	**Tool:** Information pack **Purpose:** Risk assessment, clinical management **Content**: Referral guidelines; background information; patient leaflets **Format**: Laminated summary card plus booklet, presented as part of interactive education session **Underlying guidelines**: Report of the consensus meeting on the management of women with a family history of breast cancer. London: Wellcome Trust, 1998. Eccles DM et al. J Med Genet 2000; 37: 203-9	**Study population**: Family physicians **Cancer type**: Breast/ovarian **Setting**: Family practice **Applicability:** Family practice	**Design**: Cluster randomized controlled trial **Comparison groups**: 1: Tool alone 2: None **Sample size**: Group A - Tool plus education, Practices n=56, Physicians n=225 Group B - Tool alone, Practices n=57 Physicians n=233 Group C - No intervention, Practices n=57 Physicians n=230 **Power calculation:** Maximum 122	**Practice-related outcomes:** Timing unclear, 'post-intervention' 1. Proportion of physicians making 'correct' referral decision for ≥ 5/6 vignettes • Group A: 111/140 (79%) • Group B: 100/124 (81%) • Group C: 63/162 (63%) Overall p<0.001 (one way ANOVA); group A vs C – p<0.001 (χ^2); group B vs C, p<0.001 (χ^2); group A vs B, p=0.45 (χ^2) 2. Confidence scores in four aspects of managing patients with family history of cancer, 4-point Likert scale. • Mean (SD) overall confidence scores, possible scores 0-4: Group A: 2.3 (1.0); Group B: 2.0 (1.1); Group C: 1.5 (1.0) P<0.001

Evidence Table 3: Study characteristics for studies evaluating risk assessment tools (RATS) (continued)

Author, Year, Country	Tool, Purpose, Content and Format of tool, Underlying Guidelines/Models	Study Population, Cancer Type, Clinical Setting, Applicability	Study Design, Comparison Group(s) or Interventions, Sample Size	Key Results Relating to Clinical Utility
			physicians required per group (allowing for clustering) to detect an increase in primary outcome from 15% in Group C to 35% in Group B, or from 35% in Group B to 55% in Group A	(ANOVA linear trend) **Other outcomes reports:** N/A
Wilson[55] 2005 Wilson[56]2006 UK	**Tool:** Multifaceted decision aid **Purpose:** Familial cancer risk management **Content**: Targeted family history questions; risk assessment module; background information on cancer genetics; printer-friendly patient information leaflets; weblinks; email link to cancer genetics service; automated individualized referral letter **Format**: Physician-oriented personal computer package. Implemented with offer of education session **Underlying guidelines**: Scottish Cancer Group Cancer Genetics Sub-Group. Cancer genetics services in Scotland. Guidance to support the implementation of genetics services for breast, ovarian and colorectal cancer predisposition. Edinburgh: Scottish Executive Health Department, 2001	**Study population**: Women consulting family physicians with queries about familial breast cancer; family physicians **Cancer type**: Breast, ovarian, colorectal **Setting**: Family practice **Applicability:** Family practice	**Design**: Cluster randomized controlled trial **Comparison groups**: Scottish referral guidelines mailed by Department of Health **Sample size:** Physicians Intervention group - Responders pre-intervention n=179; Responders post-intervention n=151 Control group – Responders pre-intervention n=93; Responders post-intervention n=92 Patients Intervention group – Responders pre-intervention n=133; Responders post-intervention n=75 Control group – Responders pre-intervention n=52; Responders post-intervention n=22	**Practice-related outcomes:** Family physicians 1: Self-reported physician confidence, 4-point scale Patients • very confident or confident taking FH – intervention group, 91/151 (60%), control group 56/92 (61%); p=0.93 (χ^2) • very confident or confident knowing who to refer – intervention group 60/151 (40%), control group 30/91 (33%); p=0.27 (χ^2) • very confident or confident reassuring low risk – intervention group 85/151 (57%), control group 48/92 (52%); p=0.46 (χ^2) • very confident or confident able to answer questions – intervention group 35/151 (23%), control group 20/92 (22%); p=0.77 (χ^2) 2: Genetic risk of referred patients • Proportion of referred patients assessed as elevated genetic risk Intervention group 14/29 (48%), control group 22/34 (65%), NS (reported as risk ratio) N.B. Baseline differences between groups 3: Patients' breast cancer beliefs

Evidence Table 3: Study characteristics for studies evaluating risk assessment tools (RATS) (continued)

Author, Year, Country	Tool, Purpose, Content and Format of tool, Underlying Guidelines/Models	Study Population, Cancer Type, Clinical Setting, Applicability	Study Design, Comparison Group(s) or Interventions, Sample Size	Key Results Relating to Clinical Utility
			Power calculation: 168 interventions, 84 control practices required (2:1 allocation ratio) to detect absolute difference of 20% in physicians responding very confident or confident in attitude items, 80% power, α = 0.05, ICC 0.05	Proportion of referred patients agreeing with 'incorrect' causal statement • 'Stress always increases your risk' intervention group 17/74 (23%), control group 5/22 (23%); p=0.98 (χ^2) • 'Having one close relative with breast cancer always increases your risk' – intervention group 66/75 (88%), control group 20/22 (91%); p=0.71 (χ^2) • 'Minor injury always increases your risk' – intervention group 15/75 (20%), control group 5/22 (23%); p=0.78 (χ^2). **Other outcomes measured:** N/A

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Appendix D. List of Excluded Studies

Ahsan H, Neugut AI, Garbowski GC et al. Family history of colorectal adenomatous polyps and increased risk for colorectal cancer. Ann Intern Med 1998;128(11):900-905.
Exclusion: Not about accuracy and tool not standardized

Alberto VO, Harocopos CJ, Patel AA et al. Family and personal history in colorectal cancer patients: what are we missing? Int J Colorectal Dis 2006;8(7):612-614.
Exclusion: Does not apply to any of the research questions

Altieri A, Hemminki K. Number of siblings and the risk of solid tumours: a nation-wide study. Br J Cancer 6-4-2007;96(11):1755-1759.
Exclusion: Not about accuracy and tool not standardized

American Gastroenterological Association. American Gastroenterological Association medical position statement: hereditary colorectal cancer and genetic testing. Gastroenterology 2001;121(1):195-197.
Exclusion: Study Type

Amir E, Evans DG, Shenton A et al. Evaluation of breast cancer risk assessment packages in the family history evaluation and screening programme. J Med Genet 2003;40(11):807-814.
Exclusion: Guideline or consensus statement

Andermann A, Narod SA. Genetic counselling for familial breast and ovarian cancer in Ontario. J Med Genet 2002;39(9):695-696.
Exclusion: No data reported

Anderson WF, Matsuno RK, Sherman ME et al. Estimating age-specific breast cancer risks: a descriptive tool to identify age interactions. Cancer Causes Control 2007;18(4):439-447.
Exclusion: Not about accuracy and tool not standardized

Anonymous. American Gastroenterology Association issues guidelines for colorectal cancer screening. Am Fam Physician 1997;55(8):2860-2862,2865
Exclusion: Study Type

Anonymous. Assessing hereditary breast cancer risk. Cancer Pract 1999;7(6):279-284.
Exclusion: Not about accuracy and tool not standardized

Anonymous. Colorectal cancer screening. Recommendation statement from the Canadian Task Force on Preventive Health Care. Can Fam Physician 2001;47(Sept):1811-1815.
Exclusion: Study Type

Anonymous. Colorectal cancer screening: New recommendations. Consultant 2003;43(3):318-320.
Exclusion: No data reported

Anonymous. Raising concerns about family history of breast cancer in primary care consultations: prospective, population based study. BMJ 2001;322(7277):27-28.
Exclusion: Not about accuracy and tool not standardized

Antill YC, Shanahan M, Phillips KA. The integrated, multidisciplinary clinic: A new model for the ongoing management of women at high genetic risk for breast and ovarian cancer. Cancer Forum 2005;29(2):107-110.
Exclusion: Not about accuracy and tool not standardized

Antoniou AC, Durocher F, Smith P et al. BRCA1 and BRCA2 mutation predictions using the BOADICEA and BRCAPRO models and penetrance estimation in high-risk French-Canadian families. Breast Cancer Research. 2006;8(1):R3
Exclusion: Only a mutation or prediction

Bajdik CD, Raboud JM, Schechter MT et al. A computer model to simulate family history of breast/ovarian cancer in BRCA1 mutation carriers. Math Biosci 2001;171(1):99-111.
Exclusion: Only a mutation or prediction

Balmana J, Stockwell D H, Steyerberg E W et al. Prediction of MLH1 and MSH2 mutations in Lynch syndrome. JAMA. 2006;296(12):1469-1478.
Exclusion: Guideline or consensus statement

Bankhead C, Emery J, Qureshi N et al. New developments in genetics: Knowledge, attitudes and information needs of practice nurses. Fam Pract 2001;18(5):475-486.
Exclusion: Presents only aggregate data

Barcenas CH, Hosain GM, Arun B et al. Assessing BRCA carrier probabilities in extended families. Jpn J Clin Oncol 2006;24(3):354-360.
Exclusion: Only a mutation or prediction

Bartlett S. Predictive model for hereditary colorectal cancer. Lancet Oncol 2006;7(8):624
Exclusion: Narrative only

Becher H, Chang-Claude J. Estimating disease risks for individuals with a given family history in different populations with an application to breast cancer. Genet Epidemiol 1996;13(3):229-242.
Exclusion: Only a mutation or prediction

Beckmann MW, Schnurch HG, Bodden-Heidrich R et al. Early cancer detection programmes for women at high risk for breast and ovarian cancer: a proposal of practical guidelines. Eur J Cancer Prev 1996;5(6):468-475.
Exclusion: Study type

Beebe-Dimmer JL, Drake EA, Dunn RL et al. Association between family history of prostate and breast cancer among African-American men with prostate cancer. Urology 2006;68(5):1072-1076.
Exclusion: Does not apply to any of the research questions

Bell R, Petticrew M. Screening people with a family history of cancer. Benefit of screening for ovarian cancer is unproved. BMJ 11-15-1997;315(7118):1306
Exclusion: No data reported

Benichou J. A computer program for estimating individualized probabilities of breast cancer.[erratum appears in Comput Biomed Res 1994 Feb;27(1):81]. Computers & Biomedical Research 1993;26(4):373-382.
Exclusion: Narrative only

Bennett C, Burton H, Farndon P. Competences, education and support for new roles in cancer genetics services: Outcomes from the cancer genetics pilot projects. Fam Cancer 2007;6(2):171-180.
Exclusion: Not about accuracy and tool not standardized

Bergmann M, Wolf B, Karner-Hanusch J. Hereditary colorectal cancer - Guidelines for clinical routine. European Surgery - Acta Chirurgica Austriaca Supplement 2006;38(1):59-62.
Exclusion: Study Type

Berliner JL, Fay AM. Risk assessment and genetic counseling for hereditary breast and ovarian cancer: Recommendations of the National Society of Genetic Counselors. J Genet Couns 2007;16(3):241-260.
Exclusion: Not about accuracy and tool not standardized

Bhatia S, Pratt CB, Sharp GB et al. Family history of cancer in children and young adults with colorectal cancer. Med Pediatr Oncol. 1999;33(5):470-475.
Exclusion: Population

Biswas S, Berry DA. Determining joint carrier probabilities of cancer-causing genes using Markov chain Monte Carlo methods. Genet Epidemiol 2005;29(2):141-154.
Exclusion: Study Type

Blazer KR, Grant M, Sand SR et al. Effects of a cancer genetics education programme on clinician knowledge and practice. J Med Genet 2004;41(7):518-522.
Exclusion: Not about accuracy and tool not standardized

Blazer KR, MacDonald DJ, Ricker C et al. Outcomes from intensive training in genetic cancer risk counseling for clinicians. Genetics in Medicine. 2005;7(1):40-47.
Exclusion: No cancer of interest

Bodmer D, Ligtenberg MJL, Van Der et al. Optimal selection for BRCA1 and BRCA2 mutation testing using a combination of 'easy to apply' probability models. Br J Cancer 2006;95(6):757-762.
Exclusion: Guideline or consensus statement

Bonadona V, Sinilnikova OM, Chopin S et al. Contribution of BRCA1 and BRCA2 germ-line mutations to the incidence of breast cancer in young women: results from a prospective population-based study in France. Genes Chromosomes Cancer 2005;43(4):404-413.
Exclusion: Not about accuracy and tool not standardized

Bonadona V, Sinilnikova OM, Lenoir G M et al. Re: Pretest prediction of BRCA1 or BRCA2 mutation by risk counselors and the computer model BRCAPRO (multiple letters) [2]. J Natl Cancer Inst 2002;94(20):1582-1584.
Exclusion: Only a mutation or prediction

Braithwaite D, Sutton S, Smithson WH et al. Internet-based risk assessment and decision support for the management of familial cancer in primary care: a survey of GPs' attitudes and intentions. Fam Pract 2002;19(6):587-590
Exclusion: Not about accuracy and tool not standardized

Brennan P, Claber O, Shaw T. The Teesside Cancer Family History Service: Change management and innovation at cancer network level. Fam Cancer 2007;6(2):181-187.
Exclusion: Does not apply to any of the research questions

Burke W, Daly M, Garber J et al. Recommendations for follow-up care of individuals with an inherited predisposition to cancer: II. BRCA1 and BRCA2. JAMA 1997;277(12):997-1003
Exclusion: Study Type

Burke W, Petersen G, Lynch P et al. Recommendations for follow-up care of individuals with an inherited predisposition to cancer: I. Hereditary nonpolyposis colon cancer. JAMA 1997;277(11):915-919
Exclusion: Study Type

Burrer C V, Bauer S M. Insights into genetic testing for colon cancer: the nurse practitioner role. Clin Excell Nurse Pract 2000;4(6):349-355.
Exclusion: Study type

Calzone K A, Stopfer J, Blackwood A et al. Establishing a cancer risk evaluation program. Cancer Practice: A Multidisciplinary Journal of Cancer Care 1997;5(4):228-233.
Exclusion: No data reported

Camp NJ, Slattery ML. Classification tree analysis: a statistical tool to investigate risk factor interactions with an example for colon cancer (United States). Cancer Causes Control. 2002;13(9):813-823.
Exclusion: Not about accuracy and tool not standardized

Capalbo C, Ricevuto E, Vestri A et al. Improving the accuracy of BRCA1/2 mutation prediction: validation of the novel country-customized IC software. Eur J Hum Genet 2006;14(1):49-54.
Exclusion: Only a mutation or prediction

Carayol J, Khlat M, Maccario J et al. Hereditary non-polyposis colorectal cancer: current risks of colorectal cancer largely overestimated. J Med Genet 2002;39(5):335-339.
Exclusion: Only a mutation or prediction

Casadei S, Falcini F, Naldoni C et al. Population-based screening for hereditary breast cancer in a region of North-Central Italy. Int J Mol Med 2002;10(3):299-305.
Exclusion: Guideline or consensus statement

Catherino WH, Andolsek K. Women at high risk for breast cancer: A primary care perspective. --- 1998;5(6):268-275.
Exclusion: Study type

Chang-Claude J, Becher H, Caligo M et al. Risk estimation as a decision-making tool for genetic analysis of the breast cancer susceptibility genes. Dis Markers 1999;15(1-3):53-65.
Exclusion: Only a mutation or prediction

Chatterjee N, Kalaylioglu Z, Shih J H et al. Case-control and case-only designs with genotype and family history data: estimating relative risk, residual familial aggregation, and cumulative risk. Biometrics 2006;62(1):36-48.
Exclusion: Only a mutation or prediction

Chatterjee N, Shih J, Hartge P et al. Association and aggregation analysis using kin-cohort designs with applications to genotype and family history data from the Washington Ashkenazi Study. Genet Epidemiol 2001;21(2):123-138.
Exclusion: Only a mutation or prediction

Chen S, Wang W, Lee S et al. Prediction of germline mutations and cancer risk in the Lynch syndrome. JAMA 2006;296(12):1479-1487.
Exclusion: Only a mutation or prediction

Church J M. A scoring system for the strength of a family history of colorectal cancer. Dis Colon Rectum 2005;48(5):889-896.
Exclusion: Does not apply to any of the research questions

Church J, Lowry A, Simmang C et al. Practice parameters for the identification and testing of patients at risk for dominantly inherited colorectal cancer--supporting documentation. Dis Colon Rectum 2001;44(10):1404-1412.
Exclusion: Only a mutation or prediction

Church J, McGannon E. Family history of colorectal cancer: how often and how accurately is it recorded? Dis Colon Rectum. 2000;43(11):1540-1544.
Exclusion: Not about accuracy and tool not standardized

Clark SK, Carpenter S, Broughton CIM et al. Surveillance of individuals at intermediate risk of colorectal cancer - The impact of new guidelines. Int J Colorectal Dis 2003;5(6):582-584.
Exclusion: Not about accuracy and tool not standardized

Claus EB, Stowe M, Carter D. Family history of breast and ovarian cancer and the risk of breast carcinoma in situ. Breast Cancer Res Treat 2003;78(1):7-15.
Exclusion: Guideline or consensus statement

Clough GR. Taking control of family history screening. Synergy 2003;15-7.
Exclusion: No data reported

Cochrane RA, Davies EL, Singhal H et al. The National Breast Referral Guidelines have cut down inappropriate referrals in the under 50s. Eur J Surg Oncol. 1999;25(3):251-254.
Exclusion: Not about accuracy and tool not standardized

Cohen MM. Statement of the American Society of Human Genetics on genetic testing for breast and ovarian cancer predisposition. Am J Hum Genet 1994;55(5):i-iv.
Exclusion: Study type

Colombet I, Xu Y, Jaulent MC et al. A generic computerized method for estimate of familial risks. Proceedings / AMIA ...Annual Symposium.2002:175-9
Exclusion: Presents only aggregate data

Cortesi L, Turchetti D, Marchi I et al. Breast cancer screening in women at increased risk according to different family histories: an update of the Modena Study Group experience. BMC Cancer 2006;6:210
Exclusion: Not about accuracy and tool not standardized

Cortizo-Torres ME, Duarte F, Schmitt FC et al. Criteria for definition of hereditary breast cancer in a clinic perspective. Breast J 2002;8(6):402-403.
Exclusion: Only a mutation or prediction

Coulson AS, Glasspool DW, Fox J et al. RAGs: A novel approach to computerized genetic risk assessment and decision support from pedigrees. Methods Inf Med 2001;40(4):315-322.
Exclusion: Narrative only

Couto E, Hemminki K. Estimates of heritable and environmental components of familial breast cancer using family history information. Br J Cancer 2007;96(11):1740-1742.
Exclusion: Not about accuracy and tool not standardized

Cuzick J. Epidemiology of breast cancer--selected highlights. Breast 2003;12(6):405-411.
Exclusion: Study Type

Daly MB, Axilbund JE, Bryant E et al. Genetic/familial high-risk assessment: Breast and ovarian. Clinical Practice Guidelines in Oncology. J Natl Compr Cancer Netw 2006;4(2):156-176.
Exclusion: Study Type

Daly M, Farmer J, Harrop-Stein C et al. Exploring family relationships in cancer risk counseling using the genogram. Cancer Epidemiol Biomarkers Prev 1999;8(4 Pt 2):393-398.
Exclusion: Not about accuracy and tool not standardized

Daly PA. Hereditary cancer: Guidelines in clinical practice - General overview. Ann Oncol 2004;15(SUPPL. 4):iv121-iv125.
Exclusion: Study Type

de Bock GH, van Asperen CJ, de Vries JM et al. How women with a family history of breast cancer and their general practitioners act on genetic advice in general practice: Prospective longitudinal study. Br Med J 2001;322(7277):26-27.
Exclusion: Not about accuracy and tool not standardized

de Bock GH, Vliet Vlieland TPM, Hageman GCHA et al. The assessment of genetic risk of breast cancer: A set of GP guidelines. Fam Pract 1999;16(1):71-77.
Exclusion: Does not apply to any of the research questions

de Bock GH, Vliet Vlieland TPM, Hakkeling M et al. GPs' management of women seeking help for familial breast cancer. Fam Pract 1999;16(5):463-467.
Exclusion: Not about accuracy and tool not standardized

de Bock GH, van Asperen CJ, de Vries JM et al. How women with a family history of breast cancer and their general practitioners act on genetic advice in general practice: prospective longitudinal study. BMJ 2001;322(7277):26-27.
Exclusion: Not about accuracy and tool not standardized

de Bock GH, Vlieland TP, Hakkeling M et al. GPs' management of women seeking help for familial breast cancer. Fam Pract 1999;16(5):463-467.
Exclusion: Not about accuracy and tool not standardized

de la Hoya M, Perez-Segura P, Van Orsouw,N et al. Spanish family study on hereditary breast and/or ovarian cancer: analysis of the BRCA1 gene. Int J Cancer 2001;91(1):137-140.
Exclusion: Not about accuracy and tool not standardized

DeMarco TA, Loffredo CA, Sampilo ML et al. On using a cancer center cancer registry to identify newly affected women eligible for hereditary breast cancer syndrome testing: practical considerations. J Genet Couns 2006;15(2):129-136.
Exclusion: Not about accuracy and tool not standardized

Dominguez FJ, Jones JL, Zabicki K et al. Prevalence of hereditary breast/ovarian carcinoma risk in patients with a personal history of breast or ovarian carcinoma in a mammography population. Cancer 2005;104(9):1849-1853.
Exclusion: Guideline or consensus statement

Donohue-Moore M. Commentary on Patterns of inheritance of ovarian cancer: an analysis from an ovarian cancer screening program. ONS Nursing Scan in Oncology 1994;3(2):20
Exclusion: Presents only aggregate data

Douglas FS, O'Dair LC, Robinson M et al. The accuracy of diagnoses as reported in families with cancer: a retrospective study. J Med Genet 1999;36(4):309-312.
Exclusion: Not about accuracy and tool not standardized

Eccles DM, Evans DGR, Mackay J. Guidelines for a genetic risk based approach to advising women with a family history of breast cancer. J Med Genet 2000;37(3):203-209.
Exclusion: Study Type

Eccles DM, Kennedy R, Quinn J et al. Genetic testing for BRCA1 mutation in the UK [4] (multiple letters). Lancet 2003;361(9352):178-179.
Exclusion: No data reported

Eisinger F, Horsman DE. Genetic risk assessment and BRCA mutation testing. Ann Intern Med 2006;144(5):376-377.
Exclusion: Study Type

Eisinger F, Reynier CJ, Chabal F et al. Acceptable strategies for dealing with hereditary breast/ovarian cancer risk. J Natl Cancer Inst 1997;89(10):731
Exclusion: Not about accuracy and tool not standardized

Eisinger F, Sobol H. Comments on: Current policies for surveillance and management in women at risk of breast and ovarian cancer: a survey among 16 European family cancer clinics, Vasen et al., Eur J Cancer 1998, 34, 1922-1926. Eur J Cancer 1999;35(5):859-860.
Exclusion: Narrative only

Emery J. Familial breast cancer. Fam Pract 1997;14(5):422
Exclusion: No data reported

Escher M, Sappino AP. Primary care physicians' knowledge and attitudes towards genetic testing for breast-ovarian cancer predisposition. Ann Oncol. 2000;11(9):1131-1135.
Exclusion: Not about accuracy and tool not standardized

Euhus DM, Leitch AM, Huth JF et al. Limitations of the Gail model in the specialized breast cancer risk assessment clinic. Breast J 2002;8(1):23-27.
Exclusion: Guideline or consensus statement

Euhus DM, Smith KC, Robinson L et al. Pretest prediction of BRCA1 or BRCA2 mutation by risk counselors and the computer model BRCAPRO. J Natl Cancer Inst 2002;94(11):844-851.
Exclusion: Only a mutation or prediction

Evans DG, Easton D. Family history of breast cancer: referral guidelines changed after acceptance of 10 minute consultation. BMJ 2005;330(7493):730
Exclusion: No data reported

Evans DG, Eccles DM, Rahman N et al. A new scoring system for the chances of identifying a BRCA1/2 mutation outperforms existing models including BRCAPRO. J Med Genet 2004;41(6):474-480.
Exclusion: Guideline or consensus statement

Evans DG, Lalloo F, Wallace A et al. Update on the Manchester Scoring System for BRCA1 and BRCA2 testing.. J Med Genet 2005;42(7):e39
Exclusion: Only a mutation or prediction

Evans D, Lalloo F, Shenton A et al. Uptake of screening and prevention in women at very high risk of breast cancer. Lancet 2001;358(9285):889-890.
Exclusion: Not about accuracy and tool not standardized

Evans G, Eeles R. Hereditary cancer. Lancet Oncol 2000;1(1):12-13.
Exclusion: No data reported

Evans S, Lynch HT, Fusaro RM. Clinical results using informatics to evaluate hereditary cancer risk. Proceedings - the Annual Symposium on Computer Applications in Medical Care 1995:834-8
Exclusion: Presents only aggregate data

Farraye F, Gangarosa L, Burt RW et al. American Gastroenterological Association Medical Position Statement: Hereditary colorectal cancer and genetic testing. Gastroenterology 2001;121(1):195-197.
Exclusion: Study Type

Federico M, Maiorana A, Mangone L et al. Identification of families with hereditary breast and ovarian cancer for clinical and mammographic surveillance: the Modena Study Group proposal. Breast Cancer Res Treat 1999;55(3):213-221.
Exclusion: Guideline or consensus statement

Fidalgo PO, Cravo ML, Nobre-Leitao C. Re: A National Cancer Institute Workshop on Hereditary Nonpolyposis Colorectal Cancer Syndrome: meeting highlights and Bethesda Guidelines. J Natl Cancer Inst 1998;90(12):939-940.
Exclusion: Study Type

Floderus B, Barlow L, Mack TM. Recall bias in subjective reports of familial cancer. Am J Epidemiol 1990;1(4):318-321. Exclusion: Not about accuracy and tool not standardized

Fornasarig M, Viel A, Bidoli E et al. Amsterdam criteria II and endometrial cancer index cases for an accurate selection of HNPCC families. Tumori 2002;88(1):18-20.
Exclusion: No cancer of interest

Foulkes WD, Brunet JS, Warner E et al. The importance of a family history of breast cancer in predicting the presence of a BRCA mutation. Am J Hum Genet 1999;65(6):1776-1779.
Exclusion: Not about accuracy and tool not standardized

Foulkes W, Glendon G, Narod S. Family history and risk of ovarian cancer. JAMA 1995;274(5):383
Exclusion: No data reported

Friedenson B. Assessing and managing breast cancer risk: Clinical tools for advising patients. Medgenmed [Computer File]: Medscape General Medicine 2004;6(1)8
Exclusion: Study type

Fries MH, Holt C, Carpenter I et al. Guidelines for evaluation of patients at risk for inherited breast and ovarian cancer: recommendations of the Department of Defense Familial Breast/Ovarian Cancer Research Project. Mil Med 2002;167(2):93-98. Exclusion: Study Type

Furukawa T, Konishi F, Shitoh K et al. Evaluation of screening strategy for detecting hereditary nonpolyposis colorectal carcinoma. Cancer 2002;94(4):911-920.
Exclusion: Only a mutation or prediction

Garbers V, Toniolo P G, Taioli E. Changes in self-reported family history of breast cancer with change in case-control status. Eur J Epidemiol 2001;17(6):517-520.
Exclusion: Not about accuracy and tool not standardized

Garcia-Patino E, Gomendio B, Silva JM et al. BRCA1 mutations in patients with familial risk of breast cancer. Acta Oncol (Madr) 1998;37(3):299-300.
Exclusion: Study Type

Glasspool DW, Fox J, Coulson AS et al. Risk assessment in genetics: a semi-quantitative approach. Medinfo 2001;10(Pt 1):459-463.
Exclusion: Study Type

Goelen G, Teugels E, Sermijn E et al. Comparing the performance of family characteristics and predictive models for germline BRCA1/2 mutations in breast cancer families. Archives of Public Health 2003;61(6):297-312.
Exclusion: Only a mutation or prediction

Goetsch CM, Smith SM, Olopade OI et al. Multidisciplinary rounds. Assessing hereditary breast cancer risk. Cancer Practice: A Multidisciplinary Journal of Cancer Care 1999;7(6):279-284.
Exclusion: Study Type

Gramling R, Anthony D, Simmons E et al. Self-rated breast cancer risk among women reporting a first-degree family history of breast cancer on office screening questionnaires in routine medical care: the role of physician-delivered risk feedback. Genet Med 2006;8(10):658-664.
Exclusion: Does not apply to any of the research questions

Gray E, Rothnie N, Fowler A. Family histories of cancer in primary care. Nurse led clinic may provide better service than computer program. BMJ 2000;321(7266):955
Exclusion: No data reported

Gray RE, Chart P, Carroll JC et al. Family physicians' perspectives on ovarian cancer. Cancer Prevention & Control. 1999;3(1):61-67.
Exclusion: Not about accuracy and tool not standardized

Grumet SC, Bruner DW. The identification and screening of men at high risk for developing prostate cancer. Urol Nurs 2000;20(1):15-8,23-4,46.
Exclusion: No data reported

Gui GPH, Hogben RKF, Walsh G et al. The incidence of breast cancer from screening women according to predicted family history risk: Does annual clinical examination add to mammography?. Eur J Cancer 2001;37(13):1668-1673.
Exclusion: Only a mutation or prediction

Guillem J G. Need for screening colonoscopy in first-degree relatives. Gastroenterology 1997;112(6):2161-2162.
Exclusion: No data reported

Gulzar Z, Goff S, Njindou A et al. Nurse-led cancer genetics clinics in primary and secondary care in varied ethnic population areas: Interaction with primary care to improve ascertainment of individuals from ethnic minorities. Fam Cancer 2007;6(2):205-212.
Exclusion: Does not apply to any of the research questions

Gurmankin Levy A, Shea J, Williams SV et al. Measuring perceptions of breast cancer risk. Cancer Epidemiol Biomarkers Prev 2006;15(10):1893-1898.
Exclusion: Does not apply to any of the research questions

Hakama M. Family history in colorectal cancer surveillance strategies. Lancet 2006;368(9530):101-103.
Exclusion: No data reported

Hampel H, Sweet K, Westman JA et al. Referral for cancer genetics consultation: A review and compilation of risk assessment criteria. J Med Genet 2004;41(2):81-91.
Exclusion: Presents only aggregate data

Hapgood R, Qureshi N, Allen J. Breast cancer genetics in primary care: Which GPs most accurately categorise patients at low risk?. Eur J Gen Pract 2002;8(4):146-150.
Exclusion: Not about accuracy and tool not standardized

Hartenbach EM, Becker JM, Grosen EA et al. Progress of a Comprehensive Familial Cancer Genetic Counseling Program in the Era of BRCA1 and BRCA2. Genet Test 2002;6(2):75-78.
Exclusion: Only a mutation or prediction

Hemminki K, Chen B. Familial risk for colon and rectal cancers. Int J Cancer 2004;111(5):809-810.
Exclusion: Not about accuracy and tool not standardized

Hicken GJ, Francis A, Harries SA. Hereditary breast cancer. Br J Surg 1998;85(4):570-571.
Exclusion: No data reported

Hill A, McDermott E, O'Higgins N. Hereditary breast cancer. Br J Surg 1998;85(8):1157
Exclusion: No data reported

Hodgson SV, Bishop DT, Dunlop M G et al. Suggested screening guidelines for familial colorectal cancer. J Med Screen 1995;2(1):45-51.
Exclusion: Study Type

Hodgson SV, Mohammed SN. Screening for breast cancer. Consider family history also. BMJ 1994;309(6955):664
Exclusion: Not about accuracy and tool not standardized

Hoskins KF, Zwaagstra A, Ranz M. Validation of a tool for identifying women at high risk for hereditary breast cancer in population-based screening. Cancer 2006;107(8):1769-1776.
Exclusion: Does not apply to any of the research questions

Hoskins Kent F, Stopfer Jill E, Calzone Kathleen A et al. Assessment and counseling for women with a family history of breast cancer: A guide for clinicians. JAMA 1995;273(7):577-585.
Exclusion: No data reported

Huelsman KM, Huppert J, Fiorica J. Screening your patients for inherited breast and ovarian cancer: how to collect family history data. Contemp Ob Gyn 1998;43(11):107-8,111-2,114.
Exclusion: Study type

Hughes KS, Roche CA, Whitney T et al. The management of women at high risk of experiencing hereditary breast and ovarian cancer: The lahey guidelines. Disease Management & Health Outcomes 2000;7(4):201-215.
Exclusion: Study type

Hunt L, Armitage N C. Screening for large bowel neoplasms in individuals with a family history of colorectal neoplasms. Br J Surg 1992;79(12):1384-1385.
Exclusion: No data reported

Husson G, Herrinton LJ. How accurately does the medical record capture maternal history of cancer?. Cancer Epidemiol Biomarkers Prev 2000;9(7):765-768.
Exclusion: Not about accuracy and tool not standardized

Iredale R, Brain K, Gray J et al. The information and support needs of women at high risk of familial breast and ovarian cancer: how can cancer genetic services give patients what they want?. Fam Cancer 2003;2(2):119-121.
Exclusion: Not about accuracy and tool not standardized

Irmejs A, Borosenko V, Melbarde-Gorkusa I et al. Nationwide study of clinical and molecular features of hereditary non-polyposis colorectal cancer (HNPCC) in Latvia. Anticancer Res 2007;27(1B):653-658.
Exclusion: Not about accuracy and tool not standardized

Irwin DE, Millikan RC, Stevens R et al. Genomics and public health practice: a survey of nurses in local health departments in North Carolina. J Public Health Manag Pract 2004;10(6):539-544.
Exclusion: No cancer of interest

Jacobi CE, Jonker MA, Nagelkerke NJ et al. Prevalence of family histories of breast cancer in the general population and the incidence of related seeking of health care. J Med Genet 2003;40(7):e83
Exclusion: Not about accuracy and tool not standardized

Jacobi CE, van Ierland Y, van Asperen CJ et al. Prediction of BRCA1/2 mutation status in patients with ovarian cancer from a hospital-based cohort. Genet Med 2007;9(3):173-179.
Exclusion: Not about accuracy and tool not standardized

Jacobs C, Rawson R, Campion C et al. Providing a community-based cancer risk assessment service for a socially and ethnically diverse population. Fam Cancer 2007;6(2):189-195.
Exclusion: Does not apply to any of the research questions

Jacobs LA. Author reexamines literature on genetics and hereditary nonpolyposis colon cancer. Oncol Nurs Forum 1998;25(6):975
Exclusion: Narrative only

James PA, Doherty R, Harris M et al. Optimal selection of individuals for BRCA mutation testing: A comparison of available methods. J Clin Oncol 2006;24(4):707-715.
Exclusion: Not about accuracy and tool not standardized

James PA, Parry S, Arnold J et al. Confirming a diagnosis of hereditary colorectal cancer: The impact of a familial bowel cancer registry in New Zealand. N Z Med J 2006;119(1242):1-6.
Exclusion: Does not apply to any of the research questions

Jass JR. Screening for familial colorectal cancer. Gut 1996;39(3):497
Exclusion: No data reported

John EM, Hopper JL, Beck JC et al. The Breast Cancer Family Registry: an infrastructure for cooperative multinational, interdisciplinary and translational studies of the genetic epidemiology of breast cancer. Breast Cancer Res 2004;6(4):R375-R389. Exclusion: Study Type

Johnson J, Giles RT, Larsen L et al. Utah's Family High Risk Program: bridging the gap between genomics and public health. Prev Chronic Dis 2005;2(2):A24
Exclusion: Presents only aggregate data

Jonker MA, Jacobi CE, Hoogendoorn WE et al. Modeling familial clustered breast cancer using published data. Cancer Epidemiol Biomarkers Prev 2003;12(2):1479-1485.
Exclusion: Not about accuracy and tool not standardized

Julian-Reynier C, Eisinger F, Moatti J P et al. Re: Randomized trial of a specialist genetic assessment service for familial breast cancer. J Natl Cancer Inst 2001;93(2):158-159.
Exclusion: Not about accuracy and tool not standardized

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Exclusion: Study type

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Exclusion: Guideline or consensus statement

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Exclusion: No cancer of interest

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Exclusion: Study type

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Exclusion: Study Type

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Exclusion: Study type

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Schroy PC, Barrison AF, Ling BS et al. Family history and colorectal cancer screening: A survey of physician knowledge and practice patterns. Am J Gastroenterol 2002;97(4):1031-1036.
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Exclusion: Not about accuracy and tool not standardized

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Exclusion: Study Type

Unic I, Stalmeier PFM, Peer PGM et al. A review on family history of breast cancer: Screening and counseling proposals for women with familial (non-hereditary) breast cancer. Patient Educ Couns 1997;32(1-2):117-127
Exclusion: Study Type

Vahteristo P, Eerola H, Tamminen A et al. A probability model for predicting BRCA1 and BRCA2 mutations in breast and breast-ovarian cancer families. Br J Cancer 2001;84(5):704-708.
Exclusion: Guideline or consensus statement

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Exclusion: Study type

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Exclusion: Study Type

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Exclusion: Study type

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Exclusion: Study Type

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Exclusion: Study Type

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Exclusion: Study type

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Exclusion: Only a mutation or prediction

Yusoff IF, Hoffman NE, Ee H C. Colonoscopic surveillance for family history of colorectal cancer: are NHMRC guidelines being followed? Med J Aust 2002;176(4):151-154.
Exclusion: Not about accuracy and tool not standardized

Zarchy TM, Ershoff D. Risk of colorectal cancer in families of patients with adenomatous polyps. N Engl J Med 1996;334(20):1339-1340.
Exclusion: No data reported

Appendix E. Technical Expert Panel and Peer Reviewers

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