Evidence Report/Technology Assessment
Number 179

Clinical Utility of Cancer Family History Collection in Primary Care

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. 290-02-0020

Prepared by:
McMaster University Evidence-based Practice Center, Hamilton, ON

Task Order Leaders:
Brenda Wilson, M.B., Ch.B., M.Sc, M.R.C.P.(U.K.), F.F.P.H.
Nadeem Qureshi, M.B.B.S., D.M.

Authors:
Brenda Wilson, M.B., Ch.B., M.Sc., M.R.C.P.(U.K.), F.F.P.H.
Nadeem Qureshi, M.B.B.S., D.M.
Julian Little, M.A., Ph.D.
Pasqualina Santaguida, B.Sc., P.T., Ph.D.
June Carroll, M.D., C.C.F.P., F.C.F.P.
Judith Allanson, M.B., Ch.B., F.R.C.P., F.R.C.P.(C.), F.C.C.M.G., D.A.B.M.G.
Homa Keshavarz, M.Sc., Ph.D.
Parminder Raina, B.Sc., Ph.D.

AHRQ Publication No. 09-E007
April 2009

This document is in the public domain and may be used and reprinted without permission except those copyrighted materials noted for which further reproduction is prohibited without the specific permission of copyright holders.

Suggested Citation:
Wilson B, Qureshi N, Little J, Santaguida P, Carroll J, Allanson J, Keshavarz H, Raina P. Clinical Utility of Cancer Family History Collection in Primary Care. Evidence Report/Technology Assessment No.179. (Prepared by the McMaster University Evidence-based Practice Center, under Contract No. 290-02-0020.) AHRQ Publication No. 09-E007. Rockville, MD: Agency for Healthcare Research and Quality.
April 2009.

No investigators have any affiliations or financial involvement (e.g., employment, consultancies, honoraria, stock options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in this report.

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 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.

Carolyn M. Clancy, M.D.
Director
Agency for Healthcare Research and Quality

Richard E. Besser, M.D.
Acting Director
Centers for Disease Control and Prevention

Jean Slutsky, P.A., M.S.P.H.
Director, Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Beth A. Collins Sharp, R.N., Ph.D.
Director, EPC Program
Agency for Healthcare Research and Quality

Supriya Janakiraman, M.D., M.P.H.
EPC Program Task Order Officer
Agency for Healthcare Research and Quality

Acknowledgments

The researchers at the Evidence-based Practice Center would like to acknowledge the following people for their contributions.

We are grateful to Gurvaneet Randhawa, Supriya Janakiraman and members of the technical expert panel who were instrumental in developing the questions and defining the scope of this review: Robert German, Rodolfo Valdez, Lisa Madlensky, and Louise Acheson.

We would also like to thank Maureen Rice for developing and running the search strategies; Catherine Salmon, Connie Freeborn, Robert Stevens, Lynda Booker, Solina Yoo, Kate Walker, Sara Kaffashian, and Maureen Rice for screening the citations; and Sara Shepley for managing the references in RefMan and SRS and for assistance in article retrieval.

Thank you to Rachel Morris for the many hours of screening and data abstraction.

We would like to thank Valery L'Heureux and Silvia Visentin at the University of Ottawa for their administrative assistance to the investigators.

Finally we would like to say thank you to Mary Gauld, Maureen Rice, Roxanne Cheeseman, and Cecile Royer for their invaluable input in the editing and formatting of this report.

Structured Abstract

Objectives: This systematic review aimed to evaluate, within unselected populations: the (1) performance of family history (FHx)-based models in predicting cancer risk; (2) overall benefits and harms associated with established cancer prevention interventions; (3) impact of FHx-based risk information on the uptake of preventive interventions; and (4) potential for harms associated with collecting cancer FHx.

Data Sources: MEDLINE®, EMBASE®, CINAHL® Cochrane Central®, Cochrane Database of Systematic Reviews, and PsycINFO were searched from 1990 to June 2008 inclusive. Cancer guidelines and recommendations were searched from 2002 forward and systematic reviews from 2003 to June 2008.

Review Methods: Standard systematic review methodology was employed. Eligibility criteria included English studies evaluating breast, colorectal, ovarian, or prostate cancers. Study designs were restricted to systematic review, experimental and diagnostic types. Populations were limited to those unselected for cancer risk. Interventions were limited to collection of cancer FHx; primary and/or secondary prevention interventions for breast, colorectal, ovarian, and prostate cancers.

Results: *Accuracy of models***.** Seven eligible studies evaluated systems based on the Gail model, and on the Harvard Cancer Risk Index. No evaluations demonstrated more than modest discriminatory accuracy at an individual level. No evaluations were identified relevant to ovarian or prostate cancer risk.

Efficacy of preventive interventions. From 29 eligible systematic reviews, seven found no experimental studies evaluating interventions of interest. Of the remaining 22, none addressed ovarian cancer prevention. The reviews were generally based on limited numbers of randomized or controlled clinical trials. There was no evidence either to support or refute the use of selected chemoprevention interventions, there was some evidence of effectiveness for mammography and fecal occult blood testing.

Uptake of intervention. Three studies evaluated the impact of FHx-based risk information on uptake of clinical preventive interventions for breast cancer. The evidence is insufficient to draw conclusions on the effect of FHx-based risk information on change in preventive behavior.

Potential harms of FHx taking. One uncontrolled trial evaluated the impact of FHx-based breast cancer risk information on psychological outcomes and found no evidence of significant harm.

Conclusions: Our review indicates a very limited evidence base with which to address all four of the research questions: 1) the few evaluations of cancer risk prediction models do not suggest useful individual predictive accuracy; 2) the experimental evidence base for primary and secondary cancer prevention is very limited; 3) there is insufficient evidence to assess the effect of FHx-based risk assessment on preventive behaviors; and 4) there is insufficient evidence to assess whether FHx-based personalized risk assessment directly causes adverse outcomes.

Contents

Executive Summary 1

Evidence Report 9

Chapter 1. Introduction 11
Background 11
The Potential of Family History Information in Preventing Cancer 11
Evaluating Family History for use in the Prevention of Cancers 14
Risk Stratification 15
Effectiveness of Cancer Risk Reduction Interventions 16
Scope and Purpose of the Systematic Review 17

Chapter 2. Methods 21
Analytic framework 21
Search Strategy 22
Eligibility Criteria 22
Eligibility Criteria for Research Q1: 23
Eligibility Criteria for Research Q2 24
Eligibility Criteria for Research Q3 26
Eligibility Criteria for Research Q4: 27
Study Selection 29
Data Extraction 30
Quality Assessment and Peer Review 30
Summarizing our Findings: Descriptive and Analytic Approaches 30

Chapter 3. Results 31
Research Q1: Which Risk Stratification Algorithms or Guidelines Delineate Risk Accurately, and in a Clinically Meaningful Way? 31
General Approach 31
Studies Reviewed 31
Outcomes 32
Gail Model 32
Modified Gail Model 32
CARE Model 33
Harvard Cancer Risk Index 33
Conclusion 34
Research Q2: For Which Behaviors and Clinical Preventive Services is There Evidence of Benefit in Terms of Actual Reduction of Disease Risk, and What Harms, if any, Have Been Identified? 34
General Approach 34
Studies Reviewed 34
Breast Cancer 35
Colorectal Cancer 37
Prostate Cancer 39

Quality Assessment of Studies 41
Conclusion 41
Research Q3: For Those Interventions Identified as Being Based on Reasonable Evidence, What is the Evidence That Providing Information on Risk Status Results in Behavior Change or Increased Uptake of Services on the Part of Individual Patients? 42
General Approach 42
Studies Reviewed 43
Outcomes 44
Quality Assessment of Studies 44
Conclusion 45
Research Q4: What are the Harms or Risks to Individual Patients That may Result From the Collection of Family History Information in Itself, and/or the Provision of Family History-Based Risk Information? 46
General Approach 46
Studies Reviewed 46
Outcomes 46
Conclusion 47

Chapter 4. Discussion 77
Risk Stratification Algorithms 77
Cancer Prevention Interventions 79
Family History-Based Risk Assessment and Individual Preventive Behaviors 82
Direct Harms or Risks From Family History-Based Risk Assessment 82
Limitations 83
Conclusions 84

Reference List 87

Tables

Table 1. Pooled relative risk estimates (95% confidence intervals) for cancers of interest 12
Table 2. Elements and key components of evaluation framework for family history as screening tool 15
Table 3. Family history-based risk stratification guidelines for breast, ovarian, colorectal, prostate cancers 16
Table 4. Details of risk prediction models 48
Table 5. Evaluations of risk prediction models 50
Table 6. Target interventions for review 56
Table 7. Breast cancer preventive interventions 57
Table 8. Colorectal cancer preventive interventions 61
Table 9. Prostate cancer preventive interventions 66
Table 10. Details of family history and personalized risk interventions 70
Table 11. Evaluations of family history and personalized risk 72
Table 12. Harm/risk of family history collection 76

Figures

Figure 1. Family history-based primary care activities 13

Figure 2. Analytical framework for the research questions evaluated in this review..... 21
Figure 3. Flow of studies to final number of eligible studies 29

Appendixes

Appendix A: Detailed Search Strategies
Appendix B: Forms and Guides
Appendix C: Studies Retained But Not Extracted
Appendix D: List of Excluded Studies
Appendix E: Partners, Technical Expert Panel, and Peer Reviewers

Appendixes and Evidence Tables for this report are provided electronically at http://www.ahrq.gov/downloads/pub/evidence/pdf/famhistory/famhist2.pdf.

Executive Summary

Family history reflects the combined influences of genetics, environmental exposures, and behaviors within families,[1] and is a risk factor for some clinically important chronic diseases such as cardiovascular disease, diabetes mellitus, stroke, and several cancers.[2,3] Family history reflects genomic, social and environmental risk which is shared between relatives. This 'compressed information'[4] may provide predictive information independent of other known risk factors.

Individual risk stratification systems based on family history may carry valuable predictive information for individual patients, but they need to be validated for application in routine practice. The usefulness of family history-based risk stratification systems in disease prevention depends on (a) accurate reporting and capture of family history information, (b) valid methods of risk classification, (c) effective preventive interventions to manage disease risk, and (d) evidence that the use of family history information provides incremental net benefit over and above non-family history-based alternative approaches. With the exception of accuracy of reporting, this systematic review is designed to inform all of these issues.

Scope and Purpose of the Systematic Review

This report, which builds on a previous evidence report[5] on the topic of tools for collecting and interpreting family history information, addresses the clinical utility of routinely using family history information in risk assessment and prevention for breast, ovarian, colorectal, and prostate cancers in primary care. The specific research questions are:

1. Which risk stratification algorithms or guidelines delineate risk accurately, and in a clinically meaningful way?
2. For which behaviors and clinical preventive services ('interventions') is there evidence of benefits in terms of actual reduction in disease risk, and what harms, if any, have been identified?
3. For those interventions identified as being based on reasonable evidence, what is the evidence that providing information on risk status results in behavior change or increased uptake of services on the part of individual patients?
4. What are the harms or risks to individual patients that may result from the collection of family history information in itself, and/or the provision of family history-based risk information?

These questions represent the links in the chain between taking family history and producing benefit: Does family history predict future risk of cancer? If so, are there interventions to reduce this risk, and do they also carry their own risks? Does a family history-based approach lead to higher uptake of preventive interventions? Are there any direct harms which arise from a family history-based approach?

This review's focus is therefore firmly on the application of family history taking from general populations under the care of primary care providers such as family physicians, internists, nurse practitioners, and obstetricians. We sought to examine the capture and use of

family history information as an activity practiced in primary care, where patients are not pre-selected for risk, and where the approach to capturing information is heavily influenced (often constrained) by contextual factors,[6] and where the preventive interventions available are those that can be recommended by a primary care practitioner. This is distinctly different from clinical genetics assessment, where the central focus is on extensive family history capture, validation, and assessment, where the patient population is usually pre-selected for high risk status.

Methods

Standard systematic review methodology was employed. MEDLINE®, EMBASE®, CINAHL®, Cochrane Central®, Cochrane Database of Systematic Reviews, and PsycINFO were searched from 1990 to June 2008 inclusive. Cancer guidelines and recommendations were searched from 2002 forward and systematic reviews from 2003 to June 2008.

Eligibility criteria included English studies evaluating breast, colorectal, ovarian, or prostate cancers. Study designs varied by question, but were restricted to systematic reviews of effectiveness (Question 2), and experimental (Questions 3 and 4) and diagnostic evaluation (Question 1) types. Populations were limited to those unselected for cancer risk. Interventions were the structured/systematic collection of family history (Questions 1, 3, and 4) and primary or secondary cancer prevention (screening) interventions (Question 2). The outcomes were disease incidence or proxy (Questions 1 and 2), uptake of recommended preventive interventions (Question 3), and harms (e.g., psychological distress) (Question 4).

Results

Our comprehensive search yielded 10,644 unique citations; from these 9,765 were excluded as they were not an English language publication, not on the cancers of interest, or on topic for any of the four research questions. The remaining 879 citations were screened at full text and from these a total of 12 primary studies and 29 systematic reviews were eligible.

Research Q1: Which Risk Stratification Algorithms or Guidelines, Delineate Risk Accurately and in a Clinically Meaningful Way?

General approach. The purpose of this question was to establish whether family history-based risk stratification systems (of any kind) could accurately predict risk in individual patients. We reviewed published studies that examined the discriminatory accuracy of models (algorithms, guidelines) that used family history information to predict individual risk of breast, ovarian, colorectal or prostate cancer. To be eligible, a model had to incorporate specified family history information (either alone or with other personal or clinical information which would be routinely available on all patients to a primary care practitioner), and validation data in a defined general population had to be presented. The main outcome of interest was discriminatory accuracy, which reflects the proportion of individuals correctly classified by the tool with respect to actual disease incidence. This was variously presented as a concordance statistic, the area under the curve in receiver operating characteristic (ROC) analyses, or correlation coefficient, and reflects the usefulness of the model for use in the assessment of individual patients.

Findings. Eight evaluation studies were identified as eligible after full text review.[7-14] All tools except one were designed for breast cancer risk assessment. The breast cancer tools were all generally related to the original Gail model,[15] including the model developed from the Contraceptive and Reproductive Experiences Study (the CARE model[7]). The Harvard Cancer Risk Index[16] (HCRI) was developed for application to a number of cancers, but an eligible validation study was identified only for colon cancer. No eligible studies were identified of tools based strictly on family history information alone.

The original evaluation of the Gail model was conducted in a predominantly white U.S. female population,[8] and reported discriminatory accuracy in terms of a Pearson correlation coefficient (0.67). The other breast cancer models were evaluated in white,[9] "diverse",[13] African American,[7,10] and Italian[11,12] populations. These studies reported concordance statistics in the range of 0.55-0.59, indicating very modest discriminatory accuracy.

The HCRI was evaluated for prediction of colon cancer[14] in secondary analyses of cohort data, and reported concordance statistics of 0.67 and 0.71 for women and men, respectively. This suggests moderate discriminatory accuracy (67 and 71 percent correct prediction of eventual cancer status respectively, 50 percent being that expected by chance alone).

Research Q2: For Which Behaviors and Clinical Preventive Services is There Evidence of Benefit in Terms of Actual Reduction in Disease Risk, and What Harms, if any, Have Been Identified?

General approach. The purpose of this question was to establish the link between stratifying cancer risk and being able to intervene to alter that risk, and not to conduct an exhaustive review of the extensive literature around cancer risk factors. We therefore evaluated published systematic reviews on a range of interventions which are generally recommended as part of cancer risk reduction strategies in primary care settings. Where multiple reviews addressing the same intervention were identified, we selected the most recent or most comprehensive for reporting, and considered differences in methodological quality.[17]

Findings. Twenty-nine systematic reviews were retained after full text review, addressing four chemoprevention interventions (antioxidant supplementation, calcium supplementation, non-steroidal anti-inflammatory drugs (NSAIDS), but not COX-2 inhibitors and statins) and five screening interventions (breast self-examination (BSE), screening mammography, fecal occult blood testing (FOBT), flexible sigmoidoscopy (FS), and prostate specific antigen (PSA) for three cancers (breast, colorectal, prostate). No reviews were identified for several interventions of interest, and none were relevant to ovarian cancer prevention.

Data were extracted from the 10 reviews that represented the most comprehensive, up-to-date, and high quality evidence.[18-27] Of the remainder where data were not abstracted, 12 reported overlapping data,[28-39] five did not identify primary intervention studies despite these being designed to do so,[40-44] and two did not report usable data.[45,46]

Overall quality assessment suggested low risk for bias, the main area of weakness being failure to describe adequate control of bias in study selection.[18-20,22,23,27] Other issues were incomplete description of search methods,[23,27] failure to describe criteria for assessing the validity of primary studies,[20,25,26] and failure to cite the validity assessments of included studies.[20,26]

Breast Cancer

Five systematic reviews synthesized evidence on chemoprevention (antioxidants and statins) and screening (breast self-examination (BSE) and screening mammography).

Antioxidants. One review[18] evaluated supplements that contained any combination of ß-carotene, vitamin C, vitamin E, selenium, zinc, and other antioxidants, and concluded no evidence of a protective effect of any combination against breast cancer (RR 1.00, 95 percent CI 0.90-1.09) at one year followup. A second review[19] examined vitamin E alone or in any combination in three high quality randomized controlled trials (RCT) and concluded no evidence of a reduction in breast cancer incidence (RR 0.99, 95 percent CI 0.90-1.10).

Statins. One review,[20] suggested that statins appeared to confer neither a protective nor a harmful effect on breast cancer incidence (RR 1.01, 95 percent CI 0.79-1.30).

BSE. One review[21] showed no impact of BSE on breast cancer mortality (RR 1.05, 95 percent 0.98-1.14).

Screening mammography. The most recent comprehensive review,[22] suggested that screening mammography was associated with reduced breast cancer mortality at 13 years (RR 0.80, 95 CI 0.73-0.88), although concerns were raised about inadequate bias control in some primary trials. No effect on overall mortality was noted (RR 1.00, 95 percent CI 0.96-1.04).

Colorectal Cancer

Six reviews evaluated interventions in colorectal cancer (CRC) prevention, four on chemoprevention (antioxidants, NSAIDS, statins) and two on screening (fecal occult blood testing (FOBT) and flexible sigmoidoscopy (FS)).

Antioxidants. One review[18] evaluated supplements which contained any combination of ß-carotene, vitamin C, vitamin E, selenium, zinc, and showed no evidence of a protective effect against CRC incidence (RR 1.00, 95 percent CI 0.90-1.10). A second review[19] evaluated vitamin E given in any combination and found no evidence of an effect on CRC incidence (RR 0.95, 95 percent CI 0.81-1.12).

NSAIDS. One review evaluated low dose ASA,[23] and found no evidence of an effect on CRC incidence (RR 1.02, 95 percent CI 0.84-1.25), CRC mortality (RR not reported) or adenoma incidence (RR 0.85, 95 percent CI 0.68-1.1) at 5 years.

Statins. One review[20] showed neither a protective nor harmful effect of statins on CRC incidence (pooled RR 1.02, 95 percent CI 0.89-1.16) or CRC mortality (RR 0.33, 95 percent CI 0.07-1.63).

FOBT. One review[24] examined FOBT (guaiac or immunochemical) in studies of at least two rounds of screening were compared with no screening. A statistically significant effect of screening on CRC mortality was observed (RR 0.84, 95 percent CI 0.78-0.90), and no effect on all-cause mortality (RR 1.00, 95 percent CI 0.99-1.01).

FS. A single review[25] examined the evidence for FS in CRC screening, identifying a single RCT comparing FS plus FOBT against FOBT alone. No statistically significant effect was found on CRC mortality or incidence (RR 0.78, 95 percent CI 0.36-1.73 and 1.37, 95 percent CI 0.88-2.15, respectively).

Prostate Cancer

Five reviews synthesized evidence in relation to prostate cancer prevention: four relating to chemoprevention (antioxidants, calcium, and statins) and one relating to screening (prostate-specific antigen (PSA) with digital rectal examination (DRE) and trans-urethral ultrasound (TRUS) biopsy).

Antioxidants. One review[18] evaluated supplements that contained any combination of ß-carotene, vitamin C, vitamin E, selenium, zinc, and other antioxidants. The pooled analysis of all antioxidants showed no effect on prostate cancer incidence (RR 0.87, 95 percent CI 0.74-1.02), and a reduced risk associated with vitamin E specifically (RR 0.82, 95 percent CI 0.67-0.99). A second review[19] of vitamin E in any combination showed a negative association with prostate cancer incidence (RR 0.85, 95 percent CI 0.74, 0.96).

Calcium. One review evaluated calcium supplementation and prostate cancer risk,[26] where this was a secondary outcome in a single colorectal adenoma prevention trial.[47] It suggested a statistically significantly lower incidence of prostate cancer in the supplement group until 2 years after supplementation was discontinued (rate ratio 0.52, 95 percent CI 0.28-0.98), at which point the risk in both groups converged.

Statins. One review[20] examined the effectiveness of statins on prostate cancer. The results indicated that statins appeared to neither increase nor decrease the risk of prostate cancer incidence or mortality (RR 1.00, 95 percent CI 0.85-1.17 and RR 0.99, 95 percent CI 0.14-7.01, respectively).

PSA-based screening. One review[27] examined the effectiveness of PSA-based population screening (with DRE and TRUS biopsy) in two trials, one with an annual and the other a three times yearly, screening cycle. No statistically significant impact of screening on prostate cancer mortality was found (RR 1.01, 95 percent CI 0.80-1.29).

Research Q3: For Those Interventions Identified as Being Based on Reasonable Evidence, What is the Evidence That Providing Information on Risk Status, Results in Behavior Change or Increased Uptake of Services on the Part of Individual Patients?

General approach. The focus of this question was behavior: whether giving people personalized risk advice based on their family history would lead to a higher adherence with preventive recommendations. We evaluated intervention studies in which the outcomes were actual risk-reduction behavior, focusing on interventions that were considered standard of care when the primary study was conducted.

Findings. Three studies[48-50] were eligible, all focusing on uptake of screening interventions for breast cancer as the target behavior. Two were randomized controlled trials[49,50] and examined different levels of personalization of risk information. The third[48] was an uncontrolled before-after study.

One trial[48] showed a borderline statistically significant difference (P = 0.05) in mammography uptake (about 8 percent) between intervention and control groups. The other two studies were null. The community pharmacy study[46] was the only one to examine other behaviors, and showed a statistically significant increase in self-reported BSE, but not CBE.

Research Q4: What are the Harms or Risks to Individual Patients That may Result From the Collection of Family History Information in Itself, and/or the Provision of Family History-Based Risk Information?

General approach. The purpose of this question was to identify whether the process of capturing family history and feeding back personalized risk, in and of itself, was associated with identifiable harms. We reviewed published intervention studies which examined the direct impact of family history-based risk information on quality of life, psychological, and social impact, where these could be directly attributed to this intervention and not subsequent investigations or preventive activities.

Findings. One eligible study was identified,[51] an uncontrolled before-after study designed to evaluate the psychological impact of providing family history information and receiving a personalized risk assessment for breast cancer. In all participants, no statistically significant change in anxiety or cancer worry between baseline and followup was observed. In participants whose risk assessment indicated "population risk", a small reduction in self-perceived risk was observed ($P<0.01$). In participants who required further assessment ('true' high risk and 'false positive' groups), higher baseline cancer risk perception scores were observed compared with the group assessed as population risk ($P<0.001$ for 'higher risk' group and $P=0.003$ for 'false positive' group).

Discussion and Conclusions

The purpose of this review was to establish the evidence base to answer the question, "In primary care settings, and in relation to breast, ovarian, colorectal or prostate cancers, would the routine use of family history-based risk assessment be likely to lead to net health benefits?" We identified a very limited evidence base for all four of the research questions.

While there are a number of FHx-based cancer risk stratification systems, no evaluations have been published of any based only on FHx information. Of those models which include FHx information along with other clinical variables, published validations suggest good epidemiological calibration but no more than modest individual discriminatory accuracy. The models evaluated were not necessarily developed for general clinical use.

The experimental evidence base, represented in published systematic reviews, for primary and secondary cancer prevention in general populations is very limited. The most consistent evidence supports screening mammography and FOBT-based colorectal screening strategies, with equivocal evidence for vitamin E and calcium in reducing the risk of prostate cancer. The review likely did not include some experimental evidence for interventions which have not been examined in systematic reviews, but which would be relevant to the main study questions.

There is insufficient evidence to assess the effect of FHx-based risk assessment on preventive behaviors. Very few trials have been conducted, and none in settings resembling routine primary care practice. There is also insufficient evidence to assess definitively whether FHx-based personalized risk assessment directly causes adverse outcomes; the results of the single study available indicate the need to take into account baseline psychological status and risk perception in assessing the impact of FHx-based risk information.

Conclusions

1. The evidence for the predictive accuracy of algorithms in primary care populations was very limited. Although many tools were identified that incorporated some family history information, no evaluations of solely family history-based tools. The tools on which it was possible to comment related mainly to breast cancer.

Recommendations for future research:

- The actual performance of tools based only on family history should be formally examined in primary prospective studies, and/or in secondary analysis of large cohort studies.
- The performance of individual family history components of different risk stratification models which use a wider range of factors (including those examined in this report) should be examined separately from the non-family history components, in order to determine whether they provide sufficient predictive power in the absence of the non-family history factors.
- For clinical relevance, the focus of validation should be discriminatory accuracy at the individual patient level.
- More definitive evaluation should examine the effect on health outcomes when risk stratification systems are used in combination with preventive interventions, in actual practice settings. This cannot be done with secondary analyses of observational data and requires well-designed intervention studies.

2. The evidence establishing the efficacy of interventions for primary and secondary prevention based on systematic reviews of randomized or controlled clinical studies in unselected populations is very limited. Interventions for which there were reviews include chemoprevention (antioxidants, calcium, NSAIDS, and statins) and screening interventions (BSE, mammography, FBOT, FS, and PSA) for breast, colorectal and prostate cancers. No reviews were found for ovarian cancer. It is likely that this review excluded effectiveness data available from RCTs of interventions which have not yet been the subject of systematic reviews.

Recommendations for future research:

- The large amount of evidence on potential primary cancer preventive interventions obtained from observational studies of cancer risk factors should continue to be further evaluated in well-designed randomized controlled trials.
- Further systematic reviews should be conducted to examine the full range of potentially preventive interventions

3. Within primary care populations, there is very limited evidence to support or refute the effect on risk-reducing behavior changes (e.g., lifestyle changes or uptake of recommended clinical interventions) of taking a family history and using it to personalize risk of breast, ovarian, colorectal or prostate cancer.

Recommendations for future research:

- Well-designed trials are required that compare family history-based, personalized risk advice with standard of care on risk reducing behaviors in populations at different risk levels (including population risk).

4. In primary care populations, there is very limited information to evaluate direct harm incurred from the routine practice of taking family history and using it to personalize risk information.

Recommendations for future research:

- Trials of family history taking as an intervention should include capture of data to examine the full range of potential impacts on individuals. Baseline data on psychological status should be captured so that this can formally be adjusted for in outcome analyses.

5. Research on the use of family history tools, risk stratification systems, and family history-based personalized prevention advice should take into account evidence on the factors likely to promote their effective use in practice, such as the educational needs of primary care practitioners and issues which act as barriers or constraints to their implementation in practice.

Evidence Report

Chapter 1. Introduction

Background

The Potential of Family History Information in Preventing Cancer

Family history has always been a core tool in medical practice. A person's family history reflects the combined influences of genetics, environmental exposures, and behaviors within families.[1] A large number of reports demonstrate that a positive family history is a risk factor for many chronic diseases of clinical importance, including cardiovascular disease, diabetes mellitus, stroke, and several cancers.[2,3] The greater the number of relatives affected by a disorder, the younger their ages of onset, and the closer the relationship to the individual in question, the more likely it is that the family's disease experience has a genetic basis. However, given the low population prevalence of genetic forms of common, complex disorders, a screening approach based on identifying fairly extreme family histories offers very limited public health or clinical utility in practice.

Historically, the practice of clinical genetics has been largely predicated on detecting individuals marked out by membership in families with unusual patterns of disease, and who are at significantly elevated individual risk as a result of rare genetic disorders that have relatively high penetrance. The alternative approach, which is the focus of this review, is to recognize that family clustering of disease risk reflects combinations of lower penetrance, and moderate risk alleles which are reasonably common within a population. The latter example, a high prevalence of people with slightly or moderately elevated inherited disease risk, would lead to a much higher total disease burden within a population than that associated with a low prevalence of people at very high risk.[52] Under the right circumstances, a 'genomic test' – such as the presence of particular family history characteristics - could have a significant positive predictive value.

Several years ago, Yoon and colleagues[1] illustrated this point. They demonstrated how even fairly simple family history information could be used to clarify the risk of a number of common, complex disorders. Based on published data, they suggested that a healthy 23 year old man could have the following lifetime risks of:

- 60 percent for cardiovascular disease (based on one male first degree relative (1DR) diagnosed after age 60)
- 50 percent for colorectal cancer (based on two 1DRs diagnosed before age 50); and
- 30 percent for type 2 diabetes (based on one 1DR diagnosed after age 60

Importantly, their risk prediction was based on family history information which would not be considered extreme. This application of family history information complements the vision of 'personalized medicine' which physician-geneticist Francis Collins M.D., PhD., predicted would be available in 2010, in the form of DNA-based genome profiling tests.[53] While recent research indicates that such profiling is possible in principle,[54] it is evident that this is not yet a technology ready for routine implementation in health care.[52,55] Until such time, family history represents a potential source of useful predictive information already available to any health care provider.

Discussing the role of family history in coronary heart disease risk, Kardia and colleagues describe the family history as "compressed information" which integrates risks arising from shared genomic components, and social and physical environments.[4] They expand:

> "For, example, we know that parents and children share exactly half their genes. This translates practically into sharing one copy of the 30,000 to 50,000 genes estimated to be in the human genome in the nucleus of each nucleated cell in the human body. … it is quite possible that even with our ability to measure hundreds and thousands of genes and environments we may find that family history is the best, low-cost way to identify the at-risk subgroups in the population. This will be especially true if gene-gene and gene-environment interactions play a major role in determining risk of future disease."

This perspective is supported by the work of Butterworth,[3] who recently conducted a comprehensive meta-analysis of the risk conferred by family history for a number of common, complex disorders, including the cancers of interest in this review. Table 1 summarizes his findings for colorectal, breast, ovarian, and prostate cancer.

Table 1. Pooled relative risk estimates (95% confidence intervals) for cancers of interest[3]

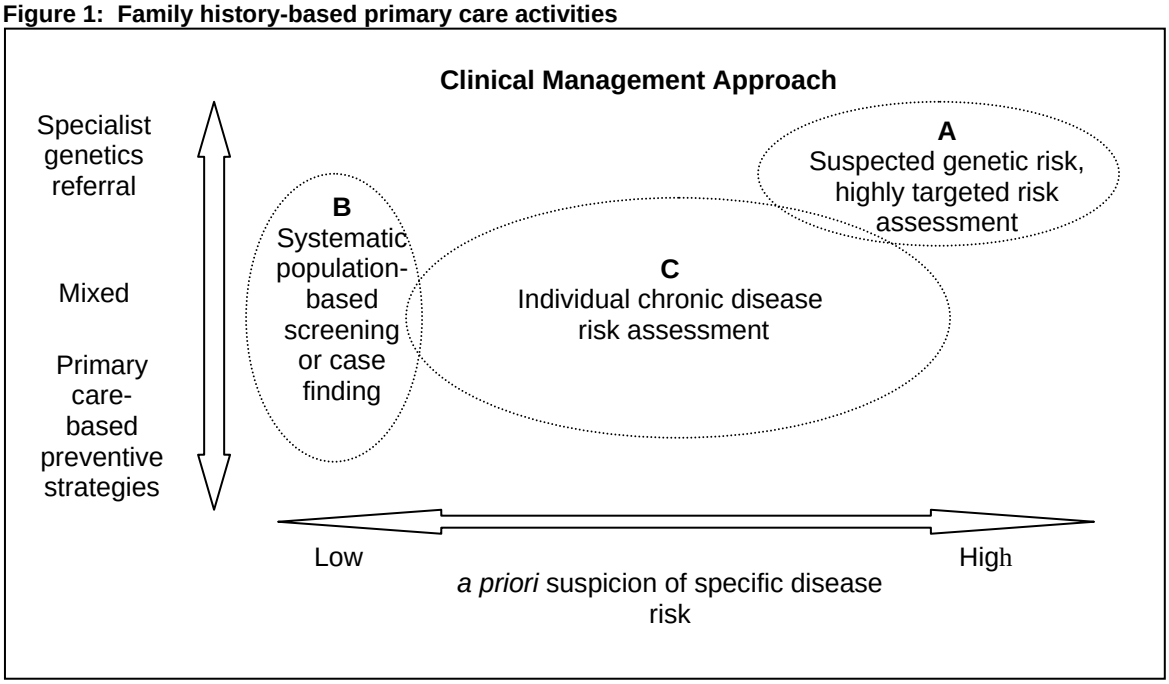
Cancer	≥1 1DR	≥2 1DRs	Age cut-off younger, older	Younger affected relative	Older affected relative
Colorectal	2.24 (2.06, 2.43)	3.97 (2.60, 6.06)	<50, ≥50	3.55 (1.84, 6.83)	2.18 (1.56, 3.04)
Breast	1.80 (1.70, 1.91)	3.01 (2.46, 3.69)	<40, >60	2.22 (1.71, 2.87)	1.55 (1.38, 1.74)
Ovarian	2.85 (2.41, 3.37)	14.74 (5.78, 37.60)	<50, ≥50	3.98 (2.53, 6.26)	2.90 (2.10, 4.01)
Prostate	2.42 (2.25, 2.60)	4.27 (3.13, 5.84)	<60, ≥60	2.91 (2.12, 4.01)	1.88 (1.47, 2.40)

1DR=first degree relative

These meticulous analyses provide direct evidence to support the association between family history and risk of cancer even when family history is captured in a less specific or extensive way than is the case in a specialist genetics consultation.

In order to understand the specific nature of family history information which might be most useful in primary care settings, it is useful to consider how family history data may serve different purposes. Figure 1 maps out different contexts for family history taking in primary care against the general locus of clinical management (primary care versus specialist referral) if elevated risk is identified. It demonstrates how the goal of family history taking may include, but is most definitely not limited to, identifying rare, high risk disease patterns in families which warrant referral for formal genetic evaluation (domain A). Domain B represents systematic screening of general patient populations for a defined range of familial or genetic diseases. Domain C represents the assessment of disease-specific family history information with other risk factor data in the assessment of chronic disease risks in individual patients. In all three domains (A, B, C), a primary care practitioner may be the key provider who captures the family history data; however, the drivers for capturing such information, and the likely decisions that will follow, vary across the three domains and extend beyond the possible identification of classical genetic disorders.

Figure 1: Family history-based primary care activities



Domain A represents the assessment of a patient in whom clinical suspicions of an inherited disorder or predisposition have arisen, for example in response to concerns about several relatives affected by cancer. In this situation, the main clinical goal would be to assess whether the individual met the criteria for referral for specialist genetics assessment and/or genetic testing. A family history 'tool' in this situation would be represented by guidelines for genetic referral or testing. Here, the focus would be on capturing specific family history information which might be rather extensive and specific, requiring attention to, for example, different combinations of diseases in the family, the lineage of affected relatives, and so forth, as illustrated in the Bethesda criteria for non-polyposis colorectal cancer.[56]

Domain B might typically represent a periodic health assessment in an otherwise healthy individual, where there would be no suspicion of underlying genetic disease and no particular indications of illness or disease susceptibility. Here, the goal would be to conduct a broad brush assessment across a range of common disorders, to identify issues which warrant further probing by the primary care practitioner. The most useful family history tool might incorporate a limited range of the most sensitive family history markers or "red flags" across a range of disorders, in the expectation that more detailed information would be collected for those conditions where an indicator item was positive.

In domain C, the primary care practitioner's goal would be to incorporate family history with other clinical and personal information to assess future risk of a specific chronic disease, with a view to ordering further investigations and advising on appropriate risk reduction strategies. In this situation, the focus would be on family history items which were either independently highly predictive of disease risk, or added useful incremental predictive value to other, established risk factors. A family history "tool" in this context might actually consist of a short set of questions within a more comprehensive disease-specific risk assessment guideline. An example of this approach would be the incorporation of information on parental history of myocardial infarction in the National Cholesterol Education Program III guidelines.[57]

These three domains are clearly not mutually exclusive. However, this approach illustrates that the demands of extensiveness and specificity of the type of information that is necessary is not uniform across all contexts. Until comprehensive and current family history information is available for patients through, for example, electronic records systems, a primary care practitioner's approach to family history-taking may be influenced by external constraints (e.g., time), their prior assessment of the patient's risk of disease, and the way in which the information will actually be used for decisionmaking.

Although this report borrows from the language and concepts of genetics and genomics (see below), its approach reflects the perspective on family history exemplified particularly by domain C described above. Its focus is on the utility of using family history information to stratify the risk of common, complex diseases in individuals who are not specifically selected for suspicion of high genetic risk.

Evaluating Family History for use in the Prevention of Cancers

The usefulness of family history stratification systems as predictive tools for common, chronic diseases can be approached using an evaluation framework originally developed by the Secretary's Advisory Committee on Genetic Testing.[58] This framework has four elements (1) analytic validity; (2) clinical validity; (3) clinical utility; and (4) ethical legal and social implications of using a test. It has been further developed for application to the evaluation of family history information in disease prevention (see Table 2 for definitions).[59] Put another way, the line of evidence between family history and individual and population benefit requires answers to the following questions:

(a) Does a positive family history (however defined) predict future risk of cancer in an individual patient sufficiently accurately to be useful in a clinical setting?
(b) If so, are there interventions available which reduce the risk of cancer? Do these interventions also carry risks?
(c) If there are interventions which help prevent cancer, does information on family history-based disease risk mean a person is more likely to adhere to them (compared with advice which is not based on knowledge of family history)?
(d) Are there any direct harms which arise from the process of taking a family history and feeding back personalized risk based on family history?

In terms of efficient health care resource use, it is also legitimate to examine the incremental benefits and costs associated with capturing and using family history information, whether it substitutes for, or adds informational value to, other risk factor information, and whether it is easier and/or cheaper to obtain.

Table 2. Elements and key components of evaluation framework for family history as screening tool [reproduced from Yoon, Scheuner, and Khoury 2003][59]

Element	Definition	Components
Analytic validity	An indicator of how well a test or tool measures the property or characteristic (disease status among relatives) that it is intended to measure	Analytical sensitivity Analytical specificity
Clinical validity	A measurement of the accuracy with which a test or tool identifies or predicts a clinical condition	Clinical sensitivity Clinical specificity Positive predictive value Negative predictive value
Clinical utility	Degree to which benefits are provided by positive and negative test results (presence and absence of family history for disease)	Availability of effective interventions Health risks and benefits Economic assessment
Ethical, legal, and social implications	Issues affecting data collection and interpretation that might negatively impact individuals, families, and society	Stigmatization Discrimination Psychological harms 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. Used with permission.

In a previous effectiveness report,[5] evidence regarding the accuracy of reporting by individuals of their family history of breast, ovarian, colorectal, and prostate cancer was synthesized, and a large number of family history tools and family history-based risk assessment tools identified and reviewed. The current review is designed to inform issues (a) to (d) above, which address the issues of clinical validity and, in part, clinical utility.

Risk Stratification

A number of risk classification systems exist, generally in the form of guidelines or algorithms developed to assist in decisionmaking around referral to genetic services or genetic testing (e.g., Rodriguez-Bigas[56]). Few risk stratification systems have been developed specifically for direct application in primary care, with a focus on recommending behavior changes and/or preventive clinical interventions in which referral for genetic counselling would be relevant for only a small sub-group of patients. One such system is that proposed by Scheuner and colleagues[60] who, in a paper predating Butterworth's analysis,[3] used available epidemiological data[61-70] to define three risk strata for a number of complex disorders (Table 3). An approach like this has the merit of appearing practical for immediate and easy application in primary care settings, but further evaluation is necessary to determine its predictive ability for the disorders of interest (clinical validity).

Table 3. Family history-based risk stratification guidelines for breast, ovarian, colorectal, prostate cancers[60]

High risk
1. Premature disease* in a 1DR 2. Two affected 1DRs 3. A 1DR with late/unknown onset of disease and an affected 2DR with premature disease from the same lineage 4. Two 2DRs, maternal or paternal, with at least one having premature onset of disease 5. Three or more affected maternal or paternal relatives 6. The presence of a 'moderate risk' family history on both sides of the pedigree 7. Pedigree demonstrating clustering of different primary cancers consistent with a family cancer syndrome
Moderate risk
1. A 1DR with late or unknown disease onset 2. Two 2DRs from the same lineage with late or unknown disease onset
Average (population) risk
1. No affected relatives 2. Only one affected 2DR 3. No known family history 4. Adopted individual with unknown family history

Scheuner M.T., Wang S.J., Raffel L.J., Larabel S.K., Rotter J.I. Family history: a comprehensive genetic risk assessment method for the chronic conditions of adulthood. Am J Med Genet 1997;71(3):315-324. Used with permission of John Wiley & Sons, Inc.
Abbreviations: 1DR=first degree relative; 2DR=second degree relative
* Breast, ovarian: premenopausal or ≤50 years; colorectal, prostate ≤50 years

Effectiveness of Cancer Risk Reduction Interventions

Even the most highly predictive and practical risk stratification system cannot change health outcomes unless effective cancer prevention interventions are available for patients at risk. While there is extensive epidemiological literature on a wide range of cancer risk factors, much of the evidence regarding cancer prevention is based on observational studies. Contradictory evidence has emerged when some apparently protective factors, identified through observational studies[71-73] were associated with increased risk of cancer in experimental studies, as was the case for alpha-tocopherol.[74] It is crucial that any assessment of the clinical utility of family history-based risk stratification take into account the highest quality evidence on the benefits and risks of recommended preventive interventions.

Effect of family history taking on uptake of interventions. Assuming that proven preventive interventions are available, the question remains whether individualized, family history-based advice actually promotes uptake of such interventions by patients. Simplistically, it might be assumed that individuals would be more motivated to act on a health care provider's advice if they know they are at higher than average risk. However, there is a body of literature in the area of predictive and predisposition genetic testing which cautions that knowledge of genetic risk might lead to fatalism in those at higher risk (failing to take up available interventions because of the 'inevitability' of disease) or complacency in those at average risk (failing to take up available interventions because of lower perceived personal risk - the 'certificate of health' effect).[75] Like any healthcare intervention, family history taking may incur incremental costs in time, energy, and money over and above standard care, therefore an examination of the incremental benefits is important.

Risks inherent in family history-based risk assessment. No healthcare intervention should be assumed to be safe without formal assessment of harms as well as benefits. While family history taking is seen as a standard activity in all areas of healthcare, the systematic capture of

more extensive information, and its purposeful use in individual risk assessment, merits objective review. The ACCE framework[58] emphasizes the assessment of both harms and benefits, and there is substantial literature that examines the impacts of predictive genetic tests beyond simple accuracy.[76] While some guidelines[77] suggest a cautionary approach, with cancer family history collection undertaken only in response to patients' enquiries, many other observers argue that family history taking is an integral part of good clinical practice.[78,79] Objective evidence on the prevalence of specific harms of family history taking, and of its use in advising patients about disease risk reduction, is necessary in order to clarify the appropriate level of caution to be exercised, and the types of situations in which patients might be most vulnerable to potential harms.

Scope and Purpose of the Systematic Review

This report is intended to build on a published evidence report focused on collection and use of family history for breast, ovarian, colorectal, and prostate cancers.[5] The key questions for that project are available at: http://www.ahrq.gov/clinic/tp/famhisttp.htm. The current systematic review addresses four key research questions relating to the clinical validity and utility of routinely using family history information in risk assessment and prevention of breast, ovarian, colorectal, and prostate cancer in primary care, as follows:

1. Which risk stratification algorithms or guidelines delineate risk accurately, and in a clinically meaningful way?
2. For which behaviors and clinical preventive services ('interventions') is there evidence of benefits in terms of actual reduction in disease risk, and what harms, if any, have been identified?
3. For those interventions identified as being based on reasonable evidence, what is the evidence that providing information on risk status results in behavior change or increased uptake of services on the part of individual patients?
4. What are the harms or risks to individual patients that may result from the collection of family history information in itself, and/or the provision of family history-based risk information?

Addressing these four key questions requires a focus on different types of evidence and different sets of literatures. The focus of key question (Q1) is not only on identifying family history-based risk prediction systems (which may be presented as guidelines, algorithms or other tools) suited to use in primary care, but also on assessing their actual predictive ability when applied to individual patients. This requires review of primary studies addressing discriminatory accuracy in cohorts representative of relevant general populations. Key question (Q2) asks whether effective cancer prevention interventions are available. While answering this question is an essential step in addressing the overall question of clinical utility of cancer family history taking, we note that the primary goal of this report is on family history taking, rather than evidence for cancer control *per se*. Given the considerable practical implications in attempting to synthesize the very extensive literature on cancer risk factors and prevention (see, for example, the reports by the World Cancer Research Fund[26,45,46]), the reasonable expectation that evidence reviews might be available for cancer prevention interventions which are considered standard of care, and direction from the sponsors of the report, the focus is therefore on reviewing systematic

reviews for primary and secondary (screening) cancer prevention. Key questions (Q3) and (Q4) are evaluative questions. Question 3 asks whether taking and using family history information is more likely to lead to desired behavior changes in patients than other approaches which do not use family history information. In addressing this question it is important to distinguish between studies which examine the behavior of people who have pre-existing perceptions of elevated disease risk because of living with a "family disease" from the *clinical strategy* of systematically capturing family history information and personalizing risk assessment for all patients, in order to promote adherence to recommended preventive behaviors. The possibility for confounding of the latter by the former cannot fully be addressed in observational studies, and steers the review towards examining evidence from well-designed intervention studies. The same issue applies in question (Q4), where adverse outcomes from the clinical strategy of taking and using family history information needs to be separated out from the psychological and social impacts of living with the implications of pre-existing *perceived* familial disease risk.

As discussed above, the focus of this review is firmly on using family history information in a primary care context. This has driven the eligibility criteria for studies towards

- study populations that resemble those in primary care – with an inherent range of disease risks but not selected because of suspicion of genetic disease
- study settings where primary care providers such as family physicians, internists, nurse practitioners, and obstetricians are taking family histories and assessing risk
- family history taking as an intervention carried out by primary care practitioners and directed primarily towards chronic disease risk assessment and prevention as an end in itself
- cancer prevention interventions evaluated in primary care or general populations with an inherent range of disease risks, but *not* selected because of special high risk (genetic or otherwise)

Even within primary care, we recognize that there is an inevitable gradation (rather than a clear cut separation) between family history taking as a means to promote effective primary care-based disease risk assessment and management (domain C, Figure 1), and family history taking as a way of identifying individuals who may be at high genetic risk, where referral to specialist genetics services is warranted (domain A). We therefore sought to include studies examining family history taking as a generalist activity, and to exclude studies which focused on family history as part of a clinical genetics assessment. Thus, even though we recognize that family history taking is a core activity in specialist genetics, this review excludes literature where the focus is primarily on the assessment of genetically high risk patients in specialist settings.

It is also important to emphasize that the focus on study populations "unselected" for high risk implies groups of participants which represent *a full range of risks*, potentially from very low to very high, with clustering around an "average" value (by definition). This criterion was adopted in an effort to reflect professional and patient decisionmaking in "typical" primary care contexts where patients with a wide range of risks (but mostly "average") are encountered. Thus, it would be expected that a predictably small proportion of patients from an unselected population would be classified by a risk stratification system into a high risk category. This situation is distinctly different from those where patients and their providers already know or suspect that they are at high disease risk, by virtue of, for example, an uncommon pattern of familial disease, a positive genetic test result in a close relative, a previous diagnosis of the condition, or diagnosis of a pre-disease state. In short, populations unselected for high risk may *include some high risk individuals* whereas populations selected for high risk definitively *exclude*

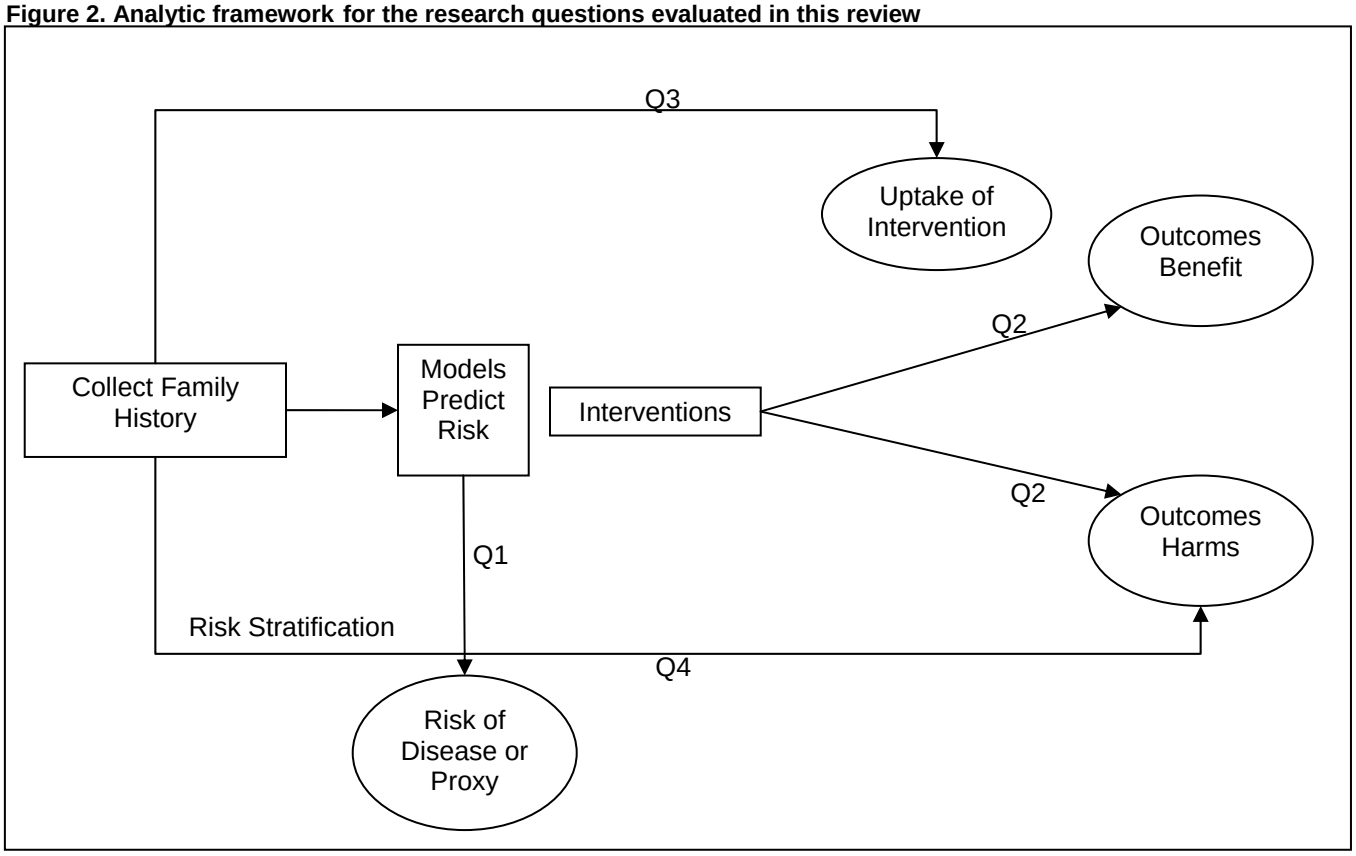
average and low risk individuals. We suggest that it cannot be assumed that findings from "selected for high risk" studies are directly applicable to the general primary care context.

Chapter 2. Methods

Analytic framework

The analytic framework is a schematic representation of the strategy for showing the relationships between the primary exposure, which is the collection of cancer family history, and the outcomes of interest for each research question. Figure 2 shows the inter-relationships among the four research questions being addressed in this systematic review. Cancer family history is an important component of algorithms, models, and guidelines used to predict risk of cancer or gene mutation; we evaluated predictive accuracy outcomes of eligible algorithms, models, or guidelines in the first research question (Q1). A large number of interventions have been implemented to address primary and secondary prevention of the cancers of interest; our second research question evaluated the evidence from systematic reviews and evaluated outcomes of benefit and harm from these interventions (Q2). Following the collection of cancer family history, the uptake of these prevention and screening interventions was the outcome of interest for our third research question (Q3). Our final research question focused on the potential for harmful outcomes as a result of collecting family history (Q4).

Figure 2. Analytic framework for the research questions evaluated in this review



Search Strategy

Bibliographic databases searched for this review included: MEDLINE®, EMBASE®, CINAHL®, Cochrane Controlled Trials Register (CCTR)® (Q1, Q3, Q4), Cochrane Database of Systematic Reviews (Q2), and PsycINFO (Q3). Years searched were 1990 to June 2008 inclusive (Q1, Q3, and Q4). We searched for cancer guidelines and recommendations from 2002 forward to ensure that the guidelines were reasonably current. We also searched the grey literature, including the National Clearing House for guidelines. Based on input from our Technical Expert Panel we searched the Guide to Community Preventive Services published by the CDC[80] and other appropriate guidelines (e.g., U. S. Preventive Services Task Force recommendations for the prevention and screening interventions for the cancers of interest).

Finally, we restricted the search for systematic reviews (Q2), from 2003 to June 2008 (Q2). As per the recommendations of our content experts, we reviewed the methods and content of the report "Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective" published by World Cancer Research Fund' from American Institute for Cancer Research (updated for breast cancer only in Spring 2008).[81] This report reflects an international initiative that has systematically reviewed the literature to evaluate the cancer prevention evidence for a range of interventions broadly including exercise and related behaviors, food and food supplements (including vitamins), and screening interventions for different types of cancer (including breast, ovarian, colorectal, and prostate cancers). Since this World Cancer Review comprehensively captured and evaluated the literature on these interventions from root to the end of 2006), we did not include any reviews on these particular interventions for this time period.

In addition we retrieved and evaluated references from eligible articles. Hand searching was not undertaken, but we reviewed the publication type "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. Finally, we formally reviewed all articles suggested by peer reviewers of the draft evidence report and incorporated those which met eligibility criteria. Detailed search strategies are listed in Appendix A.

Eligibility Criteria

A list of eligibility criteria was determined and standardized forms were developed in Systematic Review Software (SRS, 3.0, TrialStat Corporation, Ottawa, Ontario Canada) and Microsoft Excel for the purposes of this systematic review.

Publication Year, Type, and Language

Inclusion

Language: Only English language studies were eligible. (Q1, Q2, Q3, Q4)

Publication Date: 1990 to June 2008. (Q1, Q3, Q4)
2003 to June 2008 (Q1 guidelines/recommendations and Q2)

Exclusion

Publications that were editorials, comments, opinions, or abstract only (Q1, Q2, Q3, Q4)

Eligibility Criteria for Research Q1:

Population

Any patient or general populations not selected for known or suspected pre-existing elevated risk of breast, ovarian, colorectal, and/or prostate cancer

Inclusion

- populations sampled from clinical settings, including population screening programs
- participants in analytical epidemiological research studies

Exclusion

- people with a personal history of breast, ovarian, colorectal, or prostate cancer
- people at high risk of cancer, as estimated by an existing risk assessment system
- populations sampled from specialist genetic clinics or cancer family clinics
- people who have had a genetic test for a mutation related to one of the cancers of interest (irrespective of result)

Intervention

Inclusion

Any system designed

- to use family history information alone, or in combination with other information typically and universally available to primary care practitioners (i.e., personal/demographic factors, past medical history, clinical observations that do not require specialist referral)
- to stratify people into two or more risk categories OR to provide a numerical point estimate of risk of developing breast, ovarian, colorectal, and/or prostate cancer, over any time period
- for application in risk assessment of individual patients
- in which the model validation is tested on a patient sample different than the one used to develop the model

Exclusion

- Systems which do not incorporate family history information
- Systems which include data from specialist investigations which are typically unavailable in primary care settings

Design

Inclusion

1. Analytical studies examining disease risk categorization as the ‘exposure’ and cancer incidence or proxy as the ‘outcome’
   - cohort (prospective or historical)
   - case control
2. Diagnostic studies examining disease risk categorization using the algorithm as the ‘test’ and cancer incidence or proxy as the ‘reference’
3. Intervention studies examining disease risk classification system as the ‘intervention’ and correct prediction of cancer incidence or proxy as the ‘outcome’
   - randomized controlled trials (cancer risk classification system compared with any other system, or no system)

- non-randomized controlled trials (cancer risk classification system compared with any other system, or no system)
- uncontrolled before-after studies (data on prediction of patients' cancer risk before and after the introduction of a cancer risk classification system)

Exclusion

None

Outcome

Inclusion

1. Model calibration, expressed as observed versus expected cases
2. Model discriminatory accuracy, expressed as sensitivity, specificity, predictive value, likelihood ratio, concordance statistic, receiver operator characteristics (ROC), area under the curve (AUC), or other appropriate summary statistic

   For the outcomes of

   - incidence of breast, ovarian, colorectal, or prostate cancer
   - breast-, ovarian-, colorectal-, or prostate-specific mortality
   - proxies - incidence of known precancerous states, such as colorectal adenomatous polyps

   Over any defined time period

Exclusion

None

Eligibility Criteria for Research Q2

Population

Inclusion

Reviews where eligibility criteria include AND outcome data are presented separately for:

General population, primary care patients or participants in population screening programs who may or may not have been selected by age and sex criteria but not on the basis of *a priori* higher risk, such as:

- personal history of cancer
- known precancerous condition
- known disorder which increases cancer risk
- known or suspected familial cancer syndrome

Participants may have had relatives with cancer, but they are not selected specifically on the basis of suspected genetic risk

Exclusion

Reviews where the eligibility criteria focus specifically on people eligible for, or who have had, a genetic test for a cancer-associated mutation (irrespective of result)

Intervention

Inclusion

Breast

- breast self-examination
- clinical examination
- screening mammography

- chemoprevention
- magnetic resonance imaging breast screening (MRI)
- referral for genetic counseling +/- genetic testing, where criteria are met

Colorectal

- fecal occult blood (FOB) test
- screening colonoscopy
- screening sigmoidoscopy
- chemoprevention
- referral for genetic counseling +/- genetic testing, where criteria are met

Ovarian

- ultrasound screening
- referral for genetic counseling +/- genetic testing, where criteria are met

Prostate

- prostate-specific antigen (PSA) screening
- digital rectal examination
- chemoprevention
- referral for genetic counseling +/- genetic testing, where criteria are met

General behaviors for all four cancers

- vitamins, minerals, micronutrient supplementation
- regular exercise/physical activity
- high fiber diet
- increased fruit and vegetable consumption or specific food intake
- low fat diet
- smoking cessation
- reduction in alcohol intake
- seeking healthcare advice
- participation in recommended screening/surveillance

Exclusion

None

Comparator/Study Design

Inclusion

Systematic reviews of primary studies which seek to identify studies with the following designs

- randomized controlled trials
- non-randomized controlled trials
- uncontrolled before-after studies (or non-controlled trials)

Comparators:

- as reported in primary studies

Exclusion

Systematic reviews of primary studies which focus solely on the following designs

- cohort studies
- case-control studies
- case series and case reports

Outcomes

Inclusion

- cancer incidence
- cancer-related mortality
- all cause mortality
- incidence of known precancerous conditions
- complications of diagnosis, complications or side effects of treatment, psychosocial sequelae

Exclusion

All other outcomes

Eligibility Criteria for Research Q3

Population

Any patient or general populations not specifically selected for known or suspected pre-existing elevated risk of breast, ovarian, colorectal, and/or prostate cancer

Inclusion

- populations sampled from population or clinical settings, including population screening programs

Exclusion

- populations selected entirely on the basis of a personal history of breast, ovarian, colorectal, or prostate cancer
- populations selected entirely on the basis of having a high risk of cancer, as estimated by an existing risk assessment system or a genetics specialist
- populations sampled from specialist genetics clinics or cancer family clinics
- populations selected entirely because they have had a genetic test for a mutation related to one of the cancers of interest (irrespective of the result)

Intervention

Inclusion

Systematic provision of personal risk of breast, colorectal, prostate and/or ovarian cancer based on family history, *alone or combined with* individual advice on appropriate risk reduction behaviors and/or services

Exclusion

- family history taking without provision of personal risk information
- advice on risk reduction not accompanied by, or based on, family history information
- provision of general risk information
- genetic counseling

Comparator/Study Design

Inclusion

Primary studies of the following study designs:

- randomized controlled trials
- non-randomized controlled trials
- uncontrolled before-after studies (or non-controlled trials)

Comparators:

- no comparator group
- comparator group with no intervention
- comparator group receiving preventive advice without provision of family history-based information

Exclusion

- cohort studies
- case-control studies
- case series and case reports

Outcomes

Inclusion

- change in target behaviors related to cancer prevention, considered standard advice at the time of the primary study
- uptake of services identified in (Q2) or considered current/standard of care at the time of the primary study

Exclusion

None

Eligibility Criteria for Research Q4:

Population

Any patient or general populations not specifically selected for known or suspected pre-existing elevated risk of breast, ovarian, colorectal, and/or prostate cancer

Inclusion

- populations sampled from population or clinical settings, including population screening programs

Exclusion

- populations selected entirely on the basis of a personal history of breast, ovarian, colorectal, or prostate cancer
- populations selected entirely on the basis of having a high risk of cancer, as estimated by an existing risk assessment system or a genetics specialist
- populations sampled from specialist genetics clinics or cancer family clinics
- populations selected entirely because they have had a genetic test for a mutation related to one of the cancers of interest (irrespective of the result)

Intervention

Inclusion

Systematic collection of family history information and/or the provision of family history-based personal risk of breast, colorectal, prostate, and/or ovarian cancer

Exclusion

- advice on risk reduction not based on family history information
- provision of general risk information
- genetic counseling

Comparator/Study Design

Inclusion

Primary studies of the following study designs:

- randomized controlled trials
- non-randomized controlled trials
- uncontrolled before-after studies (non-controlled trials)

Comparators:

- no comparator group
- comparator group with no intervention
- comparator group with intervention not based on family history collection or family history-based preventive advice

Exclusion

- cohort studies
- case-control studies
- case series and case reports

Outcome

Inclusion

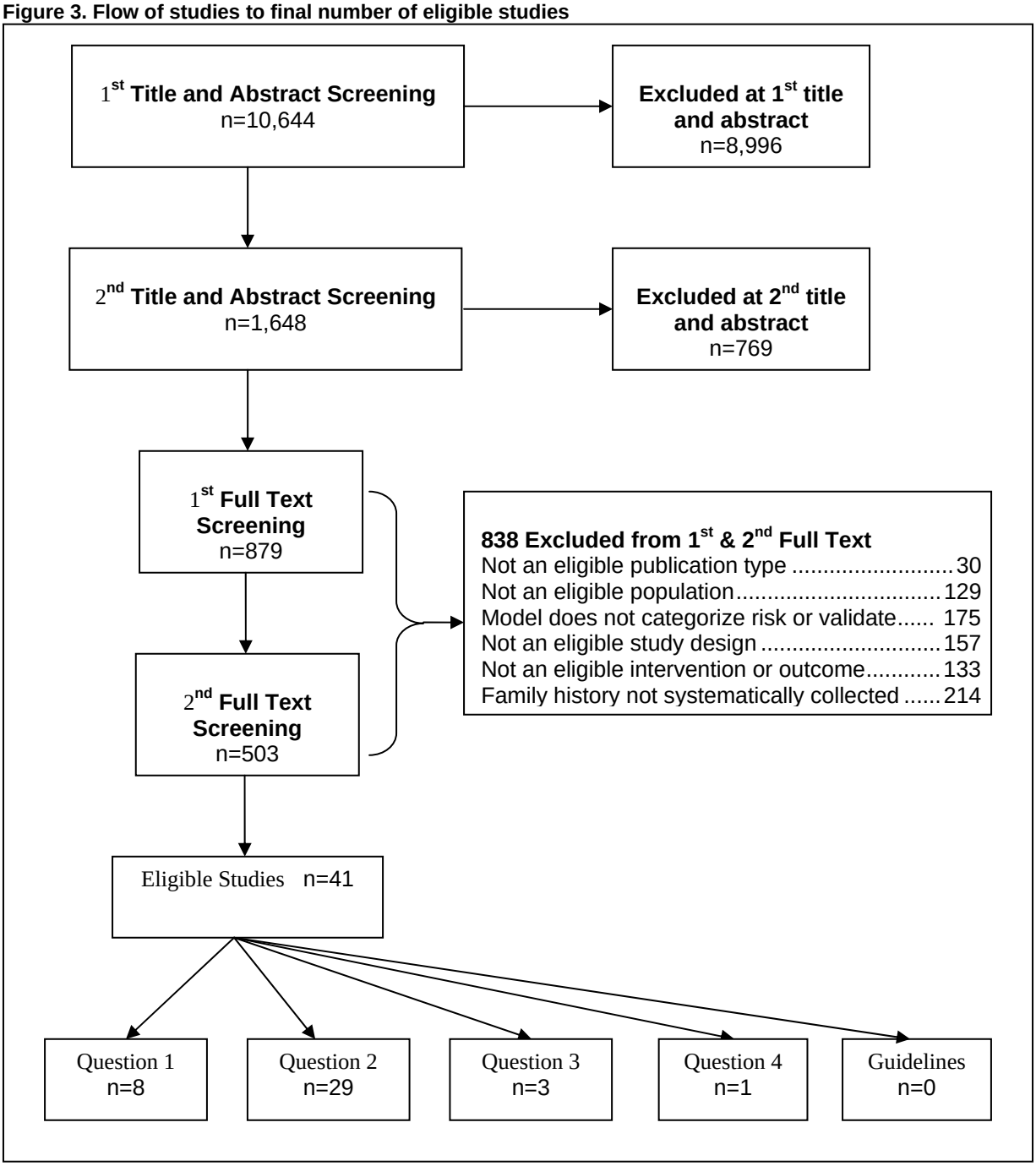
- psychological status
  - anxiety/distress
  - cancer worry
  - depression
  - inaccurate risk perception
  - other psychological outcome
- quality of life
- social impacts
  - family functioning including dynamics/communication, etc.
  - insurance or employment discrimination
  - other

Exclusion

- outcomes not listed above

Figure 3 illustrates the flow of studies based on the eligibility criteria described.

Figure 3. Flow of studies to final number of eligible studies



Study Selection

A team of study assistants was trained to apply the eligibility criteria 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.

Data Extraction

Appropriate data collection forms were developed for use in the SRS (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 and Peer Review

Quality assessment of studies was undertaken in varying forms. Studies eligible for (Q1) were evaluated for potential bias in relation to the model variables and selection bias. For the systematic reviews identified for (Q2), a modified version of the Oxman-Guyatt Overview Quality Assessment Questionnaire, a validated, 10-item assessment scale was used.[82] Studies for (Q3 and Q4) were evaluated using the Jadad scale for randomized trials.[83]

A draft version of this report was circulated to 14 peer reviewers (see Appendix E). Where possible, comments and suggestions were incorporated.

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 for (Q1, Q3, or Q4) as the clinical heterogeneity between studies was considerable.

Chapter 3. Results

Our comprehensive search yielded 10,644 unique citations; from these 9,765 were excluded as they were not an English language publication, not on the cancers of interest, or on topic for any of the four research questions (Figure 3). The remaining 879 citations were screened at full text and of these a total of 12 primary studies and 29 systematic reviews were eligible for inclusion in this review.

Research Q1: Which Risk Stratification Algorithms or Guidelines Delineate Risk Accurately, and in a Clinically Meaningful Way?

General Approach

We reviewed published studies which examined the ability of models (or algorithms, or guidelines) which used family history information to accurately predict individual risk of breast, ovarian, colorectal, or prostate cancer. To be eligible, the model had to include systematic collection of specified family history information, either alone or with other personal or clinical information which would be available for all patients and routinely available to a primary care practitioner. We examined the performance of models in relation to populations not selected for known or suspected high risk of cancer.

Model performance was assessed by predictive accuracy, in terms of calibration and discrimination. "Calibration" is a model's ability to correctly predict the number of observed events (incidence of cancer) in a population and is generally evaluated by its goodness-of-fit to observed events. The ratio of observed to expected cases provides an overall epidemiological assessment of how well a model might perform for a defined population.

"Discrimination" is the assessment of how well a model separates out individuals who will go on to develop different outcomes. Discriminatory accuracy for dichotomous outcomes (e.g., disease/no disease) is best examined through metrics such as sensitivity and specificity, predictive value, likelihood ratio, and the area under the receiver operator characteristic (ROC) curve (or area under the curve (AUC)). The AUC is also referred to as the c-statistic and is defined in the unit square with a range of 0 to 1.0. Since chance alone will follow a perfect diagonal from (0,0) to (1,1), the subsequent AUC will be 0.5 (no apparent discrimination), whereas an AUC of 1.0 indicates perfect discriminatory accuracy.

Discriminatory accuracy is a more relevant evaluation than calibration from the point of view of clinical practice, as it directly indicates how well the model predicts an individual patient's likelihood of developing cancer within a defined time scale. A model that is well calibrated at a population level may not necessarily be highly discriminating when used for individual prediction.

Studies Reviewed

Eight evaluation studies were retained for data abstraction after full text review.[7-14] All except one focused on breast cancer risk assessment. The individual breast cancer models were

all conceptually related: the "original" Gail model,[15] the modified Gail model,[84] the modified Gail model for African American populations,[10] the modified Gail model for Italian populations,[11,12] and the model developed from the Contraceptive and Reproductive Experiences (CARE) study.[7] The exception was Harvard Cancer Risk Index (HCRI),[16] which was developed for calculating the risk of a several cancers, including breast, ovary, colon, and prostate. An eligible validation[14] of the HCRI was published only for colon cancer.

The details of the models are summarized in Table 4. All of the models examined used a set of predetermined input variables in addition to family history as the basis for risk assessment. These variables included a range of personal demographic and disease-specific risk factors such as age, ethnicity, reproductive factors, diet, history of clinical investigations (e.g., breast biopsies, colonoscopies), and other risk factors such as body mass index, and alcohol consumption.

Outcomes

The details of evaluations of the models are summarized in Table 5. All evaluations were performed as secondary analyses of data derived from observational studies or trials. The sample sizes for the evaluations ranged from 1,450 to 147,916, covering a wide age range of participants. Six of the evaluations[7-10,13,14] were conducted in U.S. populations: the Nurses' Health Study (NHS)[14,85,86] (4 studies), the Women's Health Initiative (WHI)[7,87] (2 studies), the Black Women's Health Study,[88] and the Health Professionals Follow-Up Study (HPFS).[87] The remaining two evaluations[11,12] were conducted in Italian populations. Followup periods in the validation cohorts ranged from 5 to 10 years.

Gail Model

The first published version of the 'Gail Score'[15] used information on a woman's age at menarche, her age at the time of the birth of her first child, the number of her first degree relatives who had had breast cancer, and the number of previous breast biopsies that she had undergone. It was designed for women with no personal history of breast cancer who were being followed by annual screening mammography. It estimates the absolute probability of developing invasive or in situ breast cancer over a defined age interval. The model uses estimates of baseline hazard and attributable risk derived from the Breast Cancer Detection Demonstration Project (BCDDP).[89] The authors indicated that its primary application would be to "determine eligibility for entry to breast cancer prevention trials, where an important determinant of sample size is the absolute risk of breast cancer" in the study population.[15]

We identified a single study[8] which evaluated the original Gail model,[15] a secondary analysis of data from the NHS.[85,86] The ratio of expected to observed breast cancer cases was 1.33 (95 percent CI 1.28-1.39), which was a significant overestimation. Only modest discriminatory accuracy was demonstrated (Pearson correlation coefficient 0.67).

Modified Gail Model

The modified Gail model incorporated revisions to improve its validity and applicability to the North American population.[84] The key revisions were a focus on the absolute risk of invasive breast cancer only (i.e., in situ cancer was excluded): the inclusion of a diagnosis of atypical

hyperplasia on biopsy as an additional risk factor; and the substitution of age-specific invasive breast cancer rates from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI) for the BCDDP-based data used in the original model.

We identified five studies which evaluated the performance of the modified version of the Gail model, either in its originally published form, or adjusted to take account of different underlying breast cancer incidence patterns in different populations (African American,[10] Italian[11,12]). The ratios of expected to observed invasive cancer cases ranged from 0.79 to 0.96, mostly not statistically significantly different from unity. Validations, performed in a predominantly white U.S. population[9] and two Italian populations,[11,12] suggested reasonably good calibration, but poorer performance in "more diverse"[13] and African American[10] U.S. populations. These studies all suggested that the standard and modified versions all had very modest discriminatory accuracy (concordance statistic 0.58-0.59).

CARE Model

The CARE Model[7] was developed as an African American adaptation of the Gail model, using data from the Women's Contraceptive and Reproductive Experiences (CARE) Study,[90] the SEER program, and National Center for Health Statistics. It is a simpler model, in that two variables in the modified Gail model were removed and one was dichotomized.

We identified one study that validated this model, in a subset of African American women in the WHI. The model showed good calibration, with an expected observed ratio of cases not statistically significantly differently from unity. The discriminatory accuracy, expressed as AUC, was 0.555, which suggests only very modest predictive ability at best.

The authors compared the CARE Model with the MGM in classifying eligibility for a chemoprevention trial, and found that it doubled the proportion of women who met inclusion criteria (30.3 percent compared with 14.5 percent).

Harvard Cancer Risk Index

The HCRI was developed as a tool to assist clinicians in counseling patients about cancer risk reduction.[16] It addressed prediction of the most common cancers in American men and women (prostate, breast, lung, colon, bladder, endometrium, non-Hodgkin's lymphoma, ovary, kidney, leukemia, cervix, pancreas, skin melanoma, and stomach). The tool was developed using a consensus-based process in which available evidence was used to assign points for different levels of defined risk factors. Risk was stratified into a seven point categorical scale, set relative to the average U.S. population risk for each cancer. Several risk factors contributed to the score for each cancer, family history being included in all except leukemia and cervical cancer.

We identified one validation study,[87] in which the HCRI's predictive validity for colon cancer was assessed in two cohorts, the NHS (women) and the HPFS (men). Results pertaining to ovarian cancer were also reported in this publication, but family history items were lacking, therefore these data were excluded from the current review. In addition to family history, eight variables for men and eleven for women were included in the HCRI for colon cancer.

The overall ratios of observed and expected cases were not reported. For women, the ratios by initial risk stratum ranged from 0.58 to 1.79, and for men 0.75 to 2.35. A better fit was observed for women than men. The AUC was 0.67 for women and 0.71 for men, suggesting moderately good discriminatory accuracy.

Conclusion

There were essentially two families of tools on which relevant performance data were available, those based on the Gail model, and the HCRI. None of the identified studies evaluated the performance of a predictive tool or algorithm, designed for use in populations not already pre-selected for higher risk, and *using family history information alone*. No validation studies of tools designed for risk prediction for ovarian or prostate cancer were found.

Most, but not all models demonstrated good calibration for the populations for which they were developed. However, none of the models identified demonstrated more than moderate ability to correctly discriminate risk at an individual level. The highest concordance presented was 0.71: this is equivalent to the correct classification of future disease (present or absent) in 71 percent of individuals, and incorrect classification of 29 percent.

Research Q2: For Which Behaviors and Clinical Preventive Services is There Evidence of Benefit in Terms of Actual Reduction of Disease Risk, and What Harms, if any, Have Been Identified?

General Approach

For the purposes of this review, we included published quantitative and qualitative reviews of the effectiveness of personal behavioral/lifestyle and clinical interventions that are commonly recommended as part of cancer risk reduction strategies in primary care settings. The list of interventions of interest was developed by the study team in consultation with the partners and the members, and was incorporated into the eligibility criteria for the review. Table 6 lists the interventions of interest.

Where multiple reviews addressing the same intervention were identified, they were scrutinized to determine the degree of overlap, as well as for quality. We selected the most recent and/or most comprehensive review for reporting, bearing in mind any differences in quality.[17]

Studies Reviewed

Twenty-nine systematic reviews fulfilled eligibility criteria after full text review. These eligible reviews addressed evidence for four chemoprevention interventions (antioxidant supplementation, calcium supplementation, non-steroidal anti-inflammatory drugs (NSAIDS), in the form of aspirin, but not COX-2 inhibitors and statins) and five screening interventions (breast self-examination (BSE), screening mammography, fecal occult blood testing (FOBT), flexible sigmoidoscopy (FS), and prostate specific antigen (PSA), for three cancers (breast, colorectal, and prostate).

No reviews were identified which examined evidence for magnetic resonance imaging in breast screening, ultrasound ovarian screening, colonoscopy as a stand-alone screening intervention, regular exercise, dietary interventions other than supplements (reviewed under chemoprevention), reduction in alcohol consumption, smoking cessation, seeking health care advice or referral for genetic counseling and/or genetic testing. As mentioned in chapter 2, we

did not search for reviews for food, nutrition or physical activity interventions before 2006 as these were well evaluated in the World Cancer Research Fund/ American Institute for Cancer Research Second Expert Report.[81]

Of the eligible studies, data were extracted from the 10 reviews which represented the most comprehensive, up-to-date, and high quality evidence.[18-27] Twelve additional reviews reported overlapping data[28-39] but these data were not extracted. Five reviews[40-44] did not identify primary intervention studies despite being designed to do so; and two reviews[45,46] identified apparently relevant intervention studies but did not report usable data. The studies, which were not reported, on are listed in Table 1 in Appendix C.

The findings of the reviews which were included and reported are presented in Tables 7, 8, and 9. Some reviews addressed evidence related to prevention of more than one cancer type; in this situation, the results are presented separately by cancer type.

Breast Cancer

Five reviews on breast cancer prevention[18-22] are presented in Table 7 which synthesizes evidence in relation to chemoprevention (antioxidants and statins), screening (BSE), and screening mammography.

Chemoprevention. 'Chemoprevention' refers to the use of chemical compounds to arrest or reverse the earliest stages of carcinogenesis or development of pre-cancerous lesions. We apply it very broadly in this review to include the use of both recognized pharmaceutical agents (drugs) and supplements of naturally occurring elements and compounds administered in doses above those naturally encountered in typical diets, and/or administered in tablets or capsule.

Antioxidants. Antioxidants are molecules which inhibit or prevent damage to cells caused by oxidizing agents such as oxygen free radicals. It is suggested that such damage (oxidative stress) is an important early step in the development of many diseases, including cancer. It is hypothesized that antioxidant compounds could act as cancer prevention agents by preventing or inhibiting DNA damage, the earliest stage of carcinogenesis. Many observational epidemiological studies have found an inverse relationship between consumption of foods with high antioxidant content, such as fruits and vegetables, and incidence of cancer.[71-73]

Antioxidants are a diverse group of compounds and different reviews have assessed them collectively and individually. Among the many antioxidants associated with food, the most commonly studied are vitamins (A, C, and E), their precursor molecules (e.g., alpha-tocopherol and ß-carotene), and minerals (e.g., selenium and zinc).

We report the findings of two reviews that examined antioxidants and breast cancer incidence. The first review[18] evaluated supplements which contained any combination of ß-carotene, vitamin C, vitamin E, selenium, zinc, and other antioxidants, and the second review[19] focused on vitamin E in any combination. Both of these reviews also evaluated outcomes related to colorectal and prostate cancer, the results for which are presented in the relevant sections below.

The first review[18] included only placebo-controlled trials where antioxidants were given as supplements where the ingredients were fully disclosed, and which had followed up participants for at least one year. Their breast cancer analysis was based on 1,753 cancers in a total of 88,392 participants enrolled in the primary trials. No evidence was found of a protective effect of any combination of antioxidants against breast cancer (RR 1.00, 95 percent CI 0.90-1.09).

The second review[19] examined vitamin E alone or in any combination. It included randomized controlled trials (RCTs) where vitamin E, in tablet or capsule form with or without other components, was evaluated against a control group receiving placebo or no intervention. They assessed the methodological quality of all included trials as high. They identified three trials, involving 62,158 participants, in which breast cancer incidence was reported as an outcome. They concluded that there was no evidence of a protective effect of vitamin E supplementation against breast cancer (RR 0.99, 95 percent CI 0.90-1.10).

*Statins***.** Statins (hepatic 3-hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase inhibitors) are a class of lipid-lowering drugs that are widely prescribed for people at risk of cardiovascular disease. Interest in whether use of statins is associated with cancer risk was prompted by safety monitoring findings from cardiovascular prevention trials.[91] Some studies suggest that they may also have a protective effect against cancer,[92-98] while others suggest the opposite.[99-101] Setoguchi et al., (2007)[102] observed that longterm statin users tend to be healthier overall than non-users, and suggested that this might explain the positive associations.

Table 7 summarizes findings from the most comprehensive recent review[20] that examined the evidence for statins in reducing the risk of a range of cancers, including breast, colorectal, and prostate (data for the latter two presented below). This review focused on placebo-controlled trials of any statin involving any population except participants being treated for particular high risk indications (e.g., familial hypercholesterolemia). The overall analysis indicated that statins appear to confer neither a protective nor a harmful effect on breast cancer incidence (RR 1.01, 95 percent CI 0.79-1.30). The findings were unaltered in sub-group analyses comparing lipophilic and lipophobic statins, and low, medium, and high potency statins.

Screening. *Breast self-examination (BSE).* It has been believed for many years that the practice of regular BSE allows women to detect breast tumors at an early stage, and thus to seek early treatment and improve their chances of cure. It is also considered inexpensive, non-invasive, and can be done in private.[103,104] Observational evidence suggests that women diagnosed with breast cancer who have practiced BSE are more likely to have found the tumor themselves, to have smaller tumors (on average) at the time of diagnosis, and to have benefited from longer survival.[105] Critics of such analyses point to the possibility of lead-time bias, and the need to examine mortality rates as a more valid method of examining outcomes.

We report the findings of one systematic review[21] which identified primary reports of three large randomized controlled trials, in two of which the intervention was teaching BSE in general populations and, in the third, clinical breast examination followed by teaching BSE. The latter was discontinued after the first screening round because of poor compliance, so data were available for only two trials. A total of 587 breast cancer deaths were observed in a total group of participants of 388,535 across the two trials. The relative risk of breast cancer mortality was 1.05 (95 percent CI 0.90-1.14). There was no statistically significant effect on the total number of cancers identified. There was a non-significant trend towards the detection of smaller tumors (carcinoma in situ RR 1.32, 95 percent CI 0.82-2.14, tumors ≤2cm RR 1.13, 95 percent CI 0.99-1.28). There was a statistically significant increase in total number of breast biopsies and biopsies with benign pathology (RR 1.53, 95 percent CI 1.47-1.60, and 1.88, 95 percent CI 1.77-1.99, respectively). These two large, longterm, population-based trials provide robust evidence that teaching women to perform regular BSE does not translate into a lower mortality rate from breast cancer, and is associated with a higher rate of invasive investigation.

***Screening mammography*.** Mammography as an investigative technology for suspected breast pathology has been available for several decades, and has been gradually introduced, and

evaluated, as a potential screening strategy for breast cancer. The rationale for mammography is that screening may detect tumors at a stage before they are palpable through self- or clinical examination, and that these smaller tumors are less likely to have become locally invasive or metastasized. Screening mammography aims to detect early malignant tumors and, if effective, would be expected to reduce breast cancer, and overall, mortality, but not breast cancer incidence.

Screening mammography has been the focus of a relatively large number of controlled trials in a range of countries, and between 1992 and 2002, 22 systematic reviews of screening mammography were published.[106-127] This level of scrutiny reflects ongoing controversies about the quality of the primary trials, and the possibility for harm which some experts consider inadequately examined and appreciated.[106,128]

We summarize the findings of the most recent comprehensive review[22] that attempts to address these issues through analyzing the outcome of all-cause mortality as well as breast cancer mortality, by sensitivity analyses according to adequacy of allocation procedures in primary trials, and by assessing rates of different treatment modalities in screened and control groups. The data are presented in Table 7.

This review examined data from 10 completed RCTs involving about half a million women. Of these, the reviewers considered only three trials to have been adequately randomized, and conducted a meta-analysis for these three separately. The trials covered a wide range of age groups, from 39 to 74 years, although most studies focused on women within the 40-59 age group. The reported screening intervals ranged from annual to about 2 years. In some studies, screening was accompanied by clinical breast examination, physical examination, or encouragement to perform monthly BSE. In most trials, the control intervention was usual care.

The overall analysis suggested that screening mammography is associated with reduced breast cancer mortality at 13 years (RR 0.80, 95 percent CI 0.73-0.88), but the association is more marked for the trials considered 'sub-optimally randomized' (RR 0.75, 95 percent CI 0.67-0.83) than for 'adequately randomized trials (RR 0.93, 95 percent CI 0.80-1.09). When all cause mortality outcomes are considered (which would incorporate serious harms caused by over-treatment), the pooled estimates are very similar for trials considered 'adequately randomized' (RR 1.00, 95 percent CI 0.96-1.04) and 'sub-optimally randomized' (RR 0.99, 95 percent CI 0.97-1.01).

Colorectal Cancer

Six reviews are presented in Table 8 which synthesizes evidence in relation to colorectal cancer (CRC) prevention, four relating to chemoprevention (antioxidants, NSAIDS, and statins) and two relating to screening (FOBT and FS).

Chemoprevention. The rationale for chemoprevention is described in previous section on breast cancer.

Antioxidants. The background to antioxidants is described in previous section on breast cancer.

We report the findings of two reviews which examined antioxidants and CRC incidence. The first[18] evaluated supplements which contained any combination of β-carotene, vitamin C, vitamin E, selenium, zinc, and other antioxidants, and the second[19] focused on vitamin E in any combination. Further details of these reviews are included in the section on breast cancer.

The first review[18] conducted an analysis of 1,523 cancers in a total of 178,086 participants enrolled in the primary trials. No evidence was found of a protective effect of any combination of antioxidants against CRC incidence (RR 1.00, 95 percent CI 0.90-1.10).

The second review[19] identified four trials focusing on CRC. For vitamin E given in any combination (91,099 total participants), they found no evidence of an association with CRC incidence (RR 0.95, 95 percent CI 0.81-1.12). Similarly, there was no association when they examined data from two trials (24,114 participants) which evaluated vitamin E alone (RR 1.05, 95 percent CI 0.79-1.39).

Together, these reviews provide no evidence of a positive or negative association between antioxidant or vitamin E supplementation, and CRC risk.

NSAIDS. NSAIDs are a group of compounds which have an anti-inflammatory effect generally due to their action as non-selective inhibitors of the enzyme cyclooxygenase. Their potential protective effect against CRC has been observed in a number of case-control and cohort studies;[129-136] there is also evidence of their effectiveness in preventing recurrence of colorectal adenomatous polyps.[137,138]

We identified two systematic reviews that examined one specific NSAID only, ASA, in CRC prevention. We report the findings of the single review that conducted a formal meta-analysis.[23] This review identified two primary studies that evaluated CRC incidence (one at 5 years, the other at 10 years) in individuals at average risk (including no personal history of adenomas); one of these trials also reported CRC mortality and the other examined the incidence of colorectal adenomas. The intervention in both of these studies was ASA at doses recommended for cardiovascular protection (i.e., 325 mg every other day or 100 mg/day). Apparently no primary studies of standard doses (i.e., ≥325 mg/day) have examined cancer outcomes in average risk individuals. The combined number of participants in these two studies was 61,947. No statistically significant association was identified between low dose ASA and CRC incidence (pooled RR 1.02, 95 percent CI 0.84-1.25), CRC mortality (RR not reported) or adenoma incidence at 5 years (RR 0.86, 95 percent CI 0.68-1.10). These results provide no direct information on the effectiveness of either higher doses of ASA, or other NSAIDS, on colorectal neoplasia.

Statins. The background to statins is described in previous section on breast cancer. A comprehensive systematic review[20] examined the evidence for statins in reducing the risk of CRC as well as breast (reported above) and prostate cancer (reported below). Data was synthesized for nine trials which examined CRC incidence, and one which evaluated CRC mortality, as outcomes. The overall analysis indicated that statins appeared to confer neither a protective nor a harmful effect on CRC incidence (pooled RR 1.02, 95 percent CI 0.89-1.16) or mortality (RR 0.33, 95 percent CI 0.07-1.63). The findings were unaltered in sub-group analyses comparing lipophilic and lipophobic statins, and low, medium and high potency statins.

Screening. Evidence from a wide range of studies[139-141] suggests that CRC results from complex interactions between genetic and environmental factors, and that most cancers evolve from small adenomas over a period of years.[140,141] The possibility of preventing CRC cases and deaths by early intervention to remove colorectal adenomas and/or early stage cancers has led to a large number of studies of a range of screening strategies, specifically involving FOBT, colonoscopy and sigmoidoscopy.[142] There is no consensus on the optimum combination of these modalities, or on the ideal screening interval.

*FOBT***.** The most widely used approach to FOBT is the stool guaiac test, in which the presence of heme (from haemoglobin) is indicated by a color change when hydrogen peroxide is

added. This is a result of the oxidation of guaiac by the peroxide. A newer class of occult blood tests (immunochemical) rely on the detection of globin rather than heme, and it is suggested that these are more sensitive and specific than guaiac tests.[143]

A number of reviews examined FOBT-based screening strategies, of which one is reported here.[24] This review examined RCTs only of FOBT (guaiac or immunochemical) in which at least two rounds of screening were compared with no-screening controls. This review analyzed data from four trials involving a total of 329,642 participants. A statistically significant effect of screening on CRC mortality was observed (pooled RR 0.84, 95 percent CI 0.78-0.90), which remained when the three trials with biennial screening were examined separately. No effect on all-cause mortality was observed (pooled RR 1.00, 95 percent CI 0.99-1.01), but a statistically borderline association with non-CRC mortality was noted (pooled RR 1.01, 95 percent CI 1.00-1.03). The interpretation of these combined results is difficult. It is argued that effective CRC screening would have little impact on all-cause mortality because CRC makes only a small contribution to overall mortality in these populations (and screening trials are therefore inadequately powered to detect such an effect). There is also an argument that biased attribution of cause of death between screened and control groups can lead to an overestimate of the true effect of screening on mortality, therefore an assessment of all-cause mortality would provide a more valid assessment of effectiveness.[144]

We do not present data from a further systematic review[36] which focused on guaiac-based biennial FOBT screening alone; it included a non-randomized controlled trial excluded from the review reported above[24] and excluded one of the latter's included trials. The pooled results are consistent with those reported above and in Table 8.

Flexible sigmoidoscopy. Flexible sigmoidoscopy (FS) is an endocopic technique which allows visualization of the colon and rectum distal to the splenic flexure. FS has a very low complication rate.[145,146] The majority of CRCs arise in the distal colon, thus are theoretically detectable with FS, and detection of distal adenomas is an indication for full colonoscopy.[147] It is suggested that a combined strategy such as this can detect about 80 percent of CRC cases in men and about 50 percent of those in women, without recourse to more invasive colonoscopy as a primary screening modality.[148-150]

We identified one review[25] which examined the evidence for FS in CRC screening. One RCT was identified which compared FS in addition to FOBT against FOBT only (positive screens being followed up by colonoscopy). This review also considered FOBT alone as a screening strategy, but the data were not extracted as they are similar to the review reported above.[24] This trial involved 10,978 participants and showed no statistically significant effect of the combined FS plus FOBT strategy on CRC mortality or incidence (RR 0.78, 95 percent CI 0.36-1.73 and 1.37, 95 percent CI 0.88-2.15, respectively). No formal intervention studies comparing FS alone with either no screening, or FOBT only, have been identified.

Prostate Cancer

Five reviews[18-20,26,27] are presented in Table 9 which synthesizes evidence in relation to prostate cancer prevention, four relating to chemoprevention (antioxidants, calcium, and statins) and one relating to screening (PSA, digital rectal examination (DRE), and transurethral ultrasound (TRUS) biopsy).

Chemoprevention. The rationale for chemoprevention is described in previous section on breast cancer.

*Antioxidants***.** The background to antioxidants is described in previous section on breast cancer.

We report the findings of two reviews which examined antioxidants and prostate cancer incidence. The first[18] evaluated supplements which contained any combination of β-carotene, vitamin C, vitamin E, selenium, zinc, and other antioxidants, and the second[19] focused on vitamin E in any combination. Further details of these reviews are included in the section on breast cancer.

The first review[18] conducted an analysis of 2,143 new cancers in a total of 55,709 participants enrolled in the primary trials. Overall, the pooled analysis indicated a small, non-statistically significant decrease in prostate cancer incidence when all antioxidants were considered together (pooled RR 0.87, 95 percent CI 0.74-1.02). Noting high heterogeneity, a sensitivity analysis suggested that vitamin E in particular was associated with a reduced risk (pooled RR 0.82, 95 percent CI 0.67-0.99), based on three trials. The authors of this review also noted that "one trial report a decreased incidence of prostate cancer with selenium," although they did not provide relative risk data. Reporting on the same trial,[151] another review[26] (included below) estimated that, for a daily dose of 200μg of selenium (compared with placebo), the relative risk for prostate cancer incidence was 0.37 (95 percent CI 0.20-0.70).

The second review[19] evaluated the effect of vitamin E alone or in combination, and performed a meta-analysis on three primary trials. For vitamin E given in any combination (71,759 total participants), the pooled estimate for effect on prostate cancer incidence also indicated slightly reduced risk (pooled RR 0.85, 95 percent CI 0.74-0.96). Two trials examined vitamin E alone, with no evidence of an association (pooled RR 0.86, 95 percent CI 0.70, 1.06). Similarly, there was no association when they examined data from two trials (24,114 participants) which evaluated vitamin E alone (RR 1.05, 95 percent CI 0.79-1.39).

Together, these reviews suggest no evidence of an effect of combined antioxidant supplementation on prostate cancer risk, but potentially a small protective effect of vitamin E supplementation.

Calcium. The association between calcium intake and prostate cancer risk has been examined both from risk increasing and risk reducing perspectives. Observational studies have indicated a positive association between calcium intake and prostate cancer, the suggested mechanism being that calcium lowers circulating vitamin D concentrations, and this in turn alters prostate cell proliferation.[152-155] In contrast, some studies have suggested that dietary calcium decreases prostate cancer risk.[156-162]

We identified one review which analyzed intervention study data relating to calcium and prostate cancer risk.[26] This review identified a single primary trial of calcium supplementation, designed to evaluate calcium as a protective agent against recurrence of colorectal adenomas, where prostate cancer incidence was evaluated as a secondary outcome.[47] Supplements equivalent to 1,200 mg elemental calcium daily were given for 4 years and participants followed up for another 7 years. This trial observed 70 prostate cancers in 672 men with an RR for prostate cancer incidence of 0.83 (95 percent CI 0.52-1.32). Detailed review of the results suggested a statistically significantly lower incidence of prostate cancer in the supplement group until 2 years after supplementation was discontinued (RR 0.52, 95 percent CI 0.28-0.98), at which point the risk in both groups converged. It is suggested that calcium may have a slight protective effect, which is maintained only by ongoing supplementation. This finding from a single trial is insufficient to recommend calcium supplementation specifically for the purpose of

prostate cancer prevention, particularly given the contradictory findings of previous observational studies.

Statins. The background to statins is described above in previous section on breast cancer.

We present data from the comprehensive systematic review described in previous sections,[20] which examined the effectiveness of statins in reducing the risk of several cancers. Four trials examined prostate cancer incidence, and one evaluated prostate cancer mortality. The overall analysis indicated that statins appeared to neither increase nor decrease risk of prostate cancer incidence or mortality (pooled RR 1.00, 95 percent CI 0.85-1.17 and RR 0.99, 95 percent CI 0.14-7.01 respectively). No data were presented with regard to lipophilic versus lipophobic, or low, medium and high potency statins.

Screening. *Prostate-specific antigen-based strategies (PSA).* Strategies for screening for early prostate cancer have revolved around the combined use of PSA with or without DRE of the prostate, followed by needle biopsy guided transrectal ultrasound (TRUS). Digital rectal examination has limited sensitivity because it is not possible to palpate the entire prostate gland, while PSA testing produces high rates of false positive and false negative results.[163] In addition, although reductions in prostate cancer mortality have been demonstrated with early treatment,[164,165] there remains considerable concern about lead and length time bias, the overtreatment of men who have indolent disease (tumors which were never destined to be fatal),[166] and harms associated with treatment.[167-170]

We identified a single review[27] which examined the effectiveness of population-based screening in preventing death from prostate cancer. This study identified two trials of screening strategies that combined PSA testing, DRE and TRUS biopsy for diagnostic investigation, one of which used an annual, the other a 3 times yearly, screening cycle. The total number of participants randomized was 55,512, and 345 prostate cancer deaths were observed over followup periods of at least 11 years. No statistically significant impact of screening on prostate cancer mortality was found (pooled RR 1.01, 95 percent CI 0.80-1.29). No data were presented in relation to all-cause mortality. The authors of the review considered that both trials had a high risk of bias. The overall findings indicate that PSA-based screening cannot be considered to be an effective secondary prevention intervention in prostate cancer.

Quality Assessment of Studies

Standardized quality assessment checklists using a modified scoring version of the Oxman and Guyatt criteria[82] were employed for all systematic reviews. The range of scores was 11-17 out of a possible 18. The major area of weakness was failure to describe adequate control of bias in the selection of studies for review.[18-20,22,23,27] Other issues encountered in a minority of reviews were incomplete description of search methods,[23,27] and failure to describe criteria for assessing the validity of primary studies,[20,25,26] or to cite the validity assessments of included studies.[20,26]

Overall, the potential for bias in these reviews appears quite low. It is impossible to say whether failing to adequately describe search strategies, methods for controlling selection bias, or assessing validity of studies reflects methodological shortcomings or only failure to report these in published articles.

Conclusion

We were able to locate relevant systematic reviews relating to prevention, in average risk populations, of breast, colorectal, and prostate cancers, but not ovarian cancer. For all three cancers, the core primary prevention strategy for which reviews could be identified was chemoprevention. For breast and CRC, no evidence of an effect on cancer incidence of antioxidant supplements in general, vitamin E supplements in particular, or statins. For CRC, data on NSAIDS were available, with no evidence of an effect on cancer incidence. For prostate cancer, equivocal evidence was found of a possible protective effect of vitamin E supplements, selenium, and calcium supplements.

Screening strategies were also examined. For breast cancer, a review of three large population-based trials, confirm that BSE is not an effective strategy for reducing mortality from breast cancer and may increase morbidity through unnecessary investigations. Screening mammography has been evaluated in a large number of meta-analyses, which indicate that population-based screening appears to consistently reduce breast cancer mortality by about 15 percent, although there is still an open debate on whether all-cause mortality is a more valid measure of benefit of this intervention. There is concern that screening leads to higher rates of investigation and over treatment which undermine overall benefits. The analyses are based on studies with participants with a wide range of age ranges, which makes it difficult to discern the extent to which the profile of benefits and risks change according to target age. Both the technical performance of the screening test, in terms of sensitivity and specificity, and the prior risk of breast cancer, vary according to age, therefore the predictive value is not constant across all age groups. Also, the level of any risks associated with overtreatment will depend on local protocols for diagnostic investigation and treatment.

For CRC, FOBT-based screening strategies (which generally include diagnostic investigation using colonoscopy) appear to be associated with a decrease in CRC mortality, and the limited evidence available suggests that adding FS does not improve their effectiveness. As with breast screening, it is argued that all-cause mortality may provide a more valid assessment of screening effectiveness; however, since the proportion of overall mortality attributable to CRC is low, screening studies are generally underpowered to detect an effect.

With respect to prostate cancer, we found no evidence that PSA-based screening strategies are effective in reducing mortality.

Research Q3: For Those Interventions Identified as Being Based on Reasonable Evidence, What is the Evidence That Providing Information on Risk Status Results in Behavior Change or Increased Uptake of Services on the Part of Individual Patients?

General Approach

We reviewed published intervention studies (RCTs, controlled trials, and before-after studies) that examined the impact of systematic collection of family history information on one or more risk-reduction behaviors for breast, ovarian, colorectal, or prostate cancer. To be

included, the intervention had to comprise systematic collection of individual family history information, and also communication of personal risk of one or more of the cancers of interest. This could be accompanied by individualized advice on specific risk reduction behaviors, although this was not necessary for a study to be included. The target behaviors of interest were both personal/lifestyle, and adherence to recommended clinical preventive interventions such as screening; the interventions were those considered standard of care when the primary study was conducted.

Studies Reviewed

Three studies[48-50] were retained for data abstraction after full text review. These studies all focused on breast cancer risk assessment and mammography screening, with or without other behaviors, as the target intervention (Table 10). Two of the studies were RCTs[49,50] and the other[48] was an uncontrolled before-after study.

The sample sizes ranged from 188 to 2,076, and participants were recruited from a health maintenance organization (HMO),[49] community pharmacies/health promotion events,[48] and as first degree relatives (1DR) of breast cancer patients.[50] Family history information was captured by computer-assisted telephone interview,[50] postal questionnaire,[49] and interviewer-administered questionnaire.[48] In all three studies, information relating to personal medical history was collected as well as family history information. The 1DR and community pharmacy studies[48,50] specified use of the Gail model for risk calculation, which requires information on the number of 1DRs with breast cancer; the HMO study[49] used a risk stratification algorithm developed in-house, which included information on first and second degree relatives with breast cancer.[171]

The HMO study[49] had four groups, with two levels of collection of family history information (collected or not collected) and three levels of risk information included in screening invitation letters (no reinforcement, general risk messages, personalized risk messages) in the following combinations:

- no collection of individual risk information plus generic invitation for mammography
- no collection of individual risk information plus general risk messages embedded in invitation for mammography
- collection of individual risk information plus general risk messages embedded in invitation for mammography
- collection of individual risk information plus personalized risk messages embedded in invitation for mammography.

Data on the outcome of mammography uptake by 12 months were captured using the HMO's databases.

The 1DR study[50] had two groups, both of which had individual family history information collected, and personalized information on risk of breast cancer fed back. The two groups had different levels of reinforcement of the importance of, and reminders to undertake, the target behavior of screening mammography. Data on the outcome of uptake of mammography was assessed by self-report at 12 months, captured by mail or telephone survey.

The community pharmacy study[48] had one group of participants, all of whom had individual family history information collected and personalized information on risk of breast cancer fed back, along with reminders of recommended screening behaviors. Data on the outcomes of self-reported uptake of mammography, and adherence to BSE and clinical breast examination (CBE) recommendations, was captured at 6 months using telephone survey.

It should be noted that the two controlled studies (1DR and HMO[49,50]) both examined different levels of personalization of risk information, but only the HMO study[49] examined the capture of family history information as an intervention in itself. The community pharmacy study[48] did not have a control group without family history capture.

Outcomes

The findings of the evaluation studies of the interventions described above are summarized in Table 11. The 1DR study[50] showed a borderline statistically significant difference (P=0.05) in the change in mammography uptake (about 8 percent) between intervention and control groups. The other two studies were null. The community pharmacy study[48] was the only one to examine other behaviors, and showed a statistically significant increase in self-reported BSE, but not CBE. The HMO study appeared to be adequately statistically powered; this was also likely the case with the 1DR study although sample size considerations were not discussed. Although the community pharmacy study indicated an *a priori* sample size calculation, their assumptions about baseline adherence rates may have been erroneous, as they were around 70-80 percent for CBE and mammography, much higher than published general population figures and suggestive of a possible ceiling effect.

All articles reported age-specific analyses, which generally did not show meaningful differences in effectiveness of the interventions. The HMO study[49] also analyzed outcomes by breast cancer family history status (positive or negative) in the two groups that had been sent a risk questionnaire. While mammography uptake was similar between those receiving general risk and personalized risk invitations and who had a negative family history (41.4 and 39.7 percent, respectively), uptake was higher in women who had a positive family history and received a personalized invitation (66.7 percent) than women with a positive family history who received a generalized risk invitation (42.9 percent) (P=0.005). The results of the community pharmacy study[48] were unchanged when the analyses were limited to the high risk participants only.

The studies vary in the extent to which their participants were representative of the general population. The HMO study was designed to be completely representative of its own patient population, which was described in previous publication as predominantly white, slightly better educated, and having a slightly different income distribution than Washington state as a whole.[171] The proportion of participants with a positive first or second degree family history of breast cancer was about 20 percent, which is consistent with the North American female population. In contrast, the 1DR study was confined to women who had at least one first degree relative with breast cancer. The community pharmacy study drew participants from women attending pharmacies and heart health events, and no specific data are presented regarding representativeness. Their analyses indicate that 21 of 140 (15 percent) participants were assigned to the high risk category (≥1.7 percent risk of breast cancer in 5 years), which appears higher than would be expected for an unselected female population in this age group. Also, the high baseline rates of CBE and mammography compared with published figures for the general population may indicate that this study has limited external validity.

Quality Assessment of Studies

Standardized quality assessment checklists were employed on the two studies that used a randomized trial design.[49,50] The modified Jadad scores were 4 out of 8 for both studies.[83] The

main problem areas for both studies were failure to report measures to achieve blinding, and neither explicitly described randomization procedures or measures to conceal allocation. Both studies implemented the intervention through mail-outs to participants, asking them to take a specific action (schedule a mammography), and the possibility for contamination was probably rather low, particularly for the 1DR study. The potential for bias in these studies therefore appears quite low.

The third study[48] was described in the report's abstract as a 'randomized, paired, pre-post study', which is misleading. In our assessment, it was an uncontrolled pre-post study in which before-after outcomes for individual participants were analyzed as paired data. No control group was used and therefore no random allocation was possible. The potential for bias in this study is high, given that no assessment could be made of the influence of external factors, or placebo or Hawthorne effects.

Conclusion

Taken together, the three studies identified neither support nor refute the hypothesis that taking family history and using it to personalize risk of breast, ovarian, colorectal, or prostate cancer promotes lifestyle changes which reduce cancer risk, and/or greater adherence with preventive clinical interventions. All three studies focused on breast cancer, the interventions were heterogeneous, some including components beyond family history taking and personalization of risk. The interventions generally did not resemble the routine, personal interaction which might occur between a primary care professional and an individual patient, and the methodological rigor of the evaluations was variable.

The HMO study[49] was embedded in a routine screening invitation system, and therefore resembled regular clinical practice, albeit in a non-personal way. The evaluation was well-designed and had a large sample size. This study (the oldest of the three reviewed) provides no evidence that personalization of risk information would be an effective overall strategy, but suggests that it might be worth exploring as a way of promoting risk reduction behavior in high risk sub-groups.

The 1DR study[50] provided evidence of a possible modest effect on mammography uptake of personalizing risk information for a group already likely to have higher than average personal risk perceptions. The intervention had several components, and it is impossible to separate out the individual effects of the family history collection, the personalization of risk information, and the materials designed to reinforce the importance of mammography. Even this thoughtfully designed intervention produced only a small increase in screening behavior. The transferability of the approach to a clinical setting, and the absolute size of benefits that would be achieved, is unclear.

The community pharmacy study[48] showed some evidence that personalized risk information could promote cancer prevention behavior, but the lack of a control group, the questionable validity of the outcome measurement, and the likely selection bias of participants all make it impossible to judge the wider applicability of its findings.

Research Q4: What are the Harms or Risks to Individual Patients That may Result From the Collection of Family History Information in Itself, and/or the Provision of Family History-Based Risk Information?

General Approach

We reviewed published intervention studies, (RCTs, controlled trials, and before-after studies) which assessed negative impacts of systematically collecting family history information and providing patients with risk information for the cancers of interest based on their family history. The focus was on systematic collection of individual family history information, and communication of personal risk of one or more of the cancers of interest, in populations considered representative of primary care populations. Specialist genetic counseling (with or without genetic testing) for patients selected because of possible genetic risk was excluded from this definition.

The outcomes of interest were impaired quality of life, negative psychological effects (cognitive, affective, or behavioral), social impacts (e.g., negative impact on family well-being, discrimination, stigmatization), which could be directly attributed to this intervention, not subsequent clinical or other preventive activities.

Studies Reviewed

One study was identified which met all eligibility criteria.[51] This was an uncontrolled before-after study designed to evaluate the psychological impact of providing family history information and receiving a personalized risk assessment. Patients aged 35-65 registered with a single family doctor's office were invited to complete a postal cancer family history questionnaire, and were provided with individual feedback on their genetic risk of CRC and breast cancer (where appropriate). General anxiety and cancer worry was assessed at baseline and 4 to 6 weeks after risk information feedback using the Spielberger State-Trait Inventory (STAI) and a multidimensional cancer worry scale, respectively. Details of the study are summarized in Table 12.

Outcomes

This study analyzed participants in two groups. Firstly, 'lower risk' (those at no more than slightly elevated risk) participants, for whom no followup was necessary, were given feedback by letter only. No statistical difference was observed in anxiety and most other cancer worry measures following the intervention, with the exception of a small reduction in participants' perception of their own risk ($P<0.01$).

Of the remaining participants, most were interviewed to clarify details of the family history, which led to further designation into 'higher risk' and 'false positive' groups (the latter comprising patients deemed not actually to be at high risk after further enquiry). For both 'higher risk' and 'false positive' groups, no difference between baseline and followup responses to general anxiety and cancer worries scales was observed. However, both of these groups showed

higher baseline cancer risk perception scores compared to the lower risk group (P<0.001 for ‘higher risk’ group and P=0.003 for ‘false positive’ group).

Overall, the findings suggested no association between the exercise of capturing family history information and feeding back personalized risk, and anxiety or cancer worry, in patients who are close to average risk. In fact, it is possible that the intervention may have led to more realistic (lower) perceptions of personal risk. In contrast, the higher anxiety and cancer worry outcomes in the ‘true’ and ‘false positive’ high risk groups may reflect their baseline (pre-intervention) status rather than an effect of family history taking.

Conclusion

The evidence base for addressing (Q4) is limited to a single study. It suggested that structured family history collection and feedback of breast cancer risk information had no deleterious psychological effects on any of the risk groups, and in women, who were not at high risk, may have led to appropriate reductions in perceived risk. Higher average baseline levels of anxiety and cancer worry in the groups who went on to have further assessment may reflect pre-existing concerns about a positive family history and need to be taken into account when family history interventions are evaluated.

Table 4. Details of risk prediction models

System	Cancer	Family history items	Other items	Output	Relevant studies	Comments
Gail model (GM)[15]	Breast	1DRs with BC Age at first birth <20y (0, 1, ≥2) 20-24y (0, 1, ≥2) 25-29 y or nulliparous (0, 1, ≥2) ≥30y (0, 1, ≥2)	Age Ethnicity Age at menarche Age at first live birth # previous breast biopsies (0, 1, >1) Presence of atypical hyperplasia on biopsy	Risk of BC	Adams-Campbell[10](2007) Spiegelman[8](1994)	Assumes annual screening Cancer incidence rates derived from BCDDP[15]
Modified GM (MGM)[84]	Breast	As for GM	As for GM	Risk of invasive BC	Chlebowski[13](2007) Adams-Campbell[10](2007) Rockhill[9](2001) Boyle[11](2004) Decarli[12](2006)	Assumes annual screening Cancer incidence rates derived from SEER data
MGM for black/African Americans (GM-B)[10]	Breast	As for GM	As for MGM	As for MGM	Adams-Campbell[10](2007)	MGM revised using age-specific invasive rates and specific attributable risk estimates for African-American women

Abbreviations: 1DR=first degree relative; AUC=area under the curve; BC=Breast cancer; BCDDP=Breast Cancer Detection Demonstration Project; CI=confidence interval; CRC=Colorectal cancer; E=Expected events; GM=Gail Model; GM-B=GM for blacks/African Americans; IT-GM=GM for Italian population; MGM=Modified GM; O=Observed events; NHS= National Health Service; RCT=Randomized controlled trial; RR=Relative risk; SEER=Surveillance, Epidemiology and End Results; y=years;

Table 4. Details of risk prediction models (continued)						
System	**Cancer**	**Family history items**	**Other items**	**Output**	**Relevant studies**	**Comments**
MGM for Italian population (IT-GM)[11,12]	Breast	As for GM	As for MGM, except # previous breast biopsies replaced by any breast biopsy (no, yes)	As for MGM	Boyle[11](2004) Decarli[12](2006)	MGM revised using age-specific invasive rates and specific attributable risk estimates for Italian women
CARE model for African American population[7]	Breast	Number of affected relatives (mother, sisters)	Age Age at menarche # previous breast biopsies, (<50y, ≥50y) Presence of atypical hyperplasia on biopsy (Age at first live birth)	As for MGM	Gail [7]2007	MGM re-developed for African American populations using age-specific invasive rates and specific attributable risk estimates from control data from the CARE Study and SEER program.
Harvard Cancer Risk Index [16]	Colon	Brother/sister/parent with colon cancer	Red meat intake Vegetable intake Alcohol intake Multivitamin use Physical activity Body mass index Height Colonoscopy/sigmoidoscopy screening (Aspirin use)	10 year cancer risk	Kim [14] 2004	Designed to assess risk of multiple cancers Validation using family history data published only for colon cancer

Table 5. Evaluations of risk prediction models

Study Design	Tool(s)	Participants	Outcome measure(s), timing ascertainment	Algorithm performance	Conclusions
Spiegelman[8] 1994	GM	n=115,172	12 y BC incidence	**Calibration** O, E E/O (95% CI) O=2,396, E=3,196 E/O=1.33 (1.28-1.39) **Discrimination** Correlation coefficient (Pearson) 0.67 (Spearman) 0.04	Significant overestimation of overall BC risk Modest discriminatory accuracy
Rockhill[9] 2001	MGM	n=82,109	5 y BC risk	**Calibration** O, E E/O (95% CI) O=1,354, E=1,273.42 E/O=0.94 (0.89-0.99) **Discrimination** AUC (95% CI) 0.58 (0.56-0.60) RR=(95% CI) 2.83 (2.19-3.65) Sensitivity, specificity (cut point=1.67% 5 y risk): Se=0.44, Sp=0.66	Fairly well calibrated model Modest discriminatory accuracy

Abbreviations: 1DR=first degree relative; AUC=area under the curve; BC=Breast cancer; CI=confidence interval; CRC=Colorectal cancer; E=Expected events; GM=Gail Model; GM-B=GM for blacks/African Americans; IT-GM=GM for Italian population; MGM=Modified GM; O=Observed events; NHS= National Health Service; RCT=Randomized controlled trial; RR=Relative risk; Se=sensitivity; SEER=Surveillance, Epidemiology and End Results; Sp=specificity; y=years;
[1]Performance by other cut-off points also reported

Table 5. Evaluations of risk prediction models (continued)

Study Design	Tool(s)	Participants	Outcome measure(s), timing ascertainment	Algorithm performance	Conclusions
Chlebowski[13] 2007	MGM	n=147,916 Mean age 63 y (range 50-79 y) "Ethnically diverse" Excluded: History of BC, mastectomy Suspicious baseline mammogram <5 y followup	5 y invasive BC risk, assessed by annual or semi-annual ascertainment by mail or telephone questionnaire Cancer verified through pathology reports	**Calibration** O, E E/O O=3,236, E=2,562 E/O=0.79 (p<0.001) **Discrimination** AUC (95% CI) 0.58 (0.56-0.60)	Poorly calibrated, underestimated number of invasive BCs in 5 years by about 20% Modest discriminatory accuracy
Adams-Campbell[10] 2007	MGM GM-B	n=1,450 Age: 21-69 y Enrolled 1995 Diagnosed with BC 1995-2003, aged ≥35 y (cases) Age-matched, no BC by 2003	5 y invasive BC risk, assessed by biennial questionnaires	**Discrimination** Sensitivity, specificity (cut point=1.7% 5 y risk) **MGM** Se=0.18, Sp=0.86 **MGM-B** Se=0.04, Sp= 0.97	The MGM and MGM-B perform poorly at predicting risk of invasive BC in African American women Limited discriminatory accuracy

Table 5. Evaluations of risk prediction models (continued)

Study Design	Tool(s)	Participants	Outcome measure(s), timing ascertainment	Algorithm performance	Conclusions
Boyle[11] 2004 Secondary analysis of RCT data [172]	IT-GM MGM	n=5,383 Women had hysterectomies and no benign breast disease	5 y BC incidence	**Calibration** O, E E/O (95% CI) **IT-GM** O=79, E=82.5 E/O=0.92 (0.68-1.16) **MGM** O=79, E=88.4 E/O=0.86 (0.64-1.08) **Discrimination** AUC **IT-GM** 0.58	Reasonably well calibrated Modest discriminatory accuracy in the population studied Data were missing on atypical hyperplasia on biopsies

Table 5. Evaluations of risk prediction models (continued)

Study Design	Tool(s)	Participants	Outcome measure(s), timing ascertainment	Algorithm performance	Conclusions
Decarli[12] 2006	IT-GM MGM	n=10,031 Age: 35-64	5 y invasive BC risk Method of ascertainment not reported in this paper.	**Calibration** O, E E/O (95% CI) **IT-GM** O=194, E=186.11 E/O=0.96 (0.84-1.11) **MGM** O=194, E=180.1 E/O=0.93 (0.81-1.08) **Discrimination** Average age-specific AUC (95% CI) **IT-GM** 0.59 (0.54-0.63) **MGM** 0.58 (0.55-0.63)	MGM and IT-GM both well calibrated Modest discriminatory accuracy in the population studied
Gail[7] 2007	CARE	n=14,059 Age:≥50	5 y age-specific invasive BC risk	**Calibration** O/E ratio (95% CI):1.08 (0.97-1.20) **Discrimination** Unweighted average age-specific AUC (95% CI): 0.555 (0.535-0.575)	Good calibration, very modest discriminatory accuracy.

Table 5. Evaluations of risk prediction models (continued)

Study Design	Tool(s)	Participants	Outcome measure(s), timing ascertainment	Algorithm performance	Conclusions
Kim[14] 2004	HCRI	n=52,668 Females Age: median 52	10 y colon cancer incidence	**Calibration** O/E(95% CI) Overall O/E not reported **By HCRI category:** **2.10≤RR≤5.10** 1.79 (0.89-2.70) **1.10≤RR≤2.10** 1.39 (1.12-1.67) **0.90≤RR≤1.10** 1.00 (0.66-1.34) **0.50≤RR≤0.90** 0.89 (0.68-1.09) **0.20≤RR≤0.50** 0.58 (0.37-0.79) **Discrimination** AUC (95% CI): 0.67 (0.64-0.70)	Good calibration, moderate discriminatory power

Table 5. Evaluations of risk prediction models (continued)

Study Design	Tool(s)	Participants	Outcome measure(s), timing ascertainment	Algorithm performance	Conclusions
Kim [14] 2004	HCRI	n=38,953 Males Age: median 51	10 y colon cancer incidence	**Calibration** O/E(95% CI) Overall O/E not reported **By HCRI category:** **2.10≤RR≤5.10** 2.35 (1.12-3.59) **1.10≤RR≤2.10** 1.34 (1.02-1.66) **0.90≤RR≤1.10** 1.01 (0.64-1.39) **0.50≤RR≤0.90** 0.75 (0.56-0.95) **0.20≤RR≤0.50** 0.83 (0.60-1.07) **Discrimination** AUC (95% CI): 0.71 (0.68-0.74)	Poor calibration (possibly due to potential misclassification – older cohort at baseline), moderate discrimination

Table 6. Target interventions for review

Cancer	Intervention
Breast	Chemoprevention Breast self-examination Clinical breast examination Screening mammography Screening MRI
Ovarian	Screening ultrasound
Colorectal	Chemoprevention FOBT screening Screening colonoscopy Screening sigmoidoscopy
Prostate	Chemoprevention PSA screening Digital rectal examination
All	Regular exercise/physical activity Dietary interventions - high fiber diet - high fruit and vegetables - low fat Vitamin and micronutrient supplementation Limitation of alcohol intake Smoking cessation Seeking health care advice Referral for genetic counseling and/or genetic testing, where criteria are met

Abbreviations: FOBT=fecal occult blood test; MRI=magnetic resonance imaging; PSA=prostate specific antigen

Table 7. Breast cancer preventive interventions

Study	Specific intervention(s) evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type of trials	Followup duration (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Type of intervention: Chemoprevention (antioxidants, NSAIDS, and statins)										
Bardia[18] 2008	Antioxidant supplementation: β-carotene Selenium Zinc Vitamin C Vitamin E or any others	Quant	People at average risk of cancer	RCTs; Supplements with fully disclosed components and not dietary increases in nutrients; placebo-controlled; ≥1 y of followup; reported overall cancer incidence	≤12 (n not reported for cancer-specific analyses)	NR	88,392 (total across all trials)	NR	BC incidence (any antioxidant) RR=1.00 (0.90-1.09)	No evidence of protective effect of antioxidants against risk of BC

Abbreviations: BC=breast cancer; BSE=breast self-examination; DRE=digital rectal exam; e.g.=example; FOBT=fecal occult blood test; HP=High potency; LI=Lipophilic; LO=Lipophobic; LP=Low potency; mg=milligrams; MP=Medium potency; NR=not reported; PHS=Physician's Health Study; PSA=prostate specific antigen; Qual=Qualitative; Quant=Quantitative; RCT=Randomized controlled trial; RR=Relative risk; SM=Screening mammography; SR=systematic review; TRUS=transrectal ultrasound; y=year; WHS=Women's Health Study

Table 7. Breast cancer preventive interventions (continued)

Study	Specific intervention(s) evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type of trials	Followup duration (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Alkhenizan[19] 2007	Vitamin E alone Vitamin E as part of other supplements	Quant	≥18 y; range of pre-existing health states, but not high risk for BC	RCTs; Supplementation in capsule or tablet form; control = placebo or no intervention; reported total mortality, cancer mortality, cancer-specific mortality	3	≥510 days - ≤10 y (not reported separately for individual cancers)	62,158 (total across all studies)	NR	BC incidence (Vit E in any combination) RR=0.99 (0.90-1.10)	No evidence of protective effect of Vitamin E against BC
Browning[20] 2006	Statins	Quant	All populations except highly specific statin-using patients (e.g. familial hypercholesterolemia, renal transplant)	RCTs; Control = placebo; Reported all cancer, site-specific cancer incidence or mortality	1-7 (depending on analysis)	Median followup: Trials: 3.6 y Observational studies: 6.2 y	RCTs: n = 103,573 Observational studies: n = 826,854	RCTs: 18-82 y Observational studies: 30-89 y	BC incidence from use of statins: 1. All studies RR=1.01 (0.79-1.30) 2. LI (3 trials) RR=0.89 (0.62-1.27) 3. LO (4 trials) RR=1.15 (0.81-1.64) 4. LP (1 trial) RR=1.44 (0.62-3.37) 5) MP (4 trials) RR=1.15 (0.81-1.64)	No evidence of protective effect

Table 7. Breast cancer preventive interventions (continued)

Study	Specific intervention(s) evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type of trials	Followup duration (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
									6) HP (2 trials) RR=0.80 (0.54-1.19)	
Type of intervention: Screening										
Kosters[21] 2003	BSE	Quant	General population	RCTs	3 trials, 1 discontinued China Russia	10-12	122,471-266,064	30-74	1. BC mortality (longest available followup) RR=1.05 (0.90-1.14)	The trials are based on large sample sizes and the findings are robust. Uptake was high and the findings are applicable to BSE practice generally. There is no effect of BSE on breast cancer mortality, but evidence that women taught BSE were more likely to be referred for a biopsy.

Table 7. Breast cancer preventive interventions (continued)

Study	Specific intervention(s) evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type of trials	Followup duration (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Gøtzsche[22] 2006	SM	Quant	Women without previously diagnosed BC	RCTs; Controls with no SM	3 'adequately randomized' trials Canada 7 'suboptimally randomized' trials	7-13	42,482-92,934	39-74	**All trials** **BC mortality** (13 y): RR=0.80 (0.73-0.88) *Suboptimally randomized' trials* RR=0.75 (0.67-0.83) *Adequately randomized' trials* RR=0.93 (0.80-1.09) **All cause mortality** RR=1.00 (0.96-1.04) *Suboptimally randomized' trials* RR=0.99 (0.97-1.01) **All cancer mortality** RR=1.02 (0.95-1.10)	Screening likely reduced BC mortality, with a reasonable risk reduction estimate of about 15%. Screening also leads to over diagnosis and over treatment. "It is not clear whether screening does more good than harm"

Table 8. Colorectal cancer preventive interventions

Study	Specific intervention(s) evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type of trials	Followp duration (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Type of intervention: Chemoprevention (antioxidants, NSAIDS, and statins)										
Bardia[18] 2008	Antioxidant supplementation: β-carotene Selenium Zinc Vitamin C Vitamin E or any others	Quant	People at average risk of cancer	RCTs; Supplements with fully disclosed components and not dietary increases in nutrients; placebo-controlled; ≥1 y of followup; reported overall cancer incidence	≤12	NR	178,086 (total across all studies)	NR	CRC incidence (any antioxidant) RR=1.00 (0.90-1.10)	No evidence of protective effect of antioxidants against CRC

Abbreviations: ASA=acetylsalicylic acid; BC=breast cancer; BSE=breast self-examination; DRE=digital rectal exam; e.g.=example; FOBT=fecal occult blood test; HP=High potency; LI=Lipophilic; LO=Lipophobic; LP=Low potency; mg=milligrams; MP=Medium potency; NR=not reported; PHS=Physician's Health Study; PSA=prostate specific antigen; Qual=Qualitative; Quant=Quantitative; RCT=Randomized controlled trial; RR=Relative risk; SR=systematic review; TRUS=transrectal ultrasound; y=year; WHS=Women's Health Study

* Kerr review also examines FOBT screening alone, but results overlap, and are consistent, with those of Hewitson & Heresbach, therefore not reported here.

Table 8. Colorectal cancer preventive interventions (continued)

Study	Specific intervention(s) evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type of trials	Follow up duration (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Alkhenizan[19] 2007	Vitamin E alone Vitamin E as part of other supplements	Quant	≥18 y; range of pre-existing health states, but not high risk for colorectal cancer.	RCTs; Supplementation in capsule or tablet form; control = placebo or no intervention; reported total mortality, cancer mortality, cancer-specific mortality	2-4 depending on outcome	≥510 days - ≤10 y (not reported separately for individual cancers)	24,114 - 91,099 (across all trials, depending on analysis)	NR	1. CRC incidence (Vit E any combination) RR=0.95 (0.81-1.12) 2. CRC incidence (Vit E alone) RR=1.05 (0.79-1.39)	No evidence of protective effect of Vitamin E against CRC
Dubé[23] 2007	ASA	Quant and Qual	"Average' risk	RCTs, controlled clinical trials	2 PHS 325mg every other day WHS 100mg/day	5-10	22,071-39,876	NR	1. CRC mortality (WHS) "No statistically significant benefit of ASA on CRC mortality" 2. CRC incidence RR=1.02 (0.84-1.25) 3. Adenoma incidence (PHS only) RR=0.86 (0.68-1.10)	Observational data appear to indicate that ASA use reduces the risk of colorectal neoplasia, but this effect is not seen in large trials of low dose ASA use

Table 8. Colorectal cancer preventive interventions (continued)

Study	Specific intervention(s) evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type of trials	Follow up duration (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Browning[20] 2006	Statins	Quant	All populations except highly specific statin-using patients (e.g. familial hypercholesterolemia, renal transplant)	RCTs; Control = placebo; Reported all cancer, site-specific cancer incidence or mortality	1-9 (depending on analysis)	Median followup: Trials: 3.6 y	RCTs: n = 103,573	RCTs: 18-82 y	CRC incidence from use of statins: 1. All studies RR=1.02 (0.89-1.16) 2. Mortality (1 trial) RR=0.33 (0.07-1.63) 3. LI (4 trials) RR=1.0 (0.85-1.18) 4. LO (5 trials) RR=1.04 (0.85-1.30) 5. LP (2 trials) RR=1.07 (0.61-1.85) 6. MP (5 trials) RR=1.04 (0.84-1.30) 7. HP (2 trials) RR=0.99 (0.83-1.18)	No evidence of protective effect

Table 8. Colorectal cancer preventive interventions (continued)

Study	Specific intervention(s) evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type of trials	Follow up duration (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Type of intervention: Population-based screening										
Hewitson[24] 2006	FOBT (Hemoccult) investigation following positive screen result – colonoscopy or sigmoidoscopy and double contrast barium enema, with removal of colorectal cancers or adenomas found at diagnostic investigation	Quant, Qual	Adults; volunteers or individuals/households identified from primary care records or population registries	RCTs (individual or groups); control = no screening; report results based on participation in >1 screening round; report colorectal cancer mortality	4	10-17	46,551-150,251 Total 329,642	45-80 y	1. CRC mortality (all groups) RR=0.84 (0.78-0.90) 2. CRC mortality (biennial screening groups) RR=0.85 (0.78-0.92) 3. All cause mortality (all groups) RR=1.00 (0.99-1.01) 4. All cause mortality without CRC mortality (all groups) RR=1.01 (1.00-1.03). 5. CRC mortality (attended ≥1 screening) RR=0.75 (0.66-0.84)	15-16% reduction in relative risk of CRC mortality for individuals allocated to receive screening, rising to 25% risk reduction for those who actually participated at least once. No evidence of reduction in overall mortality, and borderline evidence of increased non-CRC mortality

Table 8. Colorectal cancer preventive interventions (continued)

Study	Specific intervention(s) evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type of trials	Follow up duration (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Kerr[25] 2007	Once-only flexible sigmoidoscopy in addition to FOBT test, followed by colonoscopy for investigation of positive screen result*	Quant	Not specified, but population-based implied	RCTs; control = no screening control for this study was FOBT alone	1	2-5	10,978	50-75	1. CRC mortality RR=0.78 (0.36-1.73) 2. CRC incidence RR=1.37 (0.88-2.15)	The trial was limited by short followup period and no repeat screening. Results do not support benefit of combined screening strategy of FS with FOBT over FOBT alone in asymptomatic populations Poor compliance with combined screening group

Table 9. Prostate cancer preventive interventions

Study	Specific interventions evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type trials	Followup durations (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Type of intervention: Chemoprevention										
Bardia[18] 2008	Antioxidant supplementation: β-carotene Selenium Zinc Vitamin C Vitamin E or any others	Quant	People at average risk of cancer	RCTs; Supplements with fully disclosed components and not dietary increases in nutrients; placebo-controlled; ≥1 y of followup; reported overall cancer incidence	≤12	NR	55,709 (total over all trials)	NR	Prostate cancer incidence: Any antioxidant RR=0.87 (0.74-1.02) Selenium alone (200µg daily): "decreased incidence'. [Estimated RR[26]=0.37 (0.20-0.70)]	No evidence of protective effect of antioxidants on prostate cancer risk

Abbreviations: NR=not reported; Quant=Quantitative

*This review also reported data relating to antioxidants; not included under this review's data as included in more recent included review[18]

Table 9. Prostate cancer preventive interventions (continued)

Study	Specific interventions evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type trials	Followup durations (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Alkhenizan[19] 2007	Vitamin E alone Vitamin E as part of other supplements	Quant	≥18 y; range of pre-existing health states, but not high risk for prostate cancer.	RCTs; Supplementation in capsule or tablet form; control = placebo or no intervention; reported total mortality, cancer mortality, cancer-specific mortality	2-4 (depending on outcome reported)	≥510 days - ≤10 y (not reported separately for individual cancers)	24,114-71,759 (total over all trials analyzed, depending on outcome reported)	NR	Prostate cancer incidence: 1. Any dose/ combination RR=0.85 (0.74-0.96) 2. Vit E alone RR=0.86 (0.70-1.06) 3. Vit E plus other supplements RR=0.79 (0.67-0.93) 4. Vit E ≥300mg/day RR=0.94 (0.79-1.11) 5. Vit E <300mg/day RR=0.69 (0.55-0.87)	Vitamin E may be protective against prostate cancer
Bristol SLR Team[26] 2006[*]	Calcium supplements	Quant	NR; presumed cancer free	All	1 RCT	11 (intervention duration plus followup)	672	61.8 (mean)	RR=0.83 (0.52-1.32)	No evidence of protective effect of calcium supplementation

Table 9. Prostate cancer preventive interventions (continued)

Study	Specific interventions evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type trials	Followup durations (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
Browning[20] 2006	Statins	Quant	All populations except highly specific statin-using patients (e.g. familial hypercholesterolemia, renal transplant)	RCTs; Control = placebo; Reported all cancer, site-specific cancer incidence or mortality	1 or 4 (depending on analysis	Median followup: Trials: 3.6 y Observational studies: 6.2 yrs	RCTs: n =103,573 Observational studies: n=826,854	RCTs: 18-82 yrs Observational studies: 30-89 yrs	1. Prostate cancer incidence RR=1.00 (0.85-1.17) 2. Prostate cancer mortality (1 trial) RR=0.99 (0.14-7.01)	No evidence of protective effect
Type of intervention: Screening										
Ilic[27] 2007	Any of PSA DRE TRUS biopsy	Quant	All men	RCTs, quasi-randomized, controlled trials; screening versus no screening	2 RCTs Quebec Annual screening Round 1 = PSA + DRE + TRUS where PSA >3.0ng/ml and/or abnormal DRE Later rounds = PSA with TRUS biopsy of PSA >3ng/ml or increased	11-15	9,026-46,486 Total 55,512	45-80	Prostate cancer mortality RR=1.01 (0.80-1.29)	Insufficient evidence to either support or refute the routine use of mass, selective, opportunistic, or no screening to reduce prostate cancer mortality

Table 9. Prostate cancer preventive interventions (continued)

Study	Specific interventions evaluated	Type of SR	Eligible populations	Eligible study designs	Number and type trials	Followup durations (years)	Sample sizes	Ages	Summary effect sizes	Main conclusion
					by >20% 3-yly screening Rounds 1&2=DRE Rounds 3&4=DRE + PSA. TRUS biopsy if DRE abnormal or PSA >4.0ng/ml					

*This review also reported data relating to antioxidants; please refer to more recent review included above[18]

Table 10. Details of family history and personalized risk interventions

Study and study design	Target population	Target behavior	Family history collection component of intervention	Risk personalization component of intervention	Other components	How individualized risk reduction advice communicated
Curry[49] 1993 RCT	Women eligible for SM	Having SM	Mailed self-completion questionnaire: 1. Information on 1DR and 2DR with BC 2. Other risk factors: age, age at menarche, age at first birth, menopause status, age at menopause, previous mammography, history of biopsy	Insertion of following text into a generic mammography invitation letter: "BC affects 1 in 10 women over their lifetime, but is more common with a personal history of particular risk factors. The recommendation that you schedule a comprehensive visit now is based on the answers you provided on the BC Screening Survey. From your responses, we were able to determine that your personal screening schedule is affected by your age [plus other risk factors if present]…"	None	Letter
Giles[48] 2001 BA	General female population	Having SM BSE CBE	Interviewer-administered survey: 1. Number of 1DRs with BC 2. Other risk factors: age at menarche, age at first live birth, number of breast biopsies 3. Other: history of practicing BSE, formal instruction in BSE, confidence in performing BSE, history of mammography	1. RR for developing BC in next 5y 2. RR for developing cancer in her lifetime	Encouragement to follow ACS guidelines for mammography, BSE, CBE ACS instruction card on BSE NCI brochure on BC risk factors	Individual consultation with a pharmacist

Abbreviations: 1DR=first degree relative; 2DR=second degree relative; ACS=American Cancer Society; BA=before-after; BC=breast cancer; BSE=breast self-examination; CBE=clinical breast examination; FH=family history; NCI=National Cancer Institute; RCT=randomized controlled trial; RR=relative risk; SM=screening mammogram;

Table 10. Details of family history and personalized risk interventions (continued)

Study and study design	Target population	Target behavior	Family history collection component of intervention	Risk personalization component of intervention	Other components	How individualized risk reduction advice communicated
Bastani [50] 1999 RCT	Female relatives of breast cancer patients	Having SM	Current age age at menarche, age at first live birth, number of breast biopsies, and number of first-degree relatives with breast cancer age at first biopsy, age of the index case (first degree relative listed in cancer registry) with cancer, age at menopause	List of personal risk factors for breast cancer and classification of risk in comparison with other women of the same age (“slightly”, “moderately”, or “substantially” higher risk)	Other materials tailored for high-risk women” plus message regarding the importance of regular screening mammography	Letter

Table 11. Evaluations of family history and personalized risk

Study and study design	Participants	Control intervention/group	Outcome measure(s)	Effect of FH based intervention on target behavior(s)	Modified Jadad quality score (max=8)	Conclusions
Curry[49] 1993 RCT	Women ≥50 y registered with a single HMO, eligible for SM n=2,076	1. No risk data captured, generic invitation to schedule a mammogram (C1) 2. No risk data captured, general risk information included in invitation to schedule a mammogram (C2) 3. Risk data captured, general risk information included in invitation to schedule a mammogram (C3)	Having a mammogram within 12 months of invitation	% Received a mammogram by 12 months: I: 44.6% C1: 49.2% C2: 41.1% C3: 41.8% P=0.23 (X^2) Comparison restricted to I&C3 only (risk factor questionnaire plus general risk or personalized risk invitation), stratified by family history: No family history – I: 39.7% C3: 41.4% Positive family history: I: 66.7% C3: 42.9% P=0.005. No significant interactions of personalized feedback with other risk factors	4 Allocation concealment NR	Overall, capturing risk information and/or addition of general or personalized risk information to screening mammography invitations did not increase uptake. Findings suggest that capturing risk information and personalizing risk messages may be more effective in promoting screening behavior

Abbreviations: 1DR=first degree relative; BA=before-after; BC=breast cancer; BSE=breast self-examination; CBE=clinical breast examination; FH=family history; NA=not applicable; NR=not reported; RCT=randomized controlled trial; SM=screening mammogram;
* Confidence intervals not provided in original article, calculated on basis of data presented

Table 11. Evaluations of family history and personalized risk (continued)

Study and study design	Participants	Control intervention/group	Outcome measure(s)	Effect of FH based intervention on target behavior(s)	Modified Jadad quality score (max=8)	Conclusions
Bastani[50] 1999 RCT	Women with a 1DR with BC n=901	1. Note thanking for participation in telephone survey 2. General information booklet on BC	SM measured by self-report at 1 y followup	% Had SM **All ages:** Baseline I: 55.0% C:54.9% Followup I: 65.2% C: 57.7% P=0.05 **30-40** Baseline I: 41.4% C:31.4% Followup I: 49.4% C:35.7% P=0.66 **40-50** Baseline I: 61.4% C: 57.4% Followup I: 62.3% C:67.0% P=0.26 **50-64** Baseline I: 58.9% C:68.8% Followup I: 76.8% C: 68.8% P=0.02	4 Allocation concealment NR	In a somewhat selected group of participants, and compared with the control intervention of FH taking and general information on BC, the active intervention of FH taking accompanied by individualized risk assessment and reinforcement of importance of target behavior appeared to improve adherence with screening recommendations to a modest level, equivalent to difference in increased uptake by 7% in absolute terms No comparison group which did not have FH information collected

Table 11. Evaluations of family history and personalized risk (continued)

Study and study design	Participants	Control intervention/group	Outcome measure(s)	Effect of FH based intervention on target behavior(s)	Modified Jadad quality score (max=8)	Conclusions
Giles[48] 2001 BA	Women ≥18y visiting a community pharmacy or attending a health screening event n=188	None	Adherence with ACS guidelines for BSE, CBE, and mammography, assessed at 6 months	Proportions following ACS guidelines (self-report) (% (95% CI*)) **BSE** **All:** Pre: 42/137 (31 (23-38)) Post: 77/137 (56 (48-64) P<0.001 **5 y risk≥1.7%:** Pre: 4/20 (20 (2-37)) Post: 12/20 (60 (38-81)) P<0.005 **CBE** **All:** Pre:121/140 (86 (81-92)) Post:128/140 (91 (87-96)) P<0.09 **5 y risk≥1.7%:** Pre: 17/21 (81 (61-98)) Post: 17/21 (81 (64-98)) P=1.00 **Mammography** **All:** ≥50y	NA	Findings suggest that personalized risk assessment which included family history may improve adherence with recommended screening practices The size and direction of changes were different across the three target behaviors and no uniform effect was observed in high risk participants The lack of a control intervention, the reliance on self-report data, and the small sample size for sub-group analyses severely limit the conclusions which can be drawn

Table 11. Evaluations of family history and personalized risk (continued)

Study and study design	Participants	Control intervention/group	Outcome measure(s)	Effect of FH based intervention on target behavior(s)	Modified Jadad quality score (max=8)	Conclusions
				Pre: 33/44 (75 (62-88)) Post: 31/44 (70 (57-84)) P<0.48 40-49 Pre: 18/32 (56 (39-73)) Post: 21/32 (66 (49-82)) P<0.257 **5 y risk≥1.7%:** Pre: 17/21 (81 (64-98)) Post: 15/21 (71 (52-91)) P<0.317		

Table 12. Harm/risk of family history collection

Author Year Setting	Type of cancer	Study design	Characteristic of population	1. No.recruited 2. No.completed	Time points for analysis (months)	Duration of intervention followup	Who delivered intervention?	Method of family history collection	Other intervention(s)
Leggatt[51] 2000	Colorectal/ colon/rectal Breast	Before - After uncontrolled study	Unselected patients aged 35 to 65 years	1. 666 (29% response) 2. 604	Baseline 1-1.5	Postal survey followed by single session	Lower risk group: letter from family doctor Potential increased risk groups: family doctor and/or oncologist/ geneticist	Postal cancer family history questionnaire	Participants provided with risk information

Chapter 4. Discussion

The purpose of this review was to establish the evidence base to answer the question, "In relation to the cancers of interest, would routinely taking and using family history for risk assessment in primary care settings be likely to lead to net health benefits?" Acknowledging the scope of this question, the evidence was assembled across a number of subsidiary questions, addressed individually below.

Throughout the review, the focus was the primary care context. This led to two decisions which underpinned the review's methodology, specifically the eligibility criteria. Firstly, across all questions, the populations studied had to reflect primary care populations. In practice, this meant that populations who already had cancer, a pre-cancerous condition, or who were suspected of carrying a genetic risk, were excluded. Secondly, studies of family history taking as a primary care intervention, i.e., *as an intervention in and of itself*, were included, but those where family history taking was approached as a specialist activity, and/or embedded within a larger set of clinical activities such as assessment for genetic testing, were excluded.

We also drew a distinction between "taking family history" as *a distinct activity* practiced by health care providers (of central interest in this review) and "being aware of a positive family history" *as an attribute* of study participants. A patient's ability to accurately report family history information is a prerequisite for valid family history collection. However, some people may also have a pre-existing perception of an unusually high family prevalence of cancer, leading to this being itself a cause of anxiety, quite separate from any effect of the clinical activity of taking a family history. Thus, evaluations of family history taking as an intervention need to be carefully designed to take account of this complicating factor.

Risk Stratification Algorithms

Many cancer risk stratification algorithms, models and systems exist, and the goal of this review was to identify which of those, based on family history information, performed well in primary care type populations. In approaching this question, we sought to identify evaluations of frameworks devised specifically for primary care, or which might be transferable to primary care even if originally designed for other purposes.

Further, we were interested in evaluations which assessed the ability of a system to correctly predict risk in *individuals*, not simply on studies of overall associations between family history and disease incidence at a population level. As explained in Chapter 3, to be suitable for implementation in routine clinical settings, a risk prediction system needs to differentiate between the disease risk of individuals, such that it consistently predicts higher risk of cancer in those who are truly destined to go on to develop the disease than in those who will not.

Review question (Q) 1 was therefore tightly focused on evaluations of models predicting individual risk, and this led to the exclusion of a large number of analytical epidemiological reports, descriptive clinical studies, and validation studies of models which did not present data on individual discriminatory accuracy (e.g., Constatino et al., 1999[84]). We were able to identify evaluations of only two distinct approaches, one a family of models based on the Gail model[15] (developed for breast cancer risk prediction), and the Harvard Cancer Risk Index[16] (designed to predict the risk of a range of cancers, although validation data were available only for CRC). Both included a range of variables in addition to family history.

The Gail model is publicly available on the National Cancer Institute's web site (www.cancer.gov/bcrisktool/). It should be noted that its original purpose was epidemiological – to facilitate the design of clinical trials by permitting sample size calculations to be based on improved assumptions about expected disease outcome rates – rather than for clinical decisionmaking.[15] Evaluations of this model indicated excellent performance at the population level, i.e., calibration, for predominantly white U.S. and Italian populations, judged by the ratio of expected to observed cases in the population studied. The model performed less well in more diverse U.S.[13] or African American[10] populations. The CARE model also showed good calibration.[7]

However, for all of these models, evaluations indicated generally modest discriminatory ability, with the c-statistic ranging from 0.55-0.59. Many women who would be judged to be high risk by one of these models would not go on to develop breast cancer, and vice versa.

As a contrast, family history-based risk stratification has been found to perform much better as a predictor of coronary artery disease, with a c-statistic of 0.87.[173] While family history can provide some useful predictive information on some common health conditions, the situation for breast cancer is less clear-cut. Although there are breast cancer family syndromes, these are associated with only about 5 percent of breast cancer cases. Over ninety percent of the incidence of breast cancer at a population level is not associated with a distinct familial pattern, and many women appear to develop breast cancer 'out of the blue'. The known general risk factors – e.g., younger age at menarche, and later age at birth of first child – each contribute only a little to overall incidence of the disease (individual relative risks are modest), and they are reasonably prevalent in most populations

Had the review found greater evidence of adequate discriminatory accuracy for some of these tools, this would not guarantee that their use would lead to better health outcomes in practice. A number of other conditions would need to be satisfied, for example evidence that different risk categories are matched with evidence on appropriate risk-specific preventive interventions. We note, for example, that the Gail and related models have been used primarily for assessing eligibility for cancer chemoprevention trials, although their use as more general clinical predictive tools is implied by their wider availability to the professional community and the general population. Stronger evidence is needed on the application of the tools in settings closer to routine clinical practice, and trials are required which directly assess the outcomes from risk assessment combined with risk-appropriate preventive interventions, not just assessments of the technical accuracy of risk prediction. Also, the use of tools needs to take into account standard of practice for the particular clinical context. As a hypothetical example, if guidelines were to recommend colonoscopy and polypectomy for all individuals with a family history of colorectal cancer, and this was widely implemented, and it led to a reduction in absolute colorectal cancer rates in the general population, then evaluations of risk prediction algorithms would need to consider the power implications of using cancer incidence as a primary outcome.

Since the overall purpose of this review was to assess elements of the clinical utility of family history taking, we would ideally have liked to evaluate cancer risk stratification systems based solely on family history. At the time of writing, perhaps the prototypical system of interest is Family Healthware™,[174] a Web-based tool designed to assess a person's familial risk for coronary heart disease, stroke, diabetes, and colorectal, breast, and ovarian cancer. It also provides users with personalized recommendations for lifestyle changes and screening. At the time of writing, evaluation data for this tool were not available.

In the absence of validation studies of family history-based systems, we extended the review to include tools with a family history component. Despite this, a large number of predictive tools were excluded, either because they did not include any history items, some items would not be available for all patients, or would not routinely be available to a primary care practitioner. Further details of the wider range of risk prediction systems can be found at http://riskfactor.cancer.gov/cancer_risk_prediction/.

Cancer Prevention Interventions

Review (Q2) was an assessment of the overall benefits and harms of available preventive interventions for breast, ovarian, colorectal, and prostate cancers. As noted in Chapter 1, answering this question was an essential step in addressing the overall question of clinical utility of cancer family history taking, but cancer prevention in general was not the primary focus of this report. With a focus on published reviews of evidence, we again applied the criterion of primary care applicability in terms of unselected populations, which would be expected to contain individuals at high, medium, and low risk. Reviews were excluded only where they specifically focused on studies of high risk populations such as those affected by cancer or known pre-cancerous conditions, or people at known or suspected high risk of an inherited genetic disorder. Thus, while all reviews focused on "general" populations, *none* specified having relatives with cancer (but not suspicion of inherited genetic disorder) as an exclusion criterion. Most did not in fact specify this one way or the other, except one[23] which explicitly stated that studies with participants with a positive family history of cancer were eligible. In the end, none of the reviews actually reported results separately for studies of participants with affected relatives, likely reflecting a lack of such primary studies.

We also decided to focus on reviews of intervention studies, noting (for example) how apparently clear-cut evidence from observational epidemiological studies in the areas of beta-carotene and lung cancer[71-73] and hormone replacement therapy and breast cancer[175] has been contradicted by subsequent randomized controlled trials.[74,176] Where more than one eligible review was identified, we included the data from the most recent and highest quality review. We found no reviews relating to primary or secondary prevention of ovarian cancer.

With respect to primary prevention of the cancers of interest, we found a striking lack of experimentally-derived evidence. We do not suggest, however, that this lack of evidence of effectiveness means that the interventions examined are ineffective. A number of issues and limitations must be considered.

Firstly, there is the difficulty of translating the exposures examined in many observational studies into implementable interventions in trial settings. Observations on the potential protective effect of specific antioxidants, micronutrients, and vitamins have generally been derived from analyses of dietary habits or supplements containing multiple vitamins and minerals, whereas intervention studies generally investigated the effects of one or two supplemental agents in factorial trials. Moreover, in some instances, notably the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study, the doses of these agents were substantially higher than the exposures obtained through dietary and multivitamin supplements. Hence, few intervention trials have investigated 'whole diet interventions'. To take calcium as an example, pooled analyses of cohort studies indicate an approximately 15 percent reduction in risk of colorectal neoplasia associated with higher dietary calcium intake,[45] but no reviews were available of dietary calcium as an intervention in cancer prevention. Also, chemoprevention interventions may act early in

cancer development, meaning that preventive effects may only be observable in long-term studies, not reflected in the followup timing reported in many of the primary trials contained in the reviews.

A second issue is the baseline population risk, and the power of meta-analyses to detect an intervention effect. Taking calcium as an example again, we note that reviews which have conducted pooled analyses of studies conducted in higher risk populations (e.g., patients with adenomatous polyps, therefore excluded from the present review) have demonstrated an apparent 20 percent lower recurrence rate amongst those randomized to calcium supplementation than those on placebo.[177] It is perhaps worth noting that evidence of possible preventive effects of vitamin E[19] and of calcium[26] was noted in relation to prostate cancer; although the latter review met our (Q2) eligibility criteria in that the primary studies had recruited participants not at high risk for prostate cancer, the data came from a secondary analysis of a study with participants at elevated risk of colorectal cancer (the prostate outcomes being a secondary analysis).[47] There is a current stream of thinking suggesting that there may be some common etiological pathways for prostate and colorectal cancer.[178,179] This might mean that these apparently unselected participants were *de facto* at elevated risk of prostate cancer because they were at elevated risk of colorectal cancer.

The focus on reviews also meant that we did not include large primary studies of interventions which have not yet been the subject of reviews. The report finds itself in the anomalous situation where some included reviews were based on analyses of single trials (and therefore, effectively present single trial data), but where interventions evaluated in large single trials were excluded on the basis of ineligible design (i.e., not a review). It was not possible, at the outset, to predict the results of the literature search for review (Q2) and to anticipate this situation. Extending (Q2) to include primary studies would have been a significant undertaking and was beyond the resources available for this review. We acknowledge that this has probably resulted in the exclusion of data on cancer prevention interventions which suggest protective effects. For example, one study[180] was legitimately excluded, which reported a large combined analysis of two selected RCTs along with a systematic review restricted to observational studies. This study was not eligible because the systematic review element excluded intervention studies, and the two RCTs reported represented selective reporting of all relevant trial evidence. The two RCTs were designed primarily to assess the effects of acetylsalicylic acid (ASA) on non-cancer outcomes[181,182] but had extended followup to examine the effects on cancer.[180] The pooled analysis of the two trials (ASA assigned at doses of 300mg, 500mg or 1200mg per day) suggested a protective effect on colorectal cancer incidence at ten years (pooled relative risk 0.74 (95 percent CI 0.56-0.97)). The magnitude of effect was consistent with observational studies, and no effect on the incidence of other types of cancer was observed.

Despite extensive investment in cancer research over the last four decades, underlying mechanistic pathways for individual cancers still remain to be fully elaborated. Thus, the 'risk factor' approach of many analytical observational studies is an insufficient basis for drawing definitive conclusions on biological mechanisms of cancer causation and prevention. Emphasis is now being placed on large-scale prospective cohort studies with associated biobanks that hold promise of improved exposure assessment, and that will enable joint effects of genes and exposures to be investigated with adequate statistical power.[183]

The evidence regarding screening for the cancers of interest provided greater clarity than that for primary prevention. As for secondary prevention, we found no reviews of screening or surveillance interventions relating to ovarian cancer. Regarding breast cancer, there appears to be

clear evidence, on the basis of a pooled analysis of three large population-based trials, that teaching women breast self-examination and encouraging them to carry it out regularly has no measurable effect on breast cancer mortality. In some countries, the emphasis has shifted from exhorting women to examine their breasts monthly to becoming 'breast aware' – being familiar with what is 'usual' over a monthly cycle and therefore being able to identify and act on what is not 'normal'.[184]

A large number of reviews of population-based mammography screening have been conducted, and the evidence seems to suggest that it reduces breast cancer mortality by about 15 percent. The evidence is most clear cut for women aged 50 and over, the impact being limited in younger women by greater breast density and lower baseline risk. There is debate about the validity of using cancer-specific mortality as the primary outcome for evaluations of mammography screening; arguments revolve around the possibility of bias in the coding of death between screened and control populations, and the notable lack of impact of screening on all cause mortality. Where trials have demonstrated a reduction in mortality, there is no suggestion that annual screening offers benefits over biennial screening in women aged 50 or older. This also holds for younger age groups, although the lower sensitivity of the test and evidence of the more rapid growth of tumors in younger women have led some experts to suggest more frequent screening to maximize sensitivity.[185,186]

Regarding colorectal cancer, the evidence appears to indicate that fecal occult blood testing (FOBT) and followup with colonoscopy reduces colorectal cancer mortality. The very limited evidence (one trial) suggests that flexible sigmoidoscopy does not improve this outcome, and there is no consensus on the optimum screening interval. Observers have also noted the lack of impact of screening on overall mortality, and some analyses have indicated an increase in non-colorectal cancer mortality. Although a 2008 U.S. Preventive Services Task Force (USPSTF) report[187] contains a Grade A recommendation which includes colonoscopy as a screening intervention for colorectal cancer in individuals aged 50-75 years, the background evidence report[188] indicates that no trials of colonoscopy as a stand-alone screening intervention were identified.

We found no evidence of an effect of prostate specific antigen (PSA)-based screening strategies on prostate cancer mortality. In a recent USPSTF review, two RCTs were identified that did not show a mortality benefit from PSA screening independently or in a meta-analysis; important flaws in design and analysis were noted.[189] The USPSTF review also identified one cross-sectional and two prospective cohort studies of possible psychological effects of PSA screening results. These suggested that false-positive PSA screening results cause psychological adverse effects for up to 1 year after the test.

Although we sought reviews of ultrasound screening for ovarian cancer as an intervention, we did not consider reviews of other interventions such as CA-125 screening. In retrospect, it would have been legitimate to include this since the report also reviewed PSA-based screening for prostate cancer, which is an analogous serum-based cancer screening test. We note that the USPSTF positively recommended against screening general using CA-125 in a 2004 report,[190] suggesting that the possibility of earlier detection would lead to small effects, at best, on mortality (because of the low prevalence of ovarian cancer therefore low positive predictive value), and fair evidence of important harms because of the invasive nature of diagnostic investigations.

We also did not review genetic testing as an intervention, considering this not to be in itself a preventive intervention, but we did include the broader interventions of referral for genetic

counseling and/or testing as interventions of interest applied to populations not considered high genetic risk. However, no reviews on these interventions were identified.

Family History-Based Risk Assessment and Individual Preventive Behaviors

It is postulated that knowing one's genetic risk of disease, whether through a genetic test or family history, can provide a motivation to comply with advice on preventive interventions[191] and some descriptive studies suggest that people who have a family history are overrepresented in studies of screening adherence.[192-198] Noting concerns discussed in Chapter 1 about distinguishing between the behavior of people motivated by pre-existing perceptions of elevated disease risk because of living with a "family disease" from the effects of family history-based clinical strategy, we focused on intervention studies where the effects of confounding would be less evident. We found only three relevant primary studies, all of them relating to breast cancer prevention. One of them sampled women known to have a first degree relative with breast cancer[50] (although not, by definition, formally identified as being at elevated genetic risk themselves), one was health organization-based,[49] and the third likely comprised participants who were more than typically interested and generally compliant with some screening recommendations.[48] The only study which in any way replicated a primary care consultation involving personal interaction between a health care professional and an individual patient was the third of these studies, which was in the setting of a community pharmacy,[48] but was limited by its uncontrolled design. The participants appeared to have had an atypically high average adherence rate with screening mammography recommendations at baseline, which could have resulted in apparent lack of effect because there was little room for improvement (a possible "ceiling effect"). The overall evidence was therefore equivocal, neither confirming nor undermining the hypothesis that systematic feedback of risk motivates compliance.

Direct Harms or Risks From Family History-Based Risk Assessment

All health care interventions should be assessed for evidence of harm as well as benefit. We identified only one study relevant to family history taking that was conducted in an unselected primary care population. The respondents who were not found to be at elevated cancer risk had no evidence of adverse psychological outcomes, and in fact there was some indication that the assessment was beneficial in that it promoted more realistic personal risk perceptions. In contrast, participants whose initial assessments indicated potential elevated risk had higher baseline anxiety levels than those whose initial assessments indicated population risk, irrespective of their final risk assessment. In other words, both "true positives" and "false positives" had higher average pre-test anxiety levels which might suggest that perception of family history-associated cancer risk (whether confirmed or not) rather than collection of family history information might be associated with higher levels of anxiety.

This single study is insufficient to conclude that family history taking as a deliberate clinical strategy is, in itself, likely to be harmful in terms of emotional impact, but it is consistent with findings from studies of genetic testing. It suggests that assessments of psychological status might be appropriate before embarking on family history-based risk assessments in order to identify those individuals who might be most at risk of ongoing anxiety or cancer-related worry,

and who might therefore warrant extra support or counseling, irrespective of their actual assessed disease risk.

Limitations

The eligible studies within this systematic review were limited to primary studies and systematic reviews in the English language. We restricted the search of systematic reviews to 2003 forward, to ensure that only relatively recent reviews were selected. The review was also limited to studies in adults; therefore no conclusions can be drawn with respect to children or young people specifically.

The effectiveness of family history-based tools and interventions are dependent on the accuracy of reporting of family history, and it is impossible to comment on this aspect of the topic. We did not restrict studies according to the manner in which cancer family history was collected and considerable variation in the methods used was observed. Almost universally, studies depended on self-report methods and are therefore dependent on the individual respondents' knowledge of their history. This represents a limitation on family history taking in practice rather than a limitation specifically of the review, and was explored in a previously published review.[5]

In examining the effects of family history taking on behavior (Q3), the eligibility criteria specified the intervention as feeding back family history-based risk alone, or with risk advice. We did not examine taking family history itself as an intervention without some element of feedback to a patient. The studies identified also evaluated interventions which were not terribly reflective of day-to-day primary care practice. It is therefore impossible to comment on whether the capture of family history information might lead a practitioner to consider different preventive strategies, or the incorporation of family history information into the broader knowledge of a patient might lead to changes in the nature or emphasis of preventive advice which is offered. The emphasis on very specific clinical behavioral outcomes also does not allow for exploration of other effects on the part of patients, e.g., seeking out more extensive information from family members as a result of having been asked "the first" set of questions on family history.

In regard to cancer prevention interventions, we were able to provide only an overview of classes of interventions and could not examine differences in their individual implementation (e.g., different doses). For reviews that assessed the same intervention, we selected the single best review based on several factors including number of studies and year of publications and methodological quality of the review.[17] We did not contact authors for additional clarification for QUOROM requirements. Neither did we re-abstract or re-analyze original randomized trials eligible within the systematic reviews. In addition, as discussed above, the emphasis on reviews inevitably resulted in the exclusion of RCTs which had not been incorporated into reviews, including large studies such as the Women's Health Initiative trial of a dietary modification program on the incidence of colorectal cancer in post-menopausal women.[199] We believe that, where interventions have been evaluated in primary trials which have then been included in published reviews, we have captured and reported the effectiveness evidence objectively; however, we believe that relevant effectiveness evidence for some interventions, based on well-designed trials, has been missed wholesale because primary intervention studies were not eligible for (Q2).

Conclusions

1. The evidence for the predictive accuracy of algorithms in primary care populations was very limited. Although many tools were identified that incorporated some family history information, no evaluations of solely family history-based tools were identified. The tools on which it was possible to comment related mainly to breast cancer.

Recommendations for future research:

- The actual performance of tools based only on family history should be formally examined in primary prospective studies, and/or in secondary analysis of large cohort studies.
- The performance of individual family history components of different risk stratification models which use a wider range of factors (including those examined in this report) should be examined separately from the non-family history components, in order to determine whether they provide sufficient predictive power in the absence of the non-family history factors.
- For clinical relevance, the focus of validation should be discriminatory accuracy at the individual patient level.
- More definitive evaluation should examine the effect on health outcomes when risk stratification systems are used in combination with preventive interventions, in actual practice settings. This cannot be done with secondary analyses of observational data and requires well-designed intervention studies.

2. The evidence establishing the efficacy of interventions for primary and secondary prevention based on systematic reviews of randomized or controlled clinical studies in unselected populations is very limited. Interventions for which there were reviews include chemoprevention (antioxidants, calcium, NSAIDS, and statins) and screening interventions (BSE, mammography, FBOT, flexible sigmoidoscopy, and PSA) for breast, colorectal and prostate cancers. No reviews were found for ovarian cancer. It is likely that this review excluded effectiveness data available from RCTs of interventions which have not yet been the subject of systematic reviews.

Recommendations for future research:

- The large amount of evidence on potential primary cancer preventive interventions obtained from observational studies of cancer risk factors should continue to be further evaluated in well-designed randomized controlled trials.
- Further systematic reviews should be conducted to examine the full range of potentially preventive interventions

3. Within primary care populations, there is very limited evidence to support or refute the effect on risk-reducing behavior changes (e.g., lifestyle changes or uptake of recommended clinical interventions) of taking a family history and using it to personalize risk of breast, ovarian, colorectal, or prostate cancer.

Recommendations for future research:

- Well-designed trials are required that compare family history-based, personalized risk advice with standard of care on risk reducing behaviors in populations at different risk levels (including population risk).

4. In primary care populations, there is very limited information to evaluate direct harm incurred from the routine practice of taking family history and using it to personalize risk information.

Recommendations for future research:

- Trials of family history taking as an intervention should include capture of data to examine the full range of potential impacts on individuals. Baseline data on psychological status should be captured so that this can formally be adjusted for in outcome analyses.

5. Research on the use of family history tools, risk stratification systems, and family history-based personalized prevention advice should take into account evidence on the factors likely to promote their effective use in practice, such as the educational needs of primary care practitioners and issues which act as barriers or constraints to their implementation in practice.

Reference List

1. Yoon PW, Scheuner MT, Peterson-Oehlke KL, et al. Can family history be used as a tool for public health and preventive medicine? Genetic medicine 2002;4(4):304-10.
2. Hariri S, Yoon PW, Moonesinghe R, et al. Evaluation of family history as a risk factor and screening tool for detecting undiagnosed diabetes in a nationally representative survey population. Genet Med 2006;8(12):752-9.
3. Butterworth A. Family history as a risk factor for common, complex disease. Public Health Genetics Unit (now the PHG Foundation), Cambridge, U.K.; 2007. www.phgfoundation.org/pages/family_history.htm.
4. Kardia SLR, Modell SM, Peyser PA. Family-centered approaches to understanding and preventing coronary heart disease. Am J Prev Med 2003;24(2):143-51.
5. Qureshi N, Wilson B, Santaguida P et al. Collection and use of cancer family history in primary care. Evid Rep Technol Assess No.159, AHRQ Publication No. 08-E001 (prepared by the McMaster University Evidence-based Practice Center under Contract No. 290-02-0020). Rockville, MD: Agency for Health Care Research and Quality; 2007 Oct. Available at: http://www.ahrq.gov/clinic/tp/famhisttp.htm
6. Rich EC, Burke W, Heaton CJ, et al. Reconsidering the family history in primary care. J Gen Intern Med 2004;19(3):273-80.
7. Gail MH, Costantino JP, Pee D, et al. Projecting individualized absolute invasive breast cancer risk in African American women. J Natl Cancer Inst 2007;99(23):1782-92.
8. Spiegelman D, Colditz GA, Hunter D, et al. Validation of the Gail et al. model for predicting individual breast cancer risk. J Natl Cancer Inst 1994;86(8):600-7.
9. Rockhill B, Spiegelman D, Byrne C, et al. Validation of the Gail et al. model of breast cancer risk prediction and implications for chemoprevention. J Natl Cancer Inst 2001;93(5):358-66.
10. Adams-Campbell LL, Makambi KH, Palmer JR, et al. Diagnostic accuracy of the Gail model in the Black Women's Health Study. Breast J 2007;13(4):332-6.
11. Boyle P, Mezzetti M, La Vecchia C, et al. Contribution of three components to individual cancer risk predicting breast cancer risk in Italy. Eur J Cancer Prev 2004;13(3):183-91.
12. Decarli A, Calza S, Masala G, et al. Gail model for prediction of absolute risk of invasive breast cancer: independent evaluation in the Florence-European Prospective Investigation Into Cancer and Nutrition cohort. J Natl Cancer Inst 2006;98(23):1686-93.
13. Chlebowski RT, Anderson GL, Lane DS, et al. Predicting risk of breast cancer in postmenopausal women by hormone receptor status. J Natl Cancer Inst 2007;99(22):1695-705.
14. Kim DJ, Rockhill B, Colditz GA. Validation of the Harvard Cancer Risk Index: a prediction tool for individual cancer risk. J Clin Epidemiol 2004;57(4):332-40.
15. Gail MH, Brinton LA, Byar DP, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst 1989;81(24):1879-86.
16. Colditz GA, Atwood KA, Emmons K, et al. Harvard report on cancer prevention volume 4: Harvard Cancer Risk Index. Risk Index Working Group, Harvard Center for Cancer Prevention. Cancer Causes Control 2000;11(6):477-88.
17. Whitlock EP, Lin JS, Chou R, et al. Using existing systematic reviews in complex systematic reviews. Ann Intern Med 2008;148(10):776-82.
18. Bardia A, Tleyjeh IM, Cerhan JR, et al. Efficacy of antioxidant supplementation in reducing primary cancer incidence and mortality: systematic review and meta-analysis. [Review] [73 refs]. Mayo Clin Proc 2008;83(1):23-34.
19. Alkhenizan A, Hafez K. The role of vitamin E in the prevention of cancer: a meta-analysis of randomized controlled trials. Ann Saudi Med 2007;27(6):409-14.
20. Browning DR, Martin RM. Statins and risk of cancer: A systematic review and metaanalysis. Int J Cancer 2007;120(4):833-43.
21. Kosters JP, Gotzsche PC. Regular self-examination or clinical examination for early detection of breast cancer [Review] [24 refs]. Cochrane Database Syst Rev 2003;(2):CD003373
22. Gotzsche PC, Nielsen M. Screening for breast cancer with mammography. Cochrane Database Syst Rev 2006;(4):CD001877
23. Dube C, Rostom A, Lewin G, et al. The use of aspirin for primary prevention of colorectal cancer: a systematic review prepared for the U.S. Preventive Services Task Force. Ann Intern Med 2007;146(5):365-75.

24. Hewitson P, Glasziou P, Irwig L, et al. Screening for colorectal cancer using the faecal occult blood test, Hemoccult.[update of Cochrane Database Syst Rev. 2000;(2):CD001216; PMID: 10796760]. [Review] [46 refs]. Cochrane Database Syst Rev 2007;(1):CD001216
25. Kerr J, Day P, Broadstock M, et al. Systematic review of the effectiveness of population screening for colorectal cancer. [Review] [28 refs]. N Z Medl Jl 2007;120(1258):U2629
26. Bristol SLR Team 2006. Systematic Literature Review Report. The associations between food, nutrition, physical activity and the risk of prostate cancer and underlying mechanisms. World Cancer Research Fund/American Institute for Cancer Research, Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington, DC: AICR 2007, 2006 Jun 30.
27. Ilic D, O'Connor D, Green S, et al. Screening for prostate cancer. Cochrane Database Syst Rev 2006; Issue 3, Art.No.: CD004720.DOI:10.1002/14651858.CD004720.pub2:
28. Huang HY, Caballero B, Chang S, et al. The efficacy and safety of multivitamin and mineral supplement use to prevent cancer and chronic disease in adults: a systematic review for a National Institutes of Health state-of-the-science conference. [Review] [44 refs]. Ann Intern Med 2006;145(5):372-85.
29. Moayyedi P, Achkar E. Does fecal occult blood testing really reduce mortality? A reanalysis of systematic review data.[Review] [25 refs]. Am J Gastroenterol 2006;101(2):380-4.
30. Walsh JM, Terdiman JP. Colorectal cancer screening: scientific review.[Review] [105 refs]. JAMA 2003;289(10):1288-96.
31. Bonovas S, Filioussi K, Flordellis CS, et al. Statins and the risk of colorectal cancer: a meta-analysis of 18 studies involving more than 1.5 million patients. J Clin Oncol 2007;25(23):3462-8.
32. Hoffmeister M, Chang-Claude J, Brenner H. Do older adults using NSAIDs have a reduced risk of colorectal cancer? Drugs Aging 2006;23(6):513-23.
33. Asano TK, McLeod RS. Nonsteroidal anti-inflammatory drugs and aspirin for the prevention of colorectal adenomas and cancer: a systematic review. [Review] [45 refs]. Dis Colon Rectum 2004;47(5):665-73.
34. Coulter ID, Hardy ML, Morton SC, et al. Antioxidants Vitamin C and Vitamin E for the Prevention and Treatment of Cancer. J Gen Intern Med 2006;21(7):735-44.
35. Dale KM, Coleman CI, Henyan NN, et al. Statins and cancer risk: a meta-analysis. JAMA 2006;295(1):74-80.
36. Heresbach D, Manfredi S, D'halluin PN, et al. Review in depth and meta-analysis of controlled trials on colorectal cancer screening by faecal occult blood test. [Review] [61 refs]. Eur J Gastroenterol Hepatol 2006;18(4):427-33.
37. Hackshaw AK, Paul EA. Breast self-examination and death from breast cancer: a meta-analysis. Br J Cancer 2003;88(7):1047-53.
38. Huang HY, Caballero B, Chang S et al. Multivitamin/mineral supplements and prevention of chronic disease. Evid Rep Technol Assess No.139, AHRQ Publication No.06-E012. (Prepared by The Johns Hopkins University Evidence-based Practice Center under Contract No.290-02-0018). Rockville, MD: Agency for Healthcare Research and Quality; 2006 May. PM:17764205
39. Bonovas S, Filioussi K, Tsavaris N, et al. Use of statins and breast cancer: A meta-analysis of seven randomized clinical trials and nine observational studies. J Clin Oncol 2005;23(34):8606-12.
40. Mahmud S, Franco E, Aprikian A. Prostate cancer and use of nonsteroidal anti-inflammatory drugs: systematic review and meta-analysis. [Review] [43 refs]. Br J Cancer 2004;90(1):93-9.
41. Rostom A, Dube C, Lewin G, et al. Nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors for primary prevention of colorectal cancer: a systematic review prepared for the U.S. Preventive Services Task Force. Ann Intern Med 2007;146(5):376-89.
42. Weingarten MA, Zalmanovici A, Yaphe J. Dietary calcium supplementation for preventing colorectal cancer and adenomatous polyps.[update of Cochrane Database Syst Rev. 2005;(3):CD003548; PMID: 16034903]. [Review] [38 refs]. Cochrane Database Syst Rev 2008;(1):CD003548
43. Brett J, Bankhead C, Henderson B, et al. The psychological impact of mammographic screening. A systematic review. [Review] [74 refs]. Psychooncology 2005;14(11):917-38.
44. Watson EK, Henderson BJ, Brett J, et al. The psychological impact of mammographic screening on women with a family history of breast cancer--a systematic review. [Review] [26 refs]. Psychooncology 2005;14(11):939-48.
45. Dutch Review Team 2006. Systematic Literature Review Report. The associations between food, nutrition and physical activity and the risk of colorectal cancer and underlying mechanisms. World Cancer Research Fund/American Institute for Cancer Research, Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington, DC: AICR 2007, 2007.

46. Italian Review Team 2005. Systematic Literature Review Report. The Associations between Food, Nutrition and Physical Activity and the Risk of Breast Cancer and Underlying Mechanisms. World Cancer Research Fund/American Institute for Cancer Research, Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington, DC: AICR 2007, 2007.
47. Baron JA, Beach M, Wallace K, et al. Risk of prostate cancer in a randomized clinical trial of calcium supplementation. Cancer Epidemiol Biomarkers Prev 2005;14(3):586-9.
48. Giles JT, Kennedy DT, Dunn EC, et al. Results of a community pharmacy-based breast cancer risk-assessment and education program. Pharmacotherapy 2001;21(2):243-53.
49. Curry SJ, Taplin SH, Anderman C, et al. A randomized trial of the impact of risk assessment and feedback on participation in mammography screening. Prev Med 1993;22(3):350-60.
50. Bastani R, Maxwell AE, Bradford C, et al. Tailored risk notification for women with a family history of breast cancer. Prev Med 1999;29(5):355-64.
51. Leggatt V, Mackay J, Marteau TM, et al. The psychological impact of a cancer family history questionnaire completed in general practice. J Med Genet 2000;37(6):470-2.
52. Khoury MJ, Yang Q, Gwinn M, et al. An epidemiologic assessment of genomic profiling for measuring susceptibility to common diseases and targeting interventions. Genet Med 2004;6(1):38-47.
53. Collins FS. Shattuck lecture--medical and societal consequences of the Human Genome Project. N Engl J Med 1999;341(1):28-37.
54. Levy S, Sutton G, Ng PC, et al. The diploid genome sequence of an individual human. PLoS Biol 2007;5(10):e254
55. Pharoah PD, Antoniou AC, Easton DF, et al. Polygenes, risk prediction, and targeted prevention of breast cancer. N Engl J Med 2008;358(26):2796-803.
56. Rodriguez-Bigas MA, Boland CR, Hamilton SR, et al. A National Cancer Institute Workshop on Hereditary Nonpolyposis Colorectal Cancer Syndrome: meeting highlights and Bethesda guidelines. J Natl Cancer Inst 1997;89(23):1758-62.
57. Cleeman JI, Grundy SM, Becker D, et al. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001;285(19):2486-97.
58. Haddow J, Palomaki G. Human Genome Epidemiology. Oxford: Oxford University Press; 2003. ACCE: A model process for evaluating data on emerging genetic tests.
59. Yoon PW, Scheuner MT, Khoury MJ. Research priorities for evaluating family history in the prevention of common chronic diseases. Am J Prev Med 2003;24(2):128-35.
60. Scheuner MT, Wang SJ, Raffel LJ, et al. Family history: a comprehensive genetic risk assessment method for the chronic conditions of adulthood. Am J Med Genet 1997;71(3):315-24.
61. Houlston RS, Murday V, Harocopos C, et al. Screening and genetic counselling for relatives of patients with colorectal cancer in a family cancer clinic.[erratum appears in BMJ 1990 Sep 1;301(6749):446]. BMJ 1990;301(6748):366-8.
62. Houlston RS, McCarter E, Parbhoo S, et al. Family history and risk of breast cancer. J Med Genet 1992;29(3):154-7.
63. Houlston R, Bourne TH, Davies A, et al. Use of family history in a screening clinic for familial ovarian cancer. Gynecol Oncol 1992;47(2):247-52.
64. Steinberg GD, Carter BS, Beaty TH, et al. Family history and the risk of prostate cancer. Prostate 1990;17(4):337-47.
65. Carter BS, Bova GS, Beaty TH, et al. Hereditary prostate cancer: epidemiologic and clinical features. J Urol 1993;150(3):797-802.
66. Colditz GA, Willett WC, Hunter DJ, et al. Family history, age, and risk of breast cancer. Prospective data from the Nurses' Health Study. JAMA 1993;270(3):338-43.
67. Slattery ML, Kerber RA. A comprehensive evaluation of family history and breast cancer risk. The Utah Population Database. JAMA 1993;270(13):1563-8.
68. Claus EB, Risch N, Thompson WD. Autosomal dominant inheritance of early-onset breast cancer. Implications for risk prediction. Cancer 1994;73(3):643-51.
69. Fuchs CS, Giovannucci EL, Colditz GA, et al. A prospective study of family history and the risk of colorectal cancer. N Engl J Med 1994;331(25):1669-74.
70. Spitz MR, Currier RD, Fueger JJ, et al. Familial patterns of prostate cancer: a case-control analysis. J Urol 1991;146(5):1305-7.
71. Colditz GA, Branch LG, Lipnick RJ, et al. Increased green and yellow vegetable intake and lowered cancer deaths in an elderly population. Am J Clin Nutr 1985;41(1):32-6.
72. Hertog MG, Bueno-de-Mesquita HB, Fehily AM, et al. Fruit and vegetable consumption and cancer mortality in the Caerphilly Study. Cancer Epidemiol Biomarkers Prev 1996;5(9):673-7.
73. Steinmetz KA, Potter JD. Vegetables, fruit, and cancer prevention: a review. J Am Diet Assoc 1996;96(10):1027-39.
74. Alpha-Tocopherol Beta-Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N Engl J Med 1994;330(15):1029-35.

75. Marteau TM, Lerman C. Genetic risk and behavioural change. BMJ 2001;322(7293):1056-9.
76. Heshka JT, Palleschi C, Howley H, et al. A systematic review of perceived risks, psychological and behavioral impacts of genetic testing. Genet Med 2008;10(1):19-32.
77. Sheldon TA, Cullum N, Dawson D, et al. What's the evidence that NICE guidance has been implemented? Results from a national evaluation using time series analysis, audit of patients' notes, and interviews. BMJ 2004;329(7473):999-1003.
78. Lynch HT. Cancer family history and genetic testing: are malpractice adjudications waiting to happen? Am J Gastroenterol 2002;97(3):518-20.
79. Kelly KM, Shedlosky-Shoemaker R, Porter K, et al. Cancer family history reporting: impact of method and psychosocial factors. J Genet Couns 2007;16(3):373-82.
80. Task Force on Community Preventive Services. The Guide to Community Preventive Services: What Works to Promote Health? The Community Guide 2005. http://www.thecommunityguide.org/methods/.
81. World Cancer Research Fund / American Institute for Cancer Research. Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective. 2nd Expert Report. United Kingdom: World Cancer Research Fund International; 2007 Jan 1.
82. Thoma A, Veltri K, Haines T, et al. A systematic review of reviews comparing the effectiveness of endoscopic and open carpal tunnel decompression. Plast Reconstr Surg 2004;113(4):1184-91.
83. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996;17(1):1-12.
84. Costantino JP, Gail MH, Pee D, et al. Validation studies for models projecting the risk of invasive and total breast cancer incidence. J Natl Cancer Inst 1999;91(18):1541-8.
85. Willett WC, Hunter DJ, Stampfer MJ, et al. Dietary fat and fiber in relation to risk of breast cancer. An 8-year follow-up. JAMA 1992;268(15):2037-44.
86. Colditz GA. The nurses' health study: a cohort of US women followed since 1976. J Am Med Womens Assoc 1995;50(2):40-4.
87. Anderson GL, Manson J, Wallace R, et al. Implementation of the Women's Health Initiative study design. Ann Epidemiol 2003;13(9 Suppl):S5-17.
88. Russell C, Palmer JR, Adams-Campbell LL, et al. Follow-up of a large cohort of Black women. Am J Epidemiol 2001;154(9):845-53.
89. Baker LH. Breast Cancer Detection Demonstration Project: Five-Year Summary Report. CA Cancer J Clin 1982;32(4):194-225.
90. Marchbanks PA, McDonald JA, Wilson HG, et al. The NICHD Women's Contraceptive and Reproductive Experiences Study: methods and operational results. Ann Epidemiol 2002;12(4):213-21.
91. Demierre MF, Higgins PD, Gruber SB. Statins and cancer prevention. Nat Rev Cancer 2005;5(12):930-42.
92. Kim KP, Whitehead C, Piazza G, et al. Combinatorial chemoprevention: efficacy of lovostatin and exisulind on the formation and progression of aberrant crypt foci. Anticancer Res 2004;24(3a):1805-11.
93. Agarwal B, Rao CV, Bhendwal S, et al. Lovastatin augments sulindac-induced apoptosis in colon cancer cells and potentiates chemopreventive effects of sulindac. Gastroenterology 1999;117(4):838-47.
94. Narisawa T, Fukaura Y, Terada K, et al. Prevention of 1,2-dimethylhydrazine-induced colon tumorigenesis by HMG-CoA reductase inhibitors, pravastatin and simvastatin, in ICR mice. Carcinogenesis 1994;15(9):2045-8.
95. Chan KK, Oza AM, Siu LL. The statins as anticancer agents. Clin Cancer Res 2003;9(1):10-9.
96. Graaf MR, Beiderbeck AB, Egberts AC, et al. The risk of cancer in users of statins. J Clin Oncol 2004;22(12):2388-94.
97. Poynter JN, Gruber SB, Higgins PDR, et al. Statins and the risk of colorectal cancer. N Engl J Med 2005;352(21):2184-92.
98. Shannon J, Tewoderos S, Garzotto M, et al. Statins and prostate cancer risk: a case-control study. Am J Epidemiol 2005;162(4):318-25.
99. Newman TB, Hulley SB. Carcinogenicity of lipid-lowering drugs. JAMA 1996;275(1):55-60.
100. Coogan PF, Rosenberg L, Palmer JR, et al. Statin use and the risk of breast and prostate cancer. Epidemiology 2002;13(3):262-7.
101. Pfeffer MA, Keech A, Sacks FM, et al. Safety and tolerability of pravastatin in long-term clinical trials: prospective Pravastatin Pooling (PPP) Project. Circulation 2002;105(20):2341-6.
102. Setoguchi S, Glynn RJ, Avorn J, et al. Statins and the risk of lung, breast, and colorectal cancer in the elderly. Circulation 2007;115(1):27-33.
103. Boyle P, Veronesi U, Tubiana M, et al. European School of Oncology Advisory report to the European Commission for the "Europe Against Cancer Programme" European Code Against Cancer. Eur J Cancer 1995;31A(9):1395-405.
104. Shapiro S, Coleman EA, Broeders M, et al. Breast cancer screening programmes in 22 countries: current policies, administration and guidelines. International Breast Cancer Screening Network (IBSN) and the European Network of Pilot Projects for Breast Cancer Screening. Int J Epidemiol 1998;27(5):735-42.

105. WHO. IARC Handbook of Cancer Prevention. Volume 7. Breast Cancer Screening. Lyon, France: IARC Press; 2002. Efficacy of screening by self-examination.
106. Gotzsche PC, Olsen O. Is screening for breast cancer with mammography justifiable? Lancet 2000;355(9198):129-34.
107. Blamey RW, Wilson AR, Patnick J. ABC of breast diseases: screening for breast cancer. BMJ 2000;321(7262):689-93.
108. Cox B. Variation in the effectiveness of breast screening by year of follow-up. J Natl Cancer Inst Monogr 1997;(22):69-72.
109. Elwood JM, Cox B, Richardson AK. The effectiveness of breast cancer screening by mammography in younger women. Online J Curr Clin Trials 1993;Doc No 32:23,227.
110. Glasziou PP. Meta-analysis adjusting for compliance: the example of screening for breast cancer. J Clin Epidemiol 1992;45(11):1251-6.
111. Glasziou PP, Woodward AJ, Mahon CM. Mammographic screening trials for women aged under 50. A quality assessment and meta-analysis. Med J Aust 1995;162(12):625-9.
112. Glasziou P, Irwig L. The quality and interpretation of mammographic screening trials for women ages 40-49. J Natl Cancer Inst Monogr 1997;(22):73-7.
113. Hendrick RE, Smith RA, Rutledge JH, III, et al. Benefit of screening mammography in women aged 40-49: a new meta-analysis of randomized controlled trials. J Natl Cancer Inst Monogr 1997;(22):87-92.
114. Humphrey LL, Helfand M, Chan BK, et al. Breast cancer screening: a summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2002;137(5 Part 1):347-60.
115. Kerlikowske K, Grady D, Rubin SM, et al. Efficacy of screening mammography. A meta-analysis. JAMA 1995;273(2):149-54.
116. Larsson LG, Nystrom L, Wall S, et al. The Swedish randomised mammography screening trials: analysis of their effect on the breast cancer related excess mortality. J Med Screen 1996;3(3):129-32.
117. Larsson LG, Andersson I, Bjurstam N, et al. Updated overview of the Swedish Randomized Trials on Breast Cancer Screening with Mammography: age group 40-49 at randomization. J Natl Cancer Inst Monogr 1997;(22):57-61.
118. Nystrom L, Rutqvist LE, Wall S, et al. Breast cancer screening with mammography: overview of Swedish randomised trials. Lancet 1993;341(8851):973-8.
119. Nystrom L, Larsson LG, Wall S, et al. An overview of the Swedish randomised mammography trials: total mortality pattern and the representivity of the study cohorts. J Med Screen 1996;3(2):85-7.
120. Nystrom L, Andersson I, Bjurstam N, et al. Long-term effects of mammography screening: updated overview of the Swedish randomised trials. Lancet 2002;359(9310):909-19.
121. Smart CR, Hendrick RE, Rutledge JH, III, et al. Benefit of mammography screening in women ages 40 to 49 years. Current evidence from randomized controlled trials. Cancer 1995;75(7):1619-26.
122. Kerlikowske K. Efficacy of screening mammography among women aged 40 to 49 years and 50 to 69 years: comparison of relative and absolute benefit. J Natl Cancer Inst Monogr 1997;(22):79-86.
123. Report of the Organizing Committee and Collaborators Falun Meeting. Breast-cancer screening with mammography in women aged 40-49 years. Int J Cancer 1996;68(6):693-9.
124. Nyström L. Assessment of population screening: the case of mammography [thesis] Umeå: Umeå University Medical Dissertations. 2000.
125. Wald NJ, Chamberlain J, Hackshaw A. Report of the European Society for Mastology Breast Cancer Screening Evaluation Committee (1993). The Breast 1993;2:209-16.
126. WHO. IARC Handbooks of Cancer Prevention. Volume 7. Breast Cancer Screening. Lyon: IARC Press; 2002.
127. Nyström L. Update of the overview of the Swedish randomized trials on breast cancer screening with mammography. NIH Consensus Development Conference on Breast Cancer Screening for Women Ages 40-49. Nat 1997;65-9.
128. Olsen O, Gotzsche PC. Cochrane review on screening for breast cancer with mammography. Lancet 2001;358(9290):1340-2.
129. Rosenberg L, Palmer JR, Zauber AG, et al. A hypothesis: nonsteroidal anti-inflammatory drugs reduce the incidence of large-bowel cancer. J Natl Cancer Inst 1991;83(5):355-8.
130. Thun MJ, Namboodiri MM, Heath CW, Jr. Aspirin use and reduced risk of fatal colon cancer. N Engl J Med 1991;325(23):1593-6.
131. Sandler RS. Aspirin and other nonsteroidal anti-inflammatory agents in the prevention of colorectal cancer. Important Adv Oncol 1996;123-37.
132. Friedman GD, Coates AO, Potter JD, et al. Drugs and colon cancer. Pharmacoepidemiol Drug Saf 1998;7(2):99-106.
133. Rosenberg L, Louik C, Shapiro S. Nonsteroidal antiinflammatory drug use and reduced risk of large bowel carcinoma. Cancer 1998;82(12):2326-33.
134. Giovannucci E. The prevention of colorectal cancer by aspirin use. Biomed Pharmacother 1999;53(7):303-8.
135. Kune GA. Colorectal cancer chemoprevention: aspirin, other NSAID and COX-2 inhibitors. Aust N Z J Surg 2000;70(6):452-5.

136. Garcia-Rodriguez LA, Huerta-Alvarez C. Reduced risk of colorectal cancer among long-term users of aspirin and nonaspirin nonsteroidal antiinflammatory drugs. Epidemiology 2001;12(1):88-93.
137. Baron JA, Cole BF, Sandler RS, et al. A randomized trial of aspirin to prevent colorectal adenomas. N Engl J Med 2003;348(10):891-9.
138. Sandler RS, Halabi S, Baron JA, et al. A randomized trial of aspirin to prevent colorectal adenomas in patients with previous colorectal cancer. N Engl J Med 2003;348(10):883-90.
139. Willett W. The search for the causes of breast and colon cancer. Nature 1989;338(6214):389-94.
140. Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. Cell 1990;61(5):759-67.
141. Potter JD. Reconciling the epidemiology, physiology, and molecular biology of colon cancer. JAMA 1992;268(12):1573-7.
142. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 1993;329(27):1977-81.
143. Young GP, St John DJ, Winawer SJ, et al. Choice of fecal occult blood tests for colorectal cancer screening: recommendations based on performance characteristics in population studies: a WHO (World Health Organization) and OMED (World Organization for Digestive Endoscopy) report. Am J Gastroenterol 2002;97(10):2499-507.
144. Black WC, Haggstrom DA, Welch HG. All-cause mortality in randomized trials of cancer screening. J Natl Cancer Inst 2002;94(3):167-73.
145. Levin TR, Conell C, Shapiro JA, et al. Complications of screening flexible sigmoidoscopy. Gastroenterology 2002;123(6):1786-92.
146. Segnan N, Senore C, Andreoni B, et al. Baseline findings of the Italian multicenter randomized controlled trial of "once-only sigmoidoscopy"--SCORE. J Natl Cancer Inst 2002;94(23):1763-72.
147. Gondal G, Grotmol T, Hofstad B, et al. Grading of distal colorectal adenomas as predictors for proximal colonic neoplasia and choice of endoscope in population screening: experience from the Norwegian Colorectal Cancer Prevention study (NORCCAP). Gut 2003;52(3):398-403.
148. Atkin WS, Cuzick J, Northover JM, et al. Prevention of colorectal cancer by once-only sigmoidoscopy. Lancet 1993;341(8847):736-40.
149. Lieberman DA, Weiss DG, Bond JH, et al. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. N Engl J Med 2000;343(3):162-8.
150. Schoenfeld P, Cash B, Flood A, et al. Colonoscopic screening of average-risk women for colorectal neoplasia. N Engl J Med 2005;352(20):2061-8.
151. Clark LC, Combs GF, Jr., Turnbull BW, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. JAMA 1996;276(24):1957-63.
152. Giovannucci E, Rimm EB, Wolk A, et al. Calcium and fructose intake in relation to risk of prostate cancer. Cancer Res 1998;58(3):442-7.
153. Kristal AR, Cohen JH, Qu P, et al. Associations of energy, fat, calcium, and vitamin D with prostate cancer risk. Cancer Epidemiol Biomarkers Prev 2002;11(8):719-25.
154. Rodriguez C, McCullough ML, Mondul AM, et al. Calcium, dairy products, and risk of prostate cancer in a prospective cohort of United States men. Cancer Epidemiol Biomarkers Prev 2003;12(7):597-603.
155. Chan JM, Stampfer MJ, Ma J, et al. Dairy products, calcium, and prostate cancer risk in the Physicians' Health Study. AM J Clin Nutr 2001;74(4):549-54.
156. Vlajinac HD, Marinkovic JM, Ilic MD, et al. Diet and prostate cancer: a case-control study. Eur J Cancer 1997;33(1):101-7.
157. Hayes RB, Ziegler RG, Gridley G, et al. Dietary factors and risks for prostate cancer among blacks and whites in the United States. Cancer Epidemiol Biomarkers Prev 1999;8(1):25-34.
158. Kristal AR, Stanford JL, Cohen JH, et al. Vitamin and mineral supplement use is associated with reduced risk of prostate cancer. Cancer Epidemiol Biomarkers Prev 1999;8(10):887-92.
159. Schuurman AG, van den Brandt PA, Dorant E, et al. Animal products, calcium and protein and prostate cancer risk in The Netherlands Cohort Study. Br J Cancer 1999;80(7):1107-13.
160. Chan JM, Pietinen P, Virtanen M, et al. Diet and prostate cancer risk in a cohort of smokers, with a specific focus on calcium and phosphorus (Finland). Cancer Causes Control 2000;11(9):859-67.
161. Tavani A, Gallus S, Franceschi S, et al. Calcium, dairy products, and the risk of prostate cancer. Prostate 2001;48(2):118-21.
162. Berndt SI, Carter HB, Landis PK, et al. Calcium intake and prostate cancer risk in a long-term aging study: the Baltimore Longitudinal Study of Aging. Urology 2002;60(6):1118-23.
163. Gambert SR. Screening for prostate cancer. Int Urol Nephrol 2001;33(2):249-57.
164. Holmberg L, Bill-Axelson A, Helgesen F, et al. A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer. N Engl J Med 2002;347(11):781-9.

165. Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative management of clinically localized prostate cancer. JAMA 2005;293(17):2095-101.
166. Johansson JE, Andren O, Andersson SO, et al. Natural history of early, localized prostate cancer. JAMA 2004;291(22):2713-9.
167. Coley C, Barry M, Mulley A. Clinical Guideline, Part III: Screening for Prostate Cancer. Ann Intern Med 1997;126(6):480-4.
168. Ferrini R, Woolf SH. American College of Preventive Medicine practice policy. Screening for prostate cancer in American men. Am J Prev Med 1998;15(1):81-4.
169. Harris R, Lohr KN. Screening for prostate cancer: an update of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2002;137(11):917-29.
170. Smith RA, Cokkinides V, Eyre HJ. American Cancer Society guidelines for the early detection of cancer, 2003. CA Cancer J Clin 2003;53(1):27-43.
171. Taplin SH, Thompson RS, Schnitzer F, et al. Revisions in the risk-based Breast Cancer Screening Program at Group Health Cooperative. Cancer 1990;66(4):812-8.
172. Veronesi U, Maisonneuve P, Rotmensz N, et al. Italian randomized trial among women with hysterectomy: tamoxifen and hormone-dependent breast cancer in high-risk women. J Natl Cancer Inst 2003;95(2):160-5.
173. Scheuner MT, Whitworth WC, McGruder H, et al. Familial risk assessment for early-onset coronary heart disease. Genet Med 2006;8(8):525-31.
174. Centers for Disease Control and Prevention. Family Healthware. National Office of Public Health Genomics.December 11 2007. www.cdc.gov/genomics/activities/famhx.htm.
175. Grodstein F, Stampfer MJ, Manson JE, et al. Postmenopausal estrogen and progestin use and the risk of cardiovascular disease. N Engl J Med 1996;335(7):453-61.
176. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. JAMA 2002;288(3):321-33.
177. Shaukat A, Scouras N, Schunemann HJ. Role of supplemental calcium in the recurrence of colorectal adenomas: a metaanalysis of randomized controlled trials. Am J Gastroenterol 2005;100(2):390-4.
178. Jacobs EJ, Mondul AM, Connell CJ. A large cohort study of aspirin and other nonsteroidal anti-inflammatory drugs and prostate cancer incidence. J Natl Cancer Inst 2005;97(13):975-80.
179. Haiman CA, Le Marchand L, Yamamato J, et al. A common genetic risk factor for colorectal and prostate cancer. Nat Genet 2007;39(8):954-6.
180. Flossmann E, Rothwell PM, British Doctors Aspirin Trial and the UK-TIA Aspirin Trial. Effect of aspirin on long-term risk of colorectal cancer: consistent evidence from randomised and observational studies. Lancet 2007;369(9573):1603-13.
181. Peto R. Randomised trial of prophylactic daily aspirin in british male doctors. BMJ 1988;296(6618):313-6.
182. Farrell B. The United Kingdom transient ischaemic attack (UK-TIA) aspirin trial: Final results. J Neurol Neurosurg Psychiatry 1991;54(12):1044-54.
183. Burton PR. Size matters: just how big is BIG? Quantifying realistic sample size requirements for human genome epidemiology. Int J Epidemiol 2008;1-11.
184. Austoker J. Breast self-examination. BMJ 2003;326:1-2.
185. U.S.Preventive Services Task Force. Screening for Breast Cancer. Agency for Healthcare Research and Quality, Rockville, MD.November 2003. http://www.ahrq.gov/clinic/uspstf/uspsbrca.htm.
186. Baker S, Wall M, Bloomfield A. What is the most appropriate breast-cancer screening interval for women aged 45 to 49 years in New Zealand?. [Review] [52 refs]. N Z Med J 2005;118(1221):U1636
187. U.S.Preventive Services Task Force. Screening for Colorectal Cancer. Agency for Healthcare Research and Quality, Rockville, MD.October 2008. http://www.ahrq.gov/clinic/uspstf/uspscolo.htm#related.
188. Evelyn P.Whitlock, Jennifer Lin Elizabeth Liles Tracy Beil Rongwei Fu Elizabeth O'Connor Rebecca Newton Thompson Taryn Cardenas. Screening for Colorectal Cancer: An Updated Systematic Review. Health Services/Technology Assessment Text (HSTAT. http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat3.chapter.54428.
189. Lin K, Lipsitz R. Benefits and harms of prostate-specific antigen screening for prostate cancer: an evidence update for the U.S. Preventive Services Task Force. Ann Intern Med 2008;149:192-9.
190. U.S.Preventive Services Task Force. Screening for Ovarian Cancer. Agency for Healthcare Research and Quality, Rockville, MD.May 2004. http://www.ahrq.gov/clinic/uspstf/uspsovar.htm.
191. Scheuner MT, Rotter JI. Quantifying the health benefits of genetic tests: a clinical perspective. Genet Med 2006;8(3):141-2.
192. Mandelson MT. Colorectal cancer screening participation by older women. Am J Prev Med 2000;19:149-54.
193. Slattery ML, Edwards SL, Ma KN, et al. Colon cancer screening, lifestyle, and risk of colon cancer. Cancer Causes Control 2000;11(6):555-63.

194. Madlensky L, Esplen MJ, Gallinger S, et al. Relatives of colorectal cancer patients: factors associated with screening behavior. Am J Prev Med 2003;25(3):187-94.
195. Jacobsen PB, Lamonde LA, Honour M, et al. Relation of family history of prostate cancer to perceived vulnerability and screening behavior. Psychooncology 2004;13(2):80-5.
196. Slattery ML, Kinney AY, Levin TR. Factors associated with colorectal cancer screening in a population-based study: the impact of gender, health care source, and time. Prev Med 2004;38(3):276-83.
197. Ramji F, Cotterchio M, Manno M, et al. Association between subject factors and colorectal cancer screening participation in Ontario, Canada. Cancer Detect Prev 2005;29(3):221-6.
198. Bloom JR, Stewart SL, Oakley-Girvans I, et al. Family history, perceived risk, and prostate cancer screening among African American men. Cancer Epidemiol Biomarkers Prev 2006;15(11):2167-73.
199. Beresford SA, Johnson KC, Ritenbaugh C, et al. Low-fat dietary pattern and risk of colorectal cancer: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. JAMA 2006;295(6):643-54.

Appendix A – Search Strategies Detailed

Question 1

Ovid-MEDLINE

1. claus.tw.
2. gail.tw.
3. BRCAPRO.tw.
4. BOADICEA.tw.
5. UK cancer family study group.tw.
6. UKCFSG.tw.
7. Myriad.ti,ab.
8. tyrer Cuzick.ti,ab.
9. ((Amsterdam or Bethesda or Manchester or Gilpin or Evans or Frank or Finnish or Yale or Spanish) adj5 (criteria or guideline? or scor$ or model? or protocol? or algorithm?)).ti,ab.
10. FHAT.ti,ab.
11. (Australia adj5 breast cancer cent$).tw.
12. couch.ti,ab.
13. ((mendel or LAMBDA) adj5 (criteria or guideline? or scor$ or model? or protocol? or algorithm?)).ti,ab.
14. (Dutch guideline adj7 breast).ti,ab.
15. (nice guideline? and breast cancer).ti,ab.
16. or/1-15
17. models, statistical/
18. models, theoretical/ or models, genetic/
19. 17 or 18
20. genes, brca1/ or genes, brca2/
21. BRCA$.tw.
22. 20 or 21
23. 19 and 22
24. 16 or 23
25. exp breast neoplasms/ or exp colorectal neoplasms/ or exp ovarian neoplasms/ or exp prostatic neoplasms/
26. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
27. *Neoplasms/
28. or/25-27
29. validation.ti.
30. accuracy.ti.
31. validation studies/
32. evaluation studies/
33. exp "Sensitivity and Specificity"/
34. "reproducibility of results"/
35. odds ratio/
36. multivariate analysis/
37. exp Probability/

38. predictive value?.ti,ab.
39. or/29-38
40. 24 and 28 and 39
41. animals/ not (humans/ and animals/)
42. 40 not 41
43. limit 42 to english language
44. limit 43 to yr="1990 - 2008"
45. Breast Neoplasms/
46. exp Colorectal Neoplasms/
47. exp Prostatic Neoplasms/
48. exp Ovarian Neoplasms/
49. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
50. or/45-49
51. exp Mass Screening/
52. (surveillance or screening).ti.
53. Primary Prevention/
54. Preventive Medicine/
55. prophylactic.ti.
56. prevention.ti.
57. (genetic adj2 (counsel?ing or test$)).ti.
58. Risk Assessment/
59. (risk adj (assessment? or stratification)).ti.
60. Preventive Health Services/
61. or/51-60
62. exp Pedigree/
63. limit 62 to humans
64. exp Medical History Taking/
65. ((family or familial) adj3 (histor$ or history-taking or risk$)).ti,ab.
66. anamnesis.ti.
67. (human adj2 pedigree).ti,ab.
68. (genetic adj2 (risk adj3 (assessment or evaluation))).ti,ab.
69. genogram$.ti,ab.
70. ((famil$ or heredi$ or inherit$) adj3 (cancer$ or carcinom$ or neoplasm$)).ti,ab.
71. (genetic adj2 (screening or test$)).ti,ab.
72. Family Health/
73. or/63-72
74. exp Neoplasms/
75. (neoplasm? or carcinoma? or cancer?).ti.
76. 74 or 75
77. guideline.pt.
78. practice guideline.pt.
79. guideline?.ti.
80. or/77-79
81. 73 and 76 and 80
82. 50 and 61 and 80

83. 81 or 82
84. (note or comment or editorial).pt.
85. 83 not 84
86. limit 85 to english language
87. limit 86 to yr="2003 - 2008"
88. 44 or 87

Ovid-EMBASE

1. claus.tw.
2. gail.tw.
3. BRCAPRO.tw.
4. BOADICEA.tw.
5. UK cancer family study group.tw.
6. UKCFSG.tw.
7. Myriad.ti,ab.
8. tyrer Cuzick.ti,ab.
9. ((Amsterdam or Bethesda or Manchester or Gilpin or Evans or Frank or Finnish or Yale or Spanish) adj5 (criteria or guideline? or scor$ or model? or protocol? or algorithm?)).ti,ab.
10. FHAT.ti,ab.
11. (Australia adj5 breast cancer cent$).tw.
12. couch.ti,ab.
13. ((mendel or LAMBDA) adj5 (criteria or guideline? or scor$ or model? or protocol? or algorithm?)).ti,ab.
14. (Dutch guideline adj7 breast).ti,ab.
15. (nice guideline? and breast cancer).ti,ab.
16. or/1-15
17. MATHEMATICAL MODEL/ or STATISTICAL MODEL/ or CANCER MODEL/ or GENETIC MODEL/
18. GENETIC ALGORITHM/ or ALGORITHM/
19. or/17-18
20. Brca1 Protein/ or Brca2 Protein/
21. oncogene/
22. brca2 gene/
23. BRCA$.tw.
24. or/20-23
25. 19 and 24
26. exp breast neoplasms/ or exp colorectal neoplasms/ or exp ovarian neoplasms/ or exp prostatic neoplasms/
27. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
28. *Neoplasms/
29. or/26-28
30. 16 or 25
31. 29 and 30
32. validation.ti.
33. accuracy.ti.

34. agreement.ti.
35. VALIDATION STUDY/ or INSTRUMENT VALIDATION/ or VALIDATION PROCESS/
36. diagnostic accuracy/
37. exp statistical parameters/
38. prediction/
39. "SENSITIVITY AND SPECIFICITY"/
40. predictive value?.ti,ab.
41. or/32-40
42. 31 and 41
43. limit 42 to human
44. limit 43 to english language
45. limit 44 to yr="1990 - 2008"
46. exp Neoplasms/
47. (neoplasm? or carcinoma? or cancer?).ti.
48. 46 or 47
49. exp Breast Cancer/
50. exp Colon Cancer/
51. exp Ovary Cancer/
52. exp Prostate Cancer/
53. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
54. or/49-53
55. exp anamnesis/
56. ((family or familial) adj3 (histor$ or history-taking or risk$)).ti,ab.
57. anamnesis.ti.
58. (human adj2 pedigree).ti,ab.
59. (genetic adj2 (risk adj3 (assessment or evaluation))).ti,ab.
60. ((famil$ or heredi$ or inherit$) adj3 (cancer$ or carcinom$ or neoplasm$ or tumo?r$)).ti,ab.
61. (genetic adj2 (screening or test$)).ti,ab.
62. genogram$.ti,ab.
63. or/55-62
64. prevention/ or primary prevention/ or prophylaxis/ or breast care/ or cancer prevention/ or chemoprophylaxis/ or periodic medical examination/ or personal monitoring/ or secondary prevention/
65. screening/ or screening test/ or mass screening/ or cancer screening/ or genetic screening/
66. risk/ or genetic risk/ or risk assessment/ or risk factor/ or risk management/ or risk reduction/
67. preventive medicine/
68. preventive health service/
69. prevention.ti.
70. prophylactic.ti.
71. or/64-70
72. (note or comment or editorial).pt.
73. practice guideline/
74. guideline?.ti.
75. 73 or 74
76. 48 and 63 and 75

77. 54 and 71 and 75
78. 76 or 77
79. 78 not 72
80. limit 79 to human
81. limit 80 to english language
82. limit 81 to yr="2003 - 2008"
83. 45 or 82

Ovid-CINAHL

1. claus.tw.
2. gail.tw.
3. BRCAPRO.tw.
4. BOADICEA.tw.
5. UK cancer family study group.tw.
6. UKCFSG.tw.
7. Myriad.ti,ab.
8. tyrer Cuzick.ti,ab.
9. ((Amsterdam or Bethesda or Manchester or Gilpin or Evans or Frank or Finnish or Yale or Spanish) adj5 (criteria or guideline? or scor$ or model? or protocol? or algorithm?)).ti,ab.
10. FHAT.ti,ab.
11. (Australia adj5 breast cancer cent$).tw.
12. couch.ti,ab.
13. ((mendel or LAMBDA) adj5 (criteria or guideline? or scor$ or model? or protocol? or algorithm?)).ti,ab.
14. (Dutch guideline adj7 breast).ti,ab.
15. (nice guideline? and breast cancer).ti,ab.
16. or/1-15
17. practice guidelines.pt.
18. Practice Guidelines/
19. guidelines.ti,ab.
20. or/17-19
21. exp Medical History Taking/
22. exp Family Health/
23. exp Pedigree/
24. ((family or familial) adj3 (histor$ or history-taking or risk$)).ti,ab.
25. anamnesis.ti,ab.
26. (human adj2 pedigree).ti,ab.
27. (genetic adj2 (risk adj3 (assessment or evaluation))).ti,ab.
28. ((famil$ or heredi$ or inherit$) adj3 (cancer$ or carcinom$ or neoplasm$ or tumo?r$)).ti,ab.
29. or/21-28
30. exp Breast Neoplasms/
31. exp Colorectal Neoplasms/
32. exp Ovarian Neoplasms/
33. exp Prostatic Neoplasms/
34. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.

35. or/30-34
36. cancer screening/ or genetic screening/
37. (surveillance or screening).ti.
38. Preventive Health Care/
39. Chemoprevention/
40. Risk Assessment/
41. prophylactic.ti.
42. prevention.ti.
43. (gentic adj2 (counsel?ing or test$ or screen$)).ti.
44. Genetic Counseling/
45. (risk adj (assessment? or stratification)).ti.
46. or/36-45
47. exp Neoplasms/
48. (neoplasm? or carcinoma? or cancer?).ti.
49. or/47-48
50. 20 and 29 and 49
51. 20 and 35 and 46
52. 50 or 51
53. limit 52 to (book chapter or case study or commentary or editorial)
54. 52 not 53
55. limit 54 to english
56. limit 55 to yr="2000 - 2008"
57. limit 55 to yr="2003 - 2008"
58. models, theoretical/ or models, statistical/
59. Genes, BRCA/
60. BRCA$.tw.
61. 59 or 60
62. 58 and 61
63. 16 or 62
64. exp breast neoplasms/ or exp colorectal neoplasms/ or exp ovarian neoplasms/ or exp prostatic neoplasms/
65. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
66. 64 or 65
67. 63 and 66
68. limit 67 to english
69. (book chapter or case study or commentary or editorial).pt.
70. 68 not 69
71. limit 70 to yr="1990 - 2008"
72. 57 or 71

Ovid-CCRT

1. claus.tw.
2. gail.tw.
3. BRCAPRO.tw.
4. BOADICEA.tw.

5. UK cancer family study group.tw.
6. UKCFSG.tw.
7. Myriad.ti,ab.
8. tyrer Cuzick.ti,ab.
9. ((Amsterdam or Bethesda or Manchester or Gilpin or Evans or Frank or Finnish or Yale or Spanish) adj5 (criteria or guideline? or scor$ or model? or protocol? or algorithm?)).ti,ab.
10. FHAT.ti,ab.
11. (Australia adj5 breast cancer cent$).tw.
12. couch.ti,ab.
13. ((mendel or LAMBDA) adj5 (criteria or guideline? or scor$ or model? or protocol? or algorithm?)).ti,ab.
14. (Dutch guideline adj7 breast).ti,ab.
15. (nice guideline? and breast cancer).ti,ab.
16. or/1-15
17. models, statistical/
18. models, theoretical/ or models, genetic/
19. 17 or 18
20. genes, brca1/ or genes, brca2/
21. BRCA$.tw.
22. 20 or 21
23. 19 and 22
24. 16 or 23
25. exp breast neoplasms/ or exp colorectal neoplasms/ or exp ovarian neoplasms/ or exp prostatic neoplasms/
26. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
27. *Neoplasms/
28. or/25-27
29. validation.ti.
30. accuracy.ti.
31. validation studies/
32. evaluation studies/
33. exp "Sensitivity and Specificity"/
34. "reproducibility of results"/
35. odds ratio/
36. multivariate analysis/
37. exp Probability/
38. predictive value?.ti,ab.
39. or/29-38
40. 24 and 28 and 39
41. limit 40 to yr="1990 - 2008"
42. Breast Neoplasms/
43. exp Colorectal Neoplasms/
44. exp Prostatic Neoplasms/
45. exp Ovarian Neoplasms/

46. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
47. or/42-46
48. exp Mass Screening/
49. (surveillance or screening).ti.
50. Primary Prevention/
51. Preventive Medicine/
52. prophylactic.ti.
53. prevention.ti.
54. (genetic adj2 (counsel?ing or test$)).ti.
55. Risk Assessment/
56. (risk adj (assessment? or stratification)).ti.
57. Preventive Health Services/
58. or/48-57
59. exp Pedigree/
60. limit 59 to humans
61. exp Medical History Taking/
62. ((family or familial) adj3 (histor$ or history-taking or risk$)).ti,ab.
63. anamnesis.ti.
64. (human adj2 pedigree).ti,ab.
65. (genetic adj2 (risk adj3 (assessment or evaluation))).ti,ab.
66. genogram$.ti,ab.
67. ((famil$ or heredi$ or inherit$) adj3 (cancer$ or carcinom$ or neoplasm$)).ti,ab.
68. (genetic adj2 (screening or test$)).ti,ab.
69. Family Health/
70. or/60-69
71. exp Neoplasms/
72. (neoplasm? or carcinoma? or cancer?).ti.
73. 71 or 72
74. guideline.pt.
75. practice guideline.pt.
76. guideline?.ti.
77. or/74-76
78. 70 and 73 and 77
79. 47 and 58 and 77
80. 78 or 79
81. (note or comment or editorial).pt.
82. 80 not 81
83. limit 82 to yr="2003 - 2008"
84. 41 or 83

Question 2

Ovid-MEDLINE

1. exp Diet Therapy/ or exp Nutrition Physiology/ or exp Nutritional Sciences/
2. (diet or diets or dietetic or dietary or eating or intake or nutrient$ or nutrition or vegetarian$ or vegan$ or "seventh day adventist" or macrobiotic or breastfeed$ or breast feed$ or breastfed or breast fed or breastmilk or breast milk).ti,ab.
3. exp "food and beverages"/
4. (food$ or cereal$ or grain$ or granary or wholegrain or wholewheat or roots or plantain$ or tuber or tubers or vegetable$ or fruit$ or pulses or beans or lentils or chickpeas or legume$ or soy or soya or nut or nuts or peanut$ or groundnut$ or seeds or meat or beef or pork or lamb or poultry or chicken or turkey or duck or fish or fat or fats or fatty or egg or eggs or bread or oils or shellfish or seafood or sugar or syrup or dairy or milk or herbs or spices or chilli or chillis or pepper$ or condiments).ti,ab.
5. (fluid intake or water or drinks or drinking or tea or coffee or caffeine or juice or beer or spirits or liquor or wine or alcohol or alcoholic or beverage$ or ethanol or yerba mate or ilex paraguariensis).ti,ab.
6. fertilizers/ or exp pesticides/ or Veterinary Drugs/
7. (pesticide$ or herbicide$ or DDT or fertiliser$ or fertilizer$ or organic or contaminants or contaminate$ or veterinary drug$ or polychlorinated dibenzofuran$ or PCDF$ or polychlorinated dibenzodioxin$ or PCDD$ or polychlorinated biphenyl$ or PCB$ or cadmium or arsenic or chlorinated hydrocarbon$ or microbial contamination$).ti,ab.
8. exp Food Preservation/
9. (mycotoxin$ or aflatoxin$ or pickled or bottled or bottling or canned or canning or vacuum pack$ or refrigerate$ or refrigeration or cured or smoked or preserved or preservatives or nitrosamine or hydrogenation or fortified or additive$ or colouring$ or coloring$ or flavouring$ or flavoring$ or nitrates or nitrites or solvent or solvents or ferment$ or processed or antioxidant$ or genetic modif$ or genetically modif$ or vinyl chloride or packaging or labelling or phthalates).ti,ab.
10. Cookery/
11. (cooking or cooked or grill or grilled or fried or fry or roast or bake or baked or stewing or stewed or casserol$ or broil or broiled or boiled or microwave or microwaved or re-heating or reheating or heating or re-heated or heated or poach or poached or steamed or barbecue$ or chargrill$ or heterocyclic amines or polycyclic aromatic hydrocarbons).ti,ab.
12. exp Dietary Carbohydrates/ or exp Dietary Proteins/ or exp Sweetening Agents/
13. (salt or salting or salted or fiber or fibre or polysaccharide$ or starch or starchy or carbohydrate$ or lipid$ or linoleic acid$ or sterols or stanols or sugar$ or sweetener$ or saccharin$ or aspartame or acesulfame or cyclamates or maltose or mannitol or sorbitol or sucrose or xylitol or cholesterol or protein or proteins or hydrogenated dietary oils or hydrogenated lard or hydrogenated oils).ti,ab.
14. exp Vitamins/
15. (supplements or supplement or vitamin$ or retinol or carotenoid$ or tocopherol or folate$ or folic acid or methionine or riboflavin or thiamine or niacin or pyridoxine or cobalamin or mineral$ or sodium or iron or calcium or selenium or iodine or magnesium or potassium or zinc or copper or phosphorus or manganese or chromium or phytochemical or allium or

isothiocyanate$ or glucosinolate$ or indoles or polyphenol$ or phytoestrogen$ or genistein or saponin$ or coumarin$).ti,ab.
16. Physical Fitness/ or exp Exertion/ or exp Physical Endurance/ or Walking/
17. (recreational activit$ or household activit$ or occupational activit$ or physical activit$ or physical inactivit$ or exercise or exercising or energy intake or energy expenditure or energy balance or energy density).ti,ab.
18. exp Growth/ or exp Anthropometry/ or exp Body Composition/ or exp Body Constitution/
19. (weight loss or weight gain or anthropometry or birth weight or birthweight or birth-weight or child development or height or body composition or body mass or BMI or obesity or obese or overweight or over-weight or over weight or skinfold measurement$ or skinfold thickness or DEXA or bio-impedence or waist circumference or hip circumference or waist hip ratio$).ti,ab.
20. or/1-19
21. animals/ not (humans/ and animals/)
22. 20 not 21
23. meta-analysis.pt,ti,ab,sh.
24. (meta anal$ or metaanal$).ti,ab,sh.
25. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ti,ab,sh.
26. (medline or embase or index medicus).ti,ab.
27. ((pool$ or combined or combining) adj (data or trials or studies or results)).ti,ab.
28. 25 or 26 or 27
29. review.pt,sh.
30. 28 and 29
31. 23 or 24
32. 30 or 31
33. exp Neoplasms/pc [Prevention & Control]
34. ((cancer or carcinoma$ or neoplasm$) adj3 (prevent$ or reduc$)).tw.
35. Breast Neoplasms/
36. exp Colorectal Neoplasms/
37. exp Ovarian Neoplasms/
38. exp Prostatic Neoplasms/
39. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
40. or/33-39
41. 22 and 32 and 40
42. limit 41 to english language
43. limit 42 to ed=20060101-20080425

Ovid-Medline

1. Mass Screening/
2. Smoking Cessation/
3. Alcohol Drinking/
4. Chemoprevention/
5. chemoprevention.ti.
6. (surveillance or screening).ti.
7. Primary Prevention/

8. Preventive Medicine/
9. Preventive Health Services/
10. (prophylactic or preventive or risk reduc$).ti.
11. risk reduction behavior/
12. "Referral and Consultation"/
13. medical consultation.ti.
14. (health adj3 consultation).ti.
15. or/1-14
16. Breast Neoplasms/
17. exp Colorectal Neoplasms/
18. exp Prostatic Neoplasms/
19. exp Ovarian Neoplasms/
20. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
21. or/16-20
22. self exam$.ti.
23. Breast Self-Examination/
24. exp Mammography/
25. mammog$.ti.
26. Ovariectomy/
27. risk reduction mastectomy.ti.
28. ((prophylactic or preventive or risk reduc$) adj3 (mastectomy or oophorectomy or ovariectomy)).tw.
29. ((magnetic resonance imaging or mri) adj3 breast).ti.
30. breast exam$.ti.
31. (ovarian adj3 screening).ti.
32. exp Contraceptives, Oral/
33. tamoxifen/ or raloxifene/ or toremifene/
34. (tamoxifen or raloxifene or toremifene or fareston).ti.
35. or/22-34
36. Breast Neoplasms/
37. (breast adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
38. exp Ovarian Neoplasms/
39. (ovar$ adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
40. or/36-39
41. 35 and 40
42. Fenretinide/
43. Finasteride/
44. (Fenretinide or Finasteride or proscar).ti.
45. Digital Rectal Examination/
46. Toremifene/
47. fareston.ti.
48. (avodart or dutasteride).ti.
49. Prostate-Specific Antigen/
50. (psa adj3 test$).ti.
51. prostate specific antigen.ti.

52. or/42-51
53. exp Prostatic Neoplasms/
54. (prostat$ adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
55. or/53-54
56. 52 and 55
57. Digital Rectal Examination/
58. f?ecal occult blood test$.ti.
59. (FOBT or fob test$).ti.
60. colonoscopy/ or sigmoidoscopy/
61. (sigmoidoscopy or colonoscopy).ti.
62. Hormone Replacement Therapy/
63. hrt.ti.
64. exp Anti-Inflammatory Agents, Non-Steroidal/
65. NSAID?.ti.
66. (nonsteroidal adj3 inflammatory).ti.
67. exp Hydroxymethylglutaryl-CoA Reductase Inhibitors/
68. HMG-CoA reductase inhibitors.ti.
69. statins.ti.
70. or/57-69
71. exp Colorectal Neoplasms/
72. ((colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
73. or/71-72
74. 70 and 73
75. genetic services/ or genetic counseling/ or genetic screening/
76. 21 and 75
77. 15 and 21
78. 41 or 56 or 74 or 76 or 77
79. meta-analysis.pt,ti,ab,sh.
80. (meta anal$ or metaanal$).ti,ab,sh.
81. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ti.
82. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ab.
83. (medline or embase or index medicus).ti,ab.
84. ((pool$ or combined or combining) adj (data or trials or studies or results)).ti,ab.
85. or/82-84
86. review.pt,sh.
87. 85 and 86
88. 79 or 80 or 81 or 87
89. 78 and 88
90. limit 89 to english language
91. limit 90 to yr="2000 - 2008"
92. limit 90 to yr="2003 - 2008"

Ovid-EMBASE

1. exp nutrition/
2. (diet or diets or dietetic or dietary or eating or intake or nutrient$ or nutrition or vegetarian$ or vegan$ or "seventh day adventist" or macrobiotic or breastfeed$ or breast feed$ or breastfed or breast fed or breastmilk or breast milk).ti,ab.
3. (food$ or cereal$ or grain$ or granary or wholegrain or wholewheat or roots or plantain$ or tuber or tubers or vegetable$ or fruit$ or pulses or beans or lentils or chickpeas or legume$ or soy or soya or nut or nuts or peanut$ or groundnut$ or seeds or meat or beef or pork or lamb or poultry or chicken or turkey or duck or fish or fat or fats or fatty or egg or eggs or bread or oils or shellfish or seafood or sugar or syrup or dairy or milk or herbs or spices or chilli or chillis or pepper$ or condiments).ti,ab.
4. (fluid intake or water or drinks or drinking or tea or coffee or caffeine or juice or beer or spirits or liquor or wine or alcohol or alcoholic or beverage$ or ethanol or yerba mate or ilex paraguariensis).ti,ab.
5. exp Fertilizer/
6. exp Pesticide/
7. Veterinary Drug/
8. (pesticide$ or herbicide$ or DDT or fertiliser$ or fertilizer$ or organic or contaminants or contaminate$ or veterinary drug$ or polychlorinated dibenzofuran$ or PCDF$ or polychlorinated dibenzodioxin$ or PCDD$ or polychlorinated biphenyl$ or PCB$ or cadmium or arsenic or chlorinated hydrocarbon$ or microbial contamination$).ti,ab.
9. exp food preservation/
10. (mycotoxin$ or aflatoxin$ or pickled or bottled or bottling or canned or canning or vacuum pack$ or refrigerate$ or refrigeration or cured or smoked or preserved or preservatives or nitrosamine or hydrogenation or fortified or additive$ or colouring$ or coloring$ or flavouring$ or flavoring$ or nitrates or nitrites or solvent or solvents or ferment$ or processed or antioxidant$ or genetic modif$ or genetically modif$ or vinyl chloride or packaging or labelling or phthalates).ti,ab.
11. cooking/
12. (cooking or cooked or grill or grilled or fried or fry or roast or bake or baked or stewing or stewed or casserol$ or broil or broiled or boiled or microwave or microwaved or re-heating or reheating or heating or re-heated or heated or poach or poached or steamed or barbecue$ or chargrill$ or heterocyclic amines or polycyclic aromatic hydrocarbons).ti,ab.
13. *Carbohydrate/
14. exp "peptides and proteins"/ or protein/
15. (salt or salting or salted or fiber or fibre or polysaccharide$ or starch or starchy or carbohydrate$ or lipid$ or linoleic acid$ or sterols or stanols or sugar$ or sweetener$ or saccharin$ or aspartame or acesulfame or cyclamates or maltose or mannitol or sorbitol or sucrose or xylitol or cholesterol or protein or proteins or hydrogenated dietary oils or hydrogenated lard or hydrogenated oils).ti,ab.
16. exp Vitamin/
17. (supplements or supplement or vitamin$ or retinol or carotenoid$ or tocopherol or folate$ or folic acid or methionine or riboflavin or thiamine or niacin or pyridoxine or cobalamin or mineral$ or sodium or iron or calcium or selenium or iodine or magnesium or potassium or zinc or copper or phosphorus or manganese or chromium or phytochemical or allium or

isothiocyanate$ or glucosinolate$ or indoles or polyphenol$ or phytoestrogen$ or genistein or saponin$ or coumarin$).ti,ab.
18. exp "physical activity, capacity and performance"/
19. (recreational activit$ or household activit$ or occupational activit$ or physical activit$ or physical inactivit$ or exercise or exercising or energy intake or energy expenditure or energy balance or energy density).ti,ab.
20. growth/ or exp body growth/
21. anthropometry/
22. exp body composition/
23. body constitution/
24. (weight loss or weight gain or anthropometry or birth weight or birthweight or birth-weight or child development or height or body composition or body mass or BMI or obesity or obese or overweight or over-weight or over weight or skinfold measurement$ or skinfold thickness or DEXA or bio-impedence or waist circumference or hip circumference or waist hip ratio$).ti,ab.
25. or/1-24
26. meta-analysis.ti,ab,sh.
27. (meta anal$ or metaanal$).ti,ab,sh.
28. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ti,ab,sh.
29. (medline or embase or index medicus).ti,ab.
30. ((pool$ or combined or combining) adj (data or trials or studies or results)).ti,ab.
31. 28 or 29 or 30
32. review.pt,sh.
33. 31 and 32
34. 26 or 27 or 33
35. exp Breast Cancer/
36. exp Colon Cancer/
37. exp Ovary Cancer/
38. exp Prostate Cancer/
39. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
40. exp Neoplasm/pc [Prevention]
41. cancer prevention/
42. ((cancer or carcinoma$ or neoplasm$ or tumo?r$) adj3 (prevent$ or reduc$)).tw.
43. or/35-42
44. 25 and 34 and 43
45. limit 44 to english language
46. animal/ not (human/ and animal/)
47. 45 not 46
48. limit 47 to em=200601-200817

Ovid-EMBASE

1. cancer screening/
2. genetic services/ or genetic counseling/ or genetic screening/
3. prophylaxis/ or breast care/ or cancer prevention/ or chemoprophylaxis/ or periodic medical examination/ or personal monitoring/ or secondary prevention/ or smoking cessation/

4. alcohol abstinence/ or behavioral risk factor surveillance system/ or drinking behavior/ or risk reduction/
5. (chemoprevention or chemoprophylaxis).ti.
6. (surveillance or screening).ti.
7. disease surveillance/
8. PREVENTIVE HEALTH SERVICE/ or PREVENTIVE MEDICINE/
9. (prophylactic or preventive or risk reduc$).ti.
10. patient referral/
11. medical consultation.ti.
12. (health adj3 consultation).ti.
13. or/1-12
14. exp Breast Cancer/
15. exp Colon Cancer/
16. exp Ovary Cancer/
17. exp Prostate Cancer/
18. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
19. or/14-18
20. exp breast examination/
21. self exam$.ti.
22. Ovariectomy/
23. exp mastectomy/
24. mammog$.ti.
25. ((prophylactic or preventive or risk reduc$) adj3 (mastectomy or oophorectomy or ovariectomy)).tw.
26. ((magnetic resonance imaging or mri) adj3 breast).ti.
27. breast exam$.ti.
28. (ovarian adj3 screening).ti.
29. exp Oral Contraceptive Agent/
30. raloxifene/ or tamoxifen/ or toremifene/
31. (tamoxifen or raloxifene or toremifene or fareston).ti.
32. or/20-31
33. exp Breast Cancer/
34. (breast adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
35. exp Ovary Cancer/
36. (ovar$ adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
37. or/33-36
38. 32 and 37
39. Fenretinide/
40. Finasteride/
41. (Fenretinide or Finasteride or proscar).ti.
42. digital rectal examination/
43. Toremifene/
44. fareston.ti.
45. (avodart or dutasteride).ti.
46. Prostate Specific Antigen/

47. (psa adj3 test$).ti.
48. prostate specific antigen.ti.
49. or/39-48
50. exp Prostate Cancer/
51. (prostat$ adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
52. or/50-51
53. 49 and 52
54. digital rectal examination/
55. f?ecal occult blood test$.ti.
56. (FOBT or fob test$).ti.
57. colonoscopy/ or sigmoidoscopy/
58. hormone replacement therapy.ti.
59. hrt.ti.
60. exp Hormone Substitution/
61. exp Nonsteroid Antiinflammatory Agent/
62. NSAID?.ti.
63. (nonsteroidal adj3 inflammatory).ti.
64. exp Hydroxymethylglutaryl Coenzyme a Reductase Inhibitor/
65. HMG-CoA reductase inhibitors.ti.
66. statins.ti.
67. or/54-66
68. exp Colon Cancer/
69. ((colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
70. or/68-69
71. 67 and 70
72. 13 and 19
73. 38 or 53 or 71 or 72
74. meta analysis/
75. meta-analysis.ti,ab.
76. (meta anal$ or metaanal$).ti,ab.
77. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ti.
78. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ab.
79. (medline or embase or index medicus).ti,ab.
80. ((pool$ or combined or combining) adj (data or trials or studies or results)).ti,ab.
81. or/78-80
82. review.pt,sh.
83. 81 and 82
84. or/74-77
85. 83 or 84
86. 73 and 85
87. limit 86 to english language
88. limit 87 to yr="2000 - 2008"
89. limit 87 to yr="2003 - 2008"

Ovid-CINAHL

1. Diet Therapy/
2. exp Nutrition/
3. (diet or diets or dietetic or dietary or eating or intake or nutrient$ or nutrition or vegetarian$ or vegan$ or "seventh day adventist" or macrobiotic or breastfeed$ or breast feed$ or breastfed or breast fed or breastmilk or breast milk).ti,ab.
4. exp "food and beverages"/ or food/
5. (food$ or cereal$ or grain$ or granary or wholegrain or wholewheat or roots or plantain$ or tuber or tubers or vegetable$ or fruit$ or pulses or beans or lentils or chickpeas or legume$ or soy or soya or nut or nuts or peanut$ or groundnut$ or seeds or meat or beef or pork or lamb or poultry or chicken or turkey or duck or fish or fat or fats or fatty or egg or eggs or bread or oils or shellfish or seafood or sugar or syrup or dairy or milk or herbs or spices or chilli or chillis or pepper$ or condiments).ti,ab.
6. (fluid intake or water or drinks or drinking or tea or coffee or caffeine or juice or beer or spirits or liquor or wine or alcohol or alcoholic or beverage$ or ethanol or yerba mate or ilex paraguariensis).ti,ab.
7. exp Pesticides/
8. Veterinary Medicine/
9. (pesticide$ or herbicide$ or DDT or fertiliser$ or fertilizer$ or organic or contaminants or contaminate$ or veterinary drug$ or polychlorinated dibenzofuran$ or PCDF$ or polychlorinated dibenzodioxin$ or PCDD$ or polychlorinated biphenyl$ or PCB$ or cadmium or arsenic or chlorinated hydrocarbon$ or microbial contamination$).ti,ab.
10. exp Food Preservation/
11. (mycotoxin$ or aflatoxin$ or pickled or bottled or bottling or canned or canning or vacuum pack$ or refrigerate$ or refrigeration or cured or smoked or preserved or preservatives or nitrosamine or hydrogenation or fortified or additive$ or colouring$ or coloring$ or flavouring$ or flavoring$ or nitrates or nitrites or solvent or solvents or ferment$ or processed or antioxidant$ or genetic modif$ or genetically modif$ or vinyl chloride or packaging or labelling or phthalates).ti,ab.
12. Cooking/
13. (cooking or cooked or grill or grilled or fried or fry or roast or bake or baked or stewing or stewed or casserol$ or broil or broiled or boiled or microwave or microwaved or re-heating or reheating or heating or re-heated or heated or poach or poached or steamed or barbecue$ or chargrill$ or heterocyclic amines or polycyclic aromatic hydrocarbons).ti,ab.
14. exp Dietary Carbohydrates/
15. exp Dietary Proteins/
16. exp Sweetening Agents/
17. (salt or salting or salted or fiber or fibre or polysaccharide$ or starch or starchy or carbohydrate$ or lipid$ or linoleic acid$ or sterols or stanols or sugar$ or sweetener$ or saccharin$ or aspartame or acesulfame or cyclamates or maltose or mannitol or sorbitol or sucrose or xylitol or cholesterol or protein or proteins or hydrogenated dietary oils or hydrogenated lard or hydrogenated oils).ti,ab.
18. exp Vitamins/
19. (supplements or supplement or vitamin$ or retinol or carotenoid$ or tocopherol or folate$ or folic acid or methionine or riboflavin or thiamine or niacin or pyridoxine or cobalamin or mineral$ or sodium or iron or calcium or selenium or iodine or magnesium or potassium or

zinc or copper or phosphorus or manganese or chromium or phytochemical or allium or isothiocyanate$ or glucosinolate$ or indoles or polyphenol$ or phytoestrogen$ or genistein or saponin$ or coumarin$).ti,ab.
20. Physical Fitness/
21. exp Exertion/
22. Walking/
23. (recreational activit$ or household activit$ or occupational activit$ or physical activit$ or physical inactivit$ or exercise or exercising or energy intake or energy expenditure or energy balance or energy density).ti,ab.
24. exp Growth/
25. exp "Body Weights and Measures"/
26. exp Body Composition/
27. exp Body Constitution/
28. (weight loss or weight gain or anthropometry or birth weight or birthweight or birth-weight or child development or height or body composition or body mass or BMI or obesity or obese or overweight or over-weight or over weight or skinfold measurement$ or skinfold thickness or DEXA or bio-impedence or waist circumference or hip circumference or waist hip ratio$).ti,ab.
29. or/1-28
30. meta-analysis.ti,ab,sh.
31. (meta anal$ or metaanal$).ti,ab,sh.
32. systematic review.pt.
33. systematic review.ti.
34. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ti,ab,sh.
35. (medline or embase or index medicus).ti,ab.
36. ((pool$ or combined or combining) adj (data or trials or studies or results)).ti,ab.
37. 34 or 35 or 36
38. review.pt,sh.
39. 37 and 38
40. 30 or 31 or 32 or 33
41. 39 or 40
42. exp Breast Neoplasms/
43. exp Colorectal Neoplasms/
44. exp Ovarian Neoplasms/
45. exp Prostatic Neoplasms/
46. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
47. or/42-46
48. 29 and 41 and 47
49. limit 48 to ew=2006$
50. limit 48 to ew=2007$
51. limit 48 to ew=2008$
52. 49 or 50 or 51
53. limit 52 to english

Ovid-CINAHL

1. cancer screening/ or genetic screening/
2. Genetic Counseling/
3. Chemoprevention/
4. "Referral and Consultation"/
5. Smoking Cessation/
6. Alcohol Drinking/
7. (chemoprevention or chemoprophylaxis).ti.
8. Disease Surveillance/
9. (surveillance or screening).ti.
10. Preventive Health Care/
11. (prophylactic or preventive or risk reduc$).ti.
12. medical consultation.ti.
13. (health adj3 consultation).ti.
14. Risk Management/
15. or/1-14
16. Breast Care/
17. breast examination/ or breast self-examination/
18. self exam$.ti.
19. Oophorectomy/
20. Mastectomy/
21. Mammography/
22. mammog$.ti.
23. ((prophylactic or preventive or risk reduc$) adj3 (mastectomy or oophorectomy or ovariectomy)).tw.
24. ((magnetic resonance imaging or mri) adj3 breast).ti.
25. breast exam$.ti.
26. (ovarian adj3 screening).ti.
27. exp Contraceptives, Oral/
28. raloxifene/ or tamoxifen/
29. (tamoxifen or raloxifene or toremifene or fareston).ti.
30. or/16-29
31. exp Breast Neoplasms/
32. exp Ovarian Neoplasms/
33. (breast adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
34. (ovar$ adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
35. or/31-34
36. 30 and 35
37. Finasteride/
38. (Fenretinide or Finasteride or proscar).ti.
39. Digital Rectal Examination/
40. Toremifene.ti.
41. fareston.ti.
42. (avodart or dutasteride).ti.
43. Prostate-Specific Antigen/
44. (psa adj3 test$).ti.

45. prostate specific antigen.ti.
46. or/37-45
47. exp Prostatic Neoplasms/
48. (prostat$ adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
49. or/47-48
50. 46 and 49
51. Digital Rectal Examination/
52. f?ecal occult blood test$.ti.
53. (FOBT or fob test$).ti.
54. colonoscopy/ or sigmoidoscopy/
55. Hormone Replacement Therapy/
56. hormone replacement therapy.ti.
57. hrt.ti.
58. exp Antiinflammatory Agents, Non-Steroidal/
59. NSAID?.ti.
60. (nonsteroidal adj3 inflammatory).ti.
61. exp Statins/
62. HMG-CoA reductase inhibitors.ti.
63. statins.ti.
64. or/51-63
65. exp Colorectal Neoplasms/
66. ((colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
67. or/65-66
68. 64 and 67
69. exp Breast Neoplasms/
70. exp Colorectal Neoplasms/
71. exp Prostatic Neoplasms/
72. exp Ovarian Neoplasms/
73. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti.
74. or/69-73
75. 15 and 74
76. 36 or 50 or 68 or 75
77. Meta Analysis/
78. (meta anal$ or metaanal$).ti,ab.
79. meta-analysis.ti,ab.
80. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ti.
81. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ab.
82. (medline or embase or index medicus).ti,ab.
83. ((pool$ or combined or combining) adj (data or trials or studies or results)).ti,ab.
84. or/81-83
85. review.pt,sh.
86. 84 and 85
87. "Systematic Review"/
88. systematic review.pt.
89. 78 or 79 or 80 or 86 or 87 or 88

90. 76 and 89
91. limit 90 to english
92. limit 91 to yr="2000 - 2008"
93. limit 91 to yr="2003 - 2008

Ovid-CDSR

1. (diet or diets or dietetic or dietary or eating or intake or nutrient$ or nutrition or vegetarian$ or vegan$ or "seventh day adventist" or macrobiotic or breastfeed$ or breast feed$ or breastfed or breast fed or breastmilk or breast milk).ti,ab.
2. (food$ or cereal$ or grain$ or granary or wholegrain or wholewheat or roots or plantain$ or tuber or tubers or vegetable$ or fruit$ or pulses or beans or lentils or chickpeas or legume$ or soy or soya or nut or nuts or peanut$ or groundnut$ or seeds or meat or beef or pork or lamb or poultry or chicken or turkey or duck or fish or fat or fats or fatty or egg or eggs or bread or oils or shellfish or seafood or sugar or syrup or dairy or milk or herbs or spices or chilli or chillis or pepper$ or condiments).ti,ab.
3. (fluid intake or water or drinks or drinking or tea or coffee or caffeine or juice or beer or spirits or liquor or wine or alcohol or alcoholic or beverage$ or ethanol or yerba mate or ilex paraguariensis).ti,ab.
4. (pesticide$ or herbicide$ or DDT or fertiliser$ or fertilizer$ or organic or contaminants or contaminate$ or veterinary drug$ or polychlorinated dibenzofuran$ or PCDF$ or polychlorinated dibenzodioxin$ or PCDD$ or polychlorinated biphenyl$ or PCB$ or cadmium or arsenic or chlorinated hydrocarbon$ or microbial contamination$).ti,ab.
5. (mycotoxin$ or aflatoxin$ or pickled or bottled or bottling or canned or canning or vacuum pack$ or refrigerate$ or refrigeration or cured or smoked or preserved or preservatives or nitrosamine or hydrogenation or fortified or additive$ or colouring$ or coloring$ or flavouring$ or flavoring$ or nitrates or nitrites or solvent or solvents or ferment$ or processed or antioxidant$ or genetic modif$ or genetically modif$ or vinyl chloride or packaging or labelling or phthalates).ti,ab.
6. (cooking or cooked or grill or grilled or fried or fry or roast or bake or baked or stewing or stewed or casserol$ or broil or broiled or boiled or microwave or microwaved or re-heating or reheating or heating or re-heated or heated or poach or poached or steamed or barbecue$ or chargrill$ or heterocyclic amines or polycyclic aromatic hydrocarbons).ti,ab.
7. (salt or salting or salted or fiber or fibre or polysaccharide$ or starch or starchy or carbohydrate$ or lipid$ or linoleic acid$ or sterols or stanols or sugar$ or sweetener$ or saccharin$ or aspartame or acesulfame or cyclamates or maltose or mannitol or sorbitol or sucrose or xylitol or cholesterol or protein or proteins or hydrogenated dietary oils or hydrogenated lard or hydrogenated oils).ti,ab.
8. (supplements or supplement or vitamin$ or retinol or carotenoid$ or tocopherol or folate$ or folic acid or methionine or riboflavin or thiamine or niacin or pyridoxine or cobalamin or mineral$ or sodium or iron or calcium or selenium or iodine or magnesium or potassium or zinc or copper or phosphorus or manganese or chromium or phytochemical or allium or isothiocyanate$ or glucosinolate$ or indoles or polyphenol$ or phytoestrogen$ or genistein or saponin$ or coumarin$).ti,ab.
9. (recreational activit$ or household activit$ or occupational activit$ or physical activit$ or physical inactivit$ or exercise or exercising or energy intake or energy expenditure or energy balance or energy density).ti,ab.

10. (weight loss or weight gain or anthropometry or birth weight or birthweight or birth-weight or child development or height or body composition or body mass or BMI or obesity or obese or overweight or over-weight or over weight or skinfold measurement$ or skinfold thickness or DEXA or bio-impedence or waist circumference or hip circumference or waist hip ratio$).ti,ab.
11. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
12. or/1-10
13. 11 and 12

Ovid-CDSR

1. chemoprevention.ti.
2. (surveillance or screening).ti.
3. (prophylactic or preventive or risk reduc$).ti.
4. medical consultation.ti.
5. (health adj3 consultation).ti.
6. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
7. self exam$.ti.
8. mammog$.ti.
9. risk reduction mastectomy.ti.
10. ((prophylactic or preventive or risk reduc$) adj3 (mastectomy or oophorectomy or ovariectomy)).tw.
11. ((magnetic resonance imaging or mri) adj3 breast).ti.
12. breast exam$.ti.
13. (ovarian adj3 screening).ti.
14. (tamoxifen or raloxifene or toremifene or fareston).ti.
15. (breast adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
16. (ovar$ adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
17. (Fenretinide or Finasteride or proscar).ti.
18. fareston.ti.
19. (avodart or dutasteride).ti.
20. (psa adj3 test$).ti.
21. prostate specific antigen.ti.
22. (prostat$ adj3 (cancer$ or neoplasm$ or carcinom$)).ti.
23. f?ecal occult blood test$.ti.
24. (FOBT or fob test$).ti.
25. hrt.ti.
26. NSAID?.ti.
27. (nonsteroidal adj3 inflammatory).ti.
28. HMG-CoA reductase inhibitors.ti.
29. statins.ti.
30. ((colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$)).ti,ab.
31. or/1-5
32. or/7-14
33. or/15-16

34. or/17-21
35. or/23-29
36. 6 and 31
37. 33 and 32
38. 22 and 34
39. 35 and 30
40. or/36-39

Question 3

Ovid-Medline

1. family history.ab.
2. Genetic Predisposition to Disease/
3. BRCA$.ti.
4. (relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk).ti.
5. exp Genetic Services/
6. genes, brca1/ or genes, brca2/
7. or/1-6
8. exp breast neoplasms/ or exp colorectal neoplasms/ or exp ovarian neoplasms/ or exp prostatic neoplasms/
9. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
10. *Neoplasms/
11. or/8-10
12. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (factors or behavio?r$ or intention or increase or change or impact)).ti.
13. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (mammography or test$ or screen$ or exercise or physical activity or diet or food or smoking or alcohol or utili?ation or "use")).ti.
14. ((factors or behavio?r$ or intention or increase or change or impact or risk) adj8 (mammography or test$ or screen$ or exercise or physical activity or diet or food or smoking or alcohol or utili?ation or "use")).ti.
15. (uptake or motivation or compliance or adherence or seeking or practices or patterns).ti.
16. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (change? or impact? or modification? or influence or risk)).ti.
17. ((after or following or "because of" or "due to" or "result of") adj9 (genetic test$ or genetic counsel?ing or genetic screening)).ti.
18. ((after or following or "because of" or "due to" or "result of") adj9 (mutation test$ or mutation screen$)).ti.
19. exp Health Behavior/
20. risk reduction behavior/
21. or/12-20
22. 7 and 11 and 21
23. animals/ not (humans/ and animals/)
24. 22 not 23
25. limit 24 to english language
26. (note or comment or editorial).pt.
27. 25 not 26
28. limit 27 to yr="1990 - 2008"

Ovid-EMBASE

1. exp health behavior/
2. behavior change/
3. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (factors or behavio?r$ or intention or increase or change or impact)).ti.
4. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (mammography or test$ or screen$ or exercise or physical activity or diet or food or smoking or alcohol or utili?ation or "use")).ti.
5. ((factors or behavio?r$ or intention or increase or change or impact or risk) adj8 (mammography or test$ or screen$ or exercise or physical activity or diet or food or smoking or alcohol or utili?ation or "use")).ti.
6. (uptake or motivation or compliance or adherence or seeking or practices or patterns).ti.
7. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (change? or impact? or modification? or influence or risk)).ti.
8. ((after or following or "because of" or "due to" or "result of") adj9 (genetic test$ or genetic counsel?ing or genetic screening)).ti.
9. ((after or following or "because of" or "due to" or "result of") adj9 (mutation test$ or mutation screen$)).ti.
10. or/1-9
11. Familial Cancer/
12. exp Breast Cancer/
13. exp Colon Cancer/
14. exp Ovary Cancer/
15. exp Prostate Cancer/
16. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
17. *Cancer/
18. or/11-17
19. genetic predisposition/ or genetic susceptibility/
20. family history/
21. (relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk).ti.
22. exp genetic service/
23. brca1 protein/ or brca2 protein/
24. family history.ab.
25. Familial Cancer/
26. BRCA$.ti.
27. or/19-26
28. 10 and 18 and 27
29. limit 28 to human
30. limit 29 to english language
31. (note or editorial).pt.
32. 30 not 31
33. limit 32 to yr="1990 - 2008"

Ovid-CCRT

1. family history.ab.
2. Genetic Predisposition to Disease/
3. BRCA$.ti.
4. (relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk).ti.
5. exp Genetic Services/
6. genes, brca1/ or genes, brca2/
7. or/1-6
8. exp breast neoplasms/ or exp colorectal neoplasms/ or exp ovarian neoplasms/ or exp prostatic neoplasms/
9. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
10. *Neoplasms/
11. or/8-10
12. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (factors or behavio?r$ or intention or increase or change or impact)).ti.
13. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (mammography or test$ or screen$ or exercise or physical activity or diet or food or smoking or alcohol or utili?ation or "use")).ti.
14. ((factors or behavio?r$ or intention or increase or change or impact or risk) adj8 (mammography or test$ or screen$ or exercise or physical activity or diet or food or smoking or alcohol or utili?ation or "use")).ti.
15. (uptake or motivation or compliance or adherence or seeking or practices or patterns).ti.
16. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (change? or impact? or modification? or influence or risk)).ti.
17. ((after or following or "because of" or "due to" or "result of") adj9 (genetic test$ or genetic counsel?ing or genetic screening)).ti.
18. ((after or following or "because of" or "due to" or "result of") adj9 (mutation test$ or mutation screen$)).ti.
19. exp Health Behavior/
20. risk reduction behavior/
21. or/12-20
22. 7 and 11 and 21
23. limit 22 to yr="1990 - 2008"

Ovid-CINAHL

1. health behavior/ or patient compliance/ or medication compliance/ or treatment refusal/ or help seeking behavior/
2. Behavioral Changes/
3. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (factors or behavio?r$ or intention or increase or change or impact)).ti.
4. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (mammography or test$ or screen$ or exercise or physical activity or diet or food or smoking or alcohol or utili?ation or "use")).ti.

5. ((factors or behavio?r$ or intention or increase or change or impact or risk) adj8 (mammography or test$ or screen$ or exercise or physical activity or diet or food or smoking or alcohol or utili?ation or "use")).ti.
6. (uptake or motivation or compliance or adherence or seeking or practices or patterns).ti.
7. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (change? or impact? or modification? or influence or risk)).ti.
8. ((after or following or "because of" or "due to" or "result of") adj9 (genetic test$ or genetic counsel?ing or genetic screening)).ti.
9. ((after or following or "because of" or "due to" or "result of") adj9 (mutation test$ or mutation screen$)).ti.
10. attitude to change/ or attitude to risk/
11. or/1-10
12. exp Breast Neoplasms/
13. exp Colorectal Neoplasms/
14. exp Ovarian Neoplasms/
15. exp Prostatic Neoplasms/
16. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
17. *Neoplasms/pc [Prevention and Control]
18. or/12-17
19. Genetic Screening/ or Genetic Counseling/
20. Family History/
21. (relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk).ti.
22. Genes, BRCA/
23. family history.ab.
24. BRCA$.ti.
25. or/19-24
26. 11 and 18 and 25
27. limit 26 to english
28. limit 27 to yr="1990 - 2008"

Ovid-PsycINFO

1. health behavior/
2. lifestyle changes/ or behavior change/ or health promotion/ or readiness to change/
3. preventive medicine/ or health promotion/
4. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (factors or behavio?r$ or intention or increase or change or impact)).ti.
5. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (mammography or test$ or screen$ or exercise or physical activity or diet or food or smoking or alcohol or utili?ation or "use")).ti.
6. ((factors or behavio?r$ or intention or increase or change or impact or risk) adj8 (mammography or test$ or screen$ or exercise or physical activity or diet or food or smoking or alcohol or utili?ation or "use")).ti.
7. (uptake or motivation or compliance or adherence or seeking or practices or patterns).ti.

8. ((relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk) adj8 (change? or impact? or modification? or influence or risk)).ti.
9. ((after or following or "because of" or "due to" or "result of") adj9 (genetic test$ or genetic counsel?ing or genetic screening)).ti.
10. ((after or following or "because of" or "due to" or "result of") adj9 (mutation test$ or mutation screen$)).ti.
11. risk management/
12. or/1-11
13. at risk populations/ or predisposition/ or "susceptibility (disorders)"/
14. family history.ab.
15. genetics/ or mutations/
16. (relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk).ti.
17. genetic testing/ or genetic counseling/
18. BRCA$.ti.
19. or/13-18
20. breast neoplasms/
21. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
22. *neoplasms/
23. or/20-22
24. 12 and 19 and 23
25. limit 24 to human
26. limit 25 to english language
27. limit 26 to yr="1990 - 2008"

Question 4

Ovid-MEDLINE

1. family history.ab.
2. Genetic Predisposition to Disease/
3. BRCA$.ti.
4. (relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk).ti.
5. exp Genetic Services/
6. genes, brca1/ or genes, brca2/
7. or/1-6
8. exp breast neoplasms/ or exp colorectal neoplasms/ or exp ovarian neoplasms/ or exp prostatic neoplasms/
9. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
10. *Neoplasms/
11. or/8-10
12. anxiety/ or fear/
13. depression/ or stress, psychological/
14. ((worry or anxiety or depression or distress or coping or fear) and cancer).ti.
15. ((psychological or psychosocial) and cancer).ti.
16. (perception and cancer).ti.
17. (impact and cancer).ti.
18. family relations/
19. ((insurance or employment) and cancer).ti.
20. insurance/ or exp insurance, health/
21. insurance.ti.
22. (prejudice or discrimination).ti.
23. (harm? or fatalism).tw.
24. or/12-23
25. employment/ or workplace/
26. prejudice/
27. 24 or 26
28. 7 and 11 and 27
29. animals/ not (humans/ and animals/)
30. 28 not 29
31. (note or comment or editorial).pt.
32. 30 not 31
33. limit 32 to english language
34. limit 33 to yr="1990 - 2008"

Ovid-EMBASE

1. emotional stress/ or family stress/ or interpersonal stress/
2. fear/ or anxiety/
3. exp Depression/
4. ((worry or anxiety or depression or distress or coping or fear) and cancer).ti.

5. ((psychological or psychosocial) and cancer).ti.
6. (perception and cancer).ti.
7. (impact and cancer).ti.
8. family relation/
9. family stress/
10. CANCER FAMILY/
11. ((insurance or employment) and cancer).ti.
12. exp health insurance/
13. insurance/ or exp insurance, health/
14. (prejudice or discrimination).ti.
15. (harm? or fatalism).tw.
16. employment discrimination/
17. or/2-16
18. Familial Cancer/
19. exp Breast Cancer/
20. exp Colon Cancer/
21. exp Ovary Cancer/
22. exp Prostate Cancer/
23. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
24. *Cancer/
25. or/18-24
26. genetic predisposition/ or genetic susceptibility/
27. family history/
28. (relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk).ti.
29. exp genetic service/
30. brca1 protein/ or brca2 protein/
31. family history.ab.
32. Familial Cancer/
33. BRCA$.ti.
34. or/26-33
35. 17 and 25 and 34
36. limit 35 to human
37. (note or comment or editorial).pt.
38. 36 not 37
39. limit 38 to english language
40. limit 39 to yr="1990 - 2008"

OVID-CCRT

1. family history.ab.
2. Genetic Predisposition to Disease/
3. BRCA$.ti.
4. (relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk).ti.
5. exp Genetic Services/

6. genes, brca1/ or genes, brca2/
7. or/1-6
8. exp breast neoplasms/ or exp colorectal neoplasms/ or exp ovarian neoplasms/ or exp prostatic neoplasms/
9. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
10. *Neoplasms/
11. or/8-10
12. anxiety/ or fear/
13. depression/ or stress, psychological/
14. ((worry or anxiety or depression or distress or coping or fear) and cancer).ti.
15. ((psychological or psychosocial) and cancer).ti.
16. (perception and cancer).ti.
17. (impact and cancer).ti.
18. family relations/
19. ((insurance or employment) and cancer).ti.
20. insurance/ or exp insurance, health/
21. insurance.ti.
22. (prejudice or discrimination).ti.
23. (harm? or fatalism).tw.
24. or/12-23
25. employment/ or workplace/
26. prejudice/
27. 24 or 26
28. 7 and 11 and 27
29. limit 28 to yr="1990 - 2008"

Ovid-CINAHL

1. exp 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$ or tumo?r$)).ti,ab.
6. *Neoplasms/pc [Prevention and Control]
7. or/1-6
8. Genetic Screening/ or Genetic Counseling/
9. Family History/
10. (relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk).ti.
11. Genes, BRCA/
12. family history.ab.
13. BRCA$.ti.
14. or/8-13
15. exp Coping/
16. exp "Psychosocial Aspects of Illness"/

17. stress/ or stress, psychological/
18. anxiety/ or depression/
19. Fear/
20. ((worry or anxiety or depression or distress or coping or fear) and cancer).ti.
21. ((psychological or psychosocial) and cancer).ti.
22. (perception and cancer).ti.
23. (impact and cancer).ti.
24. family functioning/ or family coping/ or family relations/
25. ((insurance or employment) and cancer).ti.
26. insurance coverage/ or insurance, health/
27. Discrimination, Employment/
28. (prejudice or discrimination).ti.
29. (harm? or fatalism).tw.
30. or/15-29
31. 7 and 14 and 30
32. limit 31 to english
33. limit 32 to yr="1990 - 2008"

Ovid-PsycINFO

1. coping behavior/ or hopelessness/
2. anxiety/
3. psychological stress/
4. emotional states/ or "depression (emotion)"/
5. fear/
6. ((worry or anxiety or depression or distress or coping or fear) and cancer).ti.
7. ((psychological or psychosocial) and cancer).ti.
8. (perception and cancer).ti.
9. (impact and cancer).ti.
10. distress/
11. family relations/ or interpersonal relationships/
12. emotional adjustment/ or coping behavior/
13. emotional adjustment/
14. or/1-13
15. at risk populations/ or predisposition/ or "susceptibility (disorders)"/
16. family history.ab.
17. genetics/ or mutations/
18. (relative? or genetic or heredit$ or famil$ or inherit$ or high$ risk or "at risk" or increased risk).ti.
19. genetic testing/ or genetic counseling/
20. BRCA$.ti.
21. or/15-20
22. breast neoplasms/
23. ((breast or ovar$ or prostate or colon or colorectal) adj3 (cancer$ or neoplasm$ or carcinom$ or tumo?r$)).ti,ab.
24. *neoplasms/
25. or/22-24

26. 14 and 21 and 25
27. limit 26 to human
28. limit 27 to english language
29. limit 28 to yr="1990 - 2008"

Appendix B – Forms and Guides

Level 1 – Title and Abstract Screening

Family History II, Screening level 1

1. **Is this article non-English or a commentary, editorial or non-systematic review?**

- ☐ Yes (Stop)
- ☐ No (Continue)

2. **Does the citation include any of the following cancers?**

- ☐ Breast/Colorectal/Colon/Rectal/Ovarian/Prostate/Cancer in general (Continue)
- ☐ None of the above (Stop)

3. **Is this a clinical practice guideline?**

- ☐ Yes (Stop)
- ☐ No (Continue)

4. **Is this a systematic review or meta-analysis?**

- ☐ Not a systematic review or meta-analysis (Continue)
- ☐ A systematic review or meta-analysis that focuses on an intervention to prevent or reduce the risk of cancer? (Stop)
- ☐ A systematic review or meta-analysis that focuses on family history? (Stop)
- ☐ A systematic review or meta-analysis on another topic? (Stop)

5. **Is this a primary study?**

- ☐ No (Stop)
- ☐ Yes/Can't Tell (Continue)

6. **Is there a reason to believe the citation FOCUSES on one or more of the following 3 topics:** Risk assessment model /risk stratification/risk algorithm **OR** awareness of cancer family history and uptake of preventative measures and/or health behavior **OR** harms or risks for individuals as a result of having their cancer family history taken.

- ☐ Yes (Include)
- ☐ No (Exclude)

Level 2 – Title and Abstract Screening

Family History II, Screening level 2

1. **Is this a cancer clinical practice guideline/recommendation?**

- ☐ Not a clinical practice guideline/recommendation (continue)
- ☐ A clinical practice guideline focus on diagnostic screening techniques (stop)
- ☐ A clinical practice guideline focus on therapeutic agents (stop)
- ☐ A clinical practice guideline focus on surgical procedure (stop)
- ☐ clinical practice guideline focus on genetic testing (stop)
- ☐ It is a clinical practice guideline/recommendation on another topic. (stop)

2. **Is this article a Systematic Review?**

- ☐ Not a systematic review (Continue)
- ☐ A systematic review on behaviors and/or clinical preventive services to change/prevent persons risk for cancer? (Stop)
- ☐ It is a non-systematic review.(Stop)
- ☐ A systematic review on another topic? (Stop)

3.

Is this a citation focused on one of the following topics:

- ☐ Risk assessment model /risk stratification/risk algorithm
- ☐ Is this about uptaking preventative measures and/or behavior change and/or clinical preventive services?
- ☐ Is this about harm/risk of collection of family history or provision of family history based risk information?
- ☐ Is this about harms/risk of genetic testing and/or genetic counseling?
- ☐ No (exclude)

Level 3 – Full Text Screening - Phase I

Family History II, Screening level 3

1. **Does this citation include the following cancers?** (Check all that apply)

- ☐ Breast
- ☐ Ovarian
- ☐ Prostate
- ☐ Colorectal/colon/Rectal
- ☐ Cancer in general
- ☐ None of the above (exclude)

2. **Does this citation describe guidelines/recommendations on diagnoses including risk assessment or risk stratification?**

- ☐ Yes (stop)
- ☐ No (continue))
- ☐ Other guideline (stop)

3. **Is this a Systematic Review?**

- ☐ Yes (continue)
- ☐ No (GO to Q6)

4. **Is this a systematic review on behaviors and /or clinical preventive services to change/reduce a person's risk for cancer?**

- ☐ Yes (continue)
- ☐ No(stop)

5. **Is this article a Systematic Review on food, nutrition, physical activity, obesity, smoking, alcohol, and the prevention on cancer* published before 2006?** (*see the list)

- ☐ Yes (stop)
- ☐ No (stop)

6. **What type of primary study is this citation?**

- ☐ Cohort
- ☐ Case Control
- ☐ Experimental
- ☐ Others

☐ It is not a primary study (stop)

7. **Does this article describe risk prediction equations/mathematical models OR risk stratification algorithms OR Risk assessment model?**

☐ Yes (continue)

☐ No (Go to Q9)

8. **Is the model based substantially on family history information?**

☐ Yes (stop)

☐ No(stop)

9. **Is this article about the uptake of behaviours or clinical preventive services to reduce risk of cancer?**

☐ Yes (continue)

☐ No (go to Q11)

10. **Does this article mention subjects have been informed of personal risk of breast, colorectal, prostate and/or ovarian cancer based on family history or at least had their family history taken?**

☐ Yes (stop)

☐ No (stop)

11. **Is this article about harm/injury/increased risk for individuals as a result of having their cancer family history taken or the provision of family history based risk information?**

☐ Yes

☐ No

12. **Is this a dissertation, conference abstract, workshop proceeding, or an old guideline?**

☐ Yes (exclude)

Level 4 – Full Text Screening – Phase II

Family History II, Screening level 4 (Q1234G)

1. **what question does this citation answer?**

- ☐ Q1 (Go to Q2---5, Blue color)
- ☉ Q2 (Go to Q6---8, -Green color)
- ☐ Q3 (Go to Q9 ---13, -Red color)
- ☐ Q4 (Go to Q14---16, Purple color)
- ☐ Guideline (Go to Q17---20, Brown color)
- ☐ none of the above

2. **Is the risk/algorithm designed to predict or categorize/stratify risk of cancer or risk of a cancer mutation?** *(Note that a model/ algorithm that focuses on treatment alone, should not be included. If the model/ algorithm also provides information on follow-up after the intervention (for example, surgery, or other treatments) that includes actions or recommendations based on family history)*

- ☐ Yes
- ☐ No (stop)

3. **Is the risk/ algorithm system designed to stratify people into >= 2 risk categories OR provide a numerical point estimate or risk?**

- ☐ Yes
- ☐ No (exclude)
- ☐ Not sure

4. **Does this study undertake validation on a sample that is unselected (for risk of cancer) and representative of a primary care sample?**

- ☐ Yes
- ☐ No (specify reason)
- ☐ Not sure (specify reason)

5. **Reviewer comments:**

6.

For SR what type of study designs are included in its eligibility criteria?

- ☐ Randomized Controlled Trials (RCT)

- ☐ Non-randomized controlled trials
- ☐ Uncontrolled trials (before-after)
- ☐ SR but None of the above
- ☐ Can not tell
- ☐ not a SR

7. **Is the intervention in this review one that is relevant for research question 2 (see list)?**

- ☐ Yes
- ☐ No (stop) ____
- ☐ Not sure ____

8.
Does this paper have the appropriate Outcomes AND unselected POPULATION:

- ☐ Yes
- ☐ Not sure ____
- ☐ No (specify reason) ____

9. **Does the POPULATION of this study include?**

- ☐ General unselected population
- ☐ Primary care patients who are unselected
- ☐ Persons who are participating in a general screening program
- ☐ People with high risk of cancer, as estimated by an existing risk assessment system or a genetics specialist OR Populations sampled from specialist genetics clinics or cancer family clinics OR People who have had a genetic test for a mutation related to one of the cancers of interest OR Persons who have cancer (exclude if any of the above criteria are met)

10. **What is the STUDY DESIGN for this citation?**

- ☐ Randomized Clinical Trial
- ☐ Non-randomized Clinical Trial
- ☐ Before After-study
- ☐ Other (exclude)

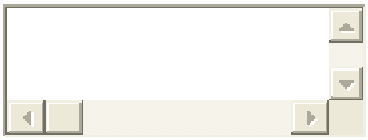
11. **Does the study include the systematic <u>provision</u> of personal risk of breast, colorectal, prostate and/or ovarian cancer based on FAMILY HISTORY?** *(WITH OR WITHOUT Individual advice on appropriate risk reduction behaviors and/or services (where recommended behavior or service was considered standard of care at the time of the study)*

- ☐ Yes (continue)
- ☐ No (exclude)
- ☐ Can't tell

12. **Does this citation also address research Q4?**

- ☐ Yes
- ☐ No
- ☐ Not sure

13. **Reviewer comments:**



14. **What is the study design of this citation?**

- ☐ Randomized Clinical Trial
- ☐ Non-randomized Clinical Trial
- ☐ Before After-study
- ☐ Other (continue to next question))

15. **Does the POPULATION of this study include?**

- ☐ General unselected population.
- ☐ Primary care patients who are unselected
- ☐ Persons who are participating in a general screening program
- ☐ People with high risk of cancer, as estimated by an existing risk assessment system or a genetics specialist OR Populations sampled from specialist genetics clinics or cancer family clinics OR People who have had a genetic test for a mutation related to one of the cancers of interest OR Persons who have cancer (exclude if any of the above criteria are met)

16. **Does this paper have the appropriate Outcomes?**

- ☐ Yes
- ☐ Not sure (specify)
- ☐ No (specify reason)

17. **Is one of the aims of the guideline designed to predict or categorize/stratify risk of cancer or risk of a cancer mutation AND does the guideline include a family history component?**

(Note that some guidelines have multiple components (treatment, screening, management) and there must be an explicit indication of collecting cancer family history).

- ☐ Yes
- ☐ No (stop)
- ☐ Not sure

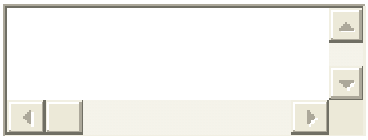
18. **Is the guideline system designed to stratify people into greater than or equal to 2 risk categories OR provide a numerical point estimate or risk?**

- ☐ Yes
- ☐ No (exclude)
- ☐ Not sure

19. **Does this guideline delineate information about the accuracy or validity of the guideline? The accuracy can be expressed as diagnostic accuracy (sensitivity, specificity, positive predictive values, etc) for either predicting cancer or cancer mutation.**

- ☐ Yes
- ☐ No (specify reason) _____
- ☐ Not sure (specify reason) _____

20. **Reviewer comments:**



Family History II, Screening level 1- Guidelines

1. Is this article non-English or a commentary, editorial or NON-systematic review?

- ☐ Yes (Stop)
- ☐ No (Continue)

Instruction:
If the citation is in a language other than English, is a commentary or editorial or is a non-systematic review (i.e. a review that is not systematic) you should answer "YES" and then go on to the next citation (don't forget to click "submit" or your answers won't be recorded).

If the citation is for a PRIMAY study, a clinical practice guideline or a systematic review (or any study type not listed above) you should answer "NO" and then continue screening

2. Does the citation include any one of the following cancers?

- ☐ Breast/Colorectal/Colon/ Rectal/Ovarian/Prostate/Cancer in general (Continue)
- ☐ None of the above (Stop)

Instruction:
Question 2: We are only interested in studies about Breast, Ovarian, Prostate and Colorectal Cancers. If the study does not specify the type of cancer, choose “cancer in general”

3. Is this a cancer clinical practice guideline?

- ☐ Yes (Stop)
- ☐ No (Continue)

4. Is this article a Systematic Review?

- ☐ Not a systematic review (Continue)
- ☐ A systematic review on an intervention to PREVENT, reduce the risk of cancer? (Stop)
- ☐ A systematic review about family history? (Stop)
- ☐ A systematic review on another topic? (Stop)

Instruction 1 for Question 4:
Please note that the word INTERVENTION is used in the generic sense to indicate a lifestyle or service obtained that will result in a **CHANGE** in a person's risk for cancer. This change can be **positive or negative** (e.g. alcohol consumption is associated with an increased risk of some cancers). The review does NOT have to show that the lifestyle change or preventive service CAUSES change in cancer risk, only that it is **ASSOCIATED** with a change in risk.

That means that for both citation A and B below you should choose would choose "A systematic review or meta-analysis that focuses on an intervention to prevent or reduce the risk of cancer?"

A. Low fat eating pattern intervention and risk of colorectal cancer in postmenopausal women: a systematic review
B. Alcohol consumption is associated with an increased risk of distal colon and rectal cancer in Japanese men: a meta-analysis

Instruction 2 for Question 4:
Look carefully for words like "systematic review", "meta analysis", "Cochrane review" or "pooling", or some description of the methods used to assemble papers:
- sort of detailed search info such as describes methods for searching 1 or more databases (MEDLINE, etc)
- discusses inclusion and exclusion criteria

NB:

- This can include people who have had cancer and are taking steps to avoid a RECURRENCE
- Exclude if the intervention is **CLEARLY** USED **ONLY** to TREAT/ MANAGE cancer patients rather than PREVENT recurrences.
- For example, if radiation therapy or drugs are being used in patients with cancer, it is likely that this study is focused on TREATING patients with cancer, not preventing cancer or RECURRENCES.

Examples of common interventions to PREVENT or reduce the risk of cancer (list is partial, include any intervention that you find)

Breast:

Specific behaviors:
- breast self-examination

Specific clinical preventive services:
- annual clinical examination
- mammography
- clinical breast examination
- cancer chemoprevention
- magnetic resonance imaging breast screening (MRI)
- genetic counseling +/- genetic testing
- risk-reduction mastectomy/oophorectomy (RRM/O)

Colorectal:

Specific clinical preventive services:
- Screening/surveillance activities

- FOB test
- sigmoidoscopy
- digital rectal exam
- colonoscopy

- genetic counseling +/- genetic testing

Ovarian:

Specific clinical preventive services:
- genetic counseling +/- genetic testing
- prophylactic oophorectomy
- ovarian screening
- genetic counseling +/- genetic testing

Prostate:

Specific clinical preventive services:
- Screening/surveillance activities:
  - PSA test
  - digital rectal examination
- chemoprevention
- genetic counseling +/- genetic testing

General behaviors for all four cancers:
- regular exercise/physical activity
- high fiber diet
- increased fruit and vegetable consumption
- low fat diet
- smoking cessation
- reduction in alcohol intake
- seeking health care advice

5. Is this a Primary Study?

☐ No (Stop)

☐ Yes (Continue)

☐ Can't Tell (Continue)

•

6. Is there a reason to believe the citation FOCUSES on one or more of the following 3 topics: Risk assessment model /risk stratification/risk algorithm **OR** awareness of cancer family history and uptake of preventative measures and/or health behavior **OR** harms or risks for individuals as a result of having their cancer family history taken.

☐ Yes (Include)

☐ No (Exclude)

Instruction: question 6.
We are including primary studies that focus on one or more of the 3 following topics:

1. Some risk assessment model /risk stratification/risk algorithm tools are listed below. Note **this is only a partial list; include any you find that you think are risk assessment tools.**

- Gail
- Claus
- Tyrer-Cuzick
- Couch
- BRCA-PRO
- UK Cancer Family Study Group
- BOADICEA
- French National agency for health evaluation
- National Breast Cancer Centre (Australia)
- Amsterdam and modified Amsterdam
- Scottish Cancer Group
- MYRIAD (Frank)
- Bethesda
- Manchester
- USPSTF
- FHAT
- Jonker
- Ontario Stratification algorithm

Definition of Risk Assessment tools (models or algorithm)
Models that stratify risk use several different pieces of information. Based on this information patients are categorized into high, medium or low risk for either getting cancer or having a high risk gene (mutation).A tool/ model/ algorithm usually has a name (see provided list) and is almost always used by physicians

2. Awareness of cancer family history and uptake of preventative measures and/or health behaviors

- Include if the abstract states that based on the participants knowing their cancer family history, are evaluated for their uptake of specific actions. These generally include either behavioral changes (e.g. changes in diet or activity level, self-exam) or clinical preventive services (e.g., chemoprevention, prophylactic surgery, screening,).
- Exclude if it is **CLEARLY** an intervention **ONLY** to improve the outcome for those WITH cancer. For example, a mastectomy that is not prophylactic (preventing the cancer from occurring) but is being undertaken to TREAT the cancer. This should be excluded as it is not showing that the preventative measure (i.e. mastectomy) was not undertaken to prevent cancer. Be careful as interventions like Tamoxifen as a treatment versus its use as a prevention measure. We are interested in it with regards to prevention.

- If there is any doubt includes the abstract OR send us a message with your queries.

3. Harms or risks for individuals as a result of having their cancer family history taken.
Examples of HARMS include:

- Psychological impacts like fear, depression, anxiety, family function impacts, discrimination in employment or insurance, fatalism, health problems, quality of life issues, deciding not to have children because of FH
- Behaviour changes due to perception or misperception of risk (i.e. fatalism or thinking you are low risk) examples: someone starts eating a high fat diet or quits exercising because they think they are going to get cancer anyway or because they believe that they aren't at risk.

Exclude articles that

- Focus on the negative impacts of HAVING cancer (there will be quite a few of these). So if spouse leaves because their partner HAS cancer, exclude.
- BUT if they leave because they learned that their partner has a family history of cancer (increased risk real or perceived), include it. If the distinction is unclear err on the side of caution and include it.
- Exclude articles if the harm is clearly secondary for example, if a person has a prophylactic mastectomy because of their family history and has surgical complications. If the distinction is unclear err on the side of caution and include it.
- Any harms that result from having undertaken a preventive measure, like a prophylactic mastectomy followed by surgical complications, should be excluded.

Appendix C – Eligible Studies Extracted and Those Retained But Not Extracted

Table 1. Eligible Studies Extracted and Those Retained But Not Extracted

Retained But Not Extracted	***Superseded by (extracted)***
Huang 2006[1] Huang 2006[2]	Bardia 2008[3]
Moayyedi 2006[4]	Hewitson 2007[5]
Walsh 2003[6]	Hewitson 2007[5]
Bonovas 2007[7] Bonovas 2005[8]	Browning 2007[9]
Hoffmeister 2006[10]	Dubé 2007[11]
Asano 2004[12]	Dubé 2007[11]
Coulter 2006[13]	Alkhenizan 2007[14]
Dale 2006[15]	Browning 2007[9]
Heresbach 2006[16]	Hewitson 2007[5]
Hackshaw 2003[17]	Kosters 2003[18]
	Gotzsche 2006[19]
	Kerr 2007[20]
	Bristol SLR Team 2006 [21]
	Ilic 2006[22]
Eligible, but did not report usable data	
Dutch Review Team, Bakker 2006[23]	
Italian Review Team, Agnoli 2005[24]	
Eligible, but no eligible intervention studies identified	
Mahmud 2004[25]	
Rostom 2007[26]	
Weingarten 2008[27]	
Brett 2005[28]	
Watson 2005[29]	

Reference List for Appendix C – Studies Retained But Not Extracted

1. Huang HY, Caballero B, Chang S et al. Multivitamin/mineral supplements and prevention of chronic disease. Evid Rep Technol Assess No.139, AHRQ Publication No.06-E012. (Prepared by The Johns Hopkins University Evidence-based Practice Center under Contract No.290-02-0018). Rockville, MD: Agency for Healthcare Research and Quality; 2006 May. PM:17764205
2. Huang HY, Caballero B, Chang S, et al. The efficacy and safety of multivitamin and mineral supplement use to prevent cancer and chronic disease in adults: a systematic review for a National Institutes of Health state-of-the-science conference. [Review] [44 refs]. Ann Intern Med 2006;145(5):372-85.
3. Bardia A, Tleyjeh IM, Cerhan JR, et al. Efficacy of antioxidant supplementation in reducing primary cancer incidence and mortality: systematic review and meta-analysis. [Review] [73 refs]. Mayo Clin Proc 2008;83(1):23-34.
4. Moayyedi P, Achkar E. Does fecal occult blood testing really reduce mortality? A reanalysis of systematic review data.[Review] [25 refs]. Am J Gastroenterol 2006;101(2):380-4.
5. Hewitson P, Glasziou P, Irwig L, et al. Screening for colorectal cancer using the faecal occult blood test, Hemoccult.[update of Cochrane Database Syst Rev. 2000;(2):CD001216; PMID: 10796760]. [Review] [46 refs]. Cochrane Database Syst Rev 2007;(1):CD001216
6. Walsh JM, Terdiman JP. Colorectal cancer screening: scientific review.[Review] [105 refs]. JAMA 2003;289(10):1288-96.
7. Bonovas S, Filioussi K, Flordellis CS, et al. Statins and the risk of colorectal cancer: a meta-analysis of 18 studies involving more than 1.5 million patients. J Clin Oncol 2007;25(23):3462-8.
8. Bonovas S, Filioussi K, Tsavaris N, et al. Use of statins and breast cancer: A meta-analysis of seven randomized clinical trials and nine observational studies. J Clin Oncol 2005;23(34):8606-12.
9. Browning DR, Martin RM. Statins and risk of cancer: A systematic review and metaanalysis. Int J Cancer 2007;120(4):833-43.
10. Hoffmeister M, Chang-Claude J, Brenner H. Do older adults using NSAIDs have a reduced risk of colorectal cancer? Drugs Aging 2006;23(6):513-23.
11. Dube C, Rostom A, Lewin G, et al. The use of aspirin for primary prevention of colorectal cancer: a systematic review prepared for the U.S. Preventive Services Task Force. Ann Intern Med 2007;146(5):365-75.
12. Asano TK, McLeod RS. Nonsteroidal anti-inflammatory drugs and aspirin for the prevention of colorectal adenomas and cancer: a systematic review. [Review] [45 refs]. Dis Colon Rectum 2004;47(5):665-73.
13. Coulter ID, Hardy ML, Morton SC, et al. Antioxidants Vitamin C and Vitamin E for the Prevention and Treatment of Cancer. J Gen Intern Med 2006;21(7):735-44.
14. Alkhenizan A, Hafez K. The role of vitamin E in the prevention of cancer: a meta-analysis of randomized controlled trials. Ann Saudi Med 2007;27(6):409-14.
15. Dale KM, Coleman CI, Henyan NN, et al. Statins and cancer risk: a meta-analysis. JAMA 2006;295(1):74-80.
16. Heresbach D, Manfredi S, D'halluin PN, et al. Review in depth and meta-analysis of controlled trials on colorectal cancer screening by faecal occult blood test. [Review] [61 refs]. Eur J Gastroenterol Hepatol 2006;18(4):427-33.
17. Hackshaw AK, Paul EA. Breast self-examination and death from breast cancer: a meta-analysis. Br J Cancer 2003;88(7):1047-53.
18. Kosters JP, Gotzsche PC. Regular self-examination or clinical examination for early detection of breast cancer [Review] [24 refs]. Cochrane Database Syst Rev 2003;(2):CD003373
19. Gotzsche PC, Nielsen M. Screening for breast cancer with mammography. Cochrane Database Syst Rev 2006;(4):CD001877
20. Kerr J, Day P, Broadstock M, et al. Systematic review of the effectiveness of population screening for colorectal cancer. [Review] [28 refs]. N Z Medl Jl 2007;120(1258):U2629
21. Bristol SLR Team 2006. Systematic Literature Review Report. The associations between food, nutrition, physical activity and the risk of prostate cancer and underlying mechanisms. World Cancer Research Fund/American Institute for Cancer Research, Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington, DC: 2006 Jun 30.
22. Ilic D, O'Connor D, Green S, et al. Screening for prostate cancer. Cochrane Database Syst Rev 2006; Issue 3, Art.No.: CD004720.DOI:10.1002/14651858.CD004720.pub 2:
23. Dutch Review Team 2006. Systematic Literature Review Report. The associations between food, nutrition and physical activity and the risk of colorectal cancer and underlying mechanisms. World Cancer Research Fund/American Institute for Cancer Research, Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington, DC: 2007.
24. Italian Review Team 2005. Systematic Literature Review Report. The Associations between Food, Nutrition and Physical Activity and the Risk of Breast Cancer and Underlying Mechanisms. World Cancer Research Fund/American Institute for Cancer Research, Food, Nutrition, Physical

Activity, and the Prevention of Cancer: a Global Perspective. Washington, DC: 2007.
25. Mahmud S, Franco E, Aprikian A. Prostate cancer and use of nonsteroidal anti-inflammatory drugs: systematic review and meta-analysis. [Review] [43 refs]. Br J Cancer 2004;90(1):93-9.
26. Rostom A, Dube C, Lewin G, et al. Nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors for primary prevention of colorectal cancer: a systematic review prepared for the U.S. Preventive Services Task Force. Ann Intern Med 2007;146(5):376-89.
27. Weingarten MA, Zalmanovici A, Yaphe J. Dietary calcium supplementation for preventing colorectal cancer and adenomatous polyps.[update of Cochrane Database Syst Rev. 2005;(3):CD003548; PMID: 16034903]. [Review] [38 refs]. Cochrane Database Syst Rev 2008;(1):CD003548
28. Brett J, Bankhead C, Henderson B, et al. The psychological impact of mammographic screening. A systematic review. [Review] [74 refs]. Psychooncology 2005;14(11):917-38.
29. Watson EK, Henderson BJ, Brett J, et al. The psychological impact of mammographic screening on women with a family history of breast cancer--a systematic review. [Review] [26 refs]. Psychooncology 2005;14(11):939-48.

Appendix D - Excluded Studies

1. Abbadessa G, Santoro A, Claudio PP. 42nd Annual Meeting of the American Society of Clinical Oncology (ASCO) (June 2-6, Atlanta) 2006. Drugs of the Future 2006;31(7):617-23. Excluded: Not an eligible study design, OVID-Embase.
2. Abdel-Fattah M, Zaki A, Bassili A, et al. Breast self-examination practice and its impact on breast cancer diagnosis in Alexandria, Egypt. East Mediterr Health J 2000;6(1):34-40. Excluded: Family history not systematically collected, OVID-Medline.
3. Absetz P, Aro AR, Sutton SR. Experience with breast cancer, pre-screening perceived susceptibility and the psychological impact of screening. Psychooncology 2003;12(4):305-18. Excluded: Family history not systematically collected, OVID-Medline.
4. Abu-Rustum NR, Herbolsheimer H. Breast cancer risk assessment in indigent women at a public hospital. Gynecol Oncol 2001;81(2):287-90. Excluded: Model does not categorize risk or validate, OVID-Medline.
5. ACOG: American College of Obstetricians and Gynecologists. ACOG practice bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 42, April 2003. Breast cancer screening. Obst Gynecol 2003;101(4):821-31. Excluded: Model does not categorize risk or validate, OVID-Medline.
6. ACOG: American College of Obstetricians and Gynecologists. ACOG practice bulletin. Breast cancer screening. Number 42, April 2003. Int J Gynaecol Obstet 2003;81(3):313-23. Excluded: Model does not categorize risk or validate, OVID-Medline.
7. ACOG: American College of Obstetricians and Gynecologists. ACOG committee opinion. Routine cancer screening. Number 247, December 2000. Int J Gynaecol Obstet 2003;82(2):241-5. Excluded: Model does not categorize risk or validate, OVID-Medline.
8. ACOG: American College of Obstetricians and Gynecologists .ACOG Committee on Gynecologic Practice. Committee opinion no. 356: Routine cancer screening. Obstet Gynecol 2006;108(6):1611-3. Excluded: Model does not categorize risk or validate, OVID-Embase.
9. Agrawal A, Fentiman IS. NSAIDs and breast cancer: A possible prevention and treatment strategy. Int J Clin Pract 2008;62(3):444-9. Excluded: Not an eligible study design, OVID-Embase.
10. Ahmed NU, Fort JG, Elzey JD, et al. Empowering factors in repeat mammography: insights from the stories of underserved women. J Ambulatory Care Manage 2004;27(4):348-55. Excluded: Family history not systematically collected, OVID-Medline.
11. Ahmed NU, Fort JG, Elzey JD, et al. Empowering factors for regular mammography screening in under-served populations: pilot survey results in Tennessee.[see comment]. Ethn Dis 2005;15(3):387-94. Excluded: Family history not systematically collected, OVID-Medline.
12. Aiken LS, Fenaughty AM, West SG, et al. Perceived determinants of risk for breast cancer and the relations among objective risk, perceived risk, and screening behavior over time. Womens Health 1995;1(1):27-50. Excluded: Family history not systematically collected, OVID-Medline.
13. Ainsworth PJ, Koscinski D, Fraser BP, et al. Family cancer histories predictive of a high risk of hereditary non-polyposis colorectal cancer associate significantly with a genomic rearrangement in hMSH2 or hMLH1. Clin Genet 2004;66(3):183-8. Excluded: Family history not systematically collected, OVID-Medline.
14. Aktan-Collan K, Mecklin JP, Jarvinen H, et al. Predictive genetic testing for hereditary non-polyposis colorectal cancer: uptake and long-term satisfaction. Int J Cancer 2000;89(1):44-50. Excluded: Not an eligible population, OVID-Medline.
15. Aktan-Collan K, Haukkala A, Pylvanainen K, et al. Direct contact in inviting high-risk members of hereditary colon cancer families to genetic counselling and DNA testing. J Med Genet 2007;44(11):732-8. Excluded: Not an eligible population, OVID-Medline.
16. Alamian A, Rouleau I, Simard J, et al. Use of dietary supplements among women at high risk of hereditary breast and ovarian cancer (HBOC) tested for cancer susceptibility. Nutr Cancer 2006;54(2):157-65. Excluded: Not an eligible population, OVID-Medline.
17. American Cancer Society. American Cancer Society issues redefined breast cancer screening guidelines. Iowa Med 93(5):27-Oct. Excluded: Model does not categorize risk or validate, OVID-Medline.
18. American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 384 November 2007: colonoscopy and colorectal cancer screening and prevention. Obstet Gynecol 2007;110(5):1199-202. Excluded: Model does not categorize risk or validate, OVID-Medline.
19. American Gastroenterological Association. American Gastroenterological Association medical position statement: hereditary colorectal cancer and genetic testing. Gastroenterology 2001;121(1):195-7. Excluded: Model does not categorize risk or validate, OVID-Medline.

20. American Society of Clinical Oncology. 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 Excluded: Model does not categorize risk or validate, OVID-Medline.
21. American Society of Clinical Oncology. American Society of Clinical Oncology policy statement update: genetic testing for cancer susceptibility. J Clin Oncol 2003;21(12):2397-406. Excluded: Model does not categorize risk or validate, OVID-Medline.
22. 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):807-14. Excluded: Model does not categorize risk or validate, OVID-Medline.
23. Andersen MR, Peacock S, Nelson J, et al. Worry about ovarian cancer risk and use of ovarian cancer screening by women at risk for ovarian cancer.[see comment]. Gynecol Oncol 2002;85(1):3-8. Excluded: Family history not systematically collected, OVID-Medline.
24. Andersen MR, Bowen D, Yasui Y, et al. Awareness and concern about ovarian cancer among women at risk because of a family history of breast or ovarian cancer. Am J Obstet Gynecol 2003;189(4:Suppl):Suppl-7.Excluded: Family history not systematically collected, OVID-Medline.
25. Andersen MR, Smith R, Meischke H, et al. Breast cancer worry and mammography use by women with and without a family history in a population-based sample. Cancer Epidemiol Biomarkers Prev 2003;12(4):314-20. Excluded: Family history not systematically collected, OVID-Medline.
26. Andersen MR, Nelson J, Peacock S, et al. Worry about ovarian cancer risk and use of screening by high-risk women: how you recruit affects what you find. Am J Med Genet 2004;Part(2):130-5. Excluded: Family history not systematically collected, OVID-Medline.
27. Anderson BO. Global Summit Consensus Conference on International Breast Health Care: Guidelines for countries with limited resources. Breast J 2003;9(SUPPL. 2):S40-S41 Excluded: Not an eligible study design, OVID-Embase.
28. Andreeva VA, Unger JB, Pentz MA. Breast cancer among immigrants: A systematic review and new research directions. J Immigr Minor Health 2007;9(4):307-22. Excluded: Not an eligible population, OVID-Embase.
29. Andrykowski MA, Zhang M, Pavlik EJ, et al. Factors associated with return for routine annual screening in an ovarian cancer screening program. Gynecol Oncol 2007;104(3):695-701. Excluded: Not an eligible study design, OVID-Medline.
30. Anonymous. Colonoscopy in the screening and surveillance of individuals at increased risk for colorectal cancer. American Society for Gastrointestinal Endoscopy. Gastrointest Endosc 1998;48(6):676-8. Excluded: Model does not categorize risk or validate, OVID-Medline.
31. Anonymous. Bilateral prophylactic mastectomy in women with an increased risk of breast cancer. Tecnologica MAP 1999;Suppl:3-6. Excluded: Family history not systematically collected, OVID-Medline.
32. Anonymous. Assessing hereditary breast cancer risk. Cancer Pract 1999;7(6):279-84. Excluded: Family history not systematically collected, OVID-Medline.
33. Anonymous. Cancer predisposition genetic testing and risk assessment counseling. Oncology Nursing Society. Oncol Nurs Forum 2000;27(9):1349 Excluded: Not an eligible study design, OVID-Medline.
34. Anonymous. Anxiety, depression in women at high risk for breast Cancer. Oncology News International 2002;11(5):50 Excluded: Not an eligible study design, OVID-Cinahl.
35. Anonymous. Colorectal cancer screening: New recommendations. Consultant 2003;43(3):318-20. Excluded: Not an eligible intervention or outcome, OVID-Embase.
36. Anonymous. Simple programme predicts who is most at risk of breast cancer. S Afr Med J 2004;Suid-Afrikaanse(5):337-8. Excluded: Not an eligible study design, OVID-Medline.
37. Anonymous. The management of colorectal cancers. Eff Health Care 2004;8(3):1-11. Excluded: Model does not categorize risk or validate, OVID-Cinahl.
38. Anonymous. Diseases: Management of patients presenting the first signs or a history of solid malignancy? Joint Bone Spine 2005;72(Suppl. 1):S31-S38 Excluded: Not an eligible intervention or outcome, OVID-Embase.
39. Anonymous. Vitamins, minerals, supplements and dietary approaches. Focus on Alternative and Complementary Therapies 2005;10(3):227-32. Excluded: Not an eligible study design, OVID-Embase.
40. Anonymous. Updated guideline provides recommendations for surveillance after colorectal cancer. ASCO News & Forum 2006;1(1):20-1. Excluded: Not an eligible intervention or outcome, OVID-Cinahl.
41. Anonymous. American Cancer Society guidelines still advise yearly mammography for women aged 40 to 49 years. CA Cancer J Clinic 2007;57(4):187-8. Excluded: Not an eligible study design, OVID-Embase.

42. Anonymous. Europe against colorectal cancer: Declaration of Brussels 9 May 2007. Z Gastroenterol 2008;46(SUPPL. 1):S2-S3
Excluded: Not an eligible publication type, OVID-Embase.
43. Antill Y, Reynolds J, Young MA, et al. Risk-reducing surgery in women with familial susceptibility for breast and/or ovarian cancer. Eur J Cancer 2006;42(5):621-8.
Excluded: Family history not systematically collected, OVID-Medline.
44. Antill YC, Reynolds J, Young MA, et al. Screening behavior in women at increased familial risk for breast cancer. Fam Cancer 2006;5(4):359-68.
Excluded: Not an eligible study design, OVID-Medline.
45. 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 Res 2006;8(1):R3
Excluded: Model does not categorize risk or validate, OVID-Medline.
46. Apicella C, Dowty JG, Dite GS, et al. Validation study of the LAMBDA model for predicting the BRCA1 or BRCA2 mutation carrier status of North American Ashkenazi Jewish women. Clin Genet 2007;72(2):87-97.
Excluded: Model does not categorize risk or validate, OVID-Medline.
47. Armstrong C. ACS recommendations on MRI and mammography for breast cancer screening. Am Fam Physician 2007;75(11):1712
Excluded: Model does not categorize risk or validate, OVID-Embase.
48. Armstrong K, Moye E. What is the evidence on screening mammography for women in their 40s? J Fam Pract 2007;56(7):530
Excluded: Model does not categorize risk or validate, OVID-Embase.
49. Armstrong K, Calzone K, Stopfer J, et al. Factors associated with decisions about clinical BRCA1/2 testing. Cancer Epidemiol Biomarkers Prev 2000;9(11):1251-4.
Excluded: Not an eligible study design, OVID-Medline.
50. Armstrong K, Weber B, FitzGerald G, et al. Life insurance and breast cancer risk assessment: adverse selection, genetic testing decisions, and discrimination. Am J Med Genet 2003;Part(3):359-64.
Excluded: Family history not systematically collected, OVID-Medline.
51. Armstrong K, Weber B, Stopfer J, et al. Early use of clinical BRCA1/2 testing: associations with race and breast cancer risk. Am J Med Genet 2003;Part(2):154-60.
Excluded: Not an eligible population, OVID-Medline.
52. Armstrong K, Micco E, Carney A, et al. Racial differences in the use of BRCA1/2 testing among women with a family history of breast or ovarian cancer. JAMA 2005;293(14):1729-36.
Excluded: Family history not systematically collected, OVID-Medline.
53. Armstrong K, Moye E, Williams S, et al. Screening mammography in women 40 to 49 years of age: a systematic review for the American College of Physicians. Ann Intern Med 2007;146(7):516-26.
Excluded: Not an eligible population, OVID-Medline.
54. Asano, TK, McLeod, et al. Vitamins and minerals for the prevention of colorectal adenomas and carcinomas [Protocol]. Cochrane Database Syst Rev 2008;(1):
Excluded: Not an eligible study design, OVID-Cochrane.
55. Asano, TK, McLeod, et al. Dietary fibre for the prevention of colorectal adenomas and carcinomas [Systematic Review]. Cochrane Database Syst Rev 2008;(1):
Excluded: Not an eligible intervention or outcome, OVID-Cochrane.
56. ASCO clinical practice guidelines highlight new strategies for breast cancer surveillance, HER-2 testing. ASCO News Forum 2007;2(1):32-3.
Excluded: Not an eligible intervention or outcome, OVID-Cinahl.
57. Association of Breast Surgery @ BASO Royal College of Surgeons of England. Guidelines for the management of symptomatic breast disease. Eur J Surg Oncol 2005;31(SUPPL.):S1-S21
Excluded: Not an eligible intervention or outcome, OVID-Embase.
58. Astorg P. Dietary n - 6 and n - 3 polyunsaturated fatty acids and prostate cancer risk: A review of epidemiological and experimental evidence. Cancer Causes Control 2004;15(4):367-86.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
59. Audrain J, Schwartz MD, Lerman C, et al. Psychological distress in women seeking genetic counseling for breast-ovarian cancer risk: the contributions of personality and appraisal. Ann Behav Med 1997;19(4):370-7.
Excluded: Family history not systematically collected, OVID-Medline.
60. Aus G, Abbou CC, Bolla M, et al. EAU guidelines on prostate cancer. Eur Urol 2005;48(4):546-51.
Excluded: Model does not categorize risk or validate, OVID-Embase.
61. Azaiza F, Cohen M. Health beliefs and rate of breast cancer screening among Arab women. J Womens Health 2006;15(5):520-30.
Excluded: Family history not systematically collected, OVID-Embase.

62. Aziz O, Athanasiou T, Fazio VW, et al. Meta-analysis of observational studies of ileorectal versus ileal pouch-anal anastomosis for familial adenomatous polyposis. Br J Surg 2006;93(4):407-17.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
63. Azzarello,L.M. Psychological factors associated with skin cancer detection behaviors in individuals with a family history of melanoma Azzarello. 2006
Excluded: Not an eligible intervention or outcome, OVID-PsycInfo.
64. Badger TM, Ronis MJJ, Simmen RCM, et al. Soy protein isolate and protection against cancer. J Am Coll Nutr 2005;24(2):146S-9S.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
65. Baider L, Ever-Hadani P, Kaplan De-Nour A. Psychological distress in healthy women with familial breast cancer: like mother, like daughter? Int J Psychiatry Med 1999;29(4):411-20.
Excluded: Family history not systematically collected, OVID-Medline.
66. Baker S, Wall M, Bloomfield A. Breast cancer screening for women aged 40 to 49 years--what does the evidence mean for New Zealand? N Z Med J 2005;118(1221):U1628
Excluded: Not an eligible study design, OVID-Medline.
67. Balmana J, Stoffel EM, Emmons KM, et al. Comparison of motivations and concerns for genetic testing in hereditary colorectal and breast cancer syndromes. J Med Genet 2004;41(4):e44
Excluded: Not an eligible study design, OVID-Medline.
68. Banerjee S, Van Dam J. CT colonography for colon cancer screening. Gastrointest Endosc 2006;63(1):121-33.
Excluded: Not an eligible population, OVID-Cinahl.
69. Bankhead CR, Brett J, Bukach C, et al. The impact of screening on future health-promoting behaviours and health beliefs: a systematic review. [Review] [264 refs]. Health Technol Assess 2003;7(42):1-92.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
70. Barcenas CH, Hosain GM, Arun B, et al. Assessing BRCA carrier probabilities in extended families. J Clin Oncol 2006;24(3):354-60.
Excluded: Model does not categorize risk or validate, OVID-Medline.
71. Barkun AN, Jobin G, Cousineau G, et al. The Quebec Association of Gastroenterology position paper on colorectal cancer screening - 2003.[erratum appears in Can J Gastroenterol. 2004 Sep;18(9):591]. Can J Gastroenterol 2004;18(8):509-19.
Excluded: Model does not categorize risk or validate, OVID-Medline.
72. Barlow WE, White E, Ballard-Barbash R, et al. Prospective breast cancer risk prediction model for women undergoing screening mammography. J Natl Cancer Inst 2006;98(17):1204-14.
Excluded: Model does not categorize risk or validate, OVID-Medline.
73. Barnsley GP, Grunfeld E, Coyle D, et al. Surveillance mammography following the treatment of primary breast cancer with breast reconstruction: a systematic review. Plast Reconstr Surg 2007;120(5):1125-32.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
74. Basch E, Bent S, Foppa I, et al. Marigold (Calendula officinalis L.): An evidence-based systematic review by the natural standard research collaboration. J Herb Pharmacother 2006;6(3-4):135-59.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
75. Bassil KL, Vakil C, Sanborn M, et al. Cancer health effects of pesticides: systematic review. Can Fam Physician 2007;53(10):1704-11.
Excluded: Not an eligible population, OVID-Medline.
76. Becker,S.T. Breast cancer screening patterns related to mammography adherence among Northern Plains Tribes American Indian women 2006
Excluded: Not an eligible publication type, OVID-Cinahl.
77. Beebe-Dimmer JL, Wood J, Gruber SB, et al. Use of complementary and alternative medicine in men with family history of prostate cancer: A pilot study. Urology 2004;63(2):282-7.
Excluded: Family history not systematically collected, OVID-Embase.
78. Beery TA, Williams JK. Risk reduction and health promotion behaviors following genetic testing for adult-onset disorders. Genet Test 2007;11(2):111-23.
Excluded: Family history not systematically collected, OVID-Medline.
79. Bellentani S, Baldoni P, Petrella S, et al. A simple score for the identification of patients at high risk of organic diseases of the colon in the family doctor consulting room. Fam Pract 1990;7(4):307-12.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
80. Benedict S, Goon G, Hoomani J, et al. Breast cancer detection by daughters of women with breast cancer.[see comment]. Cancer Pract 1997;5(4):213-9.
Excluded: Family history not systematically collected, OVID-Medline.
81. Benichou J, Gail MH, Mulvihill JJ. Graphs to estimate an individualized risk of breast cancer. J Clin Oncol 1996;14(1):103-10.
Excluded: Not an eligible study design, OVID-Medline.

82. Benjamin,O. The role of dispositional optimism, cancer specific fatalism, and psychological distress in patients participation in the brca1 and brca2 genetic testing Benjamin. 1998
Excluded: Not an eligible publication type, OVID-PsycInfo.
83. Berg AO, U.S.Preventive Services Task Force. Screening for prostate cancer: recommendations and rationale. Am J Nurs 111;103(3):107-10.
Excluded: Model does not categorize risk or validate, OVID-Medline.
84. Berg AO, U.S.Preventive Services Task Force. Screening for prostate cancer: recommendations and rationale. The American Journal for Nurse Practitioners 2003;7(1):24-6.
Excluded: Not an eligible intervention or outcome, OVID-Cinahl.
85. Berg AO, U.S.Preventive Services Task Force. Chemoprevention of breast cancer: recommendations and rationale. Am J Nurs 2003;103(5):107
Excluded: Not an eligible intervention or outcome, OVID-Cinahl.
86. Bergmann M, Wolf B, Karner-Hanusch J. Hereditary colorectal cancer - Guidelines for clinical routine. European Surgery - Acta Chirurgica Austriaca 2006;38(1):59-62.
Excluded: Model does not categorize risk or validate, OVID-Embase.
87. Bermejo-Perez MJ, Marquez-Calderon S, Llanos-Mendez A. Effectiveness of preventive interventions in BRCA1/2 gene mutation carriers: a systematic review. Int J Cancer 2007;121(2):225-31.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
88. Bermejo-Perez MJ, Marquez-Calderon S, Llanos-Mendez A. Cancer surveillance based on imaging techniques in carriers of BRCA1/2 gene mutations: a systematic review. Br J Radiol 2008;81(963):172-9.
Excluded: Not an eligible study design, OVID-Medline.
89. Bermejo JL, Eng C, Hemminki K. Cancer characteristics in Swedish families fulfilling criteria for hereditary nonpolyposis colorectal cancer. Gastroenterology 2005;129(6):1889-99.
Excluded: Model does not categorize risk or validate, OVID-Medline.
90. Berry DA, Parmigiani G, Sanchez J, et al. Probability of carrying a mutation of breast-ovarian cancer gene BRCA1 based on family history. J Natl Cancer Inst 1997;89(3):227-38.
Excluded: Model does not categorize risk or validate, OVID-Medline.
91. Berry DA, Iversen ES, Jr., Gudbjartsson DF, et al. BRCAPRO validation, sensitivity of genetic testing of BRCA1/BRCA2, and prevalence of other breast cancer susceptibility genes. J Clin Oncol 2002;20(11):2701-12.
Excluded: Model does not categorize risk or validate, OVID-Medline.
92. Bertaccini A, Fandella A, Prayer-Galetti T, et al. Systematic development of clinical practice guidelines for prostate biopsies: A 3-year Italian project. Anticancer Res 2007;27(1 B):659-66.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
93. Bevers TB, Anderson BO, Bonaccio E, et al. Breast cancer screening and diagnosis: Clinical practice guidelines in oncology[trademark]. J Natl Compr Cancer Netw 2006;4(5):480-508.
Excluded: Not an eligible publication type, OVID-Embase.
94. Bianchi F, Galizia E, Bracci R, et al. Effectiveness of the CRCAPRO program in identifying patients suspected for HNPCC. Clin Genet 2007;71(2):158-64.
Excluded: Model does not categorize risk or validate, OVID-Medline.
95. Biswas S, Berry DA. Determining joint carrier probabilities of cancer-causing genes using Markov chain Monte Carlo methods. Genet Epidemiol 2005;29(2):141-54.
Excluded: Model does not categorize risk or validate, OVID-Medline.
96. Bjelakovic G, Nikolova D, Simonetti RG, et al. Antioxidant supplements for prevention of gastrointestinal cancers: A systematic review and meta-analysis. Lancet 2004;364(9441):1219-28.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
97. Bjelakovic G. Antioxidants don't prevent GI cancers, increase overall mortality. South African Family Practice 2005;47(1):18
Excluded: Not an eligible study design, OVID-Embase.
98. Bjelakovic G, Nikolova D, Simonetti RG, et al. High-dose antioxidants to prevent cancer: Hype or hoax? Focus on Alternative and Complementary Therapies 2005;10(1):29-31.
Excluded: Not an eligible study design, OVID-Embase.
99. Bjelakovic G, Nikoloval D. Antioxidants do not prevent colorectal cancer. J Fam Pract 2006;55(10):849
Excluded: Not an eligible study design, OVID-Embase.
100. Bjelakovic G, Nagorni A, Nikolova D, et al. Meta-analysis: antioxidant supplements for primary and secondary prevention of colorectal adenoma. Aliment Pharmacol Ther 2006;24(2):281-91.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
101. Bjelakovic G, Nikolova D, Gluud LL, et al. Mortality in randomized trials of antioxidant supplements for primary and secondary prevention: Systematic review and meta-analysis. JAMA 2007;297(8):842-57.
Excluded: Not an eligible intervention or outcome, OVID-Embase.

102. Blalock SJ, DeVellis BM, Afifi RA, et al. Risk perceptions and participation in colorectal cancer screening. Health Psychol 1990;9(6):792-806.
Excluded: Not an eligible study design, OVID-PsycInfo.
103. Bleiker EM, Menko FH, Taal BG, et al. Screening behavior of individuals at high risk for colorectal cancer. Gastroenterology 2005;128(2):280-7.
Excluded: Not an eligible study design, OVID-Medline.
104. Blom J, Yin L, Liden A, et al. Toward understanding nonparticipation in sigmoidoscopy screening for colorectal cancer. Int J Cancer 2008;122(7):1618-23.
Excluded: Not an eligible study design, OVID-Medline.
105. Bloom JR, Stewart SL, Chang S, et al. Effects of a telephone counseling intervention on sisters of young women with breast cancer. Prev Med 2006;43(5):379-84.
Excluded: Family history not systematically collected, OVID-Medline.
106. Bloom JR, Stewart SL, Oakley-Girvans I, et al. Family history, perceived risk, and prostate cancer screening among African American men. Cancer Epidemiol Biomarkers Prev 2006;15(11):2167-73.
Excluded: Family history not systematically collected, OVID-Medline.
107. Bock CH, Peyser PA, Gruber SB, et al. Prostate cancer early detection practices among men with a family history of disease. Urology 2003;62(3):470-5.
Excluded: Not an eligible population, OVID-Medline.
108. Bodd TL, Reichelt J, Heimdal K, et al. Uptake of BRCA1 genetic testing in adult sisters and daughters of known mutation carriers in Norway. J Genet Couns 2003;12(5):405-17.
Excluded: Not an eligible population, OVID-Medline.
109. Bodmer D, Ligtenberg MJ, Van Der Hout AH, 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):757-62.
Excluded: Model does not categorize risk or validate, OVID-Medline.
110. Boggs BD, Stephens MM, Wallace R. How does colonoscopy compare with fecal occult blood testing as a screening tool for colon cancer? J Fam Pract 2005;54(11):996-7.
Excluded: Not an eligible study design, OVID-Embase.
111. Bondy ML, Vogel VG, Halabi S, et al. Identification of women at increased risk for breast cancer in a population-based screening program. Cancer Epidemiol Biomarkers Prev 1992;1(2):143-7.
Excluded: Model does not categorize risk or validate, OVID-Medline.
112. Bondy ML, Lustbader ED, Halabi S, et al. Validation of a breast cancer risk assessment model in women with a positive family history. J Natl Cancer Inst 1994;86(8):620-5.
Excluded: Model does not categorize risk or validate, OVID-Medline.
113. Bondy ML, Newman LA. Assessing breast cancer risk: evolution of the Gail Model. J Natl Cancer Inst 2006;98(17):1172-3.
Excluded: Not an eligible study design, OVID-Medline.
114. Bonovas S, Filioussi K, Sitaras NM. Do nonsteroidal anti-inflammatory drugs affect the risk of developing ovarian cancer? A meta-analysis. Br J Clin Pharmacol 2005;60(2):194-203.
Excluded: Not an eligible population, OVID-Embase.
115. Borry P, Stultiens L, Nys H, et al. Attitudes towards predictive genetic testing in minors for familial breast cancer: a systematic review. Crit Rev Oncol Hematol 2007;64(3):173-81.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
116. Bosserman LD, Smith JA, Hellerstedt B, et al. Hereditary cancer testing in community oncology practices. Community Oncology 2007;4(11 SUPPL.):2-8.
Excluded: Not an eligible study design, OVID-Embase.
117. Botkin JR, Smith KR, Croyle RT, et al. Genetic testing for a BRCA1 mutation: prophylactic surgery and screening behavior in women 2 years post testing. Am J Med Genet 2003;Part(3):201-9.
Excluded: Not an eligible population, OVID-Medline.
118. Bouvier A-M, Faivre J, Lejeune C. Screening strategy of colorectal cancers in high risk cases. Acta Endoscopica 2002;32(4):623-31.
Excluded: Not an eligible study design, OVID-Embase.
119. Bowen D, McTiernan A, Burke W, et al. Participation in breast cancer risk counseling among women with a family history. Cancer Epidemiol Biomarkers Prev 1999;8(7):581-5.
Excluded: Family history not systematically collected, OVID-Medline.
120. Bowen DJ, Morasca AA, Meischke H. Measures and correlates of resilience. Women Health 2003;38(2):65-76.
Excluded: Family history not systematically collected, OVID-Medline.
121. Bowen DJ, Alfano CM, McGregor BA, et al. The relationship between perceived risk, affect, and health behaviors. Cancer Detect Prev 2004;28(6):409-17.
Excluded: Family history not systematically collected, OVID-Medline.

122. Bradbury AR, Ibe CN, Dignam JJ, et al. Uptake and timing of bilateral prophylactic salpingo-oophorectomy among BRCA1 and BRCA2 mutation carriers. Genetics in Medicine 2008;10(3):161-6.
Excluded: Not an eligible population, OVID-Embase.
123. Brain K, Norman P, Gray J, et al. Anxiety and adherence to breast self-examination in women with a family history of breast cancer. Psychosom Med 1999;61(2):181-7.
Excluded: Not an eligible study design, OVID-Medline.
124. Braithwaite D, Emery J, Walter F, et al. Psychological impact of genetic counseling for familial cancer: a systematic review and meta-analysis. J Natl Cancer Inst 2004;96(2):122-33.
Excluded: Family history not systematically collected, OVID-Medline.
125. Braithwaite D, Sutton S, Mackay J, et al. Development of a risk assessment tool for women with a family history of breast cancer. Cancer Detect Prev 2005;29(5):433-9.
Excluded: Model does not categorize risk or validate, OVID-Medline.
126. Braithwaite RS, Chlebowski RT, Lau J, et al. Meta-analysis of vascular and neoplastic events associated with tamoxifen. J Gen Intern Med 2003;18(11):937-47.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
127. Bratt O, Damber JE, Emanuelsson M, et al. Risk perception, screening practice and interest in genetic testing among unaffected men in families with hereditary prostate cancer. Eur J Cancer 2000;36(2):235-41.
Excluded: Not an eligible study design, OVID-Medline.
128. Bratt O, Emanuelsson M, Gronberg H. Psychological aspects of screening in families with hereditary prostate cancer. Scand J Urol Nephrol 2003;37(1):5-9.
Excluded: Family history not systematically collected, OVID-Medline.
129. Braun L. There's no doubt: Soy protects and promotes health. Australian Journal of Pharmacy 2007;88(1044):52-3.
Excluded: Not an eligible study design, OVID-Embase.
130. Brenneman AE. Colon cancer: an update on screening. JAAPA J Am Acad Physician Assist 2008;21(3):17-8.
Excluded: Model does not categorize risk or validate, OVID-Cinahl.
131. Brewer NT, Salz T, Lillie SE. Systematic review: the long-term effects of false-positive mammograms. Ann Intern Med 2007;146(7):502-10. Excluded: Not an eligible population, OVID-Medline.
132. Broadstock M, Michie S, Marteau T. Psychological consequences of predictive genetic testing: a systematic review. Eur J Hum Genet 2000;8(10):731-8.
Excluded: Family history not systematically collected, OVID-Medline.
133. Brooks DD, Winawer SJ, Rex DK, et al. Colonoscopy surveillance after polypectomy and colorectal cancer resection. Am Fam Physician 2008;77(7):995-1002.
Excluded: Model does not categorize risk or validate, OVID-Medline.
134. Brosnan CA. Review: colorectal cancer screening with the faecal occult blood test reduced colorectal cancer mortality. Evid Based Nurs 2007;10(4):112
Excluded: Not an eligible study design, OVID-Cinahl.
135. Brown SR, Baraza W, Hurlstone P. Chromoscopy versus conventional endoscopy for the detection of polyps in the colon and rectum. Cochrane Database of Syst Rev 2007;(4):CD006439
Excluded: Not an eligible intervention or outcome, OVID-Medline.
136. Bruner DW, Baffoe-Bonnie A, Miller S, et al. Prostate cancer risk assessment program. A model for the early detection of prostate cancer. ONCOLOGY 1999;13(3):325-34. PM:10204154
Excluded: not an eligible study design,
137. Brunton M, Jordan C, Campbell I. Anxiety before, during, and after participation in a population-based screening mammography programme in Waikato Province, New Zealand. N Z Med J 2005;118(1209):U1299
Excluded: Family history not systematically collected, OVID-Medline.
138. Bryant RJ, Hamdy FC. Screening for prostate cancer: an update. Eur Urol 2008;53(1):37-44.
Excluded: Not an eligible study design, OVID-Medline.
139. Buchalter,A.J. Effects of coping on distress related to family history of breast cancer Buchalter. 2002
Excluded: Not an eligible publication type, OVID-PsycInfo.
140. Bujanda L, Sarasqueta C, Zubiaurre L, et al. Low adherence to colonoscopy in the screening of first-degree relatives of patients with colorectal cancer. Gut 2007;56(12):1714-8.
Excluded: Not an eligible study design, OVID-Medline.
141. Bunn JY, Bosompra K, Ashikaga T, et al. Factors influencing intention to obtain a genetic test for colon cancer risk: a population-based study. Prev Med 2002;34(6):567-77.
Excluded: Family history not systematically collected, OVID-Medline.

142. Burch JA, Soares-Weiser K, St John DJ, et al. Diagnostic accuracy of faecal occult blood tests used in screening for colorectal cancer: a systematic review. J Med Screen 2007;14(3):132-7. Excluded: Not an eligible population, OVID-Medline.
143. Burt RW. Impact of family history on screening and surveillance. Gastrointest Endosc 1999;49(3:Pt 2):t-4 .Excluded: Not an eligible study design, OVID-Medline.
144. Bushnell CD, Goldstein LB. Risk of ischemic stroke with tamoxifen treatment for breast cancer: a meta-analysis. Neurology 2004;63(7):1230-3. Excluded: Not an eligible intervention or outcome, OVID-Medline.
145. Butow P, Meiser B, Price M, et al. Psychological morbidity in women at increased risk of developing breast cancer: a controlled study. Psychooncology 2005;14(3):196-203. Excluded: Not an eligible study design, OVID-Medline.
146. Cairns S, Scholefield JH. Guidelines for colorectal cancer screening in high risk groups. Gut 2002;51:Suppl-2 Excluded: Not an eligible study design, OVID-Medline.
147. Calonge N. Screening for ovarian cancer: Recommendation statement. Am Fam Physician 2005;71(4):759-62. Excluded: Model does not categorize risk or validate, OVID-Embase.
148. Calonge N. U.S. preventive services task force - Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: Recommendation statement. Am Fam Physician 2006;73(5):869-77. Excluded: Model does not categorize risk or validate, OVID-Embase.
149. Calvocoressi L, Kasl SV, Lee CH, et al. A prospective study of perceived susceptibility to breast cancer and nonadherence to mammography screening guidelines in African American and White women ages 40 to 79 years. Cancer Epidemiol Biomarkers Prev 2004;13(12):2096-105. Excluded: Family history not systematically collected, OVID-Medline.
150. 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. Excluded: Model does not categorize risk or validate, OVID-Medline.
151. Capalbo C, Ricevuto E, Vestri A, et al. BRCA1 and BRCA2 genetic testing in Italian breast and/or ovarian cancer families: mutation spectrum and prevalence and analysis of mutation prediction models. Ann Oncol 2006;17:Suppl-40 Excluded: Family history not systematically collected, OVID-Medline.
152. Cappelli M, Surh L, Humphreys L, et al. Psychological and social determinants of women's decisions to undergo genetic counseling and testing for breast cancer. Clin Genet 1999;55(6):419-30. Excluded: Family history not systematically collected, OVID-Medline.
153. Cappelli M, Hunter AGW, Stern H, et al. Participation rates of Ashkenazi Jews in a colon cancer community-based screening/prevention study. Clin Genet 2002;61(2):104-14. Excluded: Family history not systematically collected, OVID-Embase.
154. Carlson RW, Moench SJ, Hammond ME, et al. HER2 testing in breast cancer: NCCN Task Force report and recommendations. J Natl Compr Cancer Netw 2004;4:Suppl-22 Excluded: Not an eligible intervention or outcome, OVID-Medline.
155. Carlsson AH, Bjorvatn C, Engebretsen LF, et al. Psychosocial factors associated with quality of life among individuals attending genetic counseling for hereditary cancer. J Genet Couns 2004;13(5):425-45. Excluded: Family history not systematically collected, OVID-Medline.
156. Carpentieri DF, Qualman SJ, Bowen J, et al. Protocol for the examination of specimens from pediatric and adult patients with osseous and extraosseous Ewing sarcoma family of tumors, including peripheral primitive neuroectodermal tumor and Ewing sarcoma. Arch Pathol Lab Med 2005;129(7):866-73. Excluded: Not an eligible intervention or outcome, OVID-Embase.
157. Ceber E, Soyer MT, Ciceklioglu M, et al. Breast cancer risk assessment and risk perception on nurses and midwives in Bornova Health District in Turkey. Cancer Nurs 2006;29(3):244-9. Excluded: Family history not systematically collected, OVID-Medline.
158. Chalmers K, Thomson K. Coming to terms with the risk of breast cancer: perceptions of women with primary relatives with breast cancer. Qual Health Res 1996;6(2):256-82. Excluded: Family history not systematically collected, OVID-Cinahl.
159. Chalmers KI, Luker KA. Breast self-care practices in women with primary relatives with breast cancer. J Adv Nurs 1996;23(6):1212-20. Excluded: Family history not systematically collected, OVID-Medline.
160. Champion VL. Compliance with guidelines for mammography screening. Cancer Detect Prev 1992;16(4):253-8. Excluded: Family history not systematically collected, OVID-Medline.

161. Chan SC. Practice of breast self-examination amongst women attending a Malaysian Well Person's Clinic. Med J Malaysia 1999;54(4):433-7. Excluded: Not an eligible study design, OVID-Medline.
162. Chao A, Connell CJ, Cokkinides V, et al. Underuse of screening sigmoidoscopy and colonoscopy in a large cohort of US adults. Am J Public Health 2004;94(10):1775-81. Excluded: Family history not systematically collected, OVID-Cinahl.
163. Chatterjee N, Wacholder S. A marginal likelihood approach for estimating penetrance from kin-cohort designs. Biometrics 2001;57(1):245-52. Excluded: Model does not categorize risk or validate, OVID-Medline.
164. Chen J, Pee D, Ayyagari R, et al. Projecting absolute invasive breast cancer risk in white women with a model that includes mammographic density. J Natl Cancer Inst 2006;98(17):1215-26. Excluded: Model does not categorize risk or validate, OVID-Medline.
165. Chen K, Qiu J-L, Zhang Y, et al. Meta analysis of risk factors for colorectal cancer. World J Gastroenterol 2003;9(7):1598-600. Excluded: Not an eligible intervention or outcome, OVID-Embase.
166. Chen S, Wang W, Lee S, et al. Prediction of germline mutations and cancer risk in the Lynch syndrome.[see comment]. JAMA 2006;296(12):1479-87. Excluded: Model does not categorize risk or validate, OVID-Medline.
167. Chen S, Parmigiani G. Meta-analysis of BRCA1 and BRCA2 penetrance. J Clin Oncol 2007;25(11):1329-33. Excluded: Not an eligible intervention or outcome, OVID-Medline.
168. Chiao EY, Giordano TP, Palefsky JM, et al. Screening HIV-infected individuals for anal cancer precursor lesions: a systematic review. Clin Infect Dis 2006;43(2):223-33. Excluded: Family history not systematically collected, OVID-Medline.
169. Chikhaoui Y, Gelinas H, Joseph L, et al. Cost-minimization analysis of genetic testing versus clinical screening of at-risk relatives for familial adenomatous polyposis. Int J Technol Assess Health Care 2002;18(1):67-80. Excluded: Not an eligible intervention or outcome, OVID-Medline.
170. Cho E, Smith-Warner SA, Ritz J, et al. Alcohol intake and colorectal cancer: a pooled analysis of 8 cohort studies. Ann Intern Med 2004;140(8):603-13. Excluded: Not an eligible intervention or outcome, OVID-Medline.
171. Christman LK, Abdulla R, Jacobsen PB, et al. Colorectal cancer screening among a sample of community health center attendees. J Health Care Poor & Underserved 2004;15(2):281-93. Excluded: Not an eligible study design, OVID-Medline.
172. 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):1404-12. Excluded: Model does not categorize risk or validate, OVID-Medline.
173. Ciliska D, Robinson P, Armour T, et al. Diffusion and dissemination of evidence-based dietary strategies for the prevention of cancer. Nutr J 2005;4:13 Excluded: Not an eligible intervention or outcome, OVID-Medline.
174. Claes E, Evers-Kiebooms G, Decruyenaere M, et al. Surveillance behavior and prophylactic surgery after predictive testing for hereditary breast/ovarian cancer. Behav Med 2005;31(3):93-105. Excluded: Family history not systematically collected, OVID-Medline.
175. Clark MA, Rakowski W, Bonacore LB. Repeat mammography: prevalence estimates and considerations for assessment. Ann Behav Med 2003;26(3):201-11. Excluded: Not an eligible intervention or outcome, OVID-Medline.
176. Clarke M. Tamoxifen for early breast cancer. Cochrane Database Syst Rev 2001;(1):CD000486 Excluded: Not an eligible intervention or outcome, OVID-Cinahl.
177. Clarke M. Tamoxifen for early breast cancer [Systematic Review]. Cochrane Database of Syst Rev 2008;(1) 2008;(1): Excluded: Not an eligible intervention or outcome, OVID-Cochrane.
178. Claus EB, Risch N, Thompson WD. The calculation of breast cancer risk for women with a first degree family history of ovarian cancer. Breast Cancer Res Treat 1993;28(2):115-20. Excluded: Model does not categorize risk or validate, OVID-Medline.
179. Claus EB, Risch N, Thompson WD. Autosomal dominant inheritance of early-onset breast cancer. Implications for risk prediction. Cancer 1994;73(3):643-51. PM:8299086 Excluded: Model does not categorize risk or validate, OVID-Medline.
180. Clavel-Chapelon F, Joseph R, Goulard H. Surveillance behavior of women with a reported family history of colorectal cancer. Prev Med 1999;28(2):174-8. Excluded: Not an eligible study design, OVID-Medline.

181. Codori AM, Petersen GM, Miglioretti DL, et al. Health beliefs and endoscopic screening for colorectal cancer: potential for cancer prevention. Prev Med 2001;33(2:Pt 1):t-36
Excluded: Family history not systematically collected, OVID-Medline.
182. Cohen M. First-degree relatives of breast-cancer patients: cognitive perceptions, coping, and adherence to breast self-examination. Behav Med 2002;28(1):15-22.
Excluded: Family history not systematically collected, OVID-Medline.
183. Cohen M. Breast cancer early detection, health beliefs, and cancer worries in randomly selected women with and without a family history of breast cancer. Psychooncology 2006;15(10):873-83.
Excluded: Family history not systematically collected, OVID-Embase.
184. Collins KS, Collins SK. Professional issues. Cancer screening recommendations. Radiat Therapist 2004;13(2):137-9.
Excluded: Not an eligible intervention or outcome, OVID-Cinahl.
185. Collins V, Meiser B, Gaff C, et al. Screening and preventive behaviors one year after predictive genetic testing for hereditary nonpolyposis colorectal carcinoma. Cancer 2005;104(2):273-81.
Excluded: Not an eligible population, OVID-Medline.
186. Colomer R, Vinas G, Beltran M, et al. Validation of the 2001 St Gallen risk categories for node-negative breast cancer using a database from the Spanish Breast Cancer Research Group (GEICAM). J Clin Oncol 2004;22(5):961-2.
Excluded: Family history not systematically collected, OVID-Medline.
187. Cormier L, Valeri A, Azzouzi R, et al. Worry and attitude of men in at-risk families for prostate cancer about genetic susceptibility and genetic testing. Prostate 2002;51(4):276-85.
Excluded: Not an eligible study design, OVID-Medline.
188. Cormier L, Reid K, Kwan L, et al. Screening behavior in brothers and sons of men with prostate cancer. J Urol 2003;169(5):1715-9.
Excluded: Family history not systematically collected, OVID-Medline.
189. Corpet DE, Pierre F. How good are rodent models of carcinogenesis in predicting efficacy in humans? A systematic review and meta-analysis of colon chemoprevention in rats, mice and men. Eur J Cancer 2005;41(13):1911-22.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
190. Costantino JP, Gail MH, Pee D, et al. Validation studies for models projecting the risk of invasive and total breast cancer incidence. J Natl Cancer Inst 1999;91(18):1541-8.
Excluded: Model does not categorize risk or validate, OVID-Medline.
191. Costanza ME, Stoddard A, Gaw VP, et al. The risk factors of age and family history and their relationship to screening mammography utilization. J Am Geriatr Soc 1992;40(8):774-8.
Excluded: Family history not systematically collected, OVID-Medline.
192. Costanza ME, Luckmann R, Stoddard AM, et al. Applying a stage model of behavior change to colon cancer screening. Prev Med 2005;41(3-4):707-19.
Excluded: Family history not systematically collected, OVID-Medline.
193. Cottet V, Pariente A, Nalet B, et al. Low compliance with colonoscopic screening in first-degree relatives of patients with large adenomas. Aliment Pharmacol Ther 2006;24(1):101-9.
Excluded: Family history not systematically collected, OVID-Medline.
194. Coughlin L. American Cancer Society releases annual guidelines for the early detection of cancer. Am Fam Physician 2005;71(11):2202-5.
Excluded: Model does not categorize risk or validate, OVID-Embase.
195. 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):315-22.
Excluded: Model does not categorize risk or validate, OVID-Medline.
196. Coyne JC, Kruus L, Racioppo M, et al. What do ratings of cancer-specific distress mean among women at high risk of breast and ovarian cancer? Am J Med Genet 2003;Part(3):222-8.
Excluded: Not an eligible study design, OVID-Medline.
197. Cravo ML, Fidalgo PO, Lage PA, et al. Validation and simplification of Bethesda guidelines for identifying apparently sporadic forms of colorectal carcinoma with microsatellite instability. Cancer 1999;85(4):779-85.
Excluded: Model does not categorize risk or validate, OVID-Medline.
198. Cui Y, Peterson NB, Hargreaves M, et al. Mammography use in the Southern Cohort Study (United States). J Health Care Poor Underserved 2007;18(4):Supplement-17
Excluded: Family history not systematically collected, OVID-Cinahl.
199. Cull A, Fry A, Rush R, et al. Cancer risk perceptions and distress among women attending a familial ovarian cancer clinic. Br J Cancer 2001;84(5):594-9.
Excluded: Not an eligible study design, OVID-Medline.
200. Cullen J, Schwartz MD, Lawrence WF, et al. Short-term impact of cancer prevention and screening activities on quality of life. J Clin Oncol 2004;22(5):943-52.
Excluded: Not an eligible intervention or outcome, OVID-Medline.

201. Culver J, Burke W, Yasui Y, et al. Participation in breast cancer genetic counseling: the influence of educational level, ethnic background, and risk perception. J Genetic Couns 2001;10(3):215-31.
Excluded: Family history not systematically collected, OVID-Cinahl.
202. Dai Z, Xu YC, Niu L. Obesity and colorectal cancer risk: a meta-analysis of cohort studies. World J Gastroenterol 2007;13(31):4199-206.
Excluded: Not an eligible population, OVID-Medline.
203. Daly MB, Lerman CL, Ross E, et al. Gail model breast cancer risk components are poor predictors of risk perception and screening behavior. Breast Cancer Res Treat 1996;41(1):59-70.
Excluded: Family history not systematically collected, OVID-Medline.
204. Davila RE, Rajan E, Baron TH, et al. ASGE guideline: colorectal cancer screening and surveillance.[erratum appears in Gastrointest Endosc. 2006 May;63(6):892 Note: Adler, Douglas G [added]; Egan, James V [added]; Faigel, Douglas O [added]; Gan, Seng-Ian [added]; Hirota, William K [added]; Leighton, Jonathan A [added]; Lichtenstein, David [added]; Qureshi, Waqar A [added]; Shen, Bo [added]; Zuckerman, Marc J [added]; VanGuilder, Trina [added]; Fanelli, Robert D [added]]. Gastrointest Endosc 2006;63(4):546-57.
Excluded: Model does not categorize risk or validate, OVID-Medline.
205. Dawson SJ, Price MA, Jenkins MA, et al. Cancer risk management practices of noncarriers within BRCA1/2 mutation positive families in the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer. J Clin Oncol 2008;26(2):225-32.
Excluded: Not an eligible population, OVID-Medline.
206. 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):26-7.
Excluded: Not an eligible study design, OVID-Medline.
207. De Bock GH, Bonnema J, Van Der Hage J., et al. Effectiveness of routine visits and routine tests in detecting isolated locoregional recurrences after treatment for early-stage invasive breast cancer: A meta-analysis and systematic review. J Clin Oncol 2004;22(19):4010-8.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
208. de la Hoya M, Diez O, Perez-Segura P, et al. Pre-test prediction models of BRCA1 or BRCA2 mutation in breast/ovarian families attending familial cancer clinics. J Med Genet 2003;40(7):503-10.
Excluded: Model does not categorize risk or validate, OVID-Medline.
209. Dearnaley DP, Kirby RS, Kirk D, et al. Diagnosis and management of early prostate cancer. Report of a British Association of Urological Surgeons Working Party. BJU Int 1999;83(1):18-33.
Excluded: Model does not categorize risk or validate, OVID-Embase.
210. Deligeoroglou E, Michailidis E, Creatsas G. Oral contraceptives and reproductive system cancer. Ann N Y Acad Sci 2003;997:199-208.
Excluded: Not an eligible study design, OVID-Embase.
211. Desch CE, Benson AB, III, Somerfield MR, et al. Colorectal cancer surveillance: 2005 update of an American Society of Clinical Oncology practice guideline.[erratum appears in J Clin Oncol. 2006 Mar 1;24(7):1224]. J Clin Oncol 2005;23(33):8512-9.
Excluded: Model does not categorize risk or validate, OVID-Medline.
212. Dettenborn L, James GD, Berge-Landry H, et al. Heightened cortisol responses to daily stress in working women at familial risk for breast cancer. Biol Psychol 2005;69(2):167-79.
Excluded: Not an eligible study design, OVID-Medline.
213. Digianni LM, Kim HT, Emmons K, et al. Complementary medicine use among women enrolled in a genetic testing program. Cancer Epidemiol Biomarkers Prev 2003;12(4):321-6.
Excluded: Not an eligible population, OVID-Medline.
214. Digianni LM, Rue M, Emmons K, et al. Complementary medicine use before and 1 year following genetic testing for BRCA1/2 mutations. Cancer Epidemiol Biomarkers Prev 2006;15(1):70-5.
Excluded: Not an eligible population, OVID-Medline.
215. DiLorenzo TA, Schnur J, Montgomery GH, et al. A model of disease-specific worry in heritable disease: the influence of family history, perceived risk and worry about other illnesses. J Behav Med 2006;29(1):37-49.
Excluded: Not an eligible study design, OVID-Medline.
216. Dimella,L.F. The relationship between beliefs about god's control over health and adherence to breast cancer screening guidelines following genetic testing Dimella. 2003
Excluded: Not an eligible intervention or outcome, OVID-PsycInfo.
217. 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):1849-53.
Excluded: Model does not categorize risk or validate, OVID-Medline.

218. Driver JA, Gaziano JM, Gelber RP, et al. Development of a risk score for colorectal cancer in men. Am J Med 2007;120(3):257-63. PM:17349449
Excluded: not an eligible study design,
219. Drossaert CC, Boer H, Seydel ER. Perceived risk, anxiety, mammogram uptake, and breast self-examination of women with a family history of breast cancer: the role of knowing to be at increased risk. Cancer Detect Prev 1996;20(1):76-85.
Excluded: Family history not systematically collected, OVID-Medline.
220. Drossaert CHC, Boer H, Seydel ER. Prospective study on the determinants of repeat attendance and attendance patterns in breast cancer screening using the theory of planned behaviour. Psychol Health 2003;18(5):551-65.
Excluded: Not an eligible study design, OVID-Cinahl.
221. DudokdeWit AC, Tibben A, Duivenvoorden HJ, et al. Distress in individuals facing predictive DNA testing for autosomal dominant late-onset disorders: comparing questionnaire results with in-depth interviews. Rotterdam/Leiden Genetics Workgroup. Am J Med Genet 1998;75(1):62-74.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
222. Duffy MJ, Bonfrer JM, Kulpa J, et al. CA125 in ovarian cancer: European Group on Tumor Markers guidelines for clinical use. Int J Gynecol Cancer 2005;15(5):679-91.
Excluded: Model does not categorize risk or validate, OVID-Embase.
223. Duffy MJ, van Dalen A, Haglund C, et al. Tumour markers in colorectal cancer: European Group on Tumour Markers (EGTM) guidelines for clinical use. Eur J Cancer 2007;43(9):1348-60.
Excluded: Model does not categorize risk or validate, OVID-Embase.
224. Eastham JA, May R, Robertson JL, et al. Development of a nomogram that predicts the probability of a positive prostate biopsy in men with an abnormal digital rectal examination and a prostate-specific antigen between 0 and 4 ng/mL. Urology 1999;54(4):709-13. PM:10510933
Excluded: Not an eligible study design
225. Eccles DM, Evans DG, Mackay J. Guidelines for a genetic risk based approach to advising women with a family history of breast cancer. UK Cancer Family Study Group (UKCFSG). J Med Genet 2000;37(3):203-9.
Excluded: Model does not categorize risk or validate, OVID-Medline.
226. Edwards A, Unigwe S, Elwyn G, et al. Effects of communicating individual risks in screening programmes: Cochrane systematic review. Br Med J 2003;327(7417):703-7.
Excluded: Family history not systematically collected, OVID-Embase.
227. Edwards A, Gray J, Clarke A, et al. Interventions to improve risk communication in clinical genetics: Systematic review. Patient Educ Couns 2008;71(1):4-25.
Excluded: Family history not systematically collected, OVID-Embase.
228. Edwards AG, Evans R, Dundon J, et al. Personalised risk communication for informed decision making about taking screening tests. Cochrane Database Syst Rev 2006;(4):CD001865
Excluded: Family history not systematically collected, OVID-Medline.
229. Eisinger F, Tarpin C, Huiart L, et al. Behavioral and economic impact of a familial history of cancers. Fam Cancer 2005;4(4):307-11.
Excluded: Family history not systematically collected, OVID-Medline.
230. Elit L. Familial ovarian cancer. Can Fam Physician 2001;47:778-84.
Excluded: Model does not categorize risk or validate, OVID-Medline.
231. Ellis P, Robinson P, Ciliska D, et al. A systematic review of studies evaluating diffusion and dissemination of selected cancer control interventions. Health Psychol 2005;24(5):488-500.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
232. Elmore JG, Armstrong K, Lehman CD, et al. Screening for breast cancer. JAMA 2005;293(10):1245-56.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
233. Emery J. The GRAIDS Trial: the development and evaluation of computer decision support for cancer genetic risk assessment in primary care. Ann Hum Biol 2005;32(2):218-27.
Excluded: Model does not categorize risk or validate, OVID-Medline.
234. Emery J, Morris H, Goodchild R, et al. The GRAIDS Trial: a cluster randomised controlled trial of computer decision support for the management of familial cancer risk in primary care. Br J Cancer 2007;97(4):486-93.
Excluded: Model does not categorize risk or validate, OVID-Medline.
235. Engstrom PF, Benson AB, III, Chen YJ, et al. Colon cancer clinical practice guidelines in oncology. J Natl Compr Cancer Netw 2005;3(4):468-91.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
236. Epstein SA, Lin TH, Audrain J, et al. Excessive breast self-examination among first-degree relatives of newly diagnosed breast cancer patients. High-Risk Breast Cancer Consortium. Psychosomatics 1997;38(3):253-61.
Excluded: Family history not systematically collected, OVID-Medline.
237. Erblich J, Bovbjerg DH, Valdimarsdottir HB. Looking forward and back: distress among women at familial risk for breast cancer. Ann

Behav Med 2000;22(1):53-9.
Excluded: Family history not systematically collected, OVID-Medline.
238. Erlick RG, Rosen BP, Bradley LN, et al. Psychological impact of screening for familial ovarian cancer: reactions to initial assessment. Gynecol Oncol 1997;65(2):197-205.
Excluded: Not an eligible population, OVID-Medline.
239. Esplen MJ, Toner B, Hunter J, et al. A supportive-expressive group intervention for women with a family history of breast cancer: results of a phase II study. Psychooncology 2000;9(3):243-52.
Excluded: Not an eligible population, OVID-Medline.
240. Esplen MJ, Hunter J, Leszcz M, et al. A multicenter study of supportive-expressive group therapy for women with BRCA1/BRCA2 mutations. Cancer 2004;101(10):2327-40.
Excluded: Not an eligible population, OVID-Embase.
241. Etminan M, FitzGerald JM, Gleave M, et al. Intake of selenium in the prevention of prostate cancer: a systematic review and meta-analysis. Cancer Causes Control 2005;16(9):1125-31.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
242. 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):23-7.
Excluded: Model does not categorize risk or validate, OVID-Medline.
243. 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):844-51.
Excluded: Model does not categorize risk or validate, OVID-Medline.
244. 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):889-90.
Excluded: Not an eligible study design, OVID-Medline.
245. Evans DG, Maher ER, Macleod R, et al. Uptake of genetic testing for cancer predisposition. J Med Genet 1997;34(9):746-8.
Excluded: Not an eligible population, OVID-Medline.
246. 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):474-80.
Excluded: Model does not categorize risk or validate, OVID-Medline.
247. Evans R, Edwards A, Brett J, et al. Reduction in uptake of PSA tests following decision aids: systematic review of current aids and their evaluations. Patient Educ Couns 2005;58(1):13-26.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
248. Fabian CJ, Kimler BF. Selective estrogen-receptor modulators for primary prevention of breast cancer. J Clin Oncol 2005;23(8):1644-55.
Excluded: Not an eligible study design, OVID-Embase.
249. Faccenda,K.A. Factors affecting the decision to have genetic testing for breast cancer Faccenda. 1999
Excluded: Not an eligible publication type, OVID-PsycInfo.
250. Fajardo LL. Screening mammography. Imaging Decisions MRI 2005;9(2):23-34.
Excluded: Not an eligible study design, OVID-Embase.
251. Fang CY, Daly MB, Miller SM, et al. Coping with ovarian cancer risk: The moderating effects of perceived control on coping and adjustment. Br J Health Psychol 2006;11(4):561-80.
Excluded: Not an eligible population, OVID-Embase.
252. Fasching PA, Bani MR, Nestle-Kramling C, et al. Evaluation of mathematical models for breast cancer risk assessment in routine clinical use. Eur J Cancer Prev 2007;16(3):216-24.
Excluded: Model does not categorize risk or validate, OVID-Medline.
253. Fernandez E, Vecchia CL, Balducci A, et al. Oral contraceptives and colorectal cancer risk: a meta-analysis. Br J Cancer 2001;84(5):722-7.
Excluded: Not an eligible population, OVID-Cochrane.
254. Figueredo A, Rumble RB, Maroun J, et al. Follow-up of patients with curatively resected colorectal cancer: A practice guideline. BMC Cancer 2003;3:26
Excluded: Model does not categorize risk or validate, OVID-Embase.
255. Finne P, Auvinen A, Aro J, et al. Estimation of prostate cancer risk on the basis of total and free prostate-specific antigen, prostate volume and digital rectal examination. Eur Urol 2002;41(6):619-26.
Excluded: Not an eligible intervention or outcome, OVID-Cochrane.
256. Finney Rutten LJ, Iannotti RJ. Health beliefs, salience of breast cancer family history, and involvement with breast cancer issues: adherence to annual mammography screening recommendations. Cancer Detect Prev 2003;27(5):353-9.
Excluded: Family history not systematically collected, OVID-Medline.
257. Finney,L.J. Health beliefs, message framing, and mammography screening compliance: Measurement development and theory testing Finney. 2001
Excluded: Not an eligible publication type, OVID-PsycInfo.

258. Fisher TJ, Kirk J, Hopper JL, et al. A simple tool for identifying unaffected women at a moderately increased or potentially high risk of breast cancer based on their family history. Breast 2003;12(2):120-7.
Excluded: Model does not categorize risk or validate, OVID-Medline.
259. Flamm CR, Ziegler KM, Aronson N. Technology evaluation center assessment synopsis: Use of magnetic resonance imaging to avoid a biopsy in women with suspicious primary breast lesions. J Am Coll Radiol 2005;2(6):485-7.
Excluded: Not an eligible population, OVID-Embase.
260. Fletcher JW, Djulbegovic B, Soares HP, et al. Recommendations on the use of PET in oncology. J Nucl Med 2008;49(3):480-508.
Excluded: Model does not categorize risk or validate, OVID-Embase.
261. Fletcher KE, Clemow L, Peterson BA, et al. A path analysis of factors associated with distress among first-degree female relatives of women with breast cancer diagnosis. Health Psychol 2006;25(3):413-24.
Excluded: Family history not systematically collected, OVID-Medline.
262. Fletcher RH, Lobb R, Bauer MR, et al. Screening patients with a family history of colorectal cancer. J Gen Intern Med 2007;22(4):508-13.
Excluded: Family history not systematically collected, OVID-Medline.
263. Fletcher SW, Elmore JG. Mammographic screening for breast cancer. N Engl J Med 2003;348(17):1672-80.
Excluded: Not an eligible study design, OVID-Embase.
264. Flook N. Colorectal cancer. Summary of Canadian screening guidelines. Can Fam Physician 2004;50:592-3.
Excluded: Model does not categorize risk or validate, OVID-Medline.
265. Flossmann E, Rothwell PM, British Doctors Aspirin Trial and the UK-TIA Aspirin Trial. Effect of aspirin on long-term risk of colorectal cancer: consistent evidence from randomised and observational studies. Lancet 2007;369(9573):1603-13.
Excluded: Not an eligible population, OVID-Medline.
266. 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.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
267. Frazier TG, Cummings PD. Motivational factors for participation in breast cancer screening. J Cancer Educ 1990;5(1):51-4.
Excluded: Not an eligible study design, OVID-Medline.
268. Friebel TM, Domchek SM, Neuhausen SL, et al. Bilateral prophylactic oophorectomy and bilateral prophylactic mastectomy in a prospective cohort of unaffected BRCA1 and BRCA2 mutation carriers. Clin Breast Cancer 2007;7(11):875-82.
Excluded: Not an eligible population, OVID-Embase.
269. Friedman LC, Webb JA, Richards CS, et al. Psychological and behavioral factors associated with colorectal cancer screening among Ashkenazim. Prev Med 1999;29(2):119-25.
Excluded: Family history not systematically collected, OVID-Medline.
270. Friedman LC, Everett TE, Peterson L, et al. Compliance with fecal occult blood test screening among low-income medical outpatients: a randomized controlled trial using a videotaped intervention. J Cancer Educ 2001;16(2):85-8.
Excluded: Family history not systematically collected, OVID-Medline.
271. Friedman LC, Webb JA, Everett TE. Psychosocial and medical predictors of colorectal cancer screening among low-income medical outpatients. J Cancer Educ 2004;19(3):180-6.
Excluded: Family history not systematically collected, OVID-Medline.
272. Fries MH, Holt C, Carpenter I, et al. Diagnostic criteria for testing for BRCA1 and BRCA2: the experience of the Department of Defense Familial Breast/Ovarian Cancer Research Project. Mil Med 2002;167(2):99-103.
Excluded: Model does not categorize risk or validate,OVID-Cinahl.
273. 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):93-8.
Excluded: Model does not categorize risk or validate, OVID-Medline.
274. Frost MH, Vockley CW, Suman VJ, et al. Perceived familial risk of cancer: Health concerns and psychosocial adjustment. J Psychosoc Oncol 2000;18(1):63-82.
Excluded: Family history not systematically collected, OVID-Embase.
275. Fuerst ML. Genetic testing plus Bethesda guidelines help screen for Lynch syndrome. Oncol Times 2005;27(18):13-4.
Excluded: Not an eligible study design, OVID-Cinahl.
276. Fung MF, Bryson P, Johnston M, et al. Screening postmenopausal women for ovarian cancer: a systematic review. J Obstet Gynaecol Can 2004;26(8):717-28.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
277. Furukawa T, Konishi F, Shitoh K, et al. Evaluation of screening strategy for detecting hereditary nonpolyposis colorectal carcinoma. Cancer 2002;94(4):911-20.
Excluded: Model does not categorize risk or validate, OVID-Medline.

278. Gagnon P, Massie MJ, Kash KM, et al. Perception of breast cancer risk and psychological distress in women attending a surveillance program. Psychooncology 1996;5(3):259-69.
Excluded: Family history not systematically collected, OVID-Cochrane.
279. Gao X, LaValley MP, Tucker KL. Prospective studies of dairy product and calcium intakes and prostate cancer risk: a meta-analysis. J Natl Cancer Inst 2005;97(23):1768-77.
Excluded: Not an eligible intervention or outcome, OVID-Cinahl.
280. Garrett MM, Fisher DA. Strategies to improve colorectal cancer screening rates. Journal of Clinical Outcomes Management 2006;13(9):512-7.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
281. Gately ST. Targeting cyclooxygenase-2 for cancer prevention and treatment. Prog Drug Res 2005;63:207-25.
Excluded: Not an eligible study design, OVID-Embase.
282. Geelen A, Schouten JM, Kamphuis C, et al. Fish consumption, n-3 fatty acids, and colorectal cancer: a meta-analysis of prospective cohort studies. Am J Epidemiol 2007;166(10):1116-25.
Excluded: Not an eligible population, OVID-Medline.
283. Geirdal AO, Reichelt JG, Dahl AA, et al. Psychological distress in women at risk of hereditary breast/ovarian or HNPCC cancers in the absence of demonstrated mutations. Fam Cancer 2005;4(2):121-6.
Excluded: Not an eligible population, OVID-Medline.
284. Geirdal AO, Maehle L, Heimdal K, et al. Quality of life and its relation to cancer-related stress in women of families with hereditary cancer without demonstrated mutation. Qual Life Res 2006;15(3):461-70.
Excluded: Not an eligible study design, OVID-Medline.
285. Geirdal AO, Dahl AA. The relationship between coping strategies and anxiety in women from families with familial breast-ovarian cancer in the absence of demonstrated mutations. Psychooncology 2008;17(1):49-57.
Excluded: Not an eligible population, OVID-Medline.
286. Geller G, Doksum T, Bernhardt BA, et al. Participation in breast cancer susceptibility testing protocols: influence of recruitment source, altruism, and family involvement on women's decisions. Cancer Epidemiol Biomarkers Prev 1999;8(4:Pt 2):t-83
Excluded: Not an eligible study design, OVID-Medline.
287. Gerdes A-M, Cruger DG, Thomassen M, et al. Evaluation of two different models to predict BRCA1 and BRCA2 mutations in a cohort of Danish hereditary breast and/or ovarian cancer families. Clin Genet 2006;69(2):171-8.
Excluded: Model does not categorize risk or validate, OVID-Embase.
288. Giardiello FM, Brensinger JD, Petersen GM. AGA technical review on hereditary colorectal cancer and genetic testing. Gastroenterology 2001;121(1):198-213.
Excluded: Model does not categorize risk or validate, OVID-Medline.
289. Giarelli E. Self-surveillance for genetic predisposition to cancer: behaviors and emotions. Oncol Nurs Forum 2006;Online.(2):221-31.
Excluded: Not an eligible population, OVID-Medline.
290. Gil F, Mendez I, Sirgo A, et al. Perception of breast cancer risk and surveillance behaviours of women with family history of breast cancer: a brief report on a Spanish cohort. Psychooncology 2003;12(8):821-7.
Excluded: Family history not systematically collected, OVID-Medline.
291. Gil KM, von Gruenigen VE. Nutrition and ovarian carcinogenesis: A critical review. Women's Oncology Review 2005;5(2):81-94.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
292. Gilbar O. Women with high risk for breast cancer: psychological symptoms. Psychol Rep 1997;80(3:Pt 1):t-2
Excluded: Family history not systematically collected, OVID-Medline.
293. Gilbar O. Coping with threat. Implications for women with a family history of breast cancer. Psychosomatics 1998;39(4):329-39.
Excluded: Family history not systematically collected, OVID-Medline.
294. Gilpin CA, Carson N, Hunter AG. A preliminary validation of a family history assessment form to select women at risk for breast or ovarian cancer for referral to a genetics center. Clin Genet 2000;58(4):299-308.
Excluded: Model does not categorize risk or validate, OVID-Medline.
295. Giuliano AE, Boolbol S, Degnim A, et al. Society of Surgical Oncology: Position statement on prophylactic mastectomy. Ann Surg Oncol 2007;14(9):2425-7.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
296. Glicksman AS, Colorectal Cancer Care Task Force. Colorectal algorithm guidelines for screening. Med Health R I 2006;89(4):149
Excluded: Not an eligible study design, OVID-Medline.
297. 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.

Excluded: Model does not categorize risk or validate, OVID-Embase.
298. Gologan A, Krasinskas A, Hunt J, et al. Performance of the revised Bethesda guidelines for identification of colorectal carcinomas with a high level of microsatellite instability. Arch Pathol Lab Med 2005;129(11):1390-7.
Excluded: Model does not categorize risk or validate, OVID-Medline.
299. Gonzalez-Perez A, Garcia Rodriguez LA, Lopez-Ridaura R. Effects of non-steroidal anti-inflammatory drugs on cancer sites other than the colon and rectum: a meta-analysis. BMC Cancer 2003;3:28
Excluded: Not an eligible population, OVID-Medline.
300. Gorham ED, Garland CF, Garland FC, et al. Optimal vitamin D status for colorectal cancer prevention: a quantitative meta analysis. Am J Prev Med 2007;32(3):210-6.
Excluded: Not an eligible population, VID-Medline.
301. Gorin SS, Albert SM. The meaning of risk to first degree relatives of women with breast cancer. Women Health 2003;37(3):97-114.
Excluded: Family history not systematically collected, OVID-Embase.
302. Goyal S, Bennett P, Sweetland HM, et al. Are surgeons effective counsellors for women with a family history of breast cancer? Eur J Surg Oncol 2002;28(5):501-4.
Excluded: Not an eligible study design, VID-Medline.
303. Gradishar WJ, Cella D. Selective estrogen receptor modulators and prevention of invasive breast cancer. JAMA 2006;295(23):2784-6.
Excluded: Not an eligible study design, OVID-Embase.
304. Gramling R, Anthony D, Lowery J, et al. Association between screening family medical history in general medical care and lower burden of cancer worry among women with a close family history of breast cancer. Genet Med 2005;7(9):640-5.
Excluded: Not an eligible study design, OVID-Medline.
305. Gramling R, Anthony D, Frierson G, et al. The cancer worry chart: a single-item screening measure of worry about developing breast cancer. Psychooncology 2007;16(6):593-7.
Excluded: Not an eligible population, OVID-Medline.
306. Greco K, Nail L, Kendall J, et al. Breast cancer screening decisions in older high-risk women. Oncol Nurs Forum 2007;34(1):205
Excluded: Not an eligible publication type, OVID-Cinahl.
307. Greco,K.E. Mammography decision-making in women age 65 or older with a family history of breast cancer.
Excluded: Not an eligible publication type, OVID-Cinahl.
308. Green BB, Taplin SH. Breast cancer screening controversies. J Am Board Fam Pract 2003;16(3):233-41.
Excluded: Not an eligible population, OVID-Medline.
309. Green RC, McLaughlin JR, Younghusband HB. SISE matters: the sum of information on seventy-yr-old equivalents measures pedigree information content when assessing the risk of HNPCC in a family. Familial Cancer 2005;4(2):169-75.
Excluded: Model does not categorize risk or validate, OVID-Medline.
310. Gronwald J, Byrski T, Huzarski T, et al. A survey of preventive measures among BRCA1 mutation carriers from Poland. Clin Genet 2007;71(2):153-7.
Excluded: Not an eligible population, OVID-Medline.
311. Gross CP, Filardo G, Singh HS, et al. The relation between projected breast cancer risk, perceived cancer risk, and mammography use: Results from the national health interview survey. J Gen Intern Med 2006;21(2):158-64.
Excluded: Family history not systematically collected, OVID-Embase.
312. Gross RE. Utilization of Breast Cancer Anxiety Scale in women at high risk for breast cancer. 18th Annual SGNO Symposium. J Gynecol Oncol Nurs 2001;11(1):24-5.
Excluded: Not an eligible study design, OVID-Cinahl.
313. Grube BJ. Barriers to diagnosis and treatment of breast cancer in the older woman. J Am Coll Surg 2006;202(3):495-508.
Excluded: Not an eligible study design, OVID-Embase.
314. Guerrero-Preston R, Chan C, Vlahov D, et al. Previous cancer screening behavior as predictor of endoscopic colon cancer screening among women aged 50 and over, in NYC 2002. J Community Health 2008;33(1):10-21.
Excluded: Family history not systematically collected, OVID-Medline.
315. Guevarra,J.S. Psychological distress, African American acculturation and family history of breast cancer: Effects on breast self-examination frequency Guevarra. 2000
Excluded: Not an eligible publication type, OVID-PsycInfo.
316. Gullini S, Matarese V, Pezzoli A, et al. Screening colonoscopy in asymptomatic increased-risk subjects. Eur J Cancer Prev 2001;10(2):175-6.
Excluded: Family history not systematically collected, OVID-Medline.
317. Haas JS, Kaplan CP, Des JG, et al. Perceived risk of breast cancer among women at average and increased risk. J Womens Health (Larchmt) 2005;14(9):845-51.
Excluded: Family history not systematically collected, OVID-Medline.
318. Hackshaw A. EUSOMA review of mammography screening. Ann Oncol

2003;14(8):1193-5.
Excluded: Not an eligible study design, OVID-Medline.
319. Hadley DW, Jenkins J, Dimond E, et al. Genetic counseling and testing in families with hereditary nonpolyposis colorectal cancer. Arch Intern Med 2003;163(5):573-82.
Excluded: Not an eligible population, OVID-Medline.
320. Hadley DW, Jenkins JF, Dimond E, et al. Colon cancer screening practices after genetic counseling and testing for hereditary nonpolyposis colorectal cancer. J Clin Oncol 2004;22(1):39-44.
Excluded: Not an eligible population, OVID-Medline.
321. Hadley DW, Jenkins JF, Steinberg SM, et al. Perceptions of cancer risks and predictors of colon and endometrial cancer screening in women undergoing genetic testing for Lynch syndrome. J Clin Oncol 2008;26(6):948-54.
Excluded: Family history not systematically collected, OVID-Medline.
322. Hagoel L, Dishon S, Almog R, et al. Proband family uptake of familial-genetic counselling. Psychooncology 2000;9(6):522-7.
Excluded: Not an eligible population, OVID-Medline.
323. Hailey BJ, Carter CL, Burnett DR. Breast cancer attitudes, knowledge, and screening behavior in women with and without a family history of breast cancer. Health Care Women Int 2000;21(8):701-15.
Excluded: Family history not systematically collected, OVID-Medline.
324. Halbert CH, Lynch H, Lynch J, et al. Colon cancer screening practices following genetic testing for hereditary nonpolyposis colon cancer (HNPCC) mutations. Arch Intern Med 2004;164(17):1881-7. Excluded: Not an eligible population, OVID-Medline.
325. Halbert CH, Brewster K, Collier A, et al. Recruiting African American women to participate in hereditary breast cancer research. J Clin Oncol 2005;23(31):7967-73.
Excluded: Family history not systematically collected, OVID-Cinahl.
326. Halbert CH, Kessler L, Wileyto EP, et al. Breast cancer screening behaviors among African American women with a strong family history of breast cancer. Prev Med 2006;43(5):385-8.
Excluded: Family history not systematically collected, OVID-Medline.
327. Halbert C, Kessler L, Collier A, et al. Psychological functioning in African American women at an increased risk of hereditary breast and ovarian cancer. Clin Genet 2005;68(3):222-7.
Excluded: Not an eligible study design, OVID-Medline.
328. Hall MJ, Neugut AI. Review: only women with specific family histories should be referred for counseling or evaluation for BRCA breast and ovarian cancer susceptibility. ACP J Club 2006;144(2):37
Excluded: Not an eligible study design, OVID-Cinahl.
329. Hallowell N, Jacobs I, Richards M, et al. Surveillance or surgery? A description of the factors that influence high risk premenopausal women's decisions about prophylactic oophorectomy. J Med Genet 2001;38(10):683-91.
Excluded: Not an eligible study design, OVID-Medline.
330. Hamann HA, Somers TJ, Smith AW, et al. Posttraumatic stress associated with cancer history and BRCA1/2 genetic testing. Psychosom Med 2005;67(5):766-72.
Excluded: Not an eligible population, OVID-Medline.
331. Hampton T. Breast cancer prevention strategies explored. JAMA 2006;295(18):2128-9.
Excluded: Not an eligible study design, OVID-Embase.
332. Hannemann M, Fox R, James M. Ovarian cancer death reduction for women at high risk: workload implications for gynaecology services. J Obstet Gynaecol 2006;26(1):42-4.
Excluded: Not an eligible study design, OVID-Medline.
333. Harmon AL, Westerberg AL, Bond DS, et al. Cancer prevention among rural youth: building a "Bridge" to better health with genealogy. J Cancer Educ 2005;20(2):103-7.
Excluded: Family history not systematically collected, OVID-Cinahl.
334. Harris L, Fritsche H, Mennel R, et al. American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer. J Clin Oncol 2007;25(33):5287-312. Excluded: Not an eligible intervention or outcome, OVID-Medline.
335. Haug U, Brenner H. New stool tests for colorectal cancer screening: a systematic review focusing on performance characteristics and practicalness. Int J Cancer 2005;117(2):169-76.
Excluded: Not an eligible population, OVID-Medline.
336. Hay JL, McCaul KD, Magnan RE. Does worry about breast cancer predict screening behaviors? A meta-analysis of the prospective evidence. Prev Med 2006;42(6):401-8.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
337. Heatley MK. Immunohistochemical and functional biomarkers of value in female genital tract lesions: A systematic review with statistical meta-analysis. Int J Gynecol Pathol 2007;26(2):177-9.
Excluded: Not an eligible study design, OVID-Embase.

338. Heikkila K, Ebrahim S, Lawlor DA. A systematic review of the association between circulating concentrations of C reactive protein and cancer. J Epidemiol Community Health 2007;61(9):824-32.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
339. Henderson BJ, Tyndel S, Brain K, et al. Factors associated with breast cancer-specific distress in younger women participating in a family history mammography screening programme. Psychooncology 2008;17(1):74-82.
Excluded: Not an eligible study design, OVID-Medline.
340. Hendriks YMC, De Jong AE, Morreau H, et al. Diagnostic approach and management of Lynch syndrome (Hereditary Nonpolyposis Colorectal Carcinoma): A guide for clinicians. CA Cancer J Clin 2006;56(4):213-25.
Excluded: Model does not categorize risk or validate, OVID-Embase.
341. Hensley ML, Robson ME, Kauff ND, et al. Pre- and postmenopausal high-risk women undergoing screening for ovarian cancer: anxiety, risk perceptions, and quality of life. Gynecol Oncol 2003;89(3):440-6.
Excluded: Not an eligible study design, OVID-Medline.
342. Herendeen JM, Lindley C. Use of NSAIDs for the chemoprevention of colorectal cancer. Ann Pharmacother 2003;37(11):1664-74.
Excluded: Not an eligible study design, OVID-Medline.
343. Heshka JT, Palleschi C, Howley H, et al. A systematic review of perceived risks, psychological and behavioral impacts of genetic testing. Genet Med 2008;10(1):19-32.
Excluded: Family history not systematically collected, OVID-Medline.
344. Hill J, Hanstock Z, Lockwood B. Keeping cancer at bay the natural way. Pharmaceutical Journal 2006;(7416):277-84.
Excluded: Not an eligible study design, OVID-Embase.
345. Hirota WK, Zuckerman MJ, Adler DG, et al. ASGE guideline: The role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. Gastrointest Endosc 2006;63(4):570-80.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
346. Hlavaty T, Lukac L, Huorka M, et al. Positive family history promotes participation in colorectal cancer screening. Bratisl Lek Listy 2005;106(10):318-23.
Excluded: Not an eligible population, OVID-Medline.
347. Ho SM, Ho JW, Chan CL, et al. Decisional consideration of hereditary colon cancer genetic test results among Hong Kong chinese adults. Cancer Epidemiol Biomarkers Prev 2003;12(5):426-32.
Excluded: Not an eligible population, OVID-Medline.
348. Ho V, Yamal JM, Atkinson EN, et al. Predictors of breast and cervical screening in Vietnamese women in Harris County, Houston, Texas. Cancer Nurs 130;28(2):119-29.
Excluded: Family history not systematically collected, OVID-Medline.
349. Hodgson SV, Bishop DT, Dunlop MG, et al. Suggested screening guidelines for familial colorectal cancer. J Med Screen 1995;2(1):45-51.
Excluded: Not an eligible publication type, OVID-Medline.
350. Hofferbert S, Worringen U, Backe J, et al. Simultaneous interdisciplinary counseling in German breast/ovarian cancer families: first experiences with patient perceptions, surveillance behavior and acceptance of genetic testing. Genet Couns 2000;11(2):127-46.
Excluded: Not an eligible population, OVID-Medline.
351. Holloway S, Porteous M, Cetnarskyj R, et al. Long-term attendance at follow-up of women assessed as being at increased risk of developing breast cancer in south-east Scotland. Community Genet 2007;10(4):252-60.
Excluded: Not an eligible population, OVID-Medline.
352. Horsman D, Wilson BJ, Avard D, et al. Clinical management recommendations for surveillance and risk-reduction strategies for hereditary breast and ovarian cancer among individuals carrying a deleterious BRCA1 or BRCA2 mutation. J Obstet Gynaecol Can 2007;29(1):45-60.
Excluded: Model does not categorize risk or validate, OVID-Medline.
353. 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):1769-76.
Excluded: Model does not categorize risk or validate, OVID-Medline.
354. Houlston RS, Murday V, Harocopos C, et al. Screening and genetic counselling for relatives of patients with colorectal cancer in a family cancer clinic.[erratum appears in BMJ 1990 Sep 1;301(6749):446]. BMJ 1990;301(6748):366-8.
Excluded: Not an eligible study design, OVID-Medline.
355. Hsia J, Kemper E, Kiefe C, et al. The importance of health insurance as a determinant of cancer screening: evidence from the Women's Health Initiative. Prev Med 2000;31(3):261-70.
Excluded: Family history not systematically collected, OVID-Medline.

356. 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 and Health Outcomes 2000;7(4):201-15.
Excluded: Model does not categorize risk or validate, OVID-Embase.
357. Humpel N, Magee C, Jones SC. The impact of a cancer diagnosis on the health behaviors of cancer survivors and their family and friends. Support Care Cancer 2007;15(6):621-30.
Excluded: Family history not systematically collected, OVID-Medline.
358. Humphrey LL, Helfand M, Chan BK. Review: Mammography reduces breast cancer mortality rates. Evid Based Med 2003;8(2):45
Excluded: Not an eligible study design, OVID-Embase.
359. Hundt S, Haug U, Brenner H. Blood markers for early detection of colorectal cancer: A systematic review. Cancer Epidemiol Biomarkers Prev 2007;16(10):1935-53.
Excluded: Not an eligible population, OVID-Embase.
360. Hunter A, Humphries SE. Family history of breast cancer and cost of life assurance: a test case comparison of current UK industry practice. BMJ 2005;331(7530):1438-9.
Excluded: Not an eligible study design, OVID-Medline.
361. Hurt GJ, McQuellon RP, Michielutte R, et al. Risk assessment of first-degree relatives of women with breast cancer: a feasibility study. Oncol Nurs Forum 2001;28(7):1097-104.
Excluded: Family history not systematically collected, OVID-Medline.
362. Husaini BA, Sherkat DE, Bragg R, et al. Predictors of breast cancer screening in a panel study of African American women. Women Health 2001;34(3):35-51.
Excluded: Family history not systematically collected, OVID-Embase.
363. Hyman RB, Baker S, Ephraim R, et al. Health Belief Model variables as predictors of screening mammography utilization. J Behav Med 1994;17(4):391-406.
Excluded: Family history not systematically collected, OVID-Medline.
364. Iannuzzi-Sucich M, Kenny AM. Preventive medicine for older women: gynecologic screening guidelines. Fam Pract Recertif 2004;26(6):53-60.
Excluded: Not an eligible intervention or outcome, VID-Cinahl.
365. Ingraham BA, Bragdon B, Nohe A. Molecular basis of the potential of vitamin D to prevent cancer. Curr Med Res Opin 2008;24(1):139-49.
Excluded: Not an eligible study design, OVID-Medline.
366. Irani S, Krevsky B. Colorectal cancer screening: Which tests, how often? Consultant 2007;47(2):138-45.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
367. 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(1 B):653-8.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
368. Irwig L, Houssami N, van Vliet C. New technologies in screening for breast cancer: a systematic review of their accuracy. Br J Cancer 2004;90(11):2118-22.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
369. Isaacs C, Peshkin BN, Schwartz M, et al. Breast and ovarian cancer screening practices in healthy women with a strong family history of breast or ovarian cancer. Breast Cancer Res Treat 2002;71(2):103-12.
Excluded: Not an eligible study design, OVID-Medline.
370. Italian Review Team 2006. Systematic Literature Review Report. The Associations between Food, Nutrition and Physical Activity and the Risk of Ovarian Cancer and Underlying Mechanisms. World Cancer Research Fund/American Institute for Cancer Research, Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington, DC: AICR, 2007.
Excluded: Not an eligible population
371. Ito H, Matsuo K, Wakai K, et al. An intervention study of smoking cessation with feedback on genetic cancer susceptibility in Japan. Prev Med 2006;42(2):102-8.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
372. Itzkowitz SH, Present DH, Binder V, et al. Consensus conference: Colorectal cancer screening and surveillance in inflammatory bowel disease. Inflamm Bowel Dis 2005;11(3):314-21.
Excluded: Model does not categorize risk or validate, OVID-Embase.
373. 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
Excluded: Family history not systematically collected, OVID-Medline.
374. Jacobs ET, Jiang R, Alberts DS, et al. Selenium and colorectal adenoma: results of a pooled analysis.[see comment]. J Natl Cancer Inst 2004;96(22):1669-75. Excluded: Family history not systematically collected, OVID-Medline.

375. Jacobsen PB, Lamonde LA, Honour M, et al. Relation of family history of prostate cancer to perceived vulnerability and screening behavior. Psychooncology 2004;13(2):80-5.
Excluded: Family history not systematically collected, OVID-Medline.
376. James GD, Berge-Landry HH, Valdimarsdottir HB, et al. Urinary catecholamine levels in daily life are elevated in women at familial risk of breast cancer. Psychoneuroendocrinology 2004;29(7):831-8.
Excluded: Family history not systematically collected, OVID-Medline.
377. James TM, Greiner KA, Ellerbeck EF, et al. Disparities in colorectal cancer screening: a guideline-based analysis of adherence. Ethn Dis 2006;16(1):228-33.
Excluded: Family history not systematically collected, OVID-Medline.
378. Janda M, Obermair A, Haidinger G, et al. Austrian women's attitudes toward and knowledge of breast self-examination. J Cancer Educ 2000;15(2):91-4.
Excluded: Not an eligible study design, VID-Cinahl.
379. Jasperson KW, Lowstuter K, Weitzel JN. Assessing the predictive accuracy of hMLH1 and hMSH2 mutation probability models. J Genet Couns 2006;15(5):339-47.
Excluded: Model does not categorize risk or validate, OVID-Medline.
380. Jeffery, M, Hickey, et al. Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev 2008;(1):
Excluded: Not an eligible intervention or outcome, OVID-Cochrane.
381. Johnson KA, Trimbath JD, Petersen GM, et al. Impact of genetic counseling and testing on colorectal cancer screening behavior. Genet Test 2002;6(4):303-6.
Excluded: Not an eligible population, OVID-Medline.
382. Johnson PM, Gallinger S, McLeod RS. Surveillance colonoscopy in individuals at risk for hereditary nonpolyposis colorectal cancer: an evidence-based review. Dis Colon Rectum 1994;49(1):80-93.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
383. Joint Test and Technology Transfer Committee Working Group ACoMG. Genetic testing for colon cancer: joint statement of the American College of Medical Genetics and American Society of Human Genetics. Joint Test and Technology Transfer Committee Working Group. Genet Med 2000;2(6):362-6.
Excluded: Model does not categorize risk or validate, OVID-Medline.
384. Jones JL, Hughes KS, Kopans DB, et al. Evaluation of hereditary risk in a mammography population. Clin Breast Cancer 2005;6(1):38-44.
Excluded: Model does not categorize risk or validate, OVID-Medline.
385. Jordan SJ, Whiteman DC, Purdie DM, et al. Does smoking increase risk of ovarian cancer? A systematic review. Gynecol Oncol 2006;103(3):1122-9.
Excluded: Not an eligible population, OVID-Medline.
386. Julian-Reynier C, Sobol H, Sevilla C, et al. Uptake of hereditary breast/ovarian cancer genetic testing in a French national sample of BRCA1 families.The French Cancer Genetic Network. Psychooncology 2000;9(6):504-10.
Excluded: Not an eligible study design, OVID-Medline.
387. Kadison P, Pelletier EM, Mounib EL, et al. Improved screening for breast cancer associated with a telephone-based risk assessment. Prev Med 1998;27(3):493-501.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
388. Kamidono S, Ohshima S, Hirao Y, et al. Evidence-based clinical practice guidelines for prostate cancer (summary - JUA 2006 edition). Int J Urol 2008;15(1):1-18.
Excluded: Model does not categorize risk or validate, OVID-Embase.
389. Kang HH, Williams R, Leary J, et al. Evaluation of models to predict BRCA germline mutations. Br J Cancer 2006;95(7):914-20.
Excluded: Model does not categorize risk or validate, OVID-Medline.
390. Kanik EA, Canbaz H, Colak T, et al. Chemopreventive effect of nonsteroidal anti-inflammatory drugs on the development of a new colorectal polyp or adenoma in a high-risk population: A meta-analysis. Current Therapeutic Research - Clinical and Experimental 2004;65(4):345-52.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
391. Kaplan KM, Weinberg GB, Small A, et al. Breast cancer screening among relatives of women with breast cancer. Am J Public Health 1991;81(9):1174-9.
Excluded: Family history not systematically collected, OVID-Medline.
392. Karazanashvili G, Abrahamsson PA. Prostate specific antigen and human glandular kallikrein 2 in early detection of prostate cancer. J Urol 2003;169(2):445-57. Excluded: Not an eligible study design, OVID-Medline.
393. Karliner LS, Napoles-Springer A, Kerlikowske K, et al. Missed opportunities: family history and behavioral risk factors in breast cancer risk assessment among a multiethnic group of women. J Gen Intern Med 2007;22(3):308-14.
Excluded: Family history not systematically collected, OVID-Medline.

394. Kash KM, Holland JC, Halper MS, et al. sychological distress and surveillance behaviors of women with a family history of breast cancer. J Natl Cancer Inst 1992;84(1):24-30.
Excluded: Not an eligible study design, OVID-Medline.
395. Kash KM, Holland JC, Osborne MP, et al. Psychological counseling strategies for women at risk of breast cancer. J Natl Cancer Inst 1995;Monographs.(17):73-9.
Excluded: Not an eligible publication type, OVID-Medline.
396. Kataja VV, Bergh J. ESMO Minimum Clinical Recommendations for diagnosis, treatment and follow-up of prostate cancer. Ann Oncol 2005;16:Suppl-6
Excluded: Model does not categorize risk or validate, OVID-Medline.
397. Kataja VV, Colleoni M, Bergh J, et al. ESMO Minimum Clinical Recommendations for diagnosis, treatment and follow-up of locally recurrent or metastatic breast cancer (MBC). Ann Oncol 2005;16:Suppl-2
Excluded: Model does not categorize risk or validate, OVID-Medline.
398. Katapodi MC, Lee KA, Facione NC, et al. Predictors of perceived breast cancer risk and the relation between perceived risk and breast cancer screening: a meta-analytic review. Prev Med 2004;38(4):388-402.
Excluded: Family history not systematically collected, OVID-Medline.
399. Katki HA. Effect of misreported family history on Mendelian mutation prediction models. Biometrics 2006;62(2):478-87.
Excluded: Model does not categorize risk or validate, OVID-Medline.
400. Katki HA. Incorporating medical interventions into carrier probability estimation for genetic counseling. BMC Medical Genetics 2007;8:13
Excluded: Model does not categorize risk or validate, OVID-Medline.
401. Kaur JS, Roubidoux MA, Sloan J, et al. Can the Gail model be useful in American Indian and Alaska Native populations? Cancer 2004;100(5):906-12.
Excluded: Model does not categorize risk or validate, OVID-Medline.
402. Kavanaugh CJ, Trumbo PR, Ellwood KC. The U.S. food and drug administration's evidence-based review for qualified health claims: Tomatoes, lycopene, and cancer. J Natl Cancer Inst 2007;99(14):1074-85.
Excluded: Not an eligible population, OVID-Embase.
403. Keinan-Boker L, Baron-Epel O, Garty N, et al. Family history of breast cancer and compliance with mammography in Israel: findings of the National Health Survey 2003-2004 (EUROHIS). Eur J Cancer Prev 2007;16(1):43-9.
Excluded: Family history not systematically collected, OVID-Medline.
404. Keller M, Jost R, Haunstetter CM, et al. Comprehensive genetic counseling for families at risk for HNPCC: impact on distress and perceptions. Genet Test 2002;6(4):291-302.
Excluded: Family history not systematically collected, OVID-Medline.
405. Kelly K, Leventhal H, Toppmeyer D, et al. Subjective and objective risks of carrying a BRCA1/2 mutation in individuals of Ashkenazi Jewish descent. J Genetic Couns 2003;12(4):351-71.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
406. Kelly K, Leventhal H, Andrykowski M, et al. The decision to test in women receiving genetic counseling for BRCA1 and BRCA2 mutations. J Genetic Couns 2004;13(3):237-57.
Excluded: Family history not systematically collected, OVID-Medline.
407. Kelly,K.M. Subjective and objective risk in individuals testing for BRCA1 and BRCA2 mutations Kelly. 2000
Excluded: Not an eligible publication type, OVID-PsycInfo.
408. Kelly RB, Shank JC. Adherence to screening flexible sigmoidoscopy in asymptomatic patients. Med Care 1992;30(11):1029-42.
Excluded: Family history not systematically collected, OVID-Medline.
409. Kenen R, Ardern-Jones A, Eeles R. Living with chronic risk: Healthy women with a family history of breast/ovarian cancer. ealth, Risk and Society 2003;5(3):315-31.
Excluded: Not an eligible study design, OVID-Embase.
410. Kerber RA, Neklason DW, Samowitz WS, et al. Frequency of familial colon cancer and hereditary nonpolyposis colorectal cancer (Lynch syndrome) in a large population database. Fam Cancer 2005;4(3):239-44.
Excluded: Model does not categorize risk or validate, OVID-Medline.
411. Key J, Hodgson S, Omar RZ, et al. Meta-analysis of studies of alcohol and breast cancer with consideration of the methodological issues. Cancer Causes Control 2006;17(6):759-70.
Excluded: Not an eligible population, OVID-Medline.
412. Key TJ, Spencer EA.Carbohydrates and cancer: an overview of the epidemiological evidence. Eur J Clin Nutr 2007;61:Suppl-21
Excluded: Not an eligible study design, OVID-Medline.
413. Khan NF, Ward A, Watson E, et al. Long-term survivors of adult cancers and uptake of primary health services: A systematic review. Eur J Cancer 2008;44(2):195-204.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
414. Khatcheressian JL, Wolff AC, Smith TJ, et al. American Society of Clinical Oncology 2006 update of the breast cancer follow-up and

management guidelines in the adjuvant setting. J Clin Oncol 2006;24(31):5091-7.
Excluded: Model does not categorize risk or validate, OVID-Medline.
415. Kievit W, de Bruin JH, Adang EM, et al. Current clinical selection strategies for identification of hereditary non-polyposis colorectal cancer families are inadequate: a meta-analysis. Clin Genet 2004;65(4):308-16.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
416. Kim SE, Perez-Stable EJ, Wong S, et al. Association between cancer risk perception and screening behavior among diverse women. Arch Intern Med 2008;168(7):728-34.
Excluded: Family history not systematically collected, OVID-Medline.
417. Kim Y, Valdimarsdottir HB, Bovbjerg DH. Family histories of breast cancer, coping styles, and psychological adjustment. J Behav Med 2003;26(3):225-43.
Excluded: Family history not systematically collected, OVID-Medline.
418. Kim Y, Duhamel KN, Valdimarsdottir HB, et al. Psychological distress among healthy women with family histories of breast cancer: effects of recent life events. Psychooncology 2005;14(7):555-63.
Excluded: Family history not systematically collected, OVID-Medline.
419. Kinney AY, Choi YA, DeVellis B, et al. Interest in genetic testing among first-degree relatives of colorectal cancer patients. Am J Prev Med 2000;18(3):249-52.
Excluded: Family history not systematically collected, OVID-Medline.
420. Kinney AY, Simonsen SE, Baty BJ, et al. Risk reduction behaviors and provider communication following genetic counseling and BRCA1 mutation testing in an African American kindred. J Genetic Couns 2006;15(4):293-305.
Excluded: Not an eligible population, OVID-Medline.
421. Kinney AY, Hicken B, Simonsen SE, et al. Colorectal cancer surveillance behaviors among members of typical and attenuated FAP families. Am J Gastroenterol 2007;102(1):153-62.
Excluded: Not an eligible study design, OVID-Medline.
422. Klimberg VS, Galandiuk S, Singletary ES, et al. Society of Surgical Oncology: statement on genetic testing for cancer susceptibilty. Committee on Issues and Governmental Affairs of the Society of Surgical Oncology. Ann Surg Oncol 1999;6(5):507-9.
Excluded: Model does not categorize risk or validate, OVID-Medline.
423. Ko C, Hyman NH, Standards Committee of The American Society of Colon and Rectal Surgeons. Practice parameter for the detection of colorectal neoplasms: an interim report (revised). Dis Colon Rectum 2006;49(3):299-301.
Excluded: Model does not categorize risk or validate, OVID-Medline.
424. Kokuer M, Naguib RN, Jancovic P, et al. Cancer risk analysis in families with hereditary nonpolyposis colorectal cancer. IEEE Trans Inf Technol Biomed 2006;10(3):581-7.
Excluded: Model does not categorize risk or validate, OVID-Medline.
425. Koo BC, Ng CS, King-Im J, et al. Minimal preparation CT for the diagnosis of suspected colorectal cancer in the frail and elderly patient. Clin Radiol 2006;61(2):127-39.
Excluded: Not an eligible population, OVID-Embase.
426. Koushik A, Hunter DJ, Spiegelman D, et al. Fruits, vegetables, and colon cancer risk in a pooled analysis of 14 cohort studies. J Natl Cancer Inst 2007;99(19):1471-83.
Excluded: Not an eligible population, OVID-Medline.
427. Kubik-Huch RA. Imaging the young breast. Breast 2006;15(Suppl 2):S35-S40
Excluded: Model does not categorize risk or validate, OVID-Embase.
428. Kubo A, Corley DA. Meta-analysis of antioxidant intake and the risk of esophageal and gastric cardia adenocarcinoma. Am J Gastroenterol 2007;102(10):2323-30.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
429. Kuhl CK. Screening of women with hereditary risk of breast cancer. Clin Breast Cancer 2004;5(4):269-71.
Excluded: Not an eligible intervention or outcome, OVID-Cinahl.
430. Kumar AS, Esserman LJ. Statins: Health-promoting agents show promise for breast cancer prevention. Clin Breast Cancer 2005;6(5):455-9.
Excluded: Not an eligible study design, OVID-Embase.
431. Kuschel B, Hauenstein E, Kiechle M, et al. Hereditary breast and ovarian cancer - Current clinical guidelines in Germany. Breast Care 2006;1(1):8-14.
Excluded: Model does not categorize risk or validate, OVID-Embase.
432. Lagerros YT, Hsieh S-F, Hsieh C-C. Physical activity in adolescence and young adulthood and breast cancer risk: A quantitative review. Eur J Cancer Prev 2004;13(1):5-12.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
433. Lancaster DR. Development and psychometric testing of the coping with breast cancer threat instrument. J Nurs Meas 2004;12(1):33-46.
Excluded: Family history not systematically collected, OVID-Medline.
434. Lancaster,D.R.N. Coping with appraised threat of breast cancer: primary prevention coping behaviors utilized by women at increased risk.
Excluded: Not an eligible publication type, OVID-Cinahl.

435. Lancaster JM, Powell CB, Kauff ND, et al. Society of Gynecologic Oncologists Education Committee statement on risk assessment for inherited gynecologic cancer predispositions. Gynecol Oncol 2007;107(2):159-62. Excluded: Model does not categorize risk or validate, OVID-Medline.
436. Lane DS, Zapka J, Breen N, et al. A systems model of clinical preventive care: the case of breast cancer screening among older women. For the NCI Breast Cancer Screening Consortium. Prev Med 2000;31(5):481-93. Excluded: Family history not systematically collected, OVID-Medline.
437. Larsson SC, Wolk A. Meat consumption and risk of colorectal cancer: a meta-analysis of prospective studies. Int J Cancer 2006;119(11):2657-64. Excluded: Not an eligible population, OVID-Medline.
438. Larsson SC, Giovannucci E, Wolk A. Folate and risk of breast cancer: a meta-analysis. J Natl Cancer Inst 2007;99(1):64-76. Excluded: Not an eligible population, OVID-Medline.
439. Lauver D, Nabholz S, Scott K, et al. Testing theoretical explanations of mammography use. Nurs Res 1997;46(1):32-9. Excluded: Family history not systematically collected, OVID-Medline.
440. Lawlor DA, Juni P, Ebrahim S, et al. Systematic review of the epidemiologic and trial evidence of an association between antidepressant medication and breast cancer. J Clin Epidemiol 2003;56(2):155-63. Excluded: Not an eligible population, OVID-Embase.
441. Leddin D, Hunt R, Champion M, et al. Canadian Association of Gastroenterology and the Canadian Digestive Health Foundation: Guidelines on colon cancer screening. Can J Gastroenterol 2004;18(2):93-9. Excluded: Model does not categorize risk or validate, OVID-Medline.
442. Lee-Lin F, Menon U, Pett M, et al. Breast cancer beliefs and mammography screening practices among Chinese American immigrants. J Obstet Gynecol Neonatal Nurs 2007;36(3):212-21. Excluded: Family history not systematically collected, OVID-Cinahl.
443. Lee-Lin,F.F. Mammography and Pap testing screening among first generation Chinese Americans DIssertation Abstract. 2006 Excluded: Not an eligible publication type, OVID-Cinahl.
444. Lee EO, Ahn SH, You C, et al. Determining the main risk factors and high-risk groups of breast cancer using a predictive model for breast cancer risk assessment in South Korea. Cancer Nurs 2004;27(5):400-6. Excluded: Model does not categorize risk or validate, OVID-Medline.
445. Lee JR, Vogel VG. Who uses screening mammography regularly? Cancer Epidemiol Biomarkers Prev 1995;4(8):901-6. Excluded: Family history not systematically collected, OVID-Medline.
446. Lee R, Localio AR, Armstrong K, et al. A meta-analysis of the performance characteristics of the free prostate-specific antigen test. Urology 2006;67(4):762-8. Excluded: Not an eligible population, OVID-Medline.
447. Lee SC, Bernhardt BA, Helzlsouer KJ. Utilization of BRCA1/2 genetic testing in the clinical setting: report from a single institution. Cancer 2002;94(6):1876-85. Excluded: Not an eligible population, OVID-Medline.
448. Legg JS. Genetic testing for inheritable cancers. Radiat Therapist 2004;13(2):99-105. Excluded: Family history not systematically collected, OVID-Cinahl.
449. Leggatt V, Mackay J, Yates JR. Evaluation of questionnaire on cancer family history in identifying patients at increased genetic risk in general practice. BMJ 1999;319(7212):757-8. Excluded: Family history not systematically collected, OVID-Medline.
450. Lemon S, Zapka J, Puleo E, et al. Colorectal cancer screening participation: comparisons with mammography and prostate-specific antigen screening. Am J Public Health 2001;91(8):1264-72. Excluded: Family history not systematically collected, OVID-Medline.
451. Lemon SC, Zapka JG, Clemow L. Health behavior change among women with recent familial diagnosis of breast cancer. Prev Med 2004;39(2):253-62. Excluded: Family history not systematically collected, OVID-Medline.
452. Lerman C, Rimer B, Trock B, et al. Factors associated with repeat adherence to breast cancer screening. Prev Med 1990;19(3):279-90. Excluded: Family history not systematically collected, OVID-Medline.
453. Lerman C, Daly M, Sands C, et al. Mammography adherence and psychological distress among women at risk for breast cancer. Natl Cancer Inst 1993;85(13):1074-80. Excluded: Family history not systematically collected, OVID-Medline.
454. Lerman C, Kash K, Stefanek M. Younger women at increased risk for breast cancer: perceived risk, psychological well-being, and surveillance behavior. J Natl Cancer Inst 1994;Monographs.(16):171-6. Excluded: Not an eligible publication type, OVID-Medline.
455. Lerman C, Narod S, Schulman K, et al. BRCA1 testing in families with hereditary breast-ovarian cancer. A prospective study of patient decision making and outcomes. JAMA 1996;275(24):1885-92. Excluded: Family history not systematically collected, OVID-Medline.

456. Lerman C, Schwartz MD, Miller SM, et al. A randomized trial of breast cancer risk counseling: interacting effects of counseling, educational level, and coping style. Health Psychol 1996;15(2):75-83.
Excluded: Not an eligible population, OVID-Medline.
457. Lerman C, Schwartz MD, Lin TH, et al. The influence of psychological distress on use of genetic testing for cancer risk. J Consult Clin Psychol 1997;65(3):414-20.
Excluded: Not an eligible population, OVID-Medline.
458. Lerman C, Hughes C, Trock BJ, et al. Genetic testing in families with hereditary nonpolyposis colon cancer. JAMA 1999;281(17):1618-22.
Excluded: Not an eligible study design, OVID-Medline.
459. Lerman C, Hughes C, Croyle RT, et al. Prophylactic surgery decisions and surveillance practices one year following BRCA1/2 testing. Prev Med 2000;31(1):75-80.
Excluded: Not an eligible population, OVID-Medline.
460. Lesniak,K.T. Psychological and sociodemographic predictors of psychological distress in BRCA1 and BRAC2 genetic testing participants within a community based genetic screening program Lesniak. 2001
Excluded: Not an eligible publication type, OVID-PsycInfo.
461. Levin B, Barthel JS, Burt RW, et al. Colorectal Cancer Screening Clinical Practice Guidelines. J Natl Compr Cancer Netw 2006;4(4):384-420.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
462. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Gastroenterology 2008;134(5):1570-95.
Excluded: Model does not categorize risk or validate, OVID-Medline.
463. Levin TR, Farraye FA, Schoen RE, et al. Quality in the technical performance of screening flexible sigmoidoscopy: Recommendations of an international multi-society task group. Gut 2005;54(6):807-13.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
464. Levine M, Moutquin JM, Walton R, et al. Chemoprevention of breast cancer. A joint guideline from the Canadian Task Force on Preventive Health Care and the Canadian Breast Cancer Initiative's Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. CMAJ 2001;164(12):1681-90.
Excluded: Model does not categorize risk or validate, VID-Medline.
465. Levy BT, Dawson J, Hartz AJ, et al. Colorectal cancer testing among patients cared for by Iowa family physicians. Am J Prev Med 2006;31(3):193-201.
Excluded: Not an eligible study design, OVID-Medline.
466. Lewis JD, Ng K, Hung KE, et al. Detection of proximal adenomatous polyps with screening sigmoidoscopy: a systematic review and meta-analysis of screening colonoscopy. Arch Intern Med 2003;163(4):413-20.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
467. Lewis SJ, Harbord RM, Harris R, et al. Meta-analyses of observational and genetic association studies of folate intakes or levels and breast cancer risk. J Natl Cancer Inst 2006;98(22):1607-22.
Excluded: Not an eligible population, OVID-Medline.
468. Liberman M, Sampalis F, Mulder DS, et al. Breast cancer diagnosis by scintimammography: a meta-analysis and review of the literature. Breast Cancer Res Treat 2003;80(1):115-26.
Excluded: Not an eligible population, OVID-Medline.
469. Liede A, Metcalfe K, Hanna D, et al. Evaluation of the needs of male carriers of mutations in BRCA1 or BRCA2 who have undergone genetic counseling. Am J Hum Genet 2000;67(6):1494-504.
Excluded: Not an eligible population, OVID-Medline.
470. Lim J, Macluran M, Price M, et al. Short- and long-term impact of receiving genetic mutation results in women at increased risk for hereditary breast cancer. J Genet Couns 2004;13(2):115-33.
Excluded: Family history not systematically collected, OVID-Medline.
471. Lin, O, Roy, et al. Screening sigmoidoscopy and colonoscopy for reducing colorectal cancer mortality in asymtomatic persons. Cochrane Database Syst Rev 2008;(1):
Excluded: Not an eligible study design, OVID-Cochrane.
472. Lin CJ, Block B, Nowalk MP, et al. Breast cancer risk assessment in socioeconomically disadvantaged urban communities. J Natl Med Assoc 2007;99(7):752-6.
Excluded: Model does not categorize risk or validate, OVID-Medline.
473. Lin OS. Clinical update: postpolypectomy colonoscopy surveillance. Lancet 2007;370(9600):1674-6.
Excluded: Model does not categorize risk or validate, OVID-Embase.

474. Lindberg NM, Wellisch D. Anxiety and compliance among women at high risk for breast cancer. Ann Behav Med 2001;23(4):298-303.
Excluded: Not an eligible study design, OVID-Medline.
475. Lindberg NM, Wellisch DK. Identification of traumatic stress reactions in women at increased risk for breast cancer. Psychosomatics 2004;45(1):7-16.
Excluded: Not an eligible study design, OVID-Medline.
476. Lindor NM, Petersen GM, Hadley DW, et al. Recommendations for the care of individuals with an inherited predisposition to Lynch syndrome: a systematic review. JAMA 2006;296(12):1507-17.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
477. Lippert MT, Eaker ED, Vierkant RA, et al. Breast cancer screening and family history among rural women in Wisconsin. Cancer Detect Prev 1999;23(3):265-72.
Excluded: Family history not systematically collected, OVID-Medline.
478. Lipton LR, Johnson V, Cummings C, et al. Refining the Amsterdam Criteria and Bethesda Guidelines: testing algorithms for the prediction of mismatch repair mutation status in the familial cancer clinic.[erratum appears in J Clin Oncol. 2005 May 20;23(15):3652]. J Clin Oncol 2004;22(24):4934-43.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
479. Lise M, Zavagno G, Meggiolaro F. Prophylactic mastectomy in women at high risk of breast cancer. FORUM - Trends in Experimental and Clinical Medicine 1997;7(1 Suppl. 2):112-6.
Excluded: Not an eligible study design, OVID-Embase.
480. Little MP, Muirhead CR, Charles MW. Describing time and age variations in the risk of radiation-induced solid tumour incidence in the Japanese atomic bomb survivors using generalized relative and absolute risk models. Stat Med 1999;18(1):17-33.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
481. Liu M, Guo Y-M, Guo X-J, et al. Evaluation of scintimammorgraphy in the diagnosis of primary breast cancer: A meta-analysis. Chinese Journal of Evidence-Based Medicine 2005;5(7):536-42.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
482. Liu X, Sennett C, Legorreta AP. Mammography utilization among California women age 40-49 in a managed care environment. Breast Cancer Res Treat 2001;67(2):181-6.
Excluded: Family history not systematically collected, OVID-Medline.
483. Loader S, Shields C, Rowley PT. Impact of genetic counseling and DNA testing on individuals with colorectal cancer with a positive family history: a population-based study. Genet Test 2005;9(4):313-9.
Excluded: Not an eligible population, OVID-Medline.
484. Locker GY, Hamilton S, Harris J, et al. ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. J Clin Oncol 2006;24(33):5313-27.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
485. Lodder L, Frets PG, Trijsburg RW, et al. Attitudes and distress levels in women at risk to carry a BRCA1/BRCA2 gene mutation who decline genetic testing. Am J Med Genet 2003;(Part 3):266-72.
Excluded: Not an eligible study design, OVID-Medline.
486. Loescher LJ. Cancer worry in women with hereditary risk factors for breast cancer. Oncol Nurs Forum 2003;Online.(5):767-72.
Excluded: Family history not systematically collected, OVID-Medline.
487. Loescher LJ, Lim K, Leitner O, et al. Risk control behaviors following BRCA genetic predisposition testing. Oncol Nurs Forum 2007;34(1):226
Excluded: Not an eligible publication type, OVID-Cinahl.
488. Longacre AV, Cramer LD, Gross CP. Screening colonoscopy use among individuals at higher colorectal cancer risk. J Clin Gastroenterol 2006;40(6):490-6.
Excluded: Family history not systematically collected, OVID-Medline.
489. Lopez ML, Iglesias JM, del Valle MO, et al. Impact of a primary care intervention on smoking, drinking, diet, weight, sun exposure, and work risk in families with cancer experience. Cancer Causes Control 2007;18(5):525-35.
Excluded: Family history not systematically collected, OVID-Medline.
490. Lord SJ, Lei W, Craft P, et al. A systematic review of the effectiveness of magnetic resonance imaging (MRI) as an addition to mammography and ultrasound in screening young women at high risk of breast cancer. Eur J Cancer 2007;43(13):1905-17.
Excluded: Family history not systematically collected, OVID-Medline.
491. Lostumbo L, Carbine N, Wallace J, et al. Prophylactic mastectomy for the prevention of breast cancer. Cochrane Database Syst Rev 2004;(4):CD002748
Excluded: Not an eligible intervention or outcome, OVID-Medline.

492. Love RR, Brown RL, Davis JE, et al. Frequency and determinants of screening for breast cancer in primary care group practice. Arch Intern Med 1993;153(18):2113-7.
Excluded: Family history not systematically collected, OVID-Embase.
493. Lubish L, Greenberg S, Friger M, et al. Breast cancer screening in two multicultural family practice teaching clinics. Isr Med Assoc J 2001;3(8):579-83.
Excluded: Family history not systematically collected, OVID-Medline.
494. Lunet N, Valbuena C, Vieira AL, et al. Fruit and vegetable consumption and gastric cancer by location and histological type: Case-control and meta-analysis. Eur J Cancer Prev 2007;16(4):312-27.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
495. Lux MP, Ackermann S, Bani MR, et al. Age of uptake of early cancer detection facilities by low-risk and high-risk patients with familial breast and ovarian cancer. Eur J Cancer Prev 2005;14(6):503-11.
Excluded: Not an eligible study design, OVID-Medline.
496. Lux MP, Ackermann S, Nestle-Kramling C, et al. Use of intensified early cancer detection in high-risk patients with familial breast and ovarian cancer. Eur J Cancer Prev 2005;14(4):399-411.
Excluded: Not an eligible population, OVID-Medline.
497. Lynch HT, Snyder C, Lynch JF, et al. Patient responses to the disclosure of BRCA mutation tests in hereditary breast-ovarian cancer families. Cancer Genet Cytogenet 2006;165(2):91-7.
Excluded: Not an eligible population, OVID-Medline.
498. MacDonald DJ, Sarna L, Uman GC, et al. Cancer screening and risk-reducing behaviors of women seeking genetic cancer risk assessment for breast and ovarian cancers. Oncol Nurs Forum 2006;Online.(2):E27-E35
Excluded: Not an eligible population, OVID-Medline.
499. MacInnis RJ, English DR. Body size and composition and prostate cancer risk: systematic review and meta-regression analysis. Cancer Causes Control 2006;17(8):989-1003.
Excluded: Not an eligible population, OVID-Medline.
500. Maciosek MV, Coffield AB, Edwards NM, et al. Priorities among effective clinical preventive services: results of a systematic review and analysis. Am J Prev Med 2006;31(1):52-61.
Excluded: Family history not systematically collected, OVID-Medline.
501. MacKarem G, Roche CA, Hughes KS. The effectiveness of the Gail model in estimating risk for development of breast cancer in women under 40 years of age. Breast J 2001;7(1):34-9.
Excluded: Model does not categorize risk or validate, OVID-Medline.
502. MacLean CH, Newberry SJ, Mojica WA, et al. Effects of omega-3 fatty acids on cancer risk: a systematic review. 2006 Apr 26;295(16):1900]. JAMA 2006;295(4):403-15.
Excluded: Not an eligible population, OVID-Medline.
503. Madalinska JB, Van Beurden M, Bleiker EM, et al. Predictors of prophylactic bilateral salpingo-oophorectomy compared with gynecologic screening use in BRCA1/2 mutation carriers. J Clin Oncol 2007;25(3):301-7.
Excluded: Not an eligible population, OVID-Cinahl.
504. Madlensky L. Screening behaviors in relatives of Ontario colorectal cancer patients: a social-ecological approach.
Excluded: Not an eligible publication type, OVID-Cinahl.
505. Madlensky L, Esplen MJ, Gallinger S, et al. Relatives of colorectal cancer patients: factors associated with screening behavior. Am J Prev Med 2003;25(3):187-94.
Excluded: Family history not systematically collected, OVID-Medline.
506. Madlensky L, Flatt SW, Bardwell WA, et al. Is family history related to preventive health behaviors and medical management in breast cancer patients? Breast Cancer Res Treat 2005;90(1):47-54.
Excluded: Family history not systematically collected, OVID-Medline.
507. Madlensky L, Vierkant RA, Vachon CM, et al. Preventive health behaviors and familial breast cancer. Cancer Epidemiol Biomarkers Prev 2005;14(10):2340-5.
Excluded: Family history not systematically collected, OVID-Medline.
508. Mahon SM, Casperson DS. Hereditary cancer syndrome: Part 2.--Psychosocial issues, concerns, and screening--results of a qualitative study. Oncol Nurs Forum 1995;22(5):775-82.
Excluded: Not an eligible study design, OVID-Medline.
509. Mahon SM. From research to clinical practice. Evidence-based practice: recommendations for the early detection of breast cancer. Clin J Oncol Nurs 2003;7(6):693-6.
Excluded: Model does not categorize risk or validate, OVID-Cinahl.
510. Mangiapane S, Blettner M, Schlattmann P. Aspirin use and breast cancer risk: A meta-analysis and meta-regression of observational studies from 2001 to 2005. Pharmacoepidemiol Drug Saf 2008;17(2):115-24. Excluded: Not an eligible population, OVID-Embase.

511. Manheimer,J. Medical risk, perceived risk, and body anxiety in women attending a high-risk breast surveillance clinic Manheimer. 1993
Excluded: Not an eligible publication type, OVID-PsycInfo.
512. Mann GJ, Thorne H, Balleine RL, et al. Analysis of cancer risk and BRCA1 and BRCA2 mutation prevalence in the kConFab familial breast cancer resource. Breast Cancer Res 2006;8(1):R12
Excluded: Model does not categorize risk or validate, OVID-Medline.
513. Marques-Vidal P, Ravasco P, Ermelinda CM. Foodstuffs and colorectal cancer risk: a review. [Review] [66 refs]. Clin Nutr 2006;25(1):14-36.
Excluded: Not an eligible population, OVID-Medline.
514. Marroni F, Aretini P, D'Andrea E, et al. Penetrances of breast and ovarian cancer in a large series of families tested for BRCA1/2 mutations. Eur J Hum Genet 2004;12(11):899-906.
Excluded: Model does not categorize risk or validate, OVID-Medline.
515. Marroni F, Aretini P, D'Andrea E, et al. Evaluation of widely used models for predicting BRCA1 and BRCA2 mutations. J Med Genet 2004;41(4):278-85.
Excluded: Model does not categorize risk or validate, OVID-Medline.
516. Marteau TM, Lerman C. Genetic risk and behavioural change. BMJ 2001;322(7293):1056-9.
Excluded: Not an eligible study design, OVID-Embase.
517. Martin RM, Middleton N, Gunnell D, et al. Breast-feeding and cancer: The Boyd Orr cohort and a systematic review with meta-analysis. J Natl Cancer Inst 2005;97(19):1446-57.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
518. Martin W, Degner L. Perception of risk and surveillance practices of women with a family history of breast cancer. Cancer Nurs 2006;29(3):227-35.
Excluded: Family history not systematically collected, OVID-Medline.
519. Masi CM, Blackman DJ, Peek ME. Interventions to enhance breast cancer screening, diagnosis, and treatment among racial and ethnic minority women. Med Care Res Rev 2007;64(5:Suppl):Suppl-242S
Excluded: Not an eligible intervention or outcome, OVID-Medline.
520. Matthews BA, Nattinger AB, Venkatesan T, et al. Objective risk, subjective risk, and colorectal cancer screening among a clinic sample. Psychol Health Med 2007;12(2):135-47.
Excluded: Family history not systematically collected, OVID-Medline.
521. Mayo MS, Kimler BF, Fabian CJ. Evaluation of models for the prediction of breast cancer development in women at high risk. J Appl Res 2001;1(1):37-44.
Excluded: Model does not categorize risk or validate, OVID-Cinahl.
522. McCarthy BD, Moskowitz MA. Screening flexible sigmoidoscopy: Patient attitudes and compliance. J Gen Intern Med 1993;8(3):120-5.
Excluded: Family history not systematically collected, OVID-Embase.
523. McCaul KD, Branstetter AD, O'Donnell SM, et al. A descriptive study of breast cancer worry. J Behav Med 1998;21(6):565-79.
Excluded: Family history not systematically collected, OVID-Medline.
524. McCormack VA, dos SS, I. Breast density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. Cancer Epidemiol Biomarkers Prev 2006;15(6):1159-69.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
525. McCullum M. Hereditary cancer risk assessment. Can Oncol Nurs J 1997;7(4):236-7.
Excluded: Not an eligible study design, OVID-Medline.
526. McDonald L. Soy food and soy supplements may not do the same thing in terms of breast cancer risk reduction. Cancer Biol Ther 2006;5(5):458-9.
Excluded: Not an eligible study design, OVID-Embase.
527. McInerney-Leo A, Hadley D, Kase RG, et al. BRCA1/2 testing in hereditary breast and ovarian cancer families III: risk perception and screening. Am J Med Genet 2006;(20):2198-206.
Excluded: Not an eligible population, OVID-Medline.
528. McKinley JM, Weideman PC, Jenkins MA, et al. Prostate screening uptake in Australian BRCA1 and BRCA2 carriers. Hereditary Cancer in Clinical Practice 2007;5(3):161-3.
Excluded: Not an eligible population, OVID-Embase.
529. McKinnon W, Naud S, Ashikaga T, et al. Results of an intervention for individuals and families with BRCA mutations: a model for providing medical updates and psychosocial support following genetic testing. J Genetic Couns 2007;16(4):433-56.
Excluded: Not an eligible population, OVID-Medline.
530. McMurrick P, Dorien S, Shapiro J. Bowel cancer - guide for the GP. Aust Fam Physician 2006;35(4):192-7.
Excluded: Model does not categorize risk or validate, OVID-Cinahl.
531. McTiernan A, Kuniyuki A, Yasui Y, et al. Comparisons of two breast cancer risk estimates in women with a family history of breast cancer. Cancer Epidemiol Biomarkers Prev 2001;10(4):333-8.
Excluded: Model does not categorize risk or validate, OVID-Medline.

532. Meijers-Heijboer H, Brekelmans CT, Menke-Pluymers M, et al. Use of genetic testing and prophylactic mastectomy and oophorectomy in women with breast or ovarian cancer from families with a BRCA1 or BRCA2 mutation. J Clin Oncol 2003;21(9):1675-81.
Excluded: Not an eligible population, OVID-Medline.
533. Meiser B, Butow P, Barratt A, et al. Attitudes toward prophylactic oophorectomy and screening utilization in women at increased risk of developing hereditary breast/ovarian cancer. Gynecol Oncol 1999;75(1):122-9.
Excluded: Family history not systematically collected, OVID-Medline.
534. Meiser B, Butow P, Barratt A, et al. Breast cancer screening uptake in women at increased risk of developing hereditary breast cancer. Breast Cancer Res Treat 2000;59(2):101-11.
Excluded: Not an eligible study design, OVID-Medline.
535. Meiser B, Butow P, Schnieden V, et al. Psychological adjustment of women at increased risk of developing hereditary breast cancer. Psychol Health Med 2000;5(4):377-88.
Excluded: Family history not systematically collected, OVID-Embase.
536. Meiser B, Halliday JL. What is the impact of genetic counselling in women at increased risk of developing hereditary breast cancer? A meta-analytic review. Soc Sci Med 2002;54(10):1463-70.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
537. Meiser B, Butow P, Price M, et al. Attitudes to prophylactic surgery and chemoprevention in Australian women at increased risk for breast cancer. J Womens Health (Larchmt) 2003;12(8):769-78.
Excluded: Not an eligible study design, OVID-Medline.
538. Meiser B, Cowan R, Costello A, et al. Prostate cancer screening in men with a family history of prostate cancer: the role of partners in influencing men's screening uptake. Urology 2007;70(4):738-42. Excluded: Not an eligible study design, OVID-Medline.
539. Meiser B, Butow P, Schnieden V, et al. Psychological adjustment of women at increased risk of developing hereditary breast cancer. Psychol Health Med 2000;5(4):377-88.
Excluded: Not an eligible population, OVID-PsycInfo.
540. Menon U, Skates SJ, Lewis S, et al. Prevalence screening for ovarian cancer using risk of ovarian cancer algorithm. Int J Gynecol Cancer 2003;13(suppl 1):1 Excluded: Not an eligible intervention or outcome, OVID-Cochrane.
541. Menon U, Skates SJ, Lewis S, et al. Prospective study using the risk of ovarian cancer algorithm to screen for ovarian cancer. J Clin Oncol 2005;23(31):7919-26.
Excluded: Not an eligible intervention or outcome, OVID-Cochrane.
542. Mertens WC, Katz D, Quinlan M, et al. Effect of oncologist-based counseling on patient-perceived breast cancer risk and psychological distress. Community Oncology 2008;5(2):108-14.
Excluded: Not an eligible population, OVID-Embase.
543. Metcalfe KA, Foulkes WD, Kim-Sing C, et al. Family history as a predictor of uptake of cancer preventive procedures by women with a BRCA1 or BRCA2 mutation. Clin Genet 2008;73(5):474-9.
Excluded: Family history not systematically collected, OVID-Embase.
544. Metcalfe KA, Birenbaum-Carmeli D, Lubinski J, et al. International variation in rates of uptake of preventive options in BRCA1 and BRCA2 mutation carriers. Int J Cancer 2008;122(9):2017-22.
Excluded: Family history not systematically collected, OVID-Medline.
545. Miller D, Livingstone V, Herbison P. Interventions for relieving the pain and discomfort of screening mammography. Cochrane Database Syst Rev 2008;(1):CD002942
Excluded: Not an eligible intervention or outcome, OVID-Medline.
546. Mistry K, Cable G. Meta-analysis of prostate-specific antigen and digital rectal examination as screening tests for prostate carcinoma. J Am Board Fam Pract 2003;16(2):95-101.
Excluded: Not an eligible population, OVID-Medline.
547. Mizoue T, Tanaka K, Tsuji I, et al. Alcohol drinking and colorectal cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol 2006;36(9):582-97.
Excluded: Not an eligible population, OVID-Medline.
548. Modan B, Hartge P, Hirsh-Yechezkel G, et al. Parity, oral contraceptives, and the risk of ovarian cancer among carriers and noncarriers of a BRCA1 or BRCA2 mutation. N Engl J Med 2001;345(4):235-40. PM:11474660
Excluded: Not an eligible study design
549. Moghaddam AA, Woodward M, Huxley R. Obesity and risk of colorectal cancer: a meta-analysis of 31 studies with 70,000 events. Cancer Epidemiol Biomarkers Prev 2007;16(12):2533-47. Excluded: Not an eligible population, OVID-Medline.
550. Moja L, Moschetti I, Liberati A, et al. Understanding systematic reviews: the meta-analysis graph (also called 'forest plot'). Intern Emerg Med 2007;2(2):140-2. Excluded: Not an eligible study design, OVID-Medline.

551. Moller P, Evans G, Haites N, et al. Guidelines for follow-up of women at high risk for inherited breast cancer: consensus statement from the Biomed 2 Demonstration Programme on Inherited Breast Cancer. Dis Markers 1999;15(1-3):207-11.
Excluded: Model does not categorize risk or validate, OVID-Medline.
552. Moller P, Evans DG, Haites NE, et al. Women at risk for inherited breast or ovarian cancer: Guidelines for follow-up. CME Journal of Gynecologic Oncology 2000;5(3):269-71.
Excluded: Model does not categorize risk or validate, OVID-Embase.
553. Monninkhof EM, Elias SG, Vlems FA, et al. Physical activity and breast cancer: a systematic review. Epidemiology 2007;18(1):137-57.
Excluded: Not an eligible population, OVID-Medline.
554. Montgomery DA, Krupa K, Cooke TG. Follow-up in breast cancer: does routine clinical examination improve outcome? A systematic review of the literature. Br J Cancer 2007;97(12):1632-41.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
555. Morantz C, American Cancer Society. ACS guidelines for early detection of cancer. Am Fam Physician 2004;69(8):2013
Excluded: Model does not categorize risk or validate, OVID-Medline.
556. Morris KT, Johnson N, Krasikov N, et al. Genetic counseling impacts decision for prophylactic surgery for patients perceived to be at high risk for breast cancer. Am J Surg 2001;181(5):431-3.
Excluded: Not an eligible population, OVID-Medline.
557. Moskal A, Norat T, Ferrari P, et al. Alcohol intake and colorectal cancer risk: a dose-response meta-analysis of published cohort studies. Int J Cancer 2007;120(3):664-71.
Excluded: Not an eligible population, OVID-Medline.
558. Moss S. Overdiagnosis in randomised controlled trials of breast cancer screening. Breast Cancer Res 2005;7(5):230-4.
Excluded: Not an eligible study design, OVID-Embase.
559. Mpofu C, Watson AJ, Rhodes JM. Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease.[update in Cochrane Database Syst Rev. 2006;(2):CD000279; PMID: 16625534]. Cochrane Database Syst Rev 2004;(2):CD000279
Excluded: Not an eligible intervention or outcome, OVID-Medline.
560. Mulhall BP, Veerappan GR, Jackson JL. Meta-analysis: computed tomographic colonography. Summary for patients in Ann Intern Med. 2005 Apr 19;142(8):I74; PMID: 15838063. Ann Intern Med 2005; Excluded: Not an eligible population, OVID-Medline.
561. Murabito JM, Evans JC, Larson MG, et al. Family breast cancer history and mammography: Framingham Offspring Study. Am J Epidemiol 2001;154(10):916-23.
Excluded: Family history not systematically collected, OVID-Medline.
562. Murff HJ, Spigel DR, Syngal S. Does this patient have a family history of cancer? An evidence-based analysis of the accuracy of family cancer history. JAMA 2004;292(12):1480-9.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
563. Murff HJ, Peterson NB, Greevy RA, et al. Early initiation of colorectal cancer screening in individuals with affected first-degree relatives. J Gen Intern Med 2007;22(1):121-6.
Excluded: Family history not systematically collected, OVID-Medline.
564. Murff HJ, Peterson NB, Fowke JH, et al. Colonoscopy screening in African Americans and whites with affected first-degree relatives. Arch Intern Med 2008;168(6):625-31.
Excluded: Family history not systematically collected, OVID-Embase.
565. Myers,M.F. Decision making regarding prophylactic mastectomy and breast cancer susceptibility testing among women at increased risk of breast cancer. Dissertation Abstract. 2000
Excluded: Not an eligible publication type, OVID-PsycInfo.
566. Myers RE, Weinberg DS, Manne SL, et al. Genetic and environmental risk assessment for colorectal cancer risk in primary care practice settings: a pilot study. Genet Med 2007;9(6):378-84. Excluded: Not an eligible intervention or outcome, OVID-Medline.
567. Nam RK, Toi A, Klotz LH, et al. Nomogram prediction for prostate cancer and aggressive prostate cancer at time of biopsy: utilizing all risk factors and tumor markers for prostate cancer. Can J Urol 2006;13 Suppl 2:2-10. PM:16672122
Excluded: Not an eligible study design,
568. Nanda R, Schumm LP, Cummings S, et al. Genetic testing in an ethnically diverse cohort of high-risk women: a comparative analysis of BRCA1 and BRCA2 mutations in American families of European and African ancestry. JAMA 2005;294(15):1925-33.
Excluded: Model does not categorize risk or validate, OVID-Medline.
569. Narod SA, Offit K. Prevention and management of hereditary breast cancer. J Clin Oncol 2005;23(8):1656-63.
Excluded: Not an eligible study design, OVID-Embase.

570. Negri E, Decarli A, La Vecchia C, et al. Identification of high risk groups for breast cancer by means of logistic models. J Clin Epidemiol 1990;43(5):413-8. Excluded: Model does not categorize risk or validate, OVID-Medline.
571. Neilson AR, Whynes DK. Determinants of persistent compliance with screening for colorectal cancer. Soc Sci Med 1995;41(3):365-74. Excluded: Not an eligible study design, OVID-Embase.
572. Neise C, Rauchfuss M, Paepke S, et al. Risk perception and psychological strain in women with a family history of breast cancer. Onkologie 2001;24(5):470-5. Excluded: Not an eligible study design, OVID-Medline.
573. Nelson HD, Huffman LH, Fu R, et al. Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: Systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med 2005;143(5):362-47. Excluded: Not an eligible intervention or outcome, OVID-Embase.
574. Ng KK, Fung SY, Chow LW. Practice of breast self-examination among high risk Chinese women in Hong Kong. Chin Med J (Engl) 2000;113(12):1100-3. Excluded: Family history not systematically collected, OVID-Medline.
575. Ngo SN, Williams DB, Cobiac L, et al. Does garlic reduce risk of colorectal cancer? A systematic review. J Nutr 2007;137(10):2264-9. Excluded: Not an eligible intervention or outcome, OVID-Medline.
576. Norman P, Brain K. An application of an extended health belief model to the prediction of breast self-examination among women with a family history of breast cancer. Br J Health Psychol 2005;10(Pt:1):1-16. Excluded: Not an eligible study design, OVID-Medline.
577. Novotny J, Pecen L, Petruzelka L, et al. Breast cancer risk assessment in the Czech female population--an adjustment of the original Gail model. Breast Cancer Res Treat 2006;95(1):29-35. Excluded: Model does not categorize risk or validate, OVID-Medline.
578. Ohori M, Swindle P. Nomograms and instruments for the initial prostate evaluation: the ability to estimate the likelihood of identifying prostate cancer. Semin Urol Oncol 2002;20(2):116-22. PM:12012297 Excluded: Not an eligible study design
579. Okasha M, McCarron P, Gunnell D, et al. Exposures in childhood, adolescence and early adulthood and breast cancer risk: a systematic review of the literature. [Review] [243 refs]. Breast Cancer Res Treat 2003;78(2):223-76. Excluded: Not an eligible intervention or outcome, OVID-Medline.
580. Oleske DM, Galvez A, Cobleigh MA, et al. Are tri-ethnic low-income women with breast cancer effective teachers of the importance of breast cancer screening to their first-degree relatives? Results from a randomized clinical trial. Breast J 2007;13(1):19-27. Excluded: Family history not systematically collected, OVID-Medline.
581. Olsen CM, Green AC, Whiteman DC, et al. Obesity and the risk of epithelial ovarian cancer: a systematic review and meta-analysis. Eur J Cancer 2007;43(4):690-709. Excluded: Not an eligible population, OVID-Medline.
582. Olsen CM, Bain CJ, Jordan SJ, et al. Recreational physical activity and epithelial ovarian cancer: A case-control study, systematic review, and meta-analysis. Cancer Epidemiol Biomarkers Prev 2007;16(11):2321-30. Excluded: Not an eligible population, OVID-Embase.
583. Optenberg SA, Clark JY, Brawer MK, et al. Development of a decision-making tool to predict risk of prostate cancer: the Cancer of the Prostate Risk Index (CAPRI) test. Urology 1997;50(5):665-72. PM:9372872 Excluded: Not an eligible study design
584. Ormondroyd E, Moynihan C, Watson M, et al. Disclosure of genetics research results after the death of the patient participant: a qualitative study of the impact on relatives. J Genet Couns 2007;16(4):527-38. Excluded: Family history not systematically collected, OVID-Medline.
585. Otto SJ, Fracheboud J, Looman CW, et al. Initiation of population-based mammography screening in Dutch municipalities and effect on breast-cancer mortality: a systematic review. Lancet 2003;361(9367):1411-7. Excluded: Not an eligible population, OVID-Medline.
586. Palmer RC, Emmons KM, Fletcher RH, et al. Familial risk and colorectal cancer screening health beliefs and attitudes in an insured population. Prev Med 2007;45(5):336-41. Excluded: Not an eligible study design, OVID-Medline.
587. Palomares MR, Machia JR, Lehman CD, et al. Mammographic density correlation with Gail model breast cancer risk estimates and component risk factors. Cancer Epidemiol Biomarkers Prev 2006;15(7):1324-30. Excluded: Model does not categorize risk or validate, OVID-Medline.
588. Papagrigoriadis S. Follow-up of patients with colorectal cancer: The evidence is in favour but we are still in need of a protocol. Int J Surg 2007;5(2):120-8. Excluded: Not an eligible study design, OVID-Embase.

589. Park JG, Vasen HF, Park YJ, et al. Suspected HNPCC and Amsterdam criteria II: evaluation of mutation detection rate, an international collaborative study. Int J Colorectal Dis 2002;17(2):109-14.
Excluded: Model does not categorize risk or validate, OVID-Medline.
590. Park,N. Effects of breast cancer risk, psychological distress, and dispositional optimism on immune responses in healthy women Excluded: Not an eligible publication type, OVID-Cinahl.
591. Parmigiani G, Chen S, Iversen ES, Jr., et al. Validity of models for predicting BRCA1 and BRCA2 mutations. Summary for patients in Ann Intern Med. 2007 Oct 2;147(7):I38; PMID: 17909202.
Excluded: Model does not categorize risk or validate, OVID-Medline.
592. Pasini B, Casalis Cavalchini GC, Genovese T, et al. Evaluating breast cancer risk: available models to assess individual breast cancer risk and probability to be a BRCA mutation carrier. J Exp Clin Cancer Res 2002;21(Suppl. 3):23-9.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
593. Patenaude AF, Schneider KA, Kieffer SA, et al. Acceptance of invitations for p53 and BRCA1 predisposition testing: Factors infleuencing potential utilization of cancer genetic testing cancer genetic testing. Psychooncology 1996;5(3):241-50.
Excluded: Not an eligible population, OVID-Embase.
594. Percesepe A, Anti M, Roncucci L, et al. The effect of family size on estimates of the frequency of hereditary non-polyposis colorectal cancer. Br J Cancer 1995;72(5):1320-3.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
595. Perkins JJ, Sanson-Fisher RW, Clarke SJ, et al. An exploration of screening practices for prostate cancer and the associated community expenditure. Br J Urol 1998;82(4):524-9.
Excluded: Not an eligible study design, OVID-Medline.
596. Perry N, Broeders M, de Wolf C, et al. European guidelines for quality assurance in breast cancer screening and diagnosis. Fourth edition--summary document. Ann Oncol 2008;19(4):614-22.
Excluded: Model does not categorize risk or validate, OVID-Medline.
597. Peshkin BN, Schwartz MD, Isaacs C, et al. Utilization of breast cancer screening in a clinically based sample of women after BRCA1/2 testing. Cancer Epidemiol Biomarkers Prev 2002;11(10:Pt 1):t-8 Excluded: Not an eligible population, OVID-Medline.
598. Pestalozzi BC, Luporsi-Gely E, Jost LM, et al. ESMO Minimum Clinical Recommendations for diagnosis, adjuvant treatment and follow-up of primary breast cancer. Ann Oncol 2005;16:Suppl-9
Excluded: Family history not systematically collected, OVID-Medline.
599. Peters NHGM, Borel R, I, Zuithoff NPA, et al. Meta-analysis of MR imaging in the diagnosis of breast lesions. Radiology 2008;246(1):116-24.
Excluded: Not an eligible population, OVID-Embase.
600. Peterson SK, Watts BG, Koehly LM, et al. How families communicate about HNPCC genetic testing: findings from a qualitative study. Am J Med Genet 2003;Part(1):78-86.
Excluded: Family history not systematically collected, OVID-Medline.
601. Petro-Nustas WI. Factors associated with mammography utilization among Jordanian women. J Transcult Nurs 2001;12(4):284-91.
Excluded: Family history not systematically collected, OVID-Cinahl.
602. Phillips KA, Jenkins MA, Lindeman GJ, et al. Risk-reducing surgery, screening and chemoprevention practices of BRCA1 and BRCA2 mutation carriers: a prospective cohort study. Clin Genet 2006;70(3):198-206.
Excluded: Not an eligible population, OVID-Medline.
603. Phillips,M.A. Reliability of a statistical instrument for predicting BRCA1/BRCA2 genetic mutation carrier status.
Excluded: Not an eligible publication type, OVID-Cinahl.
604. Pieterse K, van Dooren S, Seynaeve C, et al. Passive coping and psychological distress in women adhering to regular breast cancer surveillance. Psychooncology 2007;16(9):851-8.
Excluded: Not an eligible study design, OVID-PsycInfo.
605. Pinol V, Castells A, Andreu M, et al. Accuracy of revised Bethesda guidelines, microsatellite instability, and immunohistochemistry for the identification of patients with hereditary nonpolyposis colorectal cancer. JAMA 2005;293(16):1986-94.
Excluded: Model does not categorize risk or validate, OVID-Medline.
606. Pittler MH, Ernst E. Clinical effectiveness of garlic (Allium sativum). Mol Nutr Food Res 2007;51(11):1382-5.
Excluded: Not an eligible study design, OVID-Medline.
607. Podoloff DA, Advani RH, Allred C, et al. NCCN Task Force report: Positron Emission Tomography (PET)/Computed Tomography (CT) scanning in cancer. J Natl Compr Cancer Netw 2007;5(SUPPL. 1):S
Excluded: Not an eligible intervention or outcome, OVID-Embase.

608. Polednak AP. Knowledge of colorectal cancer and use of screening tests among higher-risk persons. J Cancer Educ 1990;5(2):115-24.
Excluded: Not an eligible population, OVID-Embase.
609. Polednak AP, Lane DS, Burg MA. Risk perception, family history, and use of breast cancer screening tests. Cancer Detect Prev 1991;15(4):257-63.
Excluded: Family history not systematically collected, OVID-Medline.
610. Potter CE, Beldock JG. Object Class Networks (OCNs) for interface-independent calculation with Gail and Claus models. Ann N Y Acad Sci 1995;768:308-11.
Excluded: Model does not categorize risk or validate, OVID-Medline.
611. Price MA, Butow PN, Lo SK, et al. Predictors of cancer worry in unaffected women from high risk breast cancer families: risk perception is not the primary issue. J Genet Couns 2007;16(5):635-44.
Excluded: Not an eligible study design, OVID-Medline.
612. Purkayastha S, Tekkis PP, Athanasiou T, et al. Magnetic resonance colonography versus colonoscopy as a diagnostic investigation for colorectal cancer: a meta-analysis.[see comment]. Clin Radiol 2005;60(9):980-9.
Excluded: Not an eligible population, OVID-Medline.
613. Pylvanainen K, Kairaluoma M, Mecklin JP. Compliance and Satisfaction with Long-Term Surveillance in Finnish HNPCC Families. Fam Cancer 2006;5(2):175-8.
Excluded: Not an eligible population, OVID-Medline.
614. Qaseem A, Snow V, Sherif K, et al. Screening mammography for women 40 to 49 years of age: a clinical practice guideline from the American College of Physicians.[summary for patients in Ann Intern Med. 2007 Apr 3;146(7):I20; PMID: 17404347]. Ann Intern Med 2007;146(7):511-5.
Excluded: Model does not categorize risk or validate, OVID-Medline.
615. Qin LQ, Xu JY, Wang PY, et al. Soyfood intake in the prevention of breast cancer risk in women: a meta-analysis of observational epidemiological studies. J Nutr Sci Vitaminol 2006;52(6):428-36.
Excluded: Not an eligible population, OVID-Medline.
616. Qin LQ, Xu JY, Wang PY, et al. Milk consumption is a risk factor for prostate cancer in Western countries: evidence from cohort studies. Asia Pac J Clin Nutr 2007;16(3):467-76.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
617. Qureshi N, Wilson B, Santaguida P, et al. Collection and use of cancer family history in primary care. Evid Rep Technol Assess No.159, AHRQ Publication No. 08-E001 (prepared by the McMaster University Evidence-based Practice Center under Contract No. 290-02-0020). Rockville, MD: Agency for Health Care Research and Quality; 2007 Oct. Available at: http://www.ahrq.gov/clinic/tp/famhisttp.htm
Excluded: Not an eligible intervention or outcome, OVID-Medline.
618. Rabeneck L, Rumble RB, Axler J, et al. Cancer Care Ontario Colonoscopy Standards: Standards and evidentiary base. Can J Gastroenterol 2007;21(Suppl. D):5D-24D.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
619. Rabin C, Pinto B. Cancer-related beliefs and health behavior change among breast cancer survivors and their first-degree relatives. Psychooncology 2006;15(8):701-12.
Excluded: Family history not systematically collected, OVID-Medline.
620. Radtke HB, Sebold CD, Allison C, et al. Neurofibromatosis type 1 in genetic counseling practice: Recommendations of the national society of genetic counselors. J Genet Couns 2007;16(4):387-407.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
621. Rahman SM, Dignan MB, Shelton BJ. Factors influencing adherence to guidelines for screening mammography among women aged 40 years and older. Ethn Dis 2003;13(4):477-84.
Excluded: Family history not systematically collected, OVID-Medline.
622. Rahman SMM, Dignan MB, Shelton BJ. A theory-based model for predicting adherence to guidelines for screening mammography among women age 40 and older. Int J Canc Prev 2005;2(3):169-79.
Excluded: Family history not systematically collected, OVID-Embase.
623. Rai T, Clements A, Bukach C, et al. What influences men's decision to have a prostate-specific antigen test? A qualitative study. Fam Pract 2007;24(4):365-71.
Excluded: Family history not systematically collected, OVID-Embase.
624. Rakowski W, Breen N, Meissner H, et al. Prevalence and correlates of repeat mammography among women aged 55-79 in the Year 2000 National Health Interview Survey. Prev Med 2004;39(1):1-10.
Excluded: Family history not systematically collected, OVID-Medline.
625. Ramji F, Cotterchio M, Manno M, et al. Association between subject factors and colorectal cancer screening participation in Ontario, Canada. Cancer Detect Prev 2005;29(3):221-6.
Excluded: Family history not systematically collected, OVID-Medline.

626. Ramsoekh D, van Leerdam ME, Tops CM, et al. The use of genetic testing in hereditary colorectal cancer syndromes: genetic testing in HNPCC, (A)FAP and MAP. Clin Genet 2007;72(6):562-7. Excluded: Not an eligible population, OVID-Medline.
627. Ray JA, Loescher LJ, Brewer M. Risk-reduction surgery decisions in high-risk women seen for genetic counseling. J Genet Couns 2005;14(6):473-84. Excluded: Not an eligible study design, OVID-Medline.
628. Rees G, Fry A, Cull A, et al. Illness perceptions and distress in women at increased risk of breast cancer. Psychol Health 2004;19(6):749-65. Excluded: Not an eligible study design, OVID-Cinahl.
629. Rees G, Gaff C, Young MA, et al. Health beliefs and behaviors of women who have received genetic counseling for breast cancer. J Genet Couns 2007;16(4):457-68. Excluded: Not an eligible population, OVID-Medline.
630. Reichelt JG, Dahl AA, Heimdal K, et al. Uptake of genetic testing and pre-test levels of mental distress in Norwegian families with known BRCA1 mutations. Dis Markers 1999;15(1-3):139-43. Excluded: Not an eligible study design, OVID-Medline.
631. Rex DK, ACG Board of Trustees. American College of Gastroenterology action plan for colorectal cancer prevention. Am J Gastroenterol 2004;99(4):574-7. Excluded: Model does not categorize risk or validate, OVID-Medline.
632. Rex DK, Kahi CJ, Levin B, et al. Guidelines for Colonoscopy Surveillance after Cancer Resection: A Consensus Update by the American Cancer Society and US Multi-Society Task Force on Colorectal Cancer. CA Cancer J Clin 2006;56(3):160-7. Excluded: Model does not categorize risk or validate, OVID-Cinahl.
633. Reyes CM, Allen BA, Terdiman JP, et al. Comparison of selection strategies for genetic testing of patients with hereditary nonpolyposis colorectal carcinoma: effectiveness and cost-effectiveness. Cancer 2002;95(9):1848-56. Excluded: Family history not systematically collected, OVID-Medline.
634. Richardson JL, Danley K, Mondrus GT, et al. Adherence to screening examinations for colorectal cancer after diagnosis in a first-degree relative. Prev Med 1995;24(2):166-70. Excluded: Family history not systematically collected, OVID-Medline.
635. Rieck GC, Lim K, Rogers MT, et al. Screening for familial ovarian cancer--management and outcome of women with moderate to high risk of developing ovarian cancer. Int J Gynecol Cancer 2006;16(Suppl.1)86-91. Excluded: Not an eligible population, OVID-Medline.
636. Rimer BK, Schildkraut JM, Lerman C, et al. Participation in a women's breast cancer risk counseling trial. Who participates? Who declines? High Risk Breast Cancer Consortium. Cancer 1996;77(11):2348-55. Excluded: Family history not systematically collected, OVID-Medline.
637. Rini C, Jandorf L, Valdimarsdottir H, et al. Distress among inflammatory bowel disease patients at high risk for colorectal cancer: a preliminary investigation of the effects of family history of cancer, disease duration, and perceived social support. sychooncology 2008;17(4):354-62. Excluded: Family history not systematically collected, OVID-Medline.
638. Ritvo P, Robinson G, Irvine J, et al. A longitudinal study of psychological adjustment to familial genetic risk assessment for ovarian cancer. Gynecol Oncol 1999;74(3):331-7. Excluded: Not an eligible population, OVID-Medline.
639. Ritvo P, Irvine J, Robinson G, et al. Psychological adjustment to familial-genetic risk assessment for ovarian cancer: predictors of nonadherence to surveillance recommendations. Gynecol Oncol 2002;84(1):72-80. Excluded: Not an eligible study design, OVID-Medline.
640. Rockhill B, Byrne C, Rosner B, et al. Breast cancer risk prediction with a log-incidence model: evaluation of accuracy. J Clin Epidemiol 2003;56(9):856-61. Excluded: Not an eligible study design, OVID-Medline.
641. Roddam AW, Duffy MJ, Hamdy FC, et al. Use of prostate-specific antigen (PSA) isoforms for the detection of prostate cancer in men with a PSA level of 2-10 ng/ml: systematic review and meta-analysis. Eur Urol 398;48(3):386-99. Excluded: Not an eligible population, OVID-Medline.
642. Rodriguez-Moranta F, Castells A, Andreu M, et al. Clinical performance of original and revised Bethesda guidelines for the identification of MSH2/MLH1 gene carriers in patients with newly diagnosed colorectal cancer: proposal of a new and simpler set of recommendations. Am J Gastroenterol 2006;101(5):1104-11. Excluded: Model does not categorize risk or validate, OVID-Medline.
643. Rodriguez C, Plasencia A, Schroeder DG. Predictive factors of enrollment and adherence in a breast cancer screening program in Barcelona (Spain). Soc Sci Med 1995;40(8):1155-60. Excluded: Family history not systematically collected, OVID-Medline.

644. Roetzheim R, Fox SA, Leake B, et al. The influence of risk factors on breast carcinoma screening of Medicare-insured older women. National Cancer Institute Breast Cancer Screening Consortium. Cancer 1996;78(12):2526-34.
Excluded: Family history not systematically collected, VID-Medline.
645. Roetzheim RG, Fox SA, Leake B. The effect of risk on changes in breast cancer screening rates in Los Angeles, 1988-1990. Cancer 1994;74(2):625-31.
Excluded: Family history not systematically collected, OVID-Medline.
646. Rojas, MP, Telaro, et al. Follow-up strategies for women treated for early breast cancer. Cochrane Database of Syst Rev 2008;(1):
Excluded: Not an eligible intervention or outcome, OVID-Cochrane.
647. Rojas MP, Telaro E, Russo A, et al. Follow-up strategies for women treated for early breast cancer. Cochrane Database Syst Rev 2005;(1):CD001768
Excluded: Not an eligible intervention or outcome, OVID-Medline.
648. Ronco AL. Use of artificial neural networks in modeling associations of discriminant factors: Towards an intelligent selective breast cancer screening. Artif Intell Med 1999;16(3):299-309.
Excluded: Model does not categorize risk or validate, OVID-Embase.
649. Ropka ME, Wenzel J, Phillips EK, et al. Uptake rates for breast cancer genetic testing: a systematic review. Cancer Epidemiol Biomarkers Prev 2006;15(5):840-55.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
650. Rosen B, Kwon J, Fung Kee FM, et al. Systematic review of management options for women with a hereditary predisposition to ovarian cancer. Gynecol Oncol 2004;93(2):280-6.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
651. Rosman AS, Korsten MA. Meta-analysis comparing CT colonography, air contrast barium enema, and colonoscopy. Am J Med 2007;120(3):203-10.
Excluded: Not an eligible population, OVID-Medline.
652. Rosolowich V, Breast Disease Committee of the Society of Obstetricians and Gynaecologists of Canada. Breast self-examination. J Obstet Gynaecol Can 2006;28(8):728-30.
Excluded: Model does not categorize risk or validate, OVID-Medline.
653. Rothemund Y, Paepke S, Flor H. Perception of risk, anxiety, and health behaviors in women at high risk for breast cancer. Int J Behav Med 2001;8(3):230-9.
Excluded: Not an eligible study design, OVID-Embase.
654. Rouleau I, Chiquette J, Plante M, et al. Changes in health-related behaviours following BRCA 1/2 genetic testing: the case of hormone replacement therapy. J Obstet Gynaecol Can 2004;26(12):1059-66.
Excluded: Not an eligible population, OVID-Medline.
655. Roumier X, Azzouzi R, Valeri A, et al. Adherence to an annual PSA screening program over 3 years for brothers and sons of men with prostate cancer. Eur Urol 45(3):280-5.
Excluded: Not an eligible study design, OVID-Medline.
656. Rowse J, Brown K, Jandorf L, et al. Breast cancer specific distress prior to genetic counseling in women of African descent at increased risk of hereditary breast and ovarian cancer. J Genet Couns 2007;16(1):11
Excluded: Family history not systematically collected, OVID-Cinahl.
657. Royak-Schaler R, Klabunde CN, Greene WF, et al. Communicating breast cancer risk: patient perceptions of provider discussions. Medscape Womens Health 7(2):2-Apr
Excluded: Not an eligible study design, OVID-Medline.
658. Royak-Schaler R, DeVellis BM, Sorenson JR, et al. Breast cancer in African-American families. Risk perception, cancer worry, and screening practices of first-degree relatives. Ann N Y Acad Sci 1995;768:281-5.
Excluded: Not an eligible study design, OVID-Medline.
659. Ruthotto F, Papendorf F, Wegener G, et al. Participation in screening colonoscopy in first-degree relatives from patients with colorectal cancer. Ann Oncol 2007;18(9):1518-22.
Excluded: Not an eligible study design, OVID-Medline.
660. Ryan EL. Risk perception, risk attribution, and risk modification beliefs among women with a family history of breast cancer Dissertation Abstract, 1998
Excluded: Not an eligible publication type, OVID-PsycInfo.
661. Sabatino SA, Burns RB, Davis RB, et al. Breast carcinoma screening and risk perception among women at increased risk for breast carcinoma: results from a national survey. Cancer 2004;100(11):2338-46.
Excluded: Family history not systematically collected, OVID-Medline.
662. Saini SD, Kim HM, Schoenfeld P. Incidence of advanced adenomas at surveillance colonoscopy in patients with a personal history of colon adenomas: a meta-analysis and systematic review. Gastrointest Endosc 2006;64(4):614-26.
Excluded: Not an eligible population, OVID-Medline.

663. Salmon PG, Swank AM. Exercise-based disease management guidelines for individuals with cancer: Potential applications in a high-risk mid-southern state. Journal of Exercise Physiology Online 2002;5(4):1-10.
Excluded: Not an eligible study design, OVID-Embase.
664. Salsman JM, Pavlik E, Boerner LM, et al. Clinical, demographic, and psychological characteristics of new, asymptomatic participants in a transvaginal ultrasound screening program for ovarian cancer. Prev Med 2004;39(2):315-22.
Excluded: Family history not systematically collected, OVID-Medline.
665. Samad AKA, Taylor RS, Marshall T, et al. A meta-analysis of the association of physical activity with reduced risk of colorectal cancer. Colorectal Dis 2005;7(3):204-13.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
666. Sanjoaquin MA, Allen N, Couto E, et al. Folate intake and colorectal cancer risk: A meta-analytical approach. Int J Cancer 2005;113(5):825-8.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
667. Saraiya M, Coughlin SS, Burke W, et al. The role of family history in personal prevention practices among US women physicians. Community Genetics 2001;4(2):102-8.
Excluded: Family history not systematically collected, OVID-Embase.
668. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography.[erratum appears in CA Cancer J Clin. 2007 May-Jun;57(3):185]. CA Cancer J Clin 2007;57(2):75-89.
Excluded: Model does not categorize risk or validate, OVID-Medline.
669. Scardino P. Update: NCCN prostate cancer Clinical Practice Guidelines. J Natl Compr Cancer Netw 2005;3(Suppl.1):S29-S33.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
670. Scherr D, Swindle PW, Scardino PT. National Comprehensive Cancer Network guidelines for the management of prostate cancer. Urology 2003;61(Suppl.2):14-24.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
671. Schildkraut JM, Lerman C, Lustbader E, et al. Adherence to mammography among subgroups of women at high risk for breast cancer. J Womens Health 1995;4(6):645-54.
Excluded: Family history not systematically collected, OVID-Embase.
672. Schmidt S, Becher H, Chang-Claude J. Breast cancer risk assessment: use of complete pedigree information and the effect of misspecified ages at diagnosis of affected relatives. Hum Genet 1998;102(3):348-56.
Excluded: Model does not categorize risk or validate, OVID-Medline.
673. Schnur JB, Valdimarsdottir HB, Montgomery GH, et al. Social constraints and distress among women at familial risk for breast cancer. Ann Behav Med 2004;28(2):142-8.
Excluded: Not an eligible study design, OVID-Medline.
674. Schnur JB, DiLorenzo TA, Montgomery GH, et al. Perceived risk and worry about prostate cancer: a proposed conceptual model. Behav Med 2006;32(3):89-96.
Excluded: Not an eligible study design, OVID-Medline.
675. Schnur JB. Social constraints, avoidance, and psychological distress in women with and without family histories of breast cancer. Dissertation abstract. 2003
Excluded: Not an eligible publication type, OVID-PsycInfo.
676. Schreer I. Early detection and diagnosis of breast cancer. Breast Care 2006;1(4):227-8.
Excluded: Model does not categorize risk or validate, OVID-Cinahl.
677. Schwartz M, Lerman C, Daly M, et al. Utilization of ovarian cancer screening by women at increased risk. Cancer Epidemiol Biomarkers Prev 1995;4(3):269-73.
Excluded: Family history not systematically collected, OVID-Medline.
678. Schwartz MD, Lerman C, Miller SM, et al. Coping disposition, perceived risk, and psychological distress among women at increased risk for ovarian cancer. Health Psychol 1995;14(3):232-5.
Excluded: Family history not systematically collected, OVID-Medline.
679. Schwartz MD, Taylor KL, Willard KS, et al. Distress, personality, and mammography utilization among women with a family history of breast cancer. Health Psychol 1999;18(4):327-32.
Excluded: Family history not systematically collected, OVID-Medline.
680. Schwartz MD, Taylor KL, Willard KS. Prospective association between distress and mammography utilization among women with a family history of breast cancer. J Behav Med 2003;26(2):105-17.
Excluded: Not an eligible study design, OVID-Medline.
681. Schwartz MD, Kaufman E, Peshkin BN, et al. Bilateral prophylactic oophorectomy and ovarian cancer screening following BRCA1/BRCA2 mutation testing. J Clin Oncol 2003;21(21):4034-41.
Excluded: Not an eligible population, OVID-Medline.

682. Seely D, Mills EJ, Wu P, et al. The effects of green tea consumption on incidence of breast cancer and recurrence of breast cancer: A systematic review and meta-analysis. Integr Cancer Ther 2005;4(2):144-55. Excluded: Not an eligible intervention or outcome, OVID-Embase.
683. Shah M, Zhu K, Palmer RC, et al. Family history of cancer and utilization of prostate, colorectal and skin cancer screening tests in U.S. men. Prev Med 2007;44(5):459-64. Excluded: Family history not systematically collected, OVID-Medline.
684. Shah M, Zhu K, Palmer RC, et al. Breast, colorectal, and skin cancer screening practices and family history of cancer in U.S. women. J Womens Health (Larchmt) 2007;16(4):526-34. Excluded: Family history not systematically collected, OVID-Medline.
685. Shaukat A, Scouras N, Schunemann HJ. Role of supplemental calcium in the recurrence of colorectal adenomas: a metaanalysis of randomized controlled trials. Am J Gastroenterol 2005;100(2):390-4.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
686. Sheinfeld GS, Albert SM. The meaning of risk to first degree relatives of women with breast cancer. Women Health 2003;37(3):97-117.
Excluded: Family history not systematically collected, OVID-Medline.
687. Shen Y, Yang Y, Inoue LY, et al. Role of detection method in predicting breast cancer survival: analysis of randomized screening trials.[see comment]. J Natl Cancer Inst 2005;97(16):1195-203.
Excluded: Family history not systematically collected, OVID-Medline.
688. Shergill AK, Terdiman JP. Refining Colorectal Cancer Screening Recommendations Based on Gender. Gastroenterology 2007;132(7):2605-6.
Excluded: Model does not categorize risk or validate, OVID-Embase.
689. Siddiqui AA, Patel A, Huerta S. Determinants of compliance with colonoscopy in patients with adenomatous colon polyps in a veteran population. Aliment Pharmacol Ther 2006;24(11-12):1623-30. Excluded: Family history not systematically collected, OVID-Medline.
690. Simard J, Dumont M, Moisan AM, et al. Evaluation of BRCA1 and BRCA2 mutation prevalence, risk prediction models and a multistep testing approach in French-Canadian families with high risk of breast and ovarian cancer.[erratum appears in J Med Genet. 2007 Jul;44(7):471]. J Med Genet 2007;44(2):107-21.
Excluded: Model does not categorize risk or validate, OVID-Medline.
691. Sinicrope PS, Vernon SW, Diamond PM, et al. Development and preliminary validation of the cancer family impact scale for colorectal cancer. Genet Test 2008;12(1):161-9.
Excluded: Family history not systematically collected, OVID-Embase.
692. Sivell S, Iredale R, Gray J, et al. Cancer genetic risk assessment for individuals at risk of familial breast cancer. [Review] [93 refs]. Cochrane Database Syst Rev 2007;(2):CD003721
Excluded: Not an eligible intervention or outcome, OVID-Medline.
693. Slattery ML, Kinney AY, Levin TR. Factors associated with colorectal cancer screening in a population-based study: the impact of gender, health care source, and time. Prev Med 2004;38(3):276-83.
Excluded: Family history not systematically collected, OVID-Medline.
694. Smith RA, Saslow D, Sawyer KA, et al. American Cancer Society guidelines for breast cancer screening: update. CA Cancer J Clin 2003;53(3):141-69.
Excluded: Model does not categorize risk or validate, OVID-Medline.
695. Smith RA, Standiford CJ, Saraiya M. Updates in colon, cervical, breast, and prostate cancer screening. Patient Care Nurse Pract 2005;7.
Excluded: Model does not categorize risk or validate, OVID-Cinahl.
696. Smith RA, Cokkinides V, Eyre HJ. American Cancer Society guidelines for the early detection of cancer. CA Cancer J Clin 2005;55(1):31-44.
Excluded: Model does not categorize risk or validate, OVID-Embase.
697. Smith RA, Cokkinides V, Eyre HJ. American Cancer Society guidelines for the early detection of cancer. CA Cancer J Clin 2006;56(1):11-25.
Excluded: Model does not categorize risk or validate, OVID-Embase.
698. Smith TJ, Khatcheressian J. Review: chemotherapy and hormonal therapy reduce recurrence and mortality at 15 years in early breast cancer. Evid Based Med 2005;10(6):169
Excluded: Not an eligible study design, OVID-Cinahl.
699. Society of Gastroenterology Nurses and Associates I. SGNA Guideline: Performance of flexible sigmoidoscopy by registered nurses for the purpose of colorectal cancer screening. Gastroenterol Nurs 2003;26(6):261-3.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
700. Sohl SJ, Moyer A. Tailored interventions to promote mammography screening: a meta-analytic review. Prev Med 2007;45(4):252-61.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
701. Song JM, Kim CB, Chung HC, et al. Prostate-specific antigen, digital rectal examination and transrectal ultrasonography: a meta-analysis for this diagnostic triad of prostate cancer in symptomatic korean men. Yonsei Med J 2005;46(3):414-24.
Excluded: Not an eligible population, OVID-Medline.

702. Sooriakumaran P, Langley SEM, Laing RW, et al. COX-2 inhibition: A possible role in the management of prostate cancer? J Chemother 2007;19(1):21-32.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
703. Sorscher S, Levonian P. BCRA 1 testing guidelines for high-risk patients. J Clin Oncol 1997;15(4):1711
Excluded: Not an eligible study design, OVID-Medline.
704. Sosna J, Morrin MM, Kruskal JB, et al. CT colonography of colorectal polyps: a metaanalysis. AJR Am J Roentgenol 2003;(6):1593-8.
Excluded: Not an eligible population, OVID-Medline.
705. Sotiriou C, Desmedt C. Gene expression profiling in breast cancer. Ann Oncol 2006;17(SUPPL. 10):259-62.
Excluded: Not an eligible study design, OVID-Embase.
706. Soyer MT, Ciceklioglu M, Ceber E. Breast cancer awareness and practice of breast self examination among primary health care nurses: influencing factors and effects of an in-service education. J Clin Nurs 2007;16(4):707-15.
Excluded: Family history not systematically collected, OVID-Cinahl.
707. Spencer BA, Babey SH, Etzioni DA, et al. A population-based survey of prostate-specific antigen testing among California men at higher risk for prostate carcinoma. Cancer 2006;106(4):765-74.
Excluded: Family history not systematically collected, OVID-Medline.
708. Stamler LL. Review: limited evidence on regular breast examination does not support its effectiveness for reducing breast cancer deaths. Evid Based Nurs 2004;7(1):15
Excluded: Not an eligible study design, OVID-Cinahl.
709. Standard TF, American Society of Colon and Rectal Surgeons, Collaborative Group of the Americas on Inherited Colorectal Cancer. Practice parameters for the identification and testing of patients at risk for dominantly inherited colorectal cancer. Dis Colon Rectum 2001;44(10):1403
Excluded: Model does not categorize risk or validate, OVID-Medline.
710. Stefanek ME, Wilcox P. First degree relatives of breast cancer patients: screening practices and provision of risk information. Cancer Detect Prev 1991;15(5):379-84.
Excluded: Not an eligible study design, OVID-Medline.
711. Stefanek ME, Helzlsouer KJ, Wilcox PM, et al. Predictors of and satisfaction with bilateral prophylactic mastectomy. Prev Med 1995;24(4):412-9.
Excluded: Not an eligible study design, OVID-Medline.
712. Stephens JH, Moore JW. Can targeted intervention in CRC patients' relatives influence screening behaviour? A pilot study. Colorectal Dis 2008;10(2):179-86.
Excluded: Family history not systematically collected, OVID-Medline.
713. Stoffel EM, Garber JE, Grover S, et al. Cancer surveillance is often inadequate in people at high risk for colorectal cancer. J Med Genet 2003;40(5):e54
Excluded: Not an eligible population, OVID-Medline.
714. Stormorken AT, Muller W, Lemkemeyer B, et al. Prediction of the outcome of genetic testing in HNPCC kindreds using the revised Amsterdam criteria and immunohistochemistry. Familial Cancer 2001;1(3-4):169-73.
Excluded: Model does not categorize risk or validate, OVID-Medline.
715. Straus WL, Mansley EC, Gold KF, et al. Colorectal cancer screening attitudes and practices in the general population: a risk-adjusted survey. J Public Health Manag Pract 2005;11(3):244-51.
Excluded: Family history not systematically collected, OVID-Cinahl.
716. Strzelczyk JJ, Dignan MB. Disparities in adherence to recommended followup on screening mammography: interaction of sociodemographic factors. Ethn Dis 2002;12(1):77-86.
Excluded: Family history not systematically collected, OVID-Medline.
717. Su X, Ma GX, Seals B, et al. Breast cancer early detection among Chinese women in the Philadelphia area. J Womens Health (Larchmt) 2006;15(5):507-19.
Excluded: Family history not systematically collected, OVID-Medline.
718. Sun C-L, Yuan J-M, Koh W-P, et al. Green tea, black tea and breast cancer risk: A meta-analysis of epidemiological studies. Carcinogenesis 2006;27(7):1310-5.
Excluded: Not an eligible population, OVID-Embase.
719. Sweetman J, Watson M, Norman A, et al. Feasibility of familial PSA screening: psychosocial issues and screening adherence. Br J Cancer 2006;94(4):507-12.
Excluded: Family history not systematically collected, OVID-Medline.

720. Syngal S, Fox EA, Eng C, et al. Sensitivity and specificity of clinical criteria for hereditary non-polyposis colorectal cancer associated mutations in MSH2 and MLH1. J Med Genet 2000;37(9):641-5.
Excluded: Model does not categorize risk or validate, OVID-Medline.
721. Takakuwa KM, Ernst AA, Weiss SJ, et al. Breast cancer knowledge and preventive behaviors: An urban emergency department-based survey. Acad Emerg Med 2000;7(12):1393-8.
Excluded: Family history not systematically collected, OVID-Medline.
722. Taplin SH, Thompson RS, Schnitzer F, et al. Revisions in the risk-based Breast Cancer Screening Program at Group Health Cooperative. Cancer 1990;66(4):812-8. PM:2386908
Excluded: Not an eligible study design
723. Tatemichi S, Miedema B, Leighton S. Breast cancer screening. First Nations communities in New Brunswick. Can Fam Physician 2002;48:1084-9.
Excluded: Family history not systematically collected, OVID-Medline.
724. Tavani A, Vecchia CL. Coffee, decaffeinated coffee, tea and cancer of the colon and rectum: A review of epidemiological studies, 1990-2003. Cancer Causes Control 2004;15(8):743-57.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
725. Taylor P, Potts HWW. Computer aids and human second reading as interventions in screening mammography: Two systematic reviews to compare effects on cancer detection and recall rate. Eur J Cancer 2008;44(6):798-807.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
726. Taylor R, Ivanov O, Page A, et al. Predictors of non-attendance from BreastScreen NSW in women who report current mammography screening. Aust N Z J Public Health 2003;27(6):581-7.
Excluded: Family history not systematically collected, OVID-Embase.
727. Taylor R, Taguchi K. Tamoxifen for breast cancer chemoprevention: low uptake by high-risk women after evaluation of a breast lump. Ann Fam Med 2005;3(3):242-7.
Excluded: Not an eligible study design, OVID-Medline.
728. Taylor SA, Laghi A, Lefere P, et al. European society of gastrointestinal and abdominal radiology (ESGAR): Consensus statement on CT colonography. Eur Radiol 2007;17(2):575-9.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
729. Tchou J, Hou N, Rademaker A, et al. Acceptance of tamoxifen chemoprevention by physicians and women at risk. Cancer 2004;100(9):1800-6.
Excluded: Not an eligible study design, OVID-Medline.
730. Teillac P. The global state of prostate cancer: New diagnostic tools, minimal requirements for diagnosis and staging, and guidelines in the second millennium. BJU Int 2004;94(Suppl 3):3-4.
Excluded: Model does not categorize risk or validate, OVID-Embase.
731. Thiel LM. Health beliefs and breast cancer screening behaviors of women religious in America. Doctoral dissertation, research.
Excluded: Not an eligible publication type, OVID-Cinahl.
732. Thirlaway K, Fallowfield L, Nunnerley H, et al. Anxiety in women "at risk' of developing breast cancer. Br J Cancer 1996;73(11):1422-4.
Excluded: Family history not systematically collected, OVID-Medline.
733. Thompson IM, Ankerst DP, Chi C, et al. Assessing prostate cancer risk: Results from the Prostate Cancer Prevention Trial. J Natl Cancer Inst 2006;98(8):529-34.
Excluded: Model does not categorize risk or validate, OVID-Embase.
734. Thomssen C. AGO recommendations for the diagnosis and therapy of breast cancer. Breast Care 2007;2(4):244-50.
Excluded: Not an eligible intervention or outcome, OVID-Cinahl.
735. Thorogood M, Simera I, Dowler E, et al. A systematic review of population and community dietary interventions to prevent cancer. Nutr Res Rev 2007;20(1):74-88.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
736. Thrasher JF, Cummings KM, Michalek AM, et al. Colorectal cancer screening among individuals with and without a family history. J Public Health Manag Pract 2002;8(2):1-9.
Excluded: Family history not systematically collected, OVID-Medline.
737. Tice JA, Cummings SR, Ziv E, et al. Mammographic breast density and the Gail model for breast cancer risk prediction in a screening population. Breast Cancer Res Treat 2005;94(2):115-22.
Excluded: Model does not categorize risk or validate, OVID-Medline.
738. Tice JA, Miike R, Adduci K, et al. Nipple aspirate fluid cytology and the Gail model for breast cancer risk assessment in a screening population. Cancer Epidemiol Biomarkers Prev 2005;14(2):324-8.
Excluded: Model does not categorize risk or validate, OVID-Medline.
739. Tice JA, Cummings SR, Smith-Bindman R, et al. Using clinical factors and mammographic breast density to estimate breast cancer risk: development and validation of a new predictive model. Ann Intern Med 2008;148(5):337-47. PM:18316752
Excluded: Not an eligible study design.

740. Tiller K, Meiser B, Butow P, et al. Psychological impact of prophylactic oophorectomy in women at increased risk of developing ovarian cancer: a prospective study. Gynecol Oncol 2002;86(2):212-9.
Excluded: Not an eligible study design, OVID-Medline.
741. Tinley ST, Houfek J, Watson P, et al. Screening adherence in BRCA1/2 families is associated with primary physicians' behavior. Am J Med Genet 2004;Part(1):5-11.
Excluded: Not an eligible population, OVID-Medline.
742. Touvier M, Kesse E, Volatier JL, et al. Dietary and cancer-related behaviors of vitamin/mineral dietary supplement users in a large cohort of French women. Eur J Nutr 2006;45(4):205-14.
Excluded: Family history not systematically collected, OVID-Medline.
743. Trafalis DTP, Athanassiou AE. A guideline for the management of women at substantially increased risk of breast cancer development. J B U ON 2005;10(4):443-58.
Excluded: Model does not categorize risk or validate, OVID-Embase.
744. Trask PC, Paterson AG, Wang C, et al. Cancer-specific worry interference in women attending a breast and ovarian cancer risk evaluation program: impact on emotional distress and health functioning. Psychooncology 2001;10(5):349-60.
Excluded: Family history not systematically collected, OVID-Medline.
745. Trepanier A, Ahrens M, McKinnon W, et al. Genetic cancer risk assessment and counseling: recommendations of the national society of genetic counselors. J Genet Couns 2004;13(2):83-114.
Excluded: Model does not categorize risk or validate, OVID-Medline.
746. Trock BJ, Hilakivi-Clarke L, Clarke R. Meta-analysis of soy intake and breast cancer risk.[see comment]. J Natl Cancer Inst 2006;98(7):459-71.
Excluded: Not an eligible population, OVID-Medline.
747. Tsouskas LI, Liaros A, Tzitzikas J, et al. The use of an expert system of composite risk factors in breast cancer screening. Stud Health Technol Inform 1997;43:t-63
Excluded: Not an eligible intervention or outcome, OVID-Medline.
748. Tsouskas LI, Noula M, Dimopoulos P. Practicing an expert system for definition of high-risk group in breast cancer screening. ICUS Nurs Web J 2005;(22):5p
Excluded: Model does not categorize risk or validate, OVID-Cinahl.
749. Turner-Cobb JM, Bloor LE, Whittemore AS, et al. Disengagement and social support moderate distress among women with a family history of breast cancer. Breast J 2006;12(1):7-15.
Excluded: Not an eligible study design, OVID-Medline.
750. Tyler CV, Jr., Snyder CW. Cancer risk assessment: examining the family physician's role. J Am Board Fam Med 2006;19(5):468-77.
Excluded: Family history not systematically collected, OVID-Medline.
751. Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors.[erratum appears in Stat Med. 2005 Jan 15;24(1):156]. Stat Med 2004;23(7):1111-30.
Excluded: Model does not categorize risk or validate, OVID-Medline.
752. U.S.Preventive Services Task Force. Screening for prostate cancer: recommendations and rationale. Am Fam Physician 2003;67(4):787-92.
Excluded: Model does not categorize risk or validate, OVID-Medline.
753. U.S.Preventive Services Task Force. Routine Vitamin Supplementation to Prevent Cancer and Cardiovascular Disease: Recommendations and Rationale. Ann Intern Med 2003;139(1):51-5.
Excluded: Model does not categorize risk or validate, OVID-Embase.
754. U.S.Preventive Services Task Force. Clinical guidelines. Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement [corrected] [published erratum appears in Ann Intern Med 2005;143(7):547]. Ann Intern Med 2005;143(5):355-61.
Excluded: Model does not categorize risk or validate, OVID-Cinahl.
755. U.S.Preventive Services Task Force. Summaries for patients. Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: U.S. Preventive Services Task Force recommendations.[see comment]. Ann Intern Med 2005;143(5):I47
Excluded: Not an eligible study design, OVID-Medline.
756. U.S.Preventive Services Task Force. Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement.[erratum appears in Ann Intern Med. 2005 Oct 4;143(7):547]. Ann Intern Med 2005;143(5):355-61.
Excluded: Model does not categorize risk or validate, OVID-Medline.
757. U.S.Preventive Services Task Force. Screening for ovarian cancer: recommendation statement. U.S. Preventive Services Task Force. Am Fam Physician 2005;71(4):759-62.
Excluded: Model does not categorize risk or validate, OVID-Medline.
758. U.S.Preventive Services Task Force. Routine aspirin or nonsteroidal anti-inflammatory drugs for the primary prevention of colorectal cancer: recommendation statement. Am Fam Physician 2007;76(1):109-13.
Excluded: Model does not categorize risk or validate, OVID-Cinahl.

759. Uyei A, Peterson SK, Erlichman J, et al. Association between clinical characteristics and risk-reduction interventions in women who underwent BRCA1 and BRCA2 testing: a single-institution study. Cancer 2006;107(12):2745-51.
Excluded: Not an eligible population, OVID-Medline.
760. Uzzo RG, Brown JG, Horwitz EM, et al. Prevalence and patterns of self-initiated nutritional supplementation in men at high risk of prostate cancer. BJU Int 2004;93(7):955-60.
Excluded: Not an eligible study design, OVID-Medline.
761. Vadaparampil ST, Jacobsen PB, Kash K, et al. Factors predicting prostate specific antigen testing among first-degree relatives of prostate cancer patients. Cancer Epidemiol Biomarkers Prev 2004;13(5):753-8.
Excluded: Not an eligible study design, OVID-Medline.
762. 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):704-8.
Excluded: Model does not categorize risk or validate, OVID-Medline.
763. Valdimarsdottir HB, Bovbjerg DH, Kash KM, et al. Psychological distress in women with a familial risk of breast cancer. Psychooncology 1995;4(2):133-41.
Excluded: Family history not systematically collected, OVID-Embase.
764. Valdimarsdottir HB, Bovbjerg DH, Brown K, et al. Cancer-specific distress is related to women's decisions to undergo BRCA1 testing. Cancer Research Therapy and Control 1999;8(1-2):61-8.
Excluded: Not an eligible publication type, OVID-Embase.
765. Valdimarsdottir HB, Zakowski SG, Gerin W, et al. Heightened psychobiological reactivity to laboratory stressors in healthy women at familial risk for breast cancer. J Behav Med 2002;25(1):51-65.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
766. van Asperen CJ, Jonker MA, Jacobi CE, et al. Risk estimation for healthy women from breast cancer families: new insights and new strategies. Cancer Epidemiol Biomarkers Prev 2004;13(1):87-93.
Excluded: Model does not categorize risk or validate, OVID-Medline.
767. Van Cutsem EJ, Oliveira J, Kataja VV, et al. ESMO Minimum Clinical Recommendations for diagnosis, treatment and follow-up of advanced colorectal cancer. Ann Oncol 2005;16:Suppl-9
Excluded: Model does not categorize risk or validate, OVID-Medline.
768. Van Cutsem EJD, Kataja VV. ESMO minimum clinical recommendations for diagnosis, adjuvant treatment and follow-up of colon cancer. Ann Oncol 2005;16(Suppl. 1):i16-i17
Excluded: Model does not categorize risk or validate, OVID-Embase.
769. van der Rhee HJ, de Vries E, Coebergh JWW. Does sunlight prevent cancer? A systematic review. Eur J Cancer 2006;42(14):2222-32.
Excluded: Not an eligible population, OVID-Embase.
770. Van Der KT, Lopes C, Santonja C, et al. Guidelines for processing and reporting of prostatic needle biopsies. J Clin Pathol 2003;56(5):336-40.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
771. van Dooren S, Rijnsburger AJ, Seynaeve C, et al. Psychological distress and breast self-examination frequency in women at increased risk for hereditary or familial breast cancer. Community Genet 2003;6(4):235-41.
Excluded: Not an eligible study design, OVID-Medline.
772. van Dooren S, Rijnsburger AJ, Seynaeve C, et al. Psychological distress in women at increased risk for breast cancer: the role of risk perception. Eur J Cancer 2004;40(14):2056-63.
Excluded: Not an eligible population, OVID-Medline.
773. van Dooren S, Seynaeve C, Rijnsburger AJ, et al. The impact of having relatives affected with breast cancer on psychological distress in women at increased risk for hereditary breast cancer. Breast Cancer Res Treat 2005;89(1):75-80.
Excluded: Family history not systematically collected, OVID-Medline.
774. van Dooren S, Seynaeve C, Rijnsburger AJ, et al. Exploring the course of psychological distress around two successive control visits in women at hereditary risk of breast cancer. Eur J Cancer 2005;41(10):1416-25.
Excluded: Family history not systematically collected, OVID-Medline.
775. van Oostrom I, Meijers-Heijboer H, Duivenvoorden HJ, et al. Comparison of individuals opting for BRCA1/2 or HNPCC genetic susceptibility testing with regard to coping, illness perceptions, illness experiences, family system characteristics and hereditary cancer distress. Patient Educ Couns 2007;65(1):58-68.
Excluded: Not an eligible population, OVID-Medline.
776. Varghese SS, Wilson DB, Penberthy LT, et al. North American perspectives. Examining the evidence for breast self examination recommendations. Clin Governance Int J 2006;11(3):225-33.
Excluded: Not an eligible study design, OVID-Cinahl.

777. Vasen HF, Moslein G, Alonso A, et al. Guidelines for the clinical management of familial adenomatous polyposis (FAP). Gut 2008;57(5):704-13.
Excluded: Model does not categorize risk or validate, OVID-Medline.
778. Vasey PA, Herrstedt J, Jelic S, et al. ESMO Minimum Clinical Recommendations for diagnosis, treatment and follow-up of epithelial ovarian carcinoma. Ann Oncol 2005;16(Suppl 1):i13-5.
Excluded: Model does not categorize risk or validate, OVID-Medline.
779. Velayos FS, Terdiman JP, Walsh JM. Effect of 5-aminosalicylate use on colorectal cancer and dysplasia risk: a systematic review and metaanalysis of observational studies. Am J Gastroenterol 2005;100(6):1345-53.
Excluded: Not an eligible population, OVID-Medline.
780. Velayos FS, Allen BA, Conrad PG, et al. Low rate of microsatellite instability in young patients with adenomas: reassessing the Bethesda guidelines. Am J Gastroenterol 2005;100(5):1143-9.
Excluded: Model does not categorize risk or validate, OVID-Medline.
781. Veschi S, Aceto G, Scioletti AP, et al. High prevalence of BRCA1 deletions in BRCAPRO-positive patients with high carrier probability. Ann Oncol 2007;18:Suppl-92
Excluded: Model does not categorize risk or validate, OVID-Medline.
782. Vicini FA, Vargas C, Abner A, et al. Limitations in the use of serum prostate specific antigen levels to monitor patients after treatment for prostate cancer. J Urol 2005;173(5):1456-62.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
783. Vogel KJ, Atchley DP, Erlichman J, et al. BRCA1 and BRCA2 genetic testing in Hispanic patients: mutation prevalence and evaluation of the BRCAPRO risk assessment model. J Clin Oncol 2007;25(29):4635-41.
Excluded: Model does not categorize risk or validate, OVID-Medline.
784. Vogel VG, Graves DS, Vernon SW, et al. Mammographic screening of women with increased risk of breast cancer. Cancer 1990;66(7):1613-20.
Excluded: Family history not systematically collected, OVID-Medline.
785. Vogel VG. Can statin therapy reduce the risk of breast cancer? J Clin Oncol 2005;23(34):8553-5.
Excluded: Not an eligible study design, OVID-Embase.
786. Vogel VG. Recent results from clinical trials using SERMs to reduce the risk of breast cancer. Ann N Y Acad Sci 2006;1089:127-42.
Excluded: Not an eligible study design, OVID-Medline.
787. Vogel VG. Chemoprevention in breast cancer. Cancer and Chemotherapy Reviews 2007;2(1):33-40.
Excluded: Not an eligible study design, OVID-Embase.
788. Von Roon AC, Karamountzos L, Purkayastha S, et al. Diagnostic precision of fecal calprotectin for inflammatory bowel disease and colorectal malignancy. Am J Gastroenterol 2007;102(4):803-13.
Excluded: Not an eligible study design, OVID-Embase.
789. Wade WM. Women receiving genetic counseling for breast cancer risk: Cancer worry, psychological distress, and risk recall accuracy. Dissertation Abstracts International: Section B: the Sciences and Engineering 2001;61(7-b):2865
Excluded: Not an eligible publication type, OVID-Cochrane.
790. Wagner A, van Kessel I, Kriege MG, et al. Long term follow-up of HNPCC gene mutation carriers: compliance with screening and satisfaction with counseling and screening procedures. Fam Cancer 2005;4(4):295-300.
Excluded: Family history not systematically collected, OVID-Medline.
791. Wahlberg SS, Schmeits J, Thomas G, et al. Evaluation of microsatellite instability and immunohistochemistry for the prediction of germ-line MSH2 and MLH1 mutations in hereditary nonpolyposis colon cancer families. Cancer Res 2002;62(12):3485-92.
Excluded: Model does not categorize risk or validate, OVID-Medline.
792. Wainberg S, Husted J. Utilization of screening and preventive surgery among unaffected carriers of a BRCA1 or BRCA2 gene mutation. [Review] [27 refs]. Cancer Epidemiol Biomarkers Prev 2004;13(12):1989-95.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
793. Walleser S, Griffiths A, Lord SJ, et al. What is the value of computered tomography colonography in patients screening positive for fecal occult blood? A systematic review and economic evaluation. [Review] [42 refs]. Clin Gastroenterol Hepatol 1368;5(12):1439-46.
Excluded: Not an eligible population, OVID-Medline.
794. Wallis M, Tarvidon A, Helbich T, et al. Guidelines from the European Society of Breast Imaging for diagnostic interventional breast procedures. Eur Radiol 2007;17(2):581-8.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
795. Walsh JME, Posner SF, Perez-Stable EJ. Colon cancer screening in the ambulatory setting. Prev Med 2002;35(3):209-18.
Excluded: Family history not systematically collected, OVID-Embase.

796. Wampler NS, Saba L, Rahman SM, et al. Factors associated with adherence to recommendations for screening mammography among American Indian women in Colorado. Ethn Dis 2006;16(4):808-14.
Excluded: Family history not systematically collected, OVID-Medline.
797. Wane D, Lengacher CA. Integrative review of lycopene and breast cancer. Oncol Nurs Forum 2006;33(1):127-37.
Excluded: Not an eligible population, OVID-Cinahl.
798. Wang P-H, Chao H-T. A reconsideration of tamoxifen use for breast cancer. Taiwan J Obstet Gynecol 2007;46(2):93-5.
Excluded: Not an eligible study design, OVID-Embase.
799. Wang Y, Sun G, Pan JG, et al. Performance of tPSA and f/tPSA for prostate cancer in Chinese. A systematic review and meta-analysis. Prostate Cancer Prostatic Dis 2006;9(4):374-8.
Excluded: Not an eligible population, OVID-Medline.
800. Wang Y-P, Pan T, Yang J-L, et al. Nonsteroidal anti-inflammatory drugs for prevention of colorectal neoplasms: A systematic review. Chinese Journal of Evidence-Based Medicine 2005;5(6):438-43.
Excluded: Not an eligible intervention or outcome, OVID-Embase
801. Wardle J. Women at risk of ovarian cancer. J Natl Cancer Inst 1995;Monographs.(17):81-5.
Excluded: Not an eligible publication type, OVID-Medline.
802. Warner E. Intensive radiologic surveillance: A focus on the psychological issues. Ann Oncol 2004;15(SUPPL. 1):i43-i47
Excluded: Family history not systematically collected, OVID-Embase.
803. Warner E, Messersmith H, Causer P, et al. Systematic review: using magnetic resonance imaging to screen women at high risk for breast cancer. [Review] [35 refs]. Ann Intern Med 2008;148(9):671-9.
Excluded: Not an eligible population, OVID-Medline.
804. Wasvary HJ. Pathology features in Bethesda guidelines predict colorectal cancer microsatellite instability: A population-based study. Dis Colon Rectum 2007;50(10):1732-3.
Excluded: Model does not categorize risk or validate, OVID-Embase.
805. Watine JC, Bunting PS. Mass colorectal cancer screening: Methodological quality of practice guidelines is not related to their content validity. Clin Biochem 2008;41(7-8):459-66.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
806. Watson, M., Kash, K. M., Homewood, J., Ebbs, S., Murday, V., and Eeles, R., Does genetic counseling have any impact on management of breast cancer risk?, Genetic Testing, 9(2), 2005, p.167 – 174.
Excluded: Not an eligible population, OVID-Embase.
807. Weik JL, Lum SS, Esquivel PA, et al. The Gail model predicts breast cancer in women with suspicious radiographic lesions. Am J Surg 2005;190(4):526-9.
Excluded: Model does not categorize risk or validate, OVID-Medline.
808. Weinberg AD, Cooper HP, Lane M, et al. Screening behaviors and long-term compliance with mammography guidelines in a breast cancer screening program. Am J Prev Med 1997;13(1):29-35.
Excluded: Family history not systematically collected, OVID-Medline.
809. Weinberg DS. In the clinic.Colorectal cancer screening. Ann Intern Med 2008;148(3):ITC2-1-16.
Excluded: Model does not categorize risk or validate, OVID-Cinahl.
810. Weinrich SP. Prostate cancer screening in high-risk men: African American Hereditary Prostate Cancer Study Network. Cancer 2006;106(4):796-803.
Excluded: Family history not systematically collected, OVID-Medline.
811. Weischer M, Bojesen SE, Ellervik C, et al. CHEK2*1100delC genotyping for clinical assessment of breast cancer risk: meta-analyses of 26,000 patient cases and 27,000 controls.[see comment]. [Review] [51 refs]. J Clin Oncol 2008;26(4):542-8.
Excluded: Not an eligible population, OVID-Medline.
812. Weitzel JN, Lagos VI, Cullinane CA, et al. Limited family structure and BRCA gene mutation status in single cases of breast cancer.[see comment]. JAMA 2007;297(23):2587-95.
Excluded: Model does not categorize risk or validate, OVID-Medline.
813. Weller DP, Owen N, Hiller JE, et al. Colorectal cancer and its prevention: prevalence of beliefs, attitudes, intentions and behaviour. Aust J Public Health 1995;19(1):19-23.
Excluded: Family history not systematically collected, OVID-Cinahl.
814. Wellisch DK, Lindberg NM. A psychological profile of depressed and nondepressed women at high risk for breast cancer. Psychosomatics 2001;42(4):330-6.
Excluded: Family history not systematically collected, OVID-Medline.

815. West DS, Greene PG, Kratt PP, et al. The impact of a family history of breast cancer on screening practices and attitudes in low-income, rural, African American women. J Womens Health (Larchmt) 2003;12(8):779-87.
Excluded: Family history not systematically collected, OVID-Medline.
816. Wiernikowski J, Mohide EA. Review: adequately randomised trials showed that mammography screening did not significantly reduce breast cancer, cancer, or all cause mortality but increased breast surgeries. Evid Based Nurs 2007;10(3):80
Excluded: Not an eligible study design, OVID-Cinahl.
817. Williams GL, Clarke P, Vellacott KD. Anxieties should not be forgotten when screening relatives of colorectal cancer patients by colonoscopy. Colorectal Dis 2006;8(9):781-4.
Excluded: Family history not systematically collected, OVID-Medline.
818. Winawer S, Fletcher R, Rex D, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale-Update based on new evidence. Gastroenterology 2003;124(2):544-60.
Excluded: Model does not categorize risk or validate, OVID-Medline.
819. Winawer SJ, Zauber AG, Fletcher RH, et al. Guidelines for colonoscopy surveillance after polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society. CA Cancer J Clin 184;56(3):143-59.
Excluded: Model does not categorize risk or validate, OVID-Medline.
820. Winawer SJ. New post-polypectomy surveillance guidelines. Practical Gastroenterology 2007;31(8):30-42.
Excluded: Model does not categorize risk or validate, OVID-Embase.
821. Wolf B, Gruber S, Henglmueller S, et al. Efficiency of the revised Bethesda guidelines (2003) for the detection of mutations in mismatch repair genes in Austrian HNPCC patients. Int J Cancer 2006;118(6):1465-70.
Excluded: Model does not categorize risk or validate, OVID-Medline.
822. Wu TY, Guthrie BJ, Bancroft JM. An integrative review on breast cancer screening practice and correlates among Chinese, Korean, Filipino, and Asian Indian American women.[erratum appears in Health Care Women Int. 2005 Oct;26(9):877. Health Care for Women Int 2005;26(3):225-46.
Excluded: Not an eligible intervention or outcome, OVID-Medline.
823. Wullenweber HP, Sutter C, Autschbach F, et al. Evaluation of Bethesda guidelines in relation to microsatellite instability. Dis Colon Rectum 2001;44(9):1281-9.
Excluded: Model does not categorize risk or validate, OVID-Medline.
824. Yan L, Spitznagel EL. Meta-analysis of soy food and risk of prostate cancer in men. Int J Cancer 2005;117(4):667-9.
Excluded: Not an eligible intervention or outcome, OVID-Embase.
825. Yang K, Allen B, Conrad P, et al. Awareness of gynecologic surveillance in women from hereditary non-polyposis colorectal cancer families. Fam Cancer 2006;5(4):405-9.
Excluded: Not an eligible study design, OVID-Medline.
826. Yasui Y, Newcomb PA, Trentham-Dietz A, et al. Familial relative risk estimates for use in epidemiologic analyses. Am J Epidemiol 2006;164(7):697-705.
Excluded: Model does not categorize risk or validate, OVID-Medline.
827. Yin LY, Wai KL, Chuan TN, et al. Factors influencing women undertaking screening mammography in primary care in Singapore. Singapore Nurs J 2007;34(3):74-80.
Excluded: Family history not systematically collected, OVID-Cinahl.
828. Yokoe T, Takei H, Horiguchi J, et al. Family history in participants of breast cancer screening. Oncol Rep 1997;4(5):973-6.
Excluded: Family history not systematically collected, OVID-Embase.
829. Yossepowitch O, Eggener SE, Bianco FJ, Jr., et al. Radical prostatectomy for clinically localized, high risk prostate cancer: critical analysis of risk assessment methods. J Urol 499;178(2):493-9.
Excluded: Family history not systematically collected, OVID-Medline.
830. Zakowski SG, Valdimarsdottir HB, Bovbjerg DH, et al. Predictors of intrusive thoughts and avoidance in women with family histories of breast cancer. Ann Behav Med 1997;19(4):362-9.
Excluded: Family history not systematically collected, OVID-PsycInfo.
831. Zakowski SG, Valdimarsdottir HB, Bovbjerg DH. Emotional expressivity and intrusive cognitions in women with family histories of breast cancer: Application of a cognitive processing model. Br J Health Psychol 2001;6(2):151-65.
Excluded: Family history not systematically collected, OVID-PsycInfo.
832. Zaloudik J, Coufal O, Kocakova I, et al. Chemoprevention of colorectal carcinoma in high-risk patients. Acta Univ Palacki Olomuc Fac Med 2000;143:109
Excluded: Family history not systematically collected, OVID-Medline.
833. Zapka J, Fisher G, Lemon S, et al. Relationship and distress in relatives of breast cancer patients. Families, Systems and Health 2006;24(2):198-212. Excluded: Family history not systematically collected, OVID-Embase.

834. Zapka JG, Stoddard A, Maul L, et al. Interval adherence to mammography screening guidelines. Med Care 1991;29(8):697-707.
Excluded: Family history not systematically collected, OVID-Medline.
835. Zapka JG, Hosmer D, Costanza ME, et al. Changes in mammography use: economic, need, and service factors. Am J Public Health 1992;82(10):1345-51.
Excluded: Family history not systematically collected, OVID-Medline.
836. Zhou B, Yang L, Wang L, et al. The association of tea consumption with ovarian cancer risk: A metaanalysis. Am J Obstet Gynecol 2007;197(6):594-6.
Excluded: Not an eligible population, OVID-Medline.
837. Zhou B, Sun Q, Cong R, et al. Hormone replacement therapy and ovarian cancer risk: A meta-analysis. Gynecol Oncol 2008;108:641-51.
Excluded: Not an eligible population, OVID-Embase.
838. Zwick YC. Outlining a pan-European colon cancer screening programme. Z Gastroenterol 2008;46(Suppl.1):S52-S53
Excluded: Not an eligible publication type, OVID-Embase.

Appendix E - Partners, Technical Expert Panel, and Peer Reviewers

Task Order Officer

Supriya Janakiraman, M.D., M.P.H.
Staff Service Fellow, Center for Outcomes and Evidence AHRQ
Rockville, MD

Partners

Robert German, Dr.P.H., M.P.H.
Associate Director for Science, Division of Cancer Prevention and Control,
Centers for Disease Control and Prevention
Atlanta, GA

Rodolfo Valdez, Ph.D., M.Sc.
National Office of Public Health Genomics
Centers for Disease Control and Prevention
Atlanta, GA

Members of the Technical Expert Panel

Lisa Madlensky, Ph.D.
Assistant Professor, Cancer Prevention & Control Program
University of San Diego
San Diego, CA

Louise Acheson, M.D., M.S.
Professor of Family Medicine and Oncology
Associate Professor of Reproductive Biology
Case Western Reserve University and University Hospitals Case Medical Center
Euclid, OH

Peer Reviewers

Louise Acheson, M.D., M.S.
Professor of Family Medicine and Oncology
Associate Professor of Reproductive Biology
Case Western Reserve University and University Hospitals Case Medical Center
Euclid, OH , U.S.A

George Browman, M.D., M.Sc.
Senior Scientist, BC Cancer Agency
Chair of the Cancer Guidelines Action Group of the Canadian Partnership Against Cancer
Victoria, BC, C.A.

W.Greg Feero, M.D., Ph.D.
Senior Advisor for Genomic Medicine
National Human Genome Research Institute
National Institutes of Health
Bethesda, MD, U.S.A.

Andrew Freedman, M.D., M.Sc.
National Cancer Institute, Epidemiologist
Bethesda, MD, U.S.A.

Joy Larsen Haidle, M.S., C.G.C.
Genetic Counselor
Hubert H. Humphrey Cancer Center
Robbinsdale, MN, U.S.A.

Lisa Madlensky, Ph.D.
Assistant Professor, Cancer Prevention & Control Program
University of San Diego
San Diego, CA. U.S.A.

Phuong Mai, M.D.
Staff Clinical, Clinical Genetics Branch
Division of Cancer Epidemiology and Genetics
National Cancer Institute, National Institutes of Health
Rockville, MD, U.S.A.

Harvey J.Murff, M.D., M.P.H.
Vanderbilt Epidemiology Center
Institute for Medicine and Public Health
Nashville, TN, U.S.A.

Suzanne O'Neill, Ph.D., C.G.C.
Associate Director, Northwestern University Graduate Program in Genetic Counseling
Assistant Professor, Northwestern University Feinberg School of Medicine
Chicago, IL, U.S.A.

Nancie Petrucelli, M.S., C.G.C.
Senior Genetic Counselor/Coordinator
Cancer Genetic Counseling Service
Barbara Ann Karmanos Cancer Institute
Detroit, MI, U.S.A.