Methods for Conducting Systematic Reviews of Evidence on Effectiveness and Economic Efficiency of Interventions to Increase Screening for Breast, Cervical, and Colorectal Cancers

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Introduction

The Task Force on Community Preventive Services (Task Force) chose to include prevention of breast, cervical, and colorectal cancer through interventions to increase screening as a topic in the *Guide to Community Preventive Services* (*Community Guide*) for several reasons. First, these cancers impose a large health burden on the U.S. population[1,2]; second, there are effective screening tests that can reduce this burden[3–6]; and third, large segments of the population still are not screened for colorectal cancers and, despite much progress, many groups have not benefited from the general rates of improvement in breast and cervical cancer screening.[7,8] Through systematic review of the literature, the Task Force sought evidence to determine effectiveness of a variety of interventions which are being applied to increase screening for these cancers.

Community Guide methods for conducting systematic reviews and for linking evidence to recommendations have been described elsewhere.[2,9,10] In brief, for each *Community Guide* topic, an interdisciplinary team (the systematic review development team), representing a range of relevant backgrounds, skills, and experiences, conducts a review by:

- developing a conceptual framework to organize, group, and select appropriate interventions for health issues under consideration;
- choosing outcomes to define effectiveness (success) of each intervention;
- systematically searching for and retrieving evidence;
- assessing quality of individual studies and summarizing strength of evidence;
- summarizing other evidence, including applicability over a range of populations and settings, other positive or negative effects, barriers to implementation, and economic efficiency of effective interventions;
- identifying and summarizing research gaps; and
- presenting findings to the Task Force for recommendation.

This report summarizes the general methodologic approach used by the *Community Guide* and adopted by the systematic review development team for conducting systematic reviews of interventions to promote screening for breast, cervical, and colorectal cancers. Any further modification to adapt these methods to a specific cancer screening intervention review will be described in the methods section of the respective review.

Systematic Review Development Team

The systematic review development team included three subgroups:

- The coordination team, which drafted the conceptual framework for reviews; managed the data collection and review process; and drafted evidence tables, summaries of evidence, and reports.
- The consultation team, which reviewed and commented on materials developed by the coordination team, and set priorities for reviews.
- The abstraction team, which collected and recorded data from studies for possible inclusion in systematic reviews.

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The names and affiliations of the Task Force members are listed at the front of this supplement and at www.thecommunityguide.org.

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Unless otherwise noted, subsequent use of the term "team" will refer to the coordination team.

Conceptual Approach

Convincing evidence shows that screening using recommended techniques improves health outcomes for breast, cervical, and colorectal cancers.[3–6] Many interventions have been applied in community and healthcare system settings to increase screening rates in populations of age-eligible individuals who have never been screened or are not screened at recommended intervals.

In developing the approach to these reviews, the team:

- identified modifiable barriers and facilitators to changing screening behavior (determinants, such as knowledge, attitudes, intentions, access, and provider-client interactions);
- conceptualized three primary strategies under which related interventions to improve screening are grouped: (1) increasing community demand for

Table 1. Interventions, to date, selected for *Community Guide* systematic review of evidence of effectiveness in increasing breast, cervical, and colorectal cancer screening. Six interventions are intended to increase client demand for screening services, three to enhance access to services, and three to improve provider and healthcare system performance in delivering screening services

Intervention	Definition
Increasing community demand for screening (client-directed)	
Mass media (education)	Informational or motivational messages delivered to large audiences through broadcast and print media (television, radio, billboards, magazines, and newspapers).
Small media (education)	Informational or motivational messages delivered to individuals through brochures, leaflets (pamphlets or flyers), newsletters, informational letters, flip-charts, or videos.
Group (education)	Informational or motivational messages delivered to an assembled group in lecture or interactive format by trained laypeople or health professionals.
One-on-one (education)	Informational or motivational messages delivered by one individual to another, either in person or by telephone. May be supported by small media or client reminders.
Client reminders and recall	Printed (letter or postcard) or telephone messages advising people they are due (reminder) or late (recall) for cancer screening. Messages may include a scheduled appointment or an offer to assist in scheduling.
Client incentives	Small, noncoercive gifts or financial rewards to motivate people to seek cancer screening for themselves or others.
Increasing community access to screening (client-directed)	
Reducing client out-of-pocket costs	Reduces client cost through reimbursement, voucher distribution, or increased third party payment for cancer screening.
Reducing structural barriers	Reduces or eliminates barriers such as location, distance, inconvenient hours of operation, or language barriers (e.g., alternative screening sites, provide transportation, expand hours of operation, assist in appointment scheduling). These interventions may be supported by reminders, educational messages, or reduced out-of-pocket client costs.
Laws to increase screening	State or federally mandated screening or insurance coverage of screening.
Increasing provider delivery or promotion of screening (provider-directed)	
Provider reminders and recall	Electronic or manual chart notations or checklists to inform or remind healthcare providers when clients are due (reminder) or overdue (recall) for screening.
Provider assessment and feedback	Evaluates provider performance in delivering a screening service (assessment) and gives the information back to providers, individually or as a group (feedback).
Provider incentives	Direct or indirect rewards (monetary or nonmonetary) to motivate providers to deliver screening services or to make appropriate referrals.

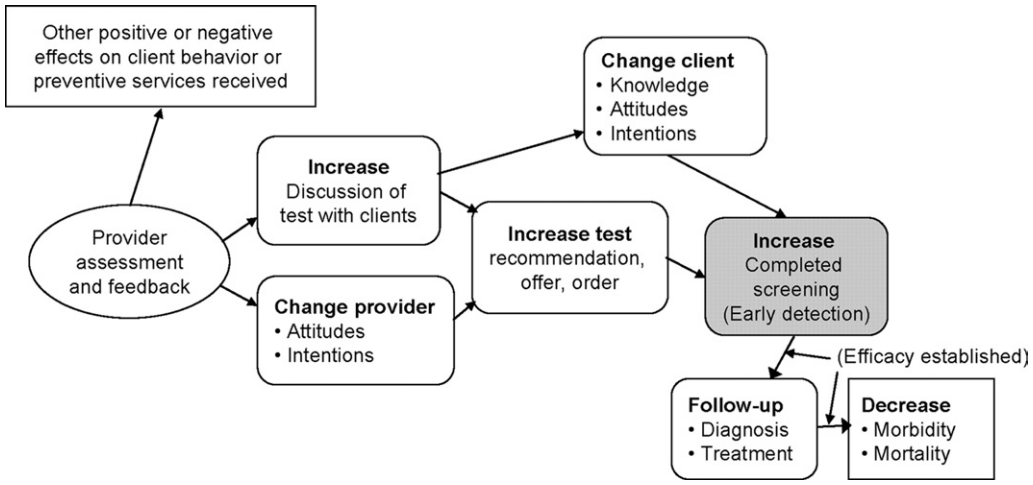

Figure 1. Example of the analytic framework used in reviews of interventions to increase screening for breast, cervical, and colorectal cancers. (Oval indicates intervention [provider assessment and feedback]; rectangles with rounded corners indicate mediators or intermediate outcomes [shaded rectangle is the outcome demonstrating intervention effectiveness]; and clear rectangle indicates desired health outcomes.)

cancer screening; (2) enhancing community access to cancer screening services; and (3) increasing healthcare provider delivery of these services;
- chose outcomes for which evidence was to be sought and which would define intervention success;
- generated a list of "candidate" interventions for improving cancer screening rates; and
- selected for review from the list of candidates, interventions that are:
  - commonly used but may be ineffective, or for which there is need for additional information;
  - commonly used and shown empirically to be effective in other areas, believed to be effective in cancer screening (e.g., client reminder/recall), or both;
  - underused and may be effective; or
  - of interest to people involved in planning, funding, and implementing population-based services and policies to improve health at the community and state levels.

The team set priorities for review of 12 classes of interventions, each addressing one of the three strategies,[11] and defined these interventions (Table 1). Six are used to increase community demand for screening services and three to enhance access; three are used in healthcare settings to influence providers to deliver or to promote use of screening services. Summaries of these reviews and Task Force recommendations will be available at www.thecommunityguide.org/cancer. Detailed reviews of interventions to increase community demand,[12] community access,[13] and provider delivery of screening (assessment and feedback and incentives),[14] along with corresponding Task Force recommendations,[15] are in accompanying articles. A detailed review of an additional intervention to increase provider delivery (reminder/recall) of or referral for screening and a review of multicomponent interventions have been completed and are being prepared for publication.

Analytic Framework

Analytic frameworks (an example of which is shown in Figure 1) were developed for each intervention to identify and map hypothesized relationships along the pathway(s) from intervention to intermediate and desired health outcomes. Completed screening (shaded) is the outcome of primary interest in these reviews. Although completed screening is an intermediate step in the model, it is the measurable criterion for intervention effectiveness because of established links to the health outcomes of ultimate interest: decreased morbidity and mortality from breast, cervical, and colorectal cancers.[4–6] The Task Force therefore based recommendation decisions on the direction, consistency, and magnitude of the change in completed screening only. Although several studies reported change in precursors to altered screening behavior (e.g., client or provider knowledge or attitude, client perception of access, provider-client interaction, or screening tests recommended or ordered), these outcomes alone were not sufficient to determine intervention effectiveness. The model also indicates that the intervention may result in other benefits or harms, such as positive or negative effects on other health behaviors or use of healthcare services.

Developing the Body of Evidence

Data Sources

To establish the evidence base the team searched five computerized databases from the earliest entries in

Table 2. Search terms used in five electronic databases to find studies for inclusion in the systematic reviews of cancer screening. Searches were conducted to find all studies of cancer screening including those specific to screening for breast, cervical, or colorectal cancer

General
Neoplasms—combined with any of the following headings:
Early detection
Mass screening
Multiphasic screening
Preventive health services
Screening
Breast cancer
Breast neoplasms
Mammography
Cervical cancer
Cervical intraepithelial neoplasia
(Uterine) cervical neoplasms
Cervix dysplasia
Vaginal smears
Colorectal cancer
Colonic neoplasms
Colorectal neoplasms
Occult blood
Sigmoid neoplasms
Sigmoidoscopy

each through November 2004: MEDLINE, database of the National Library of Medicine (from 1966); the Cumulative Index to Nursing and Allied Health database (CINAHL, from 1982); the Chronic Disease Prevention database (CDP, Cancer Prevention and Control subfield, from 1988); PsycINFO (from 1967); and the Cochrane Library databases. Medical subject headings (MeSH) searched (including all subheadings) are shown in Table 2. The team also scanned bibliographies from key articles and solicited other citations from other team members and subject-matter experts. Conference abstracts were not included because, according to *Community Guide* criteria,[9] they generally do not provide enough information to assess study validity and to address the research questions.

The search identified over 9000 citations whose titles and abstracts were screened for potential relevance to interventions and outcomes of interest; of these, 580 articles were retrieved for full-text review (see Candidate Study Selection).

Candidate Study Selection

To be considered for screening intervention review, four general inclusion criteria were assessed. Studies had to (1) be a primary investigation (as opposed to a set of guidelines, a review, or a description of process measures) of one or more interventions prioritized for review; (2) be conducted in a country with a high income economy (as defined by the World Bank)[a]; (3) provide information on one or more outcomes pre-selected by the team; and (4) include a comparison group of either pre-exposed or concurrent study participants unexposed or less exposed to the intervention. A total of 244 studies satisfying these criteria became candidates for review.

Organization of Studies by Intervention

Interventions were classified according to definitions developed as part of the review process (Table 1). The 244 candidate studies were grouped according to the class of intervention(s) described (although precise nomenclature used by a specific study sometimes differed from the corresponding term adopted by the team). Studies providing evidence for more than one intervention (e.g., multiple intervention arms that mapped to separate interventions or to multicomponent interventions) were reviewed separately for each applicable intervention.

Evaluating and Summarizing Studies Effectiveness

Qualifying studies. Each candidate study (meeting general inclusion criteria, above) was evaluated using a standardized abstraction form (available at www.thecommunityguide.org/methods/abstractionform.pdf) and assessed for suitability of study design (greatest, moderate, or least) and threats to internal and external validity.[9,10] Studies of all levels of design suitability were included in the body of evidence, except when the number of studies of greatest design suitability enabled us to analyze these alone (excluding studies of moderate and least suitable designs) without compromising internal or external validity of the resulting body of evidence. Based on the number of threats to validity, candidate studies were characterized as having good, fair, or limited quality of execution. Studies with good or fair quality of execution (minimal quality standards) qualified for final inclusion in the review of intervention effectiveness; studies with limited quality of execution did not qualify. Nonqualifying studies, however, were still considered for relevant background information, to help conceptualize the

[a]Countries with high income economies as defined by the World Bank are Andorra, Antigua and Barbuda, Aruba, Australia, Austria, The Bahamas, Bahrain, Barbados, Belgium, Bermuda, Brunei Darussalam, Canada, Cayman Islands, Channel Islands, Cyprus, Czech Republic, Denmark, Estonia, Faeroe Islands, Finland, France, French Polynesia, Germany, Greece, Greenland, Guam, Hong Kong (China), Iceland, Ireland, Isle of Man, Israel, Italy, Japan, Republic of Korea, Kuwait, Liechtenstein, Luxembourg, Macao (China), Malta, Monaco, Netherlands, Netherlands Antilles, New Caledonia, New Zealand, Norway, Portugal, Puerto Rico, Qatar, San Marino, Saudi Arabia, Singapore, Slovenia, Spain, Sweden, Switzerland, Trinidad and Tobago, United Arab Emirates, United Kingdom, United States, Virgin Islands (U.S.).

review, and to provide information on potential barriers to implementation and other benefits or harms.

Summary effect estimates. The outcome of interest in these reviews—completed screening tests—was generally ascertained in each study by record reviews or client self-reports. Results of each study were represented as change in screening attributable to the intervention; where possible, percentage point (i.e., absolute) change in completed screening from baseline or comparison value was used as the measure of effect. Percentage point changes and baseline screening rates were calculated as follows:

For studies with before-and-after measurements and concurrent comparison groups:

$(I_{post} - I_{pre}) - (C_{post} - C_{pre})$; baseline = I_{pre}

For studies with post-only measurements and concurrent comparison groups:

$(I_{post} - C_{post})$; baseline = C_{post}

For studies with before-and-after measurements and no concurrent comparison groups:

$(I_{post} - I_{pre})$; baseline = I_{pre}

Where:

I_{post} = reported percentage of intervention group screened after intervention;
I_{pre} = reported percentage of intervention group screened, immediately before intervention;
C_{post} = reported percentage of comparison group screened after intervention;
C_{pre} = reported percentage of comparison group screened, immediately before intervention; and
Baseline = the estimated study population screening rate in the absence of or prior to intervention.

When the effect was reported as an odds ratio (OR) or a percent (i.e., relative) change from baseline or comparison value, the team sought to convert the estimate to percentage point change. If this was not possible, the outcome was excluded from the summary effect measure (see below) but reported separately to reflect the complete evidence base and to assess consistency across all studies.

Studies with multiple effect estimates were handled in one of two ways. First, when there was more than one estimate for a single outcome in a single study arm, consistent rules were applied to choose the most appropriate estimate. For example, estimates adjusted for confounding were selected over crude estimates; when estimates were taken at multiple follow-up points, the estimate at longest follow-up was selected over those measured earlier. Second, when estimates differed in terms of population and intervention and therefore provided relatively independent information on effectiveness, they were treated as separate data points in the analyses. This approach was used when more than one form of the intervention of interest was evaluated in separate study groups (e.g., a client reminder might be delivered by telephone in one arm of the study and by mail in another) or when the same intervention was evaluated in distinct geographic areas or subpopulations. These estimates were used separately, because they enhanced our ability to assess for effect heterogeneity by intervention characteristics or by setting context. As a result, the number of effect estimates reported in the reviews is often greater than the number of studies.

Summarizing effectiveness evidence and translating into recommendations. Because barriers to client demand for and access to screening services can differ greatly across population subgroups and from one screening test to another, client-directed interventions were reviewed, summarized, and recommended separately for breast, cervical, or colorectal cancers.[11] In contrast, because provider behavior was thought to be less influenced by differences in client populations or by specific details of particular tests, provider-directed interventions were reviewed and recommended on the basis of evidence for all three cancer sites combined (as long as evidence did not suggest differences in effectiveness by screening test).

For each review, effect estimates across all related studies are displayed in figures or tables and summarized using the median as the descriptive statistic. When seven or more effect measures were available, interquartile intervals were used as the measure of variability; otherwise, ranges are presented.

The *Community Guide* characterizes evidence for determining intervention effectiveness as insufficient, sufficient, or strong on the basis of the number of available studies, the suitability of study design for evaluating effectiveness, the quality of execution, the overall consistency of results, and the magnitude of effect.[9] Evidence is considered sufficient or strong when the body of evidence is of sufficient size and quality to support conclusions, when reported effects are consistent and in the desired direction, and when the magnitude of effect is, in the judgment of the Task Force, large enough to be of public health importance. If these conditions are not met, evidence is considered insufficient to determine effectiveness. Insufficient evidence should not be interpreted as evidence of ineffectiveness but rather as an indication that additional research is needed.

Task Force recommendations link directly to the strength of evidence on effectiveness, as described elsewhere.[9] In brief, a finding of strong or sufficient evidence of intervention effectiveness leads to a Task Force recommendation favoring use of the intervention. Insufficient evidence leads to a recommendation for additional research.

Applicability

Applicability of effectiveness findings (i.e., the extent to which findings are thought to apply to various populations and settings) was considered by the team on both empirical and conceptual grounds. In general, several factors strengthen support for conclusions of likely applicability. One factor is individual study characteristics. Large studies with diverse populations are more likely to have broader applicability than small studies with homogenous study populations. Another factor is the character of the collective body of evidence. Larger numbers of studies with inter-study diversity of populations and settings in which the intervention has been effective add strength to evidence of its applicability. And finally, when the scope of existing empirical evidence of effectiveness is limited, strong theoretical grounds may lend weight to the likelihood of applicability to populations or settings other than those studied.

Other Positive or Negative Effects

The team sought to identify other positive or negative intervention effects to be considered when making implementation decisions and was vigilant for possible important unintended harms or benefits noted in the effectiveness literature or considered important by the team.

Evaluating Economic Efficiency

The *Community Guide* economics team conducted systematic reviews of the cost and economic efficiency (defined as achieving maximum health gain with lowest cost) of interventions that the Task Force recommended for implementation. These economic analyses are not themselves used as criteria for Task Force recommendations. Their primary purpose is to help decision makers choose among recommended interventions.

In this section, previously reported methods for conducting systematic reviews of economic efficiency are summarized,[16,17] as adapted to screening interventions for breast, cervical, and colorectal cancers. These reviews have four stages:

- searching for and retrieving evidence on economic efficiency;
- abstracting and adjusting economic data;
- assessing quality of economic evidence; and
- summarizing and interpreting evidence on economic efficiency.

Searching for and retrieving evidence on economic efficiency. Studies identified through the literature search for evidence of intervention effectiveness were included for consideration if they reported cost or cost-effectiveness information. The search was expanded by adding two economic databases, EconLit and the Social Science Citation Index in the Web of Science, and by combining economic-specific keywords with the MeSH headings listed in Table 2. Other potential sources of economic evidence included reference lists of articles selected for review and citations provided by team members and other subject-matter experts. The body of literature considered in reviews of economic efficiency included either the original reports of studies qualifying for effectiveness review or additional articles separately describing economic analyses from those studies.

To be included as a candidate for economic efficiency review, a study had to satisfy general inclusion criteria for this review (see Candidate Study Selection); employ one of four analytic techniques: cost analysis, cost-benefit analysis, cost-utility analysis, or cost-effectiveness analysis; and provide sufficient detail to enable adjustment and expression of study data, when necessary, to conform with *Community Guide* reporting protocol.

Studies reporting economic information were excluded from the review of economic efficiency when an effect size used in the cost-effectiveness estimate could not be reconciled with the data from the effectiveness study, or when cost effectiveness was estimated from only a subset of the population in the effectiveness study; when budgeted costs were used instead of actual costs; when reported costs included a range of clinical services not specific to the particular cancer screening intervention; or when other information was insufficient to enable verification of cost-effectiveness estimates, as reported.

Abstracting and adjusting economic data. Two reviewers read each study considered for inclusion in the economic review and abstracted data using a standardized form.[17] Information collected on this form includes classification of the study design and methods; description of the intervention and study population; specification of the comparator (i.e., pre-existing activity against which the intervention is being compared); measurement of intervention effectiveness; perspective (societal versus individual program); duration of intervention and analytic horizon; and total costs and benefits and economic summary measures reported.

Because the studies were designed to report changes in screening activity and did not report ultimate health outcomes (e.g., illness or deaths averted, life years gained, or quality-adjusted life years saved), economic summary measures were based on completed screening tests. For example, rather than estimating cost per life year gained, cost-effectiveness ratios were expressed as cost per additional completed screening test, an incremental measure. When a study reported cost effectiveness as cost per percentage point increase in completed screening test or as average cost, *Community Guide* staff converted the estimate to cost per additional completed screening test. *Community Guide* staff also calculated cost-effectiveness estimates for studies that did not report the summary economic measure but which

reported program cost and intervention effectiveness separately. For comparability, summary measures were adjusted to 2003 U.S. dollars using the all-item Consumer Price Index (CPI; www.bls.gov/cpi/) or the Medical Care component of the CPI (MCPI; www.bls.gov/cpi/). For international studies, purchasing power parity rates from World Development Indicators were used to convert foreign currency to U.S. dollars.[18] Finally, because the economic measure was linked to short-term cost and intermediate outcome, economic discount rates typically employed to value long-term effects were not relevant to these reviews.

Assessing quality of economic evidence. Based on an evaluation of five performance categories—study design, costs, benefit measurements, effects, and analysis—each study received a quality rating of very good, good, satisfactory, or unsatisfactory.[17] Only studies with a rating of satisfactory or better were included in the review of economic evidence. Economic quality ratings did not apply to studies reporting only intervention costs, but which otherwise qualified for the effectiveness review. These studies, although not part of the economic evidence base, are presented for cost information only.

Summarizing and interpreting evidence on economic efficiency. The findings about cost and economic efficiency based on studies qualifying for the economic review are presented in summary tables available at www.thecommunityguide.org/cancer. Tables include information on several aspects of each study. Tables and text describing the respective reviews attempt to identify important differences in assumptions and criteria used for cost ascertainment across studies (and across reviews). Some studies reflect much higher cost per additional screen (e.g., studies that included fixed costs, such as rent and utilities and start-up costs for computer systems; studies that use a societal perspective, including cost of patient time and transportation and other indirect costs for cancer screening visits; and studies that included cost of service provided and follow-up) and tend to make the intervention appear less economically attractive in comparison to studies that consider direct labor costs only. Because these sources of variability limit comparability and interpretability of findings, they are identified among the research needs for improving quality and comparability of economic data in cancer screening research and in prevention research in general.

Barriers to Implementation

Information on barriers to implementation was abstracted from reviewed studies or included if thought to be important on conceptual grounds by the team and the Task Force. Information on barriers did not affect Task Force recommendations and is provided only to assist readers contemplating intervention implementation.

Summarizing Research Gaps

Accompanying systematic reviews,[12–14] and those to follow, do more than consolidate existing information on which to base decisions about implementing cancer screening interventions. They also identify areas where information is lacking or of poor quality, to help groups such as the Cancer Prevention and Control Research Network (www.cpcrn.org) and other teams of community-based cancer prevention investigators set research priorities. The following process describes the team's approach to research gaps:

- The team identified important research questions for each cancer screening intervention reviewed.
- Where evidence on effectiveness of an intervention was sufficient or strong according to *Community Guide* criteria,[9] the team summarized remaining questions about effectiveness, applicability, other positive or negative effects, economic efficiency, and barriers to implementation.
- Where evidence was insufficient to determine intervention effectiveness, the team summarized only questions about effectiveness and other positive or negative effects. Applicability issues were summarized only if they influenced assessment of effectiveness. *Community Guide* systematic reviews do not assess research gaps related to implementation barriers or to economic costs and efficiency when evidence of effectiveness has not been demonstrated.
- For each category of evidence, members of the team used their informed judgment to identify issues that emerged from the review. Several factors informed that judgment.

  In general:
  - If information was missing or inadequate to draw conclusions about effectiveness, applicability, other positive or negative effects, or economic efficiency, the team listed these area(s) as research gaps.
  - When a conclusion was drawn about evidence, the team applied judgment to decide if additional issues remained.

  In terms of applicability:
  - If available evidence was considered broadly applicable, it was assumed additional research was not required to test the intervention in every relevant population.

  And in terms of methods:
  - Within each body of evidence, the team considered whether research into general methods

issues would improve future studies in that area.

Reviews of Evidence

This article describes methods used in systematic reviews of interventions to increase screening for breast, cervical, and colorectal cancers. The accompanying articles[12–15] and those to follow present Task Force recommendations as well as detailed findings and supporting evidence from individual intervention reviews. Each article also describes the scope and extent of the problem addressed by the intervention(s), discusses the conceptual approach for the evidence review, and presents additional methodologic details specific to that review.

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