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How do cancer screening guidelines trade off benefits versus harms and burdens of screening? A systematic survey

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ABSTRACT

Objectives Cancer screening guidelines differ in their recommendations for or against screening. To be able to provide explicit recommendations, guidelines need to specify thresholds for the magnitude of benefits of screening, given its harms and burdens. We evaluated how current cancer screening guidelines address the relative importance of benefits versus harms and burdens of screening.

Data source We searched the Guidelines International Network, International Guideline Library, ECRI Institute and Medline. Two pairs of reviewers independently performed guideline selection and data abstraction.

Eligibility criteria We included all cancer screening guidelines published in English between January 2014 and April 2019.

Results Of 68 eligible guidelines, 25 included a statement regarding the trade-off between screening benefits versus harms and burdens (14 guidelines), or a statement of direction of the net effect (defined as benefits minus harms or burdens) (13 guidelines). None of these 25 guidelines defined how large a screening benefit should be to recommend screening, given its harms and burdens. 11 guidelines performed an economic evaluation of screening. Of these, six identified a key benefit outcome; two specified a cost-effectiveness threshold for recommending a screening option. Eight guidelines commented on people's values and preferences regarding the trade-off between benefits versus harms and burdens.

Conclusions Current cancer screening guidelines fail to specify the values and preferences underlying their recommendations. No guidelines provide a threshold at which they believe the benefits of screening outweigh its harms and burdens.

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Strengths and limitations of this study

- This systematic survey adheres to the state-of-the-art systematic summary methodology.
- The report states explicit definitions of key concepts, and detailed criteria for making judgements for setting a threshold of a key beneficial outcome, that ensures reproducible and accurate inferences.
- The findings may be limited by under-reporting of methods in eligible guidelines.
- The findings may only be applicable to guidelines published in English.

INTRODUCTION

Cancer is the second leading cause of death globally, with an estimated 9.6 million deaths in 2018.[1] To reduce the mortality and burden of cancer, cancer screening programmes and associated guidelines for screening practice have been established.[2 3] However, cancer screening recommendations implemented in countries with similar levels of healthcare spending differ.[4] Even guideline panels using similarly rigorous methods for guideline development reach different conclusions.[5 6] The differences are likely to stem from variation in how guideline panels value benefits, harms and burdens of screening, and what evidence they consider.[4] People's perspective on benefits-harm trade-offs might vary according to the importance individuals place on possible benefits versus harms and burdens of screening.[7]

Ideally, guidelines should entail explicit assumptions regarding values and preferences that underlie their judgements of the trade-off between screening benefits versus its harms and burdens.[8] However, weighing these desirable and undesirable consequences, and clearly articulating the underlying values and preferences while simultaneously considering multiple outcomes, can be challenging. Researchers have developed frameworks for incorporating patients' preferences regarding benefits and harms while simultaneously considered multiple outcomes into the evaluation of health interventions.[9 10] Due

to the complexity of the process, these approaches have not seen wide use.

Cancer screening guidelines have a potential advantage over guidelines in other areas of medicine because they often have one or two key benefit outcomes: reduction in cancer mortality or cancer incidence. Therefore, the central question guideline panels face may be framed as: given the harms and burdens of screening, what magnitude of its key benefits (effect on cancer incidence and/or mortality) would people require to undergo screening? In other words, what is the threshold above which people would undergo screening and below which they would not? Some may argue that the values and preferences regarding such threshold might vary among target population. However, guideline panel could always identify the distribution of individuals' values and preferences and find the magnitude of benefit that majority of target population would require. By establishing such a threshold, a panel makes transparent, through a quantitative trade-off between benefits and harms or burdens, their assessment of the values and preferences of the target population.

We evaluated how current cancer screening guidelines address the relative importance of benefits versus harms and burdens. In particular, we evaluated:

1. The proportion of cancer screening guidelines that established a threshold for key benefit outcomes (reduction in cancer incidence or mortality) given the evidence of harms and burdens, above which people would undergo screening and below which they would not.
2. The proportion of cancer screening guidelines that qualitatively traded off the benefits versus the harms and burdens of screening.
3. The proportion of cancer screening guidelines that commented on the values and preferences of target population regarding the trade-off between the benefits versus the harms and burdens of screening.

METHODS

Design overview

We conducted a systematic survey of cancer screening guidelines published between 1 January 2014 and 30 April 2019 using the standard methodology for systematic surveys.[11]

As defined by the WHO, screening is the presumptive identification of unrecognised disease in an apparently healthy, asymptomatic population by means of tests, examinations or other procedures that can be applied rapidly and easily.[12] For this systematic survey, we defined cancer screening guideline as guidelines addressing recommendations of screening technologies for early detection or prevention of cancer, including guidelines that address the entire spectrum of screening, diagnosis and management. Ideally, guideline panels consider benefits, harms or burdens to make recommendations. Guideline panels may, if cost is in their scope, also consider cost-effectiveness to generate a cost-effectiveness ratio.[13]

For each identified screening guideline, we evaluated if the guideline included information about (1) an applied threshold for the key benefit outcome (ie, reduction in cancer mortality and/or incidence) required to balance harms or burdens of screening, and (2) an applied threshold for a beneficial cost-effectiveness ratio between benefits and costs of screening. We defined the threshold for a key benefit outcome as the threshold above which typical members of the target population would undergo screening and below which they would decline. We defined the threshold of cost-effectiveness as the magnitude of cost per unit of incremental benefit deemed acceptable to recommend a screening test.

Literature search

An experienced librarian developed a search strategy for the Guidelines International Network-International Guideline Library, ECRI Institute and Medline (online supplemental appendix 1).

The inclusion criteria were cancer screening guidelines published in full text in English between January 2014 and April 2019 including new, updated or adapted guidelines, or consolidated guidelines. We defined consolidated guidelines as those that aggregate existing guidance addressing a disease or condition, and provide recommendations that have been evaluated and found to be up to date; such guidelines may contain new recommendations.[14] We had no restriction with respect to the cancer type.

Two pairs of trained reviewers (LZ and FKN as a pair; LY and YW as another pair) independently performed the title and abstract screening of each citation for potential eligibility and full-text screening in duplicate. The reviewers abstracted data of eligible guidelines using a standardised, pilot-tested electronic form, attempted to resolve discrepancies by discussion and, if disagreement persisted, by discussion with arbitrators (LMH, RAS, GHG).

Data abstraction

We extracted information on year, institution, and country of publication, type of cancer and screening tests, target population and methods for grading quality of evidence or strength of recommendations.

Because a cancer screening guideline might address more than one key clinical question (eg, whether to recommend a particular screening test, or one test over another), we assumed that a guideline panel would apply the same approach for trading off the benefits and harms in each clinical question. Therefore, we abstracted data for one clinical question for each eligible guideline, with the following hierarchy of clinical questions: (1) recommendation for or against cancer screening; (2) a recommendation of one screening test over another(s); (3) a recommendation of a particular starting age for screening over other(s).

We established specific criteria to evaluate whether and how cancer screening guidelines defined a threshold for

Table 1 Criteria for setting a threshold for the key benefit of cancer screening in the trade-off between benefits versus harms and burdens and in cost-effectiveness evaluation in cancer screening guidelines*

Questions	Criteria or examples for judging 'yes'
Key steps for setting a threshold for the key benefit of screening given harms and burdens	
1. Does the guideline specify cancer mortality and/or incidence as the only key benefit of screening?	1. Specifying by a statement that cancer mortality and/or incidence is the 'key', 'crucial', 'most important' (or using synonyms) benefit. 2. Specifying by another statement reflecting that cancer mortality and/or incidence is the only/main benefit considered by the guideline panel. 3. Specifying by grading the importance of outcomes.
2. Does the guideline have an explicit statement of key harms and burdens of screening?	1. Specifying by a statement that certain outcomes are 'key', 'crucial' or 'most important' (or using synonyms) harms or burdens considered by the guideline panel. 2. Specifying by a statement reflecting that certain outcomes are the main harms and burdens considered by the guideline panel. 3. Specifying by grading the importance of outcomes.
3. Does the guideline specify the magnitude of effect of the key harms and burdens of screening?	1. Yes, specifies in absolute term or relative term. 2. No, not specified.
4. Does the guideline specify the magnitude of effect of the key benefit (ie, reduction in cancer mortality or cancer incidence) that would be required for recommending screening, given the evidence of key harms and burdens?	That is, specifying a threshold for the key benefit that would be required for recommending screening (vs no screening) or a particular screening option (vs other options), given the evidence of harms and burdens.
Key steps for setting a threshold for the key benefit of screening in cost-effectiveness evaluation	
1. Does the guideline consider cost-effectiveness evaluation?	1. The guideline panel performed cost-effectiveness evaluation. 2. The guideline panel identified cost-effectiveness evidence performed by other researchers.
2. Does the guideline identify the key benefit of screening in cost-effectiveness evaluation?	1. Specifying by a statement of 'key', 'crucial' or 'most important outcome' (or using synonyms). 2. Specifying by other statement reflecting that a certain outcome is the only benefit considered by the guideline panel in cost-effectiveness evaluation. 3. Specifying by grading the importance of outcomes.
3. Does the guideline specify the measurement of the cost-effectiveness ratio for the key benefit?	For example, the incremental cost-effectiveness ratio (ICER).
4. Does the guideline set a cost-effectiveness threshold that would be required for recommending screening (vs no screening) or a particular screening option (vs other options)?	For example, a threshold for ICER that would be required for recommending screening.

*Guidelines that performed each of the key steps meet the criteria of setting a threshold for the key benefit of screening in the trade-off between benefits versus harms and burdens or in cost-effectiveness evaluation.

a key benefit outcome in the trade-off between benefits versus harms and burdens, and in cost-effectiveness evaluation (table 1). We also evaluated whether the guidelines qualitatively commented on the trade-off between benefits versus harms and burdens (eg, a statement of benefits over harms and burdens, or a statement of the magnitude of net effect) or commented on the target population's values and preferences regarding the trade-off between benefits versus harms and burdens (ie, the relative importance of outcomes or health states of interest related to cancer screening) (online supplemental appendix 2).

Analyses

We conducted descriptive analyses for all variables. We summarised categorical variables with frequencies and percentages. Using univariable and multivariable logistic regression analyses, we explored the association between characteristics of guidelines and (1) performing key steps of setting thresholds for a key benefit outcome (table 1), (2) considering the values and preferences of the target population regarding trade-off between benefits and harms or burdens, (3) qualitatively commenting on the trade-off between benefits and harms. We required at least 10 events per category of variables for conducting

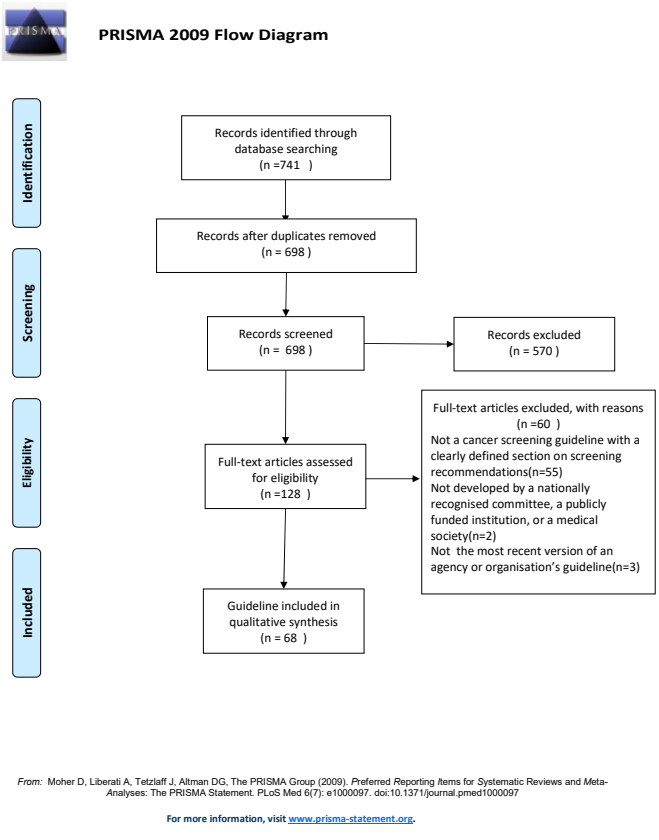

Figure 1 The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram representing the systematic literature search. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

a regression analysis. We specified a priori the following hierarchy of independent variables (ie, guideline characteristics): (1) region of guideline development (North America vs other regions), (2) use of Grading of Recommendations, Assessment, Development and Evaluations (GRADE) versus no GRADE. We presented associations using ORs and associated 95% CIs. For all analyses, we used R V.3.5.2.[15] P<0.05 provided the threshold for statistical significance.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination of our research.

RESULTS

Characteristics of included guidelines

Our search resulted in 741 records, and 68 guidelines proved eligible for analyses (figure 1). Of these, 64 (94%) were new or updated guidelines, the remaining were adapted or consolidated guidelines; 42 (62%) were from North America, and 31 (45%) in breast or colorectal cancer (table 2). online supplemental appendix 3 presents the characteristics of the eligible guidelines.

Table 2 Characteristics of cancer screening guidelines

Guideline characteristics	Total (n=68) n	%
Type of guideline		
De novo developed guideline or updated guideline	64	94.1
Adapted guideline	2	2.9
Consolidated guideline	2	2.9
Country of publication by region		
North America	42	61.8
Europe and Central Asia	15	22.1
East Asia and Pacific	6	8.8
Latin America and the Caribbean	3	4.4
Middle East and North Africa	2	2.9
Country of publication by income*		
High-income countries	63	92.6
Upper middle-income countries	5	7.4
Clinical area		
Breast	16	23.5
Colorectal	15	22.1
Cervical	8	11.8
Prostate	8	11.8
Lung	7	10.3
Ovarian	3	4.4
Thyroid	2	2.9
Others†	9	13.2
Method for rating the certainty of evidence or strength of recommendations		
GRADE	15	22.1
US Prevention Services Task Force (USPSTF) level of evidence	13	19.1
Modified GRADE	6	8.8
National Comprehensive Cancer Network (NCCN) Categories of Evidence and Consensus	3	4.4
Other methods	16	23.5
No grading for certainty of evidence and strength of recommendation	12	17.6
Not reported	3	4.4

*The category of country income is from World Bank Country and Lending Groups.
†Other clinical areas include anal, endometrial, hepatocellular carcinoma, renal, oral, pancreatic, skin—melanoma, bladder and Kaposi sarcoma (one guideline in each clinical area).
GRADE, Grading of Recommendations, Assessment, Development and Evaluations.

Setting threshold in trade-off between benefits and harms, burdens or in cost-effectiveness evaluation

None of the guidelines defined a threshold for the key

Table 3 Key steps for setting a threshold for the key benefit in cancer screening guidelines

Guideline characteristics	Total (n=68) n	%
Setting a threshold for the key benefit given harms and burdens		
Specification of cancer mortality and/or incidence as the only key benefit	22	32.4
Specification of key harms and burdens	33	48.5
Specification of the magnitude of effect of the key harms and/or burdens	26	38.2
Specification of a threshold for key benefit, given the evidence of key harms and burdens	0	0.0
Setting a threshold for the key benefit in cost-effectiveness evaluation		
Performance of an economic evaluation or identification of economic evidence	11	16.2
Identification of key benefit for economic evaluation/evidence	6	8.8
Specification of measurement of cost-effectiveness ratio for the key benefit	6	8.8
Specification of a cost-effectiveness threshold that would be required to recommend screening	2	2.9

benefit that would be required to recommend screening (or for a particular screening test or screening starting age), given screening harms and burdens. Twenty-two (32%) guidelines specified cancer mortality and/or cancer incidence as their key benefit outcome(s) (table 3). Among the 22 guidelines, 17 also specified key harms and burdens including diagnostic procedure-related harms (eg, invasive procedure, radiation exposure, infection), false-positive results, overdiagnosis, overtreatment, cost, life disruption and anxiety. Among the 17 guidelines that specified the key benefits and harms or burdens, nine specified the magnitude of the key harms and burdens, and 11 presented the magnitude of the key benefit in a quantitative way (eg, a small, moderate or large benefit).

Of the 68 guidelines, 25 (37%) included a qualitative statement of trade-off between benefits versus harms and burdens (14; 20%), or a statement of direction of net effect (defined as benefits minus harms or burdens) (13; 19%) (two of which stated both). However, none of the 25 guidelines described a quantitative approach for establishing a trade-off between benefits versus harms and burdens or a net effect of screening.

Eleven (16%) guidelines performed economic evaluation or identified economic evidence, among which six identified a key benefit outcome, and two specified a cost-effectiveness threshold required for recommending screening (table 3). Both of these two guidelines used the incremental cost-effectiveness ratio as the variable, and quantified the threshold at $100 000 per quality-adjusted life year gained.

Values and preferences

Eight (12%) guidelines commented on people's values and preferences regarding the trade-off between benefits versus harms and burdens of screening (table 4). Of these, two reported important uncertainty or variability in people's values and preferences (table 4). Because no

Table 4 Considering values and preference in cancer screening guidelines

Guideline characteristics	Total (n=68) n*	%
Explicit comment on people's values and preferences regarding the trade-off between benefits and harms/burdens of cancer screening	8	11.8
By commenting on values and preferences regarding trade-off between benefits and harms/burdens	8	11.8
By commenting on experience in shared decision-making	2	2.9
Source of information for values and preferences	8	11.8
Systematic review(s) of studies of values and preferences conducted by team(s) other than the guideline developers	4	5.9
Systematic review(s) of studies of values and preferences conducted by the guideline developers	1	1.5
Individual study(ies) of values and preferences identified by the guideline developers	1	1.5
Not reported	2	2.9
Important uncertainty or variability about people's values and preference regarding the trade-off of benefits and harms/burdens		
Yes	2	2.9
No	3	4.4
Unclear	3	4.4

*Some guidelines meet more than one category and are counted several times.

guideline set thresholds for key benefit outcomes, and few considered the values and preferences regarding trade-off between benefits versus harms and burdens, the regression analysis was minimally informative (online supplemental appendix 4).

DISCUSSION

An individual's decision to participate in cancer screening is based on personal judgement of the magnitude of benefit versus harms and burdens. Our study reveals that current cancer screening guidelines lack transparency in trading off benefits and harms or burdens, hence lack transparency in the rationale for their recommendations. Fewer than half provided quantitative estimates of the harms and burdens associated with screening, and many did not quantify key benefits. Very few guidelines explicitly addressed the issue of people's values and preferences, and none explicitly specified a threshold of key benefit given the magnitude of the harms and burdens. Few guidelines addressed economic issues. Of those that did, only two offered an explicit cost-effectiveness ratio that would justify screening.

Our study has several strengths. We used robust systematic survey methodology including explicit and reproducible broad eligibility criteria without restrictions on the type of cancers, thus ensuring generalisability; sensitive search strategies; and standardised forms for guideline screening and data abstraction. We developed explicit definitions of key concepts and detailed criteria for making judgements regarding the setting of a threshold of a key beneficial outcome. These definitions and criteria ensured reproducible and accurate inferences.

Our study also has limitations. Our evaluation was based on the reporting in guidelines. The findings may be vulnerable to under-reporting or selective reporting of guideline methods. To minimise this vulnerability, we included all published supporting documents for data abstraction. We included only guidelines published in full text in English. Generalisation to guidelines published in non-English languages is therefore limited. Because the primary aim of this study was to evaluate whether current cancer screening guidelines quantitatively trade off the benefits and harms or burdens of screening, we included only guidelines published in the last 5 years, and we did not address the qualitative approach the guideline panels used in the trade-off.

Commentators have frequently called for a requirement for a more systematic incorporation of patients' preferences in guidelines,[16–19] in particular when treatment is burdensome, benefits are limited or uncertain and harms may impact quality of life.[20] Challenges for articulating values and preferences regarding the trade-off between benefits versus harms and burdens lie in how to simultaneously consider multiple outcomes and, given the time and resource limitation in most of the guideline development, how to efficiently address the values and preferences of the target population. These challenges, however, could also be considered as opportunities to develop new and better methods. A recent BMJ Rapid Recommendation addressing colorectal cancer screening has described the first application of a method to elicit, based on the evidence of key harms and burdens, panel members' view on the target population's threshold of magnitude of key benefit for undergoing screening. This Rapid Recommendation has shown the feasibility of the method being applied to guide a formal recommendation.[21 22]

Because values and preferences regarding the threshold benefit required will certainly vary among individuals in the target population, no threshold will be right for all patients (and thus the appropriateness of weak recommendations for virtually all screening tests).[23] The goal for a guideline panel (which can only make recommendations for typical patients) is to identify the distribution of individuals' values and preferences and find the magnitude of benefit the majority of the target population would require. By establishing such a threshold for the key benefit, a panel makes their assessment of the values and preferences of the target population transparent. The recommendations that follow from the threshold will, ideally, represent the starting point for a shared decision-making discussion between patients and clinicians.

CONCLUSIONS

Cancer screening guidelines, relative to many other areas, have the advantage of being able to identify one or two key benefit outcomes. This greatly facilitates an explicit specification of thresholds for the magnitude of benefit required to justify screening given the harms and burdens. Unfortunately, current guidelines do not use this approach.

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Contributors GHG, LZ, LMH and RAS drafted the study protocol and designed the data collection forms. LZ and FKN tested the data collection forms. LZ, FKN, YW and LY screened the literature and abstracted the data. LZ, LMH, FKN, YW, LY, RAS, MB and GHG drafted and revised the manuscript. All authors have read and approved the final version of the manuscript.

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Competing interests LMH reports grants from South-Eastern Health Authority, during the conduct of the study. LMH is the first author of a guideline on colorectal cancer screening published in The BMJ 2019 (BMJ Rapid Recommendations). RAS is the coauthor of a guideline on colorectal cancer screening published in The BMJ 2019 (BMJ Rapid Recommendations). GHG is the co-founder and cochair of the GRADE working group, board member of MAGIC and the coauthor of a guideline on colorectal cancer screening published in The BMJ 2019 (BMJ Rapid Recommendations).

Patient consent for publication Not required.

Ethics approval Ethics approval for this study is not required. We will disseminate the results of this review in peer-reviewed publications and conference presentations.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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Appendix 1 Search strategy in Medline, G-I-N, and ECRI institute

Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search data:26/4/2019
Search Strategy
1 "Early Detection of Cancer"/ (20864)
2 (cancer adj3 screening).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary
concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (38693)
3 (cancer and ((detect* or diagnos) adj3 early)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word,
organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (42564)
4 or/1-3 (68736)
Annotation: cancer screening concept
5 limit 4 to (consensus development conference or consensus development conference, nih or guideline or practice guideline) (569)
6 guideline.ti,kw. (13966)
7 Practice Guideline/ or Guideline/ (31832)
8 6 or 7 (42671)
Annotation: guideline concept
9 4 and 8 (627)
10 5 or 9 (722)
Annotation: cancer screening guidelines
11 exp Neoplasms/ (3158917)
Annotation: cancer MeSH heading
12 8 and 11 (5811)
Annotation: all cancer guidelines
13 (screen* or detect*).ti,ab. (2685567)
14 12 and 13 (1019)
Annotation: cancer guidelines with mention of screen or detect
15 10 or 14 (1231)
Annotation: cancer screening GLs or GLS on cancer with screen or detect
16 limit 15 to (english language and yr="2014 -Current") (399)
17 limit 16 to (comment or editorial or letter) (10)
18 16 not 17 (389)

Database: G-I-N
Search date:26/4/2019
Search strategy:

1 limit to language: English, Publication type: Guidelines, Publication Status: Published, "cancer screening," n= 5
2 limit to language: English, Publication type: Guidelines, Publication Status: Published, (MeSH terms), n= 185
Ovarian Neoplasms (C13.371.270.750)
Neoplasms by Histologic Type (C04.557)
Head and Neck Neoplasms (C04.588.443)
Respiratory Tract Neoplasms (C04.588.894.797)
Gastrointestinal Neoplasms (C04.588.274.476)
Hematologic Neoplasms (C04.588.448)
Ovarian Neoplasms (C04.588.322.455)
Uterine Neoplasms (C04.588.945.418.948)
Skin Neoplasms (C04.588.805)
Breast Neoplasms (C04.588.180)
Urogenital Neoplasms (C04.588.945)
Liver Neoplasms (C04.588.274.623)
Lung Neoplasms (C04.588.894.797.520)
Brain Neoplasms (C04.588.614.250.195)
Central Nervous System Neoplasms (C04.588.614.250)
Bronchial Neoplasms (C04.588.894.797.265)
Bone Neoplasms (C04.588.149)
Pancreatic Neoplasms (C04.588.322.421)
Neuro-oncology / Nervous System Neoplasms (C04.588.614)
Endocrine Gland Neoplasms (C04.588.322)
Thyroid Neoplasms (C04.588.322.894)
Stomach Neoplasms (C04.588.274.476.767)
Soft Tissue Neoplasms (C04.588.839)
Prostatic Neoplasms (C04.588.945.440.770)
Bladder Neoplasms (C04.588.945.947.125)
Biliary Tract Neoplasms (C04.588.274.120)
Kidney Neoplasms (C04.588.945.947.535)
Heart Neoplasms (C04.588.894.309)
Testicular Neoplasms (C04.588.322.762)
Peritoneal Neoplasms (C04.588.033.513)
Abdominal Neoplasms (C04.588.033)
Esophageal Neoplasms (C04.588.274.476.205)
Colorectal Neoplasms (C04.588.274.476.411.307)
Testicular Neoplasms (C04.588.945.440.915)
Cancer / Neoplasms (C04)

3 limit to language: English, Publication type: Guidelines, Publication Status: Published, (MeSH terms 2015), n= 70
Diagnostic Techniques and Procedures (E01.370)
Diagnosis (E01)

Early Diagnosis (E01.390)
Diagnostic Techniques and Procedures (E01.370)
Diagnosis (E01)
Early Detection of Cancer (E01.390.500)
4 1 OR 2 OR 3 (260)
Note: Guidelines at a "Pending" (draft) state on the website are not downloaded (n=36). The total number of guidelines downloaded which are at the "Active" state is 224.

Database: ECRI institute
Search data: 26/4/2019
Search strategy: "cancer screening" (Last five year) (n=128)

Appendix 2 Criteria for qualitative tradeoff between benefits and harms, and for comment on people's values and preferences regarding tradeoff between benefits and harms

Questions	Criteria or examples for judging "yes"
Qualitative tradeoff between benefits and harms	
Is there a qualitative statement of the tradeoff between benefits and harms	a. an explicit statement of the magnitude of net effect (Net benefit = benefit minus harms or burdens) e.g. *The USPSTF concludes with high certainty that the net benefit (i.e. the benefit minus the harms) of screening for colorectal cancer in adults aged 50 to 75 years is substantial.* b. an explicit statement of tradeoff between benefits and harms or burdens e.g. *The desired effect of FS clearly outweighs the undesired effects.*
People's values and preferences regarding tradeoff between benefits and harms	
Does the guideline explicitly comment on people's values and preferences regarding the trade-off between benefits and harms or burdens of cancer screening?	a. comment on values and preferences regarding trade-off between benefits and harms or burdens e.g. *A recent study reported that veterans were less concerned about health risks from lung cancer screening and more concerned about personal risk for cancer.* b. comments on experience in shared decision-making regarding the trade-off between benefits and harms or burdens
Where does the guideline get the information on values and preferences?	a. systematic review of studies of values and preferences conducted by team(s) other than the guideline developers b. systematic review of studies of values and preferences conducted by the guideline developers c. individual study of values and preferences identified by guideline developers d. interview or focus group with patients/general population conducted by guideline developers e. survey of guideline panel to determine their view of patient's/general population's values and preferences f. experience of people on the guideline panel in shared decision-making g. other h. not reported

Appendix 3 Characteristics of included guidelines

Guideline title	Publication year	Institution	Country, Region	Income of country	Clinical area	Type of guideline	Method used for rating the certainty of evidence	Specification of cancer mortality and/or incidence as the only key benefit(Yes/No)	Specification of key harms and burdens (Yes/No)	Values and preferences regarding trad-off between benefits and harms/burdens (Yes/No)
Screening for Oral Cancer: U.S. Preventive Services Task Force (USPSTF) Recommendation Statement	2014	USPSTF	United States (US), North America	High	Oral	*de novo* developed	USPSTF level of evidence	Yes	Yes	No
Screening for Lung Cancer: USPSTF Recommendation Statement	2014	USPSTF	US, North America	High	Lung	*de novo* developed	USPSTF level of evidence	Yes	Yes	No
Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer in Women: USPSTF	2014	USPSTF	US, North America	High	Breast	*de novo* developed	USPSTF level of evidence	No	Yes	No

Recommendation Statement										
Screening for Colorectal Cancer: Updated Evidence Report and Systematic Review for the USPSTF	2016	USPSTF	US, North America	High	Colorectal	*de novo* developed	USPSTF level of evidence	Yes	Yes	No
Screening for Breast Cancer: USPSTF Recommendation Statement	2016	USPSTF	US, North America	High	Breast	*de novo* developed	USPSTF level of evidence	No	Yes	No
Screening for Skin Cancer: USPSTF Recommendation Statement	2016	USPSTF	US, North America	High	Skin - melanoma	*de novo* developed	USPSTF level of evidence	Yes	Yes	No
Screening for Thyroid Cancer: USPSTF Recommendation Statement	2017	USPSTF	US, North America	High	Thyroid	*de novo* developed	USPSTF level of evidence	No	Yes	No
Screening for Cervical Cancer: USPSTF Recommendation Statement	2018	USPSTF	US, North America	High	Cervical	*de novo* developed	USPSTF level of evidence	Yes	Yes	No

Screening for Ovarian Cancer: USPSTF Recommendation Statement	2018	USPSTF	US, North America	High	Ovarian	*de novo* developed	USPSTF level of evidence	Yes	Yes	No
Screening for Prostate Cancer: USPSTF Recommendation Statement	2018	USPSTF	US, North America	High	Prostate	*de novo* developed	USPSTF level of evidence	No	Yes	No
American College of Radiology (ACR) Appropriateness Criteria Breast Cancer Screening	2017	ACR	US, North America	High	Breast	*de novo* developed	ACR criteria	No	No	No
ACR Appropriateness Criteria Ovarian Cancer Screening	2017	ACR	US, North America	High	Ovarian	*de novo* developed	ACR criteria	No	No	No
ACR Appropriateness Criteria Colorectal Cancer Screening	2018	ACR	US, North America	High	Colorectal	*de novo* developed	ACR criteria	No	No	No
ACR Appropriateness Criteria Lung Cancer Screening	2018	ACR	US, North America	High	Lung	*de novo* developed	ACR criteria	No	No	No
Breast Cancer Screening in Women at Higher-Than-Average Risk: Recommendations from the ACR	2018	ACR	US, North America	High	Breast	*de novo* developed	ACR criteria	No	No	No

American Cancer Society(ACS) Prostate Cancer Survivorship Care Guidelines	2014	ACS	US, North America	High	Prostate	*de novo* developed	ACS criteria	No	No	No
Breast Cancer Screening for Women at Average Risk								No	Yes	No
2015 Guideline Update from the ACS	2015	ACS	US, North America	High	Breast	*de novo* developed	GRADE	No	Yes	No
ACS Head and Neck Cancer Survivorship Care Guideline	2016	ACS	US, North America	High	Lung	*de novo* developed	The working group developed the level of evidence	Yes	Yes	Yes
Colorectal Cancer Screening for Average-Risk Adults: 2018 Guideline Update from the ACS	2018	ACS	US, North America	High	Colorectal	*de novo* developed	GRADE	Yes	No	No
Prostate Cancer Early Detection	2018	National Comprehensive Cancer Network (NCCN)	US, North America	High	Prostate	*de novo* developed	NCCN Categories of Evidence and Consensus			

Colorectal Cancer Screening	2019	NCCN	US, North America	High	Colorectal	*de novo* developed	NCCN Categories of Evidence and Consensus	No	No	No
NCCN Guidelines Version 1.2020 Lung Cancer Screening	2019	NCCN	US, North America	High	Lung	*de novo* developed	NCCN Categories of Evidence and Consensus	No	Yes	Yes
Screening Pelvic Examination in Adult Women: A Clinical Practice Guideline from the American College of Physicians (ACP)	2014	ACP	US, North America	High	Ovarian	*de novo* developed	Modified GRADE	Yes	Yes	No
Cervical Cancer Screening in Average-Risk Women: Best Practice Advice from the Clinical Guidelines Committee of the ACP	2015	ACP	US, North America	High	Cervical	*de novo* developed	No rating	Yes	Yes	No
Screening for Breast Cancer in Average-Risk Women: A Guidance Statement from the ACP	2019	ACP	US, North America	High	Breast	consolidated guideline	No rating	No	Yes	No

Prostate Cancer Survivorship Care Guideline: American Society of Clinical Oncology (ASCO) Clinical Practice Guideline Endorsement	2015	ASCO	US, North America	High	Bladder	adapted guideline	Not reported	No	No	No
Evaluating Susceptibility to Pancreatic Cancer: ASCO Provisional Clinical Opinion	2019	ASCO	US, North America	High	Pancreatic	*de novo* developed	ASCO system for rating strength of recommendations, and strength of evidence	No	No	No
Early Detection for Colorectal Cancer: ASCO Resource-Stratified Guideline	2019	ASCO	US, North America	High	Colorectal	adapted guideline	ASCO system for rating strength of recommendations and strength of evidence	Yes	No	No
Practice Bulletin No. 168: Cervical Cancer Screening and Prevention	2016	American College of Obstetrici	US, North America	High	Cervical	*de novo* developed	USPSTF level of evidence	Yes	Yes	No

		ans and Gynecologists (ACOG)								
Practice Bulletin Number 179: Breast Cancer Risk Assessment and Screening in Average-Risk Women	2017	ACOG	US, North America	High	Breast	consolidated guideline	USPSTF level of evidence	No	Yes	No
Use of Primary High-Risk Human Papillomavirus Testing for Cervical Cancer Screening: Interim Clinical Guidance	2015	Society of Gynecologic Oncology, American Society for Colposcopy and Cervical Pathology	US, North America	High	Cervical	*de novo* developed	No rating	No	No	No
The Memorial Sloan Kettering Cancer Center (MSKCC) Recommendations for Prostate Cancer Screening	2016	MSKCC	US, North America	High	Prostate	*de novo* developed	No rating	Yes	Yes	No

		Cystic Fibrosis Colorectal Cancer Screening Task Force	US, North America	High	Colorectal	*de novo* developed	No rating	No	No	No
Cystic Fibrosis Colorectal Cancer Screening Consensus Recommendations	2018	Centre for Research Excellence in Polycystic Ovary Syndrome, European Society of Human Reproduction and Embryology, American Society for Reproductive Medicine,	US, North America	High	Colorectal	*de novo* developed	No rating	No	No	No
International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome	2018		US, North America	High	Endometrial	*de novo* developed	GRADE			

		Monash University								
Early Detection of Prostate Cancer: American Urological Association (AUA) Guideline	2018	AUA	US, North America	High	Prostate	*de novo* developed	Modified GRADE	Yes	Yes	Yes
The American Society of Colon and Rectal Surgeons (ASCRS) Clinical Practice Guidelines for Anal Squamous Cell Cancers	2018	ASCRS	US, North America	High	Anal	*de novo* developed	GRADE	No	No	No
Screening for Lung Cancer: American College of Chest Physicians (CHEST) Guideline and Expert Panel Report	2018	CHEST	US, North America	High	Lung	*de novo* developed	GRADE	Yes	Yes	No
Recommendations on Screening for Prostate Cancer with the PSA Test	2014	Canadian Task Force on Preventive Health Care (CTFPHC)	Canada, North America	High	Prostate	*de novo* developed	GRADE	No	Yes	Yes

Recommendations on Screening for Colorectal Cancer in Primary Care	2016	CTFPHC	Canada, North America	High	Colorectal	*de novo* developed	GRADE	No	Yes	Yes
Canadian Association of Radiologists (CAR): Guide on Computed Tomography Screening for Lung Cancer	2017	CAR	Canada, North America	High	Lung	*de novo* developed	No rating	No	No	No
Clinical Practice Guideline on Screening for Colorectal Cancer in Individuals With a Family History of Nonhereditary Colorectal Cancer or Adenoma: The Canadian Association of Gastroenterology Banff Consensus (CAGBC)	2018	CAGBC	Canada, North America	High	Colorectal	*de novo* developed	GRADE	No	Yes	Yes

							Final recommendations, the strength of each recommendation, and the quality of the evidence informing each recommendation, were arrived at by consensus of the panel members.	No	No	Yes
Balancing the Benefits and Harms of Thyroid Cancer Surveillance in Survivors of Childhood, Adolescent and Young Adult Cancer: Recommendations from the International Late Effects of Childhood Cancer Guideline Harmonization Group (IGHG) in Collaboration with the PanCareSurFup Consortium	2018	IGHG	Netherlands, North America	High	Thyroid	*de novo* developed				
Oncogenetic Testing for Lynch Syndrome and Familial Adenomatous Polyposis	2014	Belgian Health Care Knowledge Centre (KCE)	Belgium, Europe and Central Asia	High	Colorectal	*de novo* developed	No rating	No	No	No

Oncogenetic Testing and Follow-up for Women with Familial Breast/Ovarian Cancer, Li-Fraumeni Syndrome and Cowden Syndrome	2015	KCE, the College of Human Genetics and the College of Oncology	Belgium, Europe and Central Asia	High	Breast	*de novo* developed	No rating	No	No	No
Oncogenetic Testing, Diagnosis and Follow-up in Birt-Hogg-Dubé Syndrome, Familial Atypical Multiple Mole Melanoma Syndrome and Neurofibromatosis 1 and 2	2015	KCE	Belgium, Europe and Central Asia	High	Kidney	*de novo* developed	No rating	No	No	No
Association of Coloproctology of Great Britain & Ireland (ACPGBI): Guidelines for the Management of Cancer of the Colon, Rectum and Anus (2017) – Diagnosis, Investigations and Screening	2017	ACPGBI	Britain and Ireland, Europe and Central Asia	High	Colorectal	*de novo* developed	Oxford Centre for Evidence Based Medicine – levels of evidence			

Colonoscopy Surveillance for Dysplasia and Colorectal Cancer in Patients with Inflammatory Bowel Disease	2015	Society of Gastroenterology and Hepatology	Denmark, Europe and Central Asia	High	Colorectal	*de novo* developed	Oxford Centre for Evidence Based Medicine – levels of evidence	No	No	No
Clinical Indications for Computed Tomographic Colonography: European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastrointestinaland Abdominal Radiology (ESGAR) Guideline	2014	ESGE and ESGAR	Europe, Europe and Central Asia	High	Colorectal	*de novo* developed	GRADE	No	Yes	No
The European Menopause and Andropause Society (EMAS) Position Statement: Individualized Breast Cancer Screening versus Population-Based Mammography Screening Programms	2014	EMAS	Europe, Europe and Central Asia	High	Breast	*de novo* developed	No rating	No	No	No

The European Association of Urology (EAU) Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent—Update 2013	2019	EAU	Europe, Europe and Central Asia	High	Prostate	*de novo* developed	Modified GRADE	No	No	No
Prostate Cancer Screening with Prostate-Specific Antigen (PSA) Test: A Clinical Practice Guideline	2018	BMJ rapid recommendations	Finland, Europe and Central Asia	High	Prostate	*de novo* developed	GRADE	No	Yes	Yes
Prevention of Cervical Cancer	2019	German Society for Gynecology and Obstetrics and the German Knee Society	Germany, Europe and Central Asia	High	Cervical	*de novo* developed	GRADE	Yes	Yes	No
Digital Breast Tomosynthesis (DBT): Recommendations from the Italian College of	2017	ICBR, SIRM, GISMa	Italy, Europe and Central Asia	High	Breast	*de novo* developed	Oxford Centre for Evidence Based	No	No	No

Breast Radiologists (ICBR) by the Italian Society of Medical Radiology (SIRM) and the Italian Group for Mammography Screening (GISMa)							Medicine – levels of evidence			
Sociedad Española de Oncología Médica (SEOM) Guide to Primary and Secondary Prevention of Cancer: 2014	2014	SEOM	Spain, Europe and Central Asia	High	Breast	*de novo* developed	GRADE	Yes	No	No
World Health Organization (WHO) Position Paper on Mammography Screening	2014	WHO	Switzerland, Europe and Central Asia	High	Breast	*de novo* developed	GRADE	No	Yes	No
Prevention and Screening in BRCA Mutation Carriers and Other Breast/Ovarian Hereditary Cancer Syndromes: European Society for Medical Oncology (ESMO) Clinical Practice	2016	ESMO	Switzerland, Europe and Central Asia	High	Breast	*de novo* developed	Infectious Diseases Society of America–United States Public Health	No	No	No

Guidelines for Cancer Prevention and Screening										
British HIV Association (BHIV) Guidelines for HIV-Associated Malignancies 2014	2014	BHIV	United Kingdom, Europe and Central Asia	High	Kaposi sarcoma	*de novo* developed	Modified GRADE	No	No	No
China National Lung Cancer Screening Guideline with Low-Dose Computed Tomography (2015 version)	2015	National Health and Family Planning Commission	China, East Asia and Pacific	Upper-middle	Lung	*de novo* developed	No rating	No	No	No
An Updated Asia Pacific Consensus Recommendations on Colorectal Cancer Screening	2014	Asia Pacific Colorectal Cancer Working Group	China, East Asia and Pacific	Upper-middle	Colorectal	*de novo* developed	A modified Delphi process			

Recommendations on Prevention and Screening for Colorectal Cancer in Hong Kong	2018	Cancer Coordinating Committee	China (Hong Kong), East Asia and Pacific	High	Colorectal	*de novo* developed	No rating	No	No	No
The Japanese Breast Cancer Society (JBCS) Clinical Practice Guideline for Screening and Imaging Diagnosis of Breast Cancer	2014	JBCS	Japan, East Asia and Pacific	High	Breast	*de novo* developed	Not report	Yes	No	No
The Japanese Guidelines for Breast Cancer Screening	2016	National Cancer Center	Japan, East Asia and Pacific	High	Breast	*de novo* developed	Standardized method for the Japanese guidelines for cancer screening	Yes	Yes	No
The Korean Guideline for Cervical Cancer Screening	2015	Asian Society of Gynecologic Oncology, Korean Society of Gynecolog	Korea, East Asia and Pacific	High	Cervical	*de novo* developed	Modified GRADE	No	Yes	No

		ic Oncology								
Brazilian Society of Hepatology (BSH) Recommendations for the Diagnosis and Treatment of Hepatocellular Carcinoma	2015	BSH	Brazil, Latin America and the Caribbean	Upper-middle	Hepatocellular carcinoma	*de novo* developed	Modified GRADE	No	No	No
Breast Cancer Screening: Updated Recommendations of the Brazilian College of Radiology and Diagnostic Imaging (CBR), Brazilian Breast Disease Society (SBM), and Brazilian Federation of Gynecological and Obstetrical Associations (Febrasgo)	2017	CBR, SBM, and Febrasgo	Brazil, Latin America and the Caribbean	Upper-middle	Breast	*de novo* developed	Not reported	Yes	No	No

		Brazilian Association for the Lower Genital Tract Pathology and Colposcopy						No	No	No
Guidelines for HPV-DNA Testing for Cervical Cancer Screening in Brazil	2018		Brazil, Latin America and the Caribbean	Upper-middle	Cervical	*de novo* developed	USPSTF level of evidence			
National Guidelines for Colorectal Cancer Screening in Saudi Arabia with strength of Recommendations and Quality of Evidence	2015	Saudi Centre for Evidence-Based Healthcare (EBHC)	Saudi Arabia, Middle East and North Africa	High	Colorectal	*de novo* developed	GRADE	Yes	Yes	No
Clinical Practice Guidelines on the Screening and Treatment of Precancerous Lesions for Cervical Cancer Prevention in Saudi Arabia	2016	EBHC	Saudi Arabia, Middle East and North Africa	High	Cervical	*de novo* developed	GRADE	Yes	Yes	No

Appendix 4 Regression analyses of factors associated with conducting key steps of setting threshold for key beneficial outcomes

Guideline characteristics	Univariable analyses		Multivariable analyses	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Specification of key beneficial outcome				
North America vs. other regions	1.51 (0.52, 4.41)	0.45	-	-
GRADE or modified GRADE vs. no GRADE	1.45 (0.49, 4.27)	0.50	-	-
Specification of key harmful outcome				
North America vs. other regions	3.31 (1.17, 9.32)	0.024	6.82 (1.76, 26.37)	0.0055
GRADE or modified GRADE vs. no GRADE	4.03 (1.32, 12.27)	0.01	8.31 (2.00, 34.55)	0.0036
Specification of magnitude of net benefit or tradeoff between benefit and harm				
North America vs. other regions	8.43 (2.19, 32.43)	0.0019	-	-
GRADE or modified GRADE vs. no GRADE	0.81 (0.27, 2.38)	0.70	-	-