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Review Article

A synthesis of evidence for cancer-specific screening interventions: A *Preventive Medicine* Golden Jubilee Review

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ABSTRACT

The goal of cancer screening guidelines is to inform health practitioners to practice evidence-based cancer prevention. Cancer screening aims to detect treatable precancerous lesions or early-stage disease to enable actions aimed at decreasing morbidity and mortality. Continuous assessment of the available evidence for or against screening interventions by various organizations often results in conflicting recommendations and create challenges for providers and policymakers. Here we have summarized the current cancer screening recommendations by five leading organizations in North America and Europe: the National Cancer Institute's Physician Data Query (PDQ), the U.S. Preventive Services Task Force (USPSTF), the Canadian Task Force on Preventive Health Care (CTFPHC), the Cochrane Database of Systematic Reviews (CDSR), and the UK National Screening Committee for the National Health Service (UK NSC). All organizations assess evidence based on strength, quality, and quantity, and recommendations are similar although with differences with respect to screening start and stop ages. Recommendations are consistent for colorectal cancer screening with fecal occult blood test or fecal immunochemical test, cervical cancer screening with Pap-test, HPV-test, or co-testing, and breast cancer screening with mammography. However, guidelines vary with respect to age to start and end screening and testing frequency. Tests that have proven to be inefficient or whose use is capable of causing harm are routinely recommended against. Continuous review of screening guidelines is necessary to evaluate the many promising screening tests currently under investigation.

1. Introduction

Cancer is one of the leading causes of death worldwide. In 2020, 19.3 million new cases and 10.0 million cancer-related deaths were recorded (Sung et al., 2021). The global cancer burden is predicted to grow with the ageing of most populations due to decreasing fertility rates and longer life expectancy. Advances in systemic, radiation, and surgical treatments have brought substantial gains in long-term survival or even cure for many cancers. Moreover, in the last few decades, screening and early detection have proven to be effective prevention strategies for cancers, such as those of the cervix, colon, breast, and lung; however, screening remains unproven or controversial for most cancers (ACS Breast Cancer Screening Guidelines [WWW Document], 2022; Basu et al., 2018; Edwards et al., 2010; Ladabaum et al., 2020; Presant et al., 2020; World Health Organization, 2013).

The goal of cancer screening is to reduce mortality through detection of pre-invasive or early-stage disease for which treatment is more likely to be successful. Although meritorious in principle, screening for early cancer or cancer precursors often entails harmful invasive diagnostic and treatment procedures. In addition to test-related complications, false-positive test results lead to anxiety and unnecessary treatment. Likewise, overdiagnosis of cancers that would not have caused

Abbreviations: National Cancer Institute's Physician Data Query, PDQ; U.S. Preventive Services Task Force, USPSTF; Canadian Task Force on Preventive Health Care, CTFPHC; Cochrane Database of Systematic Reviews, CDSR; UK National Screening Committee, UK NSC; For the National Health Service, NHS; Human papillomavirus, HPV; Computed tomography, CT.

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symptoms or early mortality is of concern. Understanding the scientific evidence for the balance of benefits and harms is a key objective of the organizations and consortia tasked with producing clinical and public health guidelines for optimal preventive healthcare and implementation of organized screening programs. Such guideline recommendations result from coordinated cooperation among multidisciplinary teams of clinician scientists, epidemiologists, health economists, and public health policymakers that review published clinical and epidemiological evidence. As part of the review process, empirical evidence is assessed in terms of strength, quality, and consistency as well as in relation to potential and real harms.

Numerous organizations periodically or continuously assess the state of the science of screening interventions with ever more complex criteria to examine the totality of available evidence for benefits, harms, and costs. Organizations vary with respect to methodology used and each must consider local practice patterns. Complex evaluation processes and conflicting recommendations often prove challenging for healthcare professionals and public health policymakers.

This review is an expanded update to our previous publication from 2002 concerning cancer screening and prevention guidelines (Franco et al., 2002). The goal of this narrative review is to provide a synthesis of the current cancer screening recommendations from some of the most

Table 1
Organizations included for synthesis of evidence for cancer-specific screening interventions.*

Organization	What it does for cancer screening related recommendations	Responsible for cancer information/ recommendations	Meetings/updates	Evidence evaluating process	Ranking system
National Cancer Institute's Physician Data Query (PDQ)	Publishes information summaries on a range of cancer topics	The PDQ Screening and prevention editorial Board, which consists of professionals with expertise in cancer and cancer-related topics.	Meetings six times a year to update summaries.	1) study design, quality of study execution and consistency, magnitude of benefits and harms, external validity 2) level of certainty (solid, fair, inadequate)	1) RCTs 2) non-RCTs 3) cohorts, case-controls 4) ecologic and descriptive studies, 5) opinions of respected authorities based on clinical experience, descriptive studies, reports of expert committees
U.S. preventive services task force (USPSTF)	Makes evidence-based recommendations about screening, counselling, and preventive medications that improve the health of population.	Independent volunteer panel composed of national experts in prevention and evidence-based medicine including clinicians from various fields, nurses, and health behaviour specialists.	Three times per year to review and analyse various topics and assign a grade based on the strength of evidence and the benefit/harm ratio	1) A five-level grading system for the strength of recommendations and suggestions to practise 2) level of certainty (high, moderate, low)	A) Recommended, high certainty of substantial net benefit B) Recommended, high certainty of moderate to substantial benefit C) Selectively recommended, at least moderate certainty of small benefit D) Recommended against, moderate to high certainty of no benefit or harms overweighing benefits I) Current evidence insufficient to make recommendation
Canadian task force on preventive health care (CTFPHC)	Develops evidence-based clinical practice guidelines for primary care clinicians.	Independent panel of experts.	Three times per year.	Protocols are published before conducting a review to ensure transparency, repeatability, and competence. Recommendations are formulated using six criteria: The magnitude of the problem, benefits/harms, resource use required, equity, acceptability, feasibility.	Grading of recommendations assessment, development and evaluation (GRADE) system: High, moderate, low, very low And strength of the recommendation "strong", "conditional".
Cochrane database of systematic reviews (CDSR)	Publishes high-standard systematic reviews concerning evidence-based healthcare.	A network of researchers, professionals, patients, and people interested in health, there is groups that prepare reviews.	Reviews are updated regularly to account for new evidence and within two years of initial publication.	They are using meta-analysis for increasing statistical power and providing greater precision. Protocols for publications are published before conducting reviews to minimize bias.	GRADE-system; high, moderate, low, very low
UK National Screening Committee (UK NSC) for the National Health Service (NHS)	Evaluates screening programs and advises ministers of the four UK countries and the NHS on program implementation and recommendations on changes to already implemented programs.		All policies are reviewed and updated every three years, or earlier if significant new information is published.	They are using a set of internationally recognized criteria for evidence of screening recommendations including the appraisal of the viability, effectiveness, and appropriateness of their programs. Evidence from high quality RCTs.	

* References to the organizations: " (About Us – Canadian Task Force on Preventive Health Care [WWW Document], 2019); " (Grade Definitions | United States Preventive Services Taskforce, 2018) (PDQ Screening and Prevention Editorial Board, 2003); " (About Us – Canadian Task Force on Preventive Health Care [WWW Document], 2019); " (About Us – Canadian Task Force on Preventive Health Care [WWW Document], 2019), " (About the Cochrane Database of Systematic Reviews | Cochrane Library [WWW Document], 2022) (Guyatt et al., 2008).; " (About us - UK National Screening Committee - GOV.UK [WWW Document], 2022); " (UK NSC meetings and minutes - GOV.UK [WWW Document], 2021); " (Criteria for a population screening programme - GOV.UK, 2022).

influential groups in North America and Europe and to compare and contrast those recommendations.

2. Methods

We chose five leading organizations that provide information on cancer screening or issue screening recommendations in North America and Europe published in English: the National Cancer Institute's Physician Data Query (PDQ), the U.S. Preventive Services Task Force (USPSTF), the Canadian Task Force on Preventive Health Care (CTFPHC), the Cochrane Database of Systematic Reviews (CDSR), and the UK National Screening Committee for the National Health Service (UK NSC). In addition to the organizations from our previous review published 20 years ago, we have also included the UK NSC (Franco et al., 2002). These organizations all grade the strength and level of evidence based on the quality and quantity of studies. Table 1 describes all

Table 2
Guideline recommendations on screening for colorectal cancer.

Screening test	Name of the organization	Population under consideration	Recommendation	Level of evidence*	Date updated
Fecal occult blood test (guaiac-based)	PDQ	General population	Yes	1	June 2021
	USPSTF	By age			May 2021
		45–49	Yes	B	
		50–75	Yes	A	
		76–85	Yes selectively	C	
		≥ 86	No	I	
	CTFPHC	By age			March
		60–74	Yes, strong	Moderate	2016
		50–59	Yes, weak	Moderate	
		≥75	No, weak	Low	
	CDSR	Asymptomatic individuals	Yes	High	October 2013
Fecal occult blood test (fecal immunochemical based: FIT)	PDQ	General population	Yes[1]	1**	June 2021
	USPSTF	By age			May 2021
		45–49	Yes	B	
		50–75	Yes	A	
		76–85	Yes selectively	C	
		≥ 86	No	I	
	CTFPHC	By age			March
		60–74	Yes, strong	Moderate	2016
		50–59	Yes, weak	Moderate	
		≥ 75	No, weak	Low	
	CDSR	General population	Yes	Moderate***	January 2007
	UK NSC/NHS	50–74	Yes	High	August 2018
Sigmoidoscopy/ flexible sigmoidoscopy/ flexible sigmoidoscopy with FIT	PDQ	General population	Yes	1	June 2021
	USPSTF	By age			May 2021
		45–49	Yes	B	
		50–75	Yes	A	
		76–85	Yes selectively	C	
		≥ 86	No	I	
	CTFPHC	By age			March
		60–74	Yes, strong	Moderate	2016
		50–59	Yes, weak	Moderate	
		≥ 75	No, weak	Low	
	CDSR	Asymptomatic individuals	Yes	High	October 2013
Digital rectal exam	PDQ	General population	No[1]	3	June 2021
Colonoscopy	PDQ	General population	Yes[1]: ~60–70% for left colon Uncertain for right colon	3,1**	June 2021
	USPSTF	By age			May 2021
		45–49	Yes	B	
		50–75	Yes	A	
		76–85	Yes selectively	C	
		≥ 86	No	I	
	CTFPHC	All adults	No, weak	Low	March 2016
Chromoscopy	CDSR	People undergoing colonoscopy for polyp detection	Yes	Low	April 2016
Computed tomographic Colonography	USPSTF	By age			May 2021
		45–49	Yes	B	
		50–75	Yes	A	
		76–85	Yes selectively	C	
		≥ 86	No	I	

PDQ = Physician Data Query; USPSTF = US Preventive Services Task Force; CTFPCH = Canadian Task Force on Preventive Health Care; CDSR = The Cochrane Database Of Systematic Reviews; UK NSC/NHS = UK National Screening Committee for the National Health Service.

* Supplementary tables 1–4 describes the level of evidence by different organizations.

** In progress.

*** Data from RCTs.

[1] The internal validity of the studies is "fair".

included organizations and the methods they use to evaluate the efficacy, benefits, and harms of different cancer screening interventions. The Supplementary Tables provide detailed information about grading and levels of evidence and uncertainty used by PDQ (Supplementary Table 1), USPSTF (Supplementary Tables 2a and 2b), CTFPHC (Supplementary Tables 3a and 3b), and CDSR (Supplementary Table 4). It should be noted that some of the discrepancies between different organizations' recommendations may be explained, in part, by differences in their grading systems.

3. Results

Screening guidelines from the five organizations are provided in the tables by cancer site: colorectal cancer (Table 2), prostate cancer (Table 3), breast cancer (Table 4), lung cancer (Table 5), cervical cancer (Table 6), gynaecological and urothelial cancers combined (Ovarian, Endometrial, Testicular, Bladder; Table 7), cancers of the head and neck (Oral, Nasopharyngeal, Oesophageal, Thyroidal; Table 8), and the remaining sites of neuroblastoma, cancers of stomach, liver, pancreas, and skin (Table 9). Each table includes information on the utility of specific screening strategies, their target populations, the recommendation with level of evidence, and date of last update.

The recommendations are current as of April 2022 (USPSTF, CTFPHC, UK NSC). PDQ and most Cochrane reviews do not provide definitive recommendations on screening. PDQ provides information updated as of July 2021 with a statement of "solid" or "fair" if there was statistically significant evidence for beneficial impacts on cancer screening (marked as "Yes" in the tables). Strategies for which harms outweigh benefits are marked as "No" if there was lack of statistically significant evidence. Cases with "fair" internal validity are marked with a specific footnote. The external validity in these cases was mainly "solid" or "fair" and is not shown in the tables.

3.1. Consistency in guideline recommendations

All organizations issued strong recommendations for colorectal cancer screening using fecal occult blood test (Table 2) and for cervical cancer using Pap cytology, human papillomavirus (HPV) testing, or co-testing (HPV and Pap cytology together) (Table 4). Although breast cancer screening with mammography was recommended by most, Cochrane considered the data insufficient with the conclusion that although screening with mammography decreases mortality by 15%, overdiagnosis and overtreatment are of significant concern. Therefore, the recommendation is to provide a leaflet with evidence-based information to help individuals decide whether to undergo screening (Table 3). Furthermore, Cochrane considers the caveat that advances in treatment and greater cancer awareness have impacted the effect of screening (Gøtzsche & Jørgensen, 2013). There was some variation between organizations with respect to the recommended age at which to start or stop screening (Table 2). For use of fecal occult blood test for colorectal cancer screening, the recommended age to start and stop screening varied from 45 to 60 years and from 75 to 85 years, respectively, depending on the organization.

None of the organizations recommend chest X-ray, sputum cytology, or biomarker detection as screening methods for lung cancer (Table 5). Likewise, none of the organizations recommend screening for gynaecological and urothelial cancers (ovarian, endometrial, testicular, bladder) (Table 7) or neuroblastoma, and cancers of stomach, liver, pancreas, and skin, irrespective of tests (Table 9).

3.2. Variation in guideline recommendations

There was variation in guideline recommendations, specifically for some screening tests. For colorectal cancer (Table 2), only PDQ noted that digital rectal exam has no effect on colorectal cancer incidence or mortality (PDQ Screening and Prevention Editorial Board, 2022a), while other organizations did not consider this method as a screening strategy. CDSR was the only group that recommended chromoscopy for patients undergoing colonoscopy for polyp detection. Conversely, the USPSTF stated no preference for any specific test and, in contrast to others, was the only organization that recommended computed tomographic colonography as a screening method (Davidson et al., 2021). For breast cancer, a wide variety of methods and tests, such as clinical breast examination, breast self-examination, digital breast tomosynthesis, breast ultrasonography or magnetic resonance imaging, were evaluated but not recommended for screening (Table 4).

For lung cancer screening, recommendations and screening tests varied between the organizations (Table 5). Only low-dose computed tomography (CT) was recommended for high-risk populations by PDQ, USPSTF, CTFPHC and CDSR. Specifically, PDQ, USPSTF, and CTFPHC recommend screening for individuals who have a 20–30 pack-year smoking history or those who currently smoke or have quit within the past 15 years starting at age 50–55 years and stopping at age 74–80 years, whereas CDSR acknowledges that screening high-risk individuals is associated with reduction in lung cancer mortality, but that more information about cost effectiveness and harms is needed (Manser et al., 2013). UK NSC does not recommend screening for lung cancer due to lack of evidence of effective screening programs, lack of clinical trials for lung cancer screening, and lack of suitable screening tests. However, the UK NSC started review of the recommendations in February 2020 with a focus on recently published literature from the NELSON trial (Lung cancer - UK National Screening Committee (UK NSC) - GOV.UK [WWW Document], 2022)).

None of the organizations recommend screening for prostate cancer

Table 3
Guideline recommendations on screening for prostate cancer.

Screening test	Name of the organization	Age of men under consideration	Recommendation	Level of evidence*	Date updated
Prostate specific antigen (PSA)	PDQ	Any age	No[1]	3, 4, 5	March 2021
	USPSTF	55–69	Yes selectively	C	May 2018
		≥ 70	No	D	
	CTFPHC	< 55	No, strong	Low	November 2014
		55–69	No, weak	Moderate	
		≥ 70	No, strong	Low	
	CDSR	45–80	No	Moderate***	January 2013
	UK NSC/NHS	Any age	No	Moderate**	November 2020
Digital rectal exam	PDQ	Any age	Insufficient	3, 4, 5	March 2021

NA = Not Available; PDQ = Physician Data Query; USPSTF = US Preventive Services Task Force; CTFPCH = Canadian Task Force on Preventive Health Care; CDSR = The Cochrane Database of Systematic Reviews; UK NSC/NHS = UK National Screening Committee for the National Health Service.

* Supplementary Tables 1–4 describes the level of evidence by different organizations.

** Data from systematic reviews, RCTs, observational studies.

*** Data from RCTs.

[1] The internal validity of the studies is "fair".

Table 4
Guideline recommendations on screening for breast cancer.

Screening test	Name of the organization	Age of women under consideration	Recommendation	Level of evidence*	Date updated
Mammography	PDQ	40–49	No	1, 3	June 2021
		50–69	Yes	1,3	
	USPSTF	40–49	Yes selectively	C	January 2016
		50–74	Yes	B	**
		≥ 75	No	I	
	CTFPHC	40–49	No, conditional	Low	December 2018
		50–69	Yes, conditional	Very low	
		70–74	Yes, conditional	Very low	
	CDSR	Any age	Insufficient	Moderate****	June 2013
	UK NSC/NHS	50–70	Yes	High	December 2019
Clinical breast examination	PDQ	Any age	No	1**, 3	June 2021
	CTFPHC	Any age	No, conditional	No evidence	December 2018
	CDSR	Any age	No	Low***	April 2003
Breast self-examination	PDQ	Any age	No[1]	1	June 2021
	CTFPHC	Any age	No, conditional	Low	December 2018
	CDSR	Any age	No	Low***	April 2003
Digital breast tomosynthesis (DBT)	USPSTF	Any age	No	I	January 2016 **
	CTFPHC	Women not at increased risk	No, strong	No evidence	December 2018
Breast ultrasonography, magnetic resonance imaging (MRI)	USPSTF	Women with dense breasts	No	I	January 2016 **
	CTFPHC	Women not at increased risk	No, strong	No evidence	December 2018

NA = Not Available; PDQ = Physician Data Query; USPSTF = US Preventive Services Task Force; CTFPCH = Canadian Task Force on Preventive Health Care; CDSR = The Cochrane Database of Systematic Reviews; UK NSC/NHS = UK National Screening Committee for the National Health Service.
* Supplementary tables 1–4 describes the level of evidence by different organizations.
** In progress.
*** Data from two large population-based trials.
**** Data from RCTs and observational studies.

Table 5
Guideline recommendations on screening for lung cancer.

Screening test	Name of the organization	Population under consideration	Recommendation	Level of evidence*	Date updated
Low-dose computed tomography	PDQ	People aged 55–74 years with 30+ pack-year smoking history and currently smoke or have quit within the past 15 years	Yes	1	March 2021
	USPSTF	People aged 50–80 years with 20 pack-year smoking history and currently smoke or have quit within the past 15 years	Yes	B	March 2021
	CTFPHC	People aged 55–74 years with 30 pack-year smoking history and currently smoke or have quit within the past 15 years	Yes, weak	Low	April 2016
		All other adults	No, strong	Very low	
	CDSR	General population	No	Moderate***	June 2013
		High-risk smokers	Yes	Moderate***	
	UK NSC/NHS	General population	No	Very low****	December 2007
Chest X-ray	PDQ	General population	No	1	March 2021
	USPSTF	Asymptomatic adults	No	I	
	CTFPHC	All adults	No, strong	Low	April 2016
	CDSR	General population	No	Moderate***	June 2016
Sputum cytology	PDQ	General population	No	1	March 2021
	USPSTF	Asymptomatic adults	No	I	
	CTFPHC	All adults	No, strong	Low	April 2016
	CDSR	General population	No	Moderate***	June 2013
Measurement of biomarker levels	USPSTF	Asymptomatic adults	No	I	March 2021

Recommendation evidence of benefit in PDQ.
NA = Not Available; PDQ = Physician data query; USPSTF = US Preventive Services Task Force; CTFPCH = Canadian Task Force on Preventive Health Care; CDSR = The Cochrane Database of Systematic Reviews; UK NSC/NHS = UK National Screening Committee for the National Health Service.
* Supplementary tables 1–4 describes the level of evidence by different organizations; **in progress.
*** Data from RCTs (and CCTs), further data is needed.
**** Data is insufficient, two RTCs and 10 studies without comparative groups.

with prostate specific antigen (PSA) or with digital rectal exam. However, USPSTF does recommend selectively screening for prostate cancer with PSA at age 55–69 years on a case-by-case basis (Grossman et al., 2018). For oral cancer screening, CDSR concluded that visual examination reduces the mortality rate of oral cancer in high-risk individuals; however, the evidence is limited to only one study (Brocklehurst et al., 2013). The other organizations do not recommend oral cancer screening.

4. Discussion

This review summarizes the current evidence-based recommendations and policies on cancer screening among the leading organizations in North America and Europe. The three cancers for which all

Table 6
Guideline recommendations on screening for cervical cancer.

Screening test	Name of the organization	Age of women under consideration	Recommendation	Level of evidence*	Date updated
Pap cytology	PDQ	21–65	Yes	3	March 2021
		>65, with history of recent negative tests	No	3	
	USPSTF	21–65	Yes	A	August
		<21 and > 65, with adequate prior screening or who have had a hysterectomy	No	D	2018*****
	CTFPHC	< 20	No, strong	High	January 2013
		20–24	No, weak	Moderate	
		25–29	Yes, weak	Moderate	
		30–69	Yes, strong	High	
		≥ 70, with adequate screening history with 3 successive negative pap test results in the last 10 years	No, weak	Low	
	CDSR	Adult asymptomatic	Yes	Moderate to high	August 2017
	UK NSC/NHS	≥ 25	Yes	High	April 2019
HPV DNA or RNA test	PDQ	≥ 25	Yes	1	March 2021
	USPSTF	30–65	Yes	A	August 2018**
		<30 and > 65, with adequate prior screening or who have had a hysterectomy	No	D	
	CDSR	Adult asymptomatic	Yes	Moderate to high	August 2017
	UK NSC/NHS	≥ 25	Yes**	High	April 2019
Pap test and HPV DNA test (co-testing)	PDQ	≥ 30	Yes	1	March 2021
	USPSTF	30–65	Yes	A	August 2018**
		<30 and > 65, with adequate prior screening history or who have had a hysterectomy	No	D	

NA = Not Available; PDQ = Physician Data Query; USPSTF = US Preventive Services Task Force; CTFPCH = Canadian Task Force on Preventive Health Care; CDSR = The Cochrane Database of Systematic Reviews; UK NSC/NHS = UK National Screening Committee for the National Health Service.
* Supplementary tables 1–4 describes the level of evidence by different organizations.
** Since 2017 recommended to primary screening test instead of cytology.
*** In progress.

Table 7
Guideline recommendations on screening for gynaecological and urothelial cancers (ovarian, endometrial, testicular, bladder).

Cancer site	Screening test	Name of the organization	Population under consideration	Recommendation	Level of evidence*	Date updated
Ovarian cancer	Cancer antigen-125	PDQ	Women 55–74 years	No	1	June 2021
		USPSTF	Asymptomatic women	No	D	February 2018
		UK NSC/NHS	All women	No	**	July 2017
	Transvaginal ultrasound	PDQ	Women 55–74 years	No	1	June 2021
		USPSTF	Asymptomatic women	No	D	February 2018
		UK NSC/NHS	All women	No	**	July 2017
Endometrial cancer	Ultrasonography(e.g. endovaginal or transvaginal)	PDQ	All women	No	3	June 2021
	Endometrial sampling (biopsy)	PDQ	All women	No	3	June 2021
Testicular cancer	Physical examination	PDQ	All men	No	4, 5	March 2021
		USPSTF	Adolescent and adult men	No	D	April 2011
		CDSR	General population of men	No	No studies	September 2010
Bladder cancer	Cystoscopy	PDQ	General population	No	5	June 2021
	Urine cytology	PDQ	General population	No	5	June 2021
		USPSTF	Asymptomatic adults	No	I	August 2011
		UK NSC/NHS	General population	No	***	July 2020
	Hematuria (one time or repeated)	PDQ	General population	No	5	June 2021
		USPSTF	Asymptomatic adults	No	I	August 2011
		UK NSC/NHS	General population	No	***	July 2020
	Tests for urine biomarkers	USPSTF	Asymptomatic adults	No	I	August 2011
		UK NSC/NHS	General population	No	***	July 2020

PDQ = Physician Data Query; USPSTF = US Preventive Services Task Force; CTFPCH = Canadian Task Force on Preventive Health Care; CDSR = The Cochrane Database Of Systematic Reviews; UK NSC/NHS = UK National Screening Committee for the National Health Service.
* Supplementary tables 1–4 describes the level of evidence by different organizations.
** Evidence based on three systematic reviews.
*** Not enough evidence.

organizations recommend screening were also the top three most common cancers worldwide in 2020: breast 2.26 million, lung 2.2 million, and colorectal 1.93 million new cases were registered (Sung et al., 2021).

Generally, screening programs have shown to be effective for some cancers such as colorectal, breast, cervical, and lung (What Cancer Screening Tests Check for Cancer? - NCI [WWW Document], 2022) Screening programs, which rely not only on the screening modality, but also require specialized equipment and dedicated personnel, must be cost-effective to be implemented. Therefore, cancer screening tends to

Table 8
Guideline recommendations on screening for cancers of the head and neck (oral, nasopharyngeal, oesophageal, thyroidal).

Cancer site	Screening test	Name of the organization	Population under consideration	Recommendation	Level of evidence*	Date updated
Oral cancer	Visual examination	PDQ	General population	No	1, 5	June 2021
		USPSTF	Asymptomatic adults	No	I	November 2013
		CDSR	High risk individuals	Yes	Very low**	November 2013
		UK NSC/NHS	General population	No	Very low***	November 2020
	Toluidine blue	PDQ	General population	No	1, 5	June 2021
		CDSR	General population	No	No data	November 2013
	Brush biopsy/cytology	PDQ	General population	No	1, 5	June 2021
		CDSR	General population	No	No data	November 2013
	Fluorescence staining	PDQ	General population	No	1, 5	June 2021
		CDSR	General population	No	No data	November 2013
		UK NSC/NHS	General population	No	Very low***	November 2020
Nasopharyngeal cancer	Epstein-Barr virus serology, Nasopharyngoscopy	CDSR	Asymptomatic individuals	No	No data	November 2015
Oesophageal cancer	Endoscopy	PDQ	General population	No	3	March 2021
		CDSR	General population	No	No data	December 2012
	Cytology	PDQ	General population	No[1]	3	March 2021
		CDSR	General population	No	No data	December 2012
	Chromoendoscopy, laser-induced fluorescence spectroscopy	PDQ	General population	No	5	March 2021
Thyroidal cancer	Neck palpation	PDQ	General population	No	4	March 2021
		USPSTF	Asymptomatic adults	No	D	May 2017
	Ultrasound imaging	PDQ	General population	No	4	March 2021
		USPSTF	Asymptomatic adults	No	D	May 2017

PDQ = Physician Data Query; USPSTF = US Preventive Services Task Force; CTFPCH = Canadian Task Force on Preventive Health Care; CDSR = The Cochrane Database of Systematic Reviews.

* Supplementary tables 1–4 describes the level of evidence by different organizations.

** Data is limited to one study, further data is needed.

*** Not enough evidence.

[1] The interval validity of the studies is "fair".

be widely offered in high-income countries or settings where screening programs are feasible and affordable. Cancer rates are generally higher in high-income countries than in low- and middle-income countries. Cervical cancer is a notable exception; it was one of the most common cancers in women worldwide until successful screening programs were introduced, largely in high-income countries with available resources. Cervical cancer incidence and mortality are higher in low-income than high-income countries (Bray et al., 2018; Olson et al., 2016).

Screening tests for colorectal, breast and cervical cancers have been proven efficacious with high-quality evidence from RCTs, systematic reviews, meta-analyses, and observational studies while many tests for other cancers lack data on efficacy, balance of harms and benefits, or cost-effectiveness. New screening tests are constantly being developed and existing ones improved. However, for many potential tests the data on efficacy at the population level is lacking (World Health Organization: Regional Office for Europe, 2020). Due to scientific breakthroughs, cervical cancer screening has changed significantly in the past 20 years. The Pap test, the primary test used for cervical cancer screening starting in the 1960s led to a dramatic decrease in the incidence of cervical cancer. After the discovery that persistent HPV infection is necessary for development of cervical cancer (Walboomers et al., 1999), HPV DNA testing to detect the presence of HPV infection and cervical lesions was introduced alongside the Pap test and has improved cervical cancer screening due to its high reproducibility, high sensitivity, and lower cost when deployed at the population level (Bedell et al., 2020; Wentzensen & Clarke, 2021). However, health technology organizations have been slow to update their recommendations regarding adoption of HPV tests. For example, the UK NSC did not recommend a change in the primary screening test from Pap test to HPV test until 2017 (Cervical Cancer - UK National Screening Committee (UK NSC) - GOV.UK, 2019) Recently, more efficient screening tests for cervical cancer are being explored with the aim of predicting cervical cancer progression, for example DNA methylation, and are likely to replace the current tests in the future (Cuzick et al., 2012; Louvanto et al., 2015; Wajed et al., 2001).

Similar changes in recommendations have occurred with lung and prostate cancer screening. Lung cancer screening has mainly focused on individuals with substantial lifetime exposure to smoking. There is solid evidence that low-dose CT reduces mortality for lung cancer in high-risk populations, while chest X-ray shows no benefit. Bronchoscopy and molecular biomarkers seem promising tools, either independently or in addition to low-dose CT programs, but more evidence is needed (Sharma et al., 2015). For prostate cancer screening, PSA testing has shown the potential to decrease prostate cancer mortality but remains controversial due to insufficient evidence (Chou et al., 2011; Ilic et al., 2013). However, there is solid evidence of harms such as overdiagnosis, overtreatment, false-positive findings, and complications (Chou et al., 2011; Johansson et al., 2011; Loeb et al., 2013). Therefore, at this time, screening using PSA is not recommended, despite a 1994 U.S. Food and Drug Administration approval for PSA testing with digital rectal exam for screening asymptomatic men. Up to 2008, some doctors and organizations recommended yearly screening with PSA (Prostate-Specific Antigen (PSA) Test - NCI [WWW Document], 2022).

Stomach and liver cancers are also very common cancers in both sexes (Sung et al., 2021). For the latter, no successful screening test has been developed. Liver cancer screening targets mostly only individuals with elevated risk, and tumor markers to detect hepatocellular

Table 9
Guideline recommendations on screening for neuroblastoma and cancers of stomach, liver, pancreas and skin.

Cancer site	Screening test	Name of the organization	Population under consideration	Recommendation	Level of evidence*	Date updated
Neuroblastoma	Urine vanillylmandelic acic and homovanillic acid	PDQ	General population	No	2, 3, 4	June 2017
Stomach cancer	Barium-meal photofluorography	PDQ	General population	No[1]	3	March 2021
	Serum pepsinogen	PDQ	General population	No	3	March 2021
	Gastric endoscopy	PDQ	General population	No[1]	3	March 2021
Liver cancer / hepatocellular cancer	Alpha-fetoprotein	PDQ	People with elevated risk	No[1]	1	April 2021
	Ultrasound	PDQ	People with elevated risk	No[1]	1	April 2021
	Computed tomography	PDQ	People with elevated risk	No[1]	1	April 2021
Pancreatic cancer	Computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasonography (EOS)	USPSTF	Asymptomatic adults	No	D	August 2019
Skin cancers (nonmelanoma, melanoma)	Physical examination	PDQ	General population	No	4	March 2021
		USPSTF	Asymptomatic adults	No	I	July 2016 **
		CDSR	General population	No	Further data is needed***	June 2019

PDQ = Physician Data Query; USPSTF = US Preventive Services Task Force; CTFPCH = Canadian Task Force on Preventive Health Care; CDSR = The Cochrane Database of Systematic Reviews; UK NSC/NHS = UK National Screening Committee for the National Health Service.
* Supplementary tables 1–4 describes the level of evidence by different organizations.
** In progress.
*** Data based on two RCTs.
[1] The internal validity of the studies is "fair".

carcinoma, such as alfa-fetoprotein, and hepatic ultrasound, have shown promise, although with varying results (Aghoram et al., 2012; Zhang et al., 2004). For stomach cancer, a few tests have been investigated, which include barium-meal photofluorography, serum pepsinogen, and gastric endoscopy. According to a Japanese study, gastric endoscopy appears to perform better than photofluorography and could be effective in the future, while studies concerning the effect of serum pepsinogen test to be considered as a screening test are lacking (PDQ Screening and Prevention Editorial Board, 2022b; Tashiro et al., 2006).

For cancers among women, controversies remain. For example, breast examination is highly controversial as a method to screen for breast cancer and is not recommended by any organization; however, it is still taught and suggested as the only screening alternative for women in less developed countries. According to W.H·O it should not be recommended as a mass screening tool, but breast awareness should be encouraged for all women (Breast digital atlas - Breast self-Examination (BSE) [WWW Document], 2022). For ovarian cancer, screening with cancer antigen-125 (CA-125) test and transvaginal ultrasound are also not recommended by any organization, although many gynaecologists still perform regular transvaginal ultrasound for women during regular check-ups to detect possible abnormalities in the ovaries. Nevertheless, the CA-125 test can be helpful for diagnosing cancer if symptoms or findings are present or as a tool to define recurrence of ovarian cancer (What Cancer Screening Tests Check for Cancer? - NCI [WWW Document], 2022).

Non-melanoma skin cancer affects millions of people worldwide (Sung et al., 2021). As with the female cancers mentioned above, doctors often suggest that high-risk patients examine their skin regularly despite there being no recommended screening test. In addition, such self-examinations can lead to overtreatment despite many organizations promoting awareness of skin changes (What Cancer Screening Tests Check for Cancer? - NCI [WWW Document], 2022).

4.1. Practice recommendations

While specific practice recommendations regarding screening are reviewed and updated as new evidence becomes available, they vary widely among agencies and organizations. They also reflect society-specific risk perceptions. Although they reflect the state of scientific evidence at any given point in time, policy recommendations may not necessarily be implemented due to lack of buy-in from healthcare providers, opposition from the public, political parties, or professional groups. In previous studies, the percentage of clinicians that follow screening guidelines has been shown to vary. According to one study, 95% of physicians in the U.S. in 2006–2007 routinely recommended screening for colorectal cancer with colonoscopy to asymptomatic, average-risk patients, 80% recommended FOBT, and only a minority recommended other screening tests (Klabunde et al., 2009). However, another study that surveyed 1266 physicians in the U.S. in 2007 found that 19·1% of physicians made guideline-consistent recommendations across all colorectal cancer screening modalities recommended (Yabroff et al., 2011). For lung cancer, for which no screening for asymptomatic individuals is recommended, a national survey of data from 2006 to 2007 found that 55% of physicians had ordered chest X-ray, 22% low-dose spiral CT, and less than 5% sputum cytology for patients, while only 38% had ordered no lung cancer screening tests (Klabunde et al., 2012). A study that included a group of 1212 primary care physicians in the U.S. during 2006–2007 showed that surveyed physicians provided Pap tests to 91% of their eligible patients. The study also reported that primary care physicians' recommendations for Pap test screening are generally not consistent with screening guidelines (Yabroff et al., 2009). According to another study from 2004, the national screening rate for cervical cancer was 90% and for breast cancer it was 87% (Zapka et al., 2005). Although recommended screening appears to be high, there is evidence of over-screening. To ensure patient awareness of harms, guidelines suggest making decisions about participating in screening on an individual basis, especially when involving potential harms and limited benefits (Coulter & Collins, 2011).

4.2. Variation among guidelines

Healthcare providers rely on guidelines to effectively screen for cancer to save lives and be cost saving for healthcare systems by avoiding expensive cancer treatments. For a screening program to be successful, it must be relatively inexpensive, easy to administer, cause minimal discomfort, and be consistently reliable and valid. Evaluation of these criteria require many studies as more new and sophisticated tests and methods are developed for use in screening. There will be a great need to update cancer screening guidelines as new technologies appear or mature. Although new tests might be more sensitive for identifying lesions, their effectiveness must be evaluated before being included in guidelines. This review gathered the current summaries of evidence-based recommendations and policies on screening for specific types of cancer from some of the leading organizations in North America and Europe. While there are many similarities in the recommendations, noteworthy differences exist, which arguably may lead to confusion among healthcare providers, policymakers, and the public. Most discrepancies are due to differences among health technology assessment organizations on how they evaluate the evidence in terms of scientific stringency, the weight given to the potential for harms, and costs of the interventions. Another source of discrepancies is the frequency with which the organizations evaluate the peer-reviewed literature on any given screening test. Just a few years having elapsed after a completed assessment may be enough to cause recommendations to be outdated, since new evidence from RCTs or extended follow-up of screening technologies are constantly added to the medical literature.

Public health demonstration of the value of a new screening technology is a slow process. The earliest step is documenting its ability to presume the presence of disease, i.e., being positive in those who truly harbor cancer or precancerous lesions (sensitivity) while at the same time being negative among those without cancer (specificity). Demonstrating appropriate sensitivity and specificity in cross-sectional studies is thus a promising first step but much more is needed. Subsequent research may demonstrate that application of the candidate screening technique in the population leads to a shift to early-stage cancer, to an increase in survival rate, and to a decrease in the incidence of invasive cancers (for screening tests that are able to detect precancerous lesions, e.g., cervical and colorectal screening). Obviously, such research can only be done prospectively with results available only after many months, if not years, after the technique was first applied. A more stringent criterion regarding the effectiveness of screening interventions is the need to demonstrate that widescale use of the screening technology leads to a reduction of cancer-specific mortality. Obtaining such evidence takes several years, if not decades. Finally, there are those who advocate for an even more stringent level of evidence before claiming unequivocally the value of a cancer screening intervention, the demonstration of a reduction in all-cause mortality in the population (Black et al., 2002). When a health technology organization decides to assess the state of the science for a given screening technology the analysis can only reflect the current stage of clinical research trajectory for that technology. Therefore, for those technologies that are in the early stages of that research validation process, recommendations may be against their use, which should not be taken to indicate that the 'absence of evidence is evidence of absence' for the technology's public health value. When the more stringent criteria – and in consequence slowest to obtain – of screening effectiveness are fulfilled, future updates of the guidelines may become more favorable to the technique. An example of this evolution in levels of evidence was the trajectory of research on HPV testing in cervical cancer screening. Although the earliest criterion (improved sensitivity and adequate specificity in relation to Pap cytology) had been fulfilled in the 1990s (Franco, 2003), demonstrations of reductions of cervical cancer incidence and mortality (Sankaranarayanan et al., 2009), and all-cause mortality were completed decades later (Saquib et al., 2015). Consequently, guidelines moved from unfavorable recommendations in past assessments to today's favorable ones (Table 6).

A related aspect in the trajectory of a technology from initial demonstration of efficacy in detecting cancer to subsequent stages of proof in reducing mortality is with technical variants that improve on the same core technology, e.g., digital images over plain films in mammograms, liquid-based cytology over conventional Pap smears, and genotyping for HPV over simple detection of the virus. Should improvements on the same technology not require the same burden of proof as the original testing approach? Given the equivalency or improvement in disease detection relative to the basic test, accruing evidence is typically fast-tracked. Sometimes, the new variation in applying screening implies a minor loss in screening performance but with a major gain in convenience and ease of implementation. Such is the case for the advent of self-sampling for HPV testing. Although a woman's self-collected vaginal sample is inferior in quality to that of a physician-collected cervical sample, HPV testing is so sensitive that it compensates for the cellularity dilution in a self-sample (Franco, 2018). Research on the value and implementation of self-sampling for cervical cancer screening gained momentum during the COVID-19 pandemic because of the advantage of removing the need for the women to attend screening in person. The potential for increasing screening coverage is obvious. In Sweden this was demonstrated; population test coverage increased from 75 to 85% in only one year (HPV self-sampling in Sweden leading to faster elimination of cervical cancer [WWW Document], 2022).

4.2.1. Challenges in cancer screening

The value of cancer screening is not without challenges (Gøtzsche, 2015). For many cancers, screening has been traditionally viewed as a process that begins as an act of clinical presumption based on binary decision-making (negative = cancer unlikely vs. positive = cancer likely) and followed by management decisions (diagnostic work-up, treatment, and tailored follow-up). However, use of multiple approaches to screening for the same cancer, such as imaging, molecular testing in situ, exfoliative cytology, and biochemical tests for circulating tumor markers, provides the opportunity to transform this binary clinical presumption into a risk stratification algorithm, in which multiple test results are examined in combination to maximize their ability to identify existing disease or predict short-term risk. To improve prediction and assist healthcare providers in managing screen-positive individuals such algorithms can include elements of the clinical history or past test results (Perkins et al., 2020).

Cancer screening will also benefit from the advent of technologies categorized as liquid biopsies, such as blood tests for circulating cell-free tumor DNA, tumor-derived extra-cellular vesicles/exosomes (Yokoi & Ochiya, 2021). In addition to the opportunity these technologies offer for screening individual cancer types they can also be multiplexed to maximize the detection of multiple cancer types when deployed at the population level (Cohen et al., 2018).

Given the progress on cancer screening technologies and the need to accommodate the research trajectory of new screening interventions, whether for individual cancers or as complex risk-stratification algorithms, guideline development will become an increasingly complex process. Technology assessments will have to be more eclectic and agile to incorporate the totality of evidence concerning benefits and harms and the timeframe that is necessary to collect such information, in addition to actionable scientific information on cost-effectiveness as a function of the scale of screening implementation. The organizations charged with such evaluations, as the ones we covered in this review, are likely cognizant of the ever-increasing complexity and multidimensional nature of screening interventions and their contexts. Sadly, most promising new technologies and approaches are beyond the reach of low-income countries, which are increasingly bearing more of the global cancer burden. It would be useful if guideline development incorporated an analysis of affordability and resource-specific adaptations of cancer screening, as has been proposed by organizations, such as

the US National Comprehensive Cancer Network and the American Society for Clinical Oncology (Al-Sukhun et al., 2018; Koh et al., 2020). Use of resource-stratified cancer screening guidelines would be a positive step towards redressing the geographical disparities in cancer burden worldwide (Dvaladze et al., 2020; Jeronimo et al., 2016).

4.2.2. *Opportunities for low- and middle-income countries*

Implementing efficient screening programs in low- and middle-income countries (LMICs) is problematic due to absence of financial resources, coverage, and quality assurance (Sivaram et al., 2018). In consequence, many cancers are diagnosed at advanced stages in LMICs, and it has been estimated that in 2030 cancer will be the primary cause of death in the LMICs (Bray et al., 2012). For cervical cancer screening, visual inspection with acetic acid – a low-cost technique that can be implemented in the field and does not require a highly skilled workforce – has shown promise for screening or as an ancillary triage test (Sangwa-Lugoma et al., 2006; Sankaranarayanan, 2014; Santesso et al., 2016). In addition, self-sampling for HPV screening holds promises for implementation in LMICs as a cost-effective strategy because of the elimination in specialized personnel needed to collect samples (Fokom Defo & Fokom Domgue, 2020).

The burgeoning field of global oncology has brought new opportunities to improve cancer control in LMICs (Balogun et al., 2019). The establishment of equal partnerships between institutions in low-resource settings and those in high-resource ones brings capacity building, technological resources, and evidence-generating approaches to demonstrate the feasibility and value of screening in LMICs. However, screening implementation needs to be done in a holistic manner, considering local stakeholder preferences, local context and sensitivities, sustainability, and the entire continuum of cancer control and care that will be affected by the changes (Shah et al., 2019).

Ethical compliance

This manuscript is a narrative review that did not involve human subjects' research. It is exempt from ethical review.

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CRediT authorship contribution statement

Suvi Rintala: Validation, Formal analysis, Investigation, Writing – original draft, Visualization. **Kristina R. Dahlstrom:** Conceptualization, Methodology, Writing – review & editing, Visualization. **Eduardo L. Franco:** Conceptualization, Methodology, Writing – review & editing, Visualization, Supervision, Funding acquisition. **Karolina Louvanto:** Conceptualization, Methodology, Investigation, Writing – review & editing, Visualization, Supervision, Funding acquisition.

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Data availability

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Appendix A. Supplementary data

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References

About the Cochrane Database of Systematic Reviews | Cochrane Library [WWW Document], 2022. URL. https://www.cochranelibrary.com/cdsr/about-cdsr (accessed 12.14.22).

About Us – Canadian Task Force on Preventive Health Care [WWW Document], 2019. URL. https://canadiantaskforce.ca/about/ (accessed 12.14.22).

About us - UK National Screening Committee - GOV.UK [WWW Document], 2022. URL. https://www.gov.uk/government/organisations/uk-national-screening-committee/about (accessed 12.14.22).

ACS Breast Cancer Screening Guidelines [WWW Document], 2022. URL. https://www.cancer.org/cancer/breast-cancer/screening-tests-and-early-detection/american-cancer-society-recommendations-for-the-early-detection-of-breast-cancer.html (accessed 12.14.22).

Aghoram, R., Cai, P., Dickinson, J.A., 2012. Alpha-foetoprotein and/or liver ultrasonography for screening of hepatocellular carcinoma in patients with chronic hepatitis B. Cochrane Database Syst. Rev. 2012 https://doi.org/10.1002/14651858.CD002799.PUB2.

Al-Sukhun, S., Temin, S., Chavez-MacGregor, M., Denduluri, N., Oliver, T.K., Pyle, D., Shah, M.A., Gralow, J., 2018. ASCO resource-stratified guidelines: methods and opportunities. J Glob Oncol 4, 1–8. https://doi.org/10.1200/JGO.18.00113.

Balogun, O.D., Choi, A.M.K., Formenti, S.C., 2019. Shaping the path for a global oncology academic career. JAMA Oncol 5, 931–932. https://doi.org/10.1001/JAMAONCOL.2019.0555.

Basu, P., Mittal, S., Bhadra Vale, D., Chami Kharaji, Y., 2018. Secondary prevention of cervical cancer. Best Pract Res Clin Obstet Gynaecol 47, 73–85. https://doi.org/10.1016/J.BPOBGYN.2017.08.012.

Bedell, S.L., Goldstein, L.S., Goldstein, A.R., Goldstein, A.T., 2020. Cervical cancer Screening: past, present, and future. Sex Med Rev 8, 28–37. https://doi.org/10.1016/J.SXMR.2019.09.005.

Black, W.C., Haggstrom, D.A., Welch, H.G., 2002. All-cause mortality in randomized trials of cancer screening. J. Natl. Cancer Inst. 94, 167–173. https://doi.org/10.1093/JNCI/94.3.167.

PDQ Screening and Prevention Editorial Board, 2003. Levels of evidence for cancer screening and prevention studies (PDQ®). PDQ Cancer Information Summaries 1–6.

Bray, F., Jemal, A., Grey, N., Ferlay, J., Forman, D., 2012. Global cancer transitions according to the human development index (2008-2030): a population-based study. Lancet Oncol 13, 790–801. https://doi.org/10.1016/S1470-2045(12)70211-5.

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R.L., Torre, L.A., Jemal, A., 2018. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 68, 394–424. https://doi.org/10.3322/caac.21492.

Breast digital atlas - Breast self-Examination (BSE) [WWW Document], 2022. URL. https://screening.iarc.fr/breastselfexamination.php (accessed 1.31.22).

Brocklehurst, P., Kujan, O., O'Malley, L.A., Ogden, G., Shepherd, S., Glenny, A.M., 2013. Screening programmes for the early detection and prevention of oral cancer. Cochrane Database Syst. Rev. 2013 https://doi.org/10.1002/14651858.CD004150.PUB4/MEDIA/CDSR/CD004150/IMAGE_N/NCD004150-FIG-01.PNG.

Cervical Cancer - UK National Screening Committee (UK NSC) - GOV.UK [WWW Document], 2019. URL https://view-health-screening-recommendations.service.gov.uk/cervical-cancer/ (accessed 12.14.22).

Chou, R., Croswell, J.M., Dana, T., Bougatsos, C., Blazina, I., Fu, R., Gleitsmann, K., Koenig, H.C., Lam, C., Maltz, A., Rugge, J.B., Lin, K., 2011. Screening for prostate cancer: a review of the evidence for the U.S. preventive services task force. Ann. Intern. Med. 155, 762–771. https://doi.org/10.7326/0003-4819-155-11-201112060-00375.

Cohen, J.D., Li, L., Wang, Y., Thoburn, C., Afsari, B., Danilova, L., Douville, C., Javed, A.A., Wong, F., Mattox, A., Hruban, R.H., Wolfgang, C.L., Goggins, M.G., Molin, M.D., Wang, T.L., Roden, R., Klein, A.P., Ptak, J., Dobbyn, L., Schaefer, J., Silliman, N., Popoli, M., Vogelstein, J.T., Browne, J.D., Schoen, R.E., Brand, R.E., Tie, J., Gibbs, P., Wong, H.L., Mansfield, A.S., Jen, J., Hanash, S.M., Falconi, M., Allen, P.J., Zhou, S., Bettegowda, C., Diaz, L.A., Tomasetti, C., Kinzler, K.W., Vogelstein, B., Lennon, A.M., Papadopoulos, N., 2018. Detection and localization of surgically

resectable cancers with a multi-analyte blood test. Science 359, 926–930. https://doi.org/10.1126/SCIENCE.AAR3247.
Coulter, A., Collins, A., 2011. MAKING SHARED DECISION-MAKING a REALITY no Decision about me, without me.
Criteria for a population screening programme - GOV.UK, 2022. WWW Document. URL. https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes/criteria-for-appraising-the-viability-effectiveness-and-appropriateness-of-a-screening-programme (accessed 12.14.22).
Cuzick, J., Bergeron, C., von Knebel Doeberitz, M., Gravitt, P., Jeronimo, J., Lorincz, A. T., Chris, C.J.L.M., Sankaranarayanan, R., Snijders, P.J.F., Szarewski, A., 2012. New technologies and procedures for cervical cancer screening. Vaccine 30 (Suppl), 5. https://doi.org/10.1016/J.VACCINE.2012.05.088.
Davidson, K.W., Barry, M.J., Mangione, C.M., Cabana, M., Caughey, A.B., Davis, E.M., Donahue, K.E., Doubeni, C.A., Krist, A.H., Kubik, M., Li, L., Ogedegbe, G., Owens, D. K., Pbert, L., Silverstein, M., Stevermer, J., Tseng, C.W., Wong, J.B., 2021. Screening for colorectal cancer: US preventive services task force recommendation statement. JAMA - Journal of the American Medical Association 325, 1965–1977. https://doi.org/10.1001/JAMA.2021.6238.
Dvaladze, A., Duggan, C., Anderson, B.O., 2020. Phased implementation for breast cancer management in low-income and middle-income countries: a proposal for the strategic application of resource-stratified guidelines by the breast health global initiative. Cancer 126 (Suppl. 10), 2337–2338. https://doi.org/10.1002/CNCR.32942.
Edwards, B.K., Ward, E., Kohler, B.A., Eheman, C., Zauber, A.G., Anderson, R.N., Jemal, A., Schymura, M.J., Lansdorp-Vogelaar, I., Seeff, L.C., van Ballegooijen, M., Goede, S.L., Ries, L.A.G., 2010. Annual report to the nation on the status of cancer, 1975–2006, featuring colorectal trends and impact of interventions (risk factors, Screening, and treatment) to reduce future rates. Cancer 116, 544. https://doi.org/10.1002/CNCR.24760.
Fokom Defo, V., Fokom Domgue, J., 2020. Why consider self-sampling for cervical cancer Screening in low- and middle-income countries? AMA J. Ethics 22, E116–E125. https://doi.org/10.1001/AMAJETHICS.2020.116.
Franco, E.L., 2003. Chapter 13: primary screening of cervical cancer with human papillomavirus tests. J Natl Cancer Inst Monogr 89–96. https://doi.org/10.1093/OXFORDJOURNALS.JNCIMONOGRAPHS.A003488.
Franco, E.L., 2018. Self-sampling for cervical cancer screening: empowering women to lead a paradigm change in cancer control. Curr. Oncol. 25, e1 https://doi.org/10.3747/CO.25.3969.
Franco, E.L., Duarte-Franco, E., Rohan, T.E., 2002. Evidence-based policy recommendations on cancer screening and prevention. Cancer Detect. Prev. 26, 350–361. https://doi.org/10.1016/S0361-090X(02)00118-6.
Gøtzsche, P.C., 2015. Commentary: Screening: a seductive paradigm that has generally failed us. Int. J. Epidemiol. 44, 278–280. https://doi.org/10.1093/IJE/DYU267.
Gøtzsche, P.C., Jørgensen, K.J., 2013. Screening for breast cancer with mammography. Cochrane Database Syst. Rev. 2013 https://doi.org/10.1002/14651858.CD001877.PUB5/MEDIA/CDSR/CD001877/IMAGE_N/NCD001877-CMP-001-21.PNG.
Grade Definitions | United States Preventive Services Taskforce, 2018. WWW Document. URL. https://uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/grade-definitions (accessed 12.14.22).
Grossman, D.C., Curry, S.J., Owens, D.K., Bibbins-Domingo, K., Caughey, A.B., Davidson, K.W., Doubeni, C.A., Ebell, M., Epling, J.W., Kemper, A.R., Krist, A.H., Kubik, M., Seth Landefeld, C., Mangione, C.M., Silverstein, M., Simon, M.A., Siu, A. L., Tseng, C.W., 2018. Screening for prostate cancer: US preventive services task force recommendation statement. JAMA 319, 1901–1913. https://doi.org/10.1001/JAMA.2018.3710.
Guyatt, G.H., Oxman, A.D., Vist, G.E., Kunz, R., Falck-Ytter, Y., Alonso-Coello, P., Schünemann, H.J., 2008. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 336, 924–926. https://doi.org/10.1136/BMJ.39489.470347.AD.
HPV self-sampling in Sweden leading to faster elimination of cervical cancer [WWW Document], 2022. URL. https://www.who.int/europe/news/item/08-09-2022-hpv-self-sampling-in-sweden-leading-to-faster-elimination-of-cervical-cancer (accessed 12.14.22).
Ilic, D., Neuberger, M.M., Djulbegovic, M., Dahm, P., 2013. Screening for prostate cancer. Cochrane Database Syst. Rev. 2013 https://doi.org/10.1002/14651858.CD004720.PUB3/INFORMATION/EN.
Jeronimo, J., Castle, P.E., Temin, S., Denny, L., Gupta, V., Kim, J.J., Luciani, S., Murokora, D., Ngoma, T., Qiao, Y., Quinn, M., Sankaranarayanan, R., Sasieni, P., Schmeler, K.M., Shastri, S.S., 2016. Secondary prevention of cervical cancer: ASCO resource-stratified clinical practice guideline. J Glob Oncol 3, 635–657. https://doi.org/10.1200/JGO.2016.006577.
Johansson, E., Steineck, G., Holmberg, L., Johansson, J.E., Nyberg, T., Ruutu, M., Bill-Axelson, A., 2011. Long-term quality-of-life outcomes after radical prostatectomy or watchful waiting: the Scandinavian prostate cancer Group-4 randomised trial. Lancet Oncol 12, 891–899. https://doi.org/10.1016/S1470-2045(11)70162-0.
Klabunde, C.N., Lanier, D., Nadel, M.R., McLeod, C., Yuan, G., Vernon, S.W., 2009. Colorectal cancer screening by primary care physicians: recommendations and practices, 2006-2007. Am. J. Prev. Med. 37, 8–16. https://doi.org/10.1016/J.AMEPRE.2009.03.008.
Klabunde, C.N., Marcus, P.M., Han, P.K.J., Richards, T.B., Vernon, S.W., Yuan, G., Silvestri, G.A., 2012. Lung cancer screening practices of primary care physicians: results from a national survey. Ann. Fam. Med. 10, 102–110. https://doi.org/10.1370/AFM.1340.
Koh, W.J., Anderson, B.O., Carlson, R.W., 2020. NCCN resource-stratified and harmonized guidelines: a paradigm for optimizing global cancer care. Cancer 126 (Suppl. 10), 2416–2423. https://doi.org/10.1002/CNCR.32880.
Ladabaum, U., Dominitz, J.A., Kahi, C., Schoen, R.E., 2020. Strategies for colorectal cancer Screening. Gastroenterology 158, 418–432. https://doi.org/10.1053/J.GASTRO.2019.06.043.
Loeb, S., Vellekoop, A., Ahmed, H.U., Catto, J., Emberton, M., Nam, R., Rosario, D.J., Scattoni, V., Lotan, Y., 2013. Systematic review of complications of prostate biopsy. Eur. Urol. 64, 876–892. https://doi.org/10.1016/J.EURURO.2013.05.049.
Louvanto, K., Franco, E.L., Ramanakumar, A.V., Vasiljević, N., Scibior-Bentkowska, D., Koushik, A., Cuzick, J., Coutlée, F., Lorincz, A.T., 2015. Biomarkers of cervical cancer risk study team. Methylation of viral and host genes and severity of cervical lesions associated with human papillomavirus type 16. Int. J. Cancer 136, E638–E645. https://doi.org/10.1002/IJC.29196.
Lung cancer - UK National Screening Committee (UK NSC) - GOV.UK [WWW Document], 2022. URL. https://view-health-screening-recommendations.service.gov.uk/lung-cancer/ (accessed 12.14.22).
Manser, R., Lethaby, A., Irving, L.B., Stone, C., Byrnes, G., Abramson, M.J., Campbell, D., 2013. Screening for lung cancer. Cochrane Database Syst. Rev. 2013 https://doi.org/10.1002/14651858.CD001991.PUB3/MEDIA/CDSR/CD001991/IMAGE_N/NCD001991-CMP-003-02.PNG.
Olson, B., Gribble, B., Dias, J., Curryer, C., Vo, K., Kowal, P., Byles, J., 2016. Cervical cancer screening programs and guidelines in low- and middle-income countries. Int. J. Gynecol. Obstet. 134, 239–246. https://doi.org/10.1016/J.IJGO.2016.03.011.
PDQ Screening and Prevention Editorial Board, 2022a. Colorectal Cancer Screening (PDQ®). PDQ Cancer Information Summaries. https://www.ncbi.nlm.nih.gov/books/NBK65825/ (accessed 12.14.22).
PDQ Screening and Prevention Editorial Board, 2022b. Stomach (Gastric) Cancer Screening (PDQ®). PDQ Cancer Information Summaries. https://www.ncbi.nlm.nih.gov/books/NBK65730/ (accessed 12.14.22).
Perkins, R.B., Guido, R.S., Castle, P.E., Chelmow, D., Einstein, M.H., Garcia, F., Huh, W. K., Kim, J.J., Moscicki, A.B., Nayar, R., Saraiya, M., Sawaya, G.F., Wentzensen, N., Schiffman, M., 2020. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer Screening tests and cancer precursors. J Low Genit Tract Dis 24, 102–131. https://doi.org/10.1097/LGT.0000000000000525.
Presant, C.A., Salgia, R., Kulkarni, P., Tiep, B.L., Sanani, S., Leach, B., Ashing, K., Sandoval, J., Sedrak, M.S., Landau, S., Yeung, S., Raz, D., Subbiah, S., 2020. Implementing lung cancer Screening and prevention in academic Centers, affiliated network offices and collaborating care sites. J. Clin. Med. 9, 1–11. https://doi.org/10.3390/JCM9061820.
Prostate-Specific Antigen (PSA) Test - NCI [WWW Document], 2022. URL. https://www.cancer.gov/types/prostate/psa-fact-sheet (accessed 12.14.22).
Sangwa-Lugoma, G., Mahmud, S., Nasr, S.H., Liaras, J., Kayembe, P.K., Tozin, R.R., Drouin, P., Lorincz, A., Ferenczy, A., Franco, E.L., 2006. Visual inspection as a cervical cancer screening method in a primary health care setting in Africa. Int. J. Cancer 119, 1389–1395. https://doi.org/10.1002/IJC.21972.
Sankaranarayanan, R., 2014. Screening for cancer in low- and middle-income countries. Ann Glob Health 80, 412–417. https://doi.org/10.1016/J.AOGH.2014.09.014.
Sankaranarayanan, R., Nene, B.M., Shastri, S.S., Jayant, K., Muwonge, R., Budukh, A.M., Hingmire, S., Malvi, S.G., Thorat, R., Kothari, A., Chinoy, R., Kelkar, R., Kane, S., Desai, S., Keskar, V.R., Rajeshwarkar, R., Panse, N., Dinshaw, K.A., 2009. HPV Screening for cervical cancer in rural India. N. Engl. J. Med. 360, 1385–1394. https://doi.org/10.1056/nejmoa0808516.
Santesso, N., Mustafa, R.A., Schünemann, H.J., Arbyn, M., Blumenthal, P.D., Cain, J., Chirenje, M., Denny, L., de Vuyst, H., Eckert, L.O.N., Forhan, S.E., Franco, E.L., Gage, J.C., Garcia, F., Herrero, R., Jeronimo, J., Lu, E.R., Luciani, S., Quek, S.C., Sankaranarayanan, R., Tsu, V., Broutet, N., 2016. World Health Organization guidelines for treatment of cervical intraepithelial neoplasia 2-3 and screen-and-treat strategies to prevent cervical cancer. Int. J. Gynaecol. Obstet. 132, 252–258. https://doi.org/10.1016/J.IJGO.2015.07.038.
Saquib, N., Saquib, J., Ioannidis, J.P.A., 2015. Does screening for disease save lives in asymptomatic adults? Systematic review of meta-analyses and randomized trials. Int. J. Epidemiol. 44, 264–277. https://doi.org/10.1093/IJE/DYU140.
Shah, S.C., Kayamba, V., Peek, R.M., Heimburger, D., 2019. Cancer control in low- and middle-income countries: is it time to consider screening? J Glob Oncol 2019. https://doi.org/10.1200/JGO.18.00200.
Sharma, D., Newman, T.G., Aronow, W.S., 2015. Lung cancer screening: history, current perspectives, and future directions. Arch. Med. Sci. 11, 1033. https://doi.org/10.5114/AOMS.2015.54859.
Sivaram, S., Majumdar, G., Perin, D., Nessa, A., Broeders, M., Lynge, E., Saraiya, M., Segnan, N., Sankaranarayanan, R., Rajaraman, P., Trimble, E., Taplin, S., Rath, G.K., Mehrotra, R., 2018. Population-based cancer screening programmes in low-income and middle-income countries: regional consultation of the international cancer Screening network in India. Lancet Oncol 19, e113–e122. https://doi.org/10.1016/S1470-2045(18)30003-2.
Sung, H., Ferlay, J., Siegel, R.L., Laversanne, M., Soerjomataram, I., Jemal, A., Bray, F., 2021. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 71, 209–249. https://doi.org/10.3322/CAAC.21660.
Tashiro, A., Sano, M., Kinameri, K., Fujita, K., Takeuchi, Y., 2006. Comparing mass screening techniques for gastric cancer in Japan. World J. Gastroenterol. 12, 4873–4874. https://doi.org/10.3748/WJG.V12.I30.4873.
UK NSC meetings and minutes - GOV.UK [WWW Document], 2021. URL. https://www.gov.uk/government/collections/uk-nsc-meetings-and-minutes (accessed 12.14.22).
Wajed, S.A., Laird, P.W., DeMeester, T.R., 2001. DNA methylation: an alternative pathway to cancer. Ann. Surg. 234, 10. https://doi.org/10.1097/00000658-200107000-00003.
Walboomers, J.M., Jacobs, M.V., Manos, M.M., Bosch, F.X., Kummer, J.A., Shah, K.V., Snijders, P.J., Peto, J., Meijer, C.J., Muñoz, N., 1999. Human papillomavirus is a

necessary cause of invasive cervical cancer worldwide - PubMed. J. Pathol. https://doi.org/10.1002/(SICI)1096-9896(199909)189:1<12::AID-PATH431>3.0.CO;2-F.

Wentzensen, N., Clarke, M.A., 2021. Cervical cancer Screening-past, present, and future. Cancer Epidemiol. Biomark. Prev. 30, 432–434. https://doi.org/10.1158/1055-9965.EPI-20-1628.

What Cancer Screening Tests Check for Cancer? - NCI [WWW Document], 2022. URL. https://www.cancer.gov/about-cancer/screening/screening-tests#recommended-cancer-screening-tests (accessed 12.14.22).

World Health Organization, 2013. WHO guidance note: comprehensive cervical cancer prevention and control: a healthier future for girls and women [WWW Document]. URL. https://apps.who.int/iris/handle/10665/78128 (accessed 12.14.22).

World Health Organization: Regional Office for Europe, 2020. Increase effectiveness, maximize benefits and minimize harm Screening programmes: a short guide.

Yabroff, K.R., Saraiya, M., Meissner, H.I., Haggstrom, D.A., Wideroff, L., Yuan, G., Berkowitz, Z., Davis, W.W., Benard, V.B., Coughlin, S.S., 2009. Specialty differences in primary care physician reports of Papanicolaou test Screening practices: a National Survey, 2006 to 2007. Ann. Intern. Med. 151, 602. https://doi.org/10.7326/0003-4819-151-9-200911030-00005.

Yabroff, K.R., Klabunde, C.N., Yuan, G., McNeel, T.S., Brown, M.L., Casciotti, D., Buckman, D.W., Taplin, S., 2011. Are physicians' recommendations for colorectal cancer screening guideline-consistent? J. Gen. Intern. Med. 26, 177–184. https://doi.org/10.1007/S11606-010-1516-5.

Yokoi, A., Ochiya, T., 2021. Exosomes and extracellular vesicles: rethinking the essential values in cancer biology. Semin. Cancer Biol. 74, 79–91. https://doi.org/10.1016/J.SEMCANCER.2021.03.032.

Zapka, J.G., Puleo, E., Taplin, S., Solberg, L.I., Mouchawar, J., Somkin, C., Geiger, A.M., Ulcickas Yood, M., 2005. Breast and cervical cancer screening: clinicians' views on health plan guidelines and implementation efforts. J Natl Cancer Inst Monogr 46–54. https://doi.org/10.1093/jncimonographs/lgi037.

Zhang, B.H., Yang, B.H., Tang, Z.Y., 2004. Randomized controlled trial of screening for hepatocellular carcinoma. J. Cancer Res. Clin. Oncol. 130, 417–422. https://doi.org/10.1007/S00432-004-0552-0.