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Quality appraisal of documents producing recommendations for breast, colorectal and cervical cancer screening

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ABSTRACT

BACKGROUND: Breast, cervical, and colorectal cancer screening are evidence-based interventions recommended by most governmental agencies and scientific societies. The aim of this review is to assess the quality of guidelines on screening and to describe differences according to the context in which they were produced.

METHODS: A literature search of the main databases, websites on health care, and guidelines, as well as the websites of several scientific societies was carried out in order to identify the most recent guidelines (since 2000) on cervical, breast, and colorectal cancer screening. Only documents written in Italian or English were included. Two investigators independently assessed quality by using the AGREE (Appraisal of Guidelines, Research and Evaluation in Europe) instrument.

RESULTS: Thirty-three, 32, and 18 relevant documents for cervical, breast, and colorectal cancer, respectively, were identified. Only some documents (19, 12 and 13 for cervical, breast, and colorectal cancer, respectively) could be evaluated with AGREE. Items included in the domain "scope and purpose" obtained the highest scores, followed by "clarity of presentation" domain, while "applicability", "patient involvement," and "conflict of interest disclosure" domains obtained the lowest scores. The quality did not improve in more recent documents. Documents produced by governmental agencies, on average, had higher scores than documents by scientific societies, particularly for "stakeholder involvement" and "applicability".

CONCLUSIONS: Documents from different countries and health systems differ in terms of the main recommendations given and in the quality of the documents. Those produced by governmental agencies have a more multidisciplinary authorship and pay more attention to applicability than do those produced by scientific societies.

Key words: cancer screening, guidelines as topics, quality appraisal, prevention and public health guidelines

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INTRODUCTION

Screening programs for breast, cervical, and colorectal cancers are evidence-based interventions recommended by most governmental agencies and scientific society guidelines [1-3].

National and international guidelines, however, differ with regard to the main characteristics of screening organisation and implementation, such as starting and stopping age, the most efficient interval, and, in some cases, the type of screening test itself.

These differences are usually due to historical, cultural, organizational, and/ or political peculiarities of the guideline authors; what's more, guidelines can also be influenced by the context in which they have been issued.

In some industrialised countries, particularly in Western Europe, there are organised programmes that have specific protocols stemming from their own guidelines [1] that define the target population to be invited, the screening intervals, and the management for positive women. In others countries, such as the USA, screening is mostly spontaneous and based on a variety of guidelines established by national and international scientific societies. In this context, each physician chooses to adopt the guideline that is most influential in his/her community or a mix of recommendations from different guidelines based on his/her experience and, sometimes, convenience [4].

European Union (EU) Guidelines [1], as well as Italian legislation, [5] recommend the implementation of screening programs based on the active invitation of the whole target population and confirm not only the right to receive a free test, but also the National Health Service's duty to organise a clinical pathway from screening invitation all the way to treatment. Although EU guidelines have clearly recommended implementing organised programs based on their effectiveness, both of the organizational models, i.e., spontaneous screening as well as organised programs, are currently present in Italy and in many other European countries as well [6].

The Italian Ministry of Health commissioned a systematic review to describe the main recommendations on screening reported by the most influential national and international guidelines. One of the aims of this study was to collect these guidelines and analyse in detail those that could have an impact in Italy so as to better understand the major discrepancies between screening programme recommendations and spontaneous screening practice in Italy. A quality appraisal of the guidelines was also commissioned to be included in the study.

The literature proposes several instruments to assess and compare quality of guidelines [7-12]. For our assessment, we decided to use the AGREE (Appraisal of Guidelines, Research and Evaluation in Europe) instrument, [7] the result of a ten-year effort of an international group of guidelines developers to integrate all the dimensions linked to the quality of the previously existing tools. The assessment includes judgments on the methods applied to produce the guidelines, the main components of the final recommendations, and the factors linked to their uptake. Although developed mostly for clinical guidelines, [13,14] this instrument has already been applied to prevention guidelines,[15] and the most recent version, AGREE II,[16] introduced some modifications in order to increase its applicability to a wider range of health problems.

The aim of this paper is to present the results of the quality appraisal of a large sample of those guidelines on cervical, breast, and colorectal cancer screening identified as the most influential in Italian practice. We also compared the quality scores according to the type of screening, the year and country of production, and the type of organization commissioning or producing the document.

METHODS

Sources of information and guidelines selection

In order to identify the most recent guidelines (since 2000) on population screening programs for breast, cervical, and colorectal cancers, we conducted a literature search of the major databases. Specifically, we searched general websites on health care and some specific sites for guidelines and we studied the websites of several scientific societies of interest (see Appendix 1 for search methods).

The aim was to identify all the documents that may be influential in Italy. We were not able to define a systematic search because the search in the Health Authority websites

was systematic only for Italy and not for other countries. We have tried, however, to delineate the steps of our search to make it as reproducible as possible.

The search strategy was defined according to the following PICOS (Population, Intervention, Control, Outcome, Study design):

Population: healthy adult female for cervical cancer and breast cancer screening, and healthy population of both sexes for colorectal cancer.

Interventions: screening programs for early detection and treatment of cervical, breast, and colorectal cancer.

There is no comparator, since we plan to compare the quality of guidelines with each other.

Outcome: incidence and mortality reduction for cervical and colorectal cancer screening and mortality reduction for breast cancer.

Included studies are guidelines, HTA (Health Technology Assessment) reports, and other documents reporting recommendations on screening strategies.

The search was then validated by crosschecking the references of identified documents and all the experts in the working group were consulted. Finally, the results of the search were submitted to all the relevant Italian scientific societies (see Appendix 1) to receive comments and to check whether all the guidelines that they considered to be influential in Italy had been included and whether the recommendations had been extracted correctly.

The first step of the search strategy was to identify the guidelines published in the National Library (www.pubmed.com) by using the keywords selected by the Editorial Group of the Cochrane Collaboration that deals with this topic [17-20]. The keywords used, according to the kind of cancer studied, and all the scientific websites investigated, are described on the "Osservatorio Nazionale Screening" website (www.osservatorionazionalescreening.it). The search was updated on 31/12/2010.

The inclusion criteria were: to be guidelines or documents producing recommendation for screening the healthy population for breast, cervical, and colorectal cancer; to report (to refer to a document with) rationale and evidences; language - English or Italian; published from 2000 to 2010. Exclusion criteria were: to be superseded by more recent documents sponsored or authored by the same organization; focus on treatment, and no autonomous chapter or section on screening.

The identified documents were collected in PDF format and then evaluated for relevance by the working group.

Guideline quality assessment

Two investigators independently assessed the guidelines by using the instrument developed by the AGREE Collaboration [7]. AGREE is a checklist for the qualitative assessment of guidelines funded by the EU (BIOMED-2 Programme of the European Union. Project: PL96-3669) and developed in collaboration with the following countries: Belgium, The Netherlands, Switzerland, The United Kingdom, Ireland, France, Norway, Italy, Greece, Spain, Denmark, Finland, Germany, Scotland, Sweden, and Portugal.

According to AGREE, a guideline's quality is indicated by the reliability of its internal or external validity and by the practical applicability of the recommendations. The process involves the evaluation of the benefits, risks, and costs arising from the recommendations, as well as the practical issues related to them. Therefore, the process of analysis concerns an evaluation of the methods used for guideline development, the recommendations suggested, and the factors associated with their adoption.

All the documents selected as relevant were given to the two reviewers, who made a first selection of those suitable for a quality appraisal. To be included, the documents had to report the evidence on which they were based in sufficient detail, they had to have bibliographic references, they had to define their objectives, and the objectives had to include the definition of screening strategy.

Statistical analyses

Some of the items were not applicable to the guidelines under study. Accordingly, in the final summary, overall scores obtained with AGREE were standardised as percentage of the total maximum score. Furthermore, some of the included documents did not fit with the AGREE evaluation instrument for the following reasons: recommendations from the same agency were reported in different documents, making a single answer for each item impossible; the

reference to the evidence and rationale were not available (particularly frequent for laws).

We present the standardised mean scores of guidelines, overall and in each domain, according to the target cancer, their authorship (scientific societies or governmental agencies), country, and year of production. We used a t-test to compare the overall mean score between scientific societies and governmental agencies and between US and European guidelines; we performed a linear regression of the standardised mean scores using the publication year as independent variable (STATA 11.0) to test whether a time trend in quality were present.

RESULTS

Cervical cancer

Fifty documents that could be classified as guidelines, HTA reports, or other documents reporting recommendations on screening were identified (Figure 1). Twenty-three of these documents were excluded because they did not include sufficient detail on screening recommendations or because they were superseded by more recent documents.
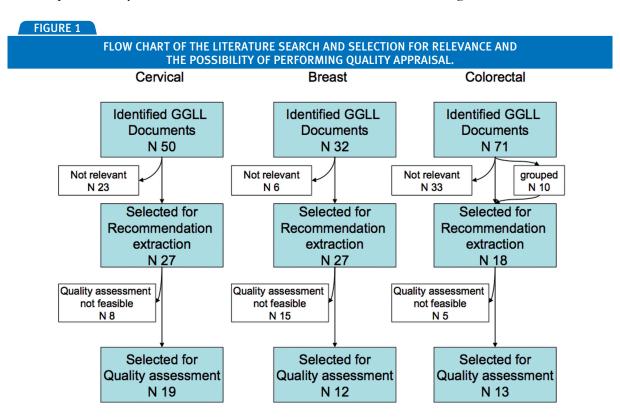
Twenty-seven reported recommendations for screening and were included in our study, presented in Table 1. Eleven of the included studies were Italian, 6 from the USA, 3 from the UK, 5 from international bodies, and one from France and from Australia each.

The language restriction (English or Italian) limited the completeness of the review. The sixteen documents in Italian identified, and some international papers that are certainly influential in Europe, such as the Dutch and Finnish recommendations, were not included due to language restriction in the search criteria.

Breast cancer

We identified 32 documents (Figure 1), 6 of which did not report any recommendation for screening and were thus excluded from the analysis. We selected 26 documents, listed in Table 2.

Apart from the Italian guidelines, most were produced in the UK, the U.S.A., and Canada, with only one from France, one from New Zealand, and one from Ireland. Two guidelines were produced by the international organizations – the WHO and the EU. Limiting the search only to documents in English or Italian excluded

FIGURE 1

FLOW CHART OF THE LITERATURE SEARCH AND SELECTION FOR RELEVANCE AND THE POSSIBILITY OF PERFORMING QUALITY APPRAISAL.

some relevant guidelines or recommendations from non-Anglophone European countries, in particular from Sweden, whose breast screening programs are influential in Italy, and from Denmark, interesting due to the strong anti-screening movement in that country.

Colorectal cancer

We identified 71 documents (Figure 1), some of which were considered as one document since they were part of a single set of recommendations issued by a single entity albeit divided into several publications or updates that presented only a few specific points. Several other documents were omitted because they were superseded by subsequent publications to which the institution itself refers.

Overall, 28 documents were included in the review, summarized in 18 extraction tables. The list of these documents is presented in Table 3.

Once again, limiting the search to documents in English or Italian excluded some colorectal cancer guidelines and recommendations from non-Anglophone countries in Europe, but in this case none was considered really influential in Italy by the expert panel.

TABLE 1

SELECTED DOCUMENTS GIVING RECOMMENDATIONS FOR CERVICAL CANCER SCREENING. AUTHOR, ACRONYM, PUBLICATION YEAR, AUTHORS' COUNTRY, AND SUITABLE FOR QUALITY APPRAISAL USING AGREE INSTRUMENT.

AUTHOR	ACRONYM	YEAR	COUNTRY	AGREE
International Federation of Gynecology and Obstetrics [21]	FIGO	2000	International	Yes
Programma Nazionale Linee Guida [22]	PNLG	2000	Italy	
Regione Lombardia [23]		2000	Italy	
American Cancer Society [24]	ACS	2002	USA	Yes
Agence Nationale d'Accréditation et d'Evaluation en Santé [25]	ANAES	2002	France	Yes
Cochrane Database of Systematic Reviews [19]	Cochrane	2002	International	
Regione Toscana [26]	PNLG	2002	Italy	Yes
National Institute for Health and Clinical Excellence [27]	NICE	2003	UK	
U.S. Preventive Services Task Force [28]	USPSTF	2003	USA	Yes
NHS Cervical Screening Programme [29]	NHSCSP	2004	UK	Yes
American Congress of Obstetricians and Gynecologists [30]	ACOG	2005	USA	
Australian Government [31]	NHMRC	2005	Australia	Yes
International Agency for Research on Cancer [32]	IARC	2005	International	Yes
Istituto Toscano Tumori [33]	ITT	2005	Italy	
Ministero della Salute [5]	ONS	2005	Italy	Yes
Regione Autonoma Friuli Venezia Giulia [34]	FVG	2005	Italy	
Institute for Clinical Systems Improvement [35-36]	ICSI	2005+2008	USA	Yes
American Society for Colposcopy and Cervical Pathology [37]	ASCCP	2006	USA	Yes
National Comprehensive Cancer Network [38]	NCCN	2007	USA	Yes
Società Italiana di Colposcopia e Patologia Cervico Vaginale [39]	SICPCV	2006	Italy	Yes
World Health Organization [40]	WHO	2006	International	Yes
Gruppo Italiano Screening del Cervicocarcinoma [41-42]	GISCI	2006+2007	Italy	Yes
European Commission [43]	EC	2008	EU	Yes
Regione Emilia-Romagna [44]	RER	2008	Italy	Yes
Scottish Intercollegiate Guidelines Network [45]	SIGN	2008	UK	
Società Italiana di Virologia [46]	SIV	2008	Italy	Yes
Regione Toscana [47]	ISPO	2010	Italy	Yes

TABLE 2

SELECTED DOCUMENTS GIVING RECOMMENDATIONS FOR BREAST CANCER SCREENING. AUTHOR, ACRONYM, PUBLICATION YEAR, AUTHORS' COUNTRY, AND SUITABLE FOR QUALITY APPRAISAL USING AGREE TOOL.				
AUTHOR	**ACRONYM**	**YEAR**	**COUNTRY**	**AGREE**
Agence Nationale d'Accréditation et d'Evaluation en Santé [48]	ANAES	2000	France	Yes
Royal College of Surgeons in Ireland [49]	RCSI	2000	Ireland	
Canadian Task Force on Preventive Health Care [50]	CTFPHC	2001	Canada	
American Cancer Society [51-52]	ACS	2003+2004	International	Yes
Regione Toscana [27]	PNLG	2003	Italy	
Società Italiana di Radiologia Medica [53]	SIRM	2004	Italy	Yes
Ministero della Salute [5]	ONS	2005	Italy	See cervical
Forza Operativa Nazionale sul Carcinoma Mammario [54]	FONCAM	2005	Italy	Yes
Agence d'évaluation des technologies et des modes d'intervention en santé [55]	AETMIS	2006	Canada	
European Commission [56]	EC	2006	EU	Yes
National Institute for Health and Clinical Excellence [57-58]	NICE	2006+2004	UK	
World Health Organization [59]	WHO	2006	International	
American College of Physicians [60]	ACP	2007	USA	Yes
Regione Piemonte [61]	CPO	2007	Italy	
Gruppo Italiano Screening Mammografico [62]	GISMA	2007	Italy	Yes
American College of Radiology [63]	ACR	2008	USA	Yes
Associazione Italiana Oncologia Medica [64]	AIOM	2008	Italy	
Institute for Clinical Systems Improvement [65]	ICSI	2008	International	
Regione Emilia-Romagna [66]	RER	2008	Italy	Yes
Australian Institute of Health and Welfare [67]	AIHW	2008	Australia	
Cochrane Database of Systematic Reviews [20]	Cochrane	2009	International	
National Institute for Health and Clinical Excellence [68]	NICE	2009	UK	
Provincia autonoma di Trento [69]	Trento	2009	Italy	
U.S. Preventive Services Task Force [70]	USPSTF	2009	USA	Yes
Regione Toscana [47]	ISPO	2010	Italy	Yes
NHS Breast Screening Programme [71]	NHSBSP	2010	UK	Yes

Quality of Guidelines

Only a few documents (19 for cervical cancer screening, 12 for breast cancer screening and 13 for colorectal cancer screening) were evaluated; we did not conduct a qualitative assessment on the remaining documents mostly for two, not mutually exclusive, reasons: first, because they were mostly legislative documents that did not address a sufficient number of areas, and/or second, because not enough methodological details were reported to make them interesting for our analysis.

The two researchers independently considered the item "applicability in a pilot study" inappropriate to most of the documents of the three types of screening programs. In fact, although a screening program's organization is very worthy of analysis through a pilot study, whether or not to conduct such a study is almost always beyond the authority of those who promote or draw up guidelines.

The assessors were not fully in agreement on the guidelines of the three cancers. Agreement was fairly consistent for guidelines on cervical cancer screening, where 58% of cases obtained identical assessments (on a scale from 1 to 4), 32% had a 1-point difference, and the remaining 10% had a difference of 2 or 3 points. As for agreement on breast cancer screening guidelines,

TABLE 3				
SELECTED DOCUMENTS GIVING RECOMMENDATIONS FOR COLORECTAL CANCER SCREENING. AUTHOR, ACRONYM, PUBLICATION YEAR, AUTHORS' COUNTRY AND SUITABLE FOR QUALITY APPRAISAL USING AGREE TOOL.				
AUTHOR	**ACRONYM**	**YEAR**	**COUNTRY**	**AGREE**
Agenzia di Sanità Pubblica della Regione Lazio [72]	ASP	2001	Italy	Yes
Canadian Task Force on Preventive Health Care [73]	CTFPHC	2001	Canada	Yes
Regione Piemonte [74]	CPO	2001	Italy	Yes
Agenzia per i Servizi Sanitari Regionali [75]	ASSR	2002	Italy	Yes
Scottish Intercollegiate Guidelines Network [76]	SIGN	2003	UK	Yes
Australian Cancer Network [77]	CAN	2005	Australia	Yes
Ministero della Salute [5]	ONS	2005	Italy	Yes
Regione Emilia-Romagna [78]	RER	2006	Italy	
Gruppo Italiano Screening ColoRettale [79]	GISCoR	2009	Italy	
American College of Gastroenterology [80]	ACG	2009	USA	Yes
Haute Autorité de Santé [81]	HAS	2008	France	
National Cancer Institute [82]	NCI	2008	USA	
US Preventive Services Task Force [83]	USPSTF	2008	USA	Yes
NHS Bowel Cancer Screening Programme [84]	NHSBCSP	2008-2010	International	Yes
American Cancer Society [85]	ACS	2008	USA	Yes
Regione Toscana [47]	ISPO	2010	Italy	Yes
European Commission [87]	IARC	2011	International	Yes
National Comprehensive Cancer Network [87]	NCCN	2011	USA	Yes

40% had identical scores, 36% differed by 1 point, 17% by 2 points, and 8% differed by 3 points. In the case of colorectal cancer screening, the agreement was similar to that obtained for breast: for individual items, 43 % had identical scores, 36% differed by 1 point, 19% by 2 points, and 4% had a difference of 3 points.

Guidelines on cervical cancer screening scored between 55% and 85% of the maximum achievable, with an average of 69% (Table 4). The document with the highest score was from Australia (ranking 1st for both reviewers),[31] while the one with the lowest score was the SICPCV document [39]. In general, the Italian documents achieved lower scores than the international ones (66.9 vs. 76.4).

Breast cancer screening guidelines scored between 34% and 76% of the maximum achievable, with an average of 61% (Table 5), significantly lower than the other screenings (p=0.016). The document with the highest score was the ISPO Tuscany (ranking 1st for both reviewers) [47], while the document from the American College of Radiologists got the lowest score [63].

Guidelines on colorectal cancer screening scored between 58% and 82% of the maximum obtainable, with an average of 70% (Table 6). These results are similar to those found for the guidelines on cervical cancer screening, but significantly better than those observed for breast cancer screening. The document with the highest score was issued by the EU in 2011 [85], and the one with the lowest score was issued by the Agency for Public Health, Lazio, Italy (ASP) in 2001[72].

The domains that obtained the best results were "scope and purpose" and "clarity of presentation".

Guidelines from governmental agencies obtained a higher score than those from scientific societies for all three screenings (overall 71.7 vs. 62.5, p= 0.005). Guidelines from the USA, mostly produced by scientific societies, had only a slightly but not significantly lower score than the average (65.6 vs. 69.3, p=0.3), as did Italian documents (66.6 vs. 69.1, p=0.5). No time trends were noted in standardised scores (i.e. the slope coefficients were very close to and not statistically different from zero: -0.005; p= 0.34; 0.002 p=0.81; 0.21; p=0.78; for cervical, breast, and colorectal cancer, respectively).

TABLE 4

AVERAGED SCORES FOR CERVICAL CANCER SCREENING GUIDELINES, BY SINGLE ITEM (CONTINUES).

	SCOPE AND PURPOSE			STAKEHOLDER INVOLVEMENT				RIGOUR OF DEVELOPMENT							TOTAL	
	OBJECTIVES OF GGLL	CLINICAL QUESTION	TARGET PATIENTS	PROFESSIONALS	PATIENTS	GGLL USERS	PILOT WITH USERS	SYSTEMATIC REVIEW	SELECTION CRITERIA	METHODS FOR RECOMMENDATIONS	HEALTH BENEFITS, RISK AND SIDE EFFECTS	LINK EVIDENCE – RECOMMENDATION	EXTERNAL REVIEW	UPDATING PROCEDURES	TOTAL	STD SCORE
ONS 2005[5]	4	4	4	4	1	4		1.5	1.5	3.5	4	3.5	1	1	64	72.7
GISCi 2006+2007[41-42]	3	3	4	3.5	1	3.5		3	3	4	3.5	3	1	2.5	69	78.4
NHMRC 2005[31]	3	3	3	4	4	4		4	4	4	4	4	4	3	74.5	84.7
EC 2008[43]	3.5	3	4	3	1	3.5		1.5	1.5	2	3.5	3	1.5	2	58.5	66.5
ANAES 2002[25]	4	3.5	3	4	1	4		2	1.5	3	3	3	4	2.5	63	71.6
IARC 2005[32]	4	3.5	3.5	3.5	2	3		3.5	2	3	4	4	1.5	1	70	79.5
USPSTF 2003[28]	3.5	4	4	3.5	1	3		3	2.5	3.5	4	3.5	2.5	2.5	61	69.3
ACS 2002[24]	4	4	4	3.5	1	2		3.5	4	4	3	3	4	3	66.5	75.6
SICPCV 2006[39]	2	3	2	2	1	2.5		1.5	1.5	1.5	3	3	1	1.5	49	55.7
ASCCP 2006[37]	3	3.5	2.5	4	1	2.5		3	2.5	2.5	2.5	3	3	3.5	54	61.4
ICSI 2005+2008[35-36]	4	4	4	3	1	3		4	2	3.5	2.5	4	3	4	68.5	77.8
FIGO 2000[21]	4	4	4	2.5	1	3		2	2.5	4	3	4	1	2.5	57.5	65.3
RER 2008[44]	4	4	2.5	3.5	1	3.5		2	2.5	3	3.5	3.5	2	3.5	65.5	74.4
SIV 2008[46]	2.5	2.5	3	2	1	2.5		2.5	2	2.5	3	3	2.5	1.5	53	60.2
NCCN 2006[38]	2.5	3	3.5	3	1	3		2	1	2	1	3	1	1	50.5	57.4
NHSCSP 2004[29]	3	2	3.5	2.5	1	2		1.5	1.5	2.5	3.5	3.5	1	2.5	55.5	63.1
PNLG 2002[26]	3	3.5	4	1.5	1	2.5		1.5	1.5	2	3	3.5	1	1.5	52.5	59.7
WHO 2006[40]	3.5	4	4	4	1	2.5		1.5	2	2.5	3	2	4	1.5	67	76.1
ISPO 2010[47]	3.5	3.5	4	4	1.5	3		3	3	3.5	4	3	3.5	1.5	66.5	75.6
Mean governmental	3.55	3.45	3.59	3.41	1.41	3.18		2.27	2.14	2.95	3.59	3.32	2.36	2.05	63.45	72.11
Mean Scientific societies	3.13	3.38	3.38	2.94	1.00	2.75		2.69	2.31	3.00	2.69	3.25	2.06	2.44	58.50	66.48
Mean USA	3.40	3.70	3.60	3.40	1.00	2.70		3.10	2.40	3.10	2.60	3.30	2.70	2.80	60.10	68.30
Mean Italian	3.14	3.36	3.36	2.93	1.07	3.07		2.14	2.14	2.86	3.43	3.21	1.71	1.86	59.93	68.10
Mean before 2005	3.61	3.50	3.67	3.22	1.44	3.06		2.50	2.33	3.28	3.50	3.56	2.22	2.17	62.72	71.28
Mean after 2005	3.15	3.35	3.35	3.20	1.05	2.95		2.40	2.10	2.70	2.95	3.05	2.25	2.25	60.15	68.35
Mean overall	3.37	3.42	3.50	3.21	1.24	3.00		2.45	2.21	2.97	3.21	3.29	2.24	2.21	61.37	69.74

TABLE 4 (CONTINUED)

AVERAGED SCORES FOR CERVICAL CANCER SCREENING GUIDELINES, BY SINGLE ITEM (CONTINUES).

	CLARITY AND PRESENTATION				APPLICABILITY			EDITORIAL INDEPENDENCE		TOTAL	
	RECOMMENDACTIONS NOT AMBIGUOUS	OPTIONS SPECIFIED	RECOMMENDACTION IDENTIFIABLE	TOOLS FOR APPLICATION	BARRIERS DISCUSSED	COSTS IMPLICATIONS IDENTIFIED	CRITERIA FOR AUDIT AND MONITORING	INDEPENDENCE	COMPETING INTEREST DISCLOSURE	TOTAL	STD SCORE
ONS 2005[5]	4	4	4	3.5	3	2	3.5	2	1	64	72.7
GiSCi 2006÷2007[41-42]	3	4	4	3.5	4	4	4	3.5	1	69	78.4
NHMRC 2005[31]	3.5	3.5	3.5	3.5	3	3	3.5	2	1	74.5	84.7
EC 2008[43]	2.5	4	2	4	4	3	4	1.5	0.5	58.5	66.5
ANAES 2002[25]	4	4	3.5	2.5	2.5	2.5	2.5	2	1	63	71.6
IARC 2005[32]	2.5	4	3.5	3	4	3.5	3	4	4	70	79.5
USPSTF 2003[28]	2	3	3	1.5	2	3	1.5	3.5	1	61	69.3
ACS 2002[24]	2.5	4	3	2	2	2.5	1.5	2	4	66.5	75.6
SICPCV 2006[39]	3.5	4	3.5	4	2	1	3	1.5	1	49	55.7
ASCCP 2006[37]	3	3	2	1.5	2	1	2	2	1	54	61.4
ICSI 2005÷2008[35-36]	4	3	4	3	2	1	2.5	3.5	3.5	68.5	77.8
FIGO 2000[21]	3	3.5	3.5	3	1	1	1	3	1	57.5	65.3
RER 2008[44]	3.5	4	4	4	2.5	2.5	3.5	2	1	65.5	74.4
SIV 2008[47]	3	3	4	2.5	1.5	2	2	2	2.5	53	60.2
NCCN 2006[38]	4	3.5	3.5	3	1	1	1	3	3.5	50.5	57.4
NHSCSP 2004[29]	3	3	2.5	4	3	3	4	2	1	55.5	63.1
PNLG 2002[26]	3	2.5	2.5	3.5	3	1.5	4	2	1	52.5	59.7
WHO 2006[40]	3.5	3	4	4	3.5	3.5	3.5	3	3.5	67	76.1
ISPO 2010[47]	3.5	2.5	3.5	2	2	2.5	2	3.5	4	66.5	75.6
Mean governmental	3.18	3.41	3.27	3.23	2.95	2.73	3.18	2.50	1.73	63.45	72.11
Mean Scientific societies	3.25	3.50	3.44	2.81	1.94	1.69	2.13	2.56	2.19	58.50	66.48
Mean USA	3.10	3.30	3.10	2.20	1.80	1.70	1.70	2.80	2.60	60.10	68.30
Mean Italian	3.36	3.43	3.64	3.29	2.57	2.21	3.14	2.36	1.64	59.93	68.10
Mean before 2005	3.06	3.50	3.22	2.94	2.61	2.44	2.72	2.50	1.67	62.72	71.28
Mean after 2005	3.35	3.40	3.45	3.15	2.45	2.15	2.75	2.55	2.15	60.15	68.35
Mean overall	3.21	3.45	3.34	3.05	2.53	2.29	2.74	2.53	1.92	61.37	69.74

TABLE 5

AVERAGED SCORES FOR BREAST CANCER SCREENING GUIDELINES, BY SINGLE ITEM (CONTINUES).

	SCOPE AND PURPOSE			STAKEHOLDER INVOLVEMENT				RIGOUR OF DEVELOPMENT							TOTAL	
	OBJECTIVES OF GGLL	CLINICAL QUESTION	TARGET PATIENTS	PROFES-SIONALS	PATIENTS	GGLL USERS	PILOT WITH USERS	SYSTEMATIC REVIEW	SELECTION CRITERIA	METHODS FOR RECOMMENDA-TIONS	HEALTH BENEFITS, RISK AND SIDE EFFECTS	LINK EVIDENCE - RECOMMENDA-TIONS	EXTERNAL REVIEW	UPDATING PROCEDURES	TOTAL	STD SCORE
FONCAM 2005[54]	2	3.5	2	1.5	1	1		1	1	1	3	1.5	1	1	41	46.6
EU 2006[56]	2.5	3.5	3	3	1	2		2.5	2	2	2	2	3.5	3	58	65.9
NHS BSP 2010[71]	3.5	3.5	4	3	2	2.5		2.5	2	2.5	3.5	3	2.5	2.5	63.5	72.2
GISMa 2006[62]	4	3	4	4	4	3.5		2.5	2	2.5	4	3.5	3	1.5	69	78.4
ACP 2007[60]	4	4	4	1	1	1		3.5	3.5	3	3	3.5	1	1	51.5	58.5
SIRM 2004[53]	3.5	3.5	2	1.5	1	1		2	1.5	2	2.5	2.5	2	1	43.5	49.4
RER 2008[66]	1.5	3	1	3	1	1.5		2	1.5	2	2.5	2	1	1	49	55.7
USPSTF 2009[70]	4	4	3.5	3	2	2.5		3.5	2.5	3.5	4	3.5	1	1	64.5	73.3
ACS 2003+2004[51-52]	4	4	4	3.5	2.5	2.5		3.5	3	2	3.5	4	3	1.5	61	69.3
ACR 2008 [63]	2.5	3	1	1	1	1		1	1	2	1.5	2	1	1.5	29.5	33.5
ANAES 2000 [48]	3	3	4	3	1	3		4	4	4	3	4	1	1	56	63.6
ISPO 2010[47]	3.5	3.5	4	4	1.5	3		3	3	3.5	4	3	3.5	1.5	66.5	75.6
Mean governmental	3.00	3.42	3.25	3.17	1.42	2.42		2.92	2.50	2.92	3.17	2.92	2.08	1.67	59.58	67.72
Mean Scientific societies	3.33	3.50	2.83	2.08	1.75	1.67		2.25	2.00	2.08	2.92	2.83	1.83	1.25	49.25	55.95
Mean USA	3.63	3.75	3.13	2.13	1.63	1.75		2.88	2.50	2.63	3.00	3.25	1.50	1.25	51.63	58.65
Mean Italian	2.90	3.30	2.60	2.80	1.70	2.00		2.10	1.80	2.20	3.20	2.50	2.10	1.20	53.80	61.14
Mean before 2005	3.13	3.50	3.00	2.38	1.38	1.88		2.63	2.38	2.25	3.00	3.00	1.75	1.13	50.38	57.23
Mean after 2005	3.19	3.44	3.06	2.75	1.69	2.13		2.56	2.19	2.63	3.06	2.81	2.06	1.63	56.44	64.14
Mean overall	3.17	3.46	3.04	2.63	1.58	2.04		2.58	2.25	2.50	3.04	2.88	1.96	1.46	54.42	61.83

TABLE 5 (CONTINUED)

AVERAGED SCORES FOR BREAST CANCER SCREENING GUIDELINES, BY SINGLE ITEM (CONTINUES).

	CLARITY AND PRESENTATION				APPLICABILITY			EDITORIAL INDEPENDENCE		TOTAL	
	RECOMMENDATIONS NOT AMBIGUOUS	OPTIONS SPECIFIED	RECOMMENDATION IDENTIFIABLE	TOOLS FOR APPLICATION	BARRIERS DISCUSSED	COSTS IMPLICATIONS IDENTIFIED	CRITERIA FOR AUDIT AND MONITORING	INDEPENDENCE	COMPETING INTEREST DISCLOSURE	TOTAL	STD SCORE
FONCAM 2005[54]	3	3.5	3	1.5	1	1.5	2.5	3	1.5	41	46.6
EU 2006[56]	2.5	2.5	1.5	4	3	2	4	4	2.5	58	65.9
NHS BSP 2010[71]	3.5	3.5	3.5	3.5	3	2.5	3.5	2.5	1	63.5	72.2
GISMa 2006[62]	4	3.5	3.5	2.5	3	3	2.5	3	2.5	69	78.4
ACP 2007[60]	3	2	3.5	2	1	1	1.5	3	1	51.5	58.5
SIRM 2004[53]	2.5	2	3	2	2	1.5	1.5	2	1	43.5	49.4
RER 2008[66]	3.5	4	3.5	3.5	2	2	3.5	3	1	49	55.7
USPSTF 2009[70]	4	3	3.5	2	2.5	3	2.5	3.5	2.5	64.5	73.3
ACS 2003+2004[51-52]	3.5	3.5	3.5	2	1	1	2	2.5	1	61	69.3
ACR 2008[63]	1	1	1	1	1.5	1	1.5	1	1	29.5	33.5
ANAES 2000[48]	3	2	3	2	1	1	2	3	1	56	63.6
ISPO 2010[44]	3.5	2.5	3.5	2	2	2.5	2	3.5	4	66.5	75.6
Mean governmental	3.33	2.92	3.08	2.83	2.25	2.17	2.92	3.25	2.00	59.58	67.72
Mean Scientific societies	2.83	2.58	2.92	1.83	1.58	1.50	1.92	2.42	1.33	49.25	55.95
Mean USA	2.88	2.38	2.88	1.75	1.50	1.50	1.88	2.50	1.38	51.63	58.65
Mean Italian	3.30	3.10	3.30	2.30	2.00	2.10	2.40	2.90	2.00	53.80	61.14
Mean before 2005	3.00	2.75	3.13	1.88	1.25	1.25	2.00	2.63	1.13	50.38	57.23
Mean after 2005	3.13	2.75	2.94	2.56	2.25	2.13	2.63	2.94	1.94	56.44	64.14
Mean overall	3.08	2.75	3.00	2.33	1.92	1.83	2.42	2.83	1.67	54.42	61.83

TABLE 6

AVERAGED SCORES FOR COLORECTAL CANCER SCREENING GUIDELINES, BY SINGLE ITEM (CONTINUES).

	SCOPE AND PURPOSE			STAKEHOLDER INVOLVEMENT				RIGOUR OF DEVELOPMENT							TOTAL	
	OBJECTIVES OF GGLL	CLINICAL QUESTION	TARGET PATIENTS	PROFESSIONALS	PATIENTS	GGLL USERS	PILOT WITH USERS	SYSTEMATIC REVIEW	SELECTION CRITERIA	METHODS FOR RECOMMENDATIONS	HEALTH BENEFITS, RISK AND SIDE EFFECTS	LINK EVIDENCE - RECOMMENDATIONS	EXTERNAL REVIEW	UPDATING PROCEDURES	TOTAL	STD SCORE
ONS 2005[5]	4	4	4	3	1	2.5		2	2	2.5	4	3	1	1	61.5	69.9
CPO 2001[74]	3.5	3.5	2	4	2	3.5		3	3	3.5	3	2.5	3.5	2.5	71	80.7
ASSR 2002[75]	2.5	3.5	2.5	3.5	1	1.5		2.5	2.5	4	3	2.5	1.5	2	60	68.2
ACS 2008[85]	2	3.5	2.5	3.5	1	2		2.5	1.5	2	4	2.5	3	3.5	57	64.8
ACN 2005[77]	4	4	3	4	2	3		3.5	3	3.5	3	3.5	4	4	71	80.7
ISPO 2010[47]	3	4	3.5	4	2	2		2	1.5	3	3.5	2.5	3	1.5	65	73.9
NHS BCSP 2008/2010[84]	4	3.5	4	2	1	1		2.5	2	2	3	1.5	1	1	53	60.2
NCCN 2011[87]	2	3.5	3.5	4	2	3		2.5	2	3.5	3.5	3	2.5	3	62	70.5
SIGN 2003[76]	3	2.5	2.5	4	3	2.5		4	4	3.5	2.5	3	4	2	64	72.7
USPSTF 2008[83]	3	4	4	4	1	1.5		4	4	4	4	3	3.5	3	72.5	82.4
CTFPHC 2001[73]	4	4	3	3.5	1	1		2.5	4	4	2.5	3	4	2.5	61.5	69.9
ACG 2009[80]	3	2	4	2	1	1		2.5	2	3	3	3	3.5	2	52	59.1
ASP 2001[72]	3.5	4	3.5	1	1	1		3	2.5	2.5	3	3.5	1	1.5	51	58.0
IARC 2010[86]	3.5	4	3.5	3.5	1	3.5		4	4	4	3.5	3.5	4	3.5	80	90.9
Mean governmental	3.50	3.73	3.23	3.32	1.45	2.09		3.00	2.95	3.32	3.18	2.86	2.77	2.23	64.59	73.41
Mean Scientific societies	2.33	3.00	3.33	3.17	1.33	2.00		2.50	1.83	2.83	3.50	2.83	3.00	2.83	57.00	64.80
Mean USA	2.50	3.25	3.50	3.38	1.25	1.88		2.88	2.38	3.13	3.63	2.88	3.13	2.88	60.88	69.20
Mean Italian	3.40	3.80	3.10	3.10	1.40	2.10		2.50	2.30	3.10	3.30	2.80	2.00	1.70	61.70	70.14
Mean before 2005	3.57	3.64	2.93	3.29	1.57	2.14		2.93	3.00	3.36	3.00	3.00	2.71	2.21	62.86	71.44
Mean after 2005	2.93	3.50	3.57	3.29	1.29	2.00		2.86	2.43	3.07	3.50	2.71	2.93	2.50	63.07	71.69
Mean overall	3.25	3.57	3.25	3.29	1.43	2.07		2.89	2.71	3.21	3.25	2.86	2.82	2.36	62.96	71.56

TABLE 6 (CONTINUED)

AVERAGED SCORES FOR COLORECTAL CANCER SCREENING GUIDELINES, BY SINGLE ITEM (CONTINUES).

	CLARITY AND PRESENTATION			APPLICABILITY			EDITORIAL INDEPENDENCE		TOTAL	
	RECOMMENDATIONS NOT AMBIGUOUS	OPTIONS SPECIFIED	RECOMMENDATION IDENTIFIABLE	TOOLS FOR APPLICATION	BARRIERS DISCUSSED	COSTS IMPLICATIONS IDENTIFIED	CRITERIA FOR AUDIT AND MONITORING	INDEPEN-DENCE	COMPETING INTEREST DISCLOSURE	TOTAL	STD SCORE
ONS 2005[5]	4	4	4	3.5	2.5	2.5	3	3	1	61.5	69.9
CPO 2001[74]	4	3.5	4	3	4	4	4	4	1	71	80.7
ASSR 2002[75]	3	3.5	3	3.5	3	3	4	3.5	1	60	68.2
ACS 2010[85]	2.5	4	2.5	2	2.5	2	1	3	4	57	64.8
National Health Australia 2005[77]	3.5	4	3.5	2.5	2.5	2.5	1.5	2.5	4	71	80.7
ISPO 2010[47]	4	3	4	2.5	2.5	2.5	3	4	4	65	73.9
NHS BCSP 2008/2010 [84]	4	1	4	4	2.5	1	4	3	1	53	60.2
NCCN 2011[87]	3	4	3	2.5	1	2	1	3.5	4	62	70.5
SIGN 2003[76]	3	2.5	3	2.5	2.5	1.5	1	3.5	4	64	72.7
USPSTF 2008[83]	3.5	4	4	3	2	3.5	1.5	4	4	72.5	82.4
CTFPHC 2001[73]	3.5	4	4	1.5	2	2	1	3.5	1	61.5	69.9
ACG 2008[80]	3.5	3.5	3	1.5	2	2	1	2.5	1	52	59.1
ASP 2001[72]	3.5	3	1.5	1.5	2.5	2.5	1	3.5	1	51	58.0
EC 2010[86]	4	4	4	3.5	4	4	4	3	4	80	90.9
Mean governmental	3.64	3.32	3.55	2.82	2.73	2.64	2.55	3.41	2.36	64.59	73.41
Mean Scientific societies	3.00	3.83	2.83	2.00	1.83	2.00	1.00	3.00	3.00	57.00	64.80
Mean USA	3.13	3.88	3.13	2.25	1.88	2.38	1.13	3.25	3.25	60.88	69.20
Mean Italian	3.70	3.40	3.30	2.80	2.90	2.90	3.00	3.60	1.60	61.70	70.14
Mean before 2005	3.50	3.50	3.29	2.57	2.71	2.57	2.21	3.36	1.86	62.86	71.44
Mean after 2005	3.50	3.36	3.50	2.71	2.36	2.43	2.21	3.29	3.14	63.07	71.69
Mean overall	3.50	3.43	3.39	2.64	2.54	2.50	2.21	3.32	2.50	62.96	71.56

DISCUSSION

This is the only study presenting a quality appraisal of a large sample of documents producing guidelines on oncologic screening.

Despite the fact that this is not a representative sample of all the existing international guidelines and other similar documents, it is interesting to note that we found some differences in quality: documents on breast cancer screening had lower scores, as had guidelines produced by scientific societies. We analysed which domain scored better in each of the three screenings for the two types of producers and why.

The fields with the highest scores for the guidelines for all three cancer screenings were those included in the *"scope and purpose"* part of the AGREE instrument, which considers the definition of the objectives, the clinical problem, and the target population. This result is the logical consequence of the attention that the scientific screening community has paid to defining the target population and the measurability of the attainable health outcomes [88].

The items included in the field *"stakeholders involvement"* were, instead, the ones that scored the lowest for all the guidelines analysed. In particular, patients were involved in the drafting of almost no document, while professionals from different disciplines were involved in the drafting of many. This reflects the scope of the guidelines analysed: in fact, screenings, as preventive interventions, are by definition directed towards a healthy population and not to *"patients"*. Instead, they are by nature multidisciplinary and thus professionals from different disciplines are always involved in writing guidelines. Nevertheless, this item had lower scores for guidelines produced by scientific societies.

For the guidelines on cervical cancer screening, the items included in the topic *"rigor of development"* (in particular, those related to the systematic review, the inclusion criteria, and methods of the recommendations) obtained low scores (slightly higher than 2 on a scale of 1 to 4), reflecting the fact that evidence on Pap test screening efficacy, based on large ecological studies and time series published decades ago, is considered a given by many guideline authors and a proper systematic review was not reported in many documents. These items greatly influenced the final score, although for many of the basic recommendations, especially in cervical screening, taking the evidence for Pap test effectiveness as a given may not affect the quality.

These results were very similar to those obtained in the assessment of the guidelines on breast cancer screening, although several trials and meta-analyses in this field are available. In particular, after the publication of the first Cochrane review written in 2001 by Olsen and Gøtzsche [89], the topic was very hot and mammography efficacy could not be considered a given.

The item on health benefits, side effects, and risks scored high in the assessment of guidelines on cervical cancer screening: almost all the documents emphasized the risk of overtreatment. Regarding breast cancer, since the international scientific community continues to debate possible risks associated with mammography due to false positives and over-diagnosis, this particular item obtained high scores.

The guidelines on colorectal cancer screening revealed scores similar to the two screening guidelines mentioned above. It is interesting to note, however, that here the item on the assessment of potential risks carried a higher average score, reflecting the attention that the scientific community has always paid to the prevention of harm in this particular screening program. This aspect is crucial especially for those guidelines recommending endoscopic tests as the first level test [82, 83, 85, 86].

The items on external review and updating were influenced by the fact that many documents were produced by government agencies as legal acts. The government approval process may conflict with periodic updates and the peer review process, particularly in Italy but also in other countries. For guidelines on colorectal cancer screening, these items scored higher than did those for breast and cervical cancers. In fact, documents of a legislative nature are less frequent for colorectal screening, meaning that the recommendations were not subject to government approval that often prevented peer review and periodic updating.

Regarding the items included in the *"clarity and presentation"* domain, the scores were quite homogeneous and high for all the documents assessed, with a few exceptions (e.g., Guidelines of the American College of Radiologists) [63]. In general, Italian documents

obtained the lowest scores for these items.

The category of *"applicability"* obtained different scores according to the kind of cancer being screened. The scores were very heterogeneous for cervical cancer screening guidelines: some of them provide tools to monitor the application [23, 43, 44, 47], while most of the others do not take them into account.

For the guidelines on breast cancer screening, this item received low mean scores. Although some guidelines provide tools to monitor the implementation and the quality of screening programs, the guidelines developed by scientific societies, especially by the American societies [60,63], do not even take into account the possible barriers to screening programme implementation.

For both cervical and breast cancer screening, documents from those national health care systems that offer organised screening programmes have better scores with regard to auditing and monitoring than U.S. documents do.

As regards the identification of barriers for colorectal cancer screening, the average score rose thanks to the documents that addressed the problem of screening participation.

Another issue considered by some documents was the sufficient availability of endoscopic resources to meet the coverage needs of the population [72, 78].

A preface is needed to explain how we interpreted the item *"independence of the editor"*. The two reviewers initially agreed that the type of conflicts of interest that most often occurs in this area is not typically due to any economic gain to the industry, but reflects those of professional groups and third party payers. So the greatest degree of independence is when none of the professional categories is dominant, there are no pressures by manufacturers of devices, and the third party payer does not directly influence the final product. When one or more of these elements is missing, the degree of independence decreases. The result is that few European documents are not directly influenced by a third party payer, while the U.S. documents are often influenced by categories of professionals who have a clear interest in providing more or fewer procedures.

Unlike the guidelines on breast and cervical cancer screening, some older government documents for colorectal cancer (mostly European and Canadian) are not directly influenced by a third party payers, as they are commissioned by government agencies to organizations for future implementation and thus do not imply immediate costs. In contrast, the documents by scientific societies (more numerous in the U.S.) are often influenced by groups of professionals who have a clear interest in providing certain procedures.

In more recent documents, the implementation of organised screening programs has led government agencies of universal health services to more strictly control the recommendations in documents directly influencing service organization, workload, and costs.

Surprisingly, more recent guidelines did not obtain higher scores, in contrast with many other fields, where clear improvements have been observed.

Also of interest is that documents produced by governmental agencies obtained higher scores in general, with many Italian regional guidelines in this group. One would expect the quality of these latter to be low due to the local level of the professionals included in the working groups yet this did not appear to be so.

The superiority of governmental agency documents is in line with the relevant literature. This appears to be due to their higher level of independence and to their multidisciplinary approach, ensured by publicly funded initiatives, compared to those by scientific societies, which may protect some professions [90].

Limitations

The major limit of this study is that it is not based on a systematic collection and review of all the documents providing recommendations for cancer screening. This is the consequence of our attempt to include documents that are truly influential on public health services, such as national and regional recommendations and laws on screening programs implementation, but which are usually only published as grey literature. To include a good representative sample of these documents and in accordance with the mandate received by the Italian Ministry of Health, we decided to limit our search to those documents that are influential in Italy, for which we had more expertise and because the vast majority were more accessible. Furthermore, the criteria to decide which documents were suitable for AGREE

appraisal were quite subjective (see appendix on excluded studies). In fact, we did not find any previous experience on using the AGREE instrument for such a broad interpretation of the documents producing recommendations.

The study started in 2007, and the first set of guidelines was evaluated in 2008. As the new version of the instrument, AGREE II, [16] had not yet been released, we used the first version.

Based on the data presented above, AGREE can be applied to guidelines for preventive interventions, as other studies have already shown [91-95], and to screening in particular [96-98]. Nevertheless, some of its items appear not to be applicable and others should be adjusted or rewritten to take into account the specific characteristics of preventive medicine guidelines. Some of the changes actually occurred in the AGREE II version: [16] item 7 on piloting was dropped, the "clinical problem" was reworded as "health problem," and "patient involvement" was changed to "patient /citizen involvement". Nevertheless, the difficulties we found in interpreting the conflict of interest items are not addressed by AGREE II, in particular how to take into account the competing interests of the third payer.

We tried to correlate the quality score obtained by the documents, overall or in singular domains, with the country of origin, or with the health system in the country, with the authorship, governmental or not. We did not have enough statistical power to prove any of these correlations and they should thus be considered mostly anecdotic.

CONCLUSIONS

Two kinds of health systems produced different guidelines and documents reporting recommendations: in the USA, most of the documents are from scientific societies, while in Europe, most are from governmental agencies. The two kinds differ in terms of the main recommendations given, in the quality of the documents, in the constraints they have, and in the competing interests of the authors and sponsors that emerge. Differences in the health system are particularly important in preventive guidelines because the role of the health provider is completely based on whether the national health system implements screening programs or not.

APPENDIX 1 - SEARCH METHODS AND SOURCES
Guideline search strategy and sources: Cervical, Breast and Colorectal cancer screening

PubMed search strategy:

Based on the strategy adopted by the colorectal cancer Cochrane group EPOC:
"guideline"[Publication Type] OR "guidelines as topic"[MeSH Terms] OR "guidelines"[All Fields] AND
"mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] ("early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields] OR ("screening"[All Fields] AND "cancer"[All Fields]) OR "screening cancer"[All Fields]))

Colorectal Cancer:
colorectal neoplasm*
colorect* neoplasm*
colorect* cancer
colorect* canc*
colorect* carcinoma
colorectal carcinom*
colorect* carcinom*
rect* neoplasms
rectal neoplasm*
rect* neoplasm*
rectal cancer
rect* cancer
rectal canc*
rect* canc*
rect* carcinoma
rectal carcinom*
rect* carcinom*
    OR/

Breast cancer (Cochrane breast cancer group)
breast neoplasms/
breast/
breast.tw.
    mammary neoplasms/

OR/
neoplasm*
cancer*
tumour*
tumor*
carcinoma*
adenocarcinoma*
sarcoma*
dcis
ductal
infiltrating
intraductal
lobular
medullary
OR/

Cervical cancer (Cochrane Gynaecological cancer group)
cervical carcinoma*
cervical cancer*
cervix carcinoma*
cervix cancer*.

The following guidelines databases and web sites were searched:
- National Guideline Clearinghouse
- National Institute Clinical Excellence
- Agency for Healthcare Research and Quality (AHRQ)
- Centre for Reviews and Dissemination
- New Zealand Guidelines Group
- ACP Guidelines Web site
- Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES)
- National Research and Development Centre for Welfare and Health (STAKES)
- Scottish Intercollegiate Guidelines Network
- Guidelines International Network GIN
- Canadian Task Force on Preventive Health Care (CTFPHC)
- National Institute for Health and Clinical Excellence (UK)
- Centers for Disease Control and Prevention (CDC)
- National Health and Medical Research Council - NHMRC (Australia)
- European Union Public Health
- Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS-Quebec)
- U.S. Preventive Services Task Force
- Scottish Intercollegiate Guidelines Network

National level Italian websites

- Ministero Salute CCM
- Istituto Superiore di Sanità
- Age.Na.S. - Agenzia Nazionale per i Servizi Sanitari Regionali
- Osservatorio Nazionale screening

Regional Italian websites
- Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica (CPO) in Piemonte
- IOV - Istituto Oncologico Veneto - IRCCS
- Istituto per lo Studio e la Prevenzione Oncologica Toscana
- ITT - Istituto Toscano Tumori
- Agenzia Sanità Pubblica Lazio
- All the regional Health Authority web sites (21)

Italian scientific societies (also consulted for checking the search results)
- GISCi - Gruppo Italiano Screening del Cervicocarcinoma
- GISMa - Gruppo Italiano Screening Mammografico
- GISCoR - Gruppo Italiano Screening del Colon Retto
- SOCIETA' ITALIANA DI COLPOSCOPIA E PATOLOGIA CERVICO VAGINALE
- Società italiana di virologia
- Società italiana di ginecologia e ostetricia
- Società Italiana di Anatomia Patologica e Citologia diagnostica
- FISMED, Federazione delle Società delle Malattie dell'Apparato Digerente: Associazione Italiana Gastroenterologi ed Endoscopisti Ospedalieri, Società Italiana Endoscopia Digestiva, Società Italiana di Gastroenterologia
- S.I.CI - Società Italiana di Citologia
- SLOG - Società Lombarda di Ostetricia e Ginecologia
- AIOM - Associazione Italiana di Oncologia Medica

International Scientific Societies
- American Cancer Society Guidelines for the Early Detection of Cancer
- National Cervical Screening Programme (New Zealand)
- NHS Cancer Screening Programmes (UK)
- WHO sezioni Cancer e Women's Health
- IARC - INTERNATIONAL AGENCY FOR RESEARCH ON CANCER
- NIHR Health Technology Assessment programme

APPENDIX 2 - EXCLUDED STUDIES

AUTHOR YEAR	TITLE	REASON FOR EXCLUSION FROM AGREE EVALUATION
WHO 2006	Guidelines for management of breast cancer	Focused only on surgical and medical treatment
Regione Piemonte 2002	Tumore della mammella. Linee guida clinico organizzative per la Regione Piemonte.	Organisational GGLL for breast units
Australia 2008	The Australian Institute of Health and Welfare and the Australian Government Department of Health and Ageing for the BreastScreen Australia Program. BreastScreen Australia monitoring report 2004–2005	The document is organised as a report of performance indicators.
Società Italiana di Radiologia Medica. 2003	Stato dell'arte della mammografia digitale.	Only for digital mammography
Regione Lombardia 2007	I programmi di screening mammografico in Regione Lombardia.	Organised as a law, does not report evidence
Provincia autonoma di Trento 2009	Il programma di diagnosi precoce del tumore della mammella: una azione di sanità pubblica a protezione dell'individuo e della comunità.	Organised as a law, does not report evidence
Associazione Italiana Oncologi Medici 2008	Linee guida. Neoplasie della mammella	Focused only on medical treatment
CDC	Mammograms & Breast Health. An Information Guide for Women.	Only informative - a public health service. Does not report evidence
Advisory Committee on Cancer Prevention 1999	Recommendations on cancer screening in the European Union.	Organised as a law, does not report evidence
Gruppo italiano screening colorettale (GISCoR). 2009	Raccomandazioni per la determinazione del sangue occulto fecale (SOF) nei programmi di screening per il carcinoma colorettale. Metodo immunologico.	Focused on laboratory quality control for FOBT
Haute Autorité de Santé. 2008	Tumeur maligne, affection maligne du tissu lymphatique ou hématopoïétique. Cancer colorectal.	Focused only on surgical and medical treatment
Regione Emilia Romagna.	Linee di indirizzo per la promozione della qualità nel II livello diagnostico-terapeutico del programma di screening dei tumori del colon retto in Regione Emilia-Romagna	Focused only on endoscopy
Regione Emilia Romagna	Programma di screening regionale per la diagnosi precoce e la prevenzione dei tumori del colon-retto: Documento di consenso per la diagnosi istopatologica delle lesioni tumorali e pre-tumorali del colon-retto	Focused only on pathology classification
Forbes et al Cochrane 2002	Interventions targeted at women to encourage the uptake of cervical screening.	Focused only on methods to increase participation.
NICE 2003	Guidance on the use of liquid-based cytology for cervical screening	Focused only on the use of liquid-based cytology
Regione autonoma Friuli Venezia Giulia 2005	Screening Oncologici in: Piano regionale della prevenzione.	Organised as a law, does not report evidence
Regione Lombardia. 2000	Linee guida generale per l'organizzazione di programmi di screening oncologico e per lo screening del carcinoma della cervice uterina	Organised as a law, does not report evidence

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