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Review Article

The association between adherence to cancer screening programs and health literacy: A systematic review and meta-analysis

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ABSTRACT

The effectiveness of a cancer screening program relies on its adherence rate. Health literacy (HL) has been investigated among the factors that could influence such participation, but the findings are not always consistent. The aim of this meta-analysis was to summarize the evidence between having an adequate level of HL (AHL) and adherence to cancer screening programs. PubMed, Scopus, and Web of Science were searched. Cross-sectional studies, conducted in any country, that provided raw data, unadjusted or adjusted odds ratio (OR) on the associations of interest were included. The quality of the studies was assessed with the Newcastle-Ottawa Scale. Inverse-variance random effects methods were used to produce pooled ORs and their associated confidence interval (CI) stratified by time interval (e.g., undergoing screening in the last period, or at least once during lifetime) for each cancer type, considering unadjusted and adjusted estimates separately. A sensitivity analysis was performed for those studies providing more estimates. Overall, 15 articles of average-to-good quality were pooled. We found a significant association between AHL and higher screening participation for breast, cervical and colorectal cancer, independently of other factors, both overall ($N = 7$, aOR = 1.73; 95% CI: 1.27–2.36; $N = 3$, aOR = 1.64; 95% CI: 1.30–2.09; and $N = 5$, aOR = 1.25, 95% CI: 1.12–1.39, respectively) and in most time-stratified analyses. The sensitivity analyses confirmed these results. Health literacy seems to be critical for an effective cancer prevention. Given the high prevalence of illiterate people across the world, a long-term action plan is needed.

1. Introduction

Population-based screening programs have been identified as a cost-effective strategy for detecting breast, cervical and colorectal cancer at an early and often treatable stage with a consequent reduction in their mortality and morbidity rates (Ratushnyak et al., 2019; Lansdorp-Vogelaar et al., 2011). Recent statistics estimate that screening every two years can reduce breast cancer deaths by 26% for every 1000 women tested (Mandelblatt et al., 2016). Similarly, the National Cancer Institute reports that screening with fecal occult blood test has a magnitude of effect on colorectal cancer mortality of 15–33% (PDQ® Screening and Prevention Editorial Board, 2021a), while regular Pap test screening decreases cervix cancer incidence and mortality by at least 80% in an appropriate population of women (PDQ® Screening and Prevention Editorial Board, 2021b). Several worldwide initiatives promote and support the implementation of organized screening programs: the 2020 World Cancer Report of the World Health Organization (WHO) International Agency for Research on Cancer identifies screening as a pillar among preventive strategies (Wild et al., 2020); in the United States, the initiative *Healthy People* 2020 advocates for a continuous improvement in screening indicators to decrease the overall burden of cancer (Healthy People, 2020); in the European Region, the WHO mentions the screening programs as one of the crucial strategies of the Action Plan for the Prevention and Control of Non-Communicable Diseases 2016–2025 (World Health Organization (WHO) Regional Office for Europe, 2016).

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Nevertheless, the effectiveness of a screening program strongly relies on its adherence rate (Chubak and Hubbard, 2016; Camilloni et al., 2013; D'Andrea et al., 2020). There are different ways to define and measure it (Chubak and Hubbard, 2016), but increasing the proportion of individuals who undergo cancer screening tests is a common long-lasting challenge (Healthy People, 2020; Camilloni et al., 2013). Several studies have attempted to identify the modifiable factors that may influence such participation (Zapka et al., 2003). Research shows that patient-level barriers include socioeconomic, cultural, and psychosocial factors (White et al., 2019; Curry et al., 2003; Pelullo et al., 2021), whose unequal distribution among populations could be responsible for the higher cancer mortality and morbidity rates registered in disadvantaged people (White et al., 2019). Lately, also health literacy (HL) has been proposed as a predictor of an individual's health status (Stormacq et al., 2019). It can be broadly defined as "[people's ability] to make judgements and take decisions in everyday life concerning healthcare, disease prevention and health promotion to maintain or improve their quality of life" (Sørensen et al., 2012), and a low level of HL has been associated with several adverse health outcomes, such as increased hospitalization, higher rates of medication non-adherence, and lower uptake of preventive interventions, including cancer screening programs (Berkman et al., 2011).

Within this context, a few studies have investigated HL and cancer screening participation over the last years (Oldach and Katz, 2014), but they have applied heterogeneous methods (Berkman et al., 2011). Also, despite some of them concluding that an adequate level of HL may be associated with higher screening participation rates for breast, cervical, and colorectal cancer (Pagán et al., 2011; Sentell et al., 2013; Kobayashi et al., 2013; Li et al., 2018), the findings are not always consistent (Oldach and Katz, 2014), especially for the latter (Miller et al., 2007; Peterson et al., 2007). Additionally, small sample sizes and a focus on racial and ethnic minorities may have limited the generalizability of the results (Horshauge et al., 2020). The aim of this systematic review and meta-analysis was to summarize the evidence on the association between adequate HL (AHL) and adherence to cancer screening programs, providing a quantitative synthesis of the results and supporting the implementation of target-specific interventions.

2. Methods

This study was performed according to the Cochrane Handbook for systematic reviews and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009; Higgins et al., 2021). The review protocol was registered at PROSPERO, identifier CRD42020175462. Because this study did not involve primary data collection, the protocol was not submitted for institutional review board approval and did not require informed consent.

2.1. Search strategy, study selection and inclusion criteria

Three reviewers searched PubMed, Scopus, and Web of Science from database inception to January 2nd, 2021 using the following terms: ("health literacy") AND (cancer* OR tumo* OR neoplasm* OR metastas* OR oncolog*). The string was adapted to fit the search criteria of each database (Supplementary Table 1). No restriction was applied. Duplicate articles were removed, and the title and abstract of all collected records were screened. Studies that clearly did not meet the inclusion criteria were excluded. Full texts of potentially relevant articles were retrieved and independently examined by two researchers. The reference lists of retrieved articles were also searched to identify other potentially relevant studies. Disagreements were resolved through discussion and reasons for exclusion recorded.

Eligible articles had a cross-sectional design, were conducted in any country, were reported in English or Italian based on co-author language abilities and investigated the association between AHL and adherence to screening programs for any cancer type providing raw data, unadjusted or adjusted odds ratios (ORs). The definition of HL proposed by Sorensen et al. (Sørensen et al., 2012) was adopted. Hence, articles that investigated only specific HL (e.g., oral literacy), that assessed only specific HL sub-domains without providing a general measurement or in which data on the association between AHL and cancer screening adherence in its target population(s) were not retrievable or were otherwise expressed were excluded.

2.2. Data collection and quality assessment

For each eligible record, two reviewers independently used a standardized data abstraction form to extract the following information: first author, year of publication, country, cancer type (breast, cervical, colorectal, or prostate), cancer screening test, sample size, key features of the target population (ethnicity, recruitment process), assessment of the screening participation (self-reported, record linkage, other), tool used to assess HL, time interval considered within the study: i) adherence to the screening program in the last period (i.e., for breast cancer, in the last 1–2 years; for cervical cancer, in the last 3 years; for colorectal cancer, fecal occult blood test [FOBT] in the last year, or sigmoidoscopy [SS] in the last 5 years, or colonoscopy [CS] in the last 10 years) or ii) at least once during lifetime, and proportion of people with AHL (if available). Supplementary Table 2 illustrates the characteristics of the HL instruments that were used to assess HL and the corresponding cut-off scores that were considered to identify people with AHL. As outcome measures, depending on data availability, we collected raw data, unadjusted and/or adjusted estimates (i.e., ORs) and their associated 95% confidence interval (CI), together with adjustment factors (if available).

Two independent authors performed the quality assessment of the articles included in the systematic review using an adapted version of the Newcastle-Ottawa Scale for Evaluating Cross-Sectional/Survey Studies (Wells et al., 2014; Modesti et al., 2016). Discrepancies were resolved by consensus. Articles were considered of high quality when the total score was ≥ 7, fair quality if the score was ≥ 5 and <7, poor quality if the score was lower than 5.

Results regarding the main features of the included records were narratively presented according to the cancer type.

2.3. Statistical analysis

When association estimates were not reported as ORs, but raw data were sufficient to compute these values (i.e., in cross-tabular format), they were transformed into ORs using Stata software, version 16. To account for between-study heterogeneity, random-effects methods with inverse-variance weighting were used to produce pooled ORs and their 95% CI considering separately unadjusted and adjusted estimates. Since in a few articles (Li et al., 2018; Sentell et al., 2015; Scott et al., 2002; Guerra et al., 2005a) the same population was investigated with respect to different cancer screening programs, we conducted separate analyses for breast, cervical, and colorectal cancer, whereas results for adherence to prostate cancer screening were narratively presented given that only one study (Li et al., 2018) quantified the relationship. Each analysis was stratified according to the time interval considered (i.e., undergoing screening in the last period or at least once during lifetime). The Cochran χ^2 test and the I^2 metric were used to test for heterogeneity (Higgins et al., 2003). Heterogeneity was considered statistically significant at p-value <0.05, and substantial heterogeneity was defined as $I^2 > 50\%$. When a study reported data on adherence to the same cancer screening program both in the last period and at least once during lifetime, we firstly pooled adherence to the screening program ever, and data from adherence to the screening program in the last period was used in sensitivity analysis. Also, since one article (Guerra et al., 2005b) provided data on adherence to screening program using two different screening tests (i.e., FOBT vs. SS or CS), we included in the main analyses the most frequently used (FOBT), whereas adherence to SS or CS was used in the sensitivity analysis. Since the number of studies retrieved was always lower than 10 within each analysis, we followed the Cochrane's suggestion (Higgins et al., 2021) and the small study effect, potentially caused by publication bias, was not assessed. For a similar reason, given the limited availability of studies across all types of cancer, meta-regression analyses were not performed. A p-value <0.05 was considered statistically significant. All analyses were performed using Stata (StataCorp LLC, 4905 Lakeway Drive, College Station, Texas, USA), version 16.0.

3. Results

3.1. Study selection

Overall, 3966 records were identified by database searching (Fig. 1). After duplicates removal and screening by title and abstract, 138 articles were assessed for eligibility, from which 125 were excluded with reasons. Five records from manual search were added to the previous 13, for a total of 18 articles meeting the inclusion criteria. However, three of them (Sentell et al., 2014; Heberer et al., 2016; Solmi et al., 2015) evaluated the same population as other articles (Kobayashi et al., 2013; Sentell et al., 2015; Komenaka et al., 2015) but in a lower number of people and therefore were excluded, for a total of 15 articles ultimately included in the meta-analysis.

3.2. Characteristics of the studies by cancer type

3.2.1. Breast cancer

Seven articles investigated the relationship between HL and adherence to breast cancer screening test, all but one (Yilmazel, 2016) conducted in the United States (US) (Pagán et al., 2011; Li et al., 2018; Sentell et al., 2015; Scott et al., 2002; Guerra et al., 2005a; Komenaka et al., 2015) (Table 1). Attendance to mammography was evaluated both in the entire life and in the last period in three studies (Pagán et al., 2011; Li et al., 2018; Guerra et al., 2005a), only in the entire life in two studies (Komenaka et al., 2015; Yilmazel, 2016) and only in the last period in other two cases (Sentell et al., 2015; Scott et al., 2002). In more than half of the studies the authors enrolled a large number of people (i. e., more than 1000 women) (Li et al., 2018; Sentell et al., 2015; Scott

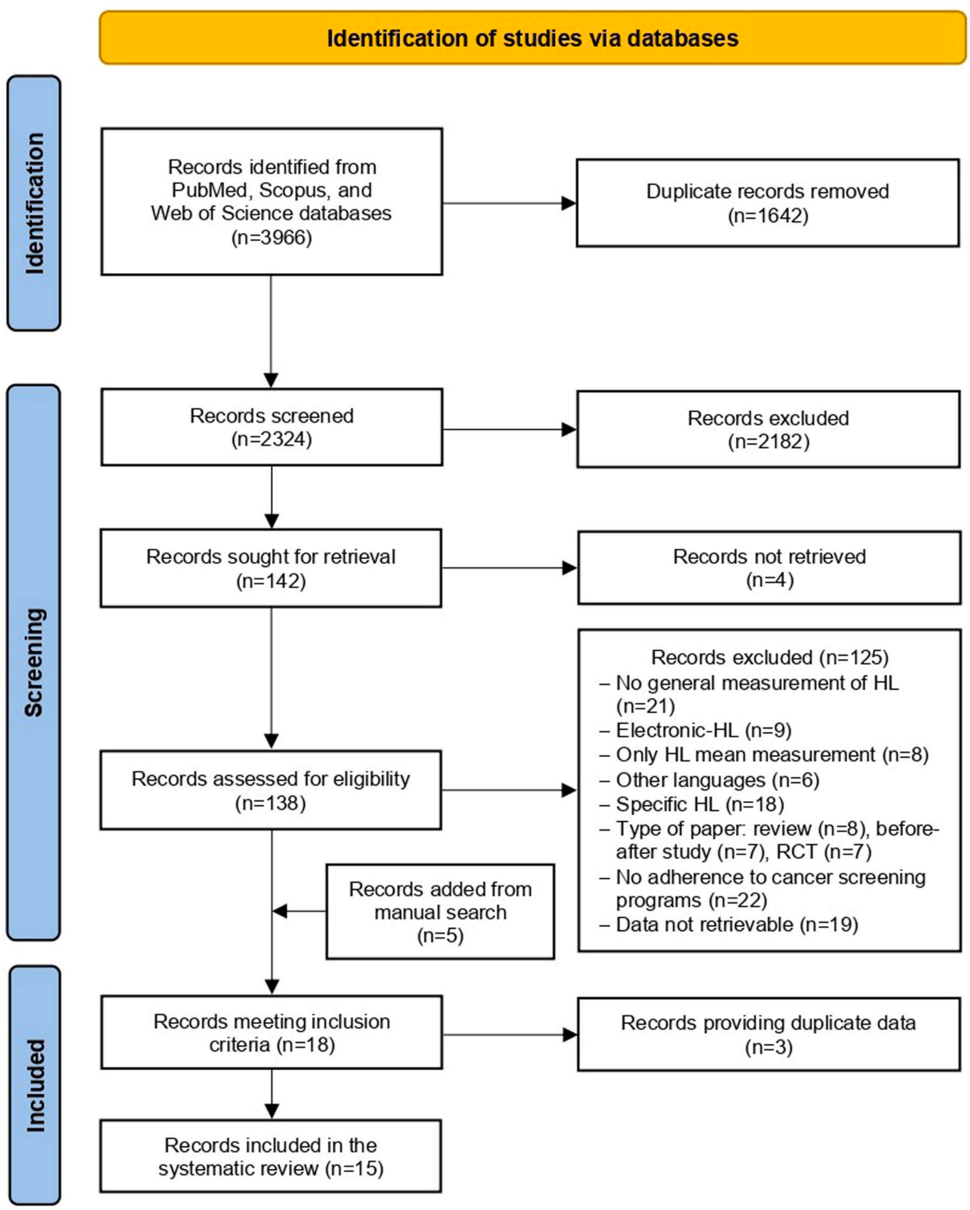

Fig. 1. PRISMA flow diagram of the review process. HL: Health Literacy. RCT: Randomized Controlled Trial.

Table 1
Key characteristics of the studies included in the systematic review by cancer type.

Author year, country	Screening test	Time interval (sample size)	Target population	Screening adherence	HL tool[§]	Adjustment factors[¥]	QS
Breast cancer							
Scott 2002, US	Mammography	In the last period* (N = 1545)	Medicare enrollees' women from a PBS	SR	s-TOFHLA	ASR, income, education, occupation, MMSE, physician visit, chronic condition	8
Guerra 2005, US	Mammography	In the entire life (N = 97) In the last period* (N = 97)	Latina women from a community clinic	SR	s-TOFHLA	Age, insurance, education, acculturation	8
Pagan 2011, US	Mammography	In the entire life (N = 722) In the last period* (N = 722)	Mexican American women from a PBS	SR	TOFHLA	AII, education, acculturation, marital status	8
Komenaka 2015, US	Mammography	In the entire life (N = 1664)	Women from clinics serving racial-ethnic minority groups	SR	NVS	AII, race, education, menopause, language, occupation, smoking status, BMI, marital status, alcohol and drug use	10
Sentell 2015, US	Mammography	In the last period* (N = 11,163)	Asian and white women from a PBS	SR	CHIS questions	AII, race, education, language, marital status, community level factors	7
Yilmazel 2016, Turkey	Mammography	In the entire life (N = 519)	Women from out-patient clinics	SR	REALM	Age, income, education, occupation, self-perceived health status, smoking status	9
Li 2018, US	Mammography	In the entire life (N = 1818) In the last period* (N = 1800)	Chinese women from a PBS	SR	REALM-R	AII, acculturation, marital status, country, language, number of children, quality of life, health status	10
Cervical cancer							
Scott 2002, US	PAP test	In the entire life (N = 1545)	Medicare enrollees' women from a PBS	SR	s-TOFHLA	ASR, income, education, occupation, MMSE, physician visit, chronic condition	8
Garbers 2004, US	PAP test	In the entire life (N = 205) In the last period* (N = 205)	Latina or Hispanic women	SR	TOFHLA	/	7
Sentell 2015, US	PAP test	In the last period* (N = 15,210)	Asian and white women from a PBS	SR	CHIS questions	AII race, education, language, marital status, community level factors	7
Li 2018, US	PAP test	In the entire life (N = 1817) In the last period* (N = 1815)	Chinese women from a PBS	SR	REALM-R	AII, acculturation, marital status, country, language, number of children, quality of life, health status	10
Colorectal cancer							
Guerra 2005, US	FOBT SS, CS	In the entire life (N = 136)	Individuals from community clinics and from university-based PCP	SR	s-TOFHLA	/	8
Miller 2007[†], US	FOBT, SS, CS	In the last period* (N = 50)	Individuals from a university-affiliated community-based PCP	SR	REALM	/	4
Peterson 2007, US	FOBT FOBT, SS, CS	In the entire life (N = 99) In the last period* (N = 99)	Individuals from a community health clinic	SR	REALM	ASR, insurance	7
Arnold 2012[†], US	FOBT	In the entire life (N = 975)	Individuals from a community health clinic	SR	REALM	/	6
Sentell 2013, US	FOBT, SS, CS	In the last period* (N = 14,410)	White individuals from a PBS	SR	CHIS questions	ASR, insurance, language, education, marital status, country, CLF	6
Sentell 2013, US	FOBT, SS, CS	In the last period* (N = 1478)	Asian individuals from a PBS	SR	CHIS questions	ASR, insurance, language, education, sex, race, marital status, country, CLF	6
Kobayashi 2013, UK	FOBT	In the entire life (N = 3087)	Individuals from a PBS	SR	IALS	ASR, education, income, health status	10
Li 2018, US	CS	In the entire life (N = 3147) In the last period* (N = 3134)	Chinese American individuals from a PBS	SR	REALM-R	AII, acculturation, marital status, country, language, number of children, quality of life, health status	10
Horshauge 2020[†], Denmark	FIT	45 days after the screening invitation (N = 6896)	Individuals from a PBS	Record linkage	HLS-EU Q16	/	10
Prostate cancer							
Li 2018, US	PSA test	In the entire life (N = 1273)	Chinese American men from a PBS	SR	REALM-R	AII, acculturation, marital status, country, language, number of children, quality of life, health condition	10

[†]: Authors conducted multivariable analyses, but data were not retrievable or usable.
In the last period*: breast cancer screening: in the last 1–2 years. Cervical cancer screening: in the last 3 years. Colorectal cancer screening: FOBT in the last year, or SS in the last 5 years, or CS in the last 10 years.
HL tool[§]: CHIS: California Health Interview Survey. HLS-EU-Q: European Health Literacy Survey Questionnaire. IALS: International Adult Literacy Survey. NVS: Newest Vital Sign. REALM: Rapid Estimate of Adult Literacy in Medicine. REALM-R: REALM Revised version. TOFHLA: Test of Functional Health Literacy in Adults. s-TOFHLA: TOFHLA Short version.
Adjustment factors[¥]: ASR: Age, Sex, Race. AII: Age, Income, Insurance. MMSE: Mini Mental State Examination. CLF: Community Level Factors.

HL: Health Literacy. QS: Quality score. SR: Self-reported. US: United States. PAP: Papanicolaou. FOBT: Fecal Occult Blood Test. SS: SigmoidoScopy. CS: ColonoScopy. FIT: Fecal Immunochemical Test. PSA: Prostate-Specific agent. PBS: Population-Based Study. PCP: Primary Care Practices.

et al., 2002; Komenaka et al., 2015) and specified the ethnicity of the target population (Hispanic, Asian or Caucasic) (Pagán et al., 2011; Li et al., 2018; Sentell et al., 2015; Guerra et al., 2005a). In four studies the patients were recruited through population-based studies (Pagán et al., 2011; Li et al., 2018; Sentell et al., 2015; Scott et al., 2002) and in three cases through clinics (Guerra et al., 2005a; Komenaka et al., 2015; Yilmazel, 2016). A low socio-economic setting was present in three studies (Scott et al., 2002; Guerra et al., 2005a; Komenaka et al., 2015). Screening adherence was always self-reported (Pagán et al., 2011; Li et al., 2018; Sentell et al., 2015; Scott et al., 2002; Guerra et al., 2005a; Komenaka et al., 2015; Yilmazel, 2016) and all but one (Sentell et al., 2015) used a tool with reading or numeracy comprehension items to assess HL (Pagán et al., 2011; Li et al., 2018; Scott et al., 2002; Guerra et al., 2005a; Komenaka et al., 2015; Yilmazel, 2016). The authors provided adjusted estimates for at least demographic and socio-economic characteristics in three studies (Pagán et al., 2011; Sentell et al., 2015; Guerra et al., 2005a) or including also health conditions in the others (Li et al., 2018; Scott et al., 2002; Komenaka et al., 2015; Yilmazel, 2016). Quality was generally quite high in all studies, ranging from 7 (Sentell et al., 2015) to 10 (Li et al., 2018; Komenaka et al., 2015) (Supplementary Table 3).

3.2.2. Cervical cancer

All studies evaluating participation in cervical cancer screening programs were conducted in the US and used PAP test as the screening method (Li et al., 2018; Sentell et al., 2015; Scott et al., 2002; Garbers and Chiasson, 2004) (Table 1). Two studies (Li et al., 2018; Garbers and Chiasson, 2004) reported estimates considering both the last period and the entire life, whereas the other two studies quantified adherence in the entire life (Scott et al., 2002) or in the last period (Sentell et al., 2015), respectively. Sample size was larger than 1000 people in the three studies that enrolled women from population-based studies (Li et al., 2018; Sentell et al., 2015; Scott et al., 2002) and that also investigated ethnic minorities (Li et al., 2018; Sentell et al., 2015; Garbers and Chiasson, 2004), whereas a low socio-economic setting was investigated in the other study (Scott et al., 2002). All surveys considered self-reported screening adherence; three of these (Li et al., 2018; Scott et al., 2002; Garbers and Chiasson, 2004) measured HL with reading or numeracy comprehension items and one with self-reported comprehension items (Sentell et al., 2015). Results were adjusted for demographic and socio-economic factors in one case (Sentell et al., 2015) and also for health conditions in two studies (Li et al., 2018; Scott et al., 2002); only one author did not provide adjusted estimates (Garbers and Chiasson, 2004). All studies were deemed of good quality (Li et al., 2018; Sentell et al., 2015; Scott et al., 2002; Garbers and Chiasson, 2004) (Supplementary Table 3).

3.2.3. Colorectal cancer

A total of eight articles examined a possible influence of HL on colorectal cancer (CRC) screening adherence, one of which considered two distinct populations, for a total of nine investigations included (Table 1). Most of them were conducted in the US (Sentell et al., 2013; Li et al., 2018; Miller et al., 2007; Peterson et al., 2007; Guerra et al., 2005b; Arnold et al., 2012), one in the United Kingdom (Kobayashi et al., 2013), and one in Denmark (Horshauge et al., 2020). Participation to CRC screening was assessed quite heterogeneously: adherence to recommendations (i.e., undergoing FOBT in the last year, or SS in the last five years, or CS in the last ten years) was investigated in three cases (Sentell et al., 2013; Miller et al., 2007); two articles considered undergoing FOBT in the entire life (Kobayashi et al., 2013; Arnold et al., 2012); one study (Li et al., 2018) investigated CS both in the last period or during lifetime; one study (Guerra et al., 2005b) quantified ever had an FOBT or ever had a SS or CS separately; one study (Peterson et al., 2007) provided data considering adherence to screening program both during lifetime (through FOBT) and in the last period (through either FOBT, SS or CS), whereas the last author (Horshauge et al., 2020) reported undergoing fecal immunochemical test within 45 days after receiving the screening invitation. The target population was enrolled from population-based studies in five investigations (Sentell et al., 2013; Kobayashi et al., 2013; Li et al., 2018; Horshauge et al., 2020), three of which targeted ethnic minorities (Asian or Caucasic) (Sentell et al., 2013; Li et al., 2018), or from community or university clinics in the remaining four studies (Miller et al., 2007; Peterson et al., 2007; Guerra et al., 2005b; Arnold et al., 2012). In all articles but one (Horshauge et al., 2020) the participants self-reported screening adherence (Sentell et al., 2013; Kobayashi et al., 2013; Li et al., 2018; Miller et al., 2007; Peterson et al., 2007; Guerra et al., 2005b; Arnold et al., 2012). Health literacy was investigated mostly with tools applying reading or numeracy comprehension items (Kobayashi et al., 2013; Li et al., 2018; Miller et al., 2007; Peterson et al., 2007; Horshauge et al., 2020; Guerra et al., 2005b; Arnold et al., 2012) and in two investigations by answering to self-reported comprehension items (Sentell et al., 2013). When retrievable or provided, adjusted estimates were controlled for demographic factors and socio-economic status in three cases (Sentell et al., 2013; Peterson et al., 2007) and also for health conditions in other two articles (Kobayashi et al., 2013; Li et al., 2018). Three records were judged as being of fair or poor quality (Sentell et al., 2013; Miller et al., 2007; Arnold et al., 2012); their main deficits were a lack of representativeness and justification for the sample size and a lack of comparability between participants and non-participants, whereas the others were considered as having average-to-high quality (Kobayashi et al., 2013; Li et al., 2018; Peterson et al., 2007; Horshauge et al., 2020; Guerra et al., 2005b) (Supplementary Table 3).

3.2.4. Prostate cancer

Only one article (Li et al., 2018) conducted in the US investigated screening for prostate cancer through prostate-specific antigen (PSA) test in Chinese American men enrolled from a population-based study (Table 1). The screening uptake was self-reported, whereas HL was assessed with reading comprehension items. The results were adjusted for demographic and socio-economic factors, as well as health conditions.

3.3. Meta-analysis of the association between AHL and adherence to cancer screening programs by cancer type

3.3.1. Breast cancer

In unadjusted pooled analysis, AHL was found to positively influence screening adherence for breast cancer ($N = 5$, OR = 1.74; 95% CI: 1.08–2.80, $I^2 = 96.8\%$) (Fig. 2A). Stratified by time interval considered, results showed a statistically significant association between AHL and undergoing mammography in the last period only ($N = 1$, OR = 1.59; 95% CI: 1.38–1.84). Similarly, in the overall adjusted pooled analysis AHL seemed to be an independent predictor of mammography adherence ($N = 7$, aOR = 1.73; 95% CI: 1.27–2.36, $I^2 = 89.1\%$), and the association was significant in both the time-stratified analyses ($N = 2$, aOR = 1.41; 95% CI: 1.18–1.67, $I^2 = 0.0\%$; and $N = 5$, aOR = 1.91; 95% CI: 1.16–3.16, $I^2 = 92.7\%$, respectively). Heterogeneity was strongly reduced in the first subgroup only (Fig. 2B).

3.3.2. Cervical cancer

Stratified by the time interval considered, the unadjusted association was significant in both cases ($N = 1$, OR = 1.42; 95% CI: 1.25–1.62; and $N = 1$, OR = 21.30; 95% CI: 2.78–163.29, respectively) but in the overall analysis people with AHL seemed to not attend cervical cancer screening visits more frequently than people with limited HL ($N = 2$, OR = 4.51;

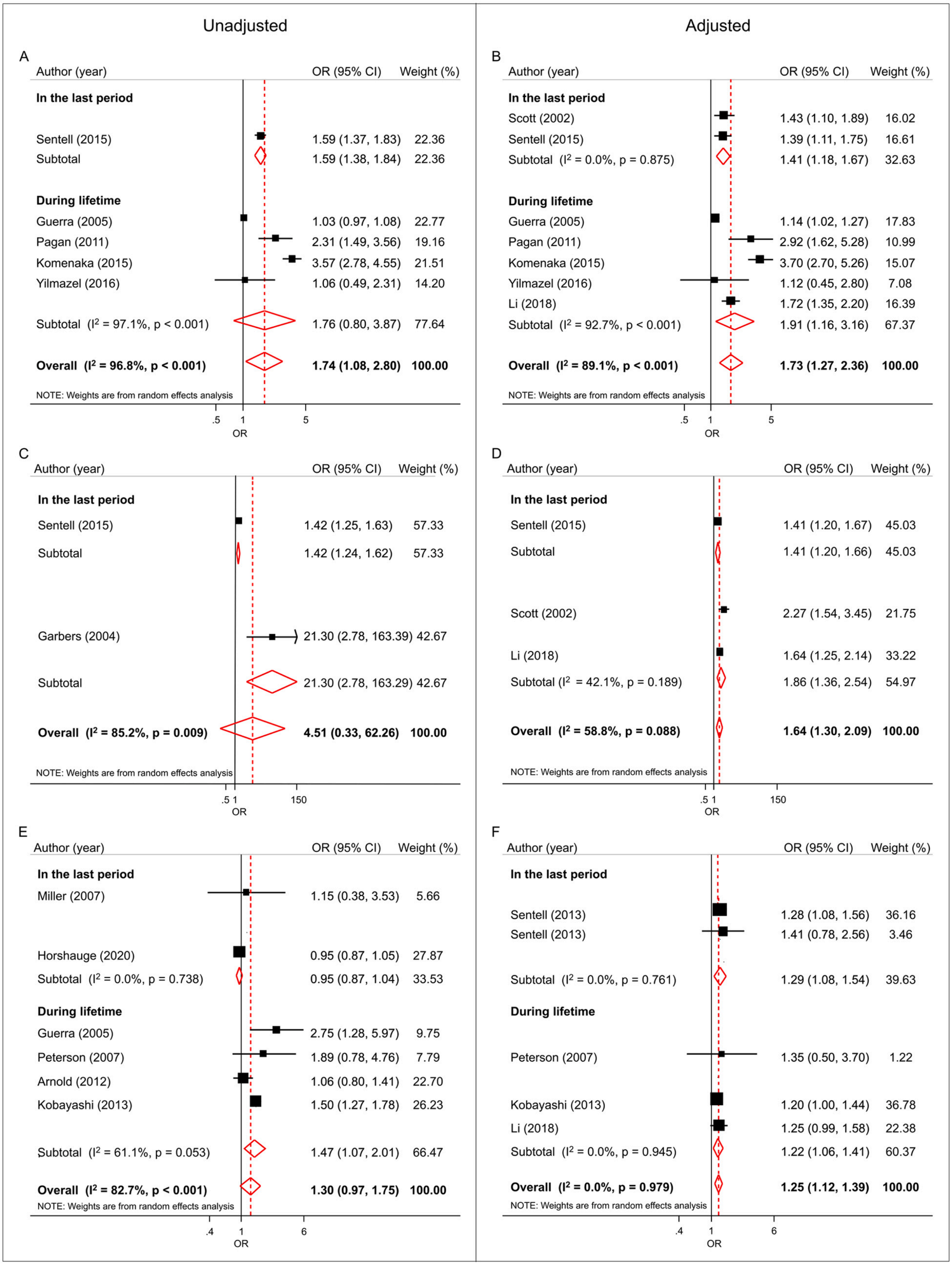

Fig. 2. Stratified inverse-variance random-effects meta-analysis of the association between adequate health literacy and adherence to screening programs for breast cancer (A, B), cervical cancer (C, D) and colorectal cancer (E, F) considering unadjusted (left panel) or adjusted estimates (right panel).

95% CI: 0.33–62.26, $I^2 = 85.2\%$) (Fig. 2C). Conversely, at the adjusted analysis, AHL was found to be a predictor of adherence to PAP test both in the overall ($N = 3$, aOR = 1.64; 95% CI: 1.30–2.09, $I^2 = 58.8\%$) and in the time-stratified analyses ($N = 1$, aOR = 1.41; 95% CI: 1.20–1.66; and $N = 2$, aOR = 1.86; 95% CI: 1.36–2.54, $I^2 = 42.1\%$, respectively), with a no longer significant heterogeneity (Fig. 2D).

3.3.3. *Colorectal cancer*

At the unadjusted pooled analysis, AHL seemed to positively influence CRC screening participation overall ($N = 6$, OR = 1.30; 95% CI: 0.97–1.75, $I^2 = 82.7\%$) and considering screening uptake once in the entire life ($N = 4$, OR = 1.47; 95% CI: 1.07–2.01, $I^2 = 61.1\%$) (Fig. 2E). Results of the adjusted analysis showed a strongly reduced heterogeneity and a significant association between AHL and CRC screening both overall ($N = 5$, aOR = 1.25, 95% CI: 1.12–1.39, $I^2 = 0.0\%$) and in the time-stratified analyses ($N = 2$, aOR = 1.29, 95% CI: 1.08–1.54, $I^2 = 0.0\%$; and $N = 3$, aOR = 1.22, 95% CI: 1.06–1.41, $I^2 = 0.0\%$, respectively) (Fig. 2F).

3.3.4. *Prostate cancer*

The only study that investigated HL and prostate cancer screening found that, after controlling for other factors, people with high HL were more likely to have ever had PSA tested compared to low HL people (aOR = 1.68, 95% CI: 1.02, 2.78).

3.4. *Sensitivity analysis*

Sensitivity analysis showed similar results with a significant association between AHL and mammography adherence in the unadjusted pooled estimate ($N = 5$, OR = 1.71; 95% CI: 1.05–2.76, $I^2 = 97.2\%$) but non-statistically significant in any time interval considered ($N = 3$, OR = 1.47; 95% CI: 0.96–2.26, $I^2 = 96.4\%$; and $N = 2$, OR = 2.06; 95% CI: 0.63–6.74, $I^2 = 88.3\%$) (Supplementary Fig. 1). A slightly reduced magnitude of the association was observed in the overall adjusted analysis ($N = 7$, aOR = 1.51; 95% CI: 1.08–2.11, $I^2 = 91.6\%$). Also, HL remained a strong predictor considering attendance in the last period ($N = 5$, aOR = 1.29; 95% CI: 1.03–1.62, $I^2 = 80.2\%$) but not in the entire life ($N = 2$, aOR = 2.20; 95% CI: 0.69–7.03, $I^2 = 82.7\%$).

As for cervical cancer, the association between AHL and PAP test became significant in unadjusted pooled analysis ($N = 2$, OR = 1.44; 95% CI: 1.24–1.68, $I^2 = 2.5\%$) in which all the studies considered screening participation in the last period (Supplementary Fig. 2). Adjusted results showed a slightly attenuated association overall ($N = 3$, aOR = 1.53; 95% CI: 1.15–2.03, $I^2 = 65.8\%$) and considering screening adherence in the last period ($N = 2$, aOR = 1.37; 95% CI: 1.18–1.59, $I^2 = 0.0\%$), whereas a slight increase was observed for undergoing PAP test at least once in the entire life ($N = 1$, aOR = 2.27; 95% CI: 1.52–3.40).

Lastly, in sensitivity analysis AHL seemed to become an independent predictor of CRC screening attendance in the crude pooled estimate ($N = 6$, OR = 1.42; 95% CI: 1.01–2.01, $I^2 = 87.4\%$), but remained non-significant considering screening participation in the last period whereas significant considering the entire life ($N = 3$, OR = 0.97; 95% CI: 0.84–1.11, $I^2 = 2.3\%$; and $N = 3$, OR = 1.77; 95% CI: 1.03–3.05, $I^2 = 87.8\%$, respectively) (Supplementary Fig. 3). Similar to the main analyses, AHL seemed to positively influence screening participation both in the overall ($N = 5$, aOR = 1.28; 95% CI: 1.14–1.43, $I^2 = 0.0\%$) and time-stratified analyses ($N = 4$, aOR = 1.33; 95% CI: 1.15–1.53, $I^2 = 0.0\%$; and $N = 1$, aOR = 1.20; 95% CI: 1.00–1.44, respectively).

4. Discussion

Previous studies have suggested that a limited or non-adequate level of HL may influence cancer screening participation (Berkman et al., 2011; Oldach and Katz, 2014), but the methods were heterogeneously applied (Berkman et al., 2011), and some results were contradictory (Oldach and Katz, 2014). In this meta-analysis, the adjusted estimates showed a strongly reduced heterogeneity compared to the unadjusted analyses, meaning that, despite our findings coming from observational studies, they could be valid estimates of the association of interest (Metelli and Chaimani, 2020). Additionally, most records reported adjusted estimates controlled for the main potential confounders (i.e., sociodemographic variables) in all cancer types, implying that our findings may have limited residual confounding (Metelli and Chaimani, 2020). Hence, considering both main and sensitivity analyses, in this review HL was found to be a predictor of mammography attendance and PAP test uptake in a similar way, whereas the significant but attenuated association with CRC screening could be due to the different type of the screening program, that in this case require individuals to personally return their sample (i.e., FOBT) or undergo more invasive procedures (i.e., SS and CS) (Lin et al., 2016), so that other barriers may hinder the participation, as already found (Hudson et al., 2012). For this reason, targeted interventions aimed at increasing HL in people with a low level should be implemented (Sørensen et al., 2020; Saulle et al., 2020), as they could be critical to increase their participation in screening programs. Devising such strategies may be particularly relevant in the current scenario, where the coronavirus disease (COVID-19) pandemic has led to reductions in the participation rates across all types of cancer programs, with consequent expected delayed diagnosis and increases in the number of avoidable deaths all over the world (Chen et al., 2021; Alkatout et al., 2021). On the one hand, these strategies could focus on enhancing the capacity of healthcare systems and health professionals to customize patient health education and meet the population's needs (Price-Haywood et al., 2014). On the other hand, the interventions could improve the ability of patients to communicate with the healthcare staff in order to increase their capacity to act on health information effectively (Simmons et al., 2017). However, in our review one study also reported a positive association between adherence to PSA testing and AHL, suggesting that people with high HL are more likely to undergo non-recommended screening, as previously hypothesized (Rutan et al., 2021). Hence, further research should consider not only the contribution of low HL as a barrier to recommended screening, but also investigate the role of high HL in non-recommended screening (Rutan et al., 2021).

Over the last years, the concept of HL has evolved in meaning (Sørensen et al., 2012). It results from everyday life (World Health Organization (WHO) Regional Office for Europe, 2013) through a multitude of social, personal, and cognitive skills (Sørensen et al., 2012). Limited participation in cancer screening programs from people with poor HL could be due to difficulty understanding risk communication and the effectiveness of preventive approaches (Koay et al., 2012). Low literacy may also influence the source and accuracy of the information received (Davis et al., 2002). However, the multifaceted nature of the concept makes it difficult to obtain an exhaustive measurement (World Health Organization (WHO) Regional Office for Europe, 2013). In our studies, different tools were used, but most of them measured the individual's capacities to read and understand actual material (Baker, 2006). These tools are preferable since people with poor HL may feel embarrassed to directly admit problems in this area and may make the self-assessment inaccurate (Koay et al., 2012). Nevertheless, developing and applying a comprehensive instrument for HL evaluation would enable a more precise estimation of the magnitude of the problem and a better comparison of evidence (Baccolini et al., 2021).

Based on the assumption that increasing participation in cancer screening programs leads to better outcomes (Chubak and Hubbard, 2016), the importance of quantifying adherence is universally recognized (Bulliard et al., 2014). In line with the cross-sectional design inclusion criterion, our studies reported data on (i) screening uptake, which was investigated through the prevalence of having been screened at least once at a given point in time, and (ii) and screening currency, that was quantified through the prevalence of being up to date for screening in the last period. Interestingly, while we found that for breast and cervical cancer the association between HL and screening uptake was slightly stronger compared to screening currency, the relationship with adherence to colorectal screening program was similar in the two time-stratified analyses, that could be the result of a larger interval considered in this case (up to the previous 10 years), but other hypotheses could be investigated. Also, all studies included in the multivariable analyses collected data on the outcome of interest through surveys without objectively verifying screening participation. Hence, given that some inaccuracies in the outcome assessment can't be excluded, as well as it is possible that a few participants were not eligible for screening (Chubak and Hubbard, 2016), consensus on definition and estimation of adherence, coupled with more standardized research, could facilitate comparison across studies, tests, and settings (Chubak and Hubbard, 2016).

Lastly, in line with the worldwide interest on HL that started at the beginning of the twenty-first century (World Health Organization (WHO) Regional Office for Europe, 2013), all studies were published in the last 20 years. Despite the pitfalls previously discussed, the study quality was generally good, but more information should be provided to how the sample is selected. Additionally, given that most studies were conducted in the US and several of them investigated population minorities or individuals from specific socio-economic settings, the generalizability of these findings may be limited. In our opinion, this is the results of the efforts made to explain the persistent socioeconomic inequalities in cancer mortality rates that have been registered over the past three decades in the US, with the widest gaps in the most preventable cancers (Siegel et al., 2019). Indeed, quantifying adherence to cancer screening programs in specific populations and identifying its determinants could help understand these differences in outcomes and map areas for improvement (Chubak and Hubbard, 2016), especially given that recent data do not show any progress in cancer screening rates between 2010 and 2013 (White et al., 2017) to which the negative impact of the COVID-19 pandemic should be added (Yong et al., 2021).

To the best of our knowledge, this is the first quantitative synthesis of data on the association between HL and cancer screening adherence that enabled an estimation of its magnitude for each cancer type. Also, by pooling unadjusted and adjusted estimates separately and by conducting time-stratified analyses, we were able to quantify the strength of the association independently from other factors and distinguish between screening uptake and being up to date with screening. Nevertheless, it is important to acknowledge the limitations of our study. First, we included only studies with a cross-sectional design and published only in English or Italian. Second, we excluded articles that provided only a mean measurement of HL, that analysed only specific sub-domains, that measured HL and cancer screening behaviours through effect measures other than ORs or that failed to report data. The other limitations are mostly related to the primary studies included in this review. As aforementioned, since our results mostly rely on self-reported adherence, the social-desirability bias could have made inaccurate our conclusions. Furthermore, several US studies specifically investigated ethnic minorities or people with a low socio-economic level. Also, in a few of these studies participants were recruited through health clinics, meaning that these individuals have already proven to be capable of accessing the healthcare system to some extent. For these reasons, since our samples may be not representative of the US population, and since Europe and the other world regions were under-investigated, further research at regional or national level should be conducted.

5. Conclusion

This review summarizes the current evidence about HL and cancer screening behaviours. Although we used stricter inclusion criteria to allow a quantitative synthesis of the results, we expanded the findings from the 2014 systematic review on the topic (Oldach and Katz, 2014) that did not report any conclusive evidence on the association. Specifically, we found that HL is an independent predictor of participation in population-based screening programs for breast, cervical and colorectal cancer, even though a slightly attenuated association was observed with the latter. Given that low HL is very frequent (Baccolini et al., 2021), there is a urgent need to implement targeted healthcare practices that effectively address this issue.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2021.106927.

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