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Lídia Maria Azevedo Faria

Gastric cancer screening: a systematic review

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Gastric cancer screening: a systematic review

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Dr. João Carlos Rocha da Silva

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DESIGNAÇÃO DA ÁREA DO PROJECTO

Gastrenterologia

TÍTULO DISSERTAÇÃO

Gastric Cancer screening: a systematic review

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ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTE TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☒
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Faculdade de Medicina da Universidade do Porto, 17/04/2020.

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Aos meus pais, irmã e avós
Por tudo.

TITLE: Gastric cancer screening: a systematic review.

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ABBREVIATIONS:

EGD: esophagogastroduodenoscopy.

FDG-PET: F-fluorodeoxyglucose-positron emission tomography.

GC: Gastric Cancer.

Hp: Helicobacter Pylori.

UGIS: Upper gastrointestinal series.

PG: Serum Pepsinogen.

ABSTRACT

Background and Aims: Population-based gastric cancer (GC) screening is recommended in high-risk populations, although screening methods and intervals vary. In intermediate-risk populations, European Society of Gastrointestinal Endoscopy guidelines suggest that esophagogastroduodenoscopy (EGD) screening may be considered depending on resources. The aim of this study was to characterize GC screening programs worldwide.

Methods: Studies regarding population-based GC screening were searched through MEDLINE and Scopus. Studies on symptomatic patients, premalignant lesions, hereditary GC and GC surveillance were excluded. The following outcomes were analysed: adherence rate, early-GC detection rate and GC detection rate. Additionally, a survey on digestive cancer screening was sent to Endoscopy/Gastroenterology societies.

Results: 44 studies were included. Population-based screening by upper gastrointestinal series (UGIS) or EGD is offered in Japan and Korea, with adherence rates between 14.31-58.01% and 7.40-74.8%, respectively. Japan reported early-GC detection rates of 0.02-0.21% and 0.35-0.66% and detection rates of 0.05-0.52% and 0.40-0.87%, for UGIS and EGD, respectively. Korea reported an EGD early-GC detection of 0.22% and detection rates between 0.01-0.29% and 0.07-0.08%, for EGD and UGIS, respectively. China offers EGD screening, with an adherence rate of 18.41% and early-GC and detection rates of 0.23-0.67% and 0.09-0.85%, respectively. In Western, several screening methods were used in pilot studies. Regarding the survey, only Serbia and Sweden reported the existence of a screening program.

Discussion: Mass screening for GC is available in Japan, Korea and China. Endoscopy-based programs seem to achieve higher early-GC and GC detection rates rather than UGIS, with variable adherence rates.

KEYWORDS: gastric cancer screening; endoscopy screening; screening program; population-based screening.

INTRODUCTION

Gastric cancer (GC) is the fourth most common malignancy worldwide and ranks third on cancer-related deaths [1]. However, its early detection can increase global 5-year survival rate up to 85-90% [2].

The incidence and mortality of GC substantially vary across geographical areas and the highest age standardized incidence-rate (ASR) and mortality rates are in Eastern Asia (22.4/100,000 and 15.9/100,000, respectively) and Central and Eastern Europe (11.4/100,000 and 9.1/100,000, respectively) [1].

At present, endoscopic screening for gastric cancer is performed solely in countries with a high-risk of disease (defined as ASR ≥ 20 per 100,000) such as Japan and Korea (29.9 and 41.3, respectively) [2, 3]. Its implementation led to early detection of GC, offering the possibility of endoscopic treatment instead of surgery as well as an improvement in disease-specific mortality and five-year survival [4, 5]. However, even in Western countries, screening methods vary and it is unclear which one is the most effective; moreover, scarce reports of population-based GC screening programs are available in Western countries. Recent studies suggested the cost-effectiveness of adding upper screening endoscopy to a scheduled colonoscopy after positive fecal occult blood tests in countries with intermediate-risk for GC, such as Portugal and other Eastern European countries [6]. European Society of Gastrointestinal Endoscopy (ESGE) recommends endoscopic screening for gastric cancer in high-risk populations, for individuals aged > 40 years old. In intermediate-risk populations, ESGE guidelines suggests that endoscopic screening may be considered depending on endoscopic resources [7]. Nevertheless, it has not been implemented.

The evaluation of previous and ongoing GC screening strategies and their results, in both Eastern and Western countries, may provide evidence for further establishment of GC screening in intermediate and low-risk populations and optimize ongoing programs in high-risk populations. The present study aimed to identify and characterize population-based GC screening programs worldwide.

METHODS

The authors performed two studies in order to access GC screening, namely: 1) A systematic review of population-based GC screening programs; 2) A cross-sectional evaluation of existing GC screening programs, through a survey sent to 311 Endoscopy and Gastroenterology societies.

1) Systematic review of Gastric Cancer Screening programs

Search Strategy:

For the current review the authors screened MEDLINE and Scopus databases (date of last search 20th December 2019) to identify relevant studies. The search query for MEDLINE was the following: ((stomach cancer) OR (gastric cancer)) AND ((cancer early diagnosis) OR (cancer screening) OR (endoscopy screening) OR (screening program)). For Scopus the following query was used: (("stomach cancer") OR ("gastric cancer")) AND (("cancer early diagnosis") OR ("cancer screening") OR ("endoscopy screening") OR ("screening program")) .

The authors further manually searched abstracts from the Gastroenterology and Endoscopy conferences proceedings. Clinical trial registries were considered. In addition, reference lists of relevant articles were reviewed to identify additional studies.

Eligibility Criteria:

This systematic review followed the PRISMA 2009 guidelines [8]. All studies on population-based GC screening programs, in asymptomatic individuals, at a national or regional level were included. Original randomized controlled trials (RCT), cohort, cross-sectional and case control studies were considered. Studies in (1) symptomatic patients, (2) premalignant conditions/lesions or (3) patients with history of GC or early-GC diagnosis, (4) hereditary GC, (5) studies with missing abstract, (6) case-series, reviews, letter and guidelines were excluded. No language or temporal restrictions were applied. If there was patient population overlap in studies, the study with the highest number of participants was included for analysis.

The primary outcome was early-GC or GC detection rate and the secondary outcome adherence rate.

Study Selection:

Two reviewers, Faria L and Silva JC independently screened title and abstracts according to a prespecified protocol, via Covidence systematic review software. In case of disagreement, Rodríguez-Carrasco M made the final decision.

Further full article reading, methodological quality evaluation and data extraction was similarly performed independently by the above-mentioned reviewers. Authors of unpublished studies or published studies in which data was not possible were missing were contacted to confirm eligibility. Authors with articles not able to translate were also contacted.

Quality evaluation:

Methodological quality and risk of bias of each study was performed by the reviewers according to the Cochrane Collaboration guidelines for RCTs [9] and to the Newcastle-Ottawa scale for observational studies [10].

Data collection process and data items:

Two reviewers (Faria L and Silva JC) independently retrieved data from full articles using a standardized, predefined form, based on Cochrane data sheets.

Data was obtained according to the target variables: (1) target population (age, sex); (2) country/region of screening program; (3) mechanisms for systematic invitation; (4) screening method used and setting (regional, national); (5) adherence rate (%); (6) detection of early-GC rate (%); (7) detection of GC rate (%); (8) study period; (9) participants; (10) year of publication; and (11) author.

2) Cross-sectional assessment of ongoing gastric cancer screening programs

An online survey (Supplementary Data - Attachment 1) on digestive cancer screening was sent to 311 Endoscopy and Gastroenterology worldwide in order to characterize ongoing GC screening programs.

The survey was sent by email in 3 different rounds, between January and March 2020, in order to maximize adherence rates. Answers were then recorded and grouped by the authors. The following domains were evaluated: (1) target population (age, sex, risk factors for GC); (2) country/region of screening program; (3) gastroenterology or endoscopy society; (4) screening setting (national; regional); (5) screening method; (6) adherence rates (%).

RESULTS

1) Systematic review in Gastric Cancer Screening

A total of 1194 articles were identified and 42 were selected for inclusion after removal of duplicates, title and abstract and full-text review. Two additional abstracts were included from manual search: 1 from Portugal and 1 from Japan and thus a total of 44 studies were included in the review (**Figure 1**). Among them, 17 reports were from Korea, 17 from Japan, 4 from China, 1 from Taiwan, 1 from Finland, 1 from Turkey, 1 from Costa Rica, 1 from Iran and 1 from Portugal.

The main characteristics of the studies included in this review are available in **Table 1**. The majority of studies are observational (41, 93%) and 3 studies are RCTs. Most of the studies were performed on a regional level (26, 59%) and 18 were national based. The majority (26, 59%) were retrospective. Quality analysis of the included studies is shown in **Table 1**. Inclusion criteria in GC screening regarding target population varied in age groups, being the majority population aged 40 or older (21, 48%), followed by group aged 40-69 years old (6, 14%). Regarding sex, 3 studies only included men, but the majority (40, 90%) included both sexes. The majority of studies evaluated GC screening performed by UGIS and EGD (20, 45%), followed by EGD (9, 20%) and UGIS (8, 18%).

Among Eastern countries, there were reports of population-based screening from three countries: Japan, Korea and China. In Japan, upper gastrointestinal series (UGIS) or esophagogastroduodenoscopy (EGD) are both first-line options for GC screening for asymptomatic individuals ≥40 years old. National Cancer Screening Program for GC in Korea started in 1999 by UGIS or EGD to individuals ≥40 years old. In China, endoscopy screening was available since 1900 only in high-risk regions. Since 2012, a population-based GC screening by EGD is available for high-risk individuals 40-74 years old. In contrast, in Western countries there are no population-based GC screening programs ongoing, yet some pilot programs attempted to address this topic.

The authors will further summarize data according to geographic location.

Eastern Countries

Japan

Gastric cancer screening was initially conducted in Miyagi Prefecture in 1960, by UGIS, and patients were recruited through community health campaigns. Population-based screening through UGIS in asymptomatic individuals aged ≥40 years old, started in 1983 in accordance with the Health Law for the Aged [11]. Photofluorography was originally performed on a mobile car in Japanese communities. Nonetheless UGIS screening has also been performed in clinical settings through several invitation methods, namely newsletter, mass health campaigns, local campaigns, house-to-house circular, personal letter or postcard, home visit and telephone recruitment. All individuals showing abnormal findings in UGIS screening were sent to further EGD.

Endoscopic screening for GC has been carried out in some Japanese prefectures since 2000. Publication of studies evaluating the effectiveness of endoscopic screening for gastric cancer lead to the revision of GC screening national guidelines. Endoscopic and radiologic screening display as first-line options for GC screening, which is now recommended for asymptomatic individuals aged 50 years or older, by the Japanese Guideline Development Group for Gastric Cancer Screening Guidelines [12].

Seventeen studies were available from Japan: 6 evaluating GC screening by UGIS, 7 comparing UGIS and EGD, 3 by serum pepsinogen (PG) and 1 by F-fluorodeoxyglucose-positron emission tomography (FDG-PET).

GC screening by UGIS:

UGIS screening adherence rates results varied from 14.3% up to 58.0% [13-19]. The highest adherence rate was reported when GC screening uptake was accessed through self-administered questionnaire**.** Yet, the proportion of cases that the authors identified by the screening reports was 38.1%. Adherence in prospective studies varied between 29.1-37.9% [13, 16-18].

A GC detection rate of 0.52% was reported [13].

GC screening by UGIS and EGD:

Adherence rate of 26.6% for UGIS screening of and 28.2% for the EGD screening was reported in a comparative study [20]. In a cross-section evaluation of GC screening uptake directed to access the effects of several invitation methods, the adherence rate ranged between 13.2-21.6% [21]. Personal and household invitation letters were the most effective and feasible strategies.

EGD early-GC detection rates ranged from 0.35-0.66% and were higher than the ones reported for UGIS (0.02-0.21%) [20, 22, 23]. EGD screening GC detection rates ranged between 0.40-0.87% and in all studies supplanted UGIS screening (0.05-0.46%) [20, 22-25]. Higher detection rates for EGD screening were obtained in a retrospective observational study [22].

GC screening by PG:

PG though to target gastric atrophy was proposed as an alternative screening method. An overall adherence rate of 40.72% is described. GC detection rate varied from 0.28% to 0.59% [26-28]. An early detection rate of 0.44% was reported in a retrospective cohort [29].

GC screening by FDG-PET:

Although FDG-PET wasn't recommended for GC screening in asymptomatic individuals, a retrospective observational study reports its use for this purpose, with low sensitivity and low GC detection rate (0.08%) [30].

Korea

A Korean National Cancer Screening Program (KNCSP) for GC is available since 1999. Men and women aged 40 or older are invited by letter to undergo EGD or UGIS, accordingly to each one preference, every two year.

Seventeen studies were selected for inclusion. 14 of them evaluated GC screening by UGIS and EGD and 3 only through EGD.

GC screening by UGIS and EGD:

Adherence rates varied from 7.40-74.8%, increasing over time [31-35]. From 2005-2015 a 5.8% annual increment in GC screening uptake was verified for all age, income and educational groups [35]. Relatives of patients with GC showed significant higher adherence rates (39.2%), comparing with participants without familiar history of GC [36]. Lifetime adherence and adherence rates in accordance to national guidelines also increased, varying from 52% to 80% and 39.2% to 73.6%, respectively [37-40]. Regarding the intention to participate in subsequent biennial GC screening, 52.2% of participants intended to participate, being the preferred method EGD (67.0%) [40].

Comparing EGD and UGIS preference, over time, participants tent to prefer EGD as screening method, varying from 25% to 72.55% [31, 32, 41, 42]. An annual percentage change for EGD of 4.2% was reported [31]. Therefore, the proportion of participants who undergone UGIS decreased during time, from 75.0% to 32.8% [31, 32, 41, 42].

Regarding the effectiveness of interventions to increase GC screening adherence, postcard intervention followed by phone call and phone calls followed by postal performed better [43, 44].

EGD detection rates varied from 0.24-0.26% and UGIS detection rates from 0.07-0.08% [41, 42]. These results show a higher probability of detecting GC with EGD, a 2.9-fold and 3.71-fold, respectively [41, 42].

GC screening by EGD:

Adherence rate of 31.3% was reported regarding screening uptake in subsequent examinations after the baseline EGD [45].

Detection rates varied from 0.01-0.29% [45, 46]. Lower rates were presented in a study performed in voluntary subjects in a single institute, as a baseline screening [45]. One study presented early-GC detection rate of 0.22% [46]. Quality assessment programs are thought to improve GC detection rates, since 80% of endoscopists reported improvement [47].

China

In China, some high-risks regions implemented GC screening programs by EGD around 1990s. Since 2012, a population-based cancer screening program for GC in urban China was initiated. Target population aged 40-74 years old was firstly recruited by phone call or personal contact to perform a cancer risk assessment. Subsequently, high-risk participants were invited to undergo EGD [48].

Four studies were included, all evaluating GC screening by EGD.

An adherence rate of 18.4% was reported [48]. Early-GC and GC detection rates ranged from 0.23-0.67% and 0.09-0.85%, respectively [48-51].

Taiwan

In Matsu Islands, a high-risk population for GC, a population-based screening using PG followed by EGD in positive cases (PG I level <30 μg/L or PG-I/II ratio <3) was implemented from 1995 to 1998. The adherence rate was 47.5% and the GC detection rate was 0.69% [52].

Western Countries

In Western countries 5 studies reported pilot projects on GC mass screening: 1 case-control from Costa-Rica; 2 prospective cohort studies from the Middle East; 1 prospective cohort from Portugal and another from Finland. European prospective studies on GC screening resorted to PG testing as primary method while Middle East programs relied in primary EGD.

Costa-Rica

In a high-risk region of Costa Rica a pilot GC screening program was undertaken through UGIS in asymptomatic individuals aged 50-75 years old, reporting an adherence rate of 78.4% and GC detection rate of 0.86% (early-GC detection rate of 0.47%) [53].

Middle East

Two Middle East programs used primary EGD as GC screening method. In a high-risk region of Iran a pilot study of EGD screening for early detection of GC among individuals older than 50 years, reported a detection rate of 0.50% [54]. Likewise a pilot EGD screening project, in a prospective cohort of 7316 individuals in Turkey reported a GC detection rate of 0.28% [55].

Portugal

Asymptomatic individuals, aged 40-79 years old, from a Portuguese high-risk region were invited to GC screening through advertisement lectures and a 10% adherence rate was estimated. PG testing was considered positive in the presence of PG I level <70 ng/L and the PG I/II ratio <3.0. Early-GC and GC detection rates were 1.10% and 2.20%, respectively [56].

Finland

A prospective observational Finnish study enrolled asymptomatic men aged 51-65 years old through mail invitation. In the presence of a PG I level ≤25 μ/L endoscopy was recommended. An adherence rate of 71.16% was obtained and a GC detection rate of 0.46% was reported [57].

2) Cross-sectional assessment of ongoing Gastric Cancer Screening Programs

Among the surveys sent to 311 Endoscopy and Gastroenterology societies, a response rate of 22 % was obtained (**Table 2)**. Data from 5 continents and 24 countries was obtained: Africa (Egypt, n=1), America (Brazil, Bolivia, Ecuador, Nicaragua and Uruguay, n=5), Asia (Jordan n=1), Europe (Slovenia, Greece, Lithuania, Czech Republic, Italy, Hungary, Slovak Republic, Sweden, Finland, Luxembourg, Norway, Albania, Serbia, Bulgaria, Spain, Azerbaijan n=16) and Oceania (New Zealand n=1).

Two countries reported the existence of GC screening program, Sweden and Serbia. In Sweden, the GC screening program is available for high-risk population, with genetic mutations, performed by EGD. In Serbia, the endoscopic GC screening program is directed to high-risk populations, for individuals younger than 65 years old, and is performed in combination with screening colonoscopy. Twenty-two countries answered no GC screening program was implemented.

DISCUSSION

Gastric cancer is still the third malignancy with more cancer-related deaths, despite the decreases in incidence and mortality rate in the last decades [1]. Screening programs have been implemented in some high-risk populations given the improvement in survival rates. Nonetheless evidence regarding its application in other high-risk or intermediate-risk populations is scarce.

The present review identified population-based GC screening programs in Eastern (Japan, Korea and China) as well as Western countries. Overall an increase in the adherence rates to GC screening programs was observed and EGD tended to be the preferred screening method. Also, endoscopic screening performed better in early and overall GC detection. In Japan and Korea, EGD and UGIS are the available screening methods, chosen by screened individuals according to their preference. Regarding early-GC and GC detection rates, the highest results were obtained in both countries through endoscopic screening, reaching an early-GC detection rate of 0.66% in Japan and 0.22% in Korea, and a detection rate up to 0.87% in Japan and 0.29% in Korea. In China GC screening is performed in urban areas though EGD and national screening program has shown an adherence rate of 18.4% and a detection rate of 0.09%. In Eastern countries GC screening through serologic testing reached adherence rates up to 41% and detection rates up to 0.59%.

In contrast, in Western countries no data on national GC programs was obtain through the review. Nonetheless there are 2 pilot studies for endoscopic screening in the Middle East, one report of radiologic screening in Costa-Rica and 2 European (Portugal and Finland) studies which relied in PG testing. Overall PG testing was associated with variable adherence and detection rates. Further studies in intermediate-risk populations are needed in order to evaluate adherence rates and define optimal GC screening strategies.

The survey sent to Gastroenterology and Endoscopy associations provided us data on endoscopic GC screening in high-risk population in 2 additional countries (Sweden and Serbia), not identified in the review process.

Our review presents some limitations. Most included studies are observational and therefore susceptible to selection bias. Economic studies were not included in this review, thus cost-effectiveness and

cost-utility of the presented screening strategies were not evaluated. Nonetheless an adequate characterization of adherence rates may largely contribute to further economic evaluation.

In conclusion, population-based screening for GC are restricted to Japan, Korea and China, and endoscopy seems to be the best method in terms of adherence and detection rates, comparing with UGIS. Further RCT are needed in order to access GC screening strategies regarding mortality, morbidity and related cost. Also, data on availability of endoscopic resources and quality assessment in GC screening must be further considered.

DISCLOSURE OF INTEREST

The authors report no conflict of interest.

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TABLES

Table 1 - Studies characteristics and GC screening adherence, early-GC and GC detection rates, within each screening method group.

First Author (Publication Year)	Country, Region	Study Period	Participants	Target population	Method invitation	Adherence rate per 100 (95% CI)	EGC detection rate per 100 (95% CI)	GC detection rate per 100 (95% CI)	Quality analysis [1]
GC screening with UGIS									
Nakamura Y. (1977) [13]	Japan	1964-1975	1115	Men and women aged 40 or older, annual	Community campaign	29.12 (28.41-29.84)		0.52 (0.33-0.77)	5
Ikeda M. (1989) [14]	Japan	1984-1989	40213	Men and women aged 40 or older, annual	Community campaign	44.20			5
Wang B. (1993) [15]	Japan	1991		Men and women aged 40 or older, annual	Newsletter; local organization; house to house circular; personal letter or postcard; home visit; telephone; mass communication	14.31 (13.03-15.67)			5
Shizuyo I. (1999) [58]	Japan	1992-1995	24134	Men and women aged 40 or older, annual	Community campaign	37.88 (37.27-38.50)			5

Mizoue T. (2003) [17]	Japan	1988-1990	87312	Men and women aged 40 or older, annual	Community campaign	35.24 (34.93-35.56)			6
Lee K.J. (2006) [18]	Japan	1990-2003	42150	Men and women aged 40-60 years old, annual		36.04 (35.58-36.50)			6
Tashiro A. (2006) [22]	Japan	2002-2004	105706	Men and women aged 40 or older, biennial			0.21 (0.15-0.28)	0.32 (0.25-0.41)	5
Matsumoto S. (2007) [20]	Japan	1996-2003	11439	Men and women aged 40 or older, biennial	Public notices; Community activities	26.60	0.02 (0.00-0.13)	0.05 (0.01-0.17)	4
Miyamoto A. (2007) [19]	Japan	1990-2001	41394	Men and women aged 40-64 years old, annual		58.01 (57.54-58.49)			6
Nakashima H. (2010) [23]	Japan	2005-2008	7942	Men and women aged 40 or older, biennial			0.07 (0.08-0.11)	0.10 (0.07-0.13)	5
Hamashima C. (2013) [25]	Japan	2002-2007	50988	Men and women aged 40-79 years old				0.46 (0.30-0.68)	6
Hamashima C. (2015) [24]	Japan	2005-2010	50521	Men and women aged 40-79 years old	Community campaign			0.43 (0.34-0.53)	5
Lee H.Y. (2010) [41]	Korea	2002-2004	1503646	Men and women aged 40 or older, biennial	Personal letter			0.08 (0.08-0.09)	5
Choi K.S. (2012) [42]	Korea	2002-2005	2250392	Men and women aged 40 or older, biennial				0.07 (0.06-0.07)	6

Rosero-Bixby L. (2007) [53]	Costa Rica	1996-2000	6828	Men and women aged 50-75 years old	Invitation letter	78.44 (77.56-79.30)	0.47 (0.32-0.66)	0.86 (0.66-1.11)	5
GC screening with UGIS or EGD									
Hamashima C. (2018) [21]	Japan	2010		Men and women aged 40-79 years old	Individual invitation letter; household invitation letter; home visits; screening in medical offices; free screening	21.58			7
Choi K.S. (2009) [40]	Korea	2005-2006	1625	Men and women aged 40 or older, biennial	Personal letter	53.42 (50.96-55.86)			6
Hahm M.I. (2010) [33]	Korea	2007	1517	Men and women aged 40-69 years old		54.91 (52.37-57.44)			6
Hahm M.I. (2011) [32]	Korea	2005-2008	4060257	Men and women aged 40 or older, biennial		20.50 (20.46-20.49)			6
Kang J.M. (2011) [36]	Korea	2005	3557	Men and women aged 40 or older, biennial		39.20 (32.39-44.51)			6
Park B. (2011) [39]	Korea	2010	4056	Men and women aged 40 or older, biennial		65.10 (63.48-66.70)			6
Lee M.H. (2012) [44]	Korea, Ilsandong-gu District	2010	2065	Men aged 40-65 years old	Phone call, postcard followed by phone call, phone call	35.71 (21.55-51.97)			Low risk

					followed by postcard, no intervention				
Hong N.S. (2014) [43]	Korea, Daegu	2012	923	Men aged 50-59 years old	No intervention, Phone call, Postal, Phone call or poster	40.53 (34.08-47.23)			Low risk
Sangeun-Lee B.N. (2015) [31]	Korea	2002-2011	5895113	Men and women aged 40 or older, biennial	Personal letter	45.40 (45.37-45.42)			7
Chang Y. (2015) [38]	Korea	2007-2009	10658	Men and women aged 40 or older, biennial		43.95 (43.00-44.90)			6
Suh M. (2016) [37]	Korea	2004-2013	30105	Men and women aged 40 or older, biennial		73.61 (72.23-74.95)			6
Suh M. (2017) [34]	Korea	2002-2012	37608375	Men and women aged 40 or older, biennial		47.32 (47.30-47.35)			7
Lee E.Y. (2018) [35]	Korea	2005-2015	28913	Men and women aged 40-74 years old		74.80 (73.32-76.25)			6
GC screening with EGD									
Tashiro A.(2006) [22]	Japan	2002-2004	105706	Men and women aged 40 or older, biennial			0.66 (0.52-0.82)	0.87 (0.71-1.06)	5
Matsumoto S. (2007) [20]	Japan	1996-2003	11439	Men and women aged 40 or older, biennial	Public notices; Community activities	28.20	0.35 (0.23-0.51)	0.40 (0.26-0.56)	4

Nakashima H. (2010) [23]	Japan	2005-2008	7942	Men and women aged 40 or older, biennial			0.43 (0.27-0.65)	0.45 (0.28-0.67)	5
Hamashima C. (2013) [25]	Japan	2002-2007	50988	Men and women aged 40-79 years old				0.87 (0.67-1.10)	6
Hamashima C. (2015) [24]	Japan	2005-2010	50521	Men and women aged 40-79 years old	Community campaign			0.63 (0.51-0.76)	5
Lee H.Y. (2010) [41]	Korea	2002-2004	1503646	Men and women aged 40 or older, biennial	Personal letter			0.24 (0.22-0.25)	5
Choi K.S. (2012) [42]	Korea	2002-2005	2250392	Men and women aged 40 or older, biennial				0.26 (0.25-0.27)	6
Kim B.J. (2013) [46]	South Korea, Chung-Ang Universitary Healthcare System	2007-2010	34416	Men and women aged 40 or older, biennial			0.22 (0.17-0.27)	0.29 (0.24-0.35)	6
Bae J.M. (2015) [45]	Korea	2007-2011	293520	Men and women aged 40-69 years old		31.29 (31.13-31.46)		0.01(0.01-0.01)	7
Cho Y.K. (2016) [47]	Korea	2004-2005							4
Lu Y.F. (2014) [49]	China, Henan Province	2009-2011	36154	Men and women aged 40-69 years old			0.67 (0.59-0.76)	0.85 (0.76-0.95)	5

Zheng X. (2015) [50]	China, Yangzhong	2006-2012	12453	Men and women aged 40-69 years old			0.48 (0.37-0.62)	0.48 (0.37-0.62)	7
Zhang M. (2016) [51]	China, Henan Province	2009-2013	88263	Men and women aged 40-69 years old			0.23 (0.20-0.26)	0.43 (0.39-0.48)	5
Guo L. (2019) [48]	China, Henan Province	2013-2017	43423	Men and women aged 40-69 years old	Phone call, personal contact	18.41 (18.05-18.78)		0.09 (0.04-0.18)	8
Mansour-Ghanaei F. (2012) [54]	Iran	2010-2011	1382	Men and women aged 50 or older	Public media; house-house direct contact			0.58 (0.25-1.14)	5
Akgul H. (2017) [55]	Turkey	2017	7316	Men and women aged 40 or older			0.05 (0.01-0.14)	0.29 (0.18-0.44)	4
GC screening with PG									
Miki K. (1993) [29]	Japan	1991	4647	Men and women aged 20 or older	Workplace screening		0.44 (0.09-1.29)	0.59 (0.16-1.51)	3
Chiang T. S. (2018) [52]	Taiwan, Matsu Islands	1995-1998	1682	Men and women aged 30 or older		47.50 (45.84-49.16)		0.69 (0.08-2.45)	6
Lomba-Viana R. (2011) [56]	Portugal	2005-2010	13118	Men and women aged 40-79 years old	Advertisement lectures and newspapers	10.00	1.10 (0.23-3.17)	2.19 (0.81-4.71)	6

Vohlonen I. (2017) [57]	Finland	1994-2011	12175	Men aged 51-65 years old	Individual invitation letter	72.16 (71.48-72.84)		0.46 (0.06-1.65)	5
GC screening with UGIS and PG									
Ohata H. (2005) [27]	Japan	1995-2002	17647	Men and women aged 40-60 years old, annual	Workplace screening			0.28 (0.21-0.37)	3
GC screening with PG and Hp									
Gotoda T. (2014) [28]	Japan	2011-2013	1206	Men and women aged 30-74 years old		40.72 (38.94-42.51)		0.49 (0.10-1.449)	Low risk
GC screening with FDG-PET									
Minamimoto R. (2014) [30]	Japan	2006-2009	153775	Men and women aged 30-80 years old				0.08 (0.07-0.10)	4

1 Cochrane Collaboration guidelines for RCT and Newcastle-Ottawa scale for observational studies .

CI, confidence interval, EGC, early-gastric cancer. GC, gastric cancer. EGD, esophagogastroduodenoscopy. UGIS, upper gastrointestinal series. PG, serum Pepsinogen; Hp, *Helicobacter Pylori* status; FDG-PET, F-fluorodeoxyglucose-positron emission tomography.

Table 2 - Online Survey Responses by Gastroenterology/Endoscopy societies worldwide.

Country	Type of GC screening	GC screening target population	GC screening method	Adherence rate to GC screening (%)	GI cancer screening programs	GI cancer screening adherence rate (%)
Countries with GI cancer screening programs						
With GC screening programs						
Sweden	High-risk individuals	Genetic high-risk individuals	EGD	No	CCR screening; FAP and Lynch syndrome	No
Serbia	Opportunistic screening	High-risk populations and age under 65 years old	EGD combined with screening colonoscopy	No	-	-
Without GC screening programs						
Slovenia	-	-	-	-	CCR screening	64
Greece	-	-	-	-	CCR screening	No
Lithuania	-	-	-	-	CCR screening	No
Czech Republic	-	-	-	-	CCR screening	41
Italy	-	-	-	-	CCR screening	30-40

Hungary	-	-	-	-	CCR screening	No
Slovak republic	-	-	-	-	CCR screening	30
Finland	-	-	-	-	CCR screening	No
Luxembourg	-	-	-	-	CCR screening	30
Norway	-	-	-	-	CCR screening	50-60.7
New Zealand	-	-	-	-	CCR screening	No
Uruguay	-	-	-	-	CCR screening	No
Countries without GI cancer screening programs						
Ecuador	-	-	-	-	-	-
Egypt	-	-	-	-	-	-
Albania	-	-	-	-	-	-
Bulgaria	-	-	-	-	-	-
Spain	-	-	-	-	-	-
Azerbaijan	-	-	-	-	-	-
Brazil	-	-	-	-	-	-
Bolivia	-	-	-	-	-	-
Nicaragua	-	-	-	-	-	-
Jordan	-	-	-	-	-	-

GC, gastric cancer.GI, gastrointestinal.EGD, esophagogastroduodenoscopy.CCR, colorectal cancer.FAP, Familial adenomatous polyposis.

FIGURES

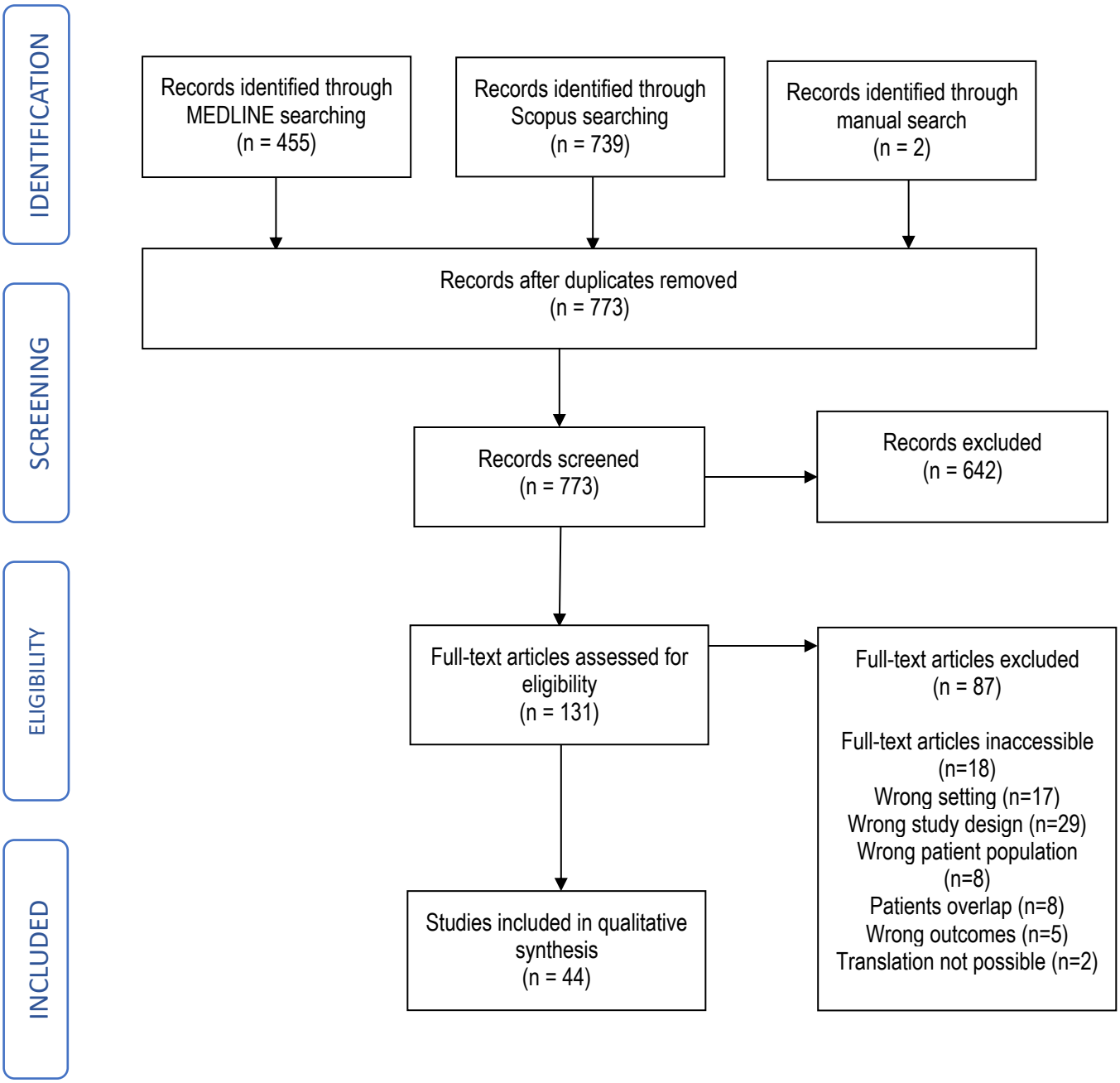

Figure 1- Flowchart of study selection included in the systematic review.

SUPPLEMENTARY DATA - ATTACHMENT I

GASTRIC CANCER SCREENING PROGRAM SURVEY

In order to approach a global understanding of gastric cancer, in specific, screening programs for early diagnosis all around the world, we address you this short questionnaire about this topic. Please answer all questions regarding gastric cancer screening in the country you are replying for.

Section 1: Gastric Cancer Screening Program

Country *

Please state the country you are answering about.

Society *

Please state the name of the society you are answering for.

Are you aware of any cancer screening program in your country? *☐ Yes ☐ No

Section 2: Gastric Cancer Screening Program Details

If you have answered YES to our previous question, please fill in the next few details about the program

itself.

Which type of screening program is offered? *

☐ Population-base screening ☐ Opportunistic screening

☐ Another:

Who is the target population? *

Please detail the characteristics of eligibility for the screening program, such as age range and specific individual characteristics (e.g high risk populations).

Which screening method is recommended? *

☐ Upper digestive endoscopy (esophagogastroduodenoscopy)

☐ Upper digestive endoscopy (esophagogastroduodenoscopy) combined with screening colonoscopy

☐ Another:

Are you aware about the adherence rate to the screening program? *□ Yes □ No

If yes, please indicate the rate of adherence.

☐ Another:

Section 3: Gastrointestinal Cancer Screening Program

Are you aware of any other gastrointestinal cancer screening programs in your country? * ☐ Yes ☐ No

If the previous answer was YES, please specify.

Are you aware about the adherence rate to the screening program?

If you have answered yes in the previous question and if you are acknowledge of this data, please indicate the rate of adherence.

☐ No

☐ Another: _____

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Anexos

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Acknowledgements

Acknowledgements should be made only to those who have made a substantial contribution to the study. Authors are responsible for obtaining written permission from people acknowledged by name in case readers infer their endorsement of data and conclusions.

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Articles in journals

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More than six authors:
Cardoso AC, Cravo C, Calçado FL, Rezende G, Campos CFF, Neto JMA, et al. The performance of M and XL probes of FibroScan for the diagnosis of steatosis and fibrosis on a Brazilian nonalcoholic fatty liver disease cohort. *Eur J Gastroentrol Hepatol* 2020;**32**: 231-238.

Supplements:
McColl KEL. Pathophysiology of duodenal ulcer disease. Eur J Gastroenterol Hepatol 2012; 9 (Suppl 1): S9-S12. McColl KEL. Pathophysiology of duodenal ulcer disease. *Eur J Gastroenterol Hepatol* 2012;**9**(Suppl 1): S9-S12.

Books

Book:
Avanduk C. *Manual of Gastroentrology: Diagnosis and Therapy*. 4th ed. 2008 Philadelphia: Lippincott Williams & Wilkins.

Chapter in a book:
Dancygier H, Lightdale CJ, Stevens PDDancygier H, Lightdale CJ. *Endoscopic ultrasonography of the upper gastrointestinal tract and colon. Endosonography in gastroenterology: principles, techniques, findings*. 1999 Stuttgart Thieme Verlag:13–175.

Online
Snyder CL, Young DO, Green PHR, Taylor AKPagon RA, Bird TC, Dolan CR, Stephens K. Celiac disease GeneReviews [Online, 03 July 2008]. 1993 Seattle University of Washington.

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