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Effectiveness of Gastric Cancer Endoscopic Screening in Intermediate-Risk Countries—A Systematic Review and Meta-Analysis

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Keywords: diagnosis | gastrointestinal neoplasms | mass screening endoscopy | meta-analysis | public health | risk factors | stomach neoplasm, early detection of cancer | survival

ABSTRACT

Background: Gastric cancer remains a major cause of cancer-related mortality in intermediate-risk countries. Although endoscopic screening is widely implemented in high-risk regions, its effectiveness and economic viability in intermediate-risk settings remain uncertain. This systematic review and meta-analysis evaluated the effectiveness and cost-effectiveness of endoscopic screening in these countries.

Methods: A systematic review and meta-analysis was conducted to assess the effectiveness and cost-effectiveness of upper gastrointestinal endoscopic screening by esophagogastroduodenoscopy (EGD) for gastric cancer. Searches were performed in Medline, Scopus, Embase, and Web of Science up to 30 September 2024. Pooled estimates were calculated for the detection of precancerous conditions, gastric cancer (overall and early-stage), and gastric cancer-specific mortality. Subgroup analyses were performed by screening strategy and geographic setting.

Results: Thirty-two studies met inclusion criteria—24 on screening effectiveness and eight on cost-effectiveness. Among 404,159 individuals screened, the pooled detection rate for precancerous conditions was 25.5%, for gastric neoplastic lesions 3.3%, and for early-stage cancer among neoplastic cases 91.6%. Gastric cancer-specific mortality was 26.1%, and 5-year survival reached 75.7%. Subgroup analyses of studies using direct EGD versus pre-selection indicated higher detection of precancerous conditions (32.5% vs. 17.0%, $p < 0.001$) and early-stage cancer (95.8% vs. 87.3%, $p < 0.001$). Comparing Chinese versus other settings, similar detection rates were found for precancerous conditions (25.3% vs. 26.0%) and early-stage detection (91.5% vs. 100%). Economic analyses suggest that endoscopic screening is cost-effective in intermediate-risk settings, particularly when combined with colorectal screening, with incremental cost-effectiveness ratios within accepted willingness-to-pay thresholds.

Abbreviations: AI, artificial intelligence; CI, confidence interval; EGC, early gastric cancer; EGD, esophagogastroduodenoscopy; GC, gastric cancer; HP, *Helicobacter pylori*; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; WTP, willingness-to-pay.

Conclusions: Endoscopic screening by EGD shows strong potential for early detection of gastric cancer in intermediate-risk countries. However, formal comparative analyses with unscreened populations are lacking, and most survival and mortality data originate from Chinese studies, limiting generalizability. Nevertheless, economic evaluations suggest implementing endoscopic screening—especially when integrated with colorectal screening or guided by risk stratification—could be a feasible and effective strategy.

Trial Registration: PROSPERO—CRD42024502174

1 | Introduction

Gastric cancer (GC) is the fifth most common and deadliest cancer worldwide, with significant geographical variation. High-risk countries such as Japan, Mongolia, and South Korea report age-standardised incidence rates ≥ 20 per 100,000 person-years, while intermediate-risk countries were defined as those with age-standardised rates between 10 and 20 per 100,000, based on GLOBOCAN 2022 data [1]. Although global incidence is declining, GC in younger individuals and proximal or diffuse types is increasing and is often associated with poorer prognosis [2, 3].

GC is typically asymptomatic in the early stages, leading to delayed diagnosis. Five-year survival exceeds 90% when detected early but remains below 40% in advanced stages [4–7]. Symptom-based detection has limited effectiveness for early diagnosis.

Esophagogastroduodenoscopy (EGD) is the gold standard for GC screening [8, 9]. In high-risk countries, national EGD-based programmes have significantly reduced GC mortality [10, 11]. However, most intermediate-risk countries lack national screening policies despite growing evidence of the benefit of endoscopic screening.

Recent studies indicate that integrating EGD with colorectal cancer screening may improve cost-effectiveness and increase participation [12, 13]. European guidelines now support EGD screening in intermediate-risk populations, provided cost-effectiveness is demonstrated and infrastructure allows [14–16]. Despite this, there is no comprehensive synthesis of the effectiveness and cost-effectiveness of EGD screening in intermediate-risk settings.

This systematic review and meta-analysis aims to address this gap by evaluating the impact of EGD screening on the detection of precancerous conditions, GC diagnosis (overall and early-stage), mortality, survival, and economic outcomes.

2 | Methods

This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and defined eligibility using the Population, Intervention, Comparison, Outcomes, and Study framework (Table 1). The protocol was registered with PROSPERO (CRD42024502174) and published [17].

A comprehensive search was conducted in Medline, Scopus, Embase, and Web of Science, supplemented by grey literature and reference lists. The search strategy adhered to the Peer Review of Electronic Search Strategies guidelines [18] and was tailored to each database (Supporting Information S2—Search strategy). We included randomised and non-randomised controlled trials, cohort, case-control, cross-sectional and other observational studies, as well as cost-effectiveness, cost-utility, and decision-analytic models published as free full-text articles in English, Portuguese or Spanish, up to 30 September 2024.

Two reviewers independently screened the title, abstracts and full texts, resolving disagreements through discussion or consultation with additional reviewers. For duplicate cohorts, the most comprehensive or recent publication was used. Inter-reviewer agreement in study selection and quality assessment was assessed with Cohen's Kappa (considered "almost perfect" when ≥ 0.81) [19, 20].

Three reviewers independently extracted data using a pre-defined form (Supporting Information S3—Variables form) and classified studies into effectiveness or economic categories. Risk of bias was assessed with appropriate tools: RoB2 for randomised controlled trials, ROBINS-I for non-randomised studies, the Newcastle-Ottawa Quality Assessment Scale [21] for case-control and cohort studies, the National Heart, Lung, and Blood Institute study quality assessment tool [22] for cross-sectional studies, and the Consensus on Health Economic Criteria list [23] for cost-effectiveness studies.

Meta-analyses were conducted in Jamovi (v2.4.8), applying a random-effects model with Restricted Maximum Likelihood estimation. Pooled effect sizes were calculated for five outcomes: detection of gastric precancerous conditions (defined as atrophic gastritis or gastric intestinal metaplasia), gastric neoplastic (low-grade intraepithelial neoplasia, high-grade intraepithelial neoplasia, carcinoma in situ, suspicious lesions, and invasive neoplasia - Vienna classification categories 3 to 5- early-stage GC (EGC) and advanced GC), 5-year survival, and GC-specific mortality [16, 24].

Statistical significance was assessed using the Z-test, with $p < 0.05$ considered significant [25]. 95% confidence intervals (CI) were reported. Heterogeneity was assessed using Cochran's Q test, and quantified via I^2 and Tau^2 [25–28].

To address potential selection bias from pre-screening strategies, a subgroup analysis compared studies using direct EGD with those using prior stratification (e.g. serological tests or questionnaires). Separate meta-analyses were performed for precancerous conditions, gastric neoplastic lesions, early-stage lesions, and GC–related mortality.

Key Summary

- What is already known about this subject
  - Gastric cancer remains a leading cause of cancer mortality worldwide, with wide regional variation in incidence.
  - Countries with intermediate-risk levels of gastric cancer face challenges in implementing organised screening programs.
  - Endoscopic screening is effective in high-risk countries, particularly in Asia, but its cost-effectiveness in intermediate-risk settings is less clear.
- What are the significant and/or new findings of this study
  - This systematic review and meta-analysis synthesises the available evidence on the effectiveness of endoscopic screening for gastric cancer in intermediate-risk countries.
  - The pooled detection rate of gastric neoplastic lesions was 3.3%, and the proportion of early-stage cancers among neoplastic cases was 91.6% in the screened populations.
  - The findings support the potential benefit of endoscopic screening in selected intermediate-risk contexts, particularly when integrated with existing colorectal cancer screening programs.

Additionally, to explore potential sources of heterogeneity, we performed a geographic subgroup analysis comparing studies from China with those from other intermediate-risk countries, focusing on pooled detection rates of precancerous conditions, gastric neoplastic lesions and early lesions.

A narrative synthesis of cost-effectiveness outcomes was conducted due to heterogeneity in models and assumptions. Currency was standardised to United States dollars (US$) at the February 2025 exchange rate (1€ = 1.04 US$ and 1CN = 0.138 US$) to facilitate comparisons between studies.

3 | Results

The search identified 1615 records; 969 remained after duplicates were removed (Supporting Information S4 and S5—All Studies; Excluded Studies) (Figure 1).

After screening, 75 articles underwent full-text review (inter-reviewer agreement: 91.0%; Cohen's kappa = 0.82), and 43 met inclusion criteria (agreement: 96%; $\kappa = 0.92$). Two additional studies were identified through reference screening, yielding 45 included articles (Supporting Information S6—Included Studies Dataset): 34 effectiveness studies and 11 cost-effectiveness studies. After risk-of-bias assessment, 24 studies were retained for effectiveness and 8 for cost-effectiveness analysis (Figure 2).

3.1 | Effectiveness Studies Analysis

A total of 404,159 individuals underwent EGD screening across 24 included effectiveness studies (Table 2).

Most studies were conducted in China [29–45], where two national screening programmes were implemented; seven often originated as pilot initiatives [46–52]. Study designs included one cluster randomised controlled trial [29], one case-control

TABLE 1 | Population, intervention, comparison, outcome and study design framework for this systematic review and meta-analysis.

Question: What is the effectiveness of endoscopic screening for gastric cancer in intermediate-risk countries?	
Population	Asymptomatic population of intermediated-risk countries (countries with incidence age-standardised rate 10–20 per 100·000 person/years: Tajikistan, Iran, Azerbaijan, Kyrgyzstan, Bhutan, Belarus, Peru, Mali, Chile, Costa Rica, Democratic People's Republic of Korea, China, Kazakhstan, Russian Federation, Vietnam, Estonia, Colombia, Portugal, Ecuador, Albania, Guadeloupe (France), Guatemala, Latvia, Armenia, Turkmenistan, Myanmar, Samoa, Turkey, Lithuania, Lao People's Democratic Republic, Sao Tome and Principe, Afghanistan, Martinique (France), Brunei Darussalam, Zimbabwe, Uzbekistan), between 40 and 80 years of age, without diagnostic of GC or precancerous conditions
Intervention	Endoscopic screening for gastric cancer
Comparison	No screening for gastric cancer
Outcome	The effectiveness of endoscopic screening of gastric cancer was defined as: detection rate of gastric precancerous conditions (atrophic gastritis, gastric intestinal metaplasia); detection rate of gastric cancer; detection rate of early gastric cancer; stage at diagnosis; mortality rate of gastric cancer of screened versus. non-screened patients; 5-year survival rate of gastric cancer screened; costs of screening programme
Studies designs	Randomised controlled trials, non-randomised controlled trials, cohort studies, case-control studies, cross-sectional studies and cost-effectiveness studies

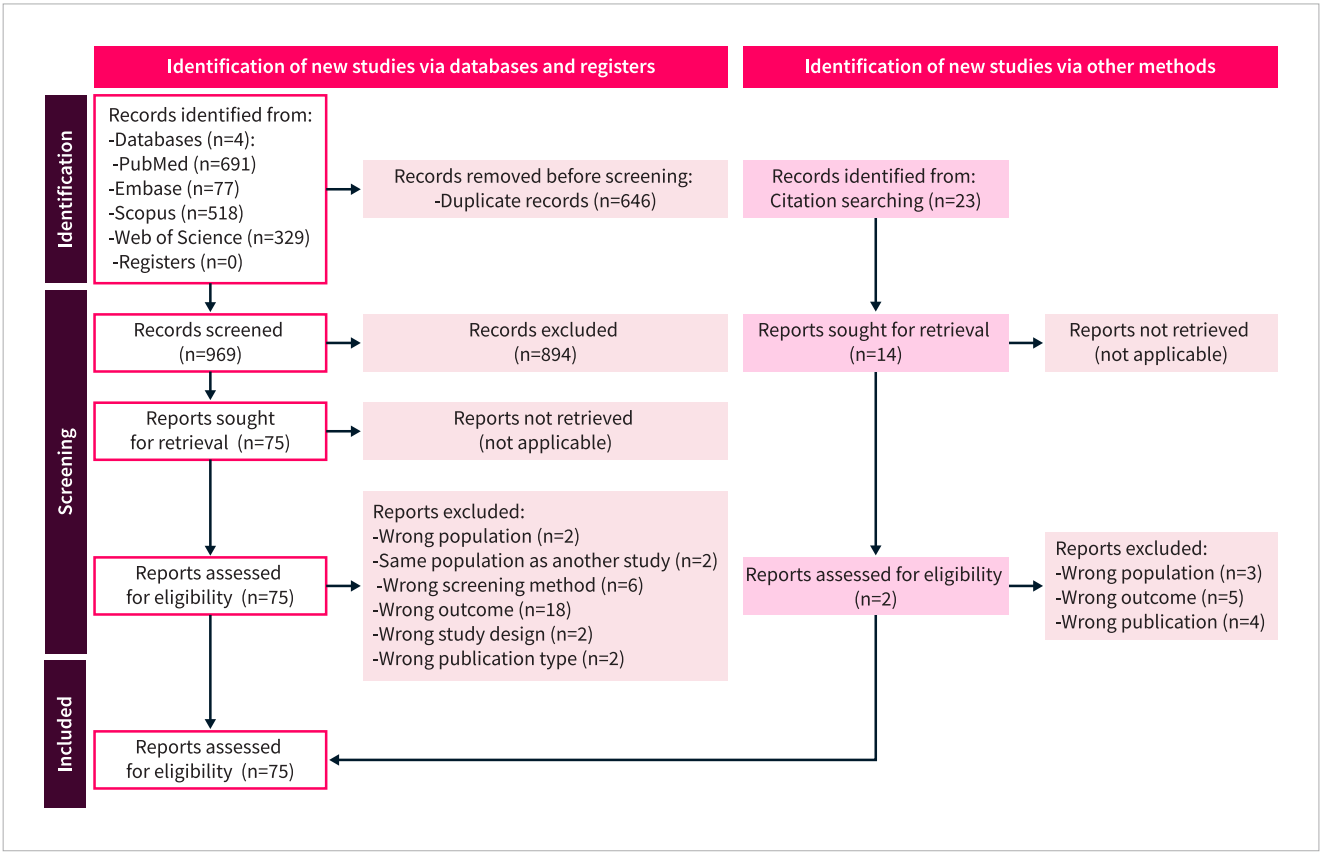

FIGURE 1 | Flowchart of the included studies according to the preferred reporting items for systematic reviews and meta-analyses guidelines.

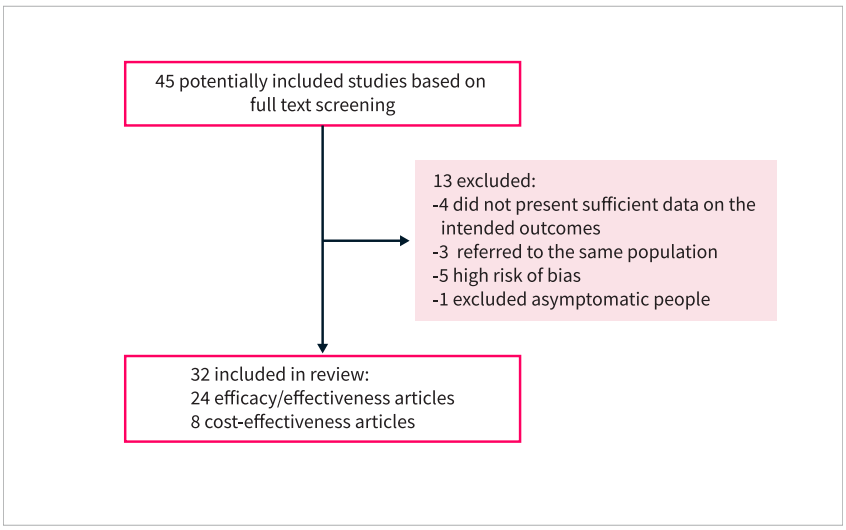

FIGURE 2 | Flowchart of the final decision to include articles in this study.

[32], four prospective [34, 37, 38, 40] and five retrospective [30, 33, 42, 51, 52] cohorts, 11 cross-sectional [31, 35, 36, 39, 43, 45–48, 50, 53], one prospective [41], and one retrospective observational study [49].

Screening was mostly offered to individuals aged ≥ 40 years, with some studies incorporating risk stratification tools prior to EGD [29, 35, 36, 38–40, 43, 44, 48, 49]. Adherence ranged from 12.7% to 94.2% (Table 2) and follow-up from 1 to 11.5 years (Supporting Information S7—Included studies outcomes dataset).

3.2 | Detection Rate of *Helicobacter Pylori* and Gastric Precancerous Conditions

Helicobacter pylori prevalence was reported in 14 studies [34–36, 38, 39, 41, 44–52], ranging from 13.1% to 89.2% (pooled effect size: 49.4% ($p < 0.001$, Tau [2] = 3.7%; $I^2 = 99.9\%$) (Supporting Information S8—*Helicobacter Pylori* Meta-analysis).

Twenty-two studies [29–31, 34–52] reported detection of gastric precancerous conditions (atrophic gastritis or gastric intestinal

TABLE 2 | Characteristics of included effectiveness studies and a description of the main outcomes.

First author, year	Country	Study design	Sample size	Adherence rate (%)	Age range (Years)	Average age (years)	Gender distribution (males %)	Screening method	Precancerous conditions (N/%)	Gastric neoplastic lesions* (N/%)	LGIN + HGIN + early GC (%)	Reduced mortality (%)	Risk of bias
Dorji, T. et al., 2024	Bhutan	Observational retrospective	53,182	94.2%	40–75			Questionnaire (high risk) + EGD	64 (0.1%)	366 (0.7%)			NHLB: Fair
Morais, R. et al., 2024	Portugal	Cohort retrospective	1364			57	45.6%	EGD	851 (62.4%)	14 (1.0%)			NOS: 4; 1; 3
Liu Y. et al., 2024	China	Cohort retrospective	17,862		> 18	53	51.3%	EGD	61 (0.3%)	76 (0.4%)	100%		NOS: 4; 1; 2
Gong, Y. et al., 2022	China	Cross-sectional	60,519		17–85	49.2	64.9%	EGD	1143 (18.9%)	1403 (2.3%)	80.2%		NHLB: Low
Li, L. et al., 2022	China	Cohort prospective	1019	12.7%	≥ 40		83.7%	Serological + questionnaire + EGD	121 (11.9%)	49 (4.8%)	71.4%		NOS: 4; 1; 2
Li, W.Q. et al., 2022	China	Cohort prospective	14,670		40–69	53.9	47.7%	EGD	5953 (40.6%)	741 (5.1%)	91.9%	33%	NOS: 4; 2;3
Yu, Z. et al., 2022	China	Cohort prospective	1957	22.3%	40–74		42.4%	Questionnaire (high risk) + EGD	145 (7.4%)	3 (0.2%)			NOS: 4; 2; 3
Ge, X. et al., 2021	China	Cross-sectional	8257		> 40		47.3%	EGD	2605 (31.6%)	621 (0.8%)	98.4%		NHLB: Low
Huang, Y. et al., 2021	China	Observational prospective	1108	93.7%	21–79	48	39.5%	EGD	1038 (93.7%)	10 (0.9%)			NHLB: Fair
Lau, J.W.L. et al., 2021	Singapore	Cohort retrospective	1414		40–88.3	60.3	52.5%	EGD	169 (12.0%)	3 (0.21%)			NOS: 3; 1; 2
Meng, T. et al., 2021	China	Cross sectional	35,525				58.2%	Questionnaire (high risk) + EGD	480 (1.4%)	280 (0.79%)			NHLB: Fair
Tong, Y. et al., 2021	China	Cross-sectional	1922		25–75	52.3	55.4%	Serological + questionnaire + EGD	717 (37.3%)	51 (2.7%)	84.3%		NHLB: Fair
Zhou, X. et al., 2021	China	Cross-sectional	14,929		40–80	56.2	49.7%	Serological + questionnaire + EGD	3651 (24.5%)	1231 (8.2%)	79.3%		NHLB: Low
Chen, R. et al., 2020	China	Cohort retrospective	113,340	33.5%	40–69		49.4%	EGD		3279 (2.9%)		62% (non-cardia)	NOS: 4; 1; 3
Ji, L. et al., 2020	China	Cross-sectional	872	69.2%	40–69	58.8	40.4%	Serological + questionnaire + EGD	169 (19.4%)	114 (13.1%)	97.4%		NHLB: Low
Xiao, H.F. et al., 2020	China	Cross-sectional	10,364	29.1%	40–74	56.1		Questionnaire (high risk) + EGD	60 (0.6%)	312 (3.0%)	100%		NHLB: Low
Zeng, H. et al., 2020	China	Cluster randomised controlled trial	37,922	43.8%	40–69	53.8	44.2%	Questionnaire (high risk) + EGD	8499 (22.4%)	284 (0.80%)	75.35%		cROB2: Low
Chen, Q. et al., 2016	China	Case-control	837		40–69	60.6		EGD				28%	NOS: 4; 1; 3
MacHaca Quea, N.R. et al., 2016	Peru	Cross-sectional	573		40–90	57	33.0%	EGD	180 (31.4%)	16 (2.8%)	100%		NHLB: Fair
Zheng, X. et al., 2015	China	Cohort retrospective	12,453		40–69	52.8	42.8%	EGD	3211 (25.8%)	85 (0.7%)	100%		NOS: 3; 1; 3

(Continues)

TABLE 2 | (Continued)

First author, year	Country	Study design	Sample size	Adherence rate (%)	Age range (Years)	Average age (years)	Gender distribution (males %)	Screening method	Precancerous conditions (N/%)	Gastric neoplastic lesions* (N/%)	LGIN + HGIN + early GC (%)	Reduced mortality (%)	Risk of bias
Mansour-Ghanaei, F. et al., 2012	Iran	Cross-sectional	1382	13.2%	50–87	61.7	49.4%	EGD	7 (0.5%)	11 (0.8%)			NHLB: Fair
Emura, F. et al., 2010	Colombia	Cross-sectional	650	81.6%	40–70	51.7	40.0%	EGD	194 (29.9%)	3 (0.5%)	100%		NHLB: Low
Malekzadeh, R. et al., 2004	Iran	Cross-sectional	1011	91.5%	40–92	53.3	48.9%	Serological + questionnaire + EGD	1051 (45.6%)	9 (0.4%)			NHLB: Low
Riecken, B. et al., 2002	China	Cohort prospective	4392		35–64	60	77.6%	EGD	2652 (60.4%)	738 (16.8%)	95.7%		NOS: 3; 1; 3

Note: Gastric neoplastic lesions: low-grade intraepithelial neoplasia, high-grade intraepithelial neoplasia, carcinoma in situ, suspicious lesions, invasive neoplasia, early-stage GC (EGC) and advanced GC.
Abbreviations: cROB2, Cochrane risk of bias tool for cluster randomised controlled trials; EGD, Esophagogastroduodenoscopy; GC, Gastric cancer; LGIN, low-grade intraepithelial neoplasia; HGIN, high-grade intraepithelial neoplasia; NHLB, National Heart, Lung and Blood Institute study quality assessment tools; NOS, Newcastle-Ottawa Quality Assessment Scale; RR, Relative risk.

metaplasia), with frequencies between 15.3% and 35.7% (pooled effect size: 25.5%; $p < 0.001$; $I^2 = 100\%$; Tau [2] = 6.0%) (Supporting Information S9—Precancerous conditions Meta-analysis). In screening methods subgroup analysis, studies using direct EGD showed a pooled detection rate of 32.5% (95% CI: 16.4%–48.7%; $p < 0.001$; Tau [2] = 8.1%; $I^2 = 100\%$, $n = 12$) (Supporting Information S10—Precancerous in direct EGD meta-analysis), versus 17.0% (95% CI: 7.3%–26.8%; $p < 0.001$; Tau [2] = 2.5%; $I^2 = 100\%$; $n = 10$) (Supporting Information S11—Precancerous in Pre-tested EGD meta-analysis) in studies with pre-selection.

In the geographic subgroup analysis, 16 studies conducted in China reported a pooled detection rate of precancerous conditions of 25.3% (95% CI: 12.3%–38.2%; $p < 0.001$; Tau [2] = 6.6%; $I^2 = 100\%$) (Supporting Information S12—Precancerous in China meta-analysis). In contrast, seven studies from other intermediate-risk countries showed a similar pooled rate of 26.0% (95% CI: 8.6%–43.3%; $p = 0.003$; Tau [2] = 5.5%; $I^2 = 99.9\%$) (Supporting Information S13—Precancerous in Other Countries meta-analysis).

3.3 | Detection Rate of Gastric Neoplastic Lesions and EGC

Regarding gastric neoplastic lesions (low-grade intraepithelial neoplasia, high-grade intraepithelial neoplasia, EGC, and advanced GC), 23 studies [29–31, 33–52] reported prevalence rates ranging from 1.5% to 5% (pooled effect size: 3.3% ($p < 0.001$; Tau [2] = 0.2%; $I^2 = 99.9\%$) (Supporting Information S14—Gastric Neoplastic Lesions Meta-analysis) (Figures 3 and 4). Among 14 studies [29–31, 34–39, 42, 44–46, 50] reporting the proportion of early-stage lesions among all neoplastic cases, the pooled estimate was 91.6% (95% CI: 86.4–96.9.0%; $p < 0.001$; Tau [2] = 0.96%; $I^2 = 100\%$) (Supporting Information S15—Early lesions Meta-analysis).

Subgroup analysis by screening strategy showed that in studies using direct EGD, the pooled gastric neoplastic lesion detection rate was 3.2% (95% CI: 0.7%–5.7%; $p < 0.012$; Tau [2] = 0.2%; $I^2 = 99.95\%$, $n = 13$) and the proportion of early-stage lesions was 95.8% (95% CI: 91.1%–100%; $p < 0.001$; Tau [2] = 0.5%; $I^2 = 100\%$, $n = 8$) (Supporting Information S16 and S17—Gastric neoplastic lesions in direct EGD meta-analysis; Early lesions in direct EGD meta-analysis). In studies applying pre-selection, the pooled detection rate for gastric neoplastic lesions was 3.4% (95% CI: 0.8%–5.9%; $p = 0.009$; Tau [2] = 0.2%; $I^2 = 99.96\%$, $n = 10$), and early-stage lesions represented 87.3% of neoplastic cases (95% CI: 76.9%–97.8%; $p < 0.001$; Tau [2] = 1.3%; $I^2 = 97.6\%$, $n = 5$) (Supporting Information S18 and S19—Gastric Neoplastic Lesions in Pretested meta-analysis; Early lesions in Pretested meta-analysis).

In the geographic subgroup analysis, 16 studies conducted in China yielded a pooled detection rate of gastric neoplastic lesions of 4.3% (95% CI: 2.0%–6.7%; $p < 0.001$; Tau [2] = 4.8%; $I^2 = 99.97\%$) and a proportion of early-stage lesions of 91.5% among neoplastic findings (95% CI: 86.0%–97.1%; $p < 0.001$; Tau [2] = 9.2%; $I^2 = 100\%$; $n = 11$) (Supporting Information S20 and S21—Gastric Neoplastic Lesions in China meta-analysis; Early lesions in

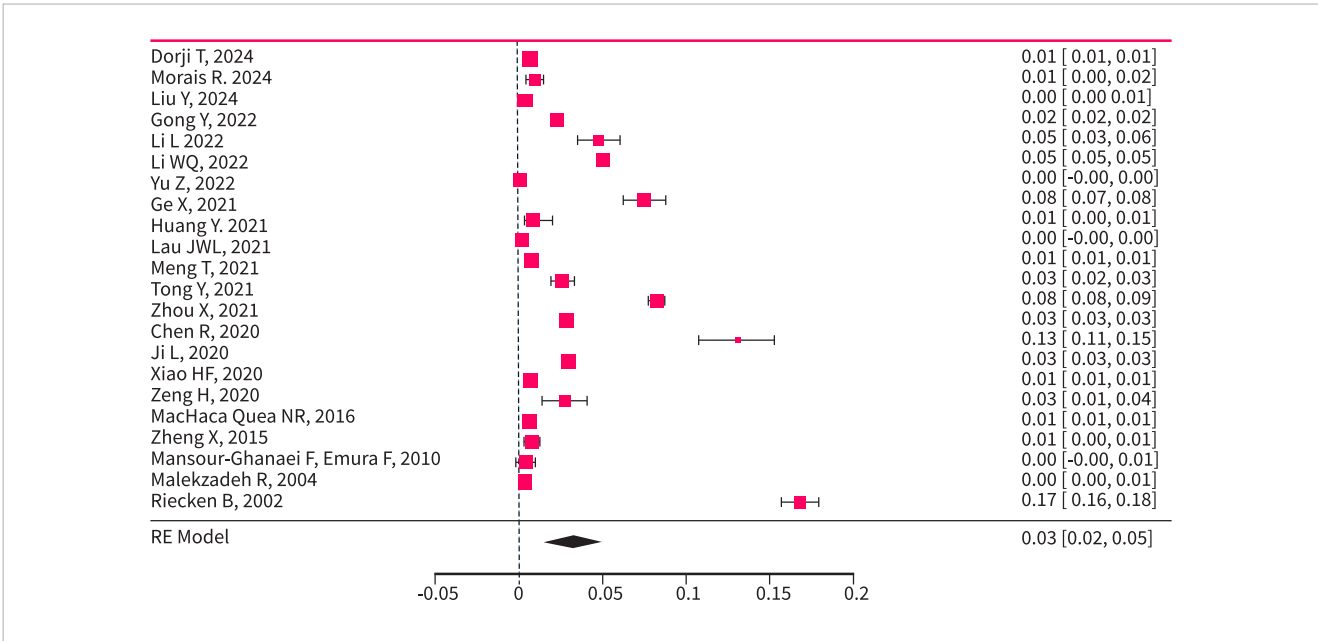

FIGURE 3 | Forest plot—Effect size of frequencies of positive lesions on endoscopic screening.

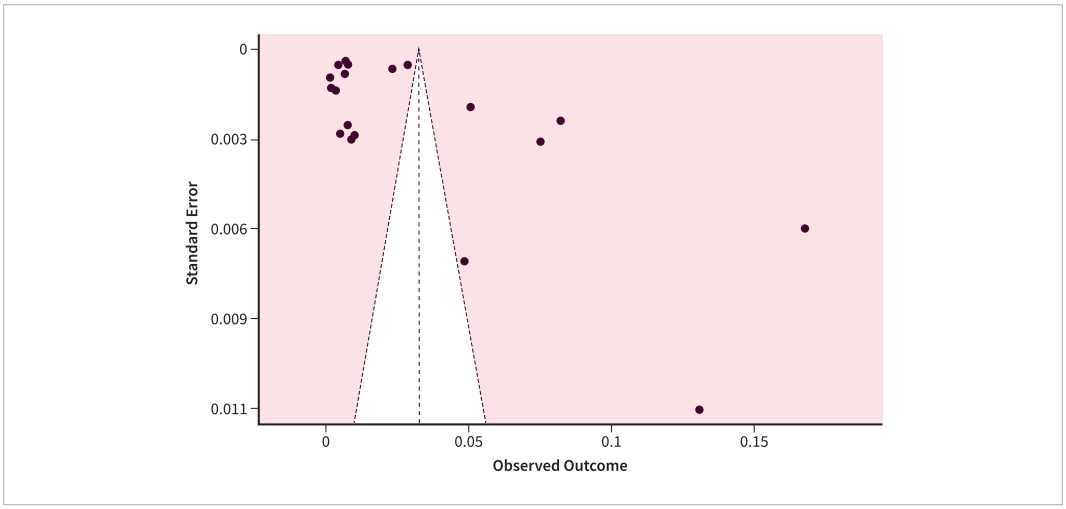

FIGURE 4 | Funnel plot for publication bias and heterogeneity in meta-analysis of positive lesions.

China meta-analysis). In contrast, seven studies from other intermediate-risk countries reported a pooled detection rate of gastric neoplastic lesions of 0.7% (95% CI: 0.3%–1.2%; $p < 0.002$; Tau [2] = 0.0%; $I^2 = 94.3\%$) (Supporting Information S22—Gastric Neoplastic Lesions in Other Countries meta-analysis). However, only two studies reported early-stage lesion data, with both indicating early-stage disease in 100% of detected neoplasms.

3.4 | Effect Size of Endoscopic Screening on GC Mortality and Five-Year Survival

GC mortality was reported in five studies [30, 32–34, 37]; one [32] lacked data on the total number of GC cases and was therefore excluded from the meta-analysis. The pooled mortality rate was 26.1% ($p < 0.001$; 95% CI: 15.5%–36.7%; Tau [2]: 1.0%; $I^2 = 91.0\%$) (Supporting Information S23—Mortality meta-analysis). Only three studies [32, 33, 37] reported relative mortality risk reduction with a pooled rate of 34.8% (95% CI: 26.1%–43.4%; $p < 0.001$; Tau [2] = 0.57%; $I^2 = 99.7\%$) (Supporting Information S24—RR mortality GC). Five-year survival was reported only in three studies [30, 34, 37]: the pooled 5-year survival rate was 75.7% (95% CI: 63.4%–88.0%; $p < 0.001$; Tau [2] = 1.2%; $I^2 = 99.9\%$) (Supporting Information S25—5Y survival meta-analysis).

All studies reporting these outcomes employed direct EGD screening and were conducted in China. Therefore, no subgroup

analyses by screening strategy or geographic setting were performed for GC-specific mortality, risk reduction mortality or 5-year survival.

3.5 | Cost-Effectiveness Studies Analysis

This review included eight cost-effectiveness studies using Markov modelling, microsimulation, or hybrid approaches. Key characteristics are presented in Table 3. Due to methodological heterogeneity, a narrative synthesis was performed.

Two studies used microsimulation [54, 55], while the remaining six applied variations of Markov models [13, 56–60]. One study integrated both methods to improve modelling of disease progression and costs [60]. Screening strategies ranged from one-time to biennial, triennial, and risk-based approaches, with some studies also assessing *Helicobacter pylori* eradication as a standalone or combined strategy.

Regarding geographical distribution, five of the studies were conducted in China [54, 55, 58–60], indicating a strong research focus in this setting. Portugal contributed two studies [13, 57], while Singapore accounted for one study [56], further emphasising the international scope of these modelling approaches.

Reductions in GC mortality risk ranged from 40% to 90%, with the highest impact reported by a Chinese study [60] using hybrid modelling (up to 90.2% reduction in mortality and 86.4% in incidence).

The impact of screening on survival was assessed in life-years saved and/or quality-adjusted life-years (QALY), and the cost-effectiveness analysis was assessed by incremental cost-effectiveness ratio (ICER) concerning the willingness-to-pay (WTP) of each country.

Despite reporting cost-effectiveness outcomes, most studies did not provide confidence intervals or standard errors for life-years saved, QALY, or ICER.

3.6 | Quality-Adjusted Life Years (QALY)

Wang et al. reported the highest QALY gain (11.99) for a combined strategy of *H. pylori* eradication and EGD screening [59]. Xia et al. [58] and Dan et al. [56] estimated gains of 10.36 and 6.86 QALYs per person, respectively, for biennial screening between ages 40 and 44, supporting frequent surveillance in high-risk groups. Qin et al. [54] assessed personalised risk-based screening and reported gains ranging from 0.068 to 1.14 QALYs. Libânio et al. [57] showed that EGD plus colonoscopy with Artificial Intelligence (AI) yielded 1.12 QALYs per person, while Areia [13] et al. reported 0.209 QALYs for combined screening every 5–10 years.

Two other studies by Qin et al. [55, 60] examined different risk-stratified screening strategies, reporting that New Gastric Cancer Screening system, screening from age 40, yielded 0.090 additional QALYs, while Gastric Cancer Risk Score Scale based screening resulted in 0.068 QALYs, highlighting the potential advantages of risk-stratified screening over uniform population-based approaches.

3.7 | Incremental Cost-Effectiveness Ratio (ICER)

ICER values varied considerably depending on the screening method, target population, and healthcare setting.

Wang et al. [59] found that *H. pylori* eradication alone yielded the lowest ICER (US$2444/QALY), well below the WTP threshold (US$9654). Xia et al. [58] reported ICERs of US$1087–4511 for biennial endoscopic screening (WTP: US$10,276/QALY). Qin et al. [55, 60] reported that Gastric Cancer Risk Score Scale screening from age 40 had an ICER of US$12,601/QALY (WTP: US$37,655/QALY), while the New Gastric Cancer Screening strategy was associated with an ICER of US$15,668/QALY (WTP: US$17,922/QALY). Another study from the same authors [54] found that personalised risk-based screening had an ICER of US $17,618/QALY, aligning with the US$18,575/QALY WTP threshold, reinforcing its cost-effectiveness compared to universal screening strategies. Areia et al. [13] reported two different ICER values based on screening frequency: endoscopic screening every 10 years combined with colorectal cancer screening had an ICER of US$16,023/QALY, whereas screening every 5 years had an ICER of US$32,144/QALY, both of which were within Portugal's US$38,480/QALY WTP threshold. Finally, Libânio et al. [57], which assessed EGD combined with colonoscopy every 5 or 10 years, reported an ICER of US$34,629/QALY and US$43,903/QALY, respectively, both remaining within the US$49,358/QALY WTP threshold. The same author reported that combined EGD and colonoscopy with AI twice per decade strategy is cost-effective as long as AI accuracy is at least 93% and the AI cost per endoscopy is ≤ US$20.8.

4 | Discussion

This systematic review and meta-analysis provide updated evidence on the effectiveness and cost-effectiveness of endoscopic screening for GC in intermediate-risk countries. The findings indicate that EGD endoscopic screening significantly increases the detection of precancerous conditions (pooled prevalence: 25.5%), gastric neoplastic lesions (3.3%) and early-stage lesions (91.6%), aligning with results from high-risk countries such as Japan and South Korea, where national screening programmes have demonstrated a similar stage shift [11, 61, 62].

In the subgroup analysis by screening method, studies using direct EGD demonstrated higher detection rates of precancerous conditions (32.5% vs. 17.0%) and early-stage gastric lesions (95.8% vs. 87.3%) compared with those using pre-selection strategies. Detection rates of gastric neoplastic lesions were similar between approaches (3.2% vs. 3.4%), suggesting that both methods can effectively identify neoplastic lesions, although direct EGD may enhance detection of earlier histological stages.

Substantial heterogeneity was observed across studies, likely driven by differences in study design, screening methodology,

TABLE 3 | Characteristics of included cost-effectiveness studies and a description of the main outcomes.

First author, year	Country	Type of study	Type(s) of screening	Periodicity	Currency	Relative risk reduction of RR of GC mortality	Additional LYS and/or QALY for best screening strategy	ICERs for best screening strategy	Conclusion	Risk of bias
Libânio, D., 2024	Portugal	Cost-effectiveness (Markov model)	Single EGD at 50 years, EGD + colonoscopy (once or twice per decade), EGD alone (once or twice per decade) with or without AI	Once, every 5 or 10 years	Euros	60%–70%		€33,297/ QALY for screening every 10 years; €42,214/ QALY for every 5 years (WTP: €47,460/ QALY)	EGD + colonoscopy twice per decade is cost-effective in Portugal	Low
Qin, S., 2024	China	Cost-effectiveness (microsimulation model)	EGD every 2, 3, 5, or 8 years; NGCS; GCRSS	Every 2, 3, 5, or 8 years; NGCS and GCRSS strategies	USD		NGCS strategy (40–60 years, no comorbidity): LYS: ~1.13/ QALY: ~1.14	US$17,618/ QALY (WTP: US$18,575/ QALY)	Personalised screening based on comorbidity is cost-effective; NGCS provides the best balance of benefits and costs	Low
Qin, S., 2022	China	Cost-effectiveness (microsimulation model)	GCRSS screening strategies starting at 40, 45, 50, 55, 60, 65, and 70 years	Once, every 2 or 3 years	USD	70.6%	40-GCRSS: LYS: 0.795/ QALY: 0.068	US$12,601/ QALYs (WTP: US$37,655/ QALY)	GCRSS screening from age 40 is cost-effective and reduces GC burden in China	Moderate
Qin, S., 2022	China	Cost-effectiveness (microsimulation and Markov model)	mNGCS, EGD (once, every 2 years, every 3 years)	Once, every 2 or 3 years	USD	90.2%	40-NGCS: LYS: 0.120/ QALY: 0.090	US$15,668/ QALYs (WTP: US$17,922/ QALY)	NGCS-based screening from 40 years is cost-effective in China, reducing GC burden significantly	Low

(Continues)

TABLE 3 | (Continued)

First author, year	Country	Type of study	Type(s) of screening	Periodicity	Currency	Relative risk reduction of RR of GC mortality	Additional LYS and/or QALY for best screening strategy	ICERs for best screening strategy	Conclusion	Risk of bias
Wang Z., 2022	China	Cost-effectiveness (Markov model)	HP eradication; EGD (one-time, annual, biennial, triennial); risk-stratified screening	Once, every 2 or 3 years	CNY	44.5%	QALY: 11.99	CNY 17,725 (WTP: 70,000 CNY/QALY)	HP eradication should be prioritised in national health plans; targeted EGD is preferable over general population screening	Low
Xia, R., 2021	China	Cost-effectiveness (Markov model)	EGD (one-time, every 2, 3, 5, or 10 years)	Once, every 2, 3, 5, or 10 years	USD		QALY: 1.087 to 10.362	US$1087 to US$4511/ QALY (WTP: US$10,276/ QALY)	EGD screening for GC and oesophageal cancer every 2 years is cost-effective in high-risk areas	Low
Areia, M., 2018	Portugal	Cost-utility analysis (Markov model)	Standalone EGD, EGD combined with screening colonoscopy, Pepsinogen serologic screening	Every 5 or 10 years (EGD + colonoscopy); every 5 years (standalone EGD); every 2 years (Pepsinogen screening)	Euros	40%–50%	QALY: 0.209	€15,407/ QALY for screening every 10 years; €30,908/ QALY for every 5 years (WTP: €37,000/ QALY)	EGD for GC screening is cost-effective in Portugal when combined with colorectal cancer screening but not as a standalone strategy.	Low
Dan YY., 2006	Singapore	Cost-utility analysis (Markov model)	EGD	Every 2 years	USD		QALY: 6.856	US$26,836/ QALY (WTP: US$28,000/ QALY)	Screening is cost-effective in high-risk subgroups but not in the general population; ICER is highly dependent on incidence and screening costs.	Low

Abbreviations: AI, Artificial Intelligence; CNY, Chinese Yuan; EGD, Esophagogastroduodenoscopy; GC, Gastric Cancer; GCRSS, Gastric Cancer Risk Score Scale; HP, *Helicobacter Pylori*; ICER, Incremental cost-effectiveness ratio; LYS, life-years saved; mNGCS, modified New Gastric Cancer Screening Scoring System; NGCS, New Gastric Cancer Screening Scoring System; QALY, quality-adjusted life-years; USD, United States Dollar; WTP, willingness-to-pay.

and population characteristics. A major contributor was the predominance of studies conducted in China, where GC incidence in some regions may approach levels typical of high-risk settings. Two large national screening programmes accounted for a substantial portion of the included data, potentially influencing pooled effect estimates.

To explore the impact of geographic variability, a subgroup analysis compared studies conducted in China with those conducted in other intermediate-risk countries. Detection rates of precancerous conditions were similar (25.3% vs. 26.0%). However, the pooled detection rate of neoplastic lesions was higher in Chinese studies (4.3% vs. 0.7%), likely reflecting the presence of organised population-based screening programmes and higher regional incidence in some areas, both of which may enhance detection and contribute to heterogeneity. These findings highlight the importance of context-specific evaluation and underscore the need for further data from diverse settings across the intermediate-risk spectrum [44].

Our meta-analysis also examined prognosis. Among the five studies, the pooled GC-specific mortality rate was 26.1%. Additionally, only three studies reported relative risk estimates comparing screened and unscreened populations. These showed a pooled relative mortality risk reduction of 34.8% (95% CI: 26.1%–43.4%), suggesting a potential benefit of screening in reducing GC-specific deaths. The most significant effect was observed in risk-stratified strategies, such as the New Gastric Cancer Screening System. Five-year survival was 75.7% across three studies, underscoring the benefit of early detection, though limited data restrict generalisability. These findings are aligned with previous meta-analyses, including Hibino et al. [63], who demonstrated a significant mortality reduction (relative risk of 0.52, 95% CI 0.39–0.79). However, the limited number of studies and the fact that all were conducted in China limit the generalisability of these findings. Moreover, no eligible studies provided sufficient data to evaluate the impact of screening on gastric cancer incidence reduction.

Although not addressed in this review, EGD endoscopic screening may also offer benefits for oesophageal cancer detection, especially in at-risk populations.

Effectiveness also depends on interval and adherence. Shorter intervals were generally associated with higher early detection rates. However, adherence varied widely across studies (12.7%–94.2%), suggesting that participation rates may significantly impact real-world effectiveness. In addition, HP prevalence also varied (13.1%–89.2%), influencing baseline risk and strategy selection. Hooi et al. [64] reported similar global variations, with rates exceeding 70% in some Asian regions but falling below 30% in Oceania. Some studies evaluated HP eradication as a complementary or alternative strategy to endoscopic screening. Morais et al. [65] found that despite declining GC mortality in Portugal, HP prevalence remains elevated among older age groups, underscoring the potential value of combined eradication and screening strategies.

Cost-effectiveness is a critical determinant in the feasibility of implementing GC screening programmes, particularly in intermediate-risk settings where healthcare resources must be carefully allocated. The eight studies included in this review applied well-established economic modelling techniques—mainly Markov models and, in some cases, microsimulation—to evaluate various screening strategies. These models consistently projected substantial reductions in GC mortality (ranging from 40% to 90%) and demonstrated that risk-stratified or combined approaches, particularly those integrating *Helicobacter pylori* eradication, are likely to be cost-effective.

QALY gains reported across studies ranged from 6.9 to 12.0 per person, and ICER generally remained below national willingness-to-pay thresholds. These results are consistent with findings from high-risk countries such as Japan and South Korea, where organised screening programmes have led to significant improvements in survival and reductions in cancer mortality [61, 66–68].

Importantly, the results of this systematic review are in line with the recently published Management of epithelial precancerous conditions and early neoplasia of the stomach III guidelines issued by the European Society of Gastrointestinal Endoscopy in 2025, which state that endoscopic screening may be considered in intermediate-risk countries, provided that cost-effectiveness has been demonstrated [16].

Nonetheless, the generalisability of economic findings is limited by heterogeneity in model assumptions, screening intervals, and especially adherence rates, which vary widely across studies. Real-world implementation may be challenged by lower participation rates and logistical constraints, potentially impacting both effectiveness and cost-efficiency. Future studies should incorporate context-specific parameters, long-term outcomes, and realistic adherence scenarios to improve the transferability of cost-effectiveness data to policy planning.

5 | Limitations

Despite the findings of this review, several limitations should be acknowledged. First, substantial heterogeneity was observed across studies, reflecting differences in design, screening protocols, population characteristics and histopathological reporting. Although subgroup analyses were conducted by screening method and geographic region, residual heterogeneity remains and may influence pooled estimates.

Second, although this review adopted the European MAPS III (2025) [16] classification to distinguish between precancerous conditions, neoplastic lesions, and early-stage disease, variability in terminology and diagnostic thresholds across studies—particularly those conducted in East Asia—may have introduced misclassification bias.

Third, the assumption that GC arises primarily from identifiable precancerous conditions (e.g., OLGA/OLGIM stage III–IV) may overlook cases arising from earlier or undetected lesions.

Fourth, adherence rates varied widely (12.7%–94.2%), which may affect the real-world effectiveness of screening programmes.

Fifth, although a meta-analysis of gastric cancer-specific mortality risk reduction was performed, only three studies contributed data, all from China. This limits the generalisability of the findings. Furthermore, no eligible studies provided sufficient data to evaluate whether screening reduces gastric cancer incidence in screened versus unscreened populations, representing a significant gap in the literature.

Finally, data on 5-year survival were again only available from Chinese studies, precluding broader comparisons of long-term outcomes across different countries.

Regarding cost-effectiveness analyses, several factors may constrain interpretation. Most cost-effectiveness analyses assumed optimal adherence and implementation, which may not reflect routine clinical settings. Differences in modelling approaches (e.g., Markov vs. microsimulation) can lead to variability in projections. Healthcare costs and willingness-to-pay thresholds differ significantly between countries, complicating extrapolation across settings. The long-term economic impact of integrating artificial intelligence remains uncertain and depends on parameters such as diagnostic accuracy and cost. Most estimates were based on modelled projections rather than long-term empirical data, highlighting the need for future validation.

Finally, relevant studies from other intermediate-risk countries may still be underway or unpublished, reinforcing the importance of continuous evidence updates to inform policy.

6 | Implications for Future Research

Future studies should focus on conducting well-designed randomised trials to establish more robust evidence on the benefits and feasibility of endoscopic screening in intermediate-risk settings. Standardising screening protocols, including risk stratification and adherence strategies, will be essential for improving comparability between studies. Additionally, economic evaluations tailored to different healthcare environments are needed to determine the feasibility of large-scale implementation.

Research on innovative screening technologies, such as AI-assisted endoscopy and non-invasive biomarkers, could further optimise cost-effectiveness by reducing costs and increasing diagnostic efficiency. Long-term impact assessments of screening on GC mortality and healthcare expenditures will also be crucial in guiding public health policies.

7 | Conclusion

This systematic review and meta-analysis supports the potential role of endoscopic screening for GC in intermediate-risk countries. Screening was associated with high detection rates of precancerous conditions (25.5%) and early-stage lesions (91.6% among neoplastic cases), as well as improved 5-year survival (75.7%) and reduced GC-specific mortality (26.1%).

Subgroup analyses by screening strategy showed that direct EGD was associated with higher proportions of precancerous conditions and early-stage detections, while geographic subgroup analysis revealed similar detection of precancerous conditions across settings, with some variation in neoplastic detection rates. These findings provide a more granular understanding of screening performance across different populations and methodologies.

Most economic evaluations suggest that endoscopic screening may be cost-effective, particularly when integrated with colorectal screening or guided by risk stratification. However, substantial heterogeneity, variable adherence, and the predominance of data from Chinese studies highlight the need for cautious interpretation.

Future research should prioritise long-term outcome data, comparative effectiveness across strategies, and context-specific economic evaluations to inform policy development in diverse intermediate-risk settings.

Author Contributions

M.B. Mourato was responsible for conceptualization, designing, investigation, formal analysis and writing the manuscript. N. Pratas provided assistance with protocol design, investigation, and writing. A. Branco Pereira was responsible for investigation, and reviewing the writing of the manuscript. R. Chança was responsible for designing the search expression in the various databases. I. Fronteira and M. Areia participated in the protocol design, systematic review process supervision, and manuscript review. R. Dinis was responsible for the revision of the manuscript.

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Ethics Statement

Ethical approval was not required for this study, as it is a systematic review and meta-analysis of previously published data. No new data involving human participants were collected or analysed.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All data generated or analysed during this study are included in this published article (and its supplementary information files).

Study Protocol Publication

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.