

ORIGINAL RESEARCH ARTICLE

Diagnostic accuracy of serum pepsinogens for detecting chronic atrophic gastritis and gastric cancer: A meta-analysis

Ganchimeg Dondov^{1,2}, Bayarmaa Nyamaa¹, Batbold Batsaikhan³, Tegshjargal Badamjav³, Sodnomtsogt Lkhagvasuren⁴, and Tulgaa Lonjid^{3*}¹Department of Gastroenterology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia²Department of Oncology, Institute of Medical Sciences, Ministry of Economy and Development, Ulaanbaatar, Mongolia³Department of Internal Medicine, Institute of Medical Sciences, Ministry of Economy and Development, Ulaanbaatar, Mongolia⁴Department of Applied Neuroscience, Institute of Brain and Psychology, Mongolian Academy of Sciences, Ulaanbaatar, Mongolia***Corresponding author:**Tulgaa Lonjid
(tulgaa.ims@mnums.edu.mn)**Citation:** Dondov G, Nyamaa B, Batsaikhan B, Badamjav T, Lkhagvasuren S, Lonjid T. Diagnostic accuracy of serum pepsinogens for detecting chronic atrophic gastritis and gastric cancer: A meta-analysis. *Eurasian J Med Oncol*. doi: 10.36922/EJMO026110126**Received:** March 12, 2026**Revised:** May 13, 2026**Accepted:** May 19, 2026**Published online:** July 7, 2026**Copyright:** © 2026 Author(s). This is an Open-Access article distributed under the terms of the Creative Commons Attribution License, permitting distribution, and reproduction in any medium, provided the original work is properly cited.**Publisher's Note:** AccScience Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.**Abstract****Introduction:** Recent studies have shown that serological biomarkers such as pepsinogens may facilitate the early detection of gastric cancer.**Objective:** This study aims to evaluate the diagnostic performance of serum pepsinogen I (PGI) and the PGI/pepsinogen II ratio (PGR) in detecting gastric cancer and chronic atrophic gastritis.**Methods:** A systematic literature search was conducted using MeSH terms related to atrophic gastritis, gastric neoplasms, pepsinogen A, sensitivity, and specificity. Twenty-one eligible studies were included in the quantitative synthesis.**Results:** For atrophic gastritis, the area under the curve was 0.74 (95% confidence interval [CI] = 0.70–0.77) for PGI and 0.78 (95% CI = 0.75–0.82) for PGR. The pooled sensitivity and specificity were 61.4% (95% CI = 48.2–73.2) and 86.4% (95% CI = 61.8–96.1), respectively, for PGI, and 72.4% (95% CI = 61.0–81.4) and 76.9% (95% CI = 49.5–91.9), respectively, for PGR. For gastric cancer detection, the area under the curve values were 0.76 (95% CI = 0.72–0.80) for PGI, 0.77 (95% CI = 0.73–0.80) for PGR, and 0.79 (95% CI = 0.75–0.83) for the combined PGI+PGR model. The pooled sensitivity and specificity were 69.8% (95% CI = 55.0–81.3) and 70.8% (95% CI = 58.7–80.6), respectively, for PGI, 76.2% (95% CI = 65.4–84.2) and 66.1% (95% CI = 56.1–74.8), respectively, for PGR, and 61.5% (95% CI = 50.9–72.1) and 86.7% (95% CI = 79.4–94.1), respectively, for PGI+PGR.**Conclusion:** Serum PGI and PGR can be used as an additional screening for high-risk subjects who may require gastroscopy or biopsy.**Keywords:** Biomarkers for gastric cancer; Gastric cancer screening; Gastric precancerous conditions; Sensitivity of pepsinogen; Specificity of pepsinogen

1. Introduction

Globally, gastric cancer remains a serious health problem, despite a dramatic reduction in incidence and mortality over the last few decades.¹ In Mongolia, gastric cancer is the second most common cancer, behind liver cancer, and has been rising.² According to statistics from the International Agency for Research on Cancer, Mongolia has the highest incidence (35.5 per 100,000) and mortality (31.5 per 100,000) of gastric cancer.³ Effective screening and early detection of gastric cancer could reduce mortality related to gastric cancer by 30–65%.⁴ Correa *et al.*⁵ have shown that gastric cancer is often caused by atrophic gastritis, which progresses to intestinal metaplasia and dysplasia, ultimately leading to cancer. Risk factors, such as *Helicobacter pylori* infection, salt intake, and other causes—such as damage and inflammation of the gastric mucosa, which triggers an immune response—lead to chronic inflammation and subsequent atrophic changes in the mucosa.⁶

Although avoiding these risk factors and effective *H. pylori* eradication can decrease the risk of gastric cancer, the cancer risk remains if precancerous lesions are already present.⁷ Therefore, early detection and regular monitoring of precancerous lesions are fundamental for early screening and effective treatment of gastric cancer.⁸ Currently, gastroscopic screening is the gold standard for the detection of gastric cancer in early stages and precancerous lesions. However, in some countries such as Mongolia, gastroscopic screening has several limitations, including a high non-attendance rate due to people's negative attitudes and apprehension about the invasiveness of the procedure, limited availability of endoscopic devices in all regions, and a shortage of well-trained endoscopists to meet the increased demands.

Recent studies have shown that serological assays, such as pepsinogens (PGs), can facilitate the early detection of gastric cancer.^{9–12} Serum pepsinogens, precursors of the enzyme pepsin, are well-established biomarkers for detecting gastric atrophy. Pepsinogen I (PGI) is exclusively produced by chief cells in the gastric corpus, whereas pepsinogen II (PGII) is released throughout the stomach and the proximal duodenum. In cases of atrophic gastritis affecting the corpus, PGI levels significantly decrease, while PGII levels remain stable. This pattern allows the reduced PGI concentration and decreased PGI/PGII ratio (PGR) to serve as effective biomarkers for detecting gastric atrophy, especially corpus atrophy.¹³ However, results from studies on the accuracy of these biomarkers have been inconsistent; therefore, this study aimed to evaluate the diagnostic value of serum PGI and PGR for identifying gastric cancer and gastric atrophy.

2. Materials and methods

This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The meta-analysis question was defined by the PIT format:

- (i) Population (P): An adult person who underwent gastroscopy in both screening and clinical settings.
- (ii) Index test (I): Serum PGI, PGII, and PGR.
- (iii) Target condition (T): Gastric cancer and chronic atrophic gastritis.

2.1. Search strategy

To identify relevant studies, the Medline database (PubMed) and ScienceDirect were searched using the keywords ((“Gastritis, Atrophic”[MeSH]) OR “Stomach Neoplasms”[MeSH]) AND “Pepsinogen A”[MeSH]) AND “Sensitivity and Specificity”[MeSH]) for publications published up to April 2025. ScienceDirect was also searched using separate synonyms of the keywords as follows:

- (i) “Neoplasm, Stomach” OR “Stomach Neoplasm” OR “Neoplasms, Stomach” OR “Gastric Neoplasms” OR “Gastric Neoplasm” OR “Neoplasm, Gastric” OR “Neoplasms, Gastric” OR “Cancer of Stomach” OR “Stomach Cancers” OR “Gastric Cancer” OR “Cancer, Gastric” OR “Cancers, Gastric” OR “Gastric Cancers” OR “Stomach Cancer” OR “Cancer, Stomach” OR “Cancers, Stomach” OR “Cancer of the Stomach” OR “Gastric Cancer, Familial Diffuse.”
- (ii) “Atrophic Gastritides” OR “Atrophic Gastritis” OR “Gastritides, Atrophic.”
- (iii) “Pepsinogen” OR “Pepsinogen I” OR “Uropepsinogen” OR “Pepsinogen 3, Group I” OR “Pepsinogen 5, Group I.”
- (iv) “Sensitivity” AND “Specificity.”

2.2. Study selection criteria

Studies were included if they met the following criteria:

- (i) Studies written in English.
- (ii) Full-text articles available.
- (iii) Studies in which gastroscopy (with biopsies) was performed as a reference test.
- (iv) Studies with available data on variables such as age, gender, and *H. pylori* infection status.
- (v) Serum or plasma PGs measured by enzyme immunoassay or radioimmunoassay were acceptable, and expressed in ng/mL or equivalent.
- (vi) All relevant studies, whether data were collected retrospectively or prospectively, that evaluated the accuracy of at least PGI or PGR in the detection of chronic atrophic gastritis or gastric cancer.

(vii) Sufficient diagnostic sensitivity, specificity, and other necessary data, or the possibility of constructing a 2×2 table of true positive (TP), false positive (FP), false negative (FN), and true negative (TN) values.

Reviews, meta-analyses, meeting abstracts, letters, editorials, and guidelines were excluded. Two authors (GD and TL) independently reviewed the title and abstract and screened the full text to identify relevant studies in accordance with the eligibility criteria. Any disagreements in study selection were resolved through discussion among all authors. The study selection process for the final analysis was presented in a PRISMA flowchart (Figure 1).

2.3. Data extraction

Data were extracted from each selected study using a Microsoft Excel data extraction form. The extracted data included the following information:

- (i) First author.
- (ii) Year of publication.
- (iii) Geographical origin of the study.
- (iv) Study design and type.
- (v) Sample size.
- (vi) Age and gender of participants.
- (vii) Index test.
- (viii) Description of reference test.
- (ix) Target conditions.
- (x) Threshold values of biomarkers.
- (xi) *H. pylori* infection status.
- (xii) Use of a proton pump inhibitor.

2.4. Risk of bias assessment

Studies that met the inclusion and exclusion criteria were entered into Review Manager 5.4.1 software (RevMan Version 5.4; The Cochrane Collaboration, United Kingdom), and the methodological assessment was performed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) questionnaire. QUADAS-2 is an instrument that assesses the bias of the study as “high,” “low,” or “uncertain” in four key domains, including participant selection, index test, reference test, and flow of participants through the study and timing.

2.5. Statistical analysis

The meta-analysis was conducted using Review Manager 5.4.1 and Stata/IC 17.0 (StataCorp LLC, United States). The TP, FP, FN, and TN parameters were extracted and calculated from each study, and a 2×2 table was entered into Review Manager 5.4.1. Given the presence of a threshold effect, the area under the curve (AUC) was prespecified as the primary outcome of overall diagnostic accuracy, while pooled sensitivity and specificity were

considered secondary outcomes. A forest plot of pooled sensitivity and specificity was generated using a bivariate model. Due to variability in diagnostic thresholds between the studies, a hierarchical summary receiver operating characteristic model was applied. Heterogeneity across the studies was evaluated by visual inspection (95% prediction contour) and the I^2 index. Additionally, publication bias was determined using Deeks' funnel plot asymmetry test.

3. Results

3.1. Search results

A total of 383 records from PubMed and ScienceDirect were identified using the keywords. During the initial screening of titles and abstracts, studies were excluded for the following reasons: review articles ($n = 50$), meta-analyses ($n = 6$), animal studies ($n = 20$), and publications not written in English ($n = 10$).

After full-text evaluation, studies were excluded for the following reasons: not found full-text articles ($n = 8$) not relevant to the research question ($n = 201$) and inappropriate study populations and outcomes ($n = 55$). However, because there was insufficient information to construct a 2×2 table, 10 studies were excluded from the quantitative analysis. One study was excluded due to duplication. Finally, a total of 22 studies were included in the qualitative synthesis (Figure 1).

3.2. Risk of bias assessment

Figure 2 presents the results from the methods section of the remaining 22 studies in the quantitative analysis, including participant selection, index and reference test methods, and the QUADAS-2 assessment of the study processes. After reviewing each study's methods and methodology, the study by Zhang *et al.*¹⁴ was considered to have a high risk of bias in index test interpretation; therefore, we excluded this study from further analysis.

3.3. Study characteristics

The included studies were conducted between 1999 and 2024 across 13 countries in Asia, Europe, and the United States. After the QUADAS-2 assessment, 21 studies were included; 7 evaluated biomarkers for chronic atrophic gastritis and 17 evaluated biomarkers for gastric cancer, with overlap between study populations assessing both conditions. The study design, population, sample size, age, and gender of participants, index test, target conditions, cut-off values, and *H. pylori* infection status of the selected studies are shown in Table 1. There were 11 cross-sectional, 4 case-control, and 6 cohort studies. Regarding index tests, five studies used the Gastropanel test as the index, and the others used serum PGI, PGII, and PGR biomarkers.

Table 1. Characteristics of the studies

Author (year)	Country	Study design	Target condition	Index test	Cut-off of PGI and PGR	Study population	Mean age (years)	Male sex, n (%)	<i>Helicobacter pylori</i> infection
Castro <i>et al.</i> ¹⁵ (2018)	Portugal	Prospective cohort	Gastric cancer	PGI, PGR	For gastric cancer: PGI = 70 ng/mL + PGR = 3	5,913	–	2,257 (38.17%)	–
Chapelle <i>et al.</i> ⁹ (2020)	France	Prospective, multicenter cross-sectional	Atrophic gastritis,	Gastropanel	For atrophic gastritis: PGI = 43.6 ng/mL; PGR = 7	344	58.8 ± 14.2	156 (45%)	13.40%
Dondov <i>et al.</i> ¹⁶ (2022)	Mongolia	Matched case-control	Atrophic gastritis, gastric cancer	PGI, PGII, PGR, G-17	For atrophic gastritis: PGI = 75.07 ng/mL; PGR = 6.25 For gastric cancer: PGI = 35.25 ng/mL; PGR = 5.27; PGI=35.25 ng/mL + PGR = 5.27	114	59.98 ± 10.88	60 (52.6%)	67 (58.8%)
Gantuya <i>et al.</i> ¹⁷ (2018)	Mongolia	Multicenter cross-sectional	Gastric cancer	PGI, PGII, HP-ab	For atrophic gastritis: PGR = 3.1 For gastric cancer: PGI = 28 ng/mL; PGR = 2.2	802	Non-cancer patients = 44 ± 13.8; cancer patients = 53.8 ± 12.1	Non-cancer = 236/752 (31.4%), cancer = 42/50 (84%)	Non-cancer = 77%, cancer = 54%
Hamashima <i>et al.</i> ¹⁸ (2017)	Japan	Matched case-control	Gastric cancer	PGI, PGII, PGR	For gastric cancer: PGI = 65 ng/mL; PGR = 3	994	57.5±7.2	66.40%	–
In <i>et al.</i> ¹⁹ (2024)	USA	Cross-sectional	Gastric cancer	PGI, PGII, PGR, Hp positivity	For gastric cancer: PGR = 5.2; PGI = 70 ng/mL + PGR = 3	92	Gastric cancer patients = 67, non-cancer patients = 56	Gastric cancer group = 71.9%, non-gastric cancer group = 33.3%	–

(cont'd...)

Table 1. (Continued)

Author (year)	Country	Study design	Target condition	Index test	Cut-off of PGI and PGR	Study population	Mean age (years)	Male sex, n (%)	<i>Helicobacter pylori</i> infection
Juan Cai <i>et al.</i> ²⁰ (2017)	Kazakhstan	Cross-sectional	Gastric cancer	PGI, PGII	For gastric cancer: PGI = 72.78 ng/mL + PGR = 4.15	464	53.3 ± 13.8	65 (61.3%)	–
Kim <i>et al.</i> ²¹ (2005)	Korea	Prospective cohort	Atrophic gastritis, gastric cancer	PGI, PGII, PGR, quinine	For gastric cancer: PGI = 70 ng/mL + PGR = 3	43	Normal patients = 33.4, atrophic gastritis patients = 47.8, cancer patients = 57	–	–
Kitahara <i>et al.</i> ²² (1999)	Japan	Cross-sectional	Gastric cancer	PGI, PGII, PGR	For gastric cancer: PGR = 3; PGI = 70 ng/mL + PGR = 3	5,113	52.5	2,456 (48%)	–
Koivurova <i>et al.</i> ²³ (2021)	Finland	Cohort	Atrophic gastritis,	Gastropanel	For atrophic gastritis: PGI = 30 ng/mL; PGR = 3	522	55.7 ± 15.4	174 (33.3%)	–
Kurilovich <i>et al.</i> ²⁴ (2016)	Russia	Prospective case-control	Gastric cancer	Gastropanel	For gastric cancer: PGI = 30 ng/mL; PGR = 3	156	Cancer patients = 60.2 ± 7.5, normal patients = 59.8 ± 7.4	96 (61.5%)	–
Lee <i>et al.</i> ²⁵ (2017)	Korea	Cross-sectional	Gastric cancer	PGR, TFF3	For gastric cancer: PGR = 4.3	104	Normal = 56 ± 26, cancer = 54 ± 24	Cancer = 53.2%, normal = 48%	Cancer = 43.9%
Mizuno <i>et al.</i> ²⁶ (2009)	Japan	Cohort	Gastric cancer	PGI, PGII, PGR	For gastric cancer: PGI = 30 ng/mL; PGR = 2	12,120	50 (median)	7,590 (62.6%)	–
Nejadi-Kelarijani <i>et al.</i> ²⁷ (2014)	Iran	Cross-sectional	Non-atrophic, atrophic gastritis, gastric cancer	Gastropanel	For atrophic gastritis and gastric cancer: PGI 80 = ng/mL; PGR = 10	234	48.5	115 (49.1%)	–

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Table 1. (Continued)

Author (year)	Country	Study design	Target condition	Index test	Cut-off of PGI and PGR	Study population	Mean age (years)	Male sex, n (%)	<i>Helicobacter pylori</i> infection
Oishi <i>et al.</i> ²⁸ (2006)	Japan	Cohort	Gastric cancer	PGI, PGII, PGR	For gastric cancer: PGI = 70 ng/mL + PGR = 3	2,446	Men = 57, women = 59	1,016 (41.5%)	71.30%
Shafaghi <i>et al.</i> ²⁹ (2013)	Iran	Multicenter, cross-sectional	Atrophy, intestinal metaplasia, dysplasia	PGI, PGII, G-17	For atrophic gastritis: PGI = 73.61 ng/mL; PGR = 6.79	1,390	61.76 ± 9.02	684 (49.2%)	66.60%
Shikata <i>et al.</i> ³⁰ (2012)	Japan	Prospective cohort	Gastric cancer	PGI, PGII, PGR	For gastric cancer: PGI = 59 ng/mL + PGR = 3.9	2,446	57.3 ± 11.4	41.50%	72%
Trivanovic <i>et al.</i> ³¹ (2022)	Croatia	Cross-sectional	Gastric cancer	PGI, PGII, PGR	For gastric cancer: PGI = 70 mg/mL + PGR = 3	116	68.34 ± 13.93	70 (60.3%)	–
Wang <i>et al.</i> ³² (2020)	China	Cross-sectional	Gastric cancer	PGI, PGII, PGR	For gastric cancer: PGI = 71.85 ng/mL; PGR = 5.04	949	49.83 ± 8.40	443 (46.7%)	–
Yakut <i>et al.</i> ³³ (2013)	Turkey	Case-control	Non-atrophic gastritis, atrophic gastritis, intestinal metaplasia, dysplasia	PGI, PGII, G-17, VEGF, IL-1 β , TLR-4, <i>Helicobacter pylori</i> CagA	For atrophic gastritis: PGI = 70 ng/mL; PGR = 3	162	54.14 ± 11.79	75 (46.3%)	60.50%
Zhang <i>et al.</i> ³⁴ (2014)	China	Cross-sectional	Non-atrophic gastritis, atrophic gastritis, gastric cancer	PGI, PGII, PGR	For gastric cancer: PGI = 70.1 ng/mL, PGR = 6, PGI = 70 ng/mL + PGR = 6	282	Normal = 52.4 ± 15.1, patients = 52.3 ± 12.3	182 (64.5%)	–

Abbreviations: G-17: Gastrin-17; HP-ab: *Helicobacter pylori* antibody; IL-1 β : Interleukin-1 β ; PGI: Pepsinogen I; PGII: Pepsinogen II; PGR: Pepsinogen I/II ratio; TFF3: Trefoil factor-3; TLR-4: Toll-like receptor-4; VEGF: Vascular endothelial growth factor.

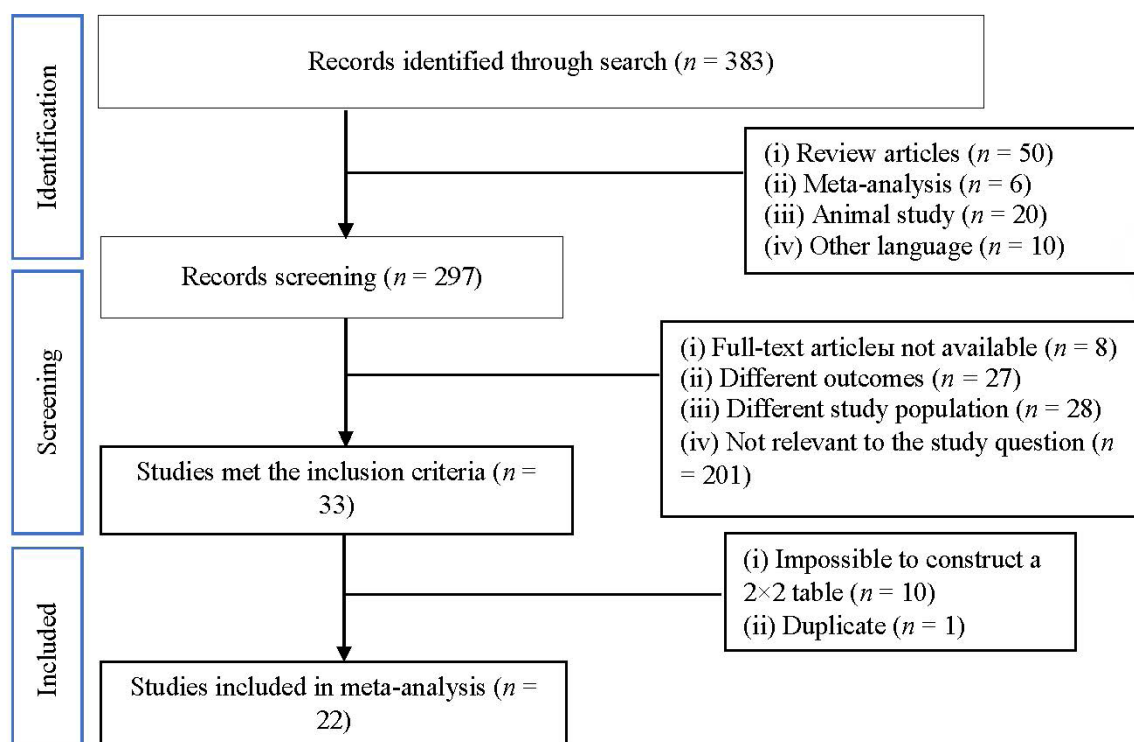


Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses flowchart of the study selection

3.4. PGI and PGR for the detection of atrophic gastritis

Since TP, FP, FN, and TN parameters were available for each of the seven studies that identified chronic atrophic gastritis, a meta-analysis was performed, and the AUC, pooled sensitivity, specificity, and positive and negative likelihood ratios were calculated. Figure 3 shows the forest plot of sensitivity and specificity with 95% confidence intervals (CIs) for PGI and PGR for the detection of chronic atrophic gastritis separately. The AUC of PGI and PGR for identifying chronic atrophic gastritis were 0.74 (95% CI = 0.70–0.77) and 0.78 (95% CI = 0.75–0.82), respectively (Figure 4).

Six studies were included in the meta-analysis for identifying chronic atrophic gastritis using PGI, with a total population of 2,447. The sensitivity and specificity of PGI biomarkers for detecting chronic atrophic gastritis in each study ranged from 38% to 77% and from 50% to 99%, respectively (Figure 3A), with a pooled sensitivity of 61.4% (95% CI = 48.2–73.2) and a pooled specificity of 86.4% (95% CI = 61.8–96.1) (Figure 4A).

Although the study by Koivurova *et al.*²³ was identified as potentially influential in the influence analysis, with a relatively high Cook's distance compared to the other studies, further sensitivity analysis demonstrated that its

exclusion did not materially alter the pooled estimates of diagnostic accuracy. Specifically, the overall sensitivity, specificity, and heterogeneity measures remained largely unchanged after removing this study. This suggests that, despite its apparent influence, the study has a relatively minor effect on the robustness or stability of the meta-analysis results. Therefore, it was retained in the final analysis to preserve the completeness of the available evidence. The diagnostic odds ratio (DOR) for the PGI biomarker in detecting atrophic gastritis was 10.1 (95% CI = 2.5–41.5), indicating that it is approximately 10-fold more likely to discriminate between patients with atrophic gastritis and healthy individuals (Table 2).

However, the meta-analysis of PGR included seven studies with a total population of 3,249 participants. The sensitivity and specificity of the PGR for detecting atrophic gastritis ranged from 50% to 90% and 38% to 99%, respectively (Figure 3B), with a pooled sensitivity of 72.4% (95% CI = 61.0–81.4) and a pooled specificity of 76.9% (95% CI = 49.5–91.9) (Figure 4B). The DOR for PGR in detecting atrophic gastritis was 8.7 (95% CI = 2.7–27.7) (Table 2).

Moreover, PGI demonstrated a positive likelihood ratio (LR+) of 4.5 (95% CI = 1.4–14.6) and a negative likelihood ratio (LR–) of 0.4 (95% CI = 0.3–0.6), while PGR showed



Figure 2. Risk of bias and applicability concerns summary. (A) Review authors' judgments for each domain across the individual included studies. (B) Proportion of studies with each level of judgment for each domain, expressed as percentages across all included studies.

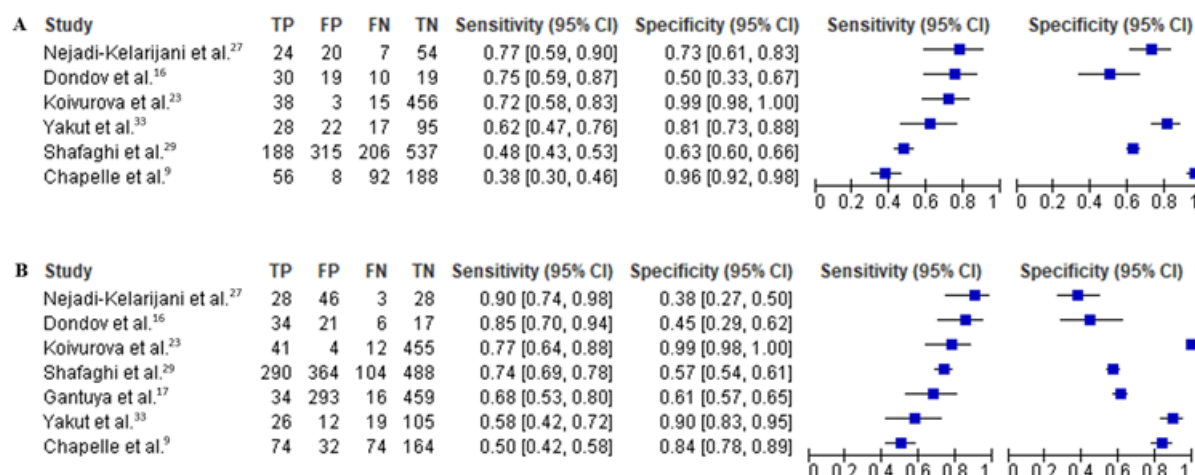


Figure 3. Forest plot showing the diagnostic performance of (A) PGI and (B) PGR biomarkers for the detection of chronic atrophic gastritis. Abbreviations: CI: Confidence interval; FN: False negative; FP: False positive; PGI: Pepsinogen I; PGR: Pepsinogen I/pepsinogen II ratio; TN: True negative; TP: True positive.

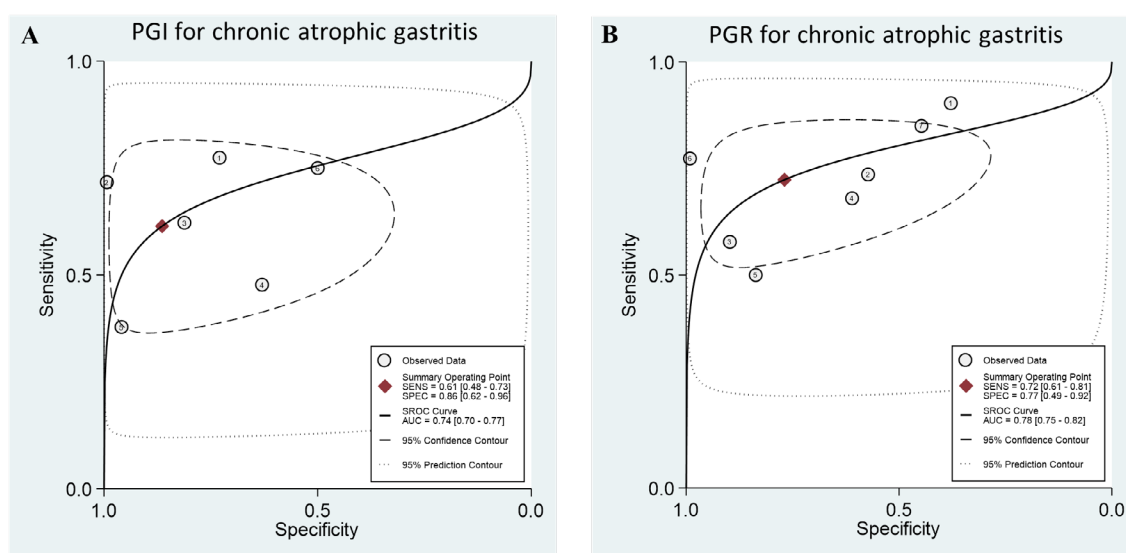


Figure 4. Summary receiver operating characteristic plots of sensitivity and specificity. (A) PGI for atrophic gastritis. (B) PGR for atrophic gastritis. Each circle represents an individual study; the red point indicates the pooled estimate of sensitivity and specificity; inner ellipses represent the 95% confidence region; outer ellipses represent the 95% prediction.

Abbreviations: AUC: Area under the curve; PGI: Pepsinogen I; PGR: Pepsinogen I/pepsinogen II ratio; SENS: Sensitivity; SPEC: Specificity; SROC: Summary of receiver operating characteristic.

an LR+ of 3.1 (95% CI = 1.3–7.7) and an LR– of 0.4 (95% CI = 0.2–0.5) (Table 2). Because the 95% prediction region in the summary receiver operating characteristic was wide, we assessed heterogeneity across studies. A significant heterogeneity was observed across the included studies, with an I^2 value of 98% (95% CI = 97–99) and 99% (95% CI = 98–99) for PGI and PGR, respectively. However, the proportion of heterogeneity attributable to threshold effects was minimal (2% for PGI, 16% for PGR), suggesting

that differences in cut-off values were not the primary source of variability.

3.5. PGI and PGR biomarkers for gastric cancer detection

A total of 17 studies were included to evaluate the diagnostic accuracy of PGI and PGR in the detection of gastric cancer. Among these, seven studies were included

in the meta-analysis of PGI biomarkers for gastric cancer detection, with a total of 3,668 participants. The forest plot demonstrated that the sensitivity and specificity of PGI for gastric cancer detection ranged from 35% to 92% and from 42% to 87%, respectively (Figure 5A). The pooled sensitivity and specificity were 69.8% (95% CI = 55.0–81.3) and 70.8% (95% CI = 58.7–80.6), respectively. The DOR for PGI in detecting gastric cancer was 5.6 (95% CI = 3.6–8.8) (Table 2).

The meta-analysis evaluating the diagnostic accuracy of PGR included 10 studies with a total of 8,568 participants. The sensitivity and specificity of PGR for gastric cancer detection ranged from 38% to 100% and from 38% to 84%, respectively (Figure 5B). The pooled sensitivity was 76.2% (95% CI = 65.4–84.2) and the pooled specificity was 66.1% (95% CI = 56.1–74.8). The DOR for gastric cancer detection of PGR was 6.2 (95% CI = 4.0–9.6) (Table 2). The AUCs of PGI and PGR for identifying gastric cancer were 0.76 (95% CI = 0.72–0.80) and 0.77 (95% CI = 0.73–0.80), respectively (Figure 6A and Figure 6B). PGI demonstrated an LR+ of 2.4 (95% CI = 1.8–3.2) and an LR– of 0.4 (95% CI = 0.3–0.6), while PGR showed an LR+ of 2.2 (95% CI = 1.8–2.8) and an LR– of 0.4 (95% CI = 0.3–0.5) for gastric cancer detection.

Additionally, considerable heterogeneity was identified among the studies, with an I^2 value of 99% (95% CI = 98–99) and 98% (95% CI = 97–98) for PGI and PGR, respectively. A large proportion of the observed heterogeneity was likely attributable to threshold effects (69% for PGI, 50% for PGR), suggesting that differences in cut-off values

contributed substantially to the variability in diagnostic performance between studies.

Furthermore, the diagnostic accuracy of combining PGI and PGR for the detection of gastric cancer was evaluated. This meta-analysis included 11 studies with a total of 28,721 participants. Forest plot analysis showed that the sensitivity and specificity of PGI+PGR ranged from 34% to 88% and from 61% to 96% (Figure 5C). Hierarchical summary receiver operating curves were built based on 11 studies, with a pooled sensitivity of 61.5% (95% CI = 50.9–72.1) and a pooled specificity of 86.7% (95% CI = 79.4–94.1). The AUC of PGI+PGR for identifying gastric cancer was 0.79 (95% CI = 0.75–0.83) (Figure 6C). The DOR for detecting gastric cancer for the PGI+PGR combination was 10.4 (95% CI = 6.6–16.6) (Table 2).

4. Discussion

Gastric cancer is one of the leading cancers, particularly in Mongolia. The systematic review found that the incidence rate of gastric cancer in patients with chronic atrophic gastritis was 1.7 cases per 1,000 person-years, ranging from 1.5 to 1.9.³⁵ Moreover, a large retrospective study evaluated the risk factors for gastric tumorigenesis in patients with underlying mucosal atrophy. Gastric neoplasms, including adenocarcinoma and dysplasia, were found to occur in 0.1% of participants without atrophic change, 1.6% of those with mild atrophic gastritis, 5.2% of those with moderate atrophic gastritis, and 12.0% of those with severe atrophic gastritis.³⁵ This suggests that as the stages of gastric atrophy increase, the probability of developing gastric neoplasm increases. In addition, the mean time intervals from gastric

Table 2. Diagnostic accuracy of pepsinogens for the detection of chronic atrophic gastritis and gastric cancer

Biomarker	Study population	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR (95% CI)
Chronic atrophic gastritis							
PGI	6/2,447	0.74 (0.70–0.77)	61.4 (48.2–73.2)	86.4 (61.8–96.1)	4.5 (1.4–14.6)	0.4 (0.3–0.6)	10.1 (2.5–41.5)
PGR	7/3,249	0.78 (0.75–0.82)	72.4 (61.0–81.4)	76.9 (49.5–91.9)	3.1 (1.3–7.7)	0.4 (0.2–0.5)	8.7 (2.7–27.7)
Gastric cancer							
PGI	7/3,668	0.76 (0.72–0.80)	69.8 (55.0–81.3)	70.8 (58.7–80.6)	2.4 (1.8–3.2)	0.4 (0.3–0.6)	5.6 (3.6–8.8)
PGR	10/8,568	0.77 (0.73–0.80)	76.2 (65.4–84.2)	66.1 (56.1–74.8)	2.2 (1.8–2.8)	0.4 (0.3–0.5)	6.2 (4.0–9.6)
PGI+PGR	11/28,721	0.79 (0.75–0.83)	61.5 (50.9–72.1)	86.7 (79.4–94.1)	4.6 (2.9–7.3)	0.4 (0.3–0.5)	10.4 (6.6–16.6)

Abbreviations: AUC: Area under the curve; CI: Confidence interval; DOR: Diagnostic odds ratio; LR+: Positive likelihood ratio; LR–: Negative likelihood ratio; PGI: Pepsinogen I; PGR: Pepsinogen I/pepsinogen II ratio.

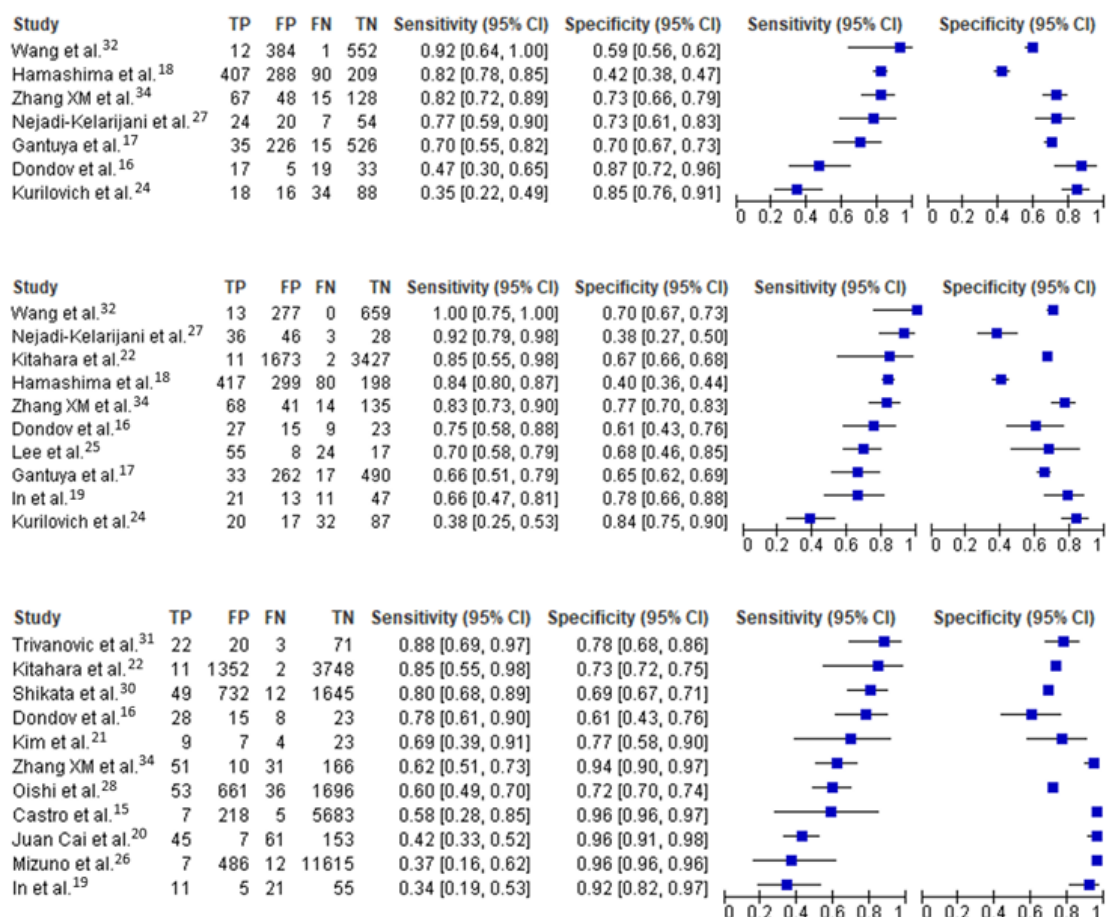


Figure 5. Forest plot showing the diagnostic performance of (A) PGI, (B) PGR, and (C) PGI+PGR biomarkers for the detection of gastric cancer. Abbreviations: CI: Confidence interval; FN: False negative; FP: False positive; PGI: Pepsinogen I; PGR: Pepsinogen I/pepsinogen II ratio; TN: True negative; TP: True positive.

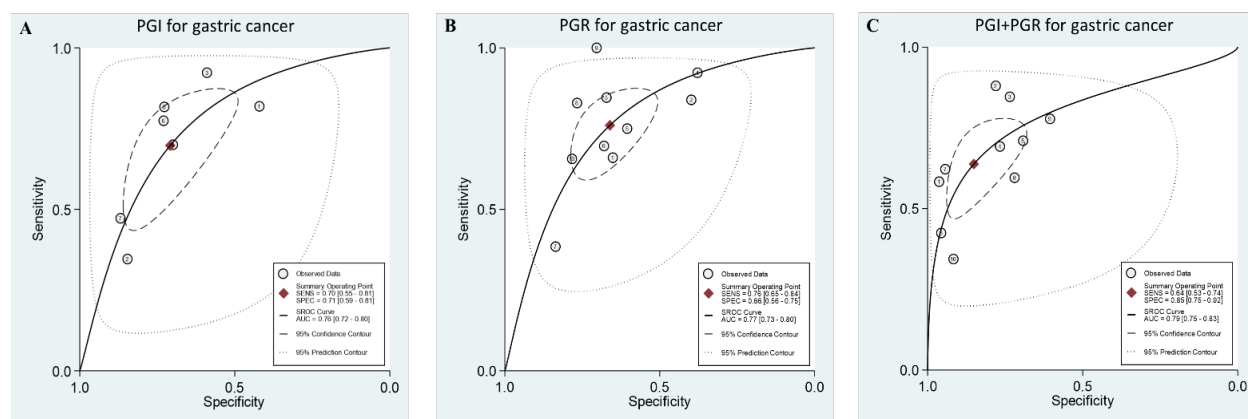


Figure 6. Summary receiver operating characteristic plots of sensitivity and specificity. (A) PGI for gastric cancer. (B) PGR for gastric cancer. (C) PGI+PGR for gastric cancer. Each circle represents an individual study; the red point indicates the pooled estimate of sensitivity and specificity; inner ellipses represent the 95% confidence region; outer ellipses represent the 95% prediction. Abbreviations: AUC: Area under the curve; PGI: Pepsinogen I; PGR: Pepsinogen I/pepsinogen II ratio; SENS: Sensitivity; SPEC: Specificity; SROC: Summary of receiver operating characteristic.

atrophy to gastric neoplasm were significantly shorter in participants with severe atrophic gastritis compared to those with mild and moderate atrophic gastritis.³⁶ Therefore, the early detection and management of atrophic gastritis are crucial to reduce the burden of gastric cancer.

In this meta-analysis, we investigated the diagnostic accuracy of serum PGI and PGR to detect gastric cancer and its precursor, chronic atrophic gastritis. The findings of this meta-analysis indicate that serum PG biomarkers demonstrate varying diagnostic performance for the detection of chronic atrophic gastritis and gastric cancer.

For chronic atrophic gastritis, PGI showed a pooled sensitivity of 61.4% and a specificity of 86.4%, while PGR demonstrated a higher sensitivity of 72.4% with a lower specificity of 76.9%. The AUC values for PGI and PGR in detecting chronic atrophic gastritis were 0.74 and 0.78, respectively, indicating moderate diagnostic accuracy. The likelihood ratio analysis supports these findings. For chronic atrophic gastritis, PGI demonstrated an LR+ of 4.5 and an LR- of 0.4, while PGR showed an LR+ of 3.1 and an LR- of 0.4. The findings of this meta-analysis indicate that both PGI and PGR demonstrate moderate diagnostic performance for the detection of atrophic gastritis and gastric cancer. The DOR for PGI and PGR were 10.1 and 8.7, respectively, suggesting a relatively strong ability of these biomarkers to distinguish between chronic atrophic gastritis patients and healthy individuals, although the wide confidence intervals may reflect heterogeneity among the included studies.

For gastric cancer detection, both PGI and PGR showed moderate diagnostic performance. PGI demonstrated a pooled sensitivity of 69.8% and specificity of 70.8%, while PGR showed a pooled sensitivity of 76.2% and specificity of 66.1%. The AUC values for PGI and PGR were 0.76 and 0.77, respectively. In addition, LR+ values (2.4 for PGI and 2.2 for PGR) suggest limited ability to confirm disease, whereas LR- values indicate moderate ability to reduce the probability of disease when the biomarkers decrease in serum. Importantly, the combined use of PGI and PGR improved diagnostic specificity for gastric cancer detection. The pooled specificity increased to 86.7%, while the sensitivity was 61.5%. The AUC for the combined biomarkers was 0.79, suggesting improved overall diagnostic performance compared with individual biomarkers. Moreover, the LR+ increased to 4.6, and the DOR reached 10.4, further supporting the potential benefit of using combined biomarker strategies for gastric cancer detection. These results highlight the limitations of using single PG biomarkers as standalone diagnostic tools for gastric cancer detection. However, combining PGI and PGR substantially improved diagnostic specificity for

gastric cancer detection.

The results of the present study are consistent with previous literature. A meta-analysis conducted by Bang *et al.*³⁷ reported sensitivity and specificity values of 59% and 89%, respectively, for detecting chronic gastritis, and 59% and 73% for detecting gastric cancer, which are comparable to the findings of this study. Similarly, a large systematic analysis by Zagari *et al.*,³⁸ which included 4,241 participants from 20 studies, reported that the Gastropanel test (including PGI, PGR, gastrin-17, and *H. pylori* immunoglobulin G) achieved a sensitivity of 74.7% and specificity of 95.6% for the detection of gastritis. In that study, threshold values of PGI ≤ 70 ng/mL and PGR ≤ 3 were considered effective for identifying both gastritis and gastric cancer. Furthermore, several studies have suggested that combining serum PG levels with other biomarkers, such as ghrelin and gastrin, may further enhance diagnostic performance by improving both sensitivity and specificity.^{29,33,39,40}

Serum PG levels may indicate the morphology and physiology of the gastric mucosa.^{41,42} PGI may be predominantly secreted by cells in the early phase of mucosal inflammation and could serve as a potent indicator of mucosal inflammation before atrophic changes occur. In the later stages of chronic atrophic gastritis, the loss of cells secreting the PGI leads to a reduction in PGI levels, consequently diminishing its diagnostic accuracy in the later stages of chronic atrophic gastritis.⁴³ The meta-analysis in this study demonstrates that PGI showed moderate diagnostic performance for atrophic gastritis. In addition, PGR plays a crucial role in detecting chronic atrophic gastritis cases across these studies, consistent with the pooled results of this meta-analysis. Numerous studies have concluded that dysregulated PG expression and a progressive decline in PGR are correlated with progression from normal gastric mucosa to precancerous lesions to gastric cancer.^{44,45} Moreover, recent studies have further highlighted the clinical importance of chronic and autoimmune-related gastric mucosal changes as precancerous conditions associated with an increased risk of gastric cancer.⁴⁶ These findings suggest that serum PGs may play an important role in the detection of early-stage atrophic changes in the gastric mucosa, in initiating effective treatment, and in preventing gastric cancer. Optimal cut-off points of serum PGs for gastric cancer may differ across different populations.⁴⁷

From a clinical perspective, serum PG testing may be particularly useful as a non-invasive screening tool for identifying individuals at increased risk of gastric mucosal pathology. Given its relatively high specificity for atrophic gastritis and improved specificity when

combined with PGR for gastric cancer detection, PG testing may be valuable in population-based screening programs, especially in regions with a high prevalence of gastric cancer. However, due to the moderate sensitivity and likelihood ratio values observed in this study, PG biomarkers have limited standalone rule-in capability. Therefore, they may be useful as a non-invasive screening tool for identifying individuals at high risk of gastric cancer and chronic atrophic gastritis and should ideally be used in combination with other diagnostic approaches, such as gastroscopy or additional serum biomarkers, to improve early detection of gastric cancer.

Gastroscopy remains essential for early detection in high-prevalence settings. Serum biomarker-based detection can be used because population-based gastroscopy is difficult to perform in rural areas due to low population density, limited endoscopic equipment and human resources, discomfort during examination, and invasiveness, even though Mongolia has the highest prevalence of gastric cancer globally.

Several limitations should be considered when interpreting the results of this study. First, significant heterogeneity was observed among the included studies, which may be attributed to differences in study population and diagnostic thresholds, particularly for specificity. With a small number of studies, meta-regression analyses may be underpowered and prone to spurious associations or overfitting. Therefore, the present meta-analysis could not quantitatively explore the potential sources of heterogeneity. Another limitation of this meta-analysis is that the literature search was restricted in scope. Consequently, some potentially eligible studies might have been missed, which may limit the comprehensiveness of the evidence included in this analysis. We assessed publication bias using Deeks' funnel plot asymmetry test. The results showed no significant evidence of publication bias among the included studies ($p > 0.05$), suggesting that the pooled estimates are unlikely to be substantially affected by small-study effects.

Overall, the findings of this meta-analysis suggest that serum PG biomarkers may be useful non-invasive tools for the detection of gastric mucosal atrophy. PGI appears to be particularly useful for identifying chronic atrophic gastritis due to its high specificity, whereas a combination of PGI and PGR may provide improved diagnostic performance for gastric cancer detection. However, the moderate sensitivity and likelihood ratio values indicate that these biomarkers may be more suitable for screening or risk stratification rather than for definitive diagnostic methods. Future studies should focus on validating serum PG levels' clinical utility as screening tools for gastric cancer, while

adjusting for differences in populations and other factors affecting PG levels, including age, sex, *H. pylori* infection, smoking, and dietary habits.

5. Conclusion

In conclusion, the moderate diagnostic value of serum PGI and PGR indicates that these non-invasive biomarkers are not suitable as a perfect alternative to gastroscopic examination for confirming the diagnosis of gastric cancer and its precancerous lesions. However, they can be useful in a multimodal screening approach or for identifying high-risk subjects who may need upper gastrointestinal endoscopy or a biopsy.

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Conflict of interest

The authors declare they have no competing interests.

Author contributions

Conceptualization: Ganchimeg Dondov, Tulgaa Lonjid

Formal analysis: Ganchimeg Dondov, Tulgaa Lonjid

Investigation: Ganchimeg Dondov, Tegshjargal Badamjav, Batbold Batsaikhan

Methodology: Tulgaa Lonjid, Bayarmaa Nyamaa, Sodnomtsogt Lkhagvasuren, Ganchimeg Dondov

Writing—original draft: Ganchimeg Dondov, Batbold Batsaikhan, Tegshjargal Badamjav

Writing—review & editing: Tulgaa Lonjid, Bayarmaa Nyamaa, Sodnomtsogt Lkhagvasuren

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Not applicable

Consent for publication

Not applicable.

Availability of data

Data is available from the corresponding author upon reasonable request.

References

1. Balakrishnan M, George R, Sharma A, *et al.* Changing Trends in Stomach Cancer Throughout the World. *Curr*

- Gastroenterol Rep.* 2017;19(8).
doi: 10.1007/s11894-017-0575-8
2. Lonjid T, Sambuu T, Tumurbat N, *et al.* Incidence of Stomach and Esophageal Cancers in Mongolia: Data from 2009 to 2018. *Euroasian J Hepato-Gastroenterol.* 2020;10(1):16-21.
doi: 10.5005/jp-journals-10018-1313
3. World Health Organization. Global Cancer Registry. Accessed February 25, 2026. <https://gco.iarc.fr/today/home>
4. Hamashima C, Ogoshi K, Okamoto M, *et al.* A community-based, case-control study evaluating mortality reduction from gastric cancer by endoscopic screening in Japan. *PLoS One.* 2013;8(11):e79088.
doi: 10.1371/journal.pone.0079088
5. Correa P, Piazuelo MB. The gastric precancerous cascade. *J Dig Dis.* 2011;13(1):2-9.
doi: 10.1111/j.1751-2980.2011.00550.x
6. Chiba T, Marusawa H, Seno H, *et al.* Mechanism for gastric cancer development by *Helicobacter pylori* infection. *J Gastroenterol Hepatol.* 2008;23(8pt1):1175-1181.
doi: 10.1111/j.1440-1746.2008.05472.x
7. Battista S, Ambrosio MR, Limarzi F, *et al.* Molecular Alterations in Gastric Preneoplastic Lesions and Early Gastric Cancer. *Int J Mol Sci.* 2021;22(13):6652.
doi: 10.3390/ijms22136652
8. Akbari A, Ashtari S, Tabaiean SP, *et al.* Overview of epidemiological characteristics, clinical features, and risk factors of gastric cancer in Asia-Pacific region. *Asia-Pac J Clin Oncol.* 2022;18(6):493-505.
doi: 10.1111/ajco.13654
9. Chapelle N, Petryszyn P, Blin J, *et al.* A panel of stomach-specific biomarkers (GastroPanel®) for the diagnosis of atrophic gastritis: A prospective, multicenter study in a low gastric cancer incidence area. *Helicobacter.* 2020;25(5).
doi: 10.1111/hel.12727
10. Liu L, Deng W. Gastric Cancer: Innovations in Screening, Diagnosis and Treatment. *J Pers Med.* 2023;13(1):127.
doi: 10.3390/jpm13010127
11. Jiang T, Mei L, Yang X, *et al.* Biomarkers of gastric cancer: current advancement. *Heliyon.* 2022;8(10):e10899.
doi: 10.1016/j.heliyon.2022.e10899
12. Tu H, Sun L, Dong X, *et al.* A Serological Biopsy Using Five Stomach-Specific Circulating Biomarkers for Gastric Cancer Risk Assessment: A Multi-Phase Study. *Am J Gastroenterol.* 2017;112(5):704-715.
doi: 10.1038/ajg.2017.55
13. Romańczyk M, Osmola M, Link A, *et al.* Non-Invasive Markers for the Detection of Gastric Precancerous Conditions. *Cancers.* 2024;16(12):2254.
doi: 10.3390/cancers16122254
14. Zhang T, Zhou X, Meng X, *et al.* The potential value of serum pepsinogen and gastrin-17 for the diagnosis of chronic atrophic gastritis at different stages of severity: a clinical diagnostic study. *BMC Gastroenterol.* 2025;25(1).
doi: 10.1186/s12876-025-03996-8
15. Castro C, Dinis-Ribeiro M, Rodrigues ANG, *et al.* Western long-term accuracy of serum pepsinogen-based gastric cancer screening. *Eur J Gastroenterol Hepatol.* 2018;30(3):274-277.
doi: 10.1097/meg.0000000000001040
16. Dondov G, Amarbayasgalan D, Batsaikhan B, *et al.* Diagnostic performances of pepsinogens and gastrin-17 for atrophic gastritis and gastric cancer in Mongolian subjects. *PLoS One.* 2022;17(10):e0274938.
doi: 10.1371/journal.pone.0274938
17. Gantuya B, Bolor D, Oyuntsetseg K, *et al.* New observations regarding *Helicobacter pylori* and gastric cancer in Mongolia. *Helicobacter.* 2018;23(4).
doi: 10.1111/hel.12491
18. Hamashima C, Sasazuki S, Inoue M, *et al.* Receiver operating characteristic analysis of prediction for gastric cancer development using serum pepsinogen and *Helicobacter pylori* antibody tests. *BMC Cancer.* 2017;17(1).
doi: 10.1186/s12885-017-3173-0
19. In H, Adams A, Ho S, *et al.* Pepsinogen and *Helicobacter pylori*: Serum biomarkers for gastric cancer risk in a diverse United States population. *Surg Oncol Insight.* 2024;1(3):100086.
doi: 10.1016/j.soi.2024.100086
20. Juan Cai W, Yin L, Kang Q, *et al.* The Serum Pepsinogen Test as a Predictor of Kazakh Gastric Cancer. *Sci Rep.* 2017;7(1).
doi: 10.1038/srep43536
21. Kim JR, Lee K, Jung WT, *et al.* Validity of serum pepsinogen levels and quininium resin test combined for gastric cancer screening. *Cancer Detect Prev.* 2005;29(6):570-575.
doi: 10.1016/j.cdp.2005.07.005
22. Kitahara F, Kobayashi K, Sato T, *et al.* Accuracy of screening for gastric cancer using serum pepsinogen concentrations. *Gut.* 1999;44(5):693-697.
doi: 10.1136/gut.44.5.693
23. Koivurova OP, Koskela R, Blomster T, *et al.* Serological Biomarker Panel in Diagnosis of Atrophic Gastritis and *Helicobacter pylori* Infection in Gastroscopy Referral Patients: Clinical Validation of the New-Generation GastroPanel(®) Test. *Anticancer Res.* 2021;41(11):5527-5537.
doi: 10.21873/anticancer.15366

24. Kurilovich S, Belkovets A, Reshetnikov O, *et al.* Stomach-specific Biomarkers (GastroPanel) Can Predict the Development of Gastric Cancer in a Caucasian Population: A Longitudinal Nested Case-Control Study in Siberia. *Anticancer Res.* 2016;36(1):247-253.
doi: 10.1007/s10238-016-0426-1
25. Lee JY, Park KS, Lee HG, *et al.* Comparison of serum trefoil factor 3 with the pepsinogen test for the screening of diffuse-type gastric cancer. *Clin Exp Med.* 2017;17(3):403-410.
doi: 10.1007/s10238-016-0426-1
26. Mizuno S, Kobayashi M, Tomita S, *et al.* Validation of the pepsinogen test method for gastric cancer screening using a follow-up study. *Gastric Cancer.* 2009;12(3):158-163.
doi: 10.1007/s10120-009-0522-y
27. Nejadi-Kelarijani F, Roshandel G, Semnani S, *et al.* Diagnostic values of serum levels of pepsinogens and gastrin-17 for screening gastritis and gastric cancer in a high risk area in northern Iran. *Asian Pac J Cancer Prev.* 2014;15(17):7433-7436.
doi: 10.7314/apjcp.2014.15.17.7433
28. Oishi Y, Kiyohara Y, Kubo M, *et al.* The serum pepsinogen test as a predictor of gastric cancer: the Hisayama study. *Am J Epidemiol.* 2006;163(7):629-637.
doi: 10.1093/aje/kwj088
29. Shafaghi A, Mansour-Ghanaei F, Joukar F, *et al.* Serum gastrin and the pepsinogen I/II ratio as markers for diagnosis of premalignant gastric lesions. *Asian Pac J Cancer Prev.* 2013;14(6):3931-3936.
doi: 10.7314/apjcp.2013.14.6.3931
30. Shikata K, Ninomiya T, Yonemoto K, *et al.* Optimal cutoff value of the serum pepsinogen level for prediction of gastric cancer incidence: the Hisayama Study. *Scand J Gastroenterol.* 2012;47(6):669-675.
doi: 10.3109/00365521.2012.658855
31. Trivanovic D, Plestina S, Honovic L, *et al.* Gastric cancer detection using the serum pepsinogen test method. *Tumori.* 2021;108(4):386-391.
doi: 10.1177/03008916211014961
32. Wang Y, Zhu Z, Liu Z, *et al.* Diagnostic value of serum pepsinogen I, pepsinogen II, and gastrin-17 levels for population-based screening for early-stage gastric cancer. *J Int Med Res.* 2020;48(3).
doi: 10.1177/0300060520914826
33. Yakut M, Örmeci N, Erdal H, *et al.* The association between precancerous gastric lesions and serum pepsinogens, serum gastrin, vascular endothelial growth factor, serum interleukin-1 Beta, serum toll-like receptor-4 levels and *Helicobacter pylori* Cag A status. *Clin Res Hepatol Gastroenterol.* 2013;37(3):302-311.
doi: 10.1016/j.clinre.2012.09.013
34. Zhang XM, Li JX, Zhang GY, *et al.* The value of serum pepsinogen levels for the diagnosis of gastric diseases in Chinese Han people in midsouth China. *BMC Gastroenterol.* 2014;14(1).
doi: 10.1186/1471-230x-14-3
35. Burke E, Harkins P, Arumugasamy M. Incidence of Gastric Adenocarcinoma in Those With Gastric Atrophy: A Systematic Review. *Cureus.* 2024;16(10):e71768.
doi: 10.7759/cureus.71768
36. Song JH, Kim SG, Jin EH, *et al.* Risk Factors for Gastric Tumorigenesis in Underlying Gastric Mucosal Atrophy. *Gut Liver.* 2017;11(5):612-619.
doi: 10.5009/gnl16488
37. Bang CS, Lee JJ, Baik GH. Prediction of Chronic Atrophic Gastritis and Gastric Neoplasms by Serum Pepsinogen Assay: A Systematic Review and Meta-Analysis of Diagnostic Test Accuracy. *J Clin Med.* 2019;8(5):657.
doi: 10.3390/jcm8050657
38. Zagari RM, Rabitti S, Greenwood DC, *et al.* Systematic review with meta-analysis: diagnostic performance of the combination of pepsinogen, gastrin-17 and anti-*Helicobacter pylori* antibodies serum assays for the diagnosis of atrophic gastritis. *Aliment Pharmacol Ther.* 2017;46(7):657-667.
doi: 10.1111/apt.14248
39. Zhao J, Tian W, Zhang X, *et al.* The diagnostic value of serum trefoil factor 3 and pepsinogen combination in chronic atrophic gastritis: a retrospective study based on a gastric cancer screening cohort in the community population. *Biomarkers.* 2024;29(6):384-392.
doi: 10.1080/1354750x.2024.2400927
40. Eun Bae S, Hoon Lee J, Soo Park Y, *et al.* Decrease of serum total ghrelin in extensive atrophic gastritis: comparison with pepsinogens in histological reference. *Scand J Gastroenterol.* 2016;51(2):137-144.
doi: 10.3109/00365521.2015.1083049
41. Qin Y, Geng JX, Huang B. Clinical value of serum pepsinogen in the diagnosis and treatment of gastric diseases. *World J Gastrointest Oncol.* 2023;15(7):1174-1181.
doi: 10.4251/wjgo.v15.i7.1174
42. Huang YK, Yu JC, Kang WM, *et al.* Significance of Serum Pepsinogens as a Biomarker for Gastric Cancer and Atrophic Gastritis Screening: A Systematic Review and Meta-Analysis. *PLoS One.* 2015;10(11):e0142080.
doi: 10.1371/journal.pone.0142080
43. Lorente S, Doiz O, Trinidad Serrano M, *et al.* *Helicobacter pylori* stimulates pepsinogen secretion from isolated human peptic cells. *Gut.* 2002;50(1):13-18.
doi: 10.1136/gut.50.1.13

44. Tong Y, Wang H, Zhao Y, *et al.* Serum pepsinogen levels in different regions of China and its influencing factors: a multicenter cross-sectional study. *BMC Gastroenterol.* 2021;21(1).
doi: 10.1186/s12876-021-01794-6
45. Xiao M, Zhang Z, Liao G, *et al.* Analysis of the Value of Helicobacter pylori Test in Combination with the Determination of Plasma Propepsin and Gastrin 17 in Screening the Precancerous Status of Gastric Cancer. *Cell Mol Biol.* 2022;68(8):110-115.
doi: 10.14715/cmb/2022.68.8.20
46. Lenti MV, Miceli E, Lahner E, *et al.* Distinguishing Features of Autoimmune Gastritis Depending on Previous Helicobacter pylori Infection or Positivity to Anti-Parietal Cell Antibodies: Results From the Autoimmune gastritis Italian network Study group (ARIOSO). *Am J Gastroenterol.* 2024;119(12):2408-2417.
doi: 10.14309/ajg.0000000000002948
47. Staynova R, Andonova D. Medicinal products under additional monitoring: a comparative analysis of market access. *Folia Med.* 2025;67(3).
doi: 10.3897/folmed.67.e151128