

EPIDEMIOLOGY OF GASTRIC CANCER: GLOBAL BURDEN, RISK FACTORS, AND TRENDS

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Abstract. Gastric cancer (GC) remains one of the most significant global health challenges, ranking among the top causes of cancer mortality worldwide. Despite declining incidence in many high-income regions, gastric cancer continues to show substantial geographical variation, with East Asia, Eastern Europe, and parts of Latin America bearing the highest burden. The disease arises from a multifactorial interaction of environmental exposures, chronic infections—especially *Helicobacter pylori*—dietary habits, genetic predisposition, and socioeconomic determinants.

This review synthesizes high-quality epidemiological evidence, incorporating global population-based registries, cohort studies, meta-analyses, and international cancer surveillance data. The article follows a hybrid systematic–narrative design to provide a comprehensive overview of incidence, mortality, risk factors, protective factors, histological patterns, and temporal trends. Special focus is given to the divergent patterns of non-cardia gastric cancer (NCGC) and cardia gastric cancer (CGC), the impact of *H. pylori* eradication, demographic transitions, and the influence of Western lifestyle patterns.

The review highlights the persistent public health importance of gastric cancer and emphasizes that early detection, infection control, dietary modification, and molecularly targeted screening strategies remain essential for reducing disease burden. These findings underscore the need for region-specific preventive policies and strengthened cancer surveillance systems.

Keywords: "Gastric cancer", "Epidemiology", "*Helicobacter pylori*", "Non-cardia gastric cancer", "Cardia gastric cancer", "Incidence trends", "Mortality", "Risk factors".

1. Introduction

Gastric cancer is the **fifth most common malignancy** and the **fourth leading cause of cancer-related death globally**. According to GLOBOCAN 2022 estimates, more than **1 million new cases** and approximately **770,000 deaths** occur annually, demonstrating the aggressive nature and late-stage presentation of most tumors.

Epidemiologically, gastric cancer displays striking geographic variation:

- **High incidence:** East Asia (Japan, Korea, China), Eastern Europe, Andean South America
- **Intermediate incidence:** Central Asia, Russia, Turkey
- **Low incidence:** North America, Scandinavia, Africa

This disparity reflects complex interactions between environmental and biological factors, notably:

- *H. pylori* infection prevalence
- Dietary consumption of salt-preserved foods, nitrates, smoked meats

- Smoking and alcohol intake
- Socioeconomic conditions
- Genetic susceptibility

Gastric cancer is broadly classified into:

1. **Non-cardia gastric cancer (NCGC)** – strongly linked to *H. pylori* and environmental factors
2. **Cardia gastric cancer (CGC)** – increasingly associated with obesity, GERD, and metabolic dysfunction

Despite declining incidence in many countries due to improved sanitation and reduced *H. pylori* prevalence, gastric cancer remains a major cause of morbidity and mortality, particularly in low- and middle-income regions.

This review aims to provide a **comprehensive epidemiological overview**, integrating global incidence patterns, risk determinants, mortality trends, and preventive strategies.

Below is an expanded, **wide, detailed, deeply academic** version of your entire **Methodology section** for the Gastric Cancer Epidemiology article.

This expanded version follows the same style and structural depth as your hepatic fibrosis article, with long paragraphs, clear scientific justification, and methodological rigor.

2. Methodology

The methodological framework for this review was developed to ensure both **scientific rigor** and **conceptual flexibility**, following the hybrid systematic–narrative model applied in the hepatic fibrosis article. This approach was intentionally selected due to the diverse and multidimensional nature of gastric cancer epidemiology, which spans global cancer surveillance systems, population-based cohort studies, molecular epidemiology, environmental exposure research, and advanced statistical modeling. Such heterogeneity necessitates a methodological structure capable of integrating quantitative evidence with qualitative interpretation, enabling a deep understanding of incidence patterns, mortality trends, risk determinants, and temporal dynamics across different populations and regions.

2.1. Study Design

This study adopts a **hybrid systematic–narrative review design**, a methodology increasingly used in public health and epidemiology research when dealing with broad, complex fields that require integration of both high-level quantitative datasets and comprehensive interpretive synthesis.

Rationale for the Hybrid Model

Gastric cancer epidemiology encompasses:

- **Population-level data** (GLOBOCAN, WHO mortality databases)
- **Regional cancer registries** (Japan, Korea, SEER, European registries)
- **Large-scale cohort studies** (JPHC, EPIC, NIH-AARP)
- **Case–control studies** analyzing risk factors
- **Meta-analyses** evaluating dietary, infectious, and genetic determinants
- **Mechanistic links** between infectious agents (*H. pylori*, EBV) and carcinogenesis

Because these sources vary in methodological design, data depth, and global representation, a traditional systematic review alone would be limiting. Conversely, a purely narrative review would lack the structural rigor required for reproducibility.

The hybrid design therefore allows:

1. **Inclusion of diverse evidence types**, ranging from molecular-pathway epidemiology to country-level incidence data.
2. **Systematic identification and critical appraisal** of core epidemiological studies.
3. **Narrative contextualization** of findings across geography, demography, socioeconomic strata, and time.
4. **Integration of heterogenous data** such as infection prevalence, dietary transitions, and health system factors.

The overall goal was to create a methodological platform that reflects the global complexity of gastric cancer while maintaining high evidence standards.

2.2. Search Strategy

A comprehensive, multilayered search strategy was developed to capture the full range of epidemiological studies relevant to gastric cancer. The search was conducted across multiple major international databases to ensure breadth, and strict search syntax was used to ensure scientific precision.

Databases Searched

- **PubMed / MEDLINE** – biomedical research, observational studies, mechanistic epidemiology
- **WHO cancer databases** – national cancer statistics, mortality, survival
- **GLOBOCAN** – global incidence and mortality estimates
- **IARC Monographs and Cancer Incidence in Five Continents (CI5)** – carcinogenic risk factors, registry-level data
- **Scopus & Web of Science** – expanded search for global public health, environmental epidemiology, and bibliographic coverage

Search Terms and Boolean Strategy

To maximize sensitivity while maintaining specificity, both MeSH terms and free-text keywords were used. Boolean operators (AND/OR/NOT) and phrase searching ensured targeted retrieval.

Key search strings included:

- **“Gastric cancer” AND “epidemiology”**
- **“Non-cardia gastric cancer” AND “risk factors”**
- **“Cardia gastric cancer” AND “incidence trends”**
- **“Helicobacter pylori infection” AND “cancer risk”**
- **“Dietary salt” OR “nitrosamines” AND “gastric cancer”**
- **“Global cancer registry trends” AND “stomach cancer”**
- **“Gastric cancer mortality decline” OR “temporal patterns”**

Filters were applied for:

- Study type (observational, cohort, registry data, systematic reviews)
- Human studies
- English-language publications
- Years 1990–2024 (to capture long-term incidence trends)

This helped avoid oversaturation with unrelated publications (e.g., basic science studies without epidemiological relevance).

2.3. Data Extraction

A structured data extraction process ensured uniformity and quality across all included studies. Extraction templates were modeled after those used in major epidemiological systematic reviews.

Extracted Variables

1. Incidence Indicators

- Age-standardized incidence rates (ASIR)
- Crude incidence rates
- Region-specific and time-trend data

2. Mortality Indicators

- Age-standardized mortality rates
- 1-year and 5-year survival (where available)

3. Risk Factors and Protective Factors

- *H. pylori* prevalence
- Dietary habits (salt intake, smoked foods)
- Tobacco and alcohol exposure
- Obesity, GERD (for cardia cancers)
- Genetic markers and family history

4. Demographic and Geographic Variation

- Sex-specific incidence patterns
- Regional differences (East Asia, Europe, Americas, Africa)
- Urban vs rural disparities

5. Subtype Trends

- Non-cardia gastric cancer vs cardia gastric cancer
- Age-based shifts (rise in young-onset gastric cancer)
- Histological variations (intestinal vs diffuse type)

6. Temporal Trends

- Declining incidence in high-income countries
- Stability or increase in some regions
- Changing patterns of risk factors

Data were cross-verified between registry databases and peer-reviewed studies to avoid inconsistencies.

2.4. Quality Assessment

Ensuring methodological quality was essential given the global heterogeneity of gastric cancer data.

Quality Assessment Tools Used

1. **Observational studies** → Newcastle–Ottawa Scale (NOS)

- Assessed cohort representativeness
- Exposure/outcome measurement validity
- Confounder adjustment
- Adequacy of follow-up

2. **Systematic reviews** → AMSTAR-2

- Evaluated comprehensiveness of search strategy
- Risk of bias assessment
- Appropriateness of statistical synthesis

3. **Cancer registry and surveillance data** → WHO/IARC quality criteria

- Completeness of case capture
- Accuracy of coding systems
- Mortality–incidence ratio consistency
- Population coverage

Studies rated **high** or **moderate quality** were included. Low-quality studies were excluded to maintain evidentiary strength.

Risk of Bias Assessment

Key domains assessed:

- Selection bias
- Misclassification bias (cardia vs non-cardia)
- Reporting bias
- Confounding (socioeconomic factors, comorbidities)
- Incomplete case recording in low-resource settings

Where necessary, sensitivity analyses were applied to weigh findings more heavily from regions with high-quality cancer registries (Japan, Korea, Scandinavia) than those with developing surveillance systems.

3. Results

3.1 Global Incidence Patterns

3.1.1 Overall Burden

- 1,050,000 new cases annually
- ASIR: **19.1 per 100,000 men, 7.2 per 100,000 women**
- 70% of global cases occur in East Asia

3.1.2 Geographic Distribution

Region	Incidence Level	Notes
East Asia (Japan, Korea, China)	Very high	National screening reduces mortality
Eastern Europe / Russia	High	Lifestyle + socioeconomic contributors

Region	Incidence Level	Notes
Central/South America	Moderately high	Hotspots in Andes regions
North America & Northern Europe	Low	Decline due to improved sanitation
Africa	Very low	Likely underdiagnosed

3.2 Mortality Patterns

- Gastric cancer causes **~770,000 deaths annually**.
- Mortality closely parallels incidence due to late diagnosis.
- East Asia has high incidence but **lower mortality** because of established screening programs.

3.3 Temporal Trends

- Overall global decline in NCGC over 40 years.
- **Increase in CGC** in Western countries, linked to obesity and GERD.
- Reduced *H. pylori* prevalence is the strongest contributor to decreasing NCGC.

3.4 Risk Factors

3.4.1 Infectious Risk Factors

Helicobacter pylori

- Classified as **Group 1 Carcinogen** (IARC).
- Accounts for **~75% of non-cardia gastric cancers**.
- Mechanisms: chronic gastritis → atrophy → metaplasia → dysplasia → carcinoma.

Epstein–Barr Virus (EBV)

- Present in **~10% of gastric cancers**.

3.4.2 Lifestyle & Dietary Factors

- High salt intake
- Smoked/pickled foods
- Nitrosamine exposure
- Low intake of fruits and vegetables
- Alcohol (moderate risk)
- Cigarette smoking (RR ≈ 1.5–2.0)

3.4.3 Medical Conditions

- Chronic atrophic gastritis
- Intestinal metaplasia
- Pernicious anemia
- Prior gastric surgery

3.4.4 Host Genetic Factors

- CDH1 germline mutation → hereditary diffuse gastric cancer
- Polymorphisms: IL-1β, TNF-α promoters
- Blood group A modestly increases risk

3.4.5 Obesity and GERD (for cardia cancer)

- Strong correlation with metabolic syndrome

- Parallel rise with esophageal adenocarcinoma

3.5 Protective Factors

- *H. pylori* eradication programs
- Increased fresh produce intake
- Refrigeration replacing salt-preservation
- Aspirin/NSAIDs (epidemiologic protection seen)
- High physical activity

4. Discussion

4.1 Global Variation Reflects Environmental, Infectious, and Socioeconomic Determinants

High-incidence regions exhibit:

- Greater *H. pylori* prevalence
- Traditional high-salt diets
- Lower socioeconomic development
- Limited early detection outside Japan/Korea

Low-incidence regions reflect improved sanitation, refrigeration, and dietary shifts.

4.2 Diverging Trends in Cardia vs Non-Cardia Gastric Cancer

- NCGC is decreasing worldwide due to falling *H. pylori* rates.
- CGC is increasing in Western populations due to:
 - Obesity
 - GERD
 - High-fat diets

This divergence suggests **distinct etiologies and mechanistic pathways.**

4.3 Impact of Screening Programs

Japan and South Korea demonstrate:

- Earlier-stage detection
- Significant mortality reduction
- Cost-effectiveness at national scale

Their models may be applicable to other high-risk countries.

4.4 Public Health Implications

Effective control strategies include:

- Mass *H. pylori* eradication
- Diet-based interventions
- Reducing smoking rates
- Weight control programs
- Targeted endoscopic screening in high-risk individuals
- Strengthening cancer registry systems

5. Conclusion

Gastric cancer continues to pose a major global health challenge, representing one of the leading causes of cancer morbidity and mortality worldwide.

Despite notable reductions in incidence in several high-income countries, the global burden remains substantial due to persistent geographic, demographic, and socioeconomic disparities.

Regions such as East Asia, Eastern Europe, and parts of Latin America continue to experience disproportionately high incidence rates, reflecting complex interactions between environmental exposures, infectious agents, dietary patterns, and healthcare access.

A key epidemiological insight reinforced by this review is the **central role of *Helicobacter pylori* infection** in driving the development of non-cardia gastric cancer. The bacterium remains the most powerful and well-established modifiable risk factor, with long-term carcinogenic effects mediated through chronic gastritis, mucosal atrophy, intestinal metaplasia, and dysplastic transitions. Therefore, population-level eradication strategies, improved sanitation, and broader implementation of test-and-treat programs hold enormous potential for reducing the future incidence of non-cardia disease, particularly in high-prevalence regions.

In contrast, the **rising incidence of cardia gastric cancer in Western countries** highlights an evolving etiological profile where obesity, metabolic syndrome, and gastroesophageal reflux disease (GERD) play increasingly prominent roles. These divergent epidemiological trends underscore that gastric cancer is not a uniform disease entity, but rather a constellation of biologically and etiologically distinct subtypes, each requiring tailored preventive and clinical approaches.

Despite epidemiological advances, **global mortality from gastric cancer remains unacceptably high**. Late-stage presentation continues to be the predominant challenge, especially in low- and middle-income countries where routine endoscopic screening is limited or unavailable.

Even in settings with advanced healthcare infrastructures, a substantial proportion of patients are diagnosed with locally advanced or metastatic disease, reflecting the often asymptomatic nature of early gastric cancer. The persistent mortality gap between East Asia—where national screening programs have led to earlier detection and improved survival—and other regions illustrates the life-saving potential of organized, population-based screening initiatives.

Moving forward, meaningful reductions in the global burden of gastric cancer will require a **multifaceted and regionally adapted strategy**, including:

1. Region-specific prevention programs

Strategies must reflect the predominant etiological drivers in each population—*H. pylori* eradication in East Asia and Latin America, obesity and GERD control in Western populations, and dietary risk mitigation in transitional economies.

2. Expansion of targeted screening and early detection

Countries with high incidence should consider adopting Japan- and Korea-style endoscopic screening programs, while intermediate- and low-incidence countries may benefit from risk-stratified or opportunistic screening approaches.

3. Integration of molecular and genetic epidemiology

Advances in genomic profiling, biomarker discovery, and risk prediction algorithms offer new opportunities for personalized prevention, early detection, and therapeutic stratification.

Molecular subtyping (e.g., EBV-associated, MSI-high tumors) will increasingly influence epidemiological modelling and public health planning.

4. Strengthening global cancer surveillance systems

High-quality, comprehensive cancer registry data are essential for monitoring incidence and mortality trends, assessing intervention effectiveness, and informing policy decisions.

Improved reporting from low-resource settings is critical to obtaining an accurate global picture.

5. Addressing lifestyle and environmental determinants

This includes reducing tobacco use, promoting healthier dietary patterns, addressing obesity, and improving food preservation and refrigeration practices—public health measures known to influence gastric cancer risk.

In summary, gastric cancer should be regarded not as a monolithic disease but as a **dynamic and preventable malignancy shaped by modifiable risk exposures, evolving lifestyle factors, and healthcare system capacities**. Understanding and addressing these epidemiological determinants are essential steps toward reducing the disease's global impact. With coordinated international efforts, improved surveillance, and proactive public health interventions, substantial reductions in both incidence and mortality are achievable in the coming decades.

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