

Original Article



Incidence, Mortality, and Future Burden of Gastrointestinal Cancers Among Older Adults in Iran: A Population-based Analysis and Projection for 2050

Yosra Vaez-Gharamaleki¹, Arman Ghahremanzadeh², Mohammad Amin Akbarzadeh^{3,4}, Mohammad-Salar Hosseini⁵

¹Hematology and Oncology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

²Department of Internal Medicine, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

³Resuscitation and Critical Care Medicine Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

⁴Research Center for Evidence-Based Medicine, Iranian EBM Center: A JBI Center of Excellence, Tabriz University of Medical Sciences, Tabriz, Iran

⁵Social Determinants of Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Article History:

Received: March 28, 2026

Revised: April 26, 2026

Accepted: April 28, 2026

ePublished: July 30, 2026

*Corresponding Author:

Mohammad-Salar Hosseini,
Emails: hosseini.msalar@gmail.
com; hosseinim@tbzmed.ac.ir

Abstract

Objectives: To evaluate the incidence and mortality of gastrointestinal cancers among older adults in Iran and to project their future burden through 2050.

Design: Population-based study.

Setting: National-level epidemiological analysis in Iran using data from the Global Cancer Observatory database.

Participants: Individuals aged 60 years and older diagnosed with major gastrointestinal malignancies, including esophageal, stomach, colorectal, anal, liver, gallbladder, and pancreatic cancers.

Outcome Measures: Estimated numbers of incident cases and deaths, age-standardized incidence and mortality rates (ASIRs and ASMRs), sex-specific distributions, and mortality-to-incidence ratios (MIRs), along with projected incidence and mortality estimates through 2050, were reported. In addition, Spearman's rank correlation analysis was performed to evaluate the association between incidence and mortality across major gastrointestinal cancer sites. A P-value of less than 0.05 was considered statistically significant.

Results: In 2022, a total of 29704 new gastrointestinal cancer cases and 24900 gastrointestinal cancer-related deaths occurred among individuals aged ≥ 60 years in Iran. The overall ASIR and ASMR were 312.5 and 259.3 per 100000 population, respectively. Men accounted for 62.23% of incident cases and 59.94% of deaths. Stomach cancer was the most common gastrointestinal malignancy. Liver, esophageal, and pancreatic cancers demonstrated disproportionately high mortality relative to incidence. By 2050, the number of new gastrointestinal cancer cases among older adults is projected to increase to over 100000 cases, while gastrointestinal cancer-related deaths are expected to rise to over 92500, with increases of more than 240% and 270%, respectively. Sensitivity analyses showed stable cancer-ranking patterns and consistent MIR estimates across alternative projection scenarios. A very strong positive correlation was observed between ASIRs and ASMRs across gastrointestinal cancer sites among older adults in Iran, indicating that gastrointestinal cancers with higher incidence account for correspondingly higher mortality burden.

Conclusions: The burden of gastrointestinal cancers is rapidly increasing among older adults in Iran, and the projected rise of incidence and mortality by 2050 highlights the urgent need for comprehensive prevention strategies, early detection programs, and expansion of geriatric oncology services to address the growing cancer burden in the aging Iranian population.

Keywords: Aging, Disparities, Epidemiology, Gastrointestinal neoplasms, GI cancers, Iran

Please cite this article as follows: Vaez-Gharamaleki Y, Ghahremanzadeh A, Akbarzadeh MA, Hosseini MS. Incidence, mortality, and future burden of gastrointestinal cancers among older adults in Iran: a population-based analysis and projection for 2050. Int J Aging 2026;4:e9147. doi:10.34172/ija.9147

Introduction

Gastrointestinal cancers are among the leading causes of cancer-related morbidity and mortality worldwide.¹ Accounting for millions of newly diagnosed cases

and deaths annually, gastrointestinal cancers show disproportionately high mortality rates compared with many other cancer types.^{1,2} Population aging, epidemiological transition, urbanization, and lifestyle-



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related risk factors have further contributed to the growing burden of gastrointestinal cancers, especially in low- and middle-income countries.^{3,4}

Advanced age is a key risk factor for the development of gastrointestinal cancers. Older adults experience cumulative exposure to carcinogenic factors, increased prevalence of chronic inflammatory and metabolic conditions, immune senescence, and age-related genomic instability, all of which contribute to elevated cancer susceptibility.^{5,6} In addition, older patients often present with advanced-stage disease, multimorbidity, frailty, and reduced tolerance to cancer therapies, resulting in poorer treatment adherence, inferior clinical outcomes, and higher mortality rates.⁷

Iran is currently undergoing a rapid demographic transition characterized by declining fertility rates and increasing life expectancy, leading to a marked expansion of the older population.⁸ Simultaneously, the country continues to face a heavy burden of gastrointestinal malignancies. Previous studies have demonstrated considerable disparities in gastrointestinal cancer incidence across Iran due to variations in environmental exposures, dietary patterns, infectious risk factors, tobacco use, socioeconomic conditions, and healthcare accessibility.^{9,10} Considering the lack of evidence on the epidemiological profile and burden of gastrointestinal cancers within this population, this study aimed to evaluate the incidence and mortality burden of major gastrointestinal cancers among individuals aged ≥ 60 years in Iran, along with the projection of their future burden through 2050.

Materials and Methods

Study Design and Data Sources

This population-based study evaluated the incidence and mortality of gastrointestinal cancers among older adults, defined as individuals aged 60 and older, in Iran using estimates from the Global Cancer Observatory (GCO) database (v 1.1) developed by the International Agency for Research on Cancer (IARC) and the World Health Organization (WHO). Data were retrieved in May 2026 from the GLOBOCAN 2022 estimates, which provide contemporary evaluations of cancer incidence and mortality for 185 countries and territories worldwide.^{11,12} The study has been reported according to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) (Supplementary Table S1).¹³

Definitions, Population, and Cancer Sites

The study population comprised individuals aged 60 and older in Iran. Analyses were stratified by gender and cancer site. Data on main gastrointestinal malignancies were retrieved according to the International Classification of Diseases, 10th Revision (ICD-10), including esophageal (C15), stomach (C16), colon (C18), rectum (C19-C20), anus and anal canal (C21), liver and intrahepatic bile ducts (C22), gallbladder (C23), and pancreatic (C25) cancers, since they collectively account for the majority

of gastrointestinal cancer incidence and mortality in Iran and the world, represent distinct anatomical and biological entities, and differ substantially with respect to risk factors, screening opportunities, clinical outcomes, and mortality patterns. Therefore, site-specific analyses allowed identification of cancers contributing most significantly to the current and future burden of disease among older adults. Data on small intestine (C17) and extrahepatic/unspecified bile duct cancers (C24) were excluded due to their exceptionally low incidence within the study population, limited contribution to the overall gastrointestinal cancer burden, histological and clinical heterogeneity, and resulting lack of statistical power, which would have resulted in unstable estimates and reduced interpretability of site-specific comparisons. The complete mapping between cancer sites and corresponding ICD-10 codes is provided in [Supplementary Table S2](#). Relative proportions of incidence and mortality attributable to each cancer site were calculated separately for males and females.

Data Extraction, Modeling, and Statistical Analysis

For each cancer type, the estimated number of new cases and deaths was extracted. Crude and age-standardized incidence and mortality rates (ASIRs and ASMRs) were extracted separately for males, females, and both genders combined. Age-standardized rates were calculated per 100000 person-year using the direct standardization method (Segi-Doll World Standard Population)^{14,15} and were used to facilitate comparisons across cancer sites and between genders while accounting for differences in the age structure of the aged population. Although the study exclusively included individuals aged 60 and older, substantial heterogeneity exists within older age groups, with cancer risks varying considerably between those aged 60–64 years and the oldest-old population. The use of age-standardized rates minimized the influence of differences in age composition and provided a more accurate measure of the underlying cancer burden than crude rates alone, enabling comparisons of incidence and mortality patterns across gastrointestinal cancer types and demographic subgroups independent of variations in age distribution.

Due to the lack of age-subgroup-specific uncertainty intervals (UIs) in the GLOBOCAN 2022 reports and in order to adhere to the GATHER, 95% UIs were reported only for estimates for which uncertainty measures were directly provided by the source database. The methods used by GLOBOCAN to calculate and adjust these UIs have been described elsewhere.¹⁴ Spearman's rank correlation analysis was performed to evaluate the association between ASIRs and ASMRs across major gastrointestinal cancer types. A *P*-value of less than 0.05 was considered statistically significant.

Future projections for the year 2050 were generated using the forecasting framework adopted by GLOBOCAN.¹² The projected numbers of incident cases and deaths were estimated by applying the age-specific incidence and

mortality rates observed in 2022 to the projected Iranian population structure for 2050. The primary projection assumed that age-specific incidence and mortality rates remained constant over time. In other words, changes in the number of cases and deaths reflected demographic shifts, including population growth and population aging. Projected estimates were analyzed overall and according to the cancer type to identify cancers expected to contribute most substantially to the future elderly cancer burden in Iran. Corresponding demographic and population projections were based on the twenty-sixth edition of the official United Nations population estimates¹⁶ and reported as ASIR and ASMR per 100,000 population-years. Subsequently, the mortality-to-incidence ratio (MIR) was employed as an indirect indicator of cancer fatality and survival patterns, with a higher MIR indicating poorer survival.

To evaluate the robustness of future projections, sensitivity analyses were conducted for gastrointestinal cancer subtypes under alternative annual incidence trend assumptions. In addition to the baseline scenario assuming stable incidence rates, conservative and accelerated growth scenarios were modeled by applying predefined annual percentage changes of -2% to +2% to the 2022 incidence rates throughout the projection period through the GLOBOCAN framework. Annual percentage changes were calculated through the data source as follows, with N symbolizing the number of cases/deaths (t_1 for the beginning and t_2 for the end of the timeframe):

$$\% \Delta = \frac{(N_{t2} - N_{t1})}{N_{t1}} \times 100$$

In addition to the baseline scenario assuming stable rates, 4 alternative scenarios were extracted assuming annual decreases of 2% and 1% and annual increases of 1% and 2%. For each scenario, adjusted rates were calculated according to the following formula, where δ denotes the assumed annual proportional change (-0.02, -0.01, 0, +0.01, or +0.02) and t represents the time period ($t = 28$ years).

$$r_{2050} = r_{2022} (1 + \delta)^t$$

Projected numbers of cases and deaths were subsequently estimated for each scenario by multiplying the adjusted age-specific rates by the projected population for each age group through the GCO module and were compared with the baseline estimates. Robustness was assessed by examining changes in the relative ranking of cancer sites, the magnitude of projected incidence and mortality, and the stability of mortality-to-incidence ratios (MIRs). Projections were considered robust when the overall epidemiological interpretation remained unchanged, and relative differences in MIRs across scenarios remained below 10%.

Results

Overview of Incidence and Mortality

In 2022, gastrointestinal cancers constituted a substantial proportion of the overall cancer burden among older adults in Iran (Figure 1). Overall, a total of 137198 (95% UI: 135556–138860) and 87247 (95% UI: 85943–88570) new cancer cases and deaths (regardless of subtype) were estimated in the total Iranian population in 2022, respectively. Gastrointestinal cancers accounted for

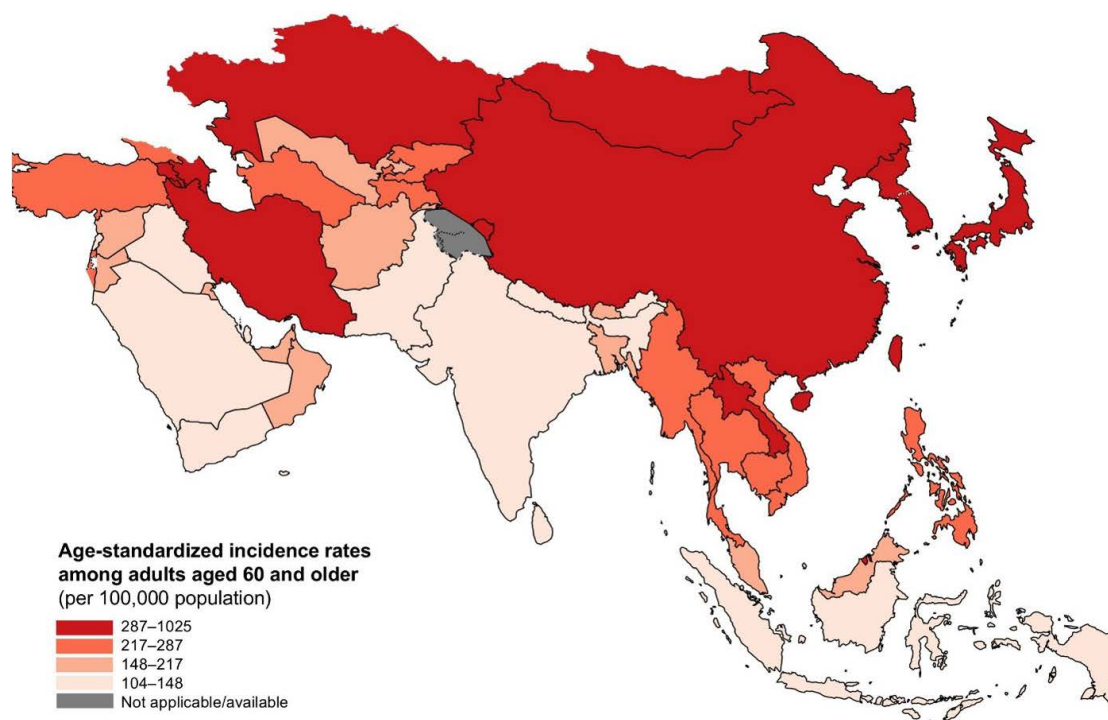


Figure 1. The Incidence of Gastrointestinal Cancers among Older Adults in Iran Compared to other Asian Countries in 2022 (data retrieved from <https://gco.iarc.who.int/today>, International Agency for Research on Cancer)

around 31.7% and 38.1% of total cancer incidence and mortality in 2022, with around 43500 new cases and around 33250 deaths. Among individuals aged 60 and above, a total of 29704 newly diagnosed gastrointestinal cancer cases and 24900 gastrointestinal cancer-related deaths were estimated nationwide, indicating that around 68.2% of new cases and 74.9% of deaths are observed in this age group. Males accounted for the majority of both incident cases and mortality, with 62.23% of new cases and 59.94% of deaths. Overall age-standardized incidence and mortality rates of 312.5 and 259.3 were estimated, respectively.

Among all gastrointestinal malignancies, stomach cancer represented the most frequently diagnosed cancer among older adults in Iran, accounting for 13562 new cases and an ASIR of 142.4 per 100000 population, followed by colon and liver cancers. Mortality patterns differed slightly, as liver cancer showed a higher absolute and age-standardized number than colon cancer, but still lower than stomach cancer, with 10649 new deaths and an ASMR of 110.8. The incidence and mortality estimates for major gastrointestinal cancers among individuals aged 60 and above in Iran were presented in Table 1.

Liver cancer, esophageal cancer, and pancreatic cancer demonstrated disproportionately high mortality relative to incidence, with MIRs of 1.132, 1.068, and 0.933, respectively. In contrast, anal and rectal cancers exhibited comparatively lower MIR values (0.462 and 0.595) (Table 2). A very strong positive monotonic correlation was observed between ASIRs and ASMRs

across gastrointestinal cancer sites among older adults in Iran ($\rho_s=0.952$, $P<0.001$), indicating that gastrointestinal cancers with higher incidence generally exhibit a correspondingly higher mortality burden in this population (Figure 2).

Gender-specific Distribution

Overall, the incidence and mortality of gastrointestinal cancers were consistently higher among males than females across almost all cancer sites. The male-to-female incidence and mortality ratios were highest for stomach (1.98 and 1.837) and pancreatic (1.966 and 1.422) cancers, whereas gender disparities were less pronounced for cancers of the anus (1 and 1.069) and gallbladder (1.19 and 0.7). The gallbladder was the only cancer site in this age group with a higher estimated number of deaths among women.

Among males aged ≥ 60 years, the leading gastrointestinal malignancy was stomach cancer with 9011 new cases and an ASIR of 188 per 100000, followed by colon cancer and liver cancer. In females, stomach cancer was also the most common gastrointestinal malignancy, accounting for 4551 new cases and an ASIR of 96.6 per 100000. Mortality rates were similarly elevated among males. The highest ASMR in both men and women was associated with stomach (140.4 and 79.9 per 100000), liver (47.1 and 38.8), and colon (39.7 and 32) cancers.

Projected Burden to 2050

The projected burden of gastrointestinal cancers among

Table 1. Incidence and Mortality Estimates for Major Gastrointestinal Cancers among Individuals Aged 60 and above in Iran, 2022-2050

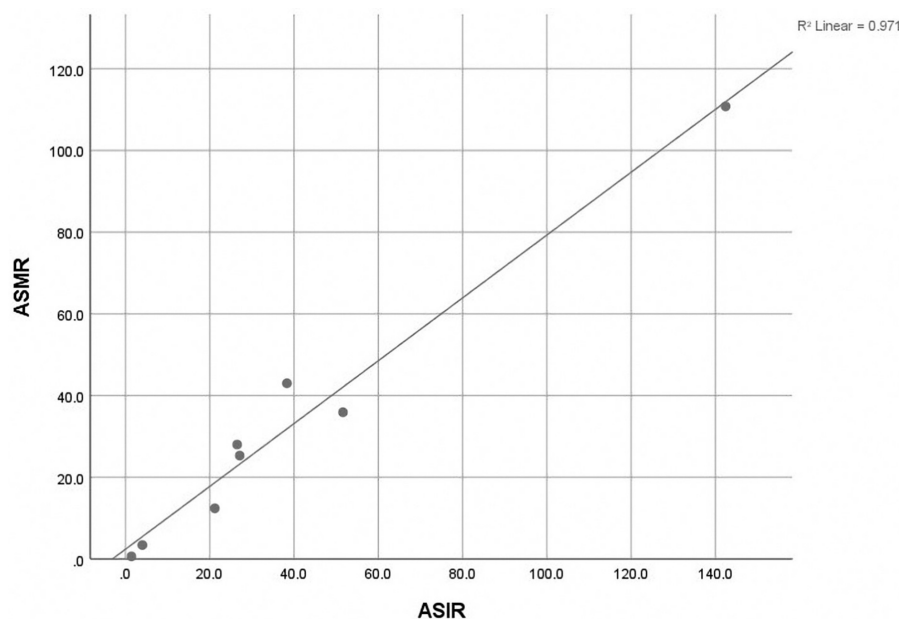
Cancer site	Indicator (point estimates)	Total population aged 60 and above				Females aged 60 and above				Males aged 60 and above			
		ASR (2022)	Estimated cases for 2022	Estimated cases for 2050	Estimated changes, 2022-2050	ASR (2022)	Estimated cases for 2022	Estimated cases for 2050	Estimated changes, 2022-2050	ASR (2022)	Estimated cases for 2022	Estimated cases for 2050	Estimated changes, 2022-2050
Esophagus	Incidence	26.5	2,521	8,712	+245.6%	23.1	1,086	4,080	+275.7%	29.8	1,435	4,633	+222.9%
	Mortality	28.0	2,692	10,144	+276.8%	25.0	1,178	5,052	+328.9%	30.8	1,514	5,091	+236.3%
Stomach	Incidence	142.4	13,562	46,333	+241.6%	96.6	4,551	17,280	+279.7%	188.0	9,011	29,053	+222.4%
	Mortality	110.8	10,649	39,395	+269.9%	79.9	3,753	16,380	+336.5%	140.4	6,896	23,015	+233.7%
Colon	Incidence	51.6	4,882	16,358	+235.1%	43.5	2,047	7,436	+263.3%	59.6	2,835	8,922	+214.7%
	Mortality	35.9	3,447	12,954	+275.8%	32.0	1,499	6,469	+331.6%	39.7	1,948	6,485	+232.9%
Rectum	Incidence	21.2	1,998	6,576	+229.1%	16.3	766	2,718	+254.8%	25.9	1,232	3,858	+213.1%
	Mortality	12.4	1,189	4,339	+264.9%	11.1	520	2,144	+312.3%	13.7	669	2,195	+228.1%
Anus	Incidence	1.4	130	501	+285.4%	1.4	65	294	+352.3%	1.4	65	207	+218.5%
	Mortality	0.62	60	239	+298.3%	0.62	29	143	+393.1%	0.65	31	96	+209.7%
Liver and intrahepatic bile ducts	Incidence	38.3	3,647	12,827	+251.7%	35.3	1,659	6,496	+291.6%	41.5	1,988	6,331	+218.5%
	Mortality	43.0	4,130	15,526	+275.9%	38.8	1,820	7,849	+331.3%	47.1	2,310	7,677	+232.3%
Gallbladder	Incidence	4.0	381	1,321	+246.7%	3.7	174	659	+278.7%	4.4	207	661	+219.3%
	Mortality	3.4	323	1,269	+292.9%	4.0	190	821	+332.1%	2.7	133	448	+236.8%
Pancreas	Incidence	27.1	2,583	8,785	+240.1%	18.5	871	3,285	+277.2%	36.0	1,712	5,500	+221.3%
	Mortality	25.3	2,410	8,725	+262.0%	21.1	987	4,086	+314.0%	29.4	1,423	4,640	+226.1%
Overall	Incidence	312.5	29,704	101,413	+241.4%	238.4	11,219	42,248	+276.6%	386.6	18,485	59,165	+220.1%
	Mortality	259.3	24,900	92,591	+271.9%	212.4	9,976	42,944	+330.5%	304.4	14,924	49,647	+232.7%

*ASR: Age-standardized rate, reported per 100000 person-years

Table 2. Projected Incidence and Mortality for Gastrointestinal Cancers under Alternative Annual Incidence-trend Assumptions

Cancer site	Indicator	Estimated number of cases in 2022	MIR*	Change percentage for the projected estimation per annual incidence trend assumption (2050)									
				-2% per year	MIR	-1% per year	MIR	Constant rate scenario	MIR	+1% per year	MIR	+2% per year	MIR
Esophagus	Incidence	2,521	1.068	4,948	1.164	6,575	1.164	8,712	1.164	11,511	1.164	15,168	1.164
	Mortality	2,692		5,761		7,656		10,144		13,403		17,660	
Stomach	Incidence	13,562	0.785	26,316	0.850	34,969	0.850	46,333	0.850	61,220	0.850	80,667	0.850
	Mortality	10,649		22,375		29,732		39,395		52,052		68,587	
Colon	Incidence	4,882	0.706	9,291	0.792	12,346	0.792	16,358	0.792	21,614	0.792	28,480	0.792
	Mortality	3,447		7,358		9,777		12,954		17,117		22,554	
Rectum	Incidence	1,998	0.595	3,735	0.660	4,963	0.660	6,576	0.660	8,689	0.660	11,449	0.660
	Mortality	1,189		2,464		3,274		4,339		5,733		7,554	
Anus	Incidence	130	0.462	285	0.477	378	0.479	501	0.477	662	0.477	873	0.478
	Mortality	60		136		181		239		316		417	
Liver and intrahepatic bile ducts	Incidence	3,647	1.132	7,285	1.211	9,680	1.211	12,827	1.210	16,948	1.210	22,331	1.211
	Mortality	4,130		8,819		11,718		15,526		20,515		27,032	
Gallbladder	Incidence	381	0.848	750	0.961	997	0.961	1,321	0.961	1,745	0.961	2,300	0.960
	Mortality	323		721		958		1,269		1,677		2,209	
Pancreas	Incidence	2,583	0.933	4,990	0.993	6,630	0.993	8,785	0.993	11,607	0.993	15,294	0.993
	Mortality	2,410		4,956		6,585		8,725		11,529		15,191	
Overall	Incidence	29,704	0.838	57,600	0.913	76,538	0.913	101,413	0.913	133,996	0.913	176,562	0.913
	Mortality	24,900		52,590		69,881		92,591		122,342		161,204	

Abbreviations: MIR: Mortality-to-incidence ratio.

**Figure 2.** Correlation between Incidence and Mortality across Gastrointestinal Cancer Sites among Older Adults in Iran

older adults in Iran is expected to increase substantially between 2022 and 2050. By 2050, the total number of new GI cancer cases among individuals aged ≥ 60 years is projected to increase from 29704 in 2022 to 101413 by 2050, indicating an increase of more than 240% (Figure 3). Similarly, gastrointestinal cancer-related deaths are projected to increase from 24900 deaths in 2022 to 92591 deaths by 2050, corresponding to a relative increase of over 270%.

Sensitivity analyses using alternative annual incidence-

trend assumptions demonstrated that projected gastrointestinal cancer burden remained substantially elevated across all modeled scenarios. Under conservative trend assumptions, the estimated number of incident cases in 2050 remained markedly higher than baseline 2022 estimates, whereas accelerated trend scenarios projected even greater increases in both incidence and mortality (Table 2). Across cancer-specific subgroup analyses, the relative ranking of major gastrointestinal cancers remained stable, with stomach cancer accounting

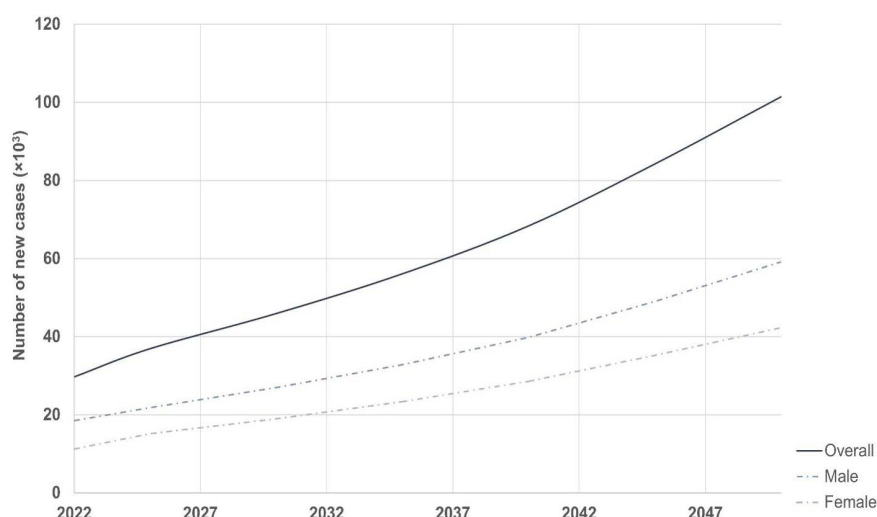


Figure 3. Estimated Number of New Gastrointestinal Cancer Cases among Individuals Older than 60 in Iran through 2050, Stratified by Gender

for the highest projected incidence and mortality burden and liver cancer maintaining the highest MIR values. The MIRs remained consistent, with relative differences across scenarios being less than 10%, indicating acceptable robustness of the primary projections.

Discussion

The current study provides a comprehensive and structured overview of the burden of gastrointestinal cancers among older adults in Iran, based on GLOBOCAN 2022 estimates and long-term demographic projections to 2050. Our findings demonstrate that gastrointestinal malignancies already constitute a major public health challenge among the Iranian older population and are expected to increase dramatically over the coming decades. In 2022 alone, almost 30000 new gastrointestinal cancer cases and approximately 25000 related deaths occurred among individuals aged ≥ 60 years, highlighting the considerable contribution of these malignancies to cancer morbidity and mortality. More importantly, projections indicate that both incidence and mortality may triple by 2050, emphasizing the urgent need for targeted prevention, early detection, geriatric oncology infrastructure, and health-system preparedness in Iran.

One of the most notable findings of the present study was the predominance of stomach cancer as the leading gastrointestinal malignancy among older adults in Iran in both incidence and mortality. This observation is consistent with previous epidemiological studies from Iran, where stomach cancer remains among the most common malignancies, especially in older populations.^{17,18} The persistently high burden of gastric cancer in Iran likely reflects the combined influence of several well-established risk factors, including high prevalence of *Helicobacter pylori* infection, dietary salt intake, consumption of smoked and preserved food, tobacco exposure, socioeconomic disparities, and regional environmental determinants.¹⁹⁻²¹

The marked burden of liver cancer observed in this

study is also of particular concern. Although liver cancer demonstrated a lower incidence compared with stomach and colon cancers, it exhibited disproportionately high mortality and the highest MIR among all gastrointestinal malignancies. The observed MIR exceeding unity may partly reflect limitations inherent to modeled estimates, delayed detection, underdiagnosis of incident disease, or rapid disease progression resulting in poor survival. In Iran, chronic hepatitis B and C infections, metabolic dysfunction-associated steatotic liver disease, cirrhosis, aflatoxin exposure, and increasing prevalence of obesity and diabetes may all contribute to the future expansion of liver cancer burden among aging populations.²² Similarly, pancreatic cancer demonstrated very high MIR values, reflecting persistently poor prognostic outcomes as observed in previous studies from Iran.²³ The high MIR observed in our analysis aligns with global epidemiological patterns and suggests that improvements in survival among older Iranian patients remain limited.²⁴ Esophageal cancer also showed higher mortality relative to incidence, which may reflect delayed presentation, regional risk-factor clustering, tobacco and opium use, and nutritional deficiencies.²⁵⁻²⁷

The MIR for esophageal and liver cancer was higher than one, indicating a higher number of estimated deaths than the overall estimated new cases in 2022. Although MIR values theoretically remain below 1, this finding may reflect limitations inherent to modeled GLOBOCAN estimates, including underdiagnosis of incident liver cancer cases, delayed detection, variations in registry completeness, and the extremely poor prognosis associated with hepatocellular carcinoma. Many liver and esophageal cancer patients are diagnosed very late or never formally diagnosed before death, especially among older populations, low-resource settings, or regions with limited surveillance. In addition, deaths in 2022 may originate from cases diagnosed earlier. Previous studies have shown that for rapidly fatal cancers with poor survival, mortality may approximate or occasionally

exceed the estimated incidence. Therefore, deaths may be captured more completely than incident diagnoses. Besides, considering that a significant rise in incidence for liver and esophageal cancers is observed in the age group of 55 to 60, a higher absolute mortality number is not unexpected.²⁸⁻³⁰ However, the MIRs for these two cancers should still be interpreted with caution, as the current investigation does not provide survival analyses.

Another finding of the present study was the pronounced gender disparity across nearly all gastrointestinal cancer sites. Men consistently exhibited higher incidence and mortality rates than women, especially for stomach and pancreatic cancers. These gender differences are likely multifactorial and may involve a higher prevalence of smoking, alcohol consumption, occupational exposures, dietary risk factors, and metabolic comorbidities among men.³¹⁻³³ Hormonal and biological differences may additionally affect both susceptibility and disease progression.³⁴ Interestingly, gallbladder cancer represented the only malignancy with higher mortality among women, a finding consistent with previous literature demonstrating increased gallstone disease and biliary pathology among females.³⁵

The strong positive correlation observed between ASIRs and ASMRs suggests that gastrointestinal cancers contributing most substantially to disease occurrence among older adults in Iran also account for the greatest mortality burden. The close alignment between incidence and mortality patterns may partly reflect delayed diagnosis, limited early detection, and suboptimal survival outcomes for this population. From a health-system perspective, these findings imply that future increases in the incidence of GI cancer are likely to translate directly into parallel increases in mortality unless substantial improvements are achieved in prevention, screening, early diagnosis, and treatment accessibility. Consequently, reducing the future mortality burden of GI cancers in Iran requires lowering incidence through primary prevention strategies.

The expected increase of more than 240% in incidence and over 270% in mortality is substantially greater than what would be anticipated from merely population growth, which largely reflects the rapid demographic aging occurring in Iran. Over the past few decades, Iran has undergone a major demographic transition characterized by declining fertility, increasing life expectancy, and an expansion of the elderly population. Considering that cancer incidence increases exponentially with age, these demographic shifts are expected to profoundly alter the national cancer landscape in the coming decades. Importantly, the projected increase in mortality exceeded the projected increase in incidence, suggesting that the future burden of gastrointestinal cancers may not only involve larger numbers of patients but also increasing numbers of advanced or fatal cases. This finding has important implications for healthcare systems, including anticipated demand for oncology services, surgical capacity, chemotherapy infrastructure, radiotherapy resources, palliative care, and long-term

survivorship support. Older patients frequently present with multimorbidity, frailty, polypharmacy, and reduced physiological reserve, all of which complicate the management of cancer and increase healthcare costs.³⁶

From a public health perspective, our findings highlight some priorities for cancer control in Iran. First, strengthening primary prevention strategies is essential. Population-level interventions targeting tobacco control, obesity reduction, dietary modification, viral hepatitis prevention, and metabolic risk-factor management may substantially reduce future gastrointestinal cancer burden. Second, expansion of inclusive screening and early detection programs could improve early-stage diagnosis and survival outcomes. Third, healthcare systems must prepare for the rapidly increasing demand for geriatric oncology services, including multidisciplinary care models.

This study has several limitations as well. First, GLOBOCAN estimates are partially model-based and rely on the availability and quality of national cancer registry and mortality data. Variability in the completeness of cancer registration and accuracy of death certification may influence estimates, especially for less common cancers. Second, the lack of subgroup-specific uncertainty intervals for older age categories limits the inferential comparisons. In addition, future projections assumed relative stability in age-specific incidence and mortality patterns and may therefore not fully capture changes in screening practices, healthcare access, environmental exposures, treatment advances, or risk-factor prevalence, although alternative scenarios have also been discussed. Lastly, MIRs, especially the high and near-unity ones, should be interpreted with caution since they represent indirect population-level indicators rather than direct survival estimates.

Conclusion

Gastrointestinal cancers represent a major and rapidly growing health burden among older adults in Iran. Stomach cancer currently accounts for the highest incidence and mortality burden, whereas liver and pancreatic cancers exhibit disproportionately high mortality relative to incidence. The projected rise in incidence and mortality of gastrointestinal cancers by 2050 highlights the urgent need for comprehensive national strategies focusing on prevention, early detection, geriatric oncology capacity, and equitable access to cancer care.

Author contributions

Conceptualization: Arman Ghahremanzadeh, Mohammad-Salar Hosseini.

Data Curation: Yosra Vaez-Gharamaleki, Mohammad-Salar Hosseini.

Formal Analysis: Mohammad Amin Akbarzadeh, Mohammad-Salar Hosseini.

Methodology: Yosra Vaez-Gharamaleki, Mohammad-Salar Hosseini.

Validation: Arman Ghahremanzadeh, Mohammad-Salar Hosseini.

Visualization: Mohammad Amin Akbarzadeh.

Writing—Original Draft: Yosra Vaez-Gharamaleki, Mohammad-Salar Hosseini.

Writing—Review & Editing: Arman Ghahremanzadeh, Mohammad

Amin Akbarzadeh.

Funding

None.

Data availability statement

The datasets used and analyzed in this study are publicly available at the Global Cancer Observatory (<https://gco.iarc.who.int/>).

Ethical approval

Not applicable.

Consent for publication

Not applicable.

Conflict of interests

The authors declare that they have no conflict of interests.

Supplementary files

Supplementary file 1 contains Table S1-S2.

References

1. Danpanichkul P, Suparan K, Tothananungroj P, Dejvajara D, Rakwong K, Pang Y, et al. Epidemiology of gastrointestinal cancers: a systematic analysis from the Global Burden of Disease Study 2021. *Gut* 2024;74(1):26-34. doi:10.1136/gutjnl-2024-333227
2. Singh A. Global burden of five major types of gastrointestinal cancer. *Prz Gastroenterol* 2024;19(3):236-54. doi:10.5114/pg.2024.141834
3. Akhondi H, Kalteh EA, Lotfi MH. Common risk factors in gastrointestinal cancers: a narrative review. *Med Princ Pract* 2025;34(6):509-26. doi:10.1159/000547241
4. McCormack VA, Boffetta P. Today's lifestyles, tomorrow's cancers: trends in lifestyle risk factors for cancer in low- and middle-income countries. *Ann Oncol* 2011;22(11):2349-57. doi:10.1093/annonc/mdq763
5. Montégut L, López-Otín C, Kroemer G. Aging and cancer. *Mol Cancer* 2024;23(1):106. doi:10.1186/s12943-024-02020-z
6. Trastus LA, d'Adda di Fagagna F. The complex interplay between aging and cancer. *Nat Aging* 2025;5(3):350-65. doi:10.1038/s43587-025-00827-z
7. Pham TT, Connor AE, Rositch AF. Multimorbidity and cancer treatment among the older patients in the United States. *PLoS One* 2026;21(1):e0338721. doi:10.1371/journal.pone.0338721
8. Azarbakhsh H, Dehghani SP. The future of Iran with a decrease in the total fertility rate. *Arch Iran Med* 2025;28(4):255-6. doi:10.34172/aim.33643
9. Vakilzadeh MM, Khayami R, Daneshdoust D, Moshfeghinia R, Sharifnezhad F, Taghiabadi Z, et al. Prevalence of tobacco use among cancer patients in Iran: a systematic review and meta-analysis. *BMC Public Health* 2024;24(1):1081. doi:10.1186/s12889-024-18594-8
10. Asgarian FS, Mahdian M, Amori N. Epidemiology and trends of gastrointestinal cancer in Iran (2004-2008). *J Cancer Res Ther* 2021;17(4):963-8. doi:10.4103/jcrt.JCRT_509_19
11. Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, et al. Global Cancer Observatory: Cancer Today (Version 1.1). Vol 2026. Lyon: International Agency for Research on Cancer; 2024.
12. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024;74(3):229-63. doi:10.3322/caac.21834
13. Stevens GA, Alkema L, Black RE, Boerma JT, Collins GS, Ezzati M, et al. Guidelines for accurate and transparent health estimates reporting: the GATHER statement. *Lancet* 2016;388(10062):e19-23. doi:10.1016/s0140-6736(16)30388-9
14. Filho AM, Laversanne M, Ferlay J, Colombet M, Piñeros M, Znaor A, et al. The GLOBOCAN 2022 cancer estimates: data sources, methods, and a snapshot of the cancer burden worldwide. *Int J Cancer* 2025;156(7):1336-46. doi:10.1002/ijc.35278
15. Doll R, Payne P, Waterhouse JA. Cancer Incidence in Five Continents: A Technical Report. Springer; 1966.
16. United Nations - Department of Economic and Social Affairs - Population Division. World Population Prospects. 2019.
17. Moradian F, Fararouei M, Karami M, Ghelichi-Ghohgh M, Gheibi Z, Nikeghbalian Z, et al. Trend of geographical distribution of stomach cancer in Iran from 2004 to 2014. *BMC Gastroenterol* 2022;22(1):4. doi:10.1186/s12876-021-02066-z
18. Mehrabian A, Esna-Ashari F, Zham H, Hadizadeh M, Bohlooli M, Khayamzadeh M, et al. Gastric cancer prevalence, according to survival data in Iran (national study-2007). *Iran J Public Health* 2010;39(3):27-31.
19. Malekzadeh R, Derakhshan MH, Malekzadeh Z. Gastric cancer in Iran: epidemiology and risk factors. *Arch Iran Med* 2009;12(6):576-83.
20. Toorang F, Sasanfar B, Hekmatdoost A, Narmcheshm S, Hadji M, Ebrahimpour-Koujan S, et al. Macronutrients intake and stomach cancer risk in Iran: a hospital-based case-control study. *J Res Health Sci* 2021;21(1):e00507. doi:10.34172/jrhrs.2021.38
21. Yusefi AR, Bagheri Lankarani K, Bastani P, Radinmanesh M, Kavosi Z. Risk factors for gastric cancer: a systematic review. *Asian Pac J Cancer Prev* 2018;19(3):591-603. doi:10.22034/apjcp.2018.19.3.591
22. Hosseini MS, Khoshbaten M, Kolahi AA, Safiri S. Liver cancer in the Middle East and North Africa: epidemiology, trends, and risk factors. *Int J Aging* 2024;2(1):e13. doi:10.34172/ija.2024.e13
23. Azizmohammad Looha M, Saberi Shahrabaki A, Zamani M, Zareie Shab Khaneh A, Javadi S, Sadeghloo Z, et al. Burden of pancreatic cancer in Iran: an analysis of Global Burden of Disease 2021. *Gastroenterol Hepatol Bed Bench* 2025;18(4):455-66. doi:10.22037/ghfbb.v18i4.3225
24. Huang K, Lan X, Chen Z, Xiao H, Jia S, Du C. Global trends and future predictions of pancreatic cancer incidence and mortality from 1990 to 2030: a comparative analysis of China, Korea, Japan, and the USA. *PLoS One* 2025;20(12):e0337181. doi:10.1371/journal.pone.0337181
25. Kamangar F, Chow WH, Abnet CC, Dawsey SM. Environmental causes of esophageal cancer. *Gastroenterol Clin North Am* 2009;38(1):27-57. doi:10.1016/j.gtc.2009.01.004
26. Sheikh M, Roshandel G, McCormack V, Malekzadeh R. Current status and future prospects for esophageal cancer. *Cancers (Basel)* 2023;15(3):765. doi:10.3390/cancers15030765
27. Zhang C, Chen L, Xiu Y, Zhang H, Zhang Y, Ying W. Burden of esophageal cancer in global, regional and national regions from 1990 to 2021 and its projection until 2050: results from the GBD study 2021. *Front Oncol* 2024;14:1518567. doi:10.3389/fonc.2024.1518567
28. Lu S, Li K, Wang K, Liu G, Han Y, Peng L, et al. Global trends of esophageal cancer among individuals over 60 years: an epidemiological analysis from 1990 to 2050 based on the Global Burden of Disease Study 1990-2021. *Oncol Rev* 2025;19:1616080. doi:10.3389/or.2025.1616080
29. Tan EY, Danpanichkul P, Yong JN, Yu Z, Tan DJ, Lim WH, et al. Liver cancer in 2021: Global Burden of Disease Study. *J Hepatol* 2025;82(5):851-60. doi:10.1016/j.jhep.2024.10.031
30. Arnold M, Abnet CC, Neale RE, Vignat J, Giovannucci EL, McGlynn KA, et al. Global burden of 5 major types of gastrointestinal cancer. *Gastroenterology* 2020;159(1):335-49.e15. doi:10.1053/j.gastro.2020.02.068

31. Li WY, Han Y, Xu HM, Wang ZN, Xu YY, Song YX, et al. Smoking status and subsequent gastric cancer risk in men compared with women: a meta-analysis of prospective observational studies. *BMC Cancer* 2019;19(1):377. doi:[10.1186/s12885-019-5601-9](https://doi.org/10.1186/s12885-019-5601-9)
32. Selvaraj RC, Cioffi G, Waite KA, Jackson SS, Barnholtz-Sloan JS. A pan-cancer analysis of age and sex differences in cancer incidence and survival in the United States, 2001-2020. *Cancers (Basel)* 2025;17(3):378. doi:[10.3390/cancers17030378](https://doi.org/10.3390/cancers17030378)
33. Andersson G, Wennersten C, Borgquist S, Jirstrom K. Pancreatic cancer risk in relation to sex, lifestyle factors, and pre-diagnostic anthropometry in the Malmö Diet and Cancer Study. *Biol Sex Differ* 2016;7:66. doi:[10.1186/s13293-016-0120-8](https://doi.org/10.1186/s13293-016-0120-8)
34. Katzke VA, Dutta S, Rasokat A, Archibugi L, Capurso G, Peduzzi G, et al. Sex disparities and female reproductive and hormonal factors associated with risk of pancreatic cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. *Cancers (Basel)* 2025;17(14):2275. doi:[10.3390/cancers17142275](https://doi.org/10.3390/cancers17142275)
35. Rawla P, Sunkara T, Thandra KC, Barsouk A. Epidemiology of gallbladder cancer. *Clin Exp Hepatol* 2019;5(2):93-102. doi:[10.5114/ceh.2019.85166](https://doi.org/10.5114/ceh.2019.85166)
36. Aggarwal P, Woolford SJ, Patel HP. Multi-morbidity and polypharmacy in older people: challenges and opportunities for clinical practice. *Geriatrics (Basel)* 2020;5(4):85. doi:[10.3390/geriatrics5040085](https://doi.org/10.3390/geriatrics5040085)