

Title of Thesis

**LONG-TERM TRENDS IN
DISEASE BURDEN AT GLOBAL,
REGIONAL, AND NATIONAL LEVELS:
FINDINGS FROM THE GLOBAL BURDEN
OF DISEASE STUDY 2019 AND THE
WORLD HEALTH ORGANIZATION
MORTALITY DATABASE**

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PUBLICATIONS RELATED TO THIS THESIS

- 1) Quynh Thi Vu, Ko Harada, Yoshito Nishimura, Hideharu Hagiya, Elizabeth Tan, Odifentse Mapula E. Lehasa, Yoshito Zamami, Toshihiro Koyama. *Burden of depressive disorders in Vietnam from 1990 to 2019: A secondary analysis of the Global Burden of Disease Study 2019*. J Psychiatr Res. 2024;172:420-426.
- 2) Quynh Thi Vu, Yoshito Nishimura, Ko Harada, Hiroki Ito, Tsukasa Higashionna, Akinari Maruo, Keisaku Harada, Tatsuaki Takeda, Hirofumi Hamano, Yoshito Zamami, Hideharu Hagiya, Toshihiro Koyama. *International trends in biliary tract cancer-related mortality, 2000–2022: An observational study of the World Health Organization Mortality Database*. Hepatology. 2025;82(3):626-637.

Large parts of this thesis are based on the above published articles.

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LIST OF ABBREVIATIONS

AAPC	Average annual percent change
ASR	Age-standardised mortality rate
BTC	Biliary tract cancer
CI	Confidence interval
DALYs	Disability-adjusted life years
DSM-IV-TR	Diagnostic and statistical manual of mental disorders- fourth edition-text revision
eCCA	Extrahepatic cholangiocarcinoma
GBC	Gallbladder cancer
GBD	Global Burden of Disease
iCCA	Intrahepatic cholangiocarcinoma
ICD	International statistical classification of diseases and related health problems
LOESS	Locally weighted regression
OR	Odds ratio
UI	Uncertainty interval
WHO	World Health Organization
YLDs	Years lived with disability
YLLs	Years of life lost

I. INTRODUCTION

This chapter is based on the previously published articles.^{1,2}

In-depth, comprehensive, and timely studies on long-term trends of disease burden at global/international, regional, and national levels are crucial for making health-related policy decisions and guiding future interventions.³ At global and regional levels, such studies enhance understanding of complex population health patterns worldwide, provide insights into disparities across regions, identify major public health challenges, and emerging global health issues. They provide scientific evidence that enables international organizations, such as the World Health Organization (WHO), to identify health priorities and formulate coordinated global responses to shared health threats. At national level, in addition to improving understanding of country-specific health patterns over time and across age groups and sexes, these studies provide context-specific evidence to support governments and policymakers in developing and implementing effective and appropriate interventions and prevention strategies in accordance with national circumstances. Furthermore, they enable more rigorous monitoring of progress toward national, regional and global health targets, particularly the United Nations Sustainable Development Goals.³ Several large-scale health databases support such studies, including the Global Burden of Disease (GBD) Study and the WHO mortality database, each with its own strengths and limitations.^{4,5}

The GBD study is one of the largest-scale and richest health-related database. The GBD study 2019 provides the estimates of the prevalence, incidence, mortality, years lived with disability (YLDs), years of life lost (YLLs), and disability-adjusted life years (DALYs) for 369 diseases and injuries across 204 countries and territories from 1990 to 2019 (available in October 2020) as a dataset.⁶ All GBD estimates are published at <https://vizhub.healthdata.org/gbd-results/>. The 369 diseases and injuries included in the GBD study 2019 were organised into a four-level cause hierarchy. The method for estimating the burden of diseases and injuries has been described previously.^{4,7} In the GBD study 2019, a systematic literature review was conducted based on peer-reviewed literature (search performed in PsycInfo, Embase, and

PubMed), grey literature, and expert consultation containing data on prevalence, incidence, remission, and/or excess mortality for diseases. The epidemiological data were modelled using DisMod-MR 2.1, a Bayesian meta-regression tool, to estimate the prevalence by location, year, age, and sex for diseases and injuries.⁴ Cause of death ensemble modelling approach was used to model most cause-specific death rates based on gathered available data. Cause of death ensemble modelling is a structured framework that runs multiple models and selects an ensemble predictive model that estimates death by location, age, sex, and year.⁴ YLDs, quantifying non-fatal health loss, were calculated by multiplying the prevalence of each sequela by disability weights. Disability weights ranged from 0 (full health state) to 1 (death state). YLDs were adjusted for comorbidities because each individual could have a combination of different diseases or sequelae at a particular time. YLLs, quantifying fatal health loss, were computed by multiplying the number of estimated deaths by the standard life expectancy at age of death.⁴ DALYs, quantifying both years lost to premature mortality and years lived with disability, were computed as the sum of YLDs and YLLs. To compare the rates between countries, and regions at the same time or in the same regions over time, age-standardised rates were estimated using the GBD 2019 World Population Age Standard.⁴

The WHO mortality database contains the number of deaths by country, year, sex, and age group since 1950, registered in national vital registration systems. It provides aggregated data for the underlying or primary cause of death listed in death certificates. Countries reporting data properly coded according to the International Statistical Classification of Diseases and Related Health Problems (ICD) (versions 7-10) have been included in this database.⁵

Non-communicable diseases have been the leading cause of death, morbidity and disability globally. According to the GBD study 2019, non-communicable diseases accounted for approximately 1,620.2 million DALYs in 2019, substantially exceeding the burden attributable to communicable diseases (420.4 million DALYs).⁸ Among non-communicable diseases, cancers and mental disorders contributed significantly to the overall non-communicable disease burden, ranking as the second

and fourth leading causes of DALYs, respectively, in 2019. Moreover, cancers were the second leading cause of death globally, following cardiovascular diseases.⁸

Depressive disorders are the most common mental disorders worldwide.^{4,9} According to the GBD study 2019, the global number of depressive disorder cases was 279.6 million (95% uncertainty interval (UI): 251.6–310.3), representing age-standardised prevalence rate of 3440.1 (95% UI: 3097.0–3817.6) per 100,000 population in 2019.⁷ Depressive disorders have been a leading cause of disability, representing the 13th leading cause of DALYs in 2019.⁴ Further, depressive disorders are closely associated with economic burden¹⁰ and suicide.¹¹ Depressive disorders are treated by either psychological or pharmacological treatments or a combination of both.^{12,13} However, the treatment rate of depressive disorders is low and only few treated patients received minimally optimal treatment, especially in low- and middle-income countries.^{14,15} Shortage of resources, a poor quality of mental health services, social stigma associated with mental diseases, high treatment costs, and poor mental health literacy are major barriers to meet the demand for mental health care worldwide.⁹ In the context of mental disorders becoming a major public health concern globally, this requires national governments to commit to actions to improve population mental health and well-being. Vietnam has strengthened national attention to this issue, as evidenced by the approval of the national plan for the prevention and control of non-communicable diseases and mental health disorders for 2022–2025.¹⁶ In Vietnam, according to National Psychiatric Hospital No.1's report to the WHO on mental disorders, the prevalence of depressive disorders was 2.45%, making it one of the top 10 common mental disorders in 2014.¹⁷ Studies in Vietnam have been conducted to analyse the prevalence of depression or depressive symptoms in specific population groups. A previous study highlighted that 31.7% of secondary and high-school students (13–17 years) had depressive symptoms.¹⁸ Another study indicated that 30.5% of industrial workers had depressive symptoms,¹⁹ whereas another study found that 31.3% of older people (≥ 60 years) had depressive symptomatology.²⁰ The prevalence of depression among patients with type 2 diabetes mellitus in the Northeast region was reported to be 32.3%.²¹ However, previous studies only focused

on specific population groups or limited locations in Vietnam or used different measuring methods, making it difficult to compare results or note the changing trend in the prevalence of depressive disorders in the country over time. Comparisons of the prevalence of depressive disorder trends in Vietnam with those in other countries are challenging, given the limited availability of context-specific studies. Moreover, no published studies have analysed the burden of depressive disorders in terms of DALYs in Vietnam. This highlights the need for studies on the burden of depressive disorders in Vietnam at the national level. This study will improve understanding of the burden of depressive disorders in Vietnam and help governments and policymakers to establish appropriate strategies to reduce the burden of these disorders by identifying the priority areas and individuals.

Among cancers, biliary tract cancers (BTCs), which are classified based on their primary anatomical location, including intrahepatic cholangiocarcinoma (iCCA), extrahepatic cholangiocarcinoma (eCCA) (subclassified as perihilar and distal cholangiocarcinoma), gallbladder cancer (GBC), and ampullary cancer, are a group of rare cancers.^{22,23} The incidence of BTCs varies widely across countries and geographical regions worldwide, with lower rates observed in Europe and higher rates observed in the Asia-Pacific and South American regions.²⁴ The GLOBOCAN 2022 database revealed that GBC was the 22nd most prevalent of 33 cancer types in terms of new cases, with an estimated 122,462 new cases in 2022.²⁵ Although BTC are relatively rare compared with more common cancers such as liver and lung cancers, they are aggressive cancers and continue to present a significant global health challenge. BTCs are known for their poor prognosis,^{26,27} with five-year survival rates ranging from 13% to 23%,^{28–30} with the lowest survival rate observed for iCCA.^{28,30} Early detection of BTCs has been a challenge, with a higher proportion of patients diagnosed at an advanced stage due to non-specific or asymptomatic clinical presentation in the early stages.^{26,27} Several risk factors for BTCs have been documented based on their subtypes. While cirrhosis and hepatitis B and C are more strongly associated with iCCA than eCCA, choledochal cyst, and choledocholithiasis have a stronger correlation with eCCA than with iCCA.²⁶ Other risk factors associated

with both iCCA and eCCA include primary sclerosing cholangitis, non-alcoholic fatty liver disease, Caroli disease, and alcohol consumption.²⁶ Liver fluke infection is an endemic risk factor for iCCA and eCCA in certain regions of specific countries. For instance, *Clonorchis sinensis* is endemic in parts of the Republic of Korea, China, Taiwan, and northern Vietnam, while *Opisthorchis viverrini* is endemic in parts of Thailand, Laos, Cambodia, Myanmar, and southern Vietnam.³¹ For GBC, gallstones are the main risk factor alongside gallbladder polyps, obesity, and diabetes.²⁷ Cigarette smoking is reportedly associated with all BTC subtypes except GBC.³² Additionally, sex influences BTC risk, such that females are more prone to GBC, whereas males are more susceptible to iCCA and eCCA.^{26,27} To mitigate the disease burden, monitoring international, regional, and national trends in mortality due to BTCs over time is crucial. A recent study examined trends in BTC-related mortality for 1990–2019 but did not include data for iCCA.³³ Other published studies analysing global trends in BTC or its subtype-related mortality exist; however, the data used are outdated.^{24,34–36} The most recent comprehensive analysis of mortality trends due to BTCs was conducted for the period up to 2016 by Baria *et al.*²⁴ Therefore, studies examining mortality trends of BTCs and their subtypes at national, regional, and global/international levels are needed.

Among available health-related databases, the GBD study, which provides health metrics such as prevalence, DALYs, is well suited for examining the burden of depressive disorders, non-fatal non-communicable diseases, in Vietnam. However, the GBD study database has inherent limitations, including limited flexibility in assessing more specific disease and injury subtypes.⁴ Notably, the GBD study provides health metrics for gallbladder and biliary tract cancers, not including iCCA, only as a broader category. Consequently, it is not possible to analyse the burden of BTCs and specific BTC subtypes using the GBD study database alone. Therefore, the WHO mortality database is more appropriate for examining the burden of BTCs and their subtypes in terms of mortality at national, regional, and global/international levels.

The objective of this research was to evaluate long-term trends in the burden of specific non-communicable diseases (i.e., depressive disorders and biliary tract cancers) using multiple health indicators at national, regional, and international levels, based on data from large-scale health databases, namely the Global Burden of Disease Study 2019 and the World Health Organization mortality database, as follows:

(1) To analyse the burden of depressive disorders in Vietnam from 1990 to 2019, stratified by sex and age, using the GBD study 2019 dataset.

(2) To examine international and regional mortality trends due to BTCs and their major subtypes between 2000 and 2022, and to analyse country-specific mortality trends over the last decade using data from the WHO mortality database.

II. METHODS

2.1. Depressive disorders

This chapter is based on the previously published article.¹

2.1.1. Definition of diseases

In GBD study 2019, depressive disorders, including major depressive disorder and dysthymia, were classified as a third-level cause hierarchy, under the broader category of mental disorders at the second-level cause hierarchy. The case definitions of major depressive disorder and dysthymia were according to the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision (DSM-IV-TR)³⁷ or the ICD-10 criteria (Table 1).³⁸ According to the GBD study 2019, depressive disorders were non-fatal diseases;⁴ therefore, YLLs, calculated based on premature mortality, were not estimated, and YLDs were equivalent to DALYs. In this study, only DALYs are shown, instead of YLDs and YLLs.

Table 1. Depressive disorders included in the GBD study 2019⁴

Cause	Corresponding DSM-IV-TR and ICD-10 codes
Major depressive disorder	DSM-IV-TR: 296.21–24, 296.31–34 ICD-10: F32.0–9, F33.0–9
Dysthymia	DSM-IV-TR: 300.4 ICD-10: F34.1

DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision; ICD-10: International Statistical Classification of Diseases and Related Health Problem-Tenth Revision

2.1.2. Data extraction and statistical analyses

This study was a secondary study using data extracted from the GBD study 2019 database. This study described the burden of depressive disorders in Vietnam in terms of prevalence and DALYs (number of cases and rate per 100,000 population) and their changing trends from 1990 to 2019. The joinpoint regression analysis was performed to identify temporal trends in prevalence and DALY rates by using the Joinpoint Regression Program software.³⁹ A log-linear model (i.e., $\ln(\text{rate}) = b_0 \times y + b_1$ where y = calendar year) was chosen. I chose the permutation test comprising 4499 permutations as the model selection method to determine the optimal number of

joinpoints.⁴⁰ Annual percent change for each segment and weighted average of the annual percent changes (i.e., average annual percent change [AAPC]) for the entire period and their 95% confidence intervals (CIs) were calculated. AAPCs were compared with zero and AAPCs were significantly different from zero at a $p < 0.05$. The rates of prevalence and DALYs were significantly increasing or decreasing if $p < 0.05$ and stable otherwise. The Joinpoint Regression Program (version 5.0.2, May 2023; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute) was used in this analysis.

2.2. Biliary tract cancers

This chapter is based on the previously published article.²

2.2.1. Definition of diseases

In accordance with the ICD-10 criteria, I identified several codes pertinent to BTCs as follows: C22.1 for iCCA; C23 for GBC; C24.0 for eCCA; C24.1 for ampullary cancer; C24.8 for overlapping lesion of BTC; and C24.9 for unspecified BTC. Moreover, I included C24 to code for other and unspecified parts of BTC.³⁸

2.2.2. Data extraction

I conducted an observational study according to the reporting of studies conducted using the observational routinely-collected health data (RECORD) statement.⁴¹ I analysed trends in BTC-related mortality using the WHO mortality database (last update, February 21, 2024), which is available at <https://www.who.int/data/data-collection-tools/who-mortality-database>.⁵ The number of deaths due to BTCs coded as C22.1, C23, C24.0, C24.1, C24.8, C24.9, and C24 were extracted from the database. Countries providing data for the period 2000–2022, categorised into 5-year age groups ranging from 0–4 to 85 years and above, were included in this study. In instances where countries reported no deaths due to BTCs, these were recorded as true zeros rather than being treated as missing data, as in the previous study.⁴² Additionally, years with missing data were treated as null values and excluded from the analysis. The quality of vital registration data from each country was classified based on a “usability” indicator developed by the WHO.⁴³ Data were categorised as high quality if the latest usability from 2008 to 2019 was

≥80%; medium quality if the latest usability was ≥60% and <80%; and low quality if the latest usability was <60%.⁴³ Only countries with medium-to-high data quality were considered for this study. Mid-year population data for these countries by year, sex, and age group were sourced from the United Nations World Population Prospects 2022.⁴⁴

2.2.3. Statistical analyses

Crude mortality rates were calculated by dividing the number of deaths by the corresponding population for each available year, stratified by age group and sex. Age-standardised mortality rates (ASRs) were calculated using the New WHO World Standard Population Distribution.⁴⁵ Mortality rates per 100,000 population are presented in this study.

This study used locally weighted regression (LOESS), a nonparametric regression procedure,⁴⁶ weighted by the individual population of countries, to produce a smoothed curve of long-term international and regional mortality rates and estimate mortality rates with 95% CIs based on available data from all included countries, similar to previous studies.^{42,47} Furthermore, sensitivity analysis was conducted by limiting the analyses to countries with varying thresholds of data quality (i.e., data usability). Geographic regions were classified according to WHO criteria.⁴⁸

Joinpoint regression analysis was applied to analyse mortality trends for individual countries.⁴⁰ To evaluate trends from the last decade of the 2000–2022 period, I used data available from 2013. Countries with data spanning at least 7 years between 2013 and 2022 met the inclusion criteria for this analysis.⁴⁹ Because the joinpoint regression analysis of age-standardised rates could not be processed if there was a zero value in any year, the analysis for those countries was not performed. A log-linear model (i.e., $\ln(\text{mortality rate}) = b_0 \times y + b_1$ where $y = \text{calendar year}$) was chosen. The Weighted Bayesian Information Criterion was chosen to identify the optimal number of joinpoints-specific years when shifts in the log-linear mortality trends occurred. The annual percent change for each segment, AAPC for the entire period, and their 95% CIs were computed. AAPCs were significantly different from

zero at the 0.05 level. Mortality rates were classified as significantly increasing or decreasing at $p < 0.05$ or stable at $p \geq 0.05$.

Data processing and aggregation were performed using Microsoft Access software from Microsoft 365 (office) (Microsoft Corporation, Redmond, WA, USA). Statistical analyses were performed using the Joinpoint Regression Program (version 5.1.0.0, April 2024; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute) and R software (version 4.3.1, R Foundation for Statistical Computing, Vienna, Austria).

2.3. Ethics considerations

The Institutional Review Board of Okayama University Hospital waived the requirement for an ethics review because this study used publicly available data that did not contain any personally identifiable information.

III. RESULTS

3.1. Burden of depressive disorders in Vietnam

This chapter is based on the previously published article.¹

3.1.1. Prevalence of depressive disorders

As shown in Table 2, depressive disorders comprised approximately 2629.1 thousand (95% UI: 2233.3–3155.9) estimated cases in Vietnam in 2019. The number of dysthymia cases was higher than that of major depressive disorder cases (1537.4 thousand [95% UI: 1175.8–2024.0] vs 1131.8 thousand [95% UI: 954.3–1336.2]). In 2019, the crude prevalence rate of depressive disorders was 2728.0 cases per 100,000 population (95% UI: 2317.3–3274.6). Major depressive disorder and dysthymia were more prevalent in females than in males.

Table 2. Prevalence (number of cases) and crude prevalence rates by sex of depressive disorders in Vietnam in 2019

	Prevalence, in thousands (95% UI)	Prevalence rate per 100,000 population (95% UI)
Depressive disorders		
Total	2629.1 (2233.3 to 3155.9)	2728.0 (2317.3 to 3274.6)
Females	1663.4 (1410.5 to 1979.2)	3421.0 (2900.8 to 4070.3)
Males	965.7 (812.5 to 1170.7)	2022.4 (1701.7 to 2451.8)
Major depressive disorder		
Total	1131.8 (954.3 to 1336.2)	1174.4 (990.2 to 1386.5)
Females	752.4 (634.4 to 894.1)	1547.3 (1304.6 to 1838.8)
Males	379.5 (314.5 to 449.3)	794.7 (658.7 to 941.0)
Dysthymia		
Total	1537.4 (1175.8 to 2024.0)	1595.2 (1220.0 to 2100.2)
Females	940.6 (714.1 to 1246.9)	1934.5 (1468.6 to 2564.3)
Males	596.8 (455.2 to 790.7)	1249.8 (953.4 to 1655.9)

UI, uncertainty interval; Adapted from the previously published article.¹

Figure 1 indicates that in 2019, the people aged ≥ 15 years had higher prevalence rates of depressive disorders than did people aged < 15 years. The 60–64-year age group had the highest rate with approximately 4791.1 (95% UI: 3537.0–6173.0) cases per 100,000 population.

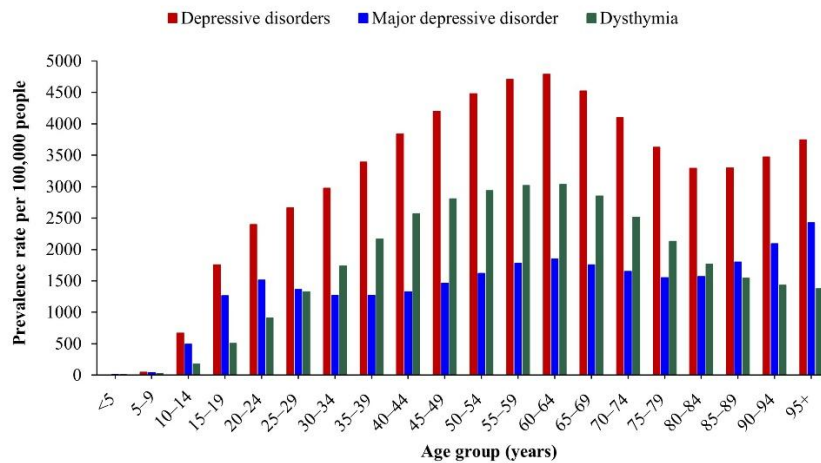


Fig. 1. Prevalence rates of depressive disorders by age group in Vietnam in 2019

Adapted from the previously published article.¹

3.1.2. DALYs of depressive disorders

Depressive disorders in Vietnam in 2019 accounted for approximately 380.6 thousand (95% UI: 258.9–533.8) estimated DALYs, representing approximately 1.5% of the total DALYs from all causes, in which major depressive disorder and dysthymia contributed 231.5 thousand (95% UI: 155.1–323.5) and 149.0 thousand (95% UI: 93.2–227.4) estimated DALYs, respectively (Supplementary Table 1). The DALY rates of depressive disorders were higher in people aged ≥ 15 years than in those aged < 15 years (Figure 2). In 2019, the 60–64-year age group had the highest DALY rate compared with the other age groups (approximately 651.0 [95% UI: 420.4–958.8] DALYs per 100,000 population).

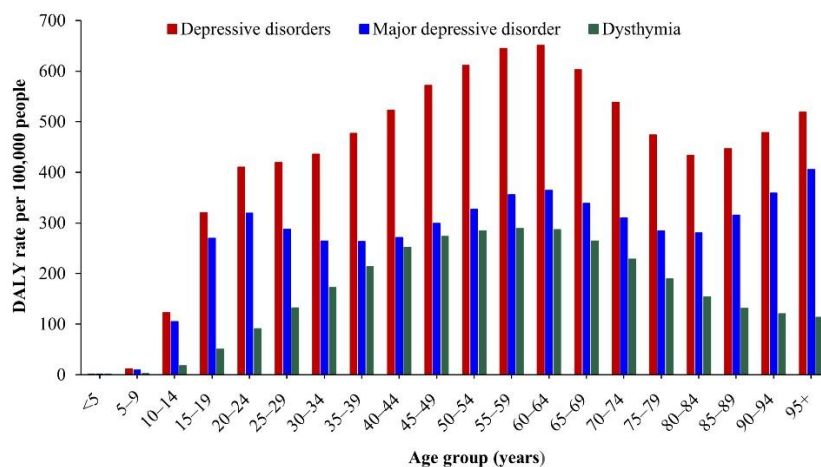


Fig. 2. DALY rates of depressive disorders by age group in Vietnam in 2019

DALY, disability-adjusted life year; Adapted from the previously published article.¹

Figure 3 presents the percentage of DALYs for depressive disorders to the total DALYs from all causes in different age groups in 2019. People aged 10–64 years had higher percentages of the total DALYs than those in other age groups. Depressive disorders accounted for the highest percentage of the total DALYs in the 15–29-year age group (approximately 3.0%). For major depressive disorder, the highest percentage of the total DALYs was in the 15–19-year age group (approximately 2.5%), whereas the percentage for dysthymia was the highest in the 35–39-year age group (approximately 1.2%).

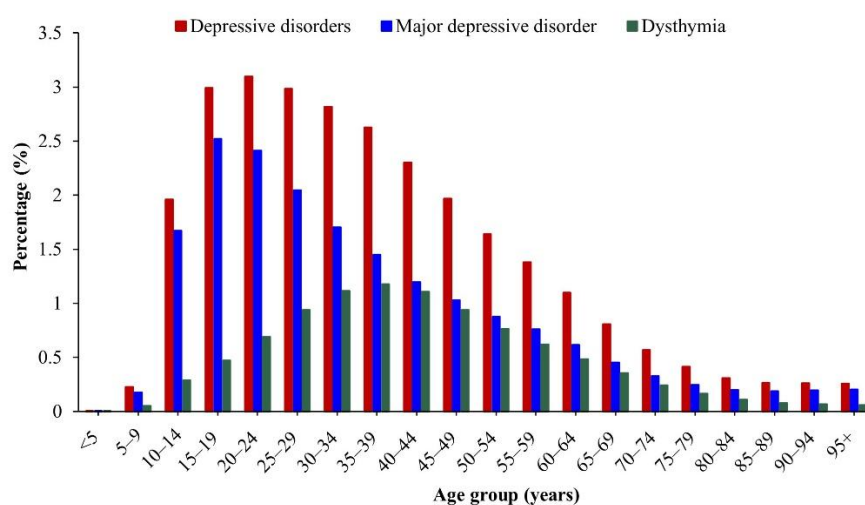


Fig. 3. Percentage of DALYs due to depressive disorders to total DALYs due to all causes by age group in Vietnam in 2019

DALY, disability-adjusted life year; Adapted from the previously published article.¹

3.1.3. Trends from 1990 to 2019

Regarding rates per 100,000 population, the crude prevalence rates of depressive disorders increased by 28.96% (95% UI: 19.92–38.71) from 2115.4 to 2728.0 during the 1990–2019 period. The crude DALY rates of depressive disorders showed a similar trend with a 21.47% (95% UI: 12.04–32.52) increase (from 325.1 to 394.9) during the same period. The increases in crude prevalence and DALY rates of depressive disorders were significant, and the respective AAPCs were 0.88% (95% CI: 0.87 to 0.89) and 0.68% (95% CI: 0.66 to 0.70) (Table 3 and Supplementary Figure 1). The results for major depressive disorder and dysthymia were in line with those observed for depressive disorders. However, after removing the effects of

different age distributions, the age-standardised prevalence and DALY rates of depressive disorders, major depressive disorder, and dysthymia decreased significantly over 30 years. Age-standardised prevalence and DALY rates of depressive disorders decreased with AAPCs: -0.20 (95% CI: -0.21 to -0.19), and -0.27% (95% CI: -0.28 to -0.25), respectively.

Table 3 Prevalence and DALY rates due to depressive disorders and their change in trends in Vietnam from 1990 to 2019

	1990	2019	Change in rate (%) (95% UI) (1990–2019)	AAPC (%) (95% CI) (1990–2019)
	Rate per 100,000 population (95% UI)			
Crude				
Depressive disorders				
Prevalence	2115.4 (1811.9 to 2481.3)	2728.0 (2317.3 to 3274.6)	28.96 (19.92 to 38.71)	0.88* (0.87 to 0.89)
DALYs	325.1 (219.3 to 453.7)	394.9 (268.6 to 553.9)	21.47 (12.04 to 32.52)	0.68* (0.66 to 0.70)
Major depressive disorder				
Prevalence	1069.3 (894.8 to 1283.9)	1174.4 (990.2 to 1386.5)	9.83 (0.51 to 21.72)	0.32* (0.30 to 0.34)
DALYs	220.4 (143.6 to 314.7)	240.2 (161.0 to 335.6)	8.99 (-1.37 to 22.23)	0.30* (0.27 to 0.33)
Dysthymia				
Prevalence	1078.5 (832.4 to 1416.5)	1595.2 (1220.0 to 2100.2)	47.92 (37.82 to 57.35)	1.36* (1.35 to 1.38)
DALYs	104.7 (64.7 to 159.6)	154.6 (96.7 to 236.0)	47.75 (35.7 to 57.82)	1.36* (1.33 to 1.38)
Age-standardised				
Depressive disorders				
Prevalence	2624.3 (2251.3 to 3088.8)	2473.1 (2117.6 to 2938.3)	-5.76 (-9.26 to -2.18)	-0.20* (-0.21 to -0.19)
DALYs	389.7 (265.0 to 544.6)	360.2 (244.4 to 502.9)	-7.56 (-12.21 to -2.52)	-0.27* (-0.28 to -0.25)
Major depressive disorder				
Prevalence	1233.6 (1046.8 to 1459.7)	1093.1 (930.4 to 1289.9)	-11.39 (-16.81 to -4.71)	-0.41* (-0.43 to -0.39)
DALYs	251.6 (168.1 to 352.3)	223.2 (150.6 to 312.3)	-11.28 (-17.73 to - 3.61)	-0.41* (-0.44 to -0.38)
Dysthymia				
Prevalence	1432.0 (1102.4 to 1872.3)	1417.7 (1091.9 to 1853.1)	-1.0 (-1.33 to -0.72)	-0.03* (-0.04 to -0.03)

	1990	2019	Change in rate (%) (95% UI) (1990–2019)	AAPC (%) (95% CI) (1990–2019)
	Rate per 100,000 population (95% UI)			
DALYs	138.1 (86.1 to 209.7)	137.1 (85.2 to 208.7)	-0.78 (-4.24 to 2.52)	-0.02* (-0.03 to -0.02)

*DALY, disability-adjusted life years; UI, uncertainty interval; AAPC, average annual percent change; CI, certainty interval; *, statistically significant with $p < 0.05$*

Adapted from the previously published article.¹

3.2. Mortality of biliary tract cancers

This chapter is based on the previously published article.²

3.2.1. Mortality rates due to BTCs by country, 2000–2022

A total of 83 countries were included in this study (Supplementary Table 2). From 2000 to 2022, the reported number of BTC-related deaths was 1,767,004. Among these, females accounted for 960,532 deaths (Table 4). Notably, 77.3% of BTC-related deaths occurred in patients aged ≥ 65 years. The predominant causes of BTC-related death were iCCA (30.9%) and GBC (29.3%), followed by eCCA (21.0%).

Table 4. Characteristics of mortality due to biliary tract cancers and their subtypes from 2000 to 2022 in 83 countries

	Males (N=806,472)	Females (N=960,532)	Total (N=1,767,004)
Age at death (years)			
<20	177 (0)	177 (0)	354 (0)
20–64	199,498 (24.7)	201,944 (21.0)	401,442 (22.7)
≥ 65	606,797 (75.2)	758,411 (79.0)	1,365,208 (77.3)
Biliary tract cancers			
Intrahepatic cholangiocarcinoma (C22.1)	284,619 (35.3)	262,209 (27.3)	546,828 (30.9)
Gallbladder cancer (C23)	169,980 (21.1)	348,180 (36.2)	518,160 (29.3)
Extrahepatic cholangiocarcinoma (C24.0)	196,162 (24.3)	174,408 (18.2)	370,570 (21.0)
Ampullary cancer (C24.1)	44,583 (5.5)	40,811 (4.2)	85,394 (4.8)
Overlapping lesion of the biliary tract (C24.8)	4,771 (0.6)	6,571 (0.7)	11,342 (0.6)
Unspecified biliary tract (C24.9)	86,670 (10.7)	114,022 (11.9)	200,692 (11.4)
Other and unspecified parts of the biliary tract (C24)	19,687 (2.4)	14,331 (1.5)	34,018 (1.9)

Data are presented as numbers (percent); Adapted from the previously published article.²

Among the countries, Chile, the Republic of Korea, and Japan had the highest ASRs due to BTCs in most years of the 2000–2022 period. ASRs in 2021 for the Republic of Korea, Chile, and Japan were 7.1, 5.9, and 4.3, respectively (Supplementary Table 3). Regarding cancer subtypes, Chile had the highest ASRs due to GBC among the 83 countries during the observation period (Supplementary Table 4). The Republic of Korea showed higher ASRs due to iCCA in most years of the 2000–2022 period, while other countries, such as Guyana (ASR 5.0 in 2009) and Mongolia (ASR 3.9 in 2018), reported higher ASRs for some years (Supplementary Table 5). Japan, Thailand, and the Republic of Korea showed the highest ASRs due to eCCA (Supplementary Table 6) during the observation period.

3.2.2. International and regional trends in mortality rates due to BTCs, 2000–2022

Figure 4 and Supplementary Figure 2 show the ASRs and crude mortality rates due to BTCs in 83 countries from 2000 to 2022. Internationally, the LOESS-smoothed crude mortality rates continuously increased from 3.8 (95% CI: 3.1–4.5) in 2000 to 5.8 (95% CI: 4.8–6.8) in 2022 (Supplementary Figure 2 and Supplementary Table 7). The LOESS-smoothed ASR due to BTCs was 2.8 (95% CI: 2.5–3.1) in 2000, reached the lowest rate in 2015 (2.5 [95% CI: 2.3–2.7]), and increased to 2.7 (95% CI: 2.3–3.1) in 2022 (Figure 4 and Supplementary Table 7). Overall, the LOESS-smoothed ASRs slightly changed between 2000 and 2022. Sensitivity analysis revealed that LOESS-smoothed ASRs derived from the redefined datasets, which applied varying data quality thresholds, demonstrated trends comparable to those observed in the primary analysis (Supplementary Figure 3).

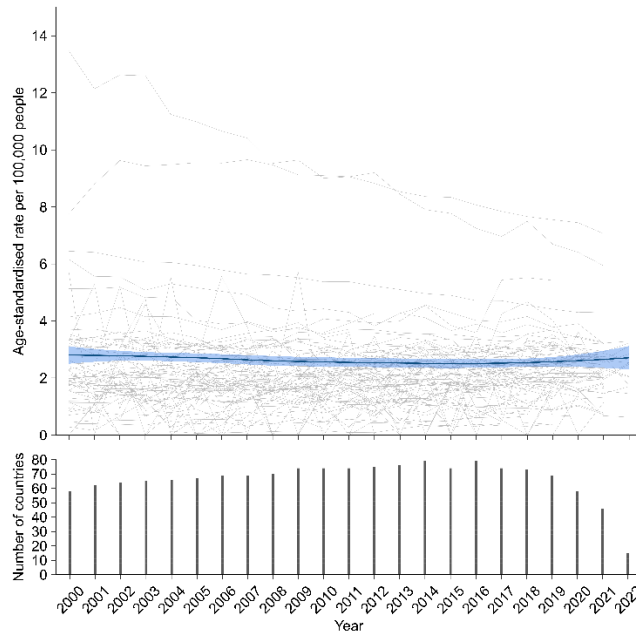


Fig. 4. Trends in age-standardised mortality rates due to biliary tract cancers for both sexes combined in 83 countries from 2000 to 2022

The locally weighted regression rates (blue line) with 95% confidence intervals (light blue shadow), weighted by country population size, are provided.

Adapted from the previously published article.²

Trends in ASRs due to BTCs by sex are illustrated in Figure 5. The LOESS-smoothed ASR for males in 2022 was 2.9 (95% CI: 2.4–3.4), while that for females was 2.5 (95% CI: 2.2–2.9) (Supplementary Table 7). The LOESS-smoothed ASRs due to BTC among males and females showed slight changes between 2000 and 2022.

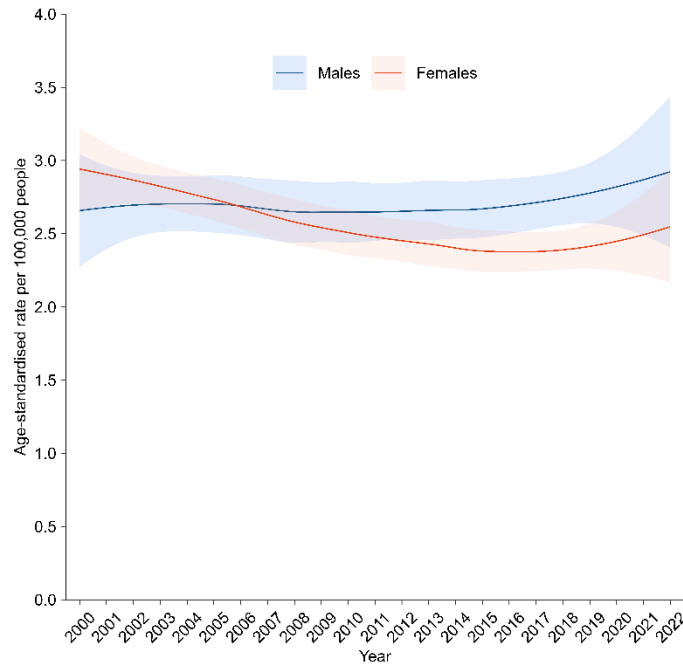


Fig. 5. Trends in age-standardised mortality rates due to biliary tract cancers for males and females in 83 countries from 2000 to 2022

The locally weighted regression rates for males (blue line) and females (red line) with 95% confidence intervals (light blue and light red shadow, respectively), weighted by country population size, are provided.

Adapted from the previously published article.²

A total of 42, 27, and eight of 83 countries in the European, American, and Western Pacific regions, respectively, were included in this study. Since only a few countries in the Southeast Asian, African, and Eastern Mediterranean regions were included, the LOESS analysis for these regions was not performed. Among the regions, the Western Pacific region had the highest LOESS-smoothed ASRs due to BTCs for the entire period (Table 5). In 2022, the LOESS-smoothed ASRs in the Western Pacific regions were 4.2 (95% CI: 1.8–6.6), which was higher than the 2.6 (95% CI: 2.3–2.9) in the European region and 2.2 (95% CI: 1.8–2.6) in the American region. Between 2000 and 2022, the LOESS-smoothed ASRs in the Western Pacific, American, and European regions showed slight changes.

Table 5. Locally weighted regression-smoothed age-standardised mortality rates due to biliary tract cancers for both sexes combined stratified by geographic region from 2000 to 2022

Year	American region	European region	Western Pacific region
2000	2.4 (2.0–2.7)	2.6 (2.4–2.8)	4.8 (3.2–6.4)
2001	2.4 (2.1–2.6)	2.6 (2.4–2.7)	4.9 (3.6–6.1)
2002	2.3 (2.1–2.5)	2.5 (2.4–2.7)	4.9 (4.0–5.9)
2003	2.3 (2.1–2.5)	2.5 (2.4–2.6)	4.9 (4.1–5.8)
2004	2.3 (2.1–2.5)	2.5 (2.4–2.6)	4.9 (4.1–5.8)
2005	2.2 (2.1–2.4)	2.5 (2.4–2.6)	4.9 (4.0–5.8)
2006	2.2 (2.0–2.4)	2.4 (2.3–2.6)	4.8 (3.9–5.7)
2007	2.2 (2.0–2.4)	2.4 (2.3–2.5)	4.7 (3.8–5.6)
2008	2.2 (2.0–2.4)	2.4 (2.3–2.5)	4.5 (3.6–5.5)
2009	2.2 (2.0–2.4)	2.4 (2.3–2.5)	4.4 (3.4–5.4)
2010	2.2 (2.0–2.3)	2.4 (2.3–2.5)	4.4 (3.5–5.4)
2011	2.2 (2.0–2.4)	2.4 (2.2–2.5)	4.5 (3.6–5.5)
2012	2.2 (2.0–2.4)	2.3 (2.2–2.5)	4.6 (3.6–5.6)
2013	2.2 (2.0–2.4)	2.4 (2.3–2.5)	4.5 (3.5–5.5)
2014	2.2 (2.0–2.4)	2.4 (2.3–2.5)	4.4 (3.4–5.5)
2015	2.2 (2.0–2.4)	2.4 (2.3–2.5)	4.2 (3.3–5.2)
2016	2.2 (2.0–2.4)	2.4 (2.3–2.5)	4.1 (3.1–5.0)
2017	2.2 (2.1–2.4)	2.4 (2.3–2.5)	4.0 (3.1–4.9)
2018	2.2 (2.1–2.4)	2.4 (2.3–2.5)	3.9 (3.1–4.8)
2019	2.2 (2.0–2.4)	2.4 (2.3–2.6)	3.9 (3.0–4.9)
2020	2.2 (2.0–2.5)	2.5 (2.3–2.6)	4.0 (2.7–5.2)
2021	2.2 (1.9–2.5)	2.5 (2.3–2.7)	4.1 (2.3–5.8)
2022	2.2 (1.8–2.6)	2.6 (2.3–2.9)	4.2 (1.8–6.6)

Data are presented as locally weighted regression rates per 100,000 population with 95% confidence intervals

Adapted from the previously published article.²

The LOESS-smoothed ASRs due to BTC subtypes during the 2000–2022 period are shown in Figure 6 and Supplementary Table 8. From 2000 to 2022, the LOESS-smoothed ASRs due to GBC for both sexes combined showed a continuous decrease from 1.1 (95% CI: 1.0–1.3) to 0.6 (95% CI: 0.4–0.8), representing a decrease

of 45.5%. The LOESS-smoothed ASR due to eCCA was 0.5 (95% CI: 0.3–0.6) in 2022 and remained stable since 2000, with a LOESS-smoothed ASR of 0.5 (95% CI: 0.4–0.7). Conversely, those due to iCCA showed a large increase at higher rates than those due to eCCA, from 0.5 (95% CI: 0.4–0.6) to 1.1 (95% CI: 1.0–1.3) (an increase of 120.0%). The same patterns were observed in both males and females. Furthermore, the LOESS-smoothed ASRs due to iCCA and eCCA among males were higher than those among females. Meanwhile, the LOESS-smoothed ASRs due to GBC were higher in females than in males.

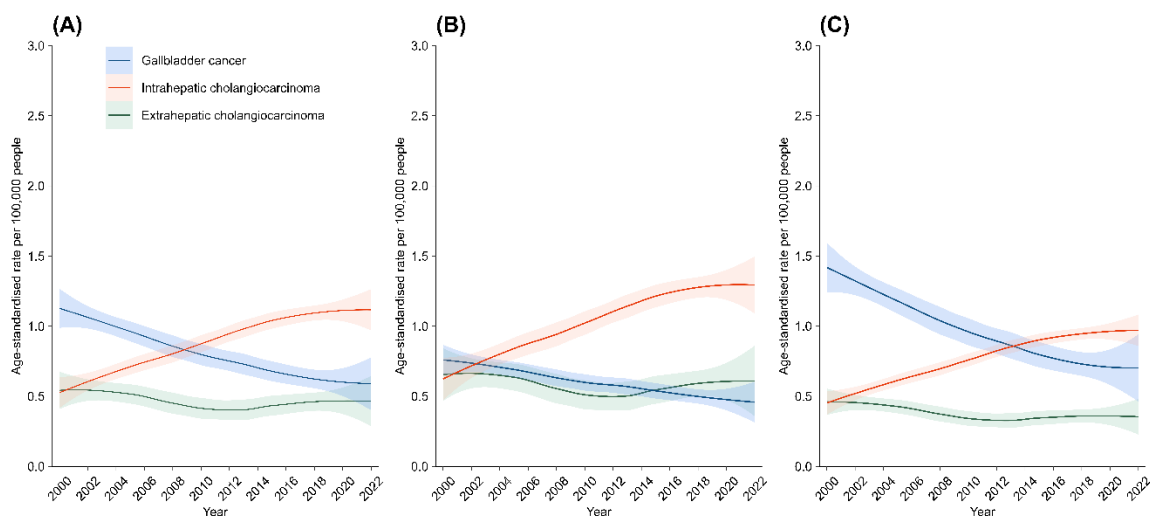


Fig. 6. Trends in age-standardised mortality rates due to gallbladder cancer, intrahepatic cholangiocarcinoma, and extrahepatic cholangiocarcinoma by sex from 2000 to 2022

The locally weighted regression rates (line) with 95% confidence intervals (shadow) for (A) both sexes combined, (B) males, and (C) females, weighted by country population size, are provided.

Adapted from the previously published article.²

3.2.3. National trends in mortality rates due to BTCs, 2013–2022

Figure 7 (A–D) and Supplementary Tables 9–12 show the AAPCs in ASRs due to BTCs and their major subtypes for males and females according to country during the last decade (2013–2022). For BTCs, most countries exhibited stability in ASRs for both males and females. The highest increases in ASRs were observed in Malta (AAPC: 16.4% [95% CI: 6.4 to 35.4]) among males and in Iceland (AAPC:

14.3% [95% CI: 3.7 to 31.5]) among females (Figure 7A and Supplementary Table 9). The largest decreases in ASRs were reported in Mauritius (AAPC -12.7% [95% CI: -19.3 to -6.1]) among males and in Cuba (AAPC -6.1% [95% CI: -10.6 to -1.7]) among females.

For GBC, most countries observed significant decreases in ASRs for both males and females during the study period. Lithuania and Greece exhibited the largest decrease in ASRs among males and females, with AAPCs of -16.4% (95% CI: -24.4 to -8.9) and -12.0% (95% CI: -20.3 to -4.3), respectively (Figure 7B and Supplementary Table 10). Georgia and the United Kingdom exhibited the largest increase in ASRs among males and females, with AAPCs of 13.1% (95% CI: 7.3 to 20.7) and 2.2% (95% CI: 0.1 to 4.4), respectively.

For iCCA, many countries reported significant increases in ASRs for both males and females. Nicaragua and Estonia reported the highest increase in ASRs among males and females, with AAPCs of 14.6% (95% CI: 3.1 to 31.3) and 15.5% (95% CI: 2.7 to 37.0), respectively (Figure 7C and Supplementary Table 11). Georgia and Singapore recorded the largest decrease in ASRs among males and females, with AAPCs of -9.0% (95% CI: -15.2 to -1.8) and -8.7% (95% CI: -12.9 to -4.9), respectively.

For eCCA, most countries remained stable in ASRs for both males and females. Georgia and Costa Rica exhibited the largest increase in ASRs among males and females, with AAPCs of 33.9% (95% CI: 19.2 to 64.1) and 28.9% (95% CI: 17.2 to 52.4), respectively (Figure 7D and Supplementary Table 12). Meanwhile, the highest decreases in ASRs were observed in Belgium and Portugal among males and females, with AAPCs of -12.7% (95% CI: -20.3 to -5.6) and -11.2% (95% CI: -20.0 to -1.7), respectively.

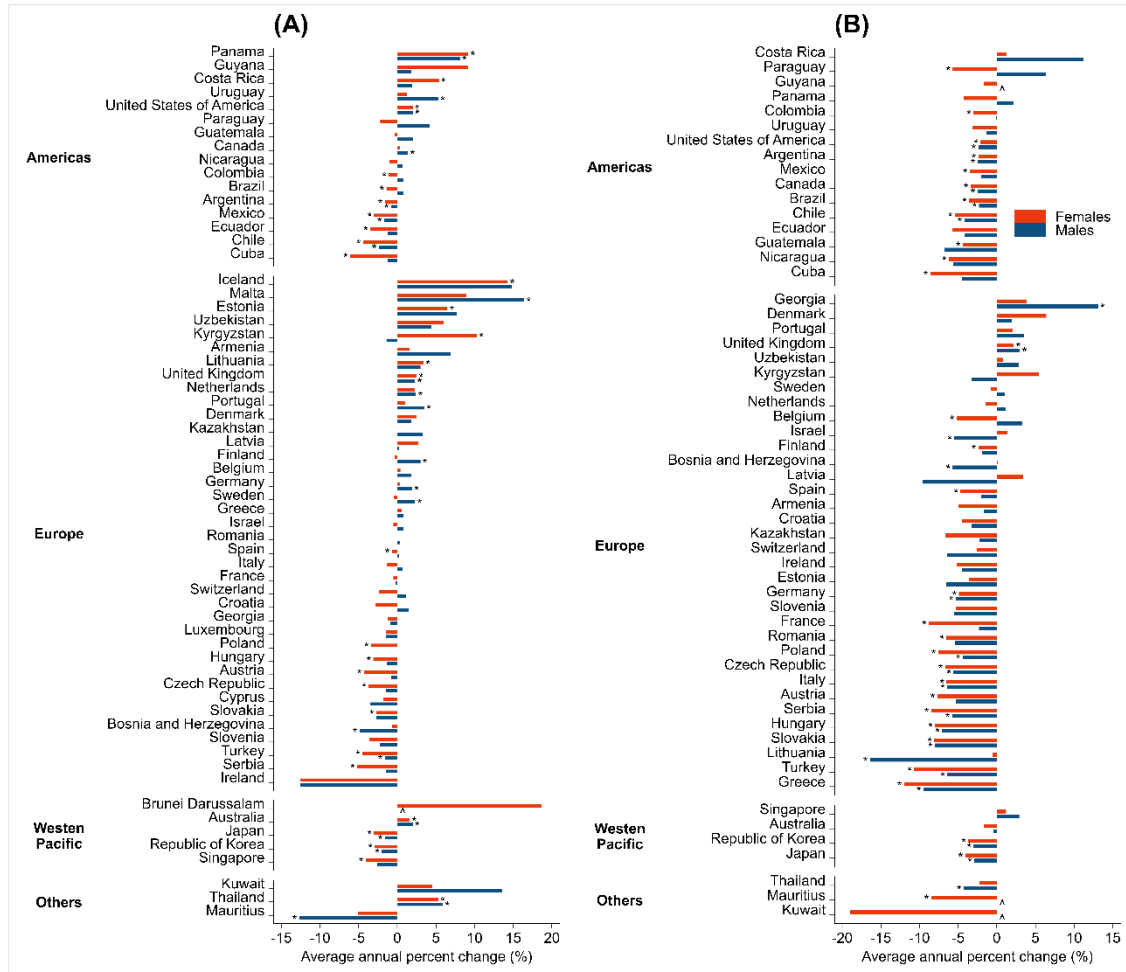


Fig. 7. Average annual percent change in age-standardised mortality rates due to (A) biliary tract cancers, (B) gallbladder cancer, (C) intrahepatic cholangiocarcinoma, and (D) extrahepatic cholangiocarcinoma for females and males by country from 2013 to 2022

**, significantly different from zero ($p < 0.05$); ^, non-available.*

Adapted from the previously published article.²

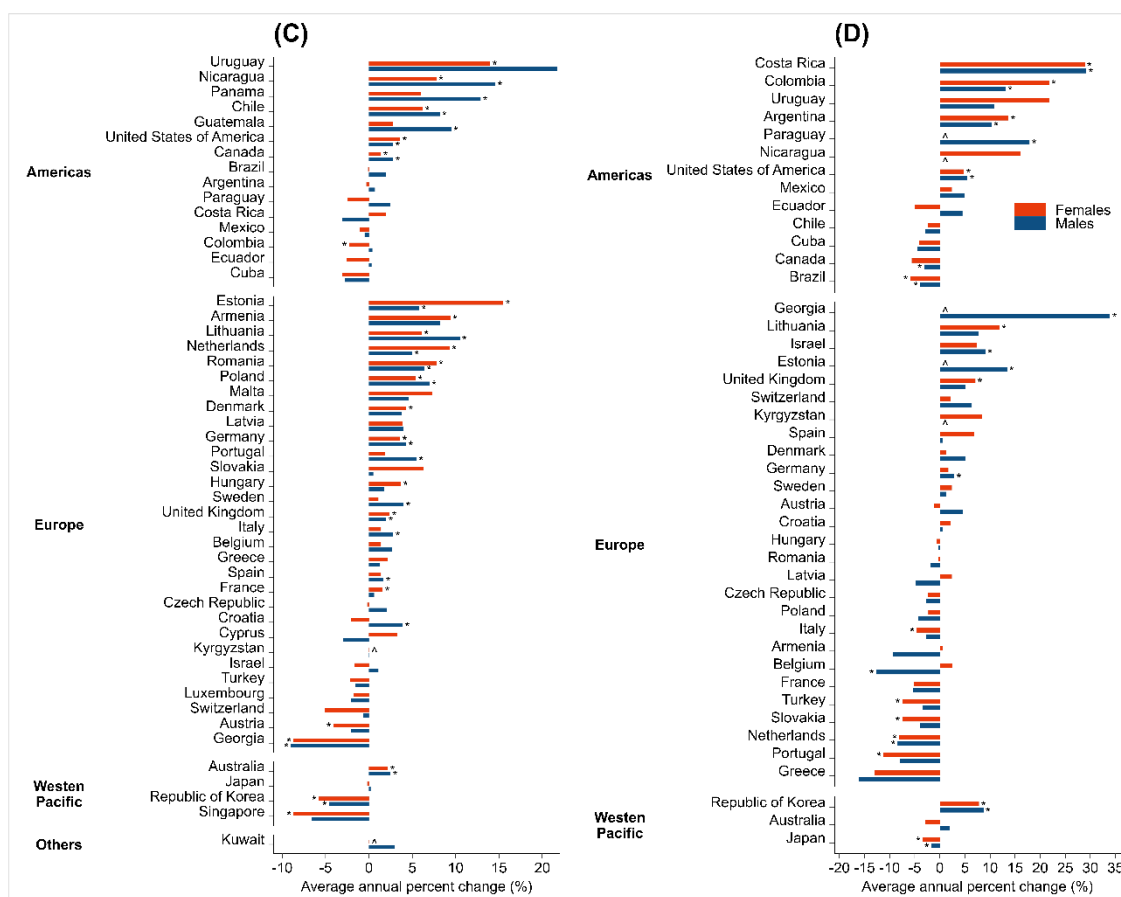


Fig. 7 (continue). Average annual percent change in age-standardised mortality rates due to (A) biliary tract cancers, (B) gallbladder cancer, (C) intrahepatic cholangiocarcinoma, and (D) extrahepatic cholangiocarcinoma for females and males by country from 2013 to 2022

**, significantly different from zero ($p < 0.05$); ^, non-available.*

Adapted from the previously published article.²

IV. DISCUSSION

4.1. Burden of depressive disorders

This chapter is based on the previously published article.¹

I conducted a detailed and comprehensive analysis of the depressive disorder-related prevalence, and DALYs in Vietnam from 1990 to 2019 by sex and age using the GBD study 2019 dataset. The findings can help the Vietnamese government or policymakers to locate priority areas and individuals for intervention to reduce the burden of these disorders.

The number of depressive disorder cases in Vietnam in 2019 was estimated to be considerably high, at approximately 2629.1 thousand, comprising approximately 2.7% of the total population (Vietnam's population in 2019 was 96.2 million),⁵⁰ higher than that reported in 2014.¹⁷ In 2019, depressive disorder cases in Vietnam accounted for approximately 0.9% of all global cases and approximately 14.2% of all Southeast Asian cases.⁷ The age-standardised prevalence rate per 100,000 population in Vietnam (2473.1) was lower than that seen globally (3440.1) and in high-income countries (3659.9), and it was almost in line with that observed in Southeast Asia (2610.6) in 2019.⁷ The age-standardised prevalence rates were lower in low- and middle-income countries than in developed countries, possibly due to the lack of relevant epidemiological data used for the GBD 2019 in these countries.⁷ These findings also showed an increasing trend in the crude prevalence rates of depressive disorders between 1990 and 2019. Despite limitations in the national epidemiological study on depressive disorders in Vietnam, recent published studies showed that rates of depressive symptoms or depression in specific population groups were more than 30%.^{18–21} These findings thus suggest that the prevalence of depressive disorders in Vietnam is considerable.

The results showed that women were more prone to depressive disorders than were men, in line with previous findings.^{51–53} Biological factors such as genetic factors and sex hormone level changes during puberty, may explain the disparity between sexes in depressive disorders. Sex-related discrimination, childhood sexual abuse, and sex-related violence may increase the risk of depressive disorders.⁵⁴

Moreover, postnatal mothers are at a higher risk of postnatal depression (14.0% pooled prevalence globally, 15.0% in developing countries, and 12.0% in developed countries).⁵⁵ In Vietnam, the postnatal depression prevalence was 8.2–37.1% in the first 3 to 6 months after childbirth.⁵⁶ Depressive disorders not only affect mothers' health but also cause adverse infant health outcomes;⁵⁷ thus, early screening and appropriate treatment are essential to improve mother and infant health.

The prevalence rate of depressive disorders in Vietnam in 2019 rose considerably after 15 years of age, which is in line with the global trend,⁹ although the median age at onset for depressive disorders was 30 (21–44).⁵⁸ Globally, the point prevalence rates of major depressive disorder and dysthymia among adolescents (aged 10–19 years) were 8% and 4%, respectively, and adolescents from Middle Eastern, African, and Asian countries were at a higher risk of depressive disorders.⁵⁹ In the USA, the prevalence of major depressive disorders increased more rapidly among young people (aged 12–17 years) than among older people from 2005 to 2015.⁵³ At present, mental health and psychosocial problems are increasing among Vietnamese children and young people.⁶⁰ In particular, Vietnamese students with depressive symptoms have a 6.64-times higher risk of suicidal ideation than those without depressive symptoms.¹⁸ Bullying, smoking and alcohol consumption, and adverse childhood experiences were among the risk factors for depressive symptoms in secondary and high-school students in Vietnam.^{18,61} Given the considerable burden of depressive disorders, the results showed a higher rate of DALYs in people aged ≥ 15 years than in those aged < 15 years. This situation demands public awareness of depressive disorders among Vietnamese children and adolescents.

DALYs owing to depressive disorders accounted for approximately 1.5% of the total DALYs due to all causes in Vietnam in 2019, with major depressive disorder as the main contributor to the burden of depressive disorders (60.8% of DALYs), despite that the prevalence rate of major depressive disorder was lower than that of dysthymia. This result was likely caused by the difference in disability weights for calculating YLDs. Dysthymia is a mood disorder, with less severe but longer-lasting symptoms than those of an episodic mood disorder (i.e., major depressive disorder).

According to the GBD 2019, the disability weight of dysthymia is equivalent to that of mild major depressive disorder.⁴ However, almost all patients with dysthymia experienced a major depressive disorder, and eventually, after recovering, patients could relapse into another period of chronic depression.⁶² I suggest that the diagnosis and treatment of dysthymia are as crucial as those of major depressive disorder.

This study highlighted that in 2019 children (aged 10–14 years) and working-age individuals (aged 15–64 years) had higher percentages of DALYs for depressive disorders to the total all-cause DALYs than those in other age groups. This result emphasised that depressive disorders were responsible for a greater burden of depressive disorders in the 10–64-year age group than in the other age groups. Therefore, raising public awareness of depressive disorders, especially among people aged 10–64 years, is essential, as these disorders affect mental health, physical health, and education and cause loss of productive work time.¹² In addition, it was noted that there were variations in the percentages of the total all-cause DALYs by age group caused by major depressive disorders and dysthymia in Vietnam in 2019. The percentages of the total all-cause DALYs caused by major depressive disorders peaked among young people aged 15–19 years, while that of dysthymia reached the largest among older people aged 35–39 years. These results suggest that chronic depression (i.e., dysthymia) is more likely to influence people's health later in life than episodic mood disorder (i.e., major depressive disorder).

In this study, the crude DALY rate of depressive disorders increased significantly with an AAPC of 0.68% (95% CI: 0.66 to 0.70) from 1990 to 2019. After removing effects of the difference in age structure, the age-standardised DALY rate showed a significant decrease with an AAPC of -0.27% (95% CI: -0.28 to -0.25). The contrasting trends between crude and age-standardised DALY rates suggest that population ageing might contributed to an increase in crude DALY rates in Vietnam, which is in line with previous reports.⁶³ These findings highlight depressive disorders as a growing public health concern in Vietnam, particularly in the context of rapid population ageing. Indeed, Vietnam is facing a rapid increase in its ageing population and is projected to become an aged population by 2036,⁵⁰ indicating the urgent need

for immediate actions to be implemented by the Vietnamese government to prepare for a rapidly ageing society with greater burdens of diseases, including depressive disorders.

Provision of mental health services, such as early diagnosis and appropriate treatment with pharmacological and non-pharmacological interventions, is crucial for care of depressive disorder patients. In Vietnam, the Ministry of Health, and the Ministry of Labor, Invalids and Social Affairs are responsible for providing community-based and hospital-based mental health services. The Vietnamese government has been actively adopting measures to improve the delivery of mental health services into the community, including the National Community Mental Health Care Project in 2000 and a national plan for the prevention and control of non-communicable diseases and mental health disorders for 2022–2025. Nonetheless, delivery of mental health services is facing many challenges, including limitations in coordination between government departments, shortage of human resources, social stigma related to mental illnesses,⁶⁰ and poor mental health literacy.⁶⁴ Mental health care is mainly provided to people with severe mental disorders (e.g., schizophrenia and epilepsy) and pays less attention to common mental disorders (e.g., depressive disorders).^{60,65} Therefore, the Vietnamese government needs to make more efforts to achieve better efficiency in the prevention and treatment of mental disorders and depressive disorders.

To the best of my knowledge, this is the first study using the GBD database to comprehensively analyse the burden of depressive disorders over the last three decades before the coronavirus disease 2019 (COVID-19) outbreak in Vietnam. However, this study has some limitations. First, this was a secondary study using data from the GBD study 2019; therefore, the study limitations were associated with those of the GBD study 2019, such as the majority of primary data for estimating using ICD-10 and DSM-IV limited epidemiological studies using the newest criteria (DSM-V and ICD-11) or other criteria, and uncertainties in the estimated results.^{4,7} Second, a lack of high-quality and up-to-date raw epidemiological data on depressive disorders in Vietnam from 1990 to 2019 caused an increase in the uncertainty

intervals of estimations.^{7,66} Therefore, high-quality epidemiological studies on depressive disorders in Vietnam are required to provide data for the estimation process. Third, this study did not analyse risk factors for depressive disorders in Vietnam. Further studies are needed to identify the risk factors for these disorders to establish strategies for preventing them in the future. Fourth, this study did not include the burden of depressive disorders due to the COVID-19 pandemic, although it is evident that the COVID-19 pandemic led to a considerable increase in the burden of depressive disorders as well as mental health issues globally.⁶⁷

4.2. Mortality of biliary tract cancers

This chapter is based on the previously published article.²

I found that: (1) Internationally, the estimated ASRs (i.e., LOESS-smoothed ASRs) due to BTCs changed slightly between 2000 and 2022, with different trends among their major subtypes; (2) BTCs showed significant variations in mortality rates across countries and regions, with the highest estimated ASRs in the Western Pacific region; (3) ASRs due to iCCA showed increasing trends internationally (2000–2022) and in many countries (2013–2022).

In this study, I found that internationally estimated ASRs due to BTCs slightly changed from 2.8 (95% CI: 2.5–3.1) in 2000 to 2.7 (95% CI: 2.3–3.1) in 2022. However, as their 95% CIs overlapped, the internationally estimated ASRs showed a stable trend during 2000–2022. A previous study using the GBD study 2019 database showed downward trends in ASRs globally during the 1990–2019 period, with an estimated annual percentage change of -0.58%. However, this study did not include iCCA in the analysis and utilized the estimated data with its uncertainty interval.³³ Notably, this study showed that the number of iCCA, eCCA, and GBC-related deaths accounted for 81.2% of total deaths due to BTCs, making those cancer subtypes major contributors to the pattern of BTCs. A disparity in trends in the estimated ASRs among BTC major subtypes was observed, highlighted by a large increase at higher rates in estimated ASRs due to iCCA over the last two decades (an increase of 120.0%). The increasing trend in iCCA-related mortality was consistent with increasing trends in iCCA incidence reported in most countries.⁶⁸ The precise causes

of this recent increase are not fully understood but may relate to established risk factors. Cirrhosis, strongly linked to iCCA (odds ratio [OR]: 15.32),²⁶ has maintained a high prevalence, and the prevalence has risen globally over the past two decades.⁶⁹ Additionally, increases in other risk factors, such as non-alcoholic fatty liver disease (OR: 2.2), alcohol consumption (OR: 3.15), and type 2 diabetes (OR:1.73), have partially contributed to increases in the risk of developing iCCA.^{26,70–72} Unfortunately, most patients with iCCA have no risk factors identified.⁷³ However, as the overall prognosis for iCCA remains relatively poor, prevention and surveillance strategies for at-risk individuals are crucial for early diagnosis with higher curative potential and improved survival.⁷⁴ Annual surveillance using non-invasive radiologic methods, such as magnetic resonance imaging plus magnetic resonance cholangiopancreatography, is suggested for patients with primary sclerosing cholangitis; biannual ultrasound surveillance is recommended for those with cirrhosis or liver flukes.⁷⁴ Depending on local disease incidence and mortality rates, considering a pilot expansion of surveillance to high-risk iCCA populations may be beneficial.

In contrast to the mortality trend due to iCCA, estimated ASRs due to GBC and eCCA showed a declining trend and a stable trend, respectively, between 2000 and 2022. Previous studies reported downward trends in mortality due to GBC and eCCA in most countries.^{34,35,75} Among various risk factors, gallstones (cholelithiasis) showed a strong association with both eCCA and GBC.^{26,27} Therefore, a decline in gallstone prevalence⁷⁶ partially decreased the risk of eCCA and GBC development. A possible explanation for the decreasing trend in GBC-related mortality is the increase in cholecystectomy use for gallbladder diseases, enabling the prevention of GBC development,⁷⁷ or an increase in incidentally detected GBC cases, and improving survival.⁷⁸

The findings indicated considerable variation in BTC-associated ASRs across different countries and regions. The Western Pacific region showed the highest estimated ASRs during the observation period, primarily driven by elevated rates in the Republic of Korea and Japan. Notably, significant discrepancies in ASRs existed

within this region, leading to broader CIs. Chile, the Republic of Korea, and Japan reported the highest ASRs in most years of the 2000–2022 period, likely linked to well-recognised risk factors. In Chile, high BTC-associated ASRs were mainly attributed to GBC, which is related to a high prevalence of gallstones⁷⁹ or aflatoxin exposure.⁸⁰ In the Republic of Korea, high ASRs were largely due to iCCA and eCCA, possibly related to *Clonorchis sinensis* infection, which exhibits higher prevalence in certain areas.⁸¹ Additionally, Thailand reported high eCCA-related ASRs, potentially caused by the high prevalence of *Opisthorchis viverrine* infection.^{82,83} A previous study reported high eCCA-related ASRs in Japan, but the exact reasons have not been fully understood.⁸⁴ Given Japan's hyper-ageing, results should be interpreted cautiously. Furthermore, disparities in ASR trends for BTCs and their major subtypes were noted across nations, with different average annual percent changes during the last decade (2013–2022). These differences potentially reflect the variations in healthcare system conditions, disease management, and healthcare strategies in each nation. For instance, the prevention program called Acceso Universal con Garantías Explicitas in Chile which prioritised cholecystectomy among young patients with gallstones since 2005 might be effective in reducing GBC-related mortality.⁷⁷ In the US, the rise in iCCA incidence rates from 1973 to 2012 might be due to improved disease detection.⁸⁵ The decline in iCCA incidence rates in the Republic of Korea since 2010 could be attributed to a reduced prevalence of risk factors such as *Clonorchis sinensis* infection and hepatitis B.⁸⁶ Notably, while upward, downward, and stable trends in mortality due to iCCA, GBC, and eCCA, respectively, were observed internationally in males, females, and both sexes combined, different trends were reported in certain countries. For instance, Georgia reported significant increases in mortality due to GBC and eCCA but a significant decrease in mortality due to iCCA during 2013–2022. In addition, countries with significant increases in ASRs due to eCCA were mostly located in the European and American regions, where the highest levels of alcohol consumption⁷¹ and a growing prevalence of obesity in the last decade were reported.⁸⁷

To my knowledge, this study is the first to use the updated WHO mortality database for a comprehensive analysis of long-term mortality trends due to BTCs and their subtypes internationally and regionally from 2000 to 2022. I also updated country-specific mortality trends for the 2013–2022 period, enhancing previous research.^{24,34–36} However, the study had few limitations that should be considered while interpreting the results. First, mortality estimates were limited to 83 countries with available data. Furthermore, not all 83 countries had available data for each year of the 2000–2022 period. Importantly, only countries with high- or medium-quality vital registration data were included to improve the robustness of the findings. Secondly, I estimated international and regional mortality rates using the LOESS procedure, weighted by each country's population, which allowed populous countries to have a significant impact on the results (Supplementary Figure 4). China and India, the most populous countries, were excluded from this study due to the lack of data from India and the outdated data from China (up to 2000) in the WHO mortality database. This analysis included countries with smaller populations, such as Saint Kitts and Nevis, and Dominica, which reported low mortality rates and had minimal impact on international or regional estimates. Additionally, data availability and data quality varied across countries and geographic regions. Most of the included countries were from the European and American regions with high data quality, with fewer from the Southeast Asian, African, or Eastern Mediterranean regions, largely due to poor data quality or unavailability for the studied period. Consequently, mortality in these regions may have been underestimated, introducing potential biases in international and regional estimated mortality rates. Third, a risk of misclassification was observed, where the Klatskin tumours were miscoded as iCCA rather than eCCA in different editions of the International Classification of Diseases for Oncology, potentially causing overestimations of iCCA-related mortality and underestimations of eCCA mortality, especially in countries with higher incidences of Klatskin tumour.^{88–90} Furthermore, some countries reported combined iCCA and hepatocellular carcinoma-related mortality under liver cancer (ICD-10 code: C22), complicating separate iCCA-related mortality analyses. Additionally, this study only

extracted BTC-related deaths coded according to the ICD-10 criteria, acknowledging the possible effect of transition from ICD-9 to ICD-10 coding on the accuracy of cause-of-death coding over time. Fourth, this study could not assess the impact of the COVID-19 pandemic on BTC-related mortality, given that cancer patients are especially vulnerable to such crises.⁹¹ Fifth, this analysis faced limitations. I used the LOESS procedure to illustrate international and regional BTC mortality trends, but it cannot compute a slope of change in rates.⁴² Moreover, joinpoint regression analysis was infeasible for countries with zero reported deaths in any observation year; consequently, several countries lacked results for this analysis. For example, Brunei Darussalam did not have an AAPC for BTC-related ASRs in males.

V. CONCLUSION

This chapter is based on the previously published articles.^{1,2}

In this research, two representative non-communicable diseases were selected to examine long-term trends in disease burden using appropriate large-scale health databases across health indicators and geographical levels. Depressive disorders, representing a non-fatal non-communicable disease, were assessed at national level in Vietnam in terms of prevalence and DALYs using data from the GBD study 2019. In contrast, biliary tract cancers, representing a fatal non-communicable disease, were evaluated in terms of mortality at national, regional, and international levels using data from the WHO mortality database. This complementary approach allowed for a comprehensive assessment of long-term trends in disease burden across different disease categories and health measures.

In conclusion, this research achieved its objective of evaluating long-term trends in the burden of two specific non-communicable diseases at national, regional, and international levels by using data from large-scale health databases. Using data from the GBD study 2019, I deeply analysed the burden of depressive disorders in term of prevalence and DALYs in Vietnam from 1990 to 2019, stratified by sex and age. I found that although the age-standardised rates decreased, the crude prevalence and DALY rates of depressive disorders showed increasing trends in Vietnam. These findings highlight the need for more attention to depressive disorders in Vietnam, especially among females and people aged 10–64 years. Accordingly, appropriate and effective interventions and prevention strategies are required to reduce the burden of depressive disorders in Vietnam. Using data from the WHO mortality database, I deeply and comprehensively examined mortality trends due to BTCs and their subtypes at national, regional and international levels from 2000 to 2022. I observed that although internationally estimated ASRs due to BTCs remained stable, a significant increase in ASRs from iCCA necessitates enhanced governmental action. Future research should develop precise screening and early diagnostic tools, especially for high-risk individuals. Overall, the research findings provide valuable scientific evidence on the burden of non-communicable diseases, supporting the

assessment of the impact of existing interventions, as well as the development and implementation of effective and appropriate interventions and prevention strategies by governments and policymakers.

Furthermore, this research demonstrates the potential and value of each database in examining long-term trends in the burden of both non-fatal diseases (e.g., depressive disorders) and fatal diseases (e.g., biliary tract cancers) across national, regional, and global/international levels using various indicators such as prevalence, mortality, and DALYs. However, it is important to recognize that each database has inherent limitations that should be carefully considered in application and interpretation.

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REFERENCES

1. Vu QT, Harada K, Nishimura Y, et al. Burden of depressive disorders in Vietnam from 1990 to 2019: A secondary analysis of the Global Burden of Disease Study 2019. *J Psychiatr Res.* 2024;172:420-426.
2. Vu QT, Nishimura Y, Harada K, et al. International trends in biliary tract cancer-related mortality, 2000–2022: An observational study of the World Health Organization Mortality Database. *Hepatology.* 2025;82(3):626-637.
3. GBD 2021 Diseases and Injuries Collaborators. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet.* 2024;403(10440):2133-2161.
4. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet.* 2020;396(10258):1204-1222.
5. World Health Organization. WHO Mortality Database (the last update 21 February 2024). 2024; <https://www.who.int/data/data-collection-tools/who-mortality-database> (accessed March 1, 2024).
6. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME). 2020; <https://vizhub.healthdata.org/gbd-results/> (accessed 10 April 2023).
7. GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Psychiatry.* 2022;9(2):137-150.
8. Shu J, Jin W. Prioritizing non-communicable diseases in the post-pandemic era based on a comprehensive analysis of the GBD 2019 from 1990 to 2019. *Sci Rep.* 2023;13(1).

9. World Health Organization. World mental health report: Transforming mental health for all. Geneva: World Health Organization. 2022.
10. Christensen MK, Lim CCW, Saha S, et al. The cost of mental disorders: a systematic review. *Epidemiol Psychiatr Sci*. 2020;29:e161.
11. Dong M, Zeng LN, Lu L, et al. Prevalence of suicide attempt in individuals with major depressive disorder: a meta-analysis of observational surveys. *Psychol Med*. 2019;49(10):1691-1704.
12. Herrman H, Patel V, Kieling C, et al. Time for united action on depression: a lancet–world psychiatric association commission. *Lancet*. 2022;399(10328):957-1022.
13. Schramm E, Klein DN, Elsaesser M, Furukawa TA, Domschke K. Review of dysthymia and persistent depressive disorder: history, correlates, and clinical implications. *Lancet Psychiatry*. 2020;7(9):801-812.
14. Mekonen T, Chan GCK, Connor JP, Hides L, Leung J. Estimating the global treatment rates for depression: A systematic review and meta-analysis. *J Affect Disord*. 2021;295:1234-1242.
15. Evans-Lacko S, Aguilar-Gaxiola S, Al-Hamzawi A, et al. Socio-economic variations in the mental health treatment gap for people with anxiety, mood, and substance use disorders: results from the WHO World Mental Health (WMH) surveys. *Psychol Med*. 2018;48(9):1560-1571.
16. The prime minister, Socialist Republic of Vietnam. The national plan for the prevention and control of non-communicable diseases and mental disorders, 2022–2025. 2022.
17. World Health Organization. Mental health in Viet Nam. n.d.; <https://www.who.int/vietnam/health-topics/mental-health> (accessed 25 May 2023).
18. Tran QA, Le VTH, Nguyen THD. Depressive symptoms and suicidal ideation among Vietnamese students aged 13–17: Results from a cross-sectional study throughout four geographical regions of Vietnam. *Health Psychol Open*. 2020;7(2):2055102920973253.

19. Do HN, Nguyen AT, Nguyen HQT, et al. Depressive symptoms, suicidal ideation, and mental health service use of industrial workers: evidence from Vietnam. *Int J Environ Res Public Health*. 2020;17(8).
20. Tran K Van, Esterman A, Saito Y, et al. Factors associated with high rates of depressive symptomatology in older people in Vietnam. *Am. J. Geriatric Psychiatry*. 2022;30(8):892-902.
21. Tran NN, Nguyen VQ, Vo HL, Hoang TPN, Bui VS, Nguyen VT. Depression among patients with type 2 diabetes mellitus: Evidence from the Northeast region of Vietnam. *Diabetes Metab. Syndr*. 2021;15(6):102293.
22. Vogel A, Bridgewater J, Edeline J, et al. Biliary tract cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up; *Annals Oncol*. 2023;34(2):127-140.
23. Nagino M, Hirano S, Yoshitomi H, et al. Clinical practice guidelines for the management of biliary tract cancers 2019: The 3rd English edition. *J Hepatobiliary Pancreat Sci*. 2021;28(1):26-54.
24. Baria K, De Toni EN, Yu B, Jiang Z, Kabadi SM, Malvezzi M. Worldwide incidence and mortality of biliary tract cancer. *Gastro Hep Advances*. 2022;1(4):618-626.
25. Bray F, Laversanne M, Sung H, 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):229-263.
26. Banales JM, Marin JJG, Lamarca A, et al. Cholangiocarcinoma 2020: the next horizon in mechanisms and management. *Nat Rev Gastroenterol Hepatol*. 2020;17(9):557-588.
27. Roa JC, García P, Kapoor VK, Maithel SK, Javle M, Koshiol J. Gallbladder cancer. *Nat Rev Dis Primers*. 2022;8(1):69.
28. Koshiol J, Yu B, Kabadi SM, Baria K, Shroff RT. Epidemiologic patterns of biliary tract cancer in the United States: 2001–2015. *BMC Cancer*. 2022;22(1):1178.
29. Minicozzi P, Casseti T, Vener C, Sant M. Analysis of incidence, mortality and survival for pancreatic and biliary tract cancers across Europe, with assessment of

influence of revised European age standardisation on estimates. *Cancer Epidemiol.* 2018;55:52-60.

30. Kang MJ, Lim J, Han SS, et al. Distinct prognosis of biliary tract cancer according to tumor location, stage, and treatment: a population-based study. *Sci Rep.* 2022;12(1):10206.

31. Brindley PJ, Bachini M, Ilyas SI, et al. Cholangiocarcinoma. *Nat Rev Dis Primers.* 2021;7(1):65.

32. McGee EE, Jackson SS, Petrick JL, et al. Smoking, alcohol, and biliary tract cancer risk: a pooling project of 26 prospective studies. *J Natl Cancer Inst.* 2019;111(12):1263-1278.

33. Su J, Liang Y, He X. Global, regional, and national burden and trends analysis of gallbladder and biliary tract cancer from 1990 to 2019 and predictions to 2030: a systematic analysis for the Global Burden of Disease Study 2019. *Front Med (Lausanne).* 2024;11.

34. Huang J, Patel HK, Boakye D, et al. Worldwide distribution, associated factors, and trends of gallbladder cancer: A global country-level analysis. *Cancer Lett.* 2021;521:238-251.

35. Bertuccio P, Malvezzi M, Carioli G, et al. Global trends in mortality from intrahepatic and extrahepatic cholangiocarcinoma. *J Hepatol.* 2019;71(1):104-114.

36. Torre LA, Siegel RL, Islami F, Bray F, Jemal A. Worldwide Burden of and Trends in Mortality From Gallbladder and Other Biliary Tract Cancers. *Clin Gastroenterol Hepatol.* 2018;16(3):427-437.

37. American psychiatric association. Diagnostic and statistical manual of mental disorders-fourth edition-text revision (DSM-IV-TR). Washington (D.C.): American Psychiatric Association. 2000.

38. World Health Organization. International statistical classification of diseases and related health problems 10th revision. 2019; <https://icd.who.int/browse10/2019/en> (accessed May 3, 2023).

39. Statistical Research and Applications Branch, National Cancer Institute. Joinpoint Regression Program (Version 5.0.2 May 2023).

40. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med*. 2000;19(3):335-351 (correction: 2001;20:655).
41. Benchimol EI, Smeeth L, Guttman A, et al. The reporting of studies conducted using observational routinely-collected health data (RECORD) statement. *PLoS Med*. 2015;12(10):e1001885.
42. Ebmeier S, Thayabaran D, Braithwaite I, Bénamara C, Weatherall M, Beasley R. Trends in international asthma mortality: analysis of data from the WHO Mortality Database from 46 countries (1993–2012). *Lancet*. 2017;390(10098):935-945.
43. World Health Organization. Data quality. n.d.; <https://platform.who.int/mortality/about/data-quality> (accessed March 5, 2024).
44. United Nations, Department of Economic and Social Affairs, Population Division. World Population Prospects 2022. 2022. <https://population.un.org/wpp/Download/Standard/CSV/> (accessed March 5, 2024).
45. Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJL, Lozano R, Inoue M. Age standardization of rates: a new WHO standard. Geneva: World Health Organization. 2001;9(10):1-14.
46. Cleveland WS, Devlin SJ. Locally Weighted Regression: An approach to regression analysis by local fitting. *J Am Stat Assoc*. 1988;83(403):596-610.
47. Barco S, Mahmoudpour SH, Valerio L, et al. Trends in mortality related to pulmonary embolism in the European Region, 2000-2015: analysis of vital registration data from the WHO Mortality Database. *Lancet Respir Med*. 2020;8(3):277-287.
48. World Health Organization. World Health Statistics 2023: Monitoring health for the SDGs, sustainable development goals. Geneva: World Health Organization; 2023:119.
49. National Cancer Institute, Surveillance Research Program. Number of Joinpoints. n.d.; <https://surveillance.cancer.gov/help/joinpoint/setting->

parameters/method-and-parameters-tab/number-of-joinpoints (accessed April 8, 2024).

50. General Statistics Office. Viet Nam population projection for the period 2019-2069. Hanoi. 2020.
51. Lu J, Xu X, Huang Y, et al. Prevalence of depressive disorders and treatment in China: a cross-sectional epidemiological study. *Lancet Psychiatry*. 2021;8(11):981-990.
52. Li S, Xu Y, Zheng L, et al. Sex difference in global burden of major depressive disorder: findings from the Global Burden of Disease Study 2019. *Front. Psychiatry*. 2022;13.
53. Weinberger AH, Gbedemah M, Martinez AM, Nash D, Galea S, Goodwin RD. Trends in depression prevalence in the USA from 2005 to 2015: widening disparities in vulnerable groups. *Psychol Med*. 2018;48(8):1308-1315.
54. Kuehner C. Why is depression more common among women than among men? *Lancet Psychiatry*. 2017;4(2):146-158.
55. Liu X, Wang S, Wang G. Prevalence and risk factors of postpartum depression in women: a systematic review and meta-analysis. *J Clin Nurs*. 2022;31(19-20):2665-267.
56. Nguyen HTT, Hoang AP, Do LTK, Schiffer S, Nguyen HTH. The rate and risk factors of postpartum depression in Vietnam from 2010 to 2020: a literature review. *Front Psychol*. 2021;12.
57. Dadi AF, Miller ER, Mwanri L. Postnatal depression and its association with adverse infant health outcomes in low- and middle-income countries: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2020;20(1):416.
58. Solmi M, Radua J, Olivola M, et al. Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Mol Psychiatry*. 2022;27(1):281-295.
59. Shorey S, Ng ED, Wong CHJ. Global prevalence of depression and elevated depressive symptoms among adolescents: A systematic review and meta-analysis. *Br. J. Clin. Psychol*. 2022;61(2):287-305.

60. UNICEF Viet Nam. Mental health and psychosocial wellbeing of children and young people in selected provinces and cities in Viet Nam. 2018 <https://www.unicef.org/vietnam/reports/mental-health-and-psychosocial-wellbeing-among-children-and-young-people-viet-nam> (accessed 10 June 2023).
61. Thai TT, Cao PLT, Kim LX, Tran DP, Bui MB, Bui HHT. The effect of adverse childhood experiences on depression, psychological distress and suicidal thought in Vietnamese adolescents: Findings from multiple cross-sectional studies. *Asian J Psychiatr.* 2020;53:102134.
62. Klein DN, Shankman SA, Rose S. Ten-year prospective follow-up study of the naturalistic course of dysthymic disorder and double depression. *Am. J. Psychiatry.* 2006;163(5):872-880.
63. India State-Level Disease Burden Initiative Mental Disorders Collaborators. The burden of mental disorders across the states of India: the Global Burden of Disease Study 1990–2017. *Lancet Psychiatry.* 2020;7(2):148-161.
64. Dang HM, Lam TT, Dao A, Weiss B. Mental health literacy at the public health level in low and middle income countries: An exploratory mixed methods study in Vietnam. *PLoS One.* 2020;15(12):e0244573.
65. Ng CH, Than PT, La CD, Van Than Q, Van Dieu C. The national community mental health care project in vietnam: a review for future guidance. *Australa. Psychiatry.* 2011;19(2):143-150.
66. Institute for Health Metrics and Evaluation. n.d.; <https://ghdx.healthdata.org/gbd-2019/data-input-sources?components=5&causes=567&locations=20> (accessed 8 May 2023).
67. COVID-19 Mental Disorders Collaborators. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *Lancet.* 2021;398(10312):1700-1712.
68. Florio AA, Ferlay J, Znaor A, et al. Global trends in intrahepatic and extrahepatic cholangiocarcinoma incidence from 1993 to 2012. *Cancer.* 2020;126(11):2666-2678.

69. Sepanlou SG, Safiri S, Bisignano C, et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol*. 2020;5(3):245-266.
70. Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology*. 2023;77(4).
71. Manthey J, Shield KD, Rylett M, Hasan OSM, Probst C, Rehm J. Global alcohol exposure between 1990 and 2017 and forecasts until 2030: a modelling study. *Lancet*. 2019;393(10190):2493-2502.
72. Ong KL, Stafford LK, McLaughlin SA, et al. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2023;402(10397):203-234.
73. Tyson GL, El-Serag HB. Risk factors for cholangiocarcinoma. *Hepatology*. 2011;54(1).
74. Alvaro D, Gores GJ, Walicki J, et al. EASL-ILCA Clinical Practice Guidelines on the management of intrahepatic cholangiocarcinoma. *J Hepatol*. 2023;79(1):181-208.
75. Miranda-Filho A, Piñeros M, Ferreccio C, et al. Gallbladder and extrahepatic bile duct cancers in the Americas: Incidence and mortality patterns and trends. *Int J Cancer*. 2020;147(4):978-989.
76. Wang X, Yu W, Jiang G, et al. Global epidemiology of gallstones in the 21st century: systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2024;22(8):1586–1595.
77. Cid V, Vargas C, Delgado I, et al. Gallbladder cancer mortality in Chile: Has the government program targeting young gallstone patients had an impact? *Am J Epidemiol*. 2024;193:1197–1202.
78. Valle JW, Kelley RK, Nervi B, Oh DY, Zhu AX. Biliary tract cancer. *Lancet*. 2021;397(10272):428-444.

79. Latorre S G, Ivanovic-Zuvic s D, Corsi S Ó, et al. Cobertura de la estrategia preventiva de cáncer de vesícula biliar en Chile: Resultados de la Encuesta Nacional de Salud 2009-2010. *Rev Med Chil.* 2015;143:158-167.
80. Nogueira L, Foerster C, Groopman J, et al. Association of aflatoxin with gallbladder cancer in Chile. *JAMA.* 2015;313(20):2075-2077.
81. Kim HS, Nam HW, Ahn HJ, Kim D, Kim YH. Relationship between *Clonorchis sinensis* infection and cholangiocarcinoma in Korea. *Korean J Parasitol.* 2022;60(4):261-271.
82. Kaewpitoon N, Kootanavanichpong N, Kompor P, et al. Review and current status of *Opisthorchis viverrini* infection at the community level in Thailand. *Asian Pac J Cancer Prev.* 2015;16(16):6825-6830.
83. Kamsa-ard S, Kamsa-ard S, Luvria V, Suwanrungruang K, Vatanasapt P, Wiangnon S. Risk factors for cholangiocarcinoma in Thailand: a systematic review and meta-analysis. *Asian Pacific Journal of Cancer Prevention.* 2018;19(3):605-614.
84. Utada M, Ohno Y, Tamaki T, Sobue T, Endo G. Long-term trends in incidence and mortality of intrahepatic and extrahepatic bile duct cancer in Japan. *J Epidemiol.* 2014;24(3):193-199.
85. Saha SK, Zhu AX, Fuchs CS, Brooks GA. Forty-year trends in cholangiocarcinoma incidence in the U.S.: intrahepatic disease on the rise. *Oncologist.* 2016;21(5):594-599.
86. Kim BW, Oh CM, Choi HY, Park JW, Cho H, Ki M. Incidence and overall survival of biliary tract cancers in South Korea from 2006 to 2015: using the national health information database. *Gut Liver.* 2019;13(1):104-113.
87. Boutari C, Mantzoros CS. A 2022 update on the epidemiology of obesity and a call to action: as its twin COVID-19 pandemic appears to be receding, the obesity and dysmetabolism pandemic continues to rage on. *Metabolism.* 2022;133:155217.
88. Khan SA, Emadossadaty S, Ladep NG, et al. Rising trends in cholangiocarcinoma: Is the ICD classification system misleading us? *J Hepatol.* 2012;56(4):848-854.

89. Walter D, Ferstl P, Waidmann O, et al. Cholangiocarcinoma in Germany: epidemiologic trends and impact of misclassification. *Liver Int.* 2019;39(2):316-323.
90. Kang MJ, Lim J, Han SS, et al. Impact of changes in the topographic classification of Klatskin tumor on incidence of intra- and extrahepatic bile duct cancer: A population-based national cancer registry study. *J Hepatobiliary Pancreat Sci.* 2021;28(9):740-750.
91. Zubiri L, Rosovsky RP, Mooradian MJ, et al. Temporal trends in inpatient oncology census before and during the covid-19 pandemic and rates of nosocomial covid-19 among patients with cancer at a large academic center. *Oncologist.* 2021;26(8):e1427-e1433.

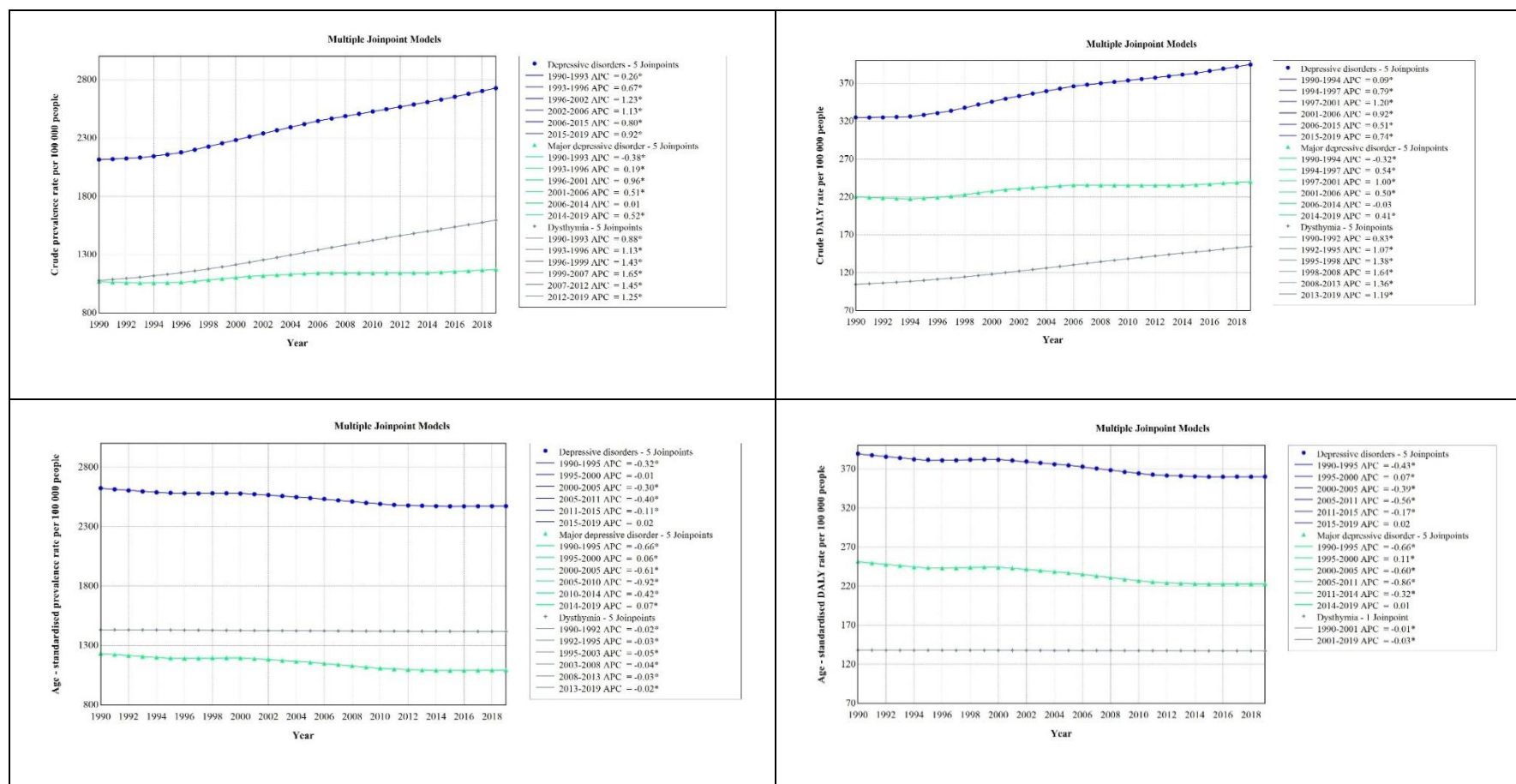
SUPPLEMENTARY MATERIALS

This chapter incorporates material previously published in articles.^{1,2}

**Supplementary Table 1. Number of DALYs of all causes and depressive disorders
by age group in Vietnam in 2019**

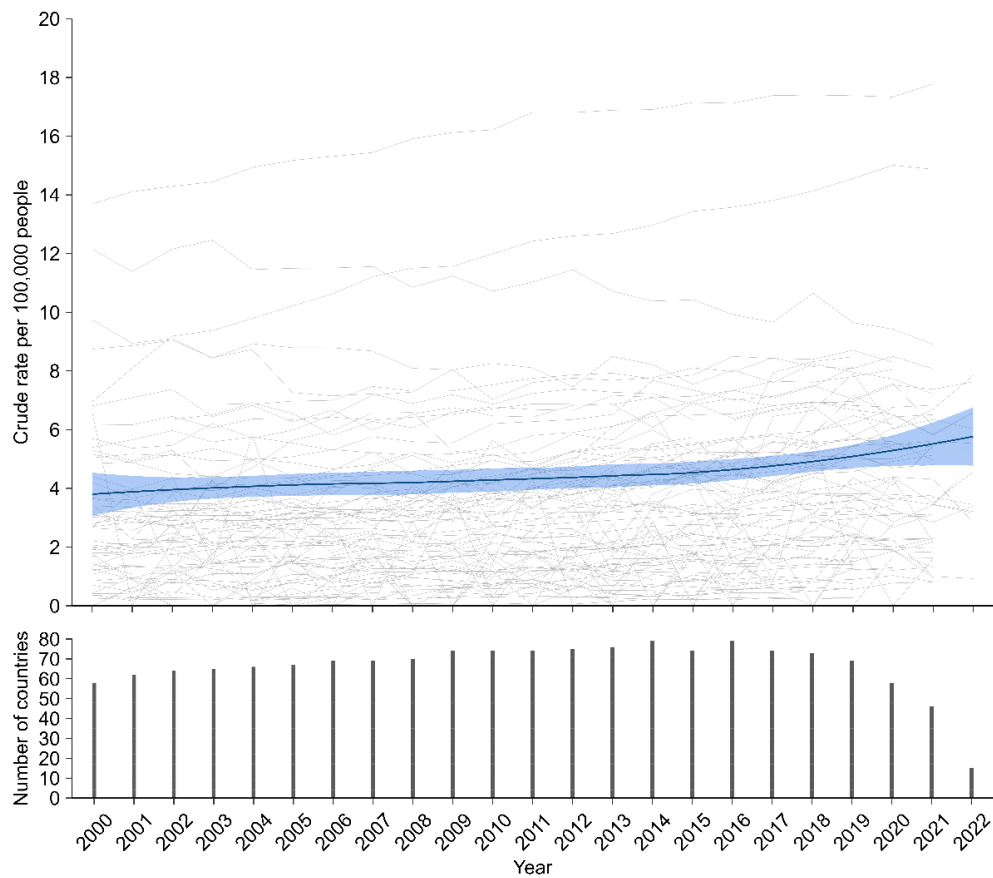
Age group (year)	Number of DALYs (95% UI)			
	All causes	Depressive disorders	Major depressive disorder	Dysthymia
<5	1707618.8 (1360262.5 to 2199659.4)	10.5 (4.5 to 22.1)	8.0 (2.6 to 19.3)	2.5 (0.5 to 6.4)
5–9	373302.5 (305902.8 to 454438.2)	836.3 (353.4 to 1561.9)	647.9 (232.9 to 1312.0)	188.4 (28.0 to 476.2)
10–14	444556.7 (351204.8 to 557387.6)	8703.6 (4566.4 to 15482.7)	7432.7 (3426.3 to 13725.9)	1270.9 (538.7 to 2471.8)
15–19	722203.5 (597039.1 to 874194.1)	21595.7 (12591.5 to 33708.8)	18206.5 (9843.2 to 29146.9)	3389.2 (1687.1 to 5692.1)
20–24	961761.2 (797418.9 to 1147777.5)	29797.9 (17428.7 to 45300.1)	23189.3 (12629.4 to 37097.8)	6608.6 (3284.6 to 11800.4)
25–29	1240466.4 (1016102.4 to 1494687.1)	37022.6 (22216.8 to 55220.8)	25376.6 (14559.9 to 39980.8)	11646.1 (6205.2 to 20579.2)
30–34	1337658.2 (1087513.8 to 1614129.5)	37658.8 (23382.1 to 56824.5)	22787.1 (12899.8 to 37221.8)	14871.7 (8597.9 to 23974.4)
35–39	1449041.9 (1177126.5 to 1750715.4)	38008.1 (24453.3 to 56472.9)	20965.9 (12983.6 to 31832.6)	17042.3 (9768.2 to 27933.8)
40–44	1597218.2 (1300870.7 to 1930423.5)	36750.5 (23171.7 to 56477.5)	19062.4 (11194.7 to 30504.7)	17688.1 (9629.8 to 29938.9)
45–49	1904807.0 (1577602.7 to 2304311.1)	37450.3 (24076.2 to 55585.5)	19560.3 (12160.8 to 28742.2)	17890.0 (9641.3 to 29767.2)
50–54	2194967.6 (1800996.4 to 2656352.4)	35969.2 (23881.6 to 52725.9)	19248.7 (12174.7 to 27837.1)	16720.5 (9722.8 to 27063.8)
55–59	2470247.8 (2041567.7 to 2951196.6)	34025.8 (22280 to 49871.9)	18790.5 (11483.3 to 28669.4)	15235.3 (8973 to 23951.1)
60–64	2430382.6 (2023694.9 to 2871809.6)	26680.1 (17231.2 to 39297.2)	14943.1 (9091.4 to 22716.3)	11737.1 (6437.4 to 19434)
65–69	1975129.8 (1664452.6 to 2285822.7)	15922.0 (10482.4 to 22898.1)	8940.4 (5682.4 to 13103.9)	6981.6 (3815.6 to 11523.9)
70–74	1494498.3 (1284616.9 to 1667079.6)	8487.9 (5491.2 to 12036.8)	4884.2 (3101.4 to 7105)	3603.7 (2016.9 to 5869.5)
75–79	1299029.6 (1157389.6 to 1417730.7)	5339.9 (3388.2 to 7752.9)	3201.3 (1899.4 to 4938.2)	2138.5 (1213.6 to 3492.1)
80–84	1135696.3 (1041611.3 to 1213680.1)	3476.2 (2174.7 to 5097.2)	2244.7 (1307.4 to 3486.4)	1231.6 (661.3 to 2098.5)
85–89	736589.2 (690384.6 to 783008.9)	1956.8 (1255.3 to 2832.6)	1381.5 (842.4 to 2063.2)	575.3 (312.6 to 955.7)
90–94	260721.8 (245457.2 to 275078.9)	680.4 (431 to 984.6)	509.4 (298.8 to 783.9)	170.9 (92.3 to 283.6)
95+	75605.9 (71023.7 to 79900.2)	194.1 (107.7 to 300.0)	151.7 (75.6 to 247.5)	42.4 (21.5 to 76.0)
Total	25811503.4 (22012142.4 to 29875885.7)	380566.8 (258903.4 to 533769.4)	231532.1 (155163 to 323452.7)	149034.7 (93223.2 to 227427.1)

DALYs, disability-adjusted life-years; 95% UI, 95% uncertainty interval; Adapted from the previously published article.¹



Supplementary Fig. 1. Annual percent changes of prevalence and DALY rates of depressive disorders in Vietnam from 1990 to 2019

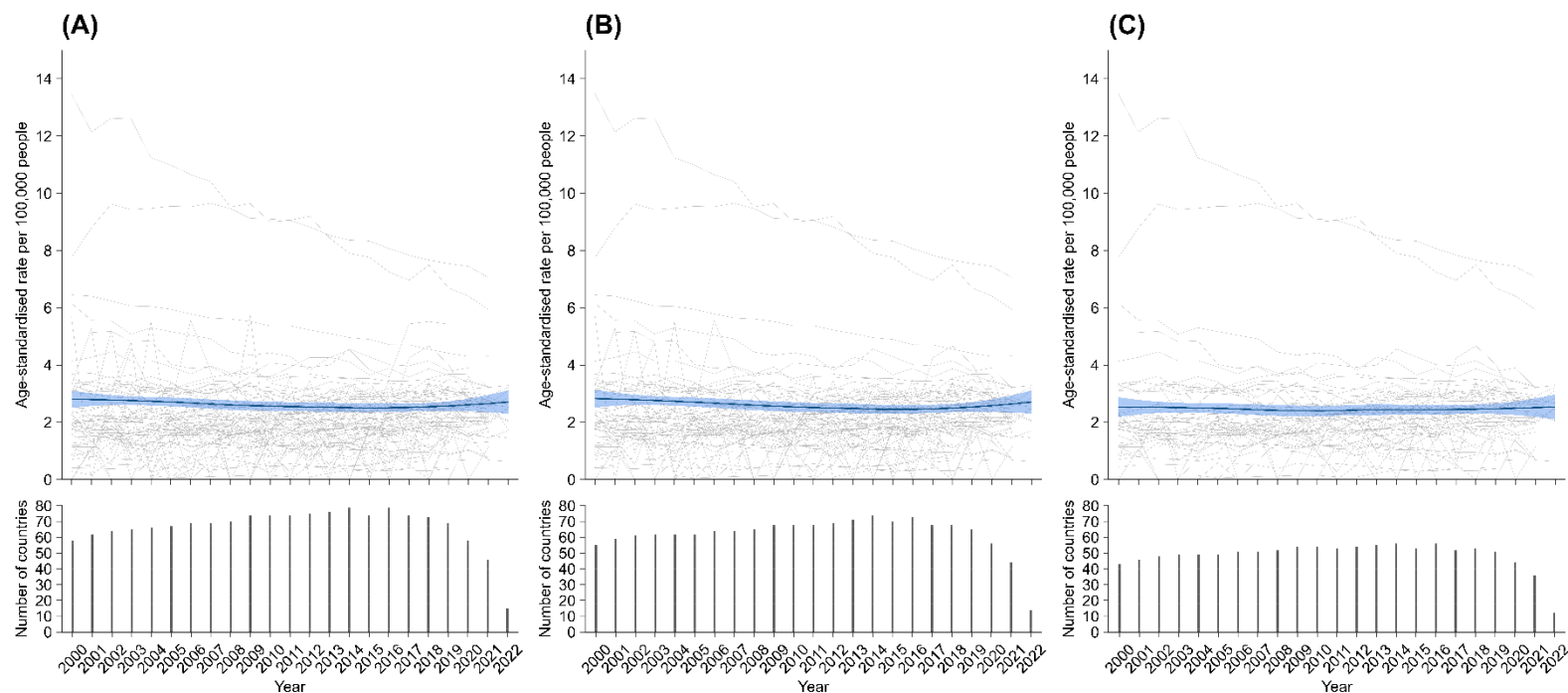
APC, annual percent change; DALYs, disability-adjusted life-years *, statistically significant with $p < 0.05$; Adapted from the previously published article.¹



Supplementary Fig. 2. Trends in crude mortality rates due to biliary tract cancers for both sexes combined in 83 countries from 2000 to 2022.

The locally weighted regression rates (blue line) with 95% confidence intervals (light blue shadow), weighted by country population size, are provided.

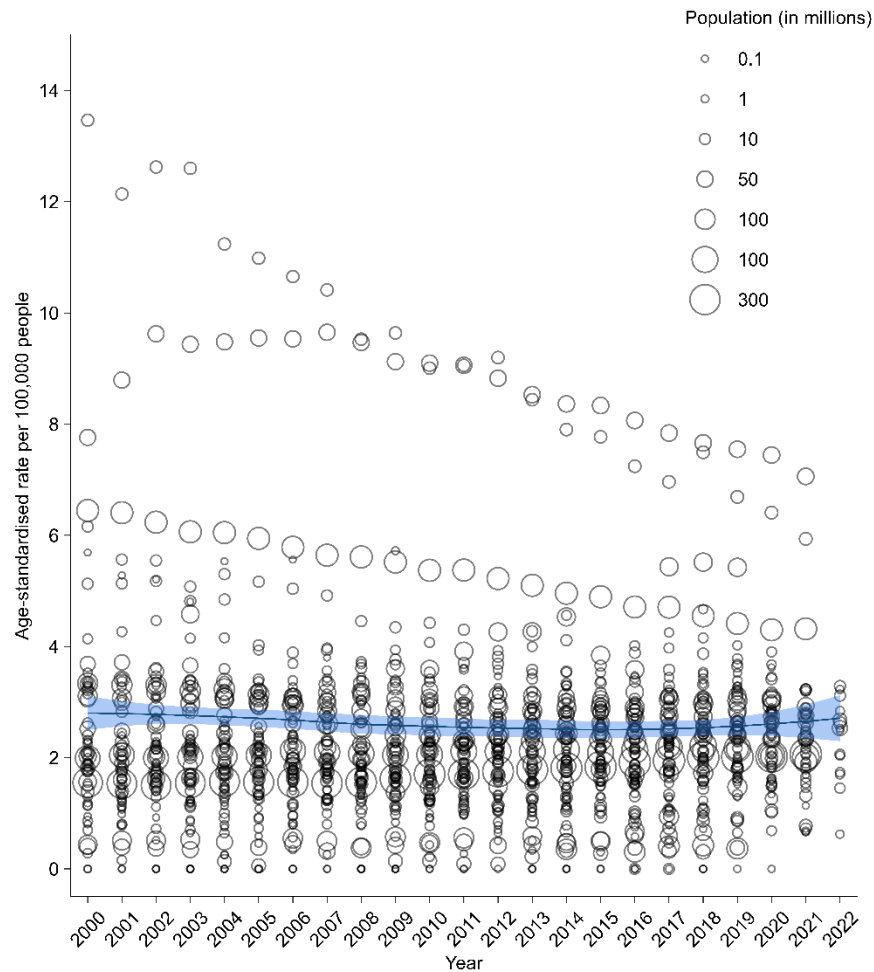
Adapted from the previously published article.²



Supplementary Fig. 3. Sensitivity analysis for trends in age-standardized mortality rates due to biliary tract cancers for both sexes combined from 2000 to 2022 according to data quality thresholds

The locally weighted regression rates (blue line) with 95% confidence intervals (light blue shadow) for (A) usability $\geq 60\%$, (B) usability $\geq 70\%$, and (C) usability $\geq 80\%$, weighted by country population size, are provided;

Adapted from the previously published article.²



Supplementary Fig. 4. Distribution and weights of age-standardized mortality rates due to biliary tract cancers for both sexes combined observed in 83 countries and contribution to the locally weighted regression curve for time trends from 2000 to 2022.

The locally weighted regression rates (blue line) with 95% confidence intervals (light blue shadow), weighted by country population size. Each circle presents the country's population size (in millions) in the corresponding year, are provided;

Adapted from the previously published article.²

Supplementary Table 2. List of countries

No.	Country name	Geographic region	No.	Country name	Geographic region
1	Mauritius	African Region	33	Norway	European Region
2	South Africa	African Region	34	Poland	European Region
3	Islamic Republic of Iran	Eastern Mediterranean Region	35	Portugal	European Region
4	Jordan	Eastern Mediterranean Region	36	Republic of Moldova	European Region
5	Kuwait	Eastern Mediterranean Region	37	Romania	European Region
6	Armenia	European Region	38	Serbia	European Region
7	Austria	European Region	39	Slovakia	European Region
8	Belarus	European Region	40	Slovenia	European Region
9	Belgium	European Region	41	Spain	European Region
10	Bosnia and Herzegovina	European Region	42	Sweden	European Region
11	Croatia	European Region	43	Switzerland	European Region
12	Cyprus	European Region	44	Tajikistan	European Region
13	Czech Republic	European Region	45	Turkey	European Region
14	Denmark	European Region	46	United Kingdom	European Region
15	Estonia	European Region	47	Uzbekistan	European Region
16	Finland	European Region	48	Antigua and Barbuda	American Region
17	France	European Region	49	Argentina	American Region
18	Georgia	European Region	50	Bahamas	American Region
19	Germany	European Region	51	Belize	American Region
20	Greece	European Region	52	Brazil	American Region
21	Hungary	European Region	53	Canada	American Region
22	Iceland	European Region	54	Chile	American Region
23	Ireland	European Region	55	Colombia	American Region
24	Israel	European Region	56	Costa Rica	American Region
25	Italy	European Region	57	Cuba	American Region
26	Kazakhstan	European Region	58	Dominica	American Region
27	Kyrgyzstan	European Region	59	Ecuador	American Region
28	Latvia	European Region	60	Grenada	American Region
29	Lithuania	European Region	61	Guatemala	American Region
30	Luxembourg	European Region	62	Guyana	American Region
31	Malta	European Region	63	Jamaica	American Region
32	Netherlands	European Region	64	Mexico	American Region

No.	Country name	Geographic region	No.	Country name	Geographic region
65	Nicaragua	American Region	75	Thailand	South-East Asia Region
66	Panama	American Region	76	Australia	Western Pacific Region
67	Paraguay	American Region	77	Brunei Darussalam	Western Pacific Region
68	Saint Kitts and Nevis	American Region	78	Japan	Western Pacific Region
69	Saint Lucia	American Region	79	Mongolia	Western Pacific Region
70	Saint Vincent and Grenadines	American Region	80	New Zealand	Western Pacific Region
71	Suriname	American Region	81	Philippines	Western Pacific Region
72	United States of America	American Region	82	Republic of Korea	Western Pacific Region
73	Uruguay	American Region	83	Singapore	Western Pacific Region
74	Venezuela	American Region			

Adapted from the previously published article.²

Supplementary Table 3. Age-standardized mortality rates due to biliary tract cancers for both sexes combined by country from 2000 to 2022.

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Antigua and Barbuda	3.3	5.3	0.9	3.3	2.6	0	0	2.8	0	0	2.3	1.9	3.5	1.3	3.3	2.7	0	2.3	0	1.7	3.6	1.7	
Argentina	3.0	3.0	2.9	2.8	2.8	2.9	2.8	2.8	2.7	2.7	2.7	2.6	2.6	2.6	2.6	2.5	2.5	2.4	2.4	2.4	2.4	2.3	
Armenia							1.0	1.3	1.7	1.5	2.0	1.6	1.6	1.6	1.2	2.2	2.1	2.2	2.6	2.5	1.9	2.3	2.0
Australia	2.1	2.0	2.0	2.0	2.0		2.0	2.0	2.2	2.1	2.2	2.1	2.2	2.3	2.4	2.5	2.4	2.5	2.6	2.7	2.6	2.7	2.7
Austria			3.5	3.4	3.6	3.4	3.0	3.1	3.0	3.4	3.4	3.2	3.2	3.4	3.3	3.0	2.9	3.1	3.1	2.6	2.8	2.8	
Bahamas	1.8	1.4	0.5	2.4	0.3	1.2	2.2	2.6	1.8	2.4	1.6	3.0	3.3	2.2	2.8	2.0							
Belarus																			1.6				
Belgium	1.9	1.7	1.7	1.7	1.9	1.7	2.0	1.9	1.7	2.0	2.0	2.2	1.9	2.1	1.9	2.2	2.1	1.9	2.1	2.3	2.1		
Belize	0.9	0.8	2.7	0	1.5	2.2	2.4	2.5	0	1.3	1.0	2.6	2.2	1.5	1.2	1.6	1.6						
Bosnia and Herzegovina												1.9			2.0		1.5	2.2	2.0	1.9	1.6	1.5	1.7
Brazil	2.0	2.0	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.0	2.1	2.1	2.1	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.0	2.0	
Brunei Darussalam												1.3	0.7	1.2	1.1	0.3	3.0	3.2	2.5	3.3			
Canada	1.8	1.9	1.7	1.8	1.8	2.0	1.9	1.9	2.0	2.0	2.1	2.3	2.3	2.4	2.5	2.6	2.5	2.6	2.5	2.5	2.6	2.6	2.5
Chile	13.5	12.1	12.6	12.6	11.2	11.0	10.7	10.4	9.5	9.6	9.0	9.1	9.2	8.4	7.9	7.8	7.2	7.0	7.5	6.7	6.4	5.9	
Colombia	3.3	3.4	3.3	3.3	3.2	3.2	3.1	3.3	3.3	3.3	3.2	2.9	2.9	3.0	3.1	3.1	2.9	3.1	2.9	3.0	3.0	2.9	
Costa Rica	2.3	2.4	2.6	2.8	2.3	2.5	2.6	2.3	1.9	1.8	2.3	2.3	1.9	2.1	2.2	2.6	2.5	2.3	2.7	2.7	2.8		
Croatia	3.3	3.1	3.1	3.4	3.0	3.1	3.4	3.6	3.7	3.9	3.4	3.6	3.6	3.5	3.5	3.5	3.4	3.4	3.5	3.4	3.5	3.2	
Cuba		1.3	1.5	1.2	1.3	1.3	1.2	1.2	1.1	1.1	1.2	1.1	1.1	1.2	1.0	1.0	1.0	1.0	0.9	0.9	1.0	0.7	
Cyprus					1.4	2.2	1.4	1.9	1.8	1.6	1.9	1.8	1.6	2.5	2.4	1.5	1.5	2.1	2.0	2.0	1.6	1.8	
Czech Republic	6.2	5.6	5.5	5.1	5.3	5.2	5.0	4.9	4.5	4.3	4.4	4.3	3.8	4.3	4.1	3.7	3.9	3.6	3.9	3.6	3.4	3.2	
Denmark	1.8	1.6	1.6	1.6	1.5	1.6	1.8	1.7	1.7	1.5	2.1	1.7	2.0	1.9	2.3	2.4	2.3	2.4	2.1	2.6	2.5	2.5	
Dominica		2.4	5.2	1.2	5.5	1.1	2.9	0	2.6	0	1.5	3.6	0	0	2.1	0	2.7	1.3	1.1	1.3	2.4		
Ecuador	3.2	2.8	2.8	2.2	2.4	2.1	2.1	2.3	2.6	2.6	2.9	2.3	2.6	2.5	2.5	2.9	2.7	2.5	2.5	2.6	2.0	2.3	
Estonia	1.2	1.2	1.9	1.2	1.2	1.7	1.8	1.6	1.4	2.0	2.9	2.3	2.3	1.6	2.5	1.9	1.4	2.7	3.0	3.5	2.9	2.9	3.2
Finland	2.0	2.0	1.8	1.7	1.8	1.9	1.6	1.9	1.9	1.7	1.8	1.7	1.6	1.8	1.7	1.8	1.9	1.7	1.9	1.9	1.9	1.9	
France	2.0	2.1	2.0	2.2	2.1	2.1	2.2	2.2	2.2	2.3	2.3	2.3	2.4	2.4	2.4	2.4	2.4	2.5	2.4	2.4	2.3		
Georgia	0.3	0.2			1.7	0.9	0.6	0.8		0.6	0.2	1.2	1.0	2.9	1.4	1.5	2.2	2.3	2.4	2.5	2.6	2.8	1.7
Germany	3.1	3.1	3.2	3.0	3.1	3.0	3.0	2.8	2.9	2.9	2.9	2.9	2.9	2.8	2.9	2.9	2.9	3.0	3.0	3.0	3.1		

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Greece															1.8	1.7	1.8	1.7	1.9	1.8	1.8		
Grenada		0	0	0	0	0	0.8	1.7	0	0	1.5	1.6	1.0	0	0	1.8	3.5	0.8	0.7	2.0	0	1.1	
Guatemala						1.4	1.4	1.2	1.3	1.3	1.4	1.6	1.1	1.3	1.3	1.1	1.0	1.1	1.1	0.9	1.3	1.3	
Guyana		1.9	2.2	0.9	1.3	0	0.3	1.2	1.6	5.7	0.4	1.0	1.3	0.5	1.5	1.3	0.8	1.1	1.0	1.6			
Hungary	5.1	5.1	5.2	4.8	4.8	4.0	3.9	3.9	3.6	3.8	3.5	3.7	3.7	3.6	3.5	3.3	3.4	3.3	3.3	3.1	3.0	2.6	3.1
Iceland	0.8	1.0	2.3	0.6	1.1	2.1	1.7	1.7	3.0	2.3	0.9	0.3	1.3	0.3	1.3	1.0	0.6	1.1	1.7	2.3	2.8	1.9	2.5
Islamic Republic of Iran														0.6	0.5	0.5	0.7	0.9					
Ireland								2.7	2.6	2.7	2.4	2.9	2.6	3.1	3.3	2.8	0.9	0.5	3.4	0.7	0.7		
Israel	1.5	1.5	1.5	1.5	1.8	1.7	1.8	1.8	1.5	1.7	1.8	1.7	1.9	1.6	1.7	1.8	1.7	1.8	1.6	1.8	1.5	1.8	
Italy				3.1	3.1	3.1	3.0	3.2	3.1	3.1	3.1	3.1	3.1	3.1	3.0	3.0	3.2	3.1	3.0	3.1	2.9		
Jamaica	1.1	1.1	1.1	1.5	1.6	2.2	1.1			1.7	1.2	1.2	1.7	1.7	1.9								
Japan	6.4	6.4	6.2	6.1	6.0	5.9	5.8	5.6	5.6	5.5	5.4	5.4	5.2	5.1	5.0	4.9	4.7	4.7	4.6	4.4	4.3	4.3	
Jordan									0.8	1.3	1.2	1.3	1.1				1.3	1.3	1.4				
Kazakhstan														0.8	0.7	0.9	0.8	0.7	0.9	0.9	1.1	0.8	
Kuwait	1.5	1.3	1.8	0.9	0.8	0.9	1.8	1.4	1.5	1.5	1.2	1.6	2.1	0.9	0.8	1.3	1.7	1.5	1.1	1.6			
Kyrgyzstan	1.2	0.8	1.3	1.1	1.0	1.3	1.0	1.3	1.2	1.1	1.2	1.6	1.1	1.3	1.1	1.9	1.5	1.7	1.6	1.3			
Latvia	1.3	1.2	1.4	1.2	1.3	1.3	1.2	1.2	1.2	1.7	1.3	1.4	1.7	1.7	2.0	1.9	1.6	1.9	2.0	2.0	1.8	2.2	
Lithuania	2.1	2.0	1.7	2.1	2.2	1.9	1.6	1.7	1.6	1.7	1.7	2.2	2.2	2.1	2.1	2.5	2.6	2.0	2.6	3.3	2.9	2.6	2.8
Luxembourg	2.1	1.3	2.3	1.2	1.7	1.5	1.9	1.7	1.9	2.8	1.7	2.4	2.3	2.8	2.1	2.6	2.1	2.2	1.5	2.3	2.0	2.0	2.5
Malta	1.9	2.1	2.1	2.2	1.9	1.9	1.5	2.0	2.1	1.5	2.3	1.6	2.1	1.0	1.9	2.3	2.7	2.4	3.3	3.2	2.6		
Mauritius						1.8	2.7	1.4	1.4	1.1	1.6	1.0	1.3	1.1	1.3	1.6	1.7	1.3	2.2	1.7	1.6	0.7	0.6
Mexico	3.3	3.3	3.3	3.2	3.2	3.1	2.9	2.6	2.5	2.4	2.4	2.3	2.4	2.3	2.4	2.3	2.3	2.2	2.1	2.2	2.0	1.9	
Mongolia																	1.9	4.3	4.7	4.0	2.7	2.8	
Netherlands	1.8	1.8	1.6	1.6	1.7	1.7	1.7	1.8	1.7	1.8	1.7	1.8	2.1	2.1	2.4	2.4	2.6	2.5	2.4	2.5	2.8	2.9	2.6
New Zealand	1.9	1.8	2.1	2.3	2.5	2.4	2.3	2.6	2.0	2.5	2.3	2.3	2.3	2.5	2.5	2.6	2.2						
Nicaragua	3.2	3.4	3.4	3.3	2.6	3.4	3.0	3.4	3.0	3.4	2.5	2.6	2.5	2.6	2.5	2.8	2.3	2.3	2.4	2.7	2.6	2.4	
Norway	1.7	1.6	1.6	1.6	1.4	1.5	1.6	1.6	1.6	1.6	1.7	2.2	2.0	1.8	2.0	2.1	2.2						
Panama	2.3	1.6	1.6	2.1	2.2	2.4	1.7	2.0	1.6	1.7	1.3	2.1	1.7	1.1	1.5	1.9	1.8	2.2	2.0	2.2		2.2	
Paraguay	0.9	1.8	1.4	1.4	0.9	1.3	1.6	1.2	1.5	1.4	1.2	1.2	1.3	1.5	1.6	1.6	1.5	1.7	1.8	1.6	1.5	1.6	
Philippines	0.4	0.5	0.5	0.5			0.6	0.5	0.4	0.6	0.5	0.6			0.4		0.3	0.4	0.4	0.4			

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Poland	3.7	3.7	3.5	3.7	3.4	3.2	3.0	3.0	3.2	3.0	3.0	2.8	3.0	2.8	2.8	2.8	2.8	2.7	2.6	2.6	2.3	2.3	
Portugal			2.2	2.0				2.3	2.2	2.1	2.3	2.1	2.2	2.7	2.8	2.9	3.1	2.8	3.0	3.2			
Republic of Korea	7.8	8.8	9.6	9.4	9.5	9.5	9.5	9.7	9.5	9.1	9.1	9.1	8.8	8.5	8.4	8.3	8.1	7.8	7.7	7.5	7.4	7.1	
Republic of Moldova	0.7	0.8	0.7	0.7	0.6	0.7	0.8	1.0	1.0	1.0	0.8	1.0	0.8	1.0	1.1	1.1	1.0	1.1	1.2				
Romania	1.4	1.4	1.5	1.6	1.7	1.6	1.6	1.6	1.5	1.7	1.6	1.7	1.7	1.8	1.8	1.9	1.7	1.9	1.7	1.8			
Saint Kitts and Nevis	5.7	0	3.1	4.8	0	2.6	5.6	3.8	1.3	2.2	0	0	2.0	0	0	1.8	1.7						
Saint Lucia	0	1.1	0	0	0	0.6	0		1.3	1.1	1.2	0	0.5	1.7	2.8	0	1.6	0.5	0	0	1.4		
Saint Vincent and Grenadines	2.3	1.5	0	0	0.7	2.1	0	0	0	0	0	1.3	0.8	2.7	0	1.7	0	0	0	1.5	1.3	0.7	
Serbia	2.6	2.2	2.2	2.2	2.2	2.1	2.2	2.2	1.8	2.3	1.9	1.9	2.2	1.9	2.0	2.2	1.9	1.8	2.0	1.9	1.5	1.5	1.5
Singapore													2.7	2.9	3.1	2.6	2.9	2.9	2.7	2.6	2.4	2.4	2.1
Slovakia	4.1	4.3	4.5	4.1	4.2	3.9	3.7	4.0	3.7	3.7	4.1		3.9	4.0	4.6		4.0	4.0	4.2	3.8	3.9	3.2	
Slovenia	3.3	3.0	3.3	2.3	2.7	3.2	3.3	3.4	3.4	2.6	2.6	2.6	2.8	2.5	3.0	2.0	2.1	2.3	2.3	2.4	2.1		
South Africa	0.4	0.4	0.4	0.3	0.5	0.4	0.5	0.3	0.4	0.4	0.5	0.5	0.4	0.4	0.5	0.5	0.6	0.6	0.7				
Spain	2.5	2.5	2.6	2.5	2.4	2.6	2.6	2.6	2.5	2.5	2.6	2.7	2.7	2.8	2.8	2.8	2.8	2.9	2.9	2.8	2.7	2.8	
Suriname	0	1.1	1.9	1.2	0.2	0.5	0.8	0.3	0.8	0.8	0.9	1.1	0.7	1.5	1.1								
Sweden	3.4	3.4	3.6	3.1	3.4	3.1	3.1	2.9	3.2	3.3	3.0	3.0	3.2	3.2	2.8	3.2	3.0	3.1	3.1	3.1	3.2	3.2	3.3
Switzerland	2.4	2.1	2.4	2.3	2.3	2.3	2.4	2.7	2.3	2.1	2.2	2.3	2.5	2.4	2.3	2.3	2.4	2.6	2.5	2.5	2.4	2.1	
Tajikistan																	0	0					
Thailand	1.6		2.6	4.6	3.0	3.0	3.1	3.0	3.2	3.6	3.6	3.9	4.3	4.3	4.5	3.8	3.6	5.4	5.5	5.4			
Turkey										1.4	1.5	1.6	1.5	1.9	1.8	1.8	1.7	1.7	1.7	1.5			
United Kingdom		1.6	1.6	1.6	1.7	1.8	1.8	1.9	2.0	2.1	2.1	2.3	2.4	2.5	2.6	2.6	2.7	2.7	2.7	2.8	3.0		
United States of America	1.6	1.5	1.5	1.5	1.6	1.6	1.6	1.5	1.6	1.6	1.7	1.7	1.8	1.8	1.8	1.8	1.9	1.9	2.0	2.0	2.0	2.1	
Uruguay	3.5	3.3	3.1	2.9	3.2	2.9	2.4	3.0	3.4	2.8	3.0		2.7	2.9	3.3	3.4	2.5	3.0	3.5	3.7	3.7		
Uzbekistan					0.1	0.1				0.1	0.1	0.1	0.1	0.2	0.3	0.3	0.4	0.3	0.3	0.4			
Venezuela	2.1	2.3	2.1	2.1	2.1	2.1	2.0	1.7	1.6	1.6	1.6	1.6	1.7	1.5	1.6	1.6	1.6						

Data are presented as age-standardized mortality rate per 100,000 population; Adapted from the previously published article.²

Supplementary Table 4. Age-standardized mortality rates due to gallbladder cancer for both sexes combined by country from 2000 to 2022.

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Antigua and Barbuda	3.3	3.9	0	0	2.6	0	0	0	0	0	0	0	0	0	0	1.8	0	1.2	0	0.8	1.6	0	
Argentina	1.3	1.2	1.2	1.2	1.1	1.1	1.1	1.1	1.1	1.1	1.0	1.0	0.9	1.0	0.9	0.9	0.8	0.9	0.8	0.8	0.8	0.8	
Armenia							0.6	0.9	1.3	0.8	1.4	1.1	1.0	1.0	0.7	1.3	0.8	1.1	0.9	1.0	0.5	0.9	0.6
Australia	0.7	0.7	0.7	0.6	0.4		0.5	0.5	0.5	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.3	0.4	0.4	0.3	0.3	0.3	0.3
Austria			1.2	1.0	1.1	1.0	0.7	0.8	0.7	0.7	0.7	0.8	0.7	0.7	0.7	0.4	0.5	0.5	0.5	0.4	0.5	0.4	
Bahamas	1.3	0.9	0.5	2.0	0	1.2	0.7	0.8	0.8	0.3	1.3	0.7	1.3	1.3	1.4	0.9							
Belarus																			0.5				
Belgium	0.5	0.4	0.4	0.3	0.4	0.3	0.4	0.4	0.3	0.3	0.3	0.2	0.3	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2		
Belize	0	0	2.7	0	1.5	1.5	2.4	1.2	0	1.3	0.4	1.2	0.6	0	0.8	0	0.4						
Bosnia and Herzegovina												1.5			1.4		1.0	1.4	1.2	1.1	1.1	1.0	1.3
Brazil	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.5	0.5	0.5	0.6	0.5	0.5	0.4	
Brunei Darussalam												0.9	0.7	0.6	1.1	0.3	1.5	0.6	0.2	0.2			
Canada	0.6	0.5	0.6	0.6	0.5	0.6	0.5	0.5	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.3	0.3	0.4	0.3	0.3
Chile	9.1	8.0	8.5	8.4	7.9	8.1	7.5	7.6	7.0	7.1	6.6	6.8	6.5	6.1	5.7	5.5	5.1	4.7	5.2	4.4	4.1	3.9	
Colombia	1.7	1.6	1.4	1.3	1.5	1.4	1.2	1.1	1.0	1.0	1.0	0.9	0.9	0.9	1.0	0.8	0.8	0.9	0.8	0.8	0.7	0.8	
Costa Rica	0.8	0.8	0.7	0.7	0.7	0.8	1.0	0.8	0.6	0.5	0.4	0.6	0.4	0.4	0.4	0.5	0.5	0.3	0.5	0.6	0.5		
Croatia	2.1	2.1	1.8	2.3	1.7	1.9	2.0	2.1	2.0	2.1	1.7	1.8	1.4	1.5	1.5	1.4	1.4	1.4	1.3	1.1	1.2	1.0	
Cuba		0.5	0.7	0.5	0.5	0.4	0.4	0.4	0.3	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.3	0.3	0.2	0.2	0.4	0.2	
Cyprus					0.6	0.8	0.7	0.3	0.4	0.3	0.4	0.2	0.3	0.3	0.3	0.3	0.2	0.2	0.1	0.4	0.1	0.1	
Czech Republic	3.7	3.4	3.1	2.9	3.2	2.9	2.6	2.5	2.3	2.2	2.1	2.2	1.7	1.7	1.7	1.5	1.5	1.3	1.3	1.2	1.1	1.0	
Denmark	0.4	0.3	0.3	0.3	0.2	0.2	0.3	0.3	0.3	0.2	0.4	0.3	0.2	0.2	0.2	0.3	0.4	0.3	0.3	0.4	0.3	0.1	
Dominica		2.4	3.5	1.2	2.7	1.1	1.7	0	2.6	0	0	2.9	0	0	0.9	0	2.7	0	1.1	1.3	0		
Ecuador	1.6	1.7	1.6	1.2	1.2	1.3	1.1	1.5	1.3	1.2	1.3	1.1	1.2	0.9	0.8	0.7	0.7	0.8	0.9	0.7	0.5	0.6	
Estonia	0.7	0.6	1.0	0.9	0.3	0.5	0.3	0.6	0.6	0.2	0.6	0.6	0.6	0.7	0.6	0.6	0.4	0.6	0.5	0.8	0.5	0.3	0.5
Finland	1.1	1.1	0.9	0.9	0.8	0.9	0.7	0.8	0.7	0.7	0.6	0.6	0.5	0.5	0.5	0.6	0.5	0.5	0.5	0.5	0.4	0.5	
France	0.5	0.5	0.5	0.4	0.4	0.3	0.4	0.3	0.3	0.3	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.1	0.1		
Georgia	0.3	0.1			1.6	0.9	0.5	0.7		0.6	0.1	0.5	0.4	0.5	0.7	0.6	1.0	1.0	0.9	1.2	0.9	1.1	0.6
Germany	1.3	1.3	1.4	1.2	1.1	1.0	0.9	0.9	0.8	0.8	0.8	0.8	0.7	0.7	0.6	0.6	0.5	0.5	0.5	0.5	0.5		

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Greece															0.3	0.2	0.2	0.2	0.2	0.1	0.1		
Grenada		0	0	0	0	0	0.8	1.7	0	0	0.6	1.6	0	0	0	1.8	2.6	0.8	0.7	1.5	0	1.1	
Guatemala						0.9	0.6	0.6	0.5	0.5	0.8	0.8	0.5	0.7	0.5	0.3	0.3	0.3	0.2	0.4	0.4	0.5	
Guyana		1.6	1.0	0	0.9	0	0.2	0.5	1.1	0.2	0.4	0.6	0.4	0.5	0.7	0.9	0.1	0.5	0.3	0.3			
Hungary	2.9	3.1	3.1	2.7	2.7	2.3	2.1	2.0	1.8	1.9	1.7	1.6	1.6	1.5	1.3	1.1	1.1	1.1	1.0	0.9	0.7	0.7	0.8
Iceland	0.3	0.2	0.9	0.2	0.4	0.5	0.2	0.2	0	0	0	0.1	0.8	0	0.3	0	0.2	0.6	0.1	0.4	1.0	0.3	0.4
Islamic Republic of Iran														0.4	0.3	0.3	0.4	0.4					
Ireland								0.6	0.6	0.4	0.3	0.4	0.5	0.4	0.5	0.5	0.6	0.2	0.5	0.4	0.3		
Israel	0.6	0.6	0.6	0.5	0.5	0.5	0.5	0.4	0.5	0.4	0.5	0.4	0.3	0.3	0.3	0.4	0.3	0.4	0.3	0.3	0.2	0.3	
Italy				1.2	1.1	1.0	0.9	1.0	0.9	0.8	0.8	0.7	0.7	0.7	0.6	0.6	0.6	0.5	0.5	0.5	0.4		
Jamaica	0.8	1.0	0.6	0.9	1.0	1.1	1.0			1.1	1.0	0.7	1.2	1.1	1.2								
Japan	2.4	2.3	2.2	2.1	2.0	1.9	1.9	1.8	1.8	1.7	1.7	1.6	1.6	1.5	1.4	1.4	1.3	1.3	1.3	1.2	1.1	1.1	
Jordan									0.3	0.5	0.4	0.4	0.4				0.5	0.6	0.6				
Kazakhstan														0.4	0.4	0.5	0.3	0.4	0.3	0.3	0.4	0.2	
Kuwait	1.5	0.5	1.4	0.6	0.5	0.9	1.6	0.8	1.0	0.6	0.5	1.4	1.2	0.5	0.2	0.3	0.7	1.0	0.4	0.1			
Kyrgyzstan	0.4	0.3	0.8	0.7	0.6	0.6	0.4	0.8	0.8	0.7	0.8	0.8	0.7	0.7	0.6	0.7	0.8	0.6	0.6	0.9			
Latvia	0.6	0.5	0.6	0.6	0.5	0.5	0.6	0.4	0.3	0.5	0.3	0.3	0.2	0.3	0.4	0.4	0.2	0.4	0.5	0.5	0.4	0.4	
Lithuania	1.4	1.1	0.8	1.0	0.9	0.8	0.5	0.8	0.6	0.6	0.6	0.7	0.5	0.6	0.7	0.8	0.5	0.3	0.7	0.6	0.5	0.4	0.6
Luxembourg	1.1	0.4	0.8	0.1	0.4	0	0	0.2	0.2	0.4	0.1	0.3	0.1	0	0.1	0.2	0.1	0.3	0.2	0.2	0	0.2	0.1
Malta	0.2	1.0	0.6	0.3	0.3	0.6	0.3	0.4	0.2	0.2	0.3	0	0.3	0.3	0.1	0.8	0.4	0.2	0.3	0.4	0.1		
Mauritius						1.0	1.8	1.0	0.7	0.7	0.9	0.8	1.3	0.9	1.0	0.6	0.9	0.6	1.0	0.6	0.5	0.5	0.2
Mexico	1.3	1.3	1.3	1.2	1.3	1.2	1.0	0.8	0.7	0.8	0.9	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	0.5	
Mongolia																	0.6	0.6	0.3	0.3	0.5	0.3	
Netherlands	0.5	0.5	0.4	0.4	0.4	0.5	0.4	0.5	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.3	0.3	0.4	0.3	0.4	0.4	0.3
New Zealand	0.6	0.6	0.7	0.7	0.8	0.6	0.4	0.6	0.5	0.6	0.6	0.4	0.6	0.6	0.7	0.6	0.6						
Nicaragua	2.0	2.5	2.3	1.8	1.8	2.4	2.0	2.6	1.9	2.2	1.4	1.7	1.6	1.6	1.5	1.5	1.0	1.1	0.9	1.1	1.0	0.9	
Norway	0.4	0.3	0.3	0.3	0.3	0.2	0.3	0.3	0.3	0.3	0.2	0.4	0.2	0.2	0.3	0.2	0.2						
Panama	0.7	0.8	0.7	1.0	0.9	0.7	0.6	1.0	0.8	0.4	0.3	0.9	0.5	0.5	0.6	0.6	0.8	0.5	0.3	0.7		0.5	
Paraguay	0.4	0.5	0.4	0.8	0.5	0.7	0.6	0.5	0.8	0.5	0.4	0.6	0.4	0.6	0.7	0.5	0.6	0.6	0.6	0.6	0.5	0.5	
Philippines	0.2	0.2	0.2	0.2			0.2	0.2	0.2	0.2	0.1	0.2			0.2		0.2	0.2	0.2	0.2			
Poland	2.8	2.7	2.6	2.5	2.2	2.1	2.0	2.0	2.0	1.9	1.8	1.6	1.7	1.5	1.4	1.3	1.3	1.2	1.1	1.1	0.9	0.8	

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Portugal			0.5	0.4				0.4	0.4	0.4	0.4	0.3	0.3	0.3	0.4	0.4	0.4	0.2	0.4	0.4			
Republic of Korea	2.2	2.5	2.8	2.7	2.6	2.7	2.5	2.6	2.5	2.6	2.3	2.4	2.2	2.2	2.1	2.1	2.0	1.9	1.8	1.9	1.8	1.7	
Republic of Moldova	0.4	0.5	0.4	0.5	0.4	0.5	0.6	0.8	0.5	0.4	0.4	0.3	0.5	0.2	0.4	0.4	0.2	0.3	0.4				
Romania	0.6	0.6	0.7	0.8	0.9	0.7	0.7	0.7	0.6	0.7	0.6	0.7	0.6	0.6	0.6	0.6	0.5	0.5	0.5	0.5			
Saint Kitts and Nevis	2.0	0	0	4.8	0	0	0	0	0	0	0	0	0	0	0	1.8	0						
Saint Lucia	0	1.1	0	0	0	0.6	0		0	0.6	0.7	0	0	1.1	1.6	0	0	0.5	0	0	0.5		
Saint Vincent and Grenadines	0	1.5	0	0	0.7	0	0	0	0	0	0	0.6	0.8	1.7	0	0	0	0	0	0.8	0.7	0	
Serbia	1.9	1.5	1.5	1.4	1.6	1.4	1.5	1.6	1.3	1.4	1.2	1.2	1.4	1.2	1.2	1.1	0.9	1.0	1.0	0.9	0.7	0.7	0.6
Singapore													0.7	0.6	0.6	0.6	0.7	0.7	0.6	0.8	0.6	0.6	0.7
Slovakia	3.1	3.0	2.9	2.8	2.7	2.6	2.3	2.3	2.2	2.3	2.0		2.0	1.8	2.2		1.6	1.6	1.4	1.1	1.1	1.1	
Slovenia	2.1	1.4	1.8	1.4	1.2	1.6	1.7	1.8	1.9	1.3	1.7	1.1	1.5	1.3	1.3	1.1	1.0	1.0	1.1	1.1	0.7		
South Africa	0.3	0.3	0.2	0.2	0.3	0.2	0.3	0.2	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.4				
Spain	0.9	0.7	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.5	0.5	0.4	0.5	0.4	0.4	0.4	0.4	0.4	0.4	0.3	0.3	0.3	
Suriname	0	0.9	0.5	0.7	0	0.2	0.5	0	0	0.3	0	0.2	0.2	0.2	0.2								
Sweden	1.4	1.3	1.2	1.1	1.2	1.1	1.0	1.0	1.1	0.8	0.8	0.9	0.9	0.8	0.6	0.7	0.7	0.7	0.8	0.7	0.6	0.6	0.7
Switzerland	0.8	0.6	0.6	0.6	0.6	0.6	0.6	0.7	0.5	0.4	0.4	0.4	0.4	0.4	0.4	0.3	0.3	0.5	0.4	0.4	0.4	0.2	
Tajikistan																	0	0					
Thailand	0.6		0.9	1.2	1.2	1.2	1.1	1.1	1.1	1.3	1.1	1.3	1.2	1.3	1.2	1.3	1.1	1.2	1.1	1.0			
Turkey										0.5	0.5	0.5	0.5	0.6	0.6	0.5	0.4	0.4	0.4	0.3			
United Kingdom		0.3	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.5	0.5		
United States of America	0.5	0.5	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.3	0.4	0.3	
Uruguay	1.7	1.5	1.6	1.3	1.5	1.4	1.1	1.3	1.9	1.3	1.6		1.4	1.2	1.5	1.6	0.9	0.9	1.3	1.4	0.9		
Uzbekistan					0.1	0				0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2			
Venezuela	0.8	0.8	0.8	0.8	0.8	0.7	0.7	0.6	0.6	0.5	0.5	0.5	0.6	0.5	0.6	0.5	0.4						

Data are presented as age-standardized mortality rate per 100,000 population; Adapted from the previously published article.²

Supplementary Table 5. Age-standardized mortality rates due to intrahepatic cholangiocarcinoma for both sexes combined by country from 2000 to 2022.

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Antigua and Barbuda	0	0	0.9	3.3	0	0	0	0	0	0	0.9	1.9	3.5	0	2.0	0.8	0	0	0	0.9	1.0	1.7	
Argentina	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.3	0.2	0.2	0.1	0.2	0.2	0.3	0.2	
Armenia								0									0.3	0.5	0.9	1.1	0.8	0.7	0.5
Australia	0.9	0.8	1.0	1.0	1.2		1.3	1.3	1.4	1.5	1.5	1.4	1.6	1.7	1.8	1.9	1.9	1.9	2.0	2.1	2.1	2.1	2.1
Austria			1.1	1.2	1.4	1.5	1.5	1.4	1.4	1.6	1.7	1.7	1.5	1.7	1.7	1.8	1.3	1.6	1.4	1.3	1.4	1.4	
Bahamas	0.5	0.5	0	0.4	0.3	0	1.1	1.0	0.3	2.1	0.3	2.3	1.3	1.0	1.2	1.1							
Belarus																			0.5				
Belgium	1.0	0.8	0.8	1.0	1.1	1.0	1.2	1.2	1.1	1.3	1.3	1.5	1.2	1.5	1.4	1.5	1.5	1.4	1.6	1.8	1.6		
Belize	0	0.8	0	0	0	0	0	0.6	0	0	0	1.3	1.1	1.0	0.4	1.6	1.2						
Brazil	0.1	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.4	0.5	0.5	
Brunei Darussalam																	1.2	1.5	1.8	2.6			
Canada	0.7	0.8	0.7	0.9	0.9	1.0	1.0	1.1	1.2	1.2	1.3	1.5	1.6	1.6	1.7	1.8	1.7	1.9	1.8	1.8	2.0	2.0	1.9
Chile	0.2	0.2	0.2	0.3	0.3	0.2	0.4	0.5	0.4	0.4	0.4	0.3	0.8	0.7	0.5	0.9	0.8	0.9	1.0	1.1	1.2	1.1	
Colombia	0.4	0.5	0.5	0.5	0.5	0.6	0.7	0.7	0.9	0.8	0.8	0.7	0.7	0.8	0.9	0.8	0.7	0.8	0.7	0.7	0.8	0.7	
Costa Rica	0.5	0.6	0.7	0.9	0.8	0.9	0.8	0.8	0.6	0.8	1.0	1.1	1.0	1.3	1.4	1.5	1.7	1.4	1.3	1.2	1.3		
Croatia	0.3	0.3	0.3	0.4	0.5	0.4	0.5	0.7	0.9	0.8	0.8	0.8	1.0	1.1	1.1	1.1	1.0	1.0	1.1	1.1	1.1	1.2	
Cuba		0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.2	0.3	0.3	0.3	0.3	0.2	0.3	0.2	
Cyprus					0.3	0.9	0.5	1.1	1.2	0.9	1.1	1.1	1.0	1.7	1.3	0.8	1.2	1.2	1.3	1.4	1.3	1.4	
Czech Republic	0.4	0.4	0.4	0.4	0.3	0.4	0.5	0.5	0.4	0.5	0.5	0.5	0.5	0.7	0.6	0.5	0.6	0.7	0.8	0.7	0.7	0.7	
Denmark	0.7	0.7	0.3	0.1	0.3	0.9	0.8	0.5	0.5	0.5	0.9	0.6	0.9	0.9	1.2	1.3	1.0	1.2	1.1	1.3	1.3	1.5	
Dominica		0	1.7	0	1.4	0	1.1	0	0	0	1.5	0.7	0	0	1.2	0	0	1.3	0	0	2.4		
Ecuador	0.4	0.4	0.3	0.1	0.2	0.2	0.2	0.2	0.6	0.6	0.7	0.5	0.6	0.7	0.6	0.9	0.8	0.6	0.5	0.7	0.6	0.8	
Estonia										1.0	1.0	0.6	0.8		0.5			1.1	1.6	1.6	1.4	1.5	1.1
France	0.8	0.9	0.9	1.0	1.0	1.2	1.2	1.2	1.4	1.4	1.5	1.5	1.6	1.7	1.7	1.7	1.8	1.9	1.8	1.8	1.8		
Georgia					0	0	0	0.1		0	0	0.6	0.3	2.2	0.5	0.4	0.5	0.7	0.8	0.8	0.9	0.8	0.5
Germany	0.5	0.6	0.7	0.7	0.7	0.9	1.0	1.0	1.1	1.2	1.2	1.1	1.1	1.1	1.1	1.1	1.2	1.3	1.3	1.4	1.4		
Greece															1.1	1.1	1.1	1.2	1.2	1.2	1.2		

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Grenada		0	0	0	0	0	0	0	0	0	0.8	0	0	0	0	0	0	0	0	0.5	0	0	
Guatemala						0.1	0.1	0	0.1	0.3	0.2	0.3	0.1	0.2	0.3	0.4	0.3	0.4	0.4	0.2	0.5	0.4	
Guyana		0.3	0.7	0.7	0.5	0	0	0.1	0.3	5.0	0	0.4	0.7	0	0.8	0.4	0.5	0.5	0.7	1.2			
Hungary	0.3	0.3	0.3	0.3	0.3	0.2	0.2	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5	0.6	0.6	0.5	0.7
Iceland	0.3	0.6	0.4	0.4	0.4	0.7	0.9	0.7	1.5	1.6									0.9	1.2	1.1	0.8	1.0
Islamic Republic of Iran																		0.2					
Ireland								1.9	1.8	2.1	2.0	2.3	1.8	2.4	2.6	2.0			2.7				
Israel	0.6	0.6	0.8	0.7	1.0	0.9	1.0	1.2	0.9	1.0	1.1	1.0	1.3	1.0	1.1	1.1	1.0	1.0	1.0	1.1	0.9	1.1	
Italy				0.5	0.6	0.6	0.7	0.7	0.8	0.8	0.9	0.9	1.0	1.0	1.0	1.0	1.1	1.1	1.1	1.2	1.1		
Jamaica	0	0	0.4	0.6	0.5	0.9	0			0.4	0.2	0.3	0.3	0.3	0.6								
Japan	0.9	0.9	0.9	0.9	1.0	0.9	0.9	0.9	1.0	0.9	0.9	1.0	0.9	0.9	0.9	1.0	1.0	1.0	0.9	1.0	0.9	1.0	
Jordan									0	0.1	0.1	0.1	0				0.1	0.1	0				
Kazakhstan																	0.1		0.1	0.2	0.3	0.2	
Kuwait	0	0.7	0.4	0.2	0.3	0	0.2	0.6	0.5	0.9	0.7	0.1	0.6	0.4	0.6	1.0	0.4	0.1	0.5	0.6			
Kyrgyzstan	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.1	0.2	0.1	0.1	0.3	0	0.1	0.2	0.5	0.5	0.6	0.5	0			
Latvia									0.2	0.3	0.4	0.6	0.7	0.9	0.7	0.9	0.7	0.9	1.0	0.8	1.0	1.2	
Lithuania		0.3	0.2	0.4	0.5	0.5	0.4	0.4	0.3	0.4	0.5	0.8	0.8	0.6	0.7	1.0	1.3	1.0	1.0	1.4	1.3	1.2	1.0
Luxembourg	0.6	0.8	1.3	1.1	0.9	1.1	1.7	1.4	1.1	1.9	1.4	1.4	1.4	2.3	1.4	1.6	1.8	1.6	0.9	1.8	1.4	1.6	1.9
Malta	0.5	0.6	1.2	1.7	1.2	1.0	0.9	0.9	1.3	0.9	1.4	1.4	1.5	0.6	1.7	0.8	2.0	1.7	2.2	2.1	1.4		
Mauritius						0.5	0.5	0.4	0.5	0.2	0.6	0.1	0.1	0.1	0.3	0.9	0.5	0.4	1.0	0.8	1.1	0.1	0.3
Mexico	0.5	0.4	0.4	0.5	0.5	0.5	0.6	0.6	0.5	0.6	0.6	0.6	0.7	0.6	0.6	0.6	0.6	0.7	0.7	0.6	0.6	0.6	
Mongolia																	0.7	2.9	3.9	2.8	1.5	2.0	
Netherlands	0.5	0.7	0.6	0.5	0.6	0.6	0.6	0.6	0.6	0.8	0.8	0.8	1.1	0.8	1.1	1.2	1.4	1.4	1.3	1.5	1.6	1.7	1.6
New Zealand	0.7	0.6	0.9	0.7	0.9	1.2	1.6	1.4	1.0	1.1	1.1	1.3	1.2	1.3	1.3	1.4	1.0						
Nicaragua	0.2	0.3	0.5	0.4	0.3	0.6	0.5	0.4	0.3	0.7	0.7	0.6	0.5	0.6	0.6	1.0	0.9	0.7	1.1	1.0	1.0	1.1	
Norway	0.4	0.4	0.2	0.3	0.8	0.9	0.9	0.7	0.9	1.0	1.0	1.3	1.3	1.1	1.2	1.4	1.3						
Panama	0.7	0.6	0.5	0.7	0.9	1.0	0.6	0.3	0.3	1.1	0.7	0.8	0.8	0.2	0.7	0.9	0.7	1.3	1.2	1.2		1.1	
Paraguay	0.1	0	0	0	0	0.1	0.2	0.2	0.3	0.1	0.3	0.1	0.3	0.4	0.4	0.4	0.4	0.4	0.4	0.2	0.3	0.4	
Philippines	0.1	0.1	0.1	0.2			0.2	0.2		0.2	0.2	0.2											
Poland	0.1	0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.3	0.3	

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Portugal			0.7	0.7				0.9	0.7	0.8	1.1	0.9	1.0	1.5	1.5	1.6	1.8	1.7	1.8	1.9			
Republic of Korea	1.4	1.6	3.1	3.0	2.9	3.0	3.2	3.5	3.6	3.2	3.7	3.6	3.6	3.5	3.4	3.3	3.0	2.7	2.6	2.6	2.5	2.3	
Republic of Moldova								0.1	0.3	0.3	0.2	0.2	0.3	0.3	0.4	0.3	0.4	0.5	0.4				
Romania	0.1	0.1	0.1	0.1	0.1	0.1	0.3	0.2	0.2	0.3	0.3	0.3	0.4	0.4	0.4	0.5	0.5	0.5	0.6	0.5			
Saint Kitts and Nevis	3.7	0	3.1	0	0	2.6	0	1.8	0	2.2	0	0	2.0	0	0	0	1.7						
Saint Lucia	0	0	0	0	0	0	0		0.6	0.5	0	0	0	0.6	0.6	0	1.1	0	0	0	0.5		
Saint Vincent and Grenadines	1.3	0	0	0	0	0	0	0	0	0	0	0	0	1.0	0	1.7	0	0	0	0.7	0.6	0.7	
Serbia																0.2							
Singapore													1.6	2.0	2.3	1.7	1.9	2.0	1.8	1.1	1.3	1.3	1.0
Slovakia											0.4		0.5	0.6	0.8		0.7	0.6	1.0	0.8	1.0	0.7	
Spain	0.8	0.8	1.0	0.9	1.0	1.1	1.2	1.2	1.3	1.3	1.4	1.5	1.5	1.6	1.6	1.6	1.7	1.8	1.8	1.8	1.8	1.8	
Suriname	0	0.2	0	0.2	0	0	0	0.3	0.3	0	0.7	0.4	0.2	0.8	0.2								
Sweden	0.4	0.4	0.5	0.5	0.5	0.4	0.5	0.4	0.5	0.7	0.7	0.6	0.8	1.0	0.8	0.9	0.7	0.7	0.9	1.0	1.0	1.2	1.2
Switzerland	0.8	0.9	1.0	0.9	1.0	1.1	1.1	1.4	1.2	1.2	1.2	1.2	1.3	1.4	1.3	1.4	1.3	1.3	1.5	1.2	1.2	1.1	
Thailand	0.2		0.1	0.2	0.1	0.1	0.1											1.6	1.6	1.7			
Turkey										0.3	0.3	0.5	0.5	0.7	0.8	0.7	0.7	0.8	0.8	0.6			
United Kingdom		1.0	1.1	1.1	1.2	1.3	1.3	1.4	1.4	1.5	1.6	1.7	1.8	1.9	1.9	2.0	2.0	2.1	2.0	2.1	2.3		
United States of America	0.7	0.7	0.7	0.8	0.8	0.8	0.8	0.8	0.9	0.9	1.0	1.0	1.1	1.1	1.1	1.2	1.2	1.3	1.3	1.3	1.3	1.4	
Uruguay	0	0.1	0.1	0.1	0.3	0.1	0.1	0.1	0.1	0.2	0.1		0.2	0.4	0.3	0.3	0.1	0.6	0.9	0.6	0.9		
Venezuela	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.4	0.3	0.4	0.4	0.4	0.5	0.4	0.4	0.4	0.5						

Data are presented as age-standardized mortality rate per 100,000 population; Adapted from the previously published article.²

Supplementary Table 6. Age-standardized mortality rates due to extrahepatic cholangiocarcinoma for both sexes combined by country from 2000 to 2022.

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Antigua and Barbuda	0	0	0	0	0	0	0	0	0	0	0	0	0	1.3	0	0	0	1.2	0	0	0	0	
Argentina	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0	0	0	0	0	0	0	0	0.1	0.1	0.1	0.1	0.1	0.1	
Armenia								0.2									0.3	0.3	0.4	0.1	0.1	0.2	0.4
Australia	0.3	0.2	0.2	0.2	0.1		0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0	0	0	0	0	0.1	0	0	0.1
Austria			0.8	0.9	0.8	0.6	0.7	0.7	0.7	0.8	0.7	0.5	0.6	0.7	0.7	0.5	0.9	0.8	0.9	0.7	0.8	0.8	
Bahamas	0	0	0	0	0	0	0	0.4	0.3	0	0	0	0.3	0	0	0							
Belarus																			0.3				
Belgium	0.1	0.1	0.1	0	0.1	0.1	0.1	0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1		
Belize	0.9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0						
Brazil	0.5	0.6	0.5	0.5	0.5	0.5	0.6	0.6	0.5	0.5	0.5	0.5	0.5	0.4	0.5	0.4	0.4	0.4	0.4	0.4	0.3	0.3	
Brunei Darussalam																	0.4	0	0	0			
Canada	0.2	0.2	0.2	0.2	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Chile	0.2	0.2	0.2	0.2	0.1	0.2	0.2	0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	
Colombia	0.2	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.1	0.1	0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.2	0.3	0.3	0.3	0.3	
Costa Rica	0.2	0.1	0.1	0.1	0.1	0.1	0	0	0	0.1	0.1	0	0	0	0.1	0.1	0	0.1	0.2	0.2	0.2		
Croatia	0.5	0.4	0.6	0.4	0.5	0.4	0.5	0.5	0.5	0.6	0.6	0.6	0.6	0.5	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	
Cuba		0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0	0.1	
Cyprus					0.1	0.1	0.1	0	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0	0.1	0.2	0.1	0	0	0.1	
Czech Republic	0.6	0.5	0.6	0.5	0.4	0.4	0.5	0.5	0.5	0.5	0.6	0.4	0.3	0.5	0.6	0.4	0.5	0.4	0.5	0.5	0.4	0.4	
Denmark	0.2	0.2	0.3	0.4	0.3	0.2	0.3	0.3	0.3	0.2	0.2	0.2	0.2	0.2	0.1	0.1	0.2	0.1	0.1	0.2	0.2	0.2	
Dominica		0	0	0	1.4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
Ecuador	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.2	0.1	0.2	0.1	0.1	0.1	0.1	0.3	0.2	0.2	0.2	0.1	0.1	0.1	
Estonia										0.2	0.4	0.3	0.3		0.2			0.3	0.3	0.5	0.7	0.6	0.9
France	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1		
Georgia					0	0	0	0		0	0	0.1	0	0	0	0	0.2	0.1	0.2	0.2	0.2	0.2	0.2
Germany	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.4	0.5	0.5	0.7	0.8	0.8	0.9	0.8	0.9	1.0	0.9	0.9	0.9		
Greece															0.1	0.2	0.1	0.1	0.1	0.1	0.1		

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Grenada		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.9	0	0	0	0	0	
Guatemala						0	0	0	0	0	0.1	0.1	0.1	0.1	0.1	0.1	0	0	0	0	0	0	
Guyana		0	0.3	0.2	0	0	0.2	0.4	0	0	0	0	0	0	0	0	0	0	0	0.2			
Hungary	0.8	0.9	0.8	0.8	0.9	0.4	0.5	0.4	0.3	0.3	0.3	0.3	0.4	1.2	1.4	1.4	1.4	1.4	1.5	1.4	1.4	1.2	1.3
Iceland	0	0	1.0	0	0.2	0.8	0.4	0.4	0.2	0.3									0.5	0.3	0.5	0.2	1.0
Islamic Republic of Iran																		0					
Ireland								0.1	0.2	0.1	0.1	0.1	0.2	0.1	0.1	0.1			0				
Israel	0.1	0.1	0	0.1	0	0	0	0.1	0.1	0.1	0.1	0.1	0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	
Italy				0.3	0.3	0.3	0.2	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.1	0.2	0.2		
Jamaica	0	0	0	0	0	0	0			0.2	0	0	0	0.1	0.1								
Japan	2.8	2.9	2.8	2.7	2.7	2.7	2.7	2.6	2.6	2.5	2.5	2.5	2.5	2.4	2.3	2.2	2.1	2.1	2.1	2.0	2.0	2.0	
Jordan									0	0	0	0	0				0	0	0				
Kazakhstan																	0.1		0.1	0.1	0.1	0.1	
Kuwait	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.1			
Kyrgyzstan	0.2	0.1	0.1	0	0	0.1	0	0.1	0.1	0	0.1	0.1	0.1	0.1	0	0.1	0.1	0	0.1	0.2			
Latvia									0.5	0.4	0.3	0.2	0.3	0.2	0.4	0.3	0.3	0.4	0.2	0.3	0.4	0.3	
Lithuania		0.5	0.4	0.5	0.5	0.4	0.4	0.3	0.4	0.3	0.2	0.4	0.3	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.4	0.2	0.5
Luxembourg	0.1	0.1	0.1	0	0.1	0	0	0	0.2	0	0.1	0.2	0	0.2	0	0.1	0	0.1	0.1	0	0.1	0.1	
Malta	0.9	0.5	0.2	0	0	0.2	0.3	0.1	0.1	0.2	0.3	0	0.1	0	0	0.4	0	0	0	0.2	0.6		
Mauritius						0.1	0.2	0	0.1	0.1	0	0.1	0	0.1	0	0	0.1	0	0	0.1	0	0	0
Mexico	0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	
Mongolia																	0.5	0.5	0.2	0.3	0.1	0.1	
Netherlands	0.5	0.4	0.5	0.5	0.4	0.5	0.4	0.5	0.5	0.4	0.4	0.4	0.4	0.5	0.5	0.4	0.4	0.4	0.3	0.2	0.3	0.3	0.2
New Zealand	0.3	0.3	0.3	0.5	0.3	0.2	0.1	0.2	0.3	0.4	0.2	0.2	0.2	0.3	0.2	0.2	0.3						
Nicaragua	0	0.1	0	0.2	0.2	0.1	0.1	0.1	0.2	0.1	0.1	0	0.1	0.1	0.1	0	0.1	0.1	0.2	0.1	0.1	0.1	
Norway	0.2	0.3	0.2	0.4	0.1	0.1	0.1	0.2	0.1	0	0.1	0.1	0	0	0.1	0.1	0.1						
Panama	0.1	0	0.1	0	0	0.2	0	0.1	0	0.1	0	0	0	0.1	0	0	0	0.1	0	0.1		0.1	
Paraguay	0.1	0.2	0.1	0.2	0	0.1	0.1	0	0	0.1	0	0.1	0	0.1	0.1	0.1	0.1	0.1	0.3	0.2	0.2	0.2	
Philippines	0	0	0	0			0	0		0	0	0											
Poland	0.2	0.2	0.2	0.2	0.1	0.1	0.1	0.2	0.1	0.2	0.2	0.2	0.2	0.1	0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.1	

Country name	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Portugal			0.6	0.5				0.5	0.6	0.4	0.5	0.4	0.5	0.3	0.1	0.1	0.1	0.1	0.1	0.2			
Republic of Korea	0.6	0.9	1.7	1.8	1.8	1.8	1.8	1.9	1.8	1.8	1.8	1.3	1.4	1.3	1.5	1.6	2.1	2.4	2.5	2.4	2.5	2.4	
Republic of Moldova								0.1	0.1	0.1	0.1	0.1	0	0.1	0.1	0.2	0.2	0.1	0.1				
Romania	0.3	0.2	0.3	0.3	0.2	0.3	0.2	0.2	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.4	0.3	0.3			
Saint Kitts and Nevis	0	0	0	0	0	0	0	2.0	0	0	0	0	0	0	0	0	0						
Saint Lucia	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0.5	0	0	0	0.4		
Saint Vincent and Grenadines	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Serbia																0.4							
Singapore													0	0	0	0	0	0	0.1	0.1	0.1	0.1	0.1
Slovakia											0.3		0.3	0.7	0.3		0.4	0.4	0.4	0.4	0.4	0.3	
Spain	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0	0	0	0	0.1	0.1	0.2	0.2	0.1	0.2	0.2	0.1	0.2	0.2	
Suriname	0	0	0	0.3	0.2	0.3	0	0	0.5	0.3	0.2	0.2	0.2	0.2	0.5								
Sweden	0.7	0.8	0.8	0.7	0.7	0.9	0.9	0.7	0.7	0.7	0.6	0.7	0.7	0.7	0.8	0.8	0.8	0.9	0.8	0.8	0.8	0.8	0.8
Switzerland	0.4	0.4	0.4	0.4	0.3	0.3	0.3	0.3	0.3	0.2	0.3	0.4	0.4	0.3	0.3	0.3	0.3	0.4	0.4	0.4	0.5	0.4	
Thailand	0.7		1.5	2.7	1.5	1.4	1.6											2.5	2.6	2.5			
Turkey										0.3	0.3	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1			
United Kingdom		0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0	0.1	0.1	0	0	0.1	0.1		
United States of America	0.2	0.2	0.2	0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	
Uruguay	0.2	0.3	0.2	0.2	0.2	0.2	0.1	0.1	0	0.1	0.1		0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.4		
Venezuela	0.1	0.2	0.1	0.2	0.1	0.1	0.1	0.1	0	0.1	0	0.1	0.1	0.1	0	0.1	0.1						

Data are presented as age-standardized mortality rate per 100,000 population; Adapted from the previously published article.²

Supplementary Table 7. Locally weighted regression-smoothed mortality rates due to biliary tract cancers by sex from 2000 to 2022.

Year	Both sexes		Males	Females
	CR (95% CI)	ASR (95% CI)	ASR (95% CI)	ASR (95% CI)
2000	3.8 (3.1–4.5)	2.8 (2.5–3.1)	2.7 (2.3–3.0)	2.9 (2.7–3.2)
2001	3.9 (3.3–4.4)	2.8 (2.6–3.0)	2.7 (2.4–3.0)	2.9 (2.7–3.1)
2002	4.0 (3.5–4.4)	2.8 (2.6–3.0)	2.7 (2.5–2.9)	2.9 (2.7–3.0)
2003	4.0 (3.6–4.4)	2.8 (2.6–2.9)	2.7 (2.5–2.9)	2.8 (2.7–3.0)
2004	4.1 (3.7–4.4)	2.7 (2.6–2.9)	2.7 (2.5–2.9)	2.8 (2.6–2.9)
2005	4.1 (3.7–4.5)	2.7 (2.6–2.9)	2.7 (2.5–2.9)	2.7 (2.6–2.9)
2006	4.2 (3.8–4.5)	2.7 (2.5–2.8)	2.7 (2.5–2.9)	2.7 (2.5–2.8)
2007	4.2 (3.8–4.6)	2.6 (2.5–2.8)	2.7 (2.5–2.9)	2.6 (2.5–2.8)
2008	4.2 (3.8–4.6)	2.6 (2.4–2.8)	2.6 (2.4–2.9)	2.6 (2.4–2.7)
2009	4.2 (3.9–4.6)	2.6 (2.4–2.7)	2.6 (2.4–2.9)	2.5 (2.4–2.7)
2010	4.3 (3.9–4.7)	2.6 (2.4–2.7)	2.6 (2.4–2.9)	2.5 (2.4–2.7)
2011	4.3 (4.0–4.7)	2.5 (2.4–2.7)	2.6 (2.5–2.8)	2.5 (2.3–2.6)
2012	4.4 (4.0–4.7)	2.5 (2.4–2.7)	2.7 (2.5–2.8)	2.5 (2.3–2.6)
2013	4.4 (4.0–4.8)	2.5 (2.4–2.7)	2.7 (2.5–2.9)	2.4 (2.3–2.6)
2014	4.5 (4.1–4.8)	2.5 (2.4–2.7)	2.7 (2.5–2.9)	2.4 (2.3–2.5)
2015	4.5 (4.2–4.9)	2.5 (2.3–2.7)	2.7 (2.5–2.9)	2.4 (2.2–2.5)
2016	4.6 (4.3–5.0)	2.5 (2.4–2.7)	2.7 (2.5–2.9)	2.4 (2.2–2.5)
2017	4.8 (4.4–5.1)	2.5 (2.4–2.7)	2.7 (2.5–2.9)	2.4 (2.2–2.5)
2018	4.9 (4.6–5.3)	2.5 (2.4–2.7)	2.7 (2.6–2.9)	2.4 (2.3–2.5)
2019	5.1 (4.7–5.5)	2.6 (2.4–2.7)	2.8 (2.6–3.0)	2.4 (2.3–2.6)
2020	5.3 (4.8–5.8)	2.6 (2.4–2.8)	2.8 (2.5–3.1)	2.4 (2.2–2.7)
2021	5.5 (4.8–6.2)	2.7 (2.4–3.0)	2.9 (2.5–3.2)	2.5 (2.2–2.8)
2022	5.8 (4.8–6.8)	2.7 (2.3–3.1)	2.9 (2.4–3.4)	2.5 (2.2–2.9)

Data are presented as locally weighted regression rates per 100,000 population with 95% confidence intervals (CIs).

ASR, age-standardized mortality rate; CR, crude mortality rate; CI, confidence interval.

Adapted from the previously published article.²

Supplementary Table 8. Locally weighted regression-smoothed mortality rates due to intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, and gallbladder cancer by sex from 2000 to 2022.

Year	ASR (95% CI)		
	Both sexes	Males	Females
Intrahepatic cholangiocarcinoma			
2000	0.5 (0.4–0.6)	0.6 (0.5–0.8)	0.5 (0.4–0.5)
2001	0.6 (0.5–0.6)	0.7 (0.6–0.8)	0.5 (0.4–0.5)
2002	0.6 (0.5–0.7)	0.7 (0.6–0.8)	0.5 (0.5–0.6)
2003	0.6 (0.6–0.7)	0.8 (0.7–0.8)	0.6 (0.5–0.6)
2004	0.7 (0.6–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.6)
2005	0.7 (0.7–0.8)	0.8 (0.8–0.9)	0.6 (0.6–0.7)
2006	0.7 (0.7–0.8)	0.9 (0.8–1.0)	0.6 (0.6–0.7)
2007	0.8 (0.7–0.8)	0.9 (0.8–1.0)	0.7 (0.6–0.7)
2008	0.8 (0.7–0.9)	0.9 (0.9–1.0)	0.7 (0.6–0.7)
2009	0.8 (0.8–0.9)	1.0 (0.9–1.1)	0.7 (0.7–0.8)
2010	0.9 (0.8–0.9)	1.0 (0.9–1.1)	0.8 (0.7–0.8)
2011	0.9 (0.9–1.0)	1.1 (1.0–1.1)	0.8 (0.7–0.8)
2012	0.9 (0.9–1.0)	1.1 (1.0–1.2)	0.8 (0.8–0.9)
2013	1.0 (0.9–1.0)	1.1 (1.1–1.2)	0.9 (0.8–0.9)
2014	1.0 (1.0–1.1)	1.2 (1.1–1.3)	0.9 (0.8–0.9)
2015	1.0 (1.0–1.1)	1.2 (1.1–1.3)	0.9 (0.9–0.9)
2016	1.1 (1.0–1.1)	1.2 (1.2–1.3)	0.9 (0.9–1.0)
2017	1.1 (1.0–1.1)	1.3 (1.2–1.3)	0.9 (0.9–1.0)
2018	1.1 (1.0–1.1)	1.3 (1.2–1.3)	0.9 (0.9–1.0)
2019	1.1 (1.0–1.2)	1.3 (1.2–1.4)	1.0 (0.9–1.0)
2020	1.1 (1.0–1.2)	1.3 (1.2–1.4)	1.0 (0.9–1.0)
2021	1.1 (1.0–1.2)	1.3 (1.1–1.4)	1.0 (0.9–1.0)
2022	1.1 (1.0–1.3)	1.3 (1.1–1.5)	1.0 (0.9–1.1)
Extrahepatic cholangiocarcinoma			
2000	0.5 (0.4–0.7)	0.7 (0.5–0.8)	0.5 (0.4–0.6)
2001	0.5 (0.4–0.6)	0.7 (0.5–0.8)	0.5 (0.4–0.5)
2002	0.5 (0.5–0.6)	0.7 (0.6–0.8)	0.5 (0.4–0.5)
2003	0.5 (0.5–0.6)	0.7 (0.6–0.8)	0.4 (0.4–0.5)
2004	0.5 (0.5–0.6)	0.6 (0.6–0.7)	0.4 (0.4–0.5)
2005	0.5 (0.4–0.6)	0.6 (0.5–0.7)	0.4 (0.4–0.5)
2006	0.5 (0.4–0.6)	0.6 (0.5–0.7)	0.4 (0.4–0.5)
2007	0.5 (0.4–0.5)	0.6 (0.5–0.7)	0.4 (0.3–0.4)
2008	0.5 (0.4–0.5)	0.6 (0.4–0.7)	0.4 (0.3–0.4)
2009	0.4 (0.4–0.5)	0.5 (0.4–0.6)	0.4 (0.3–0.4)
2010	0.4 (0.3–0.5)	0.5 (0.4–0.6)	0.3 (0.3–0.4)

Year	ASR (95% CI)		
	Both sexes	Males	Females
2011	0.4 (0.3–0.5)	0.5 (0.4–0.6)	0.3 (0.3–0.4)
2012	0.4 (0.3–0.5)	0.5 (0.4–0.6)	0.3 (0.3–0.4)
2013	0.4 (0.3–0.5)	0.5 (0.4–0.6)	0.3 (0.3–0.4)
2014	0.4 (0.3–0.5)	0.5 (0.4–0.6)	0.3 (0.3–0.4)
2015	0.4 (0.4–0.5)	0.5 (0.4–0.6)	0.3 (0.3–0.4)
2016	0.4 (0.4–0.5)	0.6 (0.5–0.7)	0.4 (0.3–0.4)
2017	0.5 (0.4–0.5)	0.6 (0.5–0.7)	0.4 (0.3–0.4)
2018	0.5 (0.4–0.5)	0.6 (0.5–0.7)	0.4 (0.3–0.4)
2019	0.5 (0.4–0.5)	0.6 (0.5–0.7)	0.4 (0.3–0.4)
2020	0.5 (0.4–0.6)	0.6 (0.5–0.7)	0.4 (0.3–0.4)
2021	0.5 (0.3–0.6)	0.6 (0.4–0.8)	0.4 (0.3–0.5)
2022	0.5 (0.3–0.6)	0.6 (0.4–0.9)	0.4 (0.2–0.5)
Gallbladder cancer			
2000	1.1 (1.0–1.3)	0.8 (0.7–0.9)	1.4 (1.2–1.6)
2001	1.1 (1.0–1.2)	0.7 (0.7–0.8)	1.4 (1.2–1.5)
2002	1.1 (1.0–1.1)	0.7 (0.7–0.8)	1.3 (1.2–1.4)
2003	1.0 (1.0–1.1)	0.7 (0.7–0.8)	1.3 (1.2–1.4)
2004	1.0 (0.9–1.1)	0.7 (0.7–0.8)	1.2 (1.1–1.3)
2005	1.0 (0.9–1.0)	0.7 (0.6–0.7)	1.2 (1.1–1.3)
2006	0.9 (0.9–1.0)	0.7 (0.6–0.7)	1.1 (1.0–1.2)
2007	0.9 (0.8–1.0)	0.7 (0.6–0.7)	1.1 (1.0–1.2)
2008	0.9 (0.8–0.9)	0.6 (0.6–0.7)	1.0 (0.9–1.1)
2009	0.8 (0.8–0.9)	0.6 (0.6–0.7)	1.0 (0.9–1.1)
2010	0.8 (0.7–0.9)	0.6 (0.5–0.7)	1.0 (0.9–1.1)
2011	0.8 (0.7–0.8)	0.6 (0.5–0.6)	0.9 (0.8–1.0)
2012	0.8 (0.7–0.8)	0.6 (0.5–0.6)	0.9 (0.8–1.0)
2013	0.7 (0.7–0.8)	0.6 (0.5–0.6)	0.9 (0.8–1.0)
2014	0.7 (0.6–0.8)	0.6 (0.5–0.6)	0.8 (0.7–0.9)
2015	0.7 (0.6–0.7)	0.5 (0.5–0.6)	0.8 (0.7–0.9)
2016	0.7 (0.6–0.7)	0.5 (0.5–0.6)	0.8 (0.7–0.9)
2017	0.6 (0.6–0.7)	0.5 (0.5–0.6)	0.7 (0.7–0.8)
2018	0.6 (0.6–0.7)	0.5 (0.4–0.5)	0.7 (0.6–0.8)
2019	0.6 (0.5–0.7)	0.5 (0.4–0.5)	0.7 (0.6–0.8)
2020	0.6 (0.5–0.7)	0.5 (0.4–0.6)	0.7 (0.6–0.8)
2021	0.6 (0.5–0.7)	0.5 (0.4–0.6)	0.7 (0.5–0.9)
2022	0.6 (0.4–0.8)	0.5 (0.3–0.6)	0.7 (0.5–0.9)

Data are presented as locally weighted regression rates per 100,000 population with 95% confidence intervals (CIs).

ASR, age-standardized mortality rate; CI, confidence interval.

Adapted from the previously published article.²

Supplementary Table 9. Average annual percent change in age-standardized mortality rates due to biliary tract cancers by country from 2013 to 2022.

Country name	Period	Both sexes		Males		Females	
		AAPC% (95% CI)	p	AAPC% (95% CI)	p	AAPC% (95% CI)	p
Argentina	2013–2021	-1.3 (-1.5 to -1.0)	<0.001	-0.8 (-1.2 to -0.4)	<0.001	-1.6 (-2.1 to -1.0)	<0.001
Armenia	2013–2022	3.4 (-0.1 to 7.6)	0.064	6.9 (-1.9 to 19.2)	0.105	1.6 (-4.3 to 8.2)	0.550
Australia	2013–2022	1.8 (1.2 to 2.5)	<0.001	2.0 (1.1 to 3.0)	<0.001	1.6 (0.7 to 2.6)	<0.001
Austria	2013–2021	-2.5 (-4.1 to -0.9)	<0.001	-0.8 (-3.3 to 1.8)	0.487	-4.3 (-7.3 to -1.4)	0.004
Belgium	2013–2020	1.1 (-2.0 to 4.5)	0.417	1.8 (-1.1 to 5.1)	0.210	0.4 (-5.1 to 6.5)	0.829
Bosnia and Herzegovina	2014–2022	-2.5 (-7.8 to 3.3)	0.322	-4.9 (-9.6 to -0.4)	0.030	-0.7 (-5.1 to 4.1)	0.726
Brazil	2013–2021	-0.6 (-1.1 to 0)	0.054	0.8 (-0.4 to 2.3)	0.159	-1.4 (-2.2 to -0.5)	0.001
Brunei Darussalam	2013–2019	18.9 (1.6 to 51.4)	0.032	N/A		18.7 (-3.7 to 63.9)	0.078
Canada	2013–2022	0.6 (-0.6 to 1.9)	0.281	1.4 (0.6 to 2.1)	<0.001	0.3 (-0.7 to 1.2)	0.543
Chile	2013–2021	-3.7 (-5.0 to -2.5)	<0.001	-2.4 (-3.9 to -0.8)	0.003	-4.4 (-5.9 to -2.8)	<0.001
Colombia	2013–2021	-0.4 (-1.6 to 1.0)	0.530	0.8 (-0.5 to 2.2)	0.237	-1.1 (-1.7 to -0.3)	0.001
Costa Rica	2013–2020	3.3 (1.3 to 5.7)	0.001	1.9 (-0.4 to 4.5)	0.106	5.4 (2.3 to 8.7)	<0.001
Croatia	2013–2021	-0.7 (-1.4 to -0.1)	0.027	1.5 (-0.8 to 4.0)	0.202	-2.8 (-6.3 to 0.7)	0.102
Cuba	2013–2021	-4.0 (-6.6 to -1.5)	0.002	-1.2 (-10.3 to 8.9)	0.716	-6.1 (-10.6 to -1.7)	0.011
Cyprus	2013–2021	-4.1 (-10.5 to 3.9)	0.235	-3.5 (-10.2 to 4.1)	0.286	-1.8 (-12.2 to 10.7)	0.657
Czech Republic	2013–2021	-2.8 (-3.9 to -1.6)	<0.001	-1.5 (-3.4 to 0.5)	0.123	-3.7 (-5.9 to -1.5)	0.001
Denmark	2013–2021	2.1 (-0.5 to 4.9)	0.100	1.8 (-1.6 to 5.7)	0.289	2.5 (-0.2 to 5.4)	0.070
Ecuador	2013–2021	-2.1 (-5.1 to 1.1)	0.203	-1.2 (-6.3 to 4.2)	0.624	-3.5 (-6.1 to -0.1)	0.044
Estonia	2013–2022	6.8 (0.2 to 15.1)	0.041	7.7 (-0.7 to 18.5)	0.067	6.5 (0.9 to 13.1)	0.022
Finland	2013–2021	1.1 (0.2 to 2.2)	0.023	3.0 (2.1 to 4.0)	<0.001	-0.3 (-1.7 to 1.1)	0.496
France	2013–2020	-0.3 (-1.0 to 0.4)	0.390	-0.2 (-1.2 to 0.8)	0.727	-0.5 (-1.2 to 0.2)	0.153
Georgia	2013–2022	1.2 (-4.4 to 7.6)	0.699	-0.9 (-5.1 to 5.5)	0.870	-1.2 (-6.8 to 5.7)	0.792
Germany	2013–2020	1.1 (0.6 to 1.5)	<0.001	1.9 (0.8 to 3.0)	0.002	0.3 (-0.3 to 0.9)	0.262
Greece	2014–2020	0.7 (-1.1 to 2.7)	0.439	0.8 (-1.3 to 3.1)	0.464	0.6 (-2.1 to 3.3)	0.708
Guatemala	2013–2021	1.0 (-2.2 to 3.3)	0.521	2.0 (-3.6 to 7.7)	0.461	-0.3 (-3.0 to 1.6)	0.621
Guyana	2013–2019	5.4 (-20.0 to 42.3)	0.500	1.8 (-17.5 to 26.7)	0.843	9.2 (-11.6 to 38.7)	0.260
Hungary	2013–2022	-2.4 (-3.6 to -1.1)	<0.001	-1.3 (-2.9 to 0.2)	0.091	-3.1 (-4.8 to -1.6)	<0.001

Country name	Period	Both sexes		Males		Females	
		AAPC% (95% CI)	p	AAPC% (95% CI)	p	AAPC% (95% CI)	p
Iceland	2013–2022	15.4 (3.4 to 35)	0.012	14.8 (-0.6 to 44.2)	0.056	14.3 (3.7 to 31.5)	0.010
Ireland	2013–2020	-12.7 (-37.6 to 14.3)	0.234	-12.5 (-38.6 to 15.7)	0.239	-12.5 (-33.2 to 8.7)	0.184
Israel	2013–2021	0.1 (-2.1 to 2.5)	0.904	0.8 (-2.9 to 4.8)	0.633	-0.5 (-3.1 to 2.1)	0.707
Italy	2013–2020	-0.2 (-1.9 to 1.5)	0.737	0.7 (-0.2 to 1.6)	0.112	-1.3 (-3.3 to 0.8)	0.203
Japan	2013–2021	-2.2 (-2.7 to -1.7)	<0.001	-1.6 (-2.2 to -1.0)	<0.001	-3.0 (-3.6 to -2.6)	<0.001
Kazakhstan	2013–2021	1.4 (-5.4 to 9.5)	0.558	3.3 (-2.5 to 10.6)	0.230	0 (-5.1 to 5.7)	0.976
Kuwait	2013–2019	8.0 (-4.1 to 24.1)	0.173	13.6 (-13.3 to 57.6)	0.248	4.5 (-7.3 to 20.0)	0.422
Kyrgyzstan	2013–2019	4.1 (-1.8 to 10.2)	0.240	-1.4 (-15.2 to 17.2)	0.870	10.3 (3.6 to 18.8)	0.004
Latvia	2013–2021	1.8 (-0.9 to 4.8)	0.194	0.2 (-4.0 to 4.6)	0.881	2.7 (-1.7 to 7.6)	0.217
Lithuania	2013–2022	3.5 (-0.5 to 7.9)	0.086	3.0 (-0.9 to 8.3)	0.131	3.4 (0.4 to 6.5)	0.023
Luxembourg	2013–2022	-1.3 (-6.3 to 3.9)	0.475	-1.5 (-6.9 to 4.3)	0.622	-1.5 (-8.0 to 5.6)	0.611
Malta	2013–2020	9.4 (4.3 to 19.2)	<0.001	16.4 (6.4 to 35.4)	<0.001	8.9 (-7.7 to 32.6)	0.267
Mauritius	2013–2022	-7.5 (-18.5 to 2.4)	0.088	-12.7 (-19.3 to -6.1)	0.001	-5.1 (-16.9 to 6.2)	0.229
Mexico	2013–2021	-2.5 (-3.4 to -1.5)	<0.001	-1.7 (-2.7 to -0.5)	0.004	-3.0 (-4.3 to -1.6)	<0.001
Netherlands	2013–2022	2.3 (0.2 to 4.6)	0.036	2.4 (0.9 to 4.0)	<0.001	2.3 (-0.3 to 5.3)	0.083
Nicaragua	2013–2021	-0.3 (-3.7 to 3.5)	0.880	0.7 (-5.0 to 7.8)	0.729	-1.0 (-3.2 to 1.5)	0.426
Panama	2013–2021	9.1 (6.6 to 11.7)	<0.001	8.1 (4.1 to 12.9)	<0.001	9.2 (3.1 to 16.3)	0.001
Paraguay	2013–2021	0.6 (-1.4 to 2.7)	0.497	4.2 (-4.6 to 15)	0.256	-2.2 (-7.4 to 3.6)	0.419
Poland	2013–2021	-2.4 (-3.2 to -1.6)	<0.001	0 (-0.8 to 0.8)	0.857	-3.4 (-4.5 to -2.4)	<0.001
Portugal	2013–2019	2.4 (0.5 to 4.4)	0.012	3.5 (1.8 to 5.3)	<0.001	1.0 (-2.1 to 4.2)	0.504
Republic of Korea	2013–2021	-2.2 (-2.6 to -1.9)	<0.001	-2.0 (-2.5 to -1.5)	<0.001	-2.9 (-3.2 to -2.6)	<0.001
Romania	2013–2019	0.1 (-1.7 to 2.1)	0.827	0.3 (-1.2 to 1.8)	0.711	0 (-2.0 to 2.1)	0.959
Serbia	2013–2022	-2.6 (-7.0 to 0.5)	0.088	-1.5 (-4.4 to 1.5)	0.278	-5.2 (-7.4 to -3.3)	<0.001
Singapore	2013–2022	-3.3 (-4.7 to -1.8)	<0.001	-2.6 (-5.8 to 0.9)	0.151	-4.1 (-6.0 to -2.2)	<0.001
Slovakia	2013–2021	-2.5 (-6.2 to 1.7)	0.222	-2.7 (-7.1 to 1.5)	0.179	-2.7 (-4.7 to -0.6)	0.017
Slovenia	2013–2020	-2.4 (-6.5 to 1.7)	0.272	-2.3 (-7.4 to 3.1)	0.391	-3.6 (-10.7 to 4.1)	0.294
Spain	2013–2021	-0.2 (-0.6 to 0.3)	0.314	0.2 (-0.7 to 1.4)	0.471	-0.7 (-1.2 to -0.2)	0.006
Sweden	2013–2022	0.8 (0 to 1.7)	0.067	2.3 (0.7 to 4.1)	0.005	-0.4 (-2.4 to 1.6)	0.637

Country name	Period	Both sexes		Males		Females	
		AAPC% (95% CI)	p	AAPC% (95% CI)	p	AAPC% (95% CI)	p
Switzerland	2013–2021	-1.1 (-2.0 to 0.2)	0.098	1.1 (-2.1 to 4.6)	0.461	-2.4 (-8.1 to 4.2)	0.284
Thailand	2013–2019	5.6 (0.6 to 11.7)	0.028	5.9 (0.8 to 12.3)	0.023	5.3 (0.5 to 11.3)	0.031
Turkey	2013–2019	-3.1 (-4.8 to -1.3)	<0.001	-1.6 (-2.5 to -0.6)	0.001	-4.5 (-7.4 to -1.4)	0.004
United Kingdom	2013–2020	2.5 (1.7 to 3.2)	<0.001	2.3 (1.2 to 3.5)	<0.001	2.5 (1.7 to 3.4)	<0.001
United States of America	2013–2021	1.9 (1.5 to 2.3)	<0.001	2.0 (1.3 to 2.8)	<0.001	2.0 (1.6 to 2.4)	<0.001
Uruguay	2013–2020	3.1 (-0.4 to 7.1)	0.079	5.3 (2.6 to 8.4)	<0.001	1.2 (-3.7 to 6.2)	0.631
Uzbekistan	2013–2019	4.8 (-4.3 to 16.1)	0.256	4.4 (-11.8 to 23.6)	0.451	6.0 (-5.4 to 21)	0.239

Data are presented as average annual percent change (AAPC) with 95% confidence intervals (CIs).

AAPC, average annual percent change; CI, confidence interval; N/A, non-available.

Adapted from the previously published article.²

Supplementary Table 10. Average annual percent change in age-standardized mortality rates due to gallbladder cancer by country from 2013 to 2022.

Country name	Period	Both sexes		Males		Females	
		AAPC% (95% CI)	p	AAPC% (95% CI)	p	AAPC% (95% CI)	p
Argentina	2013–2021	-2.4 (-3.2 to -1.6)	<0.001	-2.5 (-4.7 to -0.3)	0.024	-2.4 (-3.9 to -0.9)	0.002
Armenia	2013–2022	-4.2 (-12.1 to 3.7)	0.235	-1.7 (-12.0 to 8.8)	0.658	-5.0 (-13.7 to 3.9)	0.217
Australia	2013–2022	-1.4 (-3.1 to 0.4)	0.123	-0.4 (-3.4 to 2.8)	0.834	-1.7 (-3.8 to 0.5)	0.122
Austria	2013–2021	-7.1 (-14.3 to 0.2)	0.053	-5.3 (-16.2 to 6.2)	0.299	-7.7 (-14.8 to -0.9)	0.034
Belgium	2013–2020	-4.1 (-10.0 to 2.0)	0.166	3.3 (-3.4 to 10.9)	0.326	-5.2 (-11.2 to -1.0)	0.014
Bosnia and Herzegovina	2014–2022	-1.9 (-8.3 to 5.1)	0.437	-5.7 (-8.4 to -2.9)	<0.001	0.1 (-8.2 to 9.5)	0.965
Brazil	2013–2021	-3.4 (-4.6 to -2.0)	<0.001	-2.3 (-3.6 to -0.9)	0.007	-3.6 (-4.8 to -2.4)	<0.001
Brunei Darussalam	2013–2019	-20 (-47.1 to 16.8)	0.246	N/A		N/A	
Canada	2013–2022	-3.1 (-4.6 to -1.6)	<0.001	-2.5 (-4.5 to -0.6)	0.010	-3.4 (-5.9 to -0.9)	0.008
Chile	2013–2021	-5.1 (-6.4 to -3.8)	<0.001	-4.2 (-6.0 to -2.4)	<0.001	-5.4 (-6.9 to -3.9)	<0.001
Colombia	2013–2021	-2.3 (-4.5 to 0.1)	0.058	-0.1 (-8.5 to 9.6)	0.986	-3.0 (-5.3 to -0.6)	0.018
Costa Rica	2013–2020	3.7 (-1.5 to 10.1)	0.167	11.2 (-2.4 to 33.2)	0.099	1.3 (-3.9 to 7.1)	0.601
Croatia	2013–2021	-4.3 (-7.5 to -1.1)	0.011	-3.3 (-7.2 to 0.7)	0.09	-4.5 (-11.9 to 3.0)	0.184
Cuba	2013–2021	-7.2 (-14.6 to -0.2)	0.048	-4.5 (-12.1 to 3.2)	0.218	-8.6 (-14.1 to -3.4)	0.002
Cyprus	2013–2021	-8.5 (-22.0 to 4.4)	0.153	N/A		N/A	
Czech Republic	2013–2021	-6.4 (-8.9 to -4.2)	<0.001	-5.6 (-11.2 to -0.1)	0.046	-6.7 (-9.3 to -4.4)	<0.001
Denmark	2013–2021	-3.5 (-17.4 to 15.6)	0.69	1.9 (-11.8 to 19.9)	0.734	6.4 (-5.4 to 21.7)	0.269
Ecuador	2013–2021	-4.5 (-8.3 to -0.5)	0.029	-4.2 (-10.4 to 2.2)	0.161	-5.7 (-11.6 to 0.4)	0.068
Estonia	2013–2022	-4.0 (-9.8 to 1.3)	0.130	-6.5 (-16.7 to 3.7)	0.171	-3.6 (-10.8 to 3.1)	0.274
Finland	2013–2021	-2.4 (-6.2 to 1.4)	0.188	-1.9 (-7.5 to 4.0)	0.505	-2.4 (-4.1 to -0.7)	0.007
France	2013–2020	-6.5 (-8.3 to -4.8)	<0.001	-2.3 (-5.1 to 0.8)	0.136	-8.8 (-11.9 to -6.0)	<0.001
Georgia	2013–2022	3.8 (-3.7 to 13.6)	0.233	13.1 (7.3 to 20.7)	<0.001	3.9 (-5.6 to 14.2)	0.326
Germany	2013–2020	-5.1 (-5.9 to -4.4)	<0.001	-5.3 (-7.0 to -3.6)	<0.001	-4.9 (-7.1 to -2.7)	<0.001
Greece	2014–2020	-10.8 (-16.8 to -4.9)	<0.001	-9.5 (-15.0 to -4.7)	<0.001	-12.0 (-20.3 to -4.3)	0.001
Guatemala	2013–2021	-6.0 (-9.9 to -0.3)	0.037	-6.8 (-12.4 to 1.1)	0.102	-4.4 (-7.8 to -0.4)	0.029
Guyana	2013–2019	-15.0 (-31.3 to 1.8)	0.074	N/A		-1.7 (-13.8 to 13.2)	0.845
Hungary	2013–2022	-7.7 (-10.2 to -5.6)	<0.001	-7.1 (-11.7 to -2.9)	<0.001	-8.0 (-9.5 to -6.6)	<0.001

Country name	Period	Both sexes		Males		Females	
		AAPC% (95% CI)	p	AAPC% (95% CI)	p	AAPC% (95% CI)	p
Ireland	2013–2020	-4.7 (-18.3 to 10.4)	0.452	-4.5 (-25.6 to 22.5)	0.661	-5.2 (-13.3 to 3.4)	0.229
Israel	2013–2021	-1.3 (-4.9 to 1.6)	0.301	-5.5 (-9.4 to -1.5)	0.006	1.4 (-5.4 to 7.9)	0.582
Italy	2013–2020	-6.4 (-8.1 to -4.8)	<0.001	-6.4 (-7.6 to -5.2)	<0.001	-6.5 (-8.5 to -4.5)	<0.001
Japan	2013–2021	-3.6 (-4.2 to -3.1)	<0.001	-2.9 (-3.6 to -2.3)	<0.001	-4.1 (-4.8 to -3.4)	<0.001
Kazakhstan	2013–2021	-5.2 (-9.7 to -0.6)	0.027	-2.2 (-12.7 to 10.1)	0.699	-6.6 (-14.1 to 0.9)	0.076
Kuwait	2013–2019	-13.6 (-38.1 to 14.7)	0.276	N/A		-19.0 (-55.3 to 25.5)	0.257
Kyrgyzstan	2013–2019	3.8 (-1.0 to 9.3)	0.128	-3.3 (-15.8 to 14.2)	0.676	5.4 (-10.6 to 25.2)	0.425
Latvia	2013–2021	2.1 (-4.0 to 9.2)	0.473	-9.6 (-26.2 to 14.5)	0.244	3.4 (-3.9 to 12.1)	0.312
Lithuania	2013–2022	-3.4 (-9.0 to 2.0)	0.189	-16.4 (-24.4 to -8.9)	<0.001	-0.5 (-8.5 to 7.5)	0.836
Malta	2013–2020	-8.1 (-29.2 to 19.6)	0.533	N/A		N/A	
Mauritius	2013–2022	-8.8 (-15.7 to -2.8)	0.006	N/A		-8.5 (-17.8 to -0.2)	0.044
Mexico	2013–2021	-3.4 (-5.7 to -1.2)	0.006	-2.0 (-6.0 to 2.1)	0.284	-3.5 (-4.8 to -2.4)	<0.001
Netherlands	2013–2022	-0.7 (-3.0 to 1.6)	0.547	1.1 (-3.8 to 6.8)	0.646	-1.4 (-4.9 to 2.1)	0.407
Nicaragua	2013–2021	-6.4 (-9.6 to -3.1)	<0.001	-5.6 (-12.0 to 0.3)	0.059	-6.2 (-10.3 to -2.1)	0.002
Panama	2013–2021	-1.9 (-11.1 to 7.8)	0.710	2.2 (-7.8 to 13.5)	0.515	-4.3 (-17.8 to 9.8)	0.489
Paraguay	2013–2021	-2.3 (-5.5 to 1.2)	0.172	6.3 (-4.2 to 20.7)	0.185	-5.7 (-9.7 to -1.6)	0.008
Poland	2013–2021	-7.0 (-8.0 to -6.1)	<0.001	-4.4 (-5.7 to -3.2)	<0.001	-7.6 (-9.4 to -6.0)	<0.001
Portugal	2013–2019	2.4 (-5.9 to 11.8)	0.554	3.5 (-4.2 to 12.6)	0.394	2.0 (-6.5 to 11.6)	0.618
Republic of Korea	2013–2021	-3.1 (-4.5 to -1.7)	<0.001	-3.0 (-3.9 to -2.1)	<0.001	-3.7 (-4.5 to -2.7)	<0.001
Romania	2013–2019	-5.9 (-8.1 to -3.8)	<0.001	-5.4 (-12.7 to 2.0)	0.139	-6.5 (-9.1 to -4.1)	<0.001
Serbia	2013–2022	-7.4 (-9.0 to -6.0)	<0.001	-5.8 (-7.9 to -3.5)	<0.001	-8.5 (-10.2 to -7.1)	<0.001
Singapore	2013–2022	2.0 (-1.6 to 6.2)	0.226	2.9 (-3.0 to 10.8)	0.265	1.2 (-3.7 to 7.1)	0.497
Slovakia	2013–2021	-8.1 (-11.8 to -4.5)	<0.001	-8.0 (-13.2 to -2.9)	0.002	-8.1 (-14.7 to -1.7)	0.019
Slovenia	2013–2020	-5.0 (-12.0 to 2.6)	0.169	-5.5 (-11.6 to 0.8)	0.088	-5.3 (-14.3 to 4.6)	0.246
Spain	2013–2021	-3.7 (-5.4 to -2.0)	<0.001	-2.0 (-4.6 to 0.7)	0.128	-4.7 (-7.1 to -2.4)	<0.001
Sweden	2013–2022	-0.4 (-4.0 to 3.3)	0.823	1.0 (-2.9 to 5.5)	0.581	-0.8 (-5.5 to 4.0)	0.647
Switzerland	2013–2021	-5.0 (-12.4 to 4.8)	0.170	-6.4 (-13.1 to 1.0)	0.075	-2.6 (-8.2 to 3.6)	0.384
Thailand	2013–2019	-3.4 (-4.8 to -1.9)	<0.001	-4.3 (-7.1 to -1.4)	0.004	-2.2 (-4.8 to 0.7)	0.142

Country name	Period	Both sexes		Males		Females	
		AAPC% (95% CI)	p	AAPC% (95% CI)	p	AAPC% (95% CI)	p
Turkey	2013–2019	-9.1 (-12.6 to -5.7)	<0.001	-6.4 (-12.1 to -0.4)	0.038	-10.7 (-14.9 to -6.7)	<0.001
United Kingdom	2013–2020	2.3 (1.3 to 3.4)	<0.001	3.0 (1.6 to 4.6)	<0.001	2.2 (0.1 to 4.4)	0.042
United States of America	2013–2021	-2.3 (-3.2 to -1.3)	<0.001	-2.4 (-3.8 to -1.0)	<0.001	-2.1 (-2.9 to -1.3)	<0.001
Uruguay	2013–2020	-3.1 (-16.2 to 11.7)	0.543	-1.3 (-15.7 to 16.1)	0.853	-3.1 (-15.0 to 9.9)	0.540
Uzbekistan	2013–2019	1.4 (-4.5 to 8.0)	0.579	2.8 (-12.0 to 21.2)	0.661	0.8 (-4.9 to 7.7)	0.692

Data are presented as average annual percent change (AAPC) with 95% confidence intervals (CIs).

AAPC, average annual percent change; CI, confidence interval; N/A, non-available.

Adapted from the previously published article.²

Supplementary Table 11. Average annual percent change in age-standardized mortality rates due to intrahepatic cholangiocarcinoma by country from 2013 to 2022.

Country name	Period	Both sexes		Males		Females	
		AAPC% (95% CI)	p	AAPC% (95% CI)	p	AAPC% (95% CI)	p
Argentina	2013–2021	0.3 (-5.1 to 6.4)	0.888	0.7 (-3.4 to 5.3)	0.767	-0.3 (-10.1 to 10.6)	0.934
Armenia	2016–2022	6.1 (-1.2 to 15.0)	0.096	8.2 (-4.2 to 26.3)	0.172	9.4 (2.0 to 19.4)	0.016
Australia	2013–2022	2.4 (1.9 to 3.0)	<0.001	2.5 (1.5 to 3.6)	<0.001	2.2 (1.0 to 3.5)	<0.001
Austria	2013–2021	-2.9 (-5.5 to -0.3)	0.031	-2.1 (-4.6 to 0.5)	0.106	-4.1 (-7.7 to -0.4)	0.027
Belgium	2013–2020	2.1 (-0.3 to 4.8)	0.092	2.7 (0 to 5.5)	0.051	1.4 (-3.3 to 6.8)	0.529
Brazil	2013–2021	0.9 (-0.8 to 2.7)	0.267	2.0 (-0.7 to 5.1)	0.119	-0.1 (-1.3 to 1.3)	0.925
Canada	2013–2022	1.7 (0.5 to 3.1)	0.007	2.8 (1.2 to 4.3)	<0.001	1.4 (0.6 to 2.3)	<0.001
Chile	2013–2021	7.6 (4.5 to 11.6)	<0.001	8.2 (4.8 to 12.9)	<0.001	6.2 (3.6 to 10.7)	<0.001
Colombia	2013–2021	-1.2 (-3.7 to 1.4)	0.324	0.4 (-5.3 to 7.2)	0.802	-2.3 (-4.5 to -0.1)	0.044
Costa Rica	2013–2020	-1.0 (-4.9 to 3.4)	0.466	-3.1 (-6.4 to 0.4)	0.072	2 (-0.5 to 4.8)	0.121
Croatia	2013–2021	0.7 (-1.0 to 2.5)	0.346	3.9 (1.9 to 6.1)	<0.001	-2.1 (-5.8 to 1.0)	0.155
Cuba	2013–2021	-2.9 (-9.7 to 4.4)	0.323	-2.8 (-9.7 to 4.5)	0.354	-3.1 (-10.0 to 4.4)	0.348
Cyprus	2013–2021	-1.6 (-4.1 to 2.6)	0.415	-3.0 (-6.6 to 2.4)	0.274	3.3 (-5.8 to 15.6)	0.431
Czech Republic	2013–2021	1.0 (-1.5 to 3.7)	0.390	2.1 (-2.2 to 6.8)	0.302	-0.2 (-3.7 to 3.5)	0.885
Denmark	2013–2021	3.9 (-1.9 to 10.5)	0.155	3.8 (-4.4 to 13.4)	0.274	4.3 (0.3 to 8.9)	0.039
Ecuador	2013–2021	-1.3 (-9.5 to 8.1)	0.761	0.3 (-7.6 to 9.3)	0.899	-2.6 (-9.9 to 5.4)	0.435
Estonia	2014–2022	11.4 (7.1 to 17.2)	<0.001	5.8 (1.9 to 10.7)	0.006	15.5 (2.7 to 37.0)	0.012
France	2013–2020	1.1 (0.3 to 2.0)	0.006	0.6 (-0.5 to 1.9)	0.207	1.6 (0.8 to 2.4)	<0.001
Georgia	2013–2022	-8.9 (-14.4 to -2.4)	0.005	-9.0 (-15.2 to -1.8)	0.006	-8.7 (-15.2 to -0.6)	0.038
Germany	2013–2020	4.0 (3.2 to 4.9)	<0.001	4.3 (3.4 to 5.4)	<0.001	3.6 (0.4 to 7.1)	0.028
Greece	2014–2020	1.7 (0.5 to 2.9)	0.003	1.3 (-0.9 to 3.8)	0.214	2.2 (-1.1 to 5.8)	0.184
Guatemala	2013–2021	6.0 (-1.8 to 16.3)	0.124	9.5 (1.6 to 20.2)	0.020	2.8 (-7.1 to 15.7)	0.499
Hungary	2013–2022	2.6 (-0.7 to 6.1)	0.110	1.8 (-0.3 to 4.2)	0.092	3.7 (1.1 to 6.4)	0.002
Israel	2013–2021	-0.3 (-5.0 to 4.8)	0.894	1.1 (-1.5 to 4.0)	0.344	-1.7 (-9.2 to 6.3)	0.599
Italy	2013–2020	2.3 (0.9 to 3.8)	0.002	2.8 (2.1 to 3.7)	<0.001	1.4 (-1.3 to 4.4)	0.271
Japan	2013–2021	0.3 (-0.2 to 0.7)	0.227	0.2 (-0.9 to 1.2)	0.723	-0.2 (-1.3 to 0.9)	0.637

Country name	Period	Both sexes		Males		Females	
		AAPC% (95% CI)	p	AAPC% (95% CI)	p	AAPC% (95% CI)	p
Kuwait	2013–2019	-3.3 (-20.7 to 19.2)	0.807	3.0 (-14.8 to 26.3)	0.713	N/A	
Kyrgyzstan	2013–2019	8.8 (-24.8 to 78.4)	0.502	0 (-37.8 to 79.6)	0.853	N/A	
Latvia	2013–2021	4.3 (-0.1 to 8.1)	0.058	4.0 (-1.8 to 10.6)	0.172	3.9 (-8.6 to 19.8)	0.445
Lithuania	2013–2022	8.3 (2.3 to 15.5)	0.01	10.5 (1.0 to 22.8)	0.035	6.1 (2.0 to 10.6)	0.002
Luxembourg	2013–2022	-1.4 (-7.1 to 4.7)	0.637	-2.1 (-10.2 to 7.4)	0.636	-1.8 (-9.7 to 6.8)	0.689
Malta	2013–2020	7.4 (-7.5 to 30.2)	0.282	4.6 (-7.5 to 22.0)	0.418	7.3 (-16.4 to 45.5)	0.463
Mauritius	2013–2022	-6.7 (-32.0 to 67.9)	0.627	N/A		N/A	
Mexico	2013–2021	-0.7 (-1.6 to 0.3)	0.181	-0.5 (-2.5 to 2.0)	0.494	-1.1 (-2.6 to 0.6)	0.163
Netherlands	2013–2022	7.9 (4.1 to 11.8)	<0.001	5.0 (2.3 to 8.3)	<0.001	9.3 (4.0 to 15.3)	<0.001
Nicaragua	2013–2021	6.5 (1.0 to 13.7)	0.024	14.6 (3.1 to 31.3)	0.010	7.8 (0.9 to 17.6)	0.026
Panama	2013–2021	12.4 (5.4 to 27.1)	<0.001	12.9 (1.3 to 28.6)	0.032	6.0 (-17.0 to 38.7)	0.394
Paraguay	2013–2021	-0.7 (-6.2 to 5.3)	0.793	2.5 (-15.7 to 24.5)	0.666	-2.5 (-14.1 to 10.8)	0.630
Poland	2013–2021	6.1 (5.3 to 7.0)	<0.001	7.0 (3.1 to 11.8)	<0.001	5.4 (1.5 to 10.0)	0.007
Portugal	2013–2019	4.0 (2.9 to 5.2)	<0.001	5.5 (4.8 to 6.3)	<0.001	1.9 (-2.1 to 6.5)	0.329
Republic of Korea	2013–2021	-5.0 (-6.1 to -3.9)	<0.001	-4.6 (-5.8 to -3.6)	<0.001	-5.8 (-7.4 to -4.1)	<0.001
Romania	2013–2019	7.9 (4.4 to 12.2)	<0.001	6.4 (2.3 to 11.3)	0.003	7.8 (6.4 to 9.9)	<0.001
Singapore	2013–2022	-7.8 (-13.1 to -2.4)	0.008	-6.6 (-13.3 to 0.2)	0.058	-8.7 (-12.9 to -4.9)	<0.001
Slovakia	2013–2021	3.3 (-4.5 to 13.3)	0.357	0.5 (-10.4 to 14.8)	0.881	6.3 (-0.2 to 14.8)	0.055
Spain	2013–2021	1.4 (0.9 to 2.1)	<0.001	1.7 (0.6 to 3.1)	0.001	1.4 (-0.7 to 3.7)	0.182
Sweden	2013–2022	2.3 (0.3 to 5.4)	0.024	4.0 (2.2 to 6.5)	<0.001	1.1 (-3.3 to 6.6)	0.553
Switzerland	2013–2021	-2.7 (-5.6 to 0.4)	0.077	-0.7 (-2.6 to 1.4)	0.521	-5.1 (-10.4 to 0.2)	0.059
Turkey	2013–2019	-1.5 (-5.9 to 3.6)	0.507	-1.6 (-6.7 to 4.4)	0.521	-2.2 (-4.0 to 0.1)	0.066
United Kingdom	2013–2020	2.3 (1.7 to 2.8)	<0.001	2.0 (1.0 to 3.1)	<0.001	2.4 (1.7 to 3.2)	<0.001
United States of America	2013–2021	3.2 (2.6 to 3.8)	<0.001	2.8 (2.0 to 3.7)	<0.001	3.6 (2.0 to 5.4)	<0.001
Uruguay	2013–2020	18.7 (5.9 to 40.1)	0.004	21.7 (-1.1 to 71.1)	0.062	14.0 (0.1 to 37.4)	0.049

Data are presented as average annual percent change (AAPC) with 95% confidence intervals (CIs).

AAPC, average annual percent change; CI, confidence interval; N/A, non-available.

Adapted from the previously published article.²

Supplementary Table 12. Average annual percent change in age-standardized mortality rates due to extrahepatic cholangiocarcinoma by country from 2013 to 2022.

Country name	Period	Both sexes		Males		Females	
		AAPC% (95% CI)	p	AAPC% (95% CI)	p	AAPC% (95% CI)	p
Argentina	2013–2021	13.4 (8.8 to 20.3)	<0.001	10.3 (2.2 to 24.3)	0.012	13.7 (11.1 to 17.5)	<0.001
Armenia	2016–2022	-1.5 (-35.3 to 39.6)	0.879	-9.4 (-37.5 to 29.3)	0.387	0.6 (-37.1 to 45.2)	0.974
Australia	2013–2022	0.1 (-9.1 to 10.5)	0.961	2.0 (-10.4 to 16.6)	0.645	-2.9 (-11.8 to 6.8)	0.551
Austria	2013–2021	2.2 (-2.1 to 7.2)	0.306	4.6 (-0.5 to 11.1)	0.079	-1.2 (-7.8 to 6.2)	0.749
Belgium	2013–2020	-6.6 (-11.0 to -2.3)	0.001	-12.7 (-20.3 to -5.6)	<0.001	2.5 (-4.9 to 11.0)	0.486
Brazil	2013–2021	-4.9 (-7.5 to -2.5)	<0.001	-3.9 (-6.8 to -1.0)	0.014	-5.9 (-8.6 to -3.2)	<0.001
Canada	2013–2022	-4.0 (-8.0 to -0.2)	0.036	-3.1 (-5.6 to -0.5)	0.018	-5.6 (-14.6 to 3.3)	0.185
Chile	2013–2021	-2.9 (-12.1 to 6.8)	0.453	-2.9 (-12.1 to 7.5)	0.571	-2.4 (-14.1 to 10.3)	0.597
Colombia	2013–2021	17.7 (13.8 to 26.5)	<0.001	13.1 (9.5 to 18.4)	<0.001	21.8 (18.2 to 29.2)	<0.001
Costa Rica	2013–2020	30.3 (19.9 to 48.7)	<0.001	29.2 (17.0 to 52.0)	<0.001	28.9 (17.2 to 52.4)	<0.001
Croatia	2013–2021	1.3 (-1.7 to 4.4)	0.33	0.5 (-4.7 to 6.3)	0.835	2.1 (-5.1 to 10.3)	0.48
Cuba	2013–2021	-4.2 (-15.6 to 8.4)	0.446	-4.5 (-19.6 to 13.7)	0.489	-4.2 (-13.3 to 5.4)	0.361
Czech Republic	2013–2021	-2.4 (-6.2 to 1.6)	0.219	-2.7 (-7.3 to 2.6)	0.255	-2.4 (-6.9 to 2.4)	0.300
Denmark	2013–2021	3.5 (-4.8 to 13.6)	0.331	5.1 (-10.1 to 23.8)	0.406	1.3 (-10.6 to 17.1)	0.774
Ecuador	2013–2021	1.1 (-7.1 to 8.5)	0.801	4.5 (-15.4 to 31.8)	0.621	-5.0 (-12.2 to 2.4)	0.126
Estonia	2014–2022	22.5 (18.9 to 27.5)	<0.001	13.4 (2.1 to 28.4)	0.015	N/A	
France	2013–2020	-5.3 (-10.1 to -0.5)	0.032	-5.3 (-11.9 to 1.4)	0.119	-5.2 (-14.5 to 4.2)	0.246
Georgia	2013–2022	32.9 (22.4 to 52.2)	<0.001	33.9 (19.2 to 64.1)	<0.001	N/A	
Germany	2013–2020	2.3 (0.9 to 3.8)	<0.001	2.9 (1.0 to 4.9)	0.005	1.7 (-0.4 to 4.0)	0.12
Greece	2014–2020	-16.3 (-27.3 to -6.5)	0.004	-16.2 (-34.6 to 1.2)	0.066	-13 (-29.6 to 2.3)	0.082
Hungary	2013–2022	0.8 (-1.8 to 2.8)	0.561	-0.3 (-2.9 to 2.7)	0.869	-0.7 (-3.1 to 1.7)	0.581
Israel	2013–2021	5.6 (1.4 to 13.1)	0.011	9.1 (0.1 to 22.1)	0.047	7.3 (-5.6 to 24.7)	0.274
Italy	2013–2020	-3.6 (-7.1 to -0.1)	0.046	-2.8 (-5.7 to 0.1)	0.052	-4.6 (-8.5 to -0.9)	0.018
Japan	2013–2021	-2.4 (-2.8 to -2.0)	<0.001	-1.7 (-2.2 to -1.3)	<0.001	-3.4 (-4.1 to -2.8)	<0.001
Kyrgyzstan	2013–2019	19.3 (2.3 to 45.2)	0.025	N/A		8.4 (-8.0 to 25.7)	0.357
Latvia	2013–2021	-0.5 (-8.4 to 7.8)	0.866	-4.8 (-17.9 to 8)	0.34	2.4 (-14.9 to 22.7)	0.772

Country name	Period	Both sexes		Males		Females	
		AAPC% (95% CI)	p	AAPC% (95% CI)	p	AAPC% (95% CI)	p
Lithuania	2013–2022	10.3 (4.5 to 17.9)	<0.001	7.7 (-9.6 to 29.5)	0.238	11.9 (4.2 to 22.3)	0.001
Mexico	2013–2021	3.5 (-1.7 to 9.8)	0.178	5.0 (-6.8 to 21.0)	0.306	2.4 (-2.1 to 7.6)	0.274
Netherlands	2013–2022	-8.3 (-12.0 to -5.1)	<0.001	-8.4 (-11.9 to -5.2)	<0.001	-8.1 (-13.8 to -2.9)	0.004
Nicaragua	2013–2021	13.9 (3.3 to 29.2)	0.01	N/A		16.1 (-0.8 to 47.3)	0.060
Paraguay	2013–2021	17.4 (6.9 to 35.4)	0.002	17.9 (1.2 to 48.6)	0.042	N/A	
Poland	2013–2021	-2.7 (-7.0 to 1.7)	0.198	-4.3 (-14.2 to 6.1)	0.29	-2.3 (-4.4 to 0.1)	0.062
Portugal	2013–2019	-9 (-19.3 to 3.2)	0.136	-7.9 (-17.8 to 3.9)	0.215	-11.2 (-20 to -1.7)	0.015
Republic of Korea	2013–2021	8.5 (7.1 to 10.4)	<0.001	8.7 (6.6 to 11.9)	<0.001	7.8 (5.6 to 11.2)	<0.001
Romania	2013–2019	-1.2 (-6.8 to 4.9)	0.632	-1.9 (-8.4 to 5.3)	0.561	-0.3 (-5.4 to 5.2)	0.945
Singapore	2013–2022	18.9 (8.2 to 55.4)	<0.001	N/A		N/A	
Slovakia	2013–2021	-6.2 (-11.9 to -0.1)	0.046	-3.9 (-9.2 to 1.9)	0.184	-7.5 (-13.5 to 0)	0.049
Spain	2013–2021	3.9 (0 to 7.8)	0.053	0.5 (-4.0 to 5.4)	0.827	6.8 (-1.7 to 15.7)	0.101
Sweden	2013–2022	2.1 (-0.5 to 4.8)	0.091	1.2 (-0.5 to 3.1)	0.163	2.4 (-3.5 to 9.0)	0.251
Switzerland	2013–2021	4.6 (1.6 to 8)	0.005	6.4 (-0.2 to 14.6)	0.062	2.2 (-7.0 to 13.4)	0.528
Turkey	2013–2019	-5.6 (-8.7 to -2.4)	0.001	-3.4 (-9.4 to 3.2)	0.279	-7.5 (-12.4 to -2.4)	0.006
United Kingdom	2013–2020	6.2 (2.5 to 9.6)	<0.001	5.1 (-2.7 to 12.3)	0.196	7.1 (4.4 to 9.6)	<0.001
United States of America	2013–2021	5.2 (4.4 to 6.2)	<0.001	5.5 (4.7 to 6.6)	<0.001	4.8 (3.0 to 7.3)	<0.001
Uruguay	2013–2020	15.4 (2.8 to 29.8)	0.014	10.9 (-6.4 to 32.2)	0.192	21.8 (-9.5 to 94.2)	0.155

Data are presented as average annual percent change (AAPC) with 95% confidence intervals (CIs).

AAPC, average annual percent change; CI, confidence interval; N/A, non-available.

Adapted from the previously published article.²