BMJ Open

Impact of the COVID-19 pandemic on mortality trends in Japan: a reversal in 2021?

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-071785
Article Type:	Original research
Date Submitted by the Author:	16-Jan-2023
Complete List of Authors:	Tanaka, Hirokazu; National Cancer Center Japan, Division of Surveillance and Policy Evaluation Togawa, Kayo; National Cancer Center Japan Katanoda, Kota; National Cancer Center Japan
Keywords:	COVID-19, Epidemiology < TROPICAL MEDICINE, Public health < INFECTIOUS DISEASES, Demography < TROPICAL MEDICINE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Impact of the COVID-19 pandemic on mortality trends in Japan: a reversal in 2021?

Hirokazu Tanaka, Kayo Togawa, Kota Katanoda*

All authors: Division of Surveillance and Policy Evaluation, National Cancer Center Institute for Cancer Control, 5-1-1, Tsukiji, Chuo-ku, Tokyo, 104-0045, Japan

***Corresponding author:** Hirokazu Tanaka
Division of Surveillance and Policy Evaluation, National Cancer Center Institute for Cancer Control
5-1-1, Tsukiji, Chuo-ku, Tokyo, 104-0045, JAPAN
E-mail: hitanak@ncc.go.jp
Phone: +81335475201

Figures and Tables: 3 figures**; Word count**: 1,808 words

Declarations of interest: none

Abstract (249 words)

Objective: The COVID-19 pandemic led to an increase in mortality in most countries in 2020, deviating from prior decreasing trends. This study investigated long-term mortality trends, focusing on the period of the COVID-19 pandemic in Japan.

Design: We analysed Japanese age-standardized mortality rates (ASMRs) from 1995 to 2021 using vital statistics.

Main outcome measures: The cause-specific annual ASMR changes were calculated in comparison with the previous year.

Results: There was a general downward trend in overall ASMR for both sexes until 2020 followed by a small increase in 2021. The all-cause ASMR (per 100 000 persons) decreased from 1352.3 to 1328.8 in 2020 (-1.74% from 2019), and increased to 1356.3 in 2021 in men (+2.07% from 2020). Similarly, the all-cause ASMR decreased from 746.0 to 722.1 in 2020 (-3.20% from 2019), and increased to 737.9 (+2.19% from 2020) in 2021 in women. ASMRs from malignant neoplasms, pneumonia, accidents, and suicide (men only) continued to decrease during the COVID-19 pandemic while the trend of cardiovascular mortality increased in 2021. Analysis of ASMR changes revealed that COVID-19, senility, cardiovascular disease, and 'other causes not classified as major causes' contributed to the all-cause mortality increase in 2021.

Conclusions: In Japan, the decreasing trend in overall mortality continued in 2020 despite the COVID-19 pandemic. However, an approximately 2% mortality increase was observed in 2021, which was attributable to COVID-19, senility, cardiovascular disease, and 'other causes'. The year 2021 may be a turning point of mortality trends in Japan, although continued monitoring is warranted.

Funding: Grants-in-Aid for Cancer Control Policy from the Ministry of Health, Labor, and Welfare, Japan (20EA1017); Japan Agency for Medical Research and Development (AMED: 22ck0106778h0001)

Keywords: COVID-19 pandemic; mortality trends; vital statistics; increase in mortality; Japan

What is already known on this topic

-In most high-income countries, life expectancy in 2020 was shorter than that before 2020 due to the COVID-19 pandemic.

-No nationwide mortality data that discussed the impact of the COVID-19 pandemic on mortality trends was reported in Japan.

What this study adds

-From 1995 to 2020, we found a general downward trend in overall age-standardized mortality rates (ASMRs) for both sexes (except 2011, the year of Great East Japan earthquake) until 2020.

-An increase was observed in 2021 in the annual mortality rate in Japan, though the impact of COVID-19 pandemic on mortality still seems to be limited.

-The analysis of ASMR changes revealed that COVID-19, senility, cardiovascular disease, and 'other causes not classified as major causes' contributed to all-cause mortality increase in 2021.

-Taking the rapidly increasing number of COVID-19 cases in 2022 into consideration, further analysis is warranted for the year 2022, which may reveal increases in deaths from COVID-19 and overall mortality compared to 2020 and 2021.

Introduction

Approximately three years into the pandemic, Japan has been hit by COVID-19. Although the Japanese government did not introduce strict COVID-19 restrictions such as lockdown, people's daily lives were affected, as were the lives of health-care workers since the first declaration of a state of emergency in April 2020. Careful assessment of the impact of the pandemic on population health would aid in the evaluation of efforts during the pandemic and identify lessons, not only for Japan but also globally.

In most high-income countries, life expectancy in 2020 was shorter than before due to the pandemic.[1] For example, reductions in life expectancy in 2020 were observed in Russia, the U.S., Spain, England/Wales, Netherlands, Sweden, and France.[2] However, in Japan, life expectancy was not shortened in 2020 according to the Japanese Ministry of Health, Labour and Welfare (MHLW),[1,3] a deviation from the decreasing trend in most countries.[1]

Reasons for the prolonged life expectancy in 2020 despite the pandemic are unclear, but one reason could be that Japan did not experience as large a number of COVID-19 cases in that year. However, Japan experienced a six-fold increase in the number of reported cases from 2020 to 2021: 234 109 cases in 2020 and 1 492 874 cases in 2021.[4] Thus, annual mortality rate in 2021 in Japan may be different from the stable downward trend before 2020. This study aimed to explore the long-term mortality trends and cause-specific contributions during the COVID-19 pandemic in Japan focusing on the years 2020 and 2021.

Methods

To evaluate the trends in the number of COVID-19 cases in Japan, we extracted data on the daily number of reported COVID-19 cases from 16 January 2020 (the first case confirmed) to 28 November 2022 from Japanese government records.[4] The numbers of deaths (5-year age intervals) between 1995 and 2021 were extracted from the vital statistics (complete deaths record) in Japan managed by MHLW.[3] The 2021 complete mortality data was published in September 2022.[3] The vital statistics cover all Japanese deaths that occurred in Japan. The relevant population data were also collected from the vital statistics and population census.

We calculated age-standardized mortality rates (ASMRs) for all causes of death combined and cause-specific deaths for major causes from 1995 to 2021 to assess trends in mortality rates. ASMRs were calculated using the 2015 Japan Standard Population. We further calculated the annual percent changes in ASMRs before and during the COVID-19 pandemic (the years of 2020 and 2021). Causes of death (the International Classification of Diseases 10th revision: ICD-10) included: certain infectious and parasitic diseases (A00-B99), malignant neoplasms (C00-C97), heart diseases (I01-I02.0, I05-I09, I20-I25, I27, I30-I52), cerebrovascular diseases (I60-I69), pneumonia (J12-J18), liver disease (K70-K76), senility (R54), accidents (V01-X59), suicide (X60-X84), and COVID-19 (U07). These classifications were based on the leading causes of death reported by the official mortality statistics by MHLW.[3]

To analyse the contribution of the cause of death to annual all-cause ASMR changes, the cause-specific ASMR changes in comparison with those of the previous year were calculated for six periods from 2015–2016 to 2020–2021.

Patient and public involvement

No patients were involved in this study.

Results

Figure 1 shows trends in the daily number of reported COVID-19 cases in Japan since 16 January 2020. The peak of reported COVID-19 cases was observed in August 2022 (7th COVID-19 wave). The annual number of reported COVID-19 cases increased rapidly from 2020 to 2022.

Figure 2 shows the trends in all-cause ASMRs (per 100 000 persons) between 1995 and 2021. Supplement Table 1 shows the trends in number of deaths in Japan between 1995 and 2021. After the Great East Japan earthquake occurred in 2011, ASMRs continued decreasing until 2020, then increased in 2021 in both sexes. For men, all-cause ASMRs (per 100 000 persons) were 1352.3 in 2019 (-1.69% from 2018), 1328.8 in 2020 (-1.74% from 2019), and 1356.3 in 2021 (+2.07% from 2020). For women, all-cause ASMRs were 746.0 in 2019 (-1.39% from 2018), 722.1 in 2020 (-3.20% from 2019), and 737.9 in 2021 (+2.19% from 2020). Age-specific analyses also showed stable to slightly increased mortality trends during the period of COVID-19 pandemic (Supplement Figure 1). Supplement Figure 2 shows the trends in cause-specific ASMRs between 1995 and 2021. For men, COVID-19 ASMRs were 3.8 in 2020 and 17.5 in 2021. For women, COVID-19 ASMRs were 1.5 in 2020 and 7.7 in 2021. ASMRs from malignant neoplasms, pneumonia, accidents, and suicide (men only) decreased during the COVID-19 pandemic in Japan while the trend of cardiovascular disease (heart disease and cerebrovascular disease combined) increased in 2021. In addition, the trend of suicide in women increased in 2020. Supplement Figure 3 shows trends in malignant neoplasms ASMRs by cancer site. Trends in most malignant neoplasms were decreased or stable, which was not altered compared to the trends before 2020.

Figure 3 shows the cause-specific contribution to annual changes in all-cause ASMR. The analysis of annual ASMR changes revealed that decreases in malignant neoplasms, pneumonia, heart disease, and cerebrovascular diseases continuously contributed to substantial annual mortality reductions for both sexes during 2015–2019; however, the contributions to reduction disappeared for cardiovascular disease from 2020 to 2021. COVID-19 (+13.7 per 100 000 for men and +6.2 per 100 000 for women in comparisons with the previous year) and senility (+7.4 per 100 000 for men and +8.1 per 100,000 for women in comparisons with the previous year) largely contributed to the mortality increases from 2020 to 2021. Also, ‘other causes not classified major causes’ contributed to all-cause mortality increase as well from 2020 to 2021.

Discussion

This is the first study to comprehensively report on mortality analysis in Japan since MHLW published the 2021 complete mortality data for the Japanese population. We found that the numbers of deaths from COVID-19 were 9 732 (1.32% of all deaths) for men and 7 034 (1.00% of all deaths) for women in 2021, a substantial increase from the year 2020 (2 094 deaths for men and 1 372 deaths for women). The number of deaths in the population due to diagnosed COVID-19 was relatively low compared to many other high-income countries.[5] In both men and women, all-cause ASMR decreased gradually every year from 2011 to 2020 and increased from 2020 to 2021, with a slightly greater decrease in women than in men between 2019 and 2020. In Japan, declining trends in all-cause mortality reversed in 2021 for the first time since the Great East Japan earthquake occurred in 2011.

The mortality trend varied by cause of death. The patterns of mortality change during the COVID-19 pandemic could be classified into the following three categories: (1) stable mortality decline (e.g. certain infectious and parasitic diseases, malignant neoplasms, and pneumonia), (2) stable mortality increase (e.g. senility), and (3) reversal of decreasing mortality trend (heart diseases, cerebrovascular diseases, suicide for women). Considering these changes, a substantial mortality increase from COVID-19 and senility resulted in an all-cause mortality increase in 2021 while malignant neoplasms and pneumonia contributed to mortality declines.

Recorded mortality from malignant neoplasms declined during the COVID-19 pandemic, despite that patients diagnosed with a cancer regardless of COVID-19 status were required to postpone non-urgent surgeries, suspend outpatient visits, and change treatment methods. Indeed, the numbers of cancer diagnoses, the cancer screening, outpatient visits, and surgical procedures in 2020 have been reported to be lower than those before 2019.[6-9] Those reports have raised deep concern about potential consequences, such as delays in diagnosis and care, decreased patient survival, and increased population mortality; however, our findings revealed a decrease in 2020 and no obvious change in cancer mortality, at least in 2021. Nevertheless, further monitoring is necessary because the delays in diagnosis and treatment can exert a belated effect on mortality.

We found that the ASMR from cardiovascular disease increased in 2021. The loss of reduction trends of cardiovascular disease partially resulted in increasing all-cause mortality in 2021 for both sexes. This is supported by another study reporting excess deaths from cardiovascular disease from April to May 2021.[10] As a direct pathway, the COVID-19 pandemic may have caused an increase in the prevalence of severe heart disease for the Japanese population because COVID-19 is suggested to be a risk factor for acute myocardial infarction and ischemic stroke.[11] In addition, the pandemic might have induced a delay in emergency transport and delay in arrival at hospital, resulting in the loss of timely treatment. This may be an indirect pathway through which mortality reductions of cardiovascular disease stagnated in Japan.

A substantial increase in mortality due to senility has been occurring since the mid-2000s, independent of the pandemic. This can be interpreted as a result of the rapid aging of the Japanese

population. Although we applied age-standardization for mortality analysis, the increase in the absolute number of deaths from senility, especially for the oldest old (85 years and over), resulted in an increase in ASMR. During the pandemic, however, changes in patterns or places of medical care may have resulted in more physicians reporting senility as the cause of death, especially deaths at home. Indeed, excess deaths from senility at home have been observed since May 2020.[10] As such, for the elderly, both direct and indirect death by COVID-19 may be miscoded to senility, which contributed to excess deaths in 2021. The sharp increase in deaths by 'other causes not classified as major causes' in 2021 (Figure 3) may have occurred by a similar mechanism. Therefore, our findings suggest that senility and 'other causes not classified as major causes' may largely represent the excess deaths in Japan during the pandemic. This may also include underdiagnosis and potential misclassification of causes of death.

We found clear declines in mortality from infectious diseases (excluding COVID-19) and infectious pneumonia since the pandemic began in Japan. This is likely because the countermeasures for COVID-19 such as of wearing a mask, hand hygiene, and social distancing prevented these diseases. In addition, clear mortality declines due to accidents were observed probably because fatal traffic accidents decreased due to stay-at-home measures. These are positive outcomes of the COVID-19 measures; however, we identified an increase in suicide rate among women in 2020 and 2021. The increase did not largely impact on all-cause mortality changes for women but this is obviously a negative effect of the COVID-19 measures such as restrictions of economic activity (e.g. cancellation of events and shorter business hours for restaurants).[12,13]

In conclusion, a sign of increasing mortality was observed in 2021 in the annual mortality rate in Japan, although the impact of the COVID-19 pandemic on mortality in Japan still seems to be limited. The observed increase in mortality was attributable to COVID-19, senility, cardiovascular disease, and 'other causes not classified as major cause'. Taking the rapidly increasing rate of COVID-19 cases in 2022 into consideration, further monitoring is warranted for the year 2022, which may reveal an even larger impact of the pandemic on mortality compared to that for 2020 and 2021.

Ethics statements

Patient consent for publication

Not applicable.

Ethics approval

Ethics approval was not applicable. This study used the vital statistics data from a portal site for Japanese Government Statistics (e-Stat), data at individual level were not used.

Authors' contributions: All author had full access to all the study data. H.T. was responsible for the integrity of the data, the accuracy of the data analysis, and the drafting of the manuscript. All authors contributed to the concept and design of the study. All authors critically reviewed the manuscript. K.K. supervised the study and provided administrative, technical, and material support.

Declaration of interest statement: The authors have no conflicts of interest directly relevant to the content of this study.

Funding: This research was supported by Grants-in-Aid for Cancer Control Policy from the Ministry of Health, Labor, and Welfare, Japan (20EA1017) and Japan Agency for Medical Research and Development (AMED; Grant Number: 22ck0106778h0001).
Patient and other consents: Not applicable.
Availability of data and materials: Data are available on request.
Acknowledgment: We thank Libby Cone, MD, MA, from DMC Corp. (www.dmed.co.jp <http://www.dmed.co.jp/>) for editing English drafts of this manuscript.

Figure legends

Figure 1. Trends in the daily number of reported COVID-19 cases in Japan since 16 January 2020

Figure 2. Trends in all-cause and cause-specific age-standardized mortality rates between 1995 and 2021

Figure 3. Cause-specific contribution to changes in all-cause age-standardized mortality rates (annual comparisons with previous year): differences in changes in ASMR between 2020 and 2021 were calculated as ($ASMR_{2021}$− $ASMR_{2020}$) for each cause-specific death, where ASMR=age standardized mortality rate per 100 000 population.

Reference

1. The World Bank. Life expectancy at birth, total (years). https://data.worldbank.org/indicator/SP.DYN.LE00.IN Date accessed: December 12, 2022

2. Islam N, Jdanov DA, Shkolnikov VM, et al. Effects of covid-19 pandemic on life expectancy and premature mortality in 2020: time series analysis in 37 countries. *BMJ*. 2021;375:e066768.

3. Ministry of Health, Labour and Welfare. Vital Statistics. https://www.mhlw.go.jp/english/database/db-hw/vs01.html Date accessed: December 12, 2022

4. Ministry of Health, Labour and Welfare. Visualizing the data: information on COVID-19 infections. https://covid19.mhlw.go.jp/en/ December 12, 2022

5. World Health Organization. WHO coronavirus (COVID-19) dashboard. https://covid19.who.int December 12, 2022

6. Ikeda N, Yamamoto H, Taketomi A, et al. The impact of COVID-19 on surgical procedures in Japan: analysis of data from the National Clinical Database. *Surg Today*. 2022;52:22-35.

7. Sato Y, Fujiwara Y, Fukuda N, et al. Changes in Treatment Behavior during the COVID-19 Pandemic among Patients at a Cancer Hospital. *Cancer Cell*. 2021;39:130-131.

8. Toyoda Y, Katanoda K, Ishii K, Yamamoto H, Tabuchi T. Negative impact of the COVID-19 state of emergency on breast cancer screening participation in Japan. *Breast Cancer*. 2021;28:1340-1345.

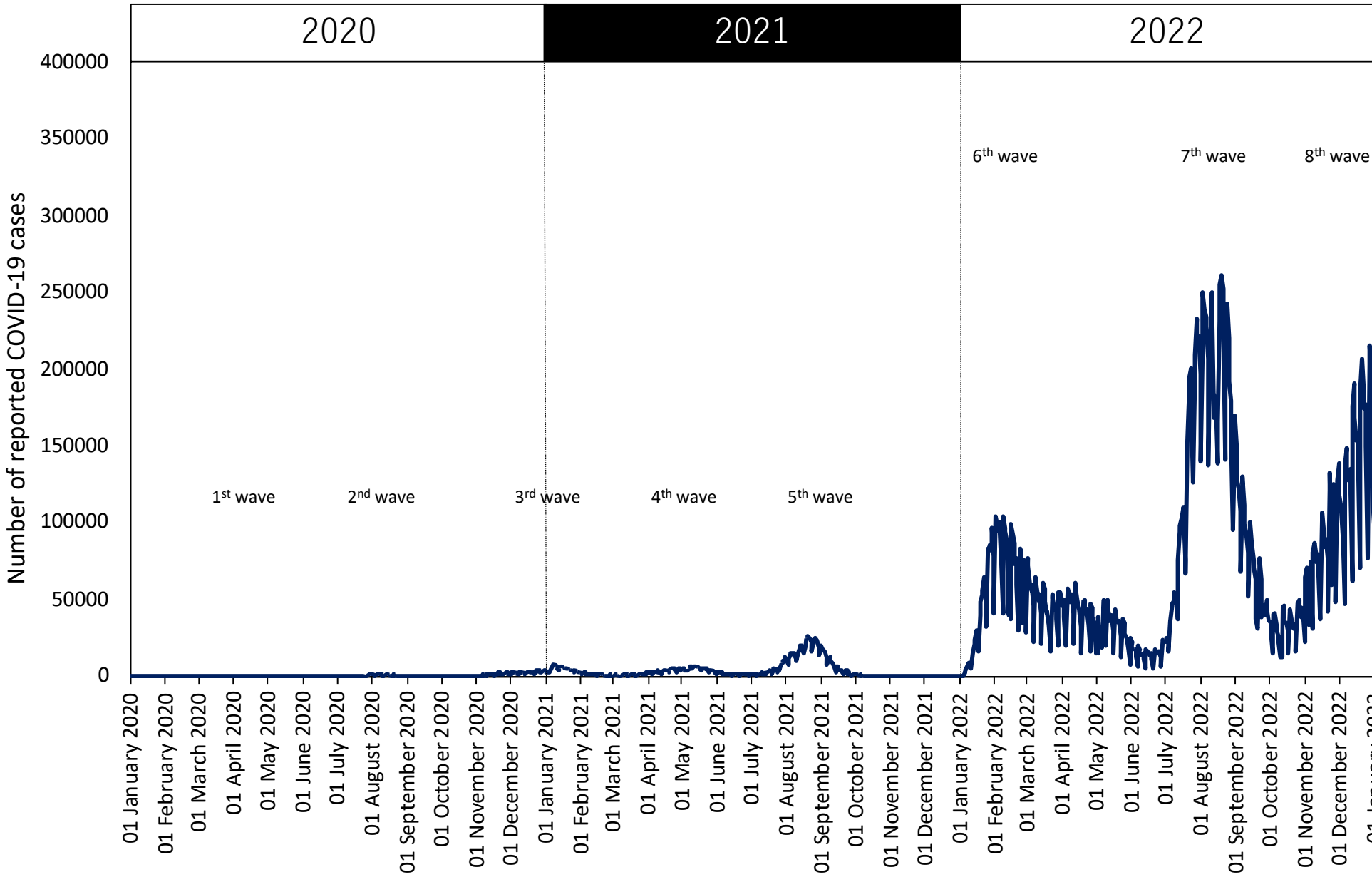
9. Okuyama A, Watabe M, Makoshi R, Takahashi H, Tsukada Y, Higashi T. Impact of the COVID-19 pandemic on the diagnosis of cancer in Japan: analysis of hospital-based cancer registries. *Jpn J Clin Oncol*. 2022;52:1215-1224.

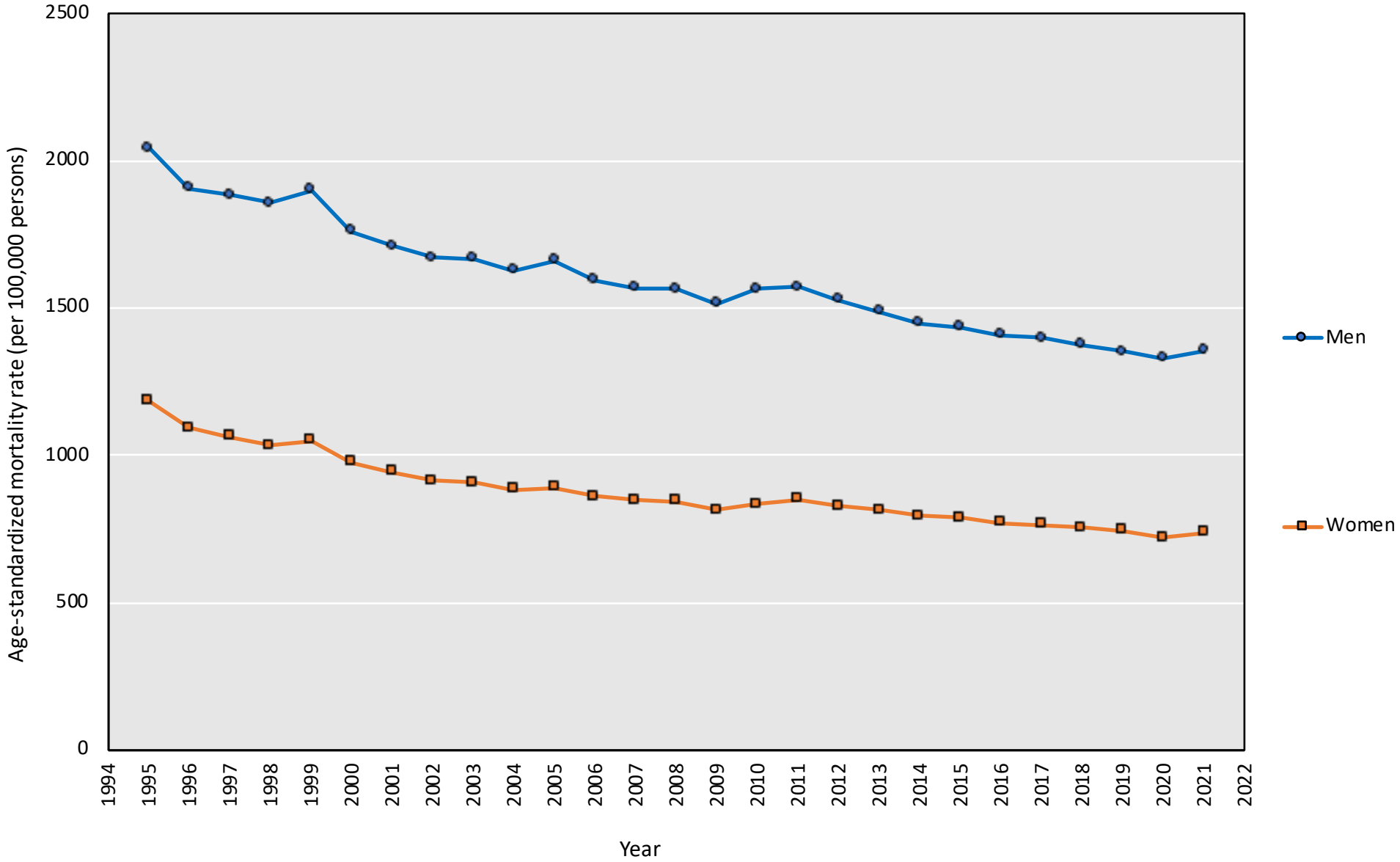
10. Nomura S, Eguchi A, Ghaznavi C, et al. Excess deaths from non-COVID-19-related causes in Japan and 47 prefectures from January 2020 through May 2021 by place of death. *SSM Popul Health*. 2022;19:101196.

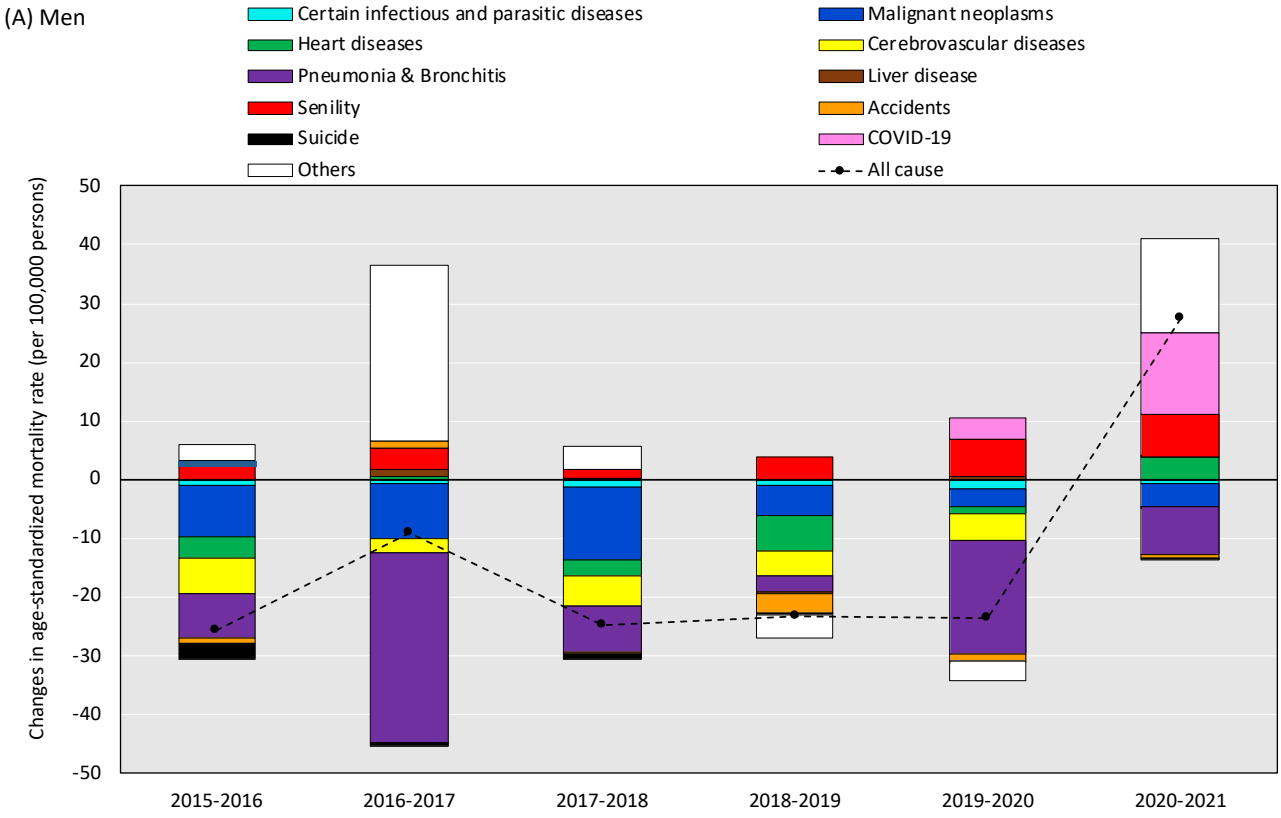
11. Katsoularis I, Fonseca-Rodriguez O, Farrington P, Lindmark K, Fors Connolly AM. Risk of acute myocardial infarction and ischaemic stroke following COVID-19 in Sweden: a self-controlled case series and matched cohort study. *Lancet*. 2021;398:599-607.

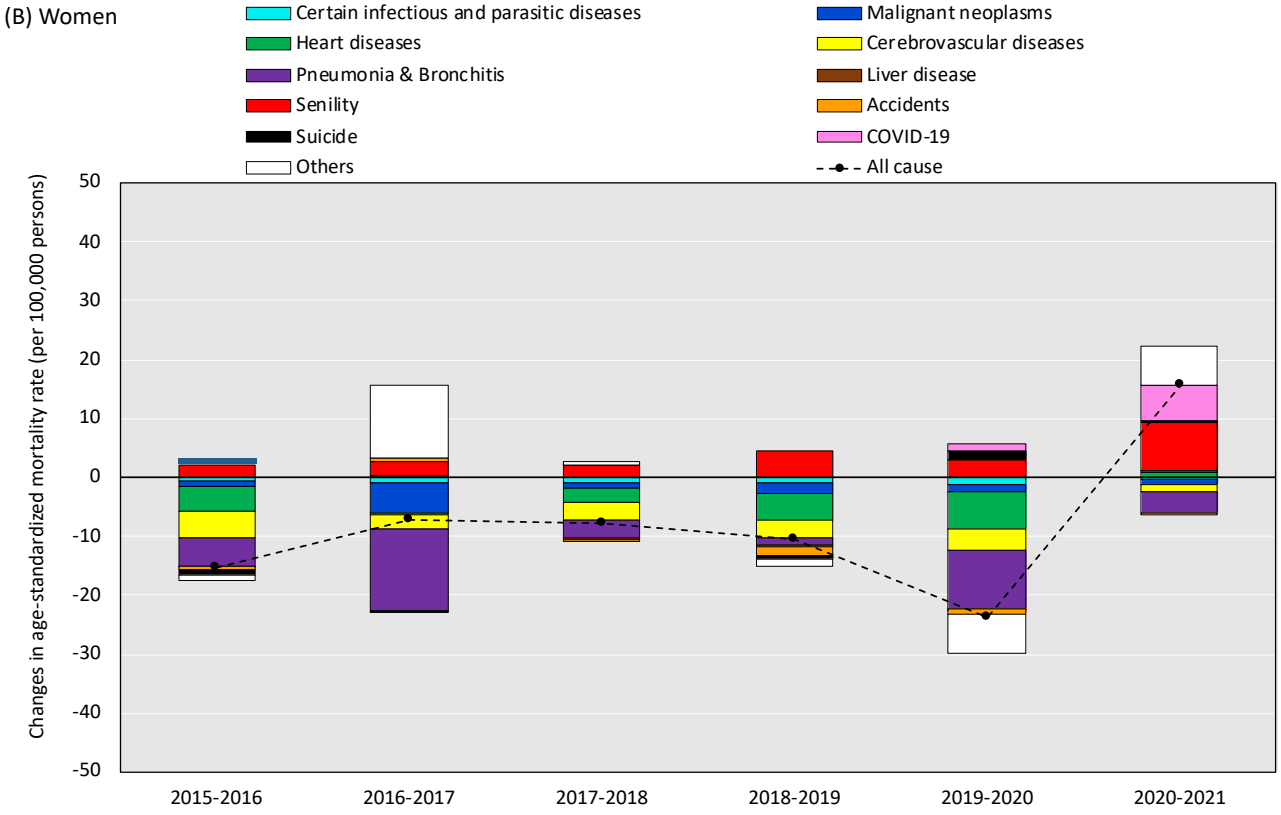
12. Sakamoto H, Ishikane M, Ghaznavi C, Ueda P. Assessment of Suicide in Japan During the COVID-19 Pandemic vs Previous Years. *JAMA Netw Open*. 2021;4:e2037378.

13. Kikuchi K, Anzai T, Takahashi K. The Unusual Increase in Suicides Among Women in Japan During The COVID-19 Pandemic: A Time-Series Analysis until October 2021. *J Epidemiol*. 2022. (in press)




2500
2000
1500
1000
500
0
Age-standardized mortality rate (per 100,000 persons)
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Year
Men
Women


(A) Men
Certain infectious and parasitic diseases
Malignant neoplasms
Heart diseases
Cerebrovascular diseases
Pneumonia & Bronchitis
Liver disease
Senility
Accidents
Suicide
COVID-19
Others
All cause
Changes in age-standardized mortality rate (per 100,000 persons)
50
40
30
20
10
0
-10
-20
-30
-40
-50
2015-2016
2016-2017
2017-2018
2018-2019
2019-2020
2020-2021

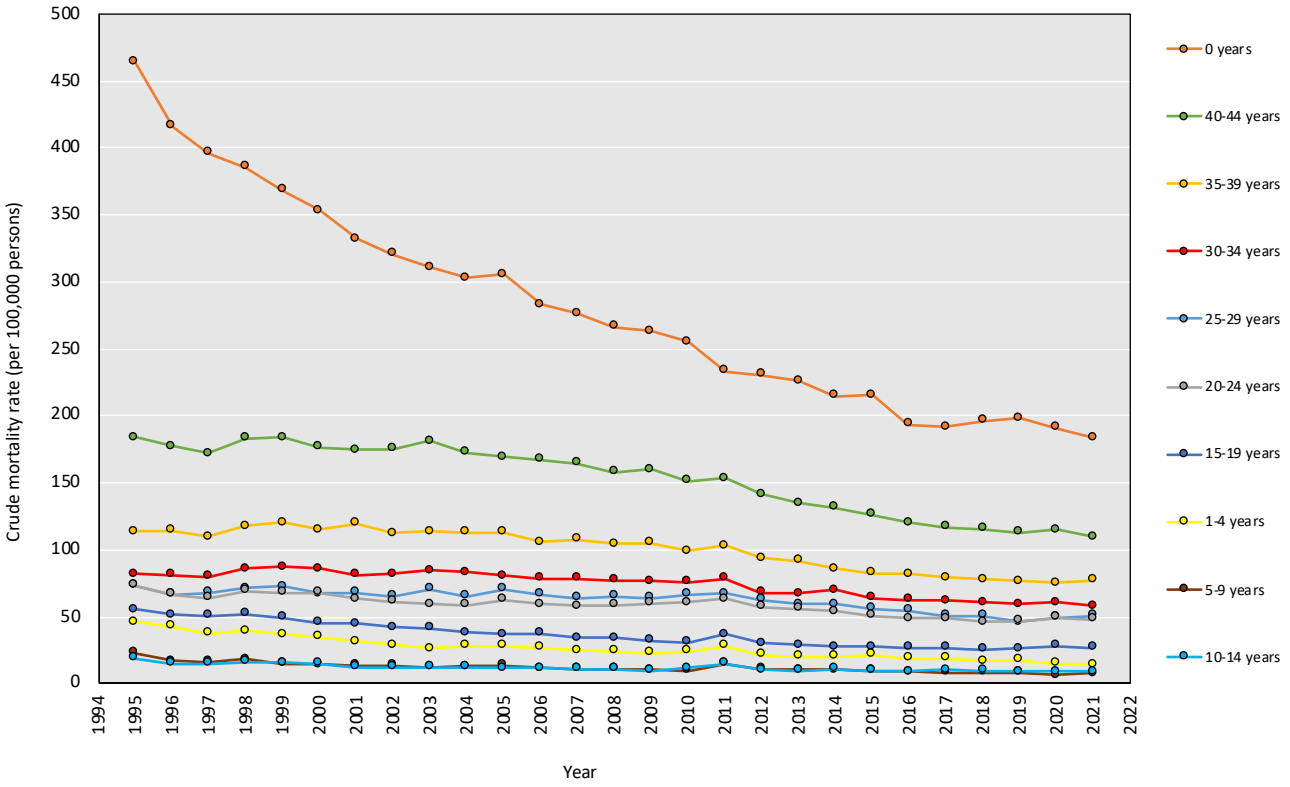

(B) Women
Certain infectious and parasitic diseases
Malignant neoplasms
Heart diseases
Cerebrovascular diseases
Pneumonia & Bronchitis
Liver disease
Senility
Accidents
Suicide
COVID-19
Others
All cause
Changes in age-standardized mortality rate (per 100,000 persons)
50
40
30
20
10
0
-10
-20
-30
-40
-50
2015-2016
2016-2017
2017-2018
2018-2019
2019-2020
2020-2021

Appendix Table 1. Number of deaths in Japan between 1995 and 2021*

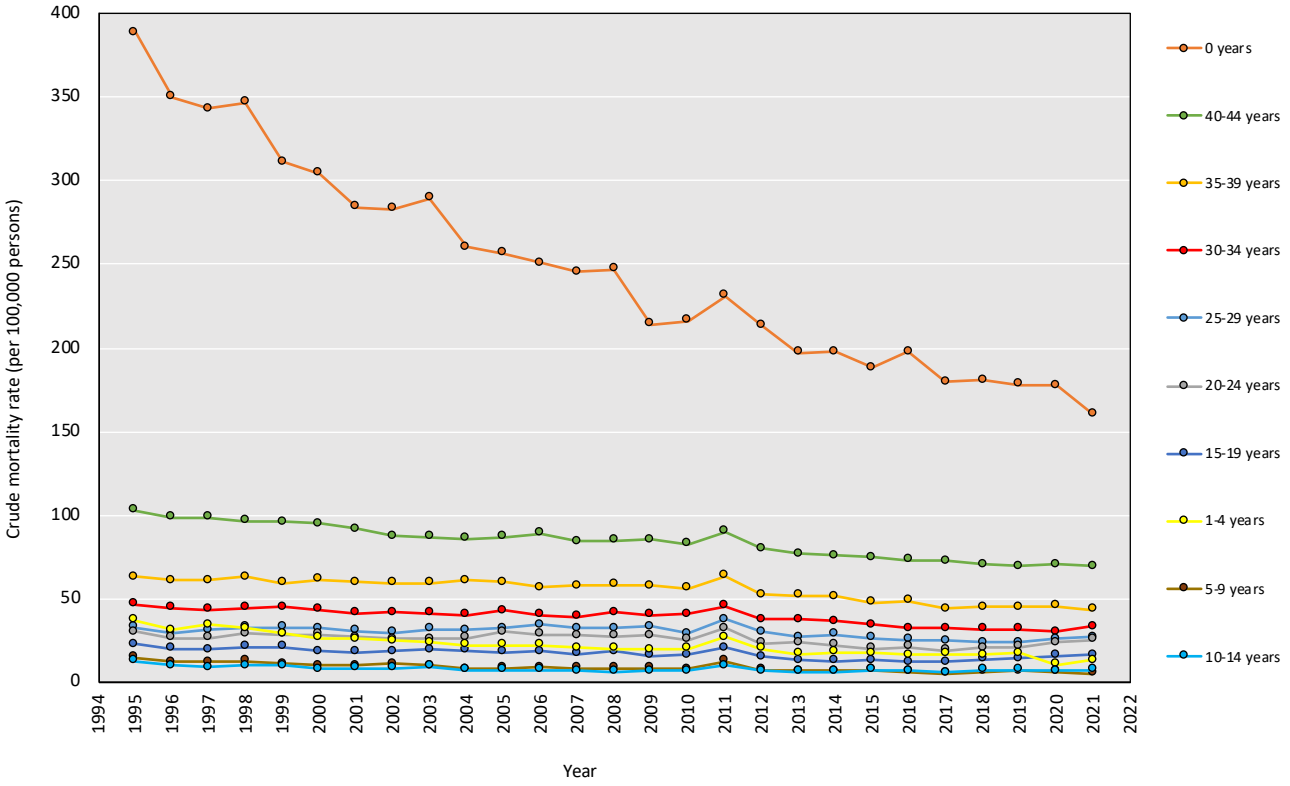
Year	Men					Women				
	All-cause	Malignant neoplasms	Heart disease	Cerebrovascular disease	COVID-19	All-cause	Malignant neoplasms	Heart disease	Cerebrovascular disease	COVID-19
1995	501276	159623	69718	69587	-	420863	103399	69488	76965	-
1996	488605	164824	68977	66479	-	407606	106359	69252	73887	-
1997	497796	167076	69776	65790	-	415606	108337	70398	72907	-
1998	512128	172306	71134	65529	-	424356	111615	71986	72290	-
1999	534778	175817	73979	66452	-	447253	114739	77100	72537	-
2000	525903	179140	72156	63127	-	435750	116344	74585	69402	-
2001	528768	181393	72727	63146	-	441563	119265	75565	68710	-
2002	535305	184033	74986	62229	-	447074	120535	77532	68028	-
2003	551746	186912	77989	63274	-	463205	122631	81556	68793	-
2004	557097	193096	77465	61547	-	471505	127262	82160	67508	-
2005	584970	196603	83979	63657	-	498826	129338	89146	69190	-
2006	581370	198052	82811	61348	-	503080	131262	90213	66920	-
2007	592784	202743	83090	60992	-	515550	133725	92449	66049	-
2008	608711	206354	86139	61121	-	533696	136609	95789	65902	-
2009	609042	206352	85543	59293	-	532823	137753	95202	63057	-
2010	633700	211435	88803	60186	-	563312	142064	100557	63275	-
2011	656540	213190	91298	59616	-	596526	144115	103628	64251	-
2012	655526	215110	92976	58625	-	600833	145853	105860	62977	-
2013	658684	216975	91445	56718	-	609752	147897	105278	61629	-
2014	660334	218397	92278	54995	-	612670	149706	104647	59212	-
2015	666707	219508	92142	53576	-	623737	150838	103971	58397	-
2016	674946	219846	93453	52718	-	633212	153242	104617	56635	-
2017	690770	220416	96330	53198	-	649797	152949	108538	56698	-
2018	699138	218625	98035	52398	-	663332	154959	110186	55788	-
2019	707421	220339	98210	51768	-	673672	156086	109504	54784	-
2020	706834	220989	99304	50390	2094	665921	157396	106292	52588	1372
2021	738141	222467	103700	51594	9732	701715	159038	111010	53001	7034

*Malignant neoplasms (ICD-10: C00-C97); Heart diseases (I01-I02.0, I05-I09, I20-I25, I27, I30-I52); Cerebrovascular diseases (I60-I69); COVID-19 (U07)

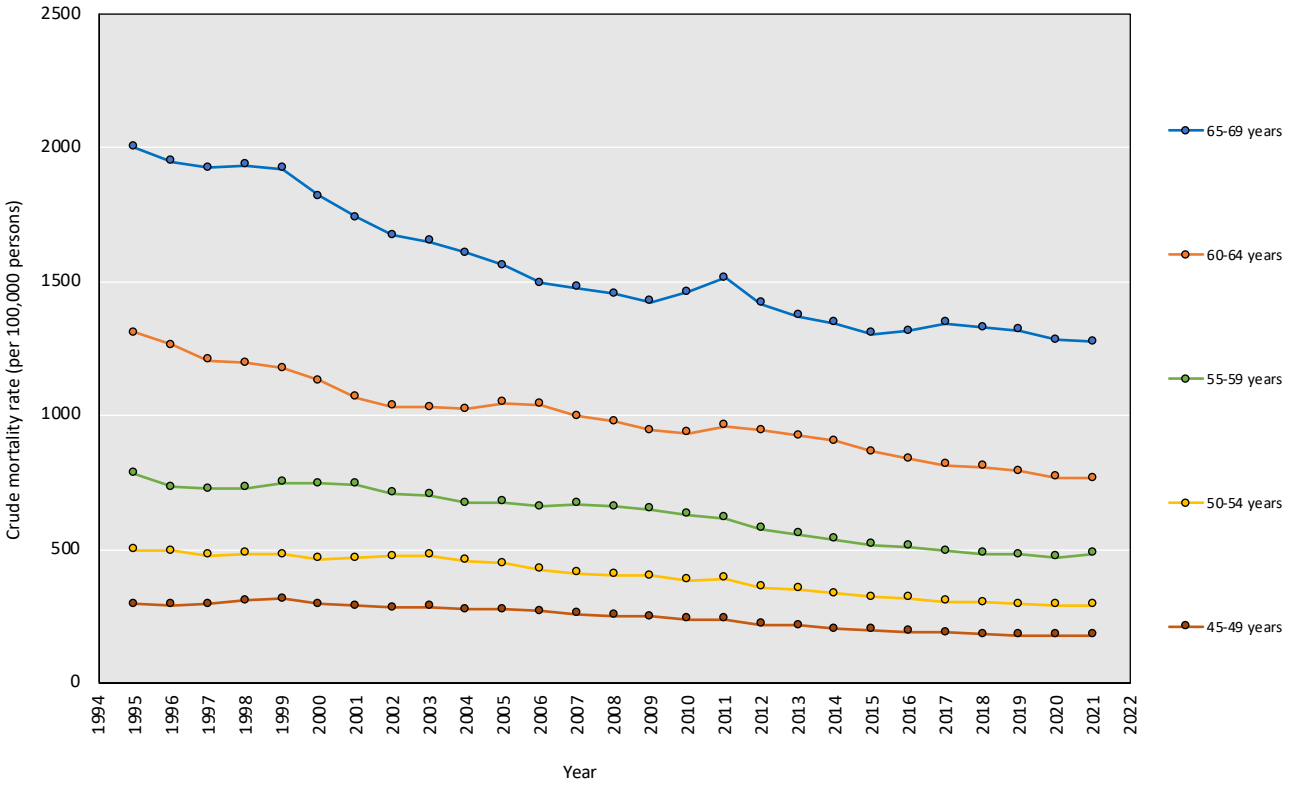
(A) All cause (men, 0-44 years)



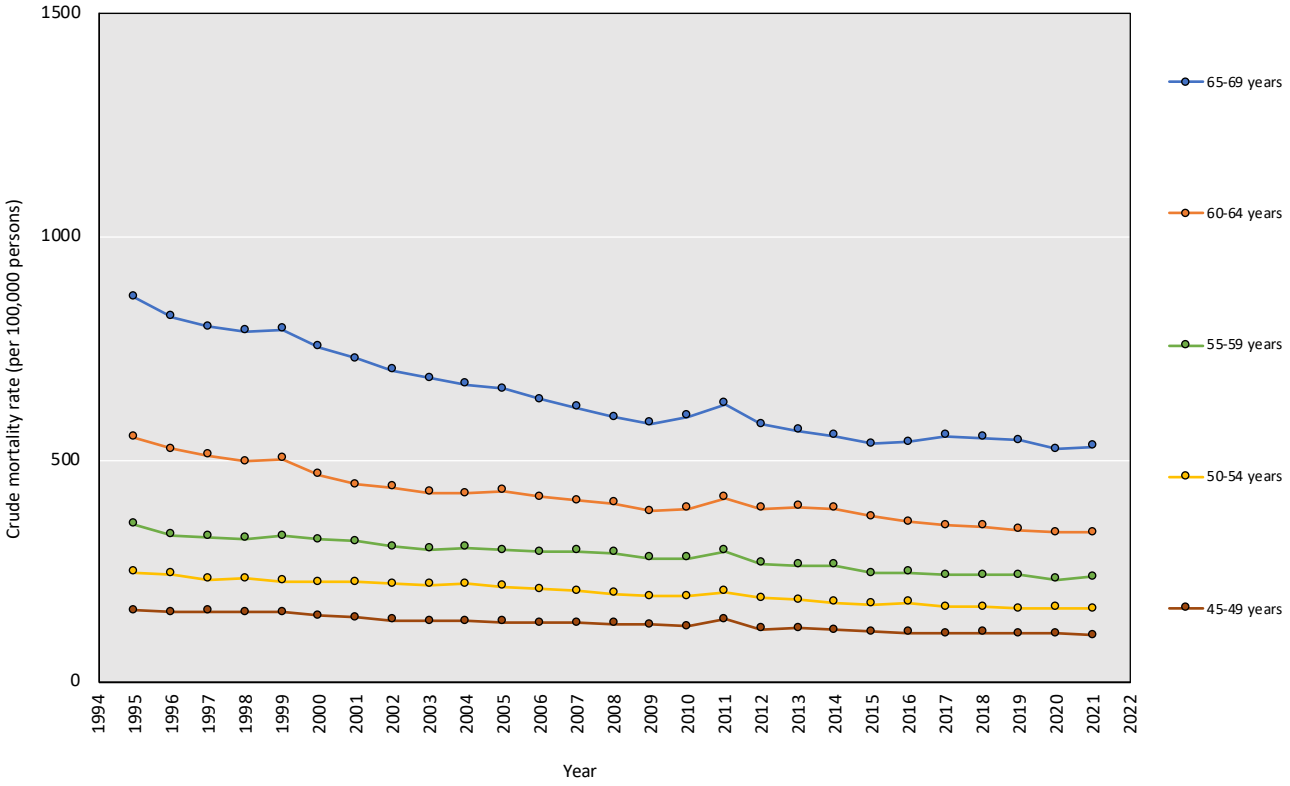
(B) All cause (women, 0-44 years)

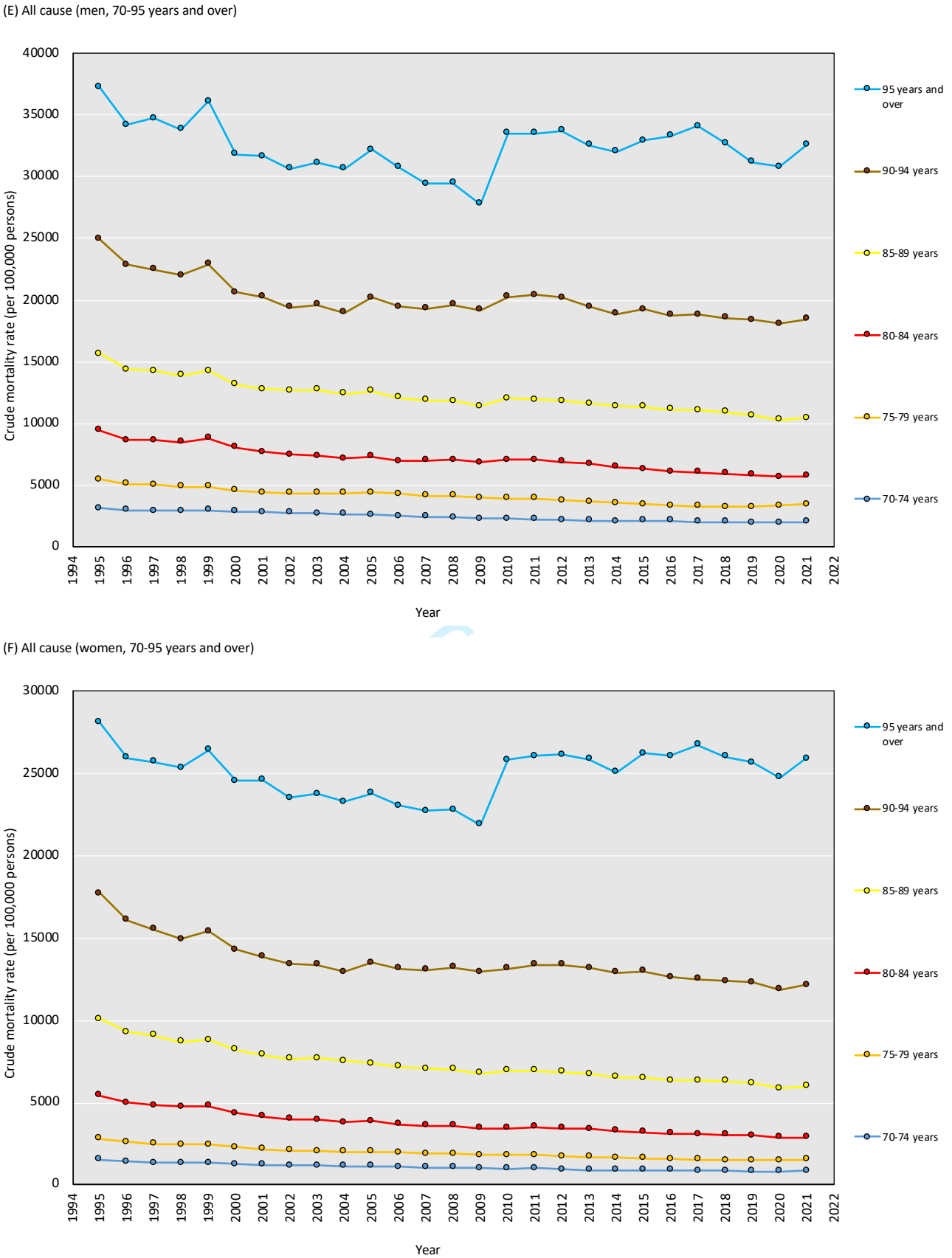


(C) All cause (men, 45-69 years)



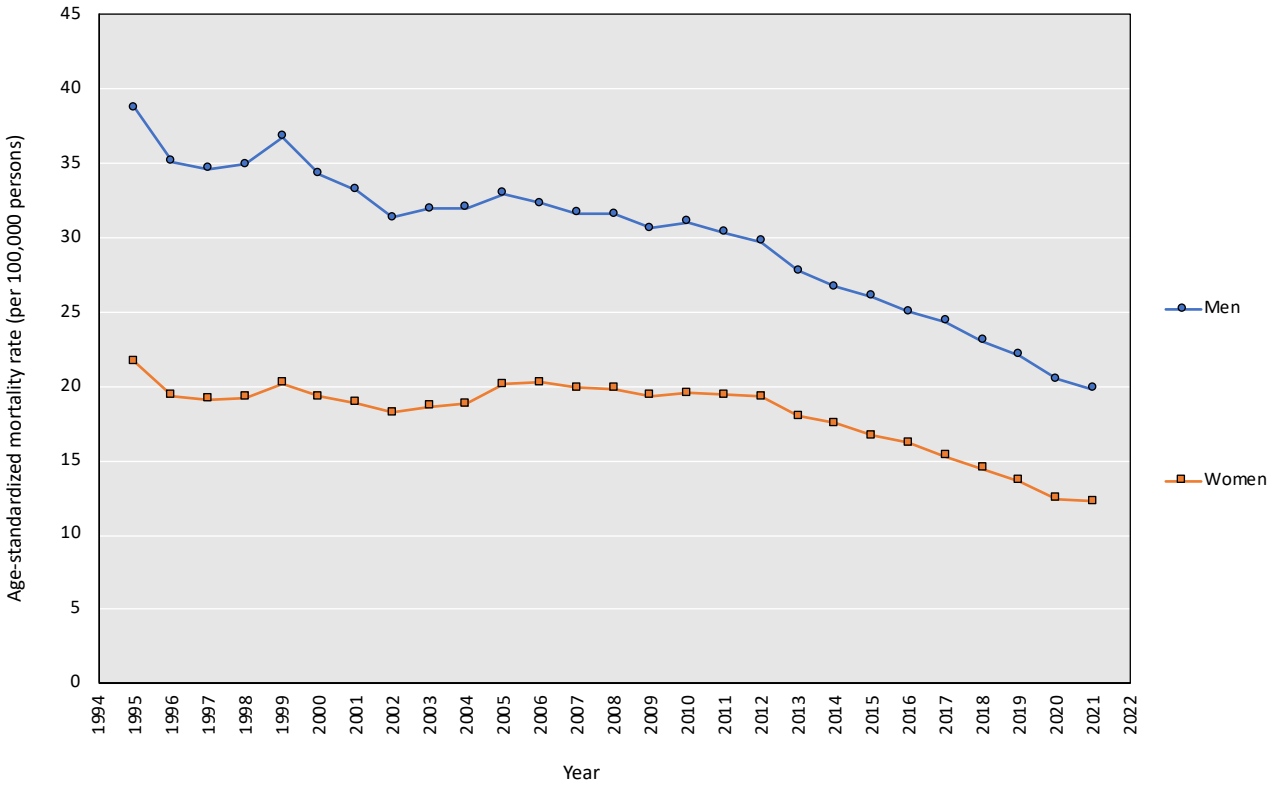
(D) All cause (women, 45-69 years)



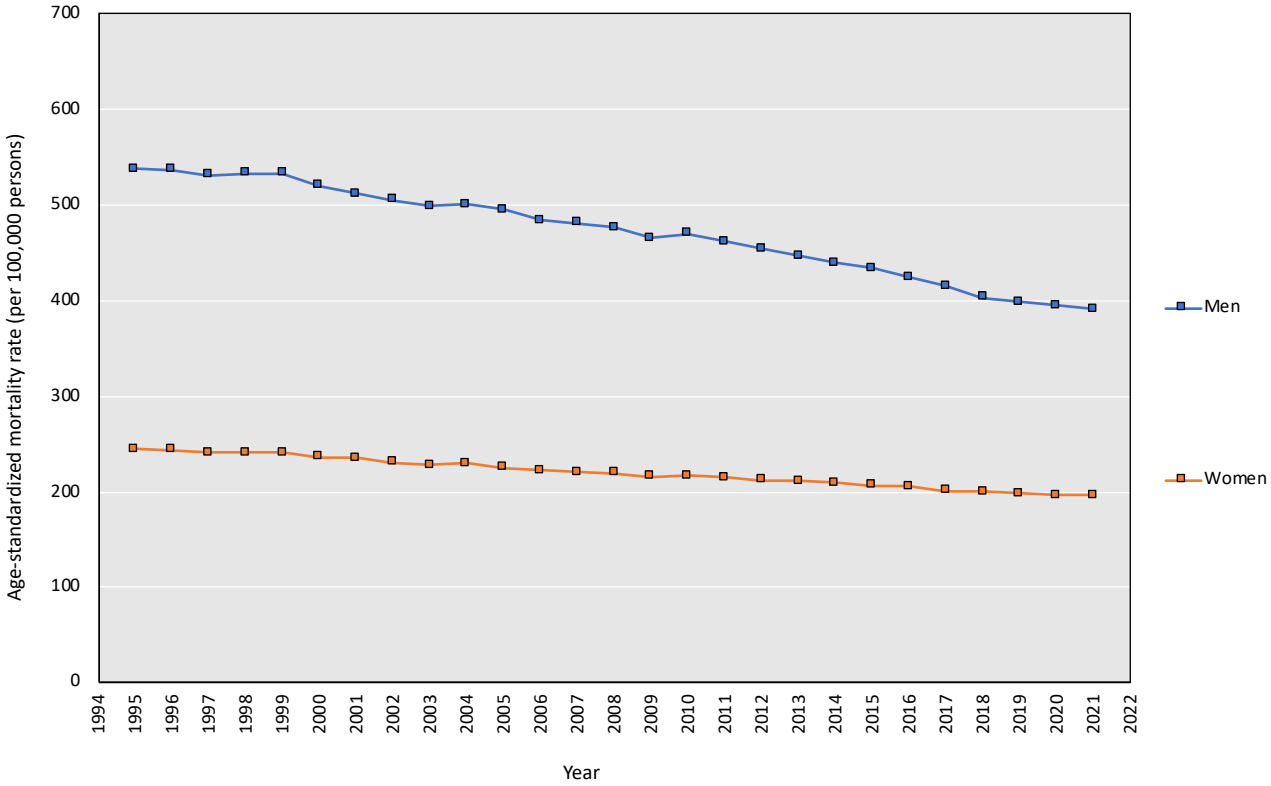


Appendix Figure 1. Trends in crude mortality rate by five-year age groups between 1995 and 2021

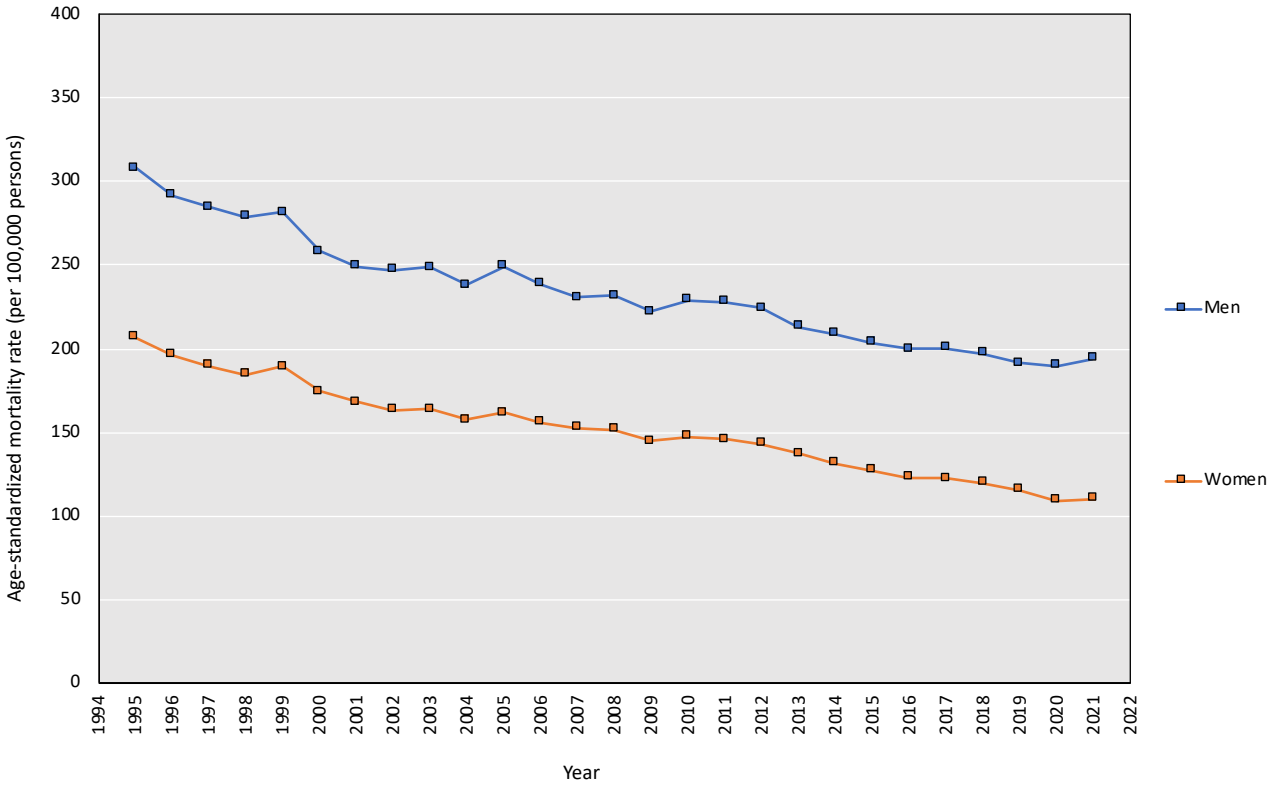
(A) Certain infectious and parasitic diseases (A00-B99)



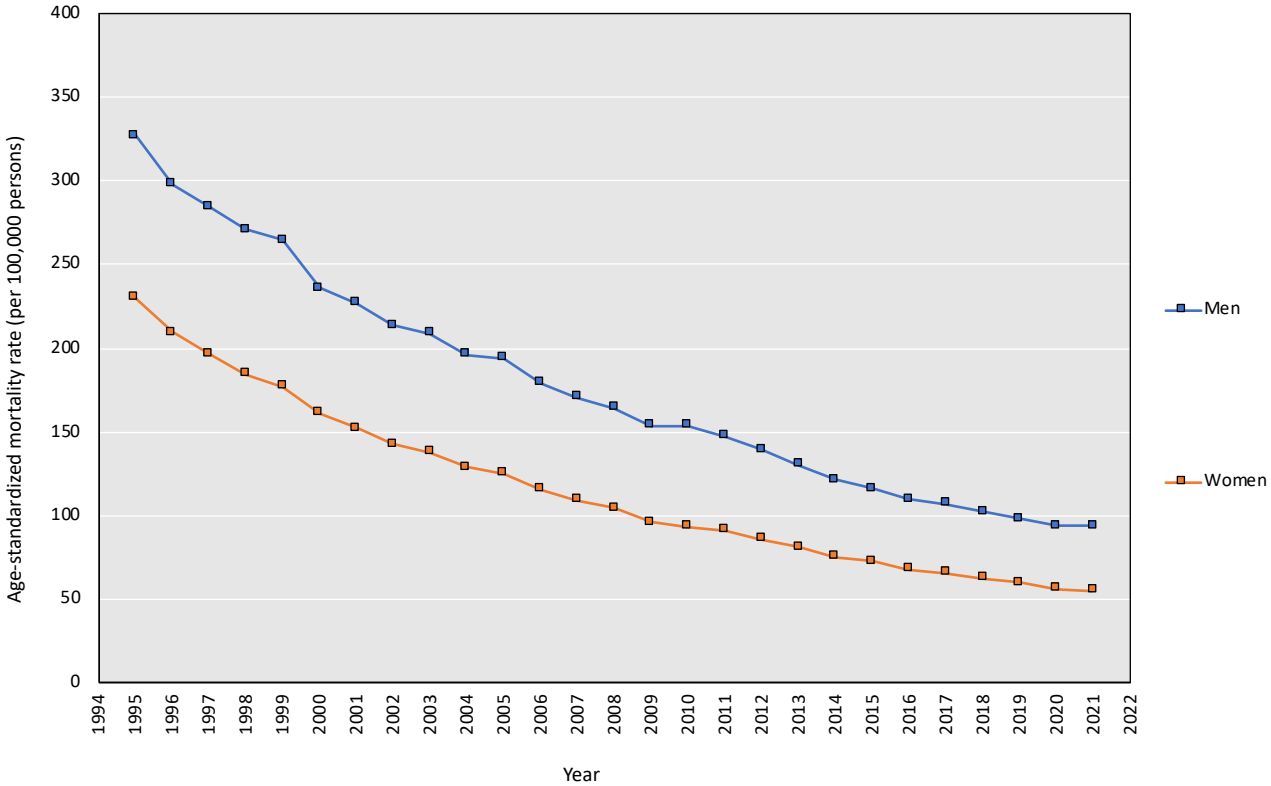
(B) Malignant neoplasms (C00-96)



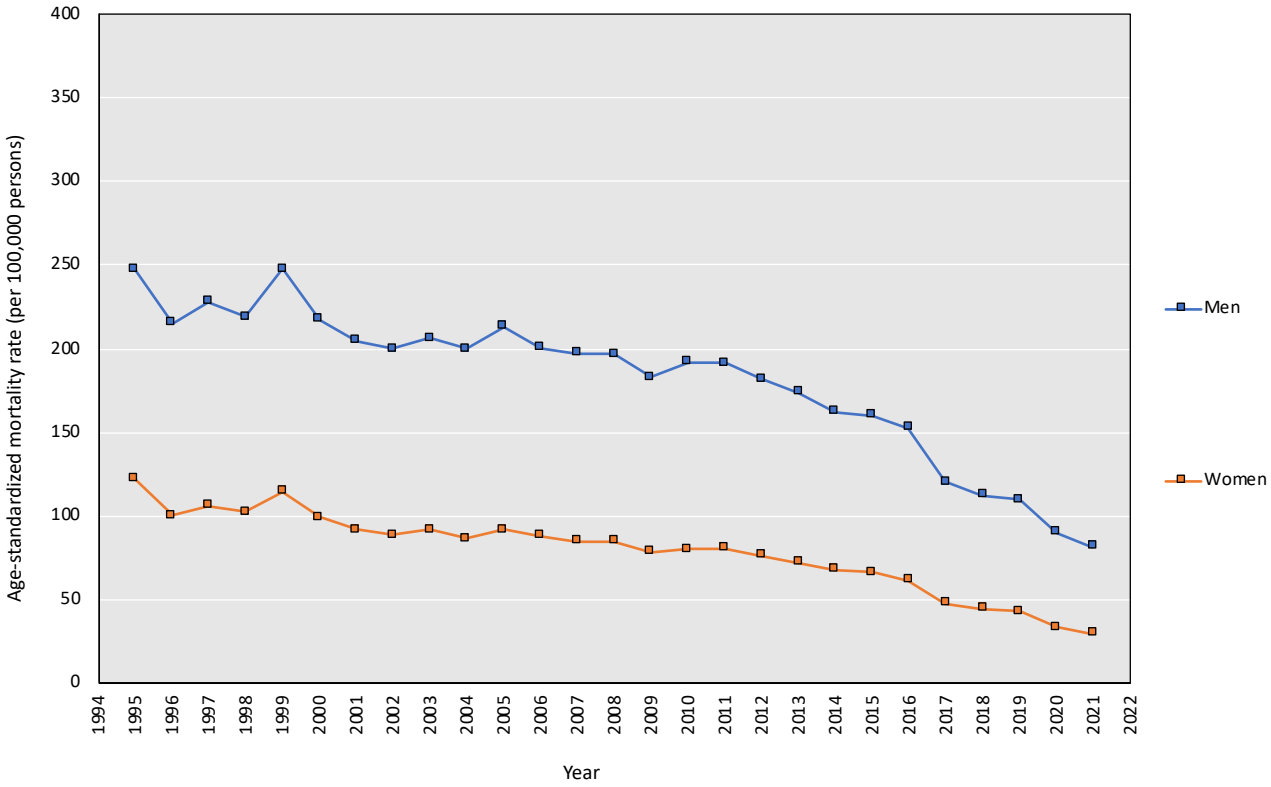
(C) Heart diseases (I05-09, I20-25, I27, I30-51)



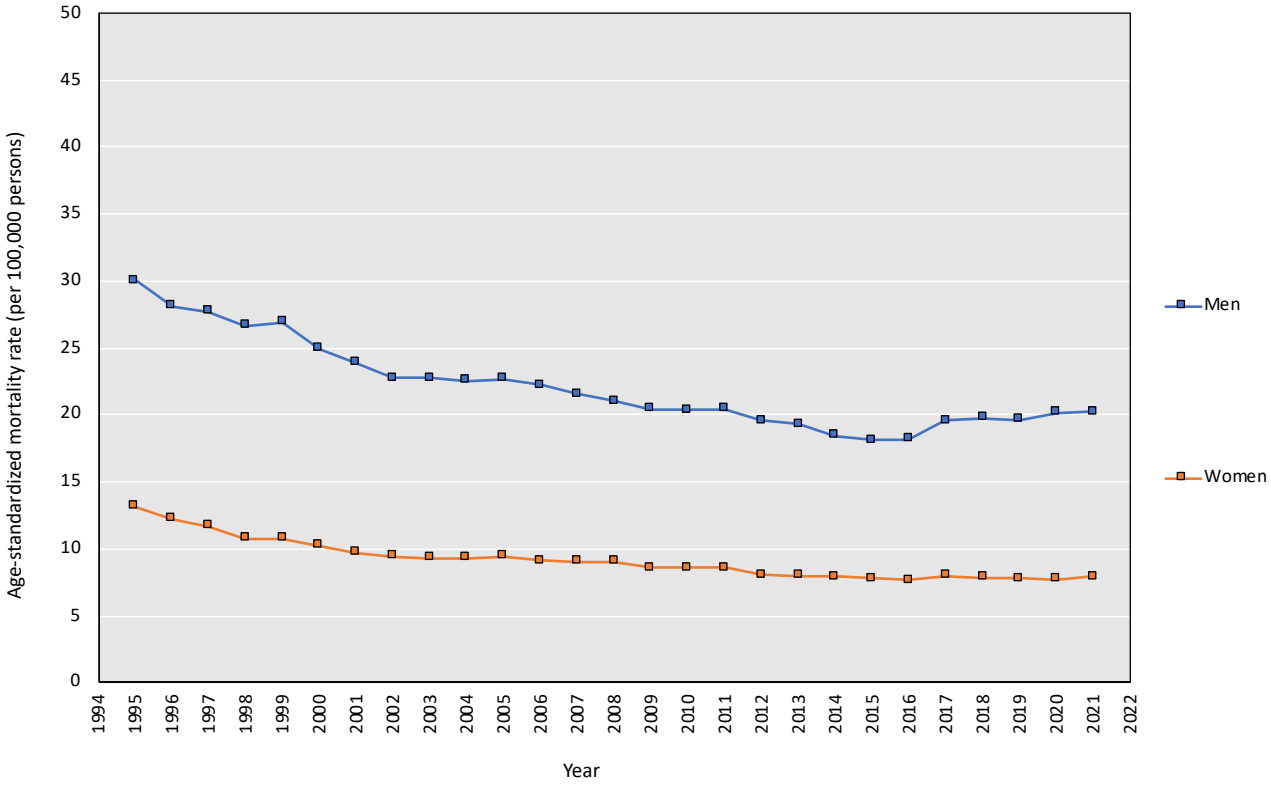
(D) Cerebrovascular diseases (I60-69)



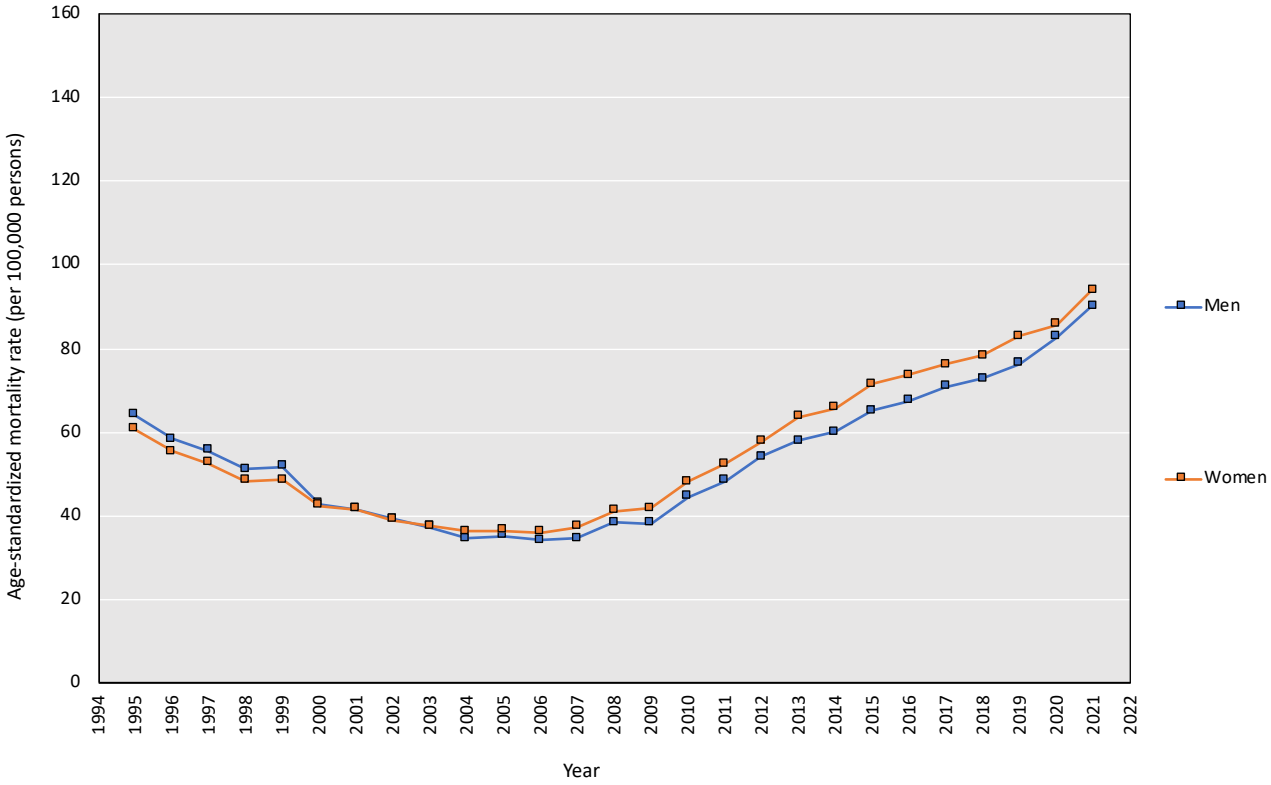
(E) Pneumonia & Bronchitis (J12-18)



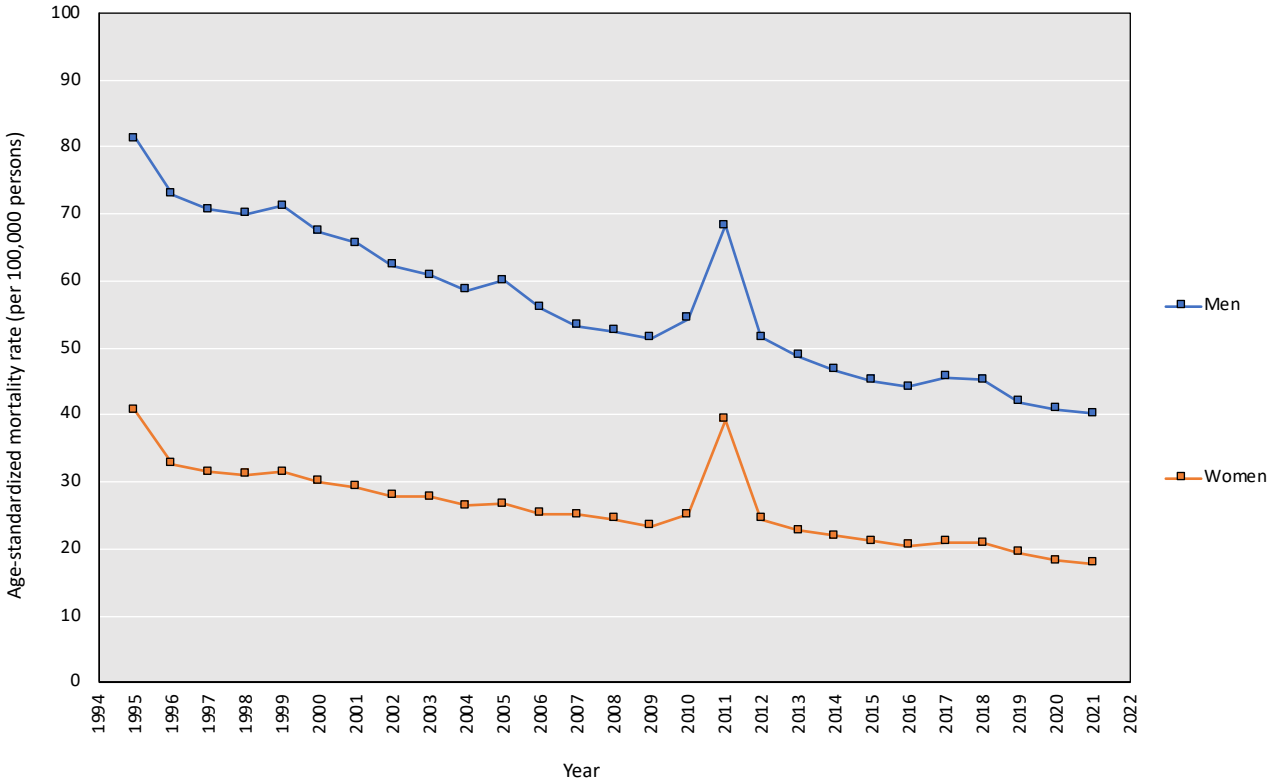
(F) Liver disease (K70-76)



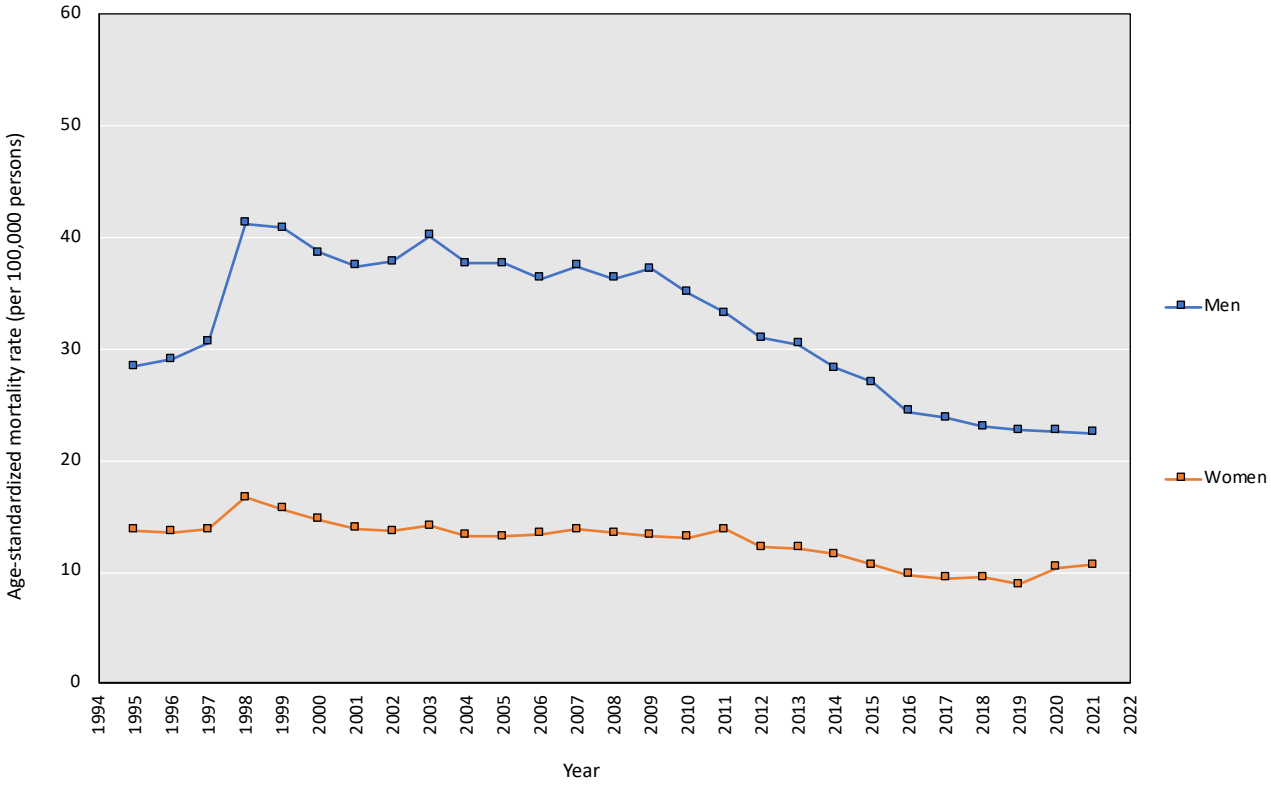
(G) Senility (R54)



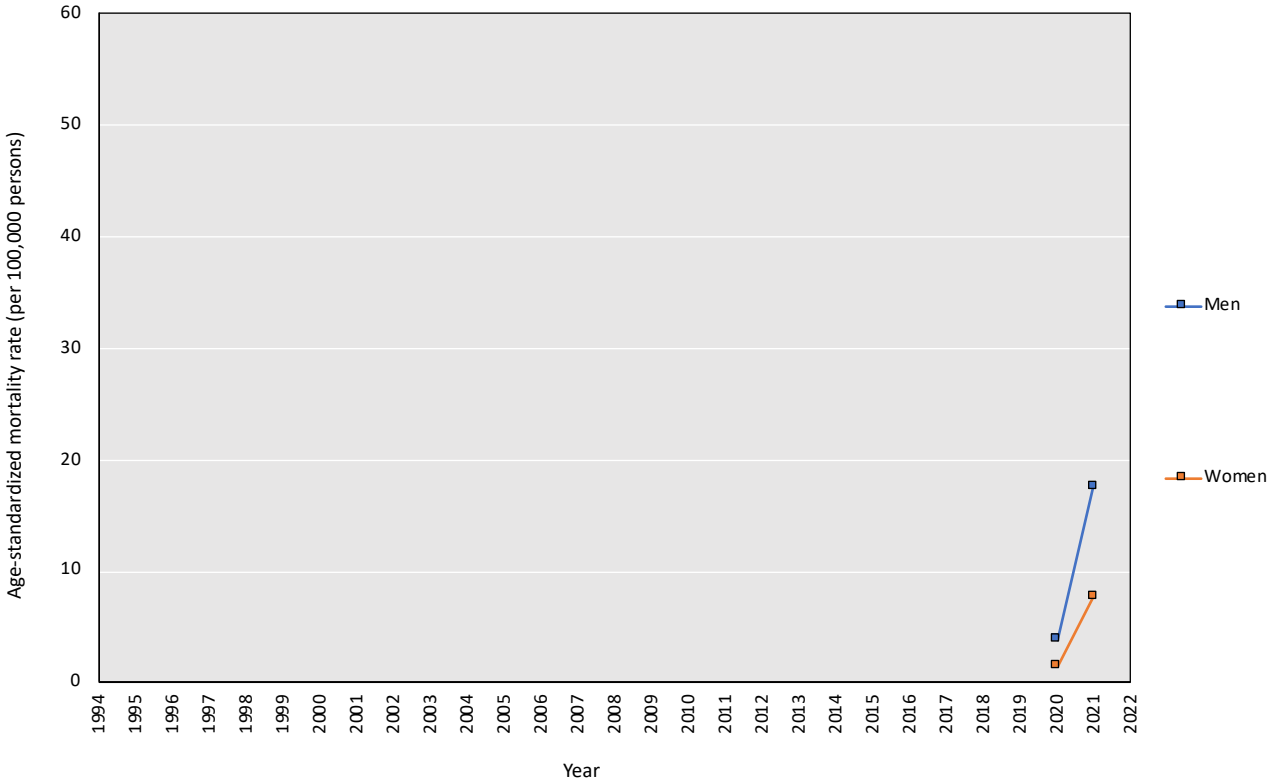
(H) Accidents (V01-X59)



(I) Suicide (X60-84)

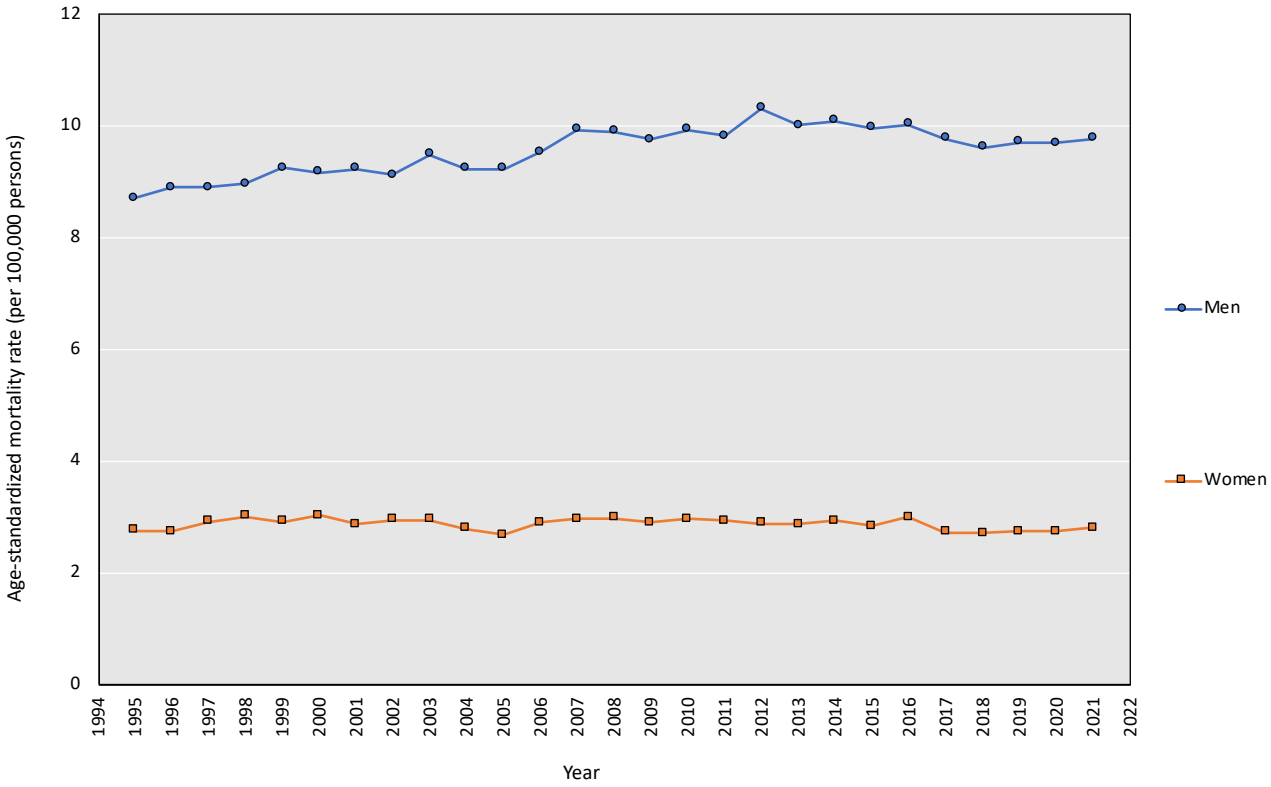


(J) COVID-19 (U07)

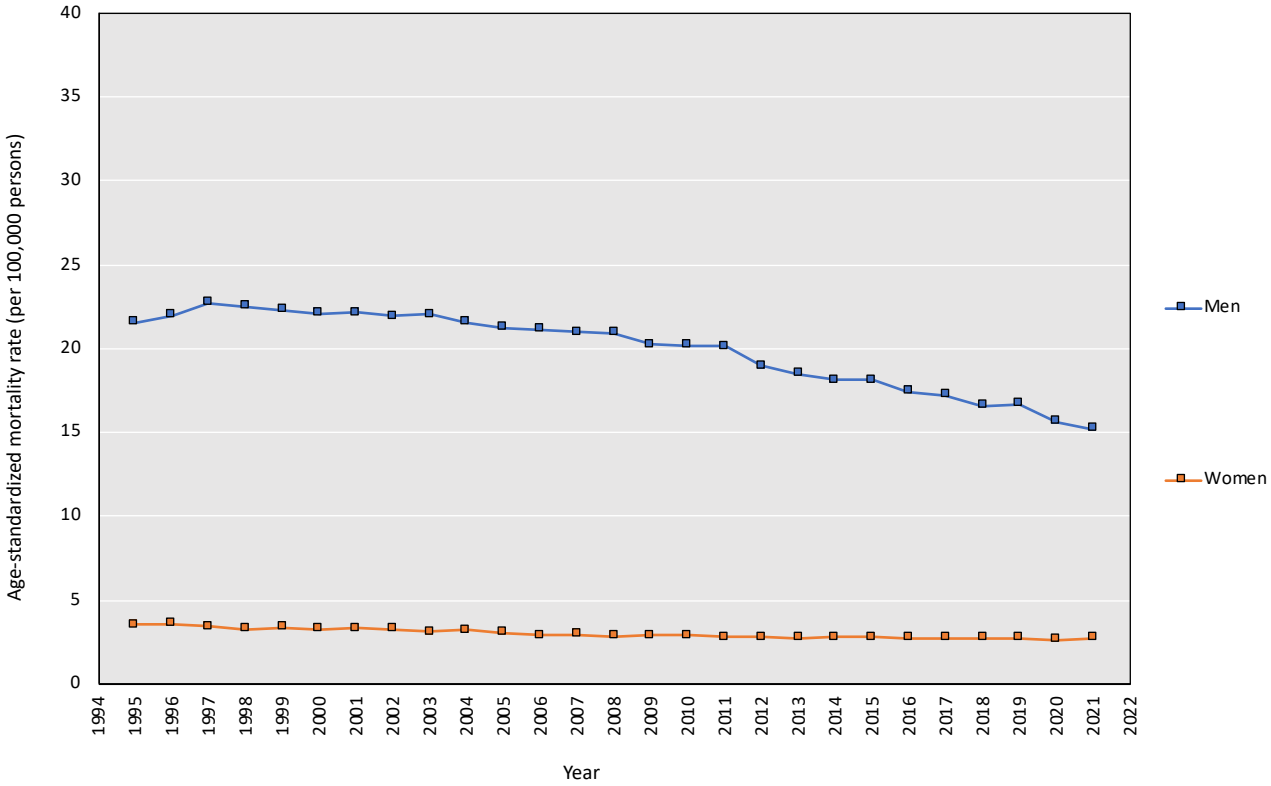


Appendix Figure 2. Trends in cause-specific age-standardized mortality rates by cancer site between 1995 and 2021

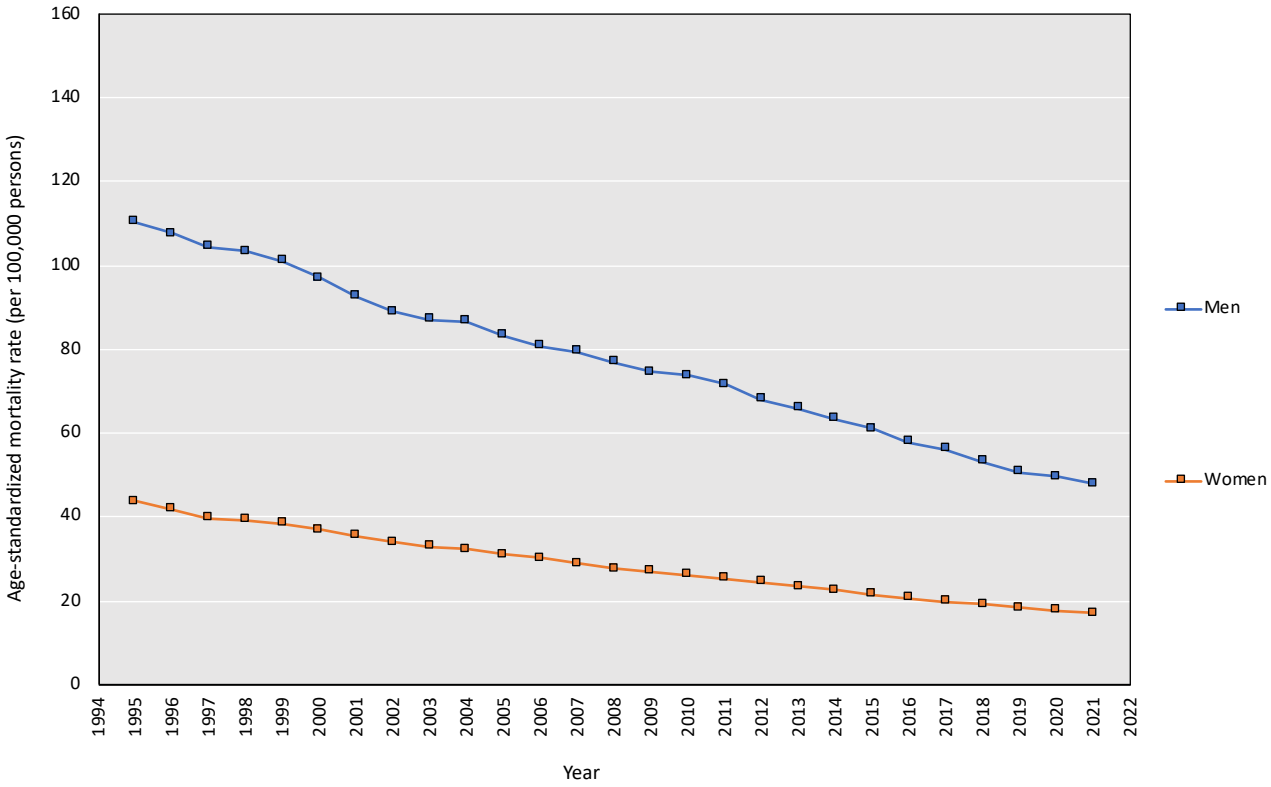
(A) Oral cavity and pharynx (C00-14)



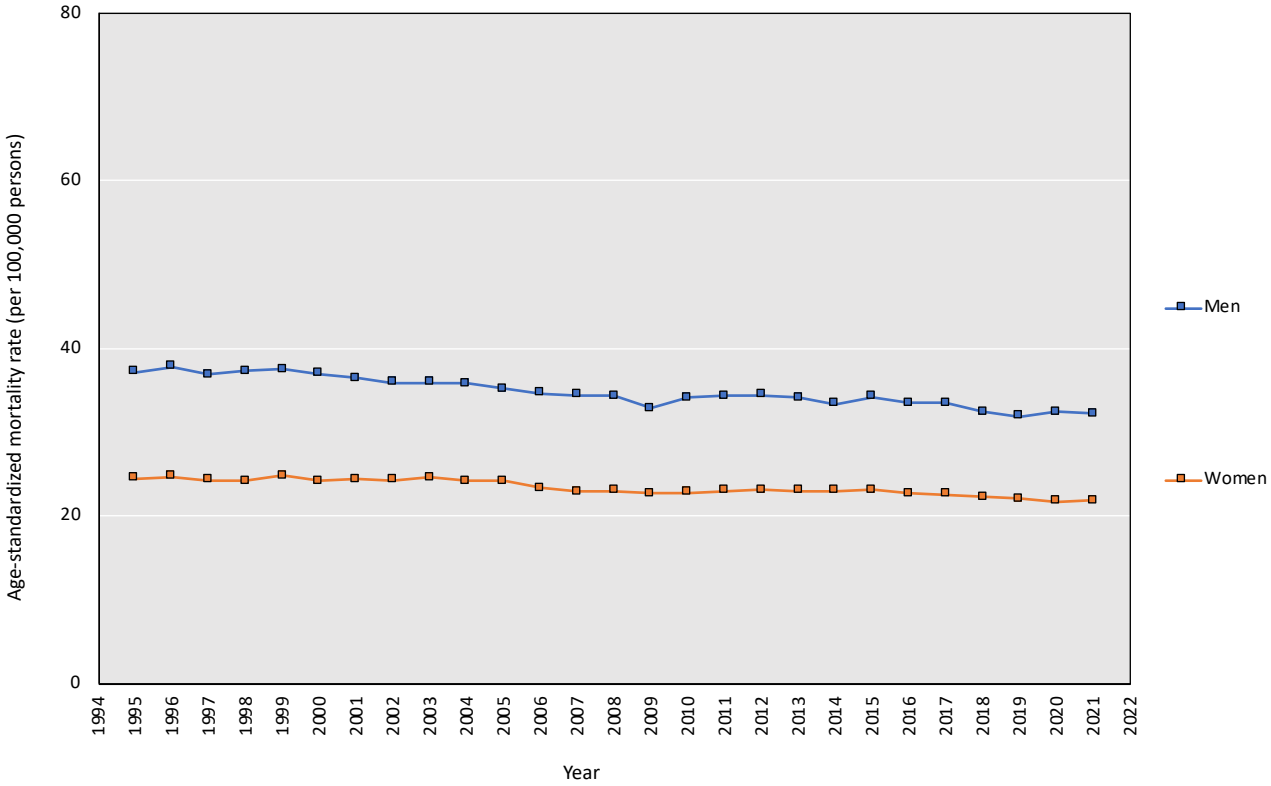
(B) Esophagus (C15)



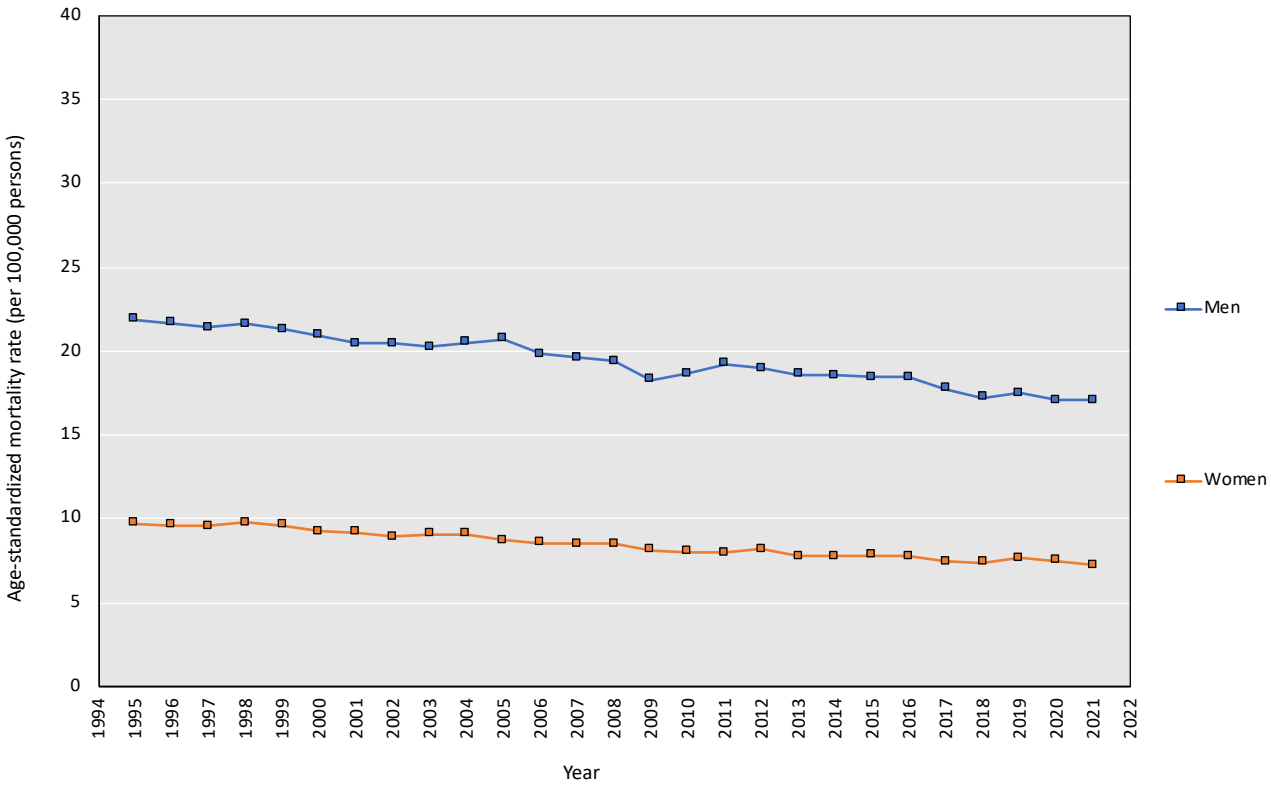
(C) Stomach (C16)



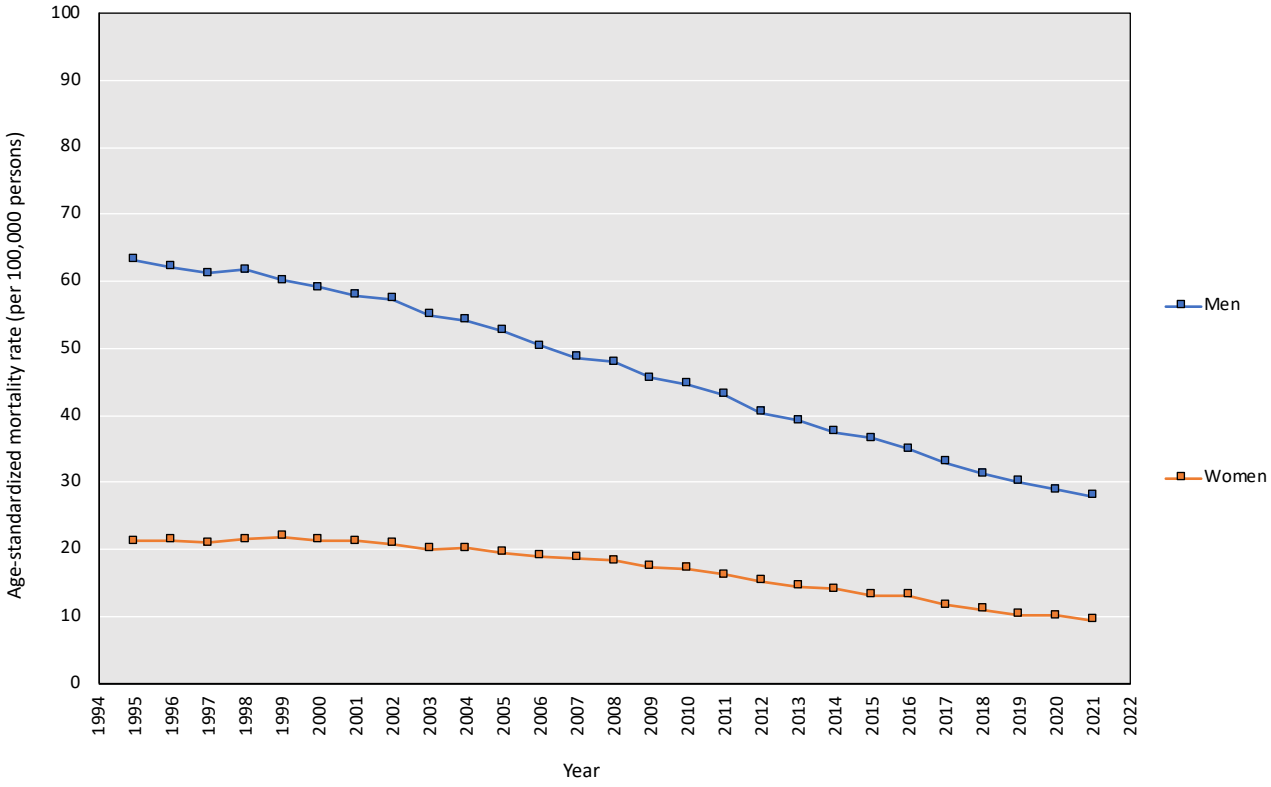
(D) Colon (C18)



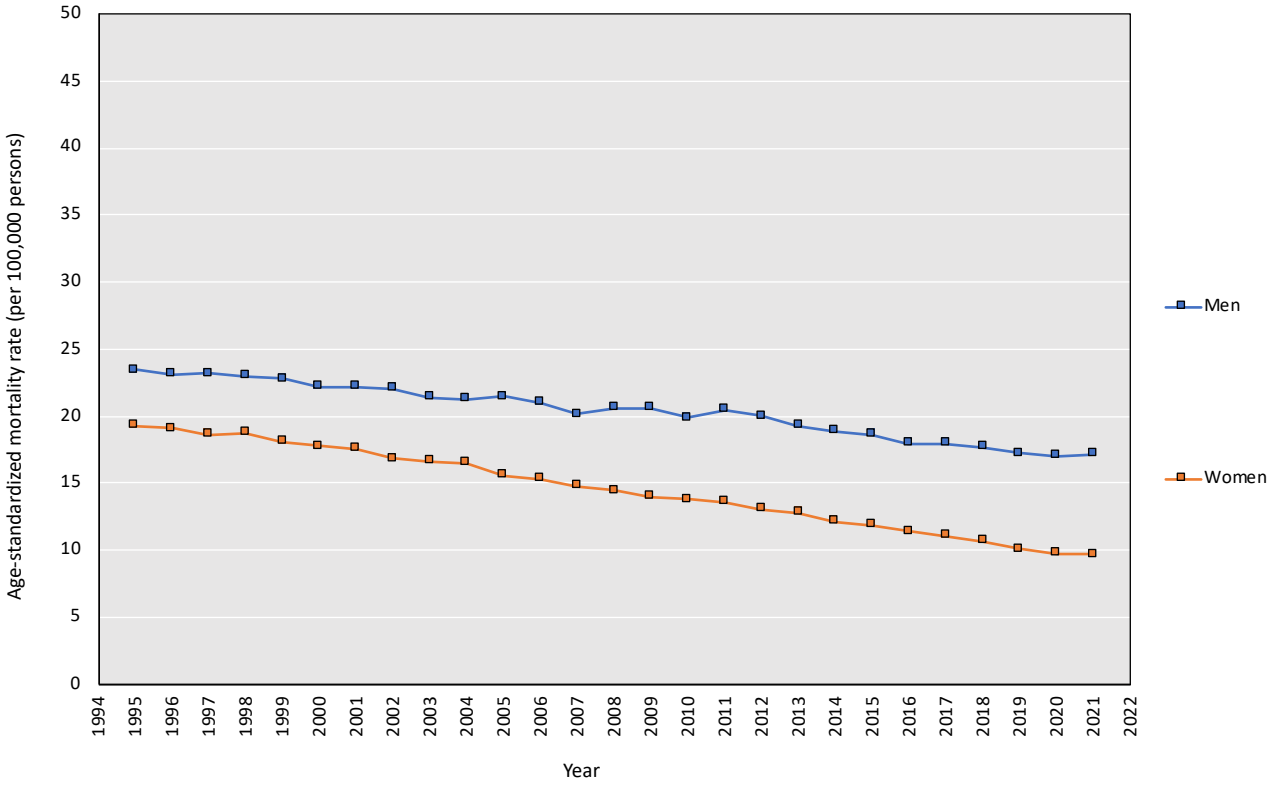
(E) Rectum (C19-20)



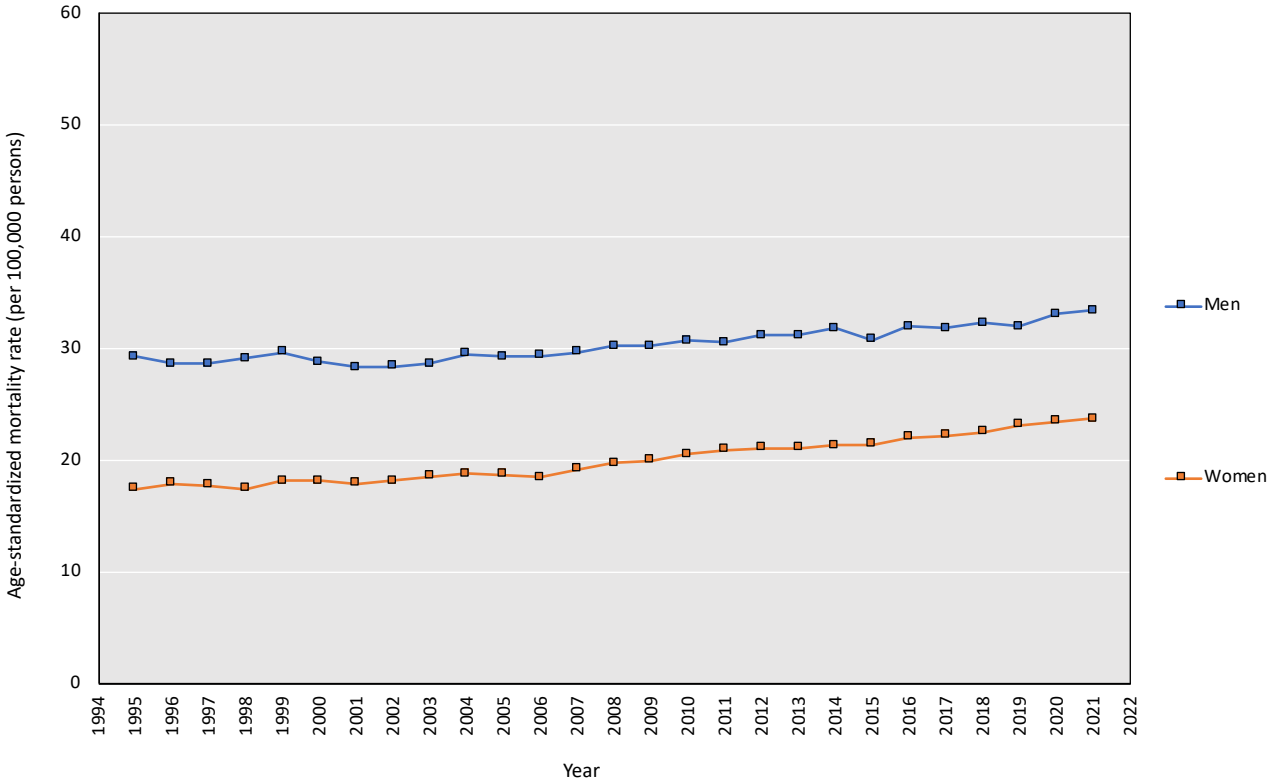
(F) Liver (C22)



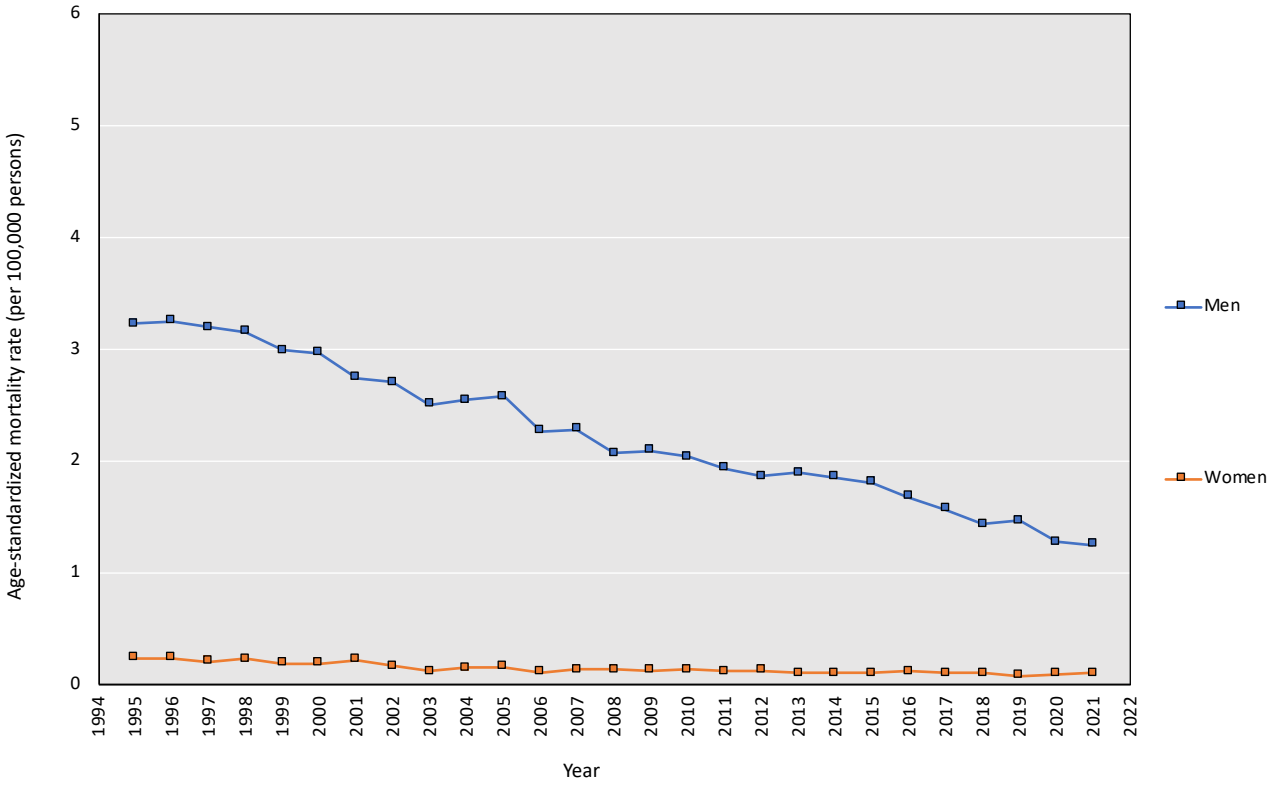
(G) Gallbladder and bile ducts (C23-24)



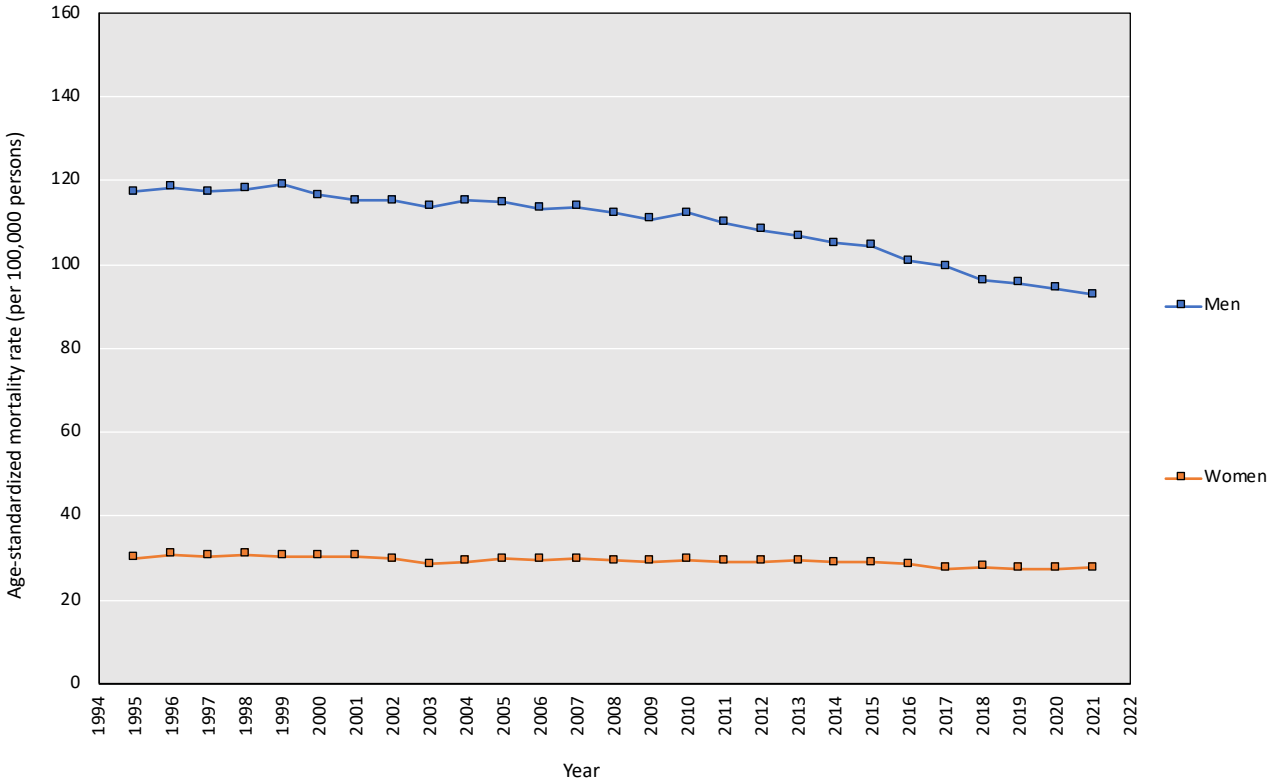
(H) Pancreas (C25)



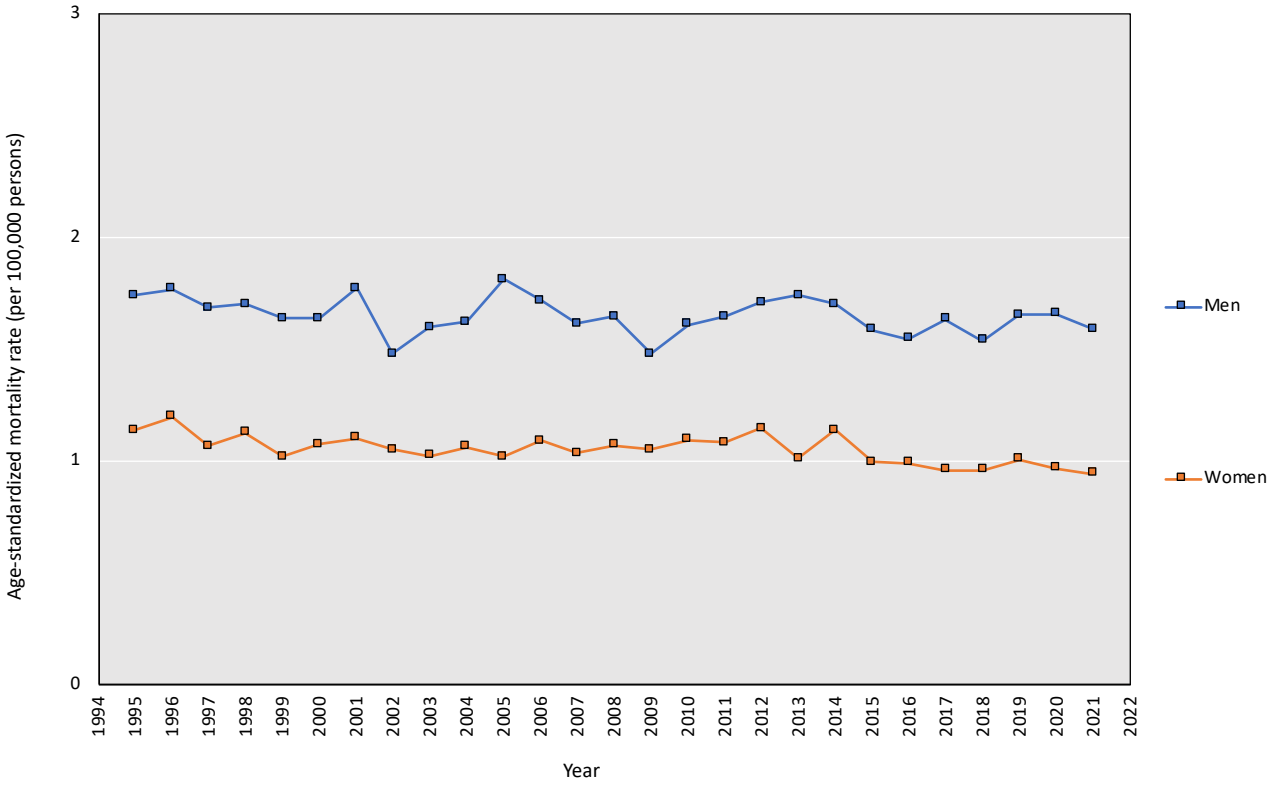
(I) Larynx (C32)



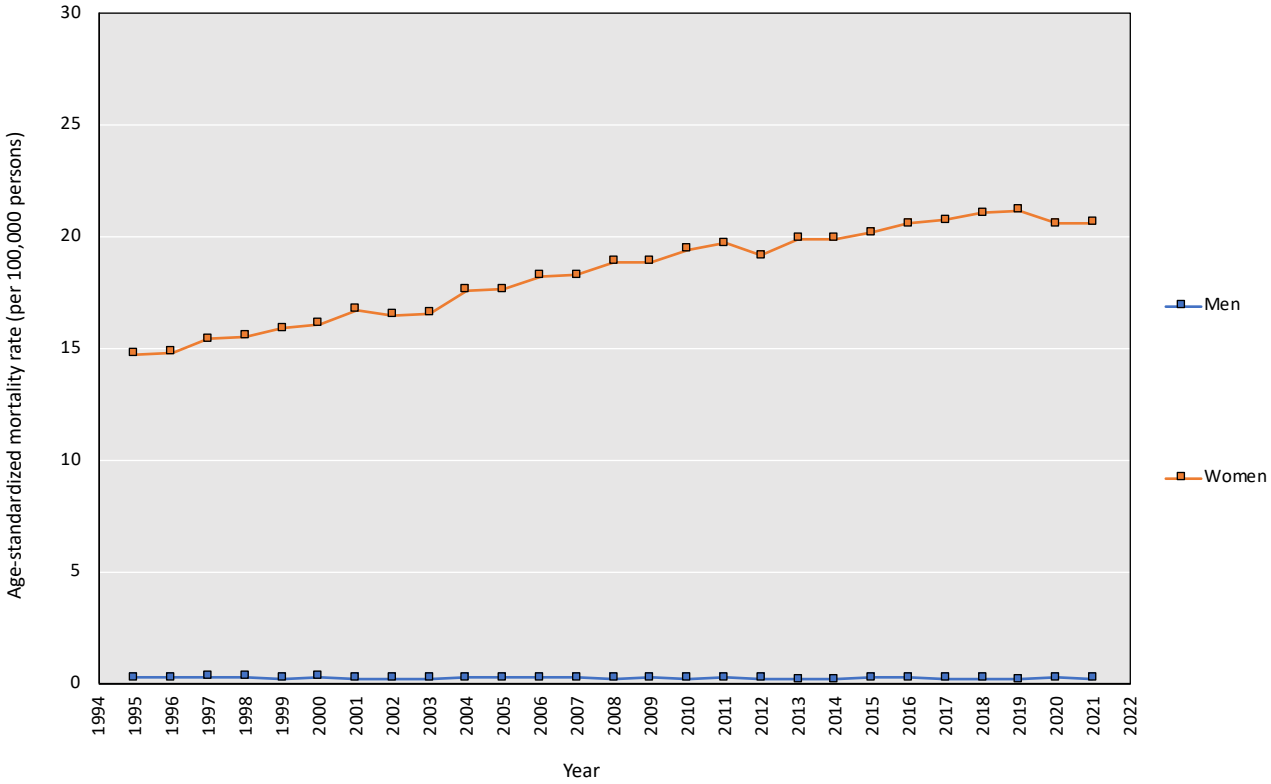
(J) Lung, trachea (C33-34)



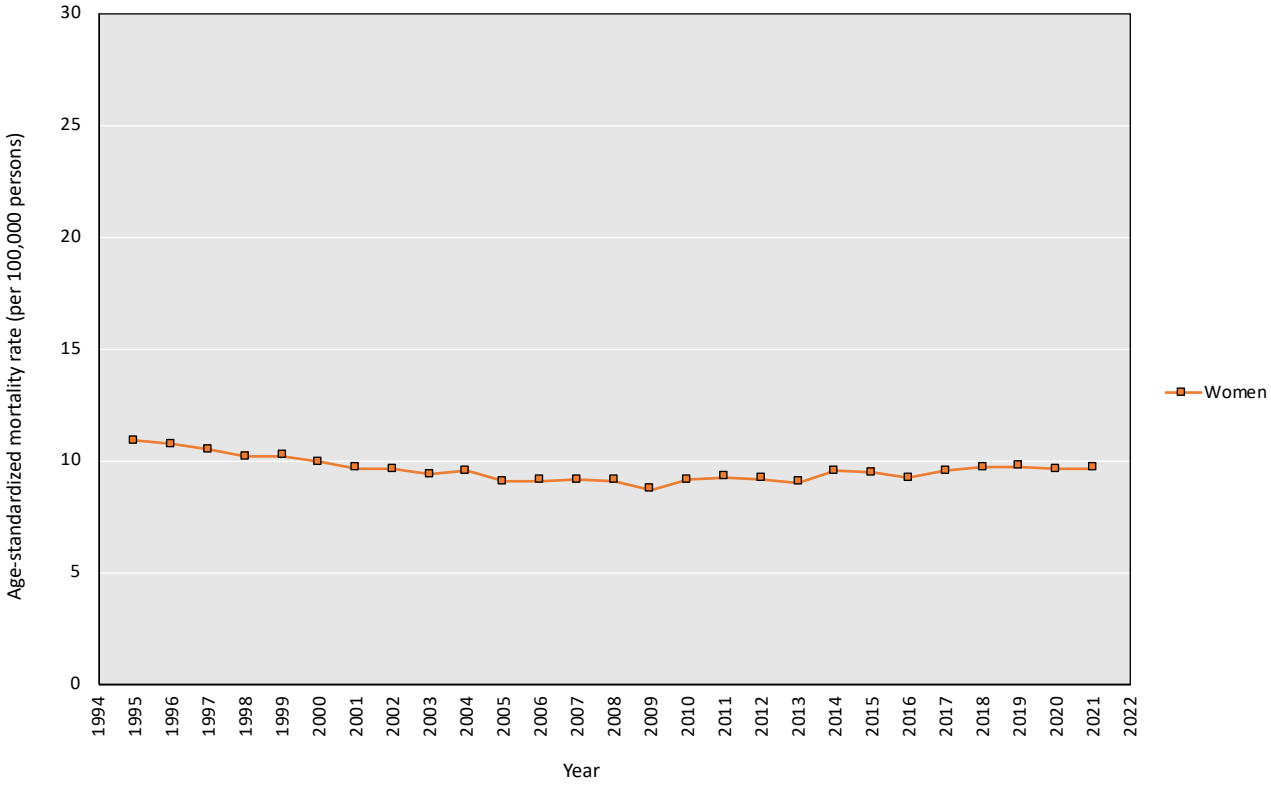
(K) Skin (C43-44)



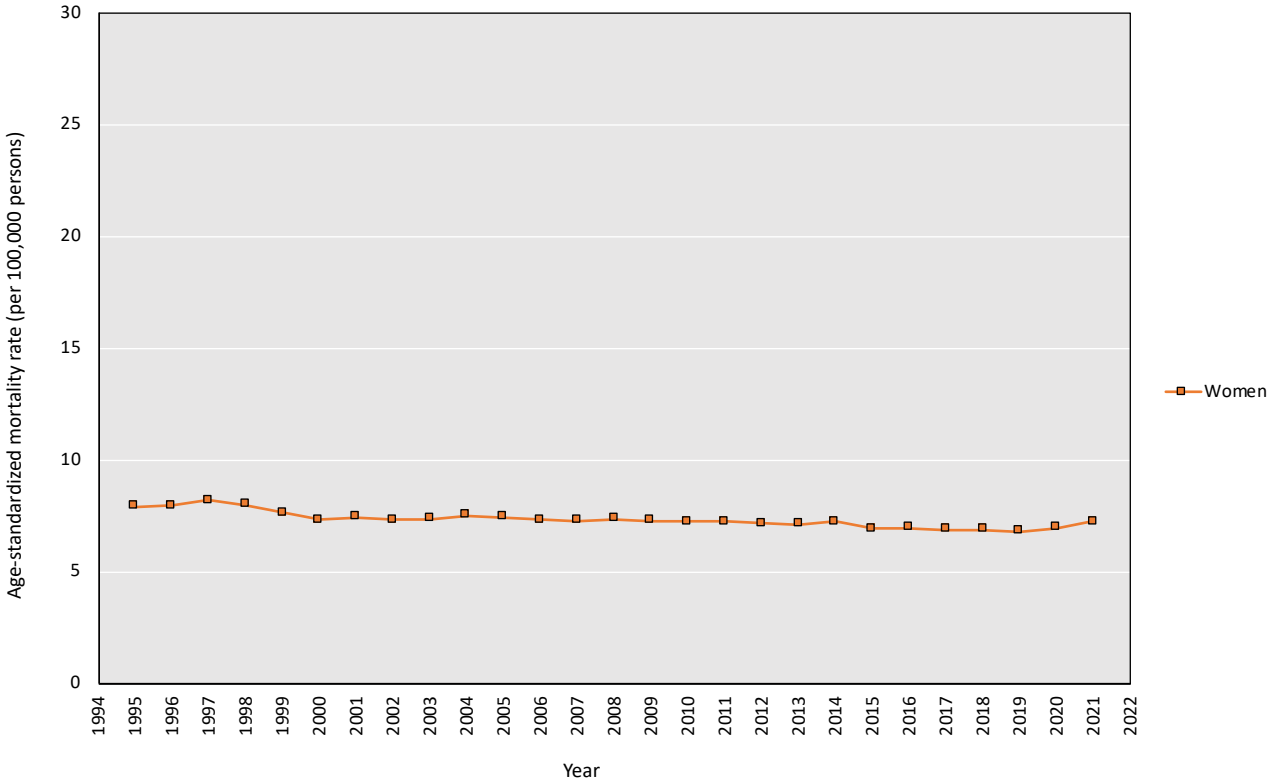
(L) Breast (C50)



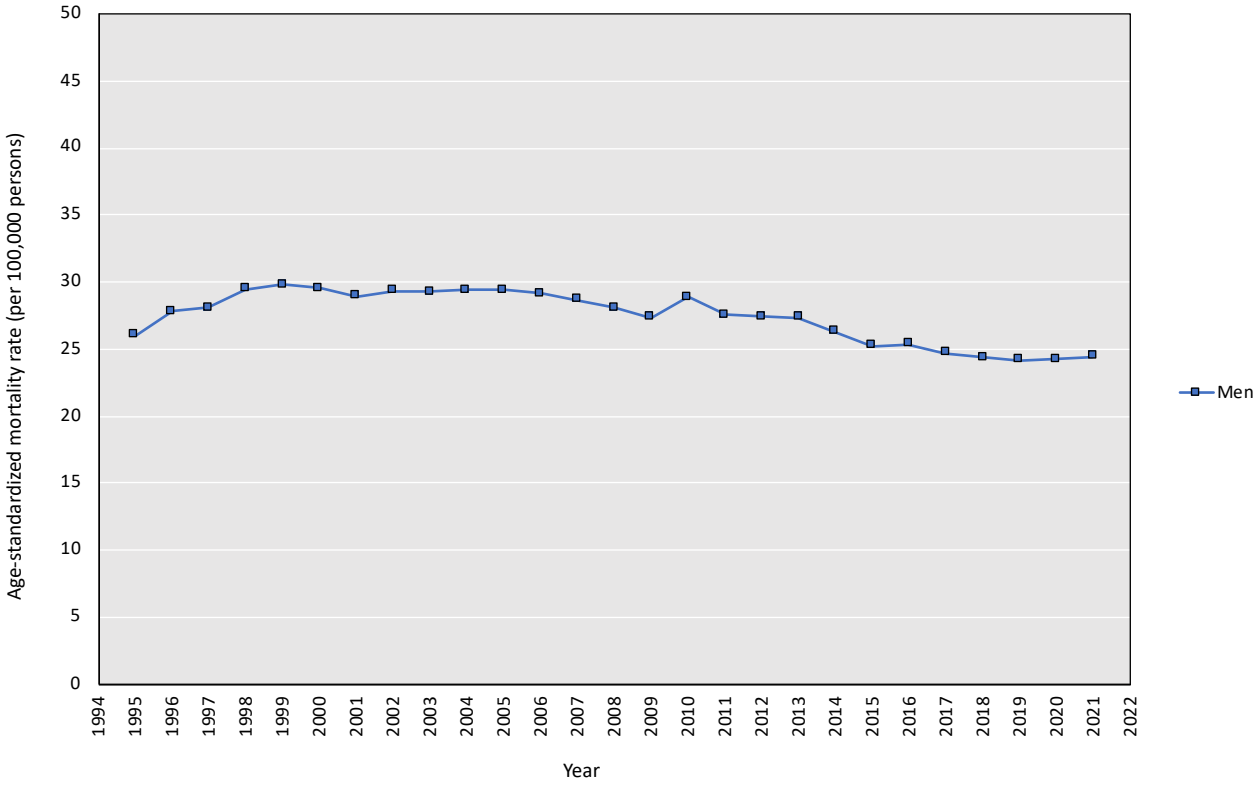
(M) Uterus (C53-55)



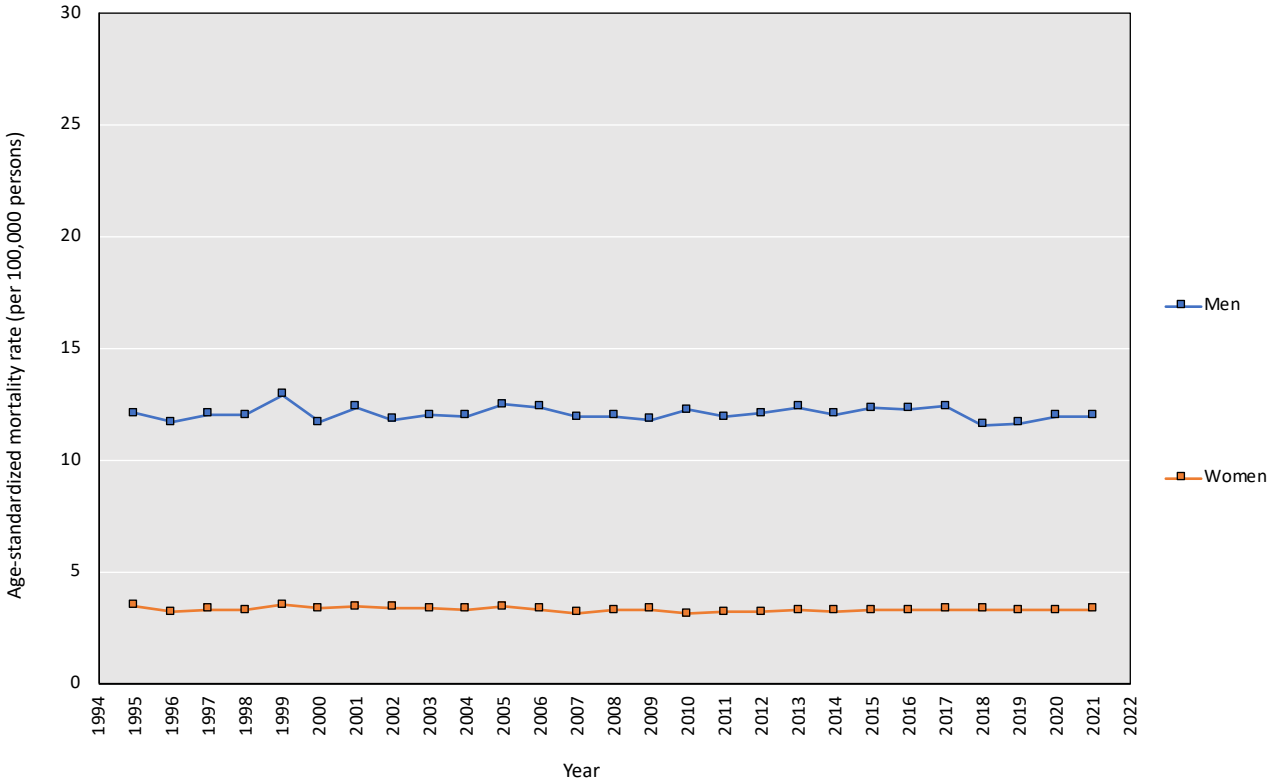
(N) Ovary (C56)



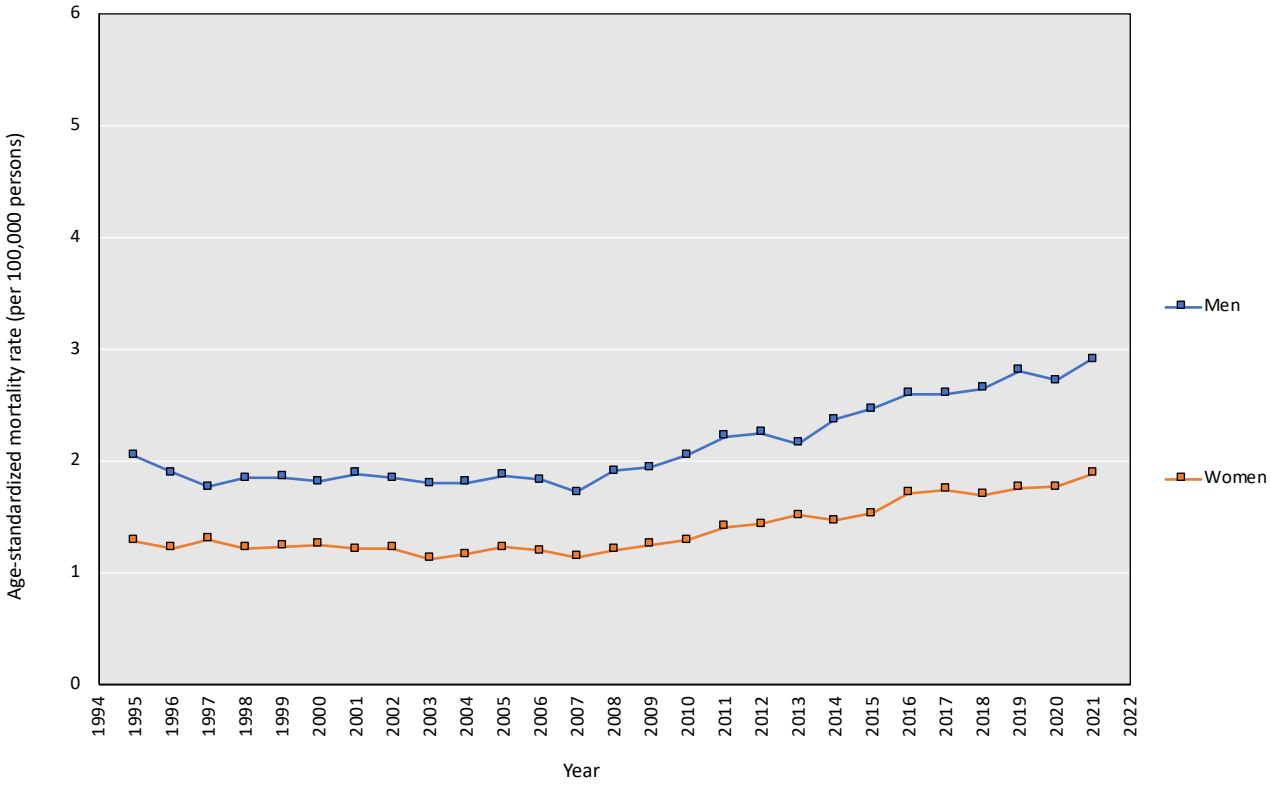
(O) Prostate (C61)



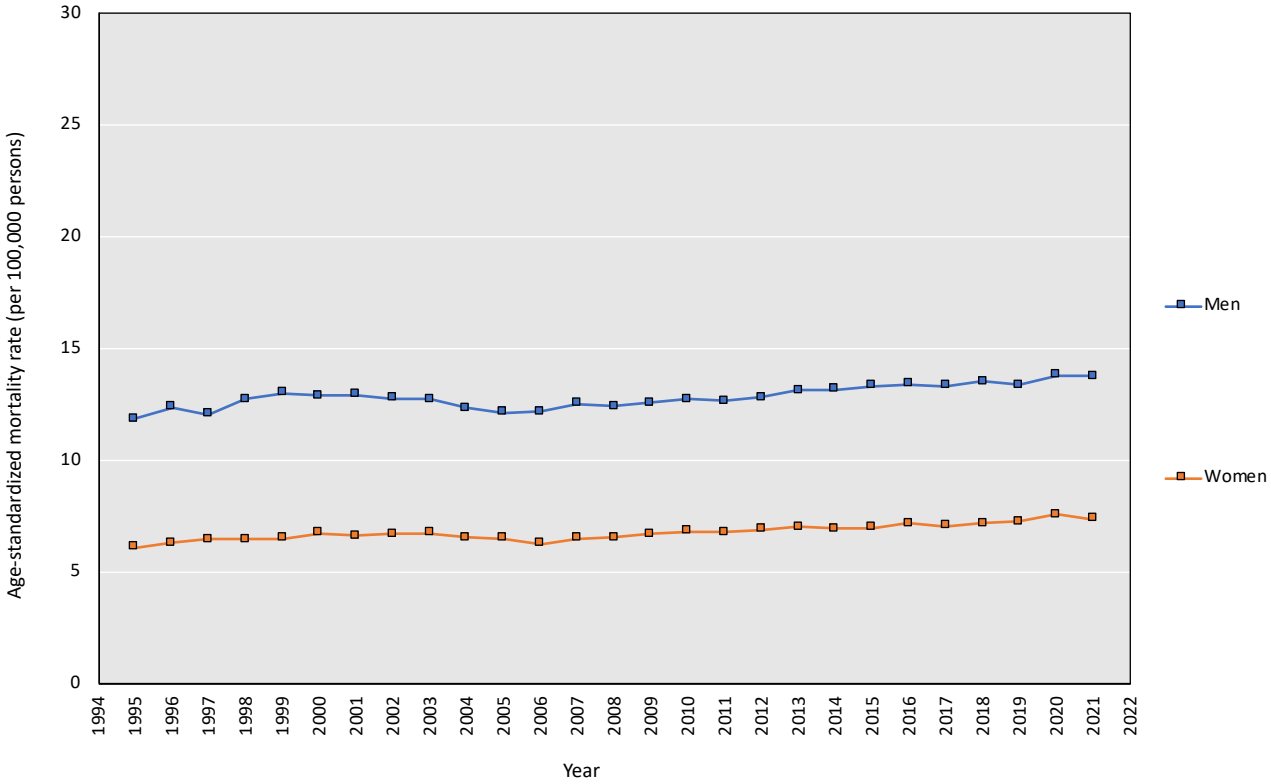
(P) Bladder (C67)

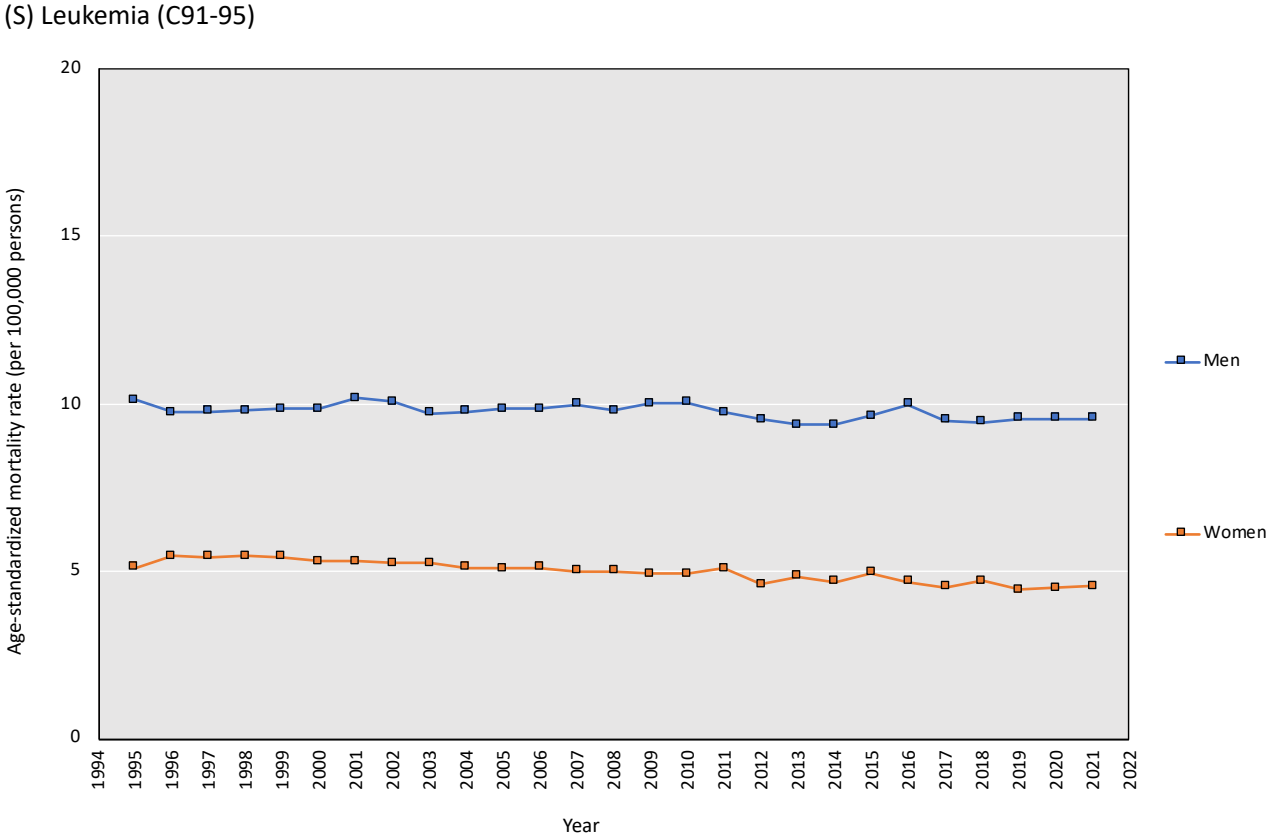


(Q) Brain, nervous system (C70-72)



(R) Malignant lymphoma (C81-85, C96)





Appendix Figure 3. Trends in cancer age-standardized mortality rates by cancer site between 1995 and 2021

BMJ Open

Impact of the COVID-19 pandemic on mortality trends in Japan: a reversal in 2021? A descriptive analysis of national mortality data, 1995-2021

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-071785.R1
Article Type:	Original research
Date Submitted by the Author:	21-Jun-2023
Complete List of Authors:	Tanaka, Hirokazu; National Cancer Center Japan, Division of Surveillance and Policy Evaluation Togawa, Kayo; National Cancer Center Japan Katanoda, Kota; National Cancer Center Japan
Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology
Keywords:	COVID-19, Epidemiology < TROPICAL MEDICINE, Public health < INFECTIOUS DISEASES, Demography < TROPICAL MEDICINE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Impact of the COVID-19 pandemic on mortality trends in Japan: a reversal in 2021? A descriptive analysis of national mortality data, 1995-2021

Hirokazu Tanaka, Kayo Togawa, Kota Katanoda*

All authors: Division of Population Data Science, National Cancer Center Institute for Cancer Control, 5-1-1, Tsukiji, Chuo-ku, Tokyo, 104-0045, Japan

***Corresponding author:** Hirokazu Tanaka
Division of Population Data Science, National Cancer Center Institute for Cancer Control
5-1-1, Tsukiji, Chuo-ku, Tokyo, 104-0045, JAPAN
E-mail: hitanak@ncc.go.jp
Phone: +81335475201

Figures and Tables: 4 figures**; Word count**: 2,012 words

Declarations of interest: none

Abstract (266 words)

Objective: The COVID-19 pandemic led to an increase in mortality in most countries in 2020, deviating from prior decreasing trends. In Japan, however, mortality was suggested to decrease in 2020. This study investigated long-term mortality trends and cause-specific contributions, focusing on the period of the COVID-19 pandemic in Japan.

Design: We analysed Japanese age-standardized mortality rates (ASMRs) from 1995 to 2021 using vital statistics.

Main outcome measures: The cause-specific annual ASMR changes were calculated in comparison with the previous year over the abovementioned period.

Results: There was a general downward trend in overall ASMR for both sexes until 2020 followed by a small increase in 2021. In men, the all-cause ASMR (per 100,000 persons) decreased from 1352.3 to 1328.8 in 2020 (−1.74% from 2019), and increased to 1356.3 in 2021 in men (+2.07% from 2020). In women, the all-cause ASMR decreased from 746.0 to 722.1 in 2020 (−3.20% from 2019), and increased to 737.9 (+2.19% from 2020) in 2021. ASMRs from malignant neoplasms, pneumonia, accidents, and suicide (men only) continued to decrease during the COVID-19 pandemic while the trend of cardiovascular mortality increased in 2021. Analysis of ASMR changes revealed that COVID-19, senility, cardiovascular disease, and 'other causes not classified as major causes' contributed to the all-cause mortality increase in 2021.

Conclusions: In Japan, the decreasing trend in overall mortality continued in 2020 despite the COVID-19 pandemic. However, approximately 2% mortality increase was observed in 2021, which was attributable to COVID-19, senility, cardiovascular disease, and 'other causes'. The year 2021 was a turning point of mortality trends in Japan, although continued monitoring is warranted.

Funding: Grants-in-Aid for Cancer Control Policy from the Ministry of Health, Labour, and Welfare, Japan (20EA1017); Japan Agency for Medical Research and Development (AMED: 22ck0106778h0001)

Keywords: COVID-19 pandemic; mortality trends; vital statistics; increase in mortality; Japan

Strengths and limitations of this study

- This is the first study to report comprehensively on mortality in Japan since the Ministry of Health, Labour, and Welfare published the 2021 complete mortality data for the Japanese population.
- From 1995 to 2020, we found a general downward trend in overall age-standardized mortality rates (ASMRs) for both sexes (except 2011, the year of the Great East Japan Earthquake) until 2020.
- An increase was observed in 2021 in the annual mortality rate, though the impact of COVID-19 pandemic on mortality still seems to be limited.
- The analysis of ASMR changes revealed that COVID-19, senility, cardiovascular disease, and 'other causes not classified as major causes' contributed to all-cause mortality increase in 2021.
- The mortality increase in 2021 may be associated with the increase of COVID-19 cases; however, further analysis is needed to clarify the quantitative impact of the increase, such as 'excess deaths'.

Introduction

Approximately three years into the pandemic, the impact of COVID-19 on Japan continues to increase. Although the Japanese government did not introduce strict COVID-19 restrictions such as lockdown, people's daily lives were affected, as were the lives of health-care workers since the first declaration of a state of emergency in April 2020. To date, however, no nationwide mortality data that discuss the impact of the COVID-19 pandemic on mortality trends have been reported in Japan. Careful assessment of the impact of the pandemic on population health would aid in the evaluation of efforts during the pandemic and identify lessons, not only for Japan but also globally.

In most high-income countries, life expectancy in 2020 was shorter than that before, attributable to both the direct and indirect effects of COVID-19.[1] For example, reductions in life expectancy in 2020 were observed in Russia, the U.S., Spain, England/Wales, Netherlands, Sweden, and France.[2] However, in Japan, life expectancy was not shortened in 2020 according to the Japanese Ministry of Health, Labour and Welfare (MHLW),[1,3] a deviation from the decreasing trend in most countries.[1]

Reasons for the prolonged life expectancy in 2020 despite the pandemic are unclear. One reason could be that Japan did not experience as large a number of COVID-19 cases that year as other countries. However, Japan experienced a six-fold increase in the number of reported cases from 2020 to 2021: 234 109 cases in 2020 and 1 492 874 cases in 2021.[4] Thus, annual mortality rate in 2021 in Japan may differ from the stable downward trend seen before 2020. This study aimed to explore the long-term mortality trends and cause-specific contributions during the COVID-19 pandemic in Japan, focusing on the years 2020 and 2021.

Methods

We illustrated changes in life expectancy between 2019 and 2020 for selected countries, including Japan, using data extracted from the World Development Indicators managed by the World Bank.[1] To evaluate the trends in the number of COVID-19 cases in Japan, we extracted data on the daily number of reported COVID-19 cases from 16 January 2020 (the first case confirmed) to 1 January 2023 from Japanese government records.[4] The numbers of deaths (5-year age intervals) between 1995 and 2021 were extracted from the vital statistics (complete deaths record) in Japan managed by MHLW.[3] The 2021 complete mortality data were published in September 2022.[3] The vital statistics cover all Japanese deaths that occurred in Japan. The relevant population data were also collected from the vital statistics and population census.

We calculated age-standardized mortality rates (ASMRs) for all causes of death combined and cause-specific deaths for major causes from 1995 to 2021 to assess trends in mortality rates. ASMRs were calculated using the 2015 Japan Standard Population.[5] We further calculated the annual percent changes in ASMRs before and during the early part of the COVID-19 pandemic (2020 and 2021). Causes of death (the International Classification of Diseases 10th revision: ICD-10) included: certain infectious and

parasitic diseases (A00-B99), malignant neoplasms (C00-C97), heart diseases (I01-I02.0, I05-I09, I20-I25, I27, I30-I52), cerebrovascular diseases (I60-I69), pneumonia (J12-J18), liver disease (K70-K76), senility (R54), accidents (V01-X59), suicide (X60-X84), and COVID-19 (U07). These classifications were based on the leading causes of death reported by the official mortality statistics from MHLW.[3] MHLW follows the algorithm for classifying the causes of death based on ICD-10.

To analyse the contribution of the cause of death to annual all-cause ASMR changes, the cause-specific ASMR changes in comparison with those of the previous year were calculated for six periods from 2015–2016 to 2020–2021.

Patient and public involvement

Actual patients were not involved in this study of data.

Results

Figure 1 shows Japan was one of the countries where life expectancy was prolonged in 2020 despite having shortened in many high-income countries such as the U.S. and France. Figure 2 shows trends in the daily number of reported COVID-19 cases in Japan since 16 January 2020. The peak of reported COVID-19 cases was observed in August 2022 (7th COVID-19 wave). While the absolute number of COVID-19 cases was very small in 2020, the annual number of reported COVID-19 cases increased rapidly in 2021 and 2022.

Figure 3 shows the trends in all-cause ASMRs (per 100 000 persons) between 1995 and 2021. Supplement Table 1 shows the trends in number of deaths in Japan between 1995 and 2021. After the Great East Japan Earthquake occurred in 2011, ASMRs continued decreasing until 2020, then increased in 2021 in both sexes. For men, all-cause ASMRs (per 100 000 persons) were 1352.3 in 2019 (-1.69% from 2018), 1328.8 in 2020 (−1.74% from 2019), and 1356.3 in 2021 (+2.07% from 2020). For women, all-cause ASMRs were 746.0 in 2019 (−1.39% from 2018), 722.1 in 2020 (−3.20% from 2019), and 737.9 in 2021 (+2.19% from 2020). Age-specific analyses also showed stable to slightly increased mortality trends during the period of COVID-19 pandemic (Supplement Figure 1). Supplement Figure 2 shows the trends in cause-specific ASMRs between 1995 and 2021. For men, COVID-19 ASMRs were 3.8 in 2020 and 17.5 in 2021. For women, COVID-19 ASMRs were 1.5 in 2020 and 7.7 in 2021. ASMRs from malignant neoplasms, pneumonia, accidents, and suicide (men only) decreased during the COVID-19 pandemic in Japan while the trend of cardiovascular disease (heart disease and cerebrovascular disease combined) increased in 2021. In addition, the trend of suicide in women increased in 2020. Supplement Figure 3 shows trends in malignant neoplasms ASMRs by cancer site. Trends in most malignant neoplasms were decreased or stable, which was not altered compared to the trends before 2020.

Figure 4 shows the cause-specific contribution to annual changes in all-cause ASMR. The analysis of annual ASMR changes revealed that decreases in malignant neoplasms, pneumonia, heart disease, and

cerebrovascular diseases continuously contributed to substantial annual mortality reductions for both sexes during 2015–2019; however, the contributions to reduction disappeared for cardiovascular disease from 2020 to 2021. COVID-19 (+13.7 per 100 000 for men and +6.2 per 100 000 for women in comparisons with the previous year) and senility (+7.4 per 100 000 for men and +8.1 per 100,000 for women in comparisons with the previous year) largely contributed to the mortality increases from 2020 to 2021. Also, 'other causes not classified major causes' contributed to all-cause mortality increase as well from 2020 to 2021.

Discussion

This is the first study to comprehensively report on mortality analysis in Japan since MHLW published the 2021 complete mortality data for the Japanese population. We found that the numbers of deaths from COVID-19 were 9 732 (1.32% of all deaths) for men and 7 034 (1.00% of all deaths) for women in 2021, a substantial increase from the year 2020 (2 094 deaths for men and 1 372 deaths for women). The number of deaths in the population due to diagnosed COVID-19 was relatively low compared to many other high-income countries.[6] In both men and women, all-cause ASMR decreased gradually every year from 2011 to 2020 and increased from 2020 to 2021, with a slightly greater decrease in women than in men between 2019 and 2020. In Japan, declining trends in all-cause mortality reversed in 2021 for the first time since the Great East Japan Earthquake occurred in 2011.

The mortality trend varied by cause of death. The patterns of mortality change during the COVID-19 pandemic could be classified into the following three categories: (1) stable mortality decline (e.g. certain infectious and parasitic diseases, malignant neoplasms, and pneumonia), (2) stable mortality increase (e.g. senility), and (3) reversal of decreasing mortality trend (heart diseases, cerebrovascular diseases, suicide for women). Considering these changes, a substantial mortality increase from COVID-19 and senility resulted in an all-cause mortality increase in 2021 while malignant neoplasms and pneumonia contributed to mortality declines.

Recorded mortality from malignant neoplasms declined during the COVID-19 pandemic, despite that patients diagnosed with a cancer regardless of COVID-19 status were required to postpone non-urgent surgeries, suspend outpatient visits, and change treatment methods. Indeed, the numbers of cancer diagnoses, the cancer screening, outpatient visits, and surgical procedures in 2020 have been reported to be lower than those before 2019.[7-10] Those reports have raised deep concern about potential consequences, such as delays in diagnosis and care, decreased patient survival, and increased population mortality; however, our findings revealed a decrease in 2020 and no obvious change in cancer mortality, at least in 2021. Nevertheless, further monitoring is necessary because the delays in diagnosis and treatment can exert a belated effect on mortality.

We found that the ASMR from cardiovascular disease increased in 2021. The loss of reduction trends of cardiovascular disease partially resulted in increasing all-cause mortality in 2021 for both sexes.

This is supported by another study reporting excess deaths from cardiovascular disease from April to May 2021.[11] As a direct pathway, the COVID-19 pandemic may have caused an increase in the prevalence of severe heart disease for the Japanese population because COVID-19 is suggested to be a risk factor for acute myocardial infarction and ischemic stroke.[12] In addition, the pandemic might have induced a delay in emergency transport and delay in arrival at hospital, resulting in the loss of timely treatment. This may be an indirect pathway through which mortality reductions of cardiovascular disease stagnated in Japan.

A substantial increase in mortality due to senility has been occurring since the mid-2000s, independent of the pandemic. This can be interpreted as a result of the rapid aging of the Japanese population. Although we applied age-standardization for mortality analysis, the increase in the absolute number of deaths from senility, especially for the oldest old (85 years and over), resulted in an increase in ASMR. During the pandemic, however, changes in patterns or places of medical care may have resulted in more physicians reporting senility as the cause of death, especially deaths at home. Indeed, excess deaths from senility at home have been observed since May 2020.[11] As such, for the elderly, both direct and indirect death by COVID-19 may be miscoded to senility, which contributed to excess deaths in 2021. The sharp increase in deaths by 'other causes not classified as major causes' in 2021 (Figure 3) may have occurred by a similar mechanism. Therefore, our findings suggest that senility and 'other causes not classified as major causes' may largely represent the excess deaths in Japan during the pandemic. This may also include underdiagnosis and potential misclassification of causes of death.

We found clear declines in mortality from infectious diseases (excluding COVID-19) and infectious pneumonia since the pandemic began in Japan. This is likely because the countermeasures for COVID-19 such as wearing a mask, hand hygiene, and social distancing prevented these diseases. In addition, clear mortality declines due to accidents were observed probably because fatal traffic accidents decreased due to stay-at-home measures. These are positive outcomes of the COVID-19 measures; however, we identified an increase in suicide rate among women in 2020 and 2021. The increase did not largely impact on all-cause mortality changes for women but this is obviously a negative effect of the COVID-19 measures such as restrictions of economic activity (e.g. cancellation of events and shorter business hours for restaurants).[13,14]

This study is a descriptive analysis of national mortality data and should accordingly be interpreted with caution. Our findings suggest that the mortality increase in 2021 may be associated with the increase in COVID-19 cases; however, further analysis is needed to clarify the quantitative impact such as 'excess deaths'. Also, long-term monitoring is necessary from 2022 onwards, especially for deaths from chronic diseases that may have long-term effects by changes in lifestyle and medical care.

In conclusion, a sign of increasing mortality was observed in 2021 in the annual mortality rate in Japan, although the impact of the COVID-19 pandemic on mortality in Japan still seems to be limited. The observed increase in mortality was attributable to COVID-19, senility, cardiovascular disease, and 'other causes not classified as major cause'. Taking the rapidly increasing rate of COVID-19 cases in

2022 into consideration, further monitoring is warranted for the year 2022, which may reveal a larger impact of the pandemic on mortality compared to that for 2020 and 2021.

Ethics statements

Patient consent for publication

Not applicable.

Ethics approval

Ethics approval was not applicable.

Data availability

This study used the vital statistics data from a portal site for Japanese Government Statistics (e-Stat: https://www.e-stat.go.jp/), and data at an individual level were not used.

Authors' contributions: All author had full access to all the study data. H.T. was responsible for the integrity of the data, the accuracy of the data analysis, and the drafting of the manuscript. All authors contributed to the concept and design of the study. All authors critically reviewed the manuscript. K.K. supervised the study and provided administrative, technical, and material support.

Declaration of interest statement: The authors have no conflicts of interest directly relevant to the content of this study.

Funding: This research was supported by Grants-in-Aid for Cancer Control Policy from the Ministry of Health, Labour, and Welfare, Japan (20EA1017) and Japan Agency for Medical Research and Development (AMED; Grant Number: 22ck0106778h0001).

Patient and other consents: Not applicable.

Availability of data and materials: Data are available on request.

Acknowledgment: We thank Libby Cone, MD, MA, from Dmed (www.dmed.co.jp <http://www.dmed.co.jp/>) for editing English drafts of this manuscript.

Figure legends

Figure 1. Changes in life expectancy between 2019 and 2020 for selected countries for both sexes

Figure 2. Trends in the daily number of reported COVID-19 cases in Japan since 16 January 2020

Figure 3. Trends in all-cause and cause-specific age-standardized mortality rates between 1995 and 2021

Figure 4. Cause-specific contribution to changes in all-cause age-standardized mortality rates (annual comparisons with previous year): differences in changes in ASMR between 2020 and 2021 were calculated as ($ASMR_{2021} - ASMR_{2020}$) for each cause-specific death, where ASMR=age standardized mortality rate per 100 000 population.

Reference

1. The World Bank. Life expectancy at birth, total (years). https://data.worldbank.org/indicator/SP.DYN.LE00.IN Date accessed: December 12, 2022

2. Islam N, Jdanov DA, Shkolnikov VM, et al. Effects of covid-19 pandemic on life expectancy and premature mortality in 2020: time series analysis in 37 countries. *BMJ*. 2021;375:e066768.

3. Ministry of Health, Labour and Welfare. Vital Statistics. https://www.mhlw.go.jp/english/database/db-hw/vs01.html Date accessed: December 12, 2022

4. Ministry of Health, Labour and Welfare. Visualizing the data: information on COVID-19 infections. https://covid19.mhlw.go.jp/en/ December 12, 2022

5. Tanaka H, Tanaka S, Togawa K, Katanoda K. Practical implications of the update to the 2015 Japan Standard Population: mortality archive from 1950 to 2020 in Japan. *J Epidemiol*. (in press)

6. World Health Organization. WHO coronavirus (COVID-19) dashboard. https://covid19.who.int December 12, 2022

7. Ikeda N, Yamamoto H, Taketomi A, et al. The impact of COVID-19 on surgical procedures in Japan: analysis of data from the National Clinical Database. *Surg Today*. 2022;52:22-35.

8. Sato Y, Fujiwara Y, Fukuda N, et al. Changes in Treatment Behavior during the COVID-19 Pandemic among Patients at a Cancer Hospital. *Cancer Cell*. 2021;39:130-131.

9. Toyoda Y, Katanoda K, Ishii K, Yamamoto H, Tabuchi T. Negative impact of the COVID-19 state of emergency on breast cancer screening participation in Japan. *Breast Cancer*. 2021;28:1340-1345.

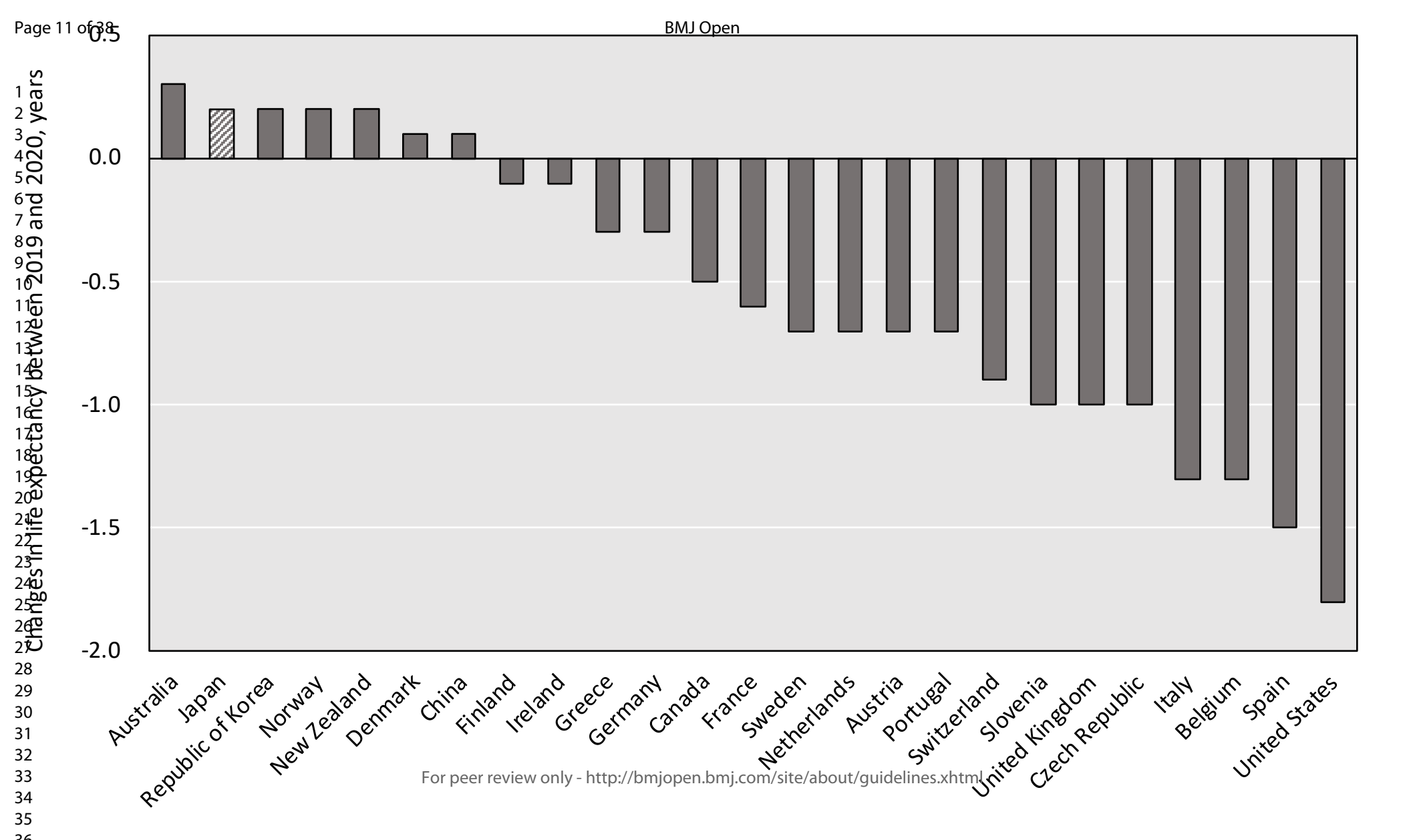
10. Okuyama A, Watabe M, Makoshi R, Takahashi H, Tsukada Y, Higashi T. Impact of the COVID-19 pandemic on the diagnosis of cancer in Japan: analysis of hospital-based cancer registries. *Jpn J Clin Oncol*. 2022;52:1215-1224.

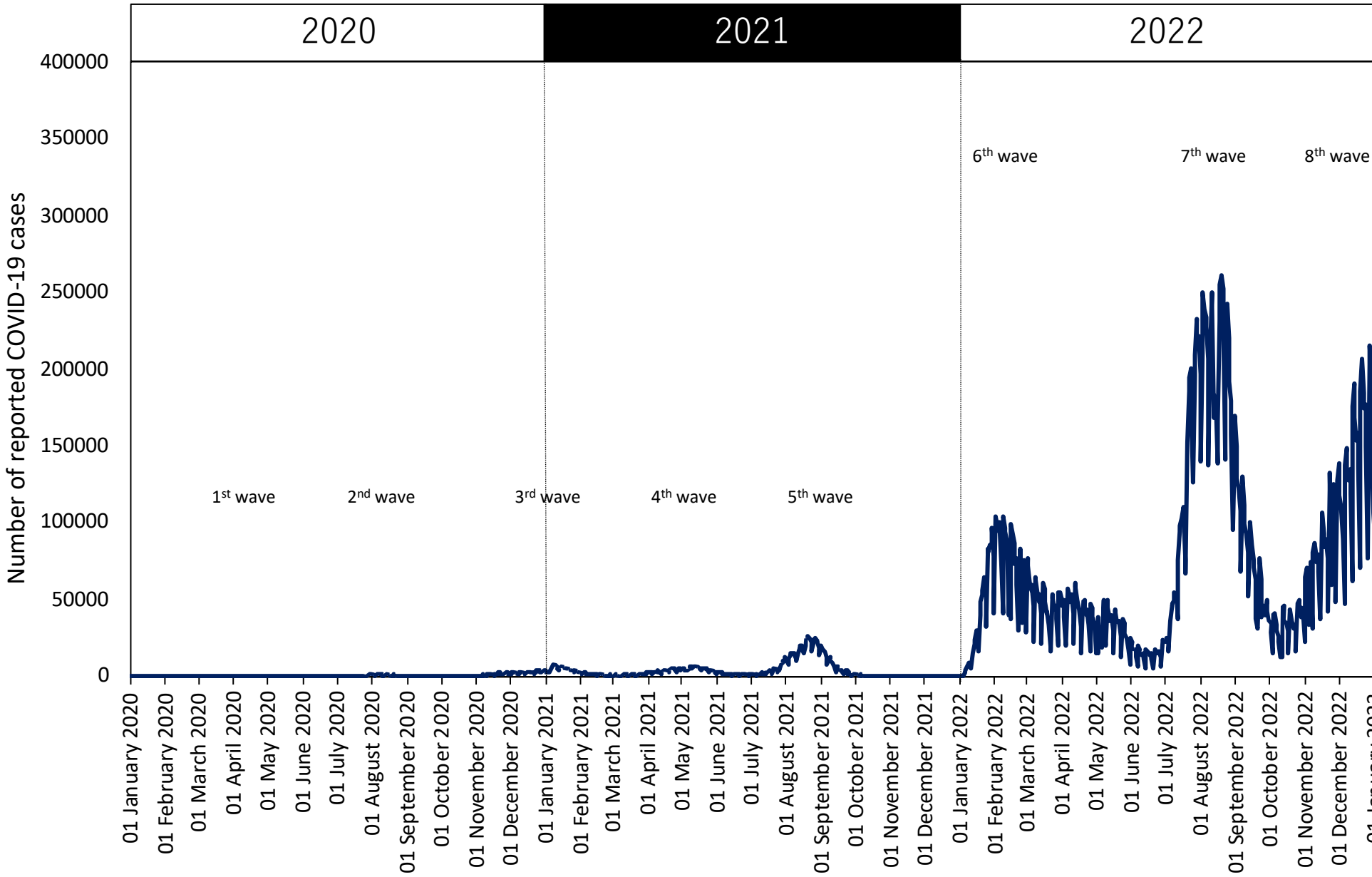
11. Nomura S, Eguchi A, Ghaznavi C, et al. Excess deaths from non-COVID-19-related causes in Japan and 47 prefectures from January 2020 through May 2021 by place of death. *SSM Popul Health*. 2022;19:101196.

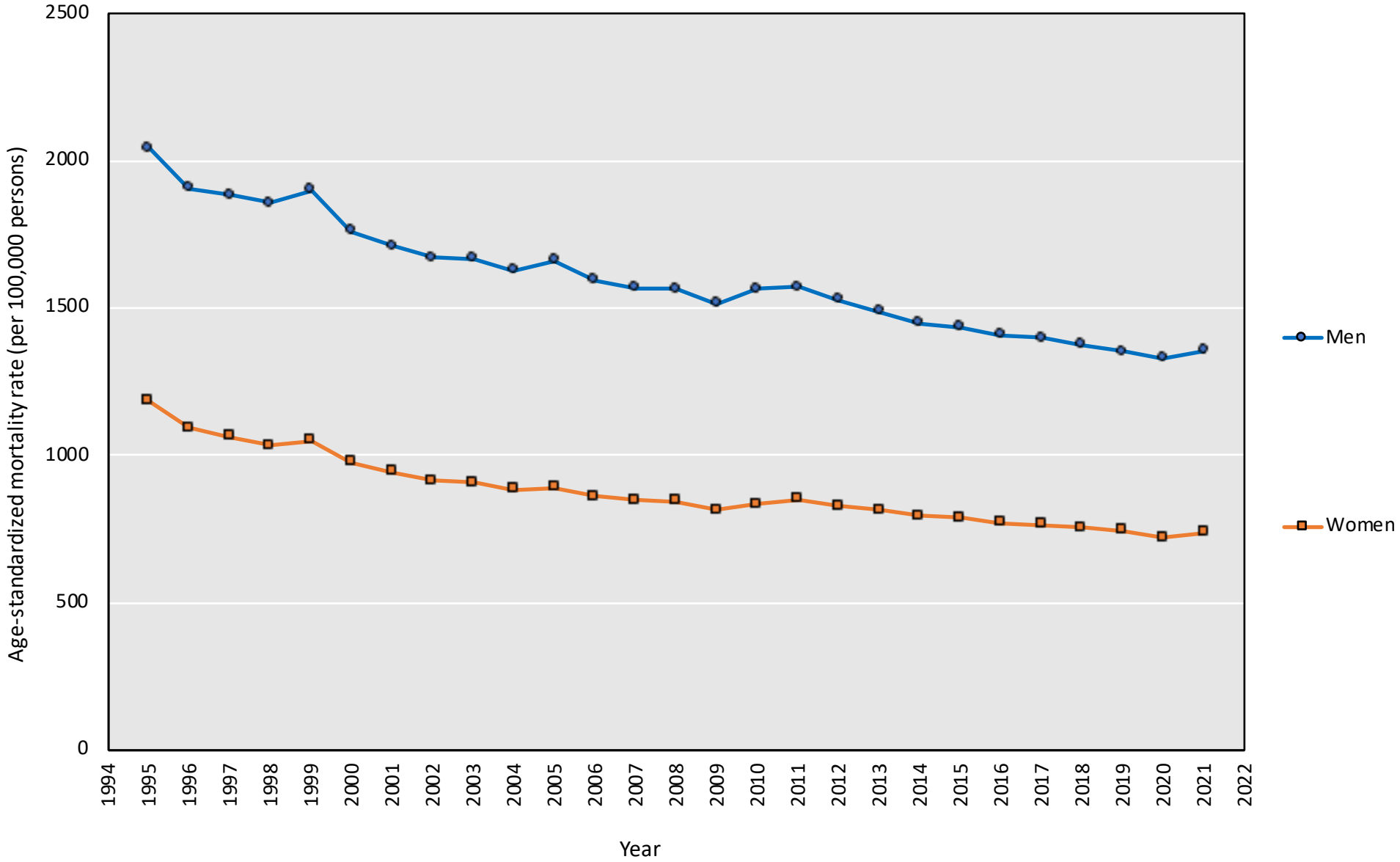
12. Katsoularis I, Fonseca-Rodriguez O, Farrington P, Lindmark K, Fors Connolly AM. Risk of acute myocardial infarction and ischaemic stroke following COVID-19 in Sweden: a self-controlled case series and matched cohort study. *Lancet*. 2021;398:599-607.

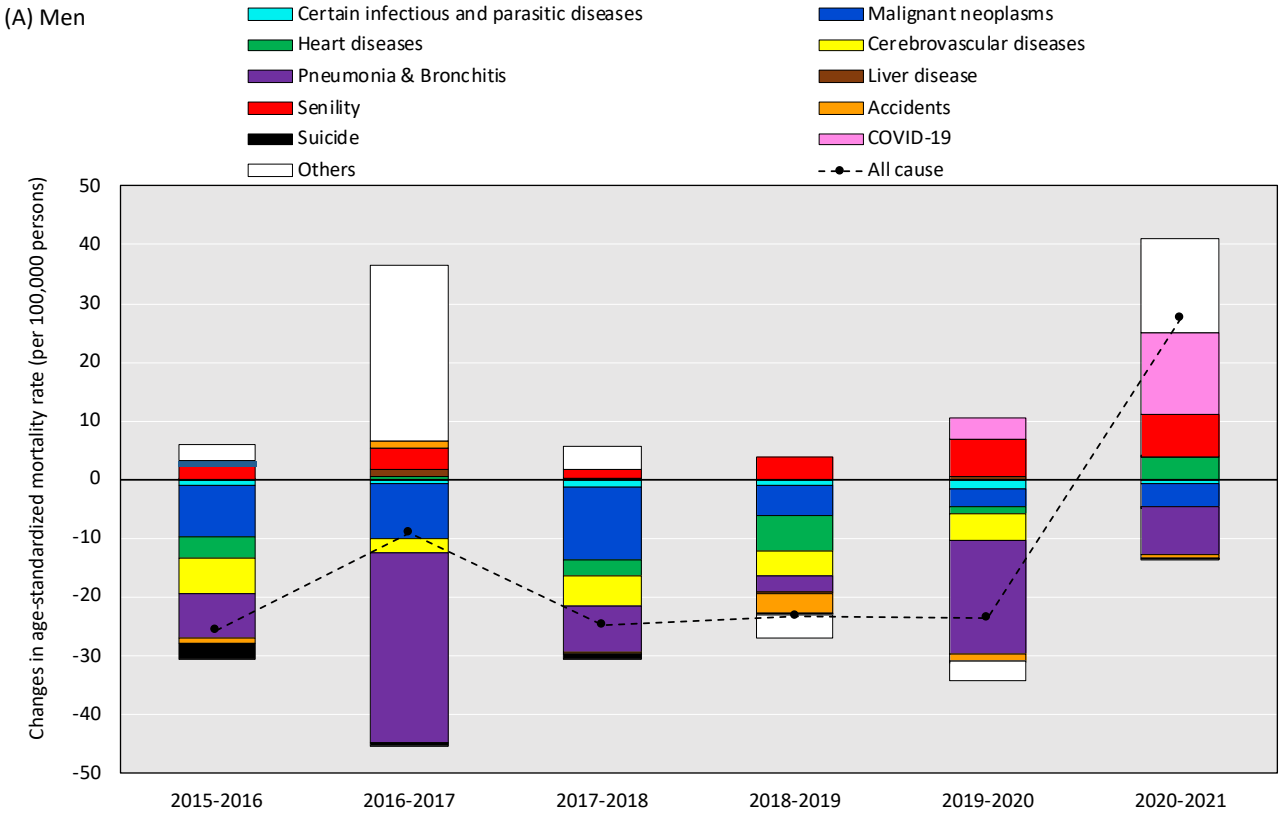
13. Sakamoto H, Ishikane M, Ghaznavi C, Ueda P. Assessment of Suicide in Japan During the COVID-19 Pandemic vs Previous Years. *JAMA Netw Open*. 2021;4:e2037378.

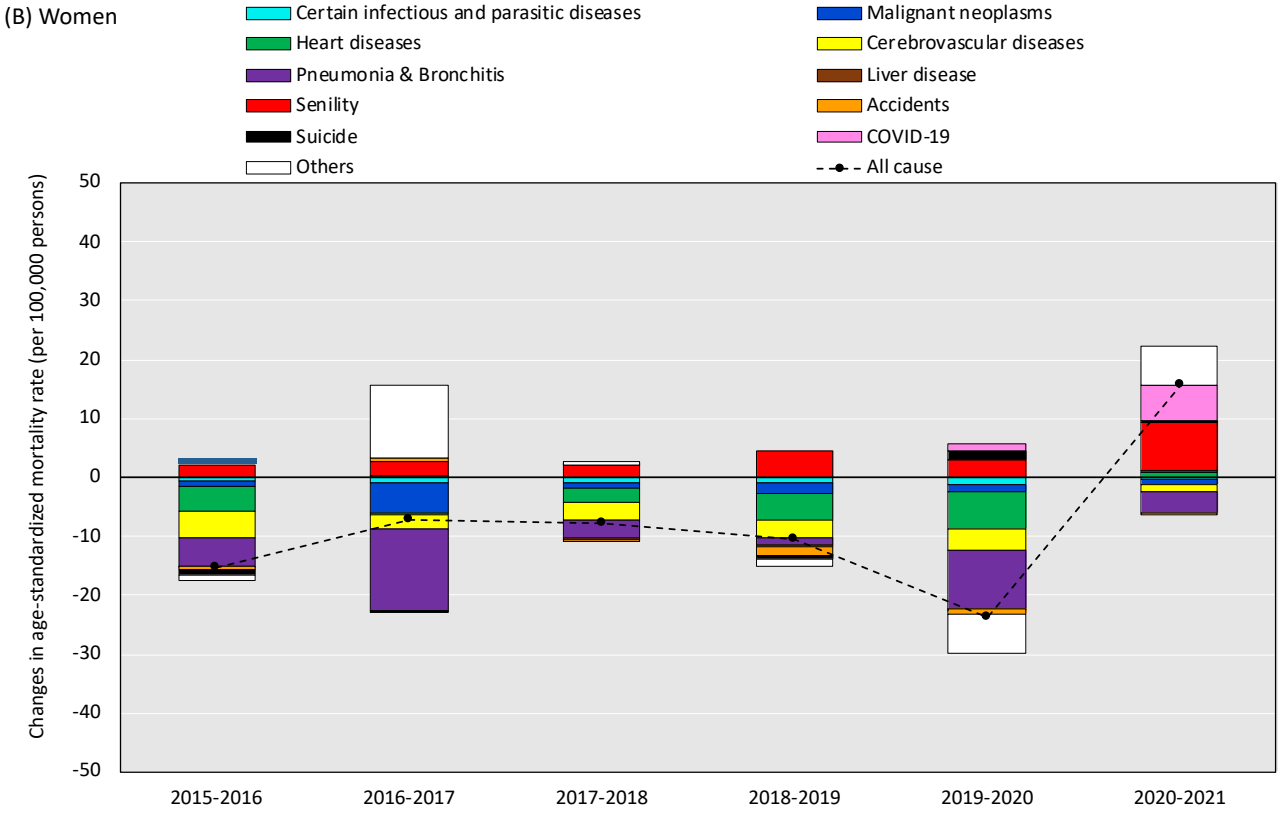
14. Kikuchi K, Anzai T, Takahashi K. The Unusual Increase in Suicides Among Women in Japan During The COVID-19 Pandemic: A Time-Series Analysis until October 2021. *J Epidemiol*. 2022. (in press)




2020
2021
2022
Number of reported COVID-19 cases
400000
350000
300000
250000
200000
150000
100000
50000
0
1st wave
2nd wave
3rd wave
4th wave
5th wave
6th wave
7th wave
8th wave
01 January 2020
01 February 2020
01 March 2020
01 April 2020
01 May 2020
01 June 2020
01 July 2020
01 August 2020
01 September 2020
01 October 2020
01 November 2020
01 December 2020
01 January 2021
01 February 2021
01 March 2021
01 April 2021
01 May 2021
01 June 2021
01 July 2021
01 August 2021
01 September 2021
01 October 2021
01 November 2021
01 December 2021
01 January 2022
01 February 2022
01 March 2022
01 April 2022
01 May 2022
01 June 2022
01 July 2022
01 August 2022
01 September 2022
01 October 2022
01 November 2022
01 December 2022
01 January 2023


2500
2000
1500
1000
500
0
Age-standardized mortality rate (per 100,000 persons)
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Year
Men
Women


(A) Men
Certain infectious and parasitic diseases
Malignant neoplasms
Heart diseases
Cerebrovascular diseases
Pneumonia & Bronchitis
Liver disease
Senility
Accidents
Suicide
COVID-19
Others
All cause
Changes in age-standardized mortality rate (per 100,000 persons)
50
40
30
20
10
0
-10
-20
-30
-40
-50
2015-2016
2016-2017
2017-2018
2018-2019
2019-2020
2020-2021

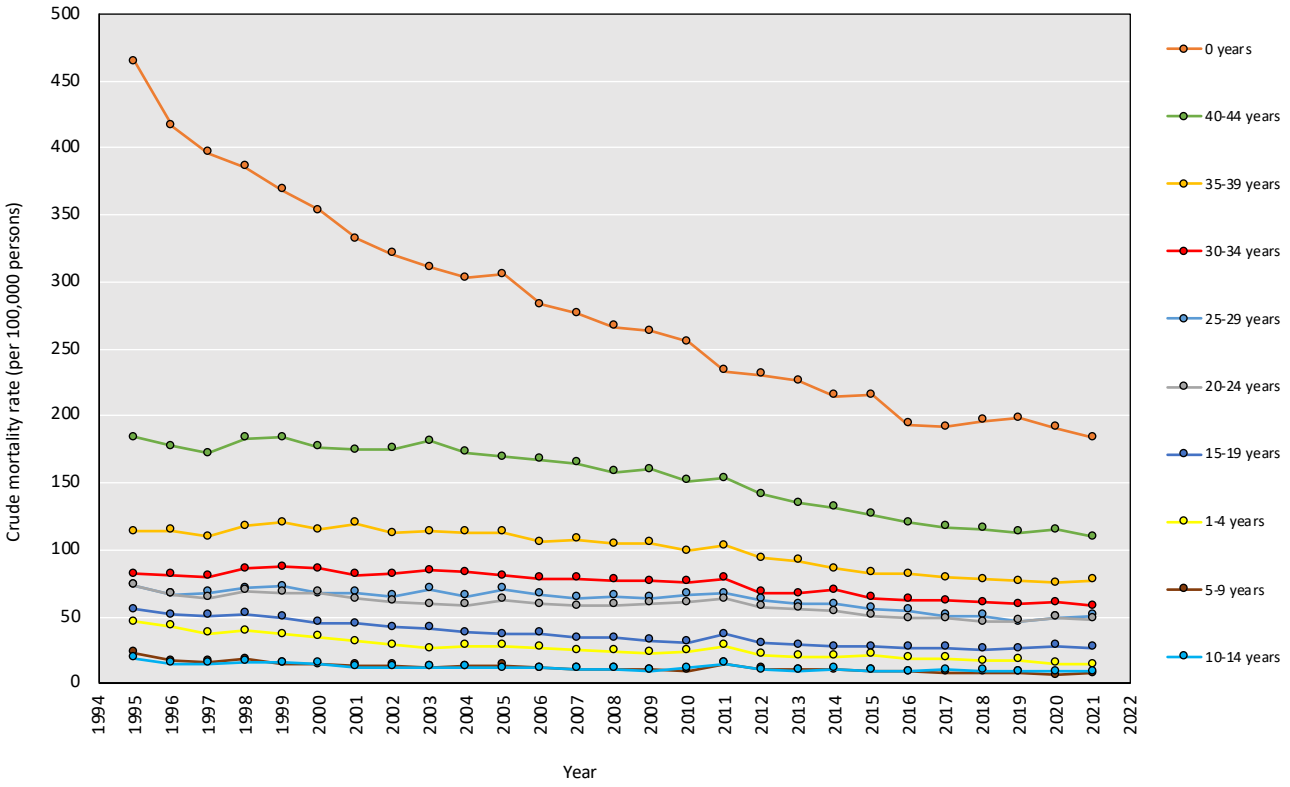

(B) Women
Certain infectious and parasitic diseases
Malignant neoplasms
Heart diseases
Cerebrovascular diseases
Pneumonia & Bronchitis
Liver disease
Senility
Accidents
Suicide
COVID-19
Others
All cause
Changes in age-standardized mortality rate (per 100,000 persons)
50
40
30
20
10
0
-10
-20
-30
-40
-50
2015-2016
2016-2017
2017-2018
2018-2019
2019-2020
2020-2021

Appendix Table 1. Number of deaths in Japan between 1995 and 2021*

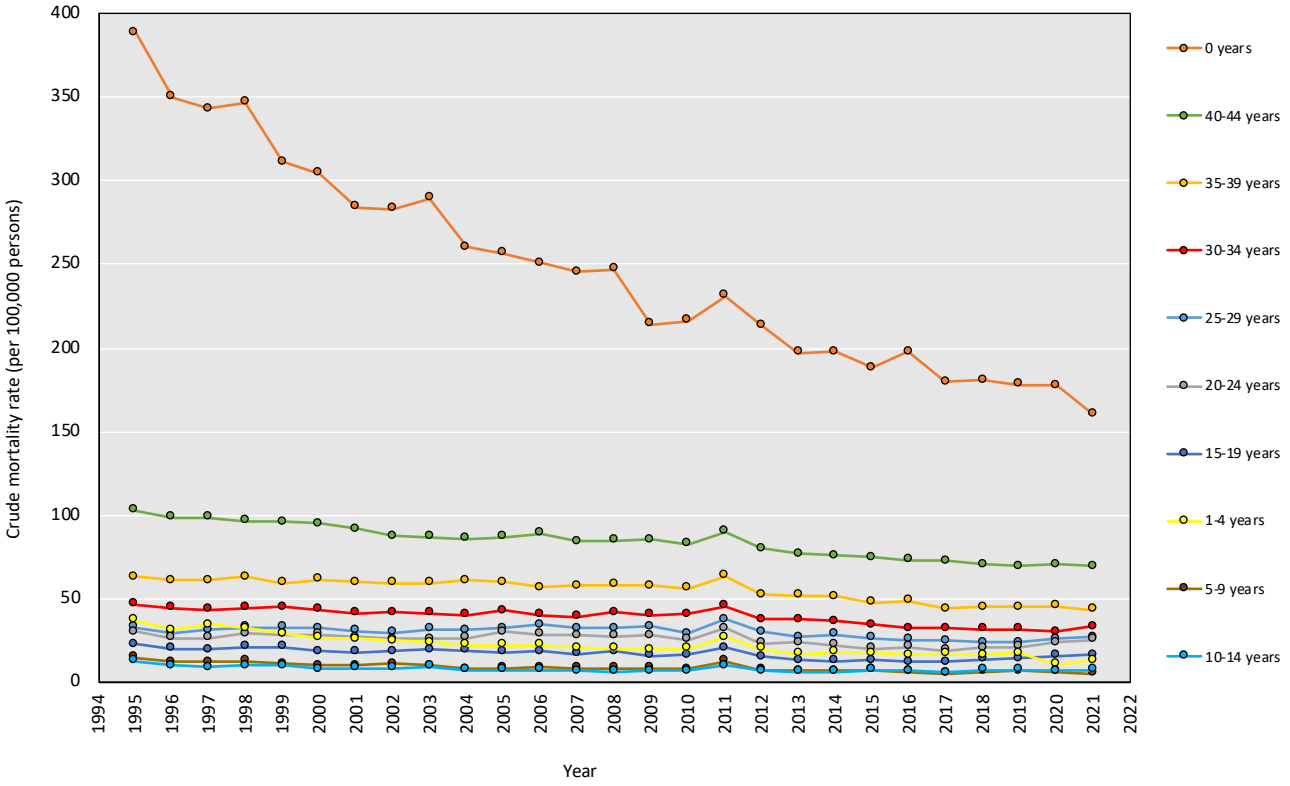
Year	Men					Women				
	All-cause	Malignant neoplasms	Heart disease	Cerebrovascular disease	COVID-19	All-cause	Malignant neoplasms	Heart disease	Cerebrovascular disease	COVID-19
1995	501276	159623	69718	69587	-	420863	103399	69488	76965	-
1996	488605	164824	68977	66479	-	407606	106359	69252	73887	-
1997	497796	167076	69776	65790	-	415606	108337	70398	72907	-
1998	512128	172306	71134	65529	-	424356	111615	71986	72290	-
1999	534778	175817	73979	66452	-	447253	114739	77100	72537	-
2000	525903	179140	72156	63127	-	435750	116344	74585	69402	-
2001	528768	181393	72727	63146	-	441563	119265	75565	68710	-
2002	535305	184033	74986	62229	-	447074	120535	77532	68028	-
2003	551746	186912	77989	63274	-	463205	122631	81556	68793	-
2004	557097	193096	77465	61547	-	471505	127262	82160	67508	-
2005	584970	196603	83979	63657	-	498826	129338	89146	69190	-
2006	581370	198052	82811	61348	-	503080	131262	90213	66920	-
2007	592784	202743	83090	60992	-	515550	133725	92449	66049	-
2008	608711	206354	86139	61121	-	533696	136609	95789	65902	-
2009	609042	206352	85543	59293	-	532823	137753	95202	63057	-
2010	633700	211435	88803	60186	-	563312	142064	100557	63275	-
2011	656540	213190	91298	59616	-	596526	144115	103628	64251	-
2012	655526	215110	92976	58625	-	600833	145853	105860	62977	-
2013	658684	216975	91445	56718	-	609752	147897	105278	61629	-
2014	660334	218397	92278	54995	-	612670	149706	104647	59212	-
2015	666707	219508	92142	53576	-	623737	150838	103971	58397	-
2016	674946	219846	93453	52718	-	633212	153242	104617	56635	-
2017	690770	220416	96330	53198	-	649797	152949	108538	56698	-
2018	699138	218625	98035	52398	-	663332	154959	110186	55788	-
2019	707421	220339	98210	51768	-	673672	156086	109504	54784	-
2020	706834	220989	99304	50390	2094	665921	157396	106292	52588	1372
2021	738141	222467	103700	51594	9732	701715	159038	111010	53001	7034

*Malignant neoplasms (ICD-10: C00-C97); Heart diseases (I01-I02.0, I05-I09, I20-I25, I27, I30-I52); Cerebrovascular diseases (I60-I69); COVID-19 (U07)

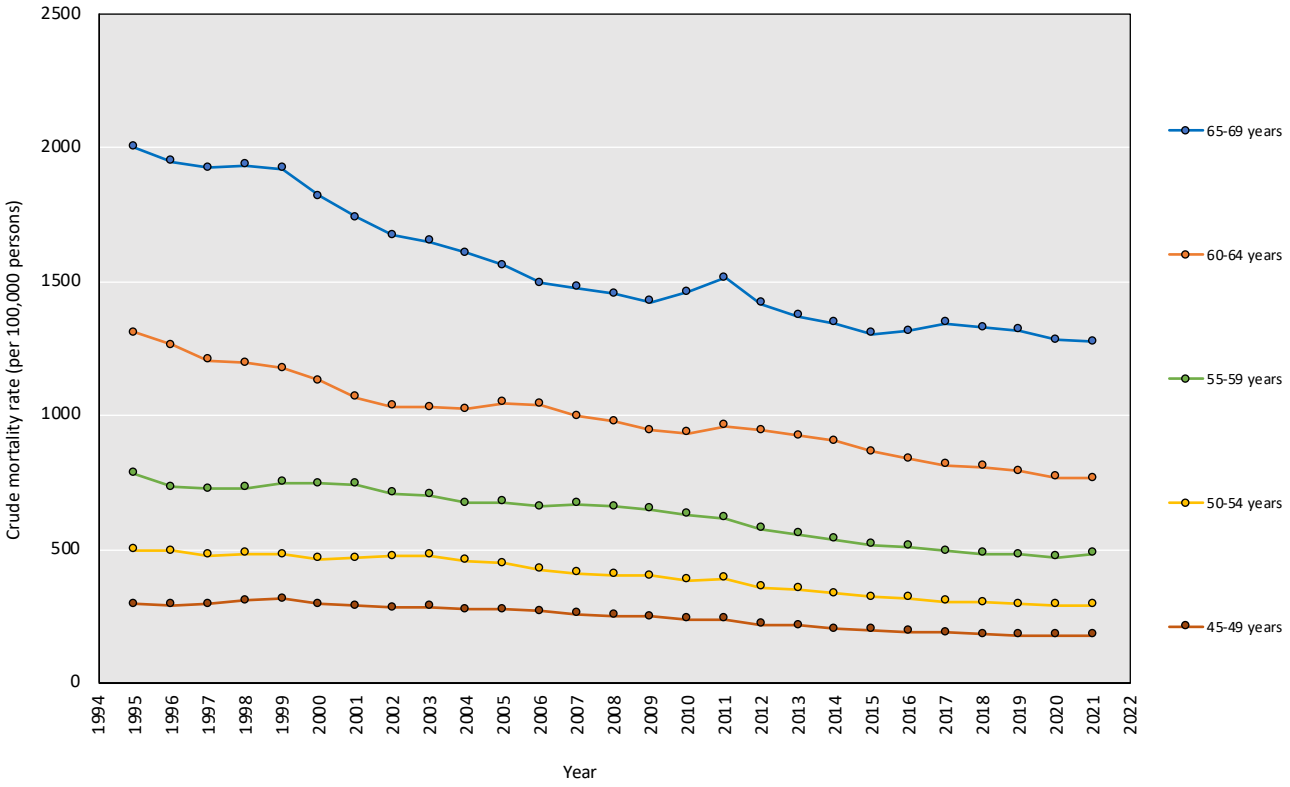
(A) All cause (men, 0-44 years)



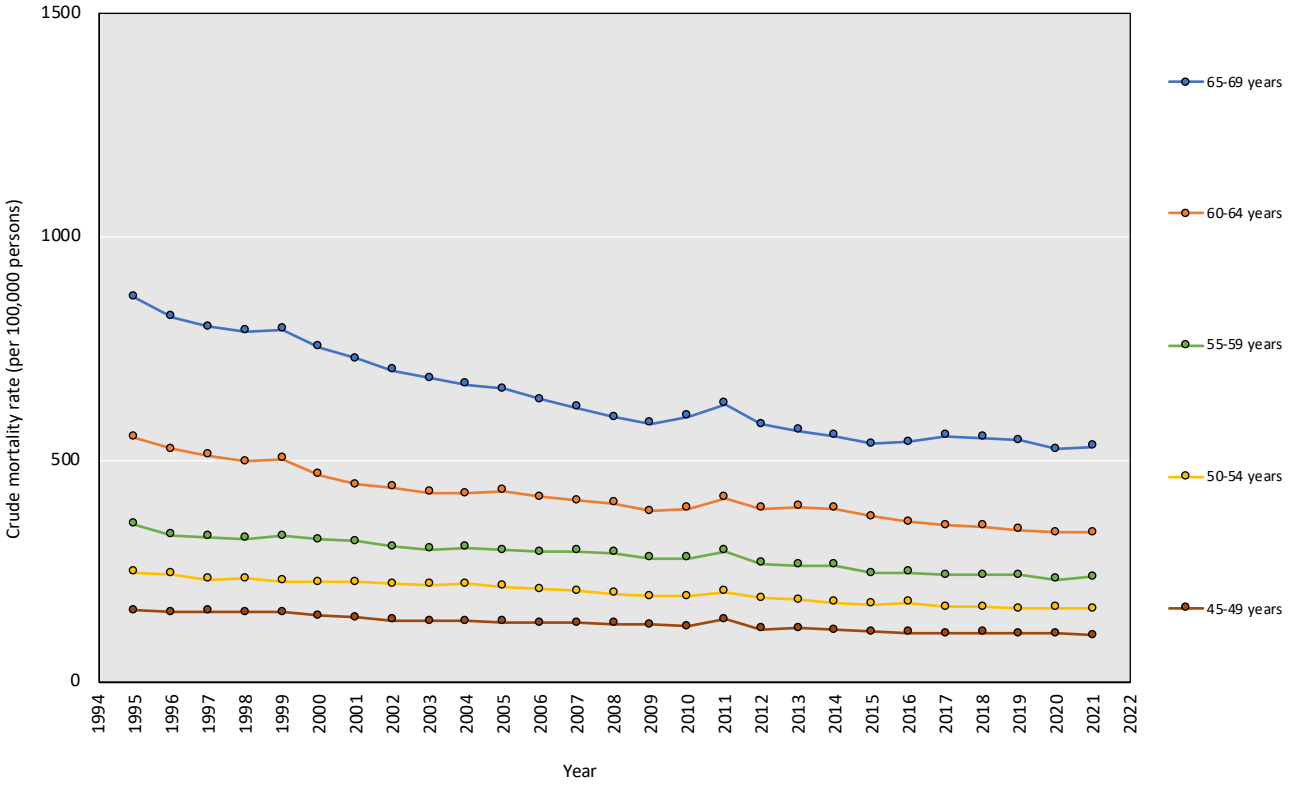
(B) All cause (women, 0-44 years)

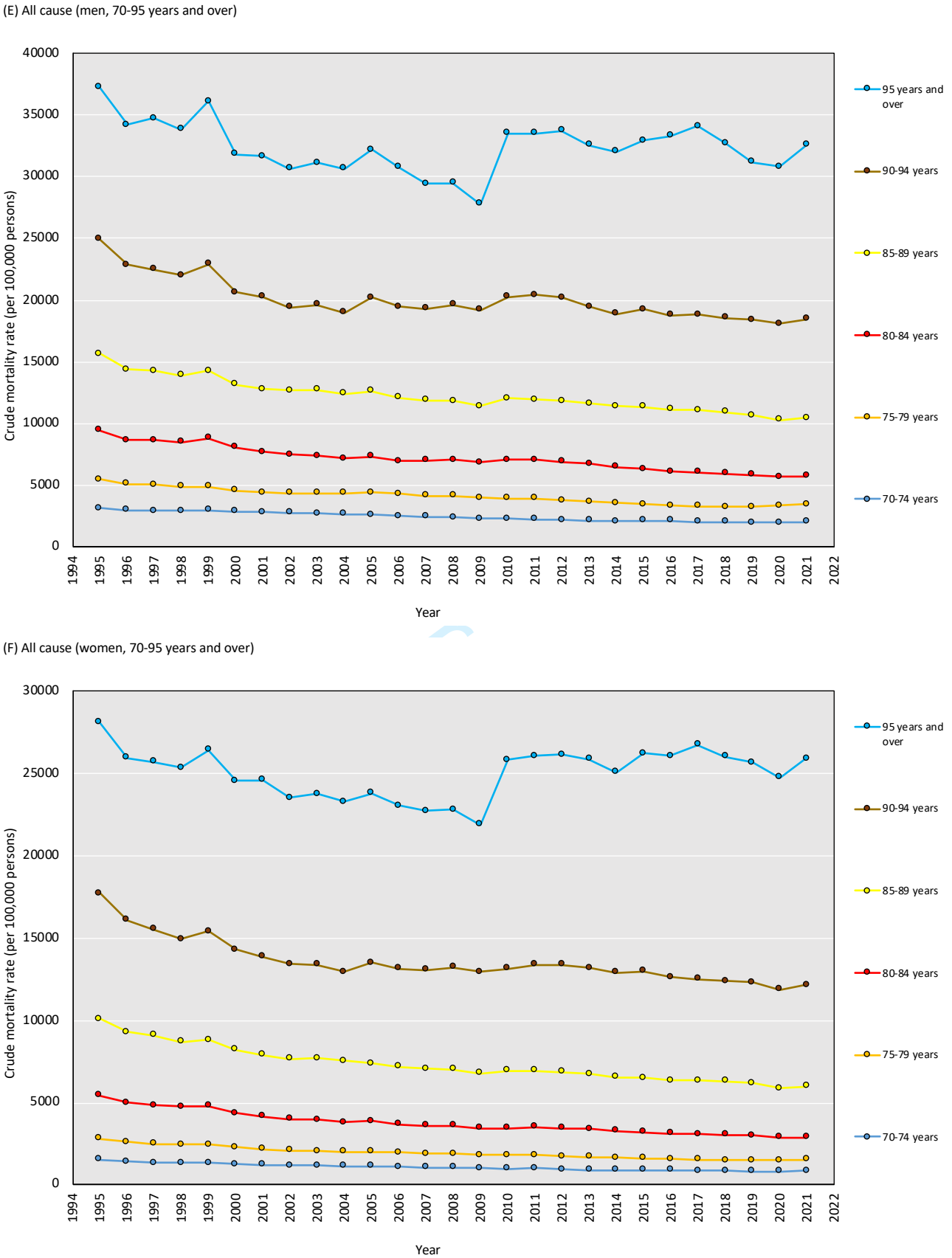


(C) All cause (men, 45-69 years)



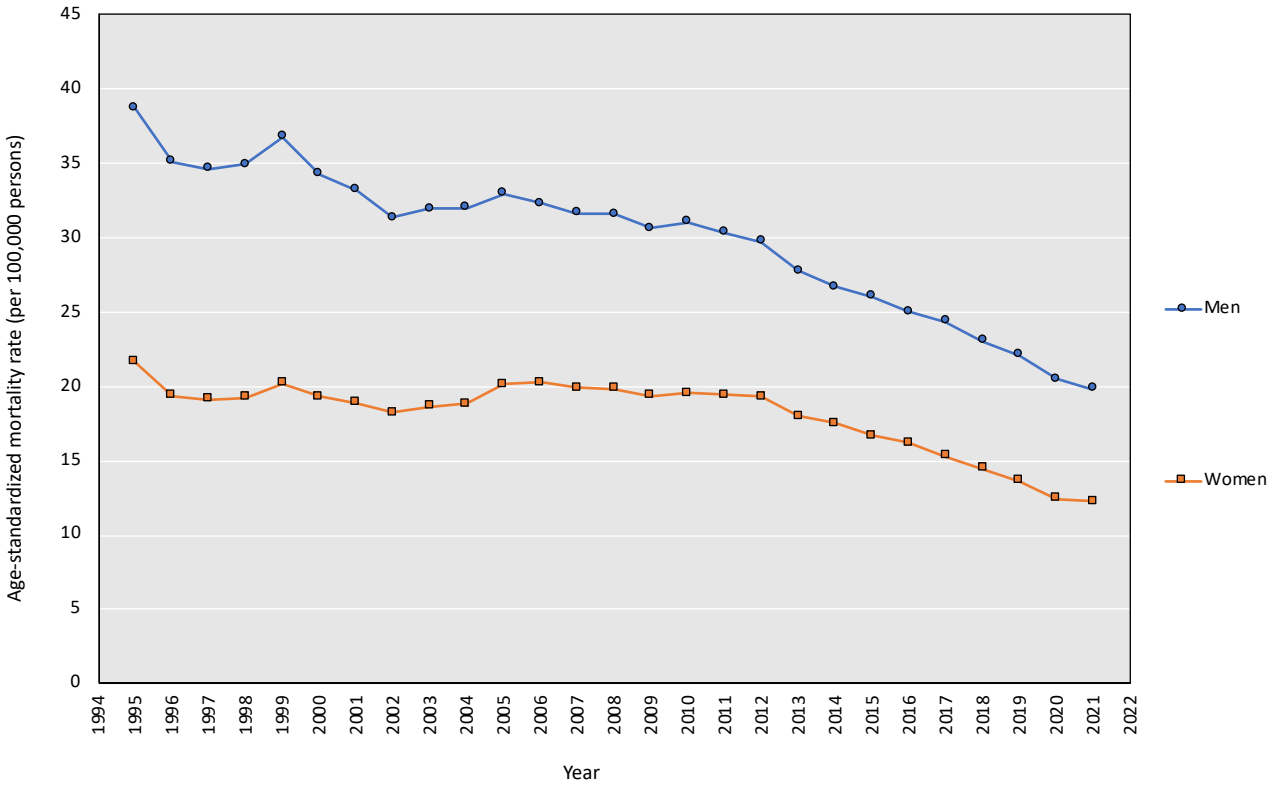
(D) All cause (women, 45-69 years)



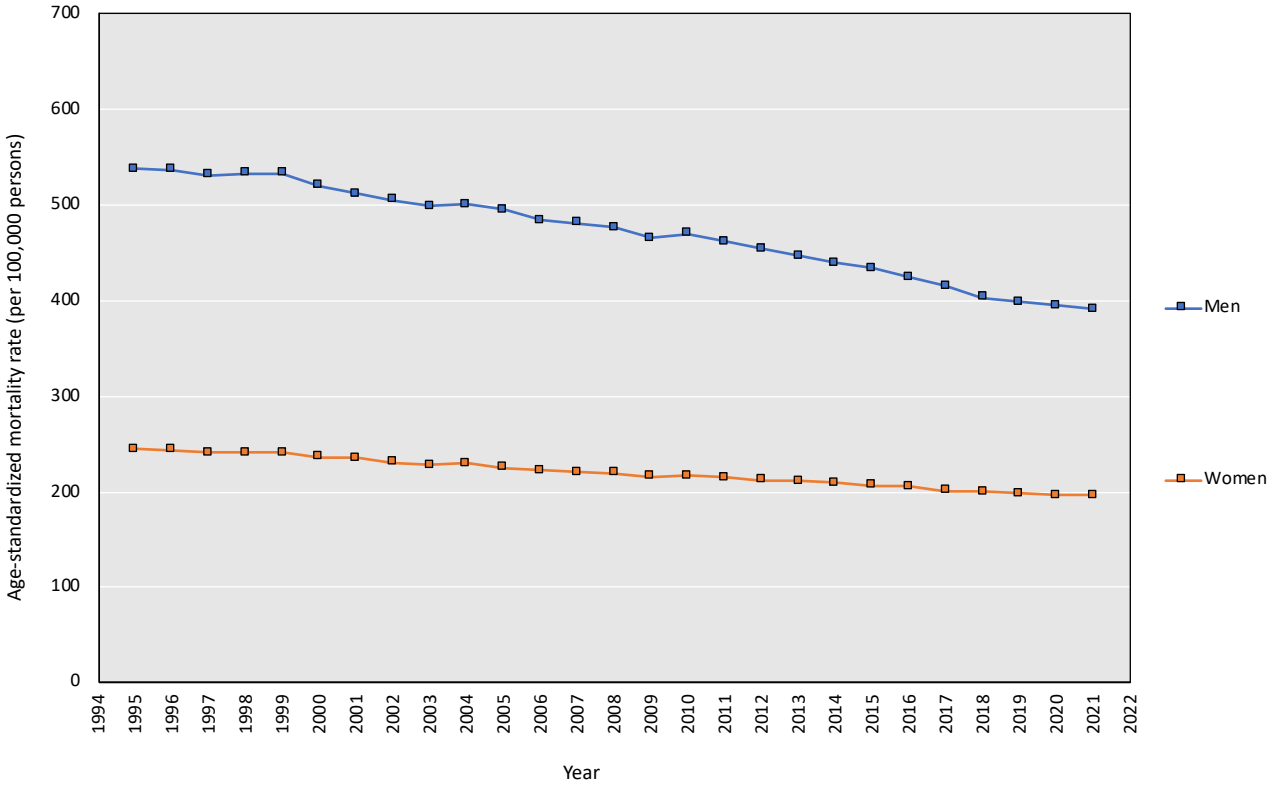


Appendix Figure 1. Trends in crude mortality rate by five-year age groups between 1995 and 2021

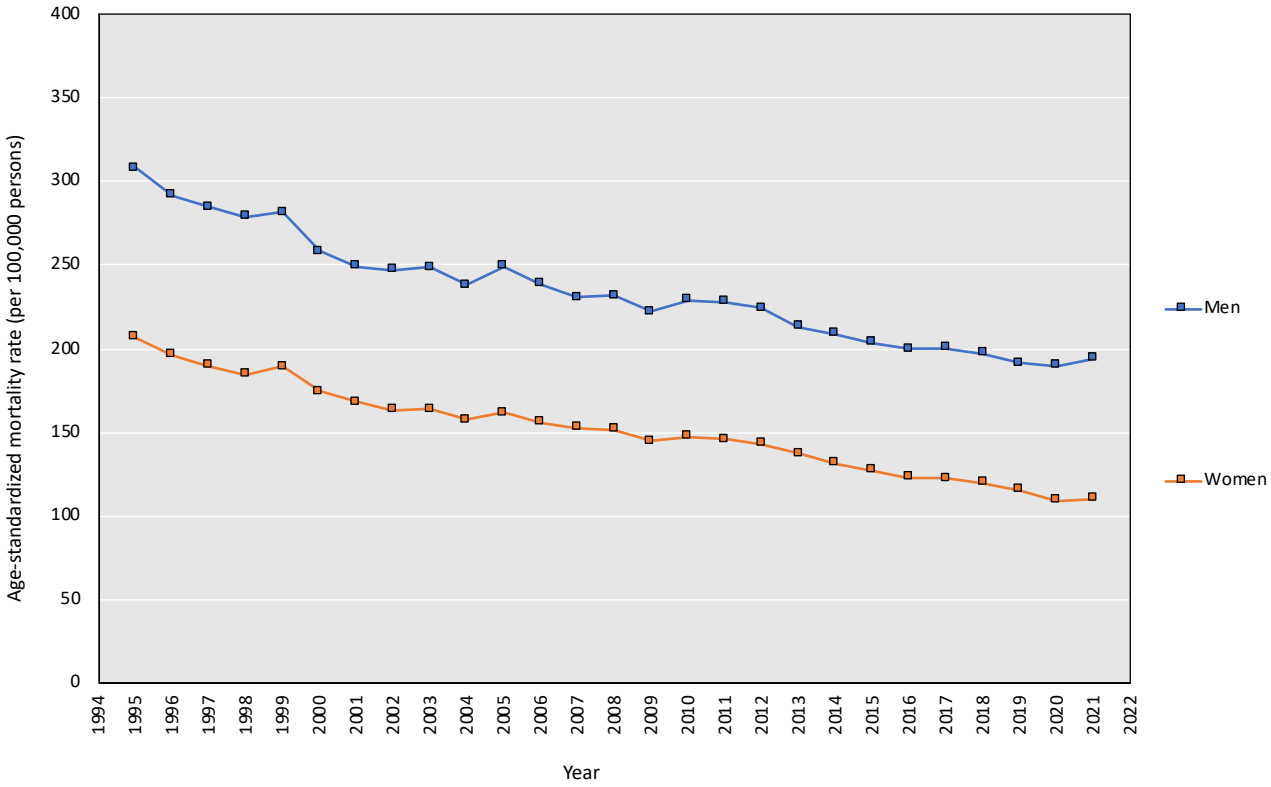
(A) Certain infectious and parasitic diseases (A00-B99)



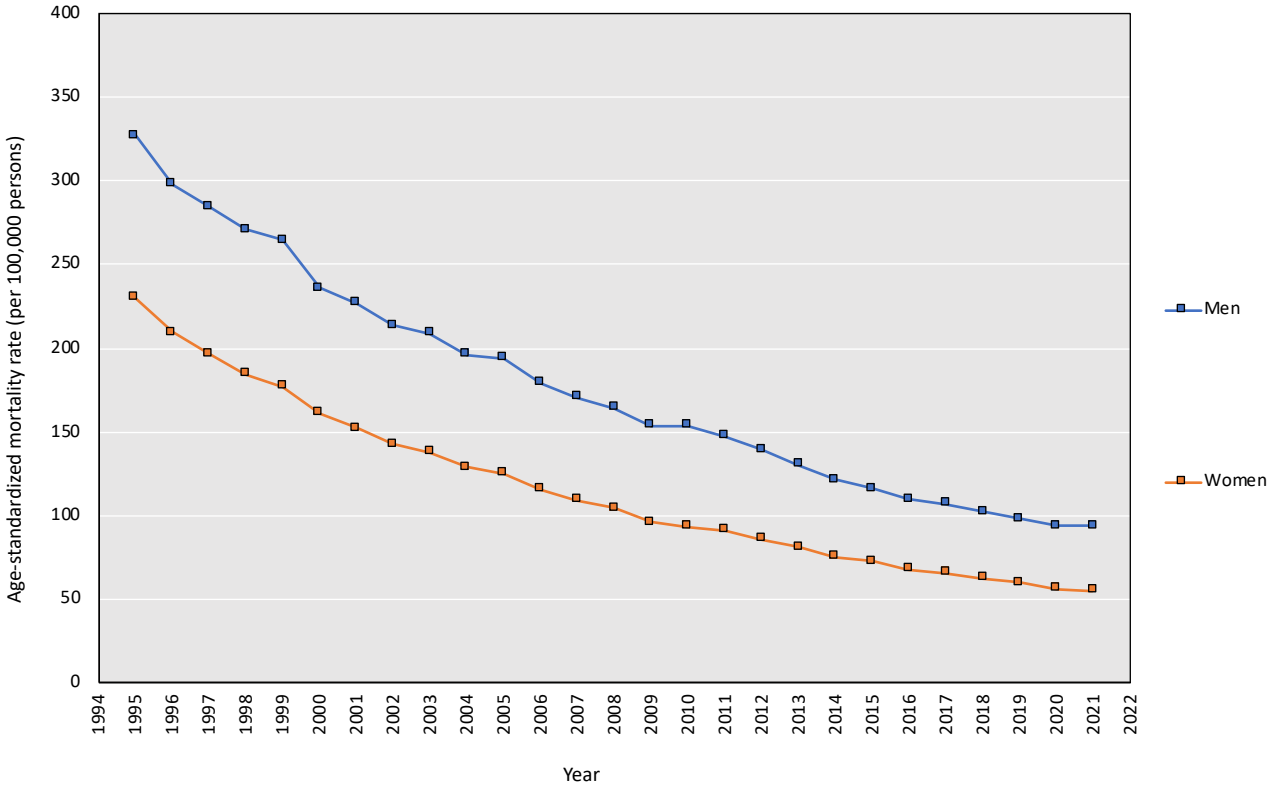
(B) Malignant neoplasms (C00-96)



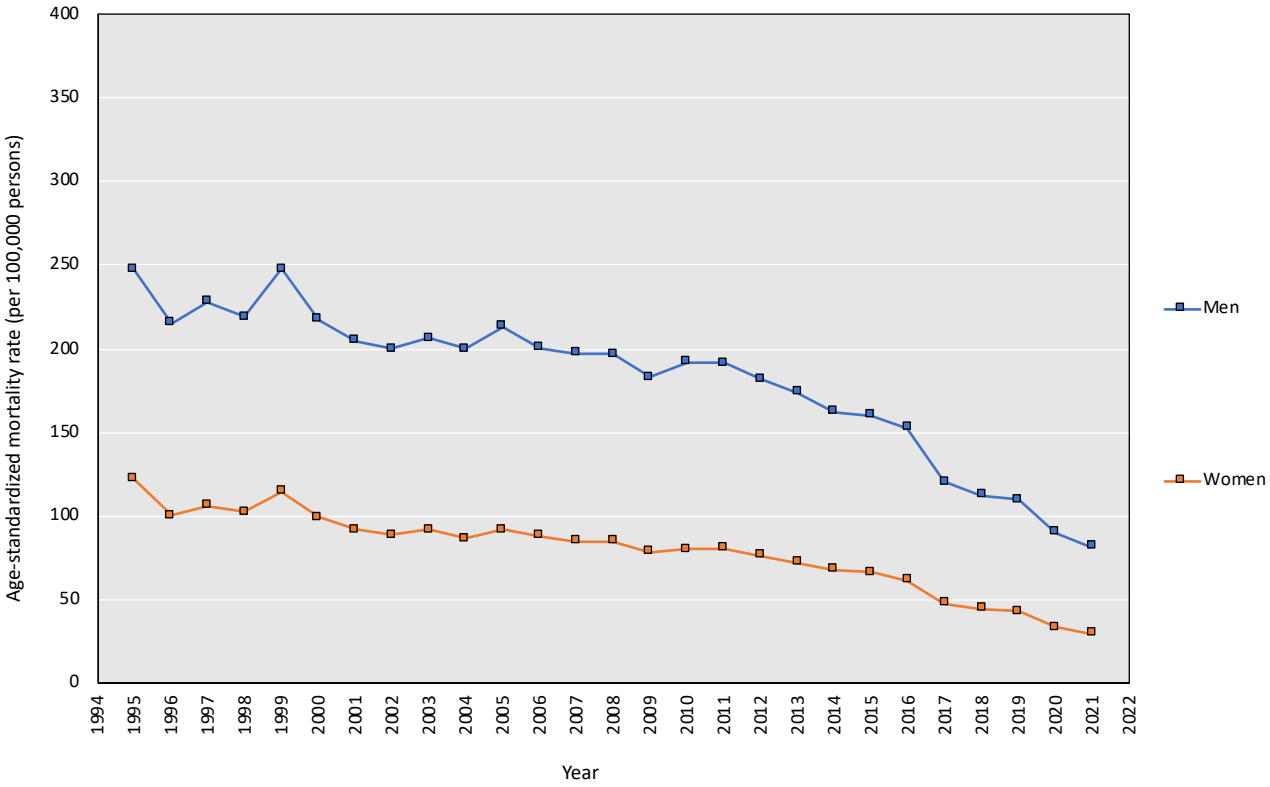
(C) Heart diseases (I05-09, I20-25, I27, I30-51)



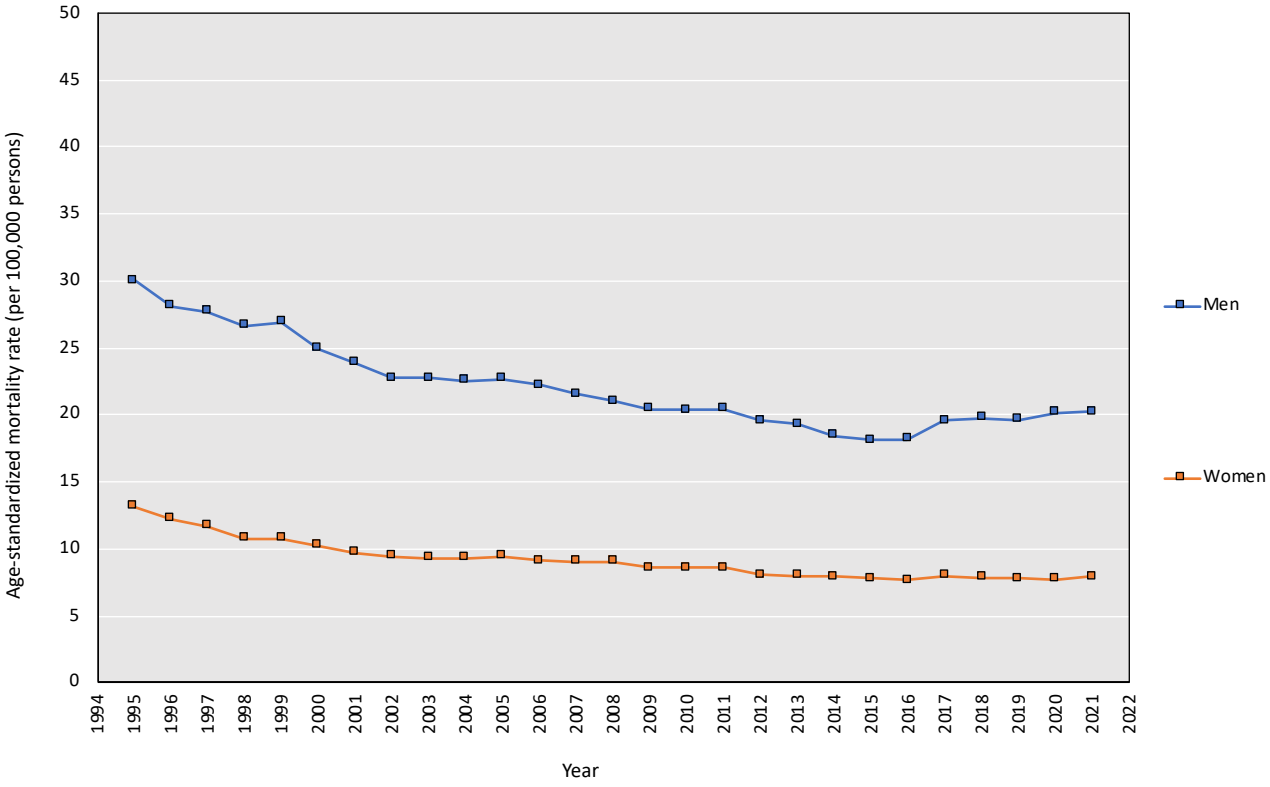
(D) Cerebrovascular diseases (I60-69)



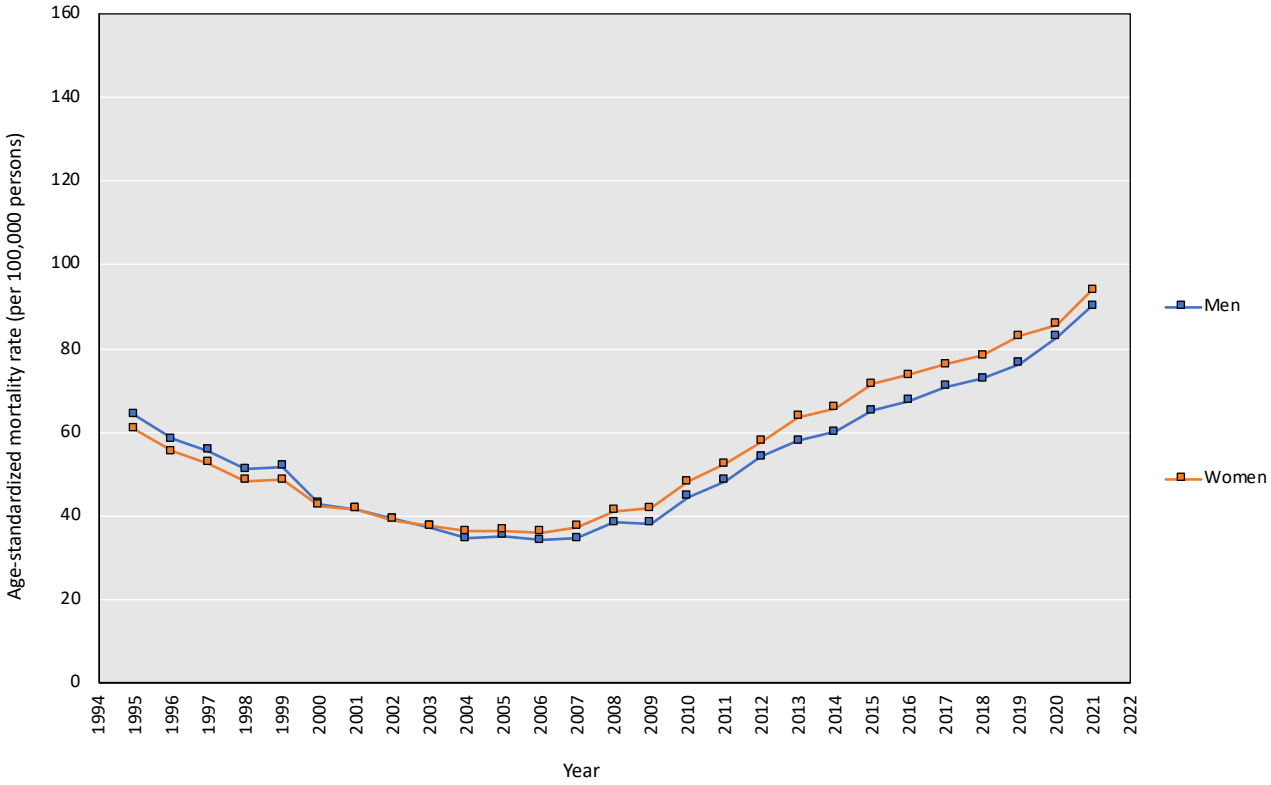
(E) Pneumonia & Bronchitis (J12-18)



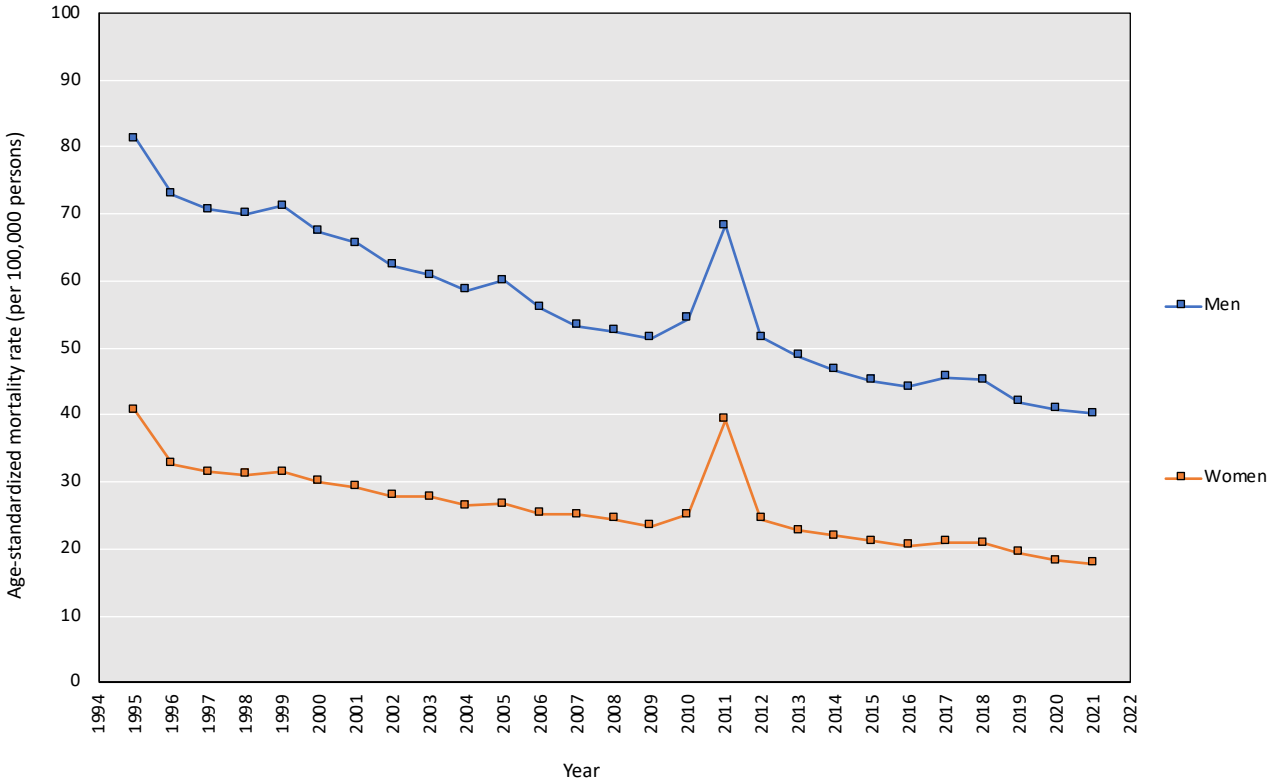
(F) Liver disease (K70-76)



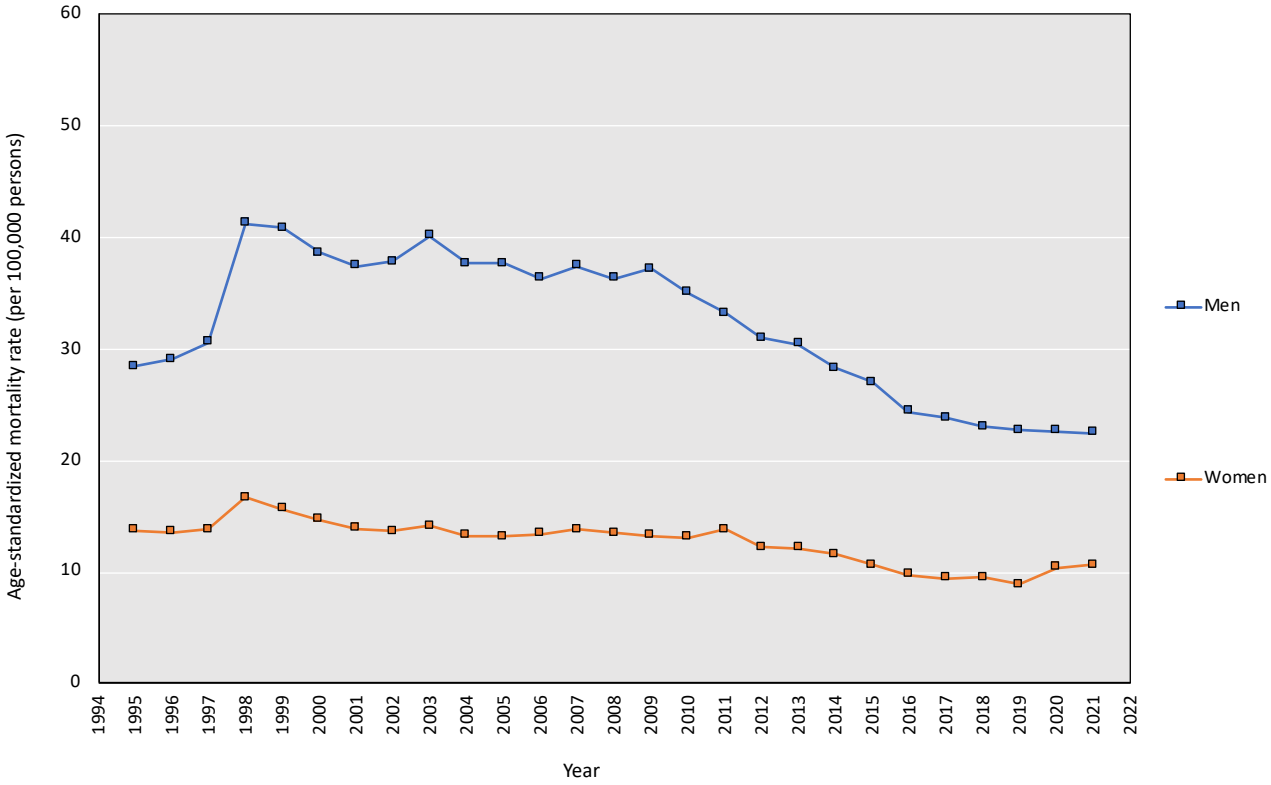
(G) Senility (R54)



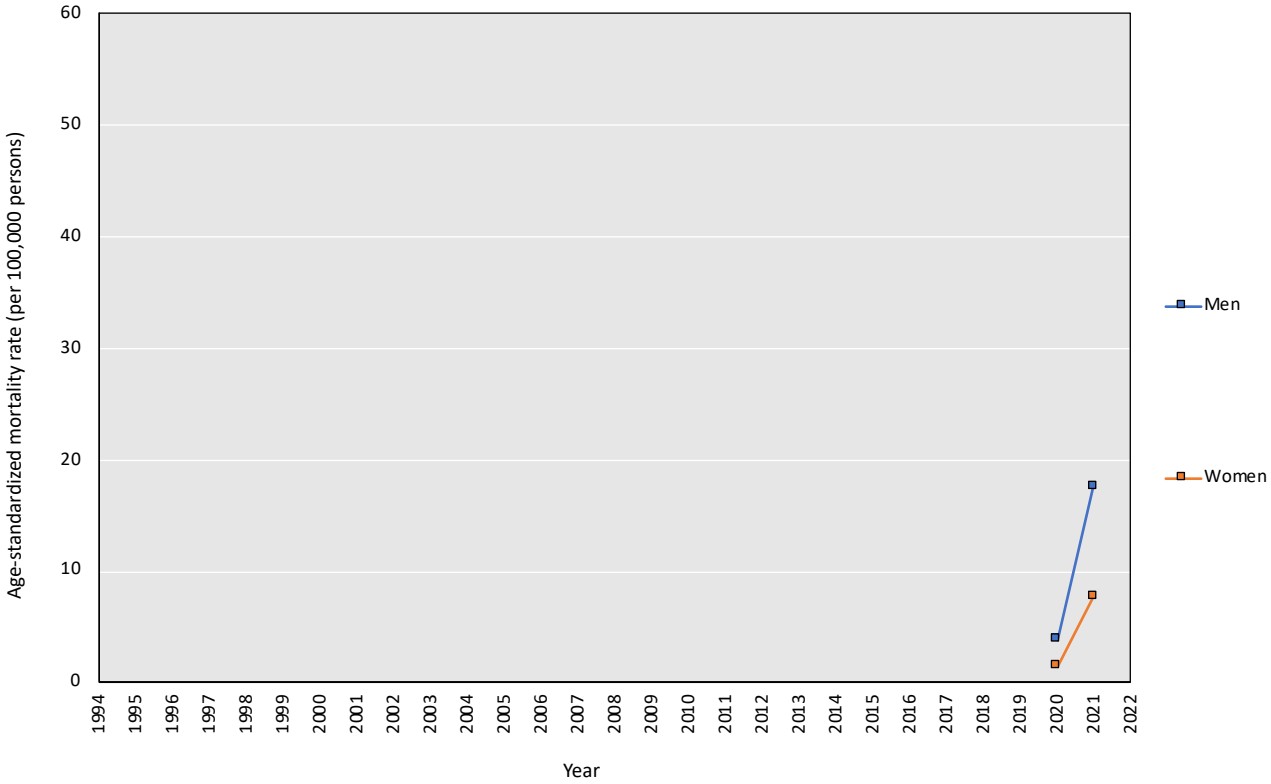
(H) Accidents (V01-X59)



(I) Suicide (X60-84)

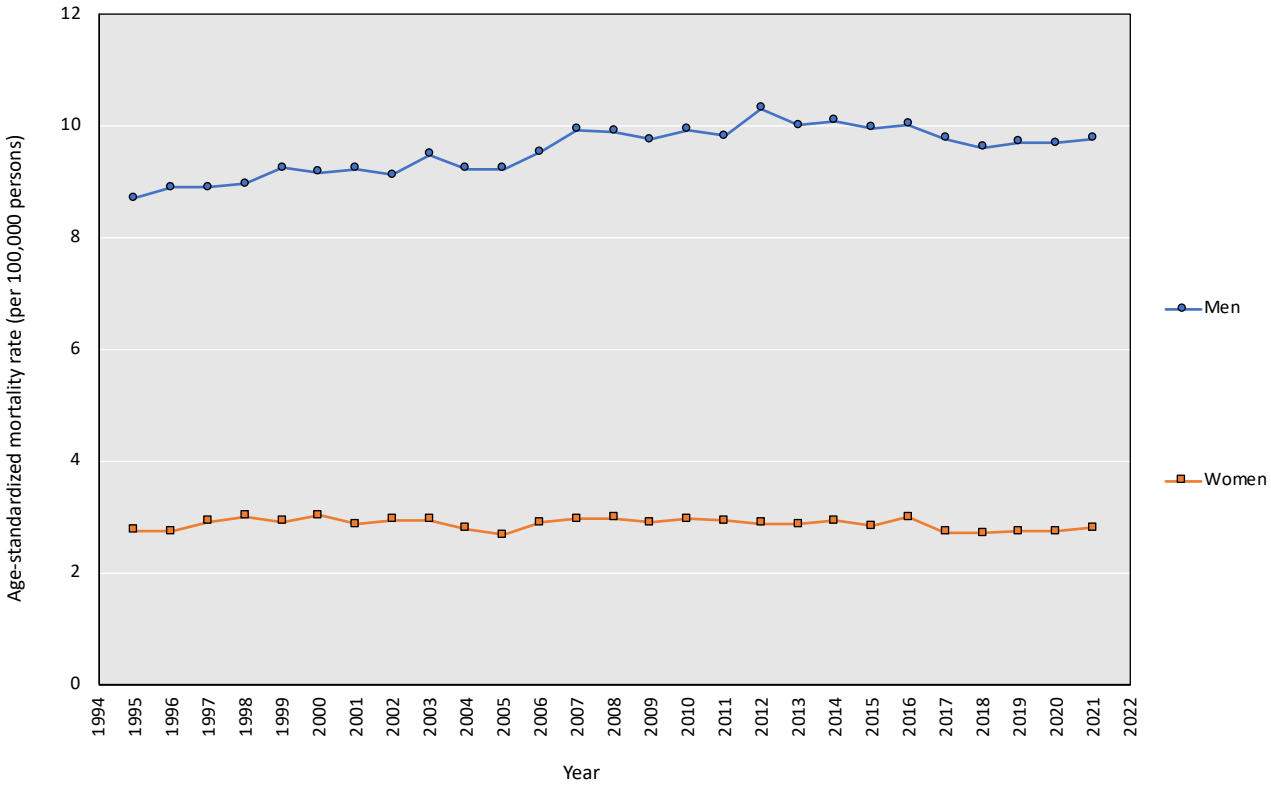


(J) COVID-19 (U07)

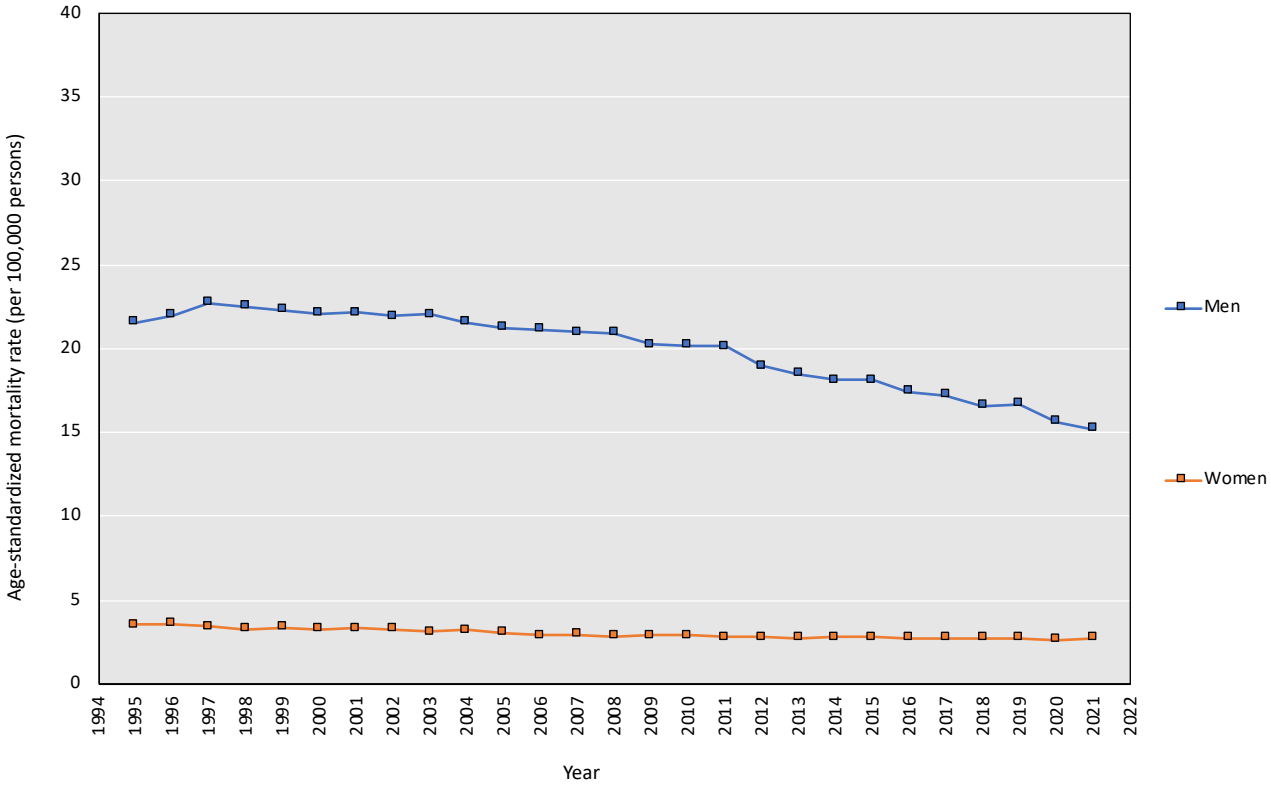


Appendix Figure 2. Trends in cause-specific age-standardized mortality rates by cancer site between 1995 and 2021

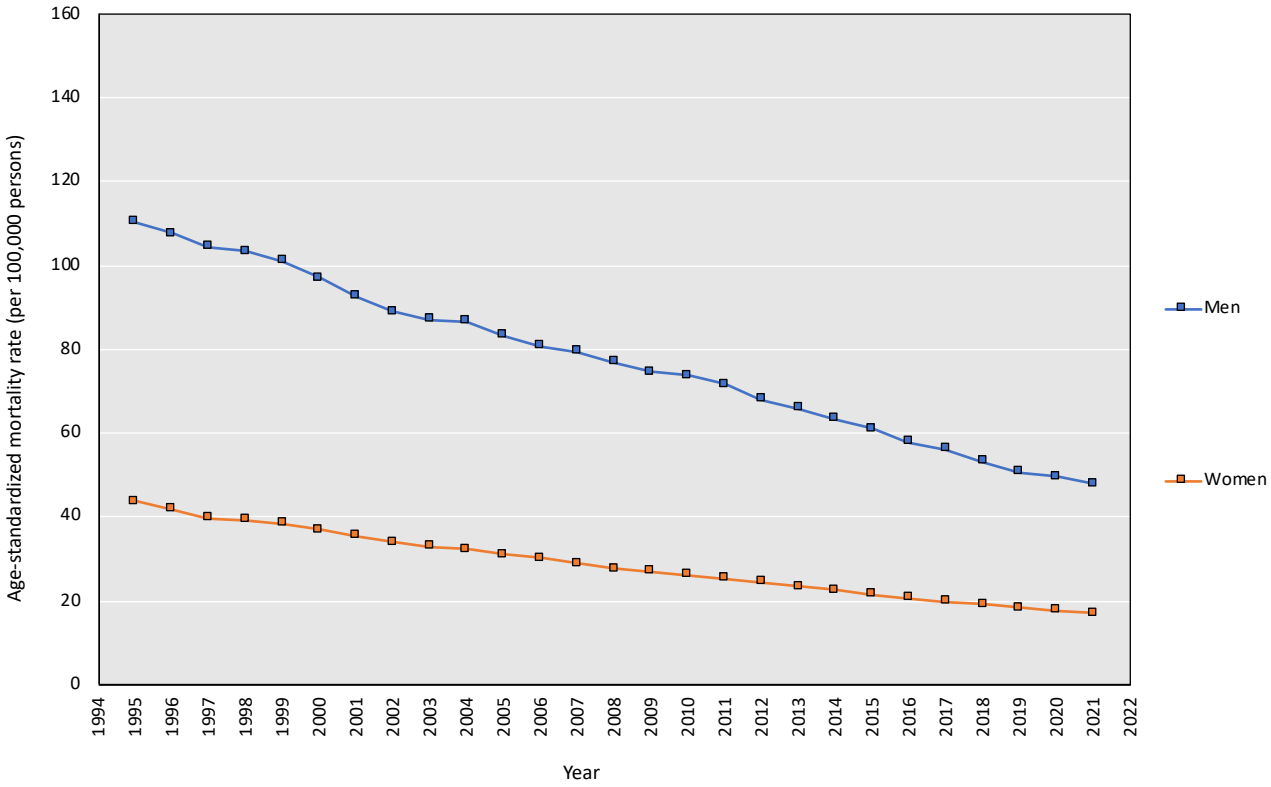
(A) Oral cavity and pharynx (C00-14)



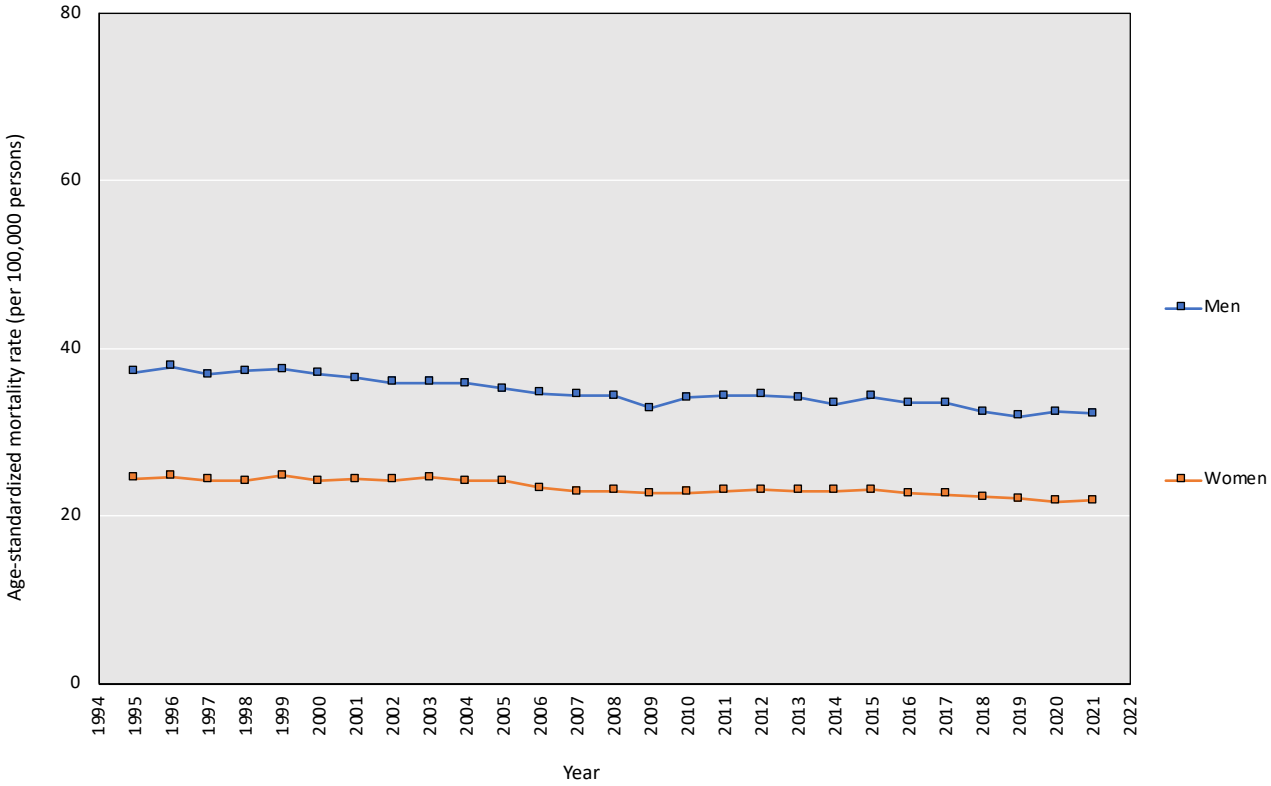
(B) Esophagus (C15)



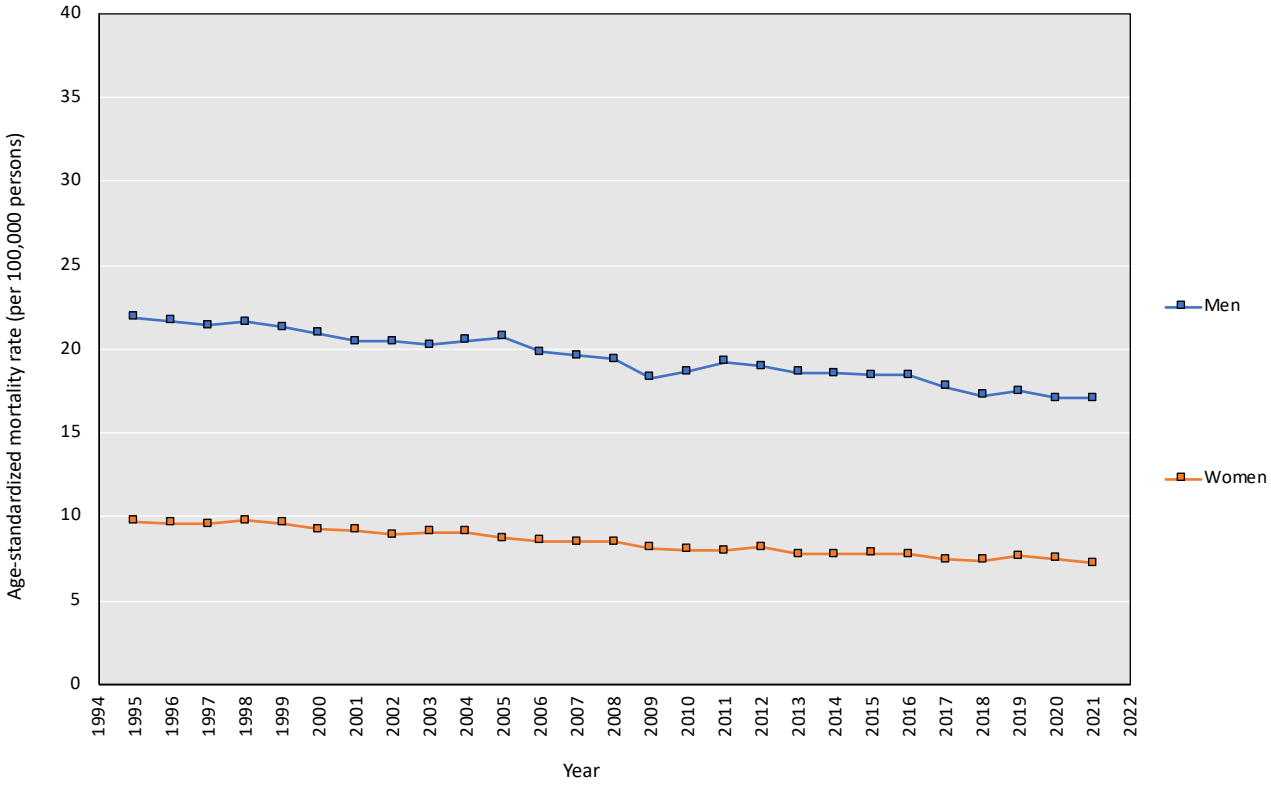
(C) Stomach (C16)



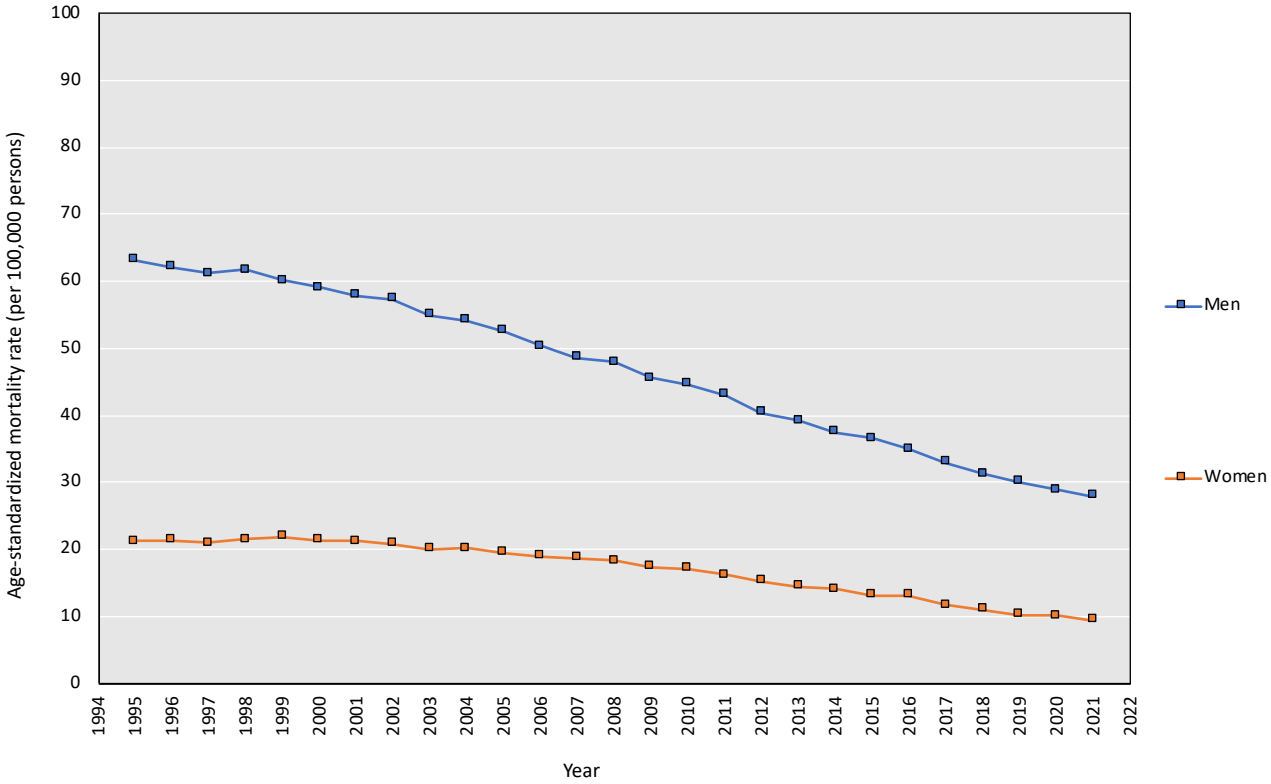
(D) Colon (C18)



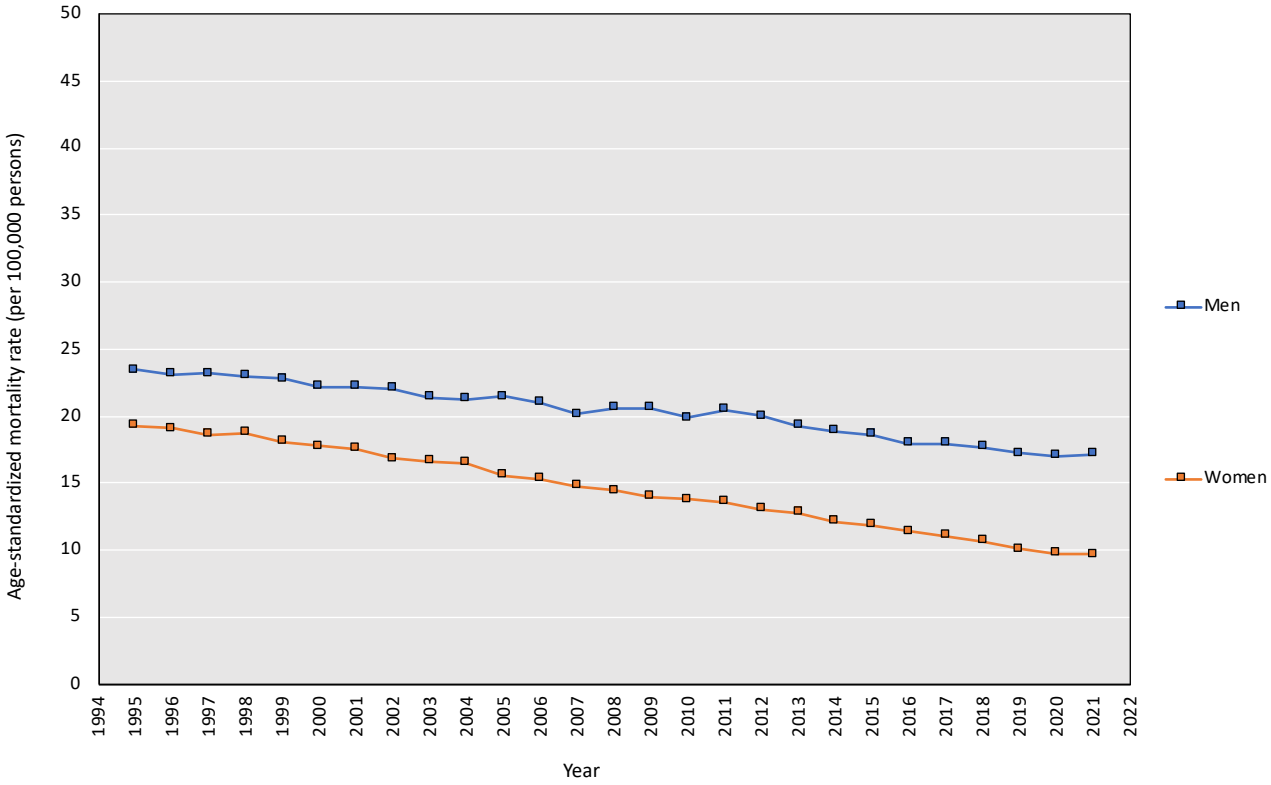
(E) Rectum (C19-20)



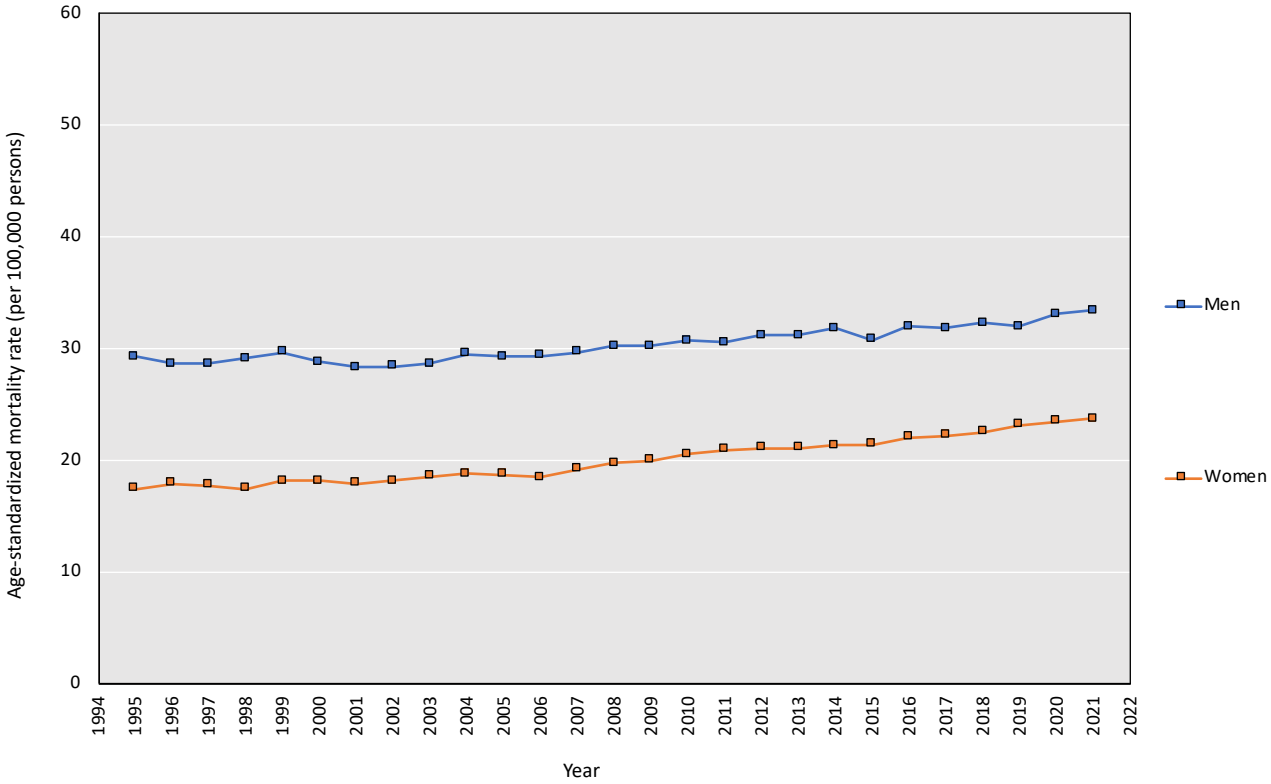
(F) Liver (C22)



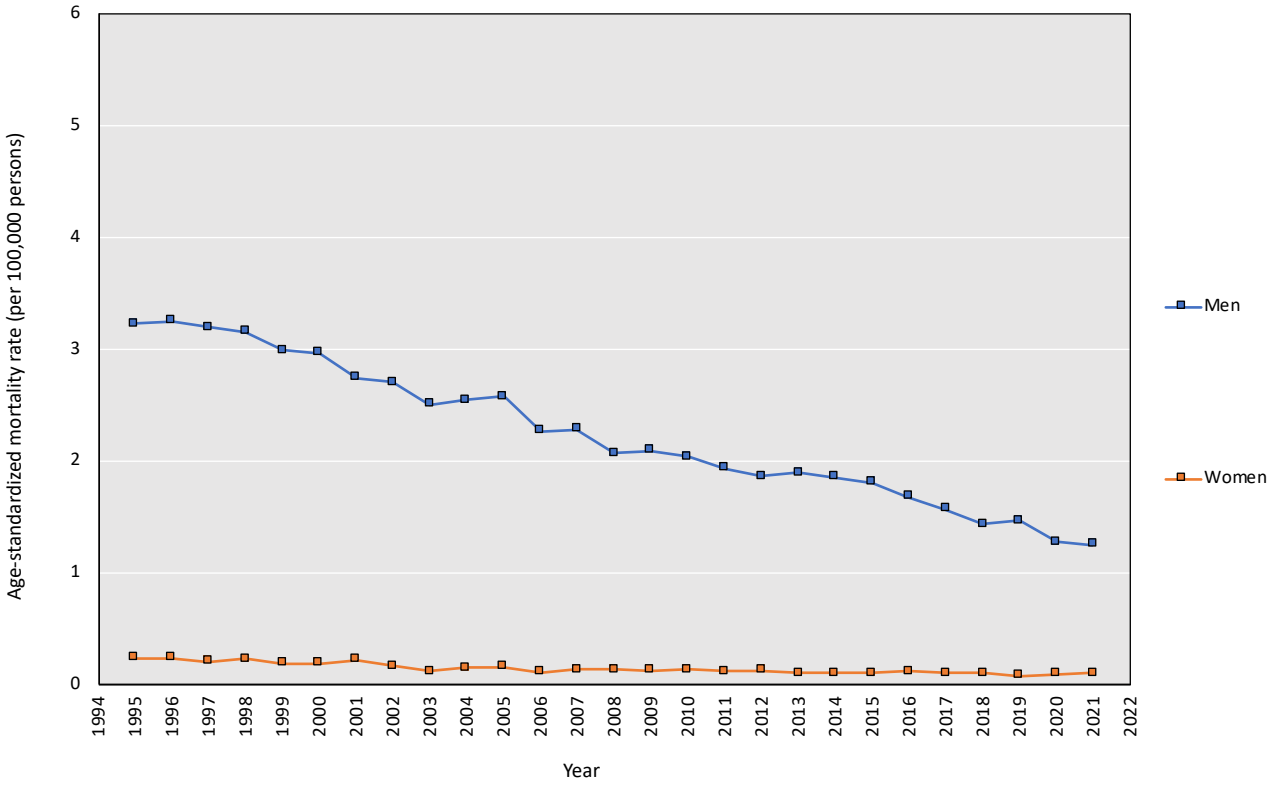
(G) Gallbladder and bile ducts (C23-24)



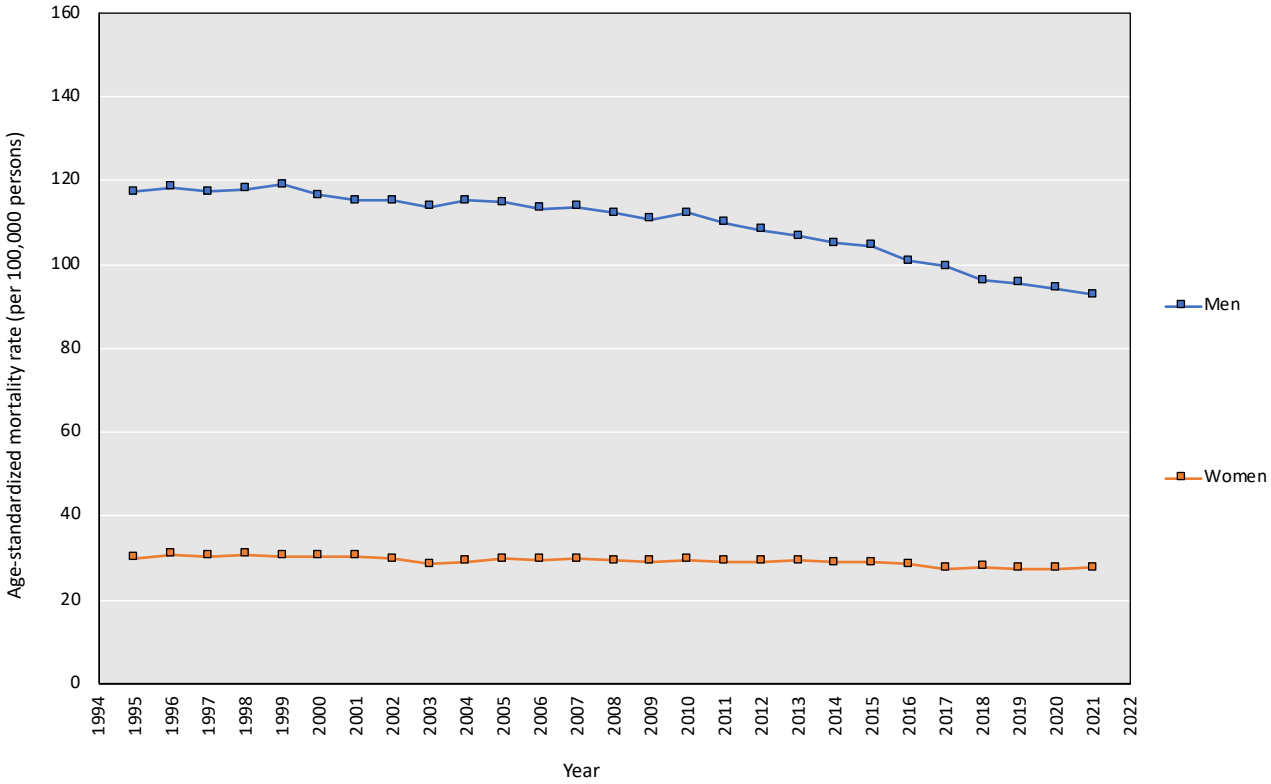
(H) Pancreas (C25)



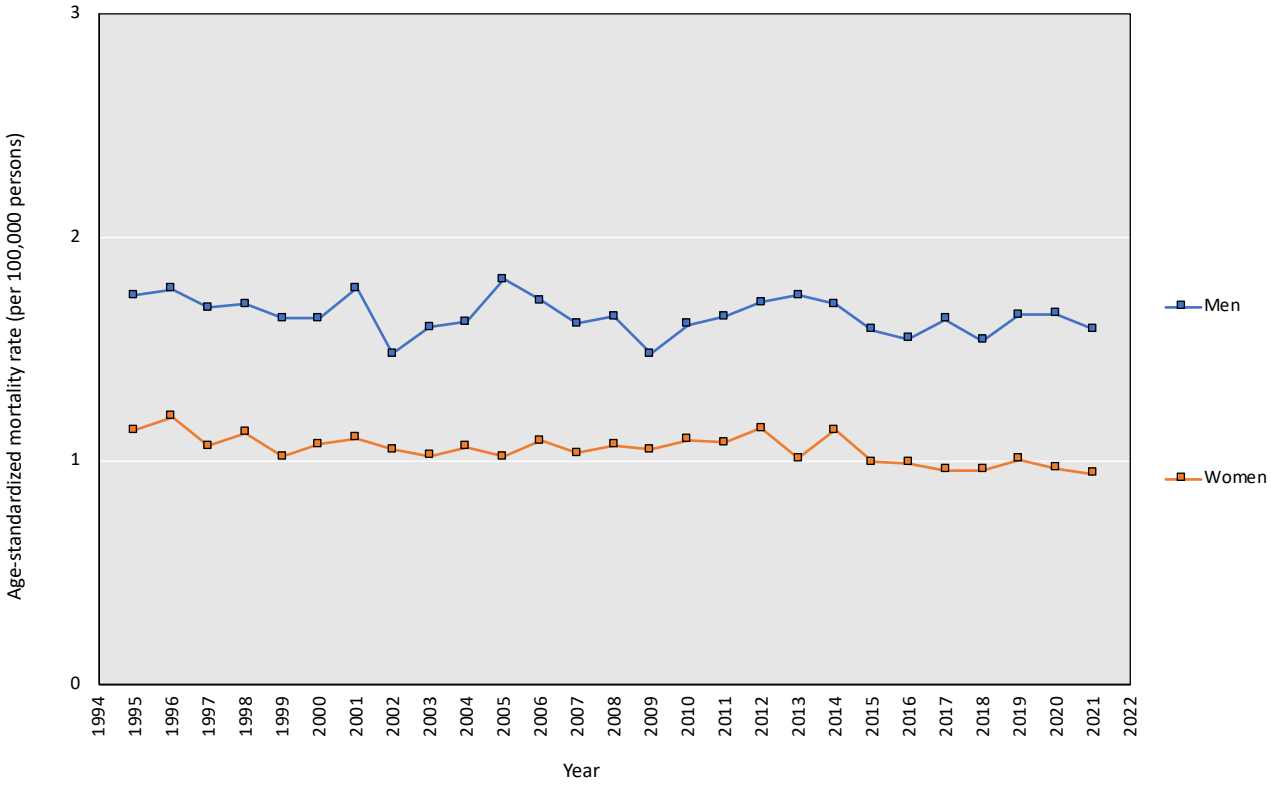
(I) Larynx (C32)



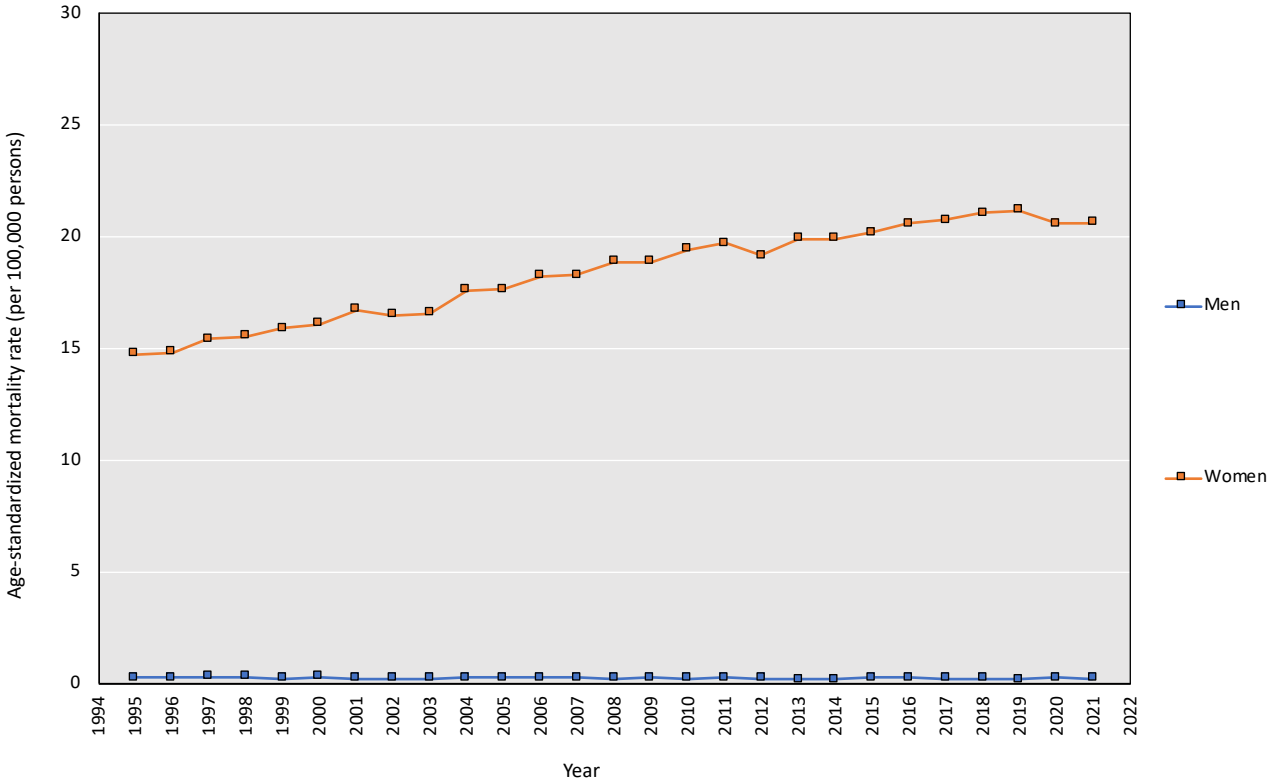
(J) Lung, trachea (C33-34)



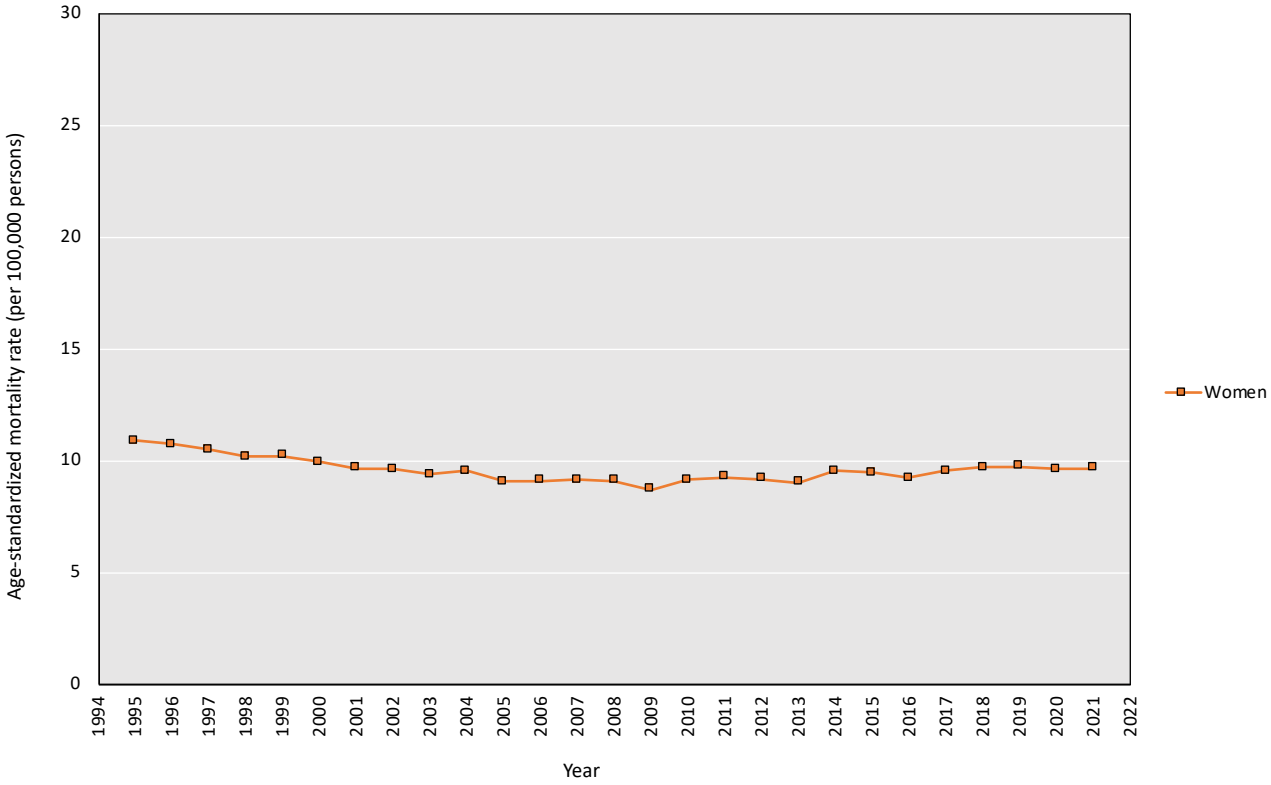
(K) Skin (C43-44)



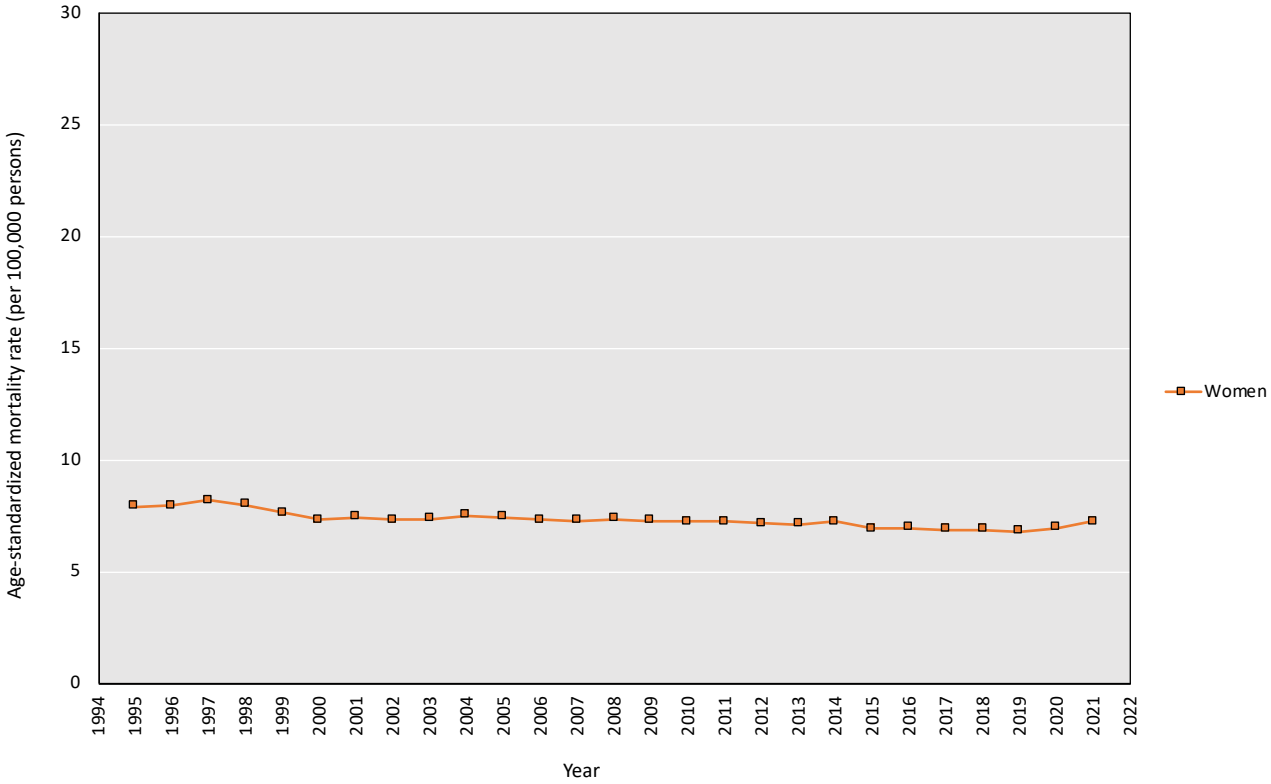
(L) Breast (C50)



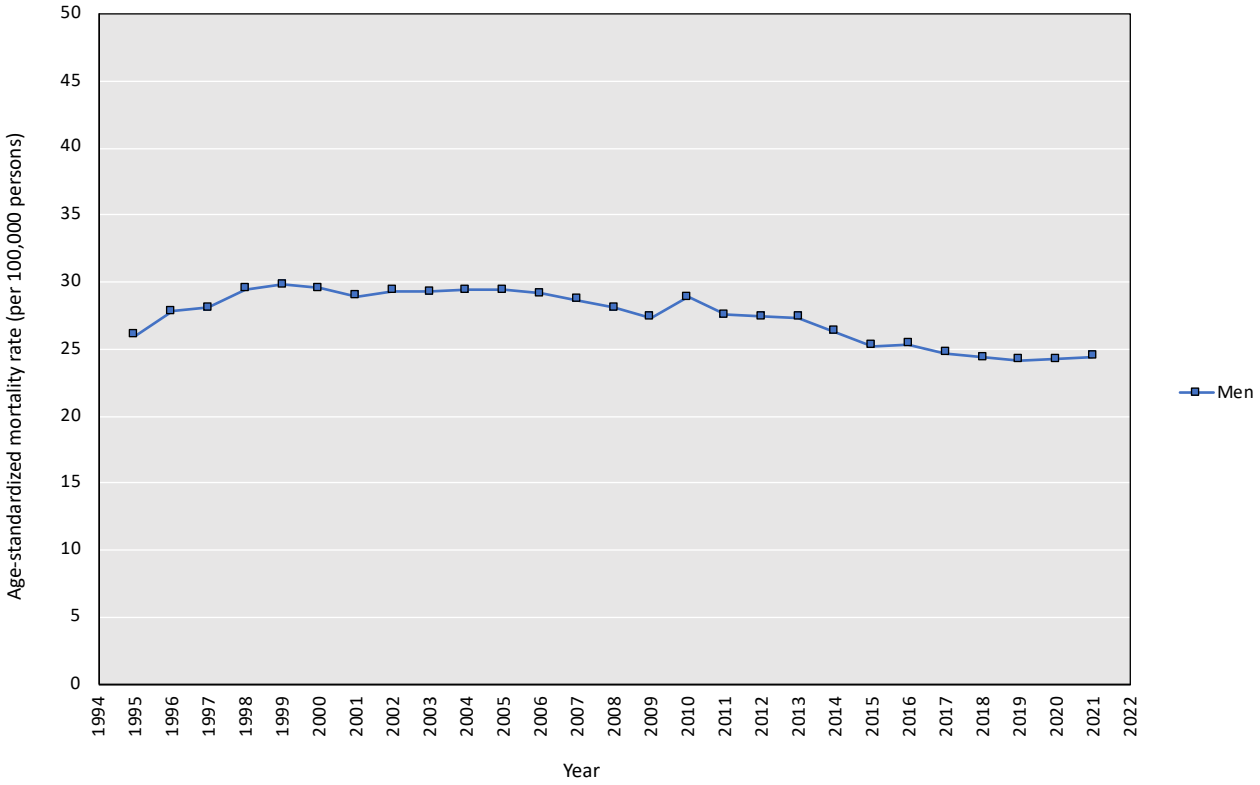
(M) Uterus (C53-55)



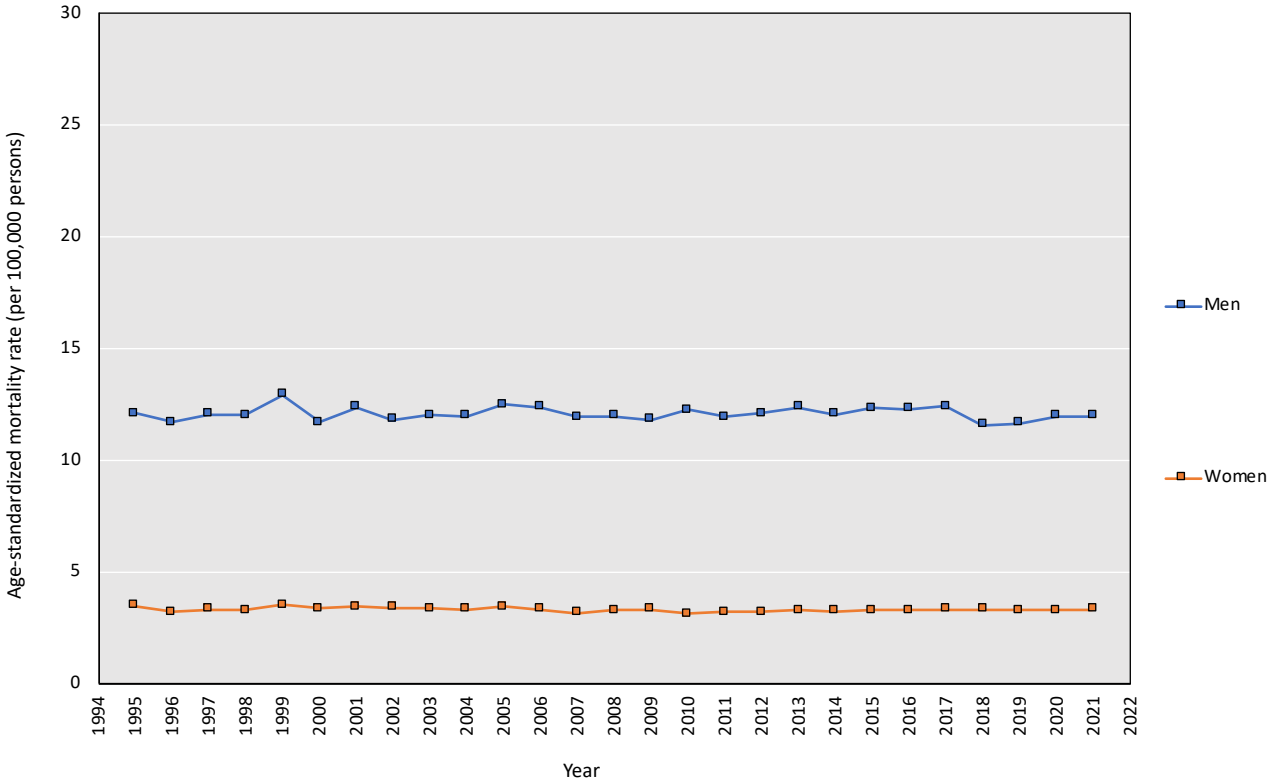
(N) Ovary (C56)



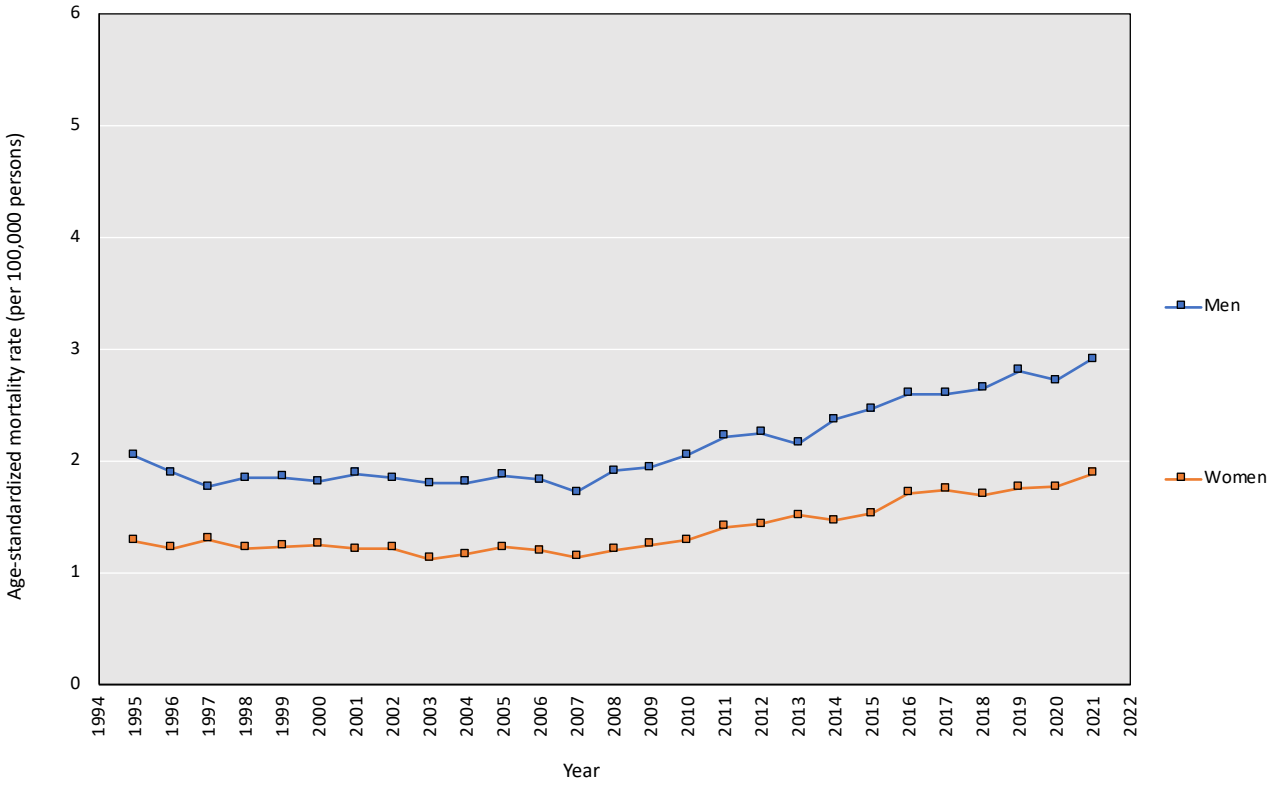
(O) Prostate (C61)



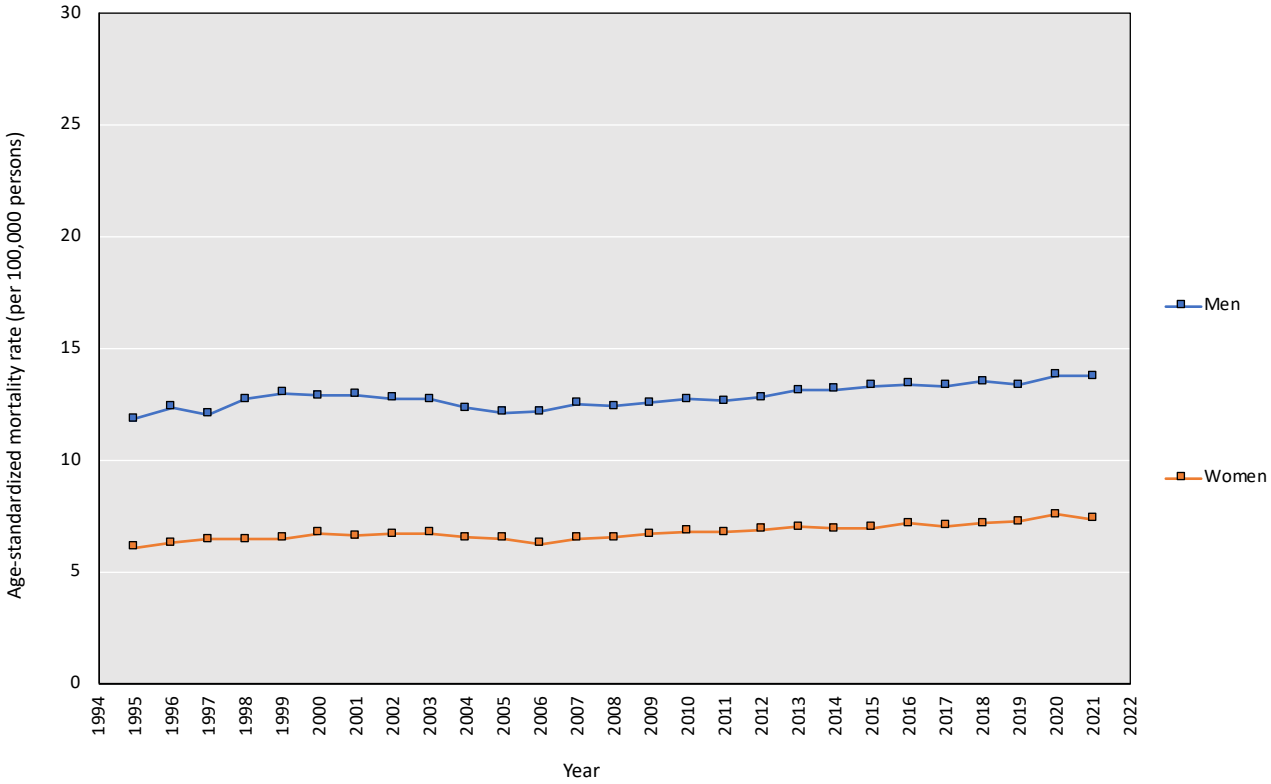
(P) Bladder (C67)

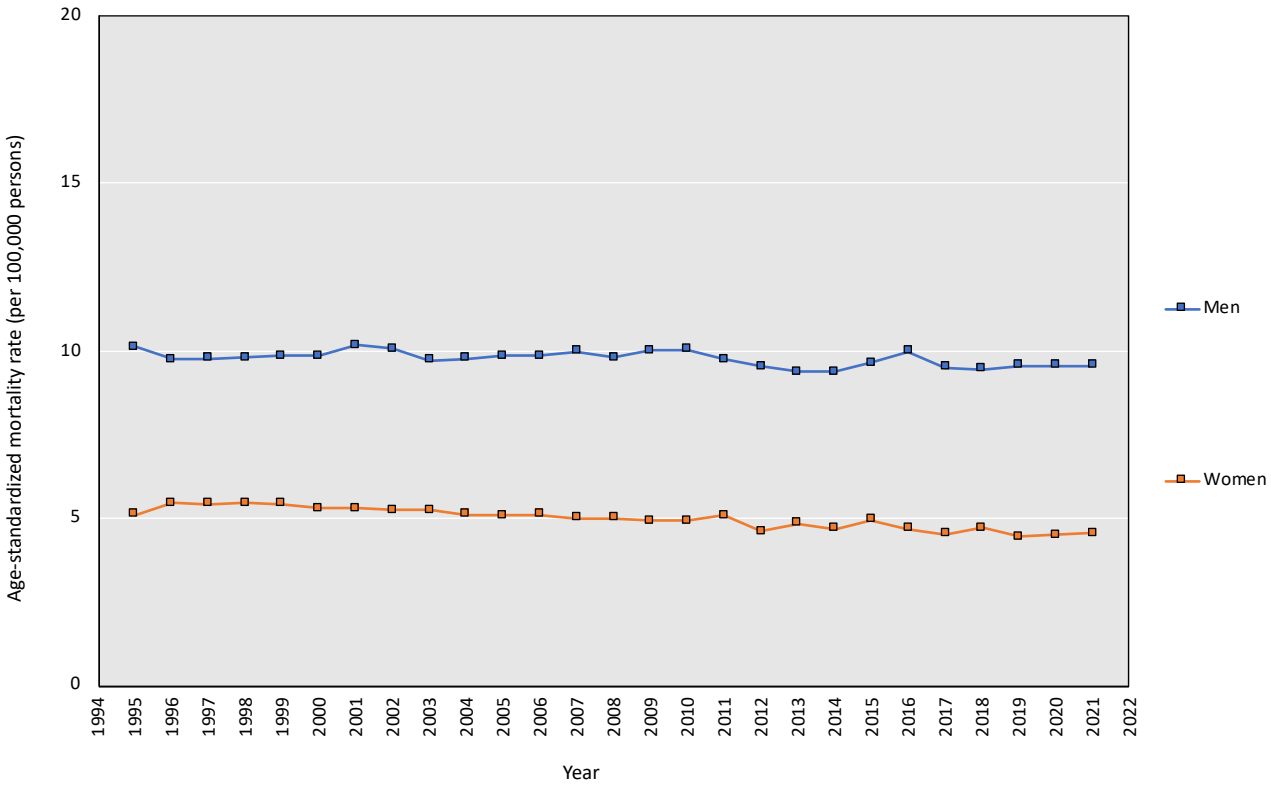


(Q) Brain, nervous system (C70-72)



(R) Malignant lymphoma (C81-85, C96)





Appendix Figure 3. Trends in cancer age-standardized mortality rates by cancer site between 1995 and 2021

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title (line 1-2), abstract (line 38-44)
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			Introduction (line 109-121)
Objectives	3	State specific objectives, including any prespecified hypotheses			Introduction (line 122-128)
Methods					
Study Design	4	Present key elements of study design early in the paper			Method (line 131-139)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			Method (line 131-139)

Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	Method (line 131-139)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.		RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Method (line 140-149)
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			Method (line 131-139)

Bias	9	Describe any efforts to address potential sources of bias			None.
Study size	10	Explain how the study size was arrived at			None.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why			Method (line 140-149)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses			Method (line 140-149)
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	Data availability (line 261-263)

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	None.
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Results (line 158-163)
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			Results (line 158-163)
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure			Results (line 164-178)

		category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			Results (line 164-187)
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses			None.
Discussion					
Key results	18	Summarise key results with reference to study objectives			Discussion (line 190-198)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Discussion (line 244-248)
Interpretation	20	Give a cautious overall interpretation of results considering objectives,			Discussion (line 199-243)

		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results			None.
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			Funding (line 271-273)
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	None.

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

BMJ Open

Impact of the COVID-19 pandemic on mortality trends in Japan: a reversal in 2021? A descriptive analysis of national mortality data, 1995-2021

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-071785.R2
Article Type:	Original research
Date Submitted by the Author:	20-Jul-2023
Complete List of Authors:	Tanaka, Hirokazu; National Cancer Center Japan, Division of Surveillance and Policy Evaluation Togawa, Kayo; National Cancer Center Japan Katanoda, Kota; National Cancer Center Japan
Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology
Keywords:	COVID-19, Epidemiology < TROPICAL MEDICINE, Public health < INFECTIOUS DISEASES, Demography < TROPICAL MEDICINE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Impact of the COVID-19 pandemic on mortality trends in Japan: a reversal in 2021? A descriptive analysis of national mortality data, 1995-2021

Hirokazu Tanaka, Kayo Togawa, Kota Katanoda*

All authors: Division of Population Data Science, National Cancer Center Institute for Cancer Control, 5-1-1, Tsukiji, Chuo-ku, Tokyo, 104-0045, Japan

***Corresponding author:** Hirokazu Tanaka
Division of Population Data Science, National Cancer Center Institute for Cancer Control
5-1-1, Tsukiji, Chuo-ku, Tokyo, 104-0045, JAPAN
E-mail: hitanak@ncc.go.jp
Phone: +81335475201

Figures and Tables: 4 figures**; Word count**: 2,012 words

Declarations of interest: none

Abstract (266 words)

Objective: The COVID-19 pandemic led to an increase in mortality in most countries in 2020, deviating from prior decreasing trends. In Japan, however, mortality was suggested to decrease in 2020. This study investigated long-term mortality trends and cause-specific contributions, focusing on the period of the COVID-19 pandemic in Japan.

Design: We analysed Japanese age-standardized mortality rates (ASMRs) from 1995 to 2021 using vital statistics.

Main outcome measures: The cause-specific annual ASMR changes were calculated in comparison with the previous year over the abovementioned period.

Results: There was a general downward trend in overall ASMR for both sexes until 2020 followed by a small increase in 2021. In men, the all-cause ASMR (per 100,000 persons) decreased from 1352.3 to 1328.8 in 2020 (−1.74% from 2019), and increased to 1356.3 in 2021 in men (+2.07% from 2020). In women, the all-cause ASMR decreased from 746.0 to 722.1 in 2020 (−3.20% from 2019), and increased to 737.9 (+2.19% from 2020) in 2021. ASMRs from malignant neoplasms, pneumonia, accidents, and suicide (men only) continued to decrease during the COVID-19 pandemic while the trend of cardiovascular mortality increased in 2021. Analysis of ASMR changes revealed that COVID-19, senility, cardiovascular disease, and 'other causes not classified as major causes' contributed to the all-cause mortality increase in 2021.

Conclusions: In Japan, the decreasing trend in overall mortality continued in 2020 despite the COVID-19 pandemic. However, approximately 2% mortality increase was observed in 2021, which was attributable to COVID-19, senility, cardiovascular disease, and 'other causes'. The year 2021 was a turning point of mortality trends in Japan, although continued monitoring is warranted.

Funding: Grants-in-Aid for Cancer Control Policy from the Ministry of Health, Labour, and Welfare, Japan (20EA1017); Japan Agency for Medical Research and Development (AMED: 22ck0106778h0001)

Keywords: COVID-19 pandemic; mortality trends; vital statistics; increase in mortality; Japan

Strengths and limitations of this study

- We comprehensively analysed mortality in Japan from the Ministry of Health, Labour, and Welfare published the 2021 complete mortality data for the Japanese population.
- To analyse the contribution of the cause of death to annual all-cause age-standardized mortality rates (ASMRs) changes, the cause-specific ASMR changes in comparison with those of the previous year were calculated.
- This study is a descriptive analysis, and therefore, further analysis is needed to clarify the quantitative impact such as 'excess deaths'.
- In addition, long-term monitoring is necessary from 2022 onwards, especially for deaths from chronic diseases that may have long-term effects by changes in lifestyle and medical care.

Introduction

Approximately three years into the pandemic, the impact of COVID-19 on Japan continues to increase. Although the Japanese government did not introduce strict COVID-19 restrictions such as lockdown, people's daily lives were affected, as were the lives of health-care workers since the first declaration of a state of emergency in April 2020. To date, however, no nationwide mortality data that discuss the impact of the COVID-19 pandemic on mortality trends have been reported in Japan. Careful assessment of the impact of the pandemic on population health would aid in the evaluation of efforts during the pandemic and identify lessons, not only for Japan but also globally.

In most high-income countries, life expectancy in 2020 was shorter than that before, attributable to both the direct and indirect effects of COVID-19.[1] For example, reductions in life expectancy in 2020 were observed in Russia, the U.S., Spain, England/Wales, Netherlands, Sweden, and France.[2] However, in Japan, life expectancy was not shortened in 2020 according to the Japanese Ministry of Health, Labour and Welfare (MHLW),[1,3] a deviation from the decreasing trend in most countries.[1]

Reasons for the prolonged life expectancy in 2020 despite the pandemic are unclear. One reason could be that Japan did not experience as large a number of COVID-19 cases that year as other countries. However, Japan experienced a six-fold increase in the number of reported cases from 2020 to 2021: 234 109 cases in 2020 and 1 492 874 cases in 2021.[4] Thus, annual mortality rate in 2021 in Japan may differ from the stable downward trend seen before 2020. This study aimed to explore the long-term mortality trends and cause-specific contributions during the COVID-19 pandemic in Japan, focusing on the years 2020 and 2021.

Methods

We illustrated changes in life expectancy between 2019 and 2020 for selected countries, including Japan, using data extracted from the World Development Indicators managed by the World Bank.[1] To evaluate the trends in the number of COVID-19 cases in Japan, we extracted data on the daily number of reported COVID-19 cases from 16 January 2020 (the first case confirmed) to 1 January 2023 from Japanese government records.[4] The numbers of deaths (5-year age intervals) between 1995 and 2021 were extracted from the vital statistics (complete deaths record) in Japan managed by MHLW.[3] The 2021 complete mortality data were published in September 2022.[3] The vital statistics cover all Japanese deaths that occurred in Japan. The relevant population data were also collected from the vital statistics and population census.

We calculated age-standardized mortality rates (ASMRs) for all causes of death combined and cause-specific deaths for major causes from 1995 to 2021 to assess trends in mortality rates. ASMRs were calculated using the 2015 Japan Standard Population.[5] We further calculated the annual percent changes in ASMRs before and during the early part of the COVID-19 pandemic (2020 and 2021). Causes of death (the International Classification of Diseases 10th revision: ICD-10) included: certain infectious and

parasitic diseases (A00-B99), malignant neoplasms (C00-C97), heart diseases (I01-I02.0, I05-I09, I20-I25, I27, I30-I52), cerebrovascular diseases (I60-I69), pneumonia (J12-J18), liver disease (K70-K76), senility (R54), accidents (V01-X59), suicide (X60-X84), and COVID-19 (U07). These classifications were based on the leading causes of death reported by the official mortality statistics from MHLW.[3] MHLW follows the algorithm for classifying the causes of death based on ICD-10.

To analyse the contribution of the cause of death to annual all-cause ASMR changes, the cause-specific ASMR changes in comparison with those of the previous year were calculated for six periods from 2015–2016 to 2020–2021.

Patient and public involvement

Actual patients were not involved in this study of data.

Results

Figure 1 shows Japan was one of the countries where life expectancy was prolonged in 2020 despite having shortened in many high-income countries such as the U.S. and France. Figure 2 shows trends in the daily number of reported COVID-19 cases in Japan since 16 January 2020. The peak of reported COVID-19 cases was observed in August 2022 (7th COVID-19 wave). While the absolute number of COVID-19 cases was very small in 2020, the annual number of reported COVID-19 cases increased rapidly in 2021 and 2022.

Figure 3 shows the trends in all-cause ASMRs (per 100 000 persons) between 1995 and 2021. Supplement Table 1 shows the trends in number of deaths in Japan between 1995 and 2021. After the Great East Japan Earthquake occurred in 2011, ASMRs continued decreasing until 2020, then increased in 2021 in both sexes. For men, all-cause ASMRs (per 100 000 persons) were 1352.3 in 2019 (-1.69% from 2018), 1328.8 in 2020 (−1.74% from 2019), and 1356.3 in 2021 (+2.07% from 2020). For women, all-cause ASMRs were 746.0 in 2019 (−1.39% from 2018), 722.1 in 2020 (−3.20% from 2019), and 737.9 in 2021 (+2.19% from 2020). Age-specific analyses also showed stable to slightly increased mortality trends during the period of COVID-19 pandemic (Supplement Figure 1). Supplement Figure 2 shows the trends in cause-specific ASMRs between 1995 and 2021. For men, COVID-19 ASMRs were 3.8 in 2020 and 17.5 in 2021. For women, COVID-19 ASMRs were 1.5 in 2020 and 7.7 in 2021. ASMRs from malignant neoplasms, pneumonia, accidents, and suicide (men only) decreased during the COVID-19 pandemic in Japan while the trend of cardiovascular disease (heart disease and cerebrovascular disease combined) increased in 2021. In addition, the trend of suicide in women increased in 2020. Supplement Figure 3 shows trends in malignant neoplasms ASMRs by cancer site. Trends in most malignant neoplasms were decreased or stable, which was not altered compared to the trends before 2020.

Figure 4 shows the cause-specific contribution to annual changes in all-cause ASMR. The analysis of annual ASMR changes revealed that decreases in malignant neoplasms, pneumonia, heart disease, and

cerebrovascular diseases continuously contributed to substantial annual mortality reductions for both sexes during 2015–2019; however, the contributions to reduction disappeared for cardiovascular disease from 2020 to 2021. COVID-19 (+13.7 per 100 000 for men and +6.2 per 100 000 for women in comparisons with the previous year) and senility (+7.4 per 100 000 for men and +8.1 per 100,000 for women in comparisons with the previous year) largely contributed to the mortality increases from 2020 to 2021. Also, 'other causes not classified major causes' contributed to all-cause mortality increase as well from 2020 to 2021.

Discussion

This is the first study to comprehensively report on mortality analysis in Japan since MHLW published the 2021 complete mortality data for the Japanese population. We found that the numbers of deaths from COVID-19 were 9 732 (1.32% of all deaths) for men and 7 034 (1.00% of all deaths) for women in 2021, a substantial increase from the year 2020 (2 094 deaths for men and 1 372 deaths for women). The number of deaths in the population due to diagnosed COVID-19 was relatively low compared to many other high-income countries.[6] In both men and women, all-cause ASMR decreased gradually every year from 2011 to 2020 and increased from 2020 to 2021, with a slightly greater decrease in women than in men between 2019 and 2020. In Japan, declining trends in all-cause mortality reversed in 2021 for the first time since the Great East Japan Earthquake occurred in 2011.

The mortality trend varied by cause of death. The patterns of mortality change during the COVID-19 pandemic could be classified into the following three categories: (1) stable mortality decline (e.g. certain infectious and parasitic diseases, malignant neoplasms, and pneumonia), (2) stable mortality increase (e.g. senility), and (3) reversal of decreasing mortality trend (heart diseases, cerebrovascular diseases, suicide for women). Considering these changes, a substantial mortality increase from COVID-19 and senility resulted in an all-cause mortality increase in 2021 while malignant neoplasms and pneumonia contributed to mortality declines.

Recorded mortality from malignant neoplasms declined during the COVID-19 pandemic, despite that patients diagnosed with a cancer regardless of COVID-19 status were required to postpone non-urgent surgeries, suspend outpatient visits, and change treatment methods. Indeed, the numbers of cancer diagnoses, the cancer screening, outpatient visits, and surgical procedures in 2020 have been reported to be lower than those before 2019.[7-10] Those reports have raised deep concern about potential consequences, such as delays in diagnosis and care, decreased patient survival, and increased population mortality; however, our findings revealed a decrease in 2020 and no obvious change in cancer mortality, at least in 2021. Nevertheless, further monitoring is necessary because the delays in diagnosis and treatment can exert a belated effect on mortality.

We found that the ASMR from cardiovascular disease increased in 2021. The loss of reduction trends of cardiovascular disease partially resulted in increasing all-cause mortality in 2021 for both sexes.

This is supported by another study reporting excess deaths from cardiovascular disease from April to May 2021.[11] As a direct pathway, the COVID-19 pandemic may have caused an increase in the prevalence of severe heart disease for the Japanese population because COVID-19 is suggested to be a risk factor for acute myocardial infarction and ischemic stroke.[12] In addition, the pandemic might have induced a delay in emergency transport and delay in arrival at hospital, resulting in the loss of timely treatment. This may be an indirect pathway through which mortality reductions of cardiovascular disease stagnated in Japan.

A substantial increase in mortality due to senility has been occurring since the mid-2000s, independent of the pandemic. This can be interpreted as a result of the rapid aging of the Japanese population. Although we applied age-standardization for mortality analysis, the increase in the absolute number of deaths from senility, especially for the oldest old (85 years and over), resulted in an increase in ASMR. During the pandemic, however, changes in patterns or places of medical care may have resulted in more physicians reporting senility as the cause of death, especially deaths at home. Indeed, excess deaths from senility at home have been observed since May 2020.[11] As such, for the elderly, both direct and indirect death by COVID-19 may be miscoded to senility, which contributed to excess deaths in 2021. The sharp increase in deaths by 'other causes not classified as major causes' in 2021 (Figure 3) may have occurred by a similar mechanism. Therefore, our findings suggest that senility and 'other causes not classified as major causes' may largely represent the excess deaths in Japan during the pandemic. This may also include underdiagnosis and potential misclassification of causes of death.

We found clear declines in mortality from infectious diseases (excluding COVID-19) and infectious pneumonia since the pandemic began in Japan. This is likely because the countermeasures for COVID-19 such as wearing a mask, hand hygiene, and social distancing prevented these diseases. In addition, clear mortality declines due to accidents were observed probably because fatal traffic accidents decreased due to stay-at-home measures. These are positive outcomes of the COVID-19 measures; however, we identified an increase in suicide rate among women in 2020 and 2021. The increase did not largely impact on all-cause mortality changes for women but this is obviously a negative effect of the COVID-19 measures such as restrictions of economic activity (e.g. cancellation of events and shorter business hours for restaurants).[13,14]

This study is a descriptive analysis of national mortality data and should accordingly be interpreted with caution. Our findings suggest that the mortality increase in 2021 may be associated with the increase in COVID-19 cases; however, further analysis is needed to clarify the quantitative impact such as 'excess deaths'. Also, long-term monitoring is necessary from 2022 onwards, especially for deaths from chronic diseases that may have long-term effects by changes in lifestyle and medical care.

In conclusion, a sign of increasing mortality was observed in 2021 in the annual mortality rate in Japan, although the impact of the COVID-19 pandemic on mortality in Japan still seems to be limited. The observed increase in mortality was attributable to COVID-19, senility, cardiovascular disease, and

'other causes not classified as major cause'. Taking the rapidly increasing rate of COVID-19 cases in 2022 into consideration, further monitoring is warranted for the year 2022, which may reveal a larger impact of the pandemic on mortality compared to that for 2020 and 2021.

Ethics statements

Patient consent for publication

Not applicable.

Ethics approval

Ethics approval was not applicable.

Data availability

This study used the vital statistics data from a portal site for Japanese Government Statistics (e-Stat: https://www.e-stat.go.jp/), and data at an individual level were not used.

Authors' contributions: All author had full access to all the study data. H.T. was responsible for the integrity of the data, the accuracy of the data analysis, and the drafting of the manuscript. All authors contributed to the concept and design of the study. All authors critically reviewed the manuscript. K.K. supervised the study and provided administrative, technical, and material support.

Declaration of interest statement: The authors have no conflicts of interest directly relevant to the content of this study.

Funding: This research was supported by Grants-in-Aid for Cancer Control Policy from the Ministry of Health, Labour, and Welfare, Japan (20EA1017) and Japan Agency for Medical Research and Development (AMED; Grant Number: 22ck0106778h0001).

Patient and other consents: Not applicable.

Availability of data and materials: Data are available on request.

Acknowledgment: We thank Libby Cone, MD, MA, from Dmed (www.dmed.co.jp <http://www.dmed.co.jp/>) for editing English drafts of this manuscript.

Figure legends

Figure 1. Changes in life expectancy between 2019 and 2020 for selected countries for both sexes

Figure 2. Trends in the daily number of reported COVID-19 cases in Japan since 16 January 2020

Figure 3. Trends in all-cause and cause-specific age-standardized mortality rates between 1995 and 2021

Figure 4. Cause-specific contribution to changes in all-cause age-standardized mortality rates (annual comparisons with previous year): differences in changes in ASMR between 2020 and 2021 were calculated as ($ASMR_{2021} - ASMR_{2020}$) for each cause-specific death, where ASMR=age standardized mortality rate per 100 000 population.

Reference

1. The World Bank. Life expectancy at birth, total (years). https://data.worldbank.org/indicator/SP.DYN.LE00.IN Date accessed: December 12, 2022

2. Islam N, Jdanov DA, Shkolnikov VM, et al. Effects of covid-19 pandemic on life expectancy and premature mortality in 2020: time series analysis in 37 countries. *BMJ*. 2021;375:e066768.

3. Ministry of Health, Labour and Welfare. Vital Statistics. https://www.mhlw.go.jp/english/database/db-hw/vs01.html Date accessed: December 12, 2022

4. Ministry of Health, Labour and Welfare. Visualizing the data: information on COVID-19 infections. https://covid19.mhlw.go.jp/en/ December 12, 2022

5. Tanaka H, Tanaka S, Togawa K, Katanoda K. Practical implications of the update to the 2015 Japan Standard Population: mortality archive from 1950 to 2020 in Japan. *J Epidemiol*. 2023;33:372-380

6. World Health Organization. WHO coronavirus (COVID-19) dashboard. https://covid19.who.int December 12, 2022

7. Ikeda N, Yamamoto H, Taketomi A, et al. The impact of COVID-19 on surgical procedures in Japan: analysis of data from the National Clinical Database. *Surg Today*. 2022;52:22-35.

8. Sato Y, Fujiwara Y, Fukuda N, et al. Changes in Treatment Behavior during the COVID-19 Pandemic among Patients at a Cancer Hospital. *Cancer Cell*. 2021;39:130-131.

9. Toyoda Y, Katanoda K, Ishii K, Yamamoto H, Tabuchi T. Negative impact of the COVID-19 state of emergency on breast cancer screening participation in Japan. *Breast Cancer*. 2021;28:1340-1345.

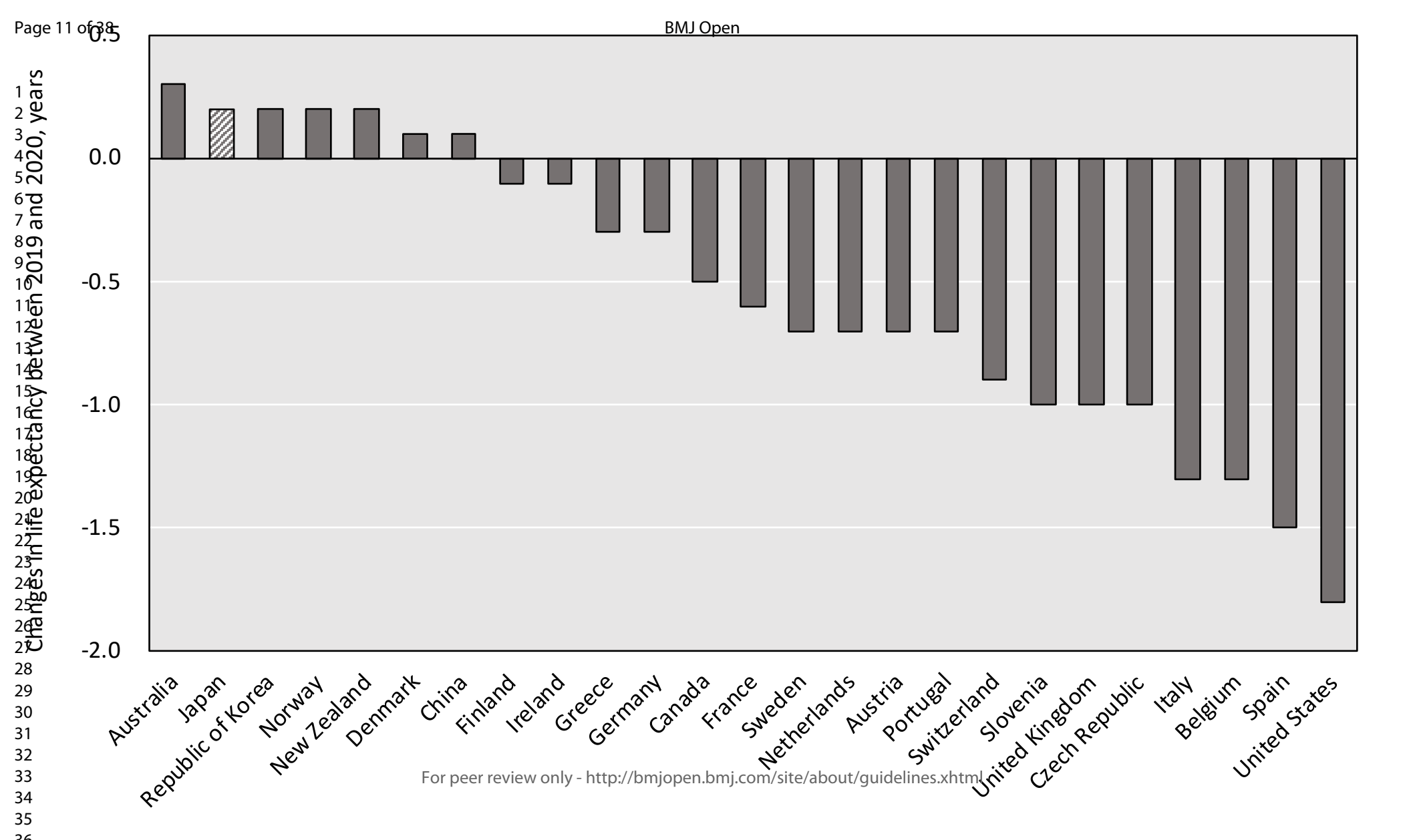
10. Okuyama A, Watabe M, Makoshi R, Takahashi H, Tsukada Y, Higashi T. Impact of the COVID-19 pandemic on the diagnosis of cancer in Japan: analysis of hospital-based cancer registries. *Jpn J Clin Oncol*. 2022;52:1215-1224.

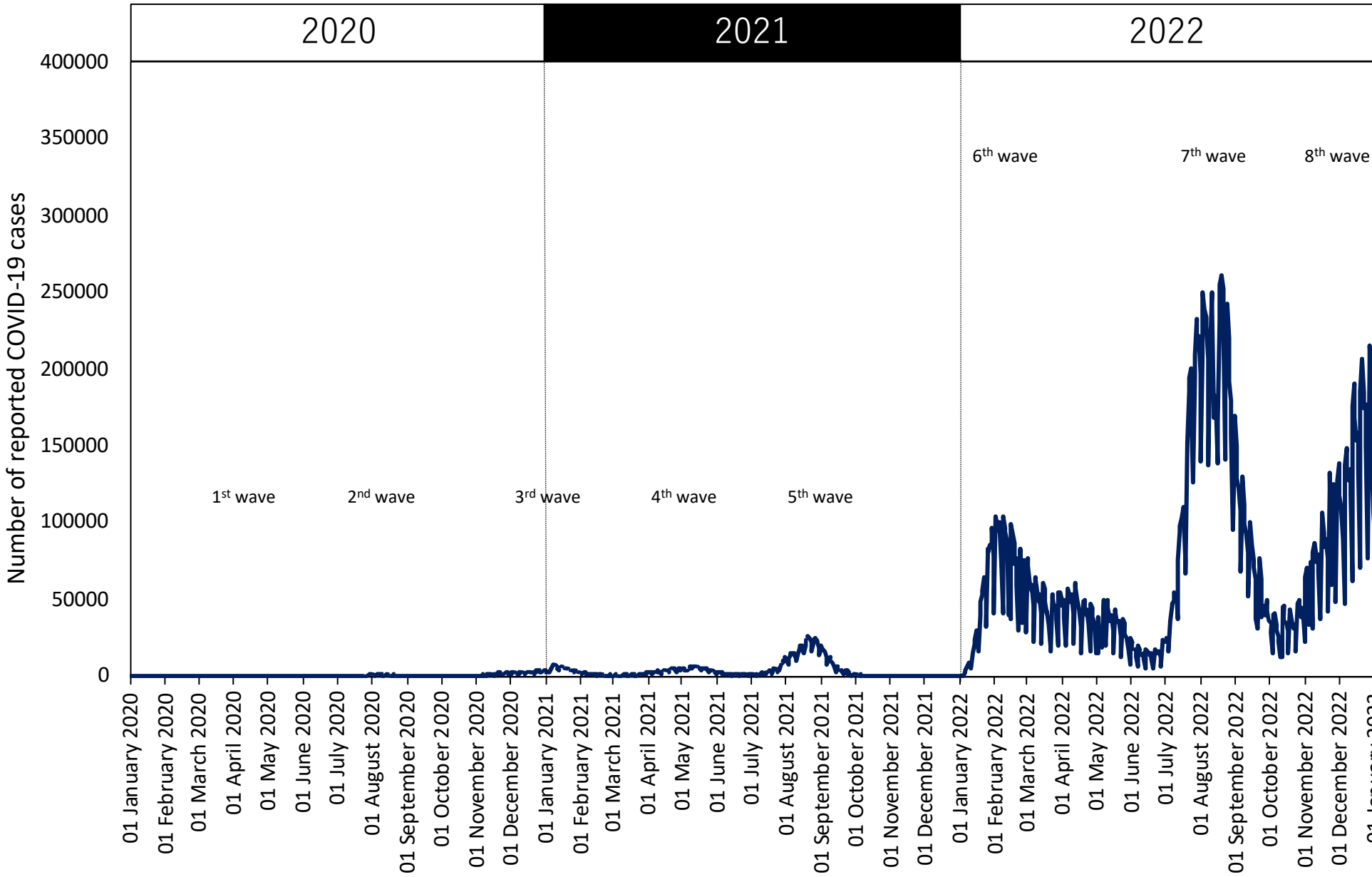
11. Nomura S, Eguchi A, Ghaznavi C, et al. Excess deaths from non-COVID-19-related causes in Japan and 47 prefectures from January 2020 through May 2021 by place of death. *SSM Popul Health*. 2022;19:101196.

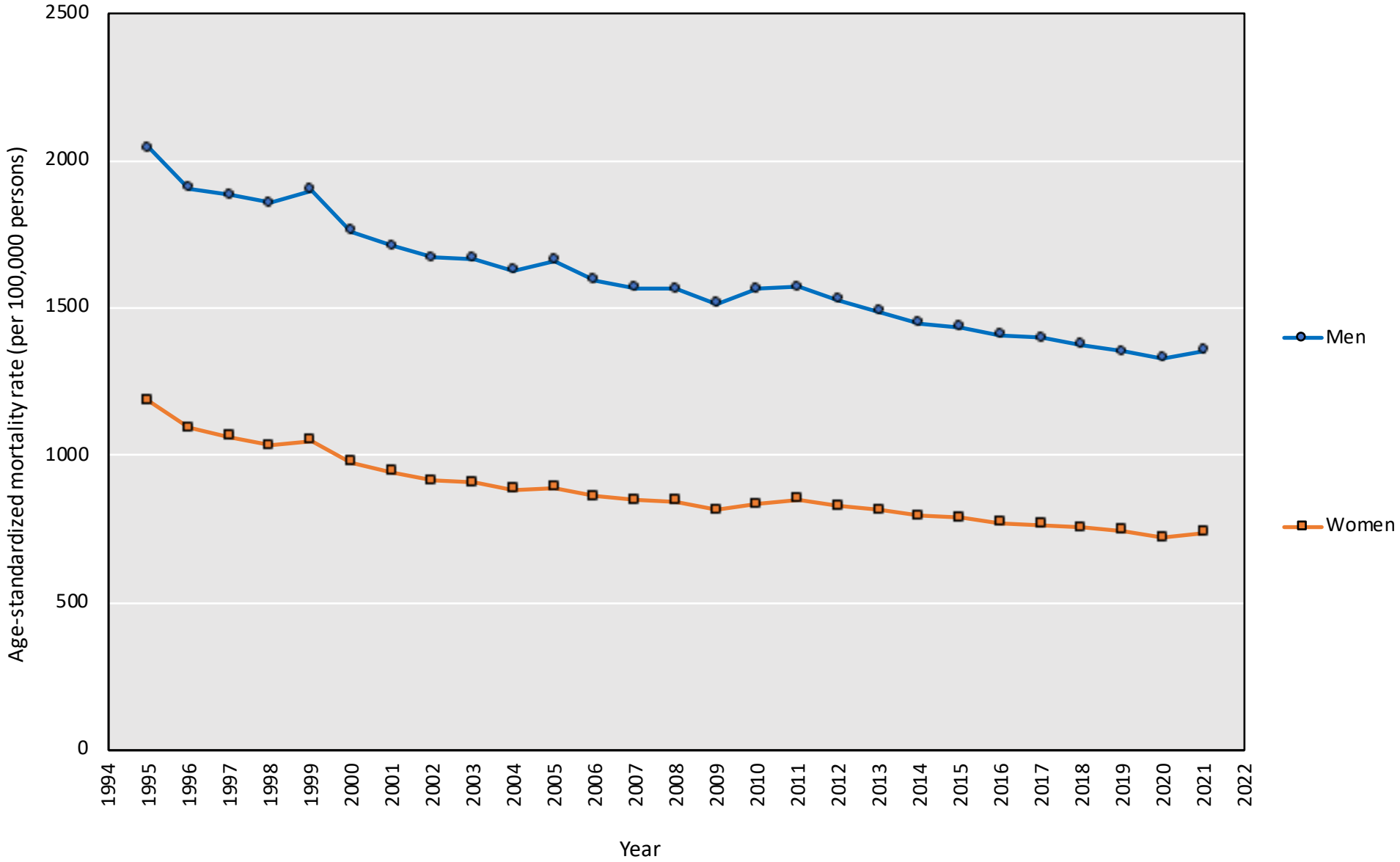
12. Katsoularis I, Fonseca-Rodriguez O, Farrington P, Lindmark K, Fors Connolly AM. Risk of acute myocardial infarction and ischaemic stroke following COVID-19 in Sweden: a self-controlled case series and matched cohort study. *Lancet*. 2021;398:599-607.

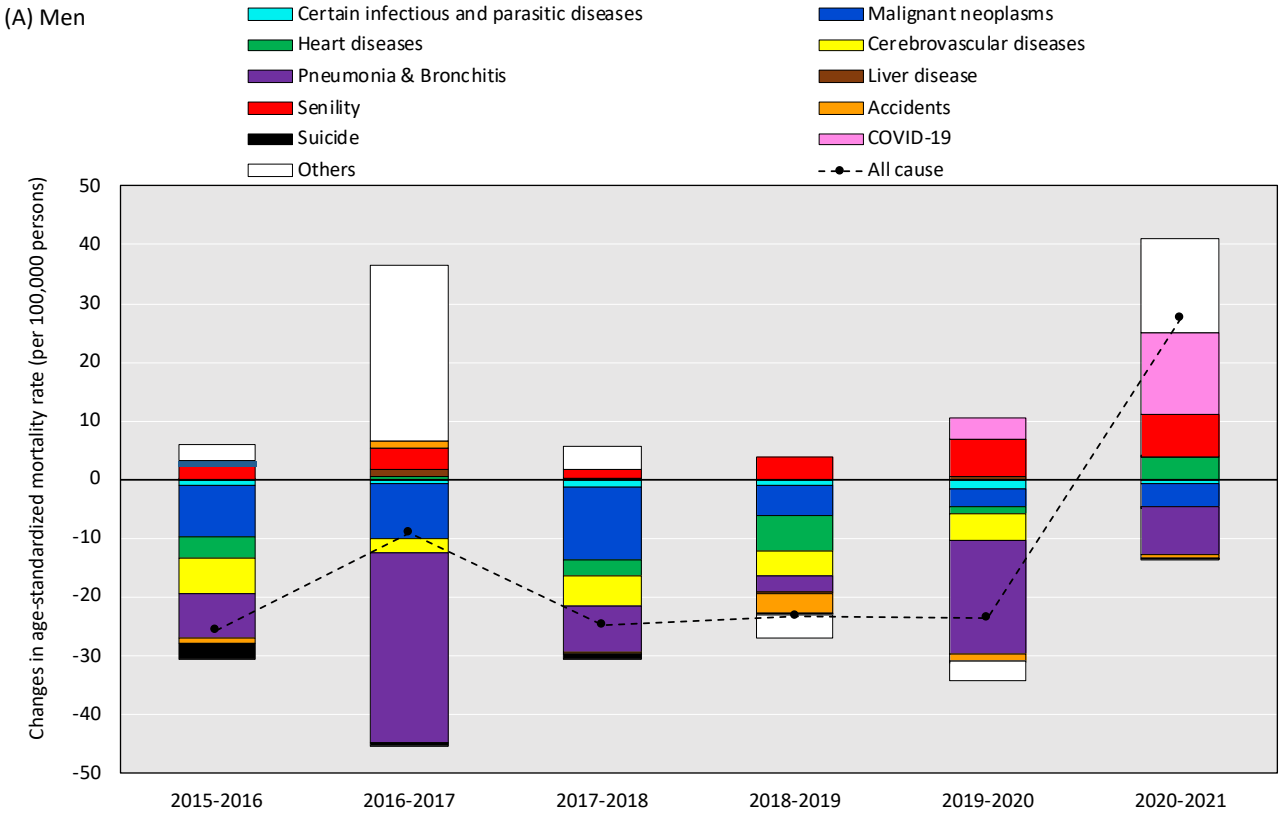
13. Sakamoto H, Ishikane M, Ghaznavi C, Ueda P. Assessment of Suicide in Japan During the COVID-19 Pandemic vs Previous Years. *JAMA Netw Open*. 2021;4:e2037378.

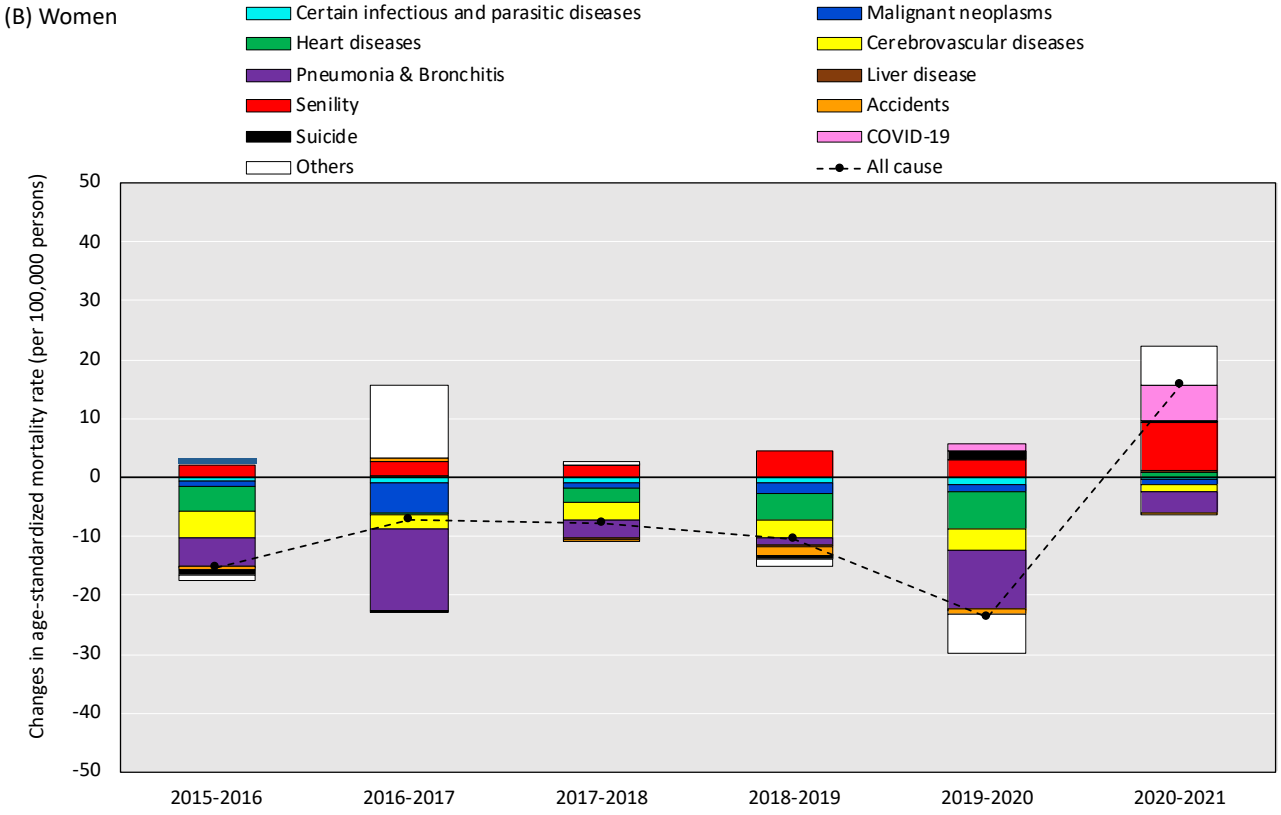
14. Kikuchi K, Anzai T, Takahashi K. The Unusual Increase in Suicides Among Women in Japan During The COVID-19 Pandemic: A Time-Series Analysis until October 2021. *J Epidemiol*. 2023; 33: 45–51.




2020
2021
2022
Number of reported COVID-19 cases
400000
350000
300000
250000
200000
150000
100000
50000
0
1st wave
2nd wave
3rd wave
4th wave
5th wave
6th wave
7th wave
8th wave
01 January 2020
01 February 2020
01 March 2020
01 April 2020
01 May 2020
01 June 2020
01 July 2020
01 August 2020
01 September 2020
01 October 2020
01 November 2020
01 December 2020
01 January 2021
01 February 2021
01 March 2021
01 April 2021
01 May 2021
01 June 2021
01 July 2021
01 August 2021
01 September 2021
01 October 2021
01 November 2021
01 December 2021
01 January 2022
01 February 2022
01 March 2022
01 April 2022
01 May 2022
01 June 2022
01 July 2022
01 August 2022
01 September 2022
01 October 2022
01 November 2022
01 December 2022
01 January 2023


2500
2000
1500
1000
500
0
Age-standardized mortality rate (per 100,000 persons)
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Year
Men
Women


(A) Men
Certain infectious and parasitic diseases
Malignant neoplasms
Heart diseases
Cerebrovascular diseases
Pneumonia & Bronchitis
Liver disease
Senility
Accidents
Suicide
COVID-19
Others
All cause
Changes in age-standardized mortality rate (per 100,000 persons)
50
40
30
20
10
0
-10
-20
-30
-40
-50
2015-2016
2016-2017
2017-2018
2018-2019
2019-2020
2020-2021

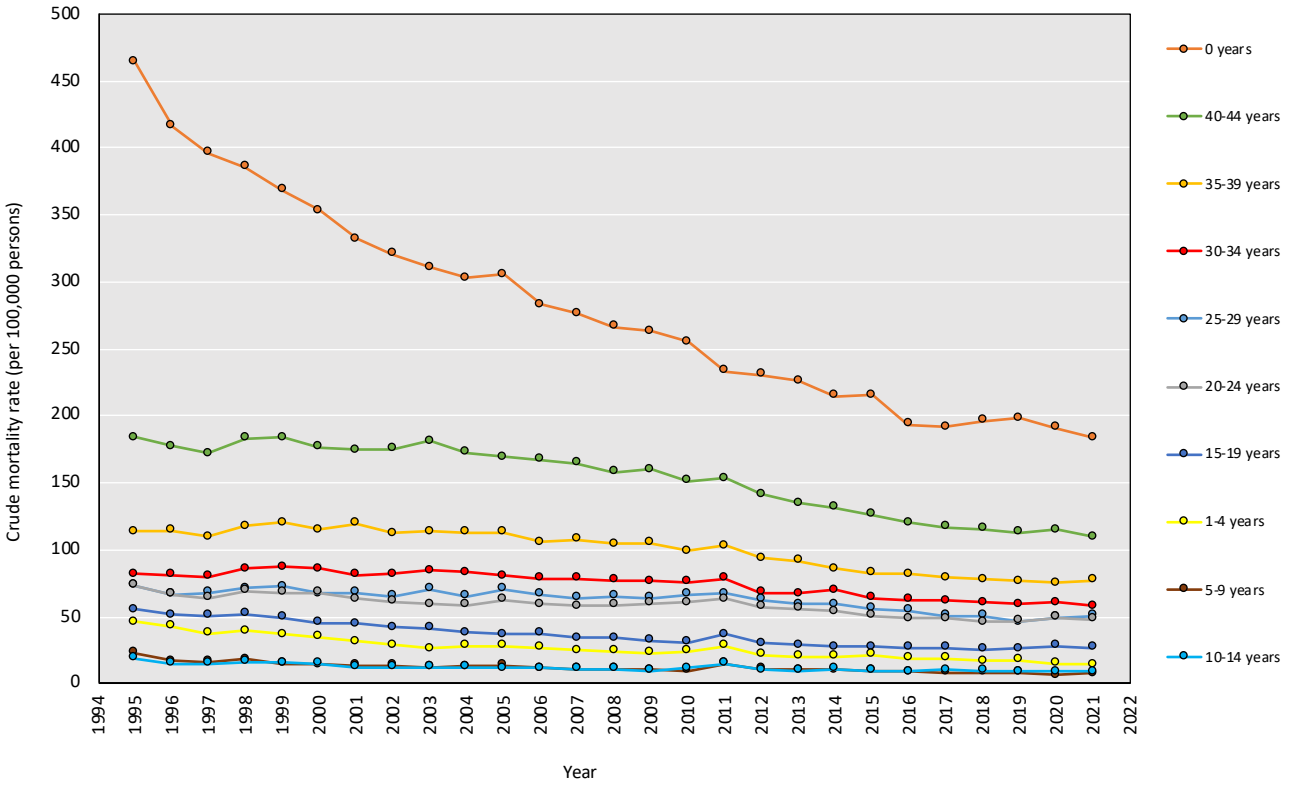

(B) Women
Certain infectious and parasitic diseases
Malignant neoplasms
Heart diseases
Cerebrovascular diseases
Pneumonia & Bronchitis
Liver disease
Senility
Accidents
Suicide
COVID-19
Others
All cause
Changes in age-standardized mortality rate (per 100,000 persons)
50
40
30
20
10
0
-10
-20
-30
-40
-50
2015-2016
2016-2017
2017-2018
2018-2019
2019-2020
2020-2021

Appendix Table 1. Number of deaths in Japan between 1995 and 2021*

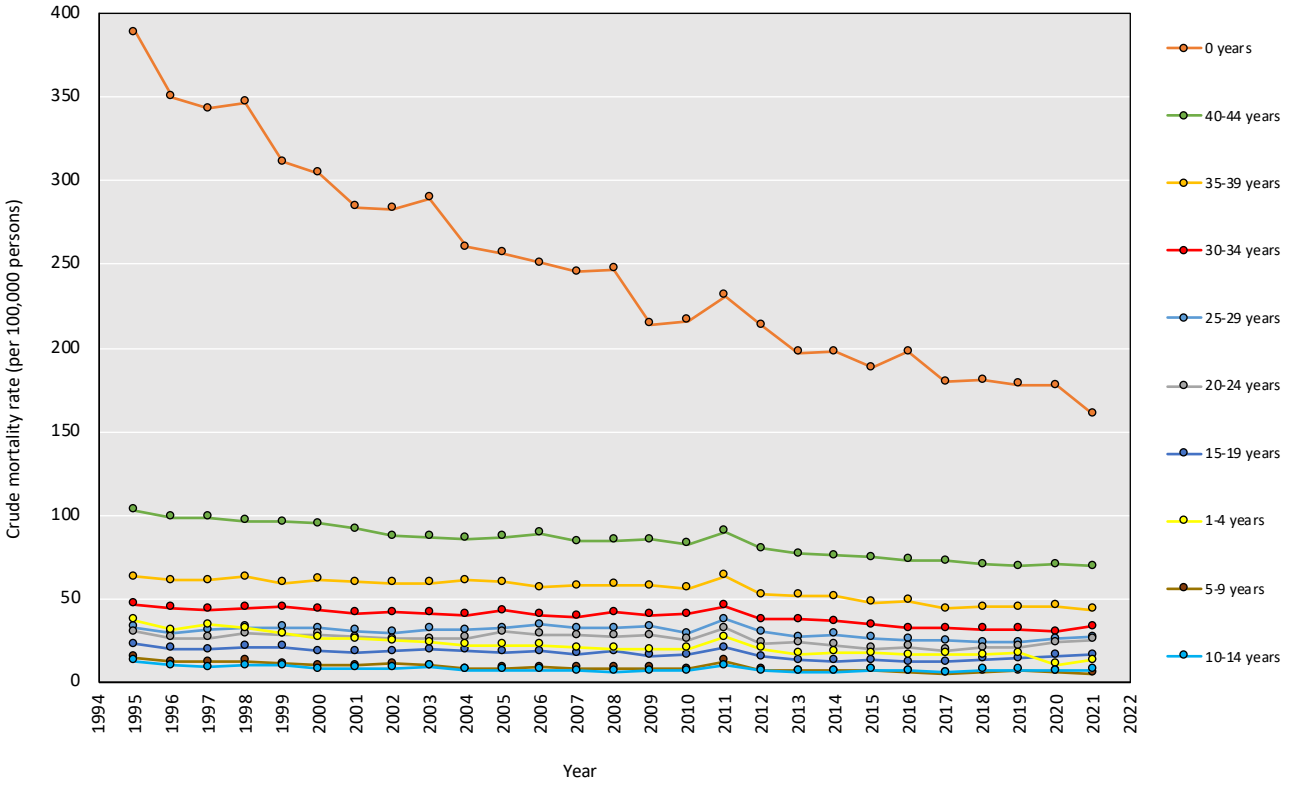
Year	Men					Women				
	All-cause	Malignant neoplasms	Heart disease	Cerebrovascular disease	COVID-19	All-cause	Malignant neoplasms	Heart disease	Cerebrovascular disease	COVID-19
1995	501276	159623	69718	69587	-	420863	103399	69488	76965	-
1996	488605	164824	68977	66479	-	407606	106359	69252	73887	-
1997	497796	167076	69776	65790	-	415606	108337	70398	72907	-
1998	512128	172306	71134	65529	-	424356	111615	71986	72290	-
1999	534778	175817	73979	66452	-	447253	114739	77100	72537	-
2000	525903	179140	72156	63127	-	435750	116344	74585	69402	-
2001	528768	181393	72727	63146	-	441563	119265	75565	68710	-
2002	535305	184033	74986	62229	-	447074	120535	77532	68028	-
2003	551746	186912	77989	63274	-	463205	122631	81556	68793	-
2004	557097	193096	77465	61547	-	471505	127262	82160	67508	-
2005	584970	196603	83979	63657	-	498826	129338	89146	69190	-
2006	581370	198052	82811	61348	-	503080	131262	90213	66920	-
2007	592784	202743	83090	60992	-	515550	133725	92449	66049	-
2008	608711	206354	86139	61121	-	533696	136609	95789	65902	-
2009	609042	206352	85543	59293	-	532823	137753	95202	63057	-
2010	633700	211435	88803	60186	-	563312	142064	100557	63275	-
2011	656540	213190	91298	59616	-	596526	144115	103628	64251	-
2012	655526	215110	92976	58625	-	600833	145853	105860	62977	-
2013	658684	216975	91445	56718	-	609752	147897	105278	61629	-
2014	660334	218397	92278	54995	-	612670	149706	104647	59212	-
2015	666707	219508	92142	53576	-	623737	150838	103971	58397	-
2016	674946	219846	93453	52718	-	633212	153242	104617	56635	-
2017	690770	220416	96330	53198	-	649797	152949	108538	56698	-
2018	699138	218625	98035	52398	-	663332	154959	110186	55788	-
2019	707421	220339	98210	51768	-	673672	156086	109504	54784	-
2020	706834	220989	99304	50390	2094	665921	157396	106292	52588	1372
2021	738141	222467	103700	51594	9732	701715	159038	111010	53001	7034

*Malignant neoplasms (ICD-10: C00-C97); Heart diseases (I01-I02.0, I05-I09, I20-I25, I27, I30-I52); Cerebrovascular diseases (I60-I69); COVID-19 (U07)

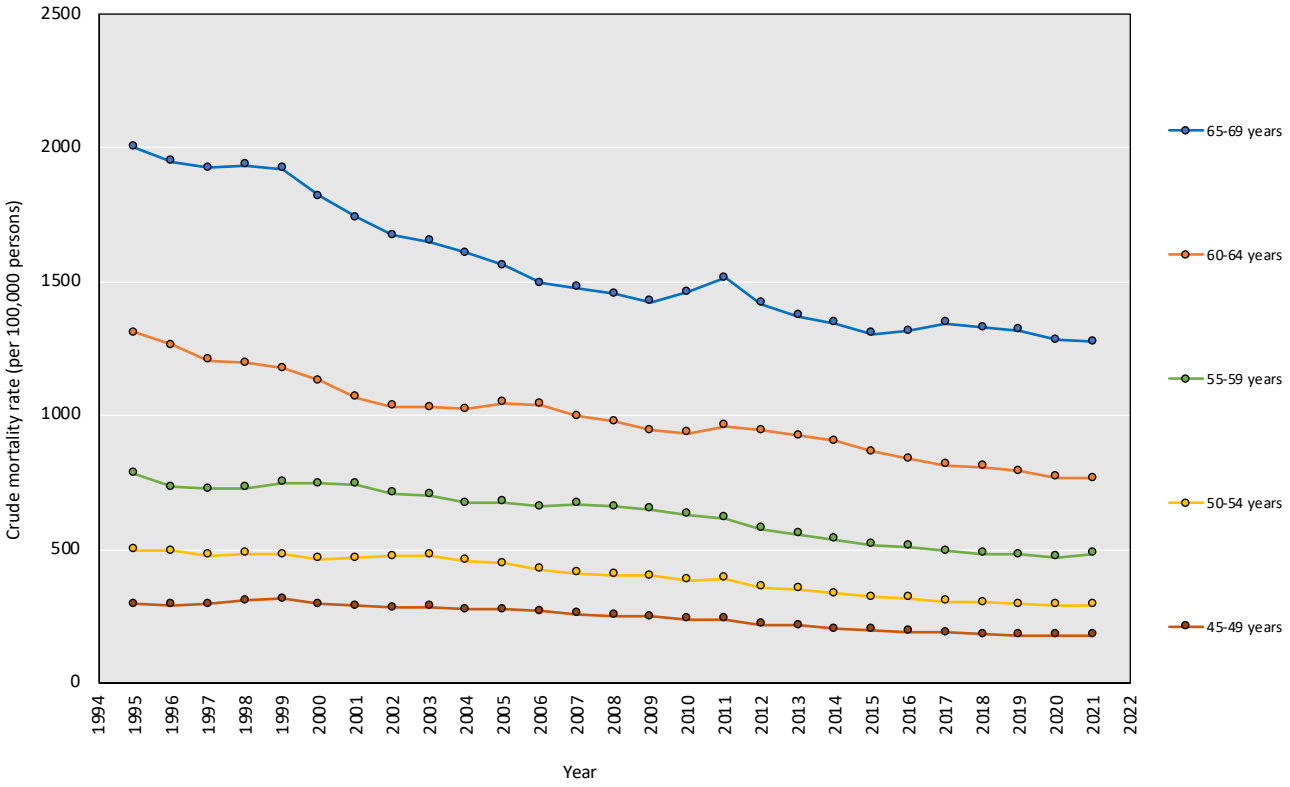
(A) All cause (men, 0-44 years)



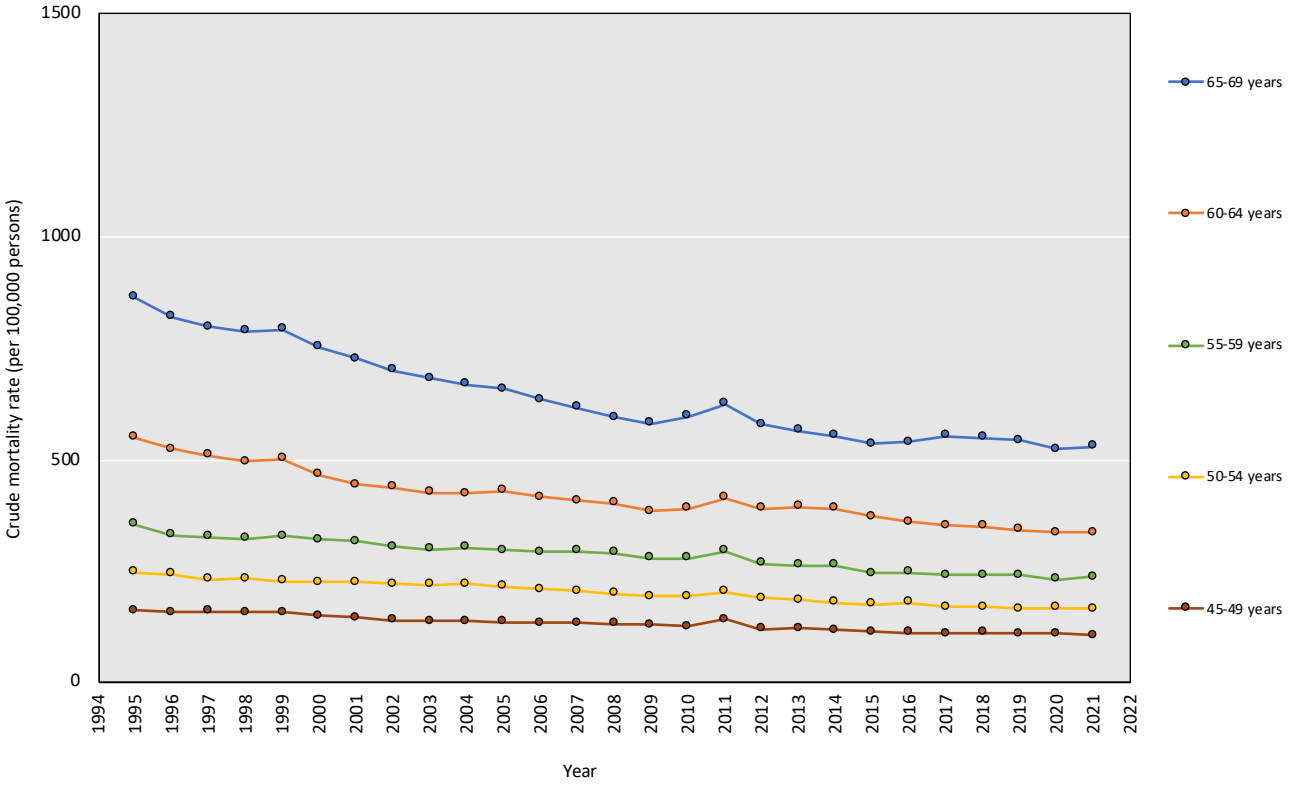
(B) All cause (women, 0-44 years)

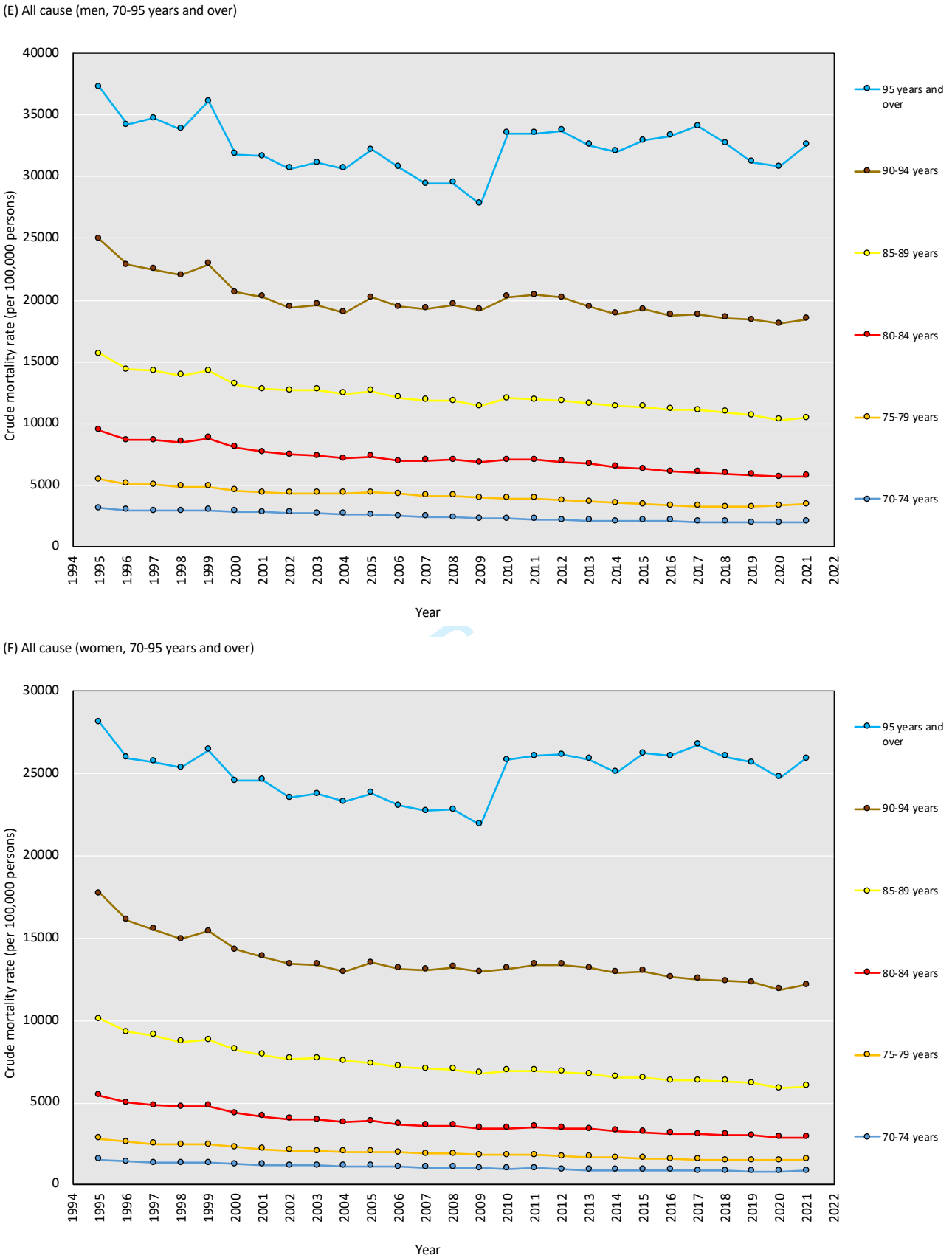


(C) All cause (men, 45-69 years)



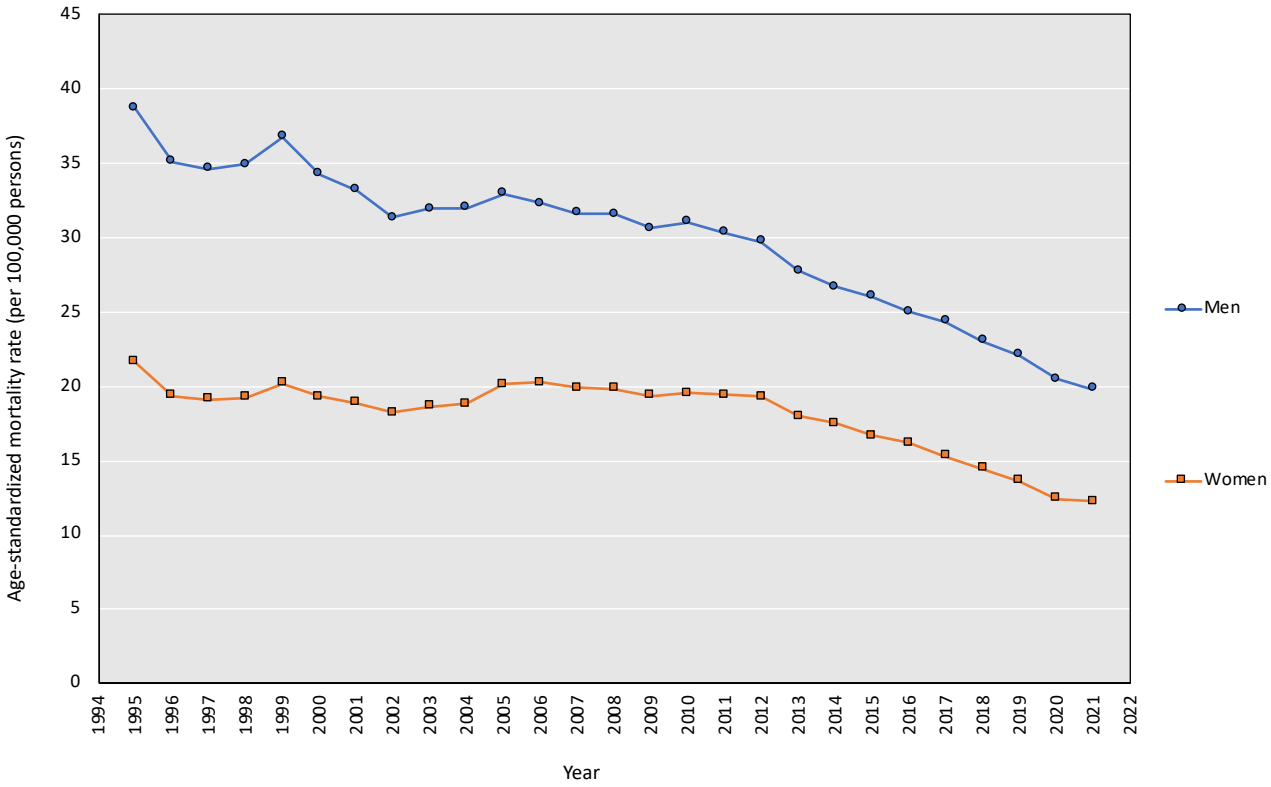
(D) All cause (women, 45-69 years)



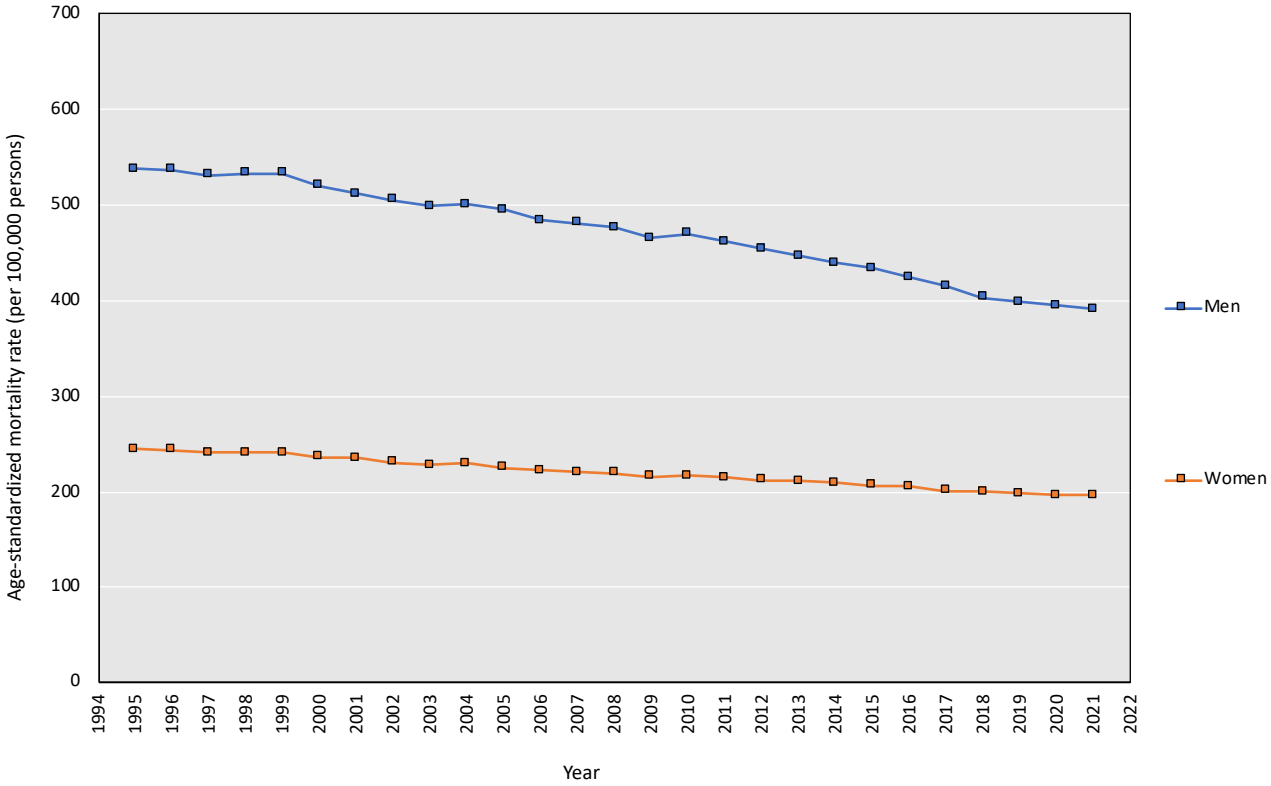


Appendix Figure 1. Trends in crude mortality rate by five-year age groups between 1995 and 2021

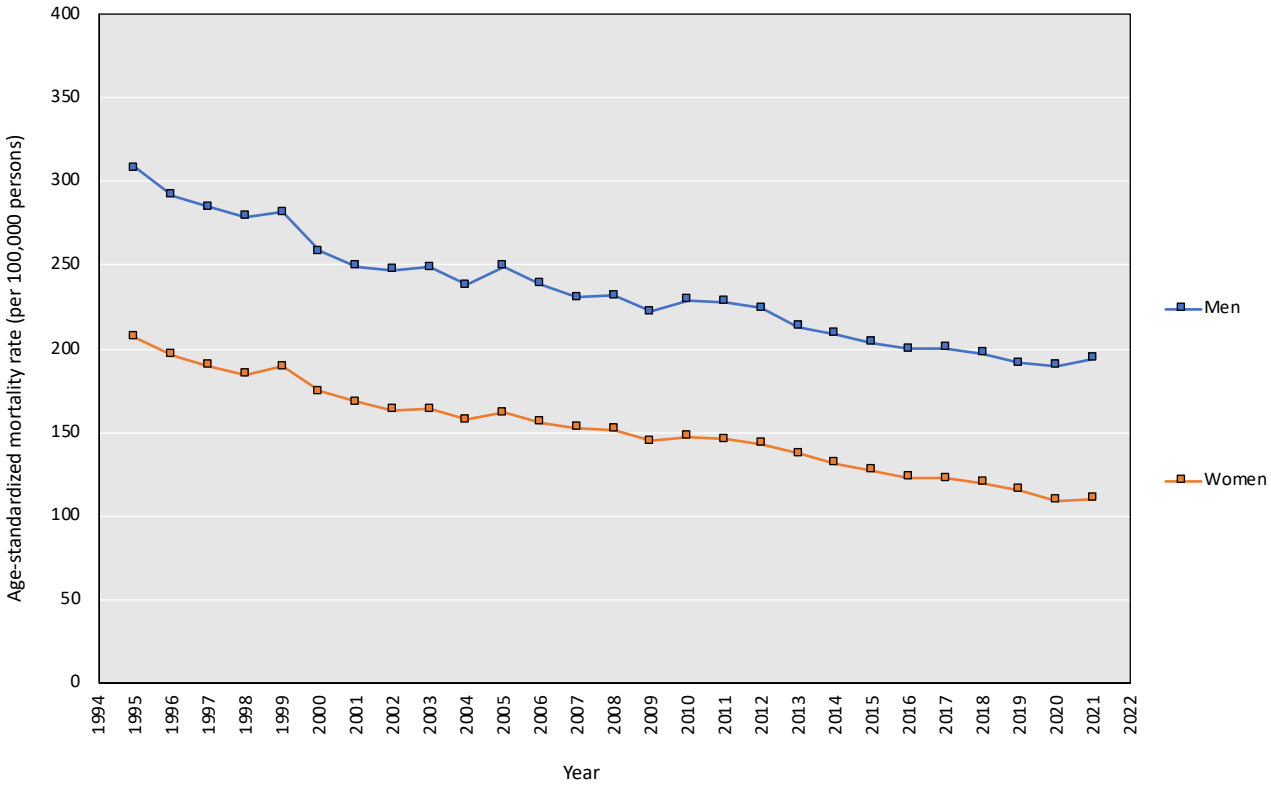
(A) Certain infectious and parasitic diseases (A00-B99)



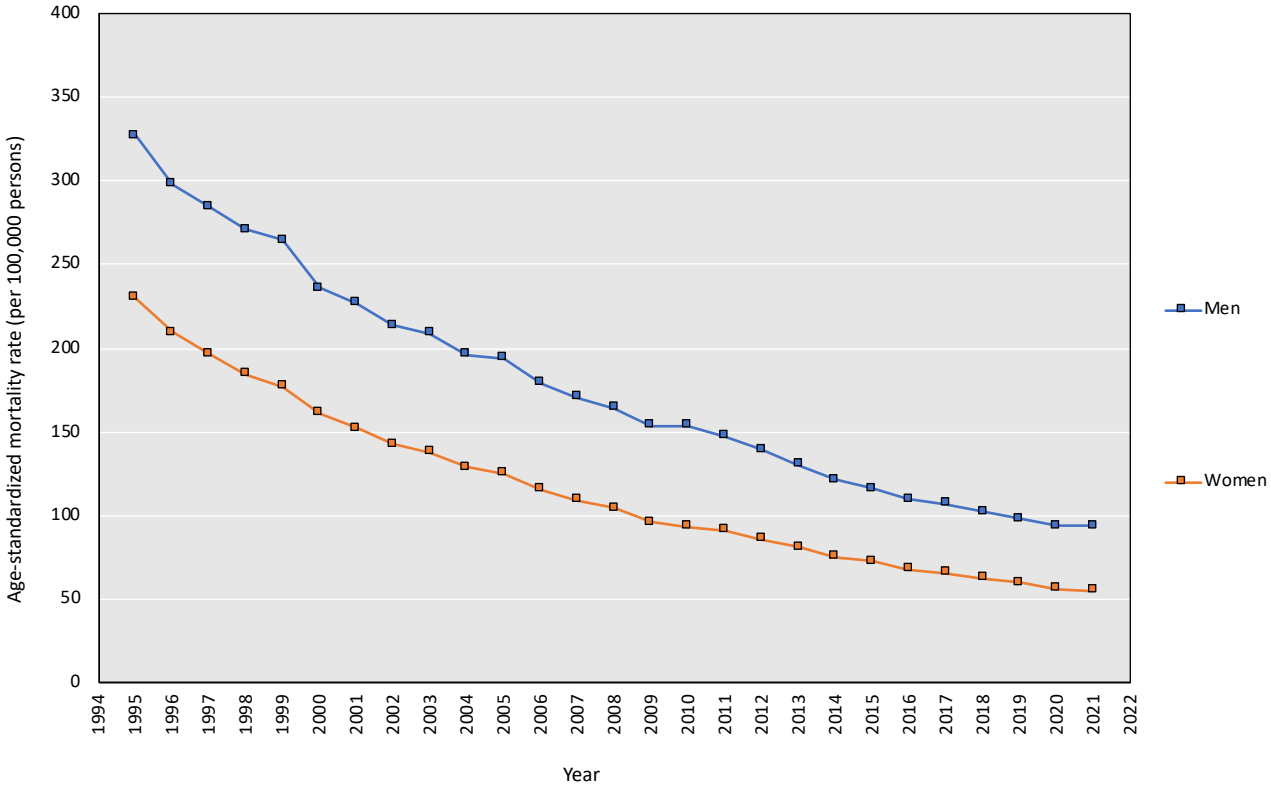
(B) Malignant neoplasms (C00-96)



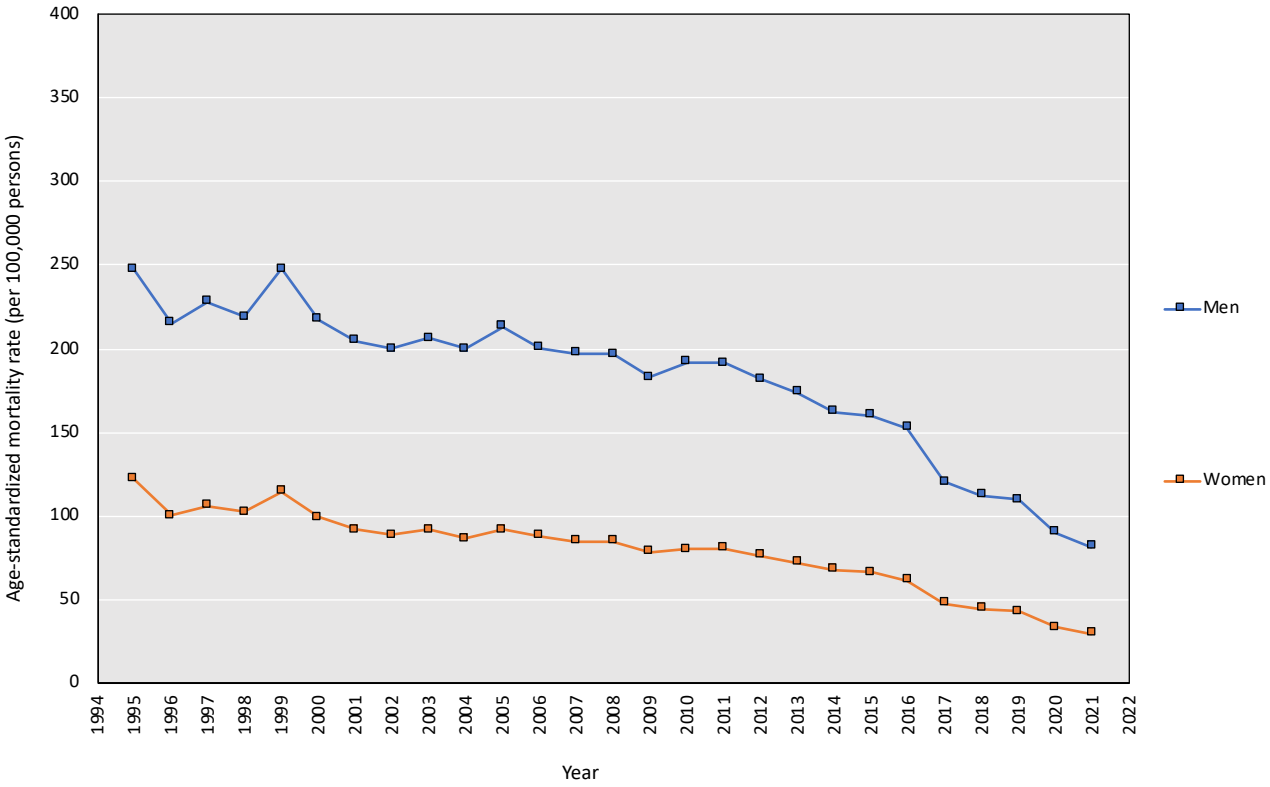
(C) Heart diseases (I05-09, I20-25, I27, I30-51)



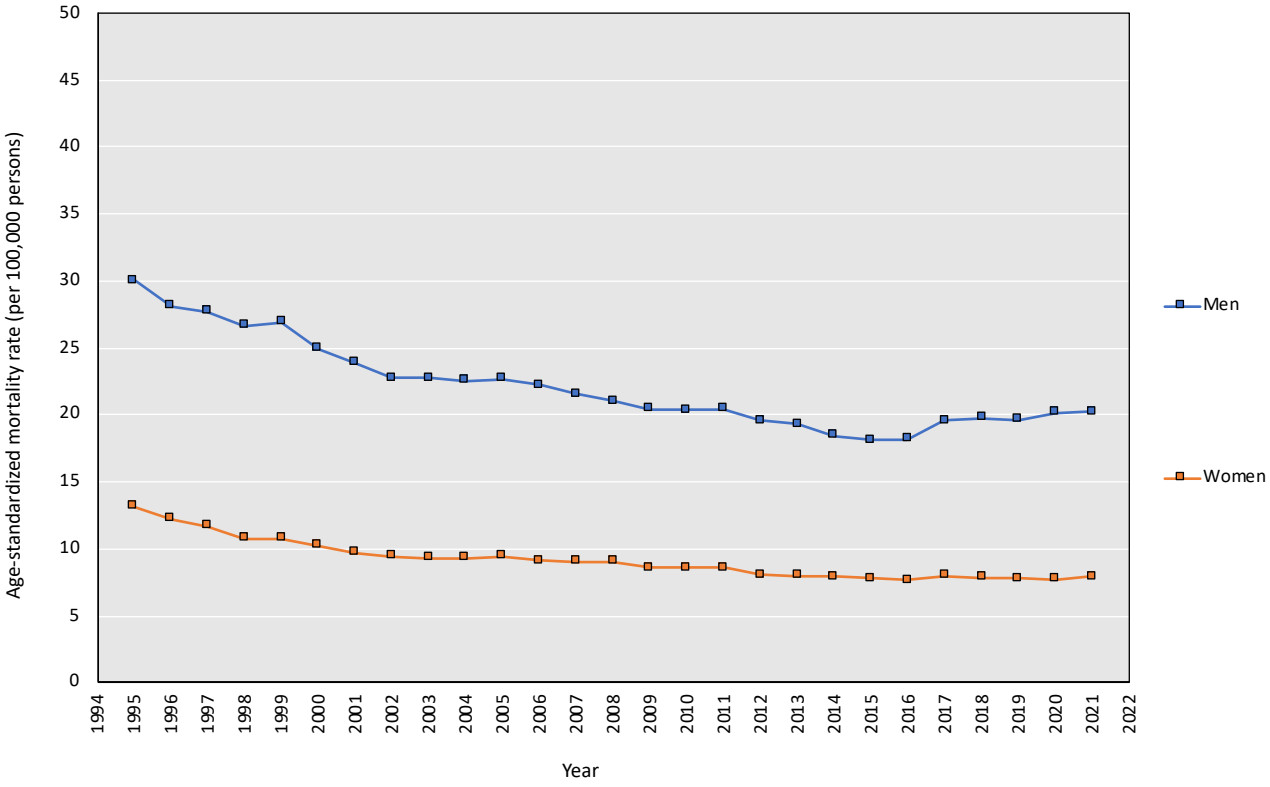
(D) Cerebrovascular diseases (I60-69)



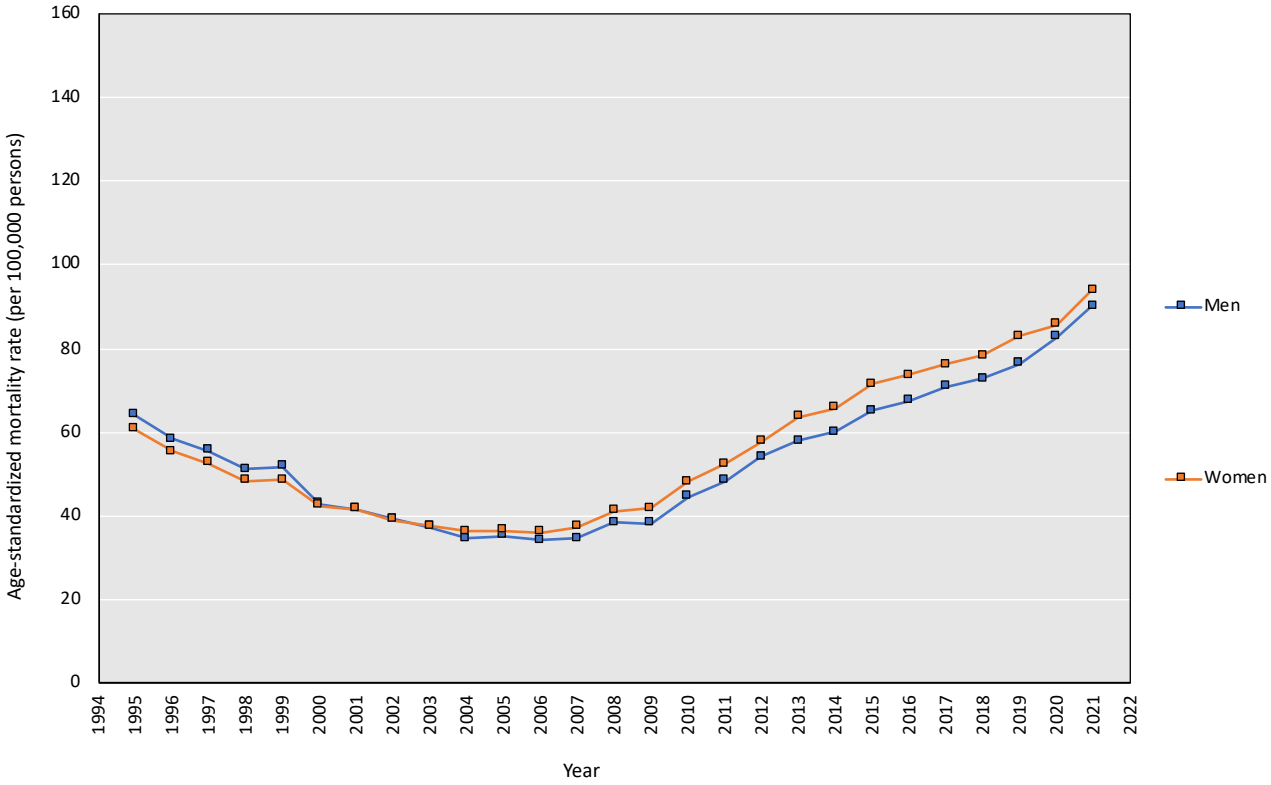
(E) Pneumonia & Bronchitis (J12-18)



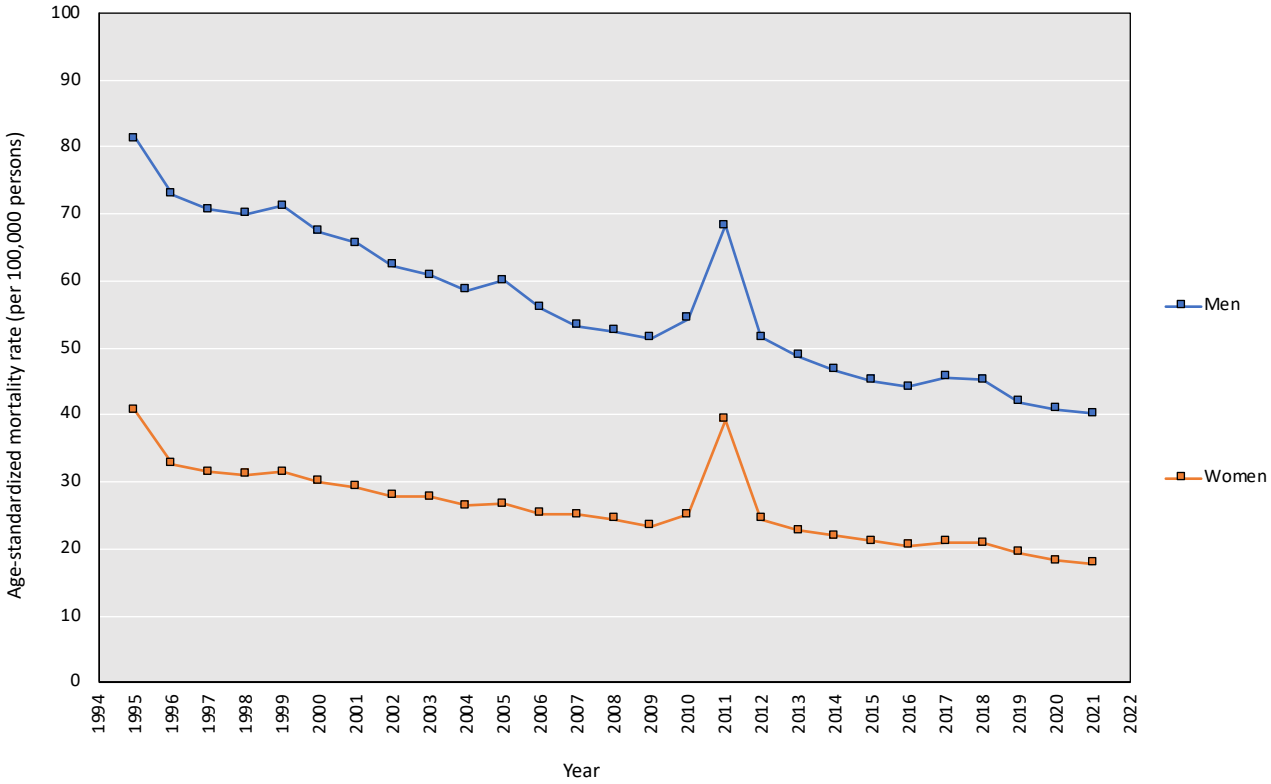
(F) Liver disease (K70-76)



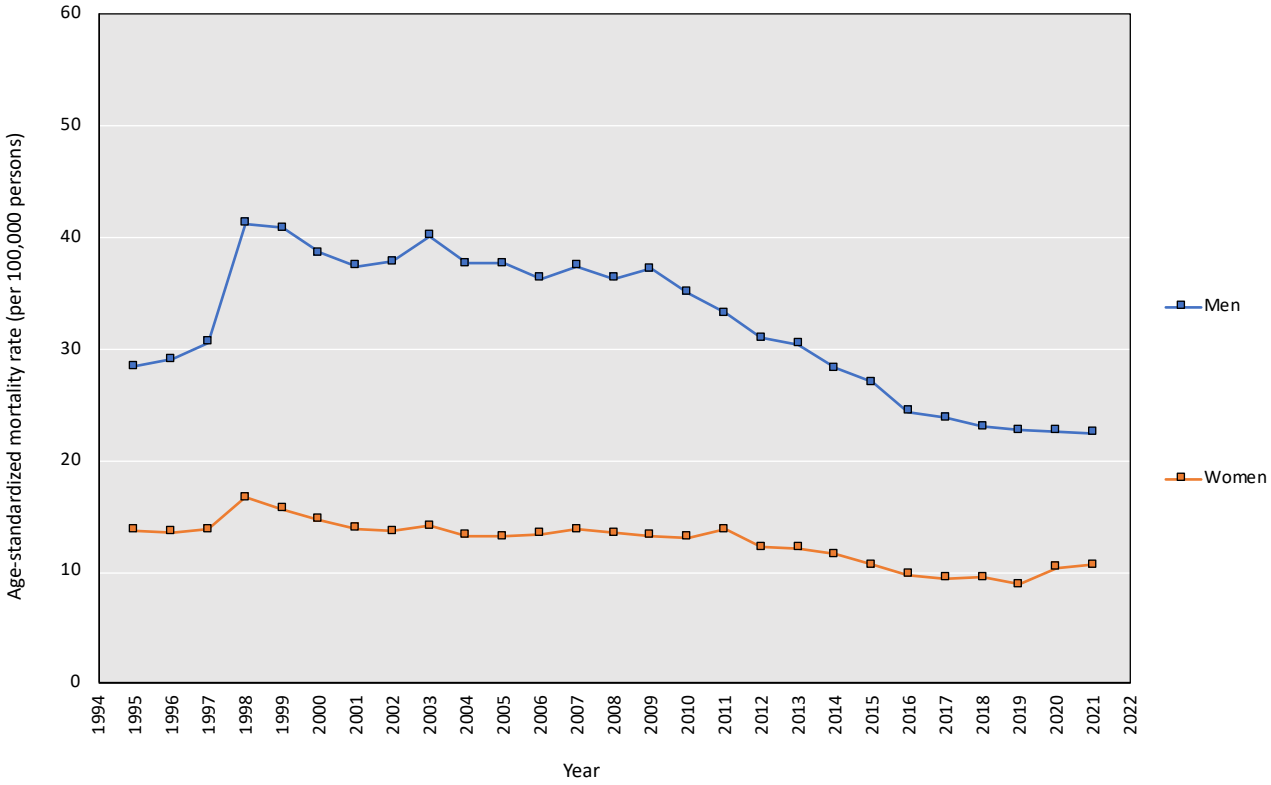
(G) Senility (R54)



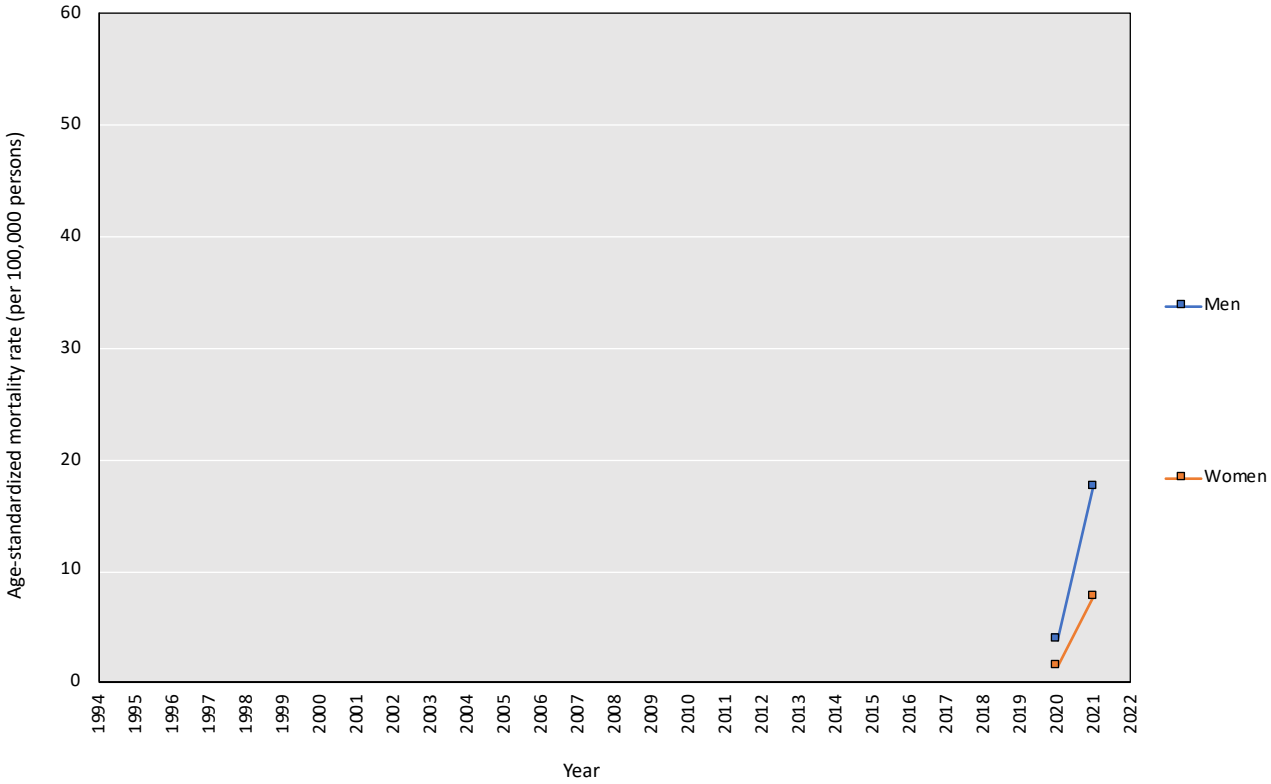
(H) Accidents (V01-X59)



(I) Suicide (X60-84)

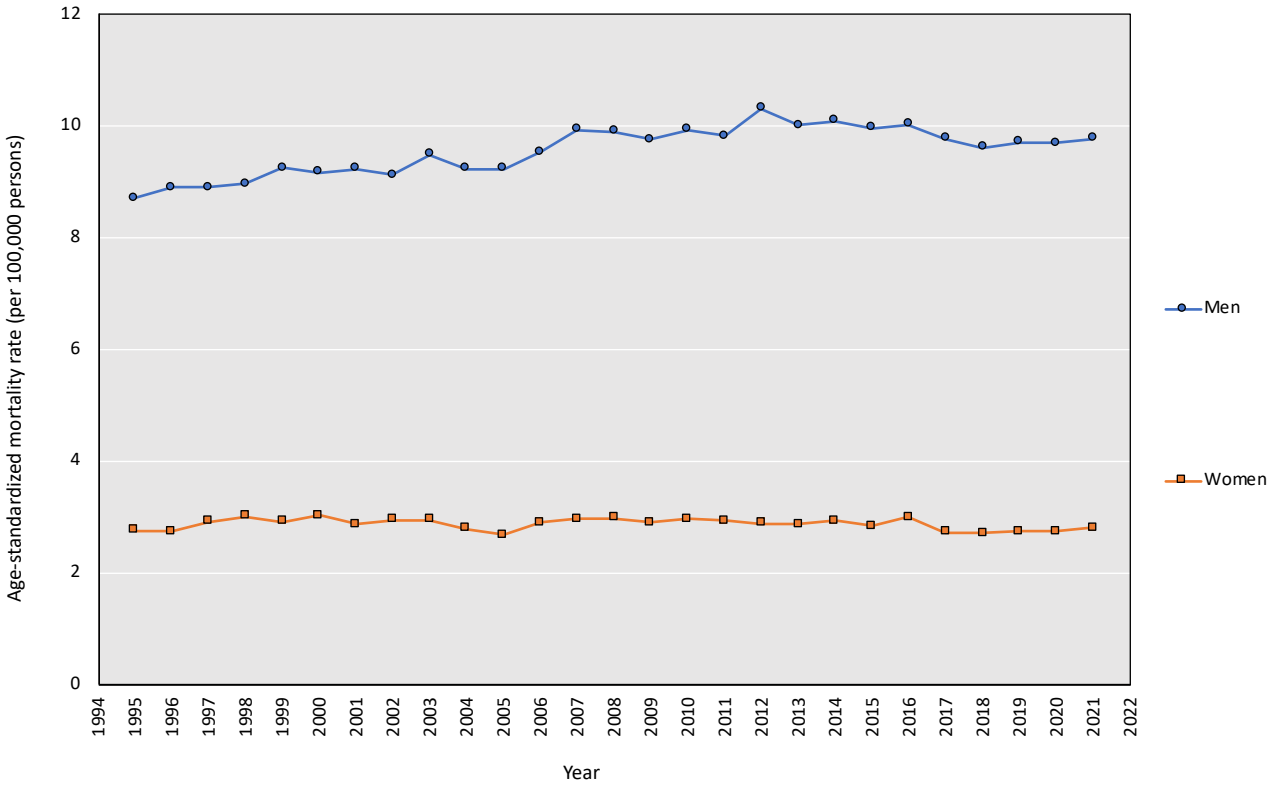


(J) COVID-19 (U07)

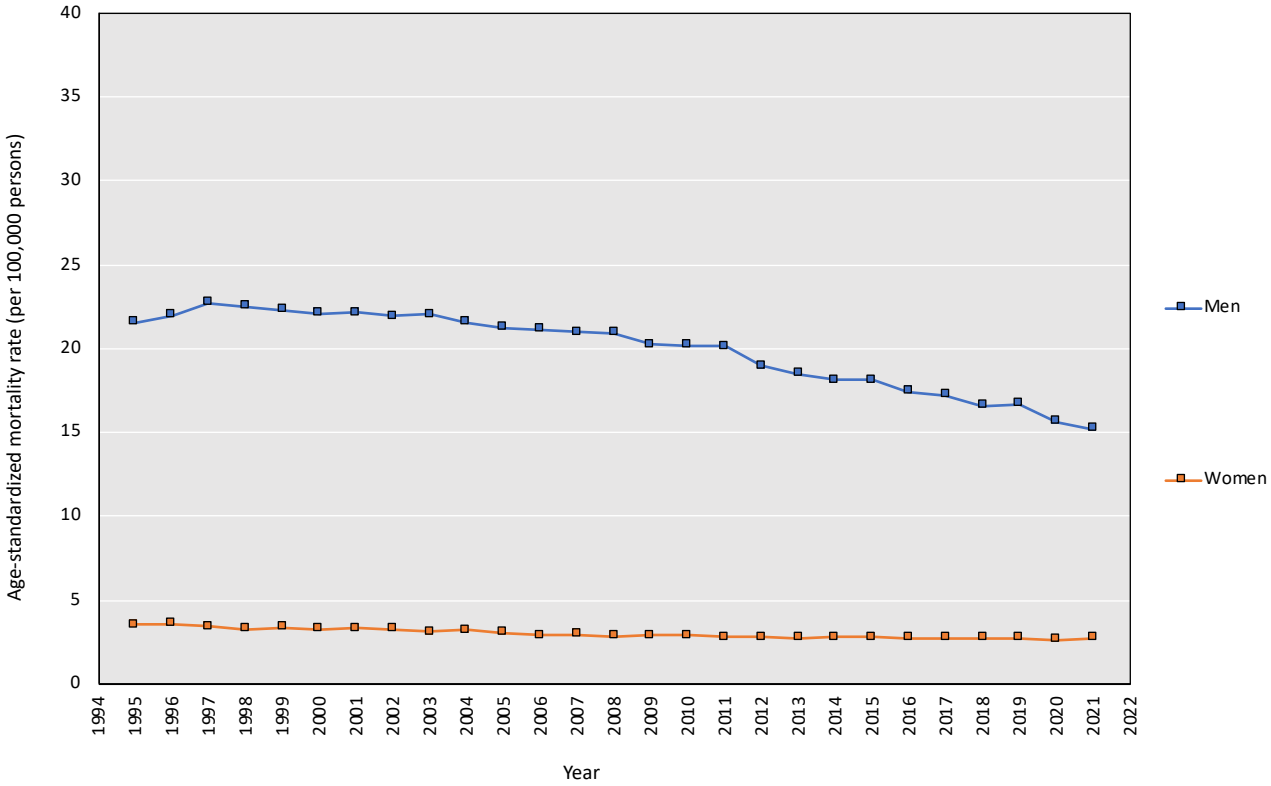


Appendix Figure 2. Trends in cause-specific age-standardized mortality rates by cancer site between 1995 and 2021

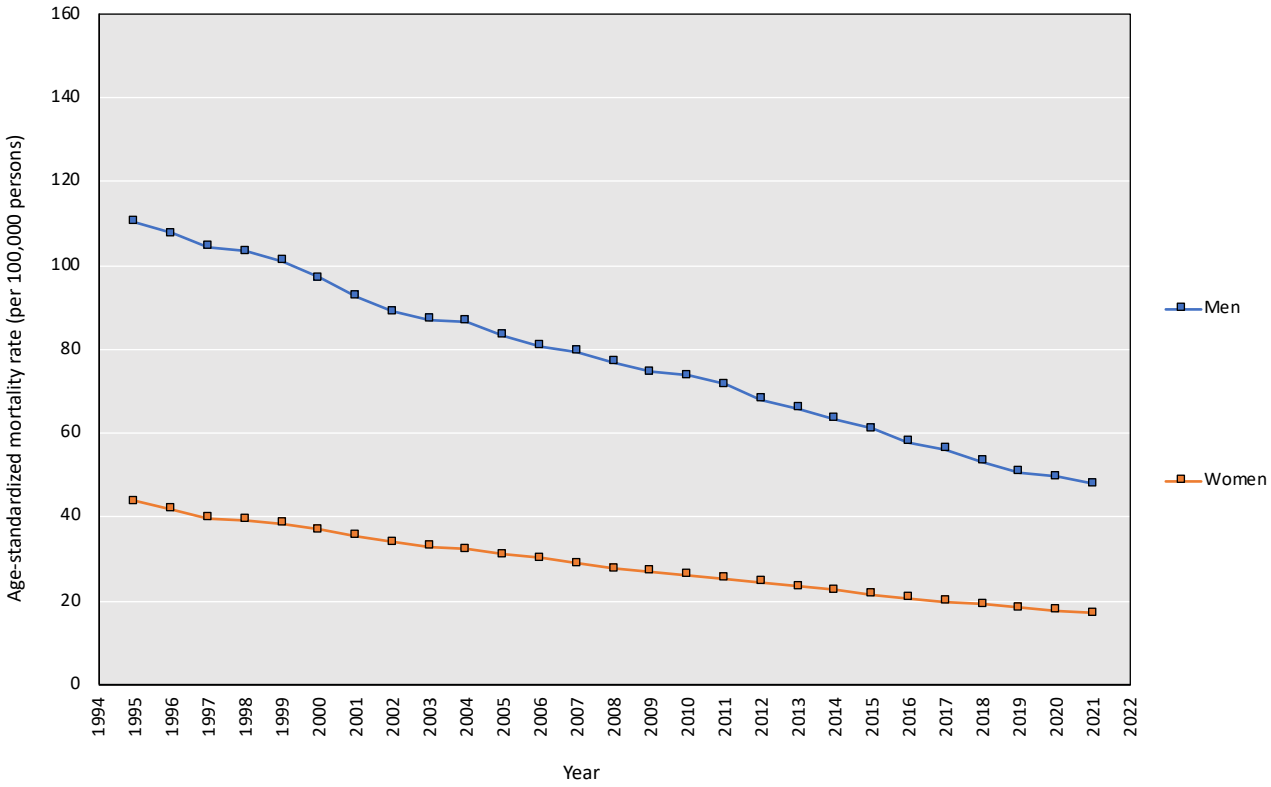
(A) Oral cavity and pharynx (C00-14)



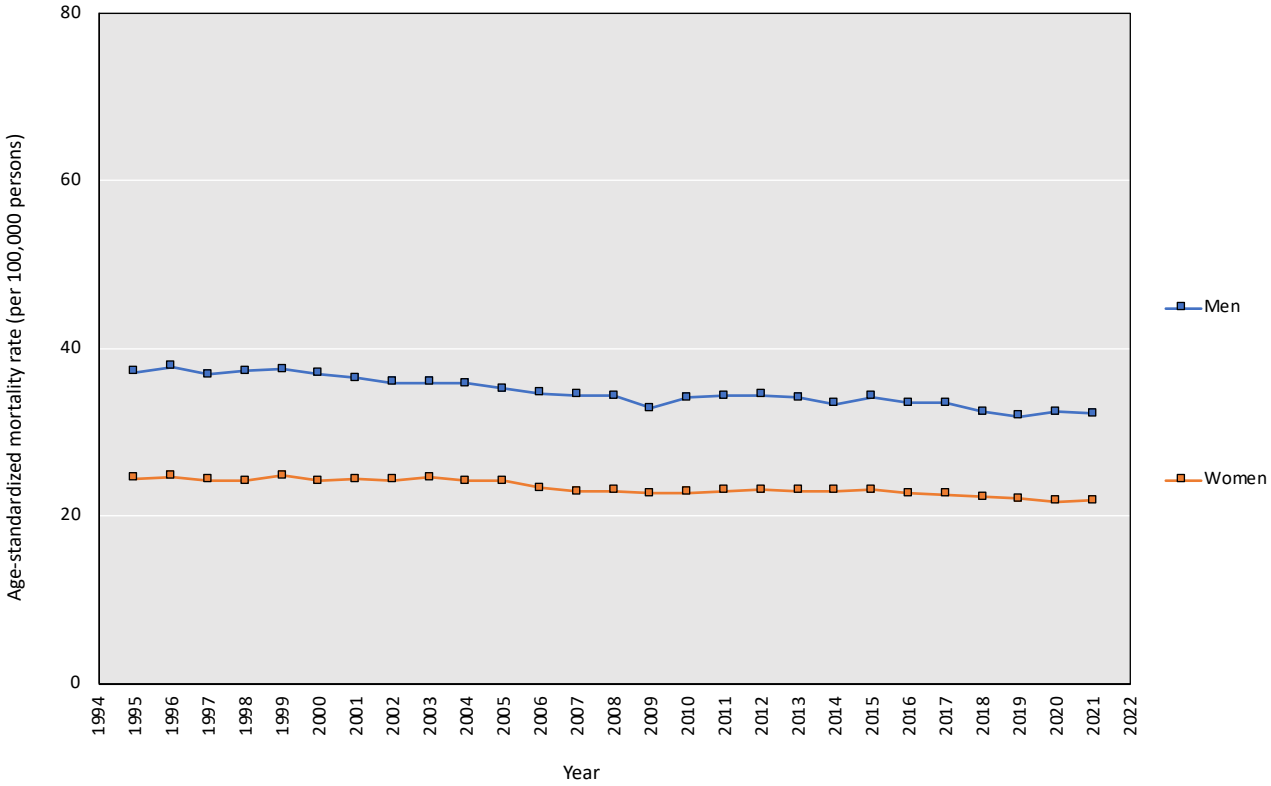
(B) Esophagus (C15)



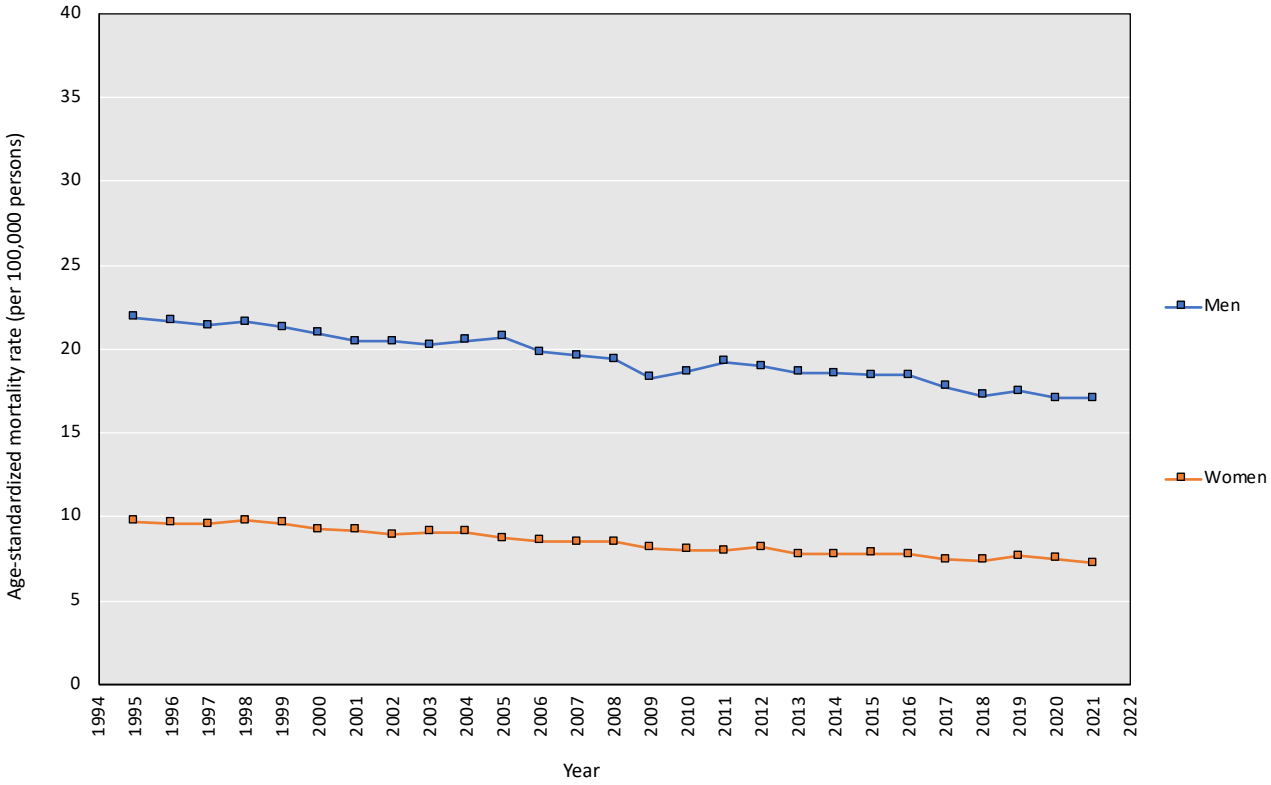
(C) Stomach (C16)



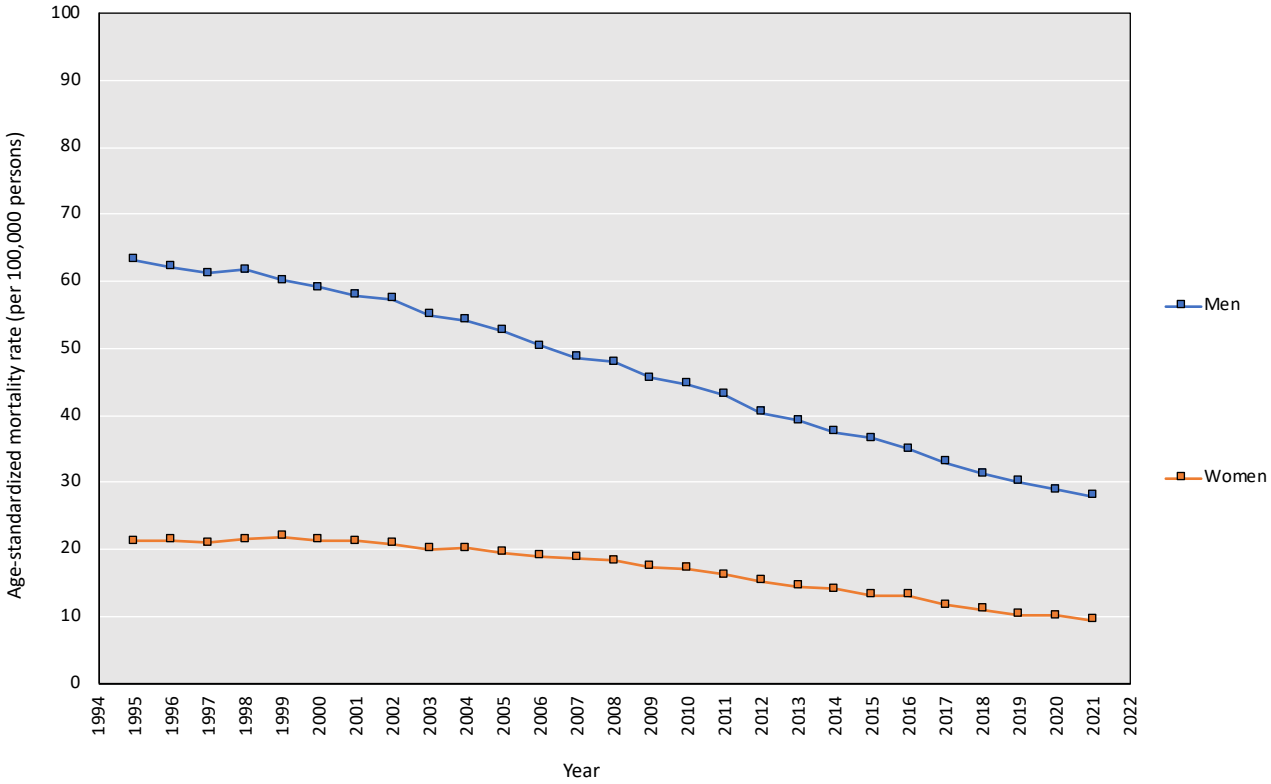
(D) Colon (C18)



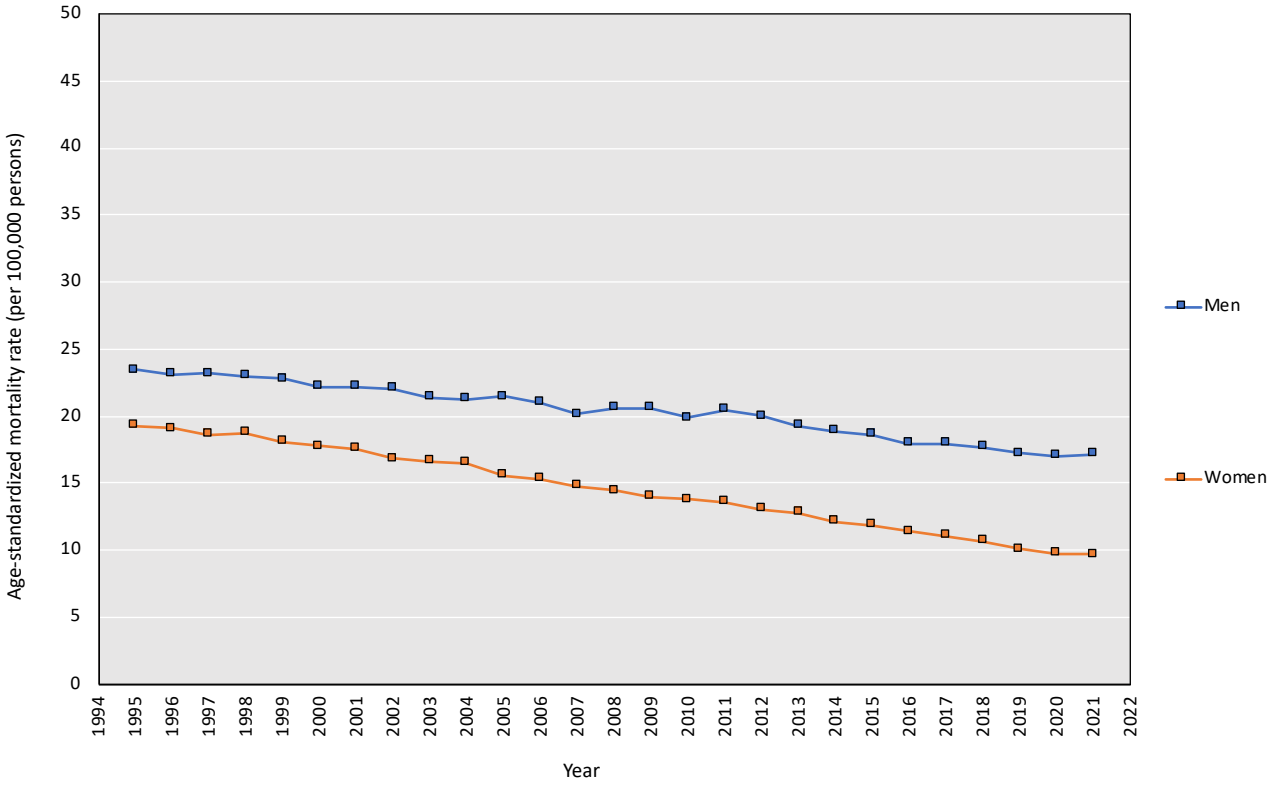
(E) Rectum (C19-20)



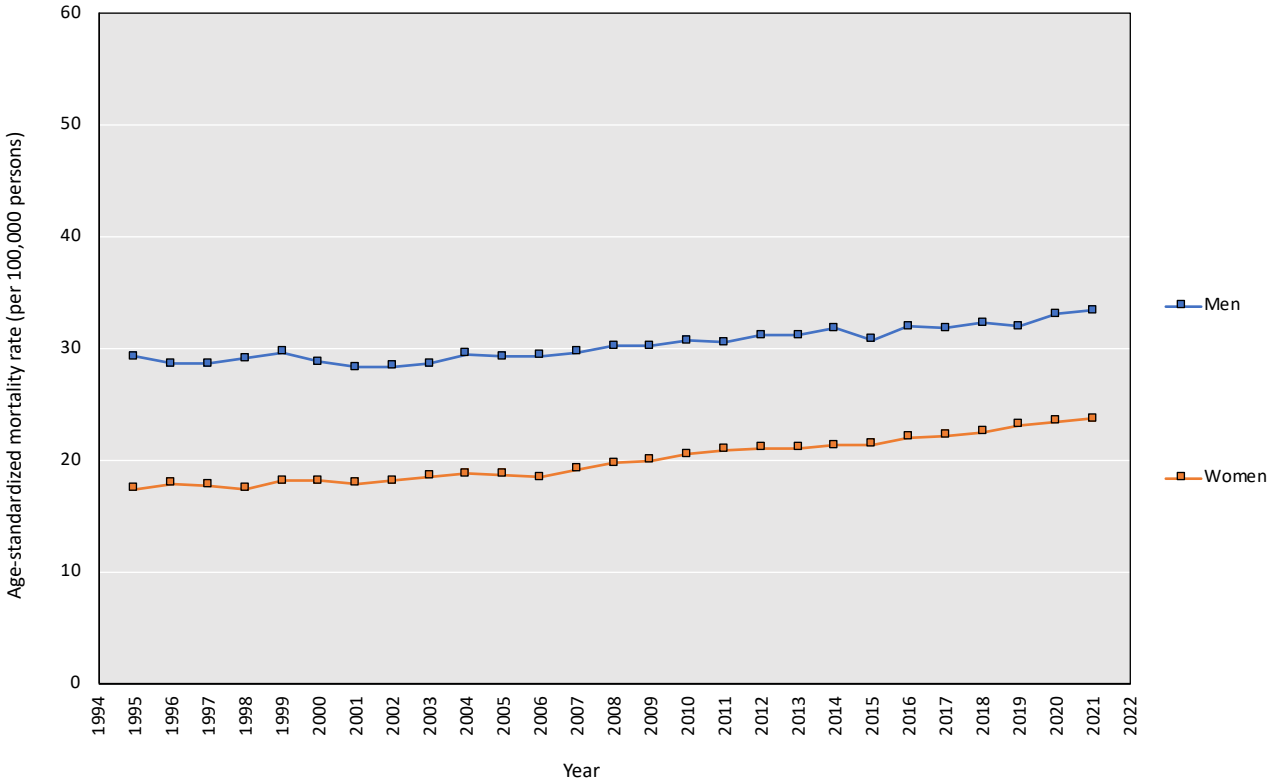
(F) Liver (C22)



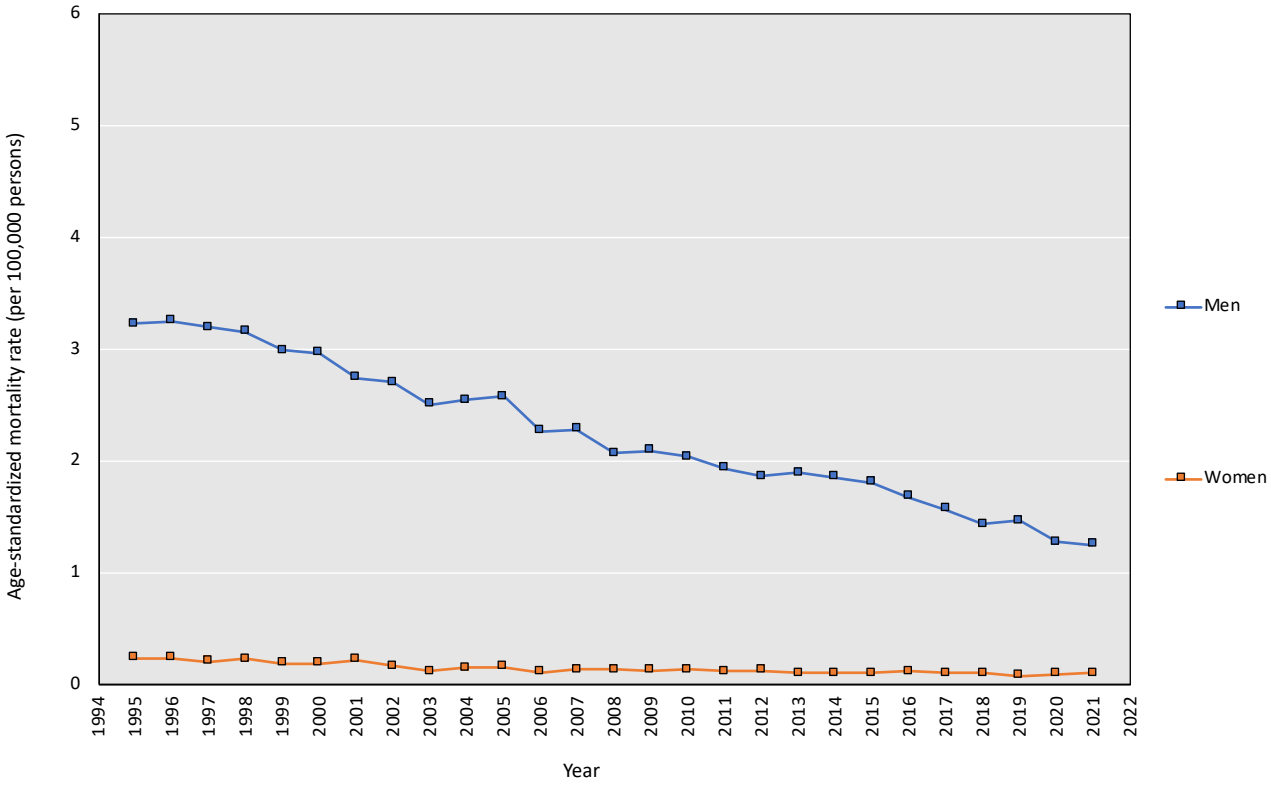
(G) Gallbladder and bile ducts (C23-24)



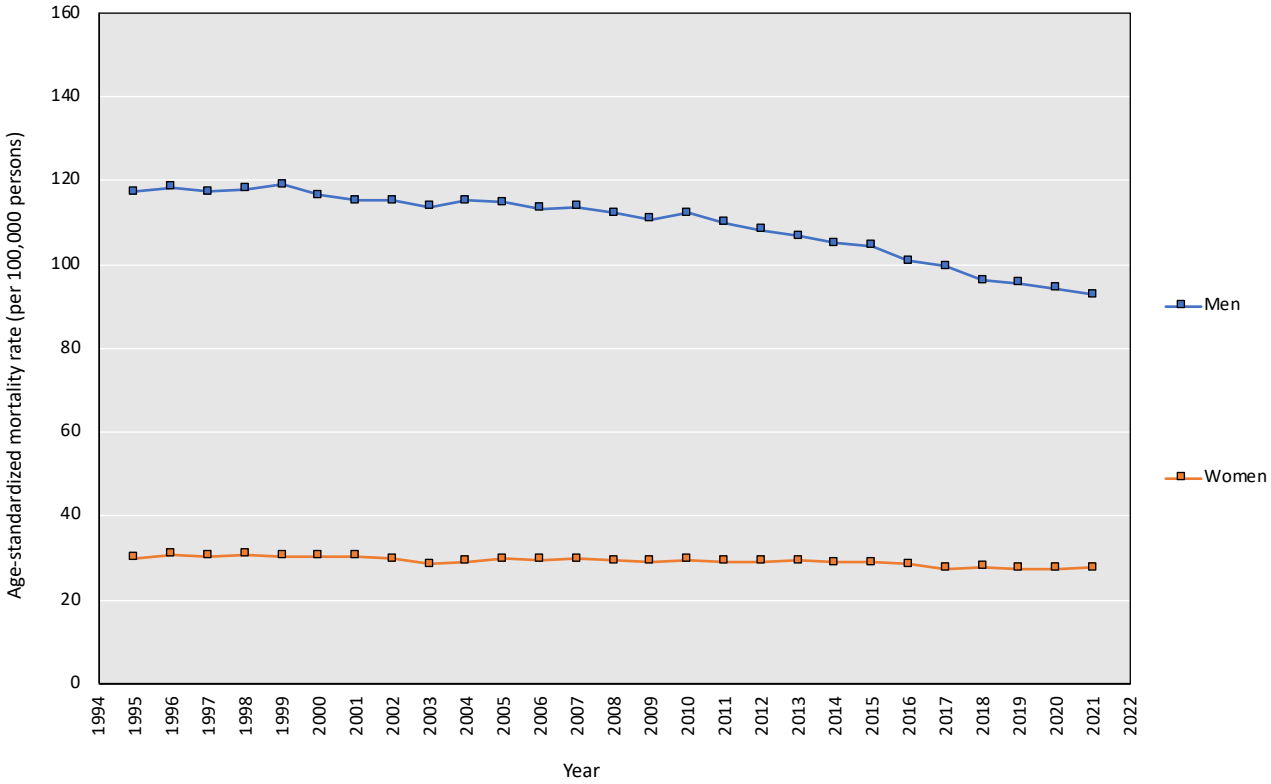
(H) Pancreas (C25)



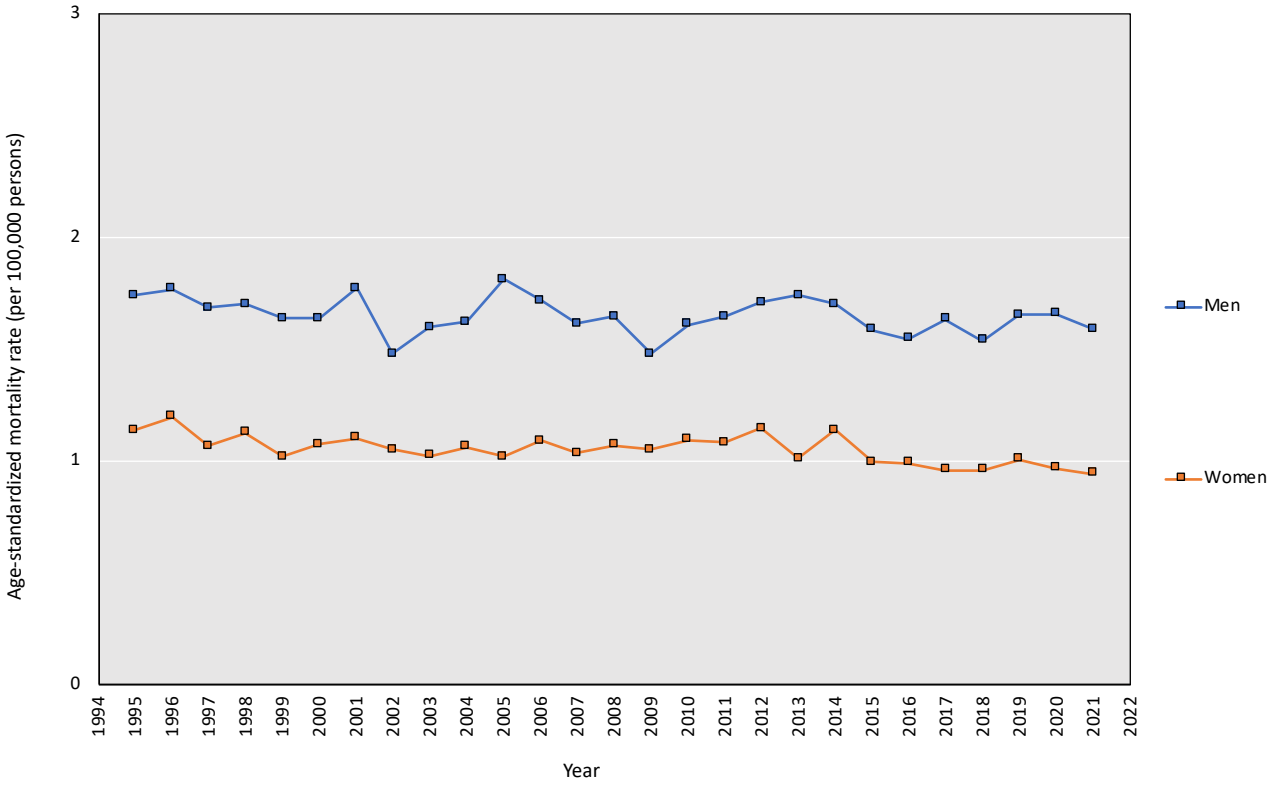
(I) Larynx (C32)



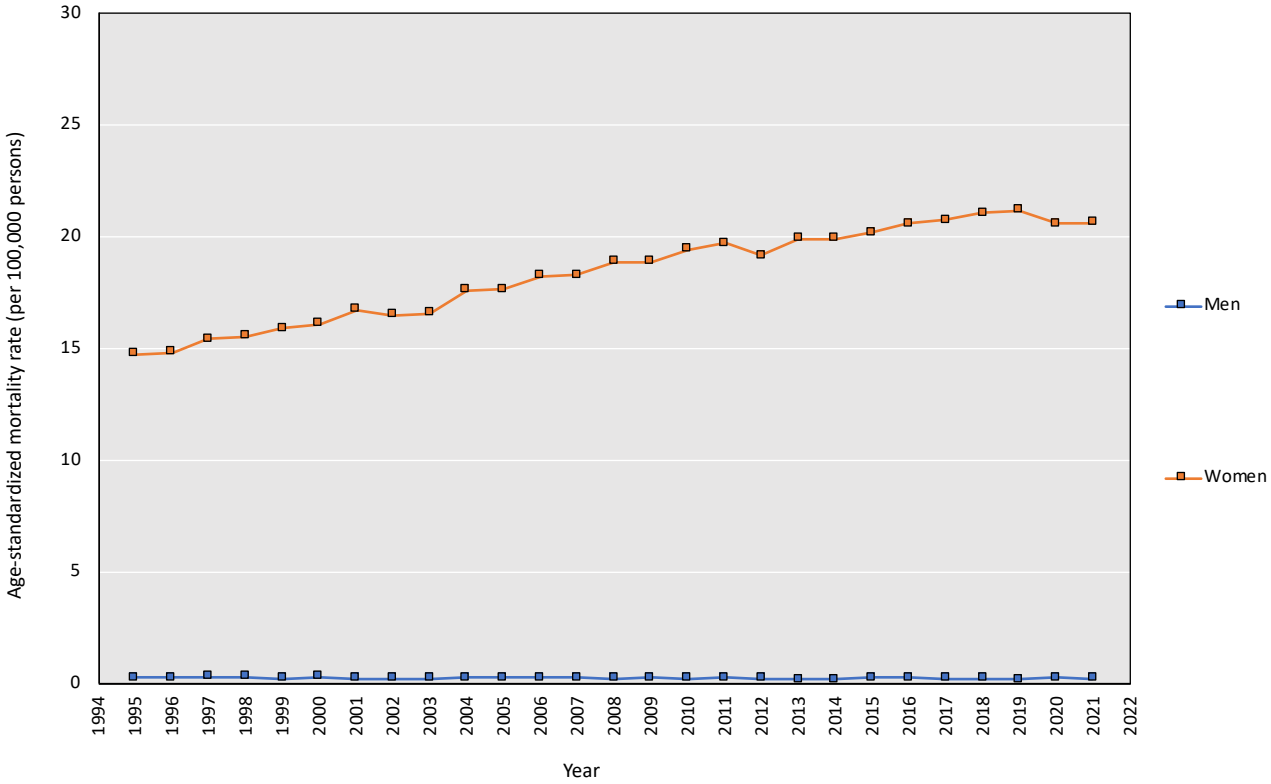
(J) Lung, trachea (C33-34)



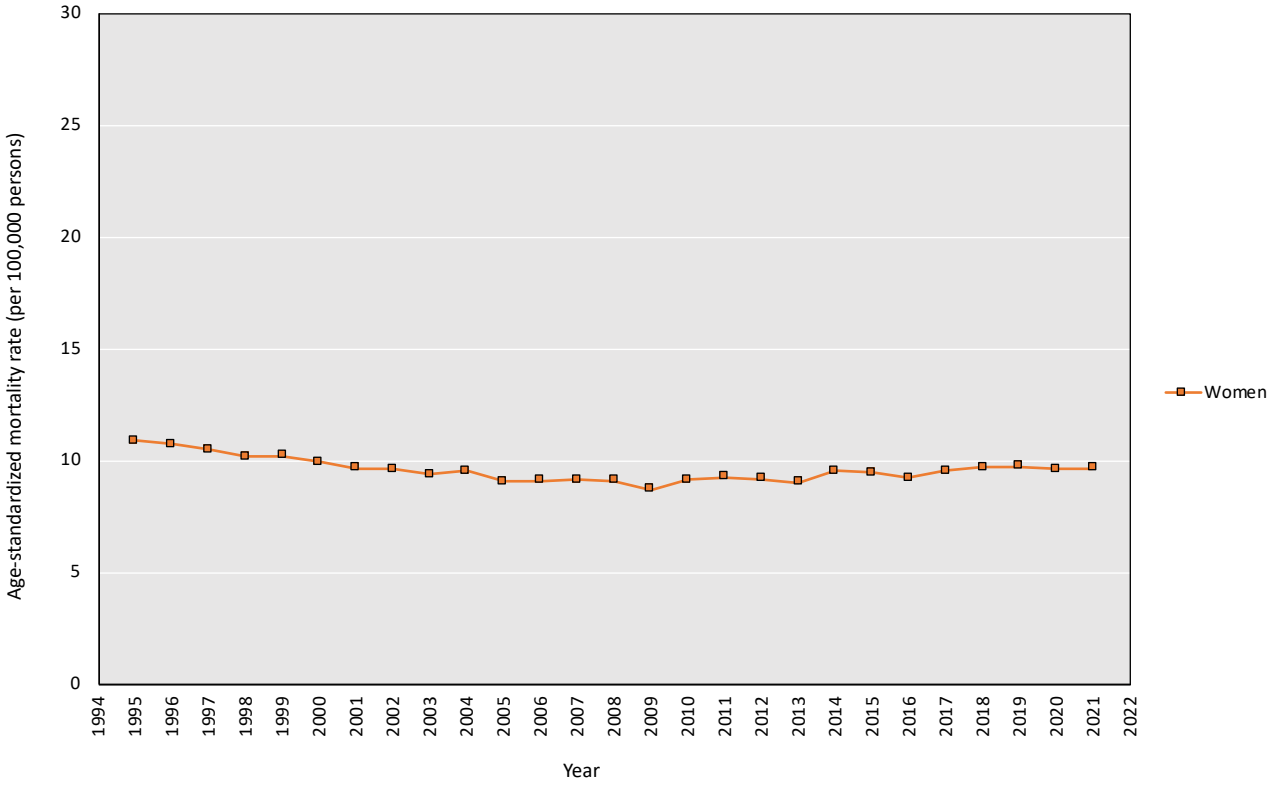
(K) Skin (C43-44)



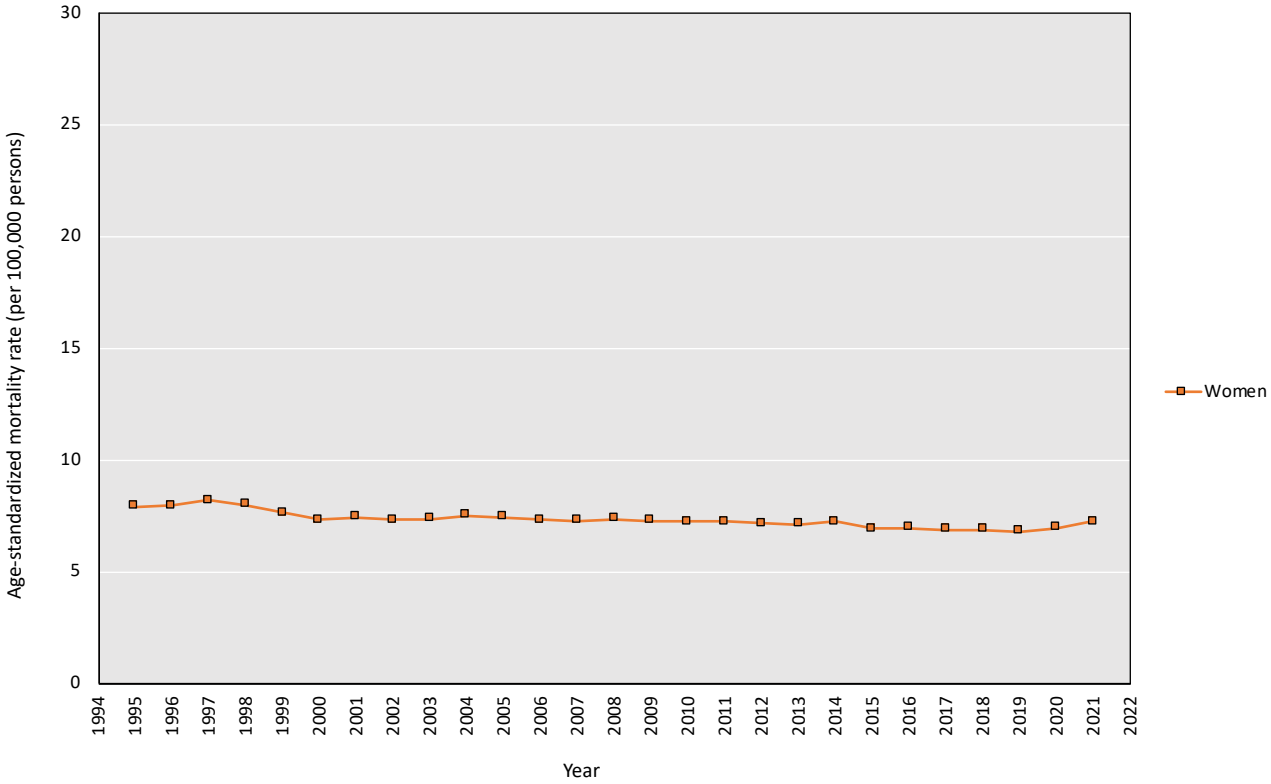
(L) Breast (C50)



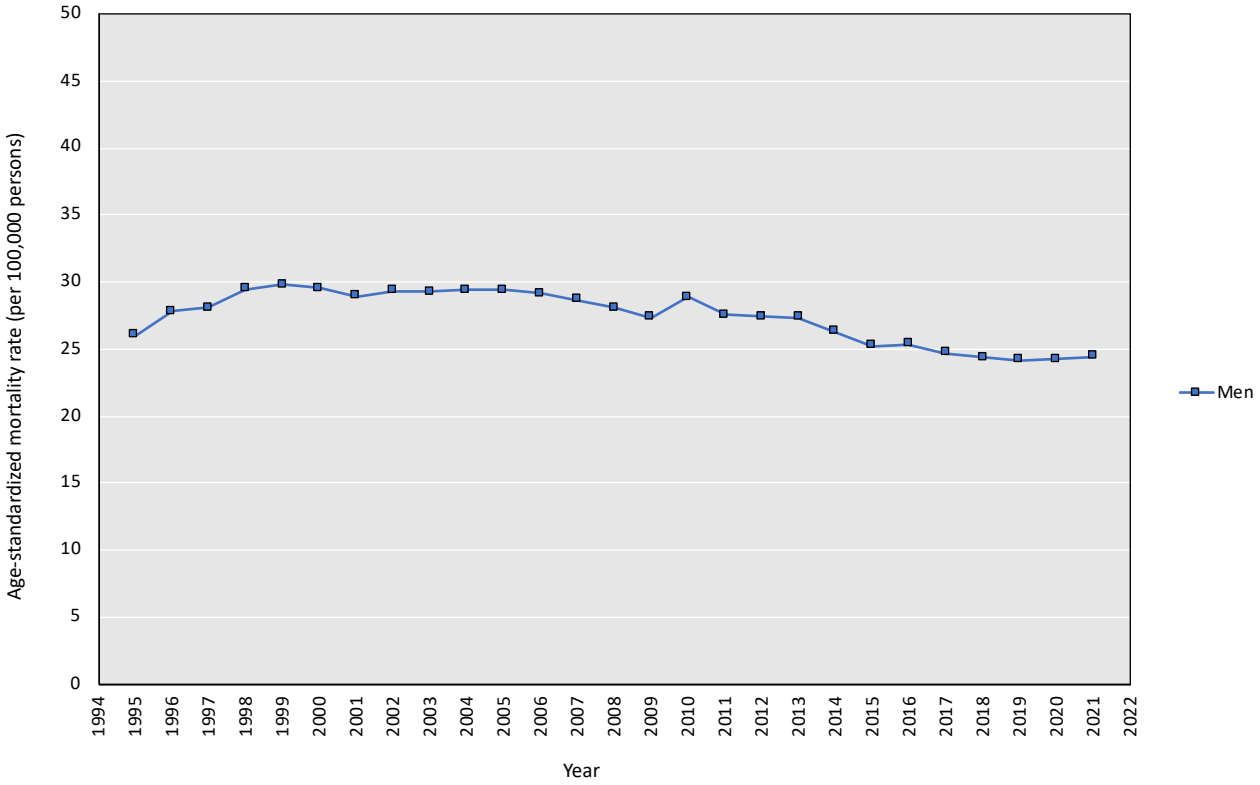
(M) Uterus (C53-55)



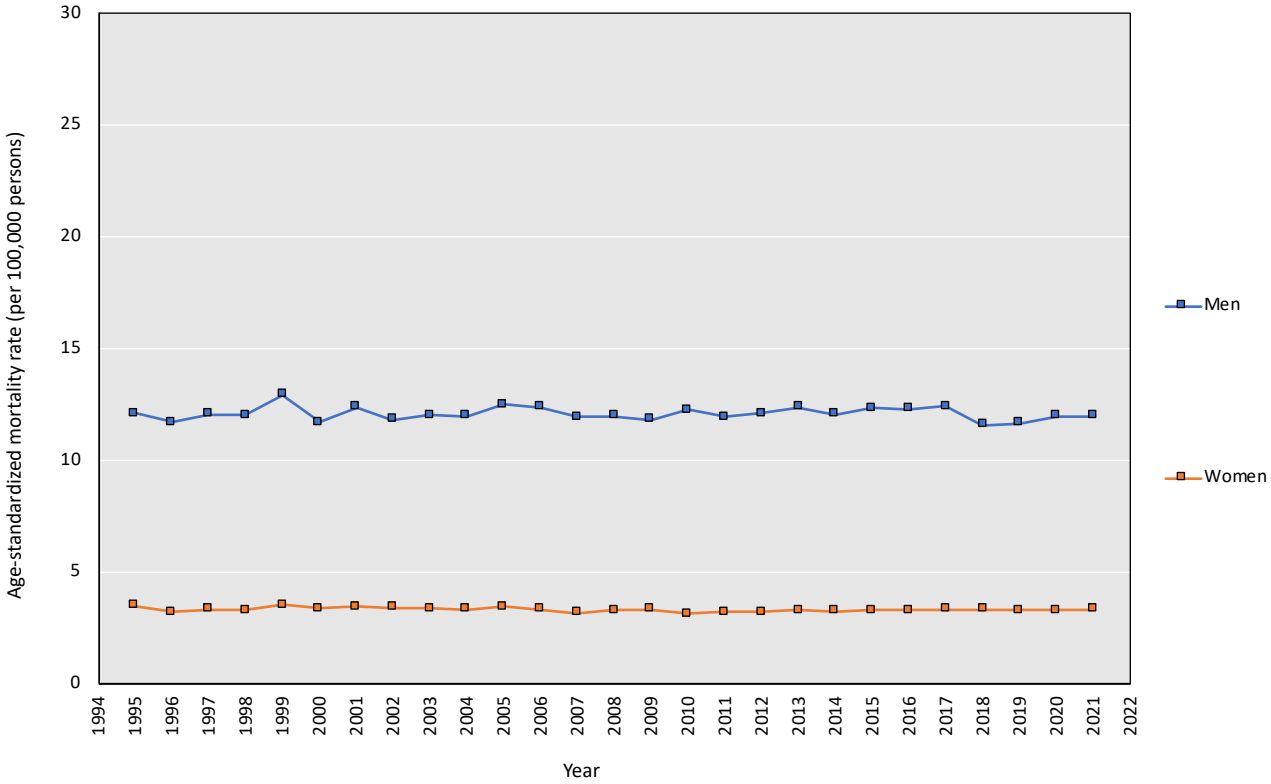
(N) Ovary (C56)



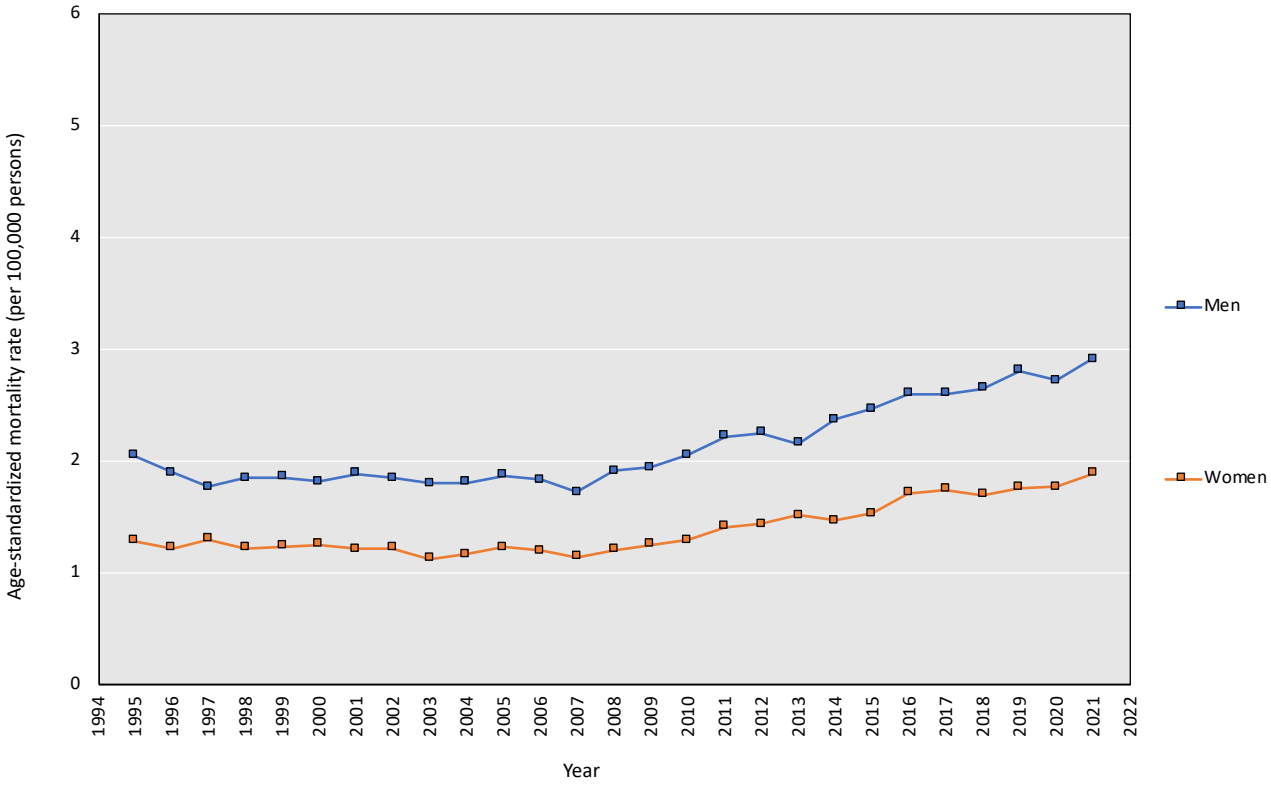
(O) Prostate (C61)



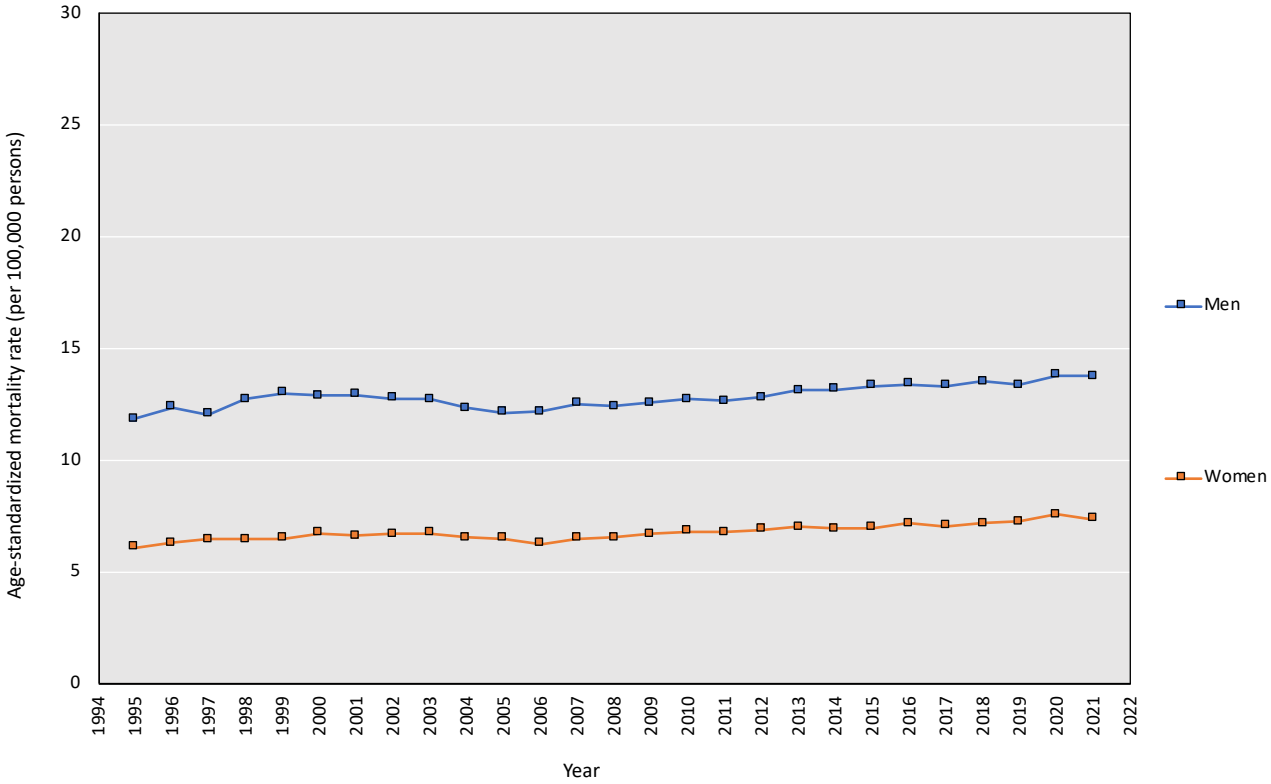
(P) Bladder (C67)

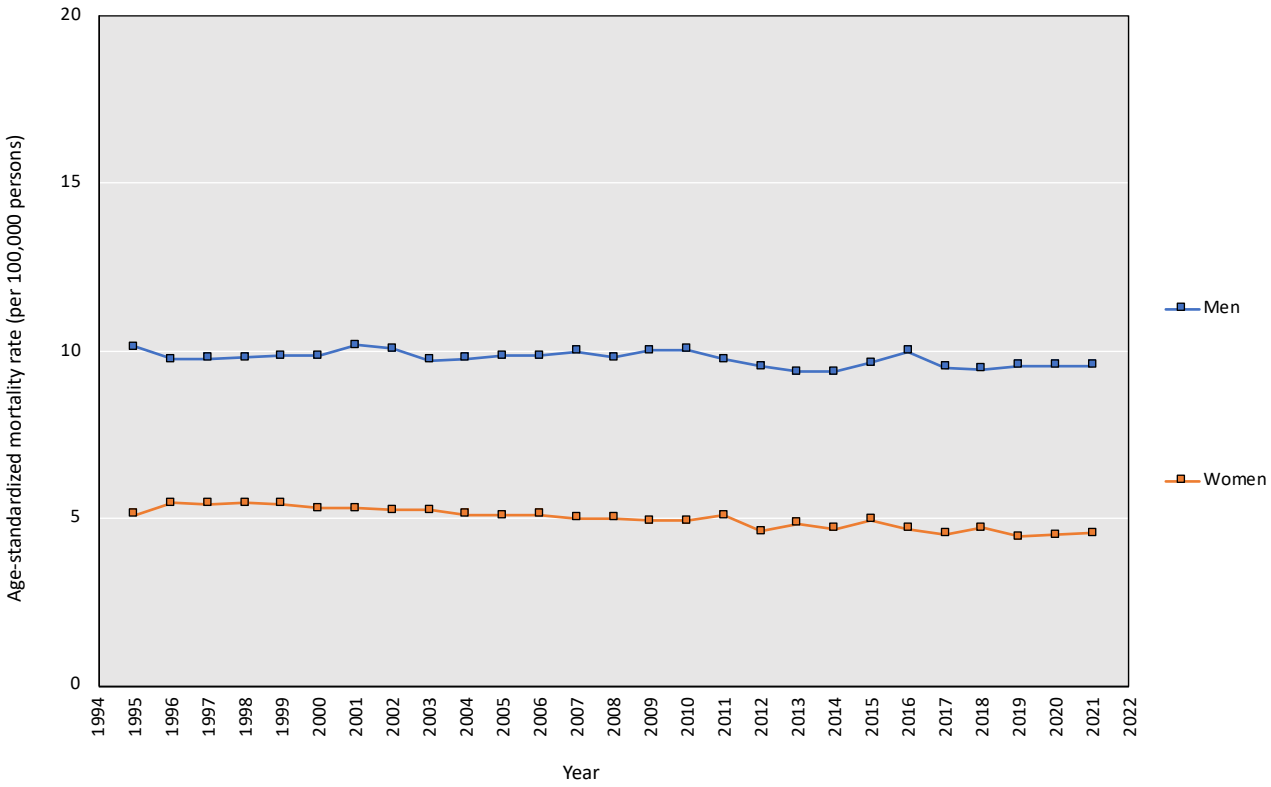


(Q) Brain, nervous system (C70-72)



(R) Malignant lymphoma (C81-85, C96)





Appendix Figure 3. Trends in cancer age-standardized mortality rates by cancer site between 1995 and 2021

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title (line 1-2), abstract (line 38-44)
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			Introduction (line 109-121)
Objectives	3	State specific objectives, including any prespecified hypotheses			Introduction (line 122-128)
Methods					
Study Design	4	Present key elements of study design early in the paper			Method (line 131-139)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			Method (line 131-139)

Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	Method (line 131-139)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.		RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Method (line 140-149)
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			Method (line 131-139)

Bias	9	Describe any efforts to address potential sources of bias			None.
Study size	10	Explain how the study size was arrived at			None.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why			Method (line 140-149)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses			Method (line 140-149)
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	Data availability (line 261-263)

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	None.
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Results (line 158-163)
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			Results (line 158-163)
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure			Results (line 164-178)

		category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			Results (line 164-187)
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses			None.
Discussion					
Key results	18	Summarise key results with reference to study objectives			Discussion (line 190-198)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Discussion (line 244-248)
Interpretation	20	Give a cautious overall interpretation of results considering objectives,			Discussion (line 199-243)

		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results			None.
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			Funding (line 271-273)
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	None.

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.