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Multinational trends in sepsis mortality between 1985 and 2019: a temporal analysis of the WHO Mortality Database

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ABSTRACT

Objectives Understanding the burden of disease of sepsis is essential for monitoring the effectiveness of international strategies to improve sepsis care. Our objective was to describe the multinational trend of sepsis-related mortality for the period 1985–2019 from the WHO Mortality Database.

Design Retrospective analysis of the WHO Mortality Database.

Setting We included data from all countries defined by the WHO as having 'high usability data' and at least 10 years of total available data.

Participants From the WHO list of 50 countries with high usability data, 14 (28%) were excluded due to excessive missingness. We included and analysed data separately for male and female.

Primary and secondary outcome measures We analysed age-standardised mortality rates (ASMR) (weighted average of the age-specific mortality rates per 100 000 people, where the weights are the proportions of people in the corresponding age groups of the WHO standard population).

Results We included 1104 country-years worth of data from 36 countries with high usability data, accounting for around 15% of the world's population. The median ASMR for men decreased from 37.8 deaths/100 000 (IQR 28.4–46.7) in 1985–1987 to 25.8 deaths/100 000 (IQR 19.2–37) in 2017–2019, an approximately 12% absolute (31.8% relative) decrease. For women, the overall ASMR decreased from 22.9 deaths/100 000 (IQR 17.7–32.2) to 16.2 deaths/100 000 (IQR 12.6–21.6), an approximately 6.7% absolute decrease (29.3% relative decrease). The analysis of country-level data revealed wide variations in estimates and trends.

Conclusions We observed a decrease in reported sepsis-related mortality across the majority of analysed nations between 1985 and 2019. However, significant variability remains between gender and health systems. System-level and population-level factors may contribute to these differences, and additional investigations are necessary to further explain these trends.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We describe sepsis-related age-standardised mortality rates (ASMR) for the period 1985–2019 and 36 countries, using the WHO Mortality Database, and include most of Europe, Israel, Australia, New Zealand, South Korea, Japan, Canada and the USA.
⇒ We used joinpoint and locally weighted smoothing regression analysis to describe trends in ASMR.
⇒ Mid-way through our analysis (in the year 2000), our data coverage represented about 15.7% of the world's population (971 million out of 6.2 billion individuals).
⇒ To limit the impact of changing sepsis definitions and International Classification of Diseases (ICD) taxonomies, we have not restricted ICD codes to 'sepsis' or 'septicaemia', but have also included the root causes of sepsis (such as pneumonia, peritonitis, etc) following previously described definitions.
⇒ This approach does not capture well low-income and middle-income countries' (LMICs) data.

BACKGROUND

Sepsis affects between 25 and 50 million people annually worldwide, making it a leading cause of death and one of the most expensive conditions treated in hospitals.[1–4] Challenges in sepsis management include early identification and diagnosis, severity classification and providing optimal targeted therapy.[2] Since the early 1990s, various efforts have been made to improve early identification and standardise the definition of the sepsis syndrome.[5–7]

In 2017, the WHO declared sepsis 'a global health priority' and urged governments to 'monitor incidence and outcomes from sepsis'.[8] Understanding the burden of disease is essential for measuring the effectiveness of international strategies to improve sepsis care. Various publications have reported trends in sepsis incidence and mortality, although ongoing discrepancies in the definition of sepsis resulted in large variability in estimates the definition of sepsis and the methods for data extraction and preprocessing resulted in substantial variability in the reported incidence and outcomes.[3 9] A uniform, consistent method has been called for, which would allow a more accurate evaluation of outcomes and clinical interventions across cohorts.[9]

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Despite wide variation in national-level estimates of sepsis, most authors reported an increasing incidence over the last decades, along with decreasing trends in case mortality.[10–12] Whether sepsis incidence has truly been increasing remains unclear, since different factors may have contributed to the trend, including increased awareness and varying definitions.[3 11] In fact, an analysis by Rudd *et al*, using data from the Global Burden of Disease Study, suggested that the age-standardised sepsis incidence had fallen by 37% between 1990 and 2017.[3] A meta-analysis of 170 sepsis studies (both interventional and observational) conducted between 2009 and 2019 only highlighted a decrease in 30-day septic shock mortality between 2009 and 2011, but not later.[13]

To provide comprehensive documentation of patterns in sepsis mortality trends, we used the WHO Mortality data from 36 countries with high usability data between 1985 and 2019 and reported country-level and multinational estimated sepsis-related deaths for both genders. We also analysed trends over time and performed sensitivity analyses using various sepsis definitions.

METHODS

Study design and data source

We conducted an observational analysis of sepsis-related mortality using data deposited in the WHO Mortality Database (https://www.who.int/data/data-collection-tools/who-mortality-database; date of access: June 2022). This database records country-level data for deaths by age, sex and cause of death from 1955 onward, as reported annually by WHO member states through their local death registration systems. Of note, deaths are not attached to a particular clinical encounter or hospital admission, so mortality cannot be defined at a given time point (eg, 'mortality at 90 days'). Primary causes of death are recorded using the International Classification of Diseases (ICD) classifications, which researchers have used in the past to abstract sepsis definitions. The WHO performs routine evaluation and verification of data deposited into the database and provides an assessment of overall data quality.[14] We obtained sepsis-related, sex-specific mortality data from countries with 'high usability data', which reflects the overall quality of death registration data (see full list of countries in online supplemental material). We included countries with at least 10 years of total available data and excluded countries that did not satisfy these criteria.

Data handling and statistical analyses

All analyses were done in SAS (V.9.4m5). Country-specific and sex-specific crude mortality data were extracted as raw SAS datafiles. For each country and year, we grouped data within the age groups provided by the World Standard Population, stratified by sex. Then, we calculated age-standardised mortality rates (ASMR) per 100 000 population using World Standard Population.[15] We performed two different analyses.

First, for the assessment of overall trends in sepsis-related mortality, we performed locally weighted scatterplot smoother (LOESS) regression analysis of the average ASMR for all available countries. LOESS is a non-parametric technique which uses local weighted regression to fit a smooth curve through points in a scatter plot and can be useful to investigate trends for data without a known parametric form and robust fitting is necessary.[16]

Next, we performed a joinpoint regression analysis for each country individually, which estimates changes in linear slope for mortality trends over time.[17] Briefly, it assesses the overall trends in mortality and identifies the best-fitting points where mortality rates change significantly (significant increase or significant decrease). The analysis initially starts with no joinpoints and tests for significant changes in the model with sequential addition of points where there is significant change in the slope of the line. Each joinpoint in the final model indicates a statistically significant change in mortality trend and Joinpoint software computes the annual percentage change for each piecewise trend by means of a generalised linear model, assuming Poisson distribution. Joinpoint regression was performed using SEER*Stat software V.8.3.6.0 provided by the US National Cancer Institute Surveillance Research Programme, and we have performed similar analyses previously using this data source and software.[18–20] For the purpose of joinpoint analysis, we imputed missing data in a last observation carried forward manner.

Sepsis definition

Sepsis is a generic clinical syndrome whose definitions have changed over time.[5–7] Since the different sepsis definitions cannot be directly translated to ICD codes, various abstractions have been proposed by different authors including Martin, Angus and Flaatten, matching the current sepsis definition and versions 9 and 10 of the ICD taxonomy.[10 21 22] While the ICD definitions required both infection criteria and organ dysfunction criteria, we only used the 'infection criteria' and assumed that any patient whose death certificate included a listed infection also had some organ dysfunction contributing to their death.

We chose the Angus definition for our main results over Martin and Flaatten definitions because it is more exhaustive and more widely used. Indeed, Angus's abstraction relied on 105 or 150 infection codes, for the ICD-9 and ICD-10 versions, respectively (see online supplemental material). In comparison, Martin's used only six or nine codes (for ICD-9 and ICD-10, respectively), whereas Flaatten used seven codes (only the ICD-10 version is available), so we did not implement those definitions (see online supplemental material).

Patient and public involvement

Our research group includes a patient advisory group which directly informs our research priorities. The members of the panel confirmed being in agreement with the 2017 WHO Resolution WHA70.7 on

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'Improving the prevention, diagnosis and clinical management of sepsis', which highlights the importance of public awareness of sepsis and estimating the global burden of sepsis.[8]

RESULTS

There were a total of 36 countries with sufficient data available during the period from 1985 to 2019 accounting for a total of 1104 country-years and 2208 potential data points from both genders for analysis, covering most of Europe, Israel, Australia, New Zealand, Japan, Canada and the USA. From the WHO list of 50 countries with high usability data, 14 (28%) were excluded due to excessive missingness. Near complete data were available for each country studied, with a total of 240 (9.8%) missing data elements. Mid-way through our analysis (in the year 2000), our data coverage represented about 15.7% of the world's population (971 million out of 6.2 billion individuals).

Multinational trends in sepsis mortality

Figure 1 presents the trend in sepsis mortality in all the included countries over the period 1985–2019, according to the Angus definition, with LOESS regression. In all countries, the ASMR was greater in men than women. The overall ASMR for men decreased from 37.8 deaths/100 000 (IQR 28.4–46.7) in 1985–1987 to 25.8 deaths/100 000 (IQR 19.2–37) in 2017–2019, an approximately 12% absolute (31.8% relative) decrease. For women, the overall ASMR decreased from 22.9 deaths/100 000 (IQR 17.7–32.2) to 16.2 deaths/100 000 (IQR 12.6–21.6), an approximately 6.7% absolute decrease (29.3% relative decrease) during the observation period. We measured a weak inverse correlation (R^2 0.25) between the ASMR during the early study period (1985–1987) and the observed relative change over the whole study period: countries with a higher early ASMR tend to be associated with a higher reduction in ASMR (see online supplemental material).

Individual country trends in sepsis mortality

Table 1 shows ASMR per 100 000 population in 1985 and 2019 (or closest year available) for men and women, and the change between the start and the end. The top three countries with the lowest estimated ASMR in the end period were Austria, Finland and Slovenia for men, and Estonia, Finland and Slovenia for women. The highest mortality rates were demonstrated in Moldova, Poland and Romania, and Denmark, Romania and the UK for males and females, respectively. The majority of the 36 countries demonstrated a decrease in sepsis-related mortality over the study period. For men, the countries with the greatest percentage change over the observation period include Finland (−89%), Slovenia (−77%) and New Zealand (−71%), while the largest increases in mortality were observed in Malta (+31%), Denmark (+19%) and Greece (+16%). For women, the greatest percentage decreases were observed in Finland (−89%), Bulgaria (−75%) and Iceland (−74%), and the largest increases were observed in Greece (+45%), Malta (+34%) and Luxembourg (+27%).

Figure 2 shows trends in ASMR of sepsis according to the Angus definition, with joinpoint regression in all 36 included countries, for men and women. Many countries showed a decreasing trend (eg, Bulgaria, Hungary, Sweden, the USA), while some others had flat estimates (eg, Australia, Germany, Switzerland) or polyphasic trends (eg, Ireland, the Netherlands, the UK). In many eastern European countries (Estonia, Latvia, Lithuania, Moldova, Poland, Romania) as well as in Japan, the gender gap was striking with male mortality far exceeding that of female. Detailed numerical results of the joinpoint analysis for all individual countries is provided in online supplemental material.

DISCUSSION

In this work, we analysed the trends of sepsis-related mortality over 3 decades and 36 countries, representing one of the largest studies to date. Overall, we observed a decrease in reported sepsis-related mortality across the majority of analysed nations between 1985 and 2019, for both genders. However, there remains significant variability between health systems and genders with respect to trends in sepsis-related mortality.

A decrease in sepsis-related ASMR may reflect several factors, since ASMR combines both the incidence of a disease (which itself depends on disease definition and coding practices) as well as case fatality, which confounds the interpretation of the trends. Only the ASMR was available to us in the dataset we used, with no direct way of disentangling the relative contribution of incidence and case fatality. Many authors have reported an increase in the incidence and mortality rates of sepsis and septic shock in recent years, along with a significant decreasing trend in case fatality rates over time.[10–12]

In this situation, the ASMR in a given country can show different profiles. It can remain flat, if the increase in incidence compensates the decrease in case fatality. If the incidence increases more than the case fatality decreases, the ASMR will increase. Finally, the ASMR can decrease if the drop in case fatality exceeds the change in reported incidence. For example, a 50% decrease in case fatality in New Zealand between 2000 and 2012 was reported,[23] while our analysis of the ASMR shows close to a flat line, which implies that the crude reported incidence may have doubled.

We confirmed that ASMR was consistently higher in males than females, which is mostly driven by a higher incidence of sepsis in men. Whether gender impacts sepsis survival is a matter of debate, with conflicting literature pointing either towards an increase or a reduction in mortality in women.[24 25]

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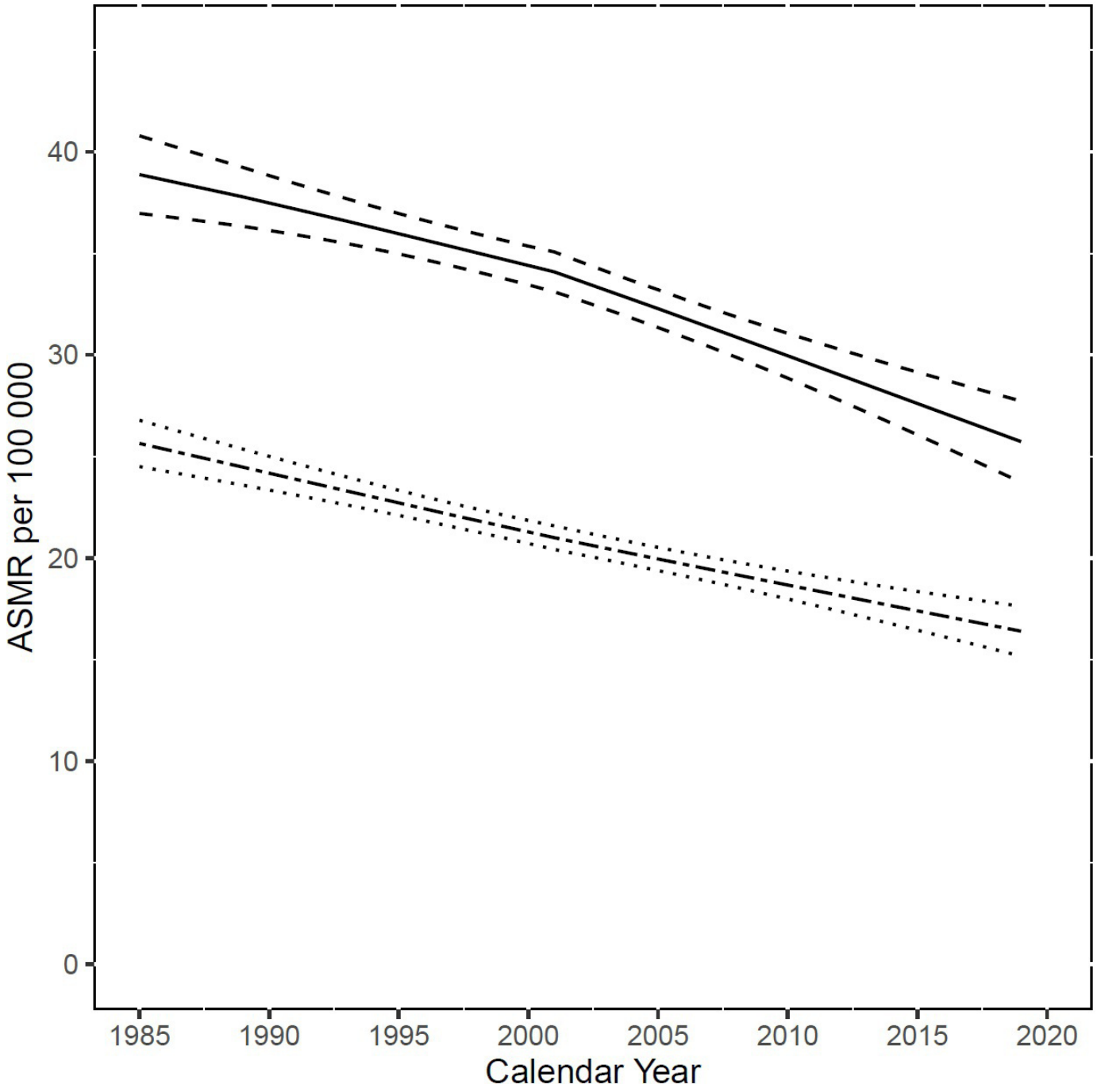


Figure 1 Multinational trend in age-standardised mortality rates (ASMR) of sepsis (Angus definition) per 100 000 population among the 36 included countries (weighted median±IQR), with LOESS regression. Full line represents male, dash-dotted line female. A decreasing trend in ASMR is observed for both genders, with ASMR decreasing faster in male.

Sepsis awareness has likely increased over the period of years, with efforts such as the Surviving Sepsis Campaign, Global Sepsis Alliance and World Sepsis Day.[26–28] As a consequence, sepsis may be diagnosed and classified more frequently, which could have contributed to both the decrease in case fatality (by including more patients with lower levels of severity) and the increase in incidence. In 2020, Rudd *et al* reported the estimated global incidence and mortality of sepsis in 195 countries, using data from the Global Burden of Disease Study.[3] Interestingly, they estimated a 37% decrease in age-standardised sepsis incidence over the 1990–2017 period, along with a 52.8% decrease in age-standardised mortality. Besides differences in data sources (Global Burden of Disease vs WHO Mortality Database), Rudd's study used a regression modelling approach to make global estimates, while this study does not use modelling and assumes the ASMR obtained from the input data is globally representative.[29] In this manuscript, the overall ASMR was significantly lower than in Rudd's study, with rates of 21 per 100 000 in 2017/2019 compared with 148.1 per 100 000. The higher burden of sepsis in low-income and middle-income

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Table 1 Average age-standardised mortality rates in 1985–1987 (start), in 2017–2019 (end) and absolute and relative change, for male and female

		Male			Female		
Country	**Data period**	**Start**	**End**	**Change (%)**	**Start**	**End**	**Change (%)**
Australia	1985–2018	19.72	17.24	−2.49 (−12.62)	16.1	14.46	−1.65 (−10.22)
Austria	1985–2019	30.33	13.8	−16.54 (−54.52)	20.21	9.95	−10.26 (−50.78)
Belgium	1985–2016	29.17	29.56	0.39 (1.34)	17.18	21.29	4.11 (23.91)
Bulgaria	1985–2018	71.37	25.01	−46.36 (−64.96)	49.32	12.22	−37.1 (−75.22)
Canada	1985–2005	30.84	21.53	−9.31 (−30.19)	19.26	17.96	−1.3 (−6.76)
Croatia	1985–2017	48.16	34.56	−13.6 (−28.24)	27.25	23.72	−3.53 (−12.95)
Czech Republic	1986–2019	46.53	37.15	−9.38 (−20.15)	36.16	24.42	−11.74 (−32.46)
Denmark	1994–2018	29.79	35.58	5.79 (19.43)	21.02	26.73	5.7 (27.13)
Estonia	1985–2016	36.16	23.42	−12.74 (−35.22)	15.83	9.74	−6.09 (−38.47)
Finland	1987–2018	51.07	5.25	−45.82 (−89.72)	31.77	3.54	−28.23 (−88.85)
France	1985–2014	26.5	18.33	−8.17 (−30.83)	15.68	11.31	−4.37 (−27.87)
Germany	1990–2019	28.22	24.2	−4.02 (−14.25)	18.72	16.66	−2.06 (−11.01)
Greece	1985–2018	17.4	20.27	2.87 (16.5)	13.48	19.63	6.15 (45.65)
Hungary	1985–2019	42.59	19.02	−23.57 (−55.35)	28.36	13.25	−15.11 (−53.27)
Iceland	1985–2019	53.36	16.56	−36.81 (−68.97)	54.17	13.85	−40.32 (−74.43)
Ireland	1985–2015	78.44	25.12	−53.32 (−67.98)	56.31	23.26	−33.05 (−58.69)
Israel	1985–2018	36.06	39.37	3.31 (9.19)	30.44	29.33	−1.1 (−3.63)
Italy	1985–2017	20.67	19.95	−0.72 (−3.47)	13.75	14.13	0.37 (2.71)
Japan	1985–2018	58.47	32.61	−25.85 (−44.22)	30.99	15.27	−15.72 (−50.73)
Latvia	1985–2018	35.96	33.59	−2.37 (−6.6)	19.41	14.62	−4.8 (−24.7)
Lithuania	1985–2019	35.34	39.55	4.22 (11.93)	16.65	18.05	1.4 (8.41)
Luxembourg	1985–2018	27.59	17.26	−10.32 (−37.42)	18.33	23.4	5.07 (27.64)
Malta	1985–2017	23.19	30.46	7.27 (31.34)	13.69	18.36	4.67 (34.11)
Moldova	1985–2018	69.48	47.16	−22.31 (−32.12)	39.16	16.07	−23.09 (−58.95)
Netherlands	1985–2018	26.19	22.16	−4.02 (−15.36)	20.63	18.15	−2.47 (−11.99)
New Zealand	1985–2016	55.01	15.83	−39.19 (−71.23)	41.9	16.58	−25.32 (−60.43)
Poland	1985–2018	41.39	44.34	2.94 (7.11)	23.95	22.39	−1.55 (−6.49)
Portugal	1985–2018	43.14	40.68	−2.46 (−5.71)	23.16	24.58	1.42 (6.15)
Romania	1985–2018	73.23	52.74	−20.49 (−27.98)	50.98	25.58	−25.4 (−49.82)
Slovakia	1992–2014	72.35	43.16	−29.19 (−40.35)	44.33	24.5	−19.83 (−44.73)
Slovenia	1985–2019	42.65	9.95	−32.7 (−76.68)	26.04	8.79	−17.24 (−66.23)
Spain	1985–2017	31.33	26.41	−4.92 (−15.71)	19.17	16.92	−2.25 (−11.72)
Sweden	1987–2018	40.23	18.61	−21.62 (−53.75)	27.58	13.44	−14.14 (−51.28)
Switzerland	1995–2019	19.12	15.43	−3.68 (−19.26)	13.44	11.41	−2.02 (−15.05)
United Kingdom	1985–2016	48.94	38.26	−10.68 (−21.82)	40.25	33.47	−6.78 (−16.84)
United States	1985–2007	37.95	28.35	−9.6 (−25.3)	24.29	23.73	−0.56 (−2.3)

We only report a percentage change for countries with complete start and end data.
NA, not available.

countries (LMICs), which were better represented in Rudd's study, may have contributed to the differences between our estimates and theirs. Nevertheless, both studies revealed comparable findings, such as higher ASMR among males than females and a decline in ASMR over a similar time period. The estimates for specific countries were also strikingly similar in both studies, such as Australia, Israel, Croatia and Japan, which all differ by less than 5 per 100 000 across both studies. This highlights the value of the current study and the accuracy of using Angus' definition in particular.

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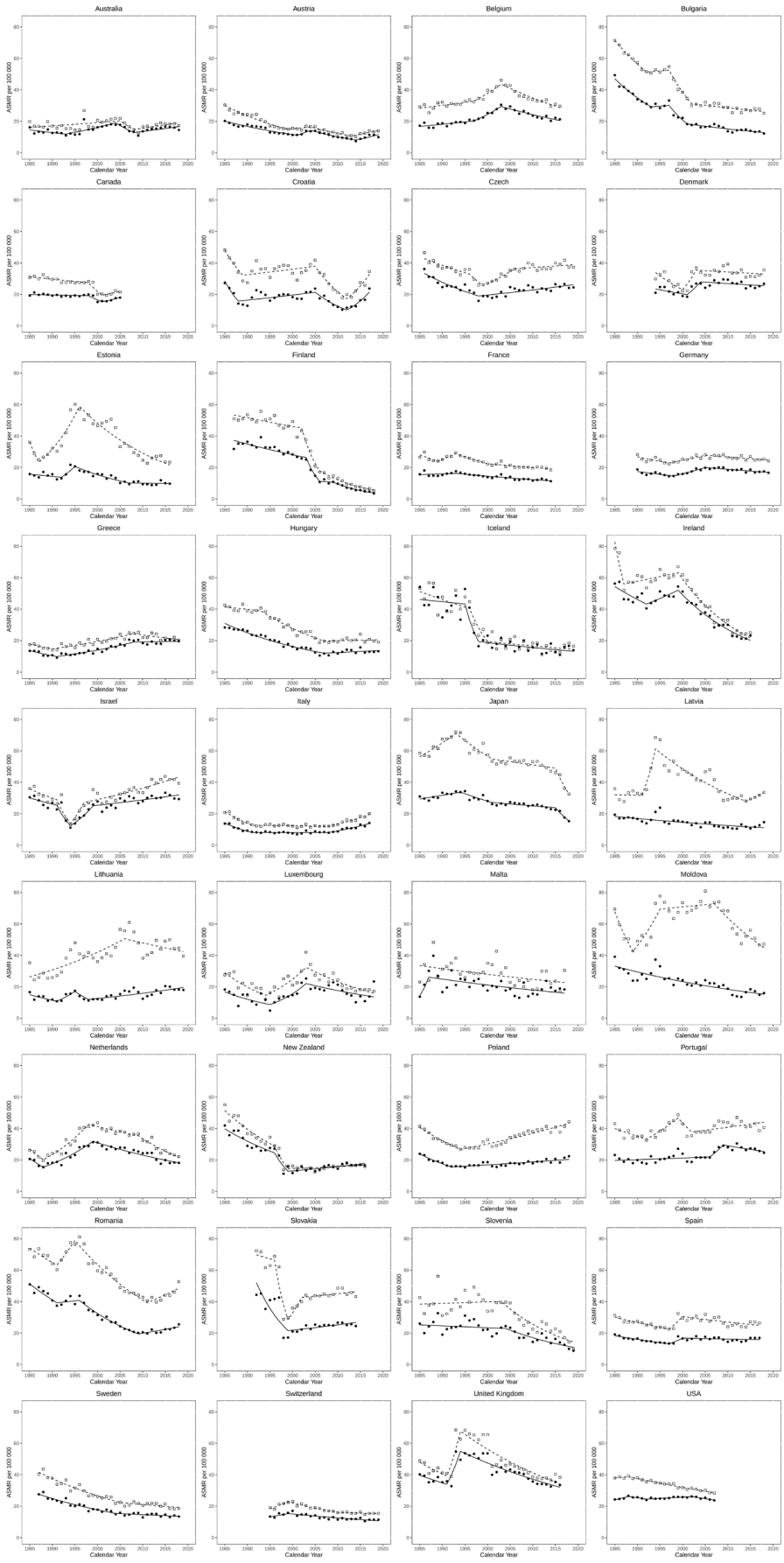


Figure 2 Age-standardised mortality rate (ASMR) of sepsis (Angus definition) and joinpoint regression analysis in 36 included countries between 1985 and 2019 (or longest period with data available). Empty squares represent male, full squares female.

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Our study has a number of limitations. The definition of sepsis and the version of the ICD taxonomy have changed over time. To limit the impact of this limitation, we have not restricted ICD codes to 'sepsis' or 'septicaemia' only but have also included the root causes of sepsis (such as pneumonia, peritonitis, etc) following previously described definitions based on ICD coding and presented sensitivity analyses from several definitions. Despite this, the transition point between versions of the ICD 9 and 10 nomenclatures are occasionally visible for some countries (eg, Iceland in 1996, Moldova in 1995 or New Zealand in 1999), which indicates that changes in ICD version have impacted our sepsis estimates.

We chose the Angus definition for our main results over Martin and Flaatten definitions because it is more exhaustive and more widely used. However, it has been reported that using the Angus definition may overestimate true sepsis incidence.[1]

In the Angus ICD abstraction of the sepsis definition, two criteria were required: a code for infection and a code for organ failure.[21 30] Only the code for primary cause of death was available to us (as a suspected cause of death). We contend that since these patients died as a consequence of an infection, it is reasonable to assume that they indeed had sepsis and organ failure. The next limitation is that we relied on ICD coding, which has been frequently criticised for being unreliable.[1 31] The practices of coding for death certificates vary across countries and within a county over time. For example, Rhee *et al* analysed sepsis incidence and mortality across 409 US hospitals, comparing clinical and claims data based on ICD-9-CM.[32] They observed a large rise in incidence (a 50% increase between 2009 and 2014) based on ICD data, which was not reflected by clinical criteria (which remained essentially flat). The WHO itself acknowledges an uncertainty in the death rates ranging from ±10% for high-income countries to ±25%–35% for sub-Saharan Africa, pertaining to a combination of uncertainty in overall mortality levels, in cause of death assignment, and in the attribution of deaths coded to ill-defined causes.[33] We only used countries with 'high usability data' as defined by the WHO itself.

We only presented aggregate national-level statistics. While our results provide valuable insights at a population level and allow for the examination of broad trends over time, they do not capture the full spectrum of variation that exists within populations, including differences in healthcare access, quality of care, socioeconomic factors and regional disparities. As such, our findings should be interpreted with caution, particularly when considering their direct applicability to individual clinical practice or policy-making.

Finally, this approach does not capture LMICs' data well, since many of these countries have major gaps in data recording. This limits the coverage of the study, since 87% of the world's population lives in LMICs. However, the validity of extrapolating data to these regions has been questioned.[3 8 29]

CONCLUSIONS

Overall, we observed a decrease in reported sepsis-related mortality across the majority of analysed nations between 1985 and 2019, when relying on the definition by Angus *et al*. However, there remains significant variability between health systems with respect to trends in sepsis-related mortality. System-level and population-level factors may contribute to these differences in mortality and additional investigations are necessary to further explain these trends.

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Contributors Conceptualisation, formal analysis, investigation and writing—review and editing: MK, JDS, JS, ACG and DCM. Methodology: JDS, JS and DCM. Writing—original draft preparation: MK. All authors read and approved the final manuscript. MK is responsible for the overall content as guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The WHO Mortality Database is a publicly available aggregated dataset for which no individual patient consent and ethics committee approval are required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. The dataset analysed for this study can be found online at: https://www.who.int/data/data-collection-tools/who-mortality-database.

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Supplementary Material

To "Multinational Trends in Sepsis Mortality between 1985 and 2019: a temporal analysis of the WHO Mortality Database"

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Online Resource 1: List of high usability countries and included countries

Online Resource 1: List of countries with high usability data and list of countries included in the analysis

Area	Country	Included?
Americas	1. Canada	Yes
	2. Dominica	No
	3. Grenada	No
	4. Mexico	No
	5. Saint Vincent and the Grenadines	No
	6. United States of America	Yes
	7. Brazil	No
	8. Chile	No
	9. Cuba	No
	10. Costa Rica	No
Europe	1. Andorra	No
	2. Austria	Yes
	3. Belgium	Yes
	4. Croatia	Yes
	5. Czechia	Yes
	6. Denmark	Yes
	7. Estonia	Yes
	8. Finland	Yes
	9. France	Yes
	10. Germany	Yes
	11. Hungary	Yes
	12. Iceland	Yes
	13. Ireland	Yes
	14. Israel	Yes
	15. Italy	Yes
	16. Luxembourg	Yes
	17. Malta	Yes
	18. Netherlands	Yes
	19. Norway	No
	20. Romania	Yes
	21. San Marino	No
	22. Slovakia	Yes
	23. Slovenia	Yes
	24. Spain	Yes
	25. Sweden	Yes
	26. Switzerland	Yes
	27. United Kingdom	Yes
	28. Lithuania	Yes
	29. The Former Yugoslav Republic of Macedonia	No
	30. Kyrgyzstan	No
	31. Latvia	Yes
	32. Republic of Moldova	Yes
	33. Uzbekistan	No
Western pacific region	1. Australia	Yes
	2. Brunei	No
	3. Darussalam	No
	4. Japan	Yes
	5. New Zealand	Yes
	6. Republic of Korea	No
Africa	Mauritius	No

Online Resource 2: Sepsis International Classification of Diseases (ICD) definitions

As defined by	ICD-9	ICD-10
Angus	X	X
Martin	X	X
Flaatten	X	

Please note that we only used the "infection criteria", and not the "organ dysfunction" criteria. We assumed that any patient whose death certificate included a listed infection also had some organ dysfunction. Because Martin's and Flaatten's definitions relied on less than 10 "infection criteria" codes, we did not implement those sepsis abstractions in our research and used only Angus's. In Online Resource 4, we showed sepsis-related ASDR for 2001-2019 according to the three definitions and confirmed that Martin's and Flaatten's abstractions lead to unreliable results,

Angus, ICD-9 definition

Infection criteria (according to the ICD-9-Clinical Modification [CM] codes of Angus adjusted to ICD-9 Swedish version)—primary and secondary codes: 001, cholera; 002, typhoid/paratyphoid fever; 003, other salmonella infection; 004, shigellosis; 005, other food poisoning; 008, intestinal infection not otherwise classified; 009 ill-defined intestinal infection; 010, primary tuberculosis; 011, pulmonary tuberculosis; 012, other respiratory tuberculosis; 013, central nervous system tuberculosis; 014, intestinal tuberculosis; 015, tuberculosis of bone and joint; 016, genitourinary tuberculosis; 017, tuberculosis in other organs; 018, miliary tuberculosis; 020, plague; 021, tularemia; 022, anthrax; 023, brucellosis; 024, glanders; 025, melioidosis; 026, rat-bite fever; 027, other bacterial zoonoses; 030, leprosy; 031, other mycobacterial disease; 032, diphtheria; 033, whooping cough; 034, streptococcal throat/scarlet fever; 035, erysipelas; 036, meningococcal infection; 037, tetanus; 038, septicemia; 039, actinomycosis; 040, other bacterial diseases; 041, bacterial infection in other diseases not otherwise specified; 090, congenital syphilis; 091, early symptomatic syphilis; 092, early syphilis latent; 093, cardiovascular syphilis; 094, neurosyphilis; 095, other late symptomatic syphilis; 096, late syphilis latent; 097, other and unspecified syphilis; 098, gonococcal infections; 100, leptospirosis; 101, Vincent's angina; 102, yaws; 103, pinta; 104, other spirochetal infection; 110, dermatophytosis; 111, dermatomycosis not otherwise classified or specified; 112, candidiasis; 114, coccidioidomycosis; 115, histoplasmosis; 116, blastomycosis; 117, other mycosis; 118, opportunistic mycoses; 320, bacterial meningitis; 322, meningitis, unspecified; 324, central nervous system abscess; 325, phlebitis and thrombophlebitis of intracranial sinus; 420, acute pericarditis; 421, acute or subacute endocarditis; 451, phlebitis and thrombophlebitis; 461, acute sinusitis; 462 acute pharyngitis; 463, acute tonsillitis; 464, acute laryngitis/tracheitis; 465, acute upper respiratory infection of multiple sites/not otherwise specified; 481, pneumococcal pneumonia; 482, other bacterial pneumonia; 485, bronchopneumonia; 486, pneumonia, organism not otherwise specified; 491, chronic bronchitis; 494, bronchiectasis; 510, empyema; 513, lung/mediastinum abscess; 540, acute appendicitis; 541, appendicitis not otherwise specified; 542, other appendicitis; 562, diverticula of intestine; 566, anal and rectal abscess; 567,

peritonitis; 569F, intestinal abscess; 572A, abscess of liver; 572B, portal pyemia; 575A, acute cholecystitis; 590, kidney infection; 597, urethritis/urethral syndrome; 599A, urinary tract infection not otherwise specified; 601, prostatic inflammation; 614, female pelvic inflammation disease; 615, uterine inflammatory disease; 616, inflammatory disease of cervix, vagina, and vulva; 681, cellulitis, finger/toe; 682, other cellulitis and abscess; 683, acute lymphadenitis; 686, other local skin infection; 711A, pyogenic arthritis; 730, osteomyelitis and periostitis; 790H, bacteremia [WHO only has 790 Nonspecific findings on examination of blood]; 996G, infection or inflammation of device/graft; 998F, postoperative infection; 999D, infection, sepsis, or septicemia due to infusion, injection, transfusion, or vaccination.

Organ dysfunction criteria (according to the ICD-9-CM codes of Angus adjusted to ICD-9 Swedish version)— primary and secondary diagnoses: cardiovascular: 458, hypotension; 785F, shock without trauma. [WHO only has code 785: “Symptoms involving cardiovascular system”]
Respiratory: V46B, mechanical ventilation. Neurologic: 293, transient organic psychosis; 348B, anoxic brain damage; 348D, encephalopathy, unspecified. Hematologic: 286G, defibrination syndrome; 286x, other/unspecified coagulation defect; 287E, secondary thrombocytopenia [WHO only has code 287 Purpura and other haemorrhagic conditions]; 287F, thrombocytopenia, unspecified. Hepatic: 570, acute and subacute necrosis of liver; 573E, hepatic infarction. Kidney: 584, acute renal failure.

Angus, ICD-10 definition

Infection criteria (according to the ICD9-CM codes of Angus adjusted to ICD-10 Swedish version)— primary and secondary diagnoses: A00, cholera; A01, typhoid/paratyphoid fever; A02, other salmonella infection; A03, shigellosis; A04, other bacterial intestinal infections; A05, other bacterial foodborne intoxications, not elsewhere classified; A09, diarrhea and gastroenteritis of presumed infectious origin; A15, respiratory tuberculosis, bacteriologically and histologically confirmed; A16, respiratory tuberculosis, not confirmed bacteriologically or histologically; A17, tuberculosis of nervous system; A18, tuberculosis of other organs; A19, miliary tuberculosis, A20, plague; A21, tularemia; A22, anthrax; A23, brucellosis; A24, glanders and melioidosis; A25, rat-bite fevers; A26, erysipeloid; A27, leptospirosis; A28, other zoonotic bacterial diseases, not elsewhere classified; A30, leprosy; A31, infection due to other mycobacteria; A32, listeriosis; A34, obstetrical tetanus; A35, other tetanus; A36, diphtheria; A37, whooping cough; A38 scarlet fever; A39, meningococcal infection; A40, streptococcal septicemia; A41, other septicemia; A42, actinomycosis; A43, nocardiosis; A44, Bartonellosis; A46, erysipelas; A48, other bacterial diseases, not elsewhere classified; A49, bacterial infection of unspecified site; A50, congenital syphilis; A51, early syphilis; A52, late syphilis; A53, other and unspecified syphilis; A54, gonococcal infection; A55, chlamydial lymphogranuloma (venereum); A56, other sexually transmitted chlamydial diseases; A57, chancroid; A58, granuloma inguinale; A59, trichomoniasis; A65, nonvenereal syphilis; A66, yaws; A67, pinta; B35, dermatophytosis; B36, other superficial mycoses; B37, candidiasis; B38, coccidioidomycosis; B39, histoplasmosis; B40, blastomycosis; B41, paracoccidioidomycosis; B42, sporotrichosis; B43, chromomycosis and phaeomycotic abscess; B44, aspergillosis; B45, cryptococcosis; B46, zygomycosis; B47, mycetoma; B48, other mycoses, not elsewhere classified; B49, unspecified mycosis; B95, streptococcus and staphylococcus as the cause of diseases classified to other chapters; B96, other bacterial agents as the cause of diseases classified to other chapters; B97, viral agents as the

cause of diseases classified to other chapters; G00, bacterial meningitis, not elsewhere classified; G01, meningitis in bacterial diseases classified elsewhere; G02, meningitis in other infectious and parasitic diseases classified elsewhere; G03, meningitis due to other and unspecified causes; G04, encephalitis, myelitis and encephalomyelitis; G05, encephalitis, myelitis, and encephalomyelitis in diseases classified elsewhere; G07, intracranial and intraspinal abscess and granuloma in diseases classified elsewhere; G08, intracranial and intraspinal phlebitis and thrombophlebitis; I30, acute pericarditis; I33, acute pericarditis; I39.8, endocarditis, valve unspecified, in diseases classified elsewhere; I80, phlebitis and thrombophlebitis; J01, acute sinusitis; J02, acute pharyngitis; J03, acute tonsillitis; J04, acute laryngitis and tracheitis; J05, acute obstructive laryngitis (croup) and epiglottitis; J06, acute upper respiratory infections of multiple and unspecified sites; J13, pneumonia due to Streptococcus pneumoniae; J14, pneumonia due to Haemophilus influenzae; J15, bacterial pneumonia, not elsewhere classified; J18, pneumonia, organism unspecified; J20, acute bronchitis; J44.0, chronic obstructive pulmonary disease with acute lower respiratory infection; J44.1, chronic obstructive pulmonary disease with acute exacerbation, unspecified; J47, bronchiectasis; J80, adult respiratory distress syndrome; J85, abscess of lung and mediastinum; J86, pyothorax; J95.1, acute pulmonary insufficiency following thoracic surgery; J95.2, acute pulmonary insufficiency following nonthoracic surgery; J96.0, acute respiratory failure; J96.9, respiratory failure, unspecified; K35, acute appendicitis; K36, other appendicitis; K37, unspecified appendicitis; K57, diverticular disease of intestine; K61, abscess of anal and rectal regions; K63.0, abscess of the intestine; K63.1, perforation of intestine (nontraumatic); K65, peritonitis; K75.0, abscess of the liver; K75.1, phlebitis of portal vein; K81, cholecystitis; L02, cutaneous abscess, furuncle, and carbuncle; L03, cellulitis; L04, acute lymphadenitis; L08, other local infections of skin and subcutaneous tissue; M00, pyogenic arthritis; M86, osteomyelitis; N10, acute tubulointerstitial nephritis; N11, chronic tubulointerstitial nephritis; N12, tubulointerstitial nephritis, not specified as acute or chronic; N20.9, urinary calculus, unspecified; N30.0, acute cystitis; N30.1, interstitial cystitis (chronic); N30.2, other chronic cystitis; N30.3, trigonitis; N30.8, other cystitis; N30.9, cystitis, unspecified; N34.1, nonspecific urethritis; N41, inflammatory diseases of prostate; N70, salpingitis and oophoritis; N71, inflammatory disease of uterus, except cervix; N72, inflammatory disease of cervix uteri; N73, other female pelvic inflammatory diseases; N75, diseases of Bartholin's gland; N76, other inflammation of vagina and vulva; O23.0, infections of kidney in pregnancy; T80.2, infections following infusion, transfusion, and therapeutic injection; T81.4, infection following a procedure, not elsewhere classified; T81.6, acute reaction to foreign substance accidentally left during a procedure; T82.6, infection and inflammatory reaction due to cardiac valve prosthesis; T82.7, infection and inflammatory reaction due to other cardiac and vascular devices, implants, and grafts; T83.5, infection and inflammatory reaction due to prosthetic device, implant, and graft in urinary system; T83.6, infection and inflammatory reaction due to prosthetic device, implant, and graft in tge genital tract; T84.5, infection and inflammatory reaction due to internal joint prosthesis; T84.6, infection and inflammatory reaction due to internal fixation device; T84.7, infection and inflammatory reaction due to other internal orthopaedic prosthetic devices, implants, and grafts; T85.7, infection and inflammatory reaction due to other internal prosthetic devices, implants, and grafts; T88.0, infection following immunization.

Organ dysfunction criteria (according to the ICD-9-CM codes of Angus adjusted to ICD-10 Swedish version)—primary and secondary diagnoses: Cardiovascular: I95, hypotension; R57, shock, not elsewhere classified. Respiratory: Z99.1, dependence on respirator. Hematologic: D65, disseminated intravascular coagulation; D68.9, coagulation defect, unspecified; D69.5, secondary

thrombocytopenia; D69.6, thrombocytopenia, unspecified. Neurologic: F05.0, delirium not superimposed on dementia; F05.8, other delirium; F05.9, delirium, unspecified; G63.1, anoxic brain damage, not elsewhere classified; G93.4, encephalopathy, unspecified; R41, other symptoms and signs involving cognitive functions and awareness. Hepatic: K72.0, acute and subacute hepatic failure; K72.9, hepatic failure, unspecified; K76.2, central hemorrhagic necrosis of liver; K76.3, infarction of the liver. Kidney: N17, acute renal failure; N99.0, postprocedural renal failure.

Martin, ICD-9 definition

Infection criteria (according to the ICD-9-CM codes of Martin et al [18] adjusted to ICD-9 Swedish version)— primary and secondary diagnoses: 038, septicemia; 020, Plague; 790H, bacteremia; 117x, other and unspecified mycoses; 112F, disseminated candidiasis; 112W, candidiasis of other specified sites.

Organ dysfunction criteria (according to the ICD-9-CM codes of Martin et al [17] adjusted to ICD-9 Swedish version)—primary and secondary diagnoses: cardiovascular: 458A, orthostatic hypotension; 458x, hypotension, unspecified; 785F, shock without mention of trauma; 796D, nonspecific low blood pressure reading. Respiratory: 518F, pulmonary insuffi- ciency following trauma and surgery; 786A, dyspnea and respiratory abnormalities; 799B, respiratory arrest; V46B, mechanical ventilation. Hematologic: 286G, defibrination syndrome; 286x, other and unspecified coagulation defects; 287D, primary thrombocytepenia; 287E, secondary thrombocytopenia; 287F, thrombocytopenia, unspecified. Neurologic: 293, transient mental disorders due to conditions classified elsewhere; 348B, anoxic brain damage; 348D, encephalopathy, not elsewhere classified; 780A, alteration of consciousness. Kidney: 584, acute renal failure; 580, acute glomerulonephritis; 586, renal failure, unspecified; V56A, extracorporeal dialysis. Hepatic: 570, acute and subacute necrosis of the liver; 572C, hepatic coma. Metabolic: 276c, acidosis.

Martin, ICD-10 definition

Infection criteria (according to the ICD-9-CM codes of Martin adjusted to ICD-10 Swedish version)— primary and secondary diagnoses: A20, plague; A40, streptococcal septicemia; A41, other septicemia; A49.9, bacterial infection, unspecified; B49, unspecified mycosis; B37.5, candidal meningitis; B37.6, candidal endocarditis; B37.7, candidal septicemia; B37.8, candidiasis of other sites.

Organ dysfunction criteria (according to the ICD-9-CM codes of Martin adjusted to ICD-10 Swedish version)—primary and secondary diagnoses: cardiovascular: I95.1, orthostatic hypotension; I95.9, hypotension, unspecified; R03.1, nonspecific low blood-pressure reading; R57, shock, not elsewhere classified. Respiratory: J95.1, acute pulmonary insufficiency following thoracic surgery; J95.2, acute pulmonary insufficiency following nonthoracic surgery; J80, adult respiratory distress syndrome; R06.0, dyspnea; R06.3, periodic breathing; R06.4, hyperventilation; R06.8, other and unspecified abnormalities of breathing; R09.2, respiratory arrest; J96.0, acute respiratory failure; J96.9, respiratory failure, unspecified. Hematologic: D65, disseminated intravascular coagulation;

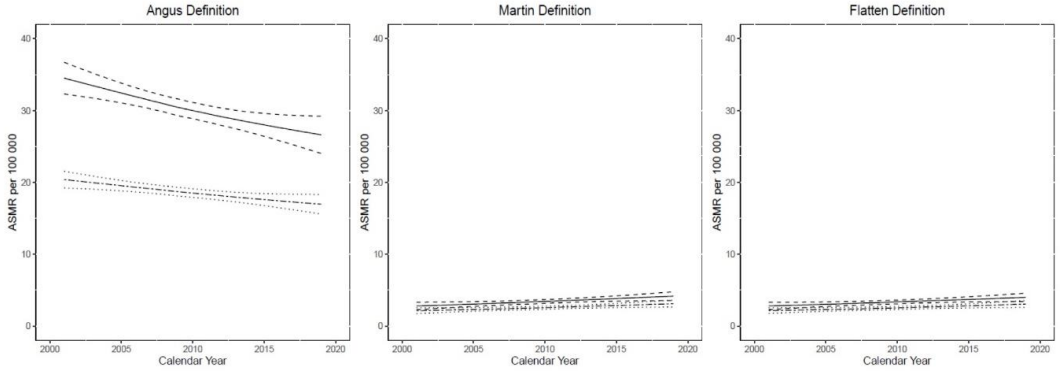
D68.9, coagulation defect, unspecified; D69.3, idiopathic thrombocytopenic purpura; D69.4, other primary thrombocytopenia; D69.5, secondary thrombocytopenia; D69.6, thrombocytopenia, unspecified. Neurologic: F05.0, delirium not superimposed on dementia; F05.8, other delirium; F05.9, delirium, unspecified; G93.1, anoxic brain damage, not elsewhere classified; G93.4, encephalopathy, unspecified; R40, somnolence, stupor and coma; R41.8, other and unspecified symptoms and signs involving cognitive functions and awareness; R41.0, disorientation, unspecified. Kidney: N00, acute nephritic syndrome; N01, rapidly progressive nephritic syndrome; N17, acute renal failure; N19, unspecified renal failure; Z49.1, extracorporeal dialysis. Hepatic: K72.0, acute and subacute hepatic failure; K72.9, hepatic failure, unspecified; K76.2, central hemorrhagic necrosis of liver. Metabolic: E87.2, acidosis.

Flaatten, ICD-10 definition

Infection criteria (according to the ICD-10 codes of Flaatten)—primary and secondary diagnoses: A26.7, Erysipelothrix septicemia; A39, meningococcal infection; A40.0, septicemia due to streptococcus, group A; A41, other septicemia; A42.7, actinomycotic septicemia; B37.7, candidal septicemia; T81.4, infection following a procedure, not elsewhere classified.

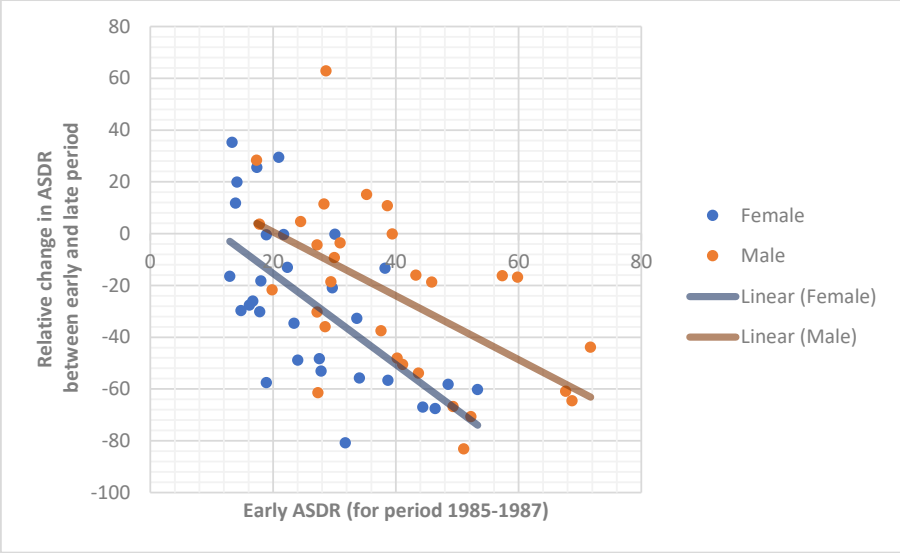
Organ dysfunction criteria (according to the ICD-10 codes of Flaatten)— only secondary diagnoses: cardiovascular: A41.9, septicemia, unspecified; I50.9, heart failure, unspecified. Respiratory: J13, pneumonia due to Streptococcus pneumoniae; J14, pneumonia due to Haemophilus influenzae; J15, bacterial pneumonia, not elsewhere classified; J16, pneumonia due to other infectious organisms, not elsewhere classified; J17, pneumonia in diseases classified elsewhere; J18, pneumonia, organism unspecified; J80, adult respiratory distress syndrome; J95, postprocedural respiratory disorders, not elsewhere classified; J96.0, acute respiratory failure. Renal: N17, acute renal failure; N99.0, postprocedural renal failure. Hematologic: D65, disseminated intravascular coagulation; D69, purpura and other hemorrhagic conditions. Other: E86, volume depletion; E87.2, acidosis; K72, hepatic failure, not elsewhere classified.

Online Resource 3: Comparison of sepsis-related ASDR for 2001-2019, according to Angus, Martin and Flaatten definitions.



Online Resource 3: Comparison of three different sepsis abstractions. The plots represent sepsis-related ASDR among the 36 included countries (weighted median +/- IQR) according to Angus, Martin and Flaatten definitions, with LOESS regression, for 2001-2019. Dashdotted lines represent females, full lines males. Definitions lead to wide differences in sepsis estimates. We confirmed that Martin and Flaatten's definitions lead to unreliable estimates, because they rely on less than 10 ICD codes for the infection criteria.

Online Resource 4: Relationship between the early ASDR for 1985-1987 and the change over the study period.



Online Resource 4: Relationship between the early ASDR (in the period 1985-1987) and the relative change over the study period, separating male in orange and female in dark blue. The linear regression trend lines are also shown. We excluded 6 countries which did not have data available for the start and/or end period. Overall, there is a weak (R coefficient -0.50 ; R-squared 0.25) inverse correlation between the ASDR during the early study period (1985-1987) and the observed relative change over the whole study period: countries with a higher early ASDR tend to be associated with a higher reduction in ASDR over the study period.

Online Resource 5: JoinPoint regression data for individual countries, Angus definition, period 1985-2019

Online Resource 5: Joinpoint regression analysis using the Angus definition, for male (table S2a) and female (table S2b) for all included countries over 1985-2019, or as indicated. We identified between one and four trends in each country.

Online Table 5a (Male):

Country	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	APC	Years	APC	Years	APC	Years	APC
Australia	1985 - 2005	1.17^	2006 - 2008	-10.12	2009 - 2019	2.65		
Austria	1985 - 1999	-4.88^	2000 - 2004	1.97	2005 - 2013	-4.70^	2014 - 2020	4.99^
Belgium	1985 - 1997	1.21^	1998 - 2003	4.88^	2004 - 2017	-3.16^		
Bulgaria	1985 - 1992	-4.59^	1993 - 1997	0.46	1998 - 2002	-9.90^	2003 - 2019	-1.09^
Ca da	1985 - 1998	-1.01^	1999 - 2001	-10.74^	2002 - 2006	3.01		
Croatia	1985 - 1989	-9.47^	1990 - 2005	1.04	2006 - 2012	-10.63^	2013 - 2018	13.64^
Czech Republic	1986 - 1996	-2.57^	1997 - 1999	-8.15	2000 - 2006	5.19^	2007 - 2020	0.51
De ngk	1994 - 2000	-6.28^	2001 - 2003	15.55	2004 - 2019	-0.49		
Estonia	1985 - 1987	-19.71	1988 - 1996	10.86^	1997 - 2017	-4.90^		
Finland	1987 - 2002	-1.12^	2003 - 2006	-20.59^	2007 - 2019	-9.22^		
France	1985 - 1989	-3.73	1990 - 1993	4.6	1994 - 2000	-3.52^	2001 - 2015	-1.16^
Germany	1990 - 1997	-2.25^	1998 - 2005	2.47^	2006 - 2020	-0.82^		

Greece	1985 - 1990	-3.72	1991 - 2008	2.86^	2009 - 2019	-1.69^		
Hungary	1985 - 1993	-0.74	1994 - 2007	-4.75^	2008 - 2020	0.35		
Iceland	1985 - 1996	-2.1	1997 - 2000	-16.78	2001 - 2020	-1.54		
Ireland	1985 - 1987	-17.75	1988 - 1999	1.01	2000 - 2016	-6.47^		
Israel	1985 - 1991	-3.46	1992 - 1994	-21.60^	1995 - 1997	24.9	1998 - 2019	2.26^
Italy	1985 - 1991	-8.31^	1992 - 2008	-0.33	2009 - 2018	5.61^		
Japan	1985 - 1993	2.95^	1994 - 2001	-3.17^	2002 - 2015	-0.80^	2016 - 2019	-12.89^
Latvia	1985 - 1991	-0.21	1992 - 1994	24.61	1995 - 2014	-3.84^	2015 - 2019	4.5
Lithuania	1985 - 2006	3.16^	2007 - 2020	-1.35				
Luxembourg	1985 - 1994	-7.36^	1995 - 2003	9.27^	2004 - 2019	-4.60^		
Malta	1985 - 2018	-1.20^						
Moldova	1985 - 1989	-11.00^	1990 - 1995	8.53^	1996 - 2007	0.4	2008 - 2019	-4.31^
Netherlands	1985 - 1988	-9.02	1989 - 1998	7.77^	1999 - 2009	-1.69^	2010 - 2019	-5.28^
New Zealand	1985 - 1996	-5.12^	1997 - 1999	-20.74^	2000 - 2017	0.89^		
Poland	1985 - 1994	-4.53^	1995 - 2019	2.04^				
Portugal	1985 - 1992	-2.62^	1993 - 1999	4.98^	2000 - 2002	-6.8	2003 - 2019	0.96^
Romania	1985 - 1991	-2.58^	1992 - 1995	5.72	1996 - 2011	-4.27^	2012 - 2019	3.08^
Slovakia	1992 - 1996	-1.22	1997 - 1999	-24.54^	2000 - 2002	14.31	2003 - 2015	0.69
Slovenia	1985 - 2003	0.25	2004 - 2020	-6.24^				

Spain	1985 - 1997	-2.38^	1998 - 2000	10.58	2001 - 2018	-1.19^		
Sweden	1987 - 2005	-3.40^	2006 - 2019	-1.14^				
Switzerland	1995 - 1999	5.44^	2000 - 2010	-3.16^	2011 - 2020	-0.54		
United Kingdom	1985 - 1991	-3.29	1992 - 1994	20.02	1995 - 2017	-3.05^		
United States	1985 - 1988	0.65	1989 - 2008	-1.60^				

Online Table 5b (Female):

Country	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	APC	Years	APC	Years	APC	Years	APC
Australia	1985 - 1993	-2.4	1994 - 2004	4.40^	2005 - 2008	-9.44	2009 - 2019	2.61
Austria	1985 - 2001	-3.64^	2002 - 2004	8.63	2005 - 2014	-5.53^	2015 - 2020	7.38^
Belgium	1985 - 1997	1.60^	1998 - 2003	6.45^	2004 - 2017	-2.76^		
Bulgaria	1985 - 1993	-5.82^	1994 - 1997	0.84	1998 - 2001	-11.67^	2002 - 2019	-2.10^
Canada	1985 - 1998	-0.27	1999 - 2001	-7.53	2002 - 2006	4.38^		
Croatia	1985 - 1988	-17.92^	1989 - 2005	1.82^	2006 - 2012	-10.24^	2013 - 2018	16.40^
Czech Republic	1986 - 1998	-4.59^	1999 - 2020	1.54^				
Denmark	1994 - 2001	-2.36	2002 - 2004	12.11	2005 - 2019	-0.66		
Estonia	1985 - 1992	-1.9	1993 - 1995	14.51	1996 - 2007	-5.75^	2008 - 2017	-0.41

Finland	1987 - 2003	-2.14^	2004 - 2006	-24.95^	2007 - 2009	-1.5	2010 - 2019	-10.83^
France	1985 - 1993	0.62	1994 - 2015	-1.63^				
Germany	1990 - 1998	-2.23^	1999 - 2005	4.63^	2006 - 2020	-1.20^		
Greece	1985 - 1991	-5.29^	1992 - 2008	3.97^	2009 - 2019	0.24		
Hungary	1985 - 2007	-4.22^	2008 - 2020	1.12				
Iceland	1985 - 1995	-0.65	1996 - 1998	-23.44	1999 - 2020	-1.80^		
Ireland	1985 - 1992	-3.23^	1993 - 1999	2.7	2000 - 2016	-5.77^		
Israel	1985 - 1991	-2.73	1992 - 1994	-21.22^	1995 - 1999	15.01^	2000 - 2019	1.30^
Italy	1985 - 1991	-8.78^	1992 - 2008	-0.02	2009 - 2018	6.15^		
Japan	1985 - 1994	1.55^	1995 - 2001	-3.05^	2002 - 2015	-0.92^	2016 - 2019	-13.58^
Latvia	1985 - 2019	-1.51^						
Lithuania	1985 - 1991	-5.26	1992 - 1995	11.96	1996 - 1998	-10.97	1999 - 2020	2.36^
Luxembourg	1985 - 1995	-6.32^	1996 - 2003	12.30^	2004 - 2019	-3.19^		
Malta	1985 - 1987	34.98	1988 - 2018	-1.62^				
Moldova	1985 - 2019	-2.32^						
Netherlands	1985 - 1988	-9.7	1989 - 1999	6.81^	2000 - 2019	-2.90^		
New Zealand	1985 - 1996	-4.30^	1997 - 1999	-19.46	2000 - 2017	1.91^		
Poland	1985 - 1992	-5.92^	1993 - 2019	1.05^				
Portugal	1985 - 2006	0.51	2007 - 2009	10.48	2010 - 2019	-1.67		

Romania	1985 - 1991	-4.32^	1992 - 1996	0.73	1997 - 2009	-5.53^	2010 - 2019	2.36^
Slovakia	1992 - 1999	-11.85^	2000 - 2015	1.46				
Slovenia	1985 - 2004	-0.49	2005 - 2020	-4.82^				
Spain	1985 - 1997	-2.75^	1998 - 2000	8.48	2001 - 2018	-0.37		
Sweden	1987 - 2004	-3.37^	2005 - 2019	-0.86^				
Switzerland	1995 - 1999	3.7	2000 - 2020	-1.76^				
United Kingdom	1985 - 1991	-2.55	1992 - 1994	17.4	1995 - 2017	-2.42^		
United States	1985 - 1988	2.98^	1989 - 1992	-1.7	1993 - 2002	0.66^	2003 - 2008	-1.79^