Electronic Supplemental Material (ESM)

This document provides supplementary material for the manuscript: Mortality trends in type 1 diabetes: a multicountry analysis of six population-based cohorts

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ESM Methods

Modified Newcastle-Ottawa Quality Assessment Scale for mortality trends in type 1 diabetes.

A study can be awarded a maximum of one or two points for each numbered item within each category.

Selection

1. Representativeness of the general population (sampling frame).
   a) National scheme with ≥80% coverage of national population (2 points)
   b) Random sample from national health insurance or national population-based survey with ≥80% response rate (1 point)
   c) Regional representative or national scheme with <80% coverage of national population (0 points)

2. Assessment of diabetes status.
   a) By blood glucose measurement (FPG, OGTT, HbA1c) or by multiple approaches / administrative algorithm where 2 or more criteria used (2 points)
   b) Clinical diagnosis (e.g. ICD code or physician-diagnosed) (1 point)
   c) Anti-diabetic medication or self-report of physician-diagnosed diabetes (0 points)

3. Exclusion of gestational diabetes
   a) Yes (1 point)
   b) No (0 points)

4. Sample size at each time point.
   a) >5,000 (1 point)
   b) ≤5,000 (0 points)

Outcome

1. Assessment of outcome
   a) By record linkage (1 point) e.g. national death registry
   b) Other – regular follow-up (0 points)

Completeness of trend data

1. How many time points are provided?
   a) ≥10 (2 points)
   b) 6 – 9 (1 point)
   c) <6 (0 points)

Total score = 9
| Country/region | Diagnostic method | Classification of diabetes type |
|---------------|-------------------|--------------------------------|
| **Australia** | Clinical diagnosis certified by a doctor, nurse or credentialed diabetes educator. | Persons were classified as having type 1 diabetes if they were registered as type 1 diabetes on the NDSS, had evidence of ongoing treatment with insulin (≥2 prescriptions on the PBS, except where time to census date/death was <2 years), and met one of the following additional criteria [1]:
1) time between diagnosis date and first insulin prescription was less than one year, or
2) registered before 45 years of age and showing evidence of insulin therapy at the time of registration (only applied to individuals with missing diagnosis date [31%]); or
3) registered before 2002 with an age at diagnosis <30 years (or age at registration <45 years if missing diagnosis date) and treatment with insulin evident from 2002; i.e. when PBS data became available (only applied to individuals with missing insulin initiation date in the NDSS database). In addition, registrants who were originally classified as type 2 on the NDSS, but whose age at diagnosis was <30 years and time to insulin was <1 year, were reclassified as type 1 diabetes. |
| **Denmark**   | Algorithm incorporating clinical diagnosis (ICD codes) from the hospitalisations or outpatient clinics, prescription of anti-diabetic medications, clinical and billing records. | Persons were classified as having type 1 diabetes in the diabetes register if any of the following criteria were met, and otherwise as type 2 diabetes:
1) Purchase of insulin before age 30, or
2) DADD: classified as having type 1 diabetes in >50% of the person’s DADD records classify the person as type 1 diabetes, and similarly for type 2 diabetes, or
3) Not classified as either type 1 or type 2 diabetes in DADD, but >50% of the patient’s records from National Patient Register classifies the person as having type 1 diabetes. Finally, a person cannot be classified as having type 1 diabetes if there is no recorded date of insulin purchase [2]. |
| Country/region | Diagnostic method | Classification of diabetes type |
|----------------|-------------------|---------------------------------|
| Latvia         | Clinical diagnosis using ICD-10 codes. | Persons were classified as having type 1 diabetes according to ICD-10 codes. |
| Scotland       | Clinical diagnosis using the Read code system. | Persons were classified as having type 1 diabetes using clinician-assigned diabetes type for each individual, which was accepted unless contradictory prescription history or age-at-diagnosis data were available (e.g. a clinician-assigned diagnosis of type 1 diabetes without any subsequent insulin prescription would not be accepted) [3]. |
| Spain (Catalonia) | Clinical diagnosis using ICD-10 codes. | Persons were classified as having type 1 diabetes according to ICD-10 codes. |
| USA (KPNW)     | Algorithm incorporating hospitalisation with diabetes as primary discharge diagnosis (ICD codes), ≥2 outpatient visits (ICD codes), anti-diabetic medications or two abnormal blood results from an integrated healthcare delivery system. | Persons were classified as having type 1 diabetes if >50% of the person’s records had a diagnosis code of type 1 diabetes within a 2-year period [4]. |

DADD, Danish Adult Diabetes Database; ICD-10, International Classification of Diseases, version 10; NDSS, National Diabetes Services Scheme; PBS, Pharmaceutical Benefits Scheme.
### ESM Table 2: Quality assessment of the included data sources

| Country/region | Origin of data                                                                 | Repres-  | Assessment  | Exclusion of | Sample size at | Assessment of | Completeness | Total Score |
|----------------|--------------------------------------------------------------------------------|----------|-------------|--------------|----------------|---------------|--------------|-------------|
|                |                                                                                 |      | tiveness of | diabetes status | time points | outcome | (no. of data |                | Score       |
|                |                                                                                 |      | population |              | (no. of type 1 |              | points)      |             |             |
|                |                                                                                 |      |             |              | diabetes)     |              |             |             |             |
| Range of allocated points | 0-2 | 0-2 | 0-1 | 0-1 | 0-1 | 0-2 | 9 |
| Australia      | National Diabetes Services Scheme | 2 | 1 | 1 | 1 | 2 | 8 |
| Denmark        | National Patient Register, prescription data base, health insurance data base, diabetes quality database, and eye screening data base | 2 | 2 | 1 | 1 | 2 | 9 |
| Latvia         | Latvian Diabetes Registry | 2 | 1 | 1 | 0 | 1 | 2 | 7 |
| Scotland       | Scottish Care Information-Diabetes database | 2 | 1 | 0 | 1 | 2 | 7 |
| Spain (Catalonia) | Information System for the Development of Research in Primary Care | 0 | 1 | 1 | 1 | 1 | 5 |
| USA (KPNW)     | KPNW (integrated managed care consortium) | 0 | 2 | 1 | 0 | 1 | 2 | 6 |
**ESM Table 3** Crude all-cause mortality rates by data source and diabetes status in male and female individuals aged 0-79 years, separately

|                      | With type 1 diabetes | Without diabetes |
|----------------------|----------------------|------------------|
|                      | Number of deaths     | Person-years (1000s) | Crude rate (per 1000 person-years) | Number of deaths | Person-years (1000s) | Crude rate (per 1000 person-years) |
| **Male**             |                      |                   |                                  |                  |                   |                                   |
| Australia            | 3587                 | 408               | 8.8                              | 404491           | 122722            | 3.3                                |
| Denmark              | 3851                 | 182               | 21.1                             | 151046           | 30783             | 4.9                                |
| Latvia               | 811                  | 30                | 27.4                             | 155529           | 13028             | 11.9                               |
| Scotland             | 2231                 | 161               | 13.9                             | 133778           | 23501             | 5.7                                |
| Spain*               | 666                  | 66                | 10.0                             | 68610            | 20380             | 3.4                                |
| USA (KPNW)           | 209                  | 14                | 15.1                             | 11010            | 3560              | 3.1                                |
| **Female**           |                      |                   |                                  |                  |                   |                                   |
| Australia            | 2140                 | 335               | 6.4                              | 260087           | 121584            | 2.1                                |
| Denmark              | 2047                 | 138               | 14.9                             | 112537           | 30812             | 3.7                                |
| Latvia               | 427                  | 24                | 17.6                             | 94686            | 14623             | 6.5                                |
| Scotland             | 1588                 | 125               | 12.7                             | 103631           | 24766             | 4.2                                |
| Spain*               | 365                  | 50                | 7.3                              | 37289            | 20481             | 1.8                                |
| USA (KPNW)           | 183                  | 13                | 14.1                             | 9376             | 3750              | 2.5                                |

*Data are from Catalonia, Spain.*
### ESM Table 4

All-cause mortality rates in people with type 1 diabetes aged 0-79 years for each calendar year

| Country/region | Calendar year | Number of deaths | Crude rate (per 1000 person-years) | Age- and sex-standardised rate (per 1000 person-years, 95% CI) |
|----------------|---------------|------------------|------------------------------------|---------------------------------------------------------------|
| **Australia**  | 2004          | 383              | 7.5                                | 8.4 (7.8, 9.0)                                                |
|                | 2005          | 366              | 7.0                                | 8.2 (7.7, 8.7)                                                |
|                | 2006          | 401              | 7.4                                | 7.9 (7.6, 8.3)                                                |
|                | 2007          | 417              | 7.4                                | 7.7 (7.4, 8.1)                                                |
|                | 2008          | 463              | 7.9                                | 7.5 (7.2, 7.9)                                                |
|                | 2009          | 466              | 7.7                                | 7.4 (7.0, 7.7)                                                |
|                | 2010          | 462              | 7.3                                | 7.2 (6.9, 7.5)                                                |
|                | 2011          | 530              | 8.1                                | 7.0 (6.7, 7.4)                                                |
|                | 2012          | 501              | 7.5                                | 6.9 (6.6, 7.2)                                                |
|                | 2013          | 549              | 7.9                                | 6.8 (6.5, 7.1)                                                |
|                | 2014          | 570              | 8.0                                | 6.7 (6.3, 7.0)                                                |
|                | 2015          | 619              | 8.4                                | 6.6 (6.1, 7.0)                                                |
| **Denmark**    | 2005          | 586              | 23.3                               | 10.4 (9.5, 11.4)                                              |
|                | 2006          | 576              | 22.7                               | 10.3 (9.6, 11.1)                                              |
|                | 2007          | 571              | 22.3                               | 10.2 (9.5, 10.8)                                              |
|                | 2008          | 562              | 21.7                               | 10.0 (9.4, 10.6)                                              |
|                | 2009          | 564              | 21.6                               | 9.7 (9.2, 10.3)                                               |
|                | 2010          | 551              | 20.8                               | 9.3 (8.8, 9.9)                                                |
|                | 2011          | 493              | 18.4                               | 8.8 (8.3, 9.3)                                                |
|                | 2012          | 440              | 16.3                               | 8.2 (7.7, 8.7)                                                |
|                | 2013          | 417              | 15.3                               | 7.5 (7.1, 8.0)                                                |
|                | 2014          | 377              | 13.6                               | 6.9 (6.4, 7.4)                                                |
|                | 2015          | 375              | 13.4                               | 6.3 (5.8, 6.9)                                                |
|                | 2016          | 386              | 13.6                               | 5.8 (5.2, 6.4)                                                |
| **Latvia**     | 2003          | 97               | 29.9                               | 27.5 (23.2, 32.5)                                              |
|                | 2004          | 89               | 26.7                               | 24.2 (21.3, 27.5)                                              |
|                | 2005          | 90               | 25.8                               | 21.4 (19.1, 23.8)                                              |
|                | 2006          | 96               | 26.5                               | 19.0 (16.9, 21.3)                                              |
|                | 2007          | 70               | 18.8                               | 17.2 (15.2, 19.5)                                              |
|                | 2008          | 83               | 21.6                               | 16.0 (14.1, 18.2)                                              |
|                | 2009          | 87               | 22.2                               | 15.4 (13.8, 17.3)                                              |
|                | 2010          | 77               | 19.6                               | 15.3 (13.7, 17.0)                                              |
|                | 2011          | 72               | 17.8                               | 15.4 (13.6, 17.4)                                              |
|                | 2012          | 89               | 21.4                               | 15.6 (13.7, 17.9)                                              |
|                | 2013          | 111              | 27.2                               | 15.9 (14.0, 18.1)                                              |
|                | 2014          | 97               | 23.5                               | 16.2 (14.3, 18.3)                                              |
|                | 2015          | 90               | 21.8                               | 16.4 (14.2, 18.9)                                              |
|                | 2016          | 90               | 21.5                               | 16.7 (13.8, 20.1)                                              |
| **Scotland**   | 2006          | 466              | 17.7                               | 12.1 (11.1, 13.2)                                              |
|                | 2007          | 408              | 15.2                               | 11.1 (10.4, 11.9)                                              |
|                | 2008          | 425              | 15.6                               | 10.2 (9.6, 10.8)                                              |
|                | 2009          | 367              | 13.2                               | 9.4 (8.9, 10.0)                                                |
|                | 2010          | 365              | 12.9                               | 8.8 (8.3, 9.4)                                                 |
|                | 2011          | 356              | 12.4                               | 8.5 (8.0, 9.0)                                                 |
|                | 2012          | 350              | 11.9                               | 8.3 (7.8, 8.7)                                                 |
| Country/region | Calendar year | Number of deaths | Crude rate (per 1000 person-years) | Age- and sex-standardised rate (per 1000 person-years, 95% CI) |
|---------------|---------------|------------------|-----------------------------------|-------------------------------------------------------------|
|                | 2013          | 350              | 11.7                              | 8.1 (7.7, 8.6)                                               |
|                | 2014          | 349              | 11.5                              | 8.1 (7.5, 8.7)                                               |
|                | 2015          | 383              | 12.4                              | 8.0 (7.3, 8.8)                                               |
| Spain (Catalonia) | 2009          | 151              | 11.5                              | 5.5 (4.6, 6.5)                                               |
|                | 2010          | 122              | 8.9                               | 5.3 (4.6, 6.1)                                               |
|                | 2011          | 144              | 10.3                              | 5.1 (4.5, 5.7)                                               |
|                | 2012          | 103              | 7.1                               | 4.9 (4.4, 5.5)                                               |
|                | 2013          | 142              | 9.6                               | 4.7 (4.3, 5.3)                                               |
|                | 2014          | 84               | 5.6                               | 4.6 (4.1, 5.2)                                               |
|                | 2015          | 152              | 9.9                               | 4.4 (3.8, 5.1)                                               |
|                | 2016          | 133              | 8.5                               | 4.3 (3.5, 5.1)                                               |
| USA (KPNW)     | 2000          | 42               | 25.7                              | 11.7 (8.4, 16.4)                                             |
|                | 2001          | 35               | 23.3                              | 11.2 (8.6, 14.6)                                             |
|                | 2002          | 29               | 20.1                              | 10.7 (8.4, 13.5)                                             |
|                | 2003          | 23               | 16.8                              | 10.2 (8.0, 13.0)                                             |
|                | 2004          | 22               | 15.8                              | 9.8 (7.6, 12.5)                                              |
|                | 2005          | 30               | 21.2                              | 9.4 (7.4, 11.9)                                              |
|                | 2006          | 13               | 8.8                               | 9.1 (7.3, 11.3)                                              |
|                | 2007          | 20               | 13.5                              | 8.8 (7.2, 10.8)                                              |
|                | 2008          | 14               | 9.2                               | 8.6 (7.0, 10.6)                                              |
|                | 2009          | 20               | 13.0                              | 8.4 (6.7, 10.6)                                              |
|                | 2010          | 23               | 14.8                              | 8.3 (6.6, 10.5)                                              |
|                | 2011          | 18               | 11.1                              | 8.2 (6.5, 10.3)                                              |
|                | 2012          | 19               | 11.3                              | 8.1 (6.5, 10.1)                                              |
|                | 2013          | 23               | 13.7                              | 8.1 (6.5, 10.0)                                              |
|                | 2014          | 18               | 10.3                              | 8.0 (6.3, 10.2)                                              |
|                | 2015          | 20               | 11.0                              | 8.0 (6.0, 10.6)                                              |
|                | 2016          | 23               | 12.0                              | 7.9 (5.6, 11.2)                                              |

Mortality rates are standardised to the age and sex distribution of the assembled population with type 1 diabetes within the six data sources, with equal weights for male and female individuals.
**ESM Table 5** Annual estimated change in all-cause mortality rates in people with type 1 diabetes and annual estimated change in SMR

| Country/region | Annual estimated change in mortality rates (%, 95% CI) | Annual estimated change in SMR (%, 95% CI) |
|----------------|------------------------------------------------------|------------------------------------------|
|                | Total | Male | Female | Total | Male | Female |
| Australia      | -2.1  | -2.1 | -2.1   | -0.4  | -0.2 | -0.6   |
|                | (-2.8, -1.3) | (-3.0, -1.1) | (-3.3, -0.8) | (-1.2, 0.4) | (-1.2, 0.8) | (-1.9, 0.7) |
| Denmark        | -5.8  | -6.0 | -5.4   | -2.4  | -2.6 | -2.0   |
|                | (-6.5, -5.1) | (-6.8, -5.1) | (-6.6, -4.2) | (-3.2, -1.7) | (-3.5, -1.7) | (-3.3, -0.8) |
| Latvia         | -2.2  | -2.3 | -2.1   | 1.1   | 1.0  | 1.0    |
|                | (-3.6, -0.8) | (-4.0, -0.6) | (-4.5, 0.3) | (-0.4, 2.5) | (-0.7, 2.8) | (-1.4, 3.5) |
| Scotland       | -4.8  | -5.0 | -4.5   | -2.3  | -2.3 | -2.4   |
|                | (-5.8, -3.7) | (-6.4, -3.6) | (-6.1, -2.8) | (-3.4, -1.2) | (-3.7, -0.9) | (-4.0, -0.7) |
| Spain (Catalonia) | -3.8  | -4.0 | -3.3   | -6.3  | -6.5 | -6.1   |
|                | (-6.3, -1.2) | (-7.1, -0.8) | (-7.5, 1.1) | (-8.8, -3.8) | (-9.5, -3.3) | (-10.2, -1.7) |
| USA (KPNW)     | -3.4  | -2.9 | -4.1   | 0.0   | 0.8  | -0.9   |
|                | (-5.3, -1.5) | (-5.4, -0.2) | (-6.8, -1.3) | (-1.9, 2.0) | (-1.9, 3.6) | (-3.7, 2.0) |

SMR, standardised mortality ratio.
ESM Fig. 1 Crude all-cause mortality rates in people with type 1 diabetes stratified by sex.

Male individuals in full lines, female individuals in broken lines. The y-axis is plotted on a natural logarithmic scale.
**ESM Fig. 2** Age-standardised all-cause mortality rates in people with type 1 diabetes stratified by sex.

Male individuals in full lines, female individuals in broken lines. Standardisation is based on annual age-specific mortality rates from age-period-cohort models fitted separately for each data source and sex. Standard population was derived from the pooled study population with type 1 diabetes within the six data sources, with equal weights for male and female individuals. Shaded areas represent 95% CI around mortality trends. The y-axis is plotted on a natural logarithmic scale.
ESM Fig. 3 Estimated mortality rates in people with type 1 diabetes by age and period in Australia.

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of mortality rates are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. The y-axis is plotted on a natural logarithmic scale.
**ESM Fig. 4** Estimated mortality rates in people with type 1 diabetes by age and period in Denmark.

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of mortality rates are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. The $y$-axis is plotted on a natural logarithmic scale.
ESM Fig. 5 Estimated mortality rates in people with type 1 diabetes by age and period in Latvia.

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of mortality rates are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. The y-axis is plotted on a natural logarithmic scale.
ESM Fig. 6 Estimated mortality rates in people with type 1 diabetes by age and period in Scotland.

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of mortality rates are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. The y-axis is plotted on a natural logarithmic scale.
ESM Fig. 7 Estimated mortality rates in people with type 1 diabetes by age and period in Spain.

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of mortality rates are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. The y-axis is plotted on a natural logarithmic scale.
**ESM Fig. 8** Estimated mortality rates in people with type 1 diabetes by age and period in the USA (KPNW).

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of mortality rates are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific rates at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific rates at different ages, as indicated by vertical lines in the upper panels. The y-axis is plotted on a natural logarithmic scale.
ESM Fig. 9 Age by time interaction of mortality rates as estimated annual change in mortality by age.

Estimated annual change in mortality was computed from a model with calendar time trend varying by age, either by smooth splines or linearly; both plotted in each panel. The curves were derived using a spline for age (a varying coefficients model), while the straight lines using the product of age and calendar time.
**ESM Fig. 10** SMR in people with type 1 diabetes compared with those without diabetes stratified by sex.

Male individuals in full lines, female individuals in broken lines. Smoothing is based on a model with SMR constant over age. SMR, standardised mortality ratio. The y-axis is plotted on a natural logarithmic scale.
ESM Fig. 11 Estimated SMR in people with type 1 diabetes compared with those without diabetes by age and period in Australia.

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of the SMRs are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. SMR, standardised mortality ratio. The y-axis is plotted on a natural logarithmic scale.
ESM Fig. 12 Estimated SMR in people with type 1 diabetes compared with those without diabetes by age and period in Denmark.

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of the SMRs are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. SMR, standardised mortality ratio. The y-axis is plotted on a natural logarithmic scale.
ESM Fig. 13 Estimated SMR in people with type 1 diabetes compared with those without diabetes by age and period in Latvia.

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of the SMRs are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. SMR, standardised mortality ratio. The y-axis is plotted on a natural logarithmic scale.
ESM Fig. 14 Estimated SMR in people with type 1 diabetes compared with those without diabetes by age and period in Scotland.

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of the SMRs are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. SMR, standardised mortality ratio. The y-axis is plotted on a natural logarithmic scale.
ESM Fig. 15 Estimated SMR in people with type 1 diabetes compared with those without diabetes by age and period in Spain.

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of the SMRs are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. SMR, standardised mortality ratio. The y-axis is plotted on a natural logarithmic scale.
ESM Fig. 16 Estimated SMR in people with type 1 diabetes compared with those without diabetes by age and period in the USA (KPNW).

Male individuals in blue (left panels), female individuals in red (right panels). Estimates of the SMRs are from age–period–cohort models, fitted separately for male and female individuals. Upper panels show age-specific SMRs at different dates, as indicated by vertical lines in the lower panels. Lower panels show period-specific SMRs at different ages, as indicated by vertical lines in the upper panels. SMR, standardised mortality ratio. The y-axis is plotted on a natural logarithmic scale.
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