

Recent Declining Trend of Incidence Rate of Subarachnoid Hemorrhage in Shimane, Japan: The Japan Incidence of Subarachnoid Hemorrhage (JIS) Study

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Abstract

The “Izumo Study” revealed the incidence rate of subarachnoid hemorrhage (SAH) in Izumo City, Shimane Prefecture, Japan, from 1980 to 1998. However, no study has been published regarding the incidence of SAH in Shimane Prefecture after 1998. Most studies reporting the incidence of SAH in Japan have been conducted before 2000, although a few have been reported after 2000. This study aimed to assess the estimated age-adjusted incidence rate (AAIR) of SAH in Shimane Prefecture after 1998, following the Izumo Study. A retrospective study was conducted to identify the estimated AAIR of SAH in Shimane Prefecture, using the age-adjusted SAH mortality rate for this population from 1999 to 2017 and assuming that the case-fatality rate of SAH decreased by 0.7% annually from 45% in 1999 to 32.4% in 2017. We used linear regression analysis for trend to the estimated AAIR of SAH. Sensitivity analyses were also conducted by various case-fatality rates of SAH using assuming case-fatality rate based on previous reports. The estimated AAIR of SAH in Shimane Prefecture declined from 33.6 (95% confidence interval [CI]: 29.7-37.9) per 100,000 person-years in 1999, by 26.5%, to 24.7 (95% CI: 21.4-28.5) in 2017 ($p < 0.01$, $r = 0.58$). Declining trend of incidence rate of SAH in Shimane Prefecture from 1999 to 2017 was confirmed in this study.

Keywords: subarachnoid hemorrhage, register-based study, aging population, incidence

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Introduction

The crude global incidence rate of subarachnoid hemorrhage (SAH) was previously reported to be 9 per 100,000 person-years, although it varied widely according to geographic location, age, sex, race, and period.¹⁻⁴⁾ A recent meta-analysis revealed that the global incidence of SAH declined by 40% between 1980 and 2010.²⁾ However, in Japan alone, in contrast to global trends, the incidence of SAH has increased by 59.1% over the last three decades.²⁾ Almost all previous studies for the incidence of SAH in Japan were conducted with data only up to 2008.^{2,5,6)} Moreover, Ikawa and colleagues recently published a register-based study and reported that the estimated age-standardized nationwide SAH incidence rate in Japan was higher than those in other countries. However, it had declined from 31.3 (95% confidence interval [CI]: 31.3-31.3) per 100,000 person-years in 2003 to 27.6 (95% CI: 27.6-27.6) in 2015.⁷⁾ Inagawa et al.'s "Izumo Study"⁸⁻¹⁰⁾ assessed the incidence rate of SAH in Izumo City, Shimane Prefecture, Japan, prior to 1998. The age-adjusted incidence rate (AAIR) of SAH in Izumo City was as high as 23 (95% CI: 20-27) per 100,000 person-years between 1980 and 1989, and thereafter it was stable, 23 (95% CI: 20-26) between 1990 and 1998.⁸⁻¹¹⁾ This area is one of the main regions of Shimane Prefecture, known to be favorable to epidemiological surveillance owing to the existence of few large industries and relatively stable social and demographic compositions of the population. There have been few reports on the most recent incidence rate of SAH in Japan.^{12,13)} Furthermore, any recent changes in the incidence rate of SAH in the local region of Izumo City, Shimane Prefecture, have not been assessed following the Izumo Study.

Following the previous studies in Shimane Prefecture,^{8-11,14)} this study aimed to assess the estimated AAIR of SAH trends according to the age-adjusted mortality rate (AAMR) of SAH in the two decades following the Izumo Study.

Materials and Methods

Ethical statement

This study was approved as the Japan Incidence of SAH (JIS) study by the Institutional Review Board (No. R19-056; Clinical registration URL: <http://www.umin.ac.jp/icdr/index.html>; title: Japan Incidence of SAH [JIS] study; ID: UMIN 000039962; No. R000045530). Owing to the anonymous nature of the data, the requirement for informed consent by patients was waived, and an opt-out method was used as a proxy for informed consent in this study. The JIS study comprised four regions, namely, Aomori, Akita, Shimane, and Kochi Prefectures, and this study in Shimane Prefecture is the first region of the JIS study.

Patient population and data source

Shimane Prefecture is located in the western part of mainland Japan and covers a rural area of 6,708 km²; further, this prefecture is favorable for epidemiological studies because of its relatively stable population composition.^{8,9)} A retrospective study of data from the Shimane Prefecture population was performed. This included examining the number of deaths¹⁵⁾ caused by SAH and changes in the Shimane Prefecture population¹⁶⁾ using the government statistics database between 1999 and 2017. The standard population of Shimane Prefecture and Japan in 2000 was adjusted for age.¹⁶⁾

Accuracy of register-based diagnosis of SAH and mortality

According to the law of Japan, all causes of death are reported to the government office and calculated in each prefecture. In Japan, computed tomography (CT) scans were pervasive, even in rural areas, and emergent or autopsy CT scans were conducted for almost all sudden deaths. Thus, the number of deaths caused by SAH based on governmental data could be considered almost accurate.

Calculation of AAMR and AAIR of SAH

The AAMR was calculated using the number of deaths caused by SAH every 5 years in Shimane Prefecture and the population data of 5-year age groups from the Shimane Prefecture population in 2000 as standard.¹⁶⁾ Additionally, the AAMR of SAH in Shimane Prefecture was calculated using data of the entire Japanese population in 2000 as standard to allow comparisons with the Izumo Study results.

The case-fatality rate of SAH was reported to range from 32% to 45%,^{17,18)} and the Izumo Study reported that the case-fatality rate of SAH in Izumo City was 39% between 1980 and 1989 and 36% between 1990 and 1998.¹⁰⁾ Therefore, in consideration of previous reports, assuming that the case-fatality rate decreased by 0.7% annually (from 45% in 1999 to 32.4% in 2017), we estimated the AAIR of SAH from the AAMR of SAH. The formula for the estimated AAIR of SAH is: (AAMR of SAH) / (case-fatality rate of SAH). Additionally, to evaluate the accuracy of the estimated AAIR of SAH in Shimane Prefecture, we conducted sensitivity analyses by changing both the case-fatality rate of SAH and annual change in the case-fatality rate of SAH, based on a range of assumed mortality and annual change rate. We used assumed case-fatality rate of SAH in 1999 from 25% to 45% at 5% intervals and annual changes in the case-fatality rate of SAH from -1% to 1% at 0.5% intervals. As a result of sensitivity analysis, it was divided into 25 patterns.

Statistical analysis

For each year, the AAMR of SAH in Shimane Prefecture,

Table 1 Population of Shimane Prefecture, percentage of the population aged 65 years or older in Shimane Prefecture, number of deaths caused by SAH, and crude mortality rate of SAH per 100,000 person-years from 1999 to 2017

| Year | Population | | | Percentage of over 65 years | | | No. of deaths | | | Crude mortality rate of SAH | | |
|------|------------|---------|---------|-----------------------------|------|--------|---------------|------|--------|-----------------------------|------|--------|
| | All | Male | Female | All | Male | Female | All | Male | Female | All | Male | Female |
| 1999 | 764,219 | 364,818 | 399,401 | 24.3 | 20.5 | 27.7 | 113 | 34 | 79 | 14.8 | 9.3 | 19.8 |
| 2000 | 763,154 | 364,490 | 398,664 | 24.8 | 20.9 | 28.4 | 116 | 43 | 73 | 15.2 | 11.8 | 18.3 |
| 2001 | 759,693 | 362,633 | 397,060 | 25.4 | 21.4 | 29.1 | 126 | 40 | 86 | 16.6 | 11.0 | 21.7 |
| 2002 | 756,657 | 361,221 | 395,436 | 26.0 | 21.9 | 29.8 | 113 | 36 | 77 | 14.9 | 10.0 | 19.5 |
| 2003 | 753,135 | 359,274 | 393,861 | 26.4 | 22.2 | 30.2 | 99 | 35 | 64 | 13.1 | 9.7 | 16.2 |
| 2004 | 749,157 | 357,232 | 391,925 | 26.7 | 22.4 | 30.6 | 105 | 32 | 73 | 14.0 | 9.0 | 18.6 |
| 2005 | 744,380 | 354,482 | 389,898 | 27.0 | 22.6 | 30.9 | 100 | 26 | 74 | 13.4 | 7.3 | 19.0 |
| 2006 | 736,882 | 350,937 | 385,945 | 27.6 | 23.1 | 31.6 | 96 | 29 | 67 | 13.0 | 8.3 | 17.4 |
| 2007 | 731,652 | 348,437 | 383,215 | 28.1 | 23.6 | 32.1 | 105 | 28 | 77 | 14.4 | 8.0 | 20.1 |
| 2008 | 725,202 | 345,360 | 379,842 | 28.5 | 24.0 | 32.6 | 86 | 31 | 55 | 11.9 | 9.0 | 14.5 |
| 2009 | 720,112 | 343,097 | 377,015 | 28.9 | 24.4 | 33.1 | 97 | 42 | 55 | 13.5 | 12.2 | 14.6 |
| 2010 | 715,438 | 341,096 | 374,342 | 29.1 | 24.5 | 33.3 | 84 | 27 | 57 | 11.7 | 7.9 | 15.2 |
| 2011 | 712,336 | 340,587 | 371,749 | 28.9 | 24.2 | 33.1 | 109 | 34 | 75 | 15.3 | 10.0 | 20.2 |
| 2012 | 707,074 | 338,296 | 368,778 | 29.8 | 25.2 | 34.0 | 84 | 31 | 53 | 11.9 | 9.2 | 14.4 |
| 2013 | 702,237 | 336,124 | 366,113 | 30.7 | 26.2 | 34.8 | 80 | 30 | 50 | 11.4 | 8.9 | 13.7 |
| 2014 | 697,015 | 333,743 | 363,272 | 31.6 | 27.2 | 35.6 | 94 | 27 | 67 | 13.5 | 8.1 | 18.4 |
| 2015 | 691,931 | 331,601 | 360,330 | 32.3 | 28.0 | 36.3 | 75 | 35 | 40 | 10.8 | 10.6 | 11.1 |
| 2016 | 689,817 | 331,423 | 358,394 | 32.7 | 28.5 | 36.6 | 77 | 20 | 57 | 11.2 | 6.0 | 15.9 |
| 2017 | 684,668 | 329,476 | 355,192 | 33.2 | 29.0 | 37.0 | 71 | 21 | 50 | 10.4 | 6.4 | 14.1 |

SAH: subarachnoid hemorrhage

with the corresponding 95% CI, was calculated using Poisson methods.¹⁹⁾ We used linear regression analysis for trend to the estimated AAIR of SAH. All p-values were two sided, and p-values of <0.05 were considered statistically significant. All statistical analyses were performed with EasyR, a modified version of R commander (version 1.6-3) that was designed to add statistical functions²⁰⁾ to R (The R Foundation for Statistical Computing, Vienna, Austria, version 2.13.0).

Results

Analyses of the entire cohort

The population in Shimane Prefecture declined by 10.4%, from 764,291 in 1999 to 684,668 in 2017. In addition to this depopulation trend, Shimane Prefecture rapidly became an aging society, wherein 24.3% and 33.2% of the population were aged 65 years or older in 1999 and 2017, respectively. Both the number of deaths by SAH and crude mortality rate of SAH in Shimane Prefecture declined from 1999 to 2017 (Table 1).

AAMR and AAIR of SAH using the Shimane Prefecture population in 2010 as standard

Using the Shimane Prefecture population in 2000 as standard, the AAMR of SAH declined by 47.0%, regardless

of sex, from 15.1 (95% CI: 12.6-18.1) per 100,000 person-years in 1999 to 8.0 (95% CI: 6.2-10.3) in 2017. Similarly, the estimated AAIR of SAH in Shimane Prefecture declined by 26.5% from 1999 to 2017, regardless of sex. It ranged from 33.6 (95% CI: 29.7-37.9) per 100,000 person-years in 1999 to 24.7 (95% CI: 21.4-28.5) in 2017 ($p < 0.01$, $r = 0.58$), after using the assumed annual change in case-fatality rate of SAH (Fig. 1 and Table 2).

AAMR and AAIR of SAH using the entire population of Japan in 2000 as standard

Using the entire population of Japan in 2000 as standard, the AAMR of SAH in Shimane Prefecture declined by 44.4% between 1999 and 2017, regardless of sex, from 11.7 (95% CI: 11.5-11.9) per 100,000 person-years in 1999 to 6.5 (95% CI: 6.4-6.6) in 2017. Similarly, the estimated AAIR of SAH in Shimane Prefecture declined by 22.7% from 26.0 (95% CI: 25.7-26.3) per 100,000 person-years in 1999 to 20.1 (95% CI: 19.8-20.3) in 2017 (Table 3).

Sensitivity analysis

Sensitivity analyses for the estimated AAIR of SAH in Shimane Prefecture using the Shimane Prefecture population in 2000 as standard showed that 92.0% of all values declined from 1999 to 2017, except for 3 patterns, and that 60.0% of all values bottomed in 2017, except for 10 pat-

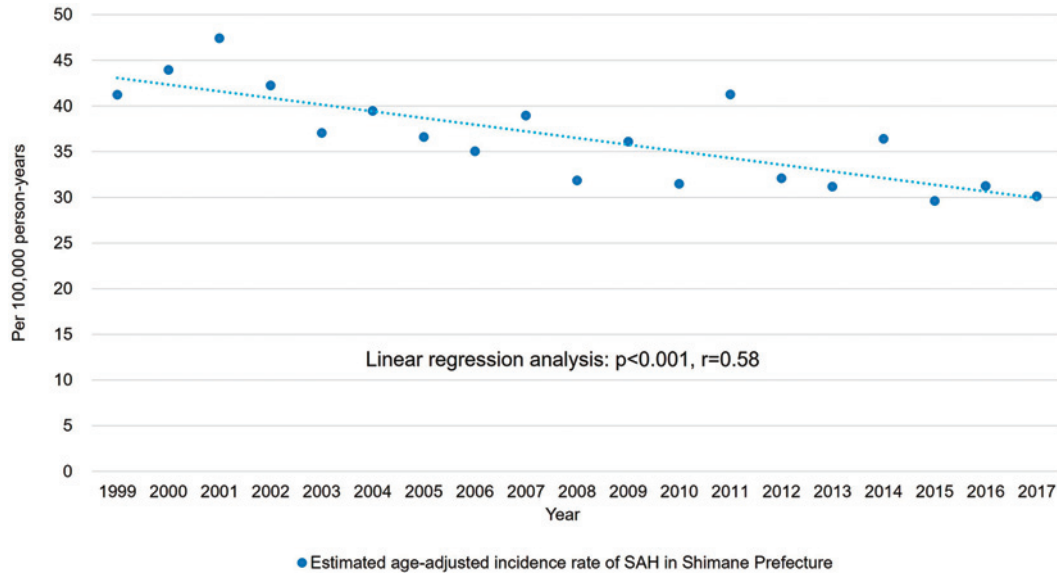


Fig. 1 Estimated age-adjusted incidence rate of subarachnoid hemorrhage in Shimane Prefecture regardless of sex from 1999 to 2017.

Table 2 Assuming case-fatality rate, age-adjusted mortality rate, and estimated age-adjusted incidence rate of subarachnoid hemorrhage in Shimane Prefecture per 100,000 person-years from 1999 to 2017 using the Shimane Prefecture population in 2000 as standard

| Year | Case-fatality rate | Age-adjusted mortality rate | | | Estimated age-adjusted incidence rate | | |
|------|--------------------|-----------------------------|-----------------|------------------|---------------------------------------|------------------|------------------|
| | | All | Male | Female | All | Male | Female |
| 1999 | 45.0 | 15.1 (12.6–18.1) | 9.4 (6.7–13.1) | 20.3 (16.4–25.3) | 33.6 (29.7–37.9) | 20.9 (16.7–26.1) | 45.1 (39.0–52.2) |
| 2000 | 44.3 | 15.2 (12.7–18.2) | 11.8 (8.8–15.9) | 18.3 (14.6–23.0) | 34.3 (30.4–38.7) | 26.6 (21.8–32.5) | 41.3 (35.5–48.1) |
| 2001 | 43.6 | 16.2 (13.6–19.3) | 10.8 (7.9–14.8) | 21.1 (17.0–26.1) | 37.2 (33.1–41.7) | 24.8 (20.2–30.4) | 48.4 (42.0–55.7) |
| 2002 | 42.9 | 14.2 (11.7–17.1) | 9.5 (6.8–13.2) | 18.4 (14.6–23.1) | 33.1 (29.3–37.4) | 22.1 (17.8–27.5) | 42.9 (36.9–49.8) |
| 2003 | 42.2 | 12.1 (9.9–14.9) | 9.0 (6.4–12.7) | 15.0 (11.6–19.3) | 28.7 (25.1–32.7) | 21.3 (17.1–26.6) | 35.5 (30.2–41.9) |
| 2004 | 41.5 | 12.5 (10.2–15.3) | 8.2 (5.8–11.7) | 16.4 (12.8–20.8) | 30.1 (26.5–34.3) | 19.8 (15.7–24.9) | 39.5 (33.8–46.2) |
| 2005 | 40.8 | 12.0 (9.7–14.7) | 6.9 (4.7–10.2) | 16.7 (13.2–21.3) | 29.4 (25.8–33.5) | 16.9 (13.2–21.7) | 40.9 (35.1–47.7) |
| 2006 | 40.1 | 11.2 (9.0–13.8) | 7.6 (5.3–11.1) | 14.5 (11.2–18.7) | 27.9 (24.4–31.9) | 19.0 (15.0–24.0) | 36.2 (30.7–42.6) |
| 2007 | 39.4 | 11.8 (9.6–14.5) | 6.9 (4.7–10.2) | 16.2 (12.7–20.6) | 29.9 (26.3–34.1) | 17.5 (13.7–22.4) | 41.1 (35.3–47.9) |
| 2008 | 38.7 | 9.5 (7.6–12.0) | 7.5 (5.1–10.9) | 11.2 (8.4–15.0) | 24.5 (21.3–28.3) | 19.4 (15.4–24.5) | 28.9 (24.1–34.7) |
| 2009 | 38.0 | 10.6 (8.6–13.2) | 10.6 (7.8–14.5) | 10.7 (7.9–14.4) | 27.9 (24.4–31.9) | 27.9 (23.0–33.9) | 28.2 (23.4–33.9) |
| 2010 | 37.3 | 9.6 (7.6–12.1) | 6.6 (4.5–9.8) | 12.4 (9.4–16.4) | 25.7 (22.4–29.6) | 17.7 (13.9–22.6) | 33.2 (28.0–39.4) |
| 2011 | 36.6 | 11.7 (9.5–14.4) | 8.4 (5.9–11.9) | 15.0 (11.6–19.3) | 32.0 (28.2–36.2) | 23.0 (18.5–28.4) | 41.0 (35.2–47.8) |
| 2012 | 35.9 | 9.1 (7.2–11.5) | 7.6 (5.2–11.0) | 10.5 (7.8–14.2) | 25.3 (22.0–29.2) | 21.2 (16.9–26.5) | 29.2 (24.4–35.1) |
| 2013 | 35.2 | 9.2 (7.3–11.7) | 8.1 (5.7–11.6) | 10.3 (7.6–14.0) | 26.1 (22.8–30.0) | 23.0 (18.6–28.5) | 29.3 (24.4–35.1) |
| 2014 | 34.5 | 10.2 (8.1–12.7) | 7.3 (5.0–10.6) | 13.1 (10.0–17.1) | 29.6 (26.0–33.7) | 21.2 (16.9–26.4) | 38.0 (32.4–44.5) |
| 2015 | 33.8 | 8.2 (6.4–10.4) | 8.8 (6.2–12.4) | 7.4 (5.2–10.6) | 24.3 (21.0–28.0) | 26.0 (21.3–31.8) | 21.9 (17.8–27.0) |
| 2016 | 33.1 | 8.3 (6.5–10.6) | 4.6 (2.9–7.4) | 11.7 (8.8–15.5) | 25.1 (21.8–28.9) | 13.9 (10.6–18.3) | 35.3 (30.0–41.7) |
| 2017 | 32.4 | 8.0 (6.2–10.3) | 5.5 (3.6–8.5) | 10.4 (7.7–14.1) | 24.7 (21.4–28.5) | 17.0 (13.2–21.8) | 32.1 (27.0–38.2) |

terns. In addition to 2017, bottom years were 2015 for five patterns, 2008 for four, and 1999 for one. The change rate of the estimated AAIR of SAH in Shimane Prefecture from 1999 to 2017 ranged from -69.2% to 90.2%, with a mean of

-34.9% (standard deviation: 36.7%) (Table 4).

Table 3 Assuming case-fatality rate, SAH mortality rate, and estimated age-adjusted incidence rate of SAH per 100,000 person-years from 1999 to 2017, using the entire population of Japan in 2000 as standard

| Year | Case-fatality rate | Age-adjusted mortality rate | | | | | | Estimated age-adjusted incidence rate | | | | | |
|------|--------------------|-----------------------------|-------------|------|-----------|--------|-------------|---------------------------------------|-------------|------|-------------|--------|-------------|
| | | All | | Male | | Female | | All | | Male | | Female | |
| 1999 | 45.0 | 11.7 | (11.5–11.9) | 7.9 | (7.7–8.1) | 15.2 | (14.9–15.5) | 26.0 | (25.7–26.3) | 17.6 | (17.2–17.9) | 33.6 | (33.3–34.2) |
| 2000 | 44.3 | 11.5 | (11.3–11.7) | 9.6 | (9.4–9.8) | 13.1 | (12.8–13.4) | 26.0 | (25.7–26.2) | 21.7 | (21.3–22.0) | 34.3 | (29.2–30.0) |
| 2001 | 43.6 | 11.8 | (11.6–12.0) | 8.4 | (8.2–8.6) | 15.1 | (14.8–15.4) | 27.1 | (26.8–27.4) | 19.3 | (18.9–19.6) | 37.2 | (34.2–35.1) |
| 2002 | 42.9 | 10.8 | (10.6–11.0) | 7.9 | (7.7–8.1) | 13.6 | (13.3–13.9) | 25.2 | (24.9–25.5) | 18.4 | (18.1–18.8) | 33.1 | (31.3–32.1) |
| 2003 | 42.2 | 9.5 | (9.3–9.7) | 7.7 | (7.5–7.9) | 11.1 | (10.8–11.4) | 22.5 | (22.3–22.8) | 18.2 | (17.9–18.6) | 28.7 | (25.9–26.7) |
| 2004 | 41.5 | 9.3 | (9.1–9.5) | 6.7 | (6.5–6.9) | 11.6 | (11.3–11.9) | 22.4 | (22.2–22.7) | 16.1 | (15.8–16.5) | 30.1 | (27.5–28.4) |
| 2005 | 40.8 | 9.1 | (8.9–9.3) | 5.6 | (5.4–5.8) | 12.4 | (12.1–12.7) | 22.3 | (22.0–22.6) | 13.7 | (13.4–14.0) | 29.4 | (30.0–30.8) |
| 2006 | 40.1 | 8.3 | (8.1–8.5) | 6.4 | (6.2–6.6) | 10.1 | (9.9–10.3) | 20.7 | (20.4–21.0) | 16.0 | (15.6–16.3) | 27.9 | (24.8–25.6) |
| 2007 | 39.4 | 8.9 | (8.7–9.1) | 5.8 | (5.6–6.0) | 11.8 | (11.5–12.1) | 22.6 | (22.3–22.9) | 14.7 | (14.4–15.0) | 29.9 | (29.5–30.4) |
| 2008 | 38.7 | 7.0 | (6.9–7.1) | 6.2 | (6.0–6.4) | 7.7 | (7.5–7.9) | 18.1 | (17.9–18.3) | 16.0 | (15.7–16.3) | 24.5 | (19.6–20.2) |
| 2009 | 38.0 | 8.4 | (8.2–8.6) | 9.2 | (9.0–9.4) | 7.6 | (7.4–7.8) | 22.1 | (21.8–22.4) | 24.2 | (23.8–24.6) | 27.9 | (19.7–20.3) |
| 2010 | 37.3 | 7.6 | (7.4–7.8) | 6.0 | (5.8–6.2) | 9.2 | (9.0–9.4) | 20.4 | (20.1–20.6) | 16.1 | (15.8–16.4) | 25.7 | (24.3–25.1) |
| 2011 | 36.6 | 8.9 | (8.7–9.1) | 7.2 | (7.0–7.4) | 10.6 | (10.4–10.9) | 24.3 | (24.0–24.6) | 19.7 | (19.3–20.0) | 32.0 | (28.6–29.4) |
| 2012 | 35.9 | 7.3 | (7.2–7.5) | 6.7 | (6.5–6.9) | 7.9 | (7.7–8.1) | 20.3 | (20.1–20.6) | 18.7 | (18.3–19.0) | 25.3 | (21.6–22.4) |
| 2013 | 35.2 | 7.4 | (7.3–7.6) | 7.0 | (6.8–7.2) | 7.7 | (7.5–7.9) | 21.0 | (20.8–21.3) | 19.9 | (19.5–20.2) | 26.1 | (21.5–22.2) |
| 2014 | 34.5 | 8.0 | (7.8–8.2) | 6.4 | (6.2–6.6) | 9.8 | (9.6–10.0) | 23.2 | (22.9–23.5) | 18.6 | (18.2–18.9) | 29.6 | (28.0–28.8) |
| 2015 | 33.8 | 6.6 | (6.5–6.7) | 7.6 | (7.4–7.8) | 5.6 | (5.4–5.8) | 19.5 | (19.3–19.8) | 22.5 | (22.1–22.9) | 24.3 | (16.3–16.9) |
| 2016 | 33.1 | 6.4 | (6.3–6.5) | 3.8 | (3.6–4.0) | 8.9 | (8.7–9.1) | 19.3 | (19.1–19.6) | 11.5 | (11.2–11.8) | 25.1 | (26.5–27.3) |
| 2017 | 32.4 | 6.5 | (6.4–6.6) | 5.0 | (4.8–5.2) | 8.0 | (7.8–8.2) | 20.1 | (19.8–20.3) | 15.4 | (15.1–15.7) | 24.7 | (24.3–25.1) |

SAH: subarachnoid hemorrhage

Discussion

Recent declining trend of AAIR after the Izumo Study

This register-based study revealed that novel results regarding the estimated AAIR of SAH in Shimane Prefecture declined by 26.5% from 33.6 (95% CI: 29.7–37.9) per 100,000 person-years in 1999 to 24.7 (95% CI: 21.4–28.5) in 2017. Therefore, the estimated AAIR of SAH in Shimane Prefecture, when combining results from the Izumo Study,^{8–10} tended to be stable as 23 per 100,000 person-years from 1980 to 1988 and afterwards showed a declining trend from 1999 to 2017. The recent declining trend of the estimated AAIR of SAH in Shimane Prefecture could be confirmed at least between 1999 and 2017, and the trends of incidence of SAH in other areas of Japan would be researched in the JIS study in the next step.

The estimated AAIR of SAH in Shimane Prefecture in this study was substantially higher than those in previous studies.^{8–10} This higher incidence rate may be attributed to the older age of the Shimane Prefecture population. The estimated AAIR of SAH was determined by the incidence rate of SAH in each 5-year age group; if the incidence rate of SAH in each 5-year age group changed drastically from that of the standard year, the estimated AAIR of SAH would change accordingly. Treatment, transport, and imaging methods of SAH were not expected to change drasti-

cally during the study period; however, the aging population accelerated in Shimane Prefecture and Japan overall. This rapidly aging population could be the reason for the remarkably higher estimated AAIR of SAH. Furthermore, because of selecting the Japanese population in 2000 as standard instead of the Shimane Prefecture population, the estimated AAIR of SAH in Shimane Prefecture during the study period could be lower value and close value to the Izumo Study standardized by the Japanese population in 1995 (Table 3). The Shimane Prefecture population was the second most aging population in Japan; therefore, the estimated AAIR of SAH in Shimane Prefecture was accordingly extremely high.¹⁶⁾

The case-fatality rate of SAH improved during the study period, although it was higher in the elderly population.^{10,17,18,21–23)} The accurate case-fatality rate in Shimane Prefecture could be calculated only by the community-based study, such as the Izumo Study, and accurate case-fatality rate was not available in the present study, which might also change each year. Therefore, the case-fatality rate in the present study was assumed in consideration of previous reports, and we conducted sensitivity analyses by changing the case-fatality rate of SAH and annual change rates to overcome this limitation. Hence, 92.0% of all values declined from 1999 to 2017, and 60.0% of all values bottomed in 2017 and 20.0% in 2015 (Table 4). Therefore,

Table 4 Sensitivity analysis of estimated age-adjusted incidence rate of SAH per 100,000 person-years using the Shimane Prefecture population in 2000 as standard year from 1999 to 2017 by the case-fatality rate of SAH and annual change in the case-fatality rate of SAH

| Case-fatality rate of SAH in 1999 | Year | Annual change of case-fatality rate per 100,000 person-years (95% confidence interval) | | | | |
|-----------------------------------|------|--|------------------|------------------|------------------|------------------|
| | | -1% | -0.5% | 0% | 0.5% | 1% |
| 45% | 1999 | 33.6 (29.7–37.9) | 33.6 (29.7–37.9) | 33.6 (29.7–37.9) | 33.6 (29.7–37.9) | 33.6 (29.7–37.9) |
| | 2017 | 29.6 (26.0–33.8) | 22.2 (19.1–25.8) | 17.8 (15.0–21.0) | 14.8 (12.3–17.8) | 12.7 (10.4–15.5) |
| Bottom year | 2008 | | 2015 | 2017 | 2017 | 2017 |
| Change rate from 1999 to 2017 (%) | | -11.9 | -33.9 | -47.0 | -56.0 | -62.2 |
| 40% | 1999 | 37.8 (33.6–42.4) | 37.8 (33.6–42.4) | 37.8 (33.6–42.4) | 37.8 (33.6–42.4) | 37.8 (33.6–42.4) |
| | 2017 | 36.4 (32.3–40.9) | 25.8 (22.4–29.7) | 20.0 (17.1–23.4) | 16.3 (13.7–19.5) | 13.8 (11.4–16.7) |
| Bottom year | 2008 | | 2015 | 2017 | 2017 | 2017 |
| Change rate from 1999 to 2017 (%) | | -3.7 | -31.7 | -47.0 | -56.9 | -63.5 |
| 35% | 1999 | 43.1 (38.7–48.1) | 43.1 (38.7–48.1) | 43.1 (38.7–48.1) | 43.1 (38.7–48.1) | 43.1 (38.7–48.1) |
| | 2017 | 47.1 (42.4–52.2) | 30.8 (27.1–35.0) | 22.9 (19.7–26.5) | 18.2 (15.4–21.5) | 15.1 (12.6–18.1) |
| Bottom year | 2008 | | 2015 | 2017 | 2017 | 2017 |
| Change rate from 1999 to 2017 (%) | | 9.3 | -28.5 | -47.0 | -57.8 | -65.0 |
| 30% | 1999 | 50.3 (45.5–55.6) | 50.3 (45.5–55.6) | 50.3 (45.5–55.6) | 50.3 (45.5–55.6) | 50.3 (45.5–55.6) |
| | 2017 | 66.7 (61.1–72.7) | 38.1 (34.0–42.7) | 26.7 (23.2–30.6) | 20.5 (17.5–24.0) | 16.7 (14.0–19.8) |
| Bottom year | 2008 | | 2015 | 2017 | 2017 | 2017 |
| Change rate from 1999 to 2017 (%) | | 32.6 | -24.3 | -47.0 | -59.2 | -66.8 |
| 25% | 1999 | 60.4 (55.1–66.2) | 60.4 (55.1–66.2) | 60.4 (55.1–66.2) | 60.4 (55.1–66.2) | 60.4 (55.1–66.2) |
| | 2017 | 114.3 (106.9–122) | 50.0 (45.2–55.3) | 32.0 (28.2–36.3) | 23.5 (20.3–27.2) | 18.6 (15.8–21.9) |
| Bottom year | 1999 | | 2015 | 2017 | 2017 | 2017 |
| Change rate from 1999 to 2017 (%) | | 90.2 | -17.2 | -47.0 | -61.1 | -69.2 |

Bottom year: bottom year of the estimated age-adjusted incidence rate of SAH between 1999 and 2017; SAH: subarachnoid hemorrhage

we could conclude that declining trend of the estimated AAIR of SAH in Shimane Prefecture from 1999 and 2017 was observed.

Limitations

Our study was limited by its retrospective register-based design. A community-based study may be desirable to assess the precise incidence rate of SAH. However, the high cost is prohibitive, and a register-based study with sensitivity analysis remains a reasonable approximation with the advantage of accounting for the entire population. Second, because the Japanese population is rapidly aging and Shimane Prefecture is one of the most rapidly aging regions, the estimated AAIR would vary according to the year selected as standard. Third, this study is limited within a relatively small geographic area in Japan.

Conclusions

The estimated AAIR of SAH in Shimane Prefecture showed a declining trend from 1999 to 2017. Further studies are warranted to evaluate the recent trend of the incidence rate of SAH at other areas in Japan.

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Conflicts of Interest Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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