Global, regional and national time trends in incidence of adverse effects of medical treatment, 1990–2019: an age–period–cohort analysis from the Global Burden of Disease 2019 study

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► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjqs-2023-016971).

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Received 29 November 2023
Accepted 1 May 2024

To cite: Lin L. *BMJ Qual Saf* Epub ahead of print: [please include Day Month Year]. doi:10.1136/bmjqs-2023-016971

ABSTRACT

Background Current adverse effects of medical treatment (AEMT) incidence estimates rely on limited record reviews and underreporting surveillance systems. This study evaluated global and national longitudinal patterns in AEMT incidence from 1990 to 2019 using the Global Burden of Disease (GBD) framework.

Methods AEMT was defined as harm resulting from a procedure, treatment or other contact with the healthcare system. The overall crude incidence rate, age-standardised incidence rate and their changes over time were analysed to evaluate temporal trends. Data were stratified by sociodemographic index (SDI) quintiles, age groups and sex to address heterogeneity across and within nations. An age–period–cohort model framework was used to differentiate the contributions of age, period and cohort effects on AEMT incidence changes. The model estimated overall and age-specific annual percentage changes in incidence rates.

Findings Although the global population increased 44.6% from 1990 to 2019, AEMT incidents rose faster by 59.3%. The net drift in the global incidence rate was 0.631% per year. The proportion of all cases accounted for by older adults and the incidence rate among older adults increased globally. The high SDI region had much higher and increasing incidence rates versus declining rates in lower SDI regions. The age effects showed that in the high SDI region, the incidence rate is higher among older adults. Globally, the period effect showed a rising incidence of risk after 2002. Lower SDI regions exhibited a significant increase in incidence risk after 2012. Globally, the cohort effect showed a continually increasing incidence risk across sequential birth cohorts from 1900 to 1950.

Conclusion As the global population ageing intensifies alongside the increasing quantity of healthcare services provided, measures need to be taken to address the continuously rising burden of AEMT among the older population.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Traditional methods for estimating adverse events from medical treatment (AEMT) incidence rates have limitations, such as under-reporting and low sensitivity, with scarce information from low-income and developing countries. Directly comparing cross-sectional estimates of AEMT incidence rates between countries in early studies is prone to problems arising from heterogeneous data sources or inherent risks within each country's healthcare delivery system.

WHAT THIS STUDY ADDS

⇒ This study uses a systematic, globally consistent method to accurately quantify AEMT incidence rates, addressing heterogeneity using sociodemographic index, age and sex, and using an age–period–cohort model framework to differentiate the contributions of age, period and cohort effects on AEMT incidence rate changes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study identifies high-risk subgroups and time intervals among the 204 nations, providing information for prioritising resources and implementing targeted preventive strategies for AEMT, and emphasises the importance of enhancing optimising geriatric medical management to reduce iatrogenic harm.

INTRODUCTION

Adverse effects of medical treatment (AEMT) and patient safety have become pressing public health concerns worldwide. AEMT refers to any harm resulting

from medical management rather than an underlying disease process.[1 2] In developed countries, over 50% of adverse events among hospitalised patients are deemed preventable, while in developing countries an even higher proportion of 83% of adverse events is judged to be highly preventable.[3] Mortality from AEMT is substantial in both developed and developing countries. In the USA, AEMT represents the third leading cause of death,[4] while in Egypt it ranks the fifth leading cause of mortality.[3] For patients, AEMT poses grave threats to health and life, resulting in detrimental impacts on quality of life and financial hardship.[5 6] At the healthcare system level, AEMT increases costs and erodes public trust.[7] Societally, AEMT represents lost productivity and uses resources that could potentially be allocated elsewhere.[8–10]

Current estimates of AEMT rely primarily on point estimates of medical harm derived from resource-intensive medical record reviews using retrospective surveillance systems,[11–14] including retrospective chart reviews of medical records,[15] which can reduce under-reporting and improve sensitivity but are resource-consuming and time-consuming. Other methods include voluntary reporting systems beset by under-reporting[16–19] or databases with limited detection sensitivity.[20–23] All of these have limitations. A systematic, globally consistent methodology is imperative to accurately quantify AEMT incidence and inform health policy priorities.

The Global Burden of Disease (GBD) study is the most comprehensive source of comparable information on the levels and trends of health loss due to all diseases and injuries worldwide. However, previous GBD research related to AEMT has only studied the USA[24] and the UK,[25] with scarce information from low-income and developing countries. Critically, we first adopt an innovative age–period–cohort (APC) modelling approach to quantify the contributions of age, secular trends and birth cohort effects to AEMT incidence rates. Our aim was to analyse longitudinal patterns in AEMT incidence rates over 30 years globally and nationally, employing the GBD framework across 204 nations categorised by their sociodemographic index (SDI) to address heterogeneity across nations.

METHODS

Data source

The data used in this study were from the public datasets of GBD 2019.[26] In GBD 2019, the definition of AEMT was harm as the result of undergoing a procedure, treatment or other contact with the healthcare system where this contact could be as an inpatient, outpatient, emergency care or during home treatment. In the GBD 2019 study, the International Classification of Diseases (ICD) codes mapped to AEMT included ICD-10 codes N30.4, Y40–Y84.9, Y88–Y88.3 and ICD-9 codes 349.0–349.1, 457.0, E870–E876, E878–E879, E930–E949.[27] The specific diseases or events corresponding to the ICD codes for AEMT have been published elsewhere.[24] The analytic unit was country. Obtained from GBD 2019 were AEMT incidence data for 204 countries and territories, stratified by age (0–94 years old), sex (female, male) and year (from 1990 to 2019). Countries were grouped into quintiles by SDI, a composite of income, education and fertility, to categorise countries into quintiles indicating socioeconomic development.[28] Based on 2019 SDIs, countries fell into high SDI (>0.81), high-middle SDI (0.70–0.81), middle SDI (0.61–0.69), low-middle SDI (0.46–0.60) and low SDI (<0.46).[27] Incidence rate was quantified as the annual number of new cases divided by the mid-year population size. The global population age distribution from GBD 2019 standardised incidence rates per 100 000 person-years. GATHER checklist was completed (online supplemental table 1).[29]

The GBD 2019 study obtained AEMT incidence data from a variety of sources, including 21 735 administrative systems that collect vital events data (vital registration sites), 825 sample-based surveillance systems (vital registration—sample sites) and 187 sites that use verbal autopsy methods to determine causes of death. These data, which cover a majority of countries globally, were derived from a mix of government records, health facility reports, sample surveys and other sources. However, some countries, especially in Africa, lacked primary data on AEMT incidence rates.[27] To address these gaps and biases, the GBD study employed data adjustments and modelling techniques. Specifically, GBD employed DisMod-MR, a Bayesian meta-regression tool, to analyse available data on incidence, prevalence, remission and mortality rates while enforcing internal consistency. This modelling approach leveraged all available quality data across time, age, geography and diseases within a Bayesian framework. This enabled generating estimates for countries lacking primary data by 'borrowing' information from reference countries and cohorts.[27] All estimates were presented with 95% uncertainty intervals obtained via repeated sampling 1000 times. Countries with limited or no primary data had larger 95% uncertainty intervals, indicating potentially lower estimate accuracy.

Analysis of overall temporal trends in AEMT incidence

The primary outcome was the temporal trends in the incidence of AEMT during 1990–2019 in this study, which used three indicators. The overall crude incidence rate (all-age incidence rate) reflected the total change, while the age-standardised incidence rate controlled for the effects of different population age structures. The percentage change in incidence rate (net drift estimated by the APC model) from 1990 to 2019 illustrated the relative change between different periods.

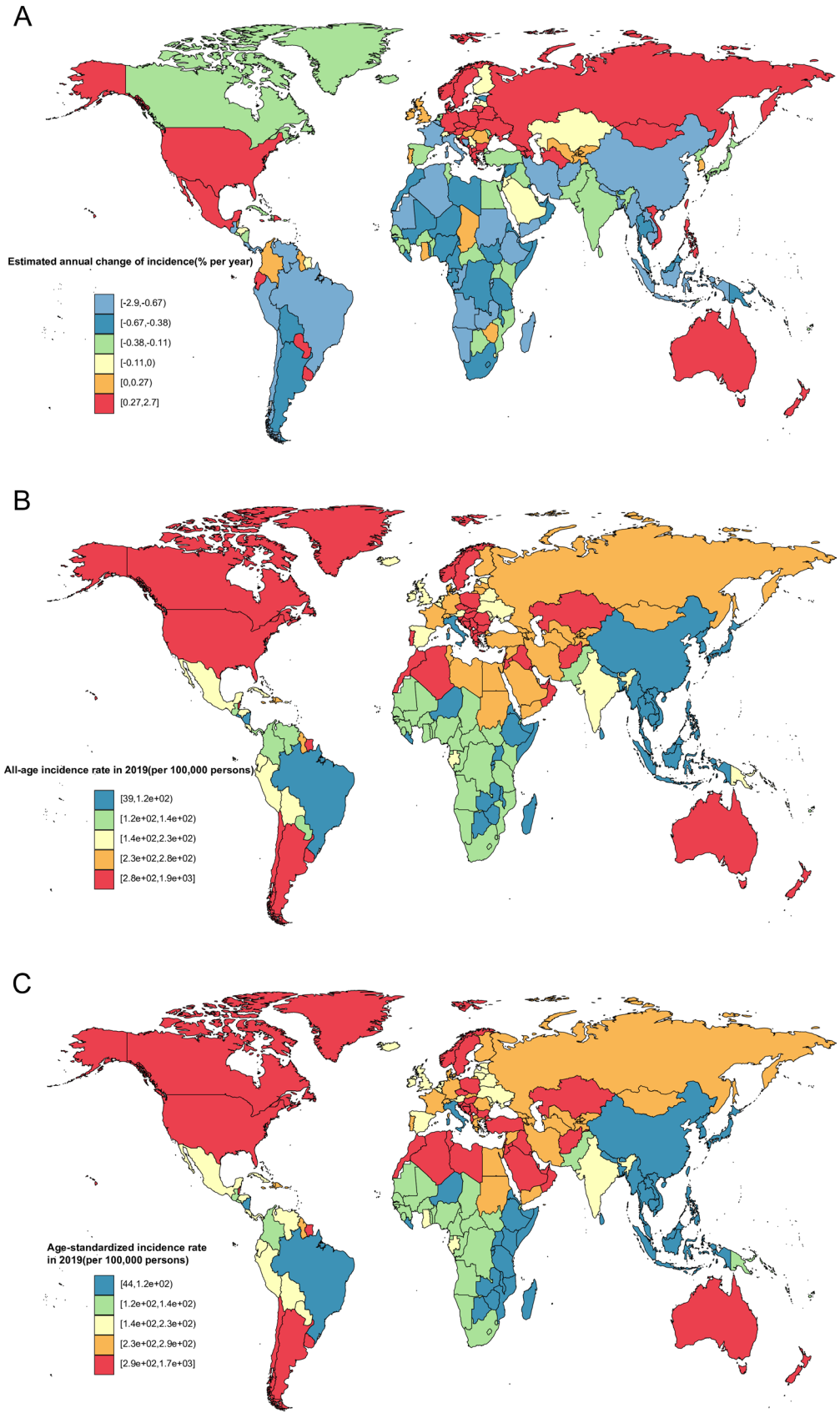

Figure 1 The net drift during 1990–2019, the all-age incidence rate in 2019 and age-standardised incidence rate in 2019 for AEMT in 204 countries and territories. (A) World map of net drifts for AEMT incidence rate. Net drift captures components of the trends attributable to calendar time and successive birth cohorts. The global net drift of AEMT incidence rate was 0.631% (95 CI: 0.493%, 0.77%). (B) World map of all-age incidence rate for AEMT in 2019. The global all-age incidence rate was 211.09 (95% UI: 172.48, 255.91) per 100 000 population. (C) World map of age-standardised incidence rate for AEMT in 2019. The global all-age incidence rate was 223.56 (95% UI: 186.25, 265) per 100 000 population. AEMT, adverse effects of medical treatment.

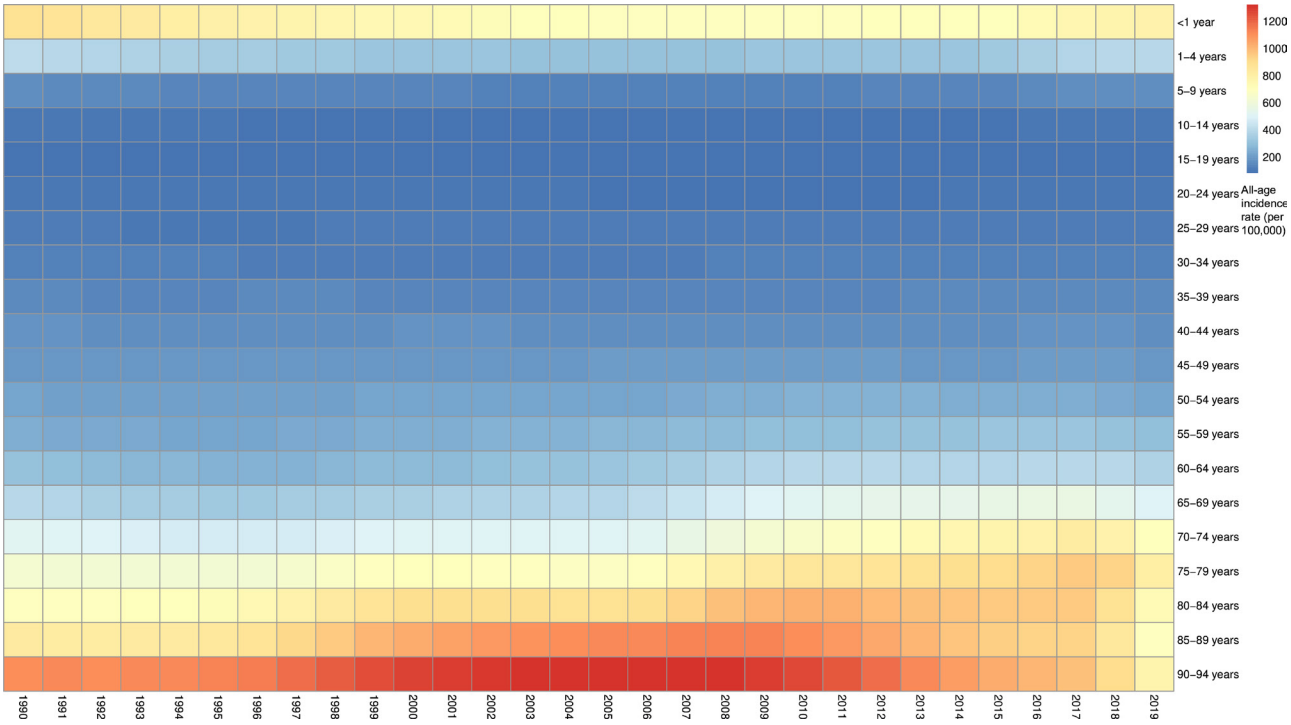

Figure 2 Heatmap displaying the global all-age incidence rate (per 100 000) of adverse effects of medical treatment. The heatmap displays the all-age incidence rates of adverse effects of medical treatment across different periods. The colour gradient ranges from blue (lowest incidence rate) to red (highest incidence rate), indicating the increasing incidence of adverse effects. The x-axis represents the years from 1990 to 2019, and the y-axis represents the age groups from 0 to 94 years.

The secondary outcome was the time trends in AEMT incidence rates stratified by SDI, age groups and sex to address heterogeneity across and within nations. Global maps of incidence rates portrayed the spatial trends. We further calculated the proportions of incidence across seven age groups (<1 year, 1–4 years, 5–9 years, 10–24 years, 25–49 years, 50–74 years and 75–94 years) to examine the age distribution of AEMT cases.

APC modelling analysis of incidence data

Another secondary outcome was the time trends in AEMT incidence rates using the APC model framework to analyse. Unlike traditional epidemiological approaches, the APC model can differentiate the contributions of age, period and cohort effects to changes in AEMT incidence. The biological and maturational age effects reflect developmental changes over the life cycle. The historical period effects capture the influence of external time-specific events like healthcare reforms. The social cohort effects represent the imprint of formative experiences shared by individuals born in the same period.[30] To address the identification problem resulting from the linear relationship among age, period and cohort in conventional APC models, the intrinsic estimator method was applied, which constructed a set of statistically independent functions and enabled reliable inference across the three time dimensions.[31]

This study utilised AEMT incidence data from the GBD 1990–2019 as inputs for the APC model. Per APC model requirements, the population was divided into 5-year age groups, and incidence and population counts from the mid-years of 6 time points (eg, (1992) 1990–1994, (1997) 1995–1999) were used as data inputs to represent specific periods. Specifically, the input data consisted of 19 age groups (0–4 to 90–94) and 21 partially overlapping 10-year birth cohorts ((1900) 1896–1904 to (2015) 2011–2019), referenced by mid-birth year. A Lexis diagram of GBD data for the APC model is presented in online supplemental table 2.

After fitting the APC model, temporal trends in AEMT incidence were estimated, including net drift and local drifts. Net drift reflected overall annual percentage change, while local drift reflected annual percentage changes within each age group. Wald χ^2 tests determined the statistical significance of parameter estimates. APC model outputs also included longitudinal age-specific incidence rates in the reference cohort, adjusted for period deviations to reflect age impacts. Also estimated were relative incidence risks across periods and cohorts, expressed as ratios of incidence rates in a given period/cohort over reference levels, after adjusting for age effects and non-linear period/cohort effects to reveal period and cohort influences. Relative risks above 1 indicated higher incidence risk in that period/cohort, while below 1

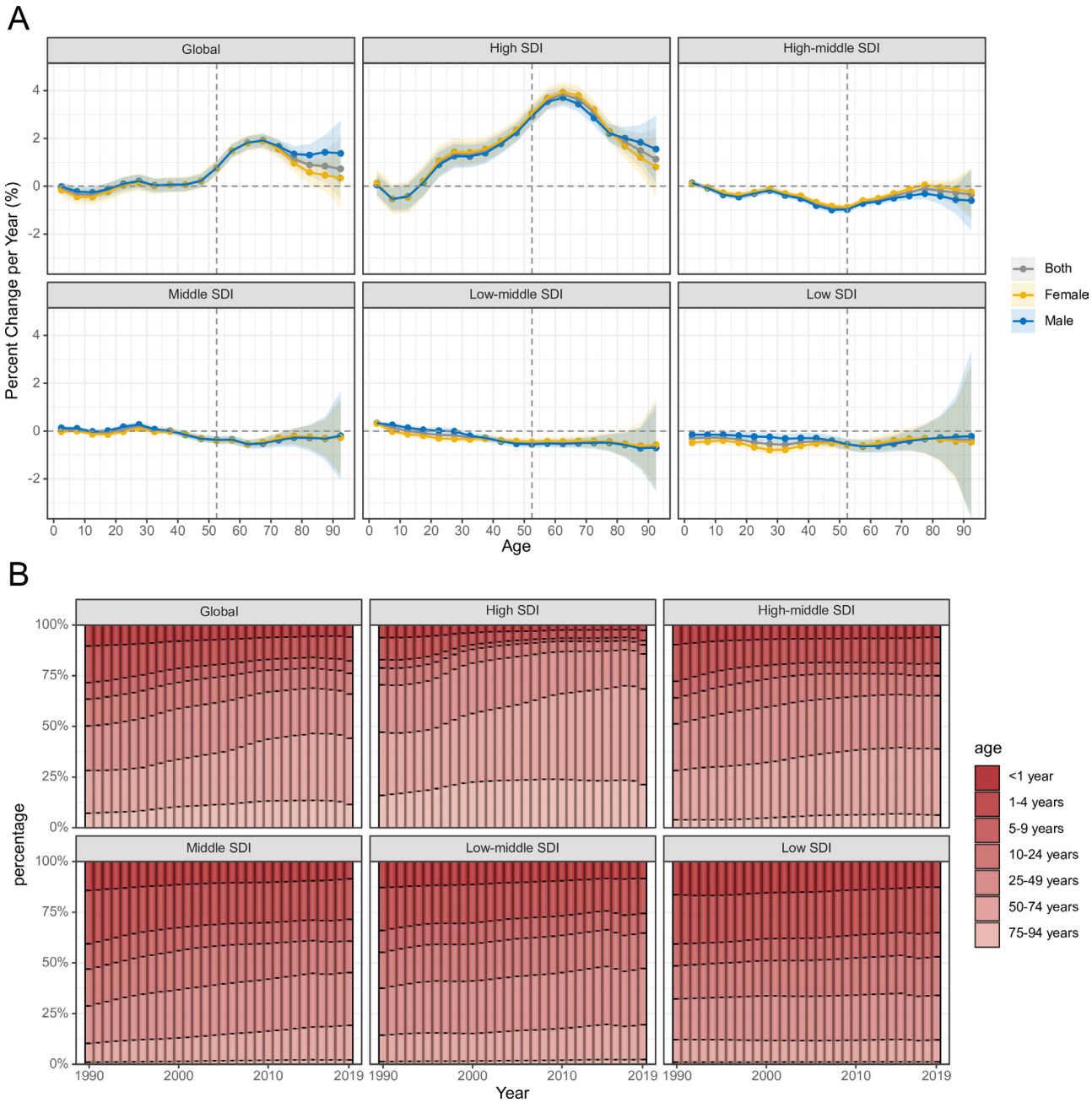

Figure 3 Local drifts of incidence rate and age distribution of cases by SDI quintiles, 1990–2019. (A) Local drifts of AEMT incidence rate (estimates from age–period–cohort models) for 19 age groups (0–4 to 90–94 years), 1990–2019. The dots and shaded areas indicate the annual percentage change of incidence rate (% per year) and the corresponding 95% CIs. (B) Temporal change in the relative proportion of AEMT cases across age groups (<1, 1–4, 5–9, 10–24, 25–49, 50–74, 75–94 years), 1990–2019. AEMT, adverse effects of medical treatment; SDI, sociodemographic index.

indicated lower risk. The APC analysis for this study used the APC Web Tool from the US National Cancer Institute.[32] All graphics were generated using R statistical software (V.4.3.1.).

RESULTS

Primary outcomes—global time trends of incidence rate of AEMT, 1990–2019

Population, total number of cases, all-age incidence rate, age-standardised incidence rate and net drift of incidence rate are presented in online supplemental table 3,4, figures 1,2. The global population has increased 44.6% from 1990 to 2019. Over the same period, AEMT cases have risen 59.3% from 11.3 million (9.2–13.7) to 18.0 million (15.0–21.3). The all-age AEMT incidence rate was 232.5 (193.8–275.3) per 100 000 in 2019, representing a 10.1% (3.9%–17.7%) increase since 1990, primarily observed among the older population (online supplemental table 2 and figure 2). The age-standardised incidence rate was 233.3 (193.6–277.6) per 100 000 in 2019, a 4.4% (1.9%–7.1%) increase over the 1990 rate. Using the APC model, the estimated global net drift in AEMT incidence rate was

0.631% per year (95% CI: 0.493, 0.77) from 1990 to 2019 (online supplemental table 3).

Secondary outcomes—time trends in AEMT incidence rate across different SDI and age groups

Regionally, the all-age incidence rate for AEMT in the high SDI region increased from 515.04 per 100 000 in 1990 to 822.73 per 100 000 in 2019, representing an increase of 59.74%. The age-standardised incidence rate increased from 501.76 to 647.57 per 100 000, an increase of 29.06%. The net drift estimated by the APC model was 2.009%, with all three indicators showing the highest incidence rates and growth among all regions. In contrast, except for the increase in per cent change of age-standardised incidence rate in low-middle SDI regions, the three indicators showed declining trends in the other four regions. The most pronounced decrease was observed in low SDI regions, where the all-age incidence rate decreased by 13.8% from 154.69 to 140.61 per 100 000, and the age-standardised incidence rate decreased by 10.11% from 146.68 to 138.4 per 100 000. The net drift was −0.462% in low SDI regions (online supplemental table 3). East Asia, Southeast Asia and East Africa exhibited relatively lower net drift, all-age incidence rates and age-standardised incidence rates (figure 1A−C).

Figure 3A shows the annual percentage change in AEMT incidence rate for each age group. Globally, before age 45–49 years, AEMT incidence remained largely unchanged across age bands. However, those aged 50–94 years exhibited increasing global trends, with the 65-year to 69-year age group having the steepest global rise of approximately 2% per year. Globally, men aged 80–94 years saw a greater increase in AEMT incidence versus females. In the high SDI region, apart from the 5–14 years group which declined, all other age groups rose, peaking at around 4% per year for 60–64 years. The remaining four regions showed relatively analogous patterns, with mostly unchanging or mildly declining AEMT incidence rates across age groups. The high-middle SDI region had the maximum decline of about 1% per year in the 50–54 years age bracket. Country-specific local drifts in incidence rates are exhibited in online supplemental figure 1.

Figure 3B illustrates the temporal shifts in the age distribution of AEMT cases. Globally, the proportion of cases in the 50-year to 74-year and 75-year to 94-year age groups increased, while those aged <1 year, 1–4 years, 5–9 years and 10–24 years declined. However, in 2019, the 0–4 years age bracket still accounted for over 17.5%. From 1990 to 2019, all five SDI regions showed analogous patterns to the global trends, with decreasing proportions in age groups <24 years and increases in those >50 years. This tendency became more pronounced with transitions from low to high SDI regions. Examining just 2019, moving from low to high SDI settings, the proportion of cases in the <1-year, 1-year to 4-year and 5-year to 9-year groups gradually diminished, while the 50–74 and 75–94 years proportions steadily rose. The country-specific age distribution of cases is displayed in online supplemental figure 2.

Tertiary outcomes—APC effects on AEMT incidence rate

Figure 4 illustrates the estimates of APC effects stratified by SDI quintile. Globally and in all five SDI regions, the 0–4 age group had a slightly higher incidence rate, around 600 per 100 000 population. In the high SDI region, the incidence rate increased markedly from the 20–24 age group, peaking at 90–94 years. From 70 years onwards, the male incidence rate was higher than the female incidence rate. In the other four SDI regions, the incidence rates were comparatively low across all age groups. Globally, the incidence rates in the 60–94 age groups were influenced by the high incidence rates in the high SDI region and also showed significant increases (figure 4A).

In the high SDI region, the period effect showed a significant rise in incidence risk from 1990 to 2015, which was brought under control from 2015 to 2019. The other four SDI regions exhibited similar trend patterns, with declining incidence risk from 1990 to 2015 but slight increases from 2015 to 2019. Across almost all periods, globally and in high, middle, middle-low and low SDI regions, the relative risk was lower in females than in males. In the high-middle SDI region after 2002, the female risk exceeded the male risk. Globally, the period effect was heavily influenced by the high SDI region, with relative risk rising after 2002 (figure 4B).

Globally, the cohort effect showed an increasing incidence risk between the 1900 and 1950 birth cohorts, with little change thereafter. In the high SDI region, the incidence risk started rising from the 1900 birth cohort, peaking around 1990 then decreasing somewhat, before gradually increasing again from birth cohorts after 2000. The other four SDI regions exhibited similar trends, with a very gradual decline in incidence risk across the 1900–2019 birth cohorts (figure 4C).

Quaternary outcomes—APC effects in exemplary countries

The graphs for the same country in online supplemental figures 1–5 can be combined and analysed in a manner similar to online supplemental figure 6 for all 204 countries. Online supplemental figure 6 shows exemplar countries from different SDI quintiles to illustrate the key trends in AEMT incidence rates when analysed by APC effects across the globe. Exemplar countries with favourable APC effects were exhibited in online supplemental figure 6A, signifying reduced AEMT risk. Those with unfavourable effects are shown in online supplemental figure 6B.

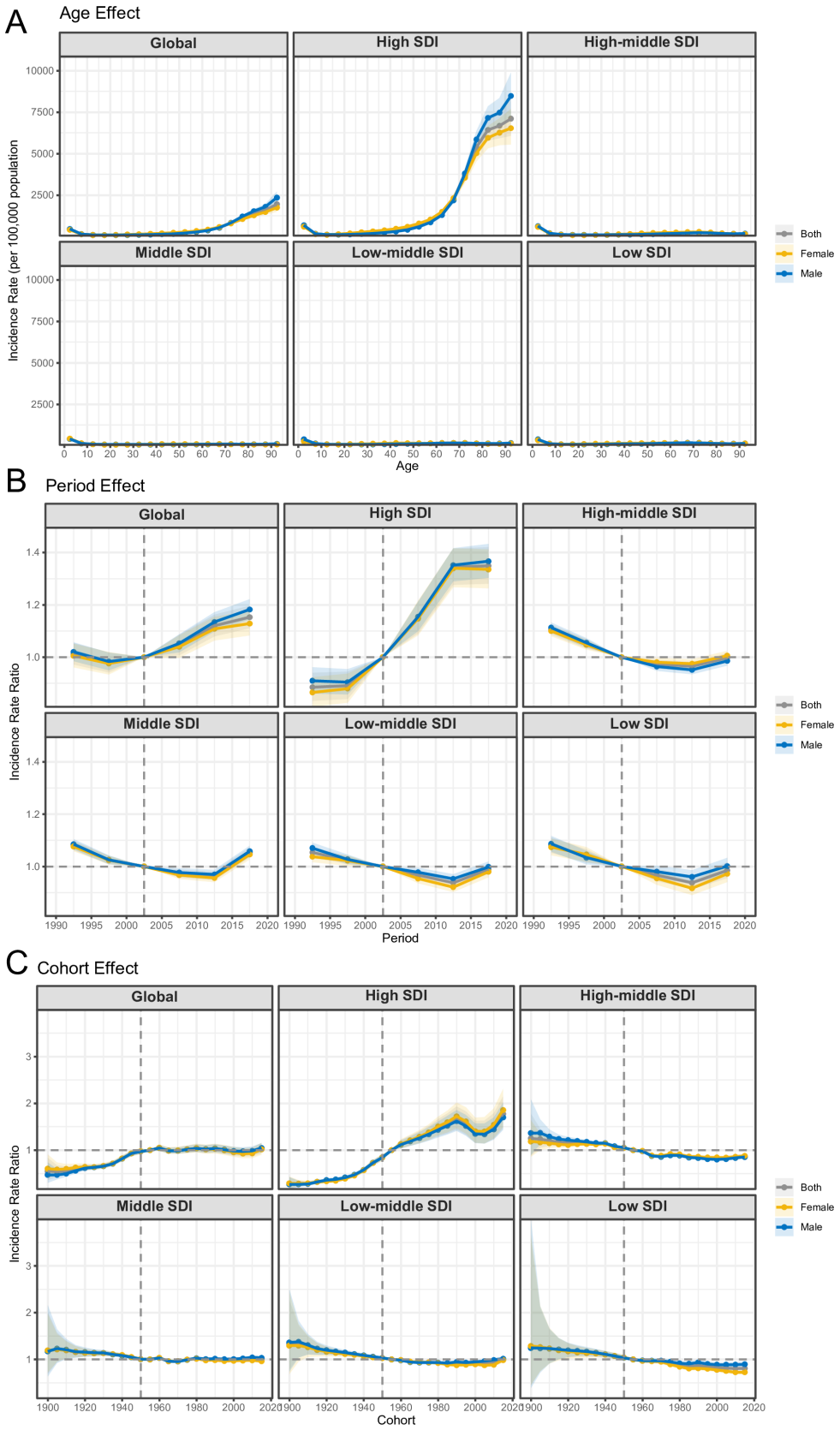

Figure 4 Age, period and cohort effects on AEMT incidence rate by SDI quintiles. (A) Age effects are shown by the fitted longitudinal age curves of incidence rate (per 100 000 person-years) adjusted for period deviations. (B) Period effects are shown by the relative risk of incidence rate (incidence rate ratio) and computed as the ratio of age-specific rates from 1990 to 1994 to 2015–2019, with the referent cohort set at 2000–2004. (C) Cohort effects are shown by the relative risk of incidence rate and computed as the ratio of age-specific rates from the 1900 cohort to the 2015 cohort, with the referent cohort set at 1950. The dots and shaded areas denote incidence rates or rate ratios and their corresponding 95% CIs. AEMT, adverse effects of medical treatment; SDI, sociodemographic index.

DISCUSSION

We used the 2019 GBD dataset to shed additional novel data on the global understanding of the importance of measuring adverse effects of healthcare treatment. We found that although policies that prioritise patient safety have been implemented,[33] the total number of AEMT incidents substantially increased by 59.3%, outpacing the 44.6% growth in population over the same period. This finding was seen mostly in older adults. In the high SDI region, incidence rates and APC effects exhibited upward trends concentrated among the old adult population. In lower SDI regions, the period risk exhibited a significant upward trend starting from 2012, and the proportion of cases among the older population increased. As population age and medical services expand with socio-economic development, addressing AEMT incidents becomes a universal imperative to safeguard patient well-being and ensure equitable access to quality healthcare.

The incidence rates of AEMT in high SDI countries demonstrate aging-associated onset, rising APC effects, contrasting with more stable or declining rates, lower proportions of old adult cases and higher proportions of childhood cases in lower SDI countries. There are several possible reasons for the higher AEMT incidence rates in high SDI countries versus other SDI countries: (1) First and foremost, the occurrence of AEMT is closely related to the amount of healthcare services provided. Countries with lower healthcare utilisation tend to have lower AEMT incidence. Healthcare expenditure is significantly positively correlated with GDP.[34] For example, according to the study's findings, the USA has about 50 times higher incidence of AEMT at all ages compared with Indonesia. However, a comparison of the healthcare delivery systems of the two countries based on 2019 OECD data shows that the USA has about three times as many hospital beds per 1000 citizens as Indonesia, and the USA has about 30 times as much healthcare expenditure per capita as Indonesia.[35] As the number of hospital beds and the expenditure of healthcare increases, the quantity and quality of healthcare provided to the population increases as well, consequently leading to increased reporting of AEMT. Therefore, simple comparisons between countries (especially between countries with different SDIs) are inappropriate. We must acknowledge worldwide heterogeneity in healthcare access and the volume of inpatient stays or care provided to populations across different countries. Higher AEMT incidence rates may reflect greater and more equitable population access to healthcare, not just poor quality or overtreatment. (2) Previous studies analysing seven common adverse events using inpatient data found that in high-income countries, the most prevalent type was adverse drug events, occurring at a rate of 5.0% (CI 2.7% to 7.2%), indicating five cases of adverse drug events per 100 hospital admissions, while the rate in low-income and middle-income countries was 2.9% (0.6% to 5.2%).[36] More advanced medical technologies in developed countries enable faster clinical trials and product launches, leading to more adverse drug effects, while developing countries have slower innovation uptake and fewer effects due to outdated systems.[37] High SDI countries experience more pronounced ageing. The larger older adult populations in developed countries are more susceptible to adverse drug reactions, unlike the younger populations in developing countries.[38–40] (3) Developed countries have more robust AEMT management and surveillance systems, whereas those in low-income and middle-income countries are often inadequate, resulting in data gaps.[3]

It is noteworthy that the six countries with unfavourable trends universally had a high older adult incidence of AEMT (online supplemental figure 6B). The USA, as a representative high SDI country with unfavourable trends, has seen substantial increases in incidence and proportion of disease burden among older adults. This relates to shifts in the societal age structure, as the baby boomer generation ages into older adulthood, currently aged 57–75 years, leading to rapid growth of the older adult population. Sweden, Croatia, Jamaica, the Dominican Republic and Haiti as countries with unfavourable trends across varying SDI levels face similar issues of rising older adult incidence and proportion of AEMT. The older adult proportion and incidence rates, as well as local drift, increase from low to high SDI. Therefore, countries with higher SDI should pay more attention to the significant impact of AEMT on older adults with multiple chronic conditions and associated geriatric syndromes. This susceptibility arises from age-related physiological changes affecting drug metabolism and clearance, multimorbidity and polypharmacy heightening drug–drug interaction risks, declines in cognitive and functional status reducing medication adherence and compounding effects of concurrent geriatric impairments like sensory deficits, malnutrition and mobility limitations.[39 40] This confluence of factors renders appropriate medication management exponentially more challenging in advanced-age populations with complex comorbidities. Old adults aged 65 and above, due to three risk factors—compromised host defenses, lifestyle considerations and living arrangements—become a well-defined population at increased risk for hospital infections and other healthcare-associated infections.[41] The 1.5 to 1.8 million residents in US nursing homes exemplify this vulnerable population.[42] A UK-based study also found that two-thirds of care home residents were exposed to one or more medication errors.[43]

In contrast, the seven countries with favourable trends all displayed a high AEMT incidence in infants and young children—indicative of a substantial age effect (online supplemental figure 6A). France was the country with the most significant declining incidence

risk among high SDI countries. France exhibited declining trends in AEMT incidence rates across all age groups, with the steepest decline in the 50–70 years group. This seems to be related to a series of patient safety policies and measures implemented in France: in 2006, France joined the WHO high 5s initiative and participated in multiple EC patient safety projects. France also spearheaded the European Network for Patient Safety project. From 2004 to 2009, French healthcare institutions devised measures to enhance patient safety.[44] Specifically, these encompassed: the adoption of proven foreign practices such as surgical checklists; improved transparency on error reporting via piloting a novel national adverse event reporting system; emphasis on clinical governance; establishment of safety metrics and early warning systems for front-line staff[45 46]; adoption of continuity of care beyond an in-hospital perspective; attention to frequent errors beyond publicly reported events; holistic medication management focusing on disease control rather than individual errors.[47] Neighbouring Italy exhibited the most pronounced favourable trends among high-middle SDI countries, with over 5% decline in the 0–20 years groups, representing the fastest decreasing incidence rates globally. However, incidence became concentrated in the 50+ years older adult groups, with almost no reduction in the 75–94 years brackets. The period risk mainly declined during 1990–2000. Other EU countries like Luxembourg, Belgium and Estonia also showed some decreasing incidence rates. Notably, similar to Italy, the period risk in these countries also declined during 1990–2000 but remained unchanged or slightly increased during 2000–2019. This could be attributed to various factors like improved medical standards, medical device regulation in the EU during 1990–2000.[48] Differences in approved medication lists between the USA and European countries may also be one reason.[37] According to Aged in Home Care (AdHOC) project (2000–2003), several potentially inappropriate medications for older adults were not approved in AdHOC European countries.[37] Nearly half of the medications on the inappropriate use list were not approved in most European countries.[37] Previous studies have documented slightly lower rates of inappropriate drug use in some European countries compared with the USA.[37] According to online supplemental figure 6, Brazil in Latin America displayed the most pronounced declining incidence trend among older adults, reflecting major progress in the quality of geriatric healthcare. Control of period effects after 2002 also evidenced policy impacts. Similar patterns occurred in Guatemala and Venezuela, other Latin American low-middle SDI countries, also with sharply declining older adult incidence. The policy focus on geriatric care within health system reforms in Latin America warrants attention. Among middle SDI Asian countries, Indonesia in Southeast Asia, China in East Asia and Iran in Western Asia exhibited analogous declining incidence trends. However, incidence declines were less remarkable in infants/children and older adults. The 0–5 age group comprised a relatively large share of incidence distribution by age. Similarities occurred for most low SDI African countries like Rwanda indicating continued efforts needed to advance paediatric and geriatric medicine in these countries.

Strengths

The study's use of overall and age-standardised incidence rates, as well as the net drift of incidence rate (estimated by APC model), provides a more comprehensive quantification of the burden of disease. Additionally, the estimation of local drift values enables the capture of time trends in incidence rates for each age group, adjusted for cyclical impacts. By linking AEMT data to SDI, the study addresses global and within-country heterogeneity based on SDI levels and population age. Furthermore, distinguishing the independent contributions of age, period and cohort effects to changes in AEMT incidence rates facilitates longitudinal insights into potential drivers of incidence rate changes. This approach reveals the contributions of age-related biological factors as well as technological and societal factors to disease trends, transcending traditional epidemiological analyses.[49]

Limitations

The research methodology employed in this study has some limitations. First, many lower SDI countries lack reliable original data on the AEMT, which may lead to bias in the results. The incidence estimates driven by covariates in these countries rely on model predictions and still have great uncertainty. This may affect the estimation of age/period/cohort trends and potentially underestimate the severity in some low SDI countries. Second, due to data limitations in the GBD study, this study only evaluated the overall incidence of AEMT, without conducting a secondary classification analysis of the types of adverse reactions. This made it impossible to identify the types of reactions that need key attention in each country. The incidence trends of different types of adverse reactions may differ, which needs further in-depth research.

CONCLUSION

In conclusion, globally, the increase in AEMT incidence outpaced population growth from 1990 to 2019, with rising old adult proportion. The high SDI region exhibited rising incidence rates and APC effects for AEMT concentrated among the old adult population. While lower SDI regions exhibited a significant increase in period risk after 2012 and the proportion of cases among the older population increased. Improvements in AEMT monitoring and reporting are imperative to obtain more accurate burden estimates, particularly for lower SDI countries. As the global

population ageing advances alongside the increasing quantity of healthcare services provided, measures need to be taken to address the continuously rising burden of AEMT among the older population.

Contributors L-QL conceived the study, accessed and acquired the raw data, performed the primary analysis, prepared tables and figures, drafted the first manuscript, interpreted the data, critically reviewed and edited the manuscript. L-QL is responsible for the overall content as guarantor.

Funding The author has not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants but the GBD study uses deidentified data aggregated by the Institute for Health Metrics and Evaluation, University of Washington. Thus, informed consent was waived per the approval of the University of Washington Institutional Review Board. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. All data used in this study can be freely accessed at the GBD 2019 portal (http://ghdx.healthdata.org/gbd2019).

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