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Original Article

Global Burden of the Adverse Effects of Medical Treatment From 1990 to 2021

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Abstract

Background: The adverse effects of medical treatment (AEMT) are unintentional injuries that occur during medical procedures and can cause significant harm, disability, and even death. AEMTs represent a global healthcare challenge with varying regional impacts. This study aimed to assess the global burden of AEMTs from 1990 to 2021 using data from the Global Burden of Disease (GBD) Study 2021.

Methods: Data from the GBD 2021 study were analyzed, and the results were reported as numbers and age-standardized rates (ASR).

Results: In 2021, the worldwide burden of AEMT was calculated to be 12.5 million incident cases (ASR: 150.4 per 100 000), marking a 5.3% decrease since 1990. AEMT-related deaths in 2021 totaled 122,330 (ASR: 1.5 per 100 000), reflecting a 36.1% reduction since 1990. The incidence rate was the highest in New Zealand (1,345.5 per 100 000), while Indonesia had the lowest rate (12.9 per 100 000). From 1990 to 2021, Brazil witnessed the highest increase in incidence (225.7%), while Israel experienced the largest decrease (50.3%). Incident cases peaked at 65–69 and 70–74 years of age for females and males, respectively, with higher rates in females aged 20–69. The burden of AEMT decreased as sociodemographic index levels rose from 1990 to 2021.

Conclusion: The global burden of AEMT remains a critical challenge characterized by regional disparities and age-related trends. While the absolute burden increased, ASRs decreased, indicating improvements in healthcare. This study highlights the need for age-specific guidelines, enhanced training, and improved reporting. Continued advancements in healthcare systems and technology are crucial for safer treatment outcomes globally.

Keywords: Patient safety, Medical errors, Adverse effects, Epidemiology, Global health

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Introduction

The adverse effects of medical treatment (AEMT) are characterized as "unintended injuries arising during medical procedures that affect a patient's diagnosis, exacerbate their pain and burden, and may result in severe long-term irreversible outcomes or even death".[1] These effects stem from errors or complications in medical care rather than the consequences of the patient's underlying illness. AEMTs are a widespread issue in healthcare, affecting approximately one in every ten patients undergoing treatment.[2-4] A systematic review of AEMT among hospitalized patients reported a median incidence rate of 9.2%, with 7.4% of these incidents resulting in patient mortality.[4]

In the United States, AEMT ranks as the third most common cause of death, with an estimated 7000 to 9000 deaths annually attributed to medication errors alone.[5,6] In low- and middle-income countries, AEMTs contribute

to around one-third of all deaths.[7] The landmark report by the US Institute of Medicine[2] catalyzed the patient safety movement by revealing that in the US, medical errors were responsible for around 98 000 deaths annually.[8] According to previous research, most AEMTs are preventable, providing hope that their associated harm could be substantially reduced or even avoided.[4,5] A meta-analysis estimated a 6% prevalence of preventable harm within various medical environments, such as hospitals, primary care, and specialized services. The most common preventable harms included drug management errors, surgical complications, healthcare-associated infections, and diagnostic inaccuracies.[9] Despite efforts to mitigate such incidents, AEMTs continue to pose significant challenges, as evidenced by statistics provided by the US Department of Health and Human Services.[10]

AEMTs impose substantial economic and social burdens. They can lead to severe harm, long-term disability, diminished quality of life, and significant financial costs, including the need for ongoing medical care and productivity losses for survivors.[11] In 2008 alone, AEMTs were estimated to have cost the US economy approximately $1 trillion in direct healthcare expenditures.[12] Furthermore, AEMTs significantly impact population health by contributing to losses in health and disability-adjusted life years (DALYs).[13]

Globally, the burden of AEMTs varies substantially by region, influenced by factors such as patient demographics (age and gender), the quality of healthcare infrastructure, socioeconomic disparities, and the availability of skilled medical professionals.[14] Analyzing global and regional patterns of AEMTs over time is important for identifying critical areas for intervention and enhancing healthcare practices. The present research aims to comprehensively investigate the global burden of AEMTs from 1990 to 2021, utilizing data from the Global Burden of Disease (GBD) Study 2021.

Methods

Overview

The GBD 2021 study, led by the Institute for Health Metrics and Evaluation, assessed AEMT across 204 countries and territories, covering seven super-regions and 21 regions from 1990 to 2021. This extensive analysis utilized methods consistent with previous GBD cycles to evaluate the disease burden and its trends over time. Interested readers can refer to earlier publications for more details on the GBD methodology and updates specific to the 2021 cycle.[15,16]

Case Definition and Data Inputs

AEMTs refer to harms caused by medical interventions, including medications, procedures, and other treatments, which lead to negative health outcomes. These adverse effects may arise from treatment errors, side effects, or complications associated with the intervention, contributing to the overall disease burden by increasing morbidity, disability, or mortality. The data recorded in the GBD database are derived from various sources, such as outpatient, inpatient, and emergency department hospital records, as well as hospital claims analyses. A total of 346 sources from 49 countries were used to estimate the non-fatal burden of AEMT. For modelling the fatal burden of AEMT in the GBD 2021 study, several site-years were utilized, including 22, 826, 825, 187, and 6 site-years from vital registration, vital registration samples, verbal autopsy, and minimally invasive tissue sampling diagnoses, respectively. These data sources were integrated to calculate the fatal burden of AEMT across diverse regions and settings.

The ICD-10 codes for AEMT cover a broad spectrum of conditions resulting from various medical interventions. For example, D69.5-D69.59 includes thrombocytopenic purpura, such as drug-induced thrombocytopenia, while D70.1-D70.2 covers agranulocytosis triggered by specific medications. Conditions such as drug-induced hypothyroidism (E03.2), drug-induced diabetes (E09-E09.9), and drug-induced hypoglycemia (E16.0) demonstrate the impact of treatments on endocrine functions. Neurological disorders due to medical treatments are represented by codes such as G21.0-G21.19 and G24.0-G24.09 for drug-induced parkinsonism and drug-induced dystonia, respectively, while G25.1 captures tremors induced by medication. Broader neurological complications are included under G97-G97.9. Ocular and auditory effects are documented with codes such as H59-H59.89 for eye complications and H91.0-H91.09 for hearing loss related to medical treatments. Gastrointestinal complications following medical procedures are covered under K91-K91.9, and skin reactions (e.g., drug-induced eruptions) are included under L23.3 and L56.0-L56.1, addressing photosensitivity. Additional conditions, including drug-induced fevers (R50.2-R50.83) and complications from medical procedures (Y40-Y84.9), are tracked as well. A comprehensive list of these codes is presented in Table S1.[15,16]

Modelling Strategy

The morbidity data were modelled using the Bayesian meta-regression method, DisMod-MR 2.1. Subsequently, the Cause of Death Ensemble Modelling software was employed to generate fatal estimates by age group, gender, cause, year, and country. Years of life lost due to AEMT were estimated using the GBD standard life table, multiplying deaths within each age range by the corresponding remaining life expectancy. DALYs were estimated as the sum of years of life lost and years lived with disability. To assess uncertainty, 1000 random samples were taken at each calculation stage, propagating uncertainties from measurement error corrections, input data, and residual non-sampling errors. The uncertainty intervals (UIs) correspond to the 2.5th and 97.5th percentiles of these ordered samples. Further details on the non-fatal and fatal burden of AEMT can be found in

other sources.[15,16]

Results

Global Level

In 2021, the worldwide burden of AEMT was calculated to be 12,481,276 incident cases (95% UI: 10 886 793 to 14 290 630), with an age-standardized rate (ASR) of 150.4 per 100 000 (95% UI: 131.2 to 171.8). This marked a 5.3% decrease (95% UI: -7.9 to -2.6) compared to 1990. The number of deaths attributable to AEMT in 2021 was 122 330 (95% UI: 103 910 to 133 911), with an ASR of 1.5 per 100 000 (95% UI: 1.3 to 1.7), reflecting a significant 36.1% decrease (95% UI: -43.7 to -28.0) since 1990. In terms of DALYs, the global burden in 2021 was estimated at 4 846 981 (95% UI: 3 914 845 to 5 494 171), with an ASR of 64.2 per 100 000 (95% UI: 51.1 to 73.1), showing a substantial 39.7% reduction (95% UI: -48.9 to -31.2) compared to 1990 (2).

Regional Level

In 2021, the regions with the highest age-standardized incidence rates for AEMT were Australasia (1,049.7 per 100 000, 95% UI: 919.1 to 1208.4), high-income North America (993.0 per 100 000, 95% UI: 855.2 to 1146.7), and Southern Latin America (471.0 per 100 000, 95% UI: 415.6 to 534.9). In contrast, the lowest incidence rates were found in Southeast Asia (23.5 per 100 000, 95% UI: 19.3 to 28.5), East Asia (24.9 per 100 000, 95% UI: 19.7 to 31.3), and Eastern Sub-Saharan Africa (57.2 per 100 000, 95% UI: 49.5 to 65.9), the details of which are provided in Table S3. In Tropical Latin America, the incidence rate of AEMT significantly increased by 215.7% (95% UI: 193.3 to 242.1). However, a 25.9% increase (95% UI: 21.2 to 31.1) and a 17.4% increase (95% UI: 12.0 to 22.8) were observed in high-income North America and Eastern Europe, respectively. Conversely, East Asia experienced the most substantial decline in the incidence rate of AEMT, with a 32.4% decrease (95% UI: -35.9 to -28.3), followed by Eastern Sub-Saharan Africa and Central Sub-Saharan Africa, with a 27.2% decrease (95% UI: -29.8 to -24.6) and a 25.0% decrease (95% UI: -28.1 to -21.7), respectively (Table S3). Sex-specific incidence rates and their percentage changes are shown in Figures S1 and S2.

In 2021, regions with the largest age-standardized death rates due to AEMT were Western sub-Saharan Africa, with a rate of 3.6 per 100 000 (95% UI: 2.3 to 4.6), South Asia at 3.4 per 100 000 (95% UI: 2.8 to 3.9), and Eastern sub-Saharan Africa at 2.9 per 100 000 (95% UI: 1.9 to 7.1). Contrarily, the lowest death rates were found in East Asia, with 0.2 per 100 000 (95% UI: 0.2 to 0.3), High-income Asia Pacific at 0.4 per 100 000 (95% UI: 0.4 to 0.5), and Australasia at 0.4 per 100 000 (95% UI: 0.4 to 0.5) (Table S4). From 1990 to 2021, East Asia experienced the most substantial decline in the death rate due to AEMT, with a decrease of 82.1% (95% UI: -86.8 to -67.8), followed by Andean Latin America and Southern Latin America with a 78.4% reduction (95% UI: -84.7 to -62.1) and a 61.8% decrease (95% UI: -63.7 to -59.5), respectively. Notably, no region exhibited an increasing trend in death rates during this period (Table S4). Figures S3 and S4 illustrate sex-specific death rates and their corresponding percentage changes.

In 2021, the highest age-standardized DALY rates due to AEMT were observed in Western sub-Saharan Africa, with a rate of 175.5 per 100 000 (95% UI: 103.3 to 219.0), Eastern sub-Saharan Africa at 114.3 per 100 000 (95% UI: 76.8 to 244.4), and the Caribbean, with a rate of 111.9 per 100 000 (95% UI: 85.6 to 142.9). In contrast, the lowest DALY rates were found in East Asia, with a rate of 10.2 per 100 000 (95% UI: 8.7 to 13.1), High-income Asia Pacific at 13.9 per 100 000 (95% UI: 13.1 to 14.8), and Central Asia, with a rate of 18.0 per 100 000 (95% UI: 15.8 to 20.4) (Table S5). East Asia experienced the largest reduction in the DALY rate during 1990–2021, with a decrease of 86.8% (95% UI: -90.0 to -76.9), followed by Andean Latin America, with an 83.0% decrease (95% UI: -87.9 to -69.9) and Southern Latin America, with a 59.5% decrease (95% UI: -61.6 to -57.1). No region demonstrated an increase in DALY rates during this period (Table S5). Sex-specific DALY rates and their corresponding percentage changes are depicted in Figures S5 and S6.

National Level

There was significant variability in the age-standardized incidence rate of AEMT between countries in 2021. New Zealand had the highest incidence rate, with 1345.5 cases per 100 000 (95% UI: 1182.8 to 1544.9), followed by the United States of America at 1,027.7 per 100 000 (95% UI: 882.1 to 1185.6) and Australia at 990.8 per 100 000 (95% UI: 861.3 to 1148.6). In contrast, the lowest incidence rates were detected in Indonesia, with an ASR of 12.9 per 100 000 (95% UI: 9.7 to 16.6), followed by China at 24.7 per 100 000 (95% UI: 19.5 to 31.0) and the Democratic People's Republic of Korea at 26.0 per 100 000 (95% UI: 21.0 to 31.8). The related data are shown in Table S3 and Figure 1A.

From 1990 to 2021, the most significant rises in the age-standardized incidence rate of AEMT were observed in Brazil, which experienced a rise of 225.7% (95% UI: 202.0 to 254.1), followed by Mauritius and Austria, with an increase of 65.9% (95% UI: 53.3 to 80.8) and a 65.7% rise (95% UI: 52.4 to 81.1), respectively. Conversely, Israel had the largest decrease in incidence, with a reduction of 50.3% (95% UI: -53.0 to -46.8), followed by Indonesia, with a 44.2% decline (95% UI: -48.2 to -41.0), and the Islamic Republic of Iran, with a similar 42.7% decrease (95% UI: -44.5 to -41.0), the results of which are summarized in Table S3.

The age-standardized mortality rate attributable to AEMT in 2021 varied considerably between countries. Grenada, Haiti, and Afghanistan had the highest death rates, with 6.5 deaths per 100 000 (95% UI: 5.7 to 7.3), 5.6 deaths per 100 000 (95% UI: 3.8 to 8.1), and 5.5 deaths per 100 000 (95% UI: 3.7 to 7.8), respectively. Contrarily,

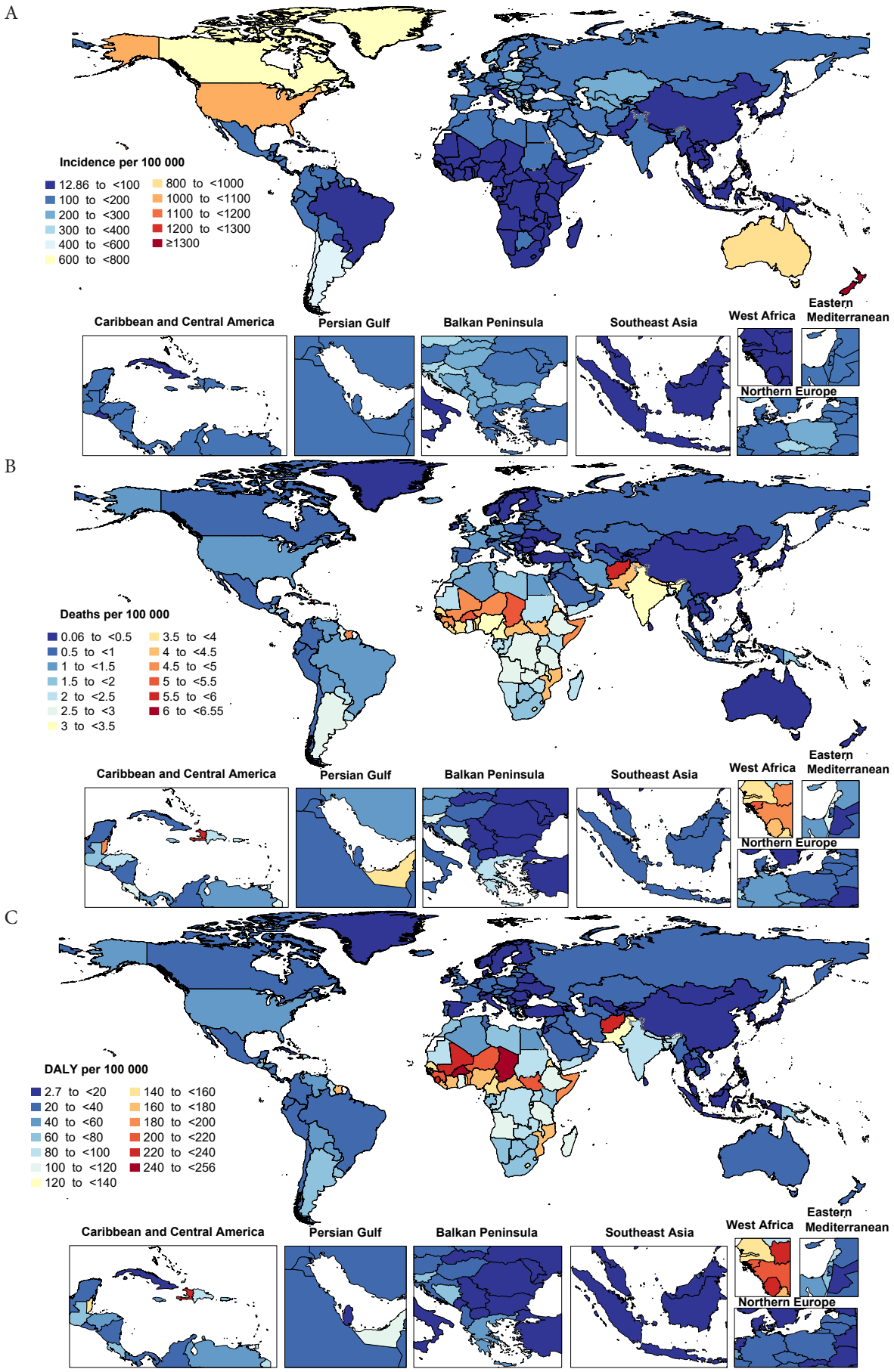

Figure 1. Age-standardized rates of incidence (A), Death (B), and Disability-Adjusted Life Years (C) Due to the Adverse Effects of Medical Treatment per 100 000 Population in 2021, by Country. *Source*. http://ghdx.healthdata.org/gbd-results-tool

the lowest death rates were found in the Cook Islands, with an ASR of 0.1 per 100 000 (95% UI: 0.0 to 0.1), followed by Kyrgyzstan and China at 0.2 per 100 000 (95% UI: 0.2 to 0.3) and 0.2 per 100 000 (95% UI: 0.2 to 0.3), respectively (Table S4 and Figure 1B). From 1990 to 2021, the most significant rises in the age-standardized death rate of AEMT were detected in Czechia, which witnessed a rise of 78.8% (95% UI: 56.9 to 101.4), followed by the United Kingdom and Japan, with an increase of 52.1% (95% UI: 47.5 to 56.4) and a 48.2% rise (95% UI: 42.1 to 53.9), respectively. In contrast, Kuwait experienced the largest decrease in death rate, with a reduction of 80.9% (95% UI: -84.7 to -76.9), followed by Peru, with an 81.4% decline (95% UI: -88.6 to -57.3), and China, with an 82.8% decrease (95% UI: -87.4 to -68.5). The related data are provided in Table S4.

In 2021, countries exhibited significant differences in the age-standardized DALY rate associated with AEMT. The highest DALY rate was related to Chad, with 255.3 per 100 000 (95% UI: 167.9 to 355.0), followed by Burkina Faso and Afghanistan, with 254.2 per 100 000 (95% UI: 153.2 to 372.9) and 235.6 per 100 000 (95% UI: 160.3 to 326.8), respectively. In contrast, the lowest DALY rates were observed in the Cook Islands, with a rate of 2.7 per 100 000 (95% UI: 1.9 to 3.4), Norway at 6.0 per 100 000 (95% UI: 5.1 to 7.1), and Montenegro at 6.6 per 100 000 (95% UI: 5.3 to 8.1) (Table S5 and Figure 1C). From 1990 to 2021, the most significant rises in the age-standardized DALY rate of AEMT were found in the United Kingdom, which witnessed a 47.7% rise (95% UI: 43.1 to 51.8), followed by Japan and Czechia, with an increase of 35.3% (95% UI: 29.1 to 41.0) and a 29.5% rise (95% UI: 14.9 to 45.7), respectively. Conversely, Kuwait, Peru, and China experienced the largest decrease in the DALY rate, with a reduction of 83.1% (95% UI: -85.9 to -80.0), an 86.2% decline (95% UI: -91.3 to -68.3), and an 87.3% decrease (95% UI: -90.4 to -77.6), respectively (Table S5).

Age and Gender Pattern

The global number of incident cases of AEMT in 2021 increased steadily across the younger age groups, peaking in the 65–69 age range for females and 70–74 among males before decreasing to the oldest age group (95$^+$ years). Incidence rates showed a consistent upward trend with age, reaching their highest levels in the 95$^+$ age group. Between the ages of 20 and 69, females demonstrated a higher total number of incidence cases and higher rates compared to males (Figure 2A).

In 2021, the global deaths related to AEMT were the highest in children under 5 years of age, followed by a decrease in the 5–9 years age group. The number of deaths then gradually rose, reaching a peak at 65–69 years and 70–74 years for males and females, respectively, before decreasing through to the 95$^+$ age group. Death rates attributable to AEMT revealed a different pattern, decreasing up to the 5–9 years age group before rising steadily with age and reaching their highest levels in the 95$^+$ years age range. In the age ranges of 15–64 years and 80–95$^+$ years, females experienced higher death rates, whereas males had higher rates in the remaining age groups (Figure 2B). A very similar pattern was observed for DALY counts and rates associated with AEMT (Figure 2C).

Association Between Adverse Effects of Medical Treatment Burden and the Socio-Demographic Index

There was a negative relationship between the SDI and the burden of AEMT. As SDI levels rose, the age-standardized DALY rate declined from 1990 to 2021. High-income North America, North Africa, the Middle East, Western Sub-Saharan Africa, the Caribbean, and Southern Latin America witnessed a higher-than-expected burden throughout the analysis period. In contrast, Central Europe, Central Asia, East Asia, the high-income Asia Pacific, Oceania, Southeast Asia, Andean Latin America, Central Latin America, and Tropical Latin America experienced a lower-than-expected burden from 1990 to 2021 (Figure 3).

Discussion

The global burden of AEMT has exhibited notable trends and variations over the past three decades, marked by differences in non-standardized and ASRs. Our analysis, utilizing the latest data, revealed a complex scenario; while the absolute burden of AEMT continues to grow, significant improvements in ASRs highlight progress in managing treatment-related adverse outcomes globally. These findings align with earlier reports[14,17] but provide a more detailed perspective on recent trends.

The total number of incident cases of AEMT rose from 7 407 310 in 1990 to 12 481 276 in 2021. This increase reflects population growth, an aging global population, and the increasing complexity of medical treatments.[18] These results are consistent with previous projections attributing the growing AEMT burden to the expanding use of medical interventions and escalating healthcare demands.[17] In 2021, global deaths attributable to AEMT totaled 122 330 cases. However, establishing a direct causal link between death and adverse events remains challenging due to various contextual factors, including healthcare services, patients, and medical teams.[19]

ASRs present a more optimistic narrative. The age-standardized incidence, DALYs, and mortality rates associated with AEMT all declined from 1990 to 2021. Specifically, the age-standardized incidence rate decreased by 5.3%, while the mortality and DALY rates witnessed reductions of 36.1% and 39.7%, respectively. These improvements likely reflect advancements in clinical care and safer medical practices.

Our analysis highlights the disproportionate burden of AEMT among specific age groups. Children under five years exhibited the highest DALY and mortality rates, underscoring the urgent need for age-specific guidelines and targeted training to ensure safer medical interventions

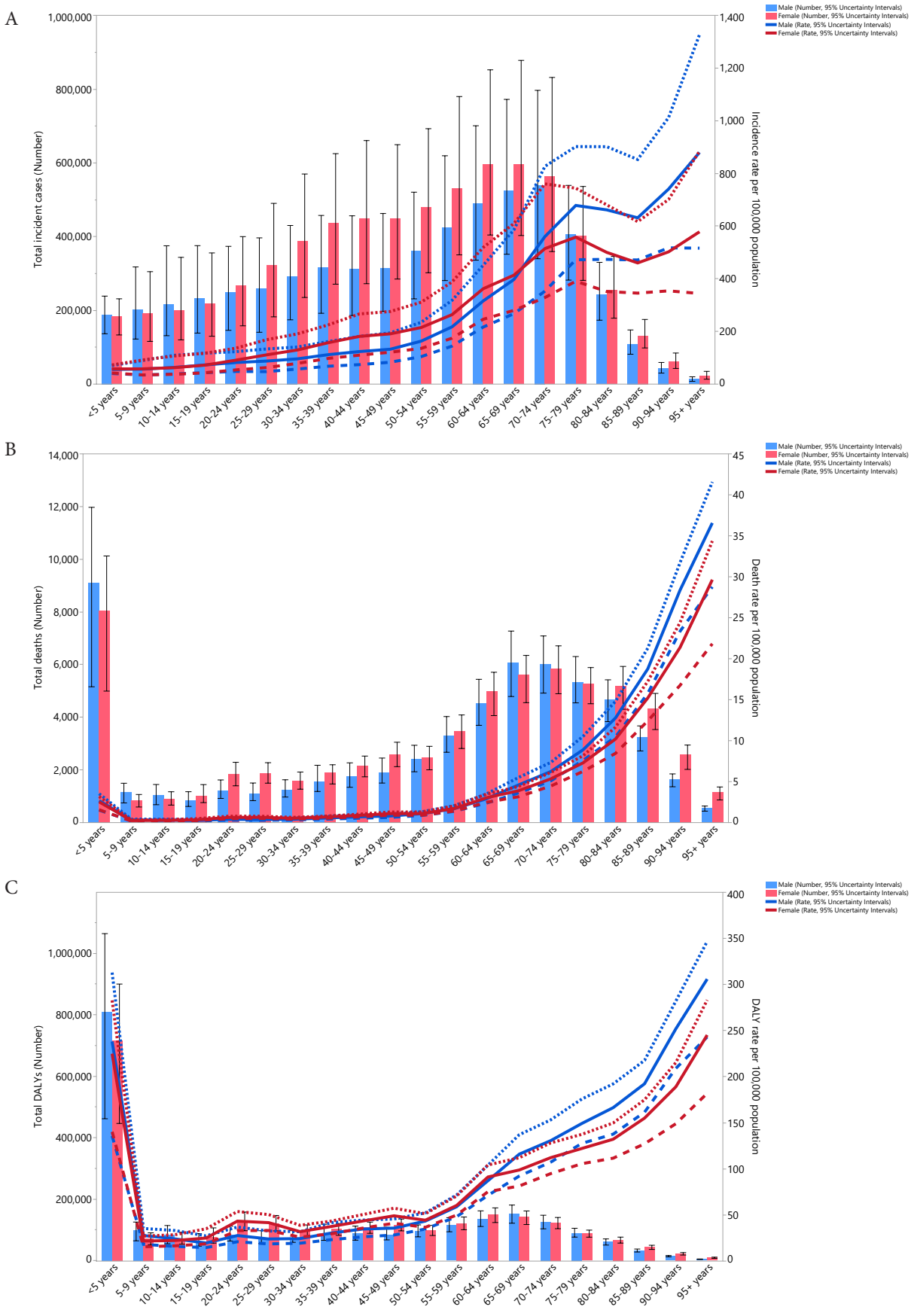

Figure 2. (A) Global Incident Cases and the age-Standardized Incidence Rate of the Adverse Effects of Medical Treatment per 100 000 Population, by Age and Gender in 2021, **(B)** Global Deaths and the Age-Standardized Death Rate Due to the Adverse Effects of Medical Treatment per 100 000 Population, by Age and Gender in 2021, **(C)** Global DALYs and the Age-Standardized DALY Rate Attributable to the Adverse Effects of Medical Treatment per 100 000 Population, by Age and Gender in 2021. *Note*. DALY: Disability-adjusted life year. The dotted and dashed lines indicate the 95% upper and lower uncertainty intervals, respectively. *Source*. http://ghdx.healthdata.org/gbd-results-tool

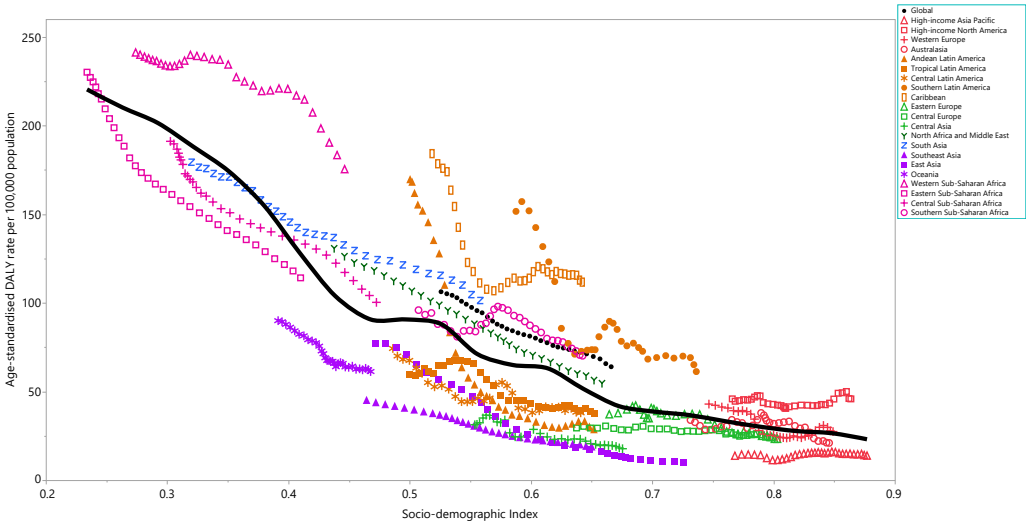

Figure 3. Age-Standardized Disability-Adjusted Life Year Rates for the Adverse Effects of Medical Treatment per 100000 Population Across the 21 Global Burden of Disease Regions, Stratified by the Sociodemographic Index From 1990 to 2021. *Note*. The black line represents the expected values based on the sociodemographic index and disease rates across all locations. *Source*. http://ghdx.healthdata.org/gbd-results-tool

during early childhood.[20,21] A high incidence rate was also observed among individuals aged 65 years and older, consistent with findings from Nauman et al[17] and Luo et al,[22] demonstrating heightened vulnerability among older adults and children in clinical trials. Common causes include inappropriate prescribing for the elderly, medication dosing errors, and pharmacological side effects in neonates.[23-25] Additionally, older patients often face challenges associated with multimorbidity, which complicates treatment plans and increases the risk of polypharmacy.[26,27] Physiological aging further compounds these risks by altering pharmacodynamics and pharmacokinetics, affecting drug absorption, metabolism, and efficacy.[28,29]

Gender differences in the AEMT burden were also apparent. Our study revealed higher AEMT incidence rates among females in most regions, consistent with previous research indicating greater susceptibility to adverse drug reactions and surgical complications in women.[14,30] Conversely, mortality rates were higher among males, which conforms to the findings of the study conducted by Shin et al.[31] Regional disparities in mortality rates are likely due to a complex interplay of factors, including healthcare infrastructure, reporting practices, and socioeconomic conditions.

Significant regional variations were also observed in the AEMT burden. Australasia and Southeast Asia reported the highest and lowest age-standardized incidence rates, respectively. These disparities may reflect underreporting in certain regions. Mortality trends were also different; East Asia represented the largest decline in the age-standardized mortality rate from 1990 to 2021, while Central Europe and the High-income Asia-Pacific experienced increases.[17] Notably, Czechia witnessed the largest rise in the age-standardized mortality rate, potentially due to healthcare challenges such as limited access to specialized care and regional inequalities.[32] In contrast, India achieved substantial reductions in age-standardized mortality rates, likely driven by recent healthcare reforms, including the expansion of health and wellness centers and the Ayushman Bharat insurance scheme.[33,34]

Implications for Public Health

Human error is an inherent aspect of medical care. Nevertheless, up to 80% of adverse events can be prevented through adherence to standard care protocols.[7] Expanding access to safer treatments, enhancing pharmacovigilance, and improving healthcare systems are essential for mitigating AEMT. Advances in machine learning, large data analysis, and artificial intelligence offer promising avenues for reducing AEMT through improved patient safety and clinical decision-making.[35] Public awareness campaigns and stricter safety regulations are equally crucial for fostering safer medical practices.

Conclusion

The global burden of AEMT remains a serious challenge, distinguished by significant regional disparities and age-related trends. Although the absolute burden has increased, reductions in ASRs reflect advancements in healthcare and safer treatment practices. This study underscores the importance of implementing age-specific guidelines, improving training, and enhancing reporting systems to mitigate AEMT. Continued efforts to strengthen healthcare systems and integrate technological innovations will be essential for ensuring safer treatment outcomes worldwide.

Ethics statement

Not applicable.

Disclosure of funding source

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Conflict of interests declaration
None declared.

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Data availability statement
The data used for these analyses are all publicly available.

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Formal analysis: Saeid Safiri.
Funding acquisition: Ali-Asghar Kolahi.
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Methodology: Saeid Safiri.
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Consent for publication
Not required.

Patient and public involvement
Patients and the public were not involved in the analyses or preparation of this manuscript.

Authors' Note
This study is based on publicly available data and solely reflects the opinion of its authors rather than that of the Institute for Health Metrics and Evaluation.

Supplementary Files
Supplementary file 1 contains Tables S1-S4 and Figures S1-S6.

References
1. Brennan TA, Leape LL, Laird NM, Hebert L, Localio AR, Lawthers AG, et al. Incidence of adverse events and negligence in hospitalized patients. Results of the Harvard Medical Practice Study I. N Engl J Med. 1991;324(6):370-6. doi: 10.1056/nejm199102073240604.
2. Institute of Medicine (US) Committee on Quality of Health Care in America. To Err is Human: Building a Safer Health System. Kohn LT, Corrigan JM, Donaldson MS, eds. Washington, DC: National Academies Press; 2000. doi: 10.7717/peerj.7702.
3. Leape LL, Lawthers AG, Brennan TA, Johnson WG. Preventing medical injury. QRB Qual Rev Bull. 1993;19(5):144-9. doi: 10.1016/s0097-5990(16)30608-x.
4. de Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. Qual Saf Health Care. 2008;17(3):216-23. doi: 10.1136/qshc.2007.023622.
5. Makary MA, Daniel M. Medical error-the third leading cause of death in the US. BMJ. 2016;353:i2139. doi: 10.1136/bmj.i2139.
6. Tariq RA, Vashisht R, Sinha A, Scherbak Y. Medication dispensing errors and prevention. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2024.
7. Wilson RM, Michel P, Olsen S, Gibberd RW, Vincent C, El-Assady R, et al. Patient safety in developing countries: retrospective estimation of scale and nature of harm to patients in hospital. BMJ. 2012;344:e832. doi: 10.1136/bmj.e832.
8. Rodziewicz TL, Houseman B, Vaqar S, Hipskind JE. Medical error reduction and prevention. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2024.
9. Panagioti M, Khan K, Keers RN, Abuzour A, Phipps D, Kontopantelis E, et al. Prevalence, severity, and nature of preventable patient harm across medical care settings: systematic review and meta-analysis. BMJ. 2019;366:l4185. doi: 10.1136/bmj.l4185.
10. Grimm CA. Adverse Events in Hospitals: A Quarter of Medicare Patients Experienced Harm in October 2018. Office of Inspector General; 2022. p. 117.
11. David G, Gunnarsson CL, Waters HC, Horblyuk R, Kaplan HS. Economic measurement of medical errors using a hospital claims database. Value Health. 2013;16(2):305-10. doi: 10.1016/j.jval.2012.11.010.
12. Slawomirski L, Auraaen A, Klazinga N. The Economics of Patient Safety: Strengthening a Value-Based Approach to Reducing Patient Harm at National Level. Paris: Organisation for Economic Co-operation and Development (OECD); 2017.
13. Khan MA, Soteriades ES, King J, Govender R, Hashim MJ, Masood-Husain S, et al. Global trends and forecast of the burden of adverse effects of medical treatment: epidemiological analysis based on the Global Burden of Disease Study. Cureus. 2020;12(3):e7250. doi: 10.7759/cureus.7250.
14. Kong X, Tao X, Li L, Zhao X, Ren J, Yang S, et al. Global trends and partial forecast of adverse effects of medical treatment from 1990 to 2019: an epidemiological analysis based on the global burden of disease study 2019. BMC Public Health. 2024;24(1):295. doi: 10.1186/s12889-023-17560-0.
15. GBD 2021 Diseases and Injuries Collaborators. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2024;403(10440):2133-61. doi: 10.1016/s0140-6736(24)00757-8.
16. GBD 2021 Causes of Death Collaborators. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2024;403(10440):2100-32. doi: 10.1016/s0140-6736(24)00367-2.
17. Nauman J, Soteriades ES, Hashim MJ, Govender R, Al Darmaki RS, Al Falasi RJ, et al. Global incidence and mortality trends due to adverse effects of medical treatment, 1990-2017: a systematic analysis from the global burden of diseases, injuries and risk factors study. Cureus. 2020;12(3):e7265. doi: 10.7759/cureus.7265.
18. Zazzara MB, Palmer K, Vetrano DL, Carfì A, Onder G. Adverse drug reactions in older adults: a narrative review of the literature. Eur Geriatr Med. 2021;12(3):463-73. doi: 10.1007/s41999-021-00481-9.
19. Bates DW, Singh H. Two decades since to err is human: an assessment of progress and emerging priorities in patient safety. Health Aff (Millwood). 2018;37(11):1736-43. doi: 10.1377/hlthaff.2018.0738.
20. Kugelman A, Inbar-Sanado E, Shinwell ES, Makhoul IR, Leshem M, Zangen S, et al. Iatrogenesis in neonatal intensive care units: observational and interventional, prospective,

multicenter study. Pediatrics. 2008;122(3):550-5. doi: 10.1542/peds.2007-2729.
21. Ligi I, Millet V, Sartor C, Jouve E, Tardieu S, Sambuc R, et al. Iatrogenic events in neonates: beneficial effects of prevention strategies and continuous monitoring. Pediatrics. 2010;126(6):e1461-8. doi: 10.1542/peds.2009-2872.
22. Luo J, Eldredge C, Cho CC, Cisler RA. Population analysis of adverse events in different age groups using big clinical trials data. JMIR Med Inform. 2016;4(4):e30. doi: 10.2196/medinform.6437.
23. Dillner P, Eggenschwiler LC, Rutjes AW, Berg L, Musy SN, Simon M, et al. Incidence and characteristics of adverse events in paediatric inpatient care: a systematic review and meta-analysis. BMJ Qual Saf. 2023;32(3):133-49. doi: 10.1136/bmjqs-2022-015298.
24. Pérez T, Moriarty F, Wallace E, McDowell R, Redmond P, Fahey T. Prevalence of potentially inappropriate prescribing in older people in primary care and its association with hospital admission: longitudinal study. BMJ. 2018;363:k4524. doi: 10.1136/bmj.k4524.
25. Kruk ME, Gage AD, Arsenault C, Jordan K, Leslie HH, Roder-DeWan S, et al. High-quality health systems in the Sustainable Development Goals era: time for a revolution. Lancet Glob Health. 2018;6(11):e1196-252. doi: 10.1016/s2214-109x(18)30386-3.
26. The Lancet Healthy Longevity. Care for ageing populations globally. Lancet Healthy Longev. 2021;2(4):e180. doi: 10.1016/s2666-7568(21)00064-7.
27. Tran PB, Kazibwe J, Nikolaidis GF, Linnosmaa I, Rijken M, van Olmen J. Costs of multimorbidity: a systematic review and meta-analyses. BMC Med. 2022;20(1):234. doi: 10.1186/s12916-022-02427-9.
28. Mangoni AA, Jackson SH. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. Br J Clin Pharmacol. 2004;57(1):6-14. doi: 10.1046/j.1365-2125.2003.02007.x.
29. Rodrigues DA, Herdeiro MT, Figueiras A, Coutinho P, Roque F. Elderly and polypharmacy: physiological and cognitive. In: Frailty in the Elderly: Understanding and Managing Complexity. IntechOpen; 2020.
30. Shan Y, Cheung L, Zhou Y, Huang Y, Huang RS. A systematic review on sex differences in adverse drug reactions related to psychotropic, cardiovascular, and analgesic medications. Front Pharmacol. 2023;14:1096366. doi: 10.3389/fphar.2023.1096366.
31. Shin E, Leibovitch E, Nishimura Y, Bhagavathula AS. Long-term trends in mortality from adverse effects of medical treatment in older populations in the United States from 1990 to 2019. J Am Pharm Assoc (2003). 2024;64(1):55-61. doi: 10.1016/j.japh.2023.09.007.
32. Bryndová L, Šlegerová L, Votápková J, Hrobon P, Shuftan N, Spranger A. Czechia: health system review. Health Syst Transit. 2023;25(1):1-216.
33. Kumar A. The transformation of the Indian healthcare system. Cureus. 2023;15(5):e39079. doi: 10.7759/cureus.39079.
34. Sriee GV, Maiya GR. Coverage, utilization, and impact of Ayushman Bharat scheme among the rural field practice area of Saveetha Medical College and Hospital, Chennai. J Family Med Prim Care. 2021;10(3):1171-6. doi: 10.4103/jfmpc.jfmpc_1789_20.
35. Ahuja AS. The impact of artificial intelligence in medicine on the future role of the physician. PeerJ. 2019;7:e7702. doi: 10.7717/peerj.7702.