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2022

Oura , P & Sajantila , A 2022 , ' A recent two-fold increase in medical adverse event deaths among US inpatients ' , Journal of Public Health Research , vol. 11 , no. 4 , 22799036221139935 . https://doi.org/10.1177/22799036221139935

http://hdl.handle.net/10138/355187
https://doi.org/10.1177/22799036221139935

Brief Report

Journal of
Public Health Research

Journal of Public Health Research
2022, Vol. 11(4), 1–4
© The Author(s) 2022
DOI: 10.1177/22799036221139935
journals.sagepub.com/home/phj
SAGE

A recent two-fold increase in medical adverse event deaths among US inpatients

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Abstract

Inpatients have a particular risk of sustaining medical adverse events (MAEs). This analysis aimed to identify patterns of change in deaths due to MAEs among US inpatients. The analysis was based on nationwide cause-of-death data from 1999 to 2019. To adjust for secular trends in overall mortality, MAE deaths were examined proportional to total deaths. Statistical analysis was performed by means of joinpoint regression modeling. Over the analysis period, a total of 18,126,135 certified deaths occurred among inpatients. MAEs were used as the underlying cause of death in 43,899 cases (0.24%). MAE deaths showed a significant increase from mid-2010s onwards; the estimated increase in MAE deaths was up to 15.6% per year (95% confidence interval 11.3–20.1) from 2014 to 2019. Procedure-related events mainly drove the trend. As the present data are insufficient to substantiate and disentangle underlying factors, future analyses are warranted.

Keywords

Adverse event, mortality, inpatient, epidemiology, US

Date received: 26 August 2022; accepted: 2 November 2022

Introduction

Medical adverse events (MAEs) are defined as unintentional harm caused by medical management.[1,2] Fatal and non-fatal MAEs have high incidence globally.[3] In the US, the number of fatal MAEs is estimated to be in the hundreds of thousands annually, and the numbers of non-fatal MAEs are even higher.[4] It is therefore crucial that further resources will be directed to the prevention of MAEs and death from medical care.[4–8]

Inpatients at medical facilities are particularly susceptible to MAEs.[5,9,10] Over the previous decades, hospitals have proceeded to improve patient safety.[4,8] For example, effective prevention and surveillance strategies have been implemented for hospital-acquired infections,[11] medication errors,[12] and surgical complications.[13] Such protocols have clearly reduced adverse event rates as long as their implementation has been successful.

At the same time, medical care has been rapidly evolving.[14] The US population is ageing, inpatient admission numbers are increasing, and novel therapies are frequently deployed. From the patient safety perspective, it is no surprise that novel MAE risk areas have been identified, health technology being one example.[4] Also the recognition and transparent reporting of MAEs have improved over the previous decades.[4,9,10]

The resultant effect of the aforementioned phenomena (e.g. effective prevention strategies, ageing population, increased admission numbers, novel sources of MAEs, and transparent reporting) on vital statistics remains ambiguous. Exploiting nationwide cause-of-death data from 1999 to 2019, this time series analysis aimed to identify patterns of change in certified MAE deaths among US inpatients.

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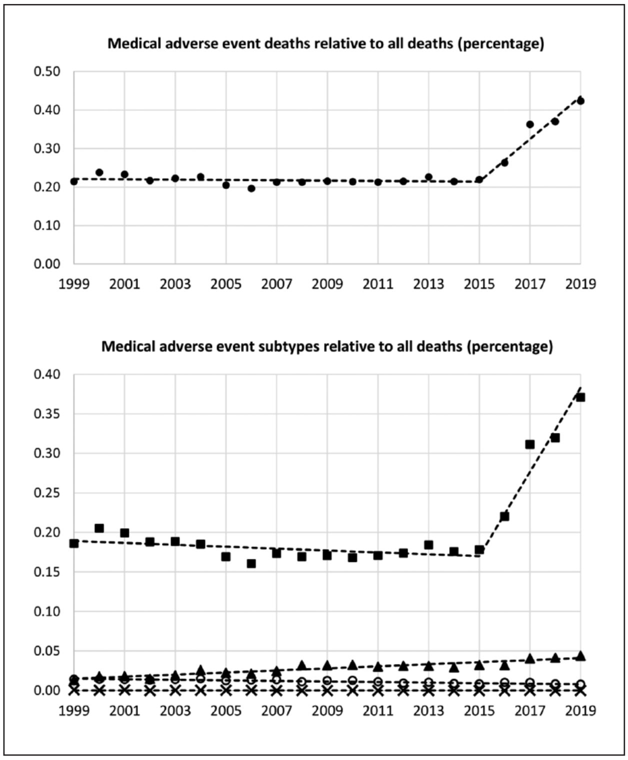

Figure 1. Medical adverse event deaths relative to all deaths over the study period. The top part of the figure shows all medical adverse event deaths in a pooled manner. The bottom part of the figure shows a breakdown of deaths by subtype: procedure-related deaths (squares), medication-related deaths (triangles), misadventure-related deaths (circles), and device-related deaths (crosses). Numeric results from jointpoint regression are presented in Table 1.

Design and methods

The analysis was based on national mortality data from National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC). Data are based on death certificates of US residents.

The publicly available "Multiple Cause of Death, 1999–2019" database was queried through the CDC Wonder system (https://wonder.cdc.gov/) on Oct 3, 2021. Queries were delimited to underlying (i.e. primary) causes of death among inpatients at medical facilities. Annual numbers of total deaths (corresponding to codes A00–Y89 in the 10th revision of the International Classification of Diseases coding system) and MAE deaths (all MAE deaths, codes Y40–Y84 and Y88; medication-related deaths, codes Y40–Y59 and Y88.0; misadventure-related deaths, codes Y60–Y69 and Y88.1; device-related deaths, codes Y70–Y82 and Y88.2; procedure-related deaths, codes Y83–Y84 and Y88.3) were obtained from the system.[15]

MAE deaths were analyzed proportional to total deaths (%) by dividing the annual number of MAE deaths by the annual number of all inpatient deaths. This proportional mortality approach was undertaken to account for secular trends in overall inpatient mortality. It was also considered to carry gross information on the magnitude of inpatient admissions on the population level.

Statistical analysis was performed by means of joinpoint regression modeling[16] (Joinpoint Regression Program version 4.8.0.1, National Cancer Institute). In general, joinpoint regression fits a prespecified number of linear segments and joinpoints in a dataset. Joinpoints are "knots" between adjacent segments. Location of the joinpoints and slopes of the linear segments are estimated by the models. Slopes are calculated as Annual Percent Changes (% change per year) within segments.

In this analysis, independent joinpoint models were run for all MAE deaths (i.e. total MAE deaths pooled) and for each MAE subtype (i.e. procedure-related deaths, medication-related deaths, misadventure-related deaths, and device-related deaths). Models with up to three joinpoints were tested each time. The most parsimonious solution according to permutation tests was selected as the final solution. Models assuming constant variance and Poisson variance yielded similar results. Estimated joinpoint locations and Annual Percent Changes withing segments were documented. Estimates were accompanied with 95% confidence intervals (CIs). CIs not including zero were considered statistically significant.

Results

A total of 18,126,135 inpatient deaths occurred over the analysis period. Of them, 43,899 (0.24%) were primarily attributed to MAEs.

Figure 1 is a graphical illustration of trends in MAE deaths in 1999 to 2019. After a relatively stable period from 1999 to mid-2010s, a steep linear increase occurred toward the end of the analysis period. Notably, the proportion of MAE deaths relative to all deaths doubled between mid-2010s and 2019.

Table 1 shows numeric estimates for joinpoint locations and Annual Percent Changes within segments. The estimated increase in all MAE deaths was up to 15.6% per year (95% CI 11.3–20.1) from 2014 to 2019. In subtype-specific analyses, procedure-related deaths were found to mainly drive the trend (estimated increase 18.2% per year, 95% CI 13.2–23.4). Medication-related deaths showed a mild increase, while misadventure-related and device-related deaths mildly decreased over the analysis period.

Conclusions

This analysis aimed to reveal patterns of change in MAE deaths among US inpatients. After a stable period, a steep two-fold increase occurred from mid-2010s onwards. The increase was mainly driven by procedure-related deaths.

Table 1. Results from joinpoint regression analysis.

Outcome	Joinpoint location (95% CI)	Annual percent change for segment 1 (95% CI)	Annual percent change for segment 2 (95% CI)
All MAE deaths	2014 (2013–2016)	0.5 (−1.2 to 0.3)	15.6 (11.3–20.1)
Procedure-related deaths	2014 (2013–2016)	−1.0 (−1.8 to −0.2)	18.2 (13.2–23.4)
Medication-related deaths	–	5.0 (4.0 to 6.1)	–
Misadventure-related deaths	–	−2.9 (−3.5 to −2.2)	–
Device-related deaths	–	−9.4 (−14.1 to −4.5)	–

CI = confidence interval.
Estimates for joinpoint locations (i.e. knots between two segments) and slopes (i.e. Annual Percent Changes within segments). A graphical illustration of joinpoints and segments is given in Figure 1.

A previous US study investigated the association between MAEs and mortality in the Global Burden of Disease (GBD) 2016 dataset.[17] Over the study period 1990–2016, age-standardized MAE mortality showed a modest decrease. Advancing age in particular was associated with higher MAE mortality, and geographic variability was observed within the US. The association of MAE mortality with higher age,[15] lower education,[18] and rurality[19] have been observed also in other US studies.

As regards the period from 1999 to mid-2010s, the findings of the present analysis were mostly in line with the GBD-based study.[17] Different datasets (NCHS vs. GBD), use of age-standardization, and proportional mortality approach are likely to account for the minor differences between the observed trends. However, from mid-2010s onwards, the MAE deaths showed a notable increasing pattern, which was only captured by the present analysis.

The present data are insufficient to identify factors explaining the steep increase in deaths attributed to MAEs. We speculate that the increasing trend may result from several concurrent phenomena such as increased admission numbers, deployment of novel therapies, ageing populations, and transparent reporting of MAEs. Importantly, it remains unclear whether the increase solely reflects technical advancements in the reporting of MAEs (in medical and surgical procedures in particular), or whether there may be an actual increase in these deaths among inpatients.

Of particular note is the US implementation of ICD-10 which took place in October 2015, approximately the same time as the increase initiated. In comparison to ICD-9, ICD-10 allowed a higher specificity at which patient-level data could be documented, thus offering a more accurate tool for capturing MAEs.[20] We speculate that a change in MAE reporting behavior due to more comprehensive ICD codes, for example, may have been reflected in recent mortality data. However, the present data are not able to substantiate and disentangle underlying factors.

The strengths of this analysis include an official data source and US-wide coverage. The dataset is publicly available for further analyses. Of note is the fact that the data were collected prior to the covid-19 pandemic. The main limitations include retrospective design and population-level approach with no patient-level data. It is also evident that MAEs are underrepresented in cause-of-death statistics.[9,15]

Acknowledgements

National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), US, is acknowledged as the data source.

Author contributions

P.O. worked on the conception of the project, data collection, analysis and interpretation of the data, and writing the manuscript. A.S. worked on the conception of the project, interpretation of the data, and writing the manuscript. Both authors approved the final version of the manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Open access funded by Helsinki University Library.

Ethics approval and consent to participate

This study did not require an ethics approval as it was based on a retrospective, anonymous, and already public dataset.

Significance for public health

Patient safety is a key priority in public health. Endeavors to reduce medical adverse events and death from medical care should be based on reliable data. This analysis found a two-fold increase in adverse event deaths among US inpatients from mid-2010s onwards. Further public health attention is required to analyze whether this finding reflects advances in transparent reporting of adverse events, or whether there may be an actual increase in adverse event deaths among US inpatients.

Availability of data and materials

Data are available from the CDC Wonder database (https://wonder.cdc.gov/).

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