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Retrospective analysis of preventable procedural adverse events (ICD-10 Y62–Y69) in the TriNetX network: a multiregional study before, during and after the COVID-19 pandemic

Rosario Caruso ,[1,2] Marco Di Muzio,[3] Emanuele Di Simone ,[4] Sara Dionisi,[5] Arianna Magon,[2] Gianluca Conte,[2] Alessandro Stievano,[6,7] Emanuele Girani,[8] Sara Boveri,[8] Pier Mario Perrone,[1] Silvana Castaldi,[1,9] Lorenzo Menicanti,[10] Mary Dolansky[11]

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjqs-2025-019077).

For numbered affiliations see end of article.

Correspondence to
Professor Rosario Caruso; rosario.caruso@unimi.it

RC and MDM are joint first authors.

Received 27 May 2025
Accepted 31 July 2025

Check for updates

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To cite: Caruso R, Di Muzio M, Di Simone E, *et al*. *BMJ Qual Saf* Epub ahead of print: [please include Day Month Year]. doi:10.1136/bmjqs-2025-019077

ABSTRACT

Background Healthcare-related procedural misadventures remain underreported despite decades of investment in patient safety. International Classification of Diseases, 10th Revision (ICD-10) codes Y62–Y69 capture defined preventable adverse events during medical and surgical care. This study aimed to examine temporal patterns in Y62–Y69-coded events using aggregated, precomputed data from the TriNetX Global Collaborative Network.

Methods We conducted a retrospective observational study using deidentified electronic health records from the TriNetX platform, encompassing over 135 million patients aged 0–89 (years: 2016–2024). Incidence rates for Y62–Y69–coded events were analysed globally and across four regional networks, USA, Europe–Middle East–Africa (EMEA), Asia-Pacific (APAC) and Latin America (LATAM), with additional sensitivity analyses in cardiovascular (ICD-10: I00–I99) and oncological (ICD-10: C00–D49) cohorts. Temporal trends were explored descriptively using polynomial regression (for visual pattern illustration) and the Mann-Kendall trend test.

Findings Globally, Y62–Y69 incidence rates increased from 0.04 to 0.09 per 100 000 patients between 2016 and 2024 (125% increase), with inflection in the early postpandemic phase. EMEA exhibited the steepest rise (414%), followed by APAC (225%). The USA showed a non-linear pattern detectable only through polynomial modelling. LATAM and APAC trends lacked statistical significance, likely due to high year-to-year variability. Sensitivity analyses in the disease-specific cohorts reflected similar patterns, reinforcing the consistency of findings.

Interpretation This is the first global, real-world analysis of ICD-10 Y62–Y69–coded adverse events. The findings reveal a notable postpandemic escalation in procedural harm, underscoring the fragility of safety systems under operational stress. Regional heterogeneity and non-linear trajectories highlight the importance of

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Procedural adverse events during medical and surgical care remain a persistent threat to patient safety, yet they are underreported in routine data sets.

⇒ International Classification of Diseases, 10th Revision (ICD-10) codes Y62–Y69 provide a structured framework for identifying such events, yet global trends, especially in relation to the COVID-19 pandemic, have not been comprehensively examined.

WHAT THIS STUDY ADDS

⇒ This is the first multinational, real-world analysis of ICD-10 Y62–Y69–coded events, revealing a significant and accelerating global rise in procedural harm, particularly in the early postpandemic period.

⇒ Regional disparities and non-linear trajectories were identified, with the sharpest increases observed in EMEA and APAC.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings highlight the need for strengthened real-time surveillance systems and tailored safety interventions across regions.

locally tailored interventions and the need to reinvigorate global patient safety efforts.

Data availability statement All data were extracted from the TriNetX Global Collaborative Network. Aggregated incidence rates and the R code used for statistical analysis are provided in online supplemental file 2.

INTRODUCTION

Patient safety remains a central pillar in the global effort to strengthen health systems and improve healthcare delivery.[1–3] Despite decades of investment and policy development, adverse events, medical errors and healthcare-related harm continue to pose significant challenges across countries.[4 5] In response, the WHO launched its Global Patient Safety Action Plan in 2021, calling for strategic and coordinated actions to minimise avoidable harm and promote a safety culture across care settings.[6] Recent comprehensive reviews and global reports further underscore that progress remains uneven and that substantial gaps persist in implementing effective safety strategies worldwide.[7–9]

However, recent data underscore that progress in this regard remains uneven.[5 6 10 11] The latest WHO report on quality and safety in Europe reveals that only one-third of member states have implemented a national plan to improve safety and/or quality of care.[11] These findings point to persistent gaps in the operationalisation of safety principles at the national and institutional levels.[2 3 6 11]

The COVID-19 pandemic further stressed healthcare systems and re-exposed vulnerabilities in patient safety.[12] The urgency of the crisis highlighted the need for tools that enable near real-time analysis of health system performance, including mechanisms to detect and respond to safety threats as they emerge.[13] Although patient safety is a well-researched topic, there remains substantial under-reporting and underestimation of the problem, limiting system-wide learning.[14–16]

In this context, health data platforms such as TriNetX, which aggregate deidentified electronic health records across institutions and regions, offer a valuable opportunity.[17] When used with standardised coding systems like the International Classification of Diseases, 10th Revision (ICD-10), these platforms support systematic detection and monitoring of healthcare-related harm.[17]

Within ICD-10, the cluster Y62–Y69 captures a defined set of adverse events and procedural errors occurring in medical and surgical care, serving as a proxy indicator of safety and quality.[18] This cluster includes failures in sterilisation (Y62), incorrect dosage or method of drug administration (Y63), incidents during infusion or transfusion (Y64), contamination or mislabelling of biological substances (Y65) and other procedural misadventures such as inappropriate surgical interventions, incorrect patient identification or lapses in aseptic technique (Y66–Y69). The cluster Y62–Y69 provides a structured and internationally recognised framework for documenting preventable harm.[18] These codes serve as retrospective markers of safety incidents and valuable inputs for trend monitoring, institutional benchmarking and the design of targeted strategies to improve care processes and outcomes. However, we acknowledge that the use of a standardised coding system alone does not resolve under-reporting. Without parallel cultural, organisational and systematic interventions to encourage accurate documentation and transparency, these codes cannot fully capture the true burden of patient safety incidents.[19–21]

The value of focusing on the Y62–Y69 cluster lies in its direct link to procedural and periprocedural adverse events, which are widely recognised as preventable and actionable safety indicators. While broader ICD-10 categories such as Y40–Y84 include drug-related adverse effects and other complications (ie, complications of medical and surgical care), Y62–Y69 uniquely capture procedural misadventures closely tied to operative and procedural care processes. Previous studies have demonstrated the relevance of this cluster as a reliable proxy for system-level procedural safety monitoring and for comparing trends across healthcare systems.[6 22] In this context, emphasising Y62–Y69 allows a focused examination of events that are clearly attributable to procedural failures and thus actionable from a quality improvement perspective.

Despite the relevance of this defined set of adverse events, little is known about how the Y62–Y69 cluster has evolved over time across different regions or in response to systemic shocks such as the COVID-19 pandemic.[18] Existing literature on patient safety trends tends to focus on individual adverse event types or institutional reporting systems, often limited in geographical scope, data granularity or standardisation.[23–26] Recent studies using the Global Burden of Disease framework have also reported a global rise in adverse effects of medical treatment, highlighting the increasing need for systematic and harmonised monitoring of procedural safety at an international level.[27 28] While broader code ranges such as Y40–Y84 capture a wide spectrum of complications, focused analyses of Y62–Y69-coded events remain scarce.[29–32]

Thus far, no prior research has comprehensively examined the incidence rate of Y62–Y69–coded events before, during and after the pandemic, nor compared trends across regional health systems.[18] Given the availability of harmonised, large-scale health data through platforms such as TriNetX, there is an opportunity to address these gaps. For these reasons, this study aims to examine temporal trends in the incidence rate of healthcare-related harm coded under ICD-10 cluster Y62–Y69 across global and regional health systems using aggregated, precomputed data from the TriNetX Global Collaborative Network.

METHODS

Study design

This study adopts an observational, retrospective design and is reported following the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.[33]

It qualifies as a big data study, leveraging the extensive and harmonised electronic health record data sets available through the TriNetX platform (TriNetX LLC, Cambridge, Massachusetts, USA). TriNetX is a global federated network that provides real-time access to deidentified electronic medical records from healthcare organisations across multiple countries.[17] The platform's big data infrastructure enables large-scale analyses, improving the robustness, scope and generalisability of study findings. Ethical approval is not required for research studies run within the TriNetX network analysis platform, due to the federated nature of the network. The TriNetX platform only receives deidentified information, which is displayed as aggregated counts and statistical summaries. In addition, TriNetX does not share with the user either the identity of Healthcare organisations (HCOs) participating in the analysis or their contributions. TriNetX is ISO 27001:2013 certified and General Data Protection Regulation (GDPR) compliant. In accordance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, all deidentification measures were appropriately implemented.

The original study protocol, which has been published elsewhere,[18] specified a temporal window from 2016 to 2023; however, the inclusion of 2024 data was deemed feasible and was incorporated to enhance trend analysis and capture the most up-to-date insights.

Setting and data source

This study uses data extracted from TriNetX, a global health research network that provides real-time access to deidentified electronic medical records from healthcare organisations across multiple countries.[17] The platform's big data infrastructure enables large-scale analyses, improving the robustness, scope and generalisability of study findings. As of the time of analysis, the TriNetX network comprised routinely collected, aggregated clinical data from approximately 250 million patients across over 140 healthcare institutions in 19 countries.

The data set includes both inpatient and outpatient encounters, and clinical data are standardised using internationally recognised terminologies, including ICD-10, Systematised Nomenclature of Medicine and Logical Observation Identifiers Names and Codes.

This retrospective analysis includes all patients aged 0–89 years who received any ICD-10-Clinical Modification diagnosis during the observation period. The primary outcome of interest is the ICD-10-CM cluster Y62–Y69, which captures 'misadventures to patients during surgical and medical care'. Incidence rates for these events were analysed from 2016 to 2024, covering periods before, during and after the COVID-19 pandemic. This segmentation was chosen because the majority of data in the TriNetX network derives from US-based institutions, making the US definition of pandemic phases the most consistent and operationally relevant framework for the overall data set.

The analysis was conducted both globally (Global Collaborative Network) and across four regional collaborative networks within TriNetX: (1) USA (US Collaborative Network), (2) Latin America (LATAM Collaborative Network), (3) Europe, Middle East and Africa (EMEA Collaborative Network) and (4) Asia-Pacific (APAC Collaborative Network).

In the current study, sensitivity analyses were also conducted in two clinical cohorts to assess whether the main temporal trends were robust across different subpopulations:[34] oncological cohort, defined by ICD-10 codes for neoplasms (C00–D49) and cardiovascular cohort, defined by ICD-10 codes for diseases of the circulatory system (I00–I99).

Study period

The analysis encompasses 9 years of data, from 2016 to 2024, with temporal segmentation designed to align with the evolving phases of the COVID-19 pandemic. For analytical purposes, the study period is divided into three distinct phases: the prepandemic phase, covering the years 2018 and 2019; the intrapandemic phase, extending from 2020 through May 2023 and corresponding to the official duration of the US federal COVID-19 public health emergency; and the early postpandemic phase, spanning from June 2023 to the end of 2024.

This phase-based structure enables a detailed examination of temporal trends in healthcare safety and quality, allowing comparisons across periods characterised by markedly different operational pressures, resource allocations and care delivery models. The chosen segmentation reflects both policy-relevant milestones and epidemiological shifts, supporting a more contextually informed interpretation of observed patterns in adverse event reporting.

Variables of interest

The primary variable of interest in this study is the incidence rate of events coded under ICD-10 cluster Y62–Y69, which captures 'Misadventures to patients during surgical and medical care'. This cluster includes a defined set of diagnostic codes representing a range of healthcare-related adverse events: lapses in sterile precautions, incorrect dosage administration, contamination or mislabelling of biological substances and other procedural errors.[18] These events serve as a meaningful proxy for the assessment of healthcare safety

and quality, providing structured data for system-wide monitoring of preventable harm.

The incidence rate is calculated using a time-sensitive approach, with the denominator reflecting the product of the number of patients at risk and the number of days within each observation interval. This method supports a dynamic and longitudinal view of how adverse event patterns evolve over time. A look-back period is applied to ensure accuracy by excluding patients who had experienced a Y62–Y69–coded event before the defined observation window, thus capturing only new (incident) cases during the study period.

To enhance data validity, incidence rates are subject to temporal alignment and demographic consistency criteria, such as age filtering and time-window overlap, allowing for meaningful subgroup comparisons and targeted analyses. The analysis also accounts for the possibility of date shifting, a practice used by healthcare organisations within TriNetX to protect patient privacy, which may introduce minor uncertainty in exact temporal attribution. While ICD-10 Y62–Y69 codes offer valuable insights, their accuracy is contingent on correct documentation, and the study acknowledges the potential for under-reporting or variability due to differences in coding practices across institutions.

Statistical analysis

The primary objective of the statistical analysis is to explore both linear and non-linear temporal trends in the incidence rates of ICD-10 Y62–Y69-coded events, with particular attention to changes occurring across the prepandemic, intrapandemic and postpandemic periods.[18] It is important to note that these analyses were performed using precomputed, aggregated annual incidence rates directly provided by the TriNetX platform. As individual-level data and raw event counts were not accessible, analyses such as Poisson regression with offset or Cochran-Armitage trend tests could not be applied. Consequently, curve-fitting approaches were employed purely for descriptive purposes to illustrate overall temporal patterns in the aggregated data.

The cornerstone of the analytical strategy involves curve-fitting techniques, particularly polynomial regression models, applied purely for descriptive and visual purposes in this study.[35] Quadratic regression was used to capture potential non-linearities in incidence trends over time, providing insights into whether rates accelerated, decelerated or remained stable.[36] These models followed the functional form $y=ax^2 + bx + c$, where y represents the incidence rate, x denotes time (in years) and a, b and c are coefficients estimated from the data. While model diagnostics such as residual analysis and goodness-of-fit measures (eg, R^2, p values and F-statistics) were examined to support interpretability, these analyses were not intended for formal inferential conclusions. To complement this, the Mann-Kendall trend test, a non-parametric method for detecting monotonic (directional) trends in time series data, was employed.[37] This dual-method approach allows for the detection of both consistent directional changes (via Mann-Kendall) and more nuanced non-linear patterns related to the shape of the trend (via quadratic regression). Overall, these trend analyses should be interpreted as exploratory visual summaries designed to illustrate general patterns in the precomputed annual incidence rates, rather than as definitive evidence of causal or statistically robust temporal effects.

Analyses were first conducted on the overall global sample, leveraging the demographic and clinical diversity available through the TriNetX platform. To ensure robustness and generalisability, the findings from the overall sample were further explored through stratified subgroup analyses to assess consistency across different regions.[34] Stratification was performed by geographical region, namely, USA, LATAM, EMEA and APAC, to evaluate regional variability in trends.

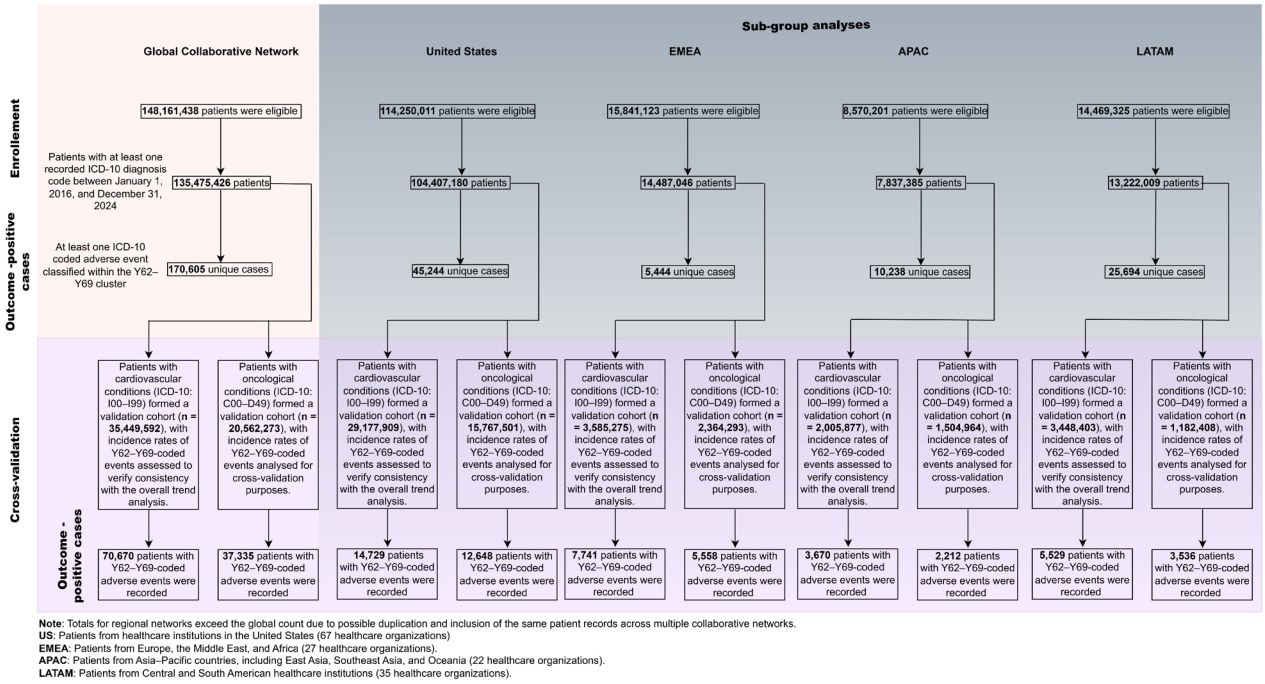
Additionally, sensitivity analyses were conducted using two disease-specific cohorts in both the overall database and region-specific databases. These cohorts were identified using ICD-10 codes for neoplasms (C00–D49) and circulatory system diseases (I00–I99) to examine whether the observed trends remained consistent in clinically meaningful subsamples compared with the broader overall population. In particular, these oncological and cardiovascular subsets were selected due to their well-established epidemiological profiles, which serve as benchmarks for assessing whether observed trends in the general population are replicated in clinically distinct groups. All statistical analyses were conducted using R V.4.5.0 for Windows (R Core Team, 2025).

RESULTS

Study population, flow and characteristics

A total of 148 161 438 patients were eligible for retrospective screening across the TriNetX Global Collaborative Network (figure 1). Of these, 135 475 426 patients had at least one recorded ICD-10 diagnosis code between 1 January 2016 and 31 December 2024, and were included in the main analysis cohort. Within this group, 170 605 unique patients experienced at least one adverse event coded within the ICD-10 cluster Y62–Y69, representing the outcome-positive population.

Subgroup analyses were conducted within the four regional TriNetX networks: USA (n=104 407 180), EMEA (n=14 487 046), APAC (n=7 837 385) and LATAM (n=13 222 009). The number of outcome-positive cases ranged from 5444 in EMEA to 45 244 in the USA. To support sensitivity analyses and contextualise the temporal trends, two disease-specific cohorts were identified: a cardiovascular cohort (ICD-10: I00–I99; n=35 449 592) and an oncological cohort (ICD-10: C00–D49; n=20 562 273). Within these cohorts,



Note: Totals for regional networks exceed the global count due to possible duplication and inclusion of the same patient records across multiple collaborative networks.
US: Patients from healthcare institutions in the United States (67 healthcare organizations)
EMEA: Patients from Europe, the Middle East, and Africa (27 healthcare organizations).
APAC: Patients from Asia–Pacific countries, including East Asia, Southeast Asia, and Oceania (22 healthcare organizations).
LATAM: Patients from Central and South American healthcare institutions (35 healthcare organizations).

Figure 1 Flow diagram of patient selection and cohort stratification. ICD-10, International Classification of Diseases, 10th Revision.

the numbers of patients with outcome-positive events were 70 670 and 37 335, respectively.

Among the 135 475 426 patients analysed (Global Collaborative Network), 56.3% were female and 43.7% male. The racial distribution was as follows: 70.9% white, 18.1% black or African American, 6.2% Asian and 4.8% Other or Unknown. Ethnicity data indicated that 13.4% of patients identified as Hispanic or Latino, 65.7% as Not Hispanic or Latino and 20.9% were reported as Unknown. Due to deidentification protocols and variations in data collection across participating institutions, detailed socioeconomic indicators were not uniformly available. These patients span all age groups from 0 to 89 years and include inpatient and outpatient encounters, offering a broad view of healthcare service use across diverse settings.

Among the 104 407 180 patients from the US Collaborative Network, 55.9% were female and 44.1% were male. The racial composition was 68.3% white, 20.7% black or African American, 5.4% Asian and 5.6% Other or Unknown. Ethnicity data showed that 14.6% of patients identified as Hispanic or Latino, 67.9% as Not Hispanic or Latino and 17.5% were reported as Unknown. As with the global data, deidentification protocols and institutional variation limited the availability of consistent socioeconomic information. The cohort comprised a wide age range from 0 to 89 years and reflected both inpatient and outpatient settings, contributing to a comprehensive representation of healthcare utilisation in the USA.

Among the 14 487 046 patients included in the EMEA Collaborative Network, 54.7% were female and 45.3% male. Race and ethnicity data were more limited due to regional documentation practices and privacy protocols; most patients were recorded as white or Other/Unknown, with granular racial or ethnic subcategories inconsistently reported. As with other networks, socioeconomic indicators were not uniformly available. Patients ranged in age from 0 to 89 years, and data encompassed both inpatient and outpatient encounters, supporting the broad representativeness of healthcare delivery across EMEA settings.

Among the 7 837 385 patients from the APAC Collaborative Network, 52.9% were female and 47.1% were male. Detailed race and ethnicity data were largely unavailable. As a result, most patients were categorised under ‘Other’ or ‘Unknown’. Socioeconomic data were not consistently captured across institutions. Patients represented a full age spectrum from 0 to 89 years and included both inpatient and outpatient settings, offering insight into healthcare service use across diverse clinical environments in the APAC region.

Among the 13 222 009 patients from the LATAM Collaborative Network, 54.7% were female and 45.3% were male. As with APAC, race and ethnicity data were inconsistently reported due to regional data standards and deidentification protocol. Socioeconomic variables were not uniformly available. The cohort included patients from across the age spectrum (0–89 years) and comprised both inpatient and outpatient encounters.

Temporal trends in the incidence of ICD-10 Y62–Y69 events across global and regional cohorts (2016–2024)

At the global level, incidence rates of Y62–Y69-coded adverse events increased from 0.04 to 0.09

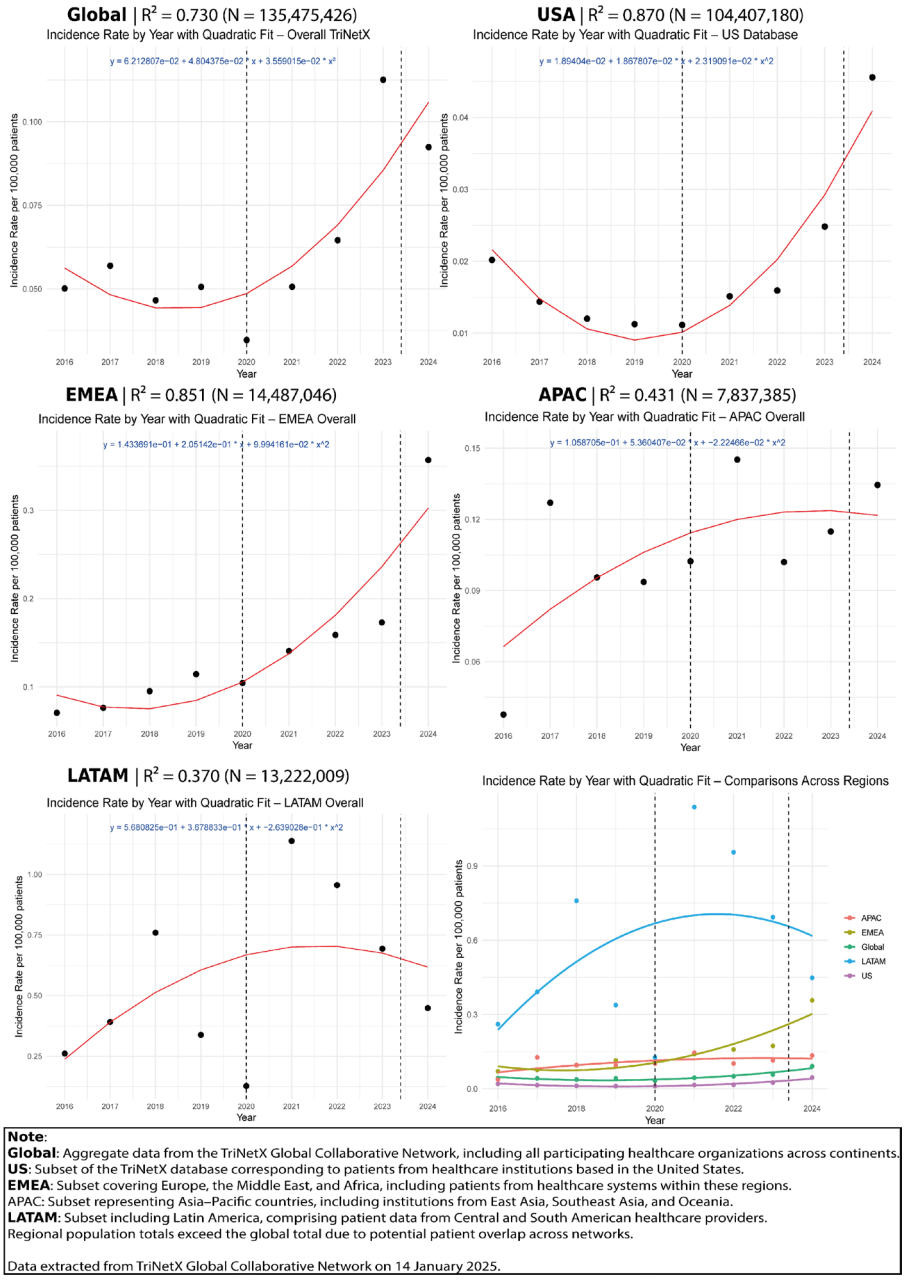


Figure 2 Temporal trends in the incidence rate of ICD-10 Y62–Y69–coded adverse events (2016–2024) across global and regional TriNetX cohorts. ICD-10, International Classification of Diseases, 10th Revision.

per 1 00 000 patients between 2016 and 2024, with a marked upward inflection observed in the early post-pandemic phase ($R^2 = 0.730$, $p<0.001$; online supplemental file 1, figure 2). Quadratic regression identified a significant non-linear trajectory, corroborated by goodness-of-fit diagnostics detailed in online supplemental file 2, along with the code used for performing the analytics. These regression-based findings should be interpreted as exploratory visual trends derived from precomputed annual incidence rates (ie, regressions are not intended to imply causal or definitive inferential conclusions in the context of this study).

Regional trends varied. EMEA exhibited a consistent and statistically significant increase ($R^2 = 0.851$, $p<0.001$). The US showed a non-linear trend identified only via polynomial modelling ($R^2 = 0.870$, $p<0.001$), with no directional consistency detected by the Mann-Kendall test ($p=0.064$). APAC and LATAM did not demonstrate significant temporal trends ($R^2 = 0.431$ and 0.370; both $p>0.05$), likely due to higher year-to-year variability (figure 2).

Sensitivity analyses within the cardiovascular cohort confirmed a strong global upward trend ($R^2 = 0.934$, $p<0.001$), which was also evident in EMEA ($R^2 = 0.876$, $p<0.001$) and APAC ($R^2 = 0.563$, $p<0.001$). No substantial trends were found in the USA or LATAM cardiovascular cohorts ($R^2 = 0.013$ and 0.096, respectively; figure 3).

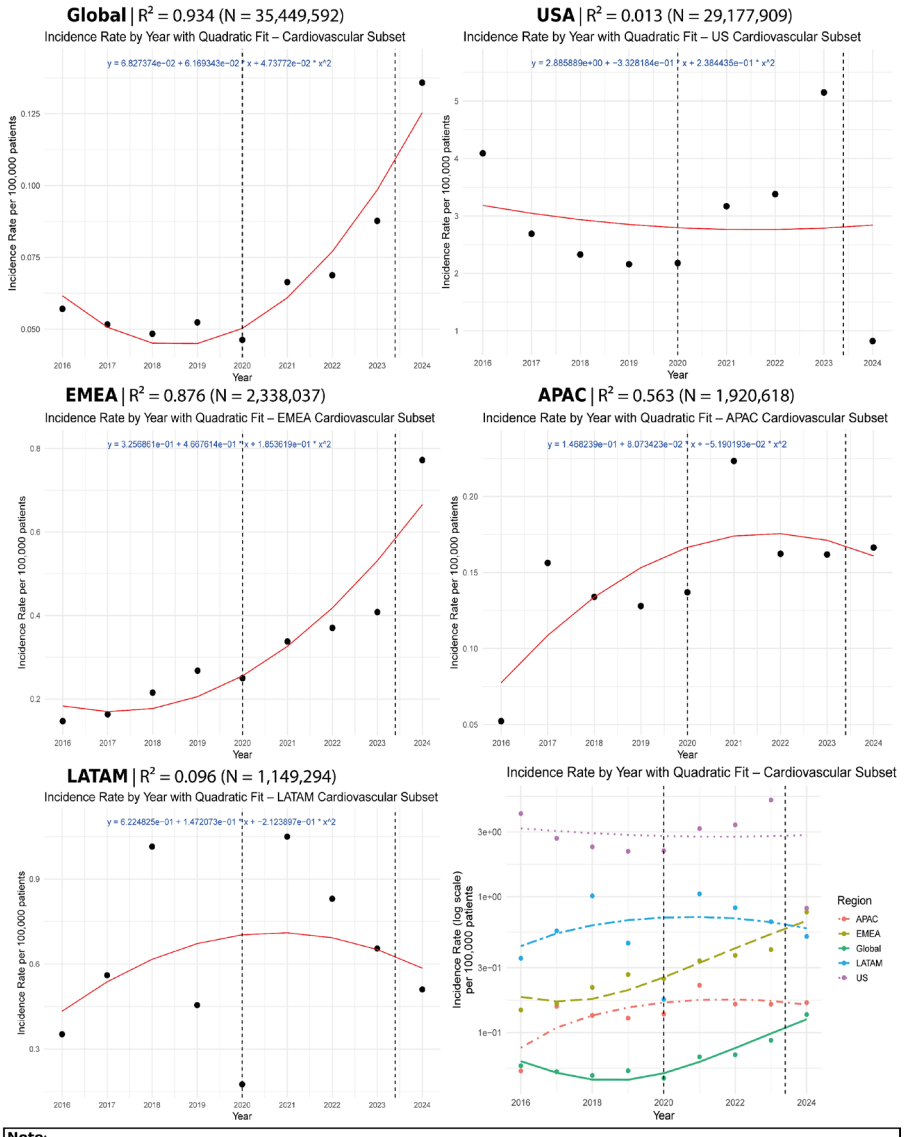


Figure 3 Sensitivity analysis of Y62–Y69 trends in the cardiovascular cohort across global and regional TriNetX data sets (2016–2024).

Similarly, the oncological cohort exhibited consistent temporal increases globally ($R^2 = 0.953$, $p<0.001$), in EMEA ($R^2 = 0.860$) and in the USA ($R^2 = 0.970$). In contrast, APAC and LATAM showed modest or unstable patterns ($R^2 = 0.370$ and 0.136; figure 4).

DISCUSSION

This study presents the first multinational, real-world analysis of ICD-10 Y62–Y69-coded adverse events, leveraging data from over 135 million patients in the TriNetX Global Collaborative Network. Our findings demonstrate a clear and accelerating global increase in healthcare-related procedural adverse events, raising urgent concerns about postpandemic safety resilience. The analysis revealed a consistent and significant increase in the incidence rates of healthcare-related misadventures globally. Between 2016 and 2024, the global incidence rate per 100 000 patients more than doubled (from 0.04 to 0.09, a 125% increase), with the steepest increases observed in EMEA (414%) and APAC (225%). Similar upward trajectories were seen in cardiovascular (133%) and oncological (140%) subsets, further reinforcing the observed trends. This trend appeared more pronounced in the early postpandemic phase, when many countries experienced systemic shifts in care delivery, documentation or exposure to procedural risk.[38–40] However, with only aggregated annual incidence rates available for modelling, we cannot determine precisely when these changes occurred. Polynomial regression analyses were

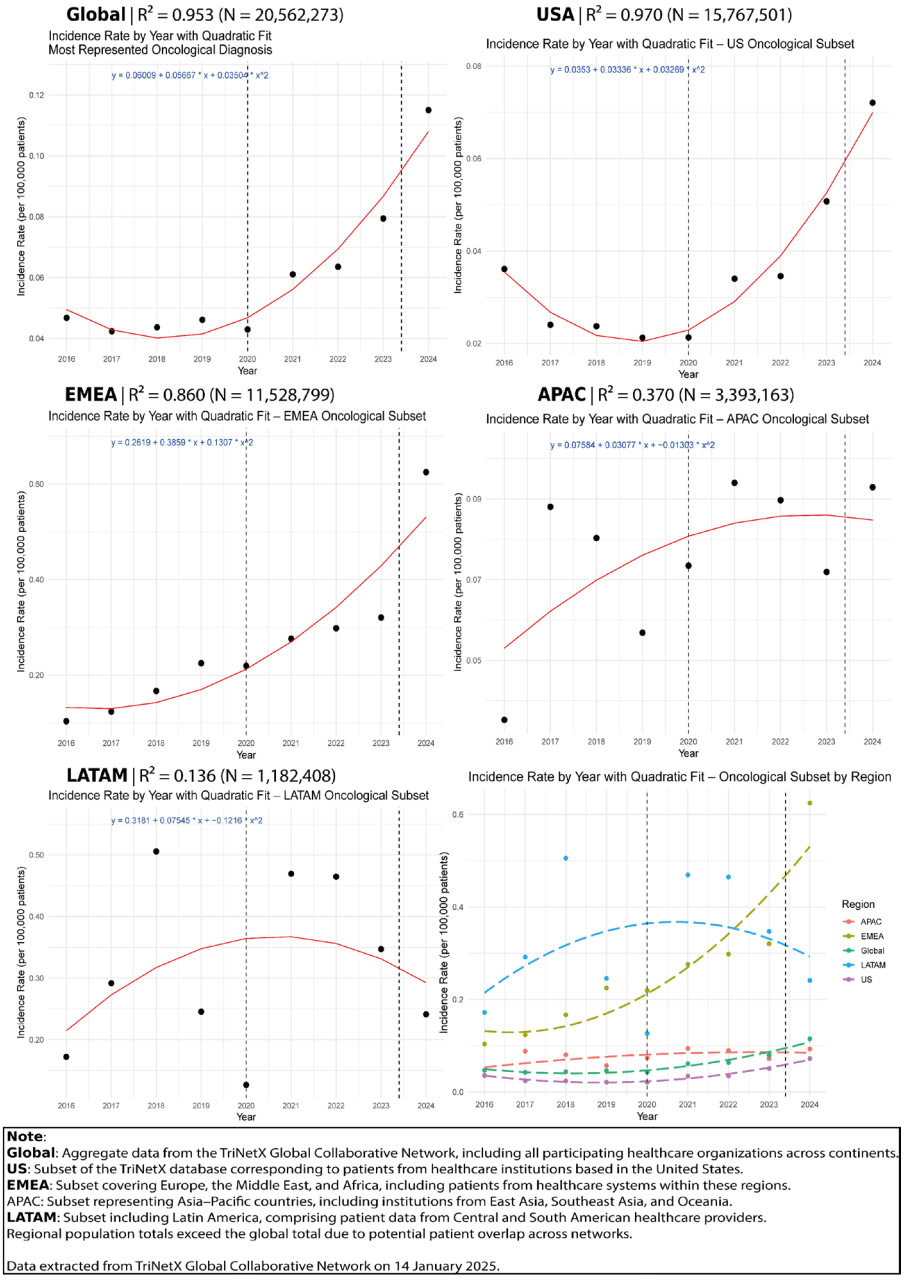


Figure 4 Sensitivity analysis of Y62–Y69 trends in the oncological cohort across global and regional TriNetX data sets (2016–2024).

employed solely for visual and descriptive purposes, to depict general temporal patterns and illustrate changes over time. These should not be interpreted as supporting inferential or causal conclusions.

Regional trends demonstrated marked heterogeneity in both the magnitude and statistical significance of incidence rate changes. In the EMEA region, incidence rates rose from 0.07 to 0.36 per 100 000 between 2016 and 2024, representing a 414% increase. The USA showed a less pronounced absolute increase (from 0.02 to 0.05 per 100 000). Still, a statistically significant non-linear trend was exhibited, and it was detectable only through polynomial regression, suggesting a more complex, non-monotonic pattern that was not captured by rank-based methods alone. Conversely, APAC and LATAM regions exhibited less consistent patterns: although APAC experienced a 225% increase (from 0.04 to 0.13) and LATAM a 73% increase (from 0.26 to 0.45), neither region showed statistically significant trends, possibly due to higher year-to-year variability within network segments. These regional disparities may reflect underlying differences in healthcare infrastructure, reporting practices, exposure to procedural risk or pandemic-related service disruptions.[41–45]

The significant upward trends identified in this study contrast with earlier assumptions that the rate of adverse procedural events had plateaued or declined in high-resource health systems.[46 47] Previous national-level analyses, often relying on institutional reporting

or claims data, have typically underestimated the frequency of medical misadventures due to underreporting, variability in coding practices or narrow definitions of adverse events.[46 48–51]

The observed postpandemic acceleration in Y62–Y69-coded events aligns with emerging literature describing the residual impacts of COVID-19 on healthcare delivery, including staff shortages, procedural backlogs, increased care complexity and disruptions in routine safety protocols.[52–54] Similar findings have been reported in surgical site infections, medication errors and diagnostic delays during the pandemic, particularly in systems strained by resource constraints.[55–58] The high concordance between overall trends and those found in clinically distinct cardiovascular and oncological subsets supports the robustness of our findings and suggests systemic patterns rather than condition-specific anomalies.

The comprehensive nature of this analysis underscores several key implications for healthcare quality and safety practices. First, the pronounced global and regional increases in Y62–Y69-coded adverse events highlight critical vulnerabilities in current patient safety monitoring frameworks, particularly under conditions of system-wide stress such as those experienced during and immediately following the COVID-19 pandemic.[59–62] The observed patterns suggest a pressing need to reinforce real-time surveillance mechanisms and strengthen institutional capacity for proactive risk management and mitigation.

Second, the variability observed between regions emphasises the necessity of context-specific interventions tailored to local infrastructure, workforce capacity and clinical practice environments.[63–65] The particularly steep rises observed in EMEA and APAC regions indicate potential gaps in standardised procedural safety practices or differences in documentation rigour, which require targeted strategies to enhance compliance and accuracy in adverse event reporting. These findings underscore the value of international benchmarking facilitated by platforms such as TriNetX, enabling the identification of best practices and promoting their dissemination across diverse healthcare settings.[66–68]

Limitations of this study warrant careful consideration. To mitigate potential sources of bias, the study applied consistent inclusion criteria across regions, used standardised ICD-10 codes for event identification and conducted sensitivity analyses in two clinically meaningful disease-specific cohorts. Despite the strengths of a large-scale, multinational data set, several factors constrain our interpretation of our findings.

First, the retrospective observational design limits causal inference and may introduce selection or documentation biases. As the analysis relies entirely on routinely collected electronic health records, data completeness and accuracy depend on the quality of clinical documentation, which varies across institutions and regions. Importantly, the ICD-10 Y62–Y69 codes, while standardised, are likely underreported in real-world data sets due to variability in coding practices, lack of awareness or institutional disincentives to report adverse events. This underreporting may lead to a systematic underestimation of the true incidence of medical misadventures, particularly in settings where patient safety surveillance is not rigorously enforced. Moreover, differences in coding practices across regions and over time may have influenced the observed trends. While ICD-10 (Y62–Y69) codes provide a standardised framework, their application can vary depending on local documentation practices, coder training, institutional safety culture and national reporting incentives. These differences may lead to either underestimation or overestimation of true adverse event rates, potentially confounding direct comparisons between regions and affecting temporal trend interpretation. Additionally, potential improvements in coding practices and increased awareness of procedural safety over time may have contributed to the observed increase in Y62–Y69-coded events.[69 70] Although this factor is unlikely to fully account for the trends observed, particularly in USA and European settings, it should be considered when interpreting temporal patterns.[71]

Second, the study spans diverse regional networks (US, EMEA, APAC, LATAM) that differ substantially in healthcare infrastructure, workforce composition, reimbursement models and reporting requirements. These contextual differences may introduce regional biases and limit direct comparability. In particular, smaller patient populations in LATAM and APAC, coupled with greater year-to-year variance, may have reduced the statistical power needed to detect significant temporal trends in those regions. This heterogeneity, while informative, necessitates caution when generalising results across or within regions. Moreover, the temporal segmentation of the pandemic phases was based on the US federal COVID-19 public health emergency timeline, which reflects the majority of the data sources used in this study. However, this approach may limit comparability and generalisability to non-US regions where different pandemic definitions and timelines apply.

Third, while polynomial regression was used to illustrate general temporal patterns in annual incidence rates, the interpretation of these visual trends should be approached with caution. Although defined inclusion criteria and sensitivity analyses in disease-specific cohorts were applied to support consistency, some unmeasured contextual factors, such as institutional safety culture or regional policy shifts, may still influence the observed patterns. However, as the regression models were not intended for inferential analysis, these factors were not formally adjusted for, and their potential influence should be interpreted in light of the study's descriptive scope.

Finally, limitations also arise from the structure of the TriNetX network itself. Although the platform is International Organization for Standardization (ISO)-certified and HIPAA-compliant, some data transformations, such as date shifting to protect patient privacy, may introduce minor inaccuracies in temporal trend alignment. Additionally, specific sociodemographic fields (such as ethnicity or socioeconomic conditions) were not consistently available for each region, limiting the scope of the analysis for different subgroups. However, despite these constraints, the internal consistency observed across multiple cohorts and analytical approaches enhances the overall credibility and relevance of the findings.

CONCLUSIONS

This study, encompassing over 135 million patients across four continents, offers exploratory insights into global patient safety patterns and sets a precedent for scalable surveillance of procedural harm using real-world data. The analysis of ICD-10 Y62–Y69-coded events supports the hypothesis of a significant and accelerating global trend in healthcare-related procedural misadventures, particularly pronounced in the early postpandemic period. The findings, especially if confirmed by further studies involving individual-event level data, underscore the enduring impact of systemic disruptions on patient safety and highlight the value of using harmonised electronic health data and complementary statistical methods to detect complex temporal patterns. Regional disparities and non-linear trajectories reinforce the need for locally tailored safety interventions, strengthened and supported surveillance infrastructure and renewed investment in global patient safety priorities.

Author affiliations
[1]Department of Biomedical Sciences for Health, University of Milan, Milan, Italy
[2]Health Professions Research and Development Unit, IRCCS Policlinico San Donato, San Donato Milanese, Italy
[3]Department of Clinical and Molecular Medicine, Sapienza University of Rome, Roma, Lazio, Italy
[4]Department of Medical and Movement Sciences and Wellness, University of Naples Parthenope, Naples, Campania, Italy
[5]Nursing, Technical and Rehabilitation Department - DaTeR, Azienda Unità Sanitaria Locale di Bologna, Bologna, Italy
[6]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[7]Centre of Excellence for Nursing Scholarship, Rome, Italy
[8]Data Management, Scientific Directorate, IRCCS Policlinico San Donato, San Donato Milanese, Italy
[9]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Lombardy, Italy
[10]Scientific Directorate, IRCCS Policlinico San Donato, San Donato Milanese, Italy
[11]Frances Payne Bolton School of Nursing and School of Medicine, Case Western Reserve University, Cleveland, Ohio, USA

Social media Rosario Caruso, LinkedIn @rosario-caruso-92b633138

Contributors RC: Conceptualisation, Methodology, Visualisation, Writing—Original Draft, Writing—Review and Editing. MDM: Conceptualisation, Methodology, Writing—Original Draft, Writing—Review and Editing. EDS: Methodology, Validation, Writing—Review and Editing. SD: Methodology, Validation, Writing—Review and Editing. AM: Methodology, Validation, Writing—Review and Editing. GC: Data Curation, Validation, Writing—Review and Editing. AS: Methodology, Supervision, Writing—Review and Editing. EG: Formal analysis, Data Curation, Investigation. SB: Formal analysis, Data Curation, Investigation. PMP: Data Curation, Validation, Writing—Review and Editing. SC: Supervision, Validation, Writing—Review and Editing. LM: Conceptualisation, Supervision, Writing—Review and Editing. MD: Conceptualisation, Supervision, Writing—Review and Editing. RC is the guarantor for this article. LM and MD are co-last authors.

Funding This study was partially supported by Ricerca Corrente funding from the Italian Ministry of Health to IRCCS Policlinico San Donato. Award/grant number: N/A.

Competing interests None declared.

Patient and public involvement statement Patients and the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. All data were extracted from the TriNetX Global Collaborative Network. Aggregated incidence rates and the R code used for statistical analysis are provided in online supplemental file 2.

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ORCID iDs
Rosario Caruso http://orcid.org/0000-0002-7736-6209
Emanuele Di Simone http://orcid.org/0000-0002-6373-8163

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