

# Errors and biases in modern healthcare: public health, medico-legal and risk management aspects

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# Errors and biases in modern healthcare: public health, medico-legal and risk management aspects

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# Editorial: Errors and biases in modern healthcare: public health, medico-legal and risk management aspects

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## KEYWORDS

risk management, legal medicine, medical error, medical bias, medical malpractice

## Editorial on the Research Topic

[Errors and biases in modern healthcare: public health, medico-legal and risk management aspects](#)

Is to err (only) human nowadays? Error is traditionally considered an unavoidable part of human life and activities, and the phrase “to err is human” has been a sort of dogma in medicine for the last decades (1). The actual genesis of human error is still largely unexplored, and the interplay between hospital organization, enforcement of policies, and human choices is still far from being decrypted (2, 3). However, we do know that teamwork is the bedrock of modern medicine and relies on human paradigms like trust (4). Can we trust artificial intelligence (AI)? The question is misleading. AI is a technology able to find correlations between input variables, but it does not currently have the capacity to infer causal relationships (at least following the traditional rules of logic). AI has no professionalism, no free will, no reputation: physicians must learn how to work with a technology suppressing the human need to trust it and how to supervise its outputs often without the possibility to understand its internal processes (4). A new kind of error—the bias (systematic error)—will emerge as a leading issue in medicine. Improving in-hospital management processes is thus the most pragmatic choice that the institutions can make now. But AI is not only a source of new kinds of errors: it does help to contain common risks in diagnosis, treatment, and prevention programs (5–7). Therefore, a constructive and pragmatic attitude is needed.

One of the biggest challenges in modern healthcare is linked to healthcare-acquired infections (HAI): multidrug-resistant bacteria are a public health threat, and HAI inflate in-hospital mortality, length of stays, direct costs of care, and disability-adjusted life years (8).

Ferorelli et al. evaluated how a new clinical risk management protocol impacted newborns, finding a reduction in umbilical venous catheter infections and an improvement in hospital stay lengths. On the other hand, exploring medical malpractice claims for HAI, Grassi, Grazzini et al. performed a cost-effectiveness analysis using epidemiological data,

including experts in infection prevention and control sitting on the hospital decisional committee. They found that improving the management of medical malpractice claims can improve the economic outcomes, containing the double cost (implementing policies against HAI and paying for the related claims) that many hospitals must face because of a public health issue (Grassi, Grazzini et al.). De Micco, Grassi et al. stressed that new technologies have already been introduced in many hospitals, but regulations are still vague and insufficient, with the borders between the liability of the manufacturer/developer, the institution, and the user still ill-defined. Instead, Kameyama et al. evaluated the impact on the drug market of a Japanese risk management plan, finding that, when specific adverse reactions and drug therapeutic categories were evaluated, it succeeded in improving patient safety.

Moreover, our special issue hosted a systematic review on the potential role of AI systems to promptly detect adverse events (making correlations that a human mind could not make or would take a longer time to make), predict future incidents, and assess risks of sentinel events like in-hospital falls (De Micco, Di Palma et al.). Regarding sentinel events, another contribution evaluated the actual impact of retained surgical foreign bodies impact, finding that, despite their health consequences, they are generally mild and have a 2-fold risk of criminal complaint, indicating that the patient blames specific professionals rather than the (impersonal) institution for the events (Grassi, Focardi et al.). Visci et al. focused on a topic of utmost relevance: can the knowledge on the causal processes related to medical errors developed by the experts in legal medicine be used to improve clinical services? Their observational study concluded that structured forensic consultation services should be incorporated into clinical practice, being able to quickly and professionally address hot topics like capacity for consent that are frequent issues that can “paralyze” hospital activities (Visci et al.). Refolo et al. analyzed another face of the term “risk”: the risk of aggressive behavior based on genetic predisposition. Aggressivity is an issue of public interest both in hospital and common social contexts, and the potential role of genes in risk profiling has a potential dual use that should lead to strong ethical barriers (Refolo et al.). Finally, Aurilio et al. discussed the birth-related long bone fractures in healthy newborns—an example of an adverse event that can be both due to unavoidable factors and to human errors, with the compliance with best practices and prevention policies being the cornerstone of medico-legal defense.

In conclusion, in medicine, there is no such thing as a rigid dichotomic difference between errors and proper conduct, but there is a risk density entangled with medical services that can be addressed/neglected, inflated/deflated, or defined/left unknown. Hunting for manipulable variables in the unknown and improving

the management of the risks are the real keywords of the papers of this special issue. To err is not only human anymore, but only humans can envision the future in healthcare and tailor new strategies to make it safe for all stakeholders.

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# Quality improvement in neonatal care through enhanced patient safety and clinical risk management: a before-and-after study about neonatal sepsis

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**Introduction:** Neonatal sepsis, classified into early-onset and late-onset based on symptom timing, poses significant risks of morbidity and mortality, especially in low birth weight infants. Effective clinical risk management protocols are crucial in reducing these risks.

**Methods:** This before-and-after study evaluated the impact of a newly implemented clinical risk management protocol in the Neonatology and Neonatal Intensive Care Unit (NICU) at Policlinico Hospital-University of Bari. The study included 399 neonates over three years, comparing pre- and post-protocol outcomes. Data collection focused on maternal and neonatal demographics, infection rates, and hospital stay lengths. Statistical analysis included t-tests, Wilcoxon-Mann-Whitney tests, and logistic regression models.

**Results:** The study found no significant differences in neonatal pathologies or demographics between pre- and post-protocol groups. However, post-protocol implementation showed a notable reduction in umbilical venous catheter (UVC) infections ( $p = 0.018$ ) and improved hospital stay lengths. Blood and urine cultures did not show significant changes in microbial patterns post-protocol.

**Discussion:** The findings underscore the effectiveness of structured clinical risk management protocols in enhancing neonatal outcomes, particularly in reducing specific infection risks. Despite the study's limitations, including its observational nature and sample size, the results advocate for broader adoption and further research on these protocols in diverse healthcare settings. The positive outcomes highlight the importance of continuous clinical risk management efforts in high-risk neonatal environments.

## KEYWORDS

neonatal sepsis, clinical risk management, patient safety, quality improvement, neonatal care

## Introduction

Sepsis is defined as a “clinical syndrome of potentially lethal organ dysfunction caused by a dysregulated response to infection” (1). Neonatal sepsis is a cause of morbidity and the third leading cause of neonatal mortality, especially in infants with low birth weight (Low Birth Weight < 2,500 g; Very Low Birth Weight < 1,500 g; Extremely Low Birth Weight < 1,000 g) (2). Neonatal sepsis can be classified into two major groups based on the timing of their presentation: Early-onset sepsis (EOS) occurs within 72 h of life, and Late-onset sepsis (LOS) occurs after 72 h of life (3). Epidemiological data about the EOS show an incidence of less than 1 per 1,000 live births when considering the entire neonatal population. However, the incidence is 10–15 per 1,000 live births among VLBW infants (4). The incidence of LOS is higher than that of EOS, especially among preterm infants, where it is estimated to be between 20–30 per 1,000 live births (3, 5).

Several factors increase the risk of neonatal sepsis, including: prolonged rupture of membranes, maternal infections, invasive procedures. Pathogens commonly involved in EOS are Group B Streptococcus (GBS), *Escherichia coli* (*E. coli*), *Listeria monocytogenes*, Other Gram-negative bacteria (Klebsiella, Pseudomonas, and Haemophilus) (6–8). Late-Onset Sepsis (LOS) The primary pathogens responsible for LOS include: Coagulase-negative Staphylococci (CONS), *Staphylococcus aureus*, Gram-negative bacteria (*E. coli*, Klebsiella, Enterobacter, and Pseudomonas), Fungal infections (*Candida* spp) (9, 10).

Several key issues in neonatal clinical risk have been described in the literature, including outdated pediatric guidelines, structural challenges, risks in departments like emergency and intensive care units, and the significant issue of drug administration errors (11). Therefore, clinical risk management tools were applied to this field in this study.

Indeed, our study underlines several key issues in pediatric clinical risk management, including the scarcity and outdated nature of pediatric guidelines, structural challenges in healthcare settings, the inherent risks of certain departments like emergency and intensive care units, and the prevalent issue of medication errors (12). Medication errors, particularly, are emphasized due to their frequency and the significant impact they have on patient safety. The discussion extends to strategies and tools for mitigating these risks and the integration of clinical pharmacists into intensive care units, showcasing their effectiveness in reducing errors (13).

Implementing procedures and protocols in clinical risk management is instrumental in reducing risks in clinical care, with various studies and analyses highlighting their effectiveness across different aspects of healthcare. According to S. Green et al. (14), such protocols provide essential training in risk management techniques for healthcare providers and establish agreed guidelines that contribute to lower rates of negligence claims and reduce malpractice insurance premiums in high-risk specialties (14).

Furthermore, the incorporation of risk management protocols into medical education promotes risk control habits among physicians, enabling them to practice quality medicine with reduced concerns for malpractice reprisal and peer review (10). M. Gulino et al. emphasize that these protocols introduce prevention and management instruments that contribute to error reduction and quality enhancement in healthcare services (15). This sentiment is echoed by J. Samanta and A. Samanta, who highlight the role of clinical

guidelines linked to the medical evidence base in enhancing care quality and minimizing treatment variations, ultimately preventing harm to patients (16).

Clinical risk management shifts the focus from litigation protection to caring for injured patients and meeting their needs, thereby improving the quality of care and reducing harm (17). R. Clements also points out the goal of decreasing adverse events and harm to patients, minimizing claims, and managing claim costs effectively through continuous improvement focused on patient welfare (18).

A protocol has been implemented in the Neonatology and Neonatal Intensive Care Unit (NICU) of the Policlinico Hospital-University of Bari to prevent healthcare-associated infections, ventilator-associated pneumonia, central line bloodstream infections (CLABSI), and epidemic events.

This study aims to evaluate whether, following the introduction of the protocol described, there is an improvement in the outcomes of neonates admitted to the Neonatology and Neonatal Intensive Care Unit (NICU).

## Study objectives

The objective of this study is to assess whether, following the introduction of the protocol described in the previous chapter, there is an improvement in the outcomes of neonates admitted to the Neonatology and Neonatal Intensive Care Unit (NICU).

## Materials and methods

This study employed an observational design to examine neonatal outcomes at the Policlinico Hospital-University of Bari, a tertiary care facility with over 1,000 beds, after protocol introduction. The protocol, implemented in the Neonatology and Neonatal Intensive Care Unit (NICU) of the Policlinico Hospital-University of Bari, consists of four documents addressing the prevention of: Healthcare-Associated Infections (HAIs) (Figure 1); Ventilator-Associated Pneumonias (VAPs) (Figure 2); central line bloodstream infections (CLABSI) (Figure 3); and epidemic events (Figure 4). The protocol applies to two areas of Neonatology and NICU (Neonatal Intensive Care and Sub-intensive Care) and is directed at all staff working in these areas (both regularly and occasionally) as well as the families of hospitalized infants.

The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines for reporting of observational studies were followed. The research protocol was approved by the local General Health Directorate (nr. 1,497 on 2020.11.19).

All patients admitted to the Neonatology and NICU of the Policlinico Hospital-University of Bari in three-year period 1 January 2019–31 December 2021 were enrolled.

The data collection period spanned from January 2019 to December 2021, encompassing the COVID-19 pandemic. This period saw an increase in healthcare-associated infections, including superinfections and co-infections, which could influence neonatal outcomes. However, none of the newborn patients in our sample, whether born to COVID-positive or COVID-negative mothers, tested positive for COVID-19 (19).

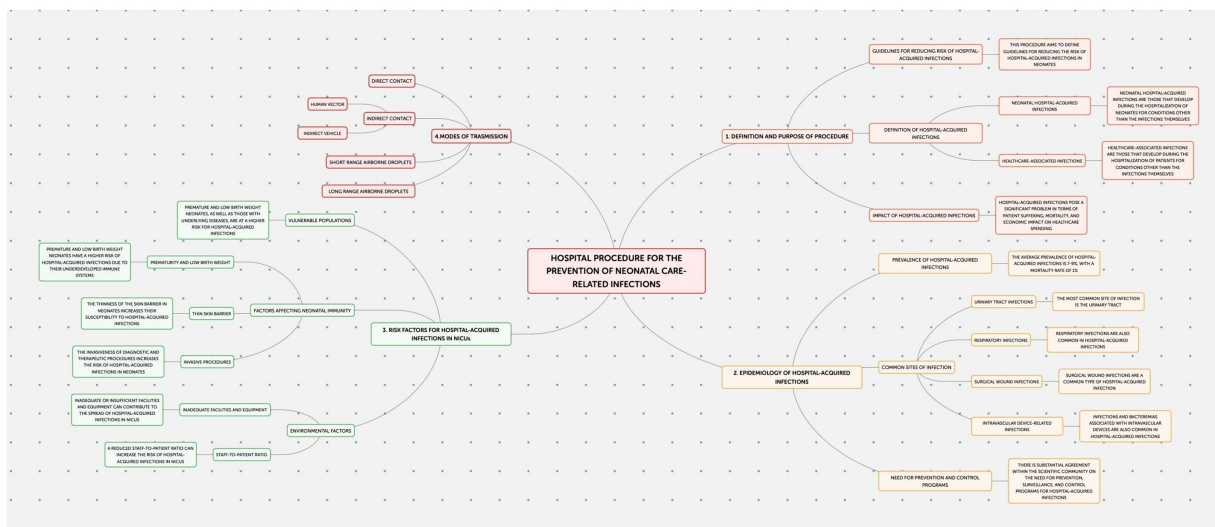


FIGURE 1  
Hospital procedure for the prevention of neonatal care-related infections.

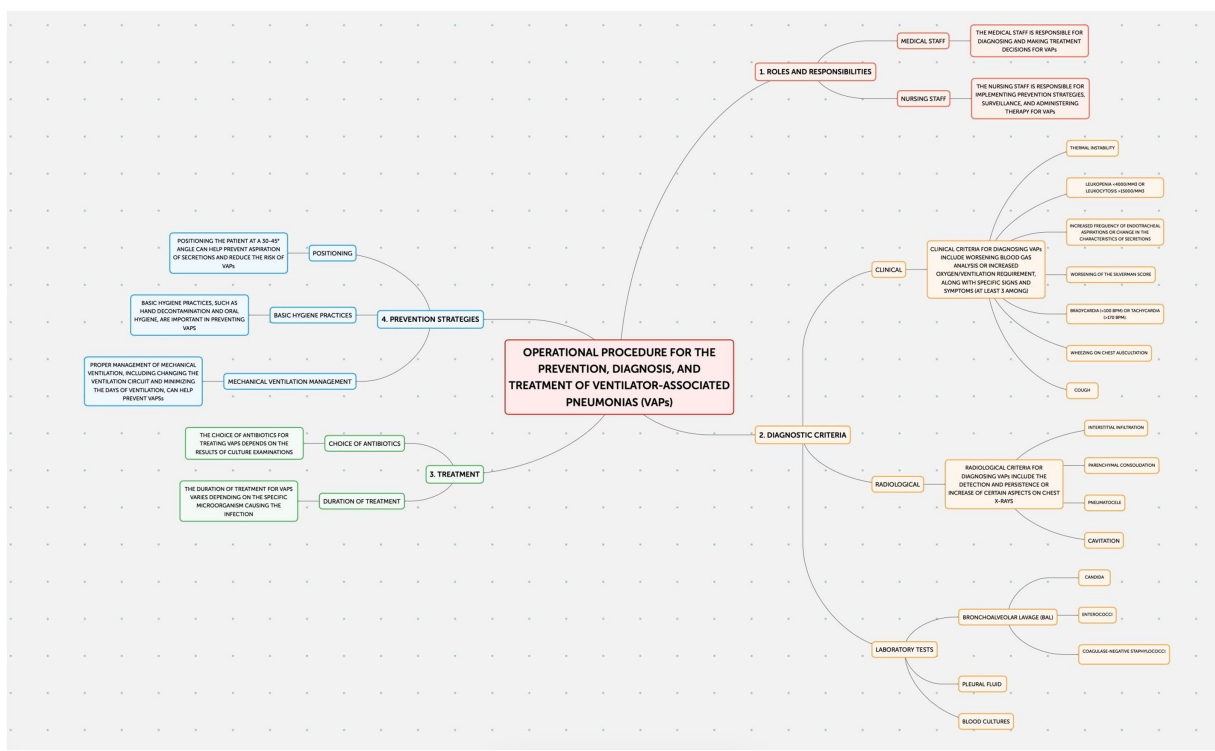


FIGURE 2  
Operational procedure for the prevention, diagnosis, and treatment of ventilator-associated pneumonias (VAPs).

For each participant, both maternal and neonatal demographic and anamnestic data regarding pregnancy, delivery and the postnatal period were systematically collected from medical charts. Data regarding neonatal urine and blood cultures, swabs, infections (i.e., sepsis; central venous catheter (CVC), peripheral venous catheter (PVC), and umbilical venous catheter (UVC) infections) and antibiotic therapy were specifically collected.

Neonates were classified as preterm if born at gestational ages <37 weeks and as low birth weight if weighing <2,500 g. Data anonymization was ensured through the use of coded keys. Based on the approval date of protocol, participants were categorized into “pre” and “post” the introduction of the protocol in July 2020. Microsoft Excel software was utilized for data collection, and Jamovi-Electron software was used for statistical processing.

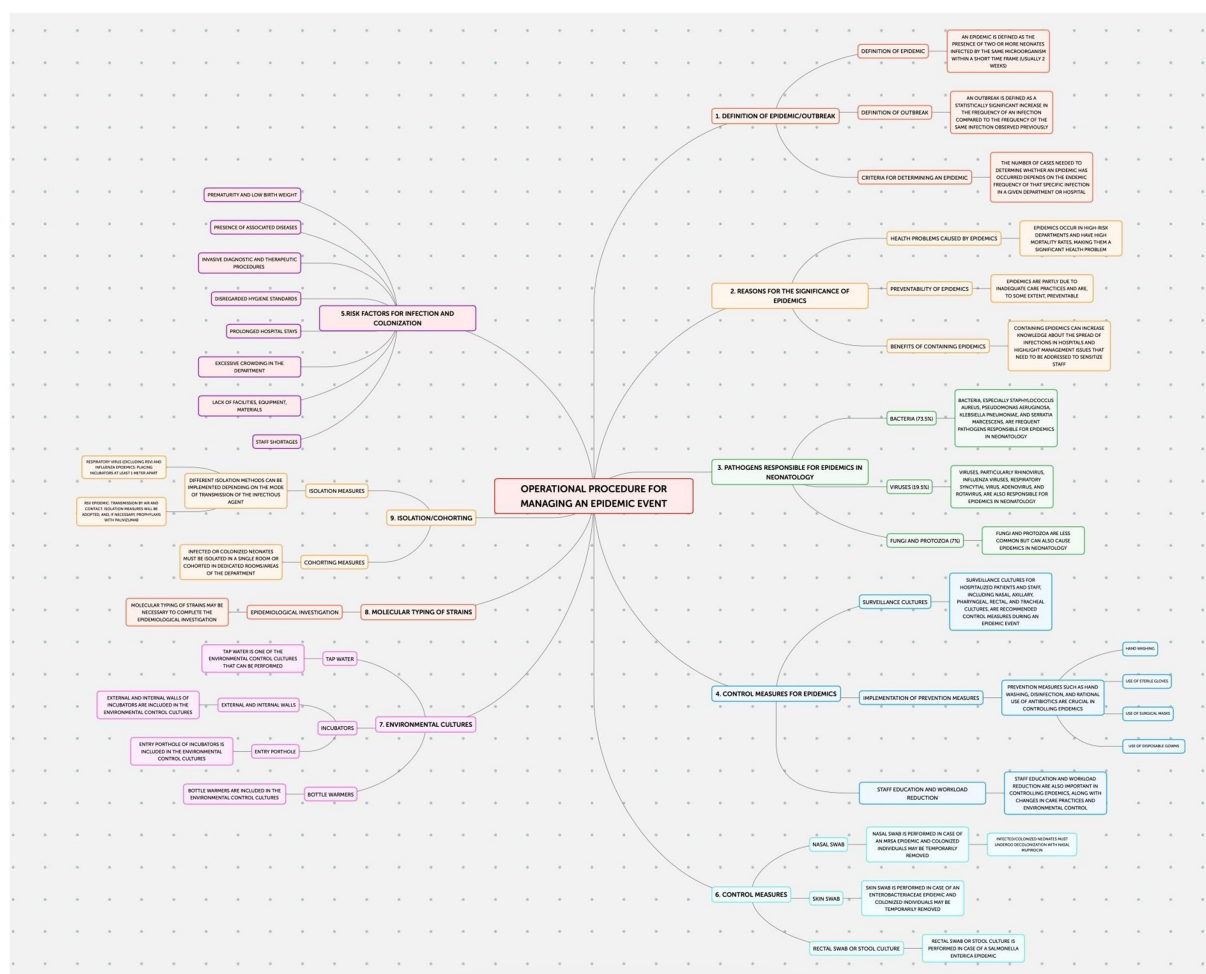


FIGURE 3  
Operational procedure for the prevention of infections associated with intravascular devices.

Quantitative variables were reported as mean, standard deviation, and interquartile ranges. The normality of distribution was assessed using Q-Q plots, skewness, kurtosis, and the Shapiro-Wilk test. The *t*-Student test was applied to parametric quantitative variables, and the Wilcoxon-Mann-Whitney test was used for non-parametric ones. Qualitative variables were presented in proportions, and their distribution was analyzed using the  $\chi^2$ -test with Fisher's correction as needed (for group sizes <5 units). Odds Ratio (OR) with 95% confidence intervals (CI95%) was calculated using logistic regression models as a measure of association. Results with  $p < 0.05$  were considered statistically significant. Correlation between variables was assessed using the Pearson Test, with significance set at  $p > 0.05$ .

## Results

Our analysis encompassed a cohort of 399 neonates, segregated into pre-protocol (39.2%,  $n = 156$ ) and post-protocol (60.8%,  $n = 243$ ) groups, aiming to evaluate the efficacy of a newly implemented neonatal care protocol. Sex distribution within the cohort was similar pre- and post-protocol, with 40.45% females ( $n = 161$ ) and 59.55%

males ( $n = 237$ ), showing no significant sex-based disparities in protocol outcomes ( $\chi^2$ -test,  $p > 0.05$ ).

Mean gestational age was 34.5 (SD 4.40) weeks for the pre-protocol group and 35.0 (SD 4.40) weeks for the post-protocol group, with distribution analyses indicating Gaussian curves for both (Shapiro-Wilk test,  $p < 0.001$ ), yet no statistically significant difference was identified between the groups (*t*-Student test,  $p = 0.128$ ).

Mean birth weight was 2,438 g (SD 947) in the pre-protocol group and 2,289 g (SD 948) in the post-protocol group, both with normal distribution (Shapiro-Wilk test,  $p < 0.01$  for post;  $p = 0.001$  for pre) and no significant difference in birth weight across groups (*t*-Student test,  $p = 0.214$ ). Birth weight categories (>2,500 g vs. <2,500 g) were similar between pre- and post-protocol groups ( $\chi^2$  test,  $p > 0.05$ ).

Delivery methods (spontaneous vs. cesarean) and the incidence of multiple gestation did not differ between pre and post protocol groups ( $\chi^2$ -test,  $p > 0.05$ ), as well as the ratio between outborn and inborn ( $\chi^2$ -test,  $p > 0.05$ ).

In assessing maternal pathologies, including gestational diabetes, gestational hypertension, preeclampsia/eclampsia, preterm premature rupture of membranes (pPROM), and other obstetric pathologies, our analyses did not reveal significant differences between the pre- and post-protocol groups ( $\chi^2$ -test,  $p > 0.05$ ) (Figure 5).



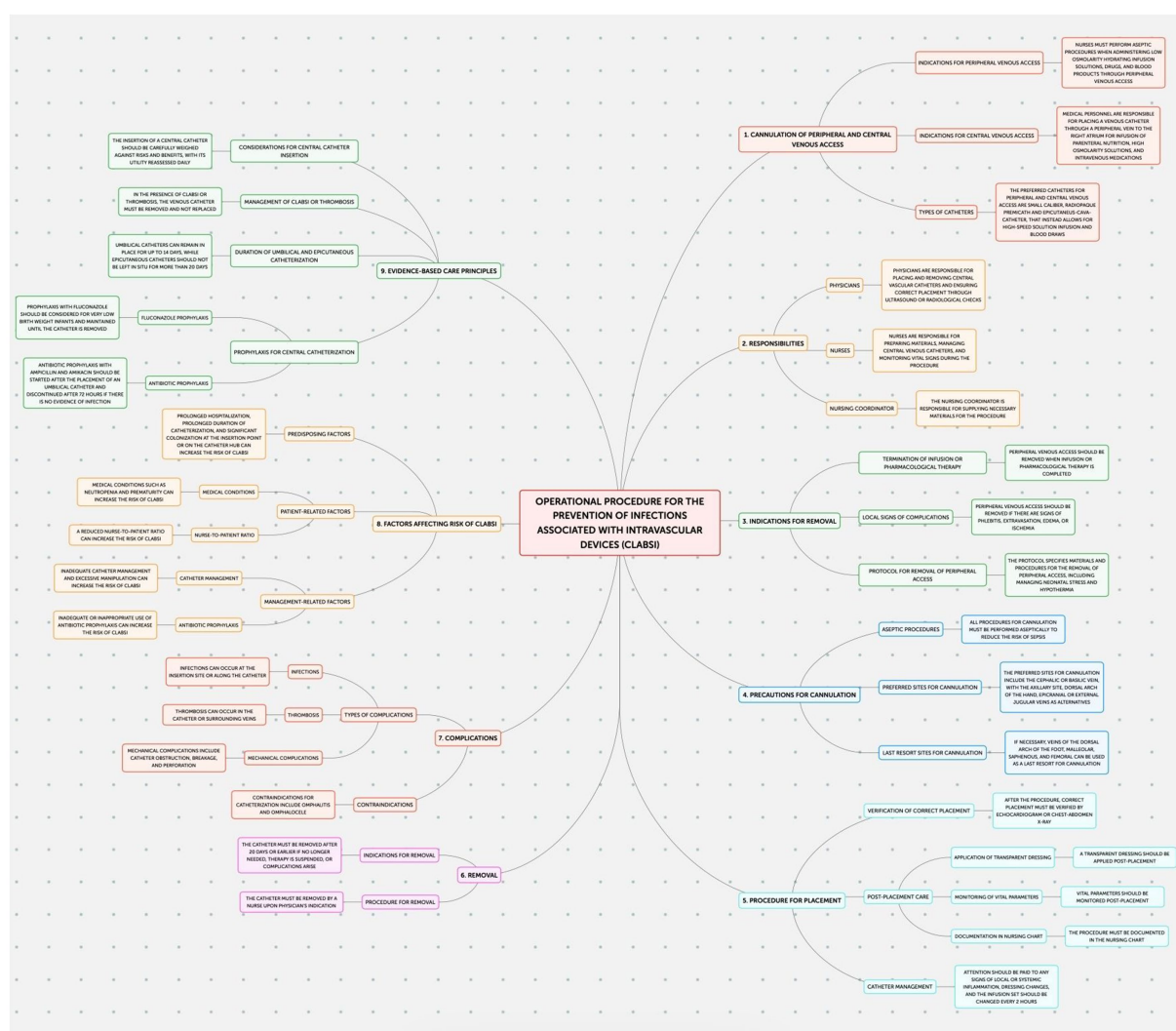


FIGURE 4  
Operational procedure for managing an epidemic event.

Neonatal pathologies and diagnoses upon admission did not exhibit statistically significant variances, suggesting the protocol's effectiveness transcends specific neonatal health conditions ( $\chi^2$ -test,  $p > 0.05$ ) (Tables 1, 2).

The microorganisms responsible for infections associated with umbilical (UVC), central (CVC), and peripheral (PVC) catheters infections were categorized as follows: Fungi: Candida. Gram-positive: Enterococcus; Staphylococcus. Gram-negative: Enterobacter; *E. coli*; Serratia. Gram-positive and Gram-negative: Staphylococcus and Klebsiella; Staphylococcus and Serratia; Staphylococcus and Pseudomonas. These findings are consistent with those reported in the literature (20).

Our evaluation of catheter infections showed no significant changes of positive cultures both for central and peripheral venous catheters between pre and post-protocol implementation, but a marked reduction of infections of umbilical venous catheter (UVC) infections ( $\chi^2$ -test,  $p = 0.018$ ) was found, indicating a targeted effect of the protocol on reducing specific infection risks (Figures 6, 7).

In the "post" group, 10.25% ( $n = 25$ ) of the blood cultures were positive, while 89.75% were negative. In the "pre" group, 7.70% ( $n = 12$ ) were positive, and 92.30% ( $n = 144$ ) were negative. The isolated microorganisms were categorized as follows: Gram-positive and Fungi: Enterococcus and Candida; Staphylococcus and Candida. Gram-positive: Bacillus; Corynebacterium; Staphylococcus; Streptococcus. Gram-negative: Enterobacter; *E. coli*; Klebsiella; Serratia. Gram-positive and Gram-negative: Staphylococcus and Klebsiella. These findings are consistent with those reported in the literature (21).

The microorganisms from urine cultures were grouped as follows: Gram-negative and Gram-negative: Klebsiella and Enterobacter; Klebsiella and *E. coli*; Klebsiella and Morganella; Pseudomonas and Klebsiella. Gram-negative and Gram-positive: *E. coli* and Enterococcus faecalis; Enterococcus and Escherichia; Klebsiella and Enterococcus; Proteus and Enterococcus; Pseudomonas and Enterococcus. Gram-negative: Enterobacter; Escherichia; Klebsiella; Pseudomonas; Serratia. Gram-positive: Enterococcus; Streptococcus. Gram-negative and Fungi: Escherichia and Candida.

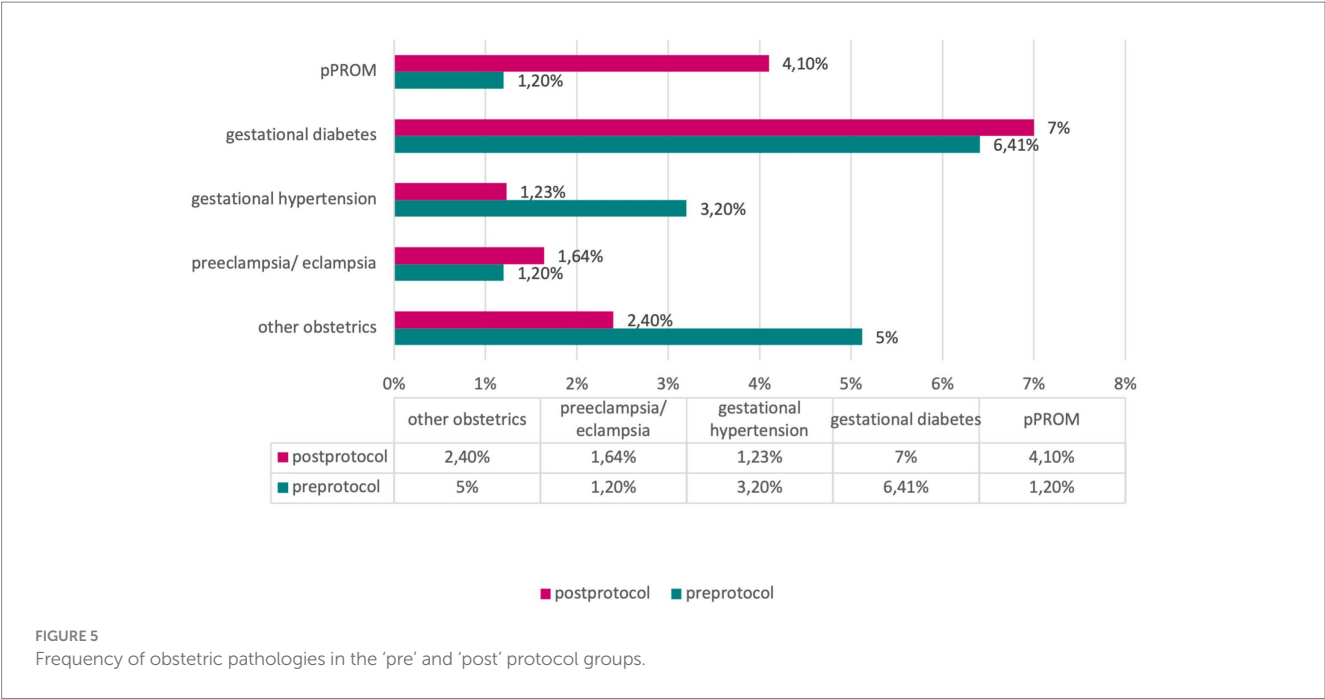


TABLE 1 Contingency table for the “admission diagnosis” variable.

Admission diagnosis	Period		Total	p-value
	post	pre		
Others	97	66	163	
Cardiovascular	12	3	15	
Gastrointestinal	24	8	32	
Infectious	6	3	9	
Malformative	25	13	38	
Metabolic	7	6	13	
Neurologic	5	4	9	
Obstetric	2	3	5	
pPROM	10	2	12	
Respiratory	54	46	100	
Total	242	154	396	0.246

The microorganisms responsible for positive swab results from various sites (surface, ear, rectal, ocular, and pharyngeal) were categorized as follows: Viruses: Respiratory Syncytial Virus. Gram-positive: Staphylococcus; Enterococcus; Streptococcus; *Enterococcus faecalis*. Gram-negative: Morganella; Pseudomonas; *E. coli*; Campylobacter; Klebsiella; Enterobacter; Proteus; Serratia; Haemophilus. Gram-positive and Gram-positive: Staphylococcus and Enterococcus. Gram-positive and Gram-negative: Staphylococcus and Pseudomonas; Streptococcus and Klebsiella; Staphylococcus and *E. coli*; Staphylococcus and Klebsiella. Gram-positive and Fungi: Streptococcus and Candida.

All these findings are consistent with those reported in the literature (22–24).

Analyzing microbial involvement in swab positivity and culture outcomes, we found no significant alterations in microbial patterns post-protocol, reinforcing the protocol’s effectiveness in maintaining a stable microbial environment within the NICU ( $\chi^2$ -test,  $p > 0.05$ ) (Figure 8).

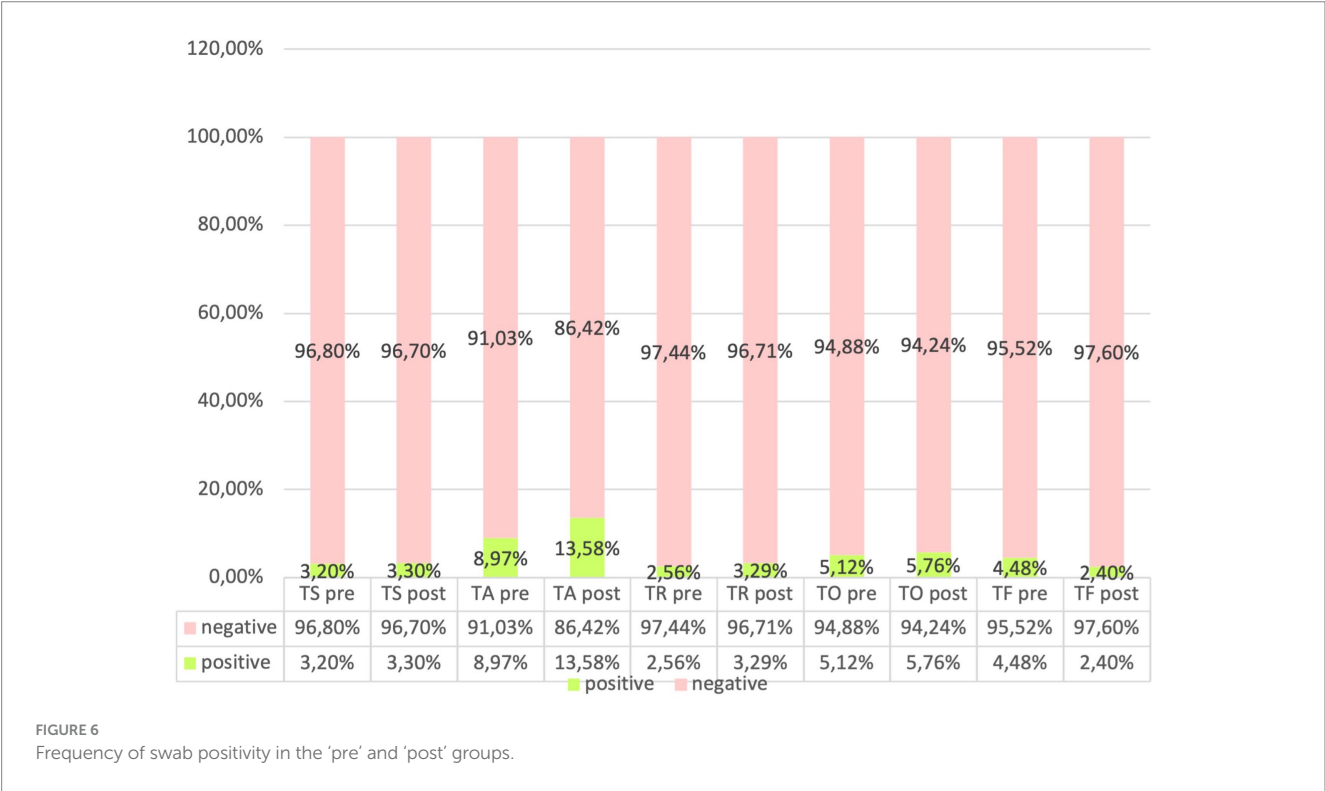
Notably, our inferential statistical analysis highlighted significant associations between gestational age and neonatal outcomes, with gestational age showing a significant correlation with birth weight (Pearson test,  $p < 0.05$ ) and inversely with hospital stay and therapy duration. Logistic regression unveiled a statistically significant improvement in outcomes related to CVC infections post-protocol ( $p = 0.012$ , OR = 0.1912), underscoring the protocol’s success in enhancing neonatal care within the NICU setting (Table 3).

Discussion

The current study offers an extensive evaluation of the effects of a newly implemented protocol on neonatal sepsis prevention outcomes. The sample comprised 399 neonates, segmented into pre-protocol (39.2%) and post-protocol (60.8%) cohorts. This segmentation

TABLE 2 Contingency table for the “neonatal pathologies” variable.

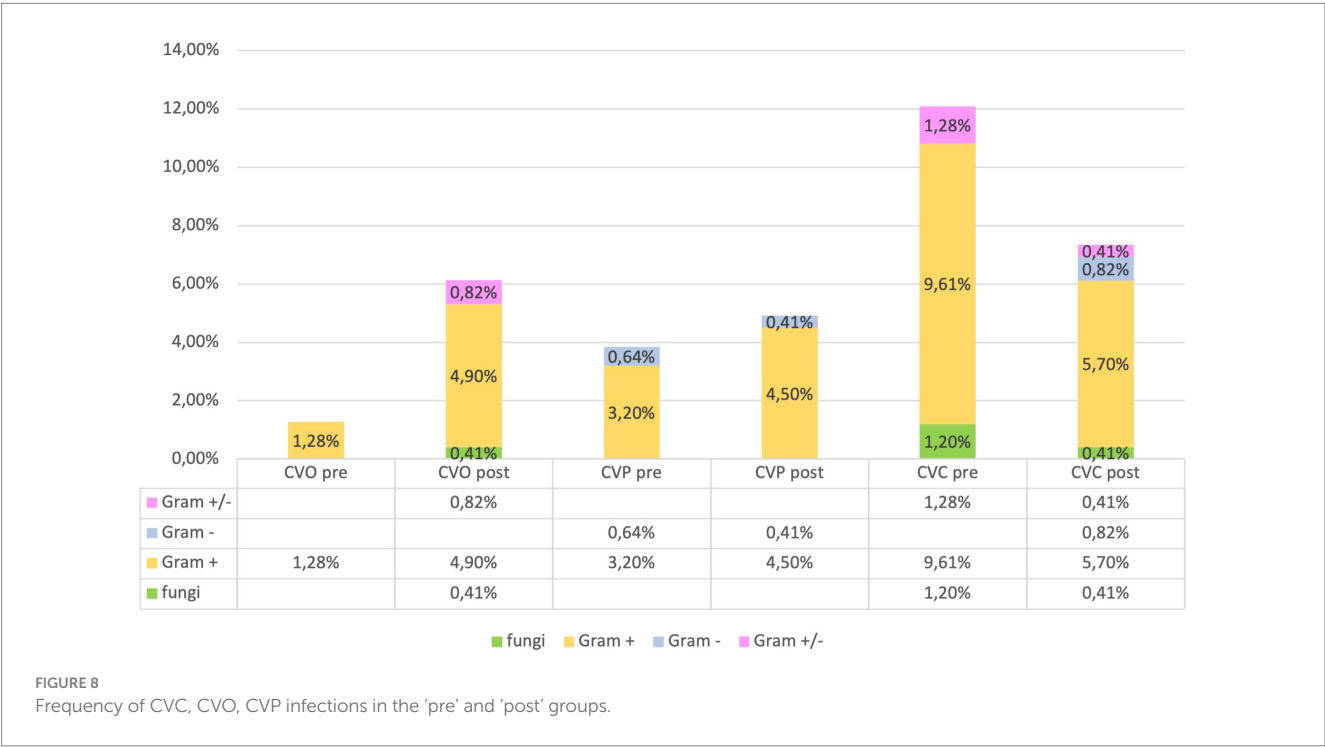
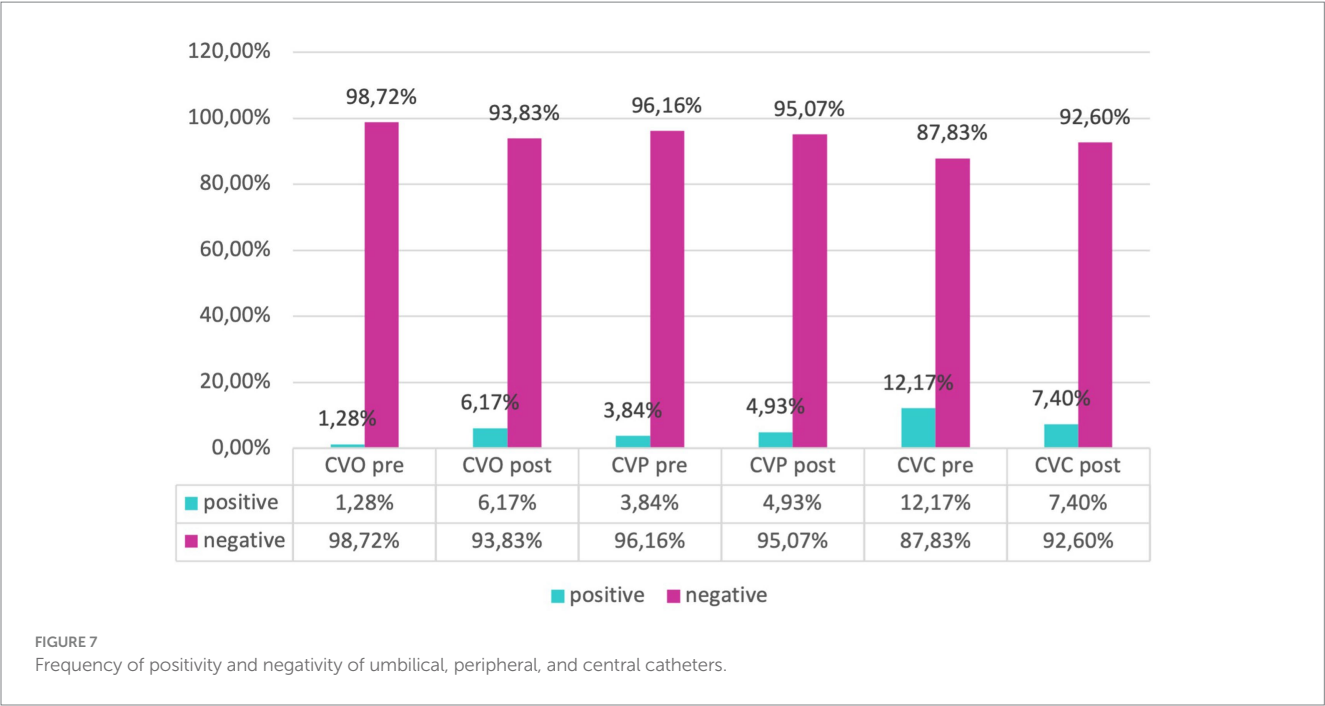
Neonatal pathology	Period		Total	p value
	post	pre		
Others	38	13	51	
Cardiovascular	11	6	17	
Gastrointestinal	17	5	22	
Genitourinary	3	2	5	
Infectious	28	18	46	
Malformative	23	16	39	
Metabolic	11	6	17	
Neurologic	7	5	12	
Ophthalmic	5	3	8	
Respiratory	97	79	176	
Total	240	153	393	0.415



facilitated a thorough comparison of outcomes prior to and subsequent to the protocol’s introduction, thereby aiming to determine its efficacy in enhancing neonatal care, consistent with the existing scientific literature (25, 26).

The two samples are homogeneous for variables such as sex (40.45% females, 59.55% males), mean gestational age (pre 34.5 weeks, post 35.0), mean birth weight (pre 2,438 g, post 2,289 g), normal weight/underweight, in/outborn, multiple gestation, type of delivery, maternal diseases (obstetric and non-obstetric), diagnosis upon admission to neonatology, and neonatal pathology. This has an undeniable advantage, as it allows for the comparison of two groups that can be considered homogeneous.

Consequently, observed variations in outcomes can be attributed with greater confidence to the effects of the intervention protocol rather than to underlying demographic or clinical disparities, in accordance with scientific evidence related to the prevention of sepsis in adults (27–30). The analysis of infections related to central venous catheters (CVC) and peripheral venous catheters (PVC) is crucial for assessing the relationship between the concentration of microorganisms and the positivity of the culture (31). Regarding infections associated with umbilical venous catheters (UVC), which are commonly inserted in neonates for vascular access and are not without complications (32), studies with similar samples have reported an incidence of related septicemia of



9.5% (33). Despite this, the use of UVC remains the standard of care in the neonatal intensive care unit (NICU) for administering fluids, medications, and parenteral nutrition (34). Our evaluation of catheter-related infections revealed no significant differences in the rate of positive cultures for both central and peripheral venous catheters following the implementation of the protocol. However, a notable reduction in umbilical venous catheter (UVC) infections was observed, suggesting that the protocol effectively targeted

specific infection risks. The NICU environment, colonized by various microorganisms, enhances the risk of developing antibiotic resistance (35). Furthermore, an increase in antibiotic-resistant organisms could lead to a rise in neonatal case fatality rates, underscoring the necessity for regular surveillance (36, 37). Analysis of microbial involvement in swab positivity and culture outcomes revealed no significant changes in microbial patterns post-protocol, supporting the protocol's effectiveness in maintaining



TABLE 3 Logistic regression model aimed at investigating the effects of the protocol on the measured clinical outcomes.

Predictor	Estimate	SE	Z	p	Odds ratio	95% Confidence Interval	
						Lower	Upper
Intercept	7.43458	3.3560	2.2153	0.027	1693.5428	2.3559	1.22e+6
UVC qual							
Yes – no	1.39212	1.2156	1.1453	0.252	4.0234	0.3715	43.578
PVC qual							
Yes – no	−0.08663	0.8802	−0.0984	0.922	0.9170	0.1634	5.148
CVC qual							
Yes – no	−1.65441	0.6554	−2.5242	0.012	0.1912	0.0529	0.691
Surface qual							
Yes – no	1.27359	0.9336	1.3642	0.172	3.5736	0.5734	22.272
Auricular qual							
Yes – no	0.76105	0.5925	1.2844	0.199	2.1405	0.6701	6.837
Rectal qual							
Yes – no	−0.13721	1.3035	−0.1053	0.916	0.8718	0.0677	11.218
Ophtalmical qual							
Yes – no	−0.56205	1.1068	−0.5078	0.612	0.5700	0.0651	4.989
Pharyngeal qual							
Yes – no	−3.31497	2.1047	−1.5750	0.115	0.0363	5.87e-4	2.248
Urine qual							
Yes – no	−0.58876	0.6659	−0.8841	0.377	0.5550	0.1505	2.047
EMO qual							
Yes – no	0.24158	0.9194	0.2628	0.793	1.2733	0.2100	7.718
Sepsis							
Yes – no	0.26171	0.7608	0.3440	0.731	1.2991	0.2925	5.771
Weight	1.65e-4	4.08e-4	0.4056	0.685	1.0002	0.9994	1.001
Recovery days	0.03182	0.0153	2.0792	0.038	1.0323	1.0018	1.064
Gestational age	−0.20336	0.1027	−1.9810	0.048	0.8160	0.6673	0.998
DOT (days of therapy)	−0.04500	0.0763	−0.5896	0.555	0.9560	0.8232	1.110
APGAR 1 min	−0.07252	0.1708	−0.4246	0.671	0.9300	0.6655	1.300
APGAR 5 min	−0.00989	0.2405	−0.0411	0.967	0.9902	0.6180	1.586

Estimates represent the log odds of “PERIOD = post” vs. “PERIOD = pre”.

a stable microbial environment within the NICU. Inferential statistical analysis showed significant associations between gestational age and neonatal outcomes, consistent with existing literature (38, 39). Specifically, gestational age was significantly correlated with birth weight and inversely correlated with the duration of hospital stay and therapy. Logistic regression analysis indicated a statistically significant improvement in outcomes related to central venous catheter (CVC) infections post-protocol, highlighting the protocol’s success in enhancing neonatal care within the NICU.

This demonstrates that proactive application of protocols aimed at improving patient safety is a virtuous activity that can also prevent neonatal sepsis (40, 41). Thus, it can be affirmed that the introduced protocol effectively reduces infection risks in neonates admitted to the NICU, critically impacting patient safety, hospital costs, and overall quality of care.

The absence of statistically significant differences in other analyzed variables, such as neonatal and maternal diseases and the type of delivery, further supports the conclusion that the observed improvements in neonatal outcomes are attributable to the protocol. The proven effectiveness of the introduced protocol allows for two considerations. Firstly, the observed results align with the objectives of the study, enhancing outcomes for hospitalized neonates, which inevitably affects costs and the entire care pathway. Secondly, consistent with international literature, clinical risk management and preventive measures are effective (42–44).

Despite these promising results, the study recognizes limitations related to sample size and suggests the potential value of repeating the study with a larger sample and possibly in a multicentric setting to provide further validation of the protocol’s effectiveness and refine its components for even greater impact on neonatal care.

This study underscores the positive impact of a targeted protocol on reducing the risk of CVC infections and the length of hospital stays in a neonatal intensive care setting. These findings emphasize the importance of evidence-based interventions in improving neonatal outcomes (45) and highlight the ongoing need for research to optimize care protocols in high-risk healthcare environments (46).

One of the major challenges in applying the protocol was the lack of comprehensive anamnestic data, which made it difficult to fully assess risk factors. Additionally, the resistance to antibiotics observed in some cases highlights the need for ongoing monitoring and adjustment of treatment protocols.

In the context of our epidemiological investigations within the neonatal intensive care unit (NICU), a specific report on neonatal nosocomial infections was not made. Consequently, there is no documented trend of nosocomial infections in the involved Department.

However, to address this lack of direct data, we used the number of umbilical venous catheter (UVC) infections as a proxy indicator. The use of UVCs is common in neonatal intensive care units for administering medications, fluids, and parenteral nutrition to premature or critically ill infants. Since infections related to UVCs represent a significant proportion of nosocomial infections in these units, their number can be considered a useful indicator to indirectly monitor the prevalence of neonatal nosocomial infections.

We collected data related to UVC infections through the NICU's internal recording system, analyzing the period between 2019 and 2021. These data provide an indicative picture of the trend of nosocomial infections and allow us to implement targeted control and prevention strategies.

Despite this limitation, the use of UVC infection as a proxy offers us a critical insight into current practices and areas needing improvement, thereby contributing to the overall quality of neonatal care in our Department.

## Conclusion

This study assessed a clinical risk management protocol implemented in the Neonatology and Neonatal Intensive Care Unit at Policlinico Hospital-University of Bari, involving 399 neonates. The protocol was designed to improve patient safety by mitigating healthcare-associated infections and other adverse events. Results indicated a significant decrease in central venous catheter infections and shorter hospital stays post-implementation, highlighting the protocol's effectiveness in enhancing neonatal outcomes and healthcare efficiency.

Despite its observational nature, the study underscores the significance of structured clinical risk management in neonatology. It posits that targeted preventive measures and staff training can substantially diminish risks associated with neonatal care. Future research involving a larger, multicentric sample is advised to further corroborate these findings and assess the protocol's adaptability across various settings, especially given that nosocomial infections are critically linked to medical liability, escalating healthcare costs, and diminishing public trust in healthcare systems (41–47).

In conclusion, the protocol shows promise as a blueprint for improving care standards in NICUs, advocating its wider adoption to establish new benchmarks in the quality and safety of neonatal care.

## Data availability statement

The datasets presented in this article are not readily available because privacy. Requests to access the datasets should be directed to [paolo.visci@uniba.it](mailto:paolo.visci@uniba.it).

## Ethics statement

The studies involving humans were approved by General Health Directorate (nr. 1497 on 2020.11.19). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

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DF: Writing – original draft, Writing – review & editing. VG: Writing – original draft, Writing – review & editing. EG: Writing – original draft, Writing – review & editing. MM: Writing – original draft, Writing – review & editing. MT: Writing – original draft, Writing – review & editing. AV: Writing – original draft, Writing – review & editing. PV: Writing – original draft, Writing – review & editing. MB: Writing – original draft, Writing – review & editing. FZ: Writing – original draft, Writing – review & editing. AF: Writing – original draft, Writing – review & editing. RP: Writing – original draft, Writing – review & editing. BS: Writing – original draft, Writing – review & editing. AD'E: Writing – original draft, Writing – review & editing. NL: Writing – original draft, Writing – review & editing.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Medico-legal management of healthcare-associated infections: a cost-effectiveness analysis in an Italian tertiary hospital

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**Introduction:** Healthcare-associated infections are the main reported adverse event in healthcare, with significant economic costs that include those caused by medical malpractice claims. In Italy, there is a fault-based compensation system, but in this specific field, the burden of proof on the hospitals is particularly heavy. Hence, we aimed to verify the economic impact of the inclusion of experts in hospital infection surveillance into internal committees for claims assessment and to evaluate what would have been the economic impact of a mandatory no-fault system rather than the current system.

**Materials and methods:** We compared two 4-year periods (T1: 2015–2018 and T2: 2019–2022), investigating the medical malpractice claims related to healthcare-associated infections in a large tertiary public hospital in Florence, Italy. Decisions of the internal committee, evolutions of the claims after the decision, and conclusions of the claims were registered. No-fault system simulations were used to evaluate the cost-effectiveness of the model.

**Results:** We observed a decrease in the number of claims after the implementation of infection prevention and control (IPC) experts into the committee (a 24% decrease in rejections and a 19% increase in admissions). We found a 6806.98 euros difference (not statistically significant) in compensations in T1 and T2. Moreover, our simulations found that a no-fault compensation system – if alternative to the traditional fault-based approach – could lead to gains or losses for the plaintiffs depending on the approach chosen. (We observed a 52% mean decrease in compensations with a 150000 euros maximal indemnity and a 134% mean increase with an indemnity tailored considering also life expectancy).

**Discussion:** Introducing experts in IPC into hospital committees for medico-legal claims management has proven to be cost-effective, offering a no-fault compensation system as an alternative to the traditional fault-based approach, supported by a properly evaluated maximal indemnity. Due to the limitations of our models, multicentric studies are recommended to verify our results.

## KEYWORDS

healthcare-associated infections (HAI), medical malpractice claims, medical malpractice, legal medicine, compensations



# 1 Introduction

Healthcare-associated infections (HAIs) are the main reported adverse event in healthcare, with a prevalence in high-income countries ranging from 3.5 to 12% (1). They have a very significant economic impact, increasing in-hospital mortality and length of stays, direct costs of care, and, in the European Economic Area, causing annually 501 disability-adjusted life years per 100000 habitants (2–4). Most HAIs are of (at least potential) medico-legal interest since they are often preventable through multimodal strategies enforced at organizational, structural, and individual levels (5). A milestone of an infection prevention and control program (IPC), according to the World Health Organization, is HAI surveillance (6). In particular, in the European Union, the supranational HAI surveillance network (HAI-NET) performs a point prevalence survey of HAIs in acute care hospitals every 5 years, and HAI surveillance programs are implemented at national, regional, and local levels (1).

When costs related to HAI are considered, the economic burden due to HAI cases of alleged medical malpractice should be taken into account.

A recent ruling of the Italian Supreme Court (6386/2023) compels hospitals to compensate patients who suffered from HAI unless they can prove 13 items (Table 1).

This significant burden of proof requires to structure a complex and articulated line of defense, a challenge for the Italian system in which, when the hospital has no insurance coverage or has high-deductible insurance coverage, medical malpractice claims are directly managed by committees composed of experts in tort law and legal medicine (7, 8). In Italy, there is a restorative justice system (no punitive damages are allowed), and permanent impairment is generally the main kind of non-economic damage related to medical malpractice. It is evaluated by an expert in legal medicine who, considering the functional history and the medico-legal physical examination of the patient, uses numerical coefficients to rate the permanent impairment of global individual functioning (the full psycho-physical integrity is equal to 100%) (9). Italian Law 210/1992 regulates no-fault compensations in cases of impairments caused by mandatory vaccinations or severe HAI (such as HIV) contracted through blood transfusions, but the patient who asks for these indemnities still has the right to also legally ask for fair compensations based on proof of fault.

TABLE 1 Hospital burden of proof (according to the Italian Supreme Court).

A. Compliance with protocols of the following:
1. Disinfection and sterilization of materials and the hospital environment;
2. Laundry management;
3. Waste management;
4. Distribution of food and water;
5. Preparation, storage, and use of disinfectants;
6. Monitoring of air quality;
7. Control and limitation of visitors;
8. Occupational injury control strategies and vaccination;
9. HAI surveillance and infection disease reporting;
10. Use of microbiological data for HAI surveillance;
11. Alert organisms surveillance.
B. The ratio between hospital staff and inpatients/outpatients
C. The time when each of the aforementioned risk management activities was performed

This study aimed to investigate the economic impact of medical malpractice claims for HAI in a tertiary public hospital and the impact of an in-house strategy to manage this issue. In detail, the primary endpoint of this study is to verify whether the inclusion of experts in IPC, specialized physicians from the Hospital Infection Prevention and Control Unit, into hospital committees for claims assessment has an impact on their performances and the mean cost of claims. The secondary endpoint is to evaluate what would have been the economic impact of hypothetical mandatory no-fault systems on public health system finances and plaintiffs rather than the fault-based system currently valid in Italy.

# 2 Materials and methods

We considered the cases in which a patient or his/her heirs requested compensation for an HAI to the Careggi University Hospital (a public 1200-bed tertiary hospital in Florence, Italy). The data source was the database of the Evaluation Committee of medical malpractice claims (MEC), an internal committee composed of hospital experts in legal medicine and tort law (loss adjusters and lawyers), whose mission is to determine whether and how much compensation should be awarded to claimant patients. In case of alleged damage due to a HAI, most compensations are related to patients' permanent impairment or death caused by the infection. Experts in IPC have constitutionally participated in MEC meetings since 2019, participating in the analysis of the cases and producing epidemiological reports (ER) for medico-legal purposes in cases of alleged HAI when the MEC evaluated that mere technical arguments were not sufficient for proper medico-legal defense.

For each case of HAI-related alleged medical malpractice claim (MMC), this information was collected from the database of the MEC: the decision of the MEC (admission or rejection of the claims), the evolution of the MMC after the MEC decision (desistance of the plaintiff or civil proceeding), and the conclusion of the MMC (also in economic terms). If the plaintiff withdrew the request before the MEC decision, this information was still noted. Although data were available since 2010 (when the hospital decided to introduce the MEC), we focused on two-time intervals composed of the same number of years (T1: 2015–2018; T2: 2019–2022) because, in 2019, the MEC started using ER for MMC evaluation and hospital legal defense. In period T2, three cases of SARS-Cov-2 infection were included.

In detail, the investigated categorical variables in T1 and T2 were as follows:

- 1 Decisions made by the MEC: Admissions (A) and rejections (R). D indicates when the plaintiff desisted before the MEC decision;
- 2 Progression of claims after the MEC decision: Cases closed by MEC (C) and cases progressed into civil proceedings (P);
- 3 Concordance between the MEC decision and the civil court decision: concordant (Co) and discordant (Di) decisions.

Finally, the economic compensations (set in an extrajudicial or judicial context) were noted, together with the percentage of permanent impairment caused by HAI.

STATA software (v. 18.0, StataCorp LLC, US) was used to perform a t-test to compare mean compensations in T1 and T2, with the cut-off of statistical significance set at  $p = 0.05$ .

Finally, we made three simulations (whose limitations are reported in the discussion) in order to predict what would have been the increase or decrease in the expenditure of the public system for MMC and the mean “loss” or “gain” for plaintiffs in three different scenarios:

- 1 In this scenario, it is hypothesized that the same amount of money actually paid by the public system is distributed using, as the sole distribution criterion, the decimal coefficient of permanent impairment evaluated by the expert in legal medicine. In this model, the maximal indemnity, i.e., the sum of money that could have been paid to a single patient with a 100% permanent impairment (in order to simplify the inferential model, death was also equaled to 100% impairment), is calculated considering the amount of money actually paid by the public system for all the cases of HAI divided by the sum of the coefficients of permanent impairment.
- 2 In this scenario, the maximal indemnity (defined as in 1) is set at 150000 euros (the indemnity given to the close relatives of fatal cases of vaccinations following Law 210/1992), and the indemnity paid to each patient is obtained by multiplying the maximal indemnity by the coefficient of permanent impairment of the specific case.
- 3 In this scenario, the maximal indemnity (same definition as before) is obtained by multiplying the Italian mean per-capita Gross Domestic Product (28200 euros) by the life expectancy when the medical malpractice was claimed. The individual indemnity – as before – is calculated by multiplying the maximal indemnity by the permanent impairment coefficient. The Italian mean per-capita Gross Domestic Product and life expectancies were obtained from the Italian National Institute of Statistics.<sup>1</sup>

## 3 Results

Regarding the primary endpoint, in T1 and T2, the hospital received 46 and 35 HAI-related MMC, respectively. (Note that hospital medical malpractice claims in general were 669 in T1 and 522 in T2.)

In T1, there were 32 rejections (70%) and 11 admissions (24%) made by the MEC and 3 cases of pre-decision desistance (6%), while in T2, there were 16 rejections (46%), 15 admissions (43%), and 4 (11%) cases of pre-decision desistance (Figure 1).

In T1, MEC managed to directly close (accepting or rejecting the claim) 17 cases (37%) and, as said, 3 cases (6%) were closed because of desistance, while in 26 cases (57%), the failure to agree on compensation led to a civil proceeding. A total of 10 cases rejected by the MEC did not progress.

In T2, MEC managed to directly close 20 cases (57%); while in 11 cases (32%), there was a civil proceeding. However, 11 cases rejected by the MEC did not progress (Figure 2).

In total, 26 MMC in T1 and 11 MMC in T2 led to civil proceedings, and concordance with MEC decisions was found in 13 cases (50%) and 3 cases (27%). In T2, in all eight cases in which the

proceeding outcome was different from the MEC decision, an ER was not formally attached (Figure 3).

Regarding mean compensation comparisons, the T1 and T2 datasets were unpaired and presented unequal variances. The mean value for T1 was 109018.78 euros (Figure 4) and for T2 was 102211.80 euros (Figure 5) (difference between T1 and T2 values: 6806.98 euros). A two-sample t-test found a *p*-value of 0.92 (> 0.05).

The secondary endpoint was evaluated through limited simulated scenarios:

- In scenario 1, we observed a 74% mean increase in compensations (maximal indemnity: 540514.78 euros).
- In scenario 2, we observed a 52% mean decrease in compensations and a 72% decrease in public expenditure (1053000 euros vs. 3794413.77 euros; maximal indemnity: 150000 euros).
- In scenario 3, we observed a 134% mean increase in compensations and a 67% increase in public expenditure (6346790.88 euros vs. 3794413.77 euros; mean maximal indemnity: 835949.23 euros).

## 4 Discussion

To the best of our knowledge, this is the first study to report a cost-effectiveness analysis of a multidisciplinary approach to HAI-related MMC.

As reported by Norelli et al., MECs can transform their organizational structure in order to enhance their economic performance (7).

In our study, comparing T1 (2015–2018) and T2 (2019–2022), we observed a decrease in the number of MMC. The fact that Italian Law grants a significant time (even higher than 10 years) to present an MMC to a health institution may limit the strength of this evidence, but in Italy, the main time interval between the event and the MMC has been reported to be 1.69 years (10). However, our institution completely retains the medico-legal risk (i.e., chose not to have insurance coverage for MMC), and the observed trend is concordant with those reported by other national institutions that retain most of the risk, as with the trend of our institution in the last decades (7, 8, 11). On the other side, Bonetti et al., who studied data from Italian insurance brokers, observed a linear increase in MMC (including those unrelated to HAI) over time, particularly pronounced in Tuscany (the region where our hospital is) (10).

We also found that the implementation of IPC experts into the team of hospital claims management experts was associated with a change in decision-making performed by MEC (a 24% decrease in rejections and a 19% increase in admissions). These data can be interpreted in different ways, but the likeliest explanation is that direct analysis of IPC data may be an objective indicator of whether the hospital can be considered liable for failing to prevent HAI, and then hospital decision-makers can be more confident to opt for early dispute resolution rather than to take chances in an expensive civil proceeding. The composition of the MEC is a crucial determinant of its performance; as shown by our data, the inclusion of experts in the IPC has had a sound impact on decision-making. These experts may be of particular help also in sub-classes of HAI of particular medico-legal complexity, such as SARS-CoV-2 infections. Indeed, as previously

<sup>1</sup> [www.istat.it/en/](http://www.istat.it/en/)

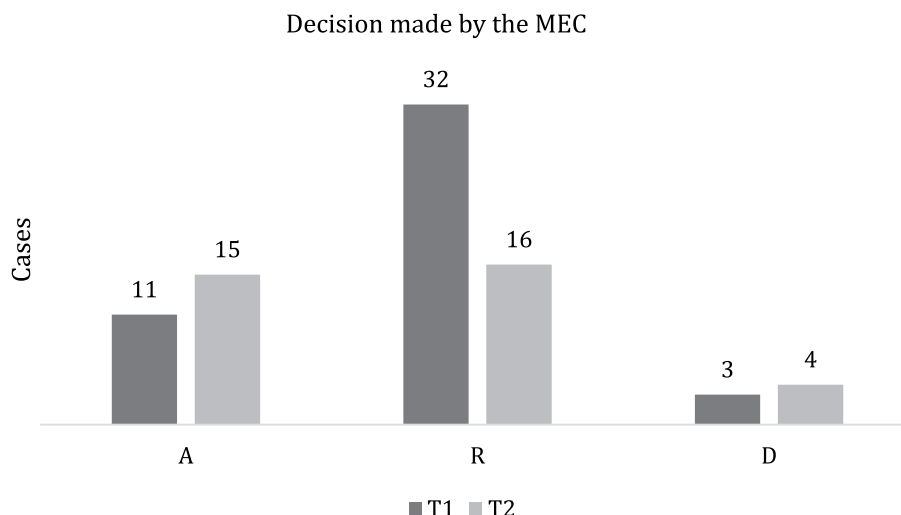


FIGURE 1  
Decision made by the MEC. Admissions (A), rejections (R), and plaintiff desisted before MEC decision (D).

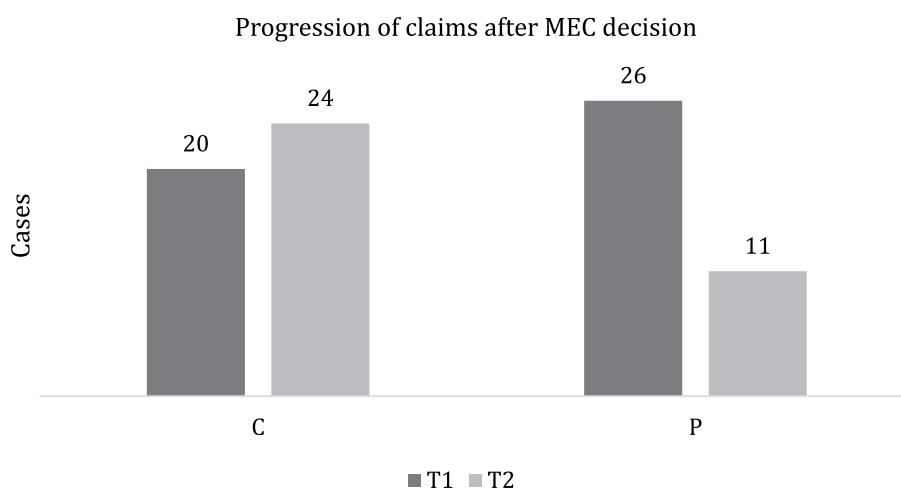


FIGURE 2  
Progression of claims after the MEC decision. Cases closed by MEC (C) and cases progressed into civil proceedings (P).

underlined, these conditions often imply specific medico-legal issues (12, 13). In our cases, only three cases concerned SARS-CoV-2 infections, and in all the cases, the MEC, also considering the ER, opted for rejection, with desistance in two cases and successful defense in a civil proceeding in the last case. Finally, implementing MEC – as in our institution – with a clinical risk manager is likely to produce a beneficial system of incident reporting that allows to promptly intercept and address organizational and individual failures (8).

T2 was also associated with a 25% increase in cases closed by MEC, an improvement in performance that can be at least partly explained by the increase in the number of accepted requests, despite the evaluated implementation could have discouraged the plaintiff from progressing through, for instance, the production of ER. However, the studied intervention is also associated with a 23% decrease in concordance between MEC and civil court decisions, meaning that when a case is not closed by the MEC, it is more likely to lead to compensation for the

plaintiff. In all cases in which the proceeding outcome was different from the MEC decision, an ER was not formally attached. This evidence could induce one to think that the absence of formal reports could jeopardize the strength of the hospital's line of defense. Regarding the likelihood of civil proceedings in these cases, in general terms, Hwang et al. reported that infectious diseases, despite being the main cause of MMC, were associated with the lowest success rate of litigations (14). However, as reported by Sage et al., litigations were strongly associated with the success of the plaintiff (15). Therefore, looking at our experience, increasing the performance of MEC and containing costs should be the two main goals of the hospital in order to avoid at-risk litigations. In this regard, it is interesting to observe the slight increase in plaintiffs' desistance before and after MEC decisions.

Regarding economic aspects, we failed to find a statistically significant difference in compensations due in T1 and T2, despite a 6806.98 euro difference between the mean values reported. This result

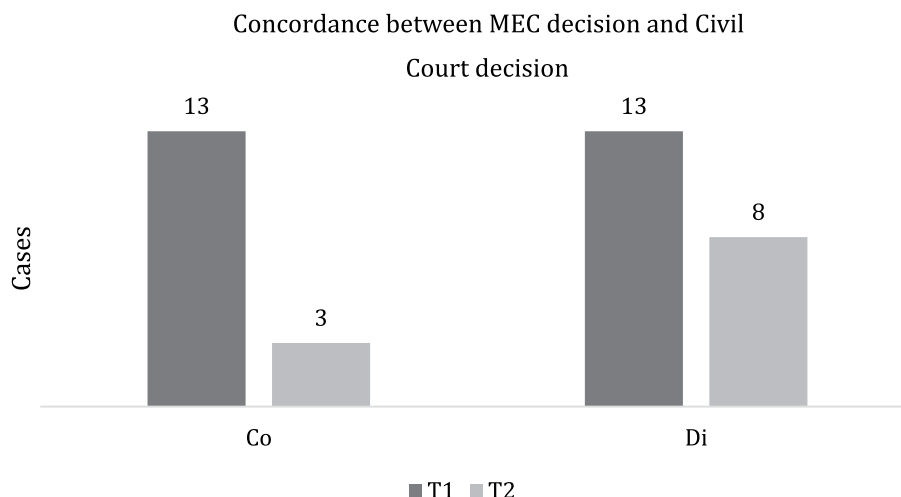


FIGURE 3

Concordance between the MEC decision and the civil court decision. Concordant (Co) and discordant decisions (Di).

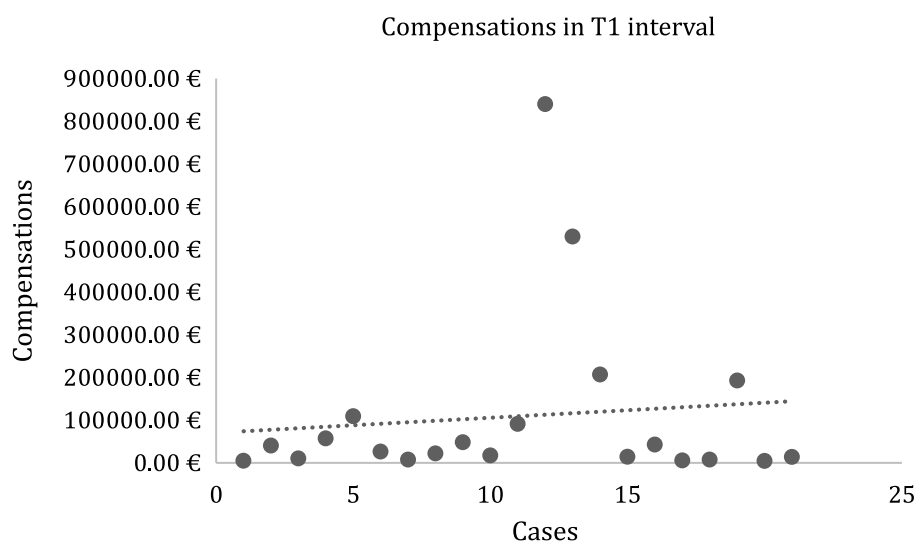


FIGURE 4

Compensations in T1 interval.

could be read as an indicator that the studied intervention radically changed the hospital's decision-making progress without an economic benefit. However, a decrease in average compensation is *per se* an indicator of good hospital performance if it is considered that in the US, China, and Italy, an increase in average payouts for MMC has been reported in the last 30 years, particularly in the last decade (8, 10, 11, 16, 17). Moreover, focusing on HAI-related MMC, it should be noted that they often represent most of the MMC costs in tertiary hospitals (11).

Regarding the secondary endpoint, we made three simulations. These simulations were intended to envision whether no-fault compensations (as a mandatory alternative to the current system) would benefit plaintiffs and the public system. These simulations were highly limited, mainly because 1) in a no-fault system, it is likely that far more patients would ask for economic indemnities (since compensation would not depend on the proof of actual failures of the hospital), 2)

compensations in Italy are calculated considering many other factors (e.g., temporary impairment and medical and legal expenses), and 3) the economic value of the coefficient of personal impairment is not homogeneous neither in absolute nor in relative terms (i.e., it can be personalized considering exceptional characteristics of the case, tends to be higher when the plaintiff is younger, and its increase with the increase in persona impairment is not proportional). That being said, in our study sample, adopting a compensation method based on relatively low caps-on-damage was associated with a foreseeable relevant decrease in compensation but also with a more significant decrease in public expenditure. In general terms, the trade-off between individual and public system economic interests (and, in general, between microeconomic and macroeconomic factors) is complex since different maximal indemnities relate to significantly diverse outcomes. Hence, a no-fault system could reduce legal expenses and the time required to



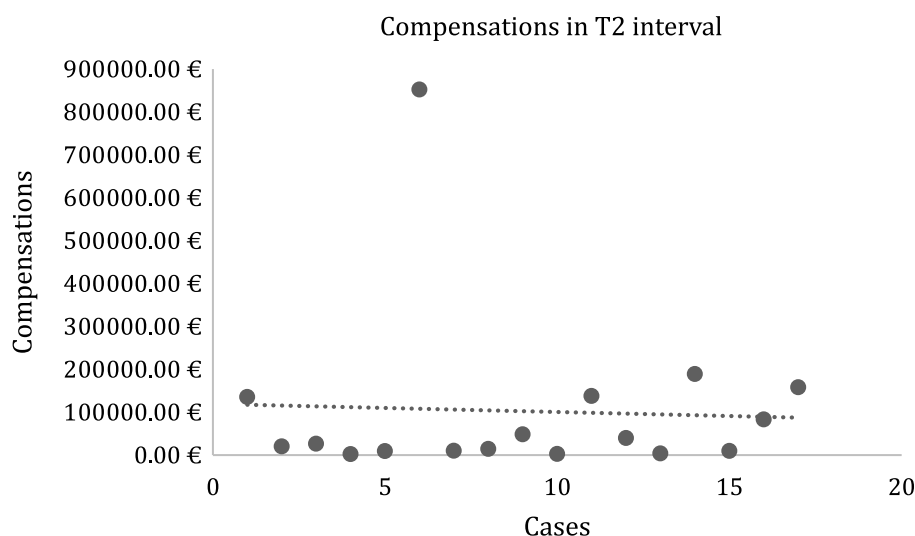


FIGURE 5  
Compensations in T2 interval.

receive compensation, but, as shown, it has several limitations. A possible solution could be obtained by capping non-economic damages, as proposed by some authors for medical malpractice (18).

Finally, regarding the use of HAI surveillance information to support decision-making in MMC management, some ethical and legal issues should be discussed. A cornerstone of good HAI surveillance is efficient incident reporting systems, and, in this regard, the Council of the European Union recommends (Council Recommendation of 9 June 2009) that they must be blame-free. However, using this information for medico-legal purposes enables hospital decision-makers to identify profiles of gross negligence. Proof of gross negligence can be used by public authorities or private institutions (e.g., insurance companies) to “penalize” the involved practitioners, for instance, by significantly increasing the insurance premiums or, in countries like Italy, by compelling the physician to compensate the institution for (at least part of) its loss. This trade-off between the interests of health institutions and physicians must still be evaluated in light of the management and economic benefits. Moreover, according to current evidence, paid MMC is not a random event, and thus the use of HAI surveillance information is also fundamental for the hospital to identify misconducts or organizational failures that can be promptly addressed through targeted interventions (19, 20).

## 5 Limitations

Our study has several limitations. The monocentric study design limited the volume of data, thus future multicentric studies are recommended. Moreover, the unpaired sets of categorical variables with unequal sample sizes impeded to reliably perform parametric statistical testing to verify whether the variations are statistically significant. Meanwhile, the sets of continuous variables considered for the t-test had different sizes. In general, the main limitation was the small sample size, a limitation due to the fact that, up to date, no Italian institution has reported the use of ER for medico-legal purposes in scientific literature. Increasing sample sizes (for

instance, by designing multicentric studies) should then be suggested.

## Data availability statement

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author.

## Author contributions

SG: Writing – review & editing, Writing – original draft. MGr: Writing – review & editing, Writing – original draft. MGU: Writing – review & editing, Writing – original draft. GB: Writing – review & editing, Writing – original draft. LP: Writing – review & editing, Writing – original draft. DP: Writing – review & editing, Writing – original draft. FN: Writing – review & editing, Writing – original draft. MF: Writing – review & editing, Writing – original draft. VP: Writing – review & editing, Writing – original draft.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Robotics and AI into healthcare from the perspective of European regulation: who is responsible for medical malpractice?

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The integration of robotics and artificial intelligence into medical practice is radically revolutionising patient care. This fusion of advanced technologies with healthcare offers a number of significant benefits, including more precise diagnoses, personalised treatments and improved health data management. However, it is critical to address very carefully the medico-legal challenges associated with this progress. The responsibilities between the different players concerned in medical liability cases are not yet clearly defined, especially when artificial intelligence is involved in the decision-making process. Complexity increases when technology intervenes between a person's action and the result, making it difficult for the patient to prove harm or negligence. In addition, there is the risk of an unfair distribution of blame between physicians and healthcare institutions. The analysis of European legislation highlights the critical issues related to the attribution of legal personality to autonomous robots and the recognition of strict liability for medical doctors and healthcare institutions. Although European legislation has helped to standardise the rules on this issue, some questions remain unresolved. We argue that specific laws are needed to address the issue of medical liability in cases where robotics and artificial intelligence are used in healthcare.

## KEYWORDS

robotics, artificial intelligence, medical liability, medical negligence, clinical decision making, accountability, tort law

## 1 Introduction

Artificial intelligence (AI) and robotics have joined forces, heralding an exhilarating and unstoppable era. Among the sectors witnessing captivating applications of robotics, healthcare stands out, solidifying its status as a domain where the integration of cutting-edge technologies has yielded significant breakthroughs (1, 2).

AI is a set of computational techniques inspired humans use their own nervous system and body to sense, learn, reason, and act (3). Robotics is the AI in action in the physical world,

also known as embodied AI. Robots are physical machines designed to address the dynamics, uncertainties, and complexities of the physical world. In robotic systems, the control architecture typically integrates capabilities for perception, reasoning, action, learning, and interaction with other systems (4).

By 2021, 42% of healthcare organisations in the European Union had already integrated artificial intelligence technologies for disease diagnosis, demonstrating a growing trend in the adoption of innovative solutions in the medical sector. In addition, a further 19% of these organisations planned to implement such technologies within the next 3 years, showing a strong inclination towards the use of AI to improve diagnostic accuracy and efficiency. At the same time, 39% of healthcare organisations planned to adopt AI-based patient monitoring tools within the same period, aiming to improve the ongoing management and monitoring of patient health, thereby optimising clinical outcomes and enhancing early intervention capability. Furthermore, 28% of organisations were already using robotics and a further 25% were planning to implement robotics-based healthcare solutions. These figures underline the growing importance of AI in healthcare and its potential transformative impact in the coming years (5, 6).

The applications of robotics in the healthcare scenario are manifold and encompass areas such as, diagnosis, therapy, and rehabilitation (7).

In the field of medical care, robotic systems allow remote patient examination, advanced diagnosis and monitoring of vital parameters (8, 9). This includes smart medical capsules, technological devices designed to administer drugs and monitor various biological parameters within the human body. The capsules are equipped with sensors, actuators and communication technologies that enable them to interact with the body and transmit real-time data to doctors or external monitoring systems (10–13).

In the therapeutic area, robotics is most widely used in robot-assisted surgery, in which human activity is supported by technological instruments capable of performing remote-controlled operations. Robot-assisted microsurgery provides a higher level of precision, eliminates the physiological tremor of the surgeon's hand and possible iatrogenic injuries, but compared to the surgeon's hand has less adaptability to soft tissue (14–16); precision robotic surgery being able to define, plan and process 3D models of the patient allows the autonomous execution of pre-programmed surgical tasks on “hard” materials such as bone (17, 18); minimally invasive robotic surgery increases the precision of surgical procedures and the speed with which they are performed, shows the surgical field in high definition, eliminates the physiological tremor of the surgeon's hands, and thanks to the ergonomics of the console, provides greater comfort for the surgeon. However, in addition to high costs, it requires high skills and special training (19–22); an interesting area for the prospects it may have is that of telesurgery, which allows remote surgical interventions such as the well-known “Lindberg Operation” in which a robot-assisted laparoscopic cholecystectomy was performed by a remote surgeon more than 14,000 km away from the patient's operating table (23). The 5G integration of telesurgery can expand the skills of the remote surgeon due to the high-speed, low-latency connectivity offered by the network and the possibility of using augmented reality (24).

There are the applications of robotics in the area of rehabilitation, to which robot-assisted rehabilitation, robot-assisted mental,

cognitive, and social therapy and robot-assisted mobility systems belong. After injuries to the central nervous system that impair motor coordination, recovery of motor function and skills involves repeated movement of the affected part and stimulation of brain plasticity. Robotics applied to rehabilitation facilitates guided movement of the upper and lower limbs, optimising therapeutic and functional effects. These technologies also provide feedback to the patient, allowing the force to be adjusted and thus maximising the effectiveness of the therapy, stimulating the recovery process (25–29). Robot-assisted rehabilitation offers muscle support therapies and repetition of basic motor activities, allowing users to perform them comfortably in the home environment through integration with personal computers. These tools often make use of technologies originally developed for other purposes, such as gaming (30–32). Robot-assisted mental, cognitive and social therapy systems are designed to interact with humans, simulating different types of social behaviour, such as communication and cooperative play. These robotic tools are applied in patients suffering from dementia, Alzheimer's disease, autism, and children's motor disabilities (33–36). Robotic wheelchairs, smart walkers, and exoskeleton are robotic mobility aid systems as alternatives to traditional tools for patients with severe motor difficulties (37, 38).

Finally, the use of Large Language Models (LLM) in the healthcare field must also be considered. Language models like ChatGPT show potential as virtual assistants in radiology, helping to streamline various tasks, but they present significant limitations. The latest version (GPT-4) cannot interpret medical images and its recommendations can be inaccurate, requiring the professional judgement of radiologists. Integration with electronic health record (EHR) systems poses challenges of privacy and coordination (39).

The integration of robotics in healthcare can lead to several benefits, including faster execution of procedures, improved diagnostic accuracy and increased efficiency in clinical operations. In addition, robotics offers the possibility of performing examinations and operations even for individuals who would otherwise be unable to access them due to geographical, political or economic limitations.

Delineate the applications of robotics and AI in healthcare and their potential, it is also necessary to highlight that there are legal and ethical challenges related to privacy and data protection, informed consent, the creation of possible new inequalities in access, the ethical implications of algorithmic decisions, and the identification of responsibilities in the event of an error committed by a surgical robot or an AI system (40, 41). Although it is often not possible to separate ethical and legal issues into distinct compartments due to their multidirectional interconnections, the topic of responsibility is the focus that this manuscript intends to address.

A robotized care process could reduce the responsibilities borne by the subjects normally involved in a non-robotized care process. If this were true, how and in what terms could the error committed by the robot be complained about? Who is responsible in case of errors or damages caused by a medical robot? If the robot is a consumer product, product liability law may apply. This question becomes even more intricate when considering that robots can operate autonomously or semi-autonomously (42–44). Liability could also extend to the developer of the software or algorithm. The answer is not so simple and immediate. Who will be liable for the tort committed by the autonomous robot-agent? Traditionally, legal liability has been attributed to human beings, who can be held responsible for their



actions under the law. In this context, can the manufacturer of the robot be held liable for the tort committed by the autonomous robot? Or, could the manufacturer be exempt from liability if it can prove that it was unable to entirely foresee the robot's actions. This raises the question of how to establish the degree of reasonable foresight that can be expected from the manufacturer of an autonomous robot. Is the liability of Healthcare Workers (HWs) limited to errors caused by misuse or mismanagement of the robot? (Figure 1).

With the increasing integration of AI and robotics into clinical practice, it is essential to examine how regulations are adapting to address emerging challenges and ensure adequate protection for patients and healthcare professionals. In this rapidly evolving context, regulations and official reports play a crucial role in ensuring that the adoption of AI and new technologies occurs in a safe, ethical, and legally compliant manner. The European overview of regulations and official reports for AI and new technologies in healthcare will provide a valuable framework of the norms and guidelines shaping the use of these advanced technologies in a healthcare setting.

We will focus on the concept of “electronic persons,” which refers to the legal consideration of artificial entities such as robots and AI systems within the legal context. The status of electronic persons raises fundamental questions regarding their legal responsibility, rights, and duties, and represents an advanced frontier in technology law. Examining this status is crucial for understanding how laws and regulations must evolve to include new forms of artificial intelligence and robotics.

Therefore, we will address the issue of strict liability, which is central to the legal and ethical debate surrounding the use of advanced technologies in healthcare. Strict liability implies that a party can be held responsible for damages caused by technologies, such as surgical robots or AI systems, regardless of proof of fault or negligence. This form of liability is particularly relevant in the healthcare context,

where technological errors can have serious and complex consequences. Exploring how strict liability norms apply to new technologies is essential for ensuring a fair and effective legal system.

In this article, we will examine in detail the European regulations and official reports regarding AI and new technologies in healthcare, analyze the concept and implications of the status of electronic persons, and discuss the implications of strict liability in the context of healthcare technology. The goal is to provide a comprehensive understanding of how regulations and legal issues intersect with technological innovation, thereby addressing the question: who is responsible for medical malpractice?

## 2 Regulations and official reports for AI and new technologies in healthcare: an European overview

Considering the complexity of the technology, the Scientific Foresight Unit (STOA) of the European Parliament Research Service (EPRS) argued that the EU legal framework needed to be updated, developing legislation based on risk analysis and making specific changes on a case-by-case basis. It was proposed that a code of conduct be established to set ethical standards to which researchers, practitioners, users and designers should adhere (45).

On 17 February 2017, the European Parliament called on the Commission to submit a legislative proposal to establish civil law rules on robotics and AI (46). Unlike other legislative resolutions, this parliamentary initiative merely laid down a set of principles. The resolution defined intelligent robots as machines capable of acquiring autonomy by interacting with their surroundings through sensors and exchanging data. This process allows them to analyse crucial information. Furthermore, these robots can learn from past events

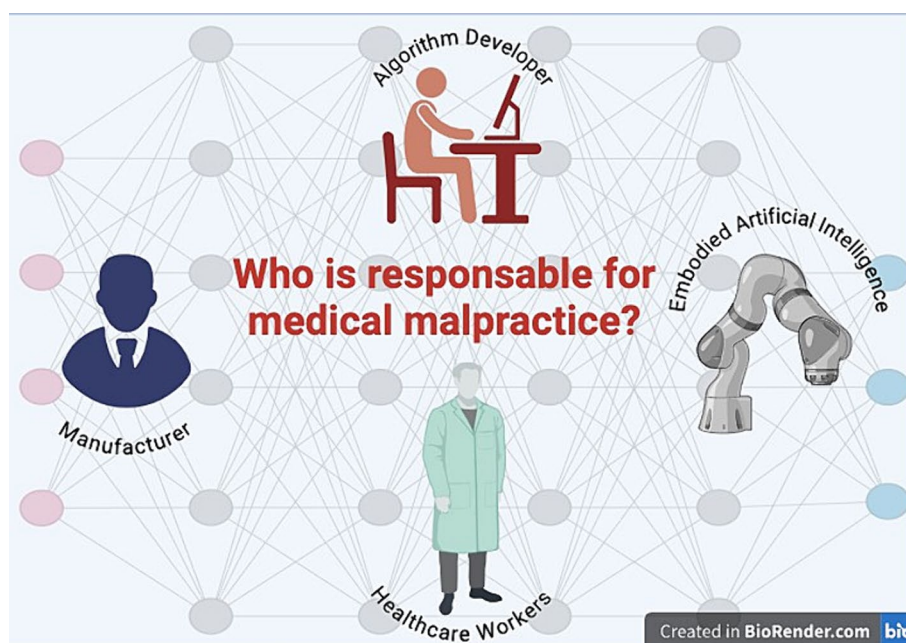


FIGURE 1

Human and non-human beings to whom medical negligence could be attributed in a robotic and AI-based care context.

and interactions, and their physical form provides the necessary tangible support. Finally, the ability to adapt behaviour and actions to their surroundings completes the picture of their powerful capabilities. The introduction of robots in healthcare should not impair the doctor-patient relationship, but provide the physician with assistance in diagnosis and/or treatment in order to reduce the risk of human error and increase quality and life expectancy. Nevertheless, the threat of the dehumanisation of care and the need to preserve the role of HWs due to the irreplaceability of the human factor in social interaction is felt. The importance of adequate education, training, and preparation is therefore emphasised, with the need to define the minimum professional requirements to be able to use surgical robots.

However, the resolution is particularly original and significant when it proposed the recognition of legal personality for robots that make autonomous decisions or interact independently with third parties so that these “electronic persons” can compensate for any damage caused by them. From this perspective, a joint human-robot action is recognisable based on the predictability and directionality of two interdependent relationships, the human and the robotic, and responsibility should be proportional to the actual level of instructions given to the robot and the latter’s degree of autonomy. Opposite to these statements is the position expressed by the European Economic and Social Committee (EESC), which called the introduction of a form of legal personality for robots or AI an unacceptable moral hazard. Among other things, the transfer of liability from the manufacturer to the robot could lead to the loss of the preventive function of correcting behaviour and to inappropriate use or abuse of the legal status (47).

In 2018, the European Union (EU) recognised the need to set high standards for AI-equipped systems in terms of safety and product liability, ensuring an appropriate legal framework (48). As regards the protection of personal data, the Commission specified that data subjects have the right to receive meaningful information on the logic used in the decision. In order to ensure fair and transparent data processing, the data subject must be provided with information on the logic used in automated decision-making as well as the possible consequences (49). Therefore, AI systems should be developed to enable humans to understand their actions and the underlying logic in order to increase transparency and minimise the risk of bias or error (50). In the document attached to the communication, the European Commission addressed the issue of liability for emerging digital technologies and stated that AI-based robots must meet the essential health and safety requirements set out in the EU regulations on machinery, radio equipment and medical devices as well as the directive protecting the health and safety of workers. Nevertheless, the limitation of the aforementioned regulations is recognised when a liability judgement must be made in situations where the damage is caused by an autonomous and self-learning technology. An example is the case of fully autonomous cars, for which it has been argued that liability for damage can be attributed to the driver/owner of the vehicle under tort law or to the manufacturer of the automated vehicle under the rules implementing the Product Liability Directive. Liability is based on fault or risk, where the holder/driver is strictly liable for opening the risk associated with the circulation of a motor vehicle on public roads (48).

Due to the lack of a specific regulatory framework concerning liability and insurance in the field of robotics and AI, the European Parliament proposed to introduce a harmonised European regulatory

framework to enable a tailor-made approach to robotics and AI. On the contrary, it is considered unsatisfactory not to develop additional measures to the existing regulatory framework or to extend the scope of the Product Liability Directive (51).

Subsequently, the Commission proposed to pursue an AI in the service of people with the ultimate goal of improving the well-being of human beings. An “anthropocentric” AI should provide for the subsistence of surveillance mechanisms, safety devices and traceability. Surveillance could be ensured by adopting an approach with human intervention (human-in-the-loop), with human supervision (human-on-the-loop) or with human control (human-in-command); safety devices should be incorporated from the design phase, to ensure the safety of AI systems in a verifiable manner during each phase, with particular attention to the physical and mental protection of all individuals involved; the algorithm used should be described and the decision-making process should be explained, recorded and documented. Finally, in the event of an unfair negative impact, accessible mechanisms should be provided to ensure adequate means of redress (52).

In 2020, the European Commission issued a white paper on AI that investigated the challenges and opportunities associated with AI and proposed guidelines for its ethical and sustainable development. According to this official report, although software intended to be used for medical purposes must be considered a medical device under the Medical Devices Regulation, two critical issues remain to be considered: whether stand-alone software can fall within the scope of EU product safety legislation and whether EU product safety legislation can also be valid and sufficient for AI-based services, such as healthcare services. The need to adapt the legal framework to digital transformations and the use of AI requires specific regulatory interventions, the drafting of which will have to be a priority following a risk assessment based on two cumulative criteria. Before anything else, we must carefully assess the domain in which AI is applied, particularly highlighting healthcare as a field where significant risks are foreseeable due to the nature of typical activities. Secondly, the way in which AI is used in the sector under consideration: a possible defect in the appointment booking system in a hospital does not present a significant risk, but AI systems that provide medical information directly to the patient or AI systems that perform medical functions on a patient may be burdened with the risk of patient injury or death.

In the first case, the risks do not justify legislative intervention, whereas in the second case, the potential impact on individual rights warrants an adjustment of the legislative framework by introducing provisions that explicitly address the new risks arising from emerging digital technologies aimed at ensuring legal certainty (53).

The European Parliament Resolution of 20 October 2020 also regulated liability for AI system users on the basis of a risk assessment approach. An AI system that works autonomously can endanger the user or the public at random and to a much greater extent than can reasonably be expected is at high risk. A strict liability is identified for high-risk AI systems, whereby users are liable for any damage or harm resulting from the use of the system, excluding only cases of force majeure. Operators cannot excuse themselves by claiming that they acted diligently or that the damage was caused independently by the AI system. It applies both to “front-end operators,” i.e., the natural or legal person who exercises a degree of control over, and benefits from, a risk associated with the operation and functioning of the AI system, and to “back-end operators,” i.e., the natural or legal person who, on

an ongoing basis, defines the characteristics of the technology and provides the essential back-end data and support service and therefore also exercises a high degree of control over a risk associated with the operation and functioning of the AI system. Both operators will have to verify the existence of civil liability insurance coverage appropriate to the amounts and scope of compensation required by the resolution: up to a maximum amount of EUR 2 million in the event of death or damage to health or physical integrity; up to a maximum amount of EUR 1 million in the event of property damage. The Resolution sets the limitation periods at 30 years from the date on which the damage occurred for personal injuries, 10 years from the date on which the damage occurred or 30 years from the date on which the harmful activity of the AI system took place for property damage. For AI systems that are not high-risk, a fault-based liability regime is identified. Whereas it is not possible to exonerate oneself from liability by claiming that the damage was caused independently by the AI system, the operator may instead prove that he is not liable if he proves that the damage was not related to a negligent action. This can occur if the AI system is activated without the operator's knowledge, provided that all reasonable security measures have been taken. Furthermore, the operator may be considered not liable if they demonstrate having diligently selected an appropriate AI system, implemented it correctly, monitored its activities closely, and maintained operational reliability by regularly installing all available updates. With regard to the apportionment of liability, the operator sees its degree of liability decrease when the damage is the result of a contribution from both the AI system and the conduct of the injured party or another party for which the injured party is responsible. If there are several operators in the AI system, they are jointly and severally liable. If the "back-end operator" is also the producer, the Product Liability Directive applies; if the "front-end operator" is also the manufacturer of the AI system, the Product Liability Directive Resolution prevails (54).

On 13 March 2024, the European Parliament approved the AI Act aimed at ensuring the smooth functioning of the EU market by harmonising the rules for placing on the market, commissioning and use of AI systems. Using a risk-based approach, AI systems are differentiated into unacceptable risk, high risk and low or minimal risk. The use of AI systems that violate the fundamental values and rights of the EU is deemed unacceptable. This encompasses those posing a risk of manipulating individuals through subliminal techniques, exploiting specific vulnerable groups, contravening current legislation on data protection, consumer protection, and digital services. Additionally, assigning a social score based on AI for general purposes by public authorities and conducting real-time remote biometric identification in public spaces for law enforcement purposes are considered unacceptable, with certain limited exceptions. At high risk are AI systems intended for use as safety components of products subject to prior conformity assessment by third parties, as well as stand-alone AI systems that primarily have fundamental rights implications. In healthcare, this category includes AI systems used by or on behalf of public authorities to assess the eligibility of individuals for public assistance benefits and services, and to grant, reduce, withdraw or recover such benefits and services; Also included in this category are AI systems used to dispatch emergency first aid services or to prioritise the dispatch of such services. However, the list may be supplemented by adding AI systems that, in addition to falling

within one of the areas already considered, also present an equivalent or higher risk of harm to health and safety than the risk of harm presented by AI systems already considered high risk. A risk management system is established for high-risk AI systems through which risks are identified, analysed and estimated, and measures are put in place for the mitigation and control of non-eliminable risks or the eradication of eliminable ones. In Article 14, the regulation deals with the human-machine interface, outlining the primary role of the human being in the decision-making process. Human surveillance will have to be planned by the provider prior to marketing and integrated into the high-risk AI system. The human being will be responsible for monitoring the functioning of the high-risk AI system, intervening promptly in the event of anomalies, malfunctions and unexpected performance, shutting down the system in good time. Furthermore, the human being must be aware of the risk of "automation bias," i.e., an excessive and uncritical reliance on the output and the need to interpret and possibly disregard the output of the high-risk AI system. For AI systems already classified as high-risk, the execution of the action must be verified and confirmed by at least two human beings. Finally, high-risk AI systems are designed and developed to ensure that their operation is transparent to the extent that users can interpret the output of the system and use it correctly (55).

The aim of the AI Act is to prevent, monitor and address the risks associated with the use of AI, but it does not include measures for the benefit of people who have been harmed by it. Therefore, the European Parliament and the Council have proposed an AI Liability Directive that aims to ensure that persons claiming compensation for damage caused by an AI system have a level of protection comparable to that guaranteed to individuals claiming compensation for damage caused without the intervention of an AI system (56). To this end, the Proposal addresses issues concerning disclosure of evidence and the burden of proof with specific reference to claims for compensation concerning damage caused by the output produced by an AI system or the failure of that system to produce an output through the fault of a person. With regard to the disclosure of evidence, in order for the alleged injured party to assess the validity of a claim for compensation, interested parties should be granted the right to request a court to order the disclosure of relevant evidence before making a claim for compensation for the damage suffered. Accordingly, in the event that the defendant in an action for damages fails to comply with the court's order to disclose the evidence at its disposal, it may be justified to create a presumption of non-compliance with the duty of care that such evidence was intended to highlight. The disclosure of evidence is limited to high-risk AI systems for which, according to the AI ACT, specific documentation, disclosure and preservation requirements apply. The causal relationship between the defendant's fault and the output or lack of output generated by an AI system may be presumed when all of the following conditions are met: the claimant has proved, or the court has presumed, fault on the part of the defendant or a person for whom the defendant is liable, consisting in the breach of a duty of care established by Union or national law, directly aimed at preventing the harm suffered; it is reasonably probable, based on the circumstances of the case, that the negligent conduct affected the output generated by the AI system or its lack of output; the claimant has proved that the harm was caused by the output produced by the AI system or its lack of output.



### 3 Discussion

The convergence of robotics and medicine has opened new frontiers in healthcare, enabling significant advances in diagnosis, surgery, rehabilitation therapies and elderly care (57). Robotics applications in medicine are radically transforming medical practice, offering more precise, efficient and customised solutions (7). In the ever-changing landscape of healthcare, the synergy between robotics and AI is opening up new frontiers, revolutionising medical practice and offering innovative solutions to improve the precision, efficiency and accessibility of care.

Despite the many benefits, there are also challenges to be addressed proactively, ensuring that technology is used responsibly to maximise benefits for patients and society. These include the identification of liability among the various parties involved in medical malpractice cases.

When AI stands between a person's action or omission and the harm, the particular characteristics of some AI systems, such as the opacity of algorithmic decisions, autonomous behaviour and complexity, can make it extremely difficult for the damaged party to meet its burden of proof. Claimants may face significantly higher initial costs and significantly longer court proceedings than in cases not involving the AI (58). On the other hand, an unfair attribution of blame may occur where physicians are wrongly blamed or blamed for errors or complications that may be beyond their control. In both cases, an injustice would be realised.

In this paragraph, the possible consequences on the determination of medical fault will be analyzed if robots were to be granted electronic personality. Then, the issues related to the potential recognition of strict liability in the context of using AI systems will be discussed.

#### 3.1 The status of electronic persons

To address this issue, in 2017 the European Parliament proposed the recognition of a joint human-robot action based on the identification of robots as “electronic persons,” with the possibility for robots to compensate for any damage caused by them (47).

Should the legal personality of robots be recognised, there could be three models in which robots could commit a crime. According to “the perpetration via another liability model” the robot is the means by which the programmer or the end user commits the crime; according to “the natural-probable-consequence liability model,” the offence is caused by the negligent conduct of the programmer or user. In this instance, if the robot/AI committed a different or additional offence, this would constitute an abnormal concurrence of offences; Finally, according to “the direct liability model,” it is viable to identify the robot's action, its causal connection with the harmful event, and its deliberate intention to perform harmful actions. The conduct may be commissive, such as the movement of the robotic arm, or omissive, such as the inertia of the robotic system. The conscious intention of the robot to commit a crime is constituted through three successive steps: the representation of the real world through the sensor-based acquisition of data and their processing; the ability of machine learning and decision-making systems to anticipate and desire a specific outcome as a consequence of their actions; the occurrence of negligent behaviour because the system does not take into account a probability that it should have taken into account on the basis of the data collected, or in the event of a calculation error during the learning process (59).

According to the European Economic and Social Committee, recognising the “electronic personality” of robots poses a significant hazard (47). However, we believe it is not only a moral, but also a bio-legal hazard, as exposed by the signatories of an open letter to the European Commission on AI and robotics (60).

The “electronic personality” concept is based on the recognition that the robot-autonomous-agent can relate to its surroundings through sensors or the constant exchange of data, learn through experience and interaction, adapt its behaviour and act through physical support. Thus, the recognition of “personality” and ownership of specific rights is conditional on the existence of characteristics such as self-awareness, self-control, ability to relate to others and communication skills. This view is definitely restrictive. Intangible personality. These include the right to one's name, image, privacy, also understood as control over the circulation of one's personal data, honour and reputation, personal identity and physical integrity. Recognition of these rights is also followed by preventive protection measures, aimed at preventing the damaging act before it occurs, and restorative measures, aimed at compensating for the prejudice linked to the injury to “personality rights.”

The recognition of an “electronic personality” is also at odds with European legislation according to which the person is at the centre of the initiatives promoted by the European Union and among the fundamental values attributed to him are the right to physical and mental integrity, without distinction (61). In addition, specific rights are attributed to the individual, first and foremost the right to life, from which follow the right to liberty and security, the right to respect for private and family life, freedom of thought, conscience and religion, freedom of expression and other relevant civil rights (62).

Therefore, should the robot-agent be granted “electronic personality,” it would also be necessary to recognise and protect “personality rights” as well as the values recognised and protected by the EU: for example, we should recognise the robot-agent's right to have its own opinion, express it, decide, without any external, even human, coercion. Otherwise, the right to freedom of thought and expression would be violated. In the healthcare area, therefore, the possibility of a relationship between patient and robot-agent should be recognised, in which the latter is given the right to formulate a medical therapy. The patient's right to freely choose whether or not to adhere would be the only limit to the medical-robotic act.

Setting the goal of an “anthropocentric” AI, although admirable, is not enough if by this term we only refer to the goal of realising AI-systems at the service of humanity and the common good, with the aim of improving the wellbeing and freedom of human beings. It becomes so when an “anthropocentric” approach expresses the recognition for the human being of a unique and inalienable moral status of primacy in the civil, political, economic and social spheres (63). Indeed, serving others is not an obstacle to the recognition of legal personality, to the same extent as it is not for the human being who is legitimately accorded “personality rights” and who considers service to another human being, to humanity and to the common good as fundamental values. The rights, duties and legal protections enjoyed by a human being due to the recognition of an inherent dignity and value as an individual cannot also be granted to a robot-agent. On these grounds, it is reasonable and well-founded to state that AI systems should be supervised and controlled by a human being, whose task it is to intervene in all potential or actual and concrete cases in which an AI system risks infringing “personality rights” (46, 52). Otherwise, if the robot-agent were recognised as



having an “electronic personality,” it would have to be given the same rights and duties as a human being. Consequently, it would be inconsistent to impose prior and continuous surveillance and control over it by human beings.

Among other things, the recognition of “electronic personality” has significant repercussions in terms of legal redress (64). The punishment meted out to a robot-agent as a result of an offence could in no way have any deterrent power towards those tempted to commit a crime or any violation of the law. Similarly, a patient victim of a negligent omissive or commissive conduct by the robot-agent could not receive any form of compensation. Finally, we consider it questionable the establishment of a specific legal status for robots by the recognition of qualities such as autonomy, learning capacity, physical support, relationality. It is not self-awareness, self-control, the ability to relate to others, the ability to communicate that make a human being the holder of inalienable rights. The human being’s status as a person persists even when the ability to think and will is absent, since self-awareness, although fundamental to human freedom, does not constitute the essence of human nature. Even when the intellectual and volitional faculties are irreversibly impaired, the human being remains a person, and human life is not determined by the expression of these faculties (65). For these reasons, we do not believe it is permissible to establish a legal status for robots, allowing sophisticated autonomous robots to be held as electronic persons responsible for the damage they cause and recognising the electronic personality of those that make autonomous decisions or interact independently with third parties.

The centrality of humans in decision-making processes, even with the assistance of AI, is crucial to ensure accountability, ethical considerations, and the integration of human capabilities with AI outcomes. Humans must interpret and wisely apply data provided by AI, as AI lacks the necessary human experience to fully grasp the context and complexities of decisions involving moral and ethical aspects. Additionally, human monitoring can identify and correct potential biases in algorithms. While AI can analyze vast amounts of data and produce rapid results, it can also be influenced by biases or distortions in training data or the decision-making process itself. Human intervention is crucial to understand the specific context in which AI operates, detect discriminatory trends or ethical distortions, and make appropriate changes to ensure AI-driven decisions are balanced, fair, and non-discriminatory. This active monitoring helps mitigate risks of negative impacts from uncontrolled AI use, promoting better adoption and acceptance of technologies that could otherwise engender mistrust or controversy. In summary, collaboration between AI and humans should enhance human capabilities, ensuring AI remains a valuable ally rather than a substitute.

### 3.2 Strict liability

A further critical issue in establishing medical malpractice in the healthcare context is the possible recognition of strict liability for HWs and healthcare organisations. The European Parliament Resolution of 20 October 2020 establishes a strict liability regime applicable to both “front-end operators” and “back-end operators” (54). Given that the “front-end operator” is defined as the natural or legal person who exercises some degree of control over a risk related to the operation and functioning of the AI system and who benefits from its operation,

we can in a healthcare scenario consider the “front-end operator” to be both the physician and the healthcare organisation.

According to the AI Liability Directive, the causal relationship between the defendant’s fault and the output or lack of output generated by an AI system can be presumed when specific conditions are met (46), which, translated, in the healthcare context can be summarised as follows: proven for alleged breach of a duty of care on the part of the physician or healthcare organisation; causal relationship between the output or lack of output of the AI system and the negligent conduct of the physician or healthcare organisation. This judgement is made on the basis of probability and not certainty; the patient’s harm is causally related to the output or lack of output of the AI system.

If the harm to a patient was caused by the inadequate, incorrect, or imperfect use of the AI system by the physician or healthcare organisation, or by a misinterpretation of the data provided by the AI system, there is no doubt that liability is attributed to the physician or healthcare organisation. Critical issues arise when the harm to the patient is causally related to the output of the AI system: who is to blame? To the manufacturer of the AI system? To the physician and the healthcare organisation? Or can they both reasonably declare their innocence because the robot-agent has the potential to autonomously increase its capacity through an appropriate deep learning system similar to human neural networks? Can strict liability also be attributed to the doctor and the healthcare organisation in such cases?

In the context of strict liability, the medical doctor or healthcare organisation is liable for harm to the patient regardless of fault, but under the rule of risk. Neither of them can be exempted from this liability, except exceptionally by proving that the harm occurred as a result of a fortuitous event. Strict liability is a type of liability designed to protect the injured party by requiring him to prove only the damage and the causation.

One limitation to the use of strict liability in the healthcare sector is the recognition of the existence of a joint human-robot activity based on two essential interdependent relationships, namely predictability and directionality (46). If we were to admit the existence of a joint human-robot action, why should strict liability of the medical doctor or healthcare organisation be recognised?

Strict liability obliges the victim to prove causation and the defendant to prove that the harm occurred due to a fortuitous event. It is required to resort to a logical procedure called the “but-for test”: for commissive conduct, a “but-for test” will be carried out based on the mental elimination of conduct from the causal course. If, by eliminating the conduct, the event would have occurred anyway, then that conduct cannot be said to have caused the event. With regard to omissive conduct, the conduct that should have been performed will be added to the causal course and it will be ascertained whether or not through this conduct the event would have occurred (66–68).

The logical reasoning just outlined is the foundation of the study of causation in both civil and criminal liability, but it is very unlikely to find application in cases where AI stands between a person’s action or omission and the harm. In fact, the latest machine learning models are like “black boxes,” as their extremely complex structure prevents users from understanding the process by which an AI system processes data to arrive at decisions (69, 70).

It would also preclude any possibility of analysing the gradation of fault by means of a procedure for assessing the seriousness of the physician’s misconduct or negligence and the corresponding level of legal liability.

Although aimed at harmonising legislation, both the European Product Liability Directive and the Directive on Liability for AI fail to close potential liability gaps (71).

We are experiencing a hybrid phase in which AI and medicine are increasingly joining forces to improve the diagnosis, treatment and management of diseases. However, at present we have many critical social, ethical and legal issues to study, address and overcome (72–74). The accelerated development of AI is far exceeding the capacity of the legal framework to fully understand its implications (75).

So, what can be done? First of all, the centrality of the relationship between physician and patient in the healthcare context must be reaffirmed. On the one hand, it is the physician's sole task to guide the diagnostic and therapeutic process, using their expertise and experience. On the other hand, the patient has the fundamental right to consciously participate in the proposed treatment, fully understanding its implications, and actively contributing to decisions concerning their own health. This balance between medical expertise and patient autonomy is essential to ensure effective care, while respecting the dignity and self-determination of each individual. With this in mind, it is crucial to avoid any distortion of automation that could undermine human autonomy by interfering with the decision-making process (4). This risk becomes even more significant considering the existence of known algorithmic biases in AI-supported clinical decision-making (76).

Therefore, in line with the current state of technology, an AI system should not be considered differently from radiology devices. Radiology as a diagnostic support tool offers multiple benefits, including more accurate and timely diagnosis, effective monitoring of treatment response and guidance during invasive procedures. However, it is essential to correctly interpret the diagnostic images and integrate them with other clinical information in order to ensure a complete and accurate assessment of the patient.

Therefore, in determining liability for medical malpractice, even when using AI systems, it is still necessary to consider the scientific dimension of causation, integrating the “but-for test” with the “covering-law model.” This approach makes it possible to assess the physician's actions on the basis of universal laws and statistical-quantitative and epidemiological rules (66–68).

Despite the revelation of the limits of linear causality by contemporary physics and mathematics and by cognitive relativism (77–79), the but-for test causality model integrated with the covering-law model can still effectively address the challenges posed by AI-integrated medicine and assist in the search for judicial truth.

In summary, the introduction of a regime of strict liability would imply that doctors and healthcare organisations are held accountable for the correct and safe use of AI systems in the healthcare sector. However, we believe that even when AI systems are used, they should be contextualized within a joint human-robotic action. Such action should be evaluated through the forensic science methodology.

## 4 Conclusion

Technological progress has played a fundamental role in medicine, revolutionising virtually every aspect, from diagnosis to therapy, and even data management. The introduction of robotics and AI have the potential to redefine the landscape of medicine, radically transforming clinical practice and improving the lives of millions of people worldwide. However, while in the past, technology's role has been explicitly to assist in medical procedures, today, for the

first time in history, new technologies can potentially enter the physician's decision-making process to the extent of replacing it.

We do not believe that an approach to analysing the problem based on a division between those who take a catastrophic attitude and fear professional deskilling and those who are carried away by easy enthusiasm is useful.

The goal of medicine is the patient's health, so if in the future robotics and AI were to pursue the objective of patient health better than the activity performed by a human being, and this is supported by solid scientific evidence, so be it.

However, we are currently in a hybrid phase where the last mile, i.e., the decision, lies with the physician. And it is at this stage that we have to deal with, and it is at this stage that those who deal with medical liability should, on the one hand, guarantee fair compensation to patients who are victims of harm, and on the other hand that doctors and health organisations should not be found objectively guilty because they have made use of AI devices.

As it turns out, the current European legislation aimed at harmonising legislation in this area leaves some questions unanswered. However, precisely on the basis of the European regulations, we believe that a specific regulation concerning medical liability in cases of the use of robotics and AI in medicine should be drawn up. To this end, it will be necessary to analyse the risk of the use of AI in health care and then assess the specific features with which AI is used. The integration of robotics in healthcare offers significant advantages, but it also presents significant ethical and medico-legal challenges. Addressing these challenges requires deep reflection and collaboration among healthcare professionals, legal experts, legislators, and stakeholders. Only through a holistic and ethically based approach can we maximise the benefits of robotics in healthcare, while ensuring the safety, privacy, and well-being of patients.

## Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

## Author contributions

FDM: Conceptualization, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. SG: Methodology, Project administration, Writing – original draft. LT: Software, Writing – original draft. GDP: Visualization, Writing – original draft. GR: Writing – original draft. RS: Investigation, Supervision, Writing – review & editing.

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# Has risk management plan system influenced the speed of package insert revisions in Japan?

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**Introduction:** The system of Risk Management Plan in Japan (J-RMP) is a relatively new system, implemented in 2013; thus, its effect on safety measures is still unclear. One of the purposes of J-RMP is to enhance the postmarketing safety measures to be ensured by publishing J-RMP and sharing information on risk management among healthcare professionals. We hypothesized that this might enable information about postmarketing adverse events to be accumulated rapidly, potentially accelerating the identification of adverse reactions (ARs). Herein, we focused on the speed of adding clinically significant ARs (CSARs) to package inserts (PIs) as an indicator of the rapidity of AR identification, investigated the impact of the J-RMP system on PI revisions.

**Methods:** We investigated the “Notice of Revision of Precautions” on the website of Pharmaceuticals and Medical Devices Agency (PMDA), targeting PI revisions with the addition of CSARs from April 2003 to March 2023, which corresponds to 10 years before and after J-RMP implementation in April 2013. We created an original database from public information of PMDA and investigated the speed of adding CSARs to PIs.

**Results:** Comparing the time lapse from drug approvals to PI revisions after J-RMP implementation (149 cases) to that before implementation (318 cases), the median value was 32 months for both. Regarding the time lapse when the additional CSARs were listed and unlisted as safety concerns at the time of approvals, it was 35 months vs. 32 months (14 cases vs. 126 cases,  $p = 0.7820$ ), with no statistically significant difference. Conversely, there were significant differences within each AR and each drug therapeutic category.

**Discussion and conclusions:** This study revealed that the rapidity of risk identification as ARs was not affected by J-RMP, and it may be affected by the characteristics of each AR and each drug therapeutic category. It is expected that other J-RMP benefits, such as risk prevention before the occurrence, will be utilized to further develop strategies for the effective utilization of the J-RMP for safety measures in Japan.

## KEYWORDS

risk management plan in Japan, risk management plan, package insert revision, adverse reaction, drug safety, pharmacovigilance

## 1 Introduction

The Risk Management Plan (RMP) in Japan is a document that indicates the risk management of drugs from the development phase to the postmarketing phase. It comprises the following three elements for individual drugs: safety concern, pharmacovigilance activities, and risk minimization activities (1). “Risk Management Plan Guidance,” which was issued in 2012, is applicable to new drugs for which approval applications were submitted on or after April 1, 2013, and requires the creation of RMP in Japan (2). The effect of the J-RMP system (which is a relatively new system) on safety measures is still unclear. Given that it has been more than 10 years since J-RMP was implemented in 2013, we believe it is meaningful to investigate the impact of J-RMP on safety measures and evaluate its effectiveness. One of the purposes of J-RMP is to enhance the postmarketing safety measures to be ensured by publishing J-RMP and sharing information on risk management among healthcare professionals, leading to understand activities as risk management (3). Consequently, it potentially increases spontaneous reports as medical professionals understand the significance of adverse event reporting or recognize it as a risk or insufficient information. Thus, we hypothesized that this might enable information about postmarketing adverse events to be accumulated faster, potentially accelerating the identification of adverse reactions (ARs). However, to the best of our knowledge, no study has been conducted to determine the impact of J-RMP on the rapidity of identifying ARs. In this study, we focused on the speed of adding clinically significant ARs (CSARs) to package inserts (PIs) as an indicator of the rapidity of AR identification and investigated the impact of the J-RMP system on PI revisions.

## 2 Materials and methods

In this study, we investigated the “Summary of Investigation Results” attached to the “Notice of Revision of Precautions” on the website of Pharmaceuticals and Medical Devices Agency (PMDA) (4). “Notice of Revision of Precautions” is a list of notification based on which manufacturers revise their PIs. We targeted PI revisions with the addition of CSARs from April 2003 to March 2023, which corresponds to the 10 years before and after J-RMP implementation in April 2013. The PI revisions from April 2013 to March 2023 were included as PI revisions after RMP implementation, and PI revisions of drugs with no RMP at the time of approval were excluded from the analysis. The PI revisions from April 2003 to March 2013 were included as PI revisions before RMP implementation. We created an original database and first checked the background characteristics of PI revisions for additional CSARs and therapeutic category of drugs. Next, we compared the speed of adding CSARs to PIs with respect to (1) before and after RMP implementation, and (2) listed and unlisted CSARs as the safety concerns at the time of approval. We also investigated the speed by each CSAR and each therapeutic category of drugs.

The speed of adding the CSAR to the PI was defined as the time from the initial approval for new active ingredients of the drug (s) to the date of issuance of the “Notice of Revision of Precautions.” When comparing such speed of PI revisions, “after RMP implementation” refers to PI revisions from April 2013 to March 2023 for products first approved after April 2013, with RMPs at the time of approval, and

“before RMP implementation” refers to PI revisions from April 2003 to March 2013 for products first approved after April 2003, with no RMPs. If “Draft drug risk management plan (5)” was included in the review report at the time of approval, it was determined that the RMP was created at the time of approval. Whether or not the CSARs were listed as the safety concerns was also checked by “Draft drug risk management plan.”

This study was conducted per the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines (6) for cross-sectional studies. All statistical analyses were performed using the analytical tools of JMP Pro 15, with two-sided  $p$ -values less than 0.05 being considered statistically significant. The Wilcoxon rank sum test was used to perform comparisons between quantitative data while the Chi-square test was used to perform comparisons between categorical data. CSARs were coded using MedDRA (7) ver. 26.0 and classified by System Organ Class. Therapeutic drug categories were classified according to the Japanese Standard Classification of Products (8).

## 3 Results

The most common CSARs after RMP implementation were “Infections and infestations,” “Skin and subcutaneous tissue disorders,” and “Hepatobiliary disorders,” classified by System Organ Class with MedDRA (7). As for CSARs before RMP implementation, “Hepatobiliary disorders,” “Nervous system disorders,” and “Skin and subcutaneous tissue disorders” were the most common. Regarding the therapeutic category of the drugs, “Other oncology drugs,” “Antidiabetic drugs,” and “Metabolic drugs not elsewhere classified,” were the most common after RMP implementation, and “Other oncology drugs,” “Metabolic drugs not classified elsewhere” and “Antiviral drugs” were the most common before RMP implementation. Table 1 shows the background characteristics of the PI revisions for the addition of CSARs.

Comparing the PI revisions after RMP implementation with before implementation, the number of CSARs added to the revised PIs was 149 vs. 318, and the median time from approvals to PI revisions was 32 months for both. Additionally, for 140 of the 149 cases after RMP implementation, excluding nine cases having no information on safety concerns at the time of approvals, we investigated the speed of PI revisions. Comparing when the additional CSARs were listed and unlisted as safety concerns at the time of approvals, the number of CSARs was 14 vs. 126, and the median time from approvals to PI revisions was 35 months vs. 32 months ( $p = 0.7820$ ), and these variables did not differ significantly from each other. A comparison of the speed of adding CSAR to the PI is shown in Table 2.

Conversely, median interval from approvals to PI revisions for each CSAR was significantly shorter for “Metabolism and nutrition disorders” (14 cases, 10 months,  $p < 0.0001$ ), and longer for “Blood and lymphatic system disorders” (9 cases, 55 months,  $p = 0.0413$ ) and “Eye disorders” (4 cases, 79.5 months,  $p = 0.0234$ ; Table 3).

The median interval from approval to PI revision by each drug category was significantly shorter for “Antidiabetic drugs” (28 cases, 17 months,  $p = 0.0106$ ) and “Antiviral drugs” (12 cases, 15 months,  $p = 0.0088$ ), and significantly longer for “Metabolic drugs not classified elsewhere” (15 cases, 59 months,  $p = 0.0143$ ) and “Drugs for digestive ulcers” (8 cases, 58 months,  $p = 0.0087$ ; Table 4).

TABLE 1 Background characteristics of package insert revisions for adding clinically significant adverse reactions.

		After RMP implementation (1)	Before RMP implementation (2)
Additional adverse reactions	Total (N)	149	318
Additional adverse reactions (SOC)	Infections and infestations	19	14
	Skin and subcutaneous tissue disorders	18	32
	Hepatobiliary disorders	17	33
	Immune system disorders	14	22
	Metabolism and nutrition disorders	14	15
	Gastrointestinal disorders	10	25
	Blood and lymphatic system disorders	9	29
	Respiratory, thoracic and mediastinal disorders	8	29
	Nervous system disorders	3	33
	Others	39	99
Therapeutic category of drugs	Other oncology drugs	66	72
	Antidiabetic drugs	28	16
	Metabolic drugs not classified elsewhere	15	31
	Antiviral drugs	12	27
	Synthetic antibacterial drugs	0	20
	Psychoneurotic drugs	1	18
	Vaccines	2	17
	Others	25	120

(1) Package insert revision for 10 years (from April 2013 to March 2023) for products first approved after April 2013 and for which the RMP was published at the time of approval. (2) Package insert revision for 10 years (from April 2003 to March 2013) for products first approved after April 2003.

TABLE 2 Comparisons of the time lapse from drug approval to the addition of adverse reactions in package insert revisions.

Addition of adverse reactions		N	Median time (month)
After RMP implementation (1)	Total	149	32
	Listed as safety concerns at the time of approval	14	35
	Unlisted as safety concerns at the time of approval	126	32
	No information	9	
Before RMP implementation (2)	Total	318	32

(1) Package insert revision for 10 years (from April 2013 to March 2023) for products first approved after April 2013 and for which the RMP was published at the time of approval. (2) Package insert revision for 10 years (from April 2003 to March 2013) for products first approved after April 2003.

4 Discussion

The speed of PI revisions is instrumental in the prompt identification of risks as ARs to improve awareness and patient safety. In this study, we investigated the impact of the J-RMP system on the revisions of PIs, focusing on PI revision speed. This is because we expected that if risks were appropriately managed using J-RMPs, they could be identified as ARs more rapidly, and PI revisions could be faster. We assumed that J-RMP potentially increase spontaneous reports as healthcare professionals understand the importance of adverse event reporting or recognize it as a risk or insufficient information, leading to fast PI revision speed. However, the results revealed that the implementation of the J-RMP system or description as safety concerns at the time of approvals did not affect the PI revision speed regarding the addition of CSARs. As a side note, in the study examining the relationship between the revision of the information in

the CSARs section in PI and the description in J-RMP at the time of drug approval, the median time from drug approval to PI revisions was 29.5 months (9), which was nearly the same as that in our study (32 months). One of the reasons for J-RMP not affecting the rapidity of risk identification as ARs in our study is potentially because healthcare professionals take precautions for reducing the risk, making ARs less likely to occur, and slowing down PI revision speed. Concerning the hypotheses of this study, we focused on the possible publication of the J-RMP that might increase the speed of collecting ARs and PI revision speed; however, risk prevention measures can slow down the PI revision speed, thereby affecting the results. Future studies on the impact of risk minimization measures on PI revision speed will be of interest.

Although the J-RMP did not affect the rapidity of risk identification for ARs, it is known to have other advantages. A study by Saito et al. revealed that there is a strong relationship between ARs

TABLE 3 Comparisons of the time lapse from drug approval to the addition of adverse reactions in package insert revisions (by each adverse reaction).

		After RMP implementation	Median time (month)	<i>p</i> -value
Additional adverse reactions	Total (N)	149	32	
Additional adverse reactions (SOC)	Infections and infestations	19	48	0.4222
	Skin and subcutaneous tissue disorders	18	36	0.4238
	Hepatobiliary disorders	17	53	0.1278
	Immune system disorders	14	29	0.6534
	Metabolism and nutrition disorders	14	10	<0.0001
	Gastrointestinal disorders	10	39	0.4168
	Blood and lymphatic system disorders	9	55	0.0413
	Respiratory, thoracic and mediastinal disorders	8	38.5	0.8234
	Cardiac disorders	8	18	0.2485
	Musculoskeletal and connective tissue disorders	6	23.5	0.1672
	Vascular disorders	5	26	0.7279
	Investigations	5	12	0.2966
	Endocrine disorders	4	48	0.1535
	Eye disorders	4	79.5	0.0234
	Nervous system disorders	3	15	0.13
	Psychiatric disorders	3	25	0.437

TABLE 4 Comparisons of the time lapse from drug approval to the addition of adverse reactions in package insert revisions (by each therapeutic category of drugs).

		After RMP implementation	Median time (month)	<i>p</i> -value
Additional adverse reactions	Total (N)	149	32	
Therapeutic category of drugs	Other oncology drugs	66	33	0.3887
	Antidiabetic drugs	28	17	0.0106
	Metabolic drugs not classified elsewhere	15	59	0.0143
	Antiviral drugs	12	15	0.0088
	Drugs for digestive ulcers	8	58	0.0087
	Other hormone drugs	7	46	0.4116
	Other central nervous system drugs	3	29	0.5565

listed as safety concerns at the time of approval and those being added to the PIs as CSARs postapproval, indicating that safety concerns could potentially induce severe ARs. This suggests that safety concerns in J-RMPs constitute important drug information, and it is expected that medical professionals will contribute to the prevention of severe ARs in patients by utilizing J-RMPs in addition to PIs (10). Furthermore, “Risk minimization activities” of the J-RMP are also important elements for healthcare professionals because they describe measures to minimize the patient’s risk (11). One of the purposes of the J-RMP is to prevent risks before they occur; however, the low usage rate of the J-RMP in clinical settings has been an issue (12). However, in Japan, the medical fee regulations were recently revised in 2024 to include a provision that medical fee points will be increased if sufficient safety instructions are provided using RMP materials at the time of dispensing (13). According to precedents, regulatory renovation had an obvious effect on Pharmacovigilance Planning (PVP). For example, the publication of the revised Good

Post-marketing Study Practice in 2017 (14, 15) and the procedure for developing Postmarketing Surveillance plans in 2018 (16) had a clear impact on PVP shown in J-RMP; the proportion of drugs with efficacy issues decreased, safety issues with additional activity also decreased, and database studies increased in contrast (17). Therefore, it is expected that the revision of medical fee regulation will also promote the use of the J-RMP in clinical settings to mitigate risks. Moreover, J-RMP consolidates risk management into one document to ensure that risk assessments are performed (3), which purpose is different from the RMP in the EU (EU-RMP) (18–21) or risk evaluation and mitigation strategies (REMS) in the US (22), as the EU-RMP lists only safety concerns that require particular attention and REMS are mandatory for only some products. One advantage of the J-RMP is that it allows both regulatory authorities and pharmaceutical companies to conduct risk assessments easily and reliably with one document. However, it has been more than a decade since the implementation of the J-RMP, and there are some preparations for



which the J-RMP has been terminated at re-examination. Therefore, a future challenge will be how to implement risk management after J-RMP termination (23).

Conversely, there were significant differences in the PI revision speed by each AR and drug category, suggesting that the speed of AR identification may be influenced by the characteristics of each AR and drug effect. The PI is revised based on AR accumulation in Japan/overseas, revisions of CCDS/overseas labeling, and information on overseas measures (24). Of these, AR accumulation in Japan is recorded in terms of the “number of domestic cases,” the “number of cases in which a causal relationship cannot be ruled out,” and the “number of fatal cases” over the last 3 years. It is possible that the accumulation speed of cases and the ease of causality assessment may influence the PI revision speed (25). In “Metabolism and nutrition disorders,” where the PI revision was faster, 12 out of the 14 CSARs were ketoacidosis and dehydration associated with antidiabetic drugs (SGLT2 inhibitors). Moreover, in “Antidiabetic drugs” with faster PI revision, 25 out of the 28 CSARs were Fournier’s gangrene, ketoacidosis, sepsis, and dehydration associated with SGLT2 inhibitors. The common denominator here is that the patients are many (26) and that causality can be easily assessed based on the drug’s mechanism of action (27, 28), which is likely why the PIs were revised quickly. As for “Antiviral drugs” with faster PI revision, four out of 12 CSARs were associated with drugs for influenza A or B virus infection, and one CSAR was associated with drugs for Herpes zoster infection, and the patients were numerous (29, 30). Regarding the two CSARs of anaphylaxis associated with drugs for SARS-CoV-2 infectious diseases, it may be easier to assess the causal relationship because anaphylaxis occurs immediately after exposure to the causative substances (31). As for CSARs with slower PI revision, seven out of nine CSARs of “Blood and lymphatic system disorders” were associated with molecular-targeted anticancer drugs, five of those were associated with immune checkpoint inhibitors, and three out of four CSARs of “Eye disorder” were uveitis associated with immune checkpoint inhibitors (32). The reason for the slower PI revision could be the relatively new mechanism of action of these drugs, which makes it difficult to assess AR causality with these drugs, and there were not many patients receiving the drugs. However, there were no clear features of other ARs or drug categories. In addition, it is possible that PI revisions regarding similar ARs associated with similar drug classes were coincidentally performed simultaneously. Further investigations using larger samples are necessary.

Nevertheless, our study has some limitations. This study targeted PI revisions with the addition of CSARs, which are clinically important and are frequently revised for analysis, and did not include the revision of other sections such as “Other adverse reactions” as well as “Precautions” or “Warnings,” etc. In addition, of the CSAR section revisions, only the new AR terms was counted, and the revision of frequency, intensity such as severity, or outcomes such as death was not counted, because the different wordings of these elements could have obscured the visual judgment to include them or not; the results may have been affected if these had been included to the analysis. In addition, regarding the comparison between findings before and after J-RMP implementation, there may be differences in the drug safety system or the procedure for PI revisions between the target periods, which may have affected the speed of the PI revision process. To minimize this effect, we also compared the PI revision speed only after

J-RMP implementation, between when additional CSARs had been included as safety concerns at the time of drug approvals and when they had not been included. Finally, the COVID-19 pandemic potentially affected the results of this study. The number of PI revisions with the addition of CSARs was 40 in 2019 (prepandemic) and 13 in 2020 (postpandemic). However, considering that the number was around 10 in other years, with not much change, the difference in numbers before and after the pandemic could be a coincidence.

## 5 Conclusion

In conclusion, the implementation of J-RMP and safety concerns did not affect PI revision and its speed. However, the J-RMP has other benefits, such as the prevention of risks before they occur and the reliability of risk assessment in one document. These benefits are expected to be utilized to further develop strategies for the effective utilization of the J-RMP for safety measures in Japan.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Author contributions

NK: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. AH: Data curation, Investigation, Writing – review & editing. HM: Conceptualization, Funding acquisition, Methodology, Resources, Supervision, Writing – review & editing.

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## Conflict of interest

NK is an employee of CMIC Co., Ltd.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Artificial intelligence in healthcare: transforming patient safety with intelligent systems—A systematic review

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**Introduction:** Adverse events in hospitals significantly compromise patient safety and trust in healthcare systems, with medical errors being a leading cause of death globally. Despite efforts to reduce these errors, reporting remains low, and effective system changes are rare. This systematic review explores the potential of artificial intelligence (AI) in clinical risk management.

**Methods:** The systematic review was conducted using the PRISMA Statement 2020 guidelines to ensure a comprehensive and transparent approach. We utilized the online tool Rayyan for efficient screening and selection of relevant studies from three different online bibliographic.

**Results:** AI systems, including machine learning and natural language processing, show promise in detecting adverse events, predicting medication errors, assessing fall risks, and preventing pressure injuries. Studies reveal that AI can improve incident reporting accuracy, identify high-risk incidents, and automate classification processes. However, challenges such as socio-technical issues, implementation barriers, and the need for standardization persist.

**Discussion:** The review highlights the effectiveness of AI in various applications but underscores the necessity for further research to ensure safe and consistent integration into clinical practices. Future directions involve refining AI tools through continuous feedback and addressing regulatory standards to enhance patient safety and care quality.

## KEYWORDS

artificial intelligence, patient safety, healthcare, intelligent systems, machine learning

## 1 Introduction

Adverse events in hospitals pose a serious threat to patient care quality and safety globally, contributing to patient distrust and impacting healthcare facility reputations (1). A significant report estimated 45,000–98,000 annual deaths in the U.S. due to medical errors (2). Despite widespread reporting systems, <10% of errors are reported, and only 15% of hospital responses prevent future incidents (3). Overcoming structural and cultural barriers is crucial for improving patient safety (4). Medical errors, defined as

actions leading to unintended results, affect patients, families, healthcare providers, and communities (5). They include drug side effects, misdiagnoses, surgical errors, and falls (7), occurring across care processes from medication to post-operative care. Healthcare risk management combines reactive systems like incident reporting with proactive methods such as Failure Mode and Effects Analysis (FMECA) (8), aiming to learn from past errors and prevent future ones through continuous improvement. Artificial Intelligence (AI) offers potential in healthcare by enhancing diagnostics, optimizing care, and predicting outcomes (9, 10). AI can detect clinical data anomalies, improving diagnostic accuracy, though integrating AI requires addressing new and existing risks (11, 12). This review provides an overview of AI applications in clinical risk management, assessing their benefits, reproducibility, and integration challenges in healthcare settings.

## 2 Materials and methods

The methodology of this systematic review was developed following the guidelines of The Preferred Reporting Items for a Systematic Review and Meta-Analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA) (13).

### 2.1 Keywords Identification

The keywords for the search (Table 1) were selected using terms related to the phrases “clinical risk management” and “artificial intelligence.” The search string used is provided in Table 1.

### 2.2 Search strategy

The search of the scientific literature was conducted in February 2024. Three online bibliographic databases were examined, which are as follows:

- Pubmed
- Scopus
- Web of Science

The first phase of the literature review was carried out using the Rayyan® tool.

### 2.3 Inclusion and exclusion criteria

This systematic review includes studies that simultaneously meet all of the following criteria: (1) Use of artificial intelligence systems, defined as any system capable of replicating complex mental processes through the use of a computer. (2) Application of the artificial intelligence system in the healthcare context. (3) Employment of the artificial intelligence system in areas of interest to clinical risk management. (4) Presence of results derived from the active experimentation of the system. (5) Prevention of an adverse event, defined as an unintentional incident resulting in

TABLE 1 Search string.

Search string
((“risk management”) OR (“clinical governance”) OR (risk assessment) OR (risk prediction)) AND ((“patient safety”) OR (“safety in healthcare”) OR (“quality in healthcare”)) AND ((artificial intelligence) OR (machine learning) OR (deep learning) OR (artificial neural networks))

harm to the patient’s health that is not directly related to the natural progression of the patient’s disease or health condition (14).

Exclusion criteria were primarily used to remove studies that, although involving the use of artificial intelligence systems to enhance care safety, addressed areas not pertinent to the concept of medical error (e.g., risk of cardiac arrest, risk of re-infarction, etc.).

## 3 Results

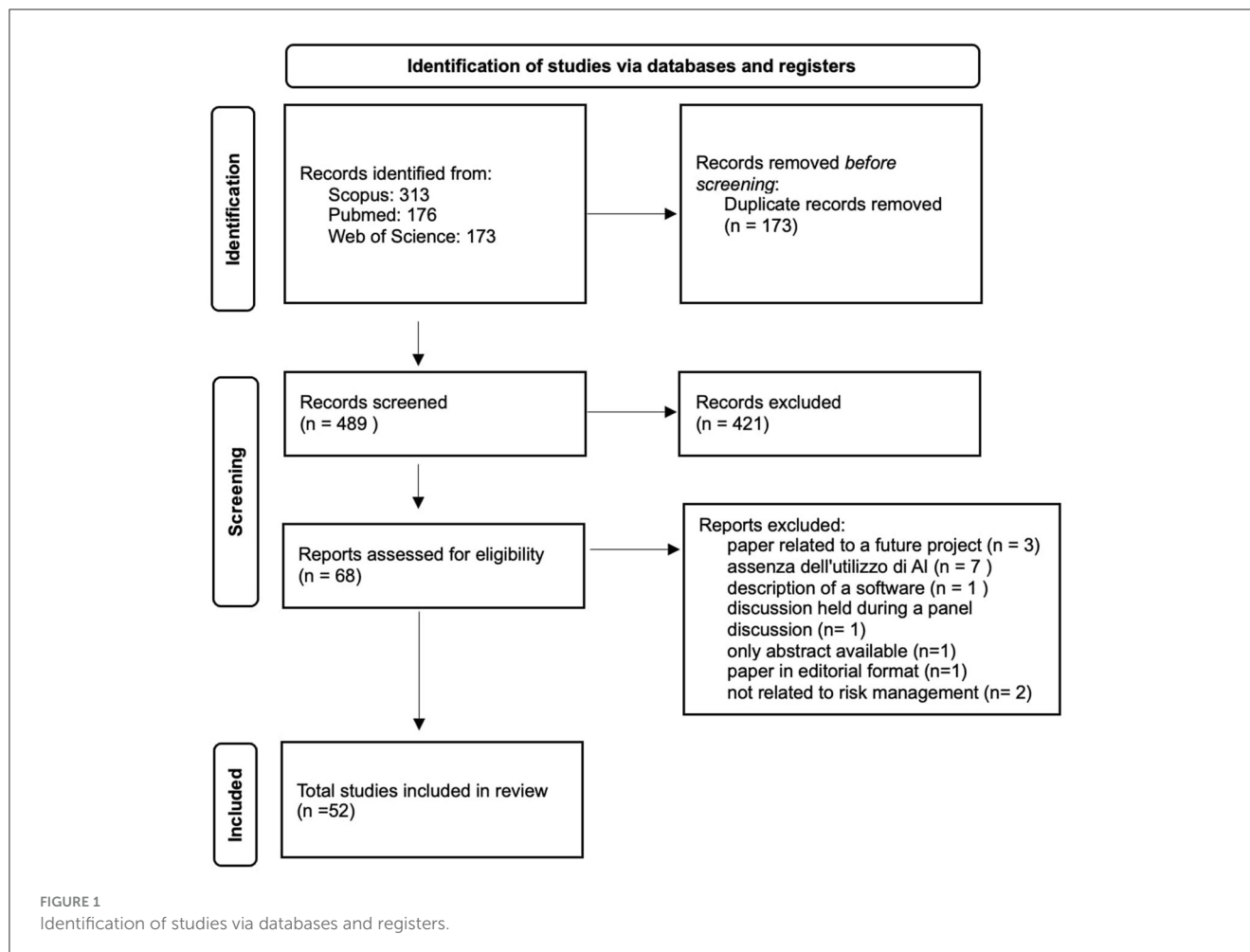
The search across the three databases yielded 662 results (Figure 1). After removing duplicates, the number was reduced to 489 studies. We excluded 421 articles as they did not meet the five established inclusion criteria. In most cases, the excluded events pertained to contexts unrelated to clinical risk management, such as complications arising from the natural progression of diseases rather than preventable adverse events. Following an initial review of the articles, 68 studies were included in the database. An additional 16 studies were excluded. One of the articles (15) was excluded because it represents a future development project for a high-performance prediction, detection, and monitoring platform for managing risks against patient safety, without providing any results. Seven of the articles (16–22) were not included as they addressed clinical risk topics but did not reference the use of artificial intelligence. One of the excluded articles (23) was only available as an abstract. Three studies were not included because, although they discussed the use of artificial intelligence in clinical risk management, they only described the software without reporting results (22, 24, 25). One article was excluded as it was a report of a discussion from a roundtable on risk management in the use of medical devices (26). Another article was not included because it was an editorial and did not meet the inclusion criteria (27). Two articles were excluded as they were not relevant to risk management in the hospital environment (28, 29).

### 3.1 Analysis and findings

The analyzed studies propose diverse methodologies in the field of risk management, offering both proactive and reactive approaches within a heterogeneous application context. The main characteristics of the reviewed articles are presented in Table 2.

### 3.2 Publication period

The articles under review were published between 2007 and 2024. As expected, the number of publications has seen a steady



increase in recent years due to growing interest, particularly in media coverage, and the development of artificial intelligence systems. Specifically, from 2019 to 2024, 36 of the analyzed studies were produced, compared to 16 from 2007 to 2008. As depicted in [Figure 2](#), the countries where the analyzed studies originated include Israel, Denmark, Netherlands, Lebanon, Brazil, United Kingdom, Switzerland, Canada, France, Italy, Spain, United Arab Emirates, South Korea, Taiwan, Japan, China, Australia, and the United States. [Figure 2](#) shows the duration in years of the studies that provided this type of information.

### 3.3 Results for single topics

In this systematic review, it emerged that the most frequently discussed topics in the scientific literature related to risk management are related to the detection of adverse events, followed by the risk of falls, and then the development of pressure ulcers.

#### 3.3.1 Detection of adverse events

In the study conducted by Barmaz Y and Ménard T (30), a hierarchical Bayesian model was employed to estimate reporting

rates at clinical sites and assess the risk of under-reporting based on anonymized public clinical trial data from Project Data Sphere. This model infers reporting behavior from patient data, enabling the detection of anomalies across clinical sites. This system has proven useful by reducing the need for audits and enhancing clinical quality assurance activities related to safety reporting in clinical trials. Bates et al. (31) conducted a scoping review evaluating the role of AI in improving patient safety through the interpretation of data collected from vital signs monitoring systems, wearables, and pressure sensors. The evidence gathered recognized significant potential in this approach, though continuous efforts are required for implementing these systems in healthcare organizations. Benin et al. (32) developed an electronic system for processing medical event reports to enhance patient safety. This system improved care safety outcomes by categorizing the same event into multiple error categories based on logical correspondences, unlike manual approaches where each error type corresponds to a single category. Elizabeth M. Borycki's work (33) addressed incident reporting related to adverse events induced by healthcare technologies, assessing the associated advantages and disadvantages. The study concluded that this experimental approach is promising. Chen H et al. (34) evaluated the effectiveness of various machine learning-based



automatic tools for adverse event classification, proposing an interface integrated with this system. The results highlighted the potential of such a system to achieve efficient and reliable report classification processes. Similarly, S. Fodeh et al. (35) proposed an automatic classification model for adverse events, combining feature detection system operations with a machine learning classifier. This model proved particularly useful for two adverse event categories: patient identification errors and weight-related issues. In contrast, Allan Fong et al. (36) advocated for the use of natural language processing (NLP) in identifying four categories of errors: Pharmacy Delivery Delay, Pharmacy Dispensing Error, Prescriber Error, and Pyxis Discrepancy. The study demonstrated that the tool's accuracy can help reduce the workload of hospital safety committees. Katsuhide Fujita et al. (37) applied NLP in incident reporting to analyze incident report texts, reinterpreting structured incident information and improving incident-related cause management. The article highlighted the tool's effectiveness, particularly for issues related to patient falls and medication management. Gerdes and Hardahl (38) tested an NLP system for reviewing clinical records to identify adverse events. The encouraging results suggest considering the systematic introduction of such automatic monitoring systems. Gupta et al. (39) proposed an automatic clinical incident classification system testing four different algorithms. Among these, the multinomial naive Bayes algorithm demonstrated particular efficiency, requiring a well-structured training phase. In another study, Gupta J et al. (40) introduced an incident reporting system based on the C4.5 decision tree algorithm and random forest, using a taxonomy from a generic system and one proposed by the WHO. The study demonstrated the superiority of the random forest algorithm and introduced a modification to the WHO taxonomy by adding another adverse event class. Hendrickx et al. (41) applied text mining techniques to highlight patient safety issues, indicating that these systems can be useful for prioritizing safety concerns and automatically classifying event severity. Liu et al. (42) proposed a text mining system for retrospective analysis of patient fall reports, reporting highly encouraging results regarding its application. Ménard et al. (43) proposed an under-reporting detection system for adverse events using a machine learning approach. Positive results from clinical trials of this approach led to the extension of this adverse event detection system to all future Roche/Genentech studies. Okamoto et al. (44) employed a machine learning system to detect unreported errors in medical records, identifying 121 incidents, with 34 subsequently selected as serious errors. In their work, Ong et al. (45) explored using Naïve Bayes and SVM text classifiers to detect extreme-risk events in clinical reports from Australian hospitals. The classifiers were evaluated on their accuracy, precision, recall, F-measure, and AUC, showing feasibility for automatic detection of high-risk incidents. Implementing a fall risk prediction tool resulted in a reduction in patient falls and an increase in risk-targeted nursing interventions in intervention units, although there was no significant difference in fall injury rates compared to control units. Saab et al. (46) proposed a machine learning model for predicting adverse events responsible for hospital readmission, aiming to reduce associated costs. The achieved accuracy levels were consistent with previous studies, highlighting the real-time feedback advantage of the tested

system. Sun et al. (47) proposed an incident reporting system combining a conversational interface with speech recognition software, concluding that socio-technical issues currently preclude its implementation. Wang et al. (48) evaluated the feasibility of using the Unified Medical Language System (UMLS) for automatically identifying patient safety incident reports by type and severity, showing its superiority over bag-of-words classifiers. In another study by Wang et al. (49), neural networks were used to assess the severity and gravity of adverse event reports. In a third study by Wang et al. (50), a multi-label incident classification system was structured for multiple incident types in individual reports. While not broadly applicable, this method proved useful in multi-label classification using a support vector machine algorithm. In a systematic review by Young et al. (51), NLP was investigated for free-text recognition in incident reporting. The review concluded that NLP can yield significant information from unstructured data in the specific domain of incident and adverse event classification, potentially enhancing adverse event learning in healthcare. Zhou et al. (52) proposed and tested an automated system for analyzing medication dispensing error reports based on machine learning algorithms. The study developed three different classifiers based on two algorithms (support vector machine and random forest), capable of identifying event causes and reorganizing them based on similarities.

### 3.3.2 Medication-related error

In a study by Corny et al. (53), a hybrid clinical decision support system was tested to reduce errors in the medication prescribing phase. Implementing this system demonstrated higher accuracy compared to existing techniques, intercepting 74% of all prescription orders requiring pharmacist intervention, with a precision of 74%. King et al. (54) used machine learning models to predict medication ordering errors and identify contributing factors. Decision trees using gradient boost achieved the highest AUROC (0.7968) and AUPRC (0.0647) among all models, showing promise for error surveillance, patient safety improvement, and targeted clinical review. Wong et al. (55) proposed a wound dressing rights detection system using NLP and deep neural networks. This system automated the identification of dressing incidents, highlighting the potential of deep learning for exploring textual reports on dressing incidents. Zheng et al. (56) focused on medication dispensing errors, reporting the development of an AI system through collaboration with pharmacists. They improved various features such as the interpretability of AI systems by adding gradual check marks, probability scores, and details on medications confused by the AI model. They also emphasized the need to build a simple and accessible system.

### 3.3.3 Patient fall risk

Stein et al. (57) evaluated the impact of a fall risk prediction system, assessing its outcomes in terms of patient outcomes and nurse feedback. The results highlighted a slight immediate reduction in the number of falls without consistent long-term effects, but the tool demonstrated intrinsic utility. Cho et al. (58) evaluated the usability of a predictive algorithm for detecting

TABLE 2 Main objective and type of approach to risk of reviewed publications.

References	Year	Risk approach	Main objective
(67)	2023	Proactive	The study reviews and evaluates research on machine learning prediction models to identify pressure injury risks in adult hospitalized patients.
(30)	2021	Reactive	The study proposes a method to compute adverse events underreporting probability, enhancing patient safety and reducing manual QA in clinical trials.
(31)	2021	Proactive and reactive	This review evaluates AI's potential to enhance patient safety in domains such as infections, adverse drug events, thromboembolism, surgical complications, pressure ulcers, falls, decompensation, and diagnostic errors.
(32)	2016	Reactive	The aim is to develop a reliable electronic approach for processing text in medical event reports to enhance patient safety.
(68)	2007	Proactive	The aim is to develop a reproducible approach integrating human qualitative coding patterns with machine learning.
(33)	2022	Proactive	The aim is to create a reproducible method for integrating human qualitative coding patterns with machine learning.
(34)	2024	Reactive	The study aims to investigate the effectiveness of machine learning classifiers trained with contextual text representations in automatically classifying patient safety event (PSE) reports.
(57)	2021	Proactive	The purpose of the study is to determine the impact of an electronic analytic tool for predicting fall risk on patient outcomes and nurses responses.
(58)	2023	Proactive	The aim is to assess whether a fall-prevention clinical decision support approach using electronic analytics that stimulates risk-targeted interventions is associated with reduced rates of falls and injurious falls.
(79)	2020	Proactive and reactive	The objective of this review is to identify and analyze quantitative studies utilizing or integrating artificial intelligence to address and report clinical-level patient safety outcomes.
(53)	2020	Proactive	The main objective is to improve patient safety and clinical outcomes by reducing the risk of prescribing errors, we tested the accuracy of a hybrid clinical decision support system in prioritizing prescription checks.
(69)	2022	Proactive	To analyze pressure injury risk factors, to identify strong predictors and to use different machine learning algorithms to classify patients with pressure injury and patients without pressure injury.
(35)	2015	Reactive	The study proposes a method to automatically classify/label event reports via semi-supervised learning which utilizes labeled as well as unlabeled event reports to complete the classification task. It focuses on classifying two types of event reports: patient mismatches and weight errors.
(36)	2017	Reactive	The aim of the paper is to develop a more efficient and streamlined method for categorizing patient safety event reports based on modeling the free text of event reports to reduce the review time of the committee.
(37)	2012	Reactive	The aim is to accumulate and reinterpret findings using structured incident information, to clarify improvements that should be made to solve the root cause of the accident, and to ensure safe medical treatment through such improvements
(38)	2013	Reactive	The aim of the study is the development of a method based on natural language processing to quickly search electronic health records for common triggers and adverse events.
(39)	2015	Reactive	The study compares the performance of different machine learning classifiers on a dataset of documents labeled by clinicians and experts.
(40)	2019	Reactive	In this study C4.5 decision tree, a single classifier, and Random Forest (RF), an ensemble classifier, are investigated to train and validate three multiclass Clinical Safety Incident taxonomies.
(41)	2021	Proactive	The aim of this study was to explore whether employing text mining techniques on patient complaint databases can help identify potential problems with patient safety at health care providers and automatically predict the severity of patient complaints.
(59)	2022	Proactive	In the study a machine learning technique is used to analyze events involving falling and establish a risk prediction model
(78)	2023	Proactive	In the study an Artificial Intelligence Clinical Assistant Decision Support System was used for venous thromboembolism prophylaxis of inpatients.
(54)	2021	Proactive	The paper proposes the use of machine learning approaches for characterizing the risk factors associated with medication ordering errors. Toward this end, we evaluated the performance of multiple machine learning methods on a large dataset of self-intercepted medication ordering errors.
(60)	2022	Proactive	The aims of this study were to create a model that detects the population at risk of falls taking into account a fall prevention variable and to know the effect on the model's performance when not considering it.

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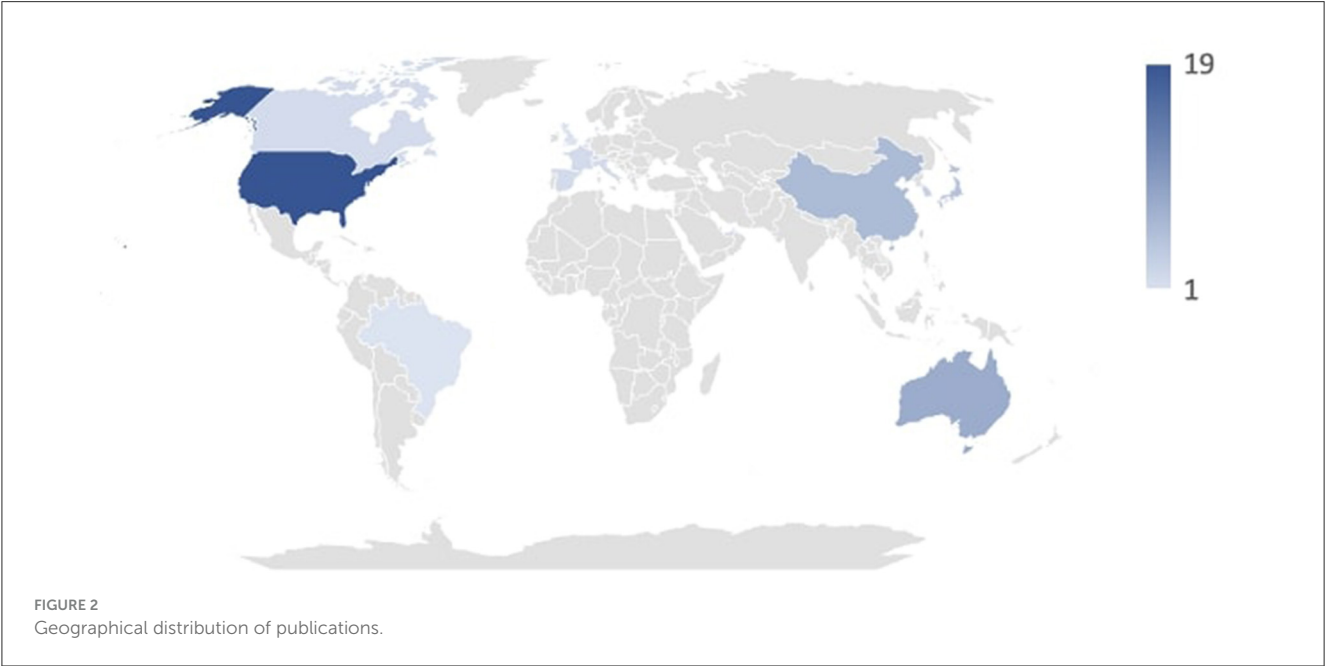
TABLE 2 (Continued)

References	Year	Risk approach	Main objective
(70)	2020	Proactive	The aim of the study is to build a model to detect pressure injury risk in intensive care unit patients and to put the model into production in a real environment.
(61)	2021	Proactive	The purpose of this study was to identify critical factors related to patient falls through the application of data mining to available data through a hospital information system.
(76)	2021	Proactive	This study evaluated whether natural language processing of psychotherapy note text provides additional accuracy over and above currently used suicide prediction models.
(62)	2021	Reactive	The presented Incident report classification framework aimed to improve the identification of the fall severity level mainly by incorporating structured features and leveraging resampling methods.
(42)	2019	Reactive	This work uses text mining to analyze fall incident reports, automatically grouping them based on semantic content for retrospective study.
(43)	2019	Reactive	The project developed a predictive model for Roche/Genentech to oversee adverse event reporting across program, study, site, and patient levels, integrating advanced analytics with traditional quality assurance approaches.
(75)	2013	Proactive	This paper aims to provide to the technology decision makers in healthcare (Health Management, Clinical Engineering and Prevention and Protection Service) a decision support system for analyzing the safety level associated to the use of technology for both patients and personnel.
(74)	2018	Reactive	The paper presents a knowledge discovery framework, the Safer Dx Trigger Tools Framework, that enables health systems to develop and implement e-trigger tools to identify and measure diagnostic errors using comprehensive electronic health record data.
(44)	2020	Reactive	The research aimed to establish a method to extract incident candidates from clinical notes in order to detect non-reported severe incidents. In addition, we implemented a reporting system that presents incident candidates extracted by using the pro- posed method.
(45)	2012	Reactive	The paper explores the feasibility of using statistical text classification to automatically detect extreme-risk events in clinical incident reports.
(46)	2020	Reactive	The main objective of the study is the construction of a model that could determine timely, on a near real time, if the patient readmission within 30 days was associated with a hospital acquired adverse event that occurred in the previous admission (response variable).
(63)	2019	Proactive	the paper developed a model for predicting falls using interpretable machine learning and integrating the model into the electronic medical record system to perform nursing interventions for each risk factor.
(77)	2021	Proactive	This research assesses the model by building a machine learning-based algorithm and altering network settings, then confirms the suggested technique using actual disinfectant supply center data.
(64)	2023	Proactive	The objective is to compare the performance of machine-learning models with the Medication Fall Risk Score in predicting fall risk related to prescription medications.
(73)	2023	Reactive	This paper assesses how staff experience impacts reported error rates in patient and staff safety using machine learning to identify key dimensions and variables influencing safety outcomes.
(71)	2021	Proactive	We used machine learning to develop an advanced tool for early assessment of pressure injury risk, leveraging extensive clinical data routinely recorded in electronic health records.
(47)	2018	Reactive	The aims of this study are two-fold. Firstly, to assess the technical feasibility of an application for reporting incidents that combines a conversational interface with speech recognition software. Secondly, to undertake a pilot study of its usability for clinical contexts.
(72)	2023	Proactive	This paper comprehensively reviews artificial intelligence and Decision Support System applications for hospital-acquired pressure injuries prediction using Electronic Health Records, including a systematic literature review and bibliometric analysis.
(65)	2019	Reactive	The purpose of this study is to build a practical system useful to predict the severity level of in-hospital falls.
(66)	2019	Proactive	The objective of this study is to develop a general predictive model for severity of falls among patient populations, using an advanced machine learning method multi-view ensemble leaning to efficiently exploit the multidimensional patient data.
(48)	2020	Reactive	The study evaluates the utility of semantic feature representation for automated identification incident reports by type and severity.
(49)	2019	Reactive	The aim is to develop a single classifier by combining word embedding with a Convolutional Neural Networks and to evaluate its feasibility to identify multiple types of incident reports and severity levels.
(50)	2017	Reactive	The paper evaluates the feasibility of using multilabel classification to automate the identification of two labels or two incident types per report.

(Continued)

TABLE 2 (Continued)

References	Year	Risk approach	Main objective
(55)	2020	Proactive	The aim of this study was to develop a medication-rights detection system to classify medication incidents using the real-world incident reports collected by the Hong Kong Hospital Authority.
(51)	2019	Reactive	The aim is to perform a systematic literature review and narrative synthesis to describe and evaluate natural language processing methods for classification of incident reports and adverse events in healthcare.
(56)	2023	Proactive	This study aimed to gather pharmacists feedback in a focus group setting to help inform the initial design of the user interface and iterative designs of the AI prototype.
(52)	2018	Proactive	In the paper a pipeline is proposed to help clinicians deal with the accumulated reports, extract valuable information and generate feedback from the reports



individual fall risk factors. Although a reduction in fall rates was observed, particularly in those over 65 years old, the intervention was not associated with a significant reduction in this rate. Huang et al. (59) employed a machine learning approach to study a 14-month fall event database aimed at developing a predictive fall risk system. This approach demonstrated particular accuracy and is used daily in one of Taiwan’s medical centers. Ladios-Martin et al. (60) developed a machine learning tool for fall risk prediction through the evaluation of a series of variables in a retrospective cohort. The Two-Class Bayes Point Machine algorithm was chosen, showing a reduction in fall events compared to the control group. Lee et al. (61) used a different approach to falls, employing data mining on hospital information system data. An artificial neural network was used to develop a predictive model that demonstrated high predictivity with a higher ROC compared to a logistic regression model. Liu et al. (62) proposed a system aimed at improving and automating severity classification models of incidents. The tool proved useful in identifying and classifying fall events, with the top two algorithms being random forest and

random oversampling. Shim et al. (63) developed and validated a machine learning model for fall prediction that is integrable into an electronic medical record system. This system, whose effectiveness was confirmed during the study, was subsequently officially integrated into the clinical record system. Silva et al. (64) proposed a machine learning model based on the Naive Bayes algorithm for developing a predictive tool for patient fall risk related to prescribed drug therapy. The Naive Bayes algorithm demonstrated superior values compared to other algorithms, particularly with an AUC of 0.678, sensitivity of 0.546, and specificity of 0.744. Wang et al. (65) proposed a tool to predict the severity of damage following a patient fall. Several machine learning algorithms were used, with the random forest algorithm proving the best with an accuracy of 0.844 and precision of 0.839. Therefore, an online severity prediction system was built using the RF algorithm and Flask package. By leveraging this predictive system, healthcare facilities can enhance patient safety and better allocate limited resources. Wang et al. (66) proposed a model to evaluate the predictability of fall events among hospitalized patients through a retrospective cohort study. A

predictive classifier developed using multi-view ensemble learning with missing values demonstrated superior predictive power compared to random forest and support vector machine, two other comparison algorithms.

### 3.3.4 Pressure injury

Barghouthi et al. (67) conducted a systematic review of prediction models for the development of pressure ulcers. The study highlighted that the most commonly employed algorithm is logistic regression. However, it also noted that none of the reviewed studies successfully used the pressure ulcer prediction model in real-world settings. Borlawsky and Hripcsak (68) proposed a similar model based on the C4.5 decision tree induction algorithm. Results showed limited application of this naive classification algorithm to automate the assessment of pressure ulcer risk. Do et al. (69) assessed the impact of an electronic predictive tool on fall risk using EHR data compared to a standard assessment tool. Conducted over 2 years in 12 nursing units, the primary outcome measured was the rate of patient falls, with secondary outcomes including injury rates and nursing interventions. The most accurate model achieved a 99.7% area under the receiver operating characteristic curve, with ten-fold cross-validation ensuring generalizability. Random forest and decision tree models had the highest prediction accuracy rates at 98%, consistent in the validation cohort. Ladios-Martin et al. (70) proposed another predictive model for the risk of developing pressure ulcers using a logistic regression algorithm. The model demonstrated a sensitivity of 0.90, specificity of 0.74, and an area under the curve of 0.89. The model performed well 1 year later in a real-world setting. Song et al. (71) employed a random forest-type predictive algorithm applied to a case study of hospital-acquired and non-hospital-acquired pressure ulcers, showing AUCs of 0.92 and 0.94 in two test sets. The study concluded that the tool could also be employed in real-world settings. Toffaha et al. (72) reviewed the literature on the prediction of pressure ulcer development, highlighting the existence of numerous predictive models, none of which have been applied in real healthcare settings but were rather trained on previous cases.

### 3.3.5 Other areas of clinical risk management

Simsekler et al. (73) employed three different machine learning algorithms to identify potential associations between organizational factors and errors affecting patient and staff safety. The results suggested that “health and wellbeing” is the main theme influencing patient and staff safety errors, with “workplace stress” being the most important factor associated with adverse outcomes for both patients and staff. Murphy et al. (74) proposed a system known as Safer Dx Trigger Tools, capable of identifying real-time and retrospective errors in the care pathway through analysis of electronic clinical data. The study concluded with the potential future application of this type of tool in daily hospital practice. Miniati et al. (75) provided a decision support system for analyzing the safety level associated with the use of

technologies for both patients and staff. The experimental tool proved useful in predicting outcomes in specific scenarios, with the authors concluding that this could be extended to other areas. Levis et al. (76) analyzed the suicide risk factor through retrospective analysis of psychiatric notes using a predictive model based on NLP. Specifically, an 8% increase in predictability was observed in the 12-month study cohort compared to more advanced available methods. Hui Jun Si et al. (77) proposed a risk management model related to the disinfection process of hospital environments using AI systems. Using a k-nearest neighbor algorithm, the results highlighted that levels of job satisfaction and work standardization achieved by nursing staff managed by an AI algorithm were significantly higher than those achieved by nurses working in traditionally managed disinfection centers. Huang et al. (78) proposed a system known as Artificial Intelligence Clinical Assistant Decision Support System (AI-CDSS) for preventing thromboembolic events; however, the tool was found to be ineffective. Choundhury et al. (79) conducted a literature review on the role of AI in ensuring patient safety, focusing on subcategories such as clinical alarms, clinical reports, and medication safety issues. Several software analyzed in this study have been designed and developed with features that can be considered medical devices, however, according to the literature reviewed, none of them have reached an official approval stage according to the EU MDR 2017/745 regulation or the US FDA. According to EU MDR 2017/745, among other aspects, software can be considered a medical device if it is intended to provide information for diagnostic and therapeutic purposes, as well as to help prevent, monitor, diagnose or even treat disease or injury (80). Based on this, the model developed by Corny et al. (53), which identifies prescriptions with a high risk of error, could fall into this category, as could the one proposed by Ladios-Martin et al. (6) for fall prevention. User acceptance and specific training are central aspects for the successful implementation of artificial intelligence (AI) systems in clinical settings. Barriers such as resistance to change, technological complexity, and lack of specific expertise can be overcome with targeted strategies such as user-centered design and dedicated training programs. Many studies included in the review highlight the importance of involving end users (physicians, nurses, pharmacists) early in development to ensure that systems meet their operational needs. Targeted training, often supported by pilot testing and simulations, has proven crucial in familiarizing users with new technologies and improving their confidence in daily use. For example, Sun et al. designed a speech recognition-based reporting system, the use of which was tested through a pilot project. The feedback highlighted the need for more detailed instructions to overcome the socio-technical difficulties encountered (47). Silva et al. developed a predictive model for fall risk and accompanied its implementation with specific training sessions. Users evaluated the approach positively, emphasizing the usefulness of ongoing support (64). Similarly, Huang et al. highlighted how practical training sessions improved the adoption of a predictive system for falls risk, facilitating the integration of the software into clinical practice and gathering suggestions for further technical improvements (59). Zheng et al. developed a system to prevent medication dispensing errors using focus groups with pharmacists. This approach allowed them to



iterate on the interface and instructions for use, significantly improving end-user satisfaction (56). According to the review, most studies did not highlight significant issues with AI, such as the lack of standards and evaluation metrics. Further research and involvement of FDA and NIST are needed to create standards that ensure patient safety.

## 4 Discussion

The reviewed studies primarily focus on incident reporting in healthcare, with two prominent approaches: automatic incident classification systems and event detection through healthcare documentation analysis. Machine learning algorithms have proven effective in automating incident classification, enhancing accuracy through past case training. Natural language processing and text mining techniques have enabled automated adverse event detection and anomaly identification in clinical data, improving care quality and reducing manual audits. Continuous implementation and system refinement are crucial for maximizing these benefits and addressing socio-technical challenges in healthcare settings. In managing medication errors, AI and machine learning have shown promise in decision support for prescription accuracy and error prevention during medication ordering. Hybrid clinical decision support systems and gradient boosting decision trees demonstrate significant accuracy in intercepting prescription errors. Deep learning techniques improve medication incident identification, emphasizing collaboration with pharmacists for system interpretability and usability in clinical practice. Regarding falls management, AI applications focus on predictive models for fall risk and severity classification systems. While predictive algorithms enhance risk assessment, their impact on reducing falls varies across age groups and implementation settings within electronic health records. Ongoing refinement is necessary to optimize predictive accuracy and practical integration into clinical workflows. Studies on predictive models for pressure ulcer development reveal varied efficacy, with machine learning algorithms like random forest showing promising predictive capability. However, the application of these models in real healthcare environments requires further validation and standardization to ensure practical clinical utility. AI and machine learning also play pivotal roles in enhancing patient and healthcare staff safety. They identify organizational factors influencing safety outcomes, support real-time error detection through tools like Safer Dx Trigger Tools, and improve predictive accuracy for technology-related risks and suicide risk. Despite successes, challenges remain, including the need for standardized evaluation metrics and regulatory oversight to ensure the efficacy and safety of AI applications in patient care. A crucial issue remains the proper and safe implementation of AI in clinical risk management practices. First, it is crucial to assess the specific needs of the clinical setting by going out and identifying all the areas where AI can provide the greatest positive impact, such as adverse event detection, falls prevention, or medication error management. This type of analysis should, in any case, involve end users so that the system is designed and designed based on their operational needs. This should be followed by a controlled pilot phase to test the technology in a protected environment to highlight possible problems related to its use; at this juncture, safety measures such as

automated monitoring and audit systems should be implemented to reduce bias and errors (81). At a second stage, user education with training programs to understand the technical operation of the system but also its limitations should be crucial. Once the system is validated, its large-scale implementation should be accompanied by continuous monitoring with periodic audits and user reporting systems. Finally, the AI system should be designed to work in perfect synergy with existing tools such as hospital information systems and electronic health records. Such a holistic approach could not only improve the safety and quality of care but could also optimize the allocation of healthcare resources.

## 5 Conclusions

The reviewed studies demonstrate that artificial intelligence (AI) and machine learning (ML) systems are transforming healthcare safety across various domains, including incident management, medication prescription, and fall prevention. Predictive algorithms and ML models have significantly improved the identification and handling of adverse events, reducing reliance on manual audits and enhancing reporting accuracy. Despite these advancements, the practical application of AI in real healthcare settings remains limited and requires ongoing refinement. Future efforts aim to enhance these systems by integrating feedback from healthcare professionals and optimizing their integration with electronic health records. Establishing uniform standards and evaluation metrics is critical to ensuring the effectiveness and safety of AI-driven solutions. Collaboration with regulatory bodies is essential to develop guidelines that support the safe and efficient use of AI technologies in everyday clinical practice. These advancements are expected to not only enhance care quality but also facilitate more effective management of healthcare resources.

## Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

## Author contributions

FD: Conceptualization, Formal analysis, Writing – original draft, Investigation, Visualization. GD: Conceptualization, Formal analysis, Methodology, Project administration, Writing – original draft, Writing – review & editing. DF: Methodology, Project administration, Software, Writing – original draft. AD: Software, Writing – original draft. LT: Software, Writing – original draft. VT: Investigation, Supervision, Writing – review & editing. MC: Investigation, Supervision, Writing – review & editing. RS: Conceptualization, Formal analysis, Investigation, Visualization, Writing – original draft.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

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# Lost and found: trends in litigation and compensation related to retained surgical foreign bodies

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**Introduction:** Retained surgical foreign bodies are supplies and devices unintentionally left at the surgical site. They are generally considered never events, albeit even full compliance with procedures can only minimize the risk of their occurrence. As never events, affected patients often allege gross negligence, and hospitals are often forced to compensate for the damages. Despite the fact that the physical consequences of the retention are usually mild and temporary, and thus the compensation paid may be hypothesized to be correspondently low, clear data on the medico-legal outcomes of these claims—both extrajudicial and judicial—and the average compensation have not yet been described.

**Materials and methods:** This paper presents a retrospective study on the related claims received between 1 January 2010 and 30 May 2024 by a large university hospital in Florence (Italy). The study aimed to deduce their incidence and mean costs, as well as the risk of medical malpractice claims leading to criminal complaints.

**Results:** We identified 27 eligible cases, with a mean compensation of €20,695.49. During the same period, the claims unrelated to retained foreign bodies, used as controls, had a mean compensation of €67,542.26. When considering only non-fatal events, criminal lawsuits were present in 12% of the cases compared to 6% in the control group, which fell within the same compensation range. The majority of the cases (63%) were directly managed by the hospital, although this was a lower percentage compared to the control cases (76%).

**Discussion:** In conclusion, even if the economic dimension of claims related to retained surgical foreign bodies is relatively contained, they are associated with a 2-fold risk of criminal lawsuits for doctors. In addition, patients are less confident about out-of-court settlements provided directly by hospital committees compared to judicial court trials. This indicates that patients perceive a retained surgical foreign body (RSFB) as a never event, which requires less justification compared to other wrongful medical care incidents. This perception is likely driven more by a breach of trust in doctors and hospitals than by the severity of consequences, which are typically mild or limited to temporary impairment.

## KEYWORDS

retained surgical foreign bodies, sentinel event, legal medicine, medical malpractice, never event, gossypiboma



## 1 Introduction

Retained surgical foreign bodies (RSFBs) are supplies and devices that are unintentionally left in the surgical site. These can include items that are usually counted after a procedure (e.g., sponges, towels, and sharps) and fragments of instruments and devices (e.g., a broken tip of a needle or catheter and a piece of a surgical device) (1). They are usually considered “never events,” i.e., events that are considered generally preventable. However, their incidence is still relatively high (up to 1.0 per 700 procedures) (2). Moreover, the incidence of RSFBs is thought to be underreported due to often delayed clinical signs and because not all RSFBs actually qualify as sentinel events—e.g., unretrieved device fragments are usually not reported (3). To date, abdominal surgery and gynecology have emerged as the most affected medical specialties, and surgical packs/sponges (in particular, surgical and vaginal sponges) (4, 5), followed by drain tubes and vascular devices (6, 7), are the most frequently RSFBs (8, 9).

Some clinical determinants of RSFBs are known, such as complex, emergency, unplanned, or prolonged surgical procedures, high body mass index, and the use of large sets of surgical instruments (10). However, the risk of RSFBs mainly depends on organizational factors, such as absent or unobserved preventive procedures, no or incorrect surgical count, or cognitive and human factors such as team communication and situational awareness (11). Although instrument counting at the beginning, during, and end of the procedure is considered the best preventive measure, most RSFBs occur after procedures with a correct count (12). Other proposed corrective interventions include taking radiographs of the surgical field immediately before or after fascial closure in the case of incorrect counting, using barcodes/radio-frequency identification tags for soft materials, and using magnetic retrieval devices and sharp detectors for metallic items (13–15). Since RSFBs are considered never events, medical malpractice is often claimed as gross negligence. Nevertheless, the reported compensations related to these cases vary widely, ranging from 37,041–2,350,000 to 150,000–5,000,000 US dollars per case (1).

All the medico-legal issues associated with RSFBs and the expenditure on related compensation to patients are currently underreported and under-discussed. Therefore, this retrospective study aimed to analyze the incidence and characteristics of medico-legal claims related to RSFBs that occurred at Careggi University Hospital, a public tertiary hospital in Florence, Italy. The study sought to compare these specific compensation claims with controls—i.e., medical malpractice claims unrelated to RSFBs. The primary endpoint was to identify trends in the incidence and costs of these specific claims, while the secondary endpoint was to evaluate if RSFBs correlate with a higher risk of healthcare personnel facing criminal court proceedings.

## 2 Materials and methods

Following approval from the Ethics Committee (code: “n.24059\_oss, date 19/03/2023”), a retrospective analysis of medical malpractice claims related to RSFBs at Careggi University Hospital (Florence, Italy) was conducted for the period from 1 January 2010 to 30 May 2024 (the years of the claims).

The inclusion criteria were as follows:

- The retained foreign body was confirmed as an RSFB.

- An RSFB was alleged by a patient who filed a medical malpractice claim against the hospital for possible compensation.

The exclusion criteria were as follows:

- RSFB occurred, but the patient did not request compensation from the hospital.
- RSFB occurred and was reported according to incident reporting procedures, but the patient did not file a claim for compensation.

As for the controls, we considered the medical malpractice claims unrelated to RSFBs received by the hospital during the same period.

While analyzing the legal and clinical documentation available for each claim, different variables were considered, including age, sex, type of procedure, and type of foreign objects/medical devices. Moreover, the intervention of the risk management service of the hospital, the medico-legal evaluation, case assessment, and out-of-court settlements Legal Medicine analyzed. The examined hospital fully retains the medico-legal risk emerging from litigation with patients, without any insurance coverage or external assistance in handling complaints and claims. These are managed by an in-hospital Medical Malpractice Claims Management Committee (MCMC), composed of medical experts in legal medicine, loss adjusters, lawyers, and the hospital's risk manager (16, 17). The MCMC can operate in three different scenarios, corresponding to the three options available in Italy for a patient to claim compensation for damages caused by a hospital:

- C1: The patient files a claim alleging hospital liability and related damage. The claim triggers the MCMC intervention, a negotiation with the claimant that can typically end either with an out-of-court settlement or with a rejection.
- C2: The patient directly opts for mediation by turning to authorized mediation bodies. A mediator tries to facilitate the composition of the litigation.
- C3: The patient directly opts for civil court proceedings. If no mediation was previously undertaken as described in C2, National Law n. 24/2017 allows the patient to file a special civil action called preventive technical inquiry. According to this special civil court proceeding, the judge appoints one or more medical experts who initially act as conciliator(s). In the event of failed conciliation, the experts write a report as court-appointed experts, answering the judge's questions regarding medical and hospital liability and related damages.

All these variables were analyzed for both RSFB-related claims and control cases, i.e., claims unrelated to RSFBs.

To compare the mean compensation, we excluded fatal cases from both groups because, in Italy, compensation for wrongful death is highly variable, depending on multiple and heterogeneous factors, such as family members or heirs entitled to receive compensation for the death of the patient.

Regarding the secondary endpoint, a comparison was made of the incidence of criminal complaints in non-fatal cases for both the RSFB-related sample and the control sample (RSFB-unrelated cases). Both cases and controls were selected if they fell within the same economic range of compensation. Indeed, by limiting the analysis to relatively low (and comparable) compensations, we aimed to exclude the possibility

that the decision to file a criminal complaint was mainly driven by economic factors or by severely invalidating health consequences. Since fatal cases were excluded from both samples (RSFB-related and RSFB-unrelated), the study also excluded cases of possible culpable homicides, for which reporting to the public prosecutor is mandatory and criminal proceedings start without any action from the patient's relatives. The non-fatal bodily injuries considered here may integrate the crime of culpable personal lesions, which in Italy can only be prosecuted when the plaintiffs file a criminal lawsuit, thereby initiating the criminal proceeding. The rate of criminal lawsuits for personal lesions against healthcare personnel, as well as the preference to directly turn to civil court for claiming compensation for an RSFB, can be considered risk indicators of intense adversarial litigation between patients and healthcare personnel and/or hospitals.

### 3 Results

We identified 27 eligible cases, half of which were reported to risk management, while a single RSFB case was excluded because it was reported but not claimed. The paid compensation ranged from €0 to €102,481.41 (Figure 1). Only one of the 27 cases was fatal.

During the same period, we identified 1,160 eligible controls, of which 646 were non-fatal cases with paid compensations not exceeding €102,481.41—consistent with the compensation amounts for such cases.

In the RSFB group, age ranged from 31 to 77 years (mean age: 50.8 years; median age: 49.5 years), and the predominant sex was male (17 male vs. 10 female individuals). In the control group, age ranged between 0 and 96 years (mean age: 52 years; median age: 53 years), and the predominant sex was female (629 female vs. 531 male individuals).

Regarding the cases, approximately a fourth of them (seven cases) occurred during orthopedic procedures, followed by emergency

surgery (five cases), neurosurgery, in particular, spine surgery (four cases), gynecology-obstetrics (three cases), abdominal surgery (two cases), and oncological procedures (two cases). Urological, maxillofacial, cardiothoracic, and vascular surgeries share the same prevalence (one case each). Most of the claims (cases) were related to elective surgery (19 cases).

Approximately two-thirds (63.0%) of the retained foreign bodies were sponges, while in 22.0% of the cases, the object was a broken part of a surgical instrument (Table 1).

As mentioned, 27 cases corresponded to medical malpractice claims: 63% of the cases were in the form of C1 (claim directly addressed to the hospital), 21% were C2 (civil mediation), and 17% were C3 (civil procedure).

In the control group, 76% of the cases were directly addressed to the hospital (C1), 16% started as civil mediations (C2), and 8% started as civil procedures (C3).

Considering only non-fatal events, the mean compensation was €20,695.49 for the RSFB-related cases (Figure 2) and €67,542.26 for the control cases. Among the cases and controls, respectively, 8 and 29% of the total were never compensated.

Regarding the secondary endpoint, considering only non-fatal events, criminal complaints were present in 12% of cases. On the other hand, when limiting our analysis to non-fatal controls with compensations not exceeding €102,481.41, criminal complaints were present in 6% of the total.

### 4 Discussion

RSFB occurrences can pose a serious threat to patient health and safety and raise serious medicolegal concerns. Despite common policies, such as surgical instrument counting, RSFBs are considered “never events,” and thus, it is extremely easy for the claimant to

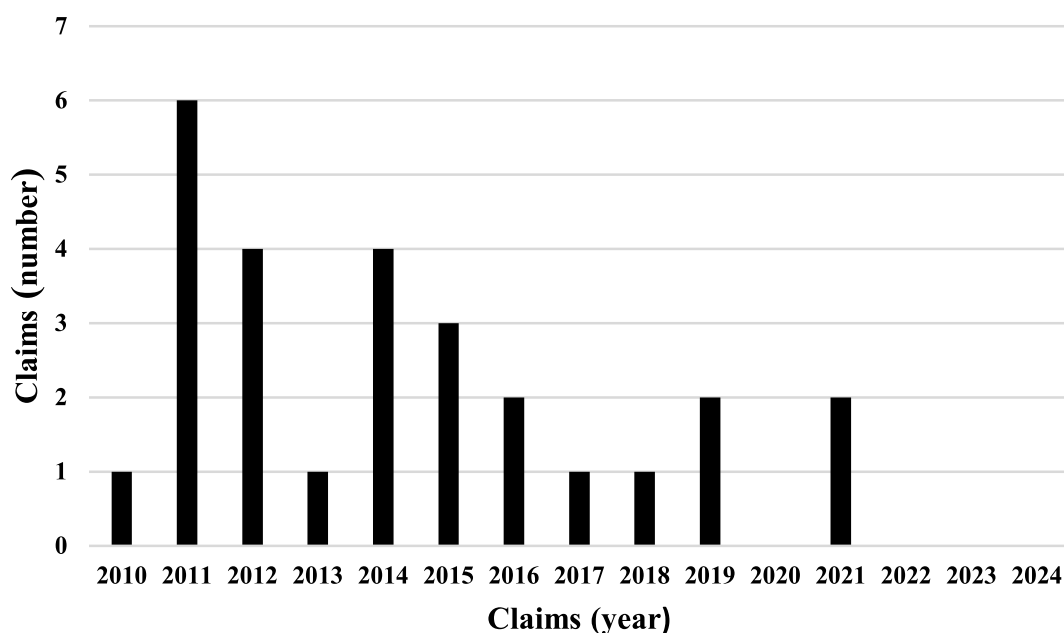


FIGURE 1  
Litigation distribution.

TABLE 1 Typology of the retained foreign bodies.

	Age	Sex	Year of the incident	Year of the claim	Retained foreign body
Case 1	67	M	2021	2021	Sponge
Case 2	39	M	2019	2021	Broken endovascular catheter
Case 3	51	F	2018	2019	Sponge
Case 4	68	F	2018	2019	Sponge
Case 5	70	M	2016	2018	Broken spinal catheter
Case 6	55	M	2016	2017	Surgical forceps
Case 7	59	F	2009	2016	Metal clip
Case 8	79	M	2014	2016	Sponge
Case 9	53	F	2006	2015	Sponge
Case 10	46	F	2014	2015	Whole needle
Case 11	61	F	2013	2014	Sponge
Case 12	56	M	2014	2014	Sponge
Case 13	68	M	2003	2014	Sponge
Case 14	60	F	2013	2014	Sponge
Case 15	89	F	2012	2013	Sponge
Case 16	63	M	2012	2012	Broken central catheter
Case 17	63	M	2011	2012	Broken surgical needle
Case 18	89	M	2011	2012	Broken drill bit
Case 19	57	F	2011	2012	Sponge
Case 20	59	M	2010	2011	Electrostimulator
Case 21	61	M	1983	2011	Sponge
Case 22	55	F	2002	2011	Broken cutter tip
Case 23	61	M	2011	2011	Sponge
Case 24	62	M	2009	2011	Sponge
Case 25	72	M	2011	2011	Sponge
Case 26	88	M	2000	2010	Sponge
Case 27	76	F	1981	2010	Sponge

obtain compensation based on the international legal principle “*res ipsa loquitur*” (18). This principle states that a rebuttable presumption of negligence is allowed if it is proven that the harm would not normally occur without the negligence of the party who has the legal duty to control the most likely cause of the harm (19). In Italy, cases of medical malpractice can be of both criminal and civil interest, even if criminal liability is regulated by a “safe harbor law” (20) that substantially limits it to cases of gross negligence (if the defendant fails to prove compliance with scientific guidelines/best practices). As a result, civil proceedings significantly outnumber criminal cases in the realm of medical malpractice (21).

In our study, we analyzed the claims that occurred at Careggi University Hospital, a large teaching hospital, which is one of the categories of health institutions (teaching hospitals and large hospitals) that have been associated with the highest incidence of RSFBs (22). We found that most cases occurred in middle-aged male patients. These findings are only partially consistent with those of Al-Qurayshi et al., who reported the largest incidence of RSFBs in female patients, with an average age of 50.9 years (23).

In almost 25% of cases, the RSFB is related to orthopedic surgical procedures, maybe because of the significant number of instruments

that are generally used in these surgeries, while relatively few cases involve gynecology and abdominal surgeries. In other studies, the most affected disciplines were abdominal surgery, followed by cardiovascular, gynecological, and orthopedic surgeries, with orthopedics prevailing only in the pediatric population (22, 23).

Consistent with previous literature (4), most RSFBs were sponges. However, unlike other reports, most of our cases occurred during elective surgery. The latter difference could be explained by the fact that we selected and included only medicolegal claims related to RSFBs rather than just incident reports. Some cases that occurred during procedures and surgeries performed under emergency conditions may be missing, as patients in these situations might be more inclined to excuse the incident, unlike in planned, routine procedures, where the occurrence of RSFBs is deemed *prima facie*, more deplorable.

The negative social perception of these events is also suggested by the fact that claims related to RSFBs—normalized for economical quantification as performed here—have a double risk of being associated with criminal lawsuits against physicians compared to control cases. Moreover, the RSFB cases were rarely found to correlate with serious health consequences, with only one case in which the

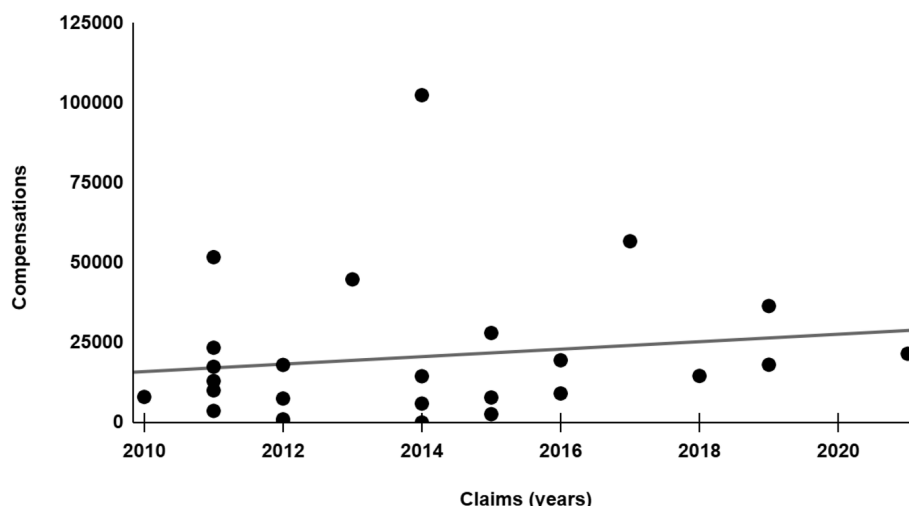


FIGURE 2  
Economic compensation.

incident resulted in the death of the patient. Similarly, Seabra et al. reported that in most of the cases, the only consequence of RSFBs was extended hospitalization, while severe injuries were often temporary, and the death of the patient occurred rarely (0.3%) (24). Therefore, the incidence of litigation due to RSFBs scarcely correlates with the severity of the consequent damage to the patient. As a result, even very minor consequences of RSFBs can give rise to litigation. Despite the low average compensations for the RSFB-related cases compared to the control sample (mean value of 22,327.12 vs. 67,542.26 euros), almost all patients who experienced an RSFB sought compensation. However, they preferred to turn to court settlements or, at least, to mediation provided by third parties in a higher percentage compared to the control sample. This tends to indicate that patients perceive an RSFB as a never event, which requires less justification compared to other wrongful medical care, generates a deeper breach of trust in hospitals and doctors, and renders patients less confident about out-of-court settlements provided directly by hospital committees compared to judicial court trials (17, 25). Furthermore, the incidence of criminal lawsuits was investigated, and it was found to be double in the RSFB cases (12%) compared to the control sample (6%). In Italy, criminal reporting of medical malpractice is mandatory only when improper care could have caused the death of the patient, and the doctor must be investigated for culpable homicide. In cases of culpable personal lesions, when patients experience only temporary or permanent injuries, the report is not mandated by law, and it is the patient's choice whether to file a criminal lawsuit against the doctor (26). Since we excluded the fatal cases, no mandatory criminal reports or penal proceedings for culpable homicides were included in the study, and the comparison between the RSFB and control samples focused only on the incidence of criminal proceedings voluntarily initiated by the patients. The significantly higher incidence of criminal lawsuits in RSFB cases indicates that the event is likely viewed by the patient as a deep breach of trust in doctors, even if the severity of the actual consequences was mild, as shown by the lower mean compensations compared to the control cases. As a consequence, the cases showed a lower tendency to directly request compensation from

the hospital. As previously mentioned, criminal proceedings for RSFBs are particularly complex for the defendant, since these “never events” are often considered evidence of gross negligence. Moreover, hospitals and practitioners risk suffering a significant loss in terms of reputation in RSFB cases, as similar events are heavily publicized and stigmatized (27). Finally, a critical finding was that the incidents were internally reported to the hospital's designated offices in less than 50% of the cases. This evidence highlights the importance of managing claims as a source of incident reporting but also unveils a reticence about admitting these types of errors, although early reporting and proper intervention are critical factors for patient safety (28). This reticence is likely due to psychological factors, as more than 80% of the involved physicians experience significant distress due to the litigation, which is often seen as indefensible, and the reputational consequences (29).

## 5 Conclusion

To the best of our knowledge, our paper is the first to analyze medical malpractice claims associated with criminal suits related to RSFBs. Our cases, compared to the controls, showed that the health consequences of these “never events” are usually mild, but in almost all the cases (27 out of 28), compensation was requested by the patient. RSFBs are associated with a 2-fold risk of criminal lawsuits and an increased tendency to turn to civil court for compensation instead of the out-of-court scheme offered by the hospital, indicating that these events cause a deeper breach of trust among patients (30). The discrepancy between relatively low health consequences and mean compensation and high litigiousness is likely due to the social stigmatization of this issue. It is recommended to address this through proper risk management strategies and extrajudicial negotiations to contain reputational damage and the psychological distress experienced by the involved professionals.

In the scientific literature, as mentioned, many preventive interventions have been reported and could be introduced to verify

their effectiveness. However, our data showed that a pivotal role must be played by risk managers, who must enhance the incident-reporting systems and promote, through internal audits, the disclosure of organizational/individual issues (including communication issues between physicians and patients) and the engagement of operating room personnel. Finally, we believe that investigating this phenomenon internally is of critical economic interest to the institution, particularly in terms of enhancing the reserve fund assessment.

## 6 Limitations

Our study has several limitations. As mentioned, the monocentric study design limited the volume of data, so future multicentric studies are recommended. Moreover, the unpaired sets of the categorical variables with unequal sample sizes prevented us from reliably performing parametric statistical tests to verify whether the variations were statistically significant. At the same time, the sets of continuous variables considered for the *t*-test had different sizes. In general, the main limitation is the small sample size, which stemmed from the fact that, to date, no Italian institution has reported this type of analysis in the scientific literature. Therefore, increasing sample sizes (for instance, by designing multicentric studies) is recommended.

## Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

## Ethics statement

The studies involving humans were approved by Comitato Etico di Area Vasta Centro (CEAVC). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

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SG: Conceptualization, Investigation, Writing – original draft, Methodology. MF: Conceptualization, Investigation, Writing – original draft. FS: Data curation, Writing – original draft. MG: Data curation, Writing – original draft. EF: Data curation, Writing – original draft. GF: Data curation, Writing – original draft. IB: Conceptualization, Writing – original draft, Investigation. FA: Conceptualization, Investigation, Writing – original draft. VP: Conceptualization, Writing – original draft, Funding acquisition, Methodology, Supervision.

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## Conflict of interest

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# Navigating the landscape of legal medicine: a 4-year analysis of forensic consultations in an Italian hospital

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**Introduction:** This study explores a comprehensive 4-year retrospective analysis of 511 forensic consultations conducted at "Policlinico" hospital in Bari, Italy. It highlights the expanding role of legal medicine within healthcare settings, an area that has traditionally been limited to expert testimony and forensic pathology. Over time, legal medicine in Italy has evolved to address a variety of clinical areas, including informed consent, disability assessment, personal injuries, and sexual violence. This research aims to examine these diverse applications and their impact on patient care.

**Methods:** Data were systematically categorized and analyzed using a multivariate multinomial regression model. The study focused on key variables, such as patient demographics and timing of shifts, to identify significant determinants that influence the types of forensic consultations conducted. The dataset consisted of 511 consultations, covering a range of clinical and legal issues.

**Results:** The analysis revealed that informed consent issues were the most prominent, with 58.7% of consultations addressing concerns related to patient autonomy and the capacity for consent, particularly in neuropsychiatric conditions. Personal injury consultations accounted for 24.3% of the total, and sexual assault cases made up 10%. These results underscore the intersection of medical practice and forensic evaluation, highlighting societal issues such as interpersonal violence and the importance of legal medicine in healthcare.

**Discussion:** The findings highlight significant gaps in the literature regarding the broader applications of legal medicine, especially in terms of integrating advanced methodologies like artificial intelligence. Such technologies could enhance patient profiling and predictive care, ultimately improving patient safety, risk management, and the protection of patient rights. The study advocates for structured forensic consultation services to be incorporated into clinical practice, emphasizing the role of legal medicine in improving patient-centered care and promoting justice. These insights are crucial for

healthcare professionals, administrators, and policymakers aiming to optimize healthcare systems.

#### KEYWORDS

legal medicine, forensic consultations, informed consent, personal injury, sexual violence, patient autonomy, clinical risk management, artificial intelligence

## 1 Introduction

Legal medicine and forensic science represent the primary interface between medicine and law within healthcare systems. Key components of legal medicine include public health, forensic science, criminology, disability assessment, privacy protection, and ethics. This medical field is interpreted and applied differently across countries worldwide. When the general public is asked, “What is legal medicine?” responses typically focus narrowly on expert witness roles in court settings (1) and forensic pathology. However, these elements form only a small part of a much broader field that encompasses numerous facets of medical practice, extending its reach into all branches of medicine. This broad applicability is driven by healthcare professionals’ heightened concerns over rising complaints and medico-legal malpractice claims (2).

In recent years, new, particularly pressing areas within legal medicine have emerged. These include defensive medicine—a practice aimed at preventing patient dissatisfaction and avoiding malpractice claims (3)—and clinical risk management, which seeks to enhance the quality and safety of healthcare services (4). In this global context, some countries adopt a holistic approach to forensic and legal medicine, integrating not only forensic pathology and court participation but also criminology, psychopathology, social medicine, and deontology. This comprehensive perspective has led to the establishment of forensic-and-legal-medicine units within hospitals, where these disciplines work collaboratively to meet the requirements of justice administration (5).

Despite the proliferation of forensic and legal medicine units and the myriad medico-legal issues in daily clinical practice, there remains a scarcity of evidence in the literature regarding the scope and nature of tasks undertaken. These gaps represent both a current issue and a future challenge, as these activities address highly sensitive issues, including personal injury, sexual violence, consent and refusal of proposed treatments, and additional clinical complexities. Moreover, structured retrospective data can enable the profiling of patient risk and, prospectively, facilitate a more refined and detailed understanding not only of specific risk profiles but also, with the aid of artificial intelligence, of potential treatment outcomes and associated complications. This article aims to present insights and outcomes from 4 years of forensic consultations within a clinical setting at a major Italian hospital.

## 2 Materials and methods

The study entailed systematically collecting and analyzing forensic consultations conducted over a 4-year period, from

1 January 2019 to 31 December 2022, at the Policlinico Hospital in Bari, which has over 1,500 beds and an Emergency Department. A total of 511 consecutive forensic consultations were gathered, with all data entered into a dedicated database. Consultations involve opinions provided by specialists in a specific medical field to colleagues in other departments regarding the management, treatment, and discharge of admitted patients (6). Following the consultation, the specialist completes a standardized form, routinely included in the patient’s medical record, which documents the consultation outcome. This form typically includes the patient’s details, date and time of consultation, requesting department, diagnostic query, and consultation outcome. These consultations were categorized as summarized in Table 1, and each consultation type was further classified based on various factors, including reported types of sexual assault, discharge protocols, informed consent and capacity for self-determination, personal injury, and other clinical matters.

This study design is retrospective observational. Data analysis was conducted using Stata MP17 software. Continuous variables were expressed as mean (SD/range), while categorical variables were expressed as proportions. The normality of continuous variables was assessed through skewness and kurtosis tests, although non-normally distributed variables could not be transformed to normality. The Dunn test, with Bonferroni correction for pairwise comparisons, was applied for comparing continuous variables across multiple groups, while the chi-square test was used for comparing categorical variables among multiple groups. Univariate multinomial regression was performed to assess determinants of consultation type, using consent-related consultations as dummy variables and including age, sex, and shift type as determinants. Relative Risk Ratios (RRR) were calculated with 95% confidence intervals (95% CI) provided. A  $p$ -value of  $< 0.05$  was considered statistically significant for all tests.

## 3 Results

The sample analyzed comprises 511 cases undergoing forensic consultation. Data analysis reveals distribution across five consultation categories: informed consent and capacity for self-determination (300 cases, 58.71%); personal injury (124 cases, 24.27%); reported sexual assault (51 cases, 9.98%); clinical discharge (26 cases, 4.89%); and other clinical issues (10 cases, 2.15%). Among the 511 consultations, 121 were requested by the Orthopedics and Traumatology department (23.68%), and 142 by the Emergency Department (27.79%). Consultations involved male patients in 213 cases (42.09%) and female patients in 298 cases (57.91%), with an average patient age of 57.67 years. This

TABLE 1 Data sample.

Variable	Consent	Clinical discharge	Personal injuries	Other clinical issues	Reported sexual assault	Total	p-value
Male; n (%)	125 (41.95)	7 (28.00)	71 (58.20)	6 (60.00)	4 (7.84)	213 (42.09)	<0.05
Age; mean (SD/range)	71.13(18.98/9–98)	65.68(19.16/15–94)	39.58 (22,07/0–93)	49.89(22.56/16–80)	21.64(14.95/2–68)	57.67(26.48/0–98)	<0.05
Shift; n (%)							<0.05
• M	• 158 (52.67)	• 9 (34.62)	• 51 (41.13)	• 6 (60.00)	• 7 (13.72)	• 231 (45.21)	
• A	• 125 (41.67)	• 15 (57.69)	• 45 (36.29)	• 4 (40.00)	• 22(43.14)	• 211 (41.29)	
• N	• 17 (5.66)	• 2 (7.69)	• 28 (22.58)	• 0 (0.00)	• 22(43.14)	• 69 (13.50)	
Requesting unit							<0.05
• Other	• 110 (36.67)	• 15 (57.69)	• 12 (9.68)	• 3 (30.00)	• 10 (19.61)	• 150 (29.35)	
• Plastic surgery	• 1 (0.33)	• 0 (0.00)	• 11 (8.87)	• 0 (0.00)	• 0 (0.00)	• 12 (2.35)	
• Internal medicine	• 38 (12.67)	• 5 (19.23)	• 3 (2.42)	• 1 (10.00)	• 0 (0.00)	• 47 (9.20)	
• Neurology	• 5 (1.67)	• 4 (15.39)	• 6 (4.84)	• 3 (30.00)	• 0 (0.00)	• 18 (3.52)	
• Orthopedics	• 119 (39.66)	• 0 (0.00)	• 2 (1.61)	• 0 (0.00)	• 0 (0.00)	• 121 (23.68)	
• ED	• 26 (8.67)	• 2 (7.69)	• 70 (56.45)	• 3 (30.00)	• 41 (80.39)	• 142 (27.79)	
• Anesthesiology	• 1 (0.33)	• 0 (0.00)	• 20 (16.13)	• 0 (0.00)	• 0 (0.00)	• 21 (4.11)	

average varied significantly across consultation categories: 71.13 years for informed consent and self-determination, 65.68 years for clinical discharge, 39.58 years for personal injury, 49.89 years for other clinical issues, and 21.64 years for reported sexual assault. Consultations occurred in 231 cases during the morning shift (45.21%), 211 in the afternoon (41.29%), and 69 at night (13.50%). Detailed sample characteristics by consultation type are provided in [Table 1](#).

### 3.1 Informed consent and capacity for self-determination

This was the most frequent consultation type over the 4-year period. Of these, 52.67% were conducted in the morning, and 39.66% were requested by the Orthopedics department. Studied characteristics included the presence of neuropsychiatric conditions, intervention type, consent capacity, the involvement of a support administrator or proxy, and the consultation’s outcome. Cognitive decline accounted for neuropsychiatric conditions in 59.70% of cases. In 32.98% of cases, the intervention involved femoral fracture reduction. Consent capacity was preserved in 24.05% of cases; however, the proposed treatment was carried out without patient consent in 75.44% of cases due to emergency conditions and the necessity of the treatment. Details on informed consent and self-determination issues are summarized in [Table 2](#).

### 3.2 Personal injuries

Consultations for personal injuries represented 24.27% of the sample. These occurred during the morning shift in 41.13% of cases, the afternoon in 36.29%, and at night in 22.58%. The Emergency Department requested 56.5% of these consultations.

A blunt object was involved in 41.57% of cases, with assault suspected in 74.23% of cases. Injuries were categorized as bruises (34.05%), abrasions (20.54%), and puncture/cut injuries (15.68%). In 90.48% of cases, the aggressor was male, with a family or romantic relationship with the victim in 59.09% and 31.81% of cases, respectively. In 22.58% of cases, injuries were inflicted by a group. [Table 3](#) presents detailed characteristics of personal injury consultations.

### 3.3 Reported sexual assault

Reported sexual assault accounted for 9.98% of consultations, with 68.63% reported as completed assaults. Over 80% of these consultations were requested by the Emergency Department, with a male aggressor involved in 92.16% of cases. A romantic relationship with the victim was present in 13.04% of cases, while the aggressor was an acquaintance in 39.13% of cases. No genital injuries were found in 76.48% of cases; the remaining 23.52% showed genital injuries (5.88% to labia majora, 3.92% perineal, 3.92% urethral, 3.92% hymenal). Other body regions presented no injuries in 48.15% of cases, while bruises appeared in 37.04%. Group assaults accounted for 29.17% of cases, while single aggressors accounted for 21.8%. [Table 4](#) details characteristics of consultations related to reported sexual assault.

### 3.4 Clinical discharge

Clinical discharge issues constituted 4.9% of consultations. Assessed variables included the reason for hospitalization, presence of prior neuropsychiatric diagnoses, any prior neurological/psychiatric consultations, discharge type, and presence of a support administrator. Among patients, 47.06% had psychiatric disorders, 41.18% had cognitive decline, and

TABLE 2 Informed consent data.

Data; n (%)	Missing data; n (%)	n	%
Neuropsychiatric pathologies			
• Cognitive decline	32 (10.67)	• 160	• 59.70
• Psychiatric disorders		• 33	• 12.30
• None		• 75	• 28.00
Type of intervention			
• Other procedure	18 (6.00)	• 156	• 55.32
• Reduction of a femoral fracture		• 93	• 32.98
• Diagnostic imaging examination		• 18	• 6.38
• Blood transfusion		• 15	• 5.32
Patient's capacity to express consent	9 (3.00)	70	24.05
Support administrator for healthcare purposes	1 (0.33)	11	3.68
Proxy to third parties	80 (26.67)	6	2.73
Decision			
• Treatment carried out without the patient's consent due to the emergency/urgent conditions	19 (6.33)	• 212	• 75.44
• Treatment with patient's consent		• 32	• 11.39
• patient's refusal respected—capable of self-determination		• 22	• 7.83
• Psychiatric evaluation		• 7	• 2.49
• Advance directives previously expressed		• 7	• 2.49
• Other procedure		• 1	• 0.36

11.76% had intellectual disabilities. Neurological and psychiatric consultations were requested in 64% of cases, with 61.54% of discharges being protected.

3.5 Other clinical issues

Consultations for other clinical issues totaled 10 cases, with assessments based on the reason for hospitalization, type of treatment, and outcome. In 80% of cases, the query related to clinical risk management, with 30% hospitalized for gynecological pathologies and another 30% for cognitive decline. Psychiatric therapy was administered in 37.5% of cases, and 33.33% resulted in corporate suicide prevention procedures.

3.6 Multivariate multinomial regression

Table 5 summarizes the findings from the multivariate multinomial regression model on the determinants of forensic

TABLE 3 Personal injuries data.

Data; n (%)	Missing data; n (%)	n	%
Mean			
• Blunt object	35 (28.23)	• 37	• 41.57
• Sharp weapon		• 24	• 26.97
• Firearm		• 14	• 15.73
• Improper weapon		• 6	• 6.74
• Traffic accident		• 4	• 4.49
• Heat-related injury		• 2	• 2.25
• Substance abuse		• 2	• 2.25
Suspected origin			
• Assault	27 (21.77)	• 72	• 74.23
• Accidental event		• 16	• 16.49
• Attempted suicide		• 9	• 9.28
Place where the injuries were made			
• Home	69 (55.65)	• 25	• 45.45
• Road		• 25	• 45.45
• Public place		• 5	• 9.10
Type of lesion			
• Bruises	9 (72.6)	• 63	• 34.05
• Abrasions		• 38	• 20.54
• Puncture and cut injuries		• 29	• 15.68
• Laceration-contusion wounds		• 17	• 9.19
• Bone fractures		• 15	• 8.11
• Firearm		• 13	• 7.03
• Defense-related injuries		• 5	• 2.70
• Thermal agent		• 2	• 1.08
• Absent		• 2	• 1.08
• Poisoning		• 1	• 0.54
Male aggressor	51 (70.83)	19	90.48
Relationship with aggressor			
Family member	50 (69.44)	• 13	• 59.09
• Romantic relationship		• 7	• 31.81
• Acquaintainance		• 1	• 4.55
• No relationship		• 1	• 4.55
Number of aggressors			
• Single	41 (56.94)	• 24	• 77.42
• Group		• 7	• 22.58

consultations. Statistically significant results ( $p < 0.05$ ) emerged in the following regressions:

- Between “injuries” and the dummy variable “consent” for age: with increasing age, it was significantly less likely for a forensic consultation to be requested for personal injuries or consent issues, suggesting that older patients are more likely



TABLE 4 Reported sexual assault data.

Data; n (%)	Missing data; n (%)	n	%
Attempted/consummated			
• Consummated	0 (0.00)	• 35	• 68.63
• Uncertain		• 12	• 23.53
• Attempted		• 4	• 7.84
Male aggressor	16 (31.37)	35	100
Relationship with aggressor			
• Acquaintance	28 (54.90)	• 9	• 39.13
• No relationship		• 6	• 26.09
• Family member		• 5	• 21.74
• Romantic relationship		• 3	• 13.04
Genital injuries			
• Absent	2 (3.92)	• 39	• 76.48
• Labia majora		• 3	• 5.88
• Perineal		• 2	• 3.92
• Urethral		• 2	• 3.92
• Hymenal		• 2	• 3.92
• Other		• 3	• 5.88
Other body region			
• Absent	1 (1.96)	• 26	• 48.15
• Bruises		• 20	• 37.04
• Lacerations		• 6	• 11.11
• Suction lesions		• 1	• 1.85
• Burns		• 1	• 1.85
Multiple aggressor	25 (49.02)	7	29.17
Use of drugs on the victim	11 (21.57)	10	25

to require interventions for which they cannot legally consent, thus necessitating forensic consultation.

- Between “clinical issues” and “consent” for age: as patient age increases, requests for forensic consultations concerning clinical issues are less likely compared to those for informed consent issues.
- Between “sexual violence” and “consent” across all determinants: younger patients are more likely to require consultations for alleged sexual violence than consent-related issues. Additionally, male patients are more likely to be involved in consent-related consultations, while consultations for alleged sexual violence are more likely during the night shift.

#### 4 Discussion

The study highlights a significant gap in the literature concerning the scope and nature of tasks performed within Forensic and Legal Medicine Units. Given the sensitive nature of the cases managed—such as personal injuries, sexual violence,

TABLE 5 Analysis of determinants of forensic consultation in a multivariate multinomial regression model.

	RRR	95% CI	p-value
Clinical discharge vs. consent			
Age	0.98	0.96–1.01	0.119
Sex (male vs. female)	0.44	0.17–1.13	0.089
Shift			
• Afternoon vs. morning	1.87	0.78–4.51	0.161
• Night vs. morning	1.73	0.32–9.20	0.521
Personal injuries vs. consent			
Age	0.94	0.93–0.95	<0.05
Sex (male vs. female)	1.05	0.62–1.80	0.851
Shift			
• Afternoon vs. morning	1.10	0.63–1.94	0.738
• Night vs. morning	1.94	0.85–4.40	0.114
Clinical issues vs. consent			
Age	0.96	0.93–0.98	0.003
Sex (male vs. female)	1.91	0.45–8.05	0.397
Shift			
• Afternoon vs. morning	0.60	0.14–2.46	0.468
• Night vs. morning	0.01	0.01–0.01	0.977
Reported sexual assault vs. consent			
Age	0.89	0.87–0.92	<0.05
Sex (male vs. female)	0.06	0.02–0.20	<0.05
Shift			
• Afternoon vs. morning	3.48	1.14–10.67	0.029
• Night vs. morning	8.67	2.38–31.54	0.001

and assessments of capacity for self-determination—the lack of supporting evidence poses a substantial challenge. This study addresses this gap by providing a comprehensive retrospective analysis of forensic consultations, exploring the intricate overlap between forensic and legal medicine and clinical practice. This domain intersects diverse fields including public health, criminology, and ethics, and involves collaboration with law enforcement (7).

Clinical challenges increasingly generate forensic considerations (8), leading to new healthcare initiatives focused on preventing harm to patients and mitigating systemic issues that can increase healthcare costs, such as defensive medicine (9). Hospitals regularly face clinically complex cases requiring a delicate balance between patient and healthcare provider rights (10). This has created a growing reliance on consultations from physicians specialized in legal medicine (11). However, data assessing the impact of medico-legal activities within hospital settings remains limited. Our study illuminates the range and complexity of forensic consultations conducted over 4 years in a major Italian hospital, highlighting contemporary healthcare challenges.

The prevalence of consultations concerning informed consent and capacity for self-determination underscores the crucial role of patient autonomy in clinical practice (12). Our findings show a considerable portion of patients with neuropsychiatric conditions, complicating the acquisition of valid consent. Notably,

many interventions were conducted without explicit consent due to urgent clinical needs, demonstrating the challenging balance between patient autonomy and timely care.

In this context, effective communication between healthcare providers and patients—or their legal representatives—is paramount. Clear, compassionate, and legally sound discussions about medical decisions, risks, and alternatives are fundamental in preserving patient rights while ensuring that necessary medical interventions are undertaken. Informed consent is not merely a procedural requirement but a cornerstone of ethical medical practice, reinforcing trust in the healthcare system and reducing medico-legal disputes (13).

Personal injury consultations formed another prominent category, reflecting the societal prevalence of violence-related incidents (14). The analysis characterizes various injury patterns, weapon types, and perpetrator demographics, with a notable portion of injuries resulting from assaults by family members or acquaintances, highlighting the complex dynamics of interpersonal violence in social and familial contexts.

Consultations for reported sexual assault present unique forensic challenges, requiring sensitive evaluation of physical and psychological trauma (15). The study reveals the diversity of circumstances in sexual violence cases, including victim-perpetrator relationships, genital injury presence, and cases involving multiple aggressors. The high incidence of cases involving known perpetrators underscores the importance of addressing interpersonal violence beyond traditional stranger assault paradigms. The regression analysis adds a valuable perspective, showing statistically significant associations between consultation types and determinants, with age, gender, and shift timing notably influencing the likelihood of consultations for personal injuries, clinical issues, and sexual violence compared to consent-related consultations. Age-related trends in consultations for personal injuries further illustrate the influence of age on the likelihood of seeking forensic advice.

These findings emphasize the indispensable role of legal medicine in navigating complex clinical scenarios and protecting patient rights and welfare (16). The establishment of structured forensic consultation services within healthcare settings supports the integration of legal and medical expertise, allowing comprehensive assessment and management of medico-legal issues. Furthermore, retrospective analysis of consultation data provides insights for risk profiling, treatment planning, and quality improvement initiatives in clinical practice. Ongoing research and interdisciplinary collaboration are vital for addressing the evolving challenges and complexities within legal medicine (17).

Despite the valuable insights provided by this study, several limitations should be acknowledged:

- Retrospective design: the study relies on previously collected data, which may be incomplete or inconsistent.
- Single-center study: The findings are based on data from a single hospital (Policlinico Hospital in Bari), limiting generalizability to other institutions, regions, or healthcare systems with different medico-legal structures.
- Lack of longitudinal follow-up: The study does not track patient outcomes or the long-term impact of forensic consultations on legal proceedings or healthcare quality.

One key outcome of our study was the detailed analysis of forensic consultations in the orthopedics department, particularly concerning patients with femoral fractures who lacked decision-making capacity. This led to the development of a hospital-wide diagnostic-therapeutic care pathway (PDTA), collaboratively designed by 11 different departments, to ensure integrated management of patients over the age of 65 with femoral fractures. Within this framework, specific provisions were made to align with Italian Law, ensuring that informed consent is obtained before surgical intervention and outlining clear guidelines for cases where patients are unable to provide valid consent. Following the implementation of this PDTA, we observed a marked reduction in requests for medico-legal consultations regarding the management of these patients, demonstrating the tangible impact of forensic clinical medicine on hospital workflows and patient care.

Future studies that utilize advanced methodologies, including artificial intelligence, hold promise for enhancing predictive capabilities and optimizing patient outcomes in the medico-legal domain (18). By embracing an interdisciplinary and innovative approach, healthcare systems can navigate the complex intersection of medicine and law, ultimately promoting justice, equity, and patient-centered care. Understanding the determinants and patterns of forensic consultations has practical implications, guiding healthcare professionals, administrators, and policymakers in developing targeted interventions, enhancing patient safety, and reducing medico-legal risks.

## Conclusion

In conclusion, this article provides an in-depth overview of legal medicine practices, filling an essential gap in the literature. The study not only presents a retrospective analysis of 4 years of forensic consultations but also offers a future-oriented perspective on integrating artificial intelligence in predicting treatment outcomes. The findings underscore the need for a global, unified approach to legal medicine that recognizes its expanding and critical role in contemporary healthcare systems (19).

## Data availability statement

The original contributions presented in this study are included in this article/supplementary material, further inquiries can be directed to the corresponding authors.

## Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed

consent from the participants was not required to participate in this study in accordance with the national legislation and the institutional requirements.

## Author contributions

PV: Writing – original draft, Writing – review & editing. GS: Writing – original draft, Writing – review & editing. AV: Writing – original draft, Writing – review & editing. FC: Writing – original draft, Writing – review & editing. FD: Writing – original draft, Writing – review & editing. MB: Writing – original draft, Writing – review & editing. BS: Writing – original draft, Writing – review & editing. AD'E: Writing – original draft, Writing – review & editing. DF: Writing – original draft, Writing – review & editing.

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# Ethical issues in the use of genetic predictions of aggressive behavior in the criminal justice system: a systematic review

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**Background:** The use of genetic predictions of aggressive behavior in the criminal justice system remains a subject of ongoing debate. Since behavioral genetic evidence is often used in criminal defense arguments, it is crucial to critically examine the ethical challenges associated with its application.

**Objective:** This article seeks to identify and analyze these ethical concerns to ensure the responsible and equitable integration of genetic testing, when deemed necessary, into the judiciary system.

**Methods:** A systematic review was conducted using PubMed, Web of Science, and Scopus, supplemented by manual searches of reference lists to identify additional relevant studies.

**Results:** The search yielded 1,023 publications, 12 of which met the inclusion criteria. Seven key ethical concerns were identified: the risks of discrimination, stigmatization, eugenic reasoning, deterministic interpretations, overestimation of dangerousness, privacy violations, and medicalization, along with the risks posed by limited scientific literacy among legal professionals.

**Conclusion:** The ethical challenges associated with genetic predictions of aggressive behavior underscore the need for a critical and multidisciplinary approach to their use in the criminal justice system. Collaboration among bioethicists, legal scholars, scientists, and communication experts is crucial to prevent misuse and reduce potential biases. Such an approach will help ensure that genetic insights are ethically applied, accurately interpreted, and used to promote justice rather than exacerbate systemic inequalities.

## KEYWORDS

genetic testing, behavioral genetics, ethics, criminal justice, MAOA gene

# 1 Introduction

Human behavioral genetics explores the origins of individual differences in psychological traits, such as intelligence and personality (Joseph, 2014). Its primary objective is to investigate the genetic foundations of behavior while accounting for the complex interaction between hereditary factors and environmental conditions (Goldsmith and Bihun, 1997).

The link between behavior and genetics, or heredity, can be traced back to the work of English scientist Sir Francis Galton (1822–1911), who introduced the concept of “nature and nurture” to describe the interplay between genetic inheritance and environmental influences.

A key focus of behavioral genetics is the investigation of genetic and environmental influences on violent behavior (Baker et al., 2006; Slutske, 2001; Viding, 2004). In the 1960s and 1970s, researchers hypothesized that the presence of an extra Y chromosome – known as XYY syndrome – heightened the risk of violent behavior. However, this theory was later discredited for its reliance on biased assumptions and flawed methodologies (Ashby, 1975; Steinfels and Levine, 1980).

A more promising link between genetic susceptibility and violent behavior emerged in 1993 when some researchers (Brunner et al., 1993) studied a Dutch family in which several male members exhibited mild cognitive impairments and impulsive aggression. Genetic analysis revealed a mutation on the X chromosome that deactivated the monoamine oxidase A (MAOA) enzyme, essential for neurotransmitter regulation. This study provided findings suggested that disruptions in neurotransmitter metabolism might contribute to aggressive tendencies.

In 2002, a study (Caspi et al., 2002) expanded on previous MAOA research, suggesting that even partial reductions in enzyme activity – linked to mutations in the gene’s promoter region – could heighten the risk of violent and antisocial behavior, particularly in unfavorable environments. As part of a large longitudinal study in Dunedin, New Zealand, researchers analyzed genetic variations in 442 males from a cohort of 1,037 individuals, using data collected up to age 26.

Subsequent studies have attempted to replicate the Dunedin findings, with most confirming the association, though some have not (Gold and Appelbaum, 2014); however, meta-analyses (Kim-Cohen et al., 2006; Byrd and Manuck, 2014) support the existence of the effect.

The MAOA gene has been cited in legal proceedings since its discovery, particularly in cases involving aggressive behavior. Already in 2017, a study (McSwiggan et al., 2017) identified 11 criminal cases where expert evidence on the MAOA gene was presented – nine in the US and two in Italy.

Behavioral genetics evidence is introduced in two legal contexts: in determining criminal responsibility and during the sentencing process. In particular, such evidence may be used to argue for diminished culpability, suggesting that a genetic predisposition to impulsivity or aggression could impair an individual’s capacity – defined as the ability to exercise self-control and make free and willful decisions. Given that capacity is a fundamental factor in assessing criminal liability, courts may consider an internal, uncontrollable drive toward aggression as grounds for excluding

or mitigating culpability in cases of aggressive behavior. More commonly, behavioral genetics evidence is introduced during sentencing, where it serves as a mitigating factor, potentially influencing the severity of the punishment imposed (Berryessa et al., 2013; Oliva et al., 2021). For instance, in the United States, behavioral genetics has frequently been presented in capital cases, where defendants facing the death penalty have sought to use genetic predispositions to violent behavior as grounds for leniency (O’Mahony and de Paor, 2017).

However, the role of genetic evidence in the criminal justice system remains highly controversial, with scholars and legal experts offering differing perspectives on its implications (Sabatello and Appelbaum, 2017). While some argue that genetic predispositions to aggressive behavior can provide valuable insights into criminal responsibility and sentencing, others warn of the risks of misuse and misinterpretation. Indeed, the scientific robustness of such evidence remains a matter of debate, with concerns raised about its validity, reliability, and predictive power (Oliva et al., 2021). Moreover, the application of genetic predictions of aggressive behavior raises significant ethical challenges, as it intersects with fundamental principles of justice, fairness, and individual rights.

The aim of this article is to identify and critically examine the ethical issues associated with the use of genetic predictions of aggressive behavior in the criminal justice system. As the field of behavioral genetics continues to evolve, this analysis may contribute to ensuring its responsible and equitable integration into legal practice. This work is part of a broader research initiative titled “Genetic Predisposition to Aggressive-Impulsive Antisocial Behavior: Forensic Aspects”, funded by the European Union (NextGenerationEU) and the Italian Ministry of University and Research.

To date, no comprehensive analysis has systematically explored the ethical issues related to the use of genetic predictions of aggressive behavior in the criminal justice system. To the best of our knowledge, this systematic review represents the first attempt to fully map the ethical debate surrounding the application of genetic predictions of aggressive behavior in legal proceedings.

# 2 Methods

This study aims to explore the ethical issues arising from the use of genetic predictions of aggressive behavior in the criminal justice system. To ensure methodological rigor and transparency, the study was designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-Ethics Reporting Guidelines (Kahrass et al., 2021).

Prior to conducting the study, four members of the research team (PR, SF, SG and AO) developed a structured protocol outlining the research objectives, search strategy, and inclusion criteria. The protocol was subsequently reviewed and approved by all researchers during a dedicated meeting on 1 August 2024. Given the thorough internal validation process, formal protocol registration was deemed unnecessary. A comprehensive literature search was conducted across three major academic databases: PubMed, Web of Science, and Scopus. These databases were selected for their broad interdisciplinary coverage, ensuring a thorough examination of the existing literature.



TABLE 1 Search string.

Database	Search string
PubMed	(((((((((“Sociobiology” [Mesh]) OR “Genetics” [Mesh]) OR “genetics” [Subheading]) OR “Forensic Genetics” [Mesh]) OR “Genetics, Behavioral” [Mesh]) OR “Human Genetics” [Mesh]) OR “Genes” [Mesh]) OR “Brunner Syndrome” [Supplementary Concept]) AND (((“Violence” [Mesh] AND “Domestic Violence” [Mesh]) OR “Aggression” [Mesh]) OR “Disruptive, Impulse Control, and Conduct Disorders” [Mesh])OR aggressive OR aggression OR violent OR violence)) AND ((“Ethics” [Mesh] OR “ethics” [Subheading] OR “Ethics, Clinical” [Mesh] OR “Bioethics” [Mesh]) OR “Morals” [Mesh] OR ethic*)

TABLE 2 Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"><li>- Focus on behavioral genetics</li><li>- Explicit reference to aggressive behavior</li><li>- Direct engagement with ethical considerations regarding the use of genetic predictions of aggression in legal settings</li></ul>	<ul style="list-style-type: none"><li>- The study addressed behavioral genetics but did not make any reference to the forensic context</li><li>- The study lacked a direct discussion on aggressive behavior</li><li>- The study did not address ethical considerations related to the implications of genetic predictions in legal settings</li></ul>

The search strategy was organized into three main thematic areas: the first centered on terminology related to “genetic predictions”, the second on “aggressive behavior”, and the third on “ethical issues”. To enhance search accuracy and scope, synonyms and alternative spellings for key terms were incorporated into each category. The PubMed search strategy is detailed in Table 1 and was subsequently adapted for Web of Science and Scopus.

The search was limited to English-language publications. All database searches were conducted in November 2024. Additionally, a manual review was performed, including an examination of reference lists from the selected studies to identify any additional relevant literature.

The inclusion and exclusion criteria were established before conducting the search (Table 2). Studies were considered eligible if they explicitly focused on behavioral genetics, included a clear reference to aggressive behavior, and directly engaged with ethical considerations concerning the use of genetic predictions of aggressive behavior in the criminal justice system. Studies were excluded if they lacked a forensic context, did not directly discuss aggressive behavior, or failed to provide a clear ethical reference on genetic predictions in legal settings.

Two independent reviewers (PR and CR) conducted the study screening process using Rayyan software<sup>1</sup>. The software facilitated the identification and removal of duplicate records, with each duplicate manually verified by both reviewers. Titles and abstracts of the retrieved documents that met the inclusion criteria were assessed separately by the reviewers. Disagreements were resolved through discussion, and unresolved cases were escalated to a third reviewer (AGS) for adjudication.

For the full-text review, PR and CR independently analyzed each study at least twice before extracting data to ensure a thorough understanding of the content. The articles were evaluated to identify ethical arguments related to the use of genetic predictions of aggressive behavior in the criminal justice system. A third researcher (AGS) cross-checked the extracted data for accuracy.

Any inconsistencies detected during this process were resolved through consultation of the primary study documents and discussions within the research team. The extracted data are detailed in the Supplementary Material S1. Given the lack of a standardized framework for evaluating ethical reasoning, no formal quality appraisal of the selected studies was conducted.

The synthesis process followed a critical interpretive synthesis approach (Dixon-Woods et al., 2006). This process enabled the research team to identify a coherent set of recurring concerns, which were further examined and refined through a series of iterative discussions. Each identified theme was subsequently developed into a dedicated paragraph, representing a distinct ethical domain. These thematic categories capture the central ethical tensions emerging from the literature and provide the analytical framework through which the results are organized and interpreted.

### 3 Results

The search process initially identified 1,023 records, and 122 duplicates were subsequently removed. During the preliminary screening phase, 817 records were excluded based on their titles and/or abstracts, as they did not meet the eligibility criteria. Although 84 full-text articles were assessed in the second-level screening, only 11 were ultimately included in the final analysis. The primary reasons for exclusion at this stage included ethical discussions that remained overly general (n = 31); studies that, although they referred to the legal domain, addressed ethical concerns in areas unrelated to criminal justice – such as education, employment, or healthcare (n = 22); and contributions that relied on outdated conceptual or ethical frameworks, limiting their relevance to current debates (n = 20). Additionally, one more article was identified through reference list screening, bringing the final selection to 12 studies (Wasserman, 2004; DeCamp and Sugarman, 2004; Rothstein, 2005; Popma and Raine, 2006; Savulescu and et al., 2006; Levitt and Manson, 2007; Berryessa et al., 2013; O’Mahony and de Paor, 2017; Specker et al., 2017; Ferioli and Picozzi, 2018; Glenn and McCauley, 2019; Meurer, 2021). A PRISMA flow diagram represented in Figure 1 illustrates the study selection process.

<sup>1</sup> Accessed on 10 January 2025 at: <https://www.rayyan.ai/>, accessed on 10 January 2025.

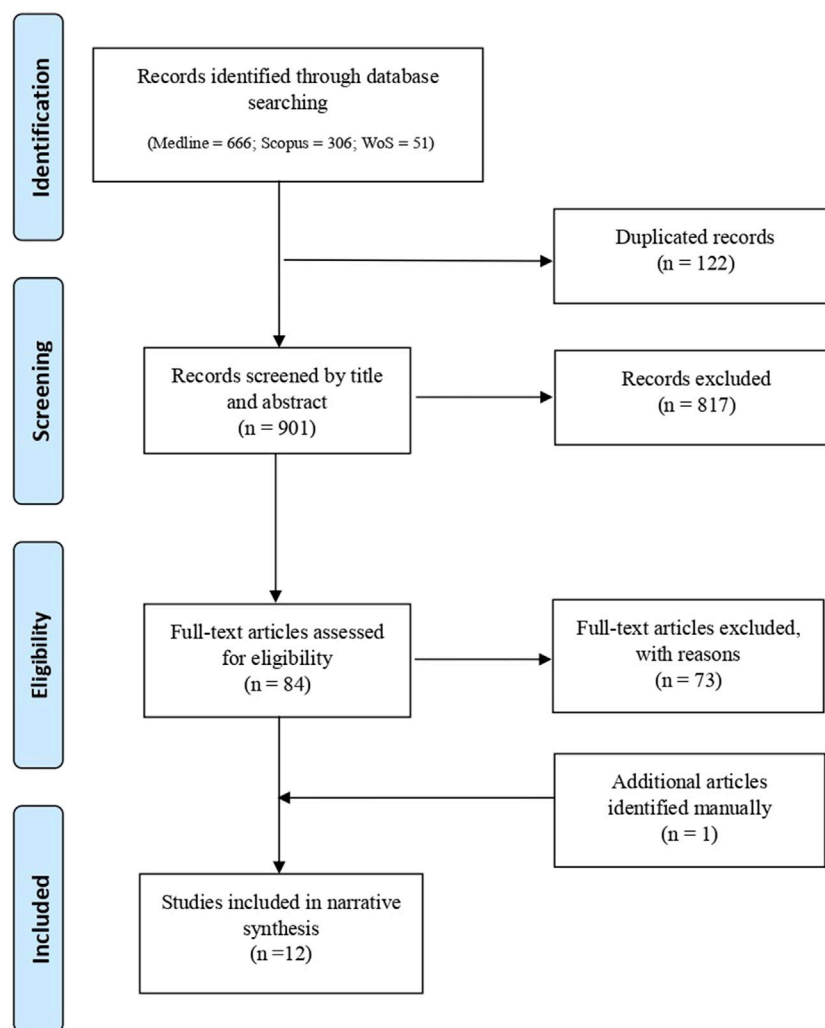


FIGURE 1  
PRISMA flow diagram.

The recurring concerns identified in the interpretative analysis coalesced into the following thematic categories: discrimination, stigmatization, resurgence of eugenic thinking, genetic determinism, overestimation of dangerousness, infringements on privacy, medicalization, and risks linked to limited scientific expertise. Below, each of these categories is discussed in detail.

### 3.1 Discrimination

Discrimination is a widely recognized ethical concern in discussions on the use of genetic predictions of aggressive behavior particularly within the criminal justice system (Wasserman, 2004; Rothstein, 2005; Popma and Raine, 2006; Savulescu and et al., 2006; Levitt and Manson, 2007; Berryessa et al., 2013; O'Mahony and de Paor, 2017; Specker et al., 2017; Ferioli and Picozzi, 2018; Glenn and McCauley, 2019). The mere identification of a genetic predisposition to violent behavior may result in social and institutional exclusion, reinforcing biases and limiting opportunities.

In the workplace, the misuse of genetic information may result in individuals being unjustly denied employment or career advancement based on perceived genetic risks rather than actual skills and competencies. This undermines the principles of merit-based hiring and professional development, further entrenching systemic inequalities. The fear of liability or workplace disruptions may drive employers to make preemptive decisions that disadvantage individuals with certain genetic profiles, even in the absence of any actual performance concern.

Similarly, in the insurance sector, concerns arise over whether private insurers should be allowed to incorporate genetic predispositions into risk assessment. Such practices could lead to higher premiums or outright denial of coverage for individuals who have never exhibited aggressive behavior, effectively penalizing them for factors beyond their control. More broadly, in healthcare, the integration of behavioral genetics into medical decision-making raises ethical concerns about the potential shift from a patient-centered approach to a predictive model that prioritizes risk management over individualized treatment.

Finally, discrimination could also extend to education, where students labeled as "at risk" based on their genetic profiles may face

reduced opportunities. If schools begin to use genetic predispositions as indicators of academic potential or behavioral tendencies, they may limit access to advanced programs, alter teaching methods, or impose additional monitoring on certain students, regardless of their actual performance or behavior. This could undermine the principle of equal educational access and deepen existing disparities, disproportionately affecting marginalized communities. By placing undue weight on genetic predispositions, educational institutions risk overlooking the significant role of personal effort, social context, and educational support in shaping student outcomes.

### 3.2 Stigmatization

A second ethical concern regarding the use of genetic predictions of aggressive behavior in the criminal justice system is the risk of stigmatization (DeCamp and Sugarman, 2004; Rothstein, 2005; Levitt and Manson, 2007; Berryessa et al., 2013; O'Mahony and de Paor, 2017; Specker et al., 2017; Ferioli and Picozzi, 2018; Glenn and McCauley, 2019; Meurer, 2021). Classifying defendants as “at risk” based on genetic markers has the potential to reinforce existing biases, shaping not only legal outcomes but also broader societal perceptions of criminality. Such labeling may contribute to disparities in sentencing, access to rehabilitative programs, and parole decisions, perpetuating cycles of exclusion rather than fostering justice.

Beyond legal consequences, genetic labeling can have profound psychological effects on those subjected to it. Being identified as having a genetic predisposition to antisocial behavior may undermine an individual's self-esteem, personal identity, and sense of agency, fostering internalized stigma and social alienation. Those labeled as genetically “high risk” may struggle with feelings of inevitability or hopelessness, believing their genetic makeup dictates their future. This psychological burden can further obstruct reintegration efforts, as individuals with such labels may face social isolation both within correctional institutions and in society at large.

A particularly concerning aspect is the reinforcement of negative stereotypes, especially against already disadvantaged and marginalized communities. If genetic or epigenetic markers associated with behavioral traits are more frequently identified within specific socioeconomic or ethnic groups, their use in risk assessment may inadvertently legitimize harmful prejudices. This could exacerbate social and health inequalities by justifying disproportionate surveillance, policing, or punitive measures against certain populations under the guise of crime prevention. Rather than advancing justice, such applications of genetic screening risk becoming instruments of social control, reinforcing existing disparities and deepening mistrust in the legal system.

To mitigate these risks, ethical frameworks must prioritize the no-stigma principle, ensuring that genetic insights do not translate into social exclusion or psychological harm.

### 3.3 Resurgence of eugenic thinking

The increasing reliance on genetic information to isolate and target specific behavioral traits raises serious concerns about the

revival of eugenic-style policies and attitudes (Wasserman, 2004; Savulescu et al., 2006; O'Mahony and de Paor, 2017). Historically, eugenic ideologies sought to classify individuals based on perceived biological “fitness,” often leading to coercive interventions, forced sterilizations, and systematic discrimination against marginalized groups. While contemporary genetic research aims to enhance the understanding of human behavior, its application in predictive justice risks reintroducing similar patterns of exclusion and control under a scientific guise.

To mitigate these ethical risks, strict regulatory and ethical safeguards must be implemented to prevent the misuse of genetic data in ways that echo eugenic ideologies. Furthermore, the ethical application of genetic insights in the criminal justice system should be subject to interdisciplinary oversight, meaning that decisions must be evaluated and guided by a diverse group of experts—including bioethicists, legal scholars, sociologists, and advocates for social justice. This collaborative supervision ensures that the development and use of genetic tools are not driven solely by scientific or technological considerations, but are also informed by ethical, legal, and societal perspectives. Such a pluralistic approach is essential to avoid repeating past injustices and to prevent the emergence of new forms of social control disguised as scientific progress.

### 3.4 Determinism

A fourth ethical issue concerns the implications of genetic predictions for free will and legal accountability (Wasserman, 2004; Popma and Raine, 2006; Savulescu et al., 2006; Levitt and Manson, 2007; Berryessa et al., 2013; O'Mahony and de Paor, 2017; Specker et al., 2017; Ferioli and Picozzi, 2018). The integration of biological factors—such as genetic markers associated with impulse control—challenges traditional conceptions of moral and legal responsibility. If certain individuals exhibit biological deficits that impair their capacity for self-regulation, should their culpability for criminal actions be reconsidered?

One of the primary risks is the reinforcement of deterministic assumptions about antisocial behavior. Perceiving criminal tendencies as innate or inherited could contribute to a self-fulfilling prophecy in which individuals labeled as genetically “predisposed to aggressive behavior” are treated as future offenders regardless of their actual conduct. Such labeling may influence legal decisions, resulting in harsher sentencing, prolonged surveillance, or restricted access to rehabilitation programs based on perceived rather than actual risk. Moreover, this perspective risks diverting attention from the social and environmental factors that contribute to criminal behavior, reinforcing a reductionist view of crime as biologically predetermined rather than as the outcome of complex social, psychological, and economic influences.

A particularly concerning development is the potential shift toward a preventive model of justice. If specific genetic or neurological markers are considered adequate grounds for state intervention, the legal system may start imposing restrictions on individuals based on predictive assessments rather than proven offenses. This could lead to increased monitoring, mandatory treatment, or even preventive detention for individuals deemed

“at risk” of criminal behavior, despite the absence of any unlawful conduct. This approach mirrors historical frameworks rooted in biological determinism, such as the 19th-century theories of criminal anthropology that attempted to classify “born criminals” based on physiological traits—a concept long discredited but now resurfacing in a more scientifically refined guise.

The ethical and legal consequences of such a shift would be profound. A system that legitimizes restrictions on individual liberty based on probabilistic genetic assessments risks violating core principles of justice, including the presumption of innocence and the right to due process.

### 3.5 Overestimation of the dangerousness

The integration of genetic screening into the criminal justice system raises significant concerns about the potential overestimation of the predictive value of genetic markers for violent behavior and, consequently, the perceived dangerousness of individuals (Rothstein, 2005; Berryessa et al., 2013; O’Mahony and de Paor, 2017). Courts and policymakers may be misled into assuming a stronger causal relationship between genetic traits and criminal tendencies than what is supported by scientific evidence.

A particularly troubling aspect is the potential labeling of individuals as future criminals based on genetic screening. If genetic predispositions are treated as deterministic indicators of future conduct, individuals could be subjected to heightened surveillance, restricted opportunities, or even preemptive legal measures despite the absence of any criminal behavior. This approach not only undermines the presumption of innocence but also penalizes individuals, limiting their social mobility and reinforcing systemic biases.

### 3.6 Privacy infringement

The collection and storage of genetic data in DNA databases raise serious ethical concerns, particularly regarding consent, confidentiality, and the potential misuse of sensitive information (Wasserman, 2004; Rothstein, 2005; Berryessa et al., 2013; O’Mahony and de Paor, 2017; Ferioli and Picozzi, 2018; Glenn and McCauley, 2019). Given the uniquely personal and immutable nature of genetic data, privacy protections must be rigorous to prevent unauthorized access, disclosure, and exploitation. Without robust safeguards, genetic information could be misused in ways that extend far beyond the original forensic purposes, posing critical challenges to the balance between security, individual rights, and ethical governance.

Moreover, the potential for misuse and secondary use of genetic data heightens concerns about discrimination and unjustified surveillance. Unauthorized access to genetic databases – whether by state authorities, private entities, or malicious actors – could lead to the exploitation of genetic profiles for purposes beyond criminal justice, including employment decisions, insurance coverage, or predictive assessments of behavior. Such applications risk reinforcing systemic biases, disproportionately affecting marginalized communities and exacerbating existing social inequalities.

The psychosocial impact of privacy breaches also warrants serious consideration. The unauthorized disclosure of genetic information can have profound consequences for individuals and their families, leading to stigma, emotional distress, and social marginalization. The awareness that one’s genetic data is permanently stored and potentially accessible by various institutions may contribute to a climate of fear and distrust in both the legal system and broader societal structures.

To address these ethical concerns, strict privacy protections and regulatory oversight must be implemented. This includes enforcing explicit and informed consent procedures, implementing data encryption and access controls, and establishing clear guidelines on the retention and deletion of genetic records. Additionally, policies must be developed to limit the scope of DNA database usage, ensuring that genetic data is employed strictly within legal and ethical boundaries and preventing its expansion into areas that could infringe upon fundamental rights.

Incorporating these safeguards is essential to maintaining trust in the forensic applications of genetics while upholding the principles of justice, autonomy, and privacy. Without comprehensive protections, the widespread use of DNA databases risks evolving into a tool for excessive state surveillance and social control, ultimately undermining the ethical foundations of the criminal justice system.

### 3.7 Medicalization

The increasing reliance on genetic and neurobiological insights in criminal justice raises concerns about the medicalization of antisocial behavior, that is the process of redefining behaviors traditionally viewed as moral or social transgressions as medical conditions requiring clinical intervention (DeCamp and Sugarman, 2004; Berryessa et al., 2013; Specker et al., 2017).

One of the primary concerns is that medicalization could undermine personal responsibility. If antisocial or violent tendencies are classified as medical disorders, defendants may increasingly be seen as patients, raising questions about the extent to which they should be held legally accountable for their actions.

Another critical issue is the use of pharmacological or neurological interventions to manage norm-defiant behavior. Treating individuals labeled as predisposed to criminal behavior with medication – whether to suppress aggression, enhance impulse control, or modify other traits – raises ethical concerns about autonomy and informed consent. The potential for coercive treatment is particularly troubling, as individuals within the criminal justice system may face pressure to undergo medical interventions as a condition for parole, reduced sentencing, or rehabilitation. This echoes past controversies surrounding forced medication, chemical castration, and other state-imposed biomedical interventions, which were often justified as measures to protect public safety but frequently resulted in serious human rights violations.

Furthermore, the expansion of medical interventions in criminal justice risks creating a system in which behavioral control takes precedence over addressing the underlying social and structural causes of crime. By attributing antisocial behavior primarily to biological or neurological dysfunctions, medicalization may divert attention from critical social, economic, and psychological factors

that contribute to criminality. This could lead to an over-reliance on biomedical solutions, while neglecting the broader need for legal, educational, and social reforms that aim to prevent crime and rehabilitate offenders.

### 3.8 Risks of limited scientific expertise

The increasing use of genetic evidence in criminal justice raises serious concerns about the scientific literacy of judges, juries, and legal professionals. While genetic insights can provide valuable information in forensic investigations, the complexity of genetics presents significant challenges for those responsible for interpreting its findings. A lack of expertise among legal decision-makers increases the risk of misinterpretation, over-reliance on expert testimony, and flawed judicial outcomes, potentially leading to miscarriages of justice (Rothstein, 2005; Berryessa et al.).

One of the primary concerns is that judges and juries often lack the necessary scientific background to critically evaluate genetic evidence. Unlike traditional forensic evidence, genetic data is highly technical and probabilistic in nature. Courts may struggle to assess the validity, reliability, and limitations of genetic findings, particularly in behavioral genetics, which remains an evolving and controversial field. This gap in understanding creates a dangerous reliance on expert testimony, where the persuasive power of scientific authority may overshadow a nuanced consideration of the evidence. Without adequate scientific literacy, legal decision-makers may either overestimate the certainty of genetic predictions, leading to unjustified conclusions about an individual's criminal responsibility, or dismiss legitimate findings due to skepticism or misunderstanding.

Another key concern is the risk of biased or misleading expert testimony. While expert witnesses play a crucial role in translating complex genetic information for the court, their interpretations may vary based on differing scientific perspectives, institutional affiliations, or even unconscious biases. In adversarial legal systems, experts may present conflicting interpretations, leaving judges and juries to choose between competing narratives without the necessary knowledge to critically assess their scientific validity. This increases the risk that legal decisions may be driven more by rhetoric than by sound scientific reasoning, ultimately undermining the fairness of the judicial process.

The absence of standardized guidelines for the use of genetic evidence further exacerbates these challenges. Unlike traditional forensic disciplines with well-established methodologies, behavioral genetics and predictive genetic profiling continue to be areas of active debate. The lack of clear legal and ethical frameworks governing the admissibility and interpretation of genetic findings creates inconsistencies in how such evidence is applied across different cases and jurisdictions, increasing the likelihood of arbitrary or unjust outcomes.

## 4 Discussion

The *MAOA* gene has been referenced in judicial proceedings since its identification, especially in cases related to aggressive behavior.

One of the earliest and most notable cases was *Mobley v. State* (1995), marking the first time the *MAOA* gene was discussed in a U.S. courtroom. A significant milestone in Europe occurred in *Bayout v. Francesco* (2009), where an Italian court reduced a convict's sentence based on genetic predisposition to violent behavior, making it the first instance in which behavioral genetics influenced a legal ruling on the continent. Additionally, *State v. Waldroup* (2011) in the United States further underscored the role of genetic evidence in criminal trials (O'Mahony and de Paor, 2017).

In addition to the *MAOA* gene, several other genes have been associated with antisocial and aggressive behavior. These include *DAT-1* (Dopamine Transporter 1), which regulates dopamine transmission; *BDNF* (Brain-Derived Neurotrophic Factor), which is crucial for brain function; and *CRHBP* (Corticotropin-Releasing Hormone Binding Protein), which influences stress response. More recent studies (Assari et al., 2018; Musci et al., 2019; Koyama et al., 2024) have also linked the low-activity variants of *5HTTLPR* (Serotonin Transporter Linked Polymorphic Region, part of the *SLC6A4* gene regulating serotonin levels), the 7-repeat allele of *DRD4* (Dopamine Receptor D4, associated with impulsivity), the A1 allele of *DRD2* (Dopamine Receptor D2, involved in reward processing), the H3 (GGA) haplotype of *CRHR1* (Corticotropin-Releasing Hormone Receptor 1, influencing stress response), and specific variants of *COMT* (Catechol-O-Methyltransferase), particularly the *Val158Met* polymorphism, which affects dopamine metabolism, with violent tendencies.

However, the debate over the use of genetic predictions of behavior remains controversial, particularly in discussions surrounding criminal responsibility. It is no coincidence that in the early stages of behavioral genetics research, scientific conferences addressing the topic were met with protests and opposition, reflecting widespread concerns about the potential misuse of genetic explanations for social and legal purposes (Birch, 1995).

Historically, fears of biological determinism have been linked to discriminatory policies, racial bias, and the erosion of personal responsibility, leading many scholars and activists to challenge the legitimacy of genetic predictions in forensic contexts. This controversy remains relevant today, as the application of behavioral genetics in criminal justice risks reviving outdated notions of "born criminals", thereby reinforcing biases rather than fostering a nuanced understanding of crime as a multidimensional phenomenon.

The review conducted in our study allowed us to identify several critical ethical concerns that were both present and emphasized in the selected articles. These concerns reflect and resonate with the main ethical frameworks that have been well established in the field of genetics. Among the most prominent issues are the risks of discrimination, stigmatization, eugenic thinking, deterministic interpretations, overestimation of dangerousness, privacy violations, medicalization, and the potential consequences of limited scientific expertise in legal decision-making.

Beyond these specific considerations, we argue that the core of this ethical debate centers on scientific reductionism – the tendency to oversimplify complex human behaviors by attributing them primarily to genetic or biological factors (Newson, 2004; Dick, 2011). While reductionist approaches once dominated scientific discourse, they are now widely recognized as inadequate for



capturing the intricate interplay between genetics, environment, and individual agency. The findings of this study reinforce the argument that predicting violent behavior solely based on genetic markers is scientifically flawed and ethically problematic. The challenge, therefore, lies in rejecting simplistic genetic explanations and adopting a more holistic, interdisciplinary approach that accounts for psychosocial, cultural, and environmental influences on behavior.

A particularly critical element for contemporary societies is the impact on public opinion. One of the greatest risks associated with genetic predictions of aggressive behavior is the public misinterpretation of scientific findings. If genetic predispositions to criminal behavior are presented without appropriate context, they could fuel misconceptions, fear, and social stigma, leading to harmful policies that undermine human rights and justice. The sensationalization of genetic research in media narratives could contribute to moral panic, reinforcing stereotypes about certain populations and justifying coercive legal measures based on speculative risk assessments. Therefore, clear, transparent, and responsible communication is essential to ensuring that both the public and policymakers understand the limitations of behavioral genetics and do not misapply genetic data in ways that perpetuate discrimination and social control (Meurer, 2021; Ferioli and Picozzi, 2018).

Despite these risks, we do not argue for the exclusion of genetic data from legal processes. On the contrary, we believe that its responsible use is possible – provided it is embedded within a robust ethical framework and interpreted through a multidisciplinary lens. Genetic evidence should inform but never determine legal outcomes, and its use must be guided by principles that protect individual rights and promote justice.

Based on the findings of our review, we propose the following recommendations for legal practitioners, particularly in complex cases involving aggressive behavior and suspected genetic predispositions:

- Contextual interpretation: genetic predispositions must never be treated as deterministic. Legal reasoning must consider social, psychological, and environmental factors.
- Scientific training: judges and legal professionals should receive adequate training in behavioral genetics and related disciplines to evaluate scientific claims critically.
- Interdisciplinary oversight: courts should consult advisory panels composed of bioethicists, neuroscientists, legal experts, and psychologists to assess the appropriateness and ethical implications of using genetic data in specific cases.
- Non-discrimination: legal decisions must avoid stigmatizing individuals based on genetic profiles and ensure that such information is not used to justify unequal treatment.
- Standards for expert testimony: clear and consistent criteria are needed to govern the admissibility and reliability of genetic evidence in court.
- Privacy protection: strict safeguards must be applied to the collection, storage, and use of genetic information, including informed consent and limitations on data sharing.
- Transparent communication: Both the legal system and media should adopt clear and responsible strategies for

communicating the meaning and limitations of genetic findings.

- Rejection of genetic-based preventive justice: measures taken against individuals must be grounded in conduct, not in probabilistic genetic assessments.

In conclusion, the ethical concerns surrounding genetic predictions of aggressive behavior underscore the importance of maintaining a critical perspective on how genetic findings are integrated into the legal system. Moving forward, a multidisciplinary approach – involving bioethicists, legal scholars, scientists, and communication experts – is crucial to ensuring that genetic insights are used ethically, interpreted accurately, and applied in ways that promote justice rather than reinforce systemic inequalities. Practically, this means establishing institutional frameworks for ongoing ethical review, such as advisory committees that include diverse disciplinary perspectives to evaluate the admissibility and use of genetic evidence in courtrooms. Legal professionals should be trained in the interpretation of scientific findings, while scientists should collaborate with ethicists to assess the societal impact of their work. Communication experts, particularly those specialized in science communication, can play a key role in translating complex genetic information for judges, juries, policymakers, and the general public, helping to prevent misinterpretations that could lead to moral panic or policy distortions.

This collaborative effort would not only ensure responsible integration of behavioral genetics into legal and policy frameworks, but also foster transparency, public trust, and the protection of fundamental human rights.

We acknowledge that this review has at least three significant limitations.

First, the way in which our research question was formulated may have inadvertently excluded some relevant studies that could have provided additional perspectives on the topic. The specific criteria used to define the scope of this review may have influenced the selection process, potentially limiting the diversity of viewpoints considered.

Second, our literature search was conducted using only three databases, which increases the possibility of having overlooked significant studies. This constraint may have led to the omission of research that could have enriched our analysis with alternative data or interpretations, thereby affecting the overall depth and comprehensiveness of our findings.

Third, most of the studies included in this review primarily reflect perspectives from the United States and Europe. This geographic concentration limits the applicability of our conclusions to a broader international context, as findings may not fully capture cultural, legal, or ethical nuances present in other regions.

To overcome these limitations, future research should expand the search methodology by incorporating a wider range of databases and adopting a more inclusive approach to study selection. Additionally, greater efforts should be made to integrate research from underrepresented regions to ensure a more comprehensive and globally relevant analysis.

## 5 Conclusion

Based on the findings of our review, the use of genetic predictions of aggressive behavior in the criminal justice system raises profound ethical concerns. These include the risks of discrimination, stigmatization, eugenic thinking, deterministic interpretations, overestimation of dangerousness, privacy violations, medicalization, and the potential consequences of limited scientific expertise in legal decision-making.

To navigate these challenges responsibly, a more holistic and interdisciplinary approach is essential. Rather than relying on reductionist explanations, future research and policy should integrate insights from genetics, neuroscience, psychology, sociology, and legal studies to develop a more nuanced understanding of crime and aggressive behavior. This approach must also be accompanied by robust ethical safeguards to prevent misuse and ensure that genetic research contributes to justice rather than reinforcing biases and inequalities.

Ultimately, these efforts are crucial to avoiding the mistakes of the past, where misguided applications of science have fueled injustice, discrimination, and ethical violations.

## Data availability statement

The original contributions presented in the study are included in the article/[Supplementary Material](#), further inquiries can be directed to the corresponding authors.

## Author contributions

PR: Methodology, Conceptualization, Formal Analysis, Writing – review and editing. SF: Conceptualization, Writing – review and editing. SG: Conceptualization, Writing – review and editing. CR: Formal Analysis, Methodology, Writing – review and editing. GM: Writing – review and editing. MZ: Writing – review and editing. GA: Writing – review and editing. AS: Methodology, Investigation, Formal Analysis, Writing – review and editing. AO: Writing – review and editing, Funding acquisition, Formal Analysis, Conceptualization, Investigation, Methodology.

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## Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fgene.2025.1599750/full#supplementary-material>

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# Birth-related long bone fractures in otherwise healthy newborns and medical professional liability: literature review and case presentation

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Birth-related long bone fractures are rare but clinically significant events that require careful evaluation to distinguish them from fractures caused by underlying pathological conditions or non-accidental trauma. Their diagnosis and management have important clinical and medico-legal implications. A selective literature review was conducted to identify relevant studies published between 2004 and 2024, regarding incidence, mode of delivery, fracture location, time to diagnosis, treatment, and outcomes. Additionally, an original case report of a female neonate diagnosed with femoral shaft fracture on the third day of life. Neonatal long bone fractures can occur even in the absence of predisposing genetic or metabolic conditions. While they generally heal without for surgical intervention, timely diagnosis through appropriate imaging is crucial to ensure proper management. Failure to do so may expose healthcare professionals and institutions to potential medico-legal liability, both during delivery and in the immediate postnatal period. Preventive strategies should focus on careful prenatal risk assessment, adherence to best practices in delivery maneuvers, and early postnatal monitoring to optimize outcomes and minimize legal risks.

## KEYWORDS

birth-related fractures, medical professional liability, clinical risk, long bone fracture, malpractice

## 1 Introduction

Birth-related fractures are an infrequent but significant complication of delivery, with an estimated incidence of approximately 2.9 per 1,000 live births, according to the latest data (1, 2). Among these, clavicular fractures are the most commonly reported, and frequently associated with challenging deliveries, such as those involving shoulder dystocia, breech presentations, or excessive traction during birth. These fractures are often accompanied by brachial plexus injuries, further complicating neonatal outcomes (3). While fractures of the skull, ribs, and long bones are substantially rarer, they remain a recognized possibility, particularly in traumatic or instrumental deliveries (4).

Neonatal long bone fractures typically involve the femur, humerus, or tibia and predominantly occur during vaginal deliveries. However, several cases of long bone fractures have been documented in the context of cesarean deliveries as well (5, 6). These injuries are more frequently observed in neonates with severe congenital or malformations, such as myofibromatosis, osteogenesis imperfecta, arthrogryposis, and muscular dystrophies. Such

underlying conditions predispose newborns to fractures even under minimal stress during delivery (7–9).

However, although rare, cases of long bone fractures have been reported in otherwise healthy newborns without malformative conditions (4). In such instances, professional liability may arise for healthcare personnel involved in delivery or in subsequent postnatal management.

The purpose of this study is to review the literature on birth-related long bone fractures in neonates without malformation or genetic or dysmetabolic conditions, present a clinical case, and discuss the medico-legal implications concerning medical professional liability.

## 2 Case presentation

We report the case of a female neonate born at 35 weeks and 4 days of gestation due to preeclampsia and a previous cesarean section, which led to the decision to perform an urgent repeat cesarean delivery. The fetus was diagnosed with intrauterine growth restriction (IUGR), with fetal doppler showing the umbilical artery flow at the 95th percentile and the cerebro-placental ratio at the 5th percentile, accompanied by abnormal cardiotocographic findings. The fetus was delivered in a cephalic presentation, and no noticeable complications were encountered during the procedure.

After birth, the neonate was entrusted to the pediatric department for initial care and cleaning, followed by placement in an incubator. On the third day of life, the neonate was found to have significant edema in the right lower limb, which was positioned in flexion and abduction, with no active movement of the thigh on the pelvis. Upon palpation, a hard swelling with crepitus was noted in the middle third of the thigh.

Further investigation through radiography revealed a fracture of the right femoral diaphysis. An orthopedic consultation was performed, which documented swelling of the thigh, absent spontaneous mobility, and movement of the foot upon stimulation and mobilization. The leg was placed in traction with a cast, which was maintained for approximately 15 days. The neonate underwent several orthopedic follow-ups, and after 2 months, no significant permanent sequelae were observed.

## 3 Methods

A selective literature review was conducted using Medline (PubMed) to identify relevant articles published in the last 20 years.

The search was performed with the following keywords: “newborn long bone fractures,” “neonatal long bone fractures,” and “birth-related long bone fractures.” Only articles published in English between 01.01.2004 and 31.12.2024 were included. Publications predating 2004 were excluded, along with studies related to fractures caused by underlying genetic or malformative conditions (e.g., osteogenesis imperfecta, myofibromatosis, muscular dystrophies) and articles focused on fractures related to child abuse. We also excluded articles for which the full text was not available.

Two of the reviewers carried out the initial search of the papers. They used the search protocol described above to identify literature. In the case of disagreements, the consensus of the research supervisors was asked. The researchers used the following research order: titles were screened first and then abstracts and full papers. A paper was considered

potentially relevant and its full text reviewed if, following discussion between the two independent reviewers, it could not be unequivocally excluded on the basis of its title and abstract. The full text of all papers not excluded on the basis of abstract or title was evaluated.

A database was created from the selected studies, focusing on the following parameters: article type, the number of cases (excluding those related to congenital, genetic or metabolic comorbidities or abuse), mode of delivery (cesarean, vaginal or not specified), fracture location, time interval between birth and diagnosis of the fracture, treatment methods, and any permanent sequelae.

## 4 Results

The literature research resulted in a total of 22 suitable papers, including 5 retrospective cohort studies and one population-based study. Key findings are summarized in Table 1.

The analysis of the selected studies identified a total of 279 cases of neonatal long bone fractures. These cases were distributed as follows: 210 cases of humeral fractures (75.3%), 61 cases of femoral fractures (21.9%), 2 cases of bilateral femoral fractures (0.7%), 2 cases of bilateral humeral fractures (0.7%), 2 cases of tibial fractures (0.7%), and 1 case involving simultaneous fractures of the femur and humerus (0.4%).

In most cases ( $n = 243$ ), the mode of delivery was not reported. Among the cases with available data, 13 fractures occurred following vaginal deliveries, while the remaining cases ( $n = 58$ ) were associated with cesarean sections. The time interval between delivery and diagnosis of the fractures ranged from immediately after delivery to 10 days postpartum.

Practically all fractures were treated conservatively, using methods such as immobilization or splinting. Only 3 cases (1.1%) required surgical intervention, specifically percutaneous pinning with Kirschner wires. Most fractures healed without permanent complications. However, two cases reported minor sequelae: one patient with a humeral fracture experienced occasional shoulder pain during sports activities, and another patient with a humeral fracture reported transient paresthesia in the fifth digit of the hand.

## 5 Discussion

The occurrence of birth-related long bone fractures, although rare, represents a clinically significant complication with implications for neonatal outcomes and potential medico-legal consequences, especially in newborns with no associated comorbidities. A few studies have highlighted the critical need to distinguish these fractures from those associated with child abuse (2). Furthermore, these cases carry notable medico-legal implications in the context of medical professional liability.

Our review of the literature revealed that both vaginal birth and cesarean section could be responsible for birth trauma, including long bone fractures.

Among the 279 cases analyzed, humeral fractures were the most frequent, followed by femoral fractures, with bilateral fractures and tibial fractures being exceedingly rare (10, 11).

The predominance of humeral fractures aligns with their anatomical vulnerability during delivery, particularly in challenging vaginal deliveries (6, 12). Interestingly, a notable proportion of fractures occurred during cesarean sections, highlighting mechanical



**TABLE 1** Summary of literature review findings.

Article	Type	Number of cases*	Delivery (n)	Fractures location (n)	Birth-diagnosis time span	Treatment	Permanent sequelae
Basha et al. (4)	Retrospective	6	Vaginal (1), Cesarean (7)	Femur (4) Humerus (2)	1–3 days	Immobilization (soft splintage)	None
Canpolat et al. (6)	Case report	1	Cesarean	Humerus bilateral	6 h	Immobilization	None
Capobianco et al. (18)	Case report	1	Cesarean	Femur	1 day	immobilization	None
Cebesoy et al. (19)	Case report	1	Cesarean	Femur (bilateral)	2 days	Immobilization (pelvipedal cast)	None
Dias (20)	Case report	1	Cesarean	Humerus bilateral	Immediately	Immobilization (splintage)	None
Farikou et al. (21)	Case report	1	Cesarean	Femur	Immediately	Immobilization (bilateral contention)	None
Galeotti et al. (2023) (13)	Case report	10	Vaginal (9), Cesarean (1)	Humerus (10)	0–9 days	Close reduction and cast immobilization; close reduction and percutaneous pinning with Kishner wires (2 cases)	Occasional elbow pain during sports (1 case) Transient fifth finger paresthesia (1 case)
Givon et al. (22)	Case report	9	Vaginal (1), Cesarean (8)	Femur (7) Femur bilateral (2)	Unknown	Immobilization (Bryant splint)	None
Goyal et al. (23)	Case report	1	Cesarean	Humerus	2 days	Immobilization	None
Hamilçikan et al. (24)	Case report	1	Vaginal	Humerus	Immediately	Immobilization	None
Hosokawa et al. (25)	Retrospective	7	Not specified	Femur (7)	Unknown	Unknown	Unknown
Kanai et al. (5)	Case report	1	Cesarean	Femur	9 days	Immobilization cast	Unknwon
Kanat Pektas et al. (26)	Retrospective	5	Cesarean	Femur (5)	1 day	Immobilization	Unknown
Kaya et al. (27)	Case report	1	Vaginal	Humerus	Immediately	Immobilization	None
Kim et al. (28)	Case report	1	Cesarean	Femur	Immediately	Immobilization (splint)	None
Matsubara et al. (29)	Case report	1	Cesarean	Femur	Immediately	Immobilization (cast)	None
Mileto et al. (10)	Case report	1	Cesarean	Tibia	Immediately	Percutaneous pinning K wires	None
Rahul et al. (2017) (16)	Case report	1	Cesarean	Femur and humerus	2 days	Immobilization	None
Rehm et al. (11)	Retrospective	15	Not specified	Humerus (13) Femur (1) Tibia (1)	Unknown	Immobilization K wires pinning (1)	Unknown
Rehmani et al. (30)	Retrospective	3	Not specified	Femur (1) Humerus (2)	Unknown	Immobilization	None
Toker et al. (31)	Case report	1	Cesarean	Femur	10 days	Immobilization	None
Von Heideken et al. (12)	Population-based	210	Not specified	Femur (30) Humerus (180)	1–7 days	Unknown	Unknown

\* Excluding those associated with congenital, genetic or metabolic comorbidities or abuse.

forces applied during extraction can still result in neonatal skeletal injuries, even in controlled surgical settings. This underscores the need for heightened vigilance and careful manipulation during delivery.

One of the most intriguing findings relates to the highly variable time span between delivery and the diagnosis of neonatal fractures. While most cases were identified immediately after birth or within the first 2–3 days postpartum, some diagnoses were delayed for up to

10 days (5, 13). It is well-established that diagnosing fractures in neonates can be particularly challenging, as these injuries often manifest with nonspecific symptoms such as irritability, excessive crying, or feeding difficulties. Such delays in diagnosis, or the premature discharge of neonates without identifying the fracture, can raise significant medico-legal concerns. Furthermore, while fractures diagnosed immediately after birth can be directly linked to maneuvers

performed during delivery, the determination of when the injury occurred becomes more complex when the diagnosis is made from the second or third day postpartum onwards.

Due to the nonspecific nature of clinical presentations, it can be difficult to discern whether the fracture was sustained during delivery but went unrecognized or occurred later as a result of improper handling, suboptimal care, or trauma during hospitalization. This ambiguity complicates the attribution of responsibility among the healthcare providers involved, posing substantial challenges in medico-legal assessments.

The clinical case presented exemplifies the challenges highlighted. Clinical records analysis did not identify any evident complications during the cesarean delivery. The diagnosis of the fracture was made 3 days after birth, triggered by the onset of significant swelling in the lower limb. From a medico-legal standpoint, this case underscores the difficulty in pinpointing the timing and mechanism of the fracture. It remains uncertain whether the injury occurred during delivery or in the days that followed, and the precise trauma responsible cannot be definitively determined. As a result, establishing liability for the healthcare professionals involved is particularly challenging in such circumstances.

One way to improve diagnostic accuracy in neonatal fractures may be to apply novel imaging techniques. Traditionally, X-ray has been the standard due to its low cost, speed, and availability. However, it has several drawbacks, including the need to reposition the infant—potentially worsening the injury—longer exam times, radiation exposure to both patient and staff, and a risk of missed diagnoses. Ultrasound, though not routinely used in this context, has recently emerged as a promising alternative. It is accurate, non-invasive, radiation-free, and allows for bedside assessment without moving the infant, thus reducing the risk of aggravating the fracture. Studies have shown its efficacy in detecting rare injuries such as Salter-Harris type I fractures of the distal humerus (14). Moreover, a recent meta-analysis highlighted its high reliability in diagnosing neonatal clavicle fractures, suggesting that ultrasound could be considered a new gold standard in selected cases (15).

Finally, findings from our review demonstrate that the vast majority of neonatal long bone fractures heal without permanent sequelae when managed conservatively, as in the case presented. This aligns with the literature emphasizing that prompt and appropriate treatment, such as immobilization or traction, is typically sufficient to achieve favorable outcomes. Surgical intervention was required in a residual number of cases, reflecting its limited necessity in this population (13, 16). From a medico-legal perspective, even if negligence on the part of healthcare professionals were to be established, the resulting claims for personal injury would generally be limited to minor temporary consequences. In only the rarest cases would there be minimal, permanent functional impairments, like transient paresthesia or Occasional pain during sports activities (13).

## 6 Conclusion

Neonatal long bone fractures are uncommon but can occur even in the absence of predisposing genetic or metabolic conditions. While most cases do not require surgical intervention and heal without permanent sequelae, accurate radiological assessment is essential to

ensure prompt and appropriate management. Failure to establish a timely diagnosis and initiate proper treatment may expose healthcare providers and institutions to potential medico-legal liability, both in relation to the delivery process and the immediate postnatal care of the newborn.

The results of this review show how in many cases there is a significant diagnostic delay and therefore greater clinical and medical-legal risk (17), for this reason the knowledge of this study can allow greater awareness of the operators and timely intercept a possible fracture avoiding further damage and, in many cases, prevent them.

## Data availability statement

The datasets presented in this article are not readily available. Requests to access the datasets should be directed to [fava.ludovico@gmail.com](mailto:fava.ludovico@gmail.com).

## Ethics statement

Written informed consent was obtained from the minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

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