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The impact of the implementation of clinical risk management tools in Pediatric or Neonatal Intensive Care Units: a systematic review.

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Abstract: Clinical risk management is a key area in terms of healthcare quality, especially within intensive-care settings and in the case of pediatric patients. The objective of this review is to assess the impact of tools for clinical risk management in pediatric intensive-care settings. Pubmed and Web of Science were queried to carry out a systematic review, using the PICO methodology (June 2019). Primary studies of applicative experiences of clinical risk management that had impacts in pediatric intensive care units were included. A total of 1178 articles were reviewed and 20 were included. Reactive risk management tools were used in 10 studies; proactive tools in 7; both reactive and proactive tools in 3. Sixteen studies out of 20 concerned drugs; other topics included: transition from hospital to primary care, hand hygiene, organizational aspects, human milk administration. Seven studies (35%) reported organizational impacts; Ten studies (50%) reported clinical and organizational impacts; Three studies (15%) reported organizational, clinical and economic impacts. The introduction of clinical risk management tools resulted in changes within the setting considered; combined use of reactive and proactive methodologies was highlighted in various studies, as well as an increasing focus on proactive tools, both drawing a growing trend over time.

Keywords: Clinical Risk Management; Safety; Pediatric Intensive Care Unit

Abstract: La gestione del rischio clinico è una funzione fondamentale per la qualità dei servizi sanitari, soprattutto nei setting ad alta intensità di cure ed in special modo per i pazienti pediatrici. Lo scopo di questa revisione è stato quello di valutare l'impatto dell'applicazione di strumenti di gestione del rischio clinico nelle terapie intensive pediatriche o neonatali. È stata condotta una revisione sistematica della letteratura, utilizzando la metodologia PICO, e sono stati interrogati i database di Pubmed e Web of Science (giugno 2019). Sono stati inclusi studi primari che riportassero l'impatto dell'applicazione di strumenti di gestione del rischio clinico nelle terapie intensive pediatriche o neonatali. Sono stati esaminati un totale di 1178 articoli e sono stati inclusi 20 articoli. Strumenti di risk management reattivi sono stati rilevati in 10 studi; strumenti proattivi in 7 studi; 3 studi riportavano l'applicazione sia di strumenti reattivi che di strumenti proattivi. Sedici studi riguardavano la gestione del rischio legato ai farmaci, altri ambiti riportati concernevano la transizione ospedale-territorio, l'igiene delle mani, la gestione del latte ed altri aspetti di natura organizzativa. Sette studi (35%) riportavano impatti organizzativi, 10 studi (50%) impatti sia clinici che organizzativi, tre studi (15%) riportavano impatti organizzativi, clinici ed economici. L'introduzione di strumenti di risk management ha avuto ripercussioni significative nel contesto considerato; l'uso combinato di strumenti reattivi e proattivi è stato evidenziato in vari studi, di pari passo al crescente interesse per gli strumenti proattivi, che è risultato in continuo aumento.

Keywords: Gestione del Rischio Clinico; Sicurezza; Unità di Terapia Intensiva Pediatrica

Introduction

According to the World Health Organization (WHO), an adverse event (AE) is defined as "an injury related to medical management, in contrast to complications of the disease"[1]. AEs may be preventable or non-preventable, with the former being caused by an error or other type of systems or equipment failure[2]. Clinical risk defines the probability of an AE occurring to a patient.

The 1999 "To err is human: Building a Safer Health System" report brought to light that 2-4% of deaths in the US were caused by preventable medical errors[3], which caused patient safety to gradually acquire the well-deserved relevance. Clinical risk management specifically is concerned with improving the quality and safety of health-care services by identifying the circumstances that put patients at risk of harm and acting to prevent or control those risks[4].

Clinical risk management activities are performed according to two main approaches: reactive, that is retrospectively analyzing incidents, in order to obtain information useful for improving healthcare processes safety; or proactive, that is analyzing organizational processes and their critical points to act on high-risk steps before an incident takes place[5].

Among reactive tools are incident reporting (IR), root cause analysis (RCA) and medical record review (MRR). The first is a method for systematically collecting data about incidents and near misses, as reported directly by operators who witnessed the event; the second is an analysis tool that focuses on causes behind the event that occurred, based on an inductive procedure; the third consists in analyzing medical records to identify indicators of adverse events. Failure Mode and Effect Analysis (FMEA), originally deployed in the industrial sector, but recently brought to the healthcare area, is an example of a proactive tool[6]. It allows to forecast potential errors, based on the analysis of each phase within the process of interest. FMECA (Failure Mode, Effects, and Criticality Analysis) methodology consists of two separate analyses: FMEA, and Criticality Analysis (CA), which ranks the significance of potential failures according to the failure rate, the severity of the failure consequences and the likelihood of detection[7]

The healthcare activities carried out in intensive care units (ICUs) often have to do with multiple urgent interventions for high-risk patients in a greatly complex and stressful environment[8], which exposes them to a high frequency of errors [9,10].

Pediatric patients have peculiar features that make them particularly exposed to AEs and to their consequences[11]: for example, specifically focusing on medication errors, pediatric patients need weight-based dosing[12], which may be a source of error[9].

Research has shown how dramatically frequent are AEs in Pediatric ICUs[13,14]. Indeed, it has been reported a rate of 2.86 AEs per 1,000 patient days in Pediatric ICUs with 62% of patients experiencing at least one AE during their hospital stay; 45% of those AEs were preventable[13].

Other reviews, before this one, have analyzed errors and clinical risk management in pediatric or neonatal ICUs, focusing mainly on defined management approaches (mainly on reactive tools such as incident reporting)[15] or focusing on a specific management tool[16] and therefore evaluating a specific impact; the results of those studies are therefore potentially limited in their generalizability to other tools and other approaches. To our knowledge, this review is the first systematic review that aims to examine the clinical and organizational impacts achieved through the application of clinical risk management tools and methods, whether reactive or proactive, in pediatric and neonatal ICUs. This review is therefore addressed to all stakeholders involved in clinical risk management and in the clinical and organizational activity of pediatric and neonatal ICUs.

Materials and Methods

A systematic review was performed according to the PRISMA statement[17] in order to summarize the existing literature about the impact of the implementation of clinical risk management tools in Pediatric or Neonatal Intensive Care Units (ICUs).

2.1. Search strategy

In order to specify the elements of the research question, the PICO (Population, Intervention, Comparison/ Control, Outcome) model was used: (P) Pediatric or Neonatal ICUs' healthcare professionals, patients and processes; (I) implementation of clinical risk management tools; (C) no clinical risk management tools implementation; (O) impact of clinical risk management tools implementation.

PubMed and Web of Science databases were queried using the following search string:

((personnel OR staff OR employee OR healthcare professional OR "healthcare professional" OR patient OR process) AND (clinical risk OR "clinical risk" OR injury OR damage OR hazard OR adverse event OR "adverse event" OR error) AND (clinical risk management OR "clinical risk management" OR "risk control" OR "risk assessment" OR "risk analysis" OR "Risk Management" OR "root cause analysis" OR rca OR FMECA OR FMEA OR decision making OR decision-making OR "Clinical Decision-Making" OR IDEF OR "Cognitive task analysis" OR HAZOP OR "Adverse Outcome Pathways" OR "Healthcare Failure Mode and Effect Analysis") AND ("Intensive Care Units" OR "Critical Care" OR ICU OR CCU) AND (Impact OR safety OR outcome OR improvement OR performance OR experience OR development) AND pediatric)

2.2. Inclusion/Exclusion criteria

The search was limited to articles focused on clinical risk management tools application experiences in Pediatric or Neonatal ICUs published from 1 January 1995 to 31 may 2019 (date of the last search made), in Italian or English language, with available full-text. Systematic reviews, editorials, commentaries, articles that did not report impacts of clinical risk management implementation were not included.

2.3. Selection process and Data synthesis

According to the PRISMA protocol, the selection of articles was performed independently by two researchers, who also carried out the data extraction; in the event of a disagreement, a third researcher has been involved as final juror. Data were collected into a database and summarized in a table reporting for each article: authors, title, year of publication, country, study design, risk management approach, risk management tool used, domain, aims, reported errors, main results and impacts, limitations, quality assessment. The software used was Microsoft Excel.

2.4. Quality appraisal

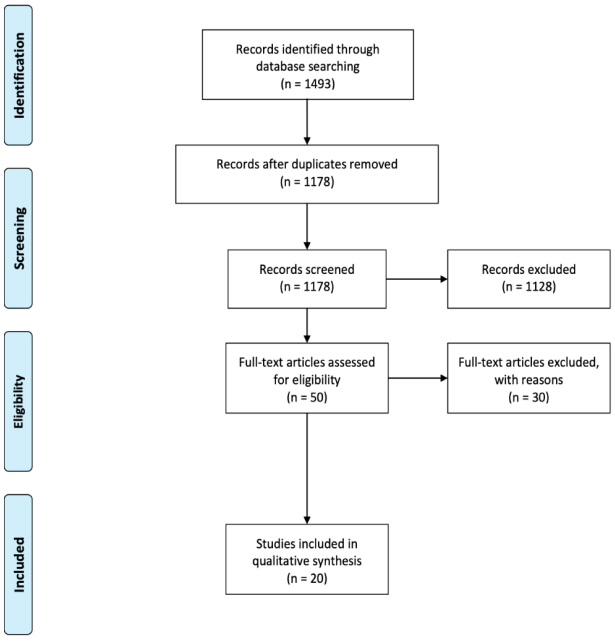
Quality appraisal was carried out through the application of the following scales, published by the US National Heart, Lung and Blood Institute: "Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group"; "Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies"[18]. The scales included items for evaluating potential flaws in study methods or implementation, including sources of bias, confounding, study power, the strength of causality in the association between interventions and outcomes, and other factors. Quality reviewers could select "yes," "no," or "cannot determine/not reported/not applicable" in response to each item on the scale[19]. The quality judgment was formulated on the basis of the three score tertile achieved on the evaluation scale by the included paper (poor, fair, good).

Two researchers independently assessed studies' quality and eventual disagreements were overcome through discussion and, if necessary, through the involvement of a final juror.

Results

Bibliographic search resulted in 750 articles from PubMed and 743 from Web of Science, with duplicates removal leading to 1178 articles. From title and abstract evaluation, 1128 studies were excluded. After assessing the remaining 50 articles, 30 more were excluded. Thus, 20 articles[20–39] were included in the review, according to the inclusion/exclusion criteria.

Figure 1 depicts the process of studies selection.



Publication years of the included studies ranged from 1998[20] until 2018[39]. Ten studies (50%) were from Europe[20,21,23,28,30,31,33–36], 6 (30%) from US[22,25,27,29,32,37], the remaining studies from Australia[26] (1 study, 5%), Brazil[39] (1 study, 5%), Israel[38] (1 study, 5%), New Zealand[24] (1 study, 5%). Based on the study design, 11 studies (55%) were classified as before-after studies[22,23,25,27,30–32,34–36,38], 6 (30%) as observational prospective studies[20,21,26,33,37,39], and 3 (15%) as cross-sectional[24,28,29].

Reactive risk management tools were used in 10 out (50%) of 20 studies[20,21,23,25–27,30,31,33,38] (some of those studies reported use of multiple reactive tools[27,33]), whereas proactive risk management tools were utilized in 7 out of 20 studies[22,24,28,29,32,34,39] (35%). Three out of 20 studies (15%) included both proactive and reactive methods[35–37]. Regarding the implemented tools, medical records review was employed in 6 studies[23,26,27,30,31,38] (30%), incident reporting in 9[20,21,23,25,27,33,35–37] (45%), FMEA/FMECA in 10[22,24,28,29,32,34–37,39] (50%), RCA in 2 studies[33,37] (10%). Fifteen studies reported the implementation of 1 tool[20–26,28–32,34,38,39] (75%), 4 studies of 2 tools[27,33,35,36], (20%), 1 study of 3 tools[37] (5%) (Table 1).

Sixteen out of 20 studies (80%) concerned clinical risk management related to drugs[20–28,30,31,34–36,38,39] the remaining studies were focused on other topics: transition from hospital to primary care[29] (1 study, 5%), hand hygiene[32] (1 study, 5%), organizational aspects[33] (1 study, 5%) human milk administration[37] (1 study, 5%).

As to the type of impact attained, 7 studies (35%) reported organizational impacts[21,22,24,26,29,33,36]; 10 studies (50%) reported clinical and organizational impacts[20,23,25,27,30,31,34,35,37,38]; 3 studies (15%) reported economic, clinical and organizational impacts[28,32,39].

The main characteristics and findings of the studies are summarized in Table 1, based on chronological order of manuscript; information shown in the table concerns: author, title, year, Country, study design, risk management approach, risk management tools, domain, aims, reported errors, main results, main impacts, limitations, quality assessment.

Regarding quality assessment results, 8 studies[23,25,27,30–32,35,38] were found to be of good quality; 12 studies[20–22,24,26,28,29,33,34,36,37,39] were found to be of fair quality. Details about quality assessment are shown in Tables 2 and Table 3.

Temporal trend of the use of each Clinical Risk Management tool is shown in figure 2. This is the trend of scientific publications relating to the application experiences of risk management tools in the setting considered by us. This trend reflects both the application use of tools and the interest of the scientific community on certain topics. The first clinical risk management tools applied in the pediatric intensive care setting were reactive tools[20,21]; since 2004[22], proactive risk management tools have been introduced with increasing frequency: looking at years from 1998 to 2009, only 2 studies[22,24] out of 8 (25%) applied proactive tools, whereas from 2010 to 2018, 8 studies[28,29,32,34–37,39] out of 12 (67%) did. All the studies that utilized more than one tool[27,33,35–37] were carried out from 2009 on, with 4[33,35–37] out of 5 being carried out in 2014 or later.

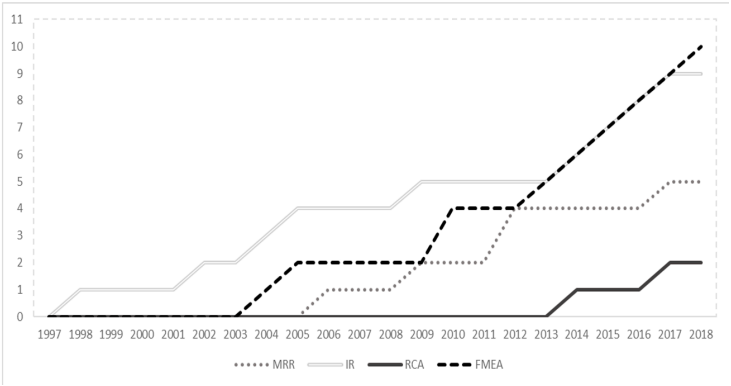


Table 1. *Characteristics of included studies*

N°	Author	Title	Year	Country	Study Design	Risk Management Approach	Risk Management Tools	Domain	Aims	Reported Errors	Main Results	Main Impacts	Limitations	Quality Assessment
1	Wilson et al.[20]	Medication errors in pediatric practice: insights from a continuous quality improvement approach.	1998	UK	Observational prospective studies	Reactive	Incident Reporting	Drugs	To assess the incidence and consequences of medication errors in a pediatric cardiac ward and a pediatric cardiac ICU and implemented changes in practice to prevent them	68% of reported errors were prescription errors and 25% administration errors.	Implementation of a Medication Error Committee periodically updating the unit staff on recommended changes in practice; Errors decreased in the second year of the study with a rate ratio of 0.44 for serious errors (95% CI = 0.29-0.66), 0.39 for administration errors (95% CI = 0.26-0.59) and 0.71 for the total number of reported errors (95% CI = 0.59-0.85). No change was registered in prescription errors (their rate doubled during months when a new junior doctor joined the team).	Clinical; Organizational.	Potential underreporting	FAIR
2	Frey et al.[21]	Does critical incident reporting contribute to medication error prevention?	2002	Switzerland	Observational prospective studies	Reactive	Incident Reporting	Drugs	To analyze medication-related critical incidents and their contribution to system changes in a neonatal-pediatric ICU	Catecholamines were most frequently involved in critical incidents (11% of reports); sedative drugs had the highest Mean Severity Score.	Introduction of standardized prescription form, compulsory double-checking for harmful drugs, new labelling of infusion syringes, guidelines.	Organizational	System changes specific to the context; no impact on outcomes reported	FAIR
3	Apkon et al.[22]	Design of a safer approach to intravenous drug infusions: failure mode effects analysis.	2004	USA	Before-After	Proactive	FMEA	Drugs	To improve patient safety and staff workflow efficiency in a pediatric ICU	NA	Redesign of drug infusion process; fewer infusions were prepared by nurses	Organizational	Actual failure rates not measured; no comparison of resources used in the two processes	FAIR
4	Simpson et al.[23]	Reducing medication errors in the neonatal intensive care unit	2004	UK	Before-After	Reactive	Incident Reporting	Drugs	To analyze medication errors in neonatal ICU	Parenteral drugs were involved in 60% of errors; poor prescribing underlay 71% of errors. Newly-hired medical staff was associated with	Introduction of prescription review by clinical pharmacist; educational program; changes in practice. Errors decreased: medication errors fell from 24.1 per 1000 neonatal activity days to 5.1 per 1000 days (p <0.001).	Clinical; Organizational.	Difficult to quantify the proportion of errors reduced by any one change in practice	GOOD

										an increase in medication errors (p=0.037).				
5	Kunac et al.[24]	Identification of priorities for medication safety in neonatal intensive care	2005	New Zeland	Cross Sectional	Proactive	FMEA	Drugs	To identify and prioritize potential failures in the Neonatal ICU medication use	The highest frequency of potential failures was found in prescription and administration phases (the majority of the 30 highest Risk Priority Scores was associated with administration); the majority of failures was caused by organizational factors.	Identification of priority measures to improve safety: medication safety training, use of oral syringes, safe storage of medications, monthly audits of medication charts	Organizational	FMEA limited to serious events; no Inclusion of a lay-per- son on their panel	FAIR
6	Larsen et al.[25]	Standard drug concentrations and smart-pump technology reduce continuous-medication-infusion errors in pediatric patients	2005	USA	Before-After	Reactive	Incident Reporting	Drugs	To analyze medication-infusion errors in a neonatal ICU	Infusion errors	Introduction of standard drug concentrations and Smart Pumps; Errors decreased: from 3.1 to 0.8 per 1000 doses for an absolute risk reduction of 2.3 errors per 1000 doses (95% CI = 1.1-3.4; p<0.001).	Clinical; Organizational.	Underreporting; impossible to determine the extent to which each individual intervention contributed to the reduction in error; little information on intervention impact on patient harm	GOOD
7	Dunn et al.[26]	Medical record review of deaths, unexpected intensive care unit admissions, and clinician referrals: detection of adverse events and insight into the system	2006	Australia	Observational prospective studies	Reactive	Medical Record Review	Drugs	To determine the insight provided by a continuous medical record review program in a large pediatric referral hospital	Operative, procedural, drug-related and intravenous fluid-related adverse events were detected	Implementation of education and training; Modification of clinical practice guidelines.	Organizational	The number of adverse events is not a true incidence of hospital-wide adverse events.	FAIR
8	Morriss et al.[27]	Effectiveness of a barcode medication administration system in reducing preventable adverse drug events in a neonatal intensive care unit: a prospective cohort study.	2009	USA	Before-After	Reactive	Medical Record Review; Incident Reporting	Drugs	To reduce drug adverse events in a neonatal ICU	NA	Introduction of a Bar Code Medication Administration System; The BCMA system reduced the relative risk of preventable adverse drug events by 47 to 50% (p=0.04).	Clinical; Organizational.	Observational design; limited generalization	GOOD
9	De Giorgi et al.[28]	Risk and pharmacoeconomic analyses of the injectable medication process in the paediatric and neonatal intensive care units.	2010	Switzerland	Cross Sectional	Proactive	FMECA	Drugs	To analyze safety risks in injectable drugs in pediatric and neonatal ICUs	The 10 most critical failure modes concerned mainly preparation, followed by administration and transcription	Generation of tools for continuous safety improvement; the safety gains predicted were: 1292 quali for ready-to-use syringes, 1201 for employment of a clinical pharmacist, 996 for double check by nurses and 984 for computerized physician order entry (1 quali= reduction of criticality index by one point) Cost-efficacy ratios of tools/measures were estimated	Organizational; Clinical Economic	Subjectivity of FMECA; impossible to assess the impact of a combination of multiple failures on a specific outcome; results not generalizable	FAIR
10	Moyer et al.[29]	Transitions from neonatal intensive care unit to ambulatory care: description and evaluation of the proactive risk assessment process.	2010	USA	Cross Sectional	Proactive	FMECA	Transition from hospital to primary care	To assess the risks of transition from the neonatal ICU to primary care	The main failure modes were neonatal ICU healthcare providers acting in isolation, inadequate preparation of parents, care-givers and community providers, lack of social support	Introduction of information sharing and specific education programs	Organizational	Conducted at a single institution; scoring matrix adapted from adult literature	FAIR
11	Martinez-Anton et al.[30]	Impact of an intervention to reduce prescribing errors in a pediatric intensive care unit.	2012	Spain	Before-After	Reactive	Medical Record Review	Drugs	To identify and reduce prescription errors in a pediatric ICU	There was a rate of deviation from good prescribing practice of 88.6%.	Standardization of prescription sources, pocket tables with dosing guidelines, prescription protocol, educational program; omission errors and readability errors had a statistically significant reduction, of 95.1 (p<0.001) and 87.5 % (p=0.002), respectively	Clinical; Organizational.	Hawthorne effect	GOOD

12	Booth et al.[31]	Zero tolerance prescribing: a strategy to reduce prescribing errors on the paediatric intensive care unit.	2012	UK	Before-After	Reactive	Medical Record Review	Drugs	To identify and reduce prescription error rate in a pediatric ICU	The baseline prescribing error rate was 892 errors per 1,000 pediatric ICU occupied bed days (OBDs) (95 % CI = 765–1.019).	New prescribing policy and introduction of daily error feedback; After the implementation of the combined two measures, a reduction in the prescribing error rate to 447 errors per 1,000 OBDs was registered (95 % CI = 389-504, p<0.0001), with an absolute risk reduction of 44.5 % (95 % CI = 40.8-48.0 %).	Clinical; Organizational.	Observational; non-blinded; restriction of data collection to weekdays; not using the most accurate denominator; errors not classified according to severity, outcome not determined; results not generalizable	GOOD
13	Song et al.[32]	Improving hand hygiene compliance in health care workers: Strategies and impact on patient outcomes	2013	USA	Before-After	Proactive	FMEA	Hand Hygiene	To analyze the impact of a systematic process for improving hand hygiene compliance among health care providers	NA	Strategic placement of hand sanitizers and implementation of educational programmes. Hand hygiene compliance rate increased from 48.6 % to 87% among physicians and from 46.5 % to 77.9% among nurses. When comparing hand hygiene compliance rates above 80% with rates below 80%, MRSA acquisition risk decreased by 48%. This reduction represents the prevention of 1.3 MRSA acquisitions per month, resulting in a saving of 11.6 NICU-days and $66,397 hospital charges	Clinical; Organizational; Economic.	Hand hygiene compliance not measured before clean/aseptic procedures and after body fluid exposure; analysis of the impact of hand hygiene on preventing MRSA acquisitions performed in a unit that had MRSA prevention measures	GOOD
14	van der Starre et al.[33]	Paediatric critical incident analysis: lessons learnt on analysis, recommendations and implementation	2014	Netherlands	Observational prospective studies	Reactive	Incident Reporting; RCA	Health work Organization	To analyze safety incidents in a pediatric ICU and a neonatal ICU	The most frequent contributing factors were related to teamwork (22%) and task factors (22%), followed by factors related to individual providers (20%), to work environment (19%), organizational factors (11%), and factors related to patient features (6%).	Development of recommendations (84, focusing on organizational factors, work environment, team and task factors) and their implementation (35% of 84, most related to task factors)	Organizational	Small number of incidents analyzed; thorough analysis of all reported critical incidents in the PICU not feasible	FAIR
15	Manrique-Rodriguez et al.[34]	Risks in the implementation and use of smart pumps in a pediatric intensive care unit: application of the failure mode and effects analysis.	2014	Spain	Before-After	Proactive	FMEA	Drugs	To identify risk points in the smart infusion pump implementation process	The highest risk scores were associated with failure to comply with protocols on standard concentrations and on administration times in intermittent infusions; slow data upload/update; slow download speed	Periodical reviews of the drug library, development of support documents, and system error alarms; Risk Points decreased, by 50-83%.	Organizational; Clinical.	Differences in smart pumps implementation from other examples in literature	FAIR
16	Daverio et al.[35]	Failure mode and effective analysis ameliorate awareness of medical errors: a 4-year prospective observational study in critically ill children.	2015	Italy	Before-After	Combined Reactive - Proactvive	Incident Reporting; FMEA	Drugs	To describe the trend of incident reporting in a pediatric ICU setting and to assess the effect of FMEA application on the number and severity of the errors detected	Medication errors reported concerned prescription in 83% of cases and preparation or administration in 17%.	Introduction of double check and sign; same references for standard doses and dilutions; use of a dedicated area during drug prescription. Changes in the number and severity of errors: 39,5% increase in reported errors (43 vs 26) with a reduction of their severity - 21% vs 8% near misses and 65% vs 38% errors with no outcome (p=0.004) - were reported. Moreover, a decrease in administration errors, an increase in prescription ones and a decrease in Risk Priority Numbers in any medication phase were observed	Clinical; Organizational.	Small sample of IR; real rate of incidents in our PICU; introduction of FMEA probably not the only factor determining change	GOOD
17	Arenas-Lopez et al.[36]	Safe implementation of standard concentration infusions in paediatric intensive care.	2016	UK	Before-After	Combined Reactive - Proactvive	Incident Reporting; FMEA	Drugs	To assess patient safety after the introduction of standard concentrations of morphine infusions in pediatric critical care	Failure modes with the highest Risk Score before the intervention were: incorrect prescription, wrong syringe selection, wrong weight band, wrong weight	Introduction of standard concentrations; Decrease of morphine-based as a percentage of total drug errors from 45% in the first year to 2.2% in the eighth year	Clinical; Organizational.	No robust electronic data capture for the years before the introduction of the standard concentrations; decrease in number of drug errors in the latter years following implementation may be due to a change in PICU reporting culture	FAIR

18	Oza-Frank et al.[37]	A Quality Improvement Project to Decrease Human Milk Errors in the NICU	2017	USA	Observational prospective studies	Combined Reactive - Proactvive	Incident Reporting; FMEA; RCA	Human Milk	To analyze a a quality improvement initiative which was associated with a decrease in human milk administration errors in a neonatal ICU setting	The most common errors identified were expired milk, wrong-milk-to-wrong-infant and preparation errors.	Human milk BCMA system and full-time milk technician. Errors decreased: from 2009 to 2015, the number of scanned errors declined from 97.1 errors per 1000 bottles to 10.8 for the whole number, from 84.0 per 1000 bottles to 8.9 for expired milk errors, from 4.8 per 1000 bottles to 2.2 for preparation errors, from 8.3 per 1000 bottles to 2.0 for wrong-milk-to-wrong-infant errors	Clinical; Organizational.	Limited generalizability; success influenced by culture of safety	FAIR
19	Kadmon et al.[38]	Case Not Closed: Prescription Errors 12 Years after Computerized Physician Order Entry Implementation	2017	Israel	Before-After	Reactive	Medical Record Review	Drugs	To identify and reduce medication prescription errors in pediatric intensive care patients	Prescription errors	Introduction of Computerized Physician Order Entry (CPOE) and Clinical Decision Support System (CDSS). The rate of prescription errors increased from 1.4% in 2007 to 3.2% in 2015 (p=0.03). A revision of the CDSS tools was brought about, the impact of which was a decrease in prescription errors rate to 1% (p<0.0001), a drop in potential adverse drug event rate from 2% to 0.7% (p=0.006), and in medication prescription error rate, from 1% to 0.2% (p=0.01).	Clinical; Organizational.	Observational; lack of control group	GOOD
20	Malfará et al.[39]	Impact of the clinical pharmacist interventions on prevention of pharmacotherapy related problems in the paediatric intensive care unit	2018	Brazil	Observational prospective studies	Proactive	FMEA	Drugs	To assess drug-related risks in the pediatric ICU to guide clinical pharmacist interventions	Seventy-five failure modes were identified by FMEA in the process of medication use in critically ill children (with the highest risks related to dispensing of medication and monitoring of drugs serum levels)	Clinical pharmacist interventions, with reduction of 16 failure modes; Cost Saving	Organizational; Economic; Clinical	Limited generalizability; impact of the clinical pharmacist interventions on the patients' clinical course not measured	FAIR

Table 2: *Quality Assessement for Before-After studies with no control group*

Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group

	Articles										
Criteria	**Apkon et al, 2004**	**Simpson et al, 2004**	**Larsen et al, 2005**	**Morriss et al, 2009**	**Martinez-Anton et al, 2012**	**Booth et al, 2012**	**Song et al, 2013**	**Daverio et al, 2015**	**Arenas-Lopez et al, 2016**	**Kadmon et al, 2017**	**Manrique-Rodriguez et al, 2014**
1. Was the study question or objective clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Were eligibility/selection criteria for the study population prespecified and clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Were all eligible participants that met the prespecified entry criteria enrolled?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Was the sample size sufficiently large to provide confidence in the findings?	NA	NA	NA	Yes	Yes	NA	NA	NA	NA	Yes	NA
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?	NR	NR	NR	No	No	No	NR	NR	NR	NR	NR
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA
EVALUATION	**FAIR**	**GOOD**	**GOOD**	**GOOD**	**GOOD**	**GOOD**	**GOOD**	**GOOD**	**FAIR**	**GOOD**	**FAIR**

Table 3: *Quality assessment for observational cohort and cross-sectional studies*

	Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies								
	Articles								
Criteria	**Wilson et al, 1998**	**Frey et al, 2002**	**Kunac et al, 2005**	**Dunn et al, 2006**	**De Giorgi et al, 2010**	**Moyer et al, 2010**	**Van der Starre, 2014**	**Oza-Frank et al, 2017**	**Malfará et al, 2018**
1. Was the research question or objective in this paper clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the study population clearly specified and defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Was the participation rate of eligible persons at least 50%?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Was a sample size justification, power description, or variance and effect estimates provided?	NA	NA	NA	NA	NA	NA	NA	NA	NA
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	NA	NA	NA	NA	NA	NA	NA	NA	NA

Beside a growing attention to the application of risk management tools in the setting considered, the systematic review also showed their effectiveness. Indeed, the application experiences of Risk Management tools described in the study often led to diverse measures being implemented in order to cut down errors. It is possible to consider the introduction of these measures as organizational impacts, among which are the introduction of standards[21,25,30,34–36], procedures[26] and automation[25,27,37,38], which emerges as a new key intervention in risk management, combined with further educational programs[23,24,26,30], aimed at emphasizing each professional's role within the healthcare process. As regards automation and Information Technology, there are numerous applications in the risk management domain, ranging from Bar Code Medication Administration System BCMA[27,37] to smart pumps[25] to Computerized Physician Order Entry System CPOE[38].

Our study also emphasized how risk management tools positively affect clinical aspects, with studies reporting, as a result of their implementation, decreases in number of errors [20,23,25,27,30,31,36–38], decreases in AEs[27], reduction of potential AEs[38], reduction of risk point scores [28,34,35], reduction of infections acquisition risk[32].

Most of the studies included in our review described risk management tools related to drugs. This specific focus is reasonably justified by the frequency and severity of AEs in this sphere [3,9,43], in addition to the known difficulties for the use of drugs in the pediatric population for various reasons, from the lack of specific clinical research, to posology, to aspects of pharmacokinetics and pharmacodynamics; tools and methodologies described for the management of drug errors are various and heterogeneous.

Several studies reported the relevance of staff and team experience with a specific focus on preventing errors, as newly-hired medical staff was associated with an increase in errors[20,23], as well as the value of multidisciplinary teams[20,22,24,26–29,31–37,39], particularly in detecting issues ranging from failure modes to instrument flaws to organizational aspects and consequently identifying interventional priorities. In some cases, an increase in reported errors has been described following the introduction of new clinical risk management tools[35] or implementation of new systems such as BCMA[27], which is attributed to the spread of risk-culture in one case[35], or to the higher detection capabilities of the new system[27]. Two studies[30,31] pointed out how the mere researcher observation could lead to an increase in patient safety over time, as a result of Hawthorne effect[30], consisting in subjects being studied changing their behavior purely in response to the fact they are being studied[41]. It is interesting to note that, in some experiences[35], the increase in the number of errors corresponds to a decrease in their severity, both in absolute and relative terms, suggesting the effectiveness of the tools applied both in detecting previously unrecognised errors and in improving patient safety.

To demonstrate that the effectiveness of risk management depends more on the application of an instrument, or rather the way in which an instrument is applied, than on the introduction of an instrument itself, the study by Kadmon et al[38] demonstrated an increasing rate of prescription errors (from 1.4% in 2007 to 3.2%, p=0.03) after the introduction of Computerized Physician Order Entry (CPOE) and Clinical Decision Support Sistem (CDSS), but, after a revision of the CDSS tools, prescription errors rate decreased to 1% (p<0.0001): the usefulness of CDSS in risk management has been demonstrated, but only on condition that it is applied appropriately.

Interestingly, one study[29] dealt with the transition from hospital to primary care, which is a fundamental area from an organizational appropriateness perspective, thus implying the wide range of potential proactive tools application to different healthcare levels and settings. This kind of issue represents a challenge for research and for the future organization of care activities, projecting clinical risk management into a care continuum that goes beyond the single episode of care.

Our review has some limits, but also some strengths. As for limits, all the included studies had an observational design, which is recognized as less robust than experimental one and more susceptible to bias. Furthermore, the high heterogeneity of the included studies did not allow us to perform a meta-analysis. Finally, none of the studies included a control group.

Concerning strengths, the systematic review was conducted according to a strict methodology; it covers a wide timespan, approximately twenty years, attempting to describe a constantly evolving scenario, with some studies indeed extending over a long period of time themselves[37,38]. Moreover, quality assessment of the included articles adds value and robustness to our review, even more so as all the included studies were assessed as fair or good quality. In light of the results of this systematic review and the above considerations, various reflections emerge needing further discussion. The reported experiences confirmed the importance of effective risk management tools implementation in the pediatric and neonatal intensive care setting. The available evidence, particularly studies focused on proactive tools, highlights the imperative of processes' safety level detection, in order to ultimately avoid and/or limit latent errors that might lead to accidents. Moreover, future risk management outlooks can be identified both at organizational and at a research level. The clear direction in the former case is marked by an increasing employment of proactive tools, which reliably allow to develop priority interventions, with highly successful impacts[34]. Furthermore such tools ought to be applied with a process management view and therefore from the perspective of the patient's whole clinical-care path through different settings, for which only one experience[29] was highlighted by our review. In this sense, it would be appropriate that the definition of pediatric and neonatal ICU risk management procedures/tools integrated with other healthcare levels/settings. Two other important aspects are represented by multidisciplinarity in risk management tools application, which is closely related to the previous one, and continuous staff education and training on the topic of specific risks associated to intensive care activities and their prevention. The development of a widespread risk culture is a pivotal component to achieve patient safety and increase detection of errors and incidents, as opposed to a still well-rooted blaming culture that often contributes to underreporting[23,24,26,30,42].

As far as research outlook is concerned, additional efforts are required to carry out experimental studies, which imply a lower risk of bias and allow to gain more targeted information. In addition, the fact that most of the studies included relate to the field of drugs makes the results in this particular field particularly consistent, but to the detriment of other particularities., However, a tendency to resort to risk management tools in different clinical activities should be encouraged, in an effort to broaden the areas of interest that could benefit from risk management initiatives.

Conclusions

The implementation of clinical risk management tools in pediatric intensive care units resulted in organizational, clinical and economic impacts, contributing not only to safety but to overall healthcare quality. Combined use of reactive and proactive methodologies had a growing trend over time, similarly to the increasing use of proactive tools.

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