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Faculty of Medicine

Department of Paediatrics, Obstetrics and Gynaecology, and Preventive Medicine and Public Health

PhD Program in Methodology of Biomedical Research and Public Health

DOCTORAL THESIS

DETECTION OF ERRORS IN HEALTH CARE AND EVALUATION OF PREVENTIVE MEASURES FOR PATIENT SAFETY

By Stefanie Chriss Suclupe Obregón

Supervisors: Dr Maria José Martinez-Zapata**,** Dr Gemma Robleda Font

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Barcelona, March 2023

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This thesis has been carried out under the supervision of Dr Maria José
Martinez-Zapata and Dr Gemma Robleda Font. It is presented as a compendium
of publications, with International Doctoral Research Component by the
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CONFLICTS OF INTEREST

The author declares that she has no conflicts of interest.

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Knowing is not enough; we must apply.

Willing is not enough; we must do it.

Goethe

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Abstract (English)

Introduction

Errors in clinical practice are a serious problem that may threaten the quality of care and patient safety, causing adverse events with harmful results. Human error is often a symptom of underlying system failures and is not primarily at fault when complex sociotechnical systems malfunction. Although many studies of interventions to prevent adverse events have been published, integrative information is necessary to guide evidence-informed decision-making.

Objectives

To analyse errors during the care process and evaluate the interventions to prevent adverse events in the hospital setting.

Methods

Three studies with different methodological designs were performed. First, to explore systems factors contributing to patient identification errors during intra-hospital transfers, a qualitative study was conducted. Second, to determine the prevalence and magnitude of medication errors and their association with patients' sociodemographic and clinical characteristics and nurses' work conditions, a cross-sectional study was undertaken. Third, to provide an overview of the effectiveness of non-pharmacological interventions aimed at preventing adverse events in the intensive care unit (ICU), a review of systematic reviews was carried out.

Results

In the qualitative study, patient identification processes did not have a uniform practice and were different from the institutional policies, particularly regarding effective and active transfer communication. The positive patient identification (PPID) process was not designed to catch failures, and not all staff were trained in this process or had knowledge of it. We also noticed that the current way of PPID is a delicate balance of all interacting studied components.

In the cross-sectional study, over half of the cases observed had medication errors in the prescription and administration of drugs, with a relevant magnitude of the error, and the nurse's workload perception was associated with an interruption during drug administration.

In the review of systematic review, some non-pharmacological interventions reduced adverse events in ICU; however, the overall methodological quality was critically low. Despite a slight overall overlap in this overview, our assessment at the outcome level showed a high overlap for some effective interventions.

Conclusions

People/teams, tools/technologies, and organisation are the main human factors involved in patient misidentification; therefore, a design adapted to current practice that integrates human factors and ongoing critical assessment is needed. Medication errors in prescription and administration still have a high prevalence, and most of them could be preventable. It is important that healthcare staff be trained to deal with interruptions and technological factors. There are nonpharmacological interventions that reduce adverse events in the intensive care setting. However, it is necessary to improve the research to deliver the safest care, so the best evidence can be incorporated into decision-making and be transferred into clinical practice.

Resumen (Español)

Introducción

Los errores en la práctica clínica son un grave problema que puede amenazar la calidad de la atención y la seguridad del paciente, provocando eventos adversos con resultados nocivos. El error humano es a menudo un síntoma de fallas subyacentes del sistema y no es el principal culpable cuando los sistemas sociotécnicos complejos funcionan mal. A pesar de que se han publicado muchos estudios de intervenciones para prevenir eventos adversos, se necesita información sintetizada para guiar la toma de decisiones basada en evidencia.

Objetivos

Analizar los errores durante el proceso de atención y evaluar las intervenciones para prevenir los eventos adversos en el ámbito hospitalario.

Métodos

Se realizaron tres estudios con diferentes diseños metodológicos. En primer lugar, se realizó un estudio cualitativo para explorar los factores del sistema que contribuyen a los errores de identificación de los pacientes durante los traslados intrahospitalarios. En segundo lugar, se realizó un estudio transversal para determinar la prevalencia y magnitud de los errores de medicación y su asociación con las características sociodemográficas y clínicas de los pacientes y las condiciones de trabajo de las enfermeras. En tercer lugar, se realizó una revisión de revisiones sistemáticas para brindar una visión general de la efectividad de las intervenciones no farmacológicas dirigidas a la prevención de eventos adversos en la unidad de cuidados intensivos (UCI).

Resultados

En el estudio cualitativo, los procesos de identificación de pacientes no tenían una práctica uniforme y eran diferentes a las políticas institucionales, particularmente en lo que se refiere a la comunicación de transferencia efectiva y activa. El proceso de identificación positiva de pacientes (PPID, por sus siglas en inglés) no fue diseñado para detectar fallas, y no todo el personal estaba capacitado en este proceso o tenía conocimiento de él. También notamos que la forma actual de PPID es un delicado equilibrio de todos los componentes del sistema que interactúan.

En el estudio transversal, más de la mitad de los casos observados presentaban errores de medicación en la prescripción y administración de medicamentos, con una magnitud del error relevante, y la percepción de la carga de trabajo del enfermero se asoció a una interrupción durante la administración de medicamentos.

En la revisión de la revisión sistemática, algunas intervenciones no farmacológicas redujeron los eventos adversos en la UCI; sin embargo, la calidad metodológica general fue críticamente baja. A pesar de una ligera superposición general en esta revisión, nuestra evaluación a nivel de desenlace mostró una alta superposición para algunas intervenciones efectivas.

Conclusiones

Las personas/equipos, las herramientas/tecnologías y la organización son los principales factores humanos involucrados en la identificación errónea del paciente; por lo tanto, se necesita un diseño adaptado a la práctica actual que integre los factores humanos y la evaluación crítica continua. Los errores de medicación en la prescripción y administración siguen teniendo una alta prevalencia, y la mayoría de ellos podrían ser prevenibles. Es importante que el personal de salud esté capacitado para hacer frente a las interrupciones y factores tecnológicos. Existen

intervenciones no farmacológicas que reducen los eventos adversos en el entorno de cuidados intensivos. Sin embargo, es necesario mejorar la investigación para brindar la atención más segura, de modo que la mejor evidencia pueda incorporarse en la toma de decisiones y transferirse a la práctica clínica.

Résumé (Français)

Introduction

Les erreurs dans la pratique clinique sont un problème grave qui peut menacer la qualité des soins et la sécurité des patients, provoquant des événements indésirables avec des résultats néfastes. L'erreur humaine est souvent un symptôme de défaillances sous-jacentes du système et n'est pas le principal responsable du dysfonctionnement de systèmes sociotechniques complexes. Malgré le fait que de nombreuses études sur les interventions visant à prévenir les événements indésirables ont été publiées, des informations synthétisées sont nécessaires pour guider la prise de décision fondée sur des preuves.

Objectifs

Analyser les erreurs au cours du processus de soins et évaluez les interventions pour prévenir les événements indésirables en milieu hospitalier.

Méthodes

Trois études avec des conceptions méthodologiques différentes ont été menées. Premièrement, une étude qualitative a été menée pour explorer les facteurs systémiques qui contribuent à l'identification erronée des patients lors des transferts intra-hospitaliers. Dans un deuxième temps, une étude transversale a été réalisée pour déterminer la prévalence et l'ampleur des erreurs médicamenteuses et leur association avec les caractéristiques sociodémographiques et cliniques des patients et les conditions de travail des infirmières. Troisièmement, une revue des revues systématiques a été réalisée pour donner un aperçu de l'efficacité des interventions non pharmacologiques visant à prévenir les événements indésirables dans l'unité de soins intensifs (USI).

Résultats

Dans l'étude qualitative, les processus d'identification des patients n'avaient pas une pratique uniforme et étaient différents des politiques institutionnelles, notamment en ce qui concerne une communication de transfert efficace et active. Le processus d'identification positive du patient (PPID) n'a pas été conçu pour détecter les échecs, et tout le personnel n'a pas été formé ou conscient de ce processus. Nous notons également que la forme actuelle de PPID est un équilibre délicat de tous les composants du système en interaction.

Dans l'étude transversale, plus de la moitié des cas observés présentaient des erreurs médicamenteuses dans la prescription et l'administration des médicaments, avec une ampleur d'erreur pertinente, et la perception de la charge de travail de l'infirmière était associée à une interruption lors de l'administration des médicaments.

Dans la revue systématique, certaines interventions non pharmacologiques ont réduit les événements indésirables en USI ; cependant, la qualité méthodologique globale était extrêmement faible. Malgré un léger chevauchement global dans cette revue, notre évaluation au niveau des résultats a montré un chevauchement élevé pour certaines interventions efficaces.

Conclusion

Les personnes/équipements, les outils/technologies et l'organisation sont les principaux facteurs humains impliqués dans l'identification erronée des patients ; par conséquent, une conception adaptée à la pratique actuelle qui intègre les facteurs humains et une évaluation critique continue est nécessaire. Les erreurs de prescription et d'administration de médicaments continuent d'être très répandues et la plupart d'entre elles pourraient être évitées. Il est important que le personnel de

santé soit formé pour faire face aux interruptions et aux facteurs technologiques. Il existe des interventions non pharmacologiques qui réduisent les événements indésirables dans le cadre des soins intensifs. Cependant, il est nécessaire d'améliorer la recherche pour fournir les soins les plus sûrs, afin que les meilleures preuves puissent être intégrées dans la prise de décision et transférées à la pratique clinique.

Resum (Catalá)

Introducció

Els errors en la pràctica clínica són un greu problema que pot amenaçar la qualitat de l'atenció i la seguretat del pacient, provocant esdeveniments adversos amb resultats nocius. L'error humà és sovint un símptoma de falles subjacents del sistema i no és el principal culpable quan els sistemes socio-técniques complexos funcionen malament. A pesar que s'han publicat molts estudis d'intervencions per a prevenir esdeveniments adversos, es necessita evidència sintetitzada per a guiar la presa de decisions basada en l'evidència.

Objectius

Analitzar els errors durant el procés d'atenció i avaluar les intervencions per prevenir esdeveniments adversos a l'àmbit hospitalari.

Mètodes

Es van realitzar tres estudis amb diferents dissenys metodològics. En primer lloc, es va realitzar un estudi qualitatiu per a explorar els factors del sistema que contribueixen als errors d'identificació dels pacients durant els trasllats intrahospitalaris. En segon lloc, es va realitzar un estudi transversal per a determinar la prevalença i magnitud dels errors de medicació i la seva associació amb les característiques sociodemogràfiques i clíniques dels pacients i les condicions de treball de les infermeres. En tercer lloc, es va realitzar una revisió de revisions sistemàtiques per a brindar una visió general de l'efectivitat de les intervencions no farmacològiques dirigides a la prevenció d'esdeveniments adversos a les unitats de cures intensives (UCI).

Resultats

A l'estudi qualitatiu, els processos d'identificació de pacients no tenien una pràctica uniforme i eren diferents a les polítiques institucionals, particularment pel que fa a la comunicació de transferència efectiva i activa. El procés d'identificació positiva de pacients (PPID, per les seves sigles en anglès) no va ser dissenyat per a detectar falles, i no tot el personal estava capacitat en aquest procés o tenia coneixement d'ell. També notem que la forma actual de PPID és un delicat equilibri de tots els components del sistema que interactuen.

A l'estudi transversal, més de la meitat dels casos observats presentaven errors de medicació en la prescripció i administració de medicaments, amb una magnitud de l'error rellevant, i la percepció de la càrrega de treball de l'infermer es va associar a una interrupció durant l'administració de medicaments.

A la revisió de la revisió sistemàtica, algunes intervencions no farmacològiques van reduir els esdeveniments adversos a l'UCI; no obstant això, la qualitat metodològica de les revisions en general va ser críticament baixa. Malgrat una lleugera superposició general en aquest revisió, la nostra avaluació a nivell de desenllaç va mostrar una alta superposició per a algunes intervencions efectives.

Conclusions

Les persones/equips, les eines/tecnologies i l'organització són els principals factors humans involucrats en la identificació errònia del pacient; per tant, es necessita un disseny adaptat a la pràctica actual que integri els factors humans i l'avaluació crítica contínua. Els errors de medicació en la prescripció i administració continuen tenint una alta prevalença, i la majoria d'ells podrien ser previsibles. És important que el personal de salut estigui capacitat per a fer front a les interrupcions i factors tecnològics. Existeixen intervencions no farmacològiques que redueixen els

esdeveniments adversos a l'entorn de les unitats de cures intensives. No obstant això, és necessari millorar la recerca per donar una atenció més segura, de manera que la millor evidència pugui incorporar-se a la presa de decisions i transferir-se a la pràctica clínica.

INTRODUCTION

1. INTRODUCTION

1.1. QUALITY OF CARE

Patient quality of care is one of the major concerns in modern medicine and is considered an essential feature of healthcare. Medical science and technology have advanced rapidly, and the healthcare system has become more complex due to the diversity of tasks involved in the delivery of patient care. However, an efficient healthcare system must ensure quality in the entire care process.[1,2]

Donabedian defined quality as "the ability to achieve desirable objectives using legitimate means".[3] The Agency for Healthcare Research and Quality (AHRQ) defines quality as "doing the right thing at the right time for the right person and having the best possible result". Over the years, people have used this term to characterise healthcare aspects.[4]

Donabedian postulated that quality of care is related to the process of care in all its parts. The goal of high-quality care is to maximise patients' welfare according to their expectations after balancing the gains and losses of the care process.[5] In 2010, The European Commission stated that good quality of care means health care that is effective, safe and responds to the needs and preferences of patients.[6]

The World Health Organization (WHO) defines the quality of care as the degree to which health services for individuals and populations increase the likelihood of desired health outcomes. It is based on evidence-based professional knowledge and is critical for universal health coverage.[7]

The definition of healthcare quality is a dynamic concept that changes over time; it is broad and varies according to the level at which it is assessed. The quality of health services, including preventive, acute, chronic and palliative care, should be effective, safe and people-centred. However, the quality of the healthcare system should focus on improved health, responsiveness, financial protection, and efficiency.[1]

1.1.1. The relevance of health care quality

In 1999 the report "To err is human" describes the quality of health care in the United States and how to achieve a threshold change in quality.[8] Quality became an issue at the international level only recently. For a long time, it was presumed that all care was of good quality, and the skills and practices in medical care were not called into question. It was only when studies and projects started to demonstrate the huge heterogeneity in medical processes and procedures, often associated with variations in clinical outcomes, as well as the high number of adverse events and medical errors, that it brought to the forefront of international attention.[9,10]

The modern quality in health care movement commenced with the publication "Crossing the Quality Chasm" by The Institute of Medicine (IoM) in the United States. This report proposed six domains for health care improvement: safe, effective, patient-centred, timely, efficient, and equitable, which should be measured by patient-desired outcomes.[11] Furthermore, the kin-centred care model has been introduced to emphasise the shared humanity of people involved in the interdependent work and to be a broader concept ensuring person-centred care rather than a separate component.[12]

More recently, the WHO has established that high-quality health services should include integration of care as one more domain, and all of them should operate inter-related in health care services.

Figure 1 visualises the seven domains to achieve quality in healthcare.[7,13] Furthermore, the core values of kindness, compassion, respect, dignity, partnership and holistic care should be inherent in health care.[14]

Figure 1. Seven domains for quality in health care

Source: Adapted from WHO, 2020[7]

In the last years, more than 5.0 million deaths have been estimated in low-and middle-income countries due to poor health care quality, representing up to 15% of overall deaths in these countries.[15,16] In most European countries, people's perceptions of the quality of healthcare services in hospitals were rated lower than in primary care.[17] This situation reduces the value of universal health, and people will not be confident in poor quality health services that lead to unexpected health outcomes. In contrast, high-quality health services attract public support, contributing to governments' sustained financing.[16]

In 2015, all the countries in the United Nations adopted the 2030 agenda for sustainable development, which included "ensuring healthy lives and promoting well-being for all at all ages" with a global commitment to advancing universal health coverage (UHC).[18] Quality in health care services is crucial in reaching this goal while ensuring access to safe, effective, and affordable essential medicines without exposing the user to financial hardship because when someone needs medical care, the worst quality is no care at all.[19]

Quality does not come automatically; it requires a culture of quality for sustainable and meaningful change that involves leadership at all levels, transparency, people-centredness, measurement and generation of information, and investment in the workforce.[2]

A commonly cited concept to address the quality of health services is the Juran trilogy which consists of three interrelated processes: *planning, assuring and improving quality*, all of which must be present in a quality strategy.[20] Although it is known that quality is considered a priority in national programs, it is important that methods and interventions address these three imperatives: *Planning for quality,* having the right policies in place to ensure the need of individuals and

populations are met; *assuring quality*, having control mechanism to ensure that services are fulfilling stated requirements for quality; and *improving quality*, using appropriate approaches for changing behaviours and implementing measurable changes, to make health services more effective, safe and people-centred.[21] Based on this trilogy, the member countries of WHO-Europe defined three domains: *legislation and regulation, monitoring and measurement, and assuring and improving the quality of healthcare services and healthcare systems* to guide governments in their identification and assessment of interventions to improve national quality strategies.[22]

1.1.2. Quality improvement

Quality improvement is the action of every person working to implement iterative, measurable changes to make health services more effective, safe and people-centred.[23] This starts with identifying an issue using various approaches and methods and implementing strategies to improve quality. Numerous strategies have emerged over the years to ensure or improve the quality of care and make a difference to patients by improving safety, clinical effectiveness, and care experience.[24,25]

The Donabedian model can be a useful approach to conceptualising quality improvement. Structures refer to the setting in which care is delivered; process relates to the provision of care, and the outcome is the measurable effect on health status.[5,23] It is a fallacy in quality improvement to go right for the outcome without previous consideration of the structure and processes that need to be in place to achieve the desired outcome.[26]

Quality Improvement Methods

There are different methods to assess quality improvement. One of them is the Plan-do-study-act (PDSA) cycle. PDSA method is widely used in healthcare improvement; however, there are few overarching evaluations of how it is applied. It is used to undertake tasks required to implement improvement and test the desired changes.

Other methods used in this field are Model for Improvement (MFI), to provide a framework for developing, testing and implementing changes leading to improvement; Total Quality Management, to long-term success through customer satisfaction; Continuous Quality Improvement (CQI), to focus on activities that are responsive to community need and improving population health; Lean, to minimise waste with ongoing process improvement; Six Sigma, to increase quality by reducing defects and costs; or Quality Improvement Collaboratives, to work in a structured way to improve an area of quality.[27–29]

Quality improvement interventions

The Agency for Healthcare Research and Quality states that "A quality improvement intervention is a change process in health care systems, services, or suppliers to increase the likelihood of optimal clinical quality of care measured by positive health outcomes for individuals and populations".[30]

Quality interventions are addressed to national priorities and to accomplish explicit quality goals.[31] Those interventions are focused on shaping the system environment, reducing harm, improving clinical care, and engaging and empowering people, and should be guided by evidence based on the impact of discrete and combined interventions.[2]

Furthermore, interventions should be adapted to the context (the national, sub-national, facility or community level of the health system), and its implementation requires a practical, effective, and sustainable plan. The implementation also needs to be evaluated in the system in a continuous improvement process.[32]

Quality measures

Measuring the quality-of-service provision builds the basis for quality assurance, accountability, and improvement strategies. Quality measures are essential for providing feedback, promoting transparency and trust, and comparative benchmarking using standardised tools to identify best practices for learning. With measurement, it is possible to determine whether quality improvement interventions are effective and whether they lead to any significant change in health outcomes. In the last years, this measurement of outcomes, especially the measurement of patient-reported outcomes, has gained interest based on the growing attention on value-based health care.[33–35] One of the best ways to measure the success of health care is to achieve safe care.[32] Although safe care does not guarantee quality, it is a prerequisite for delivering high-quality care.[8]

1.2. PATIENT SAFETY

Health care delivery contains a wide range of security problems and a certain degree of inherent unsafety. Clinicians and healthcare providers face the challenge of keeping the people they treat safe and protected from harm while delivering the right care, at the right time, in the right place, and following ethical considerations.[14,36] Therefore, safety must be central to all health care strategies and policies.[37]

The Institut National de Santé Publique du Québec defines safety as a "state in which hazards and conditions leading to physical, psychological, or material harm

are controlled to preserve the health and well-being of individuals and the community. It is an essential resource for everyday life, needed by individuals and communities to realise their aspirations".[38]

Other authors have mentioned that safety in health care does not correspond to the complete absence of risk, but these must be monitored and controlled. Moreover, safety does not only cover the protection against loss (Safety-I) but also includes the condition of excellent performance in achieving and safeguarding objectives (Safety-II).[39]

The World Health Organization defines Patient Safety as "a health care discipline that emerged with the evolving complexity in health care systems and the resulting rise of patient harm in health care facilities. It aims to prevent and reduce risks, errors and harm that occur to patients while providing health care. A cornerstone of the discipline is a continuous improvement based on learning from errors and adverse events".[40]

The Global Patient Safety states that "Patient safety is a framework of organised activities that creates cultures, processes, procedures, behaviours, technologies, and environments in healthcare that consistently and sustainably lower risks, reduce the occurrence of avoidable harm, make the error less likely and reduce its impact when it does occur".[41]

In fact, patient safety and quality are the main components of any health strategy for continuous improvement. Its concepts are dynamic and depend upon innovation and improvement within the healthcare context. What was accepted as acceptable practice ten years ago today might not be considered acceptable because if

standards improve, some adverse events could be considered, regarded as, preventable.[42]

1.2.1. The relevance of patient safety in health care

One of the earliest lessons and main principles in medicine is "first, do no harm", a famous dictum commonly attributed to Hippocrates. Another relevant principle of medical ethics is nonmaleficence, which implies an obligation to guarantee patient safety.[43] Throughout the history of medicine, there are many milestones in patient safety, such as Semmelweis's recommendations for handwashing to prevent infections in 1847 and Florence Nightingale's mandate: "the very first requirement of a hospital is that it should do the sick no harm".[14]

The rise of the patient safety movement and initiatives on patient safety are traced back to the influential report: To Err is Human, which highlighted that many patients died from adverse events. Moreover, the report also remarked that repeated errors are a significant contributing factor to patient harm, removing the traditional approach of blaming individual practitioners: "The problem is not bad people in health care; it is that good people are working in bad systems that need to be made safer". Since then, the research, prevention and safety culture have been promoted.[8]

Drawing from a concern and agreements of WHO member states, a patient safety programme was created in 2004 to raise awareness and political commitment to improving safety care and facilitate the development of patient safety policies and practices in all countries.[44]

In the European Union, the Luxembourg declaration on Patient Safety established recommendations for accessing high-quality health care.[45] Then, Eurobarometer

Survey was launched to determine the citizens' perception of medical errors in the 25 member states. The results showed that Europeans did not feel protected from medical errors and that health care was not perceived as safe as it should be.[46] In the last decade, considerable efforts have been made to improve patient safety and have contributed to the widespread acceptance and awareness of the problem of medical harm.

In the European Union, patient safety was included in the objectives of different community programs and actions, and its implementation was subsequently evaluated. The United Kingdom was one of the pioneers in patient safety, and the National Health Service (NHS) identified serious, totally preventable events that should never occur in healthcare, called "never events".[47]

In Spain, the Health Ministry included improving patient safety as a strategy in the national health plan.[48] The Patient Safety Strategy of the Spanish Healthcare System was developed to foster the implementation of safety practices, and the 30 best practices recommended in the National Quality Forum (NFQ) Safe Practices for Better Health Care were turned into indicators for measuring and evaluating healthcare outcomes.[49,50]

In Catalonia, the Department of Health created the Alliance for Patients Safety in 2005 to improve patient safety in health care. The current health plan includes strategic lines to promote a safety culture, communicate actions among all stakeholders, train everyone involved in the program and promote patient participation.[51] In addition, thematic lines in patient safety were established, such as preventing infections, identification errors, medication errors, errors during procedures, pressure ulcers and falls.[52]

Figure 2. Relevant events in the development of health care quality and patient safety

1955-56 — Barr and Mosser were concerned about the adverse consequence of medical progress

1964-81 — Schimmel and Steel found that patients in-hospital suffered iatrogenic illness relates to medication errors

1966 — A. Donabedian published "Evaluating the quality of medical care"

1994 — Leape published "Error in Medicine" in the Journal of the American Medical Association

1995 — "Quality in Australian Healthcare Study" is published

1997 — National Patient Safety Foundation is created

1999 — "To Err is Human" is published by The Institute of Medicine (IoM)

2000 — Donaldson published "An Organisation with a Memory" in UK. Spain implemented a medication error reporting program.

2001 — "Crossing the Quality Chasm" report is published

2002 — "The National Patient Safety Goals" are established by The Joint Commission. "Building a Safer System" in Canadian Health Care was published.

2004 — WHO Patient Safety Programme (World Alliance for Patient Safety) is created

2005 — "Luxembourg EU Presidency's declaration: Patient Safety - Making it Happen" is published

2006 — "Eurobarometer survey on medical errors" is launched to analyse errors based on citizens' perceptions

2007 — The WHO and Joint Commission have developed "Nine patient safety solutions" to reduce health care risks to patients

2009 — EU Member States adopted recommendations on patient safety

2017 — The OECD published "The economics of patient safety

2019 — "World Patient Safety Day" is established by the WHO

2021 — WHO launched "Global Patient Safety Action Plan" towards eliminating avoidable harm healthcare

Source: author's own compilation

Over the last few years, the importance of patient safety has been visualised and recognised as a serious global public health concern. Thus, it is a priority for modern health care and is crucial for health coverage. From this, the WHO and member countries developed a global action plan to eliminate avoidable harm in health care.[41] *Figure 2* summarises some of the most relevant events in developing health care quality and patient safety worldwide.

1.2.2. Safety Improvement

Bearing in mind the complex causes of patient harm, some organisational strategies and interventions have been widely recognised as cost-effective in addressing patient safety in health care.[1] Although many strategies may have had a positive impact on overall and preventable adverse events, the reduction of them is far from the target "zero harm".[53]

Having high-reliability organisations (HROs) in healthcare is an effective strategy for redesigning healthcare delivery organisations. These organisations manage the work in hazardous and complex environments, and their errors are analysed so that lessons learned are incorporated into design processes that reduce the likelihood of repeated errors. Moreover, they focus on standardising processes across multiple system components; therefore, the results are predictable and improve reliability.[37,54] This strategy will be helpful in an exceptional global situation as a pandemic, and an adequate approach to patient safety is crucial. Even more, when there are challenges to the health system and society, safety should be focused on public health measures, work systems measures, and clinical pathways to patients and multidisciplinary task forces.[14]

The most important component in developing a safe system relates to a ***culture of safety,*** where safety is embedded in everything we do. Patient Safety Culture, as a quality strategy, refers to how safety is approached and implemented within an organisation in its structures and processes to support and achieve desired patient outcomes. Consequently, assessing safety culture can be used to monitor change over time. Organisations with a positive safety culture are confident in the effectiveness of preventive measures, and support for the workforce.[55]

There are seven essential domains to safety culture: *leadership:* to reinforce safety as a priority in all the processes of delivering care; *teamwork:* to collaborate, cooperate and promote collegiality across the organisation to foster relationships that are open, safe, respectful, transparent, and flexible; *Evidence-based,* to standardise care interventions to reduce variance to help achieve high reliability by helping eliminate breakdowns in work processes; *Communication,* to share information in multiple ways among those involved and encourage staff to speak up on behalf of patients; *Learning,* to analyses safety data, understand how harms occur, draw conclusions, learn from mistakes and act upon recommendations; *Just,* to recognise errors as system failures rather than focusing on individual blame; and *Patient-centered,* to empower patients and families to participate actively in discussions about their care and ensure they are provided access to health information.[56]

Healthcare workers play a crucial role as individuals and teams in improving patient safety through clinical expertise and leadership in hospital quality improvement activities. However, using the best available evidence to support a safe practice is required considering a specific patient's clinical circumstances.[57]

Measuring patient safety is an important first step towards improving patient care and should be monitored over the long term. Multiple measurement methods could be used together for a greater understanding of care delivery, such as adverse event reporting, retrospective medical records review, routinely collected data and patient-reported measures.[14] Traditionally, safety has been measured by the absence of harm; however, currently, safe practices can be measured and used to predict safe outcomes. Additionally, in a framework of addressing potential harm through proactive management of risk rather than reactive management of incidents, Vincent proposed five dimensions for measuring and monitoring safety that answer the following questions: i) past harm (has patient care been safe in the past?); (ii) reliability (Are our clinical systems and processes reliable?); iii) sensitivity to operations (Is care safe today?); iv) anticipation and preparedness (Will care to be safe in the future?); and v) integration and learning (Are we responding and improving?).[58,59]

1.2.3. Incident Analysis Methods

There are various structured methods widely used in healthcare to investigate adverse events. Those methods are not only used to find out what happened but also to prevent future incidents.[14,60,61] Table 1 summarises some incident analysis methods.

Table 1. Incident analysis methods to investigate adverse events

Method	Description
Root Cause Analysis (RCA)	This aims to determine the timeline of events and underlying variation in performance that can produce undesirable outcomes.[62]
Process mapping	A visual representation of a process and assists in identifying areas to intervene to improve safety and quality. The analysis can involve either an existing, high-stakes practice or a new practice to be verified before it is implemented.[63]
System Engineering Initiative for Patient Safety Human Factors (SEIPS)	This model uses the human factors approach and examines work systems and structures (tasks, technologies, the wider environment, etc.), processes, and outcomes to understand the complex factors that contribute to adverse events.[64]
Failure Modes and effects Analysis (FMEA)	This is a systematic, proactive method for evaluating a process to identify where and how it might fail and to assess the relative impact of different failures to recognize the parts of the process that need change. It is useful for proactive and prospective identification of potential process failures.[65]
Swiss cheese model	This is a model of safety incidents to explain the occurrence of system failures. It is also used in other systems, such as aviation and engineering.[66]
AcciMap	This attempts to illustrate graphically the relationship between the various system factors contributing to errors in complex sociotechnical systems.[12]

Source: author's own compilation

1.3. RESEARCH IN PATIENT SAFETY

Research is a key component of improving patient safety and quality, as it provides an in-depth understanding of safety concerns and, thus, a basis for effective and sustainable improvement.[67]

The WHO has recommended that developed countries focus more specifically on advancing knowledge about processes and organisational factors that lead to unsafe

care, such as those related to communication, coordination, human factors and the need to improve patient safety culture.[68]

Patient safety and quality research have rapidly expanded in the past decade, with an increasing focus on preventing interventions for adverse events. Interventions in patient safety are needed and must be evaluated to achieve safer health care. It requires systematic approaches and methodologies to understand better the nature and magnitude of safety problems and their contributing factors.[69]

Research into patient safety improvement and its implementation requires looking at the healthcare system as a whole, including professionals and patients.[60] However, analysing the causes of errors and adverse events is complex because the events often relate to multiple system factors. Thus, it is required a more detailed description of interventions and outcomes, and an improved description of context to applied improvement intervention.[42]

The research strategies and methods are not sufficiently adapted to the complexities of healthcare, so it is necessary to use new multidisciplinary approaches and a variety of methods that enable an understanding of the interactive process and the factors involved in patient safety.[70]

1.3.1. Errors and adverse events definitions and related concepts

For many years medical errors and adverse events were attributable to human failure, and clinicians who provided care were blamed, however currently, there is recognised that hardworking, well-trained individuals commit most errors, and such errors are unlikely to be prevented by admonishing or by shaming and suing them.[71]

Error: An error is a failure to carry out a planned action as intended or the application of an incorrect plan to achieve what is intended. Errors may manifest by doing the wrong thing (commission) or failing to do the right thing (omission) at either the planning or execution phase.[72,73] There are many typologies to classify errors, such as human competence problem or error as a system problem;[74] normal human errors, at-risk behaviour or reckless conduct;[75] latent errors or active errors; and process errors: diagnostic, treatment and organisational or system technical errors.[37]

Adverse event: An injury caused by medical management or complication instead of the underlying disease that resulted in prolonged hospitalisation or disability at the time of discharge from medical care, or both. An undesired patient outcome may or may not be the result of an error.[72] Adverse events are injuries caused by medical intervention. When the adverse event is the result of an error, it is considered a preventable adverse event. Sometimes an error, such as giving a patient the wrong medication, may lead to no detectable adverse event. Other errors can temporarily or permanently harm the patient's health or cause the person's death.[73]

There are many causal factors for adverse events; however, the main concern is not who was wrong but how and why the defences failed.[75] *Figure 3* illustrates the classification of a patient safety incident.

Figure 3. Classification of patient safety incident
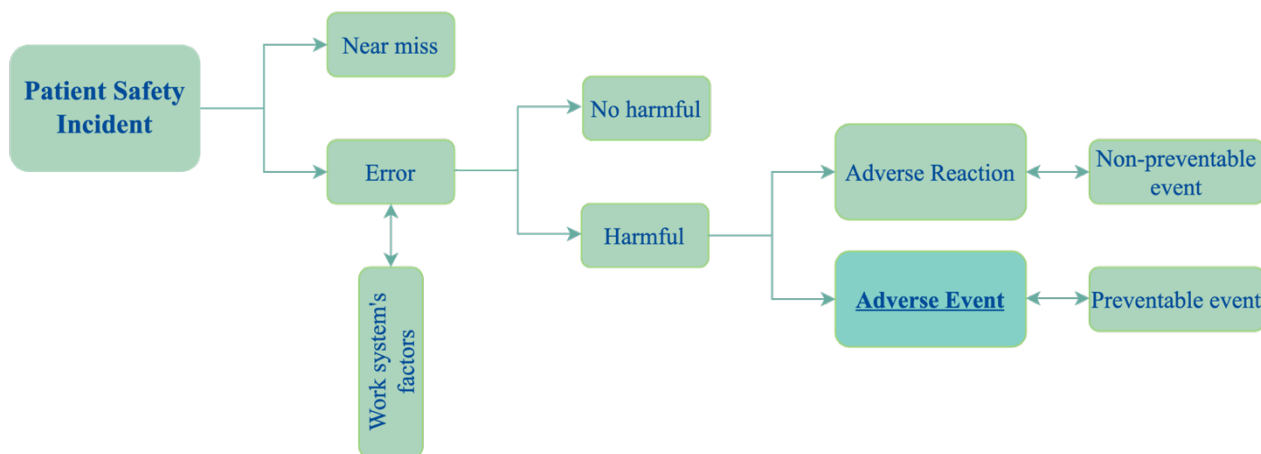
Source: Modified from WHO[72]

Table 2 shows some key definitions used in patient safety has been defined to facilitate understanding and transfer of relevant information. Those also allow us to compare patient safety data, examine the roles of system and human factors in patient safety, identify potential patient safety issues and develop priorities and safety solutions.[72]

Table 2. Key definitions in patient safety

Term	Definition
Adverse event	An incident that results in preventable harm to patient
Adverse reaction	Unexpected and non-preventable harm resulting from a justified action where the correct process was followed for the context in which the event occurred.
Causal analysis investigation	A process to investigate and analyses patient injuries and visitor incidents that identifies latent system failures and their causes.
Contributing factor	A circumstance, action or influence that is thought to have played a part in the origin or development of an incident or to increase the risk of an incident.

Detection	An action or circumstance that results in the discovery of an incident.
Error	Failure to carry out a planned action as intended or application of an incorrect plan.
Event	Something that happens to or involves a patient.
Hazard	A circumstance, agent or action with the potential to cause harm.
Incident	Any deviation from usual medical care that either causes an injury to the patient or poses a risk of harm, including errors, preventable adverse events and hazards.
Incident characteristics	Selected attributes of an incident.
Incident type	A descriptive term for a category made up of incidents of a common nature grouped because of shared, agreed features.
Near miss	An incident that did not reach the patient.
Never event	A patient safety incident that results in serious patient harm or death (this refers to particularly shocking medical errors – such as wrong-site surgery, that should never occur).
Patient characteristics	Selected attributes of a patient.
Patient outcome	The impact upon a patient that is wholly or partially attributable to an incident.
Root cause analysis	A systematic iterative process whereby the factors that contribute to an incident are identified by reconstructing the sequence of events and repeatedly asking why? Until the underlying root causes have been elucidated.

Source: Adapted from WHO[72,76]

1.3.2. Epidemiology of patient safety problems

The occurrence of an adverse event due to unsafe care is likely one of the ten leading causes of death and disability worldwide. In high-income countries, one in ten patients is harmed while receiving unsafe care, and the harm can be caused by adverse events, nearly 50% being preventable.[77] In low-and-middle-income countries, patient harm causes 2.6 million deaths each year, and most of these are avoidable.[40]

Medical practices and risks associated with health care, such as problems arising during surgery and procedures, deficiencies in monitoring and the care delivery process in a hospital setting, are the most common types of adverse events. Moreover, these are emerging as a major challenge for patient safety.[78]

In Europe, it is estimated that medical errors and health-care-related adverse events occur in between 8% and 12% of hospitalisations, and there is one death per 100,000 inhabitants annually as a result of these adverse events, representing around 5,000 deaths per year.[44] Although about two-thirds of adverse events cause little or no patient harm, about one-third of causes are from minor harm (such as prolonged hospitalisation) to permanent disability.[71]

The Spanish National Study of Adverse Events associated with hospitalisation (ENEAS), published in 2006, found that the incidence of harm to patients resulting from failures in health care processes was 8.4%. Regarding the severity of injuries, 45% were mild, 39% were moderate, and 16% were severe. The 37.4% of the adverse events were related to medication, 25.3% to nosocomial infections, and 25% to health care procedures. In addition, 31.4% of the adverse events increased hospital stays. Almost sixty-seven per cent of affected patients required additional procedures, and 69.9% other treatments. In addition, 42.8% of the adverse events were considered preventable.[79]

A national study of incidents and adverse events in intensive medicine (SYREC), published in 2007, found that the probability of a patient suffering at least one safety-related incident was 62%. The incident rate was 5.89 per 100 patients in one hour. The most frequent adverse events were related to care and nosocomial infection and were reported less frequently. The 90% of all incidents and 60% of adverse events were preventable or possibly preventable. In addition, nine out of a

thousand deaths are related to some adverse event. This study was based on the observation and reporting of adverse events in the ICU.[80] On the other hand, a national safety culture analysis study found that most professionals (77.8%) had not reported any event related to patient safety in the last year.[81]

In Catalonia, an epidemiology study of the hospital adverse events from 2010 to 2013 included 4,790 hospital discharges from 15 hospitals and identified that 7.4% of patients had an adverse event. Of these, 43.5% were considered preventable.[82]

The cost of failure in patient safety dwarfs the investment required to implement effective adverse event prevention. In Organization for Economic Cooperation and Development (OECD) countries, approximately 15% of hospital expenditure was attributable to addressing safety failures, while most of the financial burden is linked to adverse events.[16]

In Spain, a retrospective study in 12 hospitals found that approximately 6.8% of the cases studied had an adverse event related to health care, representing 16.2% of the total hospital cost. The total incremental cost of adverse events was 88.268.906 euros, an additional 6.7% of total health spending.[83] Another national study has also demonstrated that adverse events such as nosocomial infections increase the cost significantly; however, due to the heterogeneity in adverse event definitions, the total cost could not be calculated.[84]

Globally, the cost associated with medication errors has been estimated at US$ 42 billion annually, not counting lost wages, productivity, or health care costs.[85] In Europe, 7.5% of medication errors occur at the prescription stage. In hospitals, those errors represent 18.7- 56% of all adverse drug events among patients, and the estimated annual cost is between 4.5 billion and 21.8 billion euros.[86]

The COVID-19 pandemic has emphasised the magnitude of avoidable harm to patients because those were highly prevalent. The patient complexity led to longer hospital stays and other complications arising from delays in seeking care. Additionally, many safety gaps have been revealed across all core components of health systems. An adequate approach to patient safety would have been appropriate because the challenges constantly changed, and one of the higher risks in providing services was safety.[87]

In brief, despite the best efforts, medical errors still occur at different stages of the care process, and immediate and appropriate responses should be carried out. In fact, failing to do a proper patient identification could lead to a wrong medical procedure or medication error, as well as exposure to adverse events.[88] By researching the impact of errors is necessary, and it will be possible to understand the harm, both actual and potential, and this will lead to the analysis of its causes. Then, this data will be useful for identifying possible changes and preventing interventions.[58,89] Furthermore, medication errors, as much as correct patient identification, are quality indicators used to measure safety in Spain's healthcare system.[90]

1.3.3. Errors in hospitalised patients: patient misidentification

Correct identification of patients when they change location is essential not only for individualised care but also to ensure safe care.[91] Patient misidentification is considered a root cause of many errors and a major contributor to hospital adverse events, and these could be avoidable.[88,92,93] An international review disclosed that 72% of patient identification errors occur at the point of care, frequently leading to medication or blood transfusion errors.[94] Transferring patients can be a safety issue if the process is not complete and correct according to the standards.[14,95]

Many strategies have been implemented to prevent these events; for example, The Joint Commission recommends the use of at least two patient identifiers when providing care, treatment, or services.[96] Additionally, hospitals generally have institutional policies to reduce misidentification; however, there is still concern about identification errors in each hospital, particularly in intra-hospital transfer.[97]

This requires methodological approaches and perspectives that help to understand causes and adaptations, map the change, and identify processes along the patient journey.[94,98,99]

Human factors are critical to the design of safe and resilient health care, and different system models have been developed in the fields to analyse incidents in safety-critical industries such as hospital settings.[41] **Systems Engineering Initiative for Patient Safety (SEIPS)** is one of the most widely used healthcare system models.[100] The SEIPS model is based on Donabedian's structure-process-outcome model of healthcare quality and the feedback loop concept of systems theory. It means that this model explains the influence of the work system (interaction between person and work environment) in a healthcare setting and process on health outcomes.

A work system comprises five components: person(s), organisation, technologies and tools, tasks, and environment.[64] Furthermore, SEIPS 2.0 incorporates three novel concepts into the original model: *configuration,* as the interactive properties of sociotechnical systems; *engagement*, as various individuals and teams can perform health-related activities separately and collaboratively; and adaptation, as the ability of the work system to change based on feedback.[101] *Figure 4* depicts all the components of this model graphically.

In this thesis, SEIPS 2.0 is useful to gain an understanding of how different elements in the hospital system interact in intra-hospital patient transfers. This model guides the work in different clinical disciplines since it helps restructure the work system to resolve identified problems.[100,101]

Figure 4. Systems Engineering Initiative for Patient Safety (SEIPS 2.0 model)
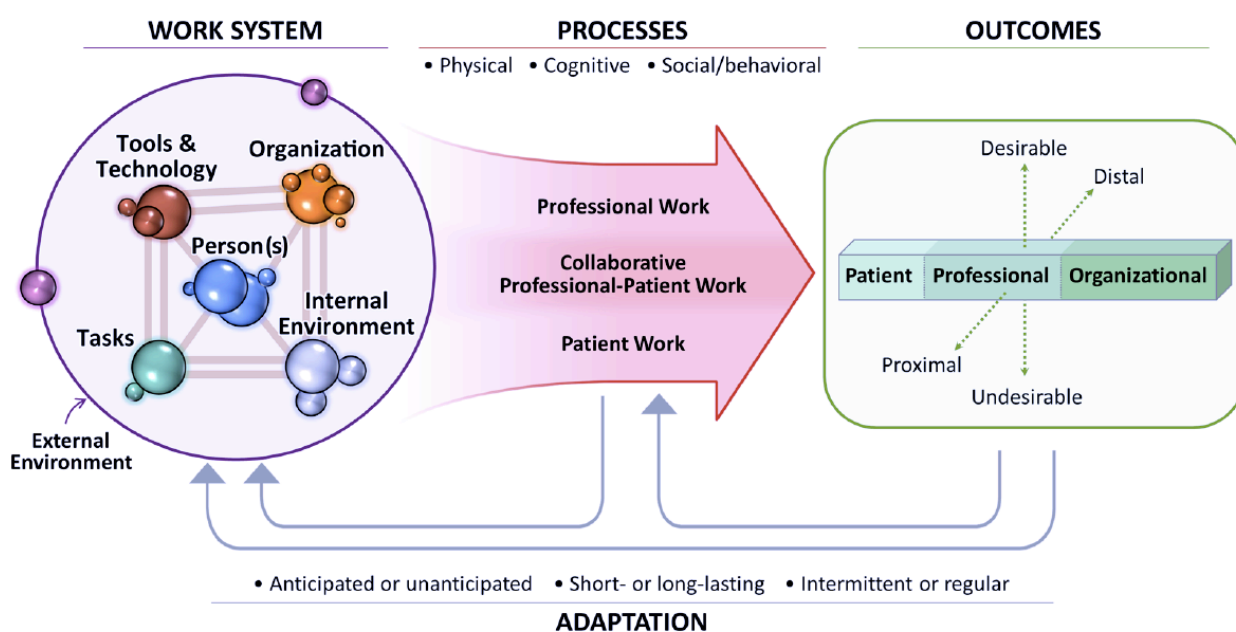
Source: Holden et al., 2013[101]

After analysing the work systems component involved, **a process map** helps to explain and illustrate all steps of the intra-hospital patient transfers, focused on the identification process in an integrated visual diagram for a better and more efficient understanding.[63] Process mapping has the capacity to show the sequence of actions, indicate who will take on each step from start to finish, and visualise the interactions between different health care providers in a specific process.[102,103]

Direct observation of the actual workflow helps to ensure that the map accurately represents the current practice, and then it is helpful to compare and identify discrepancies from policies or institutional standards. Thus, understanding vulnerabilities, delays, redundancies, deviations, or non-value steps in the current process provides a solid foundation for potential improvements.[63] Process mapping has become a more prevalent tool, it means detecting the error before it harms the patient, and it has begun to play a fundamental role in improving health care quality.[104]

The **Failure Mode and Effect Analysis (FMEA)** is a tool for a proactive risk assessment in healthcare to achieve safety.[65] FMEA allows to identify the risk of failure in patient identification during intra-hospital transfers and potential harms in this care process.[105,106] Furthermore, it emphasises prevention rather than reacting to adverse events after failures have occurred. Thus, corrective action is assigned to the process requiring a change to prevent future failures and provides a foundation for continued improvement.[65,107]

Implementation of the FMEA process requires a multidisciplinary team in its several individual steps, which are summarised in *Table 3.*

Table 3. Step to develop a Failure Mode and Effect Analysis

Define the process to analyse	A decision to begin analysis is in response to a safety event, a near miss, or sentinel event.
Identify failure modes	What could go wrong? List anything that could go wrong during that step in the process.
Identify failure causes	Why would the failure happen? List all possible causes for each of the failure modes identified
Identify failure effects	What would be the consequences of the failure? List all possible adverse consequences for each of the failure modes identified.

Introduction

Likelihood of Occurrence	On a scale of 1-10, with 10 being the most likely, what is the likelihood the failure mode will occur?
Likelihood of Detection	On a scale of 1-10, with 10 being the most likely NOT to be detected, what is the likelihood the failure will NOT be detected if it does occur?
Severity	On a scale of 1-10, with 10 being the most likely, what is the likelihood that the failure mode, if it does occur, will cause severe harm?
Risk Priority Number (RPN)	For each failure mode, multiply together the three scores the team identified (i.e., likelihood of occurrence x likelihood of detection x severity). It will help to develop a critically analysis and prioritise areas of focus.
Actions to Reduce Occurrence of Failure	List possible actions to improve safety systems, especially for failure modes with the highest RPNs.
Evaluate results for redesign improvement efforts	It should be a periodic evaluation with the team members, rounding, and observation to assess improvements in safety.

Source: authors' own compilation based on Institute of Healthcare Improvement[65]

In fact, FMEA is particularly useful in identifying high-risk failures and led to the implementation of redesign processes with the ultimate goal of improving patient safety, quality, and elimination of preventable harm.[108]

1.3.4. Errors in intensive care unit: errors in the medication process

Medication errors are the single most common preventable cause of adverse events in medication practice and a major public health burden. Although not all errors during the medication process reach the patients, these represent a high risk and can be preventable. In some countries, 70% of patients' medication histories contain errors globally.[109,110] Those errors occur when weak medication systems and human factors such as personnel fatigue, poor working conditions, workflow interruptions or staff shortages affect the practice, resulting in severe harm, disability and even death.[85,111]

The intensive care unit (ICU), due to its nature, is a setting with high-risk errors where sicker patients undergo more complex interventions. In the meantime, clinicians are expected to provide high-quality care to critical patients, often making vital decisions very quickly in a stressful environment while managing high-tech equipment and applying complex procedures.[60] In consequence, the risk of medication errors in ICU is around 2-3 times greater than in other in-hospital settings, and it has a probability of mortality that is approximately 2.5 times higher when errors occur. Moreover, interruptions during medication administration can also increase the chance of errors.[14]

1.3.5. Interventions to prevent adverse events

Once the theory and epidemiologic framework of the errors and the adverse events related to patient safety are established, it is important to evaluate the interventions carried out during clinical practice to prevent adverse events, especially in vulnerable patients.

Preventing interventions and evidence-based care to reduce adverse events have a positive impact on patient outcomes and contribute to safety improvement in health care.[112] Currently, many resources are used to ensure safe care, such as clinical guidelines, protocols, and care bundles that include interventions for preventing adverse events.

Those interventions should be reviewed and evaluated continuously according to the changes in the complex healthcare systems.[60] Due to the extended information on preventing interventions, it will be more valuable if it is synthesised and methodologically evaluated to translate the findings into hospital care.[113,114]

Developing and implementing evidence-based prevention interventions, specifically targeting preventable patient harm, could lead to major service quality improvements in medical care, which could also be more cost-effective.[115]

Implementing interventions on patient safety to improve health care requires evidence-based medicine to inform and make decisions about the care of individual patients. This means that clinical care choices undergo rigorous evaluation instead of having their effectiveness presumed based on subjective arguments relating to the health conditions or diseases.

JUSTIFICATION

2. JUSTIFICATION

Patient safety is an evolving discipline and an essential dimension of quality care. Errors and adverse events are, in the main, a reflection of how a healthcare system works and have a high impact on patient outcomes and health care quality. Although most errors are predictable and preventable, they are not completely avoidable. Therefore, knowing the conditions under those that occur will allow focus on prevention and reduction strategies.

Patient misidentification associated with system factors is experienced across all hospital departments. Thus, identifying its contributing factors using a human factors approach will lead to understanding the incident and implementing changes to make a difference.

Another common and frequent error is medication errors that potentially cause severe harm, which is more serious in critical settings. It is important to identify at which stage of the medication process it happens and consider specific patients' clinical circumstances and healthcare professional conditions to reduce them.

Although a wide variety of interventions are currently known to prevent adverse events, there is little synthesised evidence of the most effective interventions applicable in the ICU. Moreover, evaluating the methodological quality of studies that have identified these preventive interventions is important for better decision-making in patient safety.

Research in patient safety is a requirement for the best patient care. It needs to be continuously evaluated and updated for applying evidence to clinical practice and feedback to healthcare teams and across the system. In fact, to improve patient

safety, it is relevant to start identifying errors, understanding their causes, and measuring their impact, and then develop solutions which should be implemented and evaluated in hospital care. This thesis arises from the interest in analysing the multiple system factors contributing to error, measuring the impact of common errors, and evaluating preventive interventions implemented in critical settings.

For the development of its objective, this thesis has been carried out through a set of three studies following the steps of the patient safety improvement cycle: 1. exploring systems factors contributing to patient identification errors during intra-hospital transfers (Study I); 2. determining the prevalence and magnitude of medication errors and their association with patients and nurses' characteristics (Study II); 3. providing an overview of effectiveness non-pharmacological interventions aimed at preventing adverse events in the intensive care unit (Study III).

Our findings could assist hospitals and critical care settings in implementing safety care. It could also be useful to generate momentum for further safety initiatives and develop improvement projects for patient safety and quality of health care.

HYPOTHESIS AND OBJECTIVES

3. HYPOTHESIS

3.1 System factors such as people, tasks, tools/technology, environment, and organisation could contribute to patient identification errors during intra-hospital transfers.

3.2 Medication errors in the prescription and administration process could be relevant in the intensive care unit.

3.3 Non-pharmacological interventions can be useful in preventing adverse events in the intensive care unit.

4. OBJECTIVES

4.1. General objective

To analyse errors during the care process and evaluate the interventions to prevent adverse events in the hospital setting.

4.2. Specific objectives

1. To explore systems factors contributing to patient identification errors during intra-hospital transfers.

2. To determine the prevalence and magnitude of medication errors and their association with patients' sociodemographic and clinical characteristics and nurses' work conditions.

3. To provide an overview of the effectiveness of non-pharmacological interventions aimed at preventing adverse events in the intensive care unit.

METHODS

5. METHODS

This thesis is presented as a compendium of articles that have been published in indexed and peer-reviewed journals, and that respond to the stated objectives.

For a better understanding, *Figure 5* details the methodology used.

Figure 5. Methodology approach of the thesis
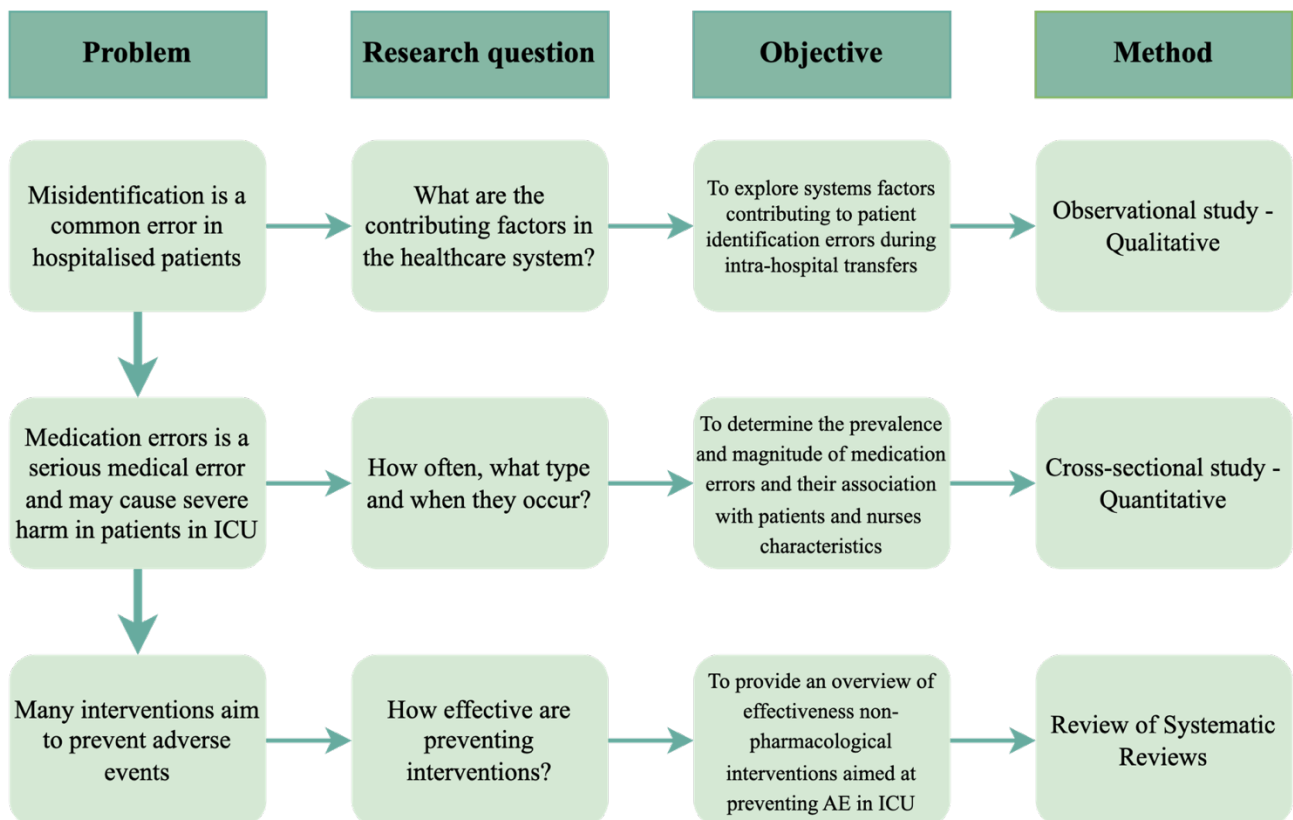
5.1. First study methodology

Evaluating patient identification practices during intra-hospital transfers: A human factors approach

This study aimed to explore systems factors contributing to identification errors during intra-hospital transfers and point to possible improvements.

Design

A qualitative study utilising direct ethnographic observation and interviews.

To understand the complex relationships between personnel and their practices, a qualitative study with a direct observation data collection method is useful to capture how patient identification during transferring patients is carried out or not. It involves a detailed observation of behaviours, watching and recording what participants do.[116,117]

This technique provides a "real life" insight into the activity performed using the human factors approach to analyse people interacting with other factors involved in the system, and therefore, risks and failures in the process could be recognised. It is important to manage the risk proactively, identifying and analysing potential failures and making recommendations for changes in the process of patient misidentification.[118] Human factors provide the framework upon which most patient safety initiatives are based.[119] Although a limitation of this type of study is that participants can modify their behaviours when they feel observed, this design helps to develop in depth-analyses of errors occurrence.[120,121]

Study population

All staff involved in patient identification during the patient transfer process of
adults between inpatient wards and departments were observed. Brief interviews
were conducted with porters. Participants were healthcare professionals (nurses,
doctors, and healthcare assistants) and staff members (porters and receptionists).

Data collection

The primary unit of analysis was the transfer process for a single patient. Transfers
were selected via convenience sampling, subject to researcher, healthcare staff and
porter availability. All data were collected between February to March 2020.

Direct structured observations were carried out through "shadowing" porters and
observing the patient handover process. Observers were assigned to a porter whom
they followed and observed during their patient transfer tasks; observations
included the actions of healthcare staff in identifying the patient leaving or entering
their department. The observations for each transfer finished when the patient was
received at the destination, and the porter informed their manager that the transfer
was completed. Observers initially characterised the practice descriptively and then
added notes on interpretations and intuitions aided by self-reflection based on their
previous training. An online form was created for collecting observation data,
incorporating free-text fields to capture factors affecting patient identification
during transfer, using the SEIPS framework, and was pilot-tested to evaluate
reliability before routine data collection. (See Appendix 2). To optimise the rigour
of the study, data were collected at different times, and observers were positioned
nearby but slightly peripheral to the porter observed to minimise the Hawthorne
effect.

Informal interviews, Brief informal interviews were conducted with each porter observed during shadowing to clarify observation data and gain insight into the patient identification process. Interviews were captured via field notes for analysis.

Data analysis

Quantitative data collected from observations were analysed using descriptive statistics, including frequencies and percentages, in SPSS (V 26.0).

Qualitative data from field notes were analysed using issues analysis, process mapping and FMEA. The SEIPS work elements were used to classify the main issues during the descriptive analysis, building up a detailed picture of the patient transfer process and potential risk areas. The analysis results informed the development of the process maps and the FMEA.

- **SEIPS analysis,** findings were categorised into work system components (people, task, tool/technology, environment, and organisation), processes, outcomes and adaption. Any potential difficulty in the completion of positive patient identification (PPID) noted was considered a potential contributing factor to inform thinking about risk controls for specific risks identified through FMEA.

- **Process map analysis** was developed to identify the parts of the patient transfer process where PPID was impacted by the system design. The process map depicts the process of patient identification during intrahospital patient transfer according to the institutional PPID to provide a visual representation of both the "work as imagined" and the process variation of the "work as done", which was observed and classified using SEIPS.

- **FMEA,** causes and effects of these potential failure modes were elicited from observation and informal interviews during shadowing to the patient identification process.

5.2. Second study methodology

Medication errors in prescription and administration in critically ill patients

This study aimed to determine the prevalence and magnitude of medication errors and their association with patients' sociodemographic and clinical characteristics and nurses' work conditions.

Design

Cross-sectional study

To know more about what types, how and when errors occur, cross-sectional studies are useful to describe, analyse and measure the prevalence of errors. It also establishes preliminary evidence for a causal relationship, more particularly to study associations between errors and their contributing factors. The limitation of this design is that it cannot establish a relationship among the variables because outcome and exposure are examined simultaneously. Thus, a cross-sectional study can infer only association, not causation. Moreover, there is no follow-up over time to know what happens after errors occur.[121,122]

Study population

Patients over 18 years who had been in intensive care unit (ICU) or the Intermediate Care Unit (IMCU) for more than 24 hours and have had the prescription and administration of at least one drug by oral or parenteral route. Patients without medical prescriptions were excluded. All patients were included consecutively except for those who met some exclusion criteria.

Data collection

We collected demographic and clinical variables from the medical records: age, sex, diagnosis at admission (medical or surgical), care unit (ICU or IMCU), comorbidity and family of drugs prescribed by the anatomical therapeutic classification (digestive and metabolic system, blood and haematopoietic organs, cardiovascular system, nervous system and others). Other variables collected in the administration stage were factors related to nurses' working situation.

We evaluated five types of errors in the prescription of medications (incorrect name, omission error, illegible handwriting, commercial name, abbreviation) and six errors in their administration (preparation, interruption, medication prepared by another professional, out of time, incompatibility using an automated dispensing cabinet, no information to patient). We also rated the overall prevalence of errors, the prevalence of each type of error and the magnitude of the errors. We designed an ad hoc questionnaire for collecting data in each stage. (See Appendix 3). We next carried out a pilot test to evaluate the reliability of this questionnaire. All data were collected from medical records between April - July 2015.

Data analysis

Categorical variables were described as frequencies and percentages, and quantitative variables as means and standard deviations (SD). In the comparative analysis, we used the chi-square test and Fisher's exact test for categorical variables, and we used the Mann– Whitney U-test for quantitative variables. The 95% confidence interval was used to express the prevalence and magnitude of the error. We performed a multivariate logistic regression to examine the association between the factors that were clinically relevant or significant and MEs. The results of the regression were expressed as odds ratios (OR) with 95% confidence intervals (95% CI).

5.3. Third study methodology

Effectiveness of non-pharmacological interventions to prevent adverse events in the intensive care unit: A review of systematic reviews

This study aimed to provide an overview of SRs assessing non-pharmacological interventions to prevent adverse events in the intensive care unit.

Design

Review of systematic reviews

This is also called an overview, a research method used to synthesise current evidence regarding a particular topic, assess the quality and highlight areas of priority in decision-making.[123,124] This systematic method has a systematic review (SR) as a unit of analysis which is considered the highest level in the hierarchy of evidence. The main purpose of overviews is to collate and appraise the methodological quality and to summarise and analyse their results across our research question identifying specific areas of available or limited evidence.[125] A comprehensive overview can provide an accurate description of the current state of research to translate into clinical practice and thus guide future research.[126] In fact, this synthesis will be useful not only to gather current evidence but also to assess the level of methodological quality of these studies and the effectiveness of interventions to prevent adverse events.[127] High-quality evidence should be provided to decision-makers to make the right choices and contribute to improving patient safety. Furthermore, when enough reliable research evidence is available, the practice should be guided by research findings in conjunction with clinical expertise and patient values.[69]

Search methods

We developed a systematic search strategy for MEDLINE, CINAHL and the Cochrane Library to identify studies published from inception until March 2022. English and Spanish languages were included. We included SRs of primary studies, including randomised controlled trials (RCTs), quasi-RCTs and controlled observational studies investigating the effect of non-pharmacological interventions (NPIs) on adverse events (AEs). Adult ICU patients aged 18 years and above were in medical and surgical ICUs. The types of interventions were any NPIs to prevent AEs focused on patient safety, described as new strategies, practices, behaviour, actions, procedures, or environment.

The primary outcomes were incidence of AEs such as infections (mechanical ventilation-associated pneumonia, bloodstream infection, central catheter infection, peripheral catheter infection), delirium, reintubation, airway occlusion, pressure ulcers, physical function deterioration, medication errors, and ICU mortality. Those adverse events were previously identified from quality indicators in intensive care and coronary units in Spain (SEMICYUC).[90] Secondary outcomes were hospital mortality, length of mechanical ventilation and stay in the ICU or hospital. Outcomes that reported consequences of AEs in terms of additional treatment(s) or readmission were not the focus of this overview.

Data extraction

Data from studies such as trial design, number of included studies, type of intervention, type of AE, comparator, and outcomes were extracted by one reviewer and checked for accuracy by a second. Disagreement was resolved through discussion, and a third reviewer was consulted if needed.

Quality appraisal

The methodological quality of the reviews was assessed using A Measurement Tool to Assess Systematic Reviews (AMSTAR-2)[128], which provides overall ratings (high, moderate, low, critically low) based on weaknesses in critical domains. A pair of reviewers independently assessed the quality of each study. A third reviewer resolved disagreements. Moreover, we described the confidence in the evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach for the primary outcomes when the SRs reported them.

Data analysis and synthesis

The study characteristics and patient outcomes for all the SRs that met our inclusion criteria were grouped by type of AE in a tabular form. To assess the overlap of primary studies among included SRs, we created a matrix of evidence as a grid, placing all the included SRs in the columns and their respective primary studies in the rows. We considered overlapping low if the corrected covered area (CCA)[129] was below 5%, moderate if CCA was between 5% and 10%, high if CCA was between 10% and 15%, and very high if CCA was above 15%. We compiled the pooled effect sizes of meta-analyses reported in the SRs and analysed the intervention components. Most of the effect sizes were expressed in OR; however, when RR was reported, these were converted to OR if the number of events per group was provided. Statistical analyses were performed using Review Manager (RevMan), V5.3. Analysis of forest plots was descriptive, and metanalysis was not performed due to the clinical diversity of intervention by outcomes.

The protocol of the review was registered in PROSPERO (CRD 42019147956). (See Appendix 4).

RESULTS

6. RESULTS

Articles published as part of the thesis:

<u>Study I</u>

Title: Evaluating patient identification practices during intra-hospital transfers: A human factors approach

Authors: Suclupe S, Kitchin J, Sivalingam R, McCulloch P

Journal: Journal of Patient Safety

Impact Factor 2020: 2.844. Q2 (51/107). Health Care Sciences & Services.

DOI: 10.1097/PTS.0000000000001074

<u>Study II</u>

Title: Medication errors in prescription and administration in critically ill patients

Authors: Suclupe S, Martinez-Zapata MJ, Mancebo J, Font-Vaquer A, Castillo-Masa AM, Viñolas I, Morán I, Robleda G.

Journal: Journal of Advanced Nursing

Impact Factor 2019: 2.561. Q1 (6/123). Nursing.

DOI: 10.1111/jan.14322

<u>Study III</u>

Title: Effectiveness of nonpharmacological interventions to prevent adverse events in the intensive care unit: A review of systematic reviews

Authors: Suclupe S, Pantoja Bustillos PE, Bracchiglione J, Requeijo C, Salas-Gama K, Solà I, Merchán-Galvis A, Uya Muntaña J, Robleda G, Martinez-Zapata MJ.

Journal: Australian Critical Care

Impact Factor 2021:3.265. Q1 (40/182). Nursing.

DOI: 10.1016/j.aucc.2022.11.003

6.1. STUDY I. Evaluating patient identification practices during intra-hospital transfers: A human factors approach

Summary of the most relevant results:

6.1.1. General characteristics

A total of 60 patient intra-hospital transfers were observed, and 51 of them were evaluable cases. *Table 4* shows Positive patient identification characteristics at the collection and delivery of patients.

6.1.2. Positive patient identification by healthcare staff and method of patient identification

Positive patient identification at patient collection

In 31 patients (60.8%), health professionals who already knew the patient identified them informally to the porter. In 17 patients (27.5%), healthcare staff used only one method of identification, or the receptionist confirmed identification when asked by the porter by pointing with her hand toward the correct patient. There was no identification in two patients (3.9%), and the porter transferred them without assistance from professional staff.

Positive patient identification at delivery

Some patient identification at the destination was performed in 18 patients (35.3%) by nurses or other staff members. The remaining 33 patients (64.7%) were not identified by the professional staff at the destination, either because the professionals responsible were not present or because they omitted it.

In none of the 51 (100%) evaluable cases observed, patient identification was conducted correctly according to hospital policy at every transfer process step.

Table 4. Positive patient identification at collection and delivery of patients

Characteristics	Ward of patient collection N=51	Ward of patient delivery N=51
Who released/received the patient?		
Nurse, No. (%)	23(45.1)	14(27.5)
Receptionist, No. (%)	6(11.8)	2(3.9)
Radiographer, No. (%)	2(3.9)	4(7.8)
HCA, No. (%)	3(5.9)	1(2.0)
Nobody, No. (%)	14(27.5)	29(56.9)
Other healthcare staff, No. (%)	3(5.9)	1(2)
Who identified the patient?		
Nurse, No. (%)	23(45.1)	13(25.5)
Receptionist, No. (%)	3(5.9)	0(0)
Radiographer, No. (%)	1(2.0)	2(3.9)
HCA, No. (%)	3(5.9)	2(3.9)
Porter, No. (%)	16(31.4)	NA
Nobody, No. (%)	2(3.9)	33(64.7)
Other healthcare staff, No. (%)	3(5.9)	1(2)

Abbreviations: SEU: Surgical Emergency Unit; CMU: Complex Medicine Unit; AAU: Ambulatory Assessment Unit; Other location: Acute General Medicine, Adult Intensive Care, Cardiology, Cardiothoracic, Emergency Assessment Unit, Gastroenterology, Gynaecology, Infectious diseases, Main reception, Neonatology, Rapid Assessment Unit, Transfer Lounge, Traumatology, Paediatric, Short Stay Unit. HCA: Healthcare assistant; Other Healthcare staff: doctor or nursing student

6.1.3. Analysis using the Systems Engineering Initiative for Patient Safety (SEIPS)

People and Teams, communication between healthcare professionals and porters was inconsistent and informal. It was common for staff to either not be available or for nurses to be overloaded to allocate attention to patient identification.

Task, porters are not expected to return to the porter's office to receive a new patient transfer task; then, they do not formally record patient information for transferring but instead, rely on memory. It was not clear who was accountable for releasing or receiving the patient.

Tools and Technology, the printing quality of paper forms was poor, making the text difficult to read, and some information was commonly omitted.

Environment, the layout of the environment and distractors, such as noise, and interruptions from other staff members, patients, or families, interfered with patient identification.

Organisation, according to the hospitals' policies, both nursing and portering staff were unclear about who was responsible for patient identification during the transfer process.

6.1.4. Processing map

Positive Patient Identification (PPID) policy was represented in 9 steps. Observations of "work as done" showed that each step of the process differed from the "work as imagined".

We found that the common deviations from the policy were: (a) only one identifier was used to identify the patient, (b) healthcare professionals relied on their knowledge to identify the patient, (c) porters received patient information on a handwritten paper slip, and (d) porters identified the patient by themselves without any input from healthcare staff.

6.1.5. Failure Modes and Effects Analysis (FMEA)

We identified 45 distinct potential pathways, and 20 conditions received a risk priority number (RPN) score of higher than 168 and were therefore considered of interest for further analysis.

The two highest-rated conditions had potential causes associated with the design or quality of information on the patient transferred slip. Nine conditions could have resulted in a patient undergoing an unnecessary procedure. The remaining conditions could lead to a patient being misidentified (but not undergoing an unwanted procedure) or to a delayed or cancelled transfer. According to the SEIPS categories, the four highest-rated conditions could be associated with people/team, tools, technology and organisation components (*Table 5*).

Table 5. The four high-risk conditions using Failure Modes and Effects Analysis

Process Map ID	Potential Failure Mode	Potential Failure Effects	SEVERITY (1 – 10)	Potential Causes	OCCURRENCE (1 – 10)	Current Controls	DETECTION (1 – 10)	RPN	SEIPS Work Elements
1	Healthcare professional misidentifies patient	Incorrect patient transferred	9	Patient Transfer Slip contains incorrect information	9	PPID policy	5	**405**	Tools/Tech
1	Healthcare professional misidentifies patient	Incorrect patient transferred	9	Patient Transfer Slip contains missing information	9	PPID policy	5	**405**	Tools/Tech

5,6,8,9	Healthcare professional misidentifies patient	Incorrect patient transferred	9	Healthcare professional confuses key patient information with another patient - attention & memory affected by high workload	9	PPID policy	4	**324**	Person / Organisation
5,6,8,9	Healthcare professional misidentifies patient	Incorrect patient transferred	9	Healthcare professional does not identify the patient in any way - actions affected by high workload	9	PPID policy	4	**324**	Person / Organisation

FULL TEXT OF ARTICLE I

Suclupe S, Kitchin J, Sivalingam R, McCulloch P. Evaluating Patient

Identification Practices During Intrahospital Transfers: A Human Factors

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Evaluating Patient Identification Practices During Intrahospital Transfers: A Human Factors Approach

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Introduction: Reliable patient identification is essential for safe care, and failures may cause patient harm. Identification can be interfered with by system factors, including working conditions, technology, organizational barriers, and inadequate communications protocols. The study aims to explore systems factors contributing to patient identification errors during intrahospital transfers.
Methods: We conducted a qualitative study through direct observation and interviews with porters during intrahospital patient transfers. Data were analyzed using the Systems Engineering Initiative for Patient Safety human factors model. The patient transfer process was mapped and compared with the institutional Positive Patient Identification policy. Potential system failures were identified using a Failure Modes and Effects Analysis.
Results: A total of 60 patient transfer handovers were observed. In none of the evaluable cases observed, patient identification was conducted correctly according to the hospital policy at every step of the process. The principal system factor responsible was organizational failure, followed by technology and team culture issues. The Failure Modes and Effects Analysis methodology revealed that miscommunication between staff and lack of key patient information put patient safety at risk.
Conclusions: Patient identification during intrahospital patient transfer is a high-risk event because several factors and many people interact. In this study, the disconnect between the policy and the reality of the workplace left staff and patients vulnerable to the consequences of misidentification. Where a policy is known to be substantially different from work as done, urgent revision is required to eliminate the serious risks associated with the unguided evolution of working practice.

Key Words: patient safety, patient identification, SEIPS, FMEA, process map

(J Patient Saf 2023;19: 117–127)

P atient safety is fundamental to strengthening the quality of the health care system. As much as we recognize the crucial importance and safety mechanisms in health care, patients still experience harm daily nationwide for several reasons within the complex sociotechnical health care system.[1,2]

Correct identification of patients when they change location is essential for safe care. Failure to do this may lead to unpredictable and harmful results.[3,4] Patients may undergo unnecessary medical procedures or incorrect drug administration with potentially serious consequences.[5–7] The risks of incorrect patient identification have led to an increased focus on preventing such incidents.[8,9]

The Positive Patient Identification (PPID) policy at the Oxford University Hospitals is based on The Joint Commission recommendations.[10] It aims to ensure a standardized approach to patient identification and reduce the number of preventable misidentification incidents. The PPID policy focuses on patient safety and uses at least 2 patient identifiers (full name and date of birth) when providing care, treatment, or services.[11]

Verbal PPID has been shown to reduce patient identification errors,[12] but this is only successful when communication is clear and accurate. Communication failures, such as omission of critical information during patient transfers, are common and constitute one of the main causes of identification errors.[7,13–16] Patient identification can be interfered with by different factors, such as working conditions, patient's functional ability and capacity, and the accuracy and clarity of the tools used.[17,18]

When reviewing adverse events in organizations, the focus tends to be on the individual's actions, commonly labeled "human error." Concluding that an adverse event is caused by a single human error is a common practice but is an inherently flawed approach.[19] The factors that lead individuals to make mistakes are often related to human cognitive and perceptual limitations, making it likely that other humans will make the same mistake under the same circumstances. Therefore, human error is often a symptom of underlying system failures,[20] which put humans in error-prone situations and should not be regarded as the primary cause of adverse events. The human factors discipline embraces the concept of system design and promotes the idea that humans are frequently not primarily at fault when complex sociotechnical systems malfunction.[21]

This study takes a human factors approach to patient misidentification in health care. It aimed to explore systems factors that contribute to identification errors during intrahospital transfers and point to possible improvements, using a hospital system that had recognized the need for improvement in its patient identification protocols as a case study. We used a human-centered model: the Systems Engineering Initiative for Patient Safety (SEIPS),[22] which frames the system in work elements, processes, and outcomes. Using this framework, observations of the "work as done" can be mapped and compared with the "work as imagined."[23] The importance of the potential system failures we identified was then estimated using the Failure Modes and Effects Analysis (FMEA) technique.[24,25] This provided a useful set of suggestions for improvement, prioritized by the risk priority assigned.

METHODS

Ethical Considerations

This study was conducted under a service evaluation agreement with the R&D Directorate at Oxford University Hospitals National Health System (NHS) Foundation Trust (OUHFT), following an approach to our human factors group by a senior manager concerned by a recent incident of misidentification in which harm to a patient was narrowly avoided. Under the ethical framework put in place by the UK Health Research Authority, such

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The authors disclose no conflict of interest.
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agreements and studies designed and conducted to evaluate current care and that do not involve either intervention or the specific research or identification of individuals are authorized at the Trust level (hospital consortium). Patients and families were not purposively studied, and no notes relating to them were kept. No personally identifiable data were collected or retained for any individual staff member or patient.

Type of Study

This is a qualitative study using direct ethnographic observation and interviews to gain a better understanding of the PPID system in use during intrahospital transfers in a large university hospital in England.

Sample and Participants

The primary unit of analysis was the transfer process for a single patient. Transfers were selected via convenience sampling, subject to researcher, health care staff, and porter availability.

Inclusion criteria

The OUHFT comprises 4 hospitals that provide specialist health care services. This study was conducted at John Radcliffe Hospital, which provides all emergency and trauma care, including general surgical and medical inpatient admissions, pediatric and maternity care, neurology, and several specialist surgical services (cardiac, vascular, and neurosurgery).

For this study, all staff involved in patient identification during the patient transfer process of adults between inpatient wards and departments at the John Radcliffe site within OUHFT were observed. Brief interviews were conducted with porters. Participants were health care professionals (nurses, doctors, and health care assistants) and staff members (porters and receptionists).

Exclusion Criteria

Health care staff and porters from the Emergency Department, Theaters and Maternity Department were excluded from this study, as those departments had a separate and dedicated patient transfer process and portering team.

Direct Observations

Direct structured observations of staff were carried out through "shadowing" porters and observing the patient handover process. Observations took place between February 2020 and March 2020 for 20 days (80 hours). They were completed before national COVID-19 precautions were instigated by the UK government on March 23. Before this date, no COVID-related changes to PPID policy were made. Two observers (medical and nursing) with health care backgrounds were trained to collect data and analyze the PPID institutional policy and procedure, using sample cases from a previous observational study to facilitate identification of deviation.

Observers were assigned to a porter whom they followed and observed during their patient transfer tasks; observations included the actions of health care staff in identifying the patient leaving or entering their department. The observations for each transfer finished when the patient was received at the destination, and the porter informed their manager that the transfer was completed.

Observers initially characterized the practice descriptively and then added notes on interpretations and intuitions aided by self-reflection based on their previous training.

An online form was created for collecting observation data, incorporating free-text fields to capture factors affecting patient identification during transfer, using the SEIPS framework (Table 1), and was pilot tested to evaluate reliability before routine data collection.

To optimize the rigor of the study, data were collected at different times, and observers were positioned nearby but slightly peripheral to the porter observed to minimize Hawthorne effect.

Data recorded for each transfer included the task assigned to the porters and the PPID process at both original location and destination ward (Table 2).

Informal Interviews

Brief informal interviews were conducted with each porter observed during shadowing to clarify observation data and gain insight into the patient identification process. Interviews were captured via field notes for analysis.

Methods of Data Analysis

Quantitative

Quantitative data collected from observations were analyzed using descriptive statistics, including frequencies and percentages, in SPSS (version 26.0; SPSS, Chicago, Illinois).

Qualitative

Qualitative data from field notes were analyzed using issues analysis,[26,27] process mapping, and FMEA. The SEIPS work elements were used to classify the main issues during the descriptive analysis, building up a detailed picture of the patient transfer process and potential risk areas. The analysis results informed the development of the process maps and the FMEA[28–32] (Fig. 1).

Descriptive Analysis

Findings were categorized using the SEIPS classification: work system components (people, task, tool/technology, environment, and organization), processes, outcomes, and adaption. Any potential difficulty in completion of PPID noted was considered a potential contributing factor to inform thinking about risk controls for specific risks identified through FMEA.

Process Map

This analysis was developed to identify the parts of the patient transfer process where PPID was impacted by the system design. The process map depicts the process of patient identification during intrahospital patient transfer according to the institutional PPID, using online diagram software (Draw.io) to provide a visual representation of both the "work as imagined" and the process variation of the "work as done,"[23] which was observed, classified using SEIPS.

Failure Modes and Effects Analysis

Failure modes are defined as ways in which a specific process step could fail. Because the patient identification process in this study is the focus of interest, the research team considered, before data collection, 2 basic failure modes: (1) a health care professional misidentifies a patient and (2) a health care professional does not identify the patient when identification should have been carried out. Causes and effects of these potential failure modes were elicited from observation and informal interviews during shadowing to the patient identification process.

Along with details of the potential failure mode, potential effect, and potential cause of each failure mode, the FMEA considers 3 main categories: *severity* (S), the potential seriousness of the outcome of the potential failure; *occurrence* (O), the likelihood of the potential error happening; and *detectability* (D), the likelihood of control measures detecting the potential failure before it occurs. For each category, a 10-point scale was used to grade S, O, and D as high or low.

TABLE 1. SEIPS Model Components (Based on Holden et al[22])

Component		Definitions	Focus of Study
Work system	People	Skills levels, experience with the procedure, cognitive function, attitudes	Health care professionals (nurses, doctors, radiographers, health care assistant) and staff members (receptionists and porters)
	Task	Difficulty, complexity, variety, and familiarity of work task or procedure	Patient identification in the original location and destination ward
	Tool/Technology	Availability or usability of technologies, health information, medical devices or equipment	Resources to assign the transfer: paper form, paper slip, wristband, patient's notes
	Environment	Internal: hygiene, lighting, air quality, noise, workspace design and layout. External: budget and cost on the quality of the technologies used and market-influenced pay levels for personnel	Design of ward where patient is collected, transferred and identified
	Organization	Whether workarounds need to be used because of lack of personnel, whether the team can work in unison, and the availability of appropriate detailed procedures for emergency situations	Hospital setting Implementation of PPID policies Standardization and training practices Role differences
Processes		These can be decomposed into physical, cognitive, and social/behavioral performance processes	Health care professionals identify details of the patient to be collected: checked against the patient's wristband, and where possible by verbally asking the patient for PPID. It should be verified that the correct notes accompany the patient where they are required.
		Many processes in health care involve collaboration between professionals and non-professionals, including patients and family.	
Outcomes		Patient: patient satisfaction and experiences	PPID or misidentification
		Professional: staff satisfaction and retention	Work overload, burnout
		Organizational: organizational results	Staffing or capacity difficulties
Adaptation		In dynamic systems, processes and their outcomes are monitored; then, adaptations are made in an attempt to decrease the gap between actual versus ideal performance	Workarounds to identify the patient

An overall *Risk Priority Number* (*RPN*) was calculated by multiplying the values (RPN = S × O × D). We selected an RPN of more than 168 (S ≥ 8; O ≥ 7; D ≤ 3) as a threshold for further analysis based on a preliminary scoping review of the data, which suggested that this cutoff point would allow us to identify the most important issues. (See Appendix 1 for severity occurrence and detectability rating tables, http://links.lww.com/JPS/A509).

A "condition" represents a potential failure mode, a potential failure effect, and a potential cause, and this is shown in a row from the FMEA matrix. Each condition was evaluated in terms of SEIPS. An additional column was added to the FMEA to indicate which

SEIPS work elements were associated with the identified conditions. Each mode condition was also linked to a step in the process map, highlighting where that potential failure could occur.

RESULTS

Quantitative

A total of 60 patient transfer handovers were observed during the 2-month inclusion period. In 9 cases, health care professionals canceled the transfer request when porters arrived at the ward

TABLE 2. Variable Definitions

Variable	Definition
Time of the transfer	Morning, afternoon, or night shift
Mode of task allocation	How the patient transfer task and patient information was allocated to porters. Modes observed included handwritten in paper slip, in printed form, or via the radio or telephone.
Health care staff who released the patient at the original location	Positions in organization were recorded as follows: nurse, health care assistant, receptionist, radiographer, or doctor. If no health care professional released the patient, this was also was recorded.
Health care staff who received the patient at the destination	Nurse, health care assistant, receptionist, radiographer, doctor. If no health care professional received the patient; it was also recorded.
Health care staff who identified the patient	Positions in organization were recorded as follows: nurse, porter, health care assistant, receptionist, radiographer, doctor or nobody.
How identification was carried out according to NHS policies[10]	In accordance with NHS policies: for this, compliance with all 3 requirements was necessary: (*a*) checking patient notes, (*b*) checking and comparing information with the wristbands, and (*c*) asking patients for their names. Not in accordance with NHS policies: when not all of the requirements mentioned above were met
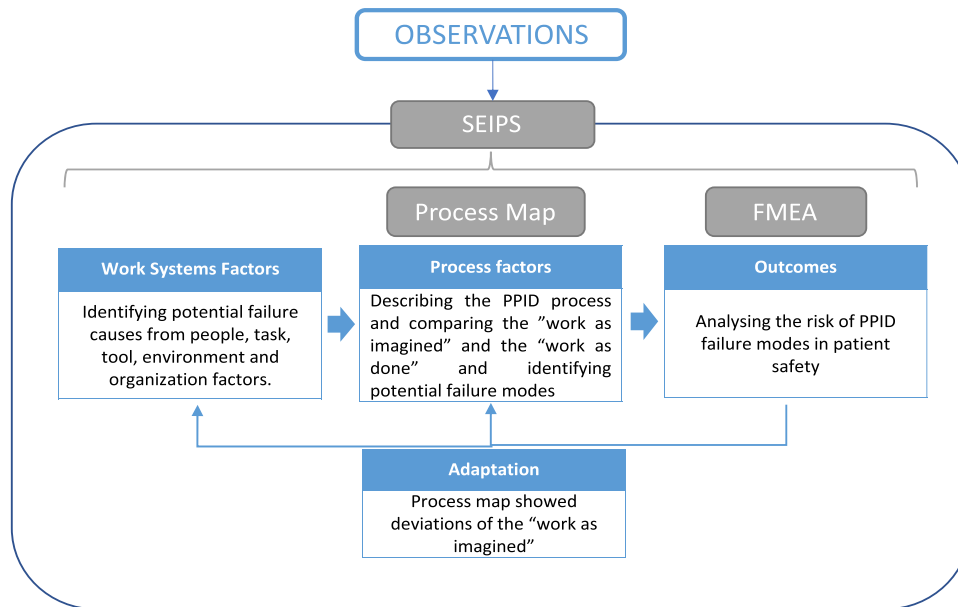
FIGURE 1. Overview of the multiple methods, with the SEIPS model as a framework.

because of patients having been transferred already or not being ready. Because these transfers did not occur and generated no observational data, they were excluded from the analysis.

Forty of 51 evaluable cases (78%) occurred in the afternoon shift, 9 (18%) in the morning shift, and 2 (4%) in the night shift. Porters received information about patients for transfer via handwritten paper slip in 28 (54.9%) cases, printed paper form in 15 (29.4%), radio in 6 (11.8%), and telephone in 2 (3.9%). All patients in this sample were conscious during transfer. Table 3 shows characteristics of the transfers.

PPID at Patient Collection

Involvement of Health Care Staff

When patients were collected, 23 patients (45%) were released to porters, which was carried out by nurses, and 14 (27.5%) by other health care professionals. Porters collected 14 patients (27.5%) without contacting any health care professionals.

PPID by Health Care Staff

Nurses identified 23 patients for transfer (45%) somehow, and other professionals identified 10 patients (19.6%). Porters actively identified 16 patients (31.4%) by themselves without assistance: in the remaining 2 cases (3.9%), the porter was not observed to make any attempt to identify the patient positively.

Method of Patient Identification

In 31 patients (60.8%), health professionals who already knew the patient identified them informally to the porter. In 6 patients (11.8%), health care staff asked the patient to confirm their name; in 5 patients (9.8%), the information in the transfer paper slip was compared with the patient medical record as the only method of identification; and in 4 patients (7.8%), the name that the patient gave when asked was compared with the patient medical record. In 3 patients (5.9%), the receptionist confirmed identification when asked by the porter by pointing with her hand toward the correct patient, and in 2 patients (3.9%), there was no identification by any ward staff, with the porter taking the patient and transferring them without assistance from others.

TABLE 3. Transfer Characteristics

Characteristics	Ward of Patient Collection (n = 51)	Ward of Patient Delivery (n = 51)
Location		
Radiology, no. (%)	21 (41.2)	19 (37.3)
SEU, no. (%)	6 (11.8)	6 (11.8)
CMU, no. (%)	3 (5.9)	0 (0)
Endoscopy, no. (%)	3 (5.9)	0 (0)
Neurology, no. (%)	3 (5.9)	1 (2.0)
Vascular surgery, no. (%)	3 (5.9)	4 (7.8)
AAU, no. (%)	2 (3.9)	3 (5.9)
Other locations, no. (%)	10 (19.5)	18 (35.2)
Who released/received the patient?		
Nurse, no. (%)	23 (45.1)	14 (27.5)
Receptionist, no. (%)	6 (11.8)	2 (3.9)
Radiographer, no. (%)	2 (3.9)	4 (7.8)
HCA, no. (%)	3 (5.9)	1 (2.0)
Nobody, no. (%)	14 (27.5)	29 (56.9)
Other health care staff, no. (%)	3 (5.9)	1 (2)
Who identified the patient?		
Nurse, no. (%)	23 (45.1)	13 (25.5)
Receptionist, no. (%)	3 (5.9)	0 (0)
Radiographer, no. (%)	1 (2.0)	2 (3.9)
HCA, no. (%)	3 (5.9)	2 (3.9)
Porter, no. (%)	16 (31.4)	NA
Nobody, no. (%)	2 (3.9)	33 (64.7)
Other health care staff, no. (%)	3 (5.9)	1 (2)

AAU, ambulatory assessment unit; CMU, complex medicine unit; HCA, health care assistant; Other health care staff, doctor or nursing student; Other location, acute general medicine, adult intensive care, cardiology, cardiothoracic, emergency assessment unit, gastroenterology, gynecology, infectious diseases, main reception, neonatology, rapid assessment unit, transfer lounge, traumatology, pediatric, short stay unit; SEU, surgical emergency unit.

PPID at Delivery

Involvement of Health Care Staff

At the transit destination, 14 patients (27.5%) were received by nurses, and 8 patients (15.7%) by doctors, radiographers, health care assistants, or receptionists. In 29 patients (56.9%), no health care staff participated in this process. The porter delivered the patients directly to their rooms or the waiting area.

PPID by Health Care Staff and Method of Patient Identification

Some patient identification at the destination was performed in 18 patients (35.3%) by nurses or other staff members. Of those, 12 were identified by either nurses or other staff members who said they knew the patient from memory and did not check any patient information from medical records. The remaining 6 cases involved patients who were simply asked verbally for their name (3 cases) or had the personal information on their paper transfer slip compared with the patient information from medical records (3 cases).

In 33 patients (64.7%), there was no identification by the professional staff at the destination, either because the professionals responsible were not present or because they omitted it. In none of the 51 (100%) evaluable cases observed, patient identification was conducted correctly according to hospital policy at every step of the transfer process.

Qualitative

Descriptive Analysis Using the SEIPS

The following issues were identified during this analysis as impacting on the PPID process. The issues have been grouped according to the SEIPS elements.

People and Teams

Communication. Communication between health care professionals and porters was inconsistent and informal. Updated information about the transfer, for example, a canceled transfer, was not always shared with the staff involved in the process. Consequently, the PPID process was not completed in any of the observations.

Workload/staff availability. It was common for staff to either not be available or nurses overloaded to allocate attention to patient identification. Porters frequently had to wait for a long time to obtain patient information.

Task

PPID process. Both at collection and delivery of patients, it was not clear who was accountable for releasing or receiving the patient from or into the department or who was responsible for patient identification. The written policy description of the PPID process was unclear.

Patient transfer task allocation. During busy times, porters are not expected to return to the porter's office to receive a new patient transfer task; instead, porters receive the next task via radio or telephone. Consequently, they do not formally record patient information for transferring but instead rely on memory. Although not observed directly, this deviation of the process was reported by multiple porters to the research team. The way this deviation from the normal process is carried out is not standardized, and new porters were not aware of this until it occurred.

Tools and Technology

Printed paper slip. Information regarding patient transfers was printed onto a paper form that the porter used as a reference for locating the patient. The printing quality of these forms was poor, making the text difficult to read, and some information was commonly omitted, for example, full name or date of birth.

Technical failure of the printer was common, and when this occurred, patient transfer slips were handwritten, introducing risks from difficulty in reading handwriting.

Patient wristband and identifiers. Porters had only compared the information on the paper slip to the patient's wristband when a health care professional was not available to identify the patient. This was sporadic rather than routine.

Environment

Layout and distractors. The layout of the environment impacted on the identification process when there were several patients in the same area. For example, the radiology department has a waiting room where multiple patients are seated, and transferred patients were commonly identified here. Potential distractors, such as noise, interruptions from other staff members, patients, or families, interfered with patient identification, especially in cognitive and physical impairment patients.

Organization

OUH PPID policy. The hospital policy for PPID and patient transfer (transfer escort policy) are not aligned with real-world activities. The PPID policies state that identifiers must be used for PPID (name, date of birth, and medical record number, if possible). However, the porter's office and therefore the patient transfer slip they issue do not have direct access to this necessary information, because the portering service is outsourced to contractors who do not have access to the electronic patient record system. The transfer escort policy states that the porter must approach a health care professional to assist in identifying the patient for transfer, but it is unclear which staff members this relates to. It was observed that, at times, porters approached receptionists, who are not accountable for patient care. According to the hospitals' policies, both nursing and portering staff were unclear about who was responsible for the patient during the transfer process.

Process Maps and SEIPS

The process map that depicts the process of patient identification according to the PPID policy has 9 steps. Observations of "work as done" showed that each step of the process was different from the "work as imagined" (Fig. 2).

Because the established PPID process as imagined was not followed, other forms of adaptation deviating from the "work as imagined" process were developed. The most common deviations were as follows: (*a*) only one identifier was used to identify the patient (the patient was just asked verbally for his/her name or wristband was checked), (*b*) health care professionals relied on their knowledge to identify the patient, (*c*) porters received patient information on a handwritten paper slip, and (*d*) porters identified the patient by themselves without any input from health care staff.

FMEA and SEIPS

We developed the FMEA considering 2 potential failure modes: (1) a health care professional misidentifies a patient, and (2) a health care professional does not identify the patient. We identified 45 distinct potential pathways combining a failure mode, effect, and severity estimate. Of these 45 unique "conditions," 20 received an RPN score of higher than 168 and were therefore considered of interest for further analysis.

The 2 highest-rated conditions had potential causes associated with the design or quality of information on the patient transferred slip. Nine conditions could have resulted in a patient undergoing an unnecessary procedure. The remaining conditions could lead to a patient being misidentified (but not undergoing an unwanted procedure) or to a delayed or canceled transfer. According to the
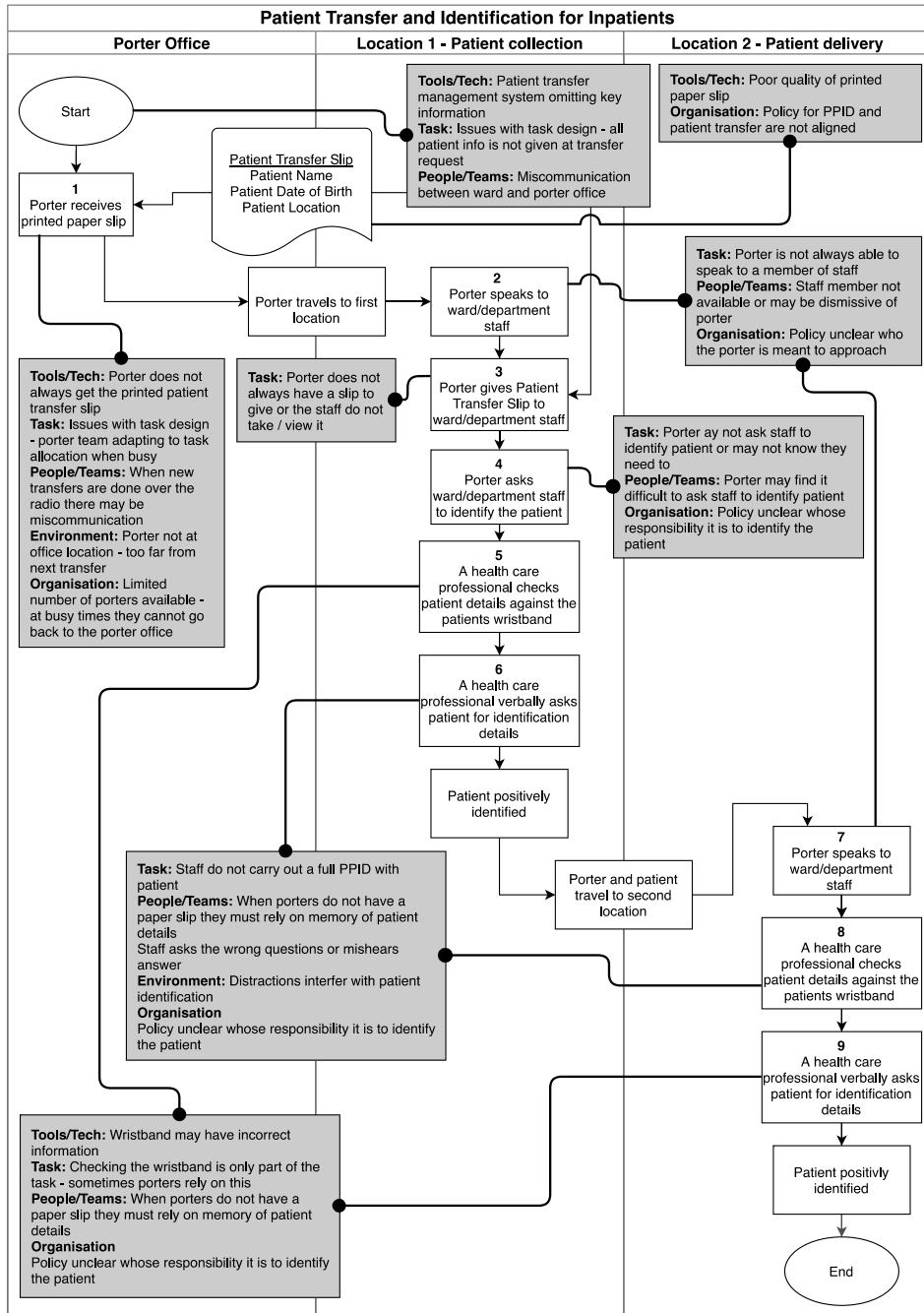
FIGURE 2. Identifying the "work as done" in each step of the process maps, according to the SEIPS work system factors.

SEIPS categories, only 2 of the conditions could be associated with individuals—that is, miscommunication between team members and reliance on memory.

Table 4 shows the 20 identified conditions from the FMEA with an RPN above the chosen threshold, along with the associated SEIPS work elements.

DISCUSSION

Because patient identification is a common process in health care and carries patient risks, hospitals generally have institutional policies to reduce misidentification. However, scientific literature on the frequency, significance, and causes of errors in PPID is scanty. A systematic review[33] identified 6 standard approaches to PPID and 3 classes of error consequences but reported that no strategies were associated with a perfect or near-perfect correct identification. A small randomized trial of a training intervention[34] found a 37% improvement in staff performance, but a Canadian study[35] in an outpatient setting recorded a 90% imperfection rate, suggesting that PPID error may be highly prevalent in a range of health care settings. A recently published study from our hospital[36] seems to be the only

TABLE 4. High-Risk Failure Modes

Process Map ID	Potential Failure Mode	Potential Failure Effects	Severity (1–10)	Potential Causes	Occurrence (1–10)	Current Controls	Detection (1–10)	RPN	SEIPS Work Elements
1	Health care professional misidentifies patient	Incorrect patient transferred	9	Patient transfer slip contains incorrect information	9	PPID	5	405	Tools/Technology
1	Health care professional misidentifies patient	Incorrect patient transferred	9	Patient transfer slip contains missing information	9	PPID	5	405	Tools/Technology
5, 6, 8, 9	Health care professional misidentifies patient	Incorrect patient transferred	9	Health care professional confuses key patient information with another patient—attention and memory affected by high workload	9	PPID	4	324	Person/Cognition/Organization
5, 6, 8, 9	Health care professional misidentifies patient	Incorrect patient transferred	9	Health care professional does not identify the patient in any way—actions affected by high workload	9	PPID	4	324	Person/Cognition/Organization
5, 6, 8, 9	Health care professional misidentifies patient	Incorrect patient transferred	9	Health care professional forgets key patient information—memory affected by high workload	8	PPID	4	288	Person/Cognition/Organization
5, 6, 8, 9	Health care professional misidentifies patient	Incorrect patient transferred	9	Health care professional confuses key patient information with another patient—attention and memory affected by distractions in the environment	7	PPID	4	252	Person/Cognition/Environment
5, 6, 8, 9	Health care professional misidentifies patient	Incorrect patient transferred	9	Health care professional does not fully hear or remember key patient information—attention and memory affected by distractions in the environment	7	PPID	4	252	Person/Cognition/Environment
1	Health care professional misidentifies patient	Patient undergoes unnecessary procedure	10	Patient transfer slip not available—printer not maintained	8	Hand write patient information	3	240	Tools/Technology
1	Health care professional misidentifies patient	Patient undergoes unnecessary procedure	10	Patient transfer slip not available—printer not connected to network or computer	8	Hand write patient information	3	240	Tools/Technology
5, 6, 8, 9	Health care professional misidentifies patient	Patient undergoes unnecessary procedure	10	Health care professional confuses key patient information with another patient—attention and memory affected by high workload	8	PPID	4	320	Person/Cognition/Organization

(Continued next page)

TABLE 4. *(Continued)*

Process Map ID	Potential Failure Mode	Potential Failure Effects	Severity (1–10)	Potential Causes	Occurrence (1–10)	Current Controls	Detection (1–10)	RPN	SEIPS Work Elements
5, 6, 8, 9	Health care professional misidentifies patient	Patient undergoes unnecessary procedure	10	Health care professional does not fully hear or remember key patient information—memory affected by high workload	8	PPID	4	320	Person/ Cognition/ Organization
5, 6, 8, 9	Health care professional misidentifies patient	Patient undergoes unnecessary procedure	10	Health care professional does not compare key patient information with wristband (partial identification)—actions affected by high workload	8	PPID	4	320	Person/ Cognition/ Organization
5, 6, 8, 9	Health care professional misidentifies patient	Patient undergoes unnecessary procedure	10	Health care professional confuses key patient information with another patient—attention and memory affected by interruptions and noisy in the environment	7	PPID	4	280	Person/ Cognition/ Environment
5, 6, 8, 9	Health care professional misidentifies patient	Patient undergoes unnecessary procedure	10	Health care professional does not compare key patient information with wristband—actions affected by distractions in the environment	7	PPID	4	280	Person/ Cognition/ Environment
5, 6, 8, 9	Health care professional misidentifies patient	Patient undergoes unnecessary procedure	10	Health care professional does not fully hear or remember key patient information—attention and memory affected by distractions in the environment	7	PPID	4	280	Person/ Cognition/ Environment
5, 6, 8, 9	Health care professional misidentifies patient	Patient undergoes unnecessary procedure	10	Health care professional does not identify the patient in any way—relies on memory of patient and patient location	7	PPID	4	280	Person/ Cognition
2, 3, 4	Health care professional does not identify patient	Incorrect patient transferred	9	Multiple patients in location waiting for transfer	7	Patient transfer slip	4	252	Environment
1, 2, 3, 7	Health care professional does not identify patient	Patient transfer canceled	8	Porter given incorrect information about patient location	8	Patient transfer slip	4	256	Team/ Communication
2, 7	Health care professional does not identify patient	Patient transfer delayed	8	It was not known by the porter who was responsible for patient identification	9	OUH policy —not available to porters	4	288	Tools/ Technology/ Task

(Continued next page)

TABLE 4. *(Continued)*

Process Map ID	Potential Failure Mode	Potential Failure Effects	Severity (1–10)	Potential Causes	Occurrence (1–10)	Current Controls	Detection (1–10)	RPN	SEIPS Work Elements
4	Health care professional does not identify patient	Patient undergoes unnecessary procedure	10	Health care professional not available to identify patient	8	OUH policy	4	320	Organization

report to date of a successful human factors–based intervention to reduce PPID errors.

We conducted an in-depth analysis using a systems and human factors engineering approach to highlight the complex patterns that affect patient identification and find out why "work as done" does not match "work as imagined."[22,23]

Our qualitative observation study shows that noncompliance with the patient identification process was widespread for transferring inpatients. Although the hospital does have a PPID policy with associated guidance, its impracticality represents a serious risk to patient safety. Through the process map, we identified that in 100% of the observations, at least 1 of the 10 steps of the PPID was incorrect. The PPID process was not designed to catch failures, and not all staff were trained in the PPID process or had knowledge of it.

The main system factor involved was the failure to anticipate or mitigate the unintended consequences of an organizational structure decision made at the highest management level. The downstream effects of this decision made the existing PPID policy unworkable and resulted in problems with technology and team culture, which played an important secondary role.

The key element underlying the discrepancies between policy and practice was the decision to outsource portering services, which meant that porters ceased to be employees of the hospital and were transferred to an external contractor. With this new status, it was decided (on the grounds of preserving patient confidentiality) that porters could not access clinical records or institutional information sources, could not be held accountable for their actions via the hospital disciplinary procedures, and could not be subjected to mandatory training. In fact, porters were not officially responsible for identifying patients at all but did carry out workarounds on their own initiative.

The knock-on consequences of these decisions for PPID explain many of the specific findings when work systems elements were analyzed using SEIPS.

People/Team and Organization

Given the porters' exclusion from the official process, it was unclear whether the nursing staff had any responsibility for "handing over" the patient to the porter. Even when health care professionals were available, the entire PPID process was never observed. This exposes staff to a risk of blame for not following policy in the case of any adverse events.[37] Other studies have also found several deviations in the patient identification process due to unclear policies and the lack of adaptation to the real world in the clinical environment.[38–40]

Tool/Technology

The PPID policy requires a health care professional to ask the patient their full name and date of birth at least,[10,11] if possible,

and cross-reference this with the procedure or transfer documentation. However, the standard paper transfer slip did not contain these identifiers and was not aligned with wristband barcodes. This was because it was not connected to the hospital's electronic patient record system. The hospital did not consider it its responsibility to provide appropriate technology to the porters and did not share key identification information with the porter's office. The technology available to the porters for producing the printed slips was obsolete and frequently malfunctioned, leading to risky workarounds.

Tool/Technology and Environment

Reliance on memory and assumptions have led to the misidentification of patients.[5,15,41] In the context of this hospital, porters sometimes used the patient wristband to identify them and cross-referenced this with the patient transfer slip or patient information by memory, either because they were under time pressure or because of distractors. However, checking wristbands alone is not effective in eliminating misidentification.[10,18,37] Furthermore, only having the name and no other patient information is a high risk because not all patients can confirm their names, which could be confused.[42]

Task and Organization Policy

According to the hospital policy, it is the health care professional's responsibility to identify patients both at the starting location before they are collected and when they are delivered at a new location. However, the situation over the status of porters led to ambiguity over who was responsible for the patient during the transfer. Hospital policy did not recognize the real-world role of nonhospital employees in the transfer process, leaving porters and clinical staff without guidance on how to hand over patients to each other. This uncertainty places health care staff and porters at risk if errors occur.[41,43] Our observations suggest that with appropriate training, porters would be well able to identify patients safely, but governance and risk issues related to their status as employees of an independent contractor would need to be resolved at a high organizational level.

Our human factors analysis highlights not only individual actions or inactions but all aspects of the work system that may impact the individual's daily practice, including the many system elements outside control.[22]

Considering the system's deficiencies, the staff showed remarkable resilience in using adaptations when they did not have the necessary resources to identify patients, which often put patient safety at risk. Individual porters showed a high degree of conscientiousness in ensuring the process worked properly, likely preventing numerous misidentification incidents.

The application of the FMEA methodology revealed that miscommunication between the staff involved and lack of key patient information put patient safety at risk. Communication and team-based

care are at the heart of health care safety,[14,44,45] but it is recognized that simply asking people to "work harder" or "do better" is not an effective or reliable solution to communication challenges.[46]

Therefore, when patients are misidentified and harm occurs, it is generally incorrect to conclude that it is due to "human error." The point of failure is a symptom of system design or "system error," as illustrated by this case study. If such system failures are not recognized through proactive analysis, harm is likely to occur, and organizations may blame individuals when the system has set them up to fail.

Recommendations for Change

The decision to outsource portering at this hospital was not unusual—political influences on the strategy of the NHS over decades have resulted in repeated attempts to introduce private enterprise and competition into the government-funded system, resulting in many hospitals seeking to outsource support services at different times. The increasing emphasis on data confidentiality in health care, however, led hospital management, in this case, to exclude non-NHS employees from systems, which could give access to personal information about patients. Some form of honorary contract for porters with the hospital, as is commonly used for research staff, might have avoided the difficulties that ensued and might provide the basis for a solution. A clear policy and process for identifying and handing over responsibility for patients as they move around the hospital are needed. This will require training for nursing staff, porters, and others who will hand off and receive patients. Technology will undoubtedly play a valuable role in providing redundancy of information via bar code scanners or similar devices that recognize the patients' unique medical record numbers. From a psychosocial viewpoint, finding ways to integrate porters into existing teams would improve communication and cooperation between them and other staff and strengthen a culture of solidarity and mutual support among hospital staff, which would likely encourage mutually supportive behavior when ensuring PPID is correctly carried out.

Limitations

Our sample of transfers was relatively small and was biased by availability—of research staff, porters, and, at night, transfers. However, our sampling strategy and methodology provided rich information from a range of patient identification during transfers in different wards and reached saturation; that is, no new themes emerged in the latter part of the study. This supports the generalizability of our findings, although the most important factor we identified (the organizational disconnect between porters and hospital staff) was specific to the hospital system studied, and the frequency with which it occurs elsewhere in the England or abroad is unknown. It is known that the researcher's presence in observational research inevitably influences the observed behavior; however, we tried to limit the observer influence by avoiding any interaction with staff to minimize our visibility and by asking the porters shadowed to continue following daily routines.

We did not include a patient perspective or interview caregivers, which would have added depth to these findings.

CONCLUSIONS

Patient identification during intrahospital patient transfer is a high-risk event because several factors and many people interact. Like any institutional policy, a PPID policy will be ineffective if it is not aligned with the realities of the workplace. The disconnect between the policy and the reality of the workplace in this case study left both health care staff and porters (and patients) vulnerable to the consequences of misidentification because a major component of the real situation was simply not accounted for in the policy. This study yielded valuable baseline data. The analytical approach can be replicated to reduce the risk of patient misidentification during patient transfer and decrease human factors affecting the PPID, ultimately improving patient safety. Future studies should analyze the effects of misidentification and portering delays and evaluate the cost-effectiveness of patient misidentification during transfer.

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6.2. STUDY II. Medication errors in prescription and administration in critically ill patients

Summary of the most relevant results:

6.2.1. General characteristics

Medication errors (ME) were analysed in 142 patients. Prescription errors were analysed in 961 prescriptions and 90 patients, 63 men and 27 women, with a mean age of 64 years (SD 16). A total of 249 drugs were analysed in 52 patients, 19 men and 33 women, with a mean age of 65 years (SD 17). *Table 6* shows errors definitions for prescription and administration.

6.2.2. Medication errors in prescriptions

The mean number of drugs prescribed per patient was 11 (SD 4.5), and we detected 7 (SD 4.1) errors per patient. The prevalence of MEs in prescription medications was 47% (CI 44%-50%), and the magnitude of error was 13.5%.

Almost 37% of the errors detected were related to the omission of the form, frequency, or route of administration of the dosage, and 29% were related to illegible handwriting on prescriptions.

ICU stay was a risk factor for omission errors (OR 2.14; 1.46-3.14: P <.01). The prescription of a cardiovascular drug showed a higher risk of omission errors than other families of drugs (OR 2.12; 1.25-3.60: P <.01).

6.2.3. Medication errors in administration

The mean number of drugs administered per patient was 4.8 (SD 5.3), and one or more errors considered in this study were observed in 3.5 (SD 3.9) drugs. We also detected 6 (SD 6.7) errors per patient. The prevalence of MEs in the administration was 73.5% (CI 68% - 79%), and the magnitude of error was 19.7%.

The most recurrent error was an interruption during the administration, found in 47% of the direct observations. The nurses reported "workload" perception in 47% (CI 41% - 54%) of the observations, and the prevalence was statistically higher in nurses on the night shift (39%) than in those on the morning (38%) and afternoon shifts (23%).

Drugs received in the morning shift (OR 2.15; 1.10-4.18: P=0.02) and workload perception of nurses (OR 3.64; 2.09-6.35: P <.01) increased the risk for interruptions.

Table 6. Variable definitions

Errors in prescription	
Type of error	**Description**
Incorrect name	The incorrect writing of the drug name
Omission error	Important elements of the prescriptions body, such as dosage form, frequency or route of administration must be left out or incomplete.
Illegible handwriting	Prescription written that are unclear or indecipherable, whether in the name, dose, frequency or route of the drug
Commercial name	Writing commercial names instead to use generic name of the drug
Abbreviation	The use of abbreviation instead of the name of the drug

Errors in administration	
Type of error	**Description**
Preparation	Preparing a drug for administration in an inappropriate space and time, as incomplete identification of the name, dose, frequency and/or route
Interruption	Interruption during preparation and/or administration of drugs as bells, telephones, calls from patients, families or colleagues.
Medication prepared by another professional	No match between the professional (nurse or physician) who prepares and who administers the drug
Out of time or without prescription	Administrating drugs after prescribed time (1 hour more before or after) or not administering. It includes verbal prescriptions as well.
Incompatibility using an automated dispensing cabinet (Pixys)	Administration of a drug that does not correspond to the prescription of the patient due to the wrong dispensation of the automated medication dispensing cabinet (Pyxis).
No information to patient	Lack of information to the patient aware about the medication administered.

FULL TEXT OF ARTICLE II

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Medication errors in prescription and administration in critically ill patients

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Abstract

Aim: To determine the prevalence and magnitude of medication errors and their association with patients' sociodemographic and clinical characteristics and nurses' work conditions.

Design: An observational, analytical, cross-sectional and ambispective study was conducted in critically ill adult patients.

Methods: Data concerning prescription errors were collected retrospectively from medical records and administration errors were identified through direct observation of nurses during drug administration. Those data were collected between April and July 2015.

Results: A total of 650 prescription errors were identified for 961 drugs in 90 patients (mean error 7[*SD* 4.1] per patient) and prevalence of 47.1% (95% CI 44–50). The most frequent error was omission of the prescribed medication. Intensive care unit stay was a risk factor associated with omission error (OR 2.14; 1.46–3.14: p < .01). A total of 294 administration errors were identified for 249 drugs in 52 patients (mean error 6 [*SD* 6.7] per patient) and prevalence of 73.5% (95% CI 68–79). The most frequent error was interruption during drug administration. Admission to the intensive care unit (OR 0.37; 0.21–0.66: p < .01), nurses' morning shift (OR 2.15; 1.10–4.18: p = .02) and workload perception (OR 3.64; 2.09–6.35: p < .01) were risk factors associated with interruption.

Conclusions: Medication errors in prescription and administration were frequent. Timely detection of errors and promotion of a medication safety culture are necessary to reduce them and ensure the quality of care in critically ill patients.

Impact: Medication errors occur frequently in the intensive care unit but are not always identified. Due to the vulnerability of seriously ill patients and the specialized care they require, an error can result in serious adverse events. The study shows that medication errors in prescription and administration are recurrent but preventable. These findings contribute to promote awareness in the proper use of medications and guarantee the quality of nursing care.

1 | INTRODUCTION

Medication errors (MEs) are a serious problem that may threaten the quality of care and patient safety and possibly lead to mistrust in the system, institution and professionals' work (Di Simone et al., 2016; Kohn, Corrigan, & Donaldson, 1999; PSNet Patient Safety Network, 2019). The problem of MEs is complex. They may occur in any phase of the medication process and can be related to different groups of healthcare workers. Of much concern is the fact that most MEs are still widely under-reported (Otero López et al., 2008; Rovinski-Wagner & Mills., 2018; Shekelle et al., 2013). Globally the impact of medication-related adverse events is nearly twice in middle-income countries compared with high-income countries, in terms of the number of year of healthy life lost. In the United States of America, medication errors cause at least one death every day and injure approximately 1.3 million people every year (World Health Organization, 2017b).

The World Health Organization launched The Third WHO Global Patient Safety Challenge: Medication Without Harm, to propose solutions to address many of the obstacles the world face today to ensure the safety of medication practices. Therefore, one of the key action area of this challenge is to promote and support research in this area as part of the overall agenda of patient safety research (World Health Organization, 2017a).

1.1 | Background

The potential of medication errors is particularly high in the prescription and administration of drugs. Several studies have shown that the risk of MEs in prescription is related to deficiency in management of dosage formulation and incomplete data (Bowdle, 2003; Grünewald & Mack, 2001; Krähenbühl-Melcher et al., 2007; Mack, Kuc, & Grünewald, 2000; Miasso et al., 2009). Errors in administration are more closely related to environmental and professional factors such as stress or work overload (Donati, Tartaglini, & Di Muzio, 2015; Elganzouri, Standish, & Androwich, 2009; Frith, 2013; Kendall-Gallagher & Blegen, 2009).

In intensive care units (ICU), MEs are particularly important due to the complexity of health care and the patients' limited physiological reserves, making them more vulnerable to the occurrence of errors (George, Henneman, & Tasota, 2010; Merino et al., 2013; Nicole Salazar, Marcela Jirón, Leslie Escobar, Tobar, & Romero, 2011). Critically ill patients receive twice as many drugs as patients in other units and most of them are intravenous. As these patients are frequently sedated and cannot participate consciously in the therapeutic process, reversal in the case of errors is difficult (Armitage & Knapman, 2003; Di Giulio, 2018; Moyen, Camiré, & Stelfox, 2008).

Studies conducted in Spain found that a patient admitted to an ICU had a 22% risk of ME's and that most of these occurred during drug prescription and administration (Merino et al., 2013). Although most MEs are predictable and preventable, they are not completely avoidable. It is thus crucial to know the conditions under which MEs occur so as to create strategies to reduce them. This study was designed to determine the prevalence and magnitude of MEs in the ICU and to analyse the association between medication errors, patients' sociodemographic and clinical factors and factors related to nurses' work.

2 | THE STUDY

2.1 | Aim

To determine the prevalence and magnitude of MEs in the ICU and to analyse the association between medication errors, patients' sociodemographic and clinical factors and factors related to nurses' work.

2.2 | Design

We conducted a single-centre, observational, cross-sectional and ambispective study.

2.3 | Sample/Participants

Inclusion criteria were patients over 18 years who had been in the ICU or the Intermediate Care Unit (IMCU) for more than 24 hr. Patients had to have the prescription and administration of at least one drug by oral or parenteral route. Patients without medical prescriptions were excluded. All patients were included consecutively except for those who met some exclusion criteria.

2.4 | Setting

The ICU in our centre has 30 beds for patients with medical or surgical illnesses requiring health care from specialist ICU physicians. The IMCU has 24-beds for critically ill medical patients who need specialist care but are not on mechanical ventilation. The nurse-patient ratio is 1:2 in the ICU and 1:4 in the IMCU. The medical prescription is written manually every day and may include one or more medications.

2.5 | Data collection

We collected the following demographic and clinical variables from the medical records: age, sex, diagnosis at admission (medical or surgical), care unit (ICU or IMCU), comorbidity and family of drugs prescribed in accordance with the anatomical therapeutic classification (digestive and metabolic system, blood and haematopoietic organs, cardiovascular system, nervous system and others). Other variables collected in the administration stage were factors related to nurses' working situation.

In accordance with Category A of the classification of the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP), we evaluated only the circumstances or events capable of causing errors or near-misses (Cousins & Heath, 2008; World Health Organization, 2009, 2010). We evaluated five types of errors in the prescription of medications and six errors in their administration (Table 1). We also rated the overall prevalence of errors, the prevalence for each type of error and the magnitude of the error for each stage of medication. The magnitude of the errors was assessed by dividing the total number of MEs in the prescription or administration between the total number of prescribed or administered drugs multiplied by the total number of possible errors.

To determine the most frequent MEs and their related factors in daily clinical practice we designed an ad hoc questionnaire for each stage through a participatory and consensus process with nurses from both participating units. We next carried out a pilot test to evaluate the reliability of this questionnaire. All data were collected from medical records between April - July 2015.

Errors in prescriptions were evaluated retrospectively using the information from the previous day (24 hr). Administration errors were analysed prospectively through direct observation and over 5 days as a maximum. Each drug administered was considered as one observation and the perception of workload was evaluated immediately after each administration. Two nurses from each unit were trained to participate in the study by the research coordinator. Nurses from the ICU and IMCU were blinded to the study hypothesis. A minimum inclusion of 500 records in total was established for accuracy of 3% and losses of 5%. This calculation was based on a pilot test and previous studies (Merino et al., 2013; Nicole Salazar et al., 2011).

2.6 | Ethical considerations

The study was approved by the Clinical Research Ethics Committee at our centre and was carried out following the ethical standards of the Declaration of Helsinki (2013). All the patients or their relatives provided written informed consent.

2.7 | Data analysis

Categorical variables were described as frequencies and percentages and quantitative variables as means and standard deviations (*SD*). In the comparative analysis, we used the chi-square test and Fisher's exact test for categorical variables and we used the Mann–Whitney U-test for quantitative variables. The 95% confidence interval was used to express prevalence and magnitude of the error.

TABLE 1 Variable definitions

Type of error	Description
Errors in prescription	
Incorrect name	The incorrect writing of the drug name
Omission error	Important elements of the prescriptions body, such as dosage form, frequency or route of administration must be left out or incomplete
Illegible handwriting	Prescription written that are unclear or indecipherable, whether in the name, dose, frequency or route of the drug
Commercial name	Writing commercial names instead to use generic name of the drug
Abbreviation	The use of abbreviation instead of the name of the drug
Errors in administration	
Preparation	Preparing a drug for administration in an inappropriate space and time, as incomplete identification of the name, dose, frequency and/or route
Interruption	Interruption during preparation and/or administration of drugs as bells, telephones, calls from patients, families or colleagues
Medication prepared by another professional	No match between the professional (nurse or physician) who prepares and who administers the drug
Out of time or without prescription	Administrating drugs after prescribed time (1 hr more before or after) or not administering. It includes verbal prescriptions as well.
Incompatibility using an automated dispensing cabinet (Pixys)	Administration of a drug that does not correspond to the prescription of the patient due to the wrong dispensation of the automated medication dispensing cabinet (Pyxis)
No information to patient	Lack of information to the patient aware about the medication administered

We performed a multivariate logistic regression to examine the association between the factors that were clinically relevant or significant and MEs. The results of the regression were expressed as odds ratios (OR) with 95% confidence intervals (95% CI). All analyses were performed with the SPSS program (V 22.0) using a bilateral approach and establishing a significance level of 5% (α = 0.05).

2.8 | Validity, reliability and rigour

We carried out a pilot test to evaluate reliability of the ad hoc questionnaire, before data collection. To optimize the rigour of the study, data on prescription and administration were collected at different times to avoid professionals modifying their behaviour in response to their awareness of being observed (Hawthorne effect). This meant that the same drugs were not evaluated in the two stages. All these data were integrated into a single database and reviewed to ensure validity and completeness.

3 | RESULTS

Medication errors were analysed in 142 patients (Figure 1). The analysis of prescription included 90 patients, 63 men and 27 women, with a mean age of 64 years (SD 16). Nine hundred and sixty-one drugs were prescribed and medical errors were identified in 453.

Administration errors were analysed in 52 patients, 19 men and 33 women, with a mean age of 65 years (SD 17). A total of 249 drugs were administered, 32.5% (81) in the morning, 31% (77) in the afternoon and 36.5% (91) at night. We identified one or more errors in 183 administrations. In 76% of observations, more than one drug was administered simultaneously. (Table 2).

3.1 | Medication errors in prescriptions and association between patients' sociodemographic factors and clinical factors

The mean number of drugs prescribed per patient was 11 (SD 4.5). Five (SD 2.7) drugs prescribed had one or more of the five types of errors included. We detected 650 MEs in 453 drugs, that is 7 (SD 4.1) errors per patient. The prevalence of MEs in the prescription of medications was 47% (CI 44%-50%) and the magnitude of error was 13.5%.

Almost 37% of the errors detected were related to the omission of the form, frequency or route of administration of the dosage and 29% were related to illegible handwriting on prescriptions. Concerning family of drugs, over 50% of errors in prescription were identified in drugs acting on the nervous system and cardiovascular system. In the assessment by type of errors, significant differences were found in prescription and administration between being admitted to ICU or to the IMCU. (Table 3).

In the bivariate analysis, ICU stay was a risk factor for omission errors (OR 2.14; 1.46–3.14: p < .01). ICU stay was also a risk factor in the multivariate analysis (OR 2.42; 1.62–3.62: p < .01). The prescription of a cardiovascular drug showed a higher risk of omission errors than other families of drugs (OR 2.12; 1.25–3.60: p < .01). (Appendix 1).
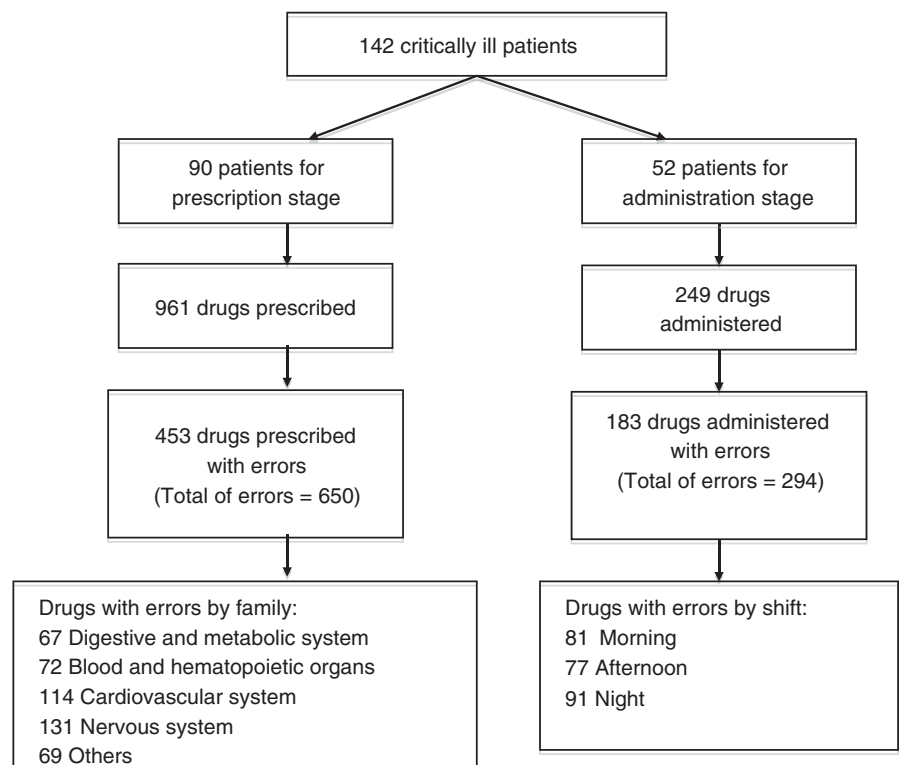
FIGURE 1 Study flow diagram

TABLE 2 Sociodemographic and clinical characteristics

Characteristics	Prescription N = 90	Administration N = 52
Age (years), M (SD)	64 (16)	65 (17)
Sex		
Women, No. (%)	27 (30)	19 (36.5)
Men, No. (%)	63 (70)	33 (63.5)
Diagnosis		
Medical, No. (%)	55 (61)	39 (75)
Surgical, No. (%)	35 (39)	13 (25)
Comorbidities, M (SD)		
>3, No. (%)	23 (26)	20 (38.5)
≤3, No. (%)	67 (74)	32 (61.5)
High blood pressure, No. (%)	43 (48)	37 (71)
Heart disease, No. (%)	20 (22)	20 (38.5)
COPD, No. (%)	9 (10)	7 (13.5)
Diabetes Mellitus, No. (%)	13 (14)	14 (27)
Dyslipaemia, No. (%)	29 (32)	23 (44)
Renal Failure, No. (%)	4 (4)	9 (17)
Smoking, No. (%)	27 (30)	13 (25)
Alcohol, No. (%)	9 (10)	5 (10)
Surgical Interventions, No. (%)	30 (33)	20 (38.5)
Depression, No. (%)	4 (4)	8 (15)
Unit		
ICU, No. (%)	59 (66)	28 (54)
Intensive Medicine, No. (%)	20 (34)	12 (43)
Anaesthesiology, No. (%)	22 (37)	10 (36)
Cardiology, No. (%)	17 (29)	6 (21)
IMCU, No. (%)	31 (34)	24 (46)
Internal Medicine	31 (100)	24 (100)

Abbreviations: M, mean; SD, standard deviation; COPD, Chronic Obstructive Disease; IQ, Surgical Interventions; ICU, Intensive Care Unit; IMCU, Intermediate Care Unit.

3.2 | Medication errors in administration and association between patients' sociodemographic and clinical factors and nurses' work factors

The mean number of drugs administered per patient was 4.8 (SD 5.3) and one or more of the 6 types of errors considered in this study were observed in 3.5 (SD 3.9) of these. The overall number of errors was 294 in 183 drugs, that is, 6 (SD 6.7) errors per patient. The prevalence of MEs in the administration was 73.5% (CI 68%–79%) and the magnitude of error was 19.7%.

The most recurrent error was interruption during the administration, found in 47% of the direct observations. (Table 3). The nurses reported 'workload' perception in 47% (CI 41%–54%) of the observations and the prevalence was statistically higher in nurses on the night shift (39%) than in those on the morning (38%) and afternoon shifts (23%).

In the bivariate analysis, ICU stay was a protector factor for interruptions (OR 0.38; 0.22–0.66: $p < .01$) and it remained significant in the multivariate analysis (OR 0.37; 0.21–0.66: $p < .01$). Furthermore, drugs received in the morning shift (OR 2.15; 1.10–4.18: $p = .02$) and workload perception of nurse (OR 3.64; 2.09–6.35: $p < .01$) increased the risk for interruptions. Patient characteristics such as sex, diagnosis and comorbidities were not associated with MEs in administration. (Appendix 2).

4 | DISCUSSION

This study shows that MEs in prescription and administration in our ICU were frequent, with a relevant magnitude of error. Furthermore, patients' clinical characteristics and nurses' work conditions were associated with medication errors both in prescribing and administering medication. Patients' sociodemographic characteristics were similar in prescription and administration and most patients had a non-surgical medical diagnosis.

The average of eleven prescribed drugs and 7.2 errors per patient differed from results in a multicentre study conducted in the United Kingdom (Ridley et al., 2004), where the average errors per patient was lower (2.2%). The overall prevalence of MEs in prescribing drugs in our study (incorrect name, omission error, illegible handwriting, commercial name and abbreviation) was 47.2% and at least one error was found in each medical prescription. These results are similar to those in a previous study (Catchpole, 2013), that reported a prevalence of 37%. However, the prescriptions in the mentioned study were evaluated separately from the transcription of medications. In our clinical practice, the physician carries out the prescription and transcription onto the patient's record sheet.

In this study, the most frequent type of error in prescription was omission of dosage form, frequency or route of administration. This represented 36.3% of the total number of errors, whereas illegible handwriting represented 28.8% of the total number of errors. In the same context, Ridley et al. (2004) found that not writing the order as standard and writing illegibly accounted for 47.9% of all errors.

In agreement with prior studies we found that MEs were more frequent in drugs with effects on the nervous system and cardiac system. In contrast, Nicole Salazar et al. (2011) found that the highest rate of MEs was related to antibacterial drugs (Carayon et al., 2014; Kuo, Phillips, Graham, & Hickner, 2008; Muroi, Shen, & Angosta, 2017).

MEs in administration of drugs were the most frequent errors in our study. We found three errors in four administered drugs. The overall prevalence of MEs in administering drugs was 73.5% in contrast with findings of Nicole Salazar et al. (2011) who reported

TABLE 3 Total of errors in prescription and administration by type and unit

Type of error		Total of errors N = 650	ICU N = 397	IMCU N = 253
Prescription[a]				
Incorrect name, No. (%)		11 (1.7)	6 (1.5)	5 (2.0)
Omission error, No. (%)		236 (36.3)	165 (41.6)	71 (28.1)
Illegible handwriting, No. (%)		187 (28.8)	65 (16.4)	122 (48.2)
Commercial name, No. (%)		115 (17.7)	77 (19.4)	38 (15.0)
Abbreviation, No. (%)		101 (15.5)	84 (21.2)	17 (6.7)
Type of error	Total of errors N = 294	ICU N = 192	IMCU N = 102	
Administration[b]				
Preparation, No. (%)	48 (16.3)	34 (17.7)	14 (13.7)	
Interruption, No. (%)	137 (46.6)	78 (40.6)	59 (57.8)	
Medication prepared by another professional, No. (%)	30 (10.2)	22 (11.5)	8 (7.8)	
Out of time or without prescription, No. (%)	62 (21.1)	42 (21.9)	20 (19.6)	
Incompatibility using an automated dispensing (Pixys), No. (%)	3 (1.0)	3 (1.6)	0 (0.0)	
No information to patient, No. (%)	14 (4.8)	13 (6.8)	1 (1.0)	

[a]In this stage of medication was evaluated 453 prescription with errors.
[b]In this stage of medication was evaluated 183 administration with errors.

a lower prevalence, 51%, in drug administration. One possible reason for these difference could be that we included interruptions as a circumstance of causing error and other authors did not consider this (Lacasa & Ayestarán, 2012; Merino et al., 2013; Nicole Salazar et al., 2011).

The most frequent type of error in administration was interruptions, most being calls from colleagues. Another author, however, noted that patient and pharmacy storage calls were the most common cause (Elganzouri et al., 2009). We found that errors related to the time and administration technique were less frequent than in studies from other countries (Romero et al., 2013; Valentin et al., 2009).

Health systems and professionals should be aware of the need to prevent such errors as this setting represents one of the riskiest moments for a serious adverse effect to occur in critically ill patients. In this regard, it is worth noting that there are evidence of effective strategies to prevent MEs as simulation-based medical education or ME identification systems as machine learning programmes that can generate patient-specific alerts (Rozenblum et al., 2019; Sarfati et al., 2019). Furthermore, computerized systems have showed a cost effective impact related to the potential occurrence of adverse events. Other strategies have demonstrated to prevent ME based on implementing tools for guiding medication use and encouraging patient care by a multidisciplinary team. (Berdot et al., 2016; De Araújo et al., 2019; Di Simone et al., 2016).

Based on our data, almost half of the nurses (47%) perceived a high workload. Interruptions were a risk factor for nurses' perception of workload. It is of note that working an afternoon shift was a protective factor for perception of workload and omission of data in the drug administration stage.

Several authors have analysed the influence of different factors associated with the occurrence of errors (Catchpole, 2013; Gurses, Ozok, & Pronovost, 2012; Henneman, 2017; Rhodes et al., 2012). In our study, patients' personal factors were not associated with MEs, but work factors of nurses such as the perception of workloads influenced the risk of MEs. Merino et al. (2013) associated MEs with patient health status and with workloads. Valentin et al. (2009) reported that workload of professionals was a contributing factors of 32% of errors.

4.1 | Limitations

This study has two main limitations. First, it was conducted in a single centre, which may reduce external validity. Second, the continuous intravenous infusions of drugs were not included in prescription and administration. The main strength of this study is that we evaluated two stages of drug use, whereas previous papers have focused on one stage only. Furthermore, collecting data through direct observation and considering all routes of drug administration allowed accurate detection of MEs.

5 | CONCLUSION

We found a higher prevalence of MES in the prescription of drugs than in their administration. The most frequent types of errors were omission of dosage form, frequency or route of administration, illegible handwriting in prescribing and interruption in administering, all of which are preventable. Other findings of note are that most MEs in the prescription stage were related to drugs that act on the nervous system or the cardiovascular system and that nurse's workload perception was associated with interruption during drug administration. As many of these events are preventable, intensifying efforts to raise awareness and promote a medication safety culture will help reduce MEs at different stages of drug use and ensure e quality care in critically ill patients.

CONFLICT OF INTEREST
No conflict of interest has been declared by the authors.

AUTHOR CONTRIBUTIONS
SS, AFV, AMCM, IV, GR: Made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; SS, MJMZ, GR, JM: Involved in drafting the manuscript or revising it critically for important intellectual content; SS, MJMZ, GR, JM, IM: Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content; SS, GR: Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONTRIBUTORSHIP STATEMENT
SS made substantial contribution to conception and design of the work, recruitment of participants, interpretation of data and drafting the manuscript. MJMZ made a substantial contribution to analysis and interpretation of data and revising it critically for important intellectual content. JM made a substantial contribution in revising it critically for important intellectual content. AFV made a substantial contribution to the acquisition of data. AMCM made a substantial contribution to the acquisition of data. IV made a substantial contribution to the acquisition of data. IM made a substantial contribution in revising it critically for important intellectual content. GR made a substantial contribution to conception and design of the work, recruitment of participants, interpretation of data and drafting the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

6.3. STUDY III. Effectiveness of non-pharmacological interventions to prevent adverse events in the intensive care unit: A review of systematic reviews

Summary of the most relevant results:

6.3.1. Characteristics of included systematic reviews

The initial search of all databases yielded 3812 articles, and 37 systematic reviews (SRs) that met the selection criteria were included in this overview. The SRs incorporated a range of study designs; however, most of them (n=30) included only randomised controlled trials (RCTs).

We found 11 different adverse events (AEs): ventilator-associated pneumonia (VAP) (11 SRs),[130–140] delirium (six SRs),[141–146] physical function deterioration (five SRs),[147–151] reintubation (four SRs),[152–155] medication error (three SRs),[156–158] artificial airway occlusion or hospital-acquired pneumonia (two SRs),[159,160] healthcare-associated infections (two SRs),[161,162] pressure injury (two SRs),[163,164] and tube displacement or tube occlusion (two SRs).[165,166] The total number of interventions evaluated was 27, and VAP was the most frequent AE studied with seven NPIs. (See Appendix 5).

6.3.2. Methodological quality assessment of systematic reviews

The AMSTAR-2 quality scores were critically low for twenty-eight SRs (75.6%), and none of the included SRs fulfilled all the AMSTAR-2 criteria. The Cochrane Risk of Bias tool (RoB) was the most-used tool to determine the methodological quality of the primary studies (62.2%).

6.3.3. Overlap assessment

The 37 included SRs comprised a total of 246 individual primary studies. Overall Corrected Covered Area (CCA), considering all SRs and all primary studies included in the reviews, was 1.0% (slight overlap). However, our overlap assessment at the outcome level showed a high and very high overlap for twelve comparisons of interventions.

6.3.4. Effects of patient-safety interventions

We found that some non-pharmacological interventions (NPI) reduced AEs in an intensive care setting. A significant effect was found for Subglottic Secretion Drainage (SSD), semi-recumbent position, and kinetic bed therapy in reducing the incidence of VAP (Figure 6); for the use of earplugs, early mobilisation, family participation and music in reducing delirium (Figure 7); for physical rehabilitation in improving muscle strength; for the use of high flow nasal cannula (HFNC) in preventing reintubation (Figure 8); for the use of a computerised physician order entry (CPOE) system in reducing ICU mortality related to medication errors, and for the use of heated water humidifier (HWH) in reducing artificial airway occlusion.

Figure 6. Incidence of ventilator-associated pneumonia

	Odds Ratio		Odds Ratio
Study or Subgroup	**IV, Fixed, 95% CI**		**IV, Fixed, 95% CI**
1.1.1 SSD vs No Drainage			
Caroff 2016	0.55 [0.46, 0.66]		
Frost 2013	0.49 [0.38, 0.63]		
Muscedere 2011	0.48 [0.38, 0.60]		
Wang 2012	0.53 [0.41, 0.69]		
1.1.2 Continuous SSD vs Intermittent SSD			
Wen 2017	0.83 [0.61, 1.13]		
1.1.3 Closed vs Open Endotracheal Suction			
Faradita 2018	0.92 [0.72, 1.18]		
Siempos 2008	0.96 [0.72, 1.28]		
1.1.4 Semirecumbent Position vs Supine Position			
Alexiou 2009	0.47 [0.27, 0.82]		
Wang Li 2016	0.42 [0.29, 0.59]		
1.1.5 Prone Position vs Supine Position			
Alexiou 2009	0.80 [0.60, 1.07]		
1.1.6 Respiratory Physiotherapy vs Usual Care			
Pozuelo 2018	0.72 [0.36, 1.43]		
1.1.7 Kinetic Bed Therapy vs Usual Care			
Delaney 2006	0.38 [0.28, 0.52]		

Favours [NPIs]   Favours [Control]

Note: SSD = Subglottic secretion drainage

Figure 7. Incidence of delirium

Study or Subgroup	Odds Ratio IV, Fixed, 95% CI	Odds Ratio IV, Fixed, 95% CI
2.1.1 Environmental Intervention vs Usual Care		
Burry 2021	0.83 [0.49, 1.41]	
Deng 2020	0.94 [0.69, 1.30]	
Herling 2018	1.22 [0.92, 1.62]	
Liang Surui 2021	1.16 [0.88, 1.53]	
2.1.2 Use of Earplugs vs Usual Care		
Litton 2016	0.59 [0.44, 0.79]	
2.1.3 Nonpharmacological interventions vs Usual Care		
Kang Lee 2018	0.66 [0.50, 0.87]	
2.1.4 Early Mobilisation vs Usual Care		
Liang Surui 2021	0.33 [0.24, 0.45]	
2.1.5 Family Participation vs Usual Care		
Liang Surui 2021	0.25 [0.18, 0.35]	
2.1.6 Music vs Usual Care		
Liang Surui 2021	0.47 [0.28, 0.79]	

Favours [NPIs]   Favours [Control]

Figure 8. Rate of reintubation

Study or Subgroup	Risk Ratio IV, Fixed, 95% CI
3.1.1 HFNC vs COT	
Granton 2020	0.46 [0.30, 0.71]
Hua-Wei 2018	0.35 [0.19, 0.64]
Liang Sujuan 2021	0.78 [0.62, 0.98]
Xiaoyang Zhou 2020	0.45 [0.27, 0.75]
3.1.2 HFNC vs NIV	
Granton 2020	1.16 [0.86, 1.56]
Hua-Wei 2018	1.19 [0.87, 1.63]
Liang Sujuan 2021	1.01 [0.77, 1.33]
Xiaoyang Zhou 2020	0.82 [0.61, 1.10]
3.1.3 NIV vs COT	
Xiaoyang Zhou 2020	0.62 [0.46, 0.84]

Note: HFNC = high flow nasal cannula; NIV = noninvasive ventilation; COT = conventional oxygen therapy.

FULL TEXT OF ARTICLE III

Review paper

Effectiveness of nonpharmacological interventions to prevent adverse events in the intensive care unit: A review of systematic reviews

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ARTICLE INFORMATION

ABSTRACT

Background: Different types of interventions have been assessed for the prevention of adverse events. However, determining which patient-safety practice is most effective can be challenging when there is no systematised evidence synthesis. An overview following the best methodological standards can provide the best reliable integrative evidence.

Objectives: The objective of this study was to provide an overview of effectiveness nonpharmacological interventions aimed at preventing adverse events in the intensive care unit.

Methods: A review of systematic reviews (SRs) was conducted according to the Cochrane Handbook and PRISMA recommendations. PubMed, CINAHL, and Cochrane Library were searched for SRs published until March 2022. Two reviewers independently assessed the study's quality, using AMSTAR-2, and extracted data on intervention characteristics and effect on prevention of adverse events.

Results: Thirty-seven SRs were included, and 27 nonpharmacological interventions were identified to prevent 11 adverse events. Most of the reviews had critically low methodological quality. Among all the identified interventions, subglottic secretion drainage, semirecumbent position, and kinetic bed therapy were effective in preventing ventilator-associated pneumonia; the use of earplugs, early mobilisation, family participation, and music in reducing delirium; physical rehabilitation in improving muscle strength; use of respiratory support in preventing reintubation; the use of a computerised physician order entry system in reducing risk of medication errors; and the use of heated water humidifier was effective in reducing artificial airway occlusion.

Conclusions: Some nonpharmacological interventions reduced adverse events in the intensive care setting. These findings should be interpreted carefully due to the low methodological quality. SRs on preventing adverse events in the intensive care unit should adhere to quality assessment tools so that best evidence can be used in decision-making.

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1. Introduction

Adverse events (AEs) are undesirable or unintended patient outcomes associated with healthcare management resulting in prolonged hospitalisation, disability at the time of hospital discharge, or death.[1] The occurrence of AEs due to unsafe care is approximately one in every 10 patients, and half of them are judged

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to be preventable. Most of these incidents are related to invasive clinical procedures and therapeutic management.[2] In addition, 12% of preventable patient harm causes permanent disability or death.[3]

Developing preventive interventions to reduce patient harm has become an international policy priority.[4] Moreover, the recognition that many AEs are not preventable has increased awareness to focus on preventable AEs.[5,6] Strengthening the focus of investigations on preventable AEs interventions can lead to greater clinical benefits and improved translation of patient-safety interventions into clinical practice.[6,7]

Patients in intensive care units (ICUs) are at a greater risk for AEs not only due to their inherent clinical conditions that lead to multiple treatments but also because they are in a highly complex environment.[8-12]

SRs are considered at the highest level in the hierarchy of evidence, reflecting the current scientific knowledge and therefore guiding evidence-informed decision-making. However, their conclusions are limited due to the methodological quality and the certainty of the evidence based on included primary studies.[13-16]

Due to the increasing number of SRs and the multiple preventive interventions being published, it is important to evaluate the current status and provide a summary of effective interventions to prevent them.[3,10,17-19] In this way, a review of SRs (overview) can provide the best reliable integrative evidence.[13] Hence, the objective of this article is to provide an overview of SRs assessing nonpharmacological interventions (NPIs) to prevent AEs in the ICU.

2. Method

2.1. Design

We conducted a review of SRs following a protocol registered in PROSPERO (CRD42019147956). Amendments to information provided in the protocol are described in Supplementary material 1.

Reviews of SRs use explicit and systematic methods to collate and appraise the methodological quality and to summarise and analyse their results across our research question identifying specific areas of available or limited evidence. A comprehensive overview can provide an accurate description of the current state of research and thus guide future research.[20-22] The overview was performed according to the Cochrane Handbook on methods for overviews,[13] and we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) checklist[23] (Supplementary material 2).

2.2. Search methods

We developed a systematic search strategy for MEDLINE, CINAHL, and the Cochrane Library to identify studies published from inception until March 2022. English and Spanish language studies were included. The reference list of included SRs was screened to identify potentially relevant studies.

The keywords were selected according to the main components of our clinical question, after a discussion between the research team and tested by an experienced systematic search reviewer before publishing the final version of the protocol. The full search strategy is available in Supplementary material 3.

A pair of trained reviewers independently assessed the inclusion eligibility of the SRs. The first screening was based on the SR title and abstract. We identified papers of peer-reviewed SRs. A full-text assessment was conducted to determine the definitive inclusion of the selected SR. Disagreements in the selection of reviews were resolved by a third reviewer.

2.3. Inclusion and exclusion criteria

2.3.1. Type of studies

SRs of primary studies, including randomised controlled trials (RCTs), quasi-RCTs and controlled observational studies, investigating the effect of NPIs on AEs were included. We considered as an SR any evidence synthesis with a clear systematic methodological approach, a detailed search strategy using at least two database sources, eligible criteria relevant to our research objective, and a narrative synthesis and/or meta-analysis.

2.3.2. Type of patients

Adult ICU patients aged 18 years and above in medical and surgical ICUs were included.

2.3.3. Type of interventions

Any NPIs to prevent AEs focused on patient safety was included, described as new strategies, practices, behaviour, actions, procedures, or environment.

We considered control interventions to be usual care or standard ICU care defined as not providing any therapy specifically aimed at preventing AEs.

2.3.4. Types of outcome measures

Primary outcomes were incidence and ICU mortality related to AEs such as infections (mechanical ventilation–associated pneumonia, bloodstream infection (BSI), central catheter infection, peripheral catheter infection), delirium, reintubation, airway occlusion, pressure ulcers, physical function deterioration, and medication errors. *Secondary outcomes* were hospital mortality, length of mechanical ventilation, and stay in the ICU or in hospital. Outcomes that reported consequences of AEs in terms of extra treatment(s) or readmission were not the focus of this overview.

2.4. Data extraction

Data from studies such as trial design, the number of included studies, type of intervention, type of AEs, comparator, and outcomes were extracted by one reviewer and checked for accuracy by a second reviewer. Disagreement was resolved through discussion, and a third reviewer was consulted if needed.

2.5. Quality appraisal

Methodological quality of the reviews was assessed using AMSTAR-2,[24] which provides overall ratings (high, moderate, low, critically low) based on weaknesses in critical domains. A pair of reviewers independently assessed the quality of each study. Disagreements were resolved by a third reviewer. Moreover, we described the confidence in the evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach for the primary outcomes when the SRs reported them.

2.6. Data analysis and synthesis

The study characteristics and patient outcomes for all the SRs that met our inclusion criteria were grouped by types of AEs in a tabular form. To assess the overlap of primary studies among included SRs, we created a matrix of evidence as a grid, placing all the included SRs in the columns and their respective primary studies in the rows. We calculated the corrected covered area (CCA) for the whole matrix and for each pair of SRs,[25] according to previously defined methods.[26] We considered overlap to be low if the CCA was below 5%, moderate if the CCA was between 5% and 10%, high if the CCA was between 10% and 15%, and very high if the CCA was above 15%. We repeated this

process for each outcome, creating custom matrices including only the SRs and primary studies providing data for each specific comparison. We reported overlap for this custom matrix using the same thresholds mentioned above.

We compiled the pooled effect sizes of meta-analyses reported in the SRs and analysed the intervention components. Most of the effect sizes were expressed in odds ratio (OR); however, when risk ratio (RR) was reported, these were converted to OR if the number of events per group was provided.

Statistical analyses were performed using Review Manager V5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2014). Analysis of forest plots was descriptive, and metanalysis was not performed due to the clinical diversity of intervention by outcomes and overlap among primary studies included in the SRs.

3. Results

3.1. Search results

The initial search of all databases yielded 3812 articles (Fig. 1). After the removal of duplicates, 3225 articles remained and were screened via review of their titles and abstracts. The screening resulted in 261 articles that underwent full-text review. A total of 224 articles were excluded because they did not meet our selection criteria. Fifty-six articles were excluded because the intervention was pharmacological, bundles, or educational interventions. A list of excluded studies with the reason for exclusion can be found in Supplementary material 4. Finally, 37 systematic reviews were included in this review.
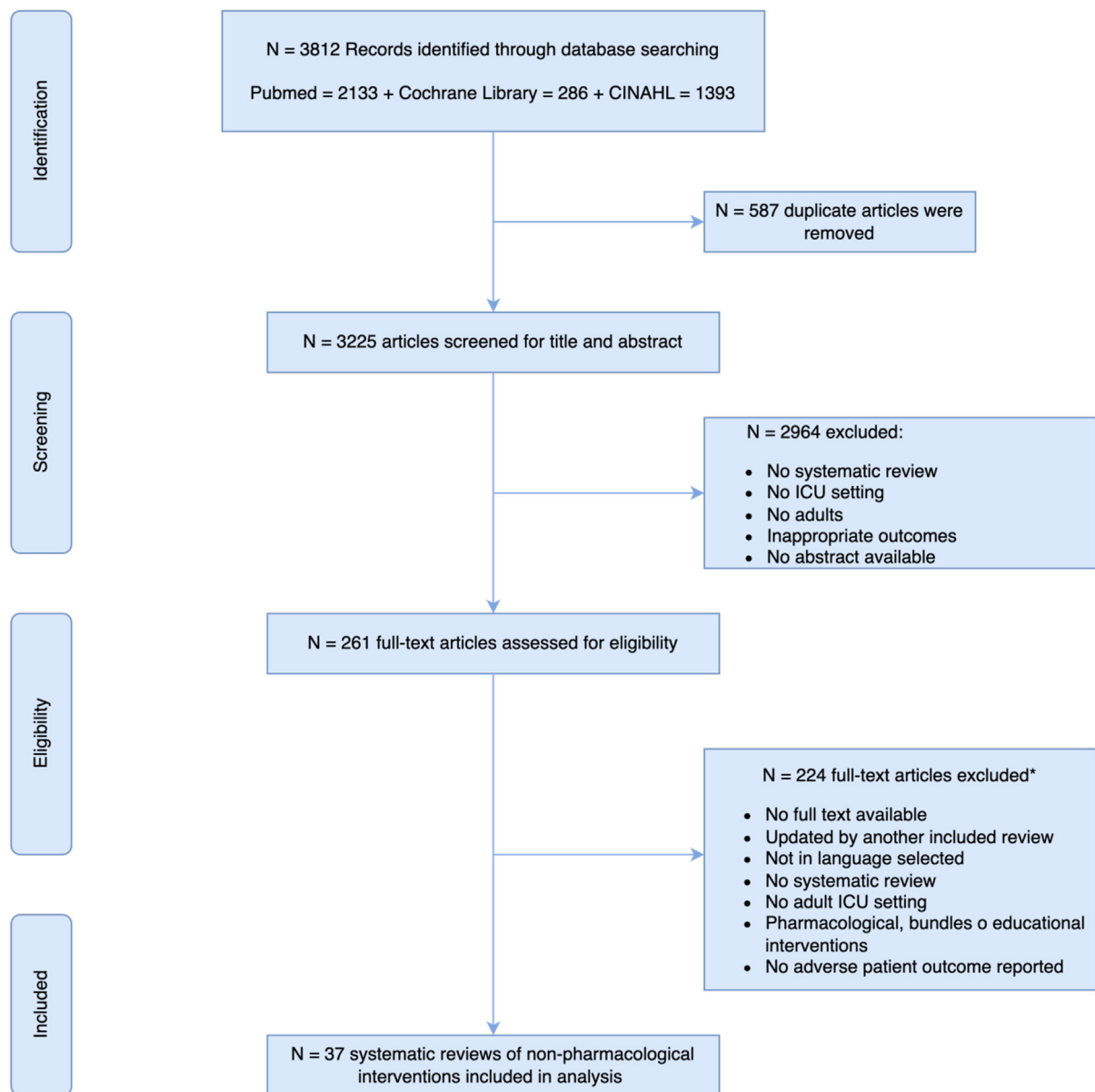
* See *supplementary file 4* for the exclusion reason per SR after full-text selection

Fig. 1. Summary of search and selection − PRISMA 2020. ICU, intensive care unit; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

3.2. Characteristics of the included systematic reviews

The characteristics of the included NPI SRs are summarised in Table 1. More than half (n = 21) of the included SRs were published after 2016. These reviews incorporated a range of study designs; however, most of them (n = 30) included only randomised controlled trials (RCTs). Thirty-two SRs performed a meta-analysis (86.4%).

The total number of eligible primary studies in the SRs ranged from 2[27–30] to 24[31] studies. The number of patients in the eligible studies ranged from 454[32] to 3369[33] and was not reported or unknown in nine (24.3%) reviews.

The included reviews covered 11 different AEs: ventilator-associated pneumonia (VAP) (11 SRs),[33–43] delirium (six SRs),[29,44–48] physical function deterioration (five SRs),[32,49–52] reintubation (four SRs),[53–56] medication error (three SRs),[31,57,58] artificial airway occlusion or hospital-acquired pneumonia (two SRs),[59,60] healthcare-associated infections (HAIs; two SRs),[61,62] pressure injury (two SRs),[30,63] and tube displacement or tube occlusion (two SRs).[27,28,54] The total number of interventions evaluated was 27, and VAP was the most frequent AE studied with seven NPIs. Usual care, defined as the standard care received by patients and determined by the treating centre during ICU admission, standard medical, and nursing care, was the most common control group.

3.3. Methodological quality of SRs

The AMSTAR-2 quality scores of the included reviews are described in Table 2. Twenty-eight (75.6%) SRs scored critically low on methodological quality, six (16.2%) SRs scored low, three (8.1%) scored moderate, and only one (2.7%) scored high. The main deficiencies noted in critical domains were failure to report a prior registered protocol, adequacy of the literature search, and justification for excluding studies, while in noncritical domains, the main deficiencies were reasons for study design selection and describing the included studies in adequate detail. None of the included SRs fulfilled all the AMSTAR-2 criteria. Regarding the certainty of the evidence, only six (16.2%) SRs reported the certainty of evidence for the primary outcomes.

3.4. Methodological quality of the primary studies included in the SRs

The Cochrane Risk of Bias tool (RoB) was the most-used tool to determine methodological quality of the primary studies (62.2%), while 10 (24.3%) SRs only provided a narrative discussion of quality, and five (13.5%) SRs did not assess RoB. Most review authors noted that results should be interpreted with caution due to methodological study limitations.

3.5. Overlap assessment

The 37 included SRs comprised a total of 246 individual primary studies. The overall CCA, considering all SRs and all primary studies included in the reviews, was 1.0% (slight overlap). Supplementary material 5 provides a detailed assessment of the overall overlap among SRs.

Six of 17 comparisons regarding VAP outcomes included at least two SRs. Considering only SRs and primary studies providing data for each specific comparison, the overall CCA and detailed CCA by pair of reviews were very high for all the comparisons. For example, comparison 1.1.1 includes four SRs, comprising a total of 17 individual primary studies. Of these, seven were included in all SRs.

This is reflected in the detailed overlap assessment, which shows that all SRs have a CCA of at least 47.1% (very high overlap).

One comparison regarding the incidence of delirium included four SRs and the overlap assessment was high (10.3%). Two comparisons regarding reintubation outcomes included at least two SRs, and the overlap assessment was high for the comparison of high flow nasal cannula (HFNC) versus conventional oxygen therapy (COT) and very high for the comparison noninvasive ventilation (NIV) versus conventional oxygen therapy (Supplementary material 6).

For other AEs studied, comparisons included only one SR; therefore, no overlap assessment was possible.

3.6. Effects of patient-safety interventions

3.6.1. Ventilator-associated pneumonia

3.6.1.1. Incidence of VAP. VAP definition varied among the studies depending on the diagnosis criteria used. Eight SRs considered VAP according to clinical, laboratory, and imaging findings, and three SRs did not provide this information.

Eleven SRs[33–43] assessed seven different NPIs for preventing VAP. Subglottic secretion drainage (SSD) compared with no drainage was assessed in four SRs, with a total of 44 RCTs and 10,193 patients. Results showed a statistically significant effect ranging from an OR of 0.48 (95% confidence interval [CI]: 0.38, 0.60) to an OR of 0.55 (95% CI: 0.46, 0.66).

Semirecumbent position compared with supine position was evaluated in two SRs[34,40] with 11 RCTs and 1096 patients. Results showed a statistically significant effect ranging from an OR of 0.42 (95% CI: 0.29, 0.59) to an OR of 0.47 (95% CI: 0.27, 0.82). Only one of them[40] assessed the certainty of the evidence, and it was graded as moderate.

Use of kinetic bed compared with usual bed was analysed in a single SR[35] and showed a statistically significant reduction in the incidence of VAP: (OR: 0.38; 95% CI: 0.28, 0.52). This effect was based on a total of 10 RCTs and 967 patients. The other comparison showed no differences between the experimental and control group for this outcome (Fig. 2a).

3.6.1.2. ICU mortality related to VAP. Five different NPIs for preventing ICU mortality related to VAP were assessed in six SRs.[35,37–40,43]

Respiratory physiotherapy compared with usual care was analysed in a single SR[38] and showed a statistically significant reduction in the ICU mortality related to VAP (OR: 0.67; 95% CI: 0.47, 0.96). This effect was based on five RCTs and 603 patients. The other comparison showed no differences between the experimental and control group for this outcome (Fig. 2b).

3.6.1.3. Hospital mortality related to VAP. Five experimental interventions for preventing hospital mortality related to VAP were assessed in eight SRs;[33,34,36,37,40–43] however, none of them showed significant results.

The comparison that drew most SRs (four)[33,37,41,43] was SSD compared with no drainage, with a total of 35 RCTs and 8520 patients. Measures of effect ranged from an OR of 0.91 (95% CI: 0.73, 1.13) to an OR of 1.03 (95% CI: 0.80, 1.32) (Fig. 2c).

3.6.2. Delirium

3.6.2.1. Incidence of delirium. Six SRs[29,44–48] assessed interventions to prevent delirium. Some authors compared environmental intervention (changes in light or sound/hearing) vs usual care in 26 RCTs. Results were not significant, ranging from an OR of 0.83 (95% CI: 0.49, 1,41) to an OR of 1.22 (95% CI: 0.92, 1.62). Only one of

Table 1
Characteristics of the included studies.

Adverse event	Author	Year	N studies included	Intervention(s)	Comparison(s)	Outcome(s)	ROB assessment	Meta-analysis
Ventilator-associated pneumonia (VAP)	Alexiou	2009	7 RCT	Semirecumbent position; prone position	Supine position	Incidence of VAP; hospital mortality; duration of mechanical ventilation; ICU length of stay	Yes	Yes
	Caroff	2016	17 RCT	SSD	Usual care (standard endotracheal tubes)	Incidence of VAP; ICU mortality; hospital mortality; duration of mechanical ventilation; ICU length of stay	Yes[a]	Yes
	Delaney	2006	15 RCT	Kinetic or rotating bed therapy	Usual care (kinetic or rotating bed therapy)	Incidence of VAP; ICU mortality; duration of mechanical ventilation; ICU length of stay	Yes[a]	Yes
	Faradita	2018	5 RCT	Closed endotracheal suctioning system	Open endotracheal suctioning system	Incidence of VAP; hospital mortality	Yes	Yes
	Frost	2013	9 RCT	SSD	Usual care (no drainage)	Incidence of VAP; ICU mortality; hospital mortality	No	Yes
	Muscedere	2011	13 RCT	SSD	Usual care (standard endotracheal tubes)	Incidence of VAP; ICU mortality; hospital mortality; ICU length of stay; duration of mechanical ventilation	No	Yes
	Pozuelo	2018	5 RCT	Respiratory physiotherapy interventions	Usual care, not receiving physiotherapy, any co-interventions	Incidence of VAP; ICU mortality; ICU length of stay	Yes[a]	Yes
	Siempos	2008	9 RCT	Closed endotracheal suctioning system	Open endotracheal suctioning system	Incidence of VAP; ICU mortality; duration of mechanical ventilation	Yes	Yes
	Wang, Li	2016	10 RCT	Semirecumbent position	Supine position	Incidence of VAP; ICU mortality; hospital mortality; ICU length of stay; duration of mechanical ventilation	Yes[a]	Yes
	Wang	2012	10 RCT	SSD	Usual care (no drainage)	Incidence of VAP; hospital mortality; ICU length of stay; duration of mechanical ventilation	Yes	Yes
	Wen	2017	8 RCT	Continuous subglottic secretion drainage	Intermittent subglottic secretion drainage	Incidence of VAP; hospital mortality; duration of mechanical ventilation	Yes[a]	Yes
Delirium	Burry	2021	12 RCT	Enviromental intervention	Usual care*	Incidence of delirium, hospital mortality; duration of mechanical ventilation; ICU length of stay	Yes[a]	Yes
	Deng Lu-Xi	2020	9 RCT	Enviromental intervention	Usual care*	Incidence of delirium, duration of ICU delirium	Yes	Yes
	Herling	2018	12 RCT	Enviromental intervention	Usual care*	Incidence of delirium	Yes[a]	Yes
	Kang	2018	15 RCT	NPhIs	Usual care*	Incidence of delirium; ICU	Yes[a]	Yes

(continued on next page)

Table 1 (*continued*)

Adverse event	Author	Year	N studies included	Intervention(s)	Comparison(s)	Outcome(s)	ROB assessment	Meta-analysis
						mortality; duration of ICU delirium; ICU length of stay		
	Litton	2016	5 RCT; 2 NRCT	Use of earplugs as a sleep hygiene strategy (physical environment)	Usual care*, other interventions	Incidence of delirium; hospital mortality	Yes[a]	Yes
	Liang Surui	2021	15 RCT	Early mobilisation, family participation, music, patient education, physical environment	Usual care*	Incidence of delirium	Yes[a]	Yes
Physical function deterioration	Adler	2012	7 NRCT; 3 RCT	Early mobilisation and physical therapy	Usual care*	Muscle strength; physical function: mobility	No	No
	Doiron	2018	4 RCT	Early mobilisation	Usual care (no mobilisation/active exercise, or mobilisation/active exercise given later than the intervention group)	Muscle strength; physical function: mobility	Yes[a]	No
	Menges	2021	4 RCT	Systematic early mobilisation standard	Early mobilisation (mobilisation initiated within 7 days but less systematically)	Muscle strength; physical function: mobility	Yes[a]	No
	Tipping	2016	14 RCT	Active mobilisation and rehabilitation	Usual care (standard physical therapy)	Muscle strength, ICU mortality; hospital mortality	Yes[a]	Yes
	Waldauf	2020	18 RCT	Physical rehabilitation	Usual Care*	Hospital mortality	Yes	Yes
Reintubation	Granton	2020	6 RCT	HFNC	Usual care (COT; NIV)	Incidence of reintubation; hospital mortality	Yes[a]	Yes
	Hua-Wei	2018	7 RCT	HFNC	Usual care (COT; NIV)	Incidence of reintubation	Yes[a]	Yes
	Liang Sujuan	2021	12 RCT	HFNC	Usual care (COT; NIV)	Incidence of reintubation; ICU mortality; hospital mortality	Yes[a]	Yes
	Xiaoyang Zhou	2020	15 RCT	HFNC; NIV	Usual care (COT; NIV)	Incidence of reintubation	Yes[a]	Yes
Medication error	Manias	2012	2 RCT and 22 QES	CPOE systems	Paper-based ordering	Rate of medication error	No	No
	Prgomet	2017	16 RCT and NRCT	CPOE systems	Paper-based ordering	Incidence of medication error; ICU mortality; ICU length of stay	Yes	Yes
	Wang	2015	8 NRCT	Pharmaceutical intervention (deliver pharmaceutical care in the ICU and not those solely involved in drug dispensing)	Usual service	Risk of general MEs	Yes[a]	Yes
Hospital-acquired pneumonia or artificial airway occlusion	Vargas	2017	18 RCT	HME	HWH	Incidence of artificial airway occlusion; incidence of hospital-acquired pneumonia; hospital mortality	Yes[a]	Yes
	Maertens	2018	6 RCT	Use of endotracheal tapered cuffs	Use of endotracheal nontapered cuffs (standard cuffed ET)	Incidence of hospital-acquired pneumonia; ICU mortality	Yes[a]	Yes
Healthcare-associated infections (VAP excluded)	Frampton	2014	5 RCT	Implementation of checklists	Usual care*	Hospital mortality related to catheter BSI	Yes[a]	No
	Chang	2019	4 RCT and BA	Universal gloving	Nongloving	Incidence of healthcare-	Yes	Yes

Table 1 (continued)

Adverse event	Author	Year	N studies included	Intervention(s)	Comparison(s)	Outcome(s)	ROB assessment	Meta-analysis
						associated infections		
Pressure injury	Lovegrove	2022	2 RCT	Reactive bed surface	Standard mattress	Incidence of pressure injury	Yes[a]	No
	Nieto-García	2021	5 RCT	Pre-early mobility programme	Post-early mobility programme	Incidence of pressure injury	Yes[a]	No
Tube displacement or tube occlusion	Gardner	2005	1RCT; 6 NRCT	ETT stabilisation (twill or cotton tape, adhesive tape, gauze, or a manufactured device)	Other ETT stabilisation	Incidence of endotracheal tube displacement	No	Yes
	Bench	2003	2 RCT	HME	HWH	Incidence of tracheal tube occlusion; incidence of VAP	Yes	No

BA = before-and-after study; QES = quasi-experimental study; NRCT = nonrandomised controlled trial; RCT = randomised controlled trial; COT = conventional oxygen therapy; CPOE = computerised physician order entry; ETT = endotracheal tube; HFNC = high-flow nasal cannula; HME = heat moisture exchange; HWH = heated water humidifier; ICU = intensive care unit; NIV = noninvasive ventilation; NPhI = nonpharmacological intervention; SSD = subglottic secretion drainage.
Usual Care*: Receiving standard care as determined by the treating centre during the ICU admission and standard medical and nursing care.
  [a] Assessment using Cochrane risk-of-bias tool (RoB: Risk of Bias).

them[48] assessed the certainty of the evidence, and it was graded as low (Fig. 3).

Litton et al.[45] found that earplug use was associated with a lower incidence of delirium than usual care: an OR of 0.59 (95% CI: 0.44, 0.79). This effect was based on five RCTs and 832 patients.

Kang et al.[44] grouped different NPIs and found these were effective in reducing incidence of delirium with an OR of 0.66 (95%

Table 2
AMSTAR-2 assessment.

Reference	AMSTAR-2 domains																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Overall quality
Adler 2012	Yes	No	No	PY	No	No	No	PY	No	No	NMA	NMA	No	No	NMA	No	Critically low
Alexiou 2009	Yes	No	No	PY	Yes	Yes	No	PY	PY	No	Yes	No	No	Yes	No	No	Critically low
Bench 2003	Yes	No	No	PY	No	No	Yes	Yes	PY	No	NMA	NMA	No	No	NMA	No	Critically low
Burry 2021	Yes	Yes	No	PY	Yes	Yes	No	PY	Yes	Yes	Yes	No	Yes	No	No	Yes	Critically low
Caroff 2016	Yes	No	Yes	PY	No	Yes	No	PY	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Critically low
Chang 2019	Yes	No	No	PY	Yes	Yes	No	Yes	PY	Yes	No	No	Yes	Yes	Yes	Yes	Critically low
Delaney 2006	Yes	PY	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low
Deng Lu-Xi 2020	Yes	PY	No	PY	Yes	Yes	No	PY	PY	No	Yes	No	No	Yes	Yes	Yes	Critically low
Doiron 2018	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NMA	NMA	Yes	Yes	NMA	Yes	High
Faradita 2018	Yes	No	Yes	No	Yes	Yes	No	No	Yes	No	No	No	No	No	No	No	Critically low
Frampton 2014	Yes	PY	No	PY	Yes	Yes	Yes	Yes	Yes	Yes	NMA	NMA	Yes	Yes	NMA	Yes	Moderate
Frost 2013	Yes	No	No	PY	No	No	No	No	No	No	Yes	No	No	Yes	Yes	No	Critically low
Gardner 2005	Yes	No	No	PY	Yes	No	No	PY	No	No	Yes	No	Yes	Yes	No	No	Critically low
Granton 2020	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Critically low
Herling 2018	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Low
Hua-Wei Huang 2018	Yes	PY	No	PY	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Kang Lee 2018	Yes	No	No	PY	Yes	Yes	No	PY	PY	Yes	No	Yes	Yes	No	Yes	Yes	Critically low
Lian Sujuan 2021	Yes	No	No	No	No	Yes	No	PY	Yes	No	Yes	No	No	Yes	Yes	Yes	Critically low
Liang Surui 2021	Yes	Yes	No	No	Yes	Yes	No	PY	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Critically low
Litton 2016	Yes	No	No	PY	Yes	Yes	No	PY	PY	No	No	No	Yes	Yes	Yes	Yes	Critically low
Lovegrove 2022	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Critically low
Maertens 2018	Yes	No	Yes	Yes	No	No	Yes	PY	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low
Manias 2012	Yes	No	No	No	Yes	Yes	No	PY	PY	Yes	NMA	NMA	No	No	NMA	Yes	Critically low
Menges 2021	Yes	Yes	Yes	PY	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Low
Muscedere 2011	Yes	No	Yes	PY	Yes	Yes	No	PY	No	No	Yes	No	No	Yes	No	Yes	Critically low
Nieto Garcia 2020	Yes	No	No	No	Yes	Yes	No	PY	Yes	No	Yes	No	No	No	No	No	Critically low
Pozuelo 2018	Yes	No	Yes	PY	Yes	Yes	No	PY	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Critically low
Prgomet 2017	Yes	PY	No	PY	Yes	No	No	PY	Yes	No	No	No	No	No	No	Yes	Critically low
Siempos 2008	Yes	No	Yes	No	Yes	Yes	No	PY	PY	Yes	No	No	No	Yes	Yes	No	Critically low
Tipping 2017	Yes	PY	Yes	Yes	Yes	Yes	No	PY	PY	No	No	Yes	Yes	Yes	No	Yes	Critically low
Vargas 2017	Yes	No	Yes	PY	Yes	Yes	No	PY	Yes	No	Yes	No	Yes	Yes	No	Yes	Critically low
Waldauf 2020	Yes	Yes	No	PY	Yes	Yes	No	PY	PY	Yes	Yes	No	No	Yes	No	Yes	Critically low
Wang F. 2012	Yes	No	Yes	PY	No	Yes	No	No	Yes	No	Yes	No	No	No	Yes	Yes	Critically low
Wang L. 2016	Yes	Yes	Yes	PY	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Wang T. 2015	Yes	No	Yes	PY	Yes	No	No	PY	PY	No	No	No	Yes	No	No	No	Critically low
Wen 2017	Yes	No	Yes	PY	Yes	Yes	No	PY	Yes	No	No	No	No	No	No	No	Critically low
Zhou Xiaoyang 2020	Yes	Yes	No	PY	Yes	Yes	Yes	PY	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Low

PY = partial yes; NMA = no meta-analysis.

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(a) Incidence of VAP   (b) ICU mortality related to VAP   (c) Hospital mortality related to VAP
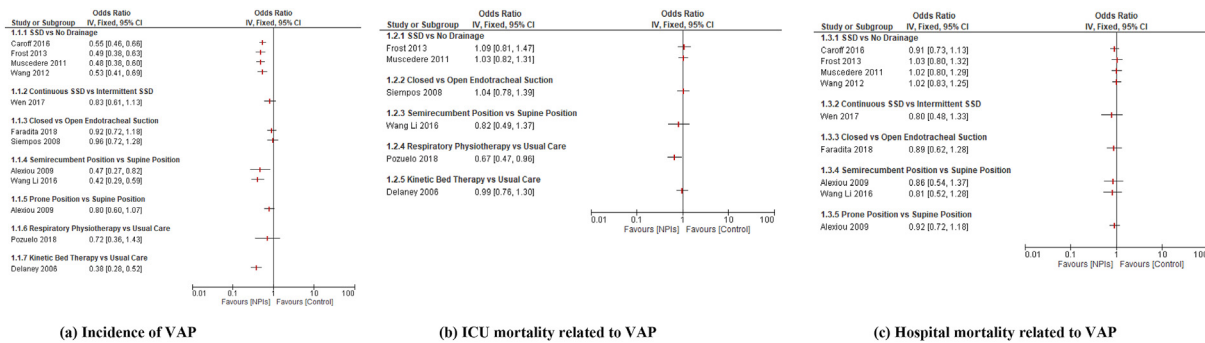
Fig. 2. Forest plot of the influence of non-pharmacological interventions to reduce ventilator-associated pneumonia (VAP). (a) Incidence of VAP. (b) ICU mortality related to VAP. (c) Hospital mortality related to VAP. CI = confidence interval; ICU, intensive care unit; SSD = subglottic secretion drainage.

CI: 0.50, 0.87). This effect was based on 14 studies (cohort and RCTs) and 3372 patients.

Liang Surui et al.[48] found that early mobilisation (moderate-certainty evidence), family participation (moderate-certainty evidence), and music (low-certainty evidence) have a statistically significant effect on decreasing delirium incidence.

3.6.2.2. *Mortality related to delirium.* Only Kang et al.[44] assessed *ICU mortality*, including three studies (cohort and RCTs), and results were not statistically significant (OR: 0.81; 95% CI: 0.61, 1.07).

Concerning the outcome *hospital mortality related to delirium*, this was reported in two SRs,[45,46] and results were not statistically significant ranging from an OR of 0.77 (95% CI: 0.54, 1.10) to an OR of 0.91 (95% CI: 0.63, 1.31).
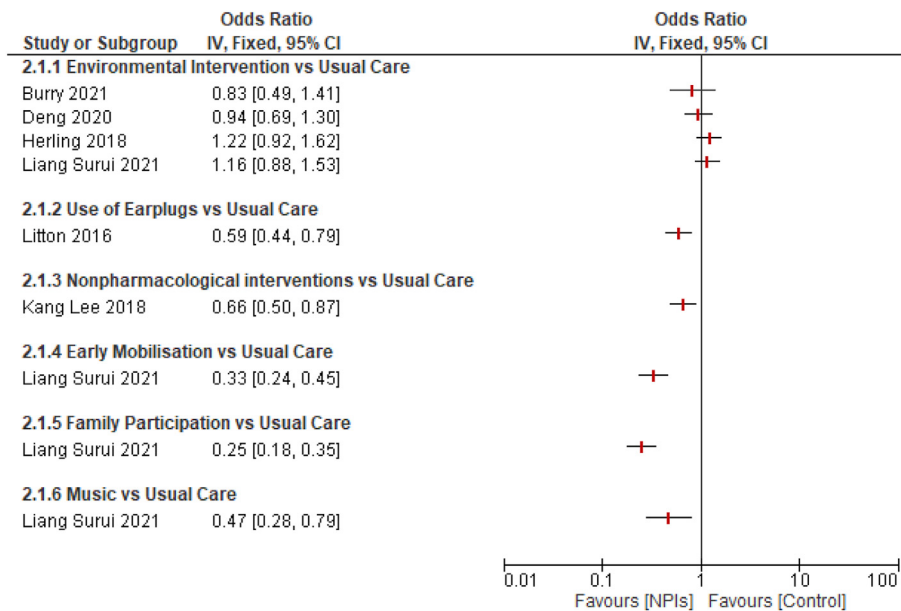
Fig. 3. Forest plot of the influence of nonpharmacological interventions to reduce incidence of delirium. CI = confidence interval.

(a) Rate of reintubation   (b) ICU mortality related to reintubation   (c) Hospital mortality related to reintubation
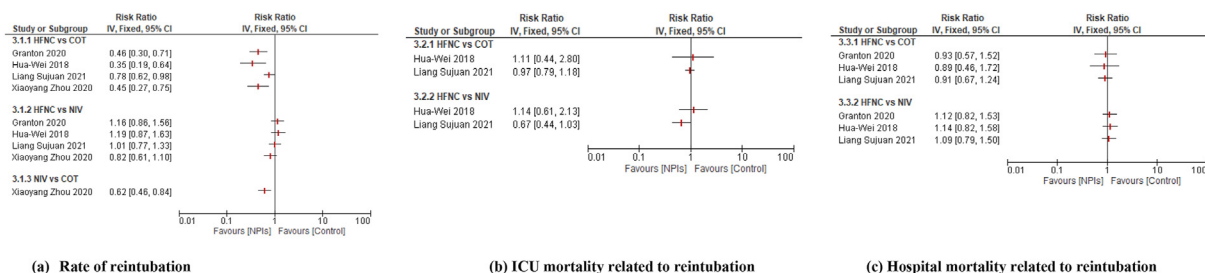
Fig. 4. Forest plot of the influence of non-pharmacological interventions to reduce reintubation. (a) Rate of reintubation. (b) ICU mortality related to reintubation. (c) Hospital mortality related to reintubation. CI = confidence interval; NPI = nonpharmacological interventions; ICU = intensive care unit; SSD = subglottic secretion drainage; HFNC = high flow nasal cannula; COT = conventional oxygen therapy; NIV = noninvasive ventilation.

3.6.3. Physical function deterioration

Five SRs reported results on physical function deterioration. Three of them[32,49,51] assessed muscle strength at ICU discharge using the Medical Research Council scale and physical function using the Barthel Index or Short Form (SF-36) questionnaire to measure mobility−disability. We could not pool results from those SRs because the interventions assessed were different.

Tipping et al.[50] assessed physical functional status and muscle strength using the WHO International Classification of Functioning, Disability and Health. Physical rehabilitation in the ICU was assessed in comparison to usual care, and the experimental group demonstrated an improvement in muscle strength (mean difference (MD): 8.62; 95% CI: 1.39, 15.86).

For early or systematic mobilisation compared with late or standard care, authors[32,49,51] found no statistically significant benefit on muscle strength. Tipping et al.[50] and Waldauf et al.[52] showed that active mobilisation and physical rehabilitation compared with usual care did not impact mortality related to physical deterioration.

3.6.4. Reintubation

3.6.4.1. Rate of reintubation.
Four SRs[53−56] assessed two different NPIs for preventing reintubation. HFNC compared with conventional oxygen therapy was assessed in six RCTs and 1558 patients. Results showed a statistically significant effect ranging from an OR of 0.35 (95% CI: 0.19, 0.64) to an OR of 0.78 (95% CI: 0.62, 0.98). The certainty of the evidence was moderate for two reviews[53,56] and low for one of them.[54]

HFNC-compared NIVs included seven RCTs and 1839 patients. Results did not demonstrate statistically significant effects on decreasing intubation rate, ranging from an OR of 0.82 (95% CI: 0.61, 1.10) to an OR of 1.19 (95% CI: 0.87, 1.63). NIV compared with conventional oxygen therapy was assessed in nine trials, and results did not show a statistically significant effect (OR: 0.62; 95% CI: 0.46, 0.84, moderate-certainty evidence) (Fig. 4a).

3.6.4.2. Mortality related to reintubation.
Two SRs[54,55] compared HFNC with conventional oxygen therapy (OR: 0.97; 95% CI: 0.79, 1.18 to OR: 1.11; 95% CI: 0.44, 2.80; 6RCTs, 1749 participants) and HFNC with NIV (OR: 0.67; 95% CI: 0.44, 1.03 to OR: 1.14; 95% CI: 0.61, 2.13; 5RCTs, 1434 participants). Results had no statistically significant effects on the ICU mortality outcome (Fig. 4b).

Concerning the outcome of hospital mortality related to reintubation, this was reported in three SRs[53−55] that compared HFNC with conventional oxygen therapy (OR: 0.89; 95% CI: 0.46, 1.72 to OR: 0.93; 95% CI: 0.57, 1.52; 6RCTs, 1321 participants) and HFNC with NIV (OR: 1.09; 95% CI: 0.79, 1.50 to OR: 1.14; 95% CI: 0.82, 1.58; 5 RCTs, 1284 participants). Results had no statistically significant effects. Only one SR, for each comparison, reported certainty evidence, and it was graded as moderate (Fig. 4c).

3.6.5. Medication error

All SRs examining medication error (ME) included RCTs and NRCTs. We found that pharmaceutical intervention vs usual care did not show significant effects.[58] However, computerised physician order entry system vs paper-based ordering was associated with a significant reduction in MEs, with an RR of 0.71 (95% CI: 0.68−0.75).[57] This result was based on 16 studies.

3.6.6. Artificial airway occlusion or hospital acquired pneumonia (non-VAP)

Heat moisture exchangers compared with heated water humidifier for preventing artificial airway occlusion were assessed in one SR,[60] including 14 RCTs and 2125 patients. Results were statistically significant, favouring heated water humidifier with an OR of 2.51 (95% CI: 1.27, 4.95), but there were no differences in the prevention of hospital-acquired pneumonia.

Endotracheal tapered cuffs vs endotracheal nontapered cuffs were also assessed in one SR,[59] which included six RCTs and 1324 patients, for prevention of ICU mortality related to hospital-acquired pneumonia, but results were not statistically significant.

3.6.7. HAIs: catheter BSI

Two SRs assessed the implementation of checklists[61] and universal gloving[62] compared with usual care for preventing HAI: catheter BSI. One SR[61] affirmed that there were insufficient data to draw conclusions, and the other SR[62] found that results were not statistically significant when only RCTs were pooled.

3.6.8. Pressure injury

Two SRs were included; one of them compared reactive bed surface with a standard mattress, and the other compared pre-early with post-early mobility programs to reduce pressure injury incidence. No one showed statistically significant results, and findings were inconclusive due to the differences in clinical characteristics and length of stay of patients.

There were other interventions to prevent AEs (tube displacement and tube occlusion), but we found few SRs included for each one. The individual results of them are summarised in Supplementary material 7.

4. Discussion

To the best of our knowledge, this is the first overview to systematically summarise and assess the quality of SRs and overlap of primary studies on NPIs for preventing AEs in ICU patients. We included 37 SRs of NPIs that evaluated 27 patient-safety interventions to reduce 11 different AEs.

We found the overall confidence of results based on the AMSTAR-2 was critically low because 73.7% of the SRs included had important methodological quality limitations. The main failures in critical domain assessment were reporting without a registered protocol, inadequacy of the literature search, and lack of justification for excluding studies, remaining the unawareness of the reason for their exclusion.[13,24]

Despite a slight overall overlap for the overview as a whole, our overlap assessment at the outcome level showed a high and very high overlap for 12 comparisons. This overlapping raises awareness of redundant SRs publications in this area.[64,65]

There were several interventions to prevent VAP, which remains among the most frequent infections in the ICU setting.[64] Most current guidelines focus on therapy and diagnosis recommendations of VAP, not prevention.[65,66] However, from seven types of NPIs, only three showed significant effects in reducing the incidence of VAP: subglottic secretion, elevating the head of the patient, and kinetic bed therapy. A literature review also found other pharmacological interventions but concluded that these implemented practices should be reviewed due to the low level of evidence.[67]

Many included SRs showed a reduction in the incidence of delirium. Early mobilisation showed a significant effect on preventing delirium; this finding is consistent with a previous clinical practice guideline that recommend performing early mobilisation of adult ICU patients whenever feasible to reduce the incidence of delirium.[68] A recent review found that multicomponent (pharmacological and nonpharmacological) interventions were optimal for preventing delirium,[47] and family participation resulted in better outcomes for reducing the incidence of delirium.[47,48] In fact, our findings are supportive of international guidelines, suggesting the

use of NPIs as part of a multimodal approach, especially in the management of delirium.[69,70]

We have not included guidelines or health technology assessments in our search; therefore, possible SRs have not been identified. We have found two guidelines, Devlin et al. (update of the Barr et al. guideline) and DAS-TASK 2015[68,69,71] that performed SRs to answer questions and made recommendations. The guideline of Devlin et al. addresses the management of pain, agitation/sedation, delirium, immobility, and sleep disruption, whereas the guideline of DAS-TASK 2015 tackles the management of delirium, analgesia, and sedation. Our overview agrees with these two guidelines in evaluating the nonpharmacological preventive measures to avoid delirium and the effects of immobility. We agree on the inclusion of most primary studies, except for the benefits of rehabilitation and mobilisation, of which Devlin included 16 RCTs, whereas we included 12 RCTs. However, the evidence was very similar.

Patients' physical rehabilitation and active mobilisation on their own combined with therapy prevents physical deterioration. However, some authors suggest that best outcomes in physical function are associated with good pain management, awakening, and breathing coordination, delirium management, and early exercise/mobility.[69,72]

HFNC or NIV compared to conventional oxygen therapy reduced the rate of reintubation, but there were no significant effects on ICU or hospital mortality. The certainty evidence varied among reviews from low to high. These findings are consistent with European Respiratory guidelines regarding the NIV in patients at high risk of reintubation as a conditional recommendation, given the low certainty of evidence.[73] Furthermore, the European Society of Intensive Care Medicine made a conditional recommendation for HFNC following extubation (moderate certainty) in reducing rates of reintubation.[74]

We found that in the ICU setting, the use of a computerised physician order entry system reduces the risk of general medication errors compared with paper-based ordering. However, computerised physician order entry systems are implemented in only about one-third of hospitals. Further research is needed to better characterise links to patient harm.[75,76]

We only found one SR that indicated that headted water humidifier significantly reduced the incidence of artificial airway occlusion. However, due to the small number of studies included and the low quality of this evidence, it is difficult to be confident about this finding.[77]

Similarl to our findings, other authors have affirmed that there is little evidence on the effects of interventions to prevent HAIs such as infection control programs.[78] For a better understanding, a more detailed analysis of the infection type and where and how this AE occurs is required.[79]

Even our findings on using reactive bed surfaces or implementing a pre-early mobility programme did not show benefits in reducing pressure injuries; the European guideline for prevention and treatment of pressure ulcers remarks that those can be a preventive measure. However, the strength of the recommendation is weak. Moreover, early mobilisation in critical patients is based on good practice statements that are not supported by evidence to be significant for clinical practice.[80] While it is true that preventing AEs should be considered a patient safety goal, comfort is the principal consideration in supportive care, especially in critical patients.[81]

4.1. Limitations

We did not search for potential SRs included in the guidelines published; thus, information on other nonpharmacological preventive interventions may have been omitted. Furthermore, our overview is limited by the methodological quality of the SRs and its

included primary studies. Results are presented descriptively using findings from SRs, but we did not conduct a meta-analysis grouping data. Participants among SRs included were heterogeneous. Even when patients were in the adult ICU, they had a wide variety of diseases, patient characteristics, reasons for ICU admission, and variation in standard intensive care practices. Furthermore, not all comparisons reported certainty of evidence, which limited drawing conclusions about NPIs.

The main strength is that the overview was carried out rigorously following the Cochrane methodology, with an updated comprehensive literature search, prespecified criteria for searching and analysis, and the selection and quality assessment of included studies evaluated independently by two authors.

Studies should be better conducted and reported to provide adequate information on preventive interventions focused on patient safety and outcomes. Future SRs should be properly designed and conducted using the AMSTAR-2 checklist, principally by providing a research protocol, performing study selection and data extraction in duplicate, providing a list of both included and excluded studies, and assessing the risk of bias in the primary studies. Moreover, we need to synthesise other types of interventions to prevent AEs, including pharmacological intervention, educational programs, and multicomponent interventions, as well as focus the intervention on patient outcomes. Some AEs studied in this overview are not yet included in standard documents or considered quality indicators to optimise patient care. Therefore, our findings could be considered in developing or updating clinical practice guidelines to prevent AEs.

One major limitation to this project is that the search strategy did not include professional guidelines that were constructed using the process of systematic review where the term 'systematic review' was not in the title. Readers are cautioned to search for guidelines and review those in addition to this summary prior to making practice changes. Future authors are cautioned to filter the search strategy by 'systematic review' instead of searching for the words 'systematic review' in the title as it is now standard practice for professional guidelines to be written using the process of systematic review.

5. Conclusions

We found some nonpharmacological interventions reduced AEs in an intensive care setting. A significant effect was found for SSD, semirecumbent position, and kinetic bed therapy in reducing the incidence of VAP; for the use of earplugs, early mobilisation, family participation, and music in reducing delirium; for physical rehabilitation in improving muscle strength; for the use of respiratory support in preventing reintubation; for use of a computerised physician order entry system in reducing ICU mortality related to medication errors; and for the use of headted water humidifier in reducing artificial airway occlusion. However, the findings are questionable due to the variety of patient characteristics, lack of certainty of evidence reported, the very high overlap for some comparisons, and the critically low quality of SRs included, making it difficult to be confident about them. In situations where strength of the evidence to support the evidence is low, clinical leaders are advised to deploy an evidence-based practice model when translating these interventions into practice to monitor quality outcomes. SRs about preventing AEs in the ICU should adhere to quality assessment tools so that best evidence can be used with greater confidence in decision-making.

Credit authorship contribution statement

Stefanie Suclupe: Conceptualisation, Writing - original draft, Formal analysis, Data curation, Writing - review & editing
Percy Efrain Pantoja Bustillos: Formal analysis, Data curation, Writing - review & editing
Javier Bracchiglione: Formal analysis, Data curation, Writing - review & editing
Carolina Requeijo: Data curation, Writing - review & editing
Karla Salas-Gama: Data curation, Writing - review & editing
Ivan Solà: Data curation, Writing - review & editing
Angela Merchán-Galvis: Data curation, Writing - review & editing
Jaume Uya Muntaña: Data curation
Gemma Robleda: Conceptualisation, Review & editing
Maria Jose Martinez−Zapata: Conceptualisation, Supervision, Writing - original draft, Formal analysis, Data curation, Writing - review & editing.

All authors approved the final version of the study.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical statement

Ethical statement not applicable the authors undertook a systematic review, no ethical statements to declare.

Registration of reviews

The protocol was registered in PROSPERO (International Prospective Register of Systematic Reviews); number CRD42019147956; https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019147956

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Appendix A. Supplementary data

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DISCUSSION

7. DISCUSSION

7.1. Joint discussion of studies

This thesis aimed to evaluate errors in health care delivery and interventions to prevent adverse events in a hospital setting. An in-depth analysis using the human factors approach to identify the complex patterns that affect patient identification was carried out (Study I), as well as a prevalence study of medication error to analyse the association between error and patient and clinical factors was developed (Study II), and the effectiveness of interventions to prevent adverse events were evaluated (Study III).

In the first study, *"Evaluating patient identification practices during intra-hospital transfers: a human factors approach"*,[167] the main finding was that the positive patient identification (PPID) processes did not have a uniform practice in the study centre, and it was different to the institutional policies. Thus, in none of the evaluable cases observed patient identification process was conducted correctly. Furthermore, the PPID process was not designed to catch failures, and not all staff knew the PPID process and less were trained. We noticed that the current way of PPID is a delicate balance of all interacting components: people, tasks, tools/technology, environment, and organisation.

Our analysis of socio-technical factors that contributed to misidentification during intra-hospital transfers was primarily attributed to **organisation factors** since it was unclear who was responsible for patient identification in releasing or receiving the patient from or into the department. Other studies have also found that the transition of care, as patient transfers, is a high-risk process which requires that organisations standardise the transfer of all relevant information.[168,169] However, an international

report states that not only identification policies are needed but also to evaluate, update and ensure that current details for patient identification are well addressed.[94]

According to the Systems Engineering Initiative for Patient Safety (SEIPS) analysis, **team and technology factors** played an important secondary role. The communication between healthcare professionals and porters was inconsistent and informal. As a team factor, these gaps in communication among the healthcare staff lead to several deviations and workarounds.[170] In addition, communication is a core clinical skill that, when it does not work, increases the risk of misidentification issues, particularly when multiple healthcare staff are involved in the care process.[171–173]

It is known that checking data in the transfer is an international recommendation that should be aligned with institutional policies.[96] However, this study found that the standard paper transfer slip, an important tool/technology factor in the PPID process, did not contain the required data to compare patient information and was not aligned with wristband barcodes. Thus, they used workarounds or adaptations, which often led patient safety at risk. In this line, a transport tool such as checklists and forms has been developed and implemented, as other studies have shown, to provide relevant patient information in the transfer process for ensuring proper care, especially in patients with critical illnesses.[95,174] In addition, the variety of patient identification methods is wide; however, current techniques have not yet provided a 100% match rate.[175]

According to our findings from FMEA, the poor-quality information and design from transfer slips were potential causes of a high risk of misidentifying patients and therefore transferring them to an incorrect destination. This analysis provided information from the current practice to find potential failures and prioritise critical

areas for safety and preventable interventions; however, some authors[118,176] have suggested that this methodology might add different sources of information to ensure its validity.

Another common error that could cause severe harm is medication error. In the Study II, *"Medication errors in prescription and administration in critically ill patients"*,[177] the main findings were medication errors in prescription and administration were frequent, with a relevant magnitude of the error, and the nurse's workload perception was associated with an interruption during drug administration.

In this research, the most frequent errors in prescribing were omission of dosage form, frequency or route of administration and illegible handwriting, all of which are preventable. Errors in this stage could be related to the fact that the prescriptions were not computerised and were made manually when the study was carried out. Different studies have shown a significant reduction in medication prescribing error rates after using computer prescriber order entry (CPOE) introduction in ICU and hospital settings.[156,157,178,179]

Consistent with our findings, Mulac et al.[180] found that dosage errors were frequent and associated with the highest severity of harm in hospitals. Mills et al.[181] also found that omission was a frequent error type, even though one of them had previously implemented an electronic prescribing and medicine administration system. This could be related to the fact that errors may still occur due to the change from prescribing on paper to prescribing in computerised records.[182] We also found that most of the errors were in drugs acting on the nervous and cardiovascular system, and other authors found that when these erroneous prescriptions reached the patients have a high risk of death.[180,183–185]

As previously discussed in Study I, implementing these technologies, such as CPOE, electronic medication administration records, and bar code medication administration, does not automatically bring safety.[183,186] Thus; hospitals should draw upon human factors principles when implementing electronic prescriptions and address local issues identified.[187]

In the administration of drugs, the overall prevalence of errors was 73.5%, and interruptions were the most frequent. However, there are differences in definitions of interruptions since some authors have considered it a circumstance of causing an error.[188,189] Even so, it is well-established that interruptions in this stage are part of work, and some of them could reduce negative events.[190] However, there are also unnecessary interruptions that can affect nursing activities and safety; therefore, they should be avoided.[191,192] Other studies highlighted that the impact of an interruption depends on its source and the type of interrupted task.[191,193]

A multicentre study found that even using a barcode wristband on the patient for checking the identification and medication to be administrated, there was a high frequency of deviations from standard procedures (workarounds), which were associated with medication administration errors.[194] This reaffirms that technology alone does not achieve error reduction.

Furthermore, similar to our findings, a recent SR reported that workload and interruptions were human cognitions and organisational factors related to medication errors.[195] Both studies I and II have described and analysed errors observed, but there also are latent errors that put patient safety at risk. Thus, the strategies mentioned in Study I, such as involving the human factor-based redesign and evaluating tasks and training to deal with interruptions, are necessary, but also

it is important to consider the complexity of the hospital system and the nurse-patient interaction to address interruptions.[192,193]

After determining the impact of errors and conditions under which they occur in clinical practice, developing preventive interventions has become a global interest in ensuring patient safety. In the third study, *"Effectiveness of nonpharmacological interventions to prevent adverse events in the intensive care unit: A review of systematic reviews"*,[196] the main finding was that some nonpharmacological interventions (NPIs) reduced adverse events in ICU.

A significant effect was found for subglottic secretion drainage (SSD), semi-recumbent position, and kinetic bed therapy in reducing the incidence of ventilator-associated pneumonia (VAP); for the use of earplugs, early mobilisation, family participation, and music in reducing delirium; for physical rehabilitation in improving muscle strength; for the use of respiratory support in preventing reintubation; for the use of a computerised physician order entry system in reducing ICU mortality related to medication errors; and for the use of heated water humidifier in reducing artificial airway occlusion. However, the overall methodological quality based on the AMSTAR-2 of the systematic reviews (SRs) assessing preventive measures was critically low. Furthermore, despite a slight overall overlap in this overview, our assessment at the outcome level showed a high overlap for some effective interventions. That means the information is redundant because no new primary evidence is produced and therefore, the most recent systematic reviews do not include new clinical trials.

Most of our findings to prevent and reduce VAP, delirium, and physical deterioration were supportive of national and international guidelines,[197–205,] and some suggested using NPIs as part of a multimodal approach.[204,205]

Concerning medication errors, we found in the overview that the CPOE system reduced the risk of general medication errors compared with paper-based ordering[156,157]. In contrast, our cross-sectional research (Study II) evaluated errors in prescriptions using handwriting orders. Therefore, the high prevalence of errors found may be related to the tools and technologies used in prescriptions, as we mentioned in Study I. This is a clear example that although the best evidence may be available, this should be transferred to clinical practice with prior consideration of the system factors involved in the development of the task.

On the other hand, the rapid expansion of SRs does not ensure methodological quality. [123,124] As we demonstrated in this overview (Study III), more than 73% of the SRs included had important methodological limitations, and the high overlap for 12 interventions raises awareness of redundant SRs publications in this area. Thus, the findings should be interpreted carefully.

The prevention of adverse events requires a comprehensive approach encompassing several strategies. This doctoral thesis highlights the use of best evidence-based care and the understanding of safety as a dynamic and continually evolving process to improve quality healthcare. Particularly the analysis of errors or potential errors that occur in hospitals and the interventions being used could benefit the redesign, implementation, and evaluation of patient safety strategies.

7.2. Strengths and limitations

Strengths

This thesis work addresses various aspects of patient safety in hospital settings. Its findings are novel and relevant for patient safety, especially when safety and quality of care are prioritised for the health system. In addition, it provides useful information to define improvement strategies for preventing errors during crucial health care processes and in critical patients.

First, Study I provided rich insights and in-depth analysis using a systems and human factors engineering approach (SEIPS) to highlight the complex patterns that affect patient identification. In addition, a process map depicted "the work as done" and was compared with the "work as imagined" to detect potential failures. Then these were analysed to prioritise the risk using the FMEA methodology.

Second, Study II evaluated two stages of medication process use where the occurrence of an error could cause serious harm and considered all routes of drug administration allowed accurate detection of medication errors.

Third, Study III synthesises effective NPIs to prevent AEs in ICU and rigorously follows the Cochrane methodology. This research was the first overview to systematically summarise and assess the quality of SRs and the overlap of primary studies in this field.

Finally, it should be noted that all the studies that are part of this thesis have been published in indexed journals and evaluated through a peer review process to guarantee the quality and validity of individual studies. The journals where these articles have been accepted are relevant in their field, with a notable level of dissemination and impact factor (range of impact factor: 2.561 to 3.265).

Limitations

The limitations of the thesis work are related to the methodological design performed. In Studies I and II, the information was collected by observation, and professionals could have modified their behaviour in response to their awareness of being observed (Hawthorne effect). However, we tried to limit the observer's influence by avoiding interaction with staff to minimise our visibility while the studies were conducted. In addition, we did not follow up with patients to assess the consequences of misidentification and medication. Both studies were conducted in a single centre, which may reduce external validity; however, our results agree with other published studies.[97,168,169,185,191]

Other limitations in the studies I and III were related to participants. In the first one, the sample was relatively small, and we did not include a patient perspective, which would have added depth to our findings. In the last study, participants among SRs and definitions of standard care practices in intensive care were heterogeneous. Furthermore, in the Study II, the ambiguity or inconsistent definitions of types of medication errors could lead to false assumptions or missing important findings.

Finally, the overview was limited by the methodological quality of the SRs and their primary studies. We did not conduct a meta-analysis due to the heterogeneity and overlap in the SRs included; however, our findings were presented descriptively and were consistent with various clinical practice guidelines.

7.3. Implications for patient safety in clinical practice

In this thesis, it was identified that all human factors systems should be aligned to detect and prevent errors, and those errors that are unavoidable must be considered in hospital system redesign. That is why the best preventive strategies should integrate their system design, resources, and evidence from clinical practice.

When applying new technologies, even when they have the best evidence, as well as the use of electronic records associated with reducing prescription errors, hospitals should monitor and evaluate them carefully to detect and reduce associated errors.

Due to medication errors in prescription and administration still recurrent, it is also necessary to intensify efforts to raise awareness, promote a safety culture and implement sustainable solutions to early identify and manage potential errors and reduce preventable errors during the medication process and patient identification.

The safety strategies and the effective interventions reported in this thesis should be implemented with caution because the evidence of the studies' methodological quality is low. Furthermore, these strategies should be supported by clear policies, adapted to the context of hospital-centred and patient-centred to guarantee the quality of care.

7.4. Implications for research in patient safety

The findings reported in this thesis are key to developing studies that explore the impact of innovative experiences for improving the capacity to detect latent health care failures. These studies should critically assess the relationship between these

experiences and error rate reduction by selecting methods that consider the complexity of health care.

Based on the current patient safety indicators, errors that arrive at the patient should be studied from more information sources such as monitoring systems and patients' perceptions and assessing individual contributions of each socio-technical factor. Furthermore, the cost-effectiveness of patient misidentification during transfer should be evaluated.

We found that there is still a concern about safe medication, so future research and international reports should join efforts to standardise the definitions of errors in this process to establish how such errors are measured to compare different contexts.

In addition, we identified effective non-pharmacological interventions to prevent adverse events (AEs). Some of them studied in this overview are not yet included in standard documents or considered quality indicators to optimise patient care. Therefore, our findings could be considered in developing or updating clinical practice guidelines to prevent AEs, and this may facilitate decision-making for health professionals in clinical practice.

It is also necessary to synthesise other types of interventions to prevent AEs, including pharmacological intervention, educational programs, and multicomponent interventions, as well as focus the intervention on patient outcomes. This evidence should be properly designed, applying high methodological quality standards.

CONCLUSION

8. CONCLUSIONS

1. Systems factors, such as people, tools/technologies, and organisation, were the main components involved in patient misidentification. The disconnection between policies and the reality of the hospital left health professionals and patients vulnerable to the consequences of errors; therefore, a design adapted to current practice that integrates human factors and ongoing critical assessment is needed.

2. Our findings highlighted that a deepened analysis could help to detect and reduce human failures to prevent errors or adverse events due to misidentification in transfers. This proves that hospitals cannot only be considered as complex systems but also as slowly adaptative systems.

3. Medication errors in prescription and administration still have a high prevalence. The omission of relevant data in prescription form was a frequent error, and most of them could be preventable.

4. Interruptions were recurrent during the administration of drugs, and these were related to the workload. It is important that healthcare staff be trained to deal with interruptions and technological factors.

5. Adverse events such as ventilator-associated pneumonia, delirium, muscular weakness, reintubation, medication errors and artificial airway occlusion, which are health care quality indicators in an intensive care setting in Spain, could be prevented by implementing non-pharmacological interventions.

6. These findings should be interpreted carefully due to the low methodological quality of included systematic reviews. The main quality deficiencies were failure to report a protocol, adequacy of the literature search and justification for excluding studies.

7. Hence, this doctoral thesis suggests that error identification based on human factors and the best evidence of preventive interventions could be applied to the clinical practice to detect and prevent errors and ultimately improve patient safety.

8. Further research on medical errors should include a clear definition of error types, error categories and information of the source and nature of interruptions. The cost-effectiveness evaluation of patient misidentification and non-pharmacological interventions should also be developed. In addition, these should involve patient experience for designing and developing solutions to improve patient safety.

9. It is necessary that future research should adhere to quality assessment tools so that the best evidence can be incorporated into decision-making.

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APPENDICES

APPENDICES

APPENDIX 1: Abbreviations

AE: Adverse Event

AHRQ: Agency for Healthcare Research and Quality

AMSTAR: A Measurement Tool to Assess Systematic Reviews

CCA: Corrected covered area

CPOE: Computerised Physician Order Entry

FMEA: Failure Modes and effects Analysis

HFNC: High flow nasal cannula

HWH: Heated Water Humidifier

ICU: Intensive Care Unit

IMCU: Intermediate Care Unit

IoM: Institute of Medicine

NPI: Non-pharmacological Intervention

PPID: Positive Patient Identification

RCT: Randomised Controlled Trials

RoB: Risk of Bias

RPN: Risk Priority Number

SEIPS: System Engineering Initiative for Patient Safety

SEMICYUC: Sociedad Española de Medicina Intensiva Crítica y Unidades Coronarias

SR: Systematic Review

SSD: Subglottic Secretion Drainage

UHC: Universal Health Coverage

VAP: Ventilator-Associated Pneumonia

WHO: World Health Organization

APPENDIX 2: Additional information of article I

Forms for data collection

**Positive Patient Identification During
Intra-hospital Transfers in John Radcliffe Hospital**

1. **Date**

(dd/MM/yyyy)   🗓

2. **Shift**

○ Morning

○ Evening

○ Afternoon

3. **Type of task allocation**

○ Radio

○ Telephone

○ Paper slip (printed)

○ Paper slip (hand written)

○ Others

Original Location

4. **Name of original location, e.g. Ward 5A, Radiology, Transfer Lounge**

5. **How busy is this original location**

   ◯ Less busy than normal

   ◯ Busier than normal

   ◯ Normal

   ◯ Unable to observe

6. **Who did the porter talk to/approach at this original location?**

○ Nurse

○ Another Porter

○ Nobody

○ Receptionist

○ Radiographer

○ Doctor

○ Healthcare Assisteant

○ Unable to observe

○ Porter goes directly to pick up the patient (go to question #9)

○ Others

7. **Was there an intermediary person involved?**

○ No

○ Yes

8. **If yes, who did the last person talk to/approach at this original location?**

◯   Nurse

◯ Another porter

◯ Healthcare Assistant

◯ Doctor

◯ Unable to observe

◯ Receptionist

◯ Others

9. **Who "gave"/"released" the patient to the porter?**

◯ Doctor

◯ Healthcare Assistant

◯ Student

◯ Nobody

◯ Unable to observe

◯ Nurse

◯ Radiographer

◯ Another Porter

◯ Receptionist

◯   Others

10. **Who identified the patient in the original location**

○
    Doctor

○
    Student

○
    Receptionist

○   Nobody

○   Nurse

○   Porter

○   Radiographer

○   Healthcare Assistant

○   Unable to observe

○   Others

11. **How was the patient identified**

○ Patient verbally asked date of birth

○ Compare asked address to paper slip

○ Professional staffs knowledge of who the patient is

○ Compare asked date of birth to paper slip

○ Patient verbally asked address

○ Compare asked name to wristband

○ Compare name on paper slip to wristband

○ Patient verbally asked name

○ Unable to observe

○ Compare asked name to paper slip

○ Compare asked name to patient notes

○ Compare name on paper slip to patient notes

○ Others

12. **Was the patient positively identified according to the hospital PPID policy?**

○ Unable to observe

○ No

○ Yes

13. **People-Team FACTORS: Were there any people or team factors affecting the patient collection? Was the porter stressed, nervous or tired? Did they have a high workload? How was the communication between the porter and porter office?**

14. **Tool-Tech FACTORS: Were there any tool or technology factors affecting patient collection? Was the paper slip legible? Did the porters radio work? Was the porter able to access this destination with their ID card? Did the patient have a wristband? Was the wristband scanned - was this possible?**

15. **Environment FACTORS: Were there any environmental factors affecting patient collection? Limited access to areas in the hospital, waiting room layout, noisy environment etc**

16. **Task FACTORS: Were there any task related factors affecting patient collection? Did the porter know what to do? Was this an unusual patient collection/handover?**

17. **Organisation FACTORS: Were there any organisational factors affecting patient collection?**

Destination

18. **Name of destination, e.g. Ward 5A, Radiology, Transfer Lounge**

19. **How busy is this destination**

◯ Less busy than normal

◯ Unable to observe

◯ Busier than normal

◯ Normal

20. **Who did the porter talk to/approach at this destination?**

◯ Doctor

◯ Nurse

◯ Nobody

◯ Healthcare Assisteant

◯ Another Porter

◯ Radiographer

◯ Receptionist

◯ Porter goes directly to pick up the patient (go to question #9)

◯ Unable to observe

◯ Others

21. **Was there an intermediary person involved?**

○ No

○ Yes

22. **If yes, who did the last person talk to/approach at this destination?**

○ Healthcare Assistant

○ Receptionist

○ Unable to observe

○   Nurse

○ Doctor

○ Another porter

○   Others

23. **Who "gave"/"released" the patient to the porter?**

    ○   Doctor

    ○   Radiographer

    ○   Student

    ○   Nobody

    ○   Healthcare Assistant

    ○   Nurse

    ○   Unable to observe

    ○   Another Porter

    ○   Receptionist

    ○   Others

24. **Who identified the patient**

○ Healthcare Assistant

○ Receptionist

○ Nobody

○ Doctor

○ Student

○ Radiographer

○ Porter

○ Nurse

○ Unable to observe

○ Others

○

25. **How was the patient identified**

○ Patient verbally asked name

○ Compare name on paper slip to patient notes

○ Compare asked name to paper slip

○ Compare asked name to wristband

○ Professional staffs knowledge of who the patient is

○ Patient verbally asked address

○ Compare asked date of birth to paper slip

○ Compare name on paper slip to wristband

○ Compare asked address to paper slip

○ Patient verbally asked date of birth

○ Unable to observe

○ Compare asked name to patient notes

○ Others

○

26. **Was the patient positively identified according to the hospital PPID policy?**

○ Unable to observe

○ No

○ Yes

27. **People-Team FACTORS: Were there any people or team factors affecting the patient collection? Was the porter stressed, nervous or tired? Did they have a high workload? How was the communication between the porter and porter office?**

28. **Tool-Tech FACTORS: Were there any tool or technology factors affecting patient collection? Was the paper slip legible? Did the porters radio work? Was the porter able to access this destination with their ID card? Did the patient have a wristband? Was the wristband scanned - was this possible?**

29. **Environment FACTORS: Were there any environmental factors affecting patient collection? Limited access to areas in the hospital, waiting room layout, noisy environment etc**

30. **Task FACTORS: Were there any task related factors affecting patient collection? Did the porter know what to do? Was this an unusual patient collection/handover?**

31. **Organisation FACTORS: Were there any organisational factors affecting patient collection?**

32. **Open ended question, if possible. How does the porter/ward staff describe the identification process?**

Severity, Occurrence and Detection rating scales for FMEA

Severity scale

Effect	Criteria: Severity of Effect	Ranking
Hazardous - Without Warning	May expose patient to loss, harm or major disruption - failure will occur **without** warning	10
Hazardous - With Warning	May expose patient to loss, harm or major disruption - failure will occur **with** warning	9
Very High	Major disruption of service involving patient interaction, resulting in either associate re-work or inconvenience to patient	8
High	Minor disruption of service involving patient interaction and resulting in either associate re-work or inconvenience to patient	7
Moderate	Major disruption of service not involving patient interaction and resulting in either associate re-work or inconvenience to patient	6
Low	Minor disruption of service not involving client interaction and resulting in either associate re-work or inconvenience to patient	5
Very Low	Minor disruption of service involving client interaction that does not result in either associate re-work or inconvenience to patient	4
Minor	Minor disruption of service not involving patient interaction and does not result in either associate re-work or inconvenience to patient	3
Very Minor	No disruption of service noticed by the client in any capacity and does not result in either associate re-work or inconvenience to patient	2
None	No Effect	1

Occurrence scale

Probability of Failure	Per Item Failure Rates*	Ranking
Very High: Failure is almost inevitable	46-51	10
	41-45	9
High: Generally associated with processes similar to previous processes that have often failed	36-40	8
	31-35	7
Moderate: Generally associated with processes similar to previous processes which have experienced occasional failures, but not in major proportions	26-30	6
	21-25	5
	16-20	4
Low: Isolated failures associated with similar processes	11-15	3
Very Low: Only isolated failures associated with almost identical processes	6-10	2
Remote: Failure is unlikely. No failures associated with almost identical processes	1-5	1
*The criteria to determinate the occurrence scale was adapted considering the number of observations evaluated (N=51)		

Detection scale

Detection	Criteria: Likelihood the existence of a defect will be detected by process controls before next or subsequent process, -OR- before exposure to a client	Ranking
Almost Impossible	No known controls available to detect failure mode	10
Very Remote	Very remote likelihood current controls will detect failure mode	9
Remote	Remote likelihood current controls will detect failure mode	8
Very Low	Very low likelihood current controls will detect failure mode	7
Low	Low likelihood current controls will detect failure mode	6
Moderate	Moderate likelihood current controls will detect failure mode	5
Moderately High	Moderately high likelihood current controls will detect failure mode	4
High	High likelihood current controls will detect failure mode	3
Very High	Very high likelihood current controls will detect failure mode	2
Almost Certain	Current controls almost certain to detect the failure mode. Reliable detection controls are known with similar processes.	1

APPENDIX 3: Additional information of article II

Case Report Forms for data collection

ANÁLISIS RETROSPECTIVO DE UNA PRÁCTICA SEGURA: ADMINISTRACIÓN DE LA MEDICACIÓN			

Fecha: ☐☐ / ☐☐ / ☐☐☐☐   ID: ☐☐☐

Servei: SEMI ☐   Critics ☐   Cama: ☐☐☐   Dx: M☐ Q☐

Edad: ☐☐☐   Sexo: D☐ H☐   Estancia: ☐ días

Co-morbilidades: Sí ☐ No ☐   Número de fármacos prescritos: ☐☐

HTA: ☐   DM: ☐   Tabaquismo: ☐   Ansiedad: ☐

Cardiopatía: ☐   DLP: ☐   Alcoholismo: ☐   Otros: ☐☐

EPOC: ☐   Insufic. Renal: ☐   IQ previas: ☐   Otros: ☐☐

Nombre del fármaco:	SÍ	NO	NP
1 Nombre del fármaco incompleto			
2 Registro de dosis incompleto/ausente			
3 Registro de frecuencia de administarción incompleto/ausente			
4 Registro de la vía de administración/ausente			
5 Letra ilegible			
6 Uso de nombres comerciales			
7 Uso de abreviaturas			
Total de errores de este fármaco		██	██

Nombre del fármaco:	SÍ	NO	NP
1 Nombre del fármaco incompleto			
2 Registro de dosis incompleto/ausente			
3 Registro de frecuencia de administarción incompleto/ausente			
4 Registro de la vía de administración/ausente			
5 Letra ilegible			
6 Uso de nombres comerciales			
7 Uso de abreviaturas			
Total de errores de este fármaco		██	██

Nombre del fármaco:	SÍ	NO	NP
1 Nombre del fármaco incompleto			
2 Registro de dosis incompleto/ausente			
3 Registro de frecuencia de administarción incompleto/ausente			
4 Registro de la vía de administración/ausente			
5 Letra ilegible			
6 Uso de nombres comerciales			
7 Uso de abreviaturas			
Total de errores de este fármaco		██	██

ANÁLISIS PROSPECTIVO DE UNA PRÁCTICA SEGURA: ADMINISTRACIÓN DE LA MEDICACIÓN			

Fecha: ☐☐ / ☐☐ / ☐☐☐☐   **ID:** ☐☐☐

Horario: | 4h | 6h | 8h | 12h | 16h | 18h | 20h | 24h |

Nº de dosis administradas: ☐☐

	Dispensación	SÍ	NO	NP
1	¿No se ha dispensado alguno de los fármacos prescritos?			
2	¿La medicación dispensada no se corresponde con la prescrita?			
3	¿No se ha dispensado la medicación antes de la hora de la administración?			
	Administración	**SÍ**	**NO**	**NP**
4	¿Se ha preparado la medicación en un espacio y momento inadecuado?			
5	¿Ha habido interrupciones de timbres durante la preparación de la medicación?			
6	¿Ha habido interrupciones de teléfono durante la preparación de la medicación?			
7	¿Ha habido interrupciones de familias/ pacientes durante la preparación de la medicación?			
8	¿Ha habido interrupciones de otros profesionales durante la preparación de la medicación?			
9	El nombre del fármaco está incompleto?			
10	¿El registro de dosis está incompleto/ausente?			
11	¿El profesional que prepara la medicación no es el mismo que la administra?			
12	¿La medicación administrada antes de la hora programada (>1h)?			
13	¿La medicación administrada después de la hora programada (>1h)?			
14	¿La medicación no fue administrada?			
15	¿Existe carga de trabajo en el momento de administración de la medicación?			
16	¿No se concilia con el paciente, el horario habitual de la medicación administrada en casa?			
17	¿Ha habido prescripciones verbales?			
18	¿Existe incompatibilidad pyxis (paciente virtual)?			
19	¿Se desconoce como se administra alguno de los fármacos?			
20	¿La enfermera no informa al paciente consciente antes de administrar la medicación?			
21	¿Ha habido interrupciones de timbres durante la administración de la medicación?			
22	¿Ha habido interrupciones de teléfono durante la administración de la medicación?			
23	¿Ha habido interrupciones de familias/ pacientes durante la administración de la medicación?			
24	¿Ha habido interrupciones de otros profesionales durante la administración de la medicación?			

Datos generales

Servicio: | Semi | Critics | **ID:** ☐☐☐

Fecha: ☐☐ / ☐☐ / ☐☐

Datos del paciente

Edad: ☐☐☐   **Sexo:** | H | M | **Dx:** | M | Q |

Co-morbilidades: | Sí | No | **Estancia:** ☐☐ días

HTA: ☐   **DM:** ☐   **Tabaquismo:** ☐   **Ansiedad:** ☐

Cardiopatía: ☐   **DL:** ☐   **Alcoholismo:** ☐   **Otros:** ☐

EPOC: ☐   **Insuf. Renal:** ☐   **IQ previas:** ☐   **Otros:** ☐

Datos del profesional

Edad: ☐☐   **Sexo:** | H | M | **Tiempo en el servicio:** ☐☐ años

1. Bivariate and multivariate logistic regression analysis of variables to determinate the association with the presence of medication errors in prescription.

Error 1: Incorrect name								
Variable		n	%	Bivariate			Multivariate	
		11	(2.4)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	6	(2.2)	0.75	0.23-2.50	0.64	--	--	--
	IMCU	5	(2.9)						
Drug[a]	Family 1	1	(1.5)	0.65	0.07-6.34	0.71			
	Family 2	3	(4.2)	1.86	0.37-9.44	0.46			
	Family 3	4	(3.5)	1.55	0.34-7.08	0.57	--	--	--
	Family 4	0	0						
	Family 5	3	(2.3)						

Error 2: Omission error								
Variable		n	%	Bivariate			Multivariate	
		236	(52.1)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	165	(59.4)	2.14	1.46-3.14	<.01	2.42	1.62-3.62	<.01
	IMCU	71	(40.6)						
Drug	Family 1	37	(55.2)	1.33	0.74-2.40	0.34	1.66	0.90-3.06	0.11
	Family 2	30	(41.7)	0.77	0.43-1.38	0.38	0.76	0.42-1.37	0.36
	Family 3	72	(63.2)	1.85	1.11-3.09	0.02	2.12	1.25-3.60	<.01
	Family 4	34	(49.3)	1.05	0.59-1.88	0.87	1.13	0.62-2.05	0.69
	Family 5	63	(48.1)						

Error 3: Illegible handwriting								
Variable		n	%	Bivariate			Multivariate	
		187	(41.3)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	65	(23.4)	0.13	0.09-0.20	<.01	0.14	0.09-0.21	<.01
	IMCU	122	(69.7)						
Drug	Family 1	36	(53.7)	2.84	1.54-5.24	<.01	2.18	1.10-4.31	0.03
	Family 2	26	(36.1)	1.38	0.75-2.55	0.29	1.52	0.77-2.30	0.23
	Family 3	52	(45.6)	2.05	1.21-3.48	<.01	1.85	1.03-3.34	0.04
	Family 4	35	(50.7)	2.52	1.38-4.61	<.01	2.62	1.34-5.14	<.01
	Family 5	38	(29)						

Error 4: Commercial name

Variable		n	%	Bivariate			Multivariate		
		115	(25.4)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	77	(27.7)	1.38	0.89-2.16	0.16	1.35	0.85-2.15	0.21
	IMCU	38	(21.7)						
Drug	Family 1	19	(16.5)	1.46	0.74-2.86	0.28	1.56	0.79-3.09	0.21
	Family 2	31	(27.0)	2.78	1.49-5.20	<.01	2.79	1.49-5.22	<.01
	Family 3	13	(11.3)	0.47	0.23-0.97	0.04	0.49	0.24-1.0	0.5
	Family 4	24	(20.9)	1.96	1.03-3.75	0.04	2.01	1.05-3.86	0.04
	Family 5	28	(21.4)						

Error 5: Abbreviation

Variable		n	%	Bivariate			Multivariate		
		101	(22.3)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	84	(30.2)	4.02	2.29-7.06	<.01	3.77	2.11-6.75	<.01
	IMCU	17	(9.7)						
Drug	Family 1	6	(9)	0.15	0.06-0.38	<.01	0.18	0.07-0.47	<.01
	Family 2	19	(26.4)	0.56	0.30-1.06	0.07	0.54	0.28-1.03	0.06
	Family 3	23	(20.2)	0.40	0.22-0.71	<.01	0.43	0.24-0.78	<.01
	Family 4	2	(2.9)	0.05	0.01-0.20	<.01	0.05	0.01-0.20	<.01
	Family 5	51	(38.9)						

Drugs[a]: Family 1 is the groups of drugs with action in Digestive and metabolic system; Family 2, Blood and hematopoietic organs; Family 3, Cardiovascular system; Family 4, (hormone therapy, anti-infective therapy, locomotors apparatus, respiratory system and others); Family 5 Nervous system.

2. Bivariate and multivariate logistic regression analysis of variables to determinate the association with the presence of medication errors in administration.

Error 1: Preparation									
Variable		n	%		Bivariate			Multivariate	
		48	(19.3)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	34	(20.6)	1.30	0.65-2.58	0.46	--	--	--
	IMCU	14	(16.7)						
Shift	Morning	17	(21.0)	2.42	1.01-5.79	0.05	2.37	0.98-5.69	0.05
	Afternoon	22	(28.6)	3.64	1.56-8.51	<.01	4.07	1.72-9.67	<.01
	Night	9	(9.9)						
Workload	Yes	27	(22.9)	1.55	0.82-2.93	0.17	1.82	0.94-3.54	0.08
	No	21	(16.0)						
Error 2: Interruption									
Variable		n	%		Bivariate			Multivariate	
		137	(55)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	78	(47.3)	0.38	0.22-0.66	<.01	0.37	0.21-0.66	<.01
	IMCU	59	(70.2)						
Shift	Morning	53	(65.4)	2.21	1.19-4.09	0.04	2.15	1.10-4.18	0.02
	Afternoon	42	(54.5)	1.40	0.76-2.57	0.28	1.79	0.92-3.47	0.09
	Night	42	(46.2)						
Workload	Yes	83	(70.3)	3.38	1.99-5.72	<.01	3.64	2.09-6.35	<.01
	No	54	(41.2)						
Error 3: Medication prepared by another professional									
Variable		n	%		Bivariate			Multivariate	
		30	(12.2)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	22	(13.5)	1.46	0.62-3.44	0.38	--	--	--
	IMCU	8	(9.6)						
Shift	Morning	5	(6.2)	0.28	0.09-0.78	0.02	0.27	0.09-0.76	0.01
	Afternoon	8	(10.4)	0.48	0.19-1.19	0.12	0.53	0.21-1.32	0.17
	Night	17	(19.3)						
Workload	Yes	18	(15.4)	1.77	0.81-3.86	0.15	1.82	0.82-4.06	0.14
	No	12	(9.3)						

Error 4: Out of time or without prescription									
Variable		n	%		Bivariate			Multivariate	
		62	(24.9)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	42	(25.5)	1.10	0.59-2.02	0.78	--	--	--
	IMCU	20	(14.3)						
Shift	Morning	21	(25.9)	0-71	0.37-1.38	0.31	0.70	0.36-1.36	0.29
	Afternoon	11	(14.3)	0.34	0.16-0.74	<.01	0.35	0.16-0.77	<.01
	Night	30	(33.0)						
Workload	Yes	34	(28.8)	1.49	0.84-2.65	0.18	1.35	0.75-2.44	0.32
	No	28	(21.4)						
Error 5: Incompatibility using an automated dispensing cabinet (Pixys)									
Variable		n	%		Bivariate			Multivariate	
		3	(1.2)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	3	(1.8)	--	--	--	--	--	--
	IMCU	0	0						
Shift	Morning	0	0	--	--	--	--	--	--
	Afternoon	0	0						
	Night	3	(3)						
Workload	Yes	2	(1.7)	--	--	--	--	--	--
	No	1	(0.8)						
Error 6: No information to patient									
Variable		n	%		Bivariate			Multivariate	
		14	(7.4)	OR	IC 95%	p	OR	IC 95%	p
Unit	ICU	13	(12.1)	11.34	1.45-88.57	0.02	13.47	1.70-106.53	0.01
	IMCU	1	(1.2)						
Shift	Morning	5	(8.3)	0.64	0.20-2.07	0.45	0.72	0.21-2.43	0.59
	Afternoon	1	(1.5)	0.11	0.01-0.89	0.04	0.09	0.01-0.75	0.03
	Night	8	(12.5)						
Workload	Yes	6	(6.6)	0.80	0.27-2.41	0.70	--	--	--
	No	8	(8.1)						

APPENDIX 4: Register of the Overview

Effects of interventions to prevent adverse event in Intensive Care Unit (ICU)

Citation

Review question

What are the effects of interventions performed to prevent or reduce adverse events in intensive care unit?

Searches

We will search the following electronic bibliographic databases: MEDLINE, EMBASE, Cochrane and CINAHL. Search terms will include any synonyms that are related to adverse events in intensive care, such as: adverse drugs events, mechanical ventilation associated pneumonia, catheter-related infections. Besides we will consider terms related to interventions to improve patient safety such as harm reduction, risk management, safety culture; and terms for the setting of the study, for example: intensive care unit and critical care. The search strategy for identifying relevant studies will be subject to the database-specific terms to enable studies appropriate to the systematic review. These terms will be derived after discussion between the research team and will be piloted and tested by an experienced systematic reviewer prior to the development of the protocol. We will not restrict searches by language or year of publication.

The corresponding author of the eligible articles may be contacted if additional information is needed.

Types of study to be included

Systematic reviews and meta-analyses, which take into account randomized control trials (RCTs), non-RCTs, quasi-RCTs and other controlled studies investigating the effect of intervention to prevent or reduce adverse events. We will consider Cochrane or non-Cochrane systematic reviews of controlled studies for inclusion in the overview where they have employed a clear systematic approach, have a detailed search strategy using at least two sources searched, have included eligible criteria relevant to our research objective, and include an assessment of the quality of the methodological elements of the included trials with a narrative synthesis and/or meta-analysis.

Condition or domain being studied

Adverse events that occur in Intensive Care Unit. The definition of Adverse Events by The World Alliance for Patient Safety (from the World Health Organization) that we are using is: "an injury related to medical management in the healthcare setting, which includes all aspects of care, in contrast to complications of disease".

Participants/population

Adult critically ill patients in Intensive Care Unit

Intervention(s), exposure(s)

Interventions to prevent adverse events focused on patient safety

Comparator(s)/control

Control group receiving usual care, it can mean not receiving prevent interventions as well.

Control group receiving another preventive intervention.

Main outcome(s)

We will include the most frequent adverse events in ICU. We had chosen a-priori those:

• Adverse drugs events related to medication errors

• Infections: mechanical ventilation-associated pneumonia, bloodstream infection, central catheter infection, peripheral catheter infection

• Delirium

• Pressure ulcers

Those adverse event will be measured by:

• Mortality

• Length of stay

• Type of Harm (physical, psychological)

Measures of effect

We will gather data on each of the 3 primary outcomes measured over time, noting the time. Effect sizes will be noted but not aggregated in a meta-analysis because of the diversity of the interventions we anticipate identifying.

Additional outcome(s)

None

Measures of effect

Not applicable

Data extraction (selection and coding)

Two reviewers will screen review titles and abstracts to identify potentially relevant studies. They will then screen the full text of reviews deemed to be potentially relevant. Disagreements will be resolved by discussion with a third author.

Data from studies that meet the inclusion criteria, will be extracted into a review-specific data extraction tool by a lead reviewer and checked for accuracy by a second researcher who will be unaware of the findings of the lead reviewer.

Intervention characteristics to be extracted are: study setting (country, type of ICU), participants (gender, age, medical or surgical diagnosis), type of adverse event, type of intervention, comparator, duration of the intervention, and outcome measures.

Risk of bias (quality) assessment

We will perform an assessment of the quality of reporting of the systematic reviews using the Assessment of multiple systematic reviews (AMSTAR) checklist. We will also report the risk of bias tables pertaining to individual RCTs where these are reported within systematic reviews.

To assess the degree of overlap in the inclusion of primary studies between systematic reviews, the citation matrix will be generated by one reviewer and checked by a second for accuracy. The degree of overlap will be calculated with use of the corrected cover area (CCA).

Strategy for data synthesis [2 changes]

Presentation of results of overview will align guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the Cochrane Handbook of Systematic Reviews of Interventions. A PRISMA flow diagram will be used to summarize search results. Descriptive summaries about the efficacy of the interventions will be generated. Data will be presented as a synthesis and will be supplemented by series of summary tables and figures.

Eligible studies will be grouped according to the type of intervention to prevent adverse events. These could be pharmacological, non-pharmacological, educational, or group of mixed interventions. If there are more than 30 studies included in a single type of intervention, other specifics overviews will be carried out and published for the other types of interventions.

We do not plan a data analysis because it is an overview. However, we will describe the results of interest extracted from the included reviews. The measures of effects presented will be expressed as the original review, for example: frequency measures, Risk Ratio (RR), Odds Ratio (OR) with their 95% Confidence Interval.

If the included reviews present results by a GRADE Summary of Findings table, we will also describe them.

Analysis of subgroups or subsets [1 change]

Subsets will include grouping by type of adverse events as well as domain of interventions to improve patient safety.

Contact details for further information

Stefanie Suclupe

stefanie.suclupe@gmail.com

Organisational affiliation of the review

Iberoamerican Cochrane Centre

https://es.cochrane.org/iberoamerican-cochrane-network

Review team members and their organisational affiliations [2 changes]

Ms Stefanie Suclupe. Iberoamerican Cochrane Centre. Barcelona, Spain. Instituto de Investigación Biomédica Sant Pau (IIB Sant Pau). Barcelona, España. Universitat Autònoma de Barcelona. Spain.

Mr Percy Efrain Pantoja Bustillos. Iberoamerican Cochrane Centre. Barcelona, Spain. Instituto de Investigación Biomédica Sant Pau (IIB Sant Pau). Barcelona, España. Universitat Autònoma de Barcelona. Spain.

Dr Gemma Robleda. Iberoamerican Cochrane Centre. Barcelona, Spain. Mar University School of Nursing - Pompeu Fabra University.

Mr Ivan Solà. Servicio de Epidemiología Clínica y Salud Pública, Hospital de la Santa Creu i Sant Pau. Instituto de Investigación Biomédica Sant Pau (IIB Sant Pau). Barcelona, España. CIBERESP, España.

Ms Carolina Requeijo. Servicio de Epidemiología Clínica y Salud Pública, Hospital de la Santa Creu i Sant Pau. Instituto

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Karla Salas-Gama. Servicio de Epidemiología Clínica y Salud Pública, Hospital de la Santa Creu i Sant Pau. Instituto de Investigación Biomédica Sant Pau (IIB Sant Pau). Barcelona, España.

Dr Maria Jose Martinez Zapata. Servicio de Epidemiología Clínica y Salud Pública, Hospital de la Santa Creu i Sant Pau. Instituto de Investigación Biomédica Sant Pau (IIB Sant Pau). Barcelona, España. CIBERESP, España.

Type and method of review

Intervention, Meta-analysis, Systematic review

Anticipated or actual start date

01 September 2019

Anticipated completion date [2 changes]

31 December 2020

Funding sources/sponsors

None

Conflicts of interest

Language

English

Country

Spain

Stage of review

Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Humans; Intensive Care Units

Date of registration in PROSPERO

16 December 2019

Date of first submission

20 August 2019

Stage of review at time of this submission [1 change]

Stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	Yes	No
Risk of bias (quality) assessment	Yes	No
Data analysis	No	No

Revision note

There is an update of strategy for data synthesis, since the authors have decided that, in case we find a high number of eligible studies, we will group them by type of intervention and different overviews and publications will be conducted.

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

16 December 2019

06 January 2020

10 March 2021

APPENDIX 5: Additional information of article III

Supplementary Material 1: Differences between protocol and review

We made the following changes to the published protocol:

1. In the protocol we planned to search in four different database, but in the review we did not include EMBASE.

2. In protocol, we mentioned methodological quality assessment as an inclusion criteria for SRs but we did not consider this criteria in the review

Supplementary Material 2: PRISMA 2020 Checklist

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	2,3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	4, supplementary file 3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	4,5,6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	4,5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in	5

Section and Topic	Item #	Checklist item	Location where item is reported
		each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	6, 7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	6,7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	n/a
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	n/a
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	n/a
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	6,7
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	7, 8, fig 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Fig 1, Supplementary file 4

Section and Topic	Item #	Checklist item	Location where item is reported
Study characteristics	17	Cite each included study and present its characteristics.	8, Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	n/a
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	13 -23
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	n/a
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	13-23, fig 2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	n/a
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	n/a
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	n/a
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	13, table 2
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	28
	23b	Discuss any limitations of the evidence included in the review.	31
	23c	Discuss any limitations of the review processes used.	31
	23d	Discuss implications of the results for practice, policy, and future research.	32
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Supplementary

Section and Topic	Item #	Checklist item	Location where item is reported
			file 1
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	n/a
Competing interests	26	Declare any competing interests of review authors.	32
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Supplementary files

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Supplementary Material 3: Search strategy

MEDLINE

#1	medication error*[Title/Abstract] OR drug error*[Title] OR inappropriate prescri*[Title/Abstract] OR inappropriate administrati*[Title/Abstract] OR adverse drug event*[Title/Abstract] OR "Medication Errors"[Mesh] OR "Inappropriate Prescribing"[Mesh] OR "Drug-Related Side Effects and Adverse Reactions"[MAJR]	112,563
#2	"Pneumonia, Ventilator-Associated"[Mesh] OR "Pneumonia, Aspiration"[Mesh] OR "Healthcare-Associated Pneumonia"[Mesh] OR "Airway Obstruction"[Mesh] OR "Airway Extubation"[Mesh] OR "Intubation"[Mesh] OR "Airway Management"[Mesh] OR nosocomial pneumonia[Title/Abstract] OR healthcare-associated pneumonia[Title/Abstract] OR intubation[Title/Abstract] OR reintubation[Title/Abstract] OR re intubation[Title/Abstract] OR airway manage*[Title/Abstract]	199,437
#3	catheter related infect*[Title/Abstract] OR catheter infect*[Title/Abstract] OR bloodstream infect*[Title/Abstract] OR blood stream infect*[Title/Abstract] OR bacteremia*[Title/Abstract] OR urinary infection*[Title/Abstract] OR thrombosis[Title] OR phlebitis[Title/Abstract] OR "Catheter-Related Infections"[Mesh] OR "Bacteremia"[Mesh] OR "Phlebitis"[MAJR] OR "Urinary Tract Infections"[Mesh] OR "Embolism and Thrombosis"[MAJR]	296,092
#4	pressure ulcer*[Title/Abstract] OR ulcer*[Title] OR wound infect*[Title/Abstract] OR "Pressure Ulcer"[Mesh] OR "Wound Infection"[Mesh]	184,131
#5	deliri*[Title] OR "Delirium"[MAJR]	11,671
#6	adverse event*[Title/Abstract] OR error*[Title] OR mistake*[Title] OR harm*[Title] OR incident*[Title] OR infection*[Title] OR sepsis[Title] OR complication[Title] OR healthcare-associated infection*[Title/Abstract] OR health care-associated infection*[Title/Abstract] OR "Medical Errors"[Mesh] OR "Cross Infection"[Mesh] OR "Infectious Disease Transmission, Professional-to-Patient"[Mesh] OR "Sepsis"[Mesh] OR "Patient Harm"[Mesh]	1,082,467
#7	safety[Title] OR patient safety[Title/Abstract] OR harm reduction[Title/Abstract] OR "Patient Safety"[Mesh] OR "Safety Management"[Mesh] OR "Harm Reduction"[Mesh] OR "Risk Management"[Mesh] OR "Quality of Health Care"[MAJR] OR "Infection Control"[MAJR] OR "Accident Prevention"[Mesh]	1,459,738
#8	"Intensive Care Units"[Mesh] OR "Critical Care"[Mesh] OR "Critical Illness"[Mesh] OR critical care*[Title/Abstract] OR intensive care*[Title/Abstract] OR intensive care unit*[Title/Abstract] OR critical ill*[Title/Abstract] OR ICU*[Title/Abstract] OR critical care unit*[Title/Abstract]	285,605
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	3,031,678
#10	#9 AND #8	110,083
#11	#10 AND systematic[sb]	2,133

COCHRANE LIBRARY

#1	MeSH descriptor: [Medication Errors] explode all trees	450
#2	(medication error OR drug error OR inappropriate prescription OR inappropriate administration OR adverse drug event):ti,ab,kw	31,495
#3	MeSH descriptor: [Healthcare-Associated Pneumonia] explode all trees	343
#4	(nosocomial pneumonia OR healthcare-associated pneumonia OR intubation OR reintubation OR re intubation OR airway manage):ti,ab,kw	23,091
#5	MeSH descriptor: [Catheter-Related Infections] explode all trees	327
#6	(catheter related NEXT (infection*) OR bloodstream NEXT (infect*) OR bacteremia):ti,ab,kw	3,920
#7	MeSH descriptor: [Delirium] explode all trees	850
#8	MeSH descriptor: [Pressure Ulcer] explode all trees	775
#9	(adverse event OR error OR mistake OR harm OR incident OR infection OR healthcare-associated infection OR health care-associated infection):ti,ab,kw	354,822
#10	MeSH descriptor: [Patient Safety] explode all trees	685
#11	#1 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	372,694
#12	MeSH descriptor: [Intensive Care Units] explode all trees	3,801
#13	(Critical Care OR Critical Illness OR critical care OR intensive care OR intensive care unit OR critical ill OR ICU OR critical care unit):ti,ab,kw	44,270
#14	#12 OR #13	44,504
#15	(neonatal intensive care OR neonatal OR child OR children OR pediatric OR paediatric):ti,ab,kw	181,409
#16	#14 NOT #15	286

CINAHL

S1	(MH "Medication Errors") OR (MH "Health Care Errors")	18,472
S2	(MH "Inappropriate Prescribing")	3,183
S3	(MH "Adverse Health Care Event")	8,787
S4	(TI medication error* OR AB medication error*)	8,091
S5	(TI drug error* OR AB drug error*)	4,555
S6	(TI inappropriate prescri* OR AB inappropriate prescri*)	3,348
S7	(TI adverse drug event* OR AB adverse drug event*)	17,917
S8	(TI inappropriate administrati* OR AB inappropriate administrati*)	1,049
S9	(MH "Pneumonia, Ventilator-Associated") OR (MH "Healthcare-Associated Pneumonia")	3,565
S10	(MH "Extubation") OR (MH "Airway Obstruction")	6,739
S11	(MH "Intubation/AE/NU")	198
S12	(MH "Airway Management/AE/NU")	324
S13	(TI nosocomial pneumonia OR AB nosocomial pneumonia)	1,368
S14	(TI healthcare-associated pneumonia OR AB healthcare-associated pneumonia)	539
S15	((TI intubation OR AB intubation)) OR ((TI re intubation OR AB re intubation)) OR ((TI reintubation OR AB reintubation)) OR ((TI extubation OR AB extubation)) OR ((TI airway manage* OR AB airway manage*))	25,185

S16	(MH "Urinary Tract Infections, Catheter-Related") OR (MH "Catheter-Related Bloodstream Infections") OR (MH "Catheter-Related Infections") OR (MH "Central Venous Catheters/AE/NU")	7,626
S17	(MH "Catheter-Related Thrombosis/CO/PC") OR (MH "Catheter-Related Complications") OR (MH "Catheterization, Peripheral/AE")	2,040
S18	(MH "Phlebitis")	763
S19	((TI catheter related infect* OR AB catheter related infect*)) OR ((TI bacteremia* OR AB bacteremia*)) OR ((TI bacteraemia* OR AB bacteraemia*)) OR ((TI blood stream infection* OR AB blood stream infection*)) OR ((TI urinary infection* OR AB urinary infection*)) OR ((TI phlebitis* OR AB phlebitis*))	22,399
S20	(MH "Pressure Ulcer")	15,112
S21	(MH "Wound Infection")	4,289
S22	((TI pressure ulcer* OR AB pressure ulcer*)) OR ((TI ulcer* OR AB ulcer*)) OR ((TI wound infect* OR AB wound infect*))	55,661
S23	(MH "Delirium")	7,560
S24	(TI deliri* OR AB deliri*)	9,546
S25	(MH "Adverse Drug Event/PC")	2,710
S26	(MH "Cross Infection")	26,323
S27	(MH "Disease Transmission, Professional-to-Patient")	580
S28	((TI adverse event* OR AB adverse event*)) OR ((TI healthcare-associated infection* OR AB healthcare-associated infection**)) OR ((TI harm* OR AB harm*)) OR ((TI error* OR AB error*)) OR ((TI incident* OR AB incident*))	256,080
S29	(MH "Patient Safety")	68,738
S30	(MH "Safety")	30,356
S31	(MH "Harm Reduction")	4,709
S32	(MH "Risk Management")	16,427
S33	(MH "Quality of Health Care")	80,492
S34	(TI safety) OR ((TI patient safety OR AB patient safety)) OR ((TI harm reduction OR AB harm reduction))	161,667
S35	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34	668,278
S36	(MH "Intensive Care Units")	42,448
S37	(MM "Critical Care")	15,642
S38	((TI intensive care unit* OR AB intensive care unit*)) OR ((TI ICU* OR AB ICU*)) OR ((TI critical care unit* OR AB critical care unit*)) OR ((TI critical ill* OR AB critical ill*))	97,127
S39	S36 OR S37 OR S38	116,306
S40	S35 AND S39	29,055
S41	(MH "Meta Analysis" OR MH "Systematic Review" OR PT Systematic Review OR TI systematic review* OR AB systematic review*)	205,417
S42	S40 AND S41	1393

Supplementary Material 4: Excluded systematic reviews after full text (N=167)

Year	Authors	Title	Reason for exclusion
1998	D'Amico	Effectiveness of antibiotic prophylaxis in critically ill adult patients: systematic review of randomised controlled trials	No NPhI
2000	Liberati	Antibiotics for preventing respiratory tract infections in adults receiving intensive care	No adverse patient outcomes reported
2000	Cullum	Beds, mattresses and cushions for pressure sore prevention and treatment	Wrong population
2002	Geerts	Venous thromboembolism and its prevention in critical care	No NPhI
2003	Klerk	Thrombosis prophylaxis in patient populations with a central venous catheter: a systematic review	No NPhI
2003	Geerts	Prevention of venous thromboembolism in the ICU	No NPhI
2003	Bucknall	Research review. Preventing ventilator-associate pneumonia (VAP) in critically ill patients	Wrong study design
2003	Petrucci	Ventilation with lower tidal volumes versus traditional tidal volumes in adults for acute lung injury and acute respiratory distress syndrome	Wrong outcome
2003	Marik	Gastric versus post-pyloric feeding: a systematic review	No NPhI
2003	Hawkes	Early extubation for adult cardiac surgical patients	Wrong setting
2004	García Fernández	Utility and cost-effectiveness of air suspension bed in the prevention of pressure ulcers	Wrong study design
2004	Liberati	Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care	No adverse patient outcomes reported
2004	Gramlich	Does enteral nutrition compared to parenteral nutrition result in better outcomes in critically ill adult patients? A systematic review of the literature	No NPhI
2004	Celik	Nosocomial infections in neurosurgery intensive care units	Wrong study design
2005	Blackwood	Review: subglottic secretion drainage reduces ventilator associated pneumonia	Wrong outcome
2005	Silvestri	Handwashing in the intensive care unit: a big measure with modest effects	Wrong study design
2005	Carroll	Review: noninvasive positive-pressure ventilation reduces intubation and length of ICU stay in acute respiratory failure	Wrong study design
2006	de Laat	Epidemiology, risk and prevention of pressure ulcers in critically ill patients: a literature review	Wrong study design
2006	Playford	Antifungal agents for preventing fungal infections in non-neutropenic critically ill and surgical patients: systematic review and meta-analysis of randomized clinical trials	No NPhI
2007	Niel-Weise	Humidification policies for mechanically ventilated intensive care patients and prevention of ventilator-associated pneumonia: a systematic review of randomized controlled trials	No NPhI
2007	Berry	Systematic literature review of oral hygiene practices for intensive care patients receiving mechanical ventilation	Wrong study design, wrong population
2007	Watkinson	The use of pre- pro- and synbiotics in adult intensive care unit patients: systematic review	No NPhI
2007	Silvestri	Selective decontamination of the digestive tract reduces bacterial bloodstream infection and mortality in critically ill patients. Systematic review of randomized, controlled trials	No NPhI
2007	Siddiqi	Interventions for preventing delirium in hospitalised patients	Wrong setting
2007	Niel-Weise	Anti-infective-treated central venous catheters: a systematic review of randomized controlled trials	No NPhI
2007	Landoni	Beneficial impact of fenoldopam in critically ill patients with or at risk for acute renal failure: a meta-analysis of randomized clinical trials	Wrong outcome
2008	Safdar	Educational interventions for prevention of healthcare-associated infection: a systematic review	Wrong setting
2008	Ramritu	A systematic review comparing the relative effectiveness of antimicrobial-coated catheters in intensive care units	No NPhI
2008	Siempos	Closed tracheal suction systems for prevention of ventilator-associated pneumonia	Duplicated. This study was included
2008	Krau	Review: some interventions may reduce catheter-related bloodstream infections and colonisation in the ICU	Wrong study design
2008	O'Keefe-McCarthy	Ventilator-associated pneumonia bundled strategies: an evidence-based practice	Wrong study design
2008	Jones	Oral care and the risk of bloodstream infections in mechanically ventilated adults: a review	Wrong study design
2009	Hermans	Interventions for preventing critical illness polyneuropathy and critical illness myopathy	No NPhI
2009	McCaffrey	Corticosteroids to prevent extubation failure: a systematic review and meta-analysis	No NPhI

2010	Moola	A systematic review of the management of short-term indwelling urethral catheters to prevent urinary tract infections	No NPhI
2010	Marik	Stress ulcer prophylaxis in the new millennium: a systematic review and meta-analysis	No NPhI
2010	Siempos	Impact of the administration of probiotics on the incidence of ventilator-associated pneumonia: A meta-analysis of randomized controlled trials	No NPhI
2010	Harada	Closed suctioning system: critical analysis for its use	Wrong study design
2010	Carlet	Anti-, pre-, or . . . probiotics to prevent ventilator-associated pneumonia in the intensive care unit?	Wrong study design
2011	Zamora	Effectiveness of oral care in the prevention of ventilator-associated pneumonia. Systematic review and meta-analysis of randomised clinical trials	No NPhI
2011	Roberts	Chlorhexidine and tooth-brushing as prevention strategies in reducing ventilator-associated pneumonia rates	No NPhI
2011	Chamberlain	The severe sepsis bundles as processes of care: A meta-analysis	Wrong study design
2012	O'Horo	The efficacy of daily bathing with chlorhexidine for reducing healthcare-associated bloodstream infections: a meta-analysis	No NPhI
2012	Gu	Impact of oral care with versus without toothbrushing on the prevention of ventilator-associated pneumonia: a systematic review and meta-analysis of randomized controlled trials	No NPhI
2012	Petrof	Probiotics in the critically ill: a systematic review of the randomized trial evidence	No NPhI
2012	Liu	Probiotics' effects on the incidence of nosocomial pneumonia in critically ill patients: a systematic review and meta-analysis	No NPhI
2012	Márquez Rivero	Evidence-based protocol on the urinary catheter cares in intensive care units	Wrong study design
2012	Lip	Prevention of Venous Thromboembolism with New Oral Anticoagulants versus Standard Pharmacological Treatment in Acute Medically 111 Patients	Wrong outcome
2012	Glossop	Non-invasive ventilation for weaning, avoiding reintubation after extubation and in the postoperative period: a meta-analysis	No NPhI
2012	Artur Ferreira de Sousa	Contributions of the electronic health records to the safety of intensive care unit patients: An integrative review	Wrong study design
2013	Wang	Probiotics for preventing ventilator-associated pneumonia: a systematic review and meta-analysis of high-quality randomized controlled trials	No NPhI
2013	Li	Oral topical decontamination for preventing ventilator-associated pneumonia: a systematic review and meta-analysis of randomized controlled trials	No NPhI
2013	Galvin	Partial liquid ventilation for preventing death and morbidity in adults with acute lung injury and acute respiratory distress syndrome	No NPhI
2013	Alhazzani	Proton pump inhibitors versus histamine 2 receptor antagonists for stress ulcer prophylaxis in critically ill patients: a systematic review and meta-analysis	Wrong outcome
2013	Afonso	The value of chlorhexidine gluconate wipes and prepacked washcloths to prevent the spread of pathogens--a systematic review	Wrong population
2013	Giron Camerini	Preventive strategies of adverse events with potentially dangerous medications	Wrong study design
2013	Crespo	Ventilator-Associated Pneumonia. Influence of the implementation of preventive nursing measures in critical patients	Wrong study design
2013	Xia	Clinical benefits of dexmedetomidine versus propofol in adult intensive care unit patients: a meta-analysis of randomized clinical trials	No adverse patient outcomes reported
2013	Teslyar	Prophylaxis with antipsychotic medication reduces the risk of post-operative delirium in elderly patients: a meta-analysis	No NPhI
2013	Li	Active mobilization for mechanically ventilated patients: a systematic review	No NPhI
2013	Flodgren	Interventions to improve professional adherence to guidelines for prevention of device-related infections	No NPhI
2013	Barraud	Impact of the administration of probiotics on mortality in critically ill adult patients: a meta-analysis of randomized controlled trials	Wrong outcome
2014	Clark	Systematic review of the use of prophylactic dressings in the prevention of pressure ulcers	No NPhI
2014	Tabak	Meta-analysis on central line–associated bloodstream infections associated with a needleless intravenous connector with a new engineering design	No NPhI
2014	Howell	Reducing the burden of surgical harm: a systematic review of the interventions used to reduce adverse events in surgery	Wrong setting
2014	Hermans	Interventions for preventing critical illness polyneuropathy and critical illness myopathy	No NPhI
2014	Blackwood	Protocolized versus non-protocolized weaning for reducing the duration of mechanical ventilation in critically ill adult patients	Wrong outcome

2014	Alikhan	Heparin for the prevention of venous thromboembolism in acutely ill medical patients (excluding stroke and myocardial infarction)	Wrong population
2014	Hurley	Ventilator-associated pneumonia prevention methods using topical antibiotics: herd protection or herd peril?	Wrong study design
2014	Hui-Chun	Effects of Prone Positioning on Oxygenation and Complications in Patients With Acute Respiratory Distress Syndrome (ARDS) in the Intensive Care Unit: A Systematic Review and Meta-Analysis	Not in English or Spanish
2015	Rivosecchi	Nonpharmacological interventions to prevent delirium: an evidence-based systematic review	Wrong study design
2015	El-Rabbany	Prophylactic oral health procedures to prevent hospital-acquired and ventilator-associated pneumonia: a systematic review	No NPhI
2015	Wei	Meta analysis of influence of brushing teeth on incidence of ventilator - associated pneumonia in patients with mechanical ventilation	Not in English or Spanish
2015	Ullman	Dressings and securement devices for central venous catheters (CVC)	Wrong study design
2015	Trogrlic	A systematic review of implementation strategies for assessment, prevention, and management of ICU delirium and their effect on clinical outcomes	No NPhI
2015	Nelson	Defining the Role of Dexmedetomidine in the Prevention of Delirium in the Intensive Care Unit	Wrong study design: integrative review
2015	Mu	Pharmacologic agents for the prevention and treatment of delirium in patients undergoing cardiac surgery: systematic review and metaanalysis	Wrong setting
2015	Makam	Diagnostic accuracy and effectiveness of automated electronic sepsis alert systems: A systematic review	No NPhI
2015	Liu	Early versus late tracheostomy: a systematic review and meta-analysis	No NPhI
2015	Damiani	Effect of performance improvement programs on compliance with sepsis bundles and mortality: a systematic review and meta-analysis of observational studies	Wrong population, wrong outcome
2015	Chou	Ultrasonography for confirmation of endotracheal tube placement: a systematic review and meta-analysis	Wrong outcome
2015	Campbell	Warming of intravenous and irrigation fluids for preventing inadvertent perioperative hypothermia	Wrong setting
2015	Bloomfield	Prone position for acute respiratory failure in adults	Wrong outcome
2015	Allingstrup	Selenium supplementation for critically ill adults	Wrong outcome
2016	Shah	Bathing With 2% Chlorhexidine Gluconate: Evidence and Costs Associated With Central Line-Associated Bloodstream Infections	No NPhI
2016	Schrijver	Efficacy and safety of haloperidol for in-hospital delirium prevention and treatment: A systematic review of current evidence	No NPhI
2016	Nair	Clinical Effectiveness of Mupirocin for Preventing Staphylococcus aureus Infections in Nonsurgical Settings: A Meta-analysis	No NPhI
2016	Lai	Skin antisepsis for reducing central venous catheter-related infections	No NPhI
2016	Lai	Catheter impregnation, coating or bonding for reducing central venous catheter-related infections in adults	No NPhI
2016	Krag	Stress ulcer prophylaxis in the intensive care unit	No NPhI
2016	Hua	Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia	Wrong population
2016	Hewitt	Lateral positioning for critically ill adult patients	No NPhI
2016	Guerra	[VAP and oral hygiene.A systematic review]	Not in English or Spanish
2016	Gavin	Frequency of dressing changes for central venous access devices on catheter-related infections	No NPhI
2016	Alshamsi	Efficacy and safety of proton pump inhibitors for stress ulcer prophylaxis in critically ill patients: a systematic review and meta-analysis of randomized trials	No adverse patient outcomes reported
2016	Afonso	Prevention of hospital-acquired bloodstream infections through chlorhexidine gluconate-impregnated washcloth bathing in intensive care units: a systematic review and meta-analysis of randomised crossover trials	Wrong population
2016	Şanlı	Yoğun Bakım Hastalarında Kateter İlişkili Kan Dolaşımı Enfeksiyonlarının Önlenmesinde Kanıta Dayalı Önerilerin Etkinliğinin İncelenmesi	Not in English or Spanish
2016	Palombi	Efficacia del bagno con clorexidina gluconato al 2% nella prevenzione delle batteriemie associate a catetere intravascolare in terapia intensiva: una revisione sistematica	Not in English or Spanish
2016	Martínez	Prevención del delirium en pacientes ingresados en unidades de críticos	No NPhI
2016	Huang	Systemic evaluation on efficacy of chlorhexidine sponge bath for preventing catheter-associated urinary tract infections for adult patients in intensive care unit	Not in English or Spanish
2016	Estepa del Árbol	Eficacia de los programas de seguridad del paciente	Wrong study design
2016	Ullman	Dressing and securement for central venous access devices (CVADs): A Cochrane systematic review	No NPhI
2016	Siddiqi	Interventions for preventing delirium in hospitalised non-ICU patients	Wrong setting

2016	Pedersen	The effectiveness of systematic perioperative oral hygiene in reduction of postoperative respiratory tract infections after elective thoracic surgery in adults: a systematic review	Wrong setting
2016	Neufeld	Antipsychotic Medication for Prevention and Treatment of Delirium in Hospitalized Adults: A Systematic Review and Meta-Analysis	Wrong setting
2016	Muller	Antimicrobial surfaces to prevent healthcare-associated infections: a systematic review	No NPhI
2016	Hockey	Does objective measurement of tracheal tube cuff pressures minimise adverse effects and maintain accurate cuff pressures? A systematic review and meta-analysis	No NPhI
2016	Flannery	The Impact of Interventions to Improve Sleep on Delirium in the ICU: A Systematic Review and Research Framework	No NPhI
2016	Cortegiani	Antifungal agents for preventing fungal infections in non-neutropenic critically ill patients	Wrong population
2016	Zuckerman	Oral Chlorhexidine Use to Prevent Ventilator-Associated Pneumonia in Adults: Review of the Current Literature	Wrong study design, wrong outcome
2016	Marang-van de Mheen	Meta-analysis of the central line bundle for preventing catheterrelated infections: a case study in appraising the evidence in quality improvement	No NPhI
2016	Mao	Subglottic secretion suction for preventing ventilator-associated pneumonia: an updated meta-analysis and trial sequential analysis	No NPhI
2017	Teerawattanapong	Prevention and Control of Multidrug-Resistant Gram-Negative Bacteria in Adult Intensive Care Units: A Systematic Review and Network Meta-analysis	No NPhI
2017	Silvestri	Impact of Oral Chlorhexidine on Bloodstream Infection in Critically Ill Patients: Systematic Review and Meta-Analysis of Randomized Controlled Trials	No NPhI
2017	Lin	[Chlorhexidine Bed-Bath Improves CLABSI: A Meta-Analysis]	Not in English or Spanish
2017	Kramer	Are antimicrobial peripherally inserted central catheters associated with reduction in central line-associated bloodstream infection? A systematic review and meta-analysis	No NPhI
2017	Mohammad Ali Heydari	Nursing preventive measures against the incidence of delirium in hospitalized patients: a narrative review	Wrong study design
2017	Lima Benevides	Nursing strategies for the prevention of pressure ulcers in intensive therapy: Integrative review	Wrong study design: integrative review
2017	Klompas	Oropharyngeal Decontamination with Antiseptics to Prevent Ventilator-Associated Pneumonia: Rethinking the Benefits of Chlorhexidine	Wrong outcome
2017	Akanji	Effectiveness of formal hand hygiene education and feedback on healthcare workers' hand hygiene compliance and hospital-associated infections in adult intensive care units: a systematic review protocol	Wrong outcome
2017	Woo	The impact of the advanced practice nursing role on quality of care, clinical outcomes, patient satisfaction, and cost in the emergency and critical care settings: a systematic review	No adverse patient outcomes reported
2017	Teeple	Outcomes of safe patient handling and mobilization programs: A meta-analysis	Wrong setting
2017	Schieren	Continuous lateral rotational therapy in trauma-A systematic review and meta-analysis	Wrong setting
2017	Rose	Cough augmentation techniques for extubation or weaning critically ill patients from mechanical ventilation	No NPhI
2017	Putzu	Vitamin D and outcomes in adult critically ill patients. A systematic review and meta-analysis of randomized trials	No NPhI
2017	Munshi	Prone Position for Acute Respiratory Distress Syndrome. A Systematic Review and Meta-Analysis	Wrong population
2017	Costa	Identifying Barriers to Delivering the Awakening and Breathing Coordination, Delirium, and Early Exercise/Mobility Bundle to Minimize Adverse Outcomes for Mechanically Ventilated Patients: A Systematic Review	Wrong outcome
2017	West	22 Apneic Oxygenation Via Conventional Nasal Cannula to Prevent Oxygen Desaturation During Rapid Sequence Intubation in the Emergency Department and Intensive Care Unit: A Systematic Review and Meta-Analysis	No full text available
2018	Serraes	Prevention of pressure ulcers with a static air support surface: A systematic review	No NPhI
2018	Alshehari	Strategies to improve hand hygiene compliance among healthcare workers in adult intensive care units: a mini systematic review	Wrong population
2018	강현욱	중환자실의 욕창 예방 중재 프로그램의 효과 : 메타 분석	Not in English or Spanish
2018	Wang	Postoperative tight glycemic control significantly reduces postoperative infection rates in patients undergoing surgery: a meta-analysis	No NPhI
2018	Teo Kai	Evaluating the effectiveness of silicone multilayer foam dressing in preventing heel pressure injury among critically ill patients in Singapore	No NPhI
2018	Rabello	Effectiveness of oral chlorhexidine for the prevention of nosocomial pneumonia and ventilator-associated pneumonia in intensive care units: Overview of systematic reviews	No NPhI
2018	Nguyen	Effectiveness of dexmedetomidine versus propofol on extubation times, length of stay and mortality rates in adult cardiac surgery patients: a systematic review and meta-analysis	No NPhI
2018	Kumari	Oral Care in Intubated Patients Whether or not on Mechanical Ventilation: A Systemic Review	No NPhI

2018	Ghaeli	Preventive Intervention to Prevent Delirium in Patients Hospitalized in Intensive Care Unit	Wrong study design
2018	Floyd	Effectiveness of Pressure Ulcer Protocols with the Braden Scale for Elderly Patients in the Intensive Care Unit: A Systematic Review	Wrong population
2018	Bisaio Quillici	Importância dos cuidados de enfermagem para a prevenção de pneumonia associada à ventilação mecânica	Wrong study design: integrative review
2018	Warttig	Automated monitoring compared to standard care for the early detection of sepsis in critically ill patients	No NPhI
2018	Smit	Bedside ultrasound to detect central venous catheter misplacement and associated iatrogenic complications: a systematic review and meta-analysis	No NPhI
2018	Shen	Effects of Haloperidol on Delirium in Adult Patients: A Systematic Review and Meta-Analysis	Wrong setting
2018	Ni	The effect of high-flow nasal cannula in reducing the mortality and the rate of endotracheal intubation when used before mechanical ventilation compared with conventional oxygen therapy and noninvasive positive pressure ventilation. A systematic review and meta-analysis	No NPhI
2018	Lee	A Systematic Review of Early Warning Systems' Effects on Nurses' Clinical Performance and Adverse Events Among Deteriorating Ward Patients	No adverse patient outcomes reported
2018	Guay	Intraoperative use of low volume ventilation to decrease postoperative mortality, mechanical ventilation, lengths of stay and lung injury in adults without acute lung injury	Wrong population
2018	Driscoll	The effect of nurse-to-patient ratios on nurse-sensitive patient outcomes in acute specialist units: a systematic review and meta-analysis	Wrong outcome
2018	Wu	Perioperative dexmedetomidine reduces delirium after cardiac surgery: A meta-analysis of randomized controlled trials	Wrong population
2018	Gomes da Silva	Impacto da implementação dos bundles na redução das infecções da corrente sanguínea: uma revisão integrativa	Not in English or Spanish
2018	Binda	Efficacia dell'ossigenoterapia con le cannule nasali ad alto flusso nella prevenzione della reintubazione del paziente critico: revisione della letteratura	Wrong study design, wrong outcome
2019	Ray-Barruel	Effectiveness of insertion and maintenance bundles in preventing peripheral intravenous catheter-related complications and bloodstream infection in hospital patients: A systematic review	Wrong setting
2019	Musuuza	The impact of chlorhexidine bathing on hospital-acquired bloodstream infections: a systematic review and meta-analysis	No NPhI
2019	김남영	클로르헥시딘 구강간호법이 인공호흡기 관련 폐렴 발생률과 사망률에 미치는 효과: 체계적 문헌고찰 및 메타분석	Not in English or Spanish
2019	Alecrim	Estratégias para prevenção de pneumonia associada à ventilação mecânica: revisão integrativa	Not in English or Spanish
2019	Torres	Non-invasive positive pressure ventilation for prevention of complications after pulmonary resection in lung cancer patients	No NPhI
2019	Barbateskovic	Stress ulcer prophylaxis with proton pump inhibitors or histamin-2 receptor antagonists in adult intensive care patients: a systematic review with meta-analysis and trial sequential analysis	Wrong outcome
2019	Bannon	The effectiveness of non-pharmacological interventions in reducing the incidence and duration of delirium in critically ill patients: a systematic review and meta-analysis	Wrong population
2019	Wang	Chest physiotherapy for the prevention of ventilator-associated pneumonia: A meta-analysis	No NPhI
2019	Ratelle	Implementing bedside rounds to improve patient-centred outcomes: a systematic review	No NPhI
2019	Rahimi	Prevention and management catheter-associated urinary tract infection in intensive care unit	No NPhI
2019	Jonsson	Bleeding and thrombosis in intensive care patients with thrombocytopenia-Protocol for a topical systematic review	This is a protocol
2019	Garry	Do nurse-led critical care outreach services impact inpatient mortality rates?	No NPhI
2020	Worraphan	Effects of Inspiratory Muscle Training and Early Mobilization on Weaning of Mechanical Ventilation: A Systematic Review and Network Meta-analysis	Wrong outcome
2020	Deemer	Effect of early cognitive interventions on delirium in critically ill patients: a systematic review	No NPhI
2020	Hong-Jie	High-flow nasal cannula therapy as apneic oxygenation during endotracheal intubation in critically ill patients in the intensive care unit: a systematic review and meta-analysis	Wrong outcome
2020	Zang	The effect of early mobilization in critically ill patients: A meta-analysis	Wrong outcome
2021	Lewis	High-flow nasal cannulae for respiratory support in adult intensive care patients	Wrong outcome
2022	Fernando	Noninvasive respiratory support following extubation in critically ill adults: a systematic review and network meta-analysis	Results reported in network metanalysis

Supplementary Material 5: Assessment of overall overlap among SRs

666	=	Total nodes (pairs of reviews)
629	=	Slight overlap (<5%)
8	=	Moderate overlap (5% to <10%)
9	=	High overlap (10% to <15%)
20	=	Very High overlap (≥15%)

	Adler 2012	Alexiou 2009	Bench 2003	Caroff 2016	Chang 2019	Delaney 2006	Doiron 2018	Faradita 2018	Frampton 2014	Frost 2014	Gardner 2005	Herling 2018	Hua-Wei 2018	Kang Lee 2018	Litton 2016	Maertens 2018	Manias	Muscedere 2011	Pozuelo 2018	Prgomet 2017	Siempos 2008	Tipping 2016	Vargas 2017	Wang 2015	Wang Li 2016	Wang 2012	Wen 2017	Burry 2021	Deng 2020	Granton 2022	Liang Sujuan 2021	Lovegrove 2022	Menges 2021	Nieto-García 2020	Liang Surui 2021	Waldauf 2020
Alexiou 2009	0.0%																																			
Bench 2003	0.0%	0.0%																																		
Caroff 2016	0.0%	0.0%	0.0%																																	
Chang 2019	0.0%	0.0%	0.0%	0.0%																																
Delaney 2006	0.0%	0.0%	0.0%	0.0%	0.0%																															
Doiron 2018	8.3%	0.0%	0.0%	0.0%	0.0%	0.0%																														
Faradita 2018	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%																													
Frampton 2014	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%																												
Frost 2014	0.0%	0.0%	0.0%	52.9%	0.0%	0.0%	0.0%	0.0%	0.0%																											
Gardner 2005	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%																										
Herling 2018	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%																									
Hua-Wei 2018	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%																								
Kang Lee 2018	4.2%	0.0%	0.0%	0.0%	0.0%	0.0%	5.9%	0.0%	0.0%	0.0%	0.0%	13.3%	0.0%																							
Litton 2016	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	12.5%	0.0%	4.8%																						
Maertens 2018	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%																					
Manias	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%																				
Muscedere 2011	0.0%	0.0%	0.0%	66.7%	0.0%	0.0%	0.0%	0.0%	0.0%	69.2%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%																			
Pozuelo 2018	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%																		
Prgomet 2017	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	10.0%	0.0%	0.0%																	
Siempos 2008	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	27.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%																
Tipping 2016	8.7%	0.0%	0.0%	0.0%	0.0%	0.0%	20.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	3.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%															
Vargas 2017	0.0%	0.0%	11.1%	0.0%	0.0%	0.0%	4.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	3.8%														
Wang 2015	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	10.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%													
Wang Li 2016	0.0%	21.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%												
Wang 2012	0.0%	0.0%	0.0%	58.8%	0.0%	0.0%	0.0%	0.0%	0.0%	72.7%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	76.9%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%											
Wen 2017	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%										
Burry 2021	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	20.0%	0.0%	13.6%	6.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%									
Deng 2020	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	28.6%	0.0%	22.2%	7.7%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	41.7%								
Granton 2022	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	18.2%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%							
Liang Sujuan 2021	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	5.6%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	12.5%						
Lovegrove 2022	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%					
Menges 2021	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	16.7%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	18.8%	0.0%	0.0%	0.0%	0.0%				
Nieto-García 2020	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%			
Liang Surui 2021	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	6.3%	0.0%	11.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	4.2%	4.8%	0.0%	0.0%	0.0%		
Waldauf 2020	3.7%	0.0%	0.0%	0.0%	0.0%	0.0%	16.7%	0.0%	0.0%	0.0%	0.0%	3.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	43.5%	0.0%	0.0%	0.0%	0.0%	15.8%	0.0%	0.0%	
Zhou 2020	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	10.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	31.3%	8.0%	0.0%	0.0%	0.0%	0.0%	0.0%

Supplementary Material 6: Detailed overlap assessment for each specific comparison. CCA was calculated for a matrix containing only relevant SRs for the specific comparison. The detailed assessment provides a figure showing CCA for a matrix containing each possible pair of SRs within the comparison

Adverse event	Outcome	Comparison	Systematic reviews	Overlap assessment	
				CCA†	Detailed CCA by pairs of reviews
1. Ventilation acquired pneumonia (VAP)	1.1 Incidence of VAP	1.1.1 Subglottic secretion drainage vs no drainage	Caroff 2016 Frost 2014 Muscedere 2011 Wang 2012	52.9% Very high	
		1.1.3 Closed vs open endotracheal suction	Faradita 2018 Siempos 2008	27.3% Very high	
		1.1.4 Semirecumbent vs supine position	Alexiou 2009 Wang Li 2016	22,2% Very high	

1.2 ICU Mortality		1.2.1 Subglottic secretion drainage vs no drainage	Frost 2013 Muscedere 2011	42,9% Very high
1.3 Hospital mortality		1.3.1 Subglottic secretion drainage vs no drainage	Caroff 2016 Frost 2014 Muscedere 2011 Wang 2012	42,9% Very high
		1.3.4 Semirecumbent vs supine position	Alexiou 2009 Wang Li 2016	66,7% Very high
2. Delirium	2.1 Incidence of delirium	2.1.1 Environmental intervention vs usual care	Burry 2021 Deng 2020 Herling 2018 Liang Surui 2021	10.3% High

1.2.1 chart:
- Muscedere 2011 / Frost 2014: 42.9%

1.3.1 chart:
- Frost 2014 / Caroff 2016: 28.6%
- Muscedere 2011 / Caroff 2016: 42.9%; Muscedere 2011 / Frost 2014: 66.7%
- Wang 2012 / Caroff 2016: 57.1%; Wang 2012 / Frost 2014: 33.3%; Wang 2012 / Muscedere 2011: 55.6%

1.3.4 chart:
- Wang.Li 2016 / Alexiou 2009: 66.7%

2.1.1 chart:
- Burry 2021 / Herling 2018: 20.0%
- Deng 2020 / Herling 2018: 28.6%; Deng 2020 / Burry 2021: 41.7%
- Liang Surui 2021 / Herling 2018: 6.3%; Liang Surui 2021 / Burry 2021: 4.2%; Liang Surui 2021 / Deng 2020: 4.8%

3. Reintubation	3.1 Rate of Reintubation	3.1.1 High-flow nasal cannula vs Conventional oxygen therapy	Granton 2022 Hua-Wei 2018 Liang Sujuan 2021 Zhou 2020	38.9% Very high	
		3.1.2 Noninvasive ventilation vs Conventional oxygen therapy	Granton 2022 Hua-Wei 2018 Liang Sujuan 2021 Zhou 2020	14.3% High	
	3.2 ICU Mortality	3.2.1 High-flow nasal cannula vs Conventional oxygen therapy	Hua-Wei 2018 Liang Sujuan 2021	16.7% Very high	
	3.3 Hospital Mortality	3.3.1 High-flow nasal cannula vs Conventional oxygen therapy	Granton 2022 Hua-Wei 2018 Liang Sujuan 2021	33.3% Very high	

3.1.1:
Granton 2022 — Hua-Wei 2018: 50.0%
Liang Sujuan 2021 — Hua-Wei 2018: 0.0%, Granton 2022: 16.7%
Zhou 2020 — Hua-Wei 2018: 50.0%, Granton 2022: 100.0%, Liang Sujuan 2021: 16.7%

3.1.2:
Granton 2022 — Hua-Wei 2018: 33.3%
Liang Sujuan 2021 — Hua-Wei 2018: 0.0%, Granton 2022: 0.0%
Zhou 2020 — Hua-Wei 2018: 0.0%, Granton 2022: 20.0%, Liang Sujuan 2021: 20.0%

3.2.1:
Liang Sujuan 2021 — Hua-Wei 2018: 16.7%

3.3.1:
Granton 2022 — Hua-Wei 2018: 66.7%
Liang Sujuan 2021 — Hua-Wei 2018: 16.7%, Granton 2022: 33.3%

		3.3.1 High-flow nasal cannula vs Noninvasive ventilation	Granton 2022 Hua-Wei 2018 Liang Sujuan 2021	12.5% High	

Supplementary Material 7:

Adverse event	Author	Intervention(s)	Comparison(s)	Outcome/Measure	Effect size (95% CI)	p value	N studies	GRADE
Ventilator-associated pneumonia	Muscedere 2011	Subglottic secretion drainage (SSD)	No drainage	Duration of MV	MD= -1.08 days (95% CI -2.04 , -0.12 days)	0.03	7 RCT	NR
	Wang 2012	Subglottic secretion drainage (SSD)	No drainage	Duration of MV	MD= -1.55 days (95% CI -2.40 , -0.71 days)	< 0.001	5 RCT	NR
	Caroff 2016	Subglottic secretion drainage (SSD)	No drainage	Duration of MV	WMD= -0.65 days (95% CI -1.59 , 0.28 days)	0.17	8 RCT	NR
	Wen 2017	Continuous SSD	Intermittent SSD	Duration of MV	WMD= -0.89 days (95% CI -2.72 , 0.94 days)	-	4 RCT	NR
	Siempos 2008	Closed tracheal suction systems	Open tracheal suction systems	Duration of MV	WMD= 0.65 days (95% CI 0.28 , 1.03 days)	-	5 RCT	NR
	Alexiou 2009	Semirecumbent position	Supine position	Duration of MV	WMD= -0.45 days (95% CI -1.58 , 0.68 days)	-	1 RCT	NR
	Wang_Li 2016	Semirecumbent position	Supine position	Duration of MV	MD= -3.35 days (95% CI -7.80 , 1.09 days)	0.14	4 RCT	NR
	Alexiou 2009	Prone position	Supine position	Duration of MV	WMD= -0.45 days (95% CI -1.58 , 0.68 days)	-	3 RCT	NR
	Delaney 2006	Kinetic bed therapy	Standard manual turning	Duration of MV	SMD = -0.14 days (95%CI -0.29 , 0.02 days)	0.08	7 RCT	NR
	Muscedere 2011	Subglottic secretion drainage (SSD)	No drainage	ICU length of stay	MD= -1.52 days (95% CI -2.94 , - 0.11 days)	0.03	7 RCT	NR
	Wang 2012	Subglottic secretion drainage (SSD)	No drainage	ICU length of stay	WMD = -2.04 days (95% CI -4.18 , 0.09)	0.06	4 RCT	NR
	Caroff 2016	Subglottic secretion drainage (SSD)	No drainage	ICU length of stay	WMD= −1.04 days (95% CI −2.40 , 0.33 days)	0.14	7 RCT	NR
	Wang_Li 2016	Semirecumbent position	Supine position	ICU length of stay	MD= -1.64 days (95% CI -4.41 , 1.14 days)	0.21	3 RCT	Moderate
	Alexiou 2009	Prone position	Supine position	ICU length of stay	WMDs= 1.54 days (95% CI −1.54 , 4.62 days)	-	3 RCT	NR
	Pozuelo 2018	Respiratory physiotherapy	Usual care	ICU length of stay	WMD= -0.33, 95% CI -2.31 , 1.66)	-	5 RCT	NR
	Delaney 2006	Kinetic bed therapy	Usual care	ICU length of stay	SMD = -0.064 days (95%CI -0.21 , 0.086 days)	0.40	8 RCT	NR
Delirium	Kang Lee 2018	Nonpharmacological interventions	Usual care	ICU mortality	OR = 0.81 (95% CI 0.61 , 1.07)	0.14	14 (RCT; CCT)	NR
	Litton 2016	Use of earplugs	Usual care	Hospital mortality	RR = 0.77 (95% CI 0.54 , 1.11)	< 0.001	3RCT; 1NRCT	NR
	Burry 2021	Environmental intervention	Usual care	Hospital mortality	OR = 0.91(95% CI 0.63 , 1.30)	0.61	3RCT	NR
	Kang Lee 2018	Nonpharmacological interventions	Usual care	ICU length of stay	OR = 0.85 (95% CI 0.67 , 1.09)	0.19	4 (RCT; CCT)	NR
	Burry 2021	Environmental intervention	Usual care	ICU length of stay	OR = 0.05 (95% CI -0.07 , 0.18)	0.41	5 RCT	NR
	Kang Lee 2018	Nonpharmacological interventions	Usual care	Duration of ICU delirium	OR = 0.31 (95% CI 0.10 , 0.94)	0.04	6 (RCT; CCT)	NR
	Deng 2020	Environmental intervention	Usual care	Duration of ICU delirium	MD = -0.11 (95% CI, -0.36 , 0.15)	-	2 RCT	NR
Physical function deterioration	Adler 2012	Early mobilisation and physical therapy	Usual care	Muscle strength, physical function	Results were not pooled	-	4 NRCT	NR
	Doiron 2018	Early Mobilisation	Usual care	Improvement of muscle strength	MD = 6.10 (95% CI 11.85 , 24.05)	-	3 RCT	Low

	Menges 2021	Systematic early mobilisation	Usual care	Improvement of muscle strength	MD = 5.80 (-1.41 , 13.02)	0.115	4 RCT	Very Low
	Tipping 2016	Active mobilisation and rehabilitation	Usual care	Improvement of muscle strength	MD = 8.62 (95% CI 1.39 , 15.86)	0.02	3 RCT	NR
	Tipping 2016	Active mobilisation and rehabilitation	Usual care	ICU mortality	OR = 1.08 (95% CI 0.64 , 1.80)	0.81	8 RCT	NR
	Waldauf 2020	Physical rehabilitation	Usual care	Hospital mortality	OR =0.91 (95% CI 0.71 , 1.12)	0.43	18 RCT	NR
	Tipping 2016	Active mobilisation and rehabilitation	Usual care	Hospital mortality	OR= 0.93(95% CI 0.69 , 1.27)	0.65	10 RCT	NR
Reintubation	Granton 2020	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)	Rate of reintubation	RR = 0.46 (95% CI 0.30 , 0.70)	< 0.0003	4RCT	Moderate
	Hua-Wei 2018	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)	Rate of reintubation	RR= 0.35 (95% CI 0.19 , 0.64)	< 0.001	2 RCT	Low
	Liang Sujuan 2021	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)	Rate of reintubation	RR = 0.78 (95% CI 0.62 , 0.98)	0.03	3RCT	NR
	Xiaoyang Zhou 2020	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)	Rate of reintubation	RR = 0.45 (95% CI 0.27 , 0.73)	< 0.002	4RCT	Moderate
	Granton 2020	High-flow nasal cannula (HFNC)	Noninvasive ventilation (NIV)	Rate of reintubation	RR = 1.16 (95% CI, 0.86 , 1.57)	0.32	3RCT	Low
	Hua-Wei 2018	High-flow nasal cannula (HFNC)	Noninvasive ventilation (NIV)	Rate of reintubation	RR= 1.19 (95% CI 0.87 , 1.63)	0.27	1 RCT	High
	Liang Sujuan 2021	High-flow nasal cannula (HFNC)	Noninvasive ventilation (NIV)	Rate of reintubation	RR= 1.01 (95% CI 0.77 , 1.33)	0.14	3 RCT	NR
	Xiaoyang Zhou 2020	High-flow nasal cannula (HFNC)	Noninvasive ventilation (NIV)	Rate of reintubation	RR= 0.82 (95% CI 0.61 , 1.12)	0.19	3 RCT	Low
	Xiaoyang Zhou 2020	Noninvasive ventilation (NIV)	Conventional oxygen therapy (COT)	Rate of reintubation	RR = 0.62 (95% CI 0.46 , 0.83)	< 0.002	9 RCT	Moderate
	Hua-Wei 2018	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)	ICU mortality	RR= 1.11 (95% CI 0.44 , 2.79)	0.82	2 RCT	NR
	Liang Sujuan 2021	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)	ICU mortality	RR = 0.97 (95% CI 0.79 , 1.18)	0.72	5 RCT	NR
	Hua-Wei 2018	High-flow nasal cannula (HFNC)	Noninvasive ventilation (NIV)	ICU mortality	RR= 1.14 (95% CI 0.61 , 2.13)	0.68	1 RCT	NR
	Liang Sujuan 2021	High-flow nasal cannula (HFNC)	Noninvasive ventilation (NIV)	ICU mortality	RR= 0.67 (95% CI 0.44 , 1.03)	0.07	4 RCT	NR
	Granton 2020	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)	Hospital mortality	RR = 0.93 (95% 0.57 , 1.52)	0.77	3 RCT	Moderate
	Hua-Wei 2018	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)	Hospital mortality	RR= 0.89 (95% CI 0.46 ,1.71)	0.72	2 RCT	NR
	Liang Sujuan 2021	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)	Hospital mortality	RR= 0.91 (95% CI 0.67 , 1.24)	0.54	5 RCT	NR

	Granton 2020	High-flow nasal cannula (HFNC)	Noninvasive ventilation (NIV)	Hospital mortality	RR = 1.12 (95% CI, 0.82 , 1.53)	0.48	2 RCT	Moderate
	Hua-Wei 2018	High-flow nasal cannula (HFNC)	Noninvasive ventilation (NIV)	Hospital mortality	RR= 1.14 (95% CI 0.82 , 1.59)	0.43	1 RCT	NR
	Liang Sujuan 2021	High-flow nasal cannula (HFNC)	Noninvasive ventilation (NIV)	Hospital mortality	RR = 1.09 (95% CI, 0.79 , 1.50)	0.60	2 RCT	NR
Medication error	Wang 2015	Pharmaceutical intervention	Usual service	Risk of MEs	RR = 0.61 (95% CI 0.11 , 3.55)	0.57	4 RCT	NR
	Prgomet 2017	Commercial CPOE systems	Paper-based ordering	Risk of MEs	RR= 0.71 (95% CI 0.68 , 0.75)	< 0.001	5 (RCT; BAS)	NR
	Prgomet 2017	Commercial CPOE systems	Paper-based ordering	ICU mortality	RR= 0.89 (95% CI 0.77 , 1.03)	0.11	2 BAS	NR
	Prgomet 2017	Commercial CPOE systems	Paper-based ordering	ICU length of stay	RR= -0.01 (95% CI -1.16 , 1.13)	0.70	5 (RCT; BAS)	NR
Artificial airway occlusion	Vargas 2017	Heat moisture exchangers (HME)	Heated water humidifiers (HWH)	Incidence of artificial airway occlusion	OR= 2.51(95% CI 1.27 , 4.95)	0.008	14 RCT	NR
Hospital-acquired pneumonia (HAP)	Vargas 2017	Heat moisture exchangers (HME)	Heated water humidifiers (HWH)	Incidence of HAP	OR= 0.92(95% CI 0.73 , 1.15)	0.45	18 RCT	NR
	Maertens 2018	Endotracheal tapered cuffs	Endotracheal nontapered cuffs	Incidence of HAP	OR= 0.96(95% CI 0.72 , 1.27)	0.81	6 RCT	NR
	Maertens 2018	Endotracheal tapered cuffs	Endotracheal nontapered cuffs	ICU mortality	OR= 0.89(95% CI 0.57 , 1.40)	0.63	2 RCT	NR
	Vargas 2017	Heat moisture exchangers (HME)	Heated water humidifiers (HWH)	Hospital mortality	OR = 1.04 (95% CI 0.85 , 1.28)	0.68	11 RCT	NR
Healthcare-associated infections (HAI)-Catheter bloodstream infection	Frampton 2014	Implementation of checklists	Usual care	Hospital Mortality	Results were not pooled	-	5 RCT	NR
	Chang 2019	Universal gloving	Non-gloving	Incidence of HAI	IRR= 1.01 (95% CI 0.91 , 1.13)	0.55	4 (RCT, BAQS)	NR
Pressure injury	Lovegrove 2022	Reactive bed surface	Standard Mattress	Incidence of pressure injury	RR = 0.24 (95% CI 0.004 , 1.46)	0.12	2 RCT	NR
	Nieto-García 2021	Pre-early mobility programme	Post-early mobility programme	Incidence of pressure injury	OR = 0.97 (95% CI 0.49 , 1.91)	0.93	5 RCT	NR
Tube displacement/ occlusion	Gardner 2005	ETT stabilisation	Other ETT stabilisation	Incidence of tube displacement	Results were not pooled	-	2 NRCT	NR
	Bench 2003	Heat moisture exchangers (HME)	Heated water humidifiers (HWH)	Incidence of tube occlusion	Results were not pooled	-	2 RCT	NR

NR: No Reported