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Can an early mobilisation programme prevent hospital-acquired pressure injures in an intensive care unit?: A systematic review and meta-analysis

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Abstract

A systematic review and meta-analysis were conducted to clarify the effect of an early mobilisation programme on the prevention of hospital-acquired pressure injuries in an intensive care unit as opposed to standard care. We searched a total of 11 databases until 1 May 2020 and included seven studies (n = 7.520) related to the effect of early mobilisation protocol in the prevention of hospital-acquired pressure injuries (five quasi-experimental and two random comparative). The five quasi-experimental studies were significantly heterogeneous ($P = .02$ for Q test and 66% for I^2), and the odds ratio was 0.97 (95% CI: 0.49-1.91) with a non-significant statistical difference between both groups ($P = .93$). Our study shows inconclusive outcomes related to the effect of the implementation of an early mobility programme in the prevention of pressure injuries in critical patients. Future research is needed considering the small number of articles on the topic.

KEYWORDS

early mobility programme, intensive care unit, pressure injuries, prevention, systematic review

1 | INTRODUCTION

Pressure injury (PI), also known as pressure ulcer, is defined as a "localized damage to the skin and underlying soft tissue, usually over a bony prominence or related to a medical or other device; resulting from intense and/or prolonged pressure or pressure in combination with shear."[1] In general, it is understood that hospital-acquired pressure injuries (HAPIs) are a preventable problem; for this reason, they are used as a negative indicator of the quality of care and patient safety. These are associated with increased mortality and mobility and decreased quality of life. Moreover, it is correlated with an increase in health care resource utilisation and significant health care costs. The development of HAPIs has a multifactorial aetiology,[2,3] and according to a recent review, critically ill patients have particularly high risk factors for PIs related to age, perfusion, mobility/activity, and vasopressor infusion.[4]

International clinical practice guidelines for the prevention and treatment of PIs focus on evidence-based recommendations in repositioning and early mobilisation among other topics.[5] Latest recommendations of health care in the intensive care unit (ICU) are based on the ABCDEF bundle[6] (Awaken from sedation, Breathe independently of the

ventilator, Choice of sedation, Delirium management, Early Mobilization and Exercise, and Family engagement and empowerment) and Pain, Agitation/sedation, Delirium, Immobility (rehabilitation/mobilization), and Sleep (disruptions) (PADIS) guideline.[7] Note that, in this context, both share the early mobilisation component. A recent systematic review shows that there is no consensus on the definition of the term "early mobilisation" (EM),[8] with a wide timeframe from the beginning of EM activities. Currently, there are several EM protocols[9-15] covering a wide range of interventions, including positioning, range-of-motion exercises (ROM), electrical muscle stimulation, cycle ergometers, tilt tables, transfer training, progressive resistance exercises, ambulating, and functional mobilisation.[15]

ICU early mobility programmes (EMP) are associated with an improvement in clinical outcomes, such as decrease in days of delirium, increase of functional status, decreased hospital and ICU length of stay (LOS), decreased mortality, significant economic cost, and patient and family satisfaction with care.[7,16] This study aims to establish whether the implementation of an EMP could reduce the development of HAPIs in an ICU.

2 | MATERIAL AND METHODS

2.1 | Study design

This systematic review was planned in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement.[17] Study eligibility was defined according to the conventional Population-Intervention-Comparison-Outcomes-Study type (PICOS) criteria,[18,19] which were determined a priori, including the following: *Population* (intensive care adult patient); *Intervention* (early mobilisation programme); *Comparators* (standard care); *Outcomes* (HAPIs); and *Study design* (randomised controlled trial, non-randomised controlled trial, controlled quasi-experimental studies, empirical observational studies). Therefore, we considered the following review question: *Can an EMP improve HAPI prevention in ICU patients as opposite to a standard care protocol?*

2.2 | Search strategy

An extensive systematic search has been carried out across relevant databases and evidence summaries related to the health care area: *Trypdatabase, Cochrane Library, Epistemonikos, National Guideline Clearinhouse (NGC), National Institute for Health and Care Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN), PubMed (Medline), Scopus, Cumulative Index to Nursing and Allied*

Key Messages

- this is one of the first reports to analyse the effects of the implementation of an early mobilisation protocol on the prevalence of hospital-acquired pressure injuries in the intensive care unit
- a systematic review identified seven studies on the prevalence of hospital-acquired pressure injuries after implementation of an early mobility protocol in the intensive care unit
- the meta-analysis did not show significant effects on prevention, and an early mobilisation protocol may improve other clinical outcomes
- future studies with rigorous designs are recommended in order to gather better evidence and improve critical care quality

Health Literature (CINAHL), Embase, and Physiotherapy Evidence Database (PEDro). The search will be performed for studies from inception to May 1, 2020.

The following search key words or MeSH vocabulary thesaurus and Boolean operators were entered: ["early ambulation" OR "early mobilization" OR "early mobility program" OR "early mobility protocol"] AND ["pressure ulcer" OR "pressure injury"] AND ["Intensive Care Unit" OR "ICU"]. A sample search is included in Appendix A.

2.3 | Selection criteria

All relevant studies, edited in English or Spanish, that reported the assessment of the effects of an EMP in an ICU and included PI rates and were published in a peer-reviewed journal were considered for analysis and classified according to levels of evidence and grades of recommendation proposed by the Oxford Centre for Evidence-Based Medicine (OCEBM).[20]

The *inclusion criteria* covers studies published in peer-reviewed journals involving adult patients (≥18 years old) hospitalised in the ICU, where an early mobility protocol/programme is implemented, its success is compared against usual care, and the development of HAPIs is treated as a clinical outcome; it also includes prospective or retrospective observational studies or clinical trials [OCEBM Levels of evidence 1-4, Grades of Recommendation A-C].

On the other hand, the *exclusion criteria* discard studies involving paediatric populations; publications in languages

other than English or Spanish; and data from editorials, letters to editors, reports of expert committees, and opinions of respected authorities based on clinical experience because these designs do not have the same value, impact, or power to make decisions or make recommendations [OCEBM Level of Evidence 5, Grade of Recommendation D].

2.4 | Selection of studies, data extraction, and quality assessment

First, initial screenings were performed by title followed by abstract; then, the full text was read, and articles were assessed independently for fulfilment of the inclusion criteria by two authors (L. N. G. and M. A. S.). Disagreements regarding the inclusion or exclusion of articles were resolved by discussion.

A systematic method was applied to data collection from each included study. All relevant texts, tables, and figures were reviewed for data extraction. The data collected were the first author's name, year of publication, country of origin, study objective, study design, trial time period, number of patients, population characteristics, EMP, frequency and duration of EMP sessions, EMP team, HAPI incidence or prevalence rates, HAPI data records source, ICU LOS, hospital LOS, adverse events, and other significant clinical outcomes.

Two team members (L. N. G and M. A. S.) independently reviewed each eligible study and extracted the information and data necessary to carry out the qualitative analysis and the meta-analysis. They followed the methodological standards recommended by the *Committee on Standards for Systematic Reviews of Comparative Effectiveness Research* for finding and assessing individual studies: They worked independently, screened and selected articles, and extracted quantitative and other critical data from included studies.

Each eligible study was systematically appraised for risk of bias, relevance to the study's populations, and outcome measures. To evaluate risk of bias, we used the seven item-based Risk Of Bias In Non-randomized Studies—of Interventions (ROBINS-I)[21] risk-of-bias assessment tool. Moreover, OCEBM Levels of Evidence and Grades of Recommendation[20] were applied to determine the certainty of evidence generated and strength of recommendations. We used the recommendations of the PRISMA declaration as a guide. Disagreements were resolved by consensus among all authors.

2.5 | Meta-analysis methods

Meta-analysis was performed using the *Cochrane Review Manager* (Rev Man 5.3) software. To combine studies to find a summary effect, we resorted to Mantel-Haenselz statistical weights. Heterogeneity across studies was assessed using the *Cochrane Q-statistic* ($P < .05$ was considered statistically significant), and homogeneity of studies was rejected. Statistical heterogeneity was measured using the I^2 statistic: $I^2 = 0\%$ to 25%, no heterogeneity; $I^2 = 25\%$ to 50%, moderate heterogeneity; $I^2 = 50\%$ to 75%, large heterogeneity; $I^2 = 75\%$ to 100%, extreme heterogeneity. A *fixed-effect model* was applied if there was no significant heterogeneity across studies ($I^2 < 50\%$). Otherwise, a *random-effect model* was used when significant heterogeneity was detected between studies ($I^2 > 50\%$). The significance of the pooled odds ratio was evaluated with the *Z test* and its two-tailed *P* value. *Forest plots* with odds ratios and their 95% confidence intervals were used to visualise all results. In addition, a *funnel plot* was performed to analyse the publication bias.

3 | RESULTS

3.1 | Search results

A PRISMA flow diagram of the literature search is given in Figure 1. By searching the electronic databases, we identified 803 records related to the effects of EM in the ICU. Finally, we included seven studies fulfilling the inclusion criteria and added them to the qualitative synthesis. Only five of them were included in the quantitative analysis.

3.2 | Study characteristics

Seven articles[22-28] researching the effect of EMP on ICU and PI rates were selected and classified by type of study design. Included studies were prospective or retrospective two-group comparative and pre-post quasi-experimental research. Table 1 summarises the main methodological data of these studies in alphabetical order. According to the OCEBM classification, the level of evidence of the selected articles ranged between levels 2a and 2c.

The oldest publication dates back to 2012 from *Titsworth* et al,[28] while the most recent was published in 2016 by Floyd et al.[26] The geographic location of all studies was centred in the United States. The total sample size of the included studies was 7.520.

The ROBINS-I tool was used to assess the risk of bias in the included articles. Of all the studies of interventions analysed, only one study showed a low risk of bias (RoB), while four showed a moderate RoB, and two studies were classified as serious RoB (Table 2).
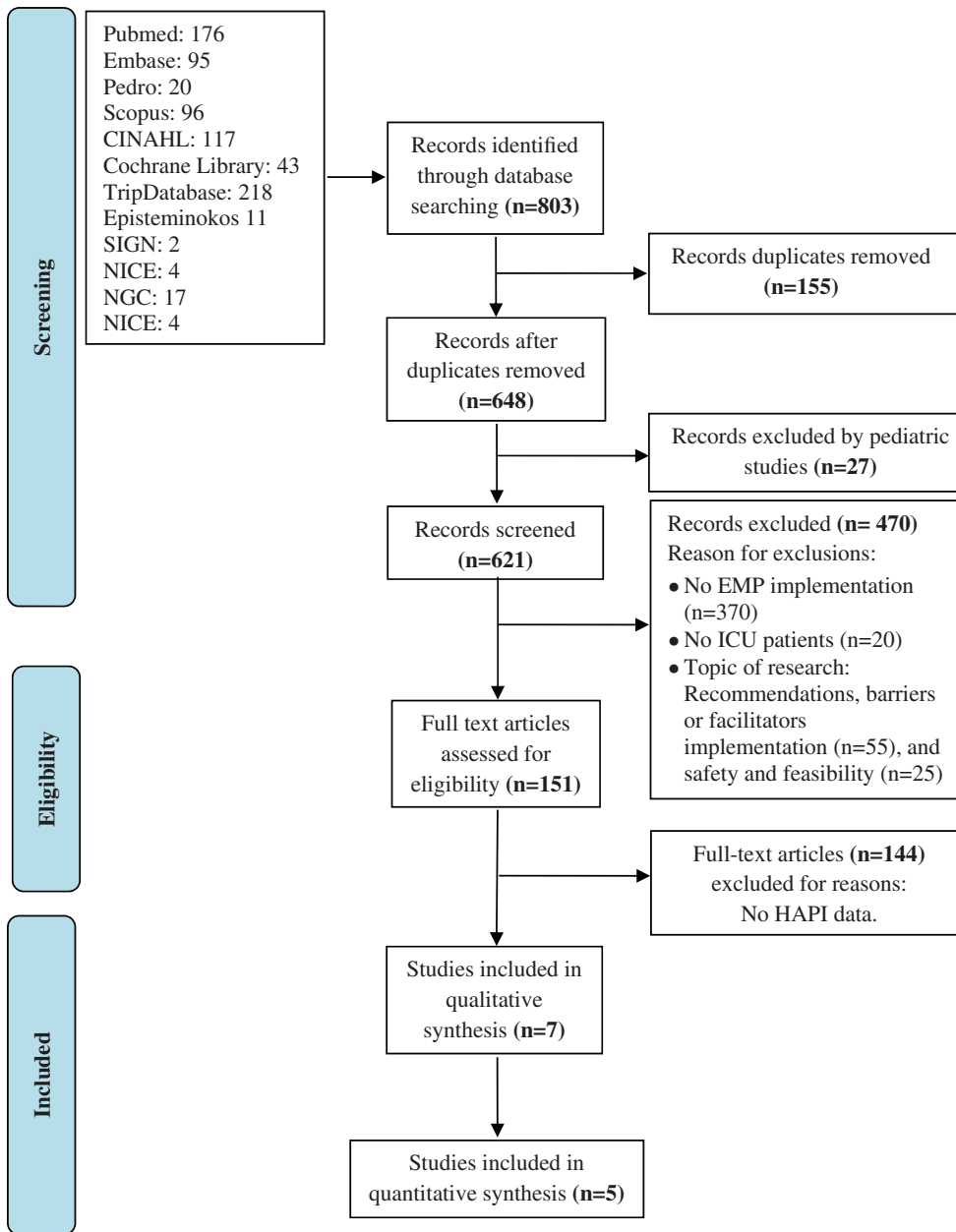
Screening

Pubmed: 176
Embase: 95
Pedro: 20
Scopus: 96
CINAHL: 117
Cochrane Library: 43
TripDatabase: 218
Episteminokos 11
SIGN: 2
NICE: 4
NGC: 17
NICE: 4

Records identified through database searching (**n=803**)

Records duplicates removed (**n=155**)

Records after duplicates removed (**n=648**)

Records excluded by pediatric studies (**n=27**)

Records screened (**n=621**)

Records excluded (**n= 470**)
Reason for exclusions:
- No EMP implementation (n=370)
- No ICU patients (n=20)
- Topic of research: Recommendations, barriers or facilitators implementation (n=55), and safety and feasibility (n=25)

Eligibility

Full text articles assessed for eligibility (**n=151**)

Full-text articles (**n=144**) excluded for reasons:
No HAPI data.

Included

Studies included in qualitative synthesis (**n=7**)

Studies included in quantitative synthesis (**n=5**)

FIGURE 1 Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram summarising the results for this systematic review and meta-analysis

3.3 | Qualitative synthesis outcomes

3.3.1 | EMP Characteristics

Table 3 summarises the main qualitative data collected from the studies that were analysed, and Table 4 shows others relevant outcomes related to the implementation of the EMP.

Those EMPs were implemented in different subspecialties of intensive care: neurological ICU,[27,28] medical ICU,[22,26] coronary ICU,[26] surgical ICU,[24,26] thoracic and cardiovascular ICU,[25] and burn and trauma ICU.[23]

Several types of EMP were identified, each structured in different levels or phases. Each programme is detailed extensively according to its levels and mobility

techniques in Appendix Table B1. However, all of them showed similar treatment progression according to the clinical evolution of the patients and included widespread techniques such as ROM, repositioning, transferring, staying, and walking. No adverse effects were reported among patients in the mobility group.[22,23,26,28]

In all EMPs, the frequency of mobilisation is daily, while the number of repetitions and the duration of each exercise are different. Even so, the progression of the patient through the levels or phases of mobility is dependent on the patient's overall physical and clinical stability and tolerance.

The development of these mobilisation programmes usually involved an interdisciplinary team, often comprised of physiotherapists (PT), nurses, occupational therapists, physicians, rehabilitators, and care assistants.

TABLE 1 Main methodological data of included studies

Author/s (Ref)] Year	Country	ICU setting	Follow-up period	Study Design	Level of evidence (OCEBM)	Sample (n)	G1 (n)	G2 (n)
Azuh et al[22] (2016)	United States	MICU (Braden scale score < 19)	Pre-EMP: 1 year Post-EMP: 1 year	Pre and post quasi-experimental design.	2c	3.233	NA	NA
Clark et al[23] (2013)	United States	TBICU	Pre-EMP: 11 months Post-EMP: 11 months	Pre and post quasi-experimental design	2c	2.176	1.044	1.132
Dickinson et al[24] (2013)	United States	SICU	Pre-EMP: 6 months Post-EMP: 5 months	Pre and post quasi-experimental design	2c	1.112	555	557
Floyd et al[25] (2016)	Unites States	TCV ICU	1-year period	Randomised matched pairs design	2b	60	30	30
Fraser et al[26] (2015)	United States	MICU, SICU and Coronary ICU	2 month-control group 11 month-mobilisation group	Two-group random comparative study (retrospective)	2b	132	66	66
Klein et al[27] (2015)	United States	NICU	Pre-EMP: 4 months Post-EMP: 4 months	Pre and post quasi-experimental design	2c	637	260	377
Titsworth et al[28] (2012)	United States	NICU	Pre-EMP: 10 months Post-EMP: 6 months	Pre and post quasi-experimental design	2c	170	77	93

Abbreviations: G1, control group or pre-intervention group sample; G2, intervention/mobilisation group sample; MICU, medical intensive care unit; NA, no data available; NICU, neurological intensive care unit; SICU, surgical intensive care unit; TBICU, burn and trauma intensive care unit; TCV ICU, thoracic cardiovascular intensive care unit.

3.3.2 | HAPI outcomes

Most of the studies collect incidence or prevalence data from electronic medical or nursing records while specifying the staging system used. Only two studies describe in detail the frequency of skin assessment and who performs it.[22,28]

From a qualitative assessment of the seven studies, three of the studies found that the correlation between HAPI prevalence rates and EMP implementation was not statistically significant,[23,24,28] three of them reported a decrease of HAPI rates with statistical significance,[22,26,27] and only one observed reduced HAPI rates but without statistical significance.[25] Within the statistically significant quasi-experimental studies, HAPI rates decreased by 2.7%[27] and 3.1%.[22]

3.4 | Quantitative synthesis using meta-analysis

Figure 2 shows the results obtained from comparing the pre-EMP group with the post-EMP group for the quasi-experimental studies. These five studies are significantly heterogeneous ($P = .02$ for Q test and 66% for I^2); therefore, a random-effects model was used. In addition, the summary odds ratio found in the meta-analysis shows a value of .97 (95% CI:0.49, 1.91). The test for overall effect shows a non-significant statistical correlation between both groups ($P = .93$).

To assess publication bias, we examined the funnel plot of the observed effect (Figure 3), which revealed asymmetry, suggesting publication bias.

TABLE 2 ROBINS-I risk-of-bias assessment

Studies/ First author	Confounding	Selection bias	Classification of intervention	Intended intervention	Missing data	Measurement of outcomes	Reported results	Overall
Azuh[22]	Serious	Moderate	Low	Low	No information	Low	Low	Serious RoB
Clark[23]	Low	Low	Low	Low	No information	Low	Low	Moderate RoB
Dickinson[24]	Low	Low	Low	Serious risk	No information	Low	Low	Serious RoB
Floyd[25]	Low	Low	Moderate	Low	Low	Low	Low	Moderate RoB
Fraser[26]	Low	Low	Moderate	Low	Low	Low	Low	Moderate RoB
Klein[27]	Low	Low	Low	Low	Low	Low	Low	Low of RoB
Titsworth[28]	Low	Low	Low	Moderate	Low	Low	Low	Moderate RoB

Abbreviation: ROBINS, Risk Of Bias In Non-randomized Studies.

4 | DISCUSSION

The identification of the physiological benefits of increased mobility in ICU patients has been trending in recent studies, although they are mostly focused on ventilated medical ICU wards. In fact, despite the interest aroused in the last decade in relation to EM in critical patients, there are only a few studies in which HAPIs are analysed. The present meta-analysis and systematic review only encountered seven articles investigating the effects of EMP in the prevention of PIs in patients with critical illness.

The qualitative analysis showed a positive trend towards the decrease in HAPI rates after the implementation of an EMP in only three included studies, while another three reported the opposite. Within the latter results, Dickinson et al[24] discussed some possible reasons why the EMP may have failed to reduce the PI rate. A possible explanation might lie in the clinical status of the patients; the post-implementation mobility group's overall health was probably worse as indicated by longer ICU and hospital LOS, although pre- and post-implementation mobility groups had similar Acute Physiology and Chronic Health Evaluation (APACHE) scores. In addition, Titsworth et al[28] related the lack of significant results with overall lower PI rates in both groups.

The meta-analysis carried out includes only five of the seven articles that meet the inclusion criteria. Clark et al,[23] Dickinson et al,[24] Klein et al,[27] and Titsworth et al[28] share the same methodology, a pre-post intervention design. The study carried out by Floyd et al[25] was included in the meta-analysis even though it was a matched pair design. When we analysed its design in depth, we observed similar methodological characteristics as the remaining quasi-experimental articles included, as it shows a pre-intervention compared with post-intervention group. The article by Fraser et al[26] was excluded because it used a different methodological design; while it is a two-group comparative study, it does not include pre- and post-intervention groups but instead has control and intervention groups. On the other hand, the study by Azuh et al,[22] even though it features a pre-post intervention design, does not provide quantitative data on the specific sample sizes of each group; therefore, a numerical meta-analysis is possible.

Although literature in this field is lacking, in a recent meta-analysis, Zang et al[30] studied the relationship between any type of EM or early rehabilitation compared with standard ICU care; there is no overlap in the literature with the present study because of different inclusion criteria. Zang et al only found four randomised control trials demonstrating the association between EM with a significantly lower ICU-HAPI incidence in the intervention group. They were evaluated with excellent homogeneity according to the Q test.

Our results highlight the improved outcomes related to pulmonary complications or pneumonias,[23,28] infections,[26-28] and deep vein thrombosis (DVT)[23,25] following the implementation of an EMP; however, the analysis of these clinical conditions needs caution as they require complex diagnostic procedures. Even though HAPI rates are usually associated with the

TABLE 3 Main qualitative outcomes of included studies

Study [Ref.] (year)	Early mobilisation protocol	Frequency/duration	HAPI data-recording sources	HAPI outcomes
Azuh et al[22] (2016)	Five-point mobility scale was developed by authors + Education (patient/family) about the need for mobility.	The daily duration and number of repetitions in each exercise is dependent on the level assigned by the evaluation scale.	Skin care nurse performed a visual skin assessment on admission and follow up daily until discharge. Data collection included number of all PI (stages 1-4, unstageable and deep tissue injury).	Pre-EMP: 9.2% Post-EMP: 6.1% (P = .04)
Clark et al[23] (2013)	Progressive early mobility programme adapted in literature[29] based on 4 levels.	Daily/Duration and number of repetitions depends on exercise and level.	Electronic record medical documentation.	Pre-EMP: 7% Post-EMP: 7.3% (P = .77)
Dickinson et al[24] (2013)	Developed the mobility protocol ("Moving and Grooving") with 3 phases + Family education.	Each exercise: 3 times/day; 10 repetitions.	A PI was defined as any ulcer documented in the medical record as a stage I or greater, according the NPUAP rating scale.	Pre-EMP: n = 20 (3.6%) Post-EMP: 41 (7.4%) (P = .7)
Floyd et al[25] (2016)	PMP adaptation,[11] comprised of 7 levels.	Daily/No duration data available.	Retrospective analysis of the electronic records of patients, codified by ICD-9.	Pre-EMP: 1 Post-EMP: 0 (P = .313)
Fraser et al[26] (2015)	EMP team designed the programme (with 4 phases) based on intervention described in literature + Education to the patient and family.	Once/day, Monday to Friday. 30 to 45 min/session	Data extracted from hospital's database. Followed the NDNQI guidelines to indicate the presence of HAPI	Routine Care group: 2 (3%) Mobility group: 0 (P < .001)
Klein et al[27] (2015)	An early mobility protocol was developed by nurse clinician leaders with four progressive mobility milestones from 16 mobility levels.	Daily mobility for 13 days (initiated on the day of admission). The duration and number of repetitions in each exercise is dependent on the level assigned.	Data were defined based on National Quality Forum and other national quality sources (Centers for Disease Control) used to assess quality care.	Pre-EMP: 10 (3.8%) Post-EMP: 4 (1.1%) (P = .026)
Titsworth et al[28] (2012)	PUMP plus algorithm, developed and modified using existing evidence and guidelines.	Each step must be implemented at least 3 times/day and more frequently as tolerated. Progress each step from 30 to 60 min.	Data were collected by an Ostomy and Wound Liaison nurse during weekly "Skin Rounds." HAPI was categorised according to the NPUAP rating scale. The results presented are Stage II and higher.	Pre EMP: 2.6% ± 0.03 Post EMP: 4.6% ± 0.02 (P = .22)

Abbreviations: ICD-9, International Classification of Diseases; *NDNQI*, National Database of Nursing Quality Indicators; NPUAP, National Pressure Ulcer Advisory Panel; PMP, Progressive Mobility Protocol; PUMP, Progressive Upright Mobility Protocol.

analysis of other complications, also secondary to immobility, we could not find the same variables in all the studies; therefore, it is difficult to properly analyse the correlation between their presence and variation of HAPI rates.

Through all these articles, hospital LOS and ICU LOS show conflicting results. In general, ICU LOS[22,25,27,28] and hospital LOS[25,27,28] decrease with the implementation of an EMP. Although these outcomes are in agreement with most of the current literature, we found one

TABLE 4 Other relevant outcomes and adverse events

Study (Ref.) (year)	Other relevant outcomes	Adverse event related to EMP
Azuh et al[22] (2016)	MICU LOS decreased by 1 day after implementation of EMP ($P = .165$). Hospital readmission of ICU decreased from 17.1% to 11.5% ($P = .001$).	No adverse events reported (defined as fall, injuries, unwitnessed disconnections, and coincidental change in the patient's clinical status).
Clark et al[23] (2013)	• Decreased airway complications ($P = .001$). • Decreased cardiovascular complication ($P = .04$). • Decreased pulmonary complications ($P = .001$) and pneumonia rates ($P = .01$). • Decreased DVT and vascular ($P = <.001$).	No adverse event reported (categorised as involuntary or self-extubation, fall, cardiac event or respiratory event).
Dickinson et al[24] (2013)	Hospital and ICU LOS significant longer in the mobility group ($P = .002$ and $P \leq .001$).	No reported information.
Floyd et al[25] (2016)	Not statistically significant, but it shows clinical significance in a reduction in hospital LOS and ICU LOS, in ICU readmission rate and DVT.	No reported information.
Fraser et al[26] (2015)	• Decreased hospital readmission of ICU ($P < .001$). • Reduced falls, ventilator-associated events, and CAUTIs ($P < .001$). • Fewer delirium days ($P = .05$).	No adverse event (defined as fall, a cardiac event, an extubation, a decannulation, or a respiratory event).
Klein et al[27] (2015)	• Decreased ICU LOS by 45% ($P < .001$). • Decreased Hospital LOS by 33% ($P < .001$). • Decreased anxiety scores ($P = .03$). • Decreased bloodstream infection prevalence by 3% ($P = .015$).	No reported information.
Titsworth et al[28] (2012)	• Increased mobility by 300% ($P < .0001$). • Decreased NICU LOS by 13% ($P < .004$). • Decreased Hospital LOS ($P < .004$). • Decreased hospital-acquired infection by 60% ($P < .05$). • Decreased ventilator-associated pneumonias ($P < .001$). • Decrease days in restraints ($P < .05$).	No increase in adverse events (measured by fall or inadvertent line disconnections).

Abbreviations: CAUTIs, catheter-associated urinary tract infections; DRS, disability rating scale; DVT, deep vein thrombosis; ERBI, Early Rehabilitation Barthel Index.
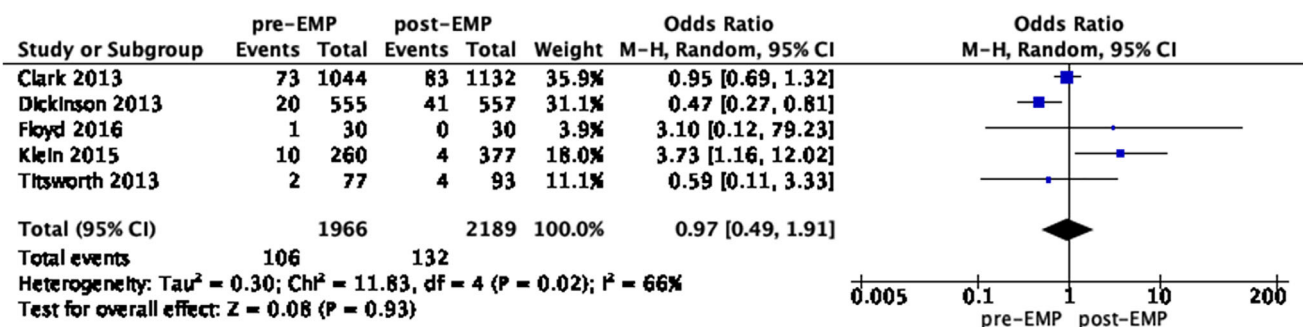

FIGURE 2 Forest plot for comparison: pre-early mobility programme (pre-EMP) vs post-EMP, outcome (event = PI). Statistical method: Mantel-Haenszel. Analysis model: random effects. Effect measure: odds ratio. 95% confidence interval
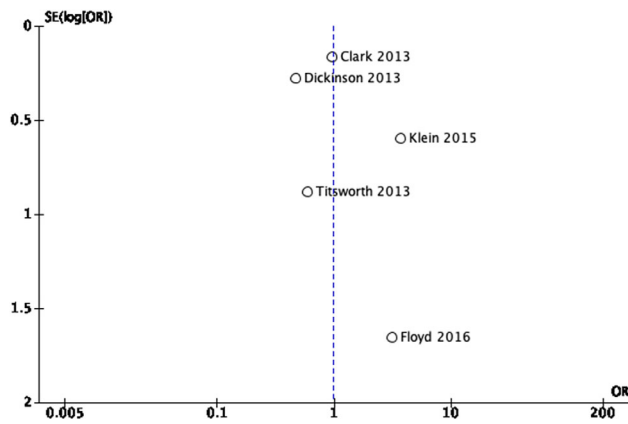
FIGURE 3 Funnel plots for quasi-experimental (pre-post) studies' meta-analysis

article, Dickinson et al,[24] that shows contradictory data, that is, an increase in the days of hospitalisation, which may be explained by the reasoning illustrated early in the discussion. It is worth mentioning that ICU readmissions after the implementation of the EMP follows a decreasing trend in all studies that measure this variable.[22,25,26]

Although it is true that there are certain barriers that complicate the implementation of an EMP, such as haemodynamic or pulmonary instability of patients, ICU culture of mobility, and lack of resources among clinicians,[31] the EMP is inherently safe according to a recent meta-analysis.[32] In fact, our systematic review agrees that EMP was safe in at least four of the seven articles included.

4.1 | Strengths and limitations

There were several potential limitations in this meta-analysis that should be acknowledged. First, the main limitation of this study was the lack of data; only seven articles met the inclusion criteria to answer the research question. Second, some of the included studies had a relatively low methodological quality, and our conclusion may be limited by this point. Third, substantial heterogeneity was identified in the included meta-analysis, which made the findings complicated to interpret. Likewise, some confounding factors, such as the definition of EM, timing of EM, and the differences in critically ill patients, may not be consistent across the included studies and account for the heterogeneity. In addition, the limitations associated with the variability in the definition of PI, the lack of description of the staging system used in some of the articles, and the differences between the inclusion criteria of the PI stage used in the calculation of the incidence or prevalence rates for each article must also be taken into account.

Finally, although this review improves the current lack of information, more studies are necessary to obtain conclusive evidence. Despite these limitations, this systematic review sought to analyse the available information to date related to how an EMP improves HAPI prevention.

5 | CONCLUSIONS

Existing literature cannot answer the review question. The discrepancies between studies and the scant number of them related to the assessment of PIs after the implementation of an EMP make the answer to whether EMP versus usual care is more effective in reducing the incidence of HAPI in ICU inconclusive. Thus, more large-scale and well-performed randomised control trials are needed to verify our results.

CONFLICT OF INTEREST
The authors declare no potential conflicts of interest.

AUTHOR CONTRIBUTIONS
Leticia Nieto-García and **Montserrat Alonso-Sardón:** Conceived and designed the study. **Leticia Nieto-García:** Developed the search strategy and performed the literature search. **Leticia Nieto-García** and **Montserrat Alonso-Sardón:** Carried out the study selection, extraction, and assessment of data for the systematic review. **Leticia Nieto-García** and **Montserrat Alonso-Sardón:** Wrote the first draft of the manuscript. **Adela Carpio-Pérez** and **María Teresa Moreiro-Barroso:** Contributed to interpretation of data and critical revision of the manuscript. **Montserrat Alonso-Sardón:** Supervised the study. All authors approved the final manuscript. All authors confirm the accuracy or integrity of the work.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT
This study was reviewed and approved by the *Clinical Research Ethics Committee for Clinical Investigation of the University Hospital of Salamanca*. (Code: CEIm PI 2019 03208).

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APPENDIX A: SAMPLE SEARCH STRATEGY

The electronic search strategy was as follow:

1. "pressure ulcer" [MeSH Terms] OR "pressure injury" [All Fields]
2. "intensive care unit" [MeSH Terms] OR "ICU" [All Fields]
3. "early ambulation" [MeSH Terms] OR "early mobilization" [All Fields] OR "early mobility program" [All Fields] OR "early mobility protocol" [All Fields]
4. #1 AND #2 AND #3
5. "randomized controlled trials" [Publication type] OR "clinical trial" [Publication type] OR "systematic review" [Publication type] OR "meta-analysis" [Publication type]
6. #4 AND #5
7. Limit to English and Spanish language

TABLE B1 Different EMPs applied in each study

Author, year	EMP description	Intervention
Azuh et al, 2016	Five-point mobility scale devised by the authors based on previous experience and reviews.	• *Level 1 (bedrest)*: Reposition every 2 h, ROM based on restrictions every 4 h. • *Level 2 (edge of bed)*: Sitting bedside unsupported (up to 3 times per day for 5-30 min), initiate assisted or active exercises, assistance with activities of daily living. • *Level 3 (stand to chair)*: Transfer from bed to chair. • *Level 4*: Exercise while seated. Walk 3 times per day with assistance. • *Level 5*: Independent ambulation and stationary bicycle.
Clark et al, 2013	Adapted progressive mobility program.[29]	• *Level 1*: repositioning every 2 h and daily routine passive ROM. • *Level 2*: active-assisted to active exercises. • *Level 3 y 4*: Use of weights and resistance bands.
Dickinson et al, 2013	Developed a new EMP: "Moving and Grooving."	• *Phase 0*: active/passive ROM (3×/day, 10 repetitions), HOB elevated 30° to 45° or reverse Trendelenburg, reposition (every 2 h), CLR (18-24 h per day). • *Phase 1*: Phase 0 + chair position or OOB with sling (3×/day) and dangling (3×/day). • *Phase 2*: Resisting ROM (3×/day, 10 repetitions), HOB elevated 30° to 45° and reposition (every 2 h), standing (3×/day) and walking (3×/day).
Floyd et al, 2016	Progressive Mobility Protocol (PMP) adapted from Zomorodi.[11]	• *Level 1*. Active/passive ROM in bed, HOB > 30°. • *Level 2*. Sitting on edge of bed. • *Level 3*. Stand up and lateral side step along the bed. • *Level 4*. OOB to chair via stand pivot transfer. • *Level 5*. Ambulation < 50 ft. • *Level 6*. Ambulation 100 ft. • *Level 7*. Ambulation > 100 ft.

(Continues)

TABLE B1 (Continued)

Author, year	EMP description	Intervention
Fraser et al, 2015	Designed the EMP based on interventions described in the literature.	• *Phase 1*: Passive ROM and repositioning every 2 h. • *Phase 2*: Sitting on edge of bed and standing. • *Phase 3*: Transferring from bed to chair. • *Phase 4*: Ambulation.
Klein et al, 2015	Created an early mobility protocol with four progressive mobility milestones from 16 mobility levels.	*Level 1.* 1. Bed rest without passive ROM. 2. Bed rest with passive ROM. 3. Bed rest with active ROM. 4. Turn and position every 2 h. 5. HOB routinely < 30°. 6. HOB elevated > 30°. 7. CLR. *Level 2* (HOB elevated and dangle at bedside). 1. HOB elevated ≥45° o < 65° × 60 min. 2. HOB elevated ≥45° o < 65° + legs in a dependent position × 60 min. 3. HOB elevated ≥65° + legs in a dependent position x 60 min (beach chair). 4. Meets ≠ 9 o 10 but for > 60 min. 5. Dangle with assistance. *Level 3* (stand at bedside). 1. Stand at side of bed. 2. Stand and pivot to chair. *Level 4* (walking). 1. Walk with assistance. 2. Walk independently.
Titsworth et al, 2012	Developed a PUMP plus algorithm (Progressive Upright Mobility Protocol).	• *Step 1*: HOB elevated at 45°. • *Step 2*: HOB elevated at 45° plus legs in dependent position (partial chair mode/cardiac chair). • *Step 3*: HOB elevated at 45° plus legs in full dependent position (full bed chair mode/cardiac chair). • *Step 4*: HOB elevated at 65° plus legs in full dependent position and feet on floor; standing in place. • *Step 5*: Initial stand position/pivot and into chair. • *Step 6 (plus)*: Transfer standing from bed to chair for 2 to 3 meals with sitting time not to exceed 45 min. • *Step 7 (plus)*: Ambulate within room using assistive devices and extra personnel PRN (goal = 20 ft). • *Step 8 (plus)*: Ambulate within hallway using assistive devices and extra personnel PRN (goal = 50 ft). • *Step 9 (plus)*: Ambulate within hallway using assistive devices and extra personnel PRN (goal = 100 ft). • *Step 10 (plus)*: Ambulate 150 ft with contact guard (hands on only for balance) or personal supervision/assistance (coaching only). • *Step 11 (plus)*: Ambulate without coaching or supervision, may use device if necessary.

Abbreviations: CLR, continuous lateral rotation; HOB, head-of-bed elevation; OOB, out of bed; PRN, as needed; ROM, range of motion.