HHS Public Access

Author manuscript

Int J Nurs Stud. Author manuscript; available in PMC 2018 June 01.

Published in final edited form as:

Int J Nurs Stud. 2017 June ; 71: 97–114. doi:10.1016/j.ijnurstu.2017.03.012.

RISK FACTORS FOR PRESSURE INJURIES AMONG CRITICAL-CARE PATIENTS: A SYSTEMATIC REVIEW

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Abstract

Objective—To identify risk factors independently predictive of pressure injury (also known as pressure ulcer) development among critical-care patients

Design—We undertook a systematic review of primary research based on standardized criteria set forth by the Institute of Medicine.

Data Sources—We searched the following databases: CINAHL (EBSCOhost), the Cochrane Library (Wilson), Dissertations & Theses Global (ProQuest), PubMed (National Library of Medicine), and Scopus. There was no language restriction.

Method—A research librarian coordinated the search strategy. Articles that potentially met inclusion criteria were screened by two investigators. Among the articles that met selection criteria, one investigator extracted data and a second investigator reviewed the data for accuracy. Based on a literature search, we developed a tool for assessing study quality using a combination of currently available tools and expert input. We used the method developed by Coleman and colleagues in 2014 to generate evidence tables and a summary narrative synthesis by domain and subdomain.

Results—Of 1753 abstracts reviewed, 158 were identified as potentially eligible and 18 fulfilled eligibility criteria. Five studies were classified as high quality, two were moderate quality, nine were low quality, and two were of very low quality. Age, mobility/activity, perfusion, and vasopressor infusion emerged as important risk factors for pressure injury development, whereas results for risk categories that are theoretically important, including nutrition, and skin/pressure injury status, were mixed. Methodological limitations across studies limited the generalizability of

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the results, and future research is needed, particularly to evaluate risk conferred by altered nutrition and skin/pressure injury status, and to further elucidate the effects of perfusion-related variables.

Conclusions—Results underscore the importance of avoiding overinterpretation of a single study, and the importance of taking study quality into consideration when reviewing risk factors. Maximal pressure injury prevention efforts are particularly important among critical-care patients who are older, have altered mobility, experience poor perfusion, or who are receiving a vasopressor infusion.

Keywords

Critical Care; Pressure Injury; Risk factor; Skin

Introduction

Hospital-acquired pressure injuries (formerly called pressure ulcers) are localized areas of damage to the skin, underlying tissue, or both, as a result of pressure. Hospital-aquired pressure injuries occur in 3% to 34% of hospitalized patients worldwide and result in longer hospital stays, increased morbidity, and increased human suffering.[1–4]

Due to negative outcomes associated with pressure injuries, standards of practice include a recommendation to conduct pressure injury risk assessment and comprehensive skin assessment upon admission and at any time there is a significant change in a patient's condition.[5] Accurate risk assessment along with comprehensive skin assessment enables prompt recognition and treatment of pressure injuries that occur among high-risk patients, which is important because early (Category 1) pressure injuries are highly treatable[6]; however, discernment of which individuals are at highest risk for pressure injuries in the intensive care unit (ICU) is problematic because the risk-assessment scales currently used for critical-care patients tend to identify almost all patients as "high risk."[7]

Critical-care patients represent a highly specialized patient population, and risk for pressure injuries in this population is likely to be different than risk in other populations, particularly as it relates to perfusion and general skin status due to severity of illness and treatments, including vasopressor infusion, that are unique to critical-care patients.[8] The purpose of the current review is to identify factors that are independently associated with increased risk for pressure injuries among critical-care patients specifically. An independent risk factor retains its statistical association with the outcome variable when other risk factors are included in the model; note that independence is a statistical concept and does not imply causality.[9,10]

We evaluated identified independent risk factors in relation to clinical relevance and in relation to recent pressure injury conceptual and theoretical frameworks.[5,11] We also evaluated risk factors in relation to study quality, as a recent pressure injury study conducted in a general population determined that most of the included studies were of low or very low quality.[9]

Methods

Research Protocol

We undertook a systematic review of primary research. Our approach was based on the standardized criteria set forth by the Institute of Medicine[12] for comparative effectiveness reviews and modified to appraise risk-factor/observational studies.[9]

Eligibility Criteria

We adapted inclusion criteria based on the method employed by Coleman and colleagues,[9] to include *(a)* primary research; *(b)* adult sample; *(c)* ICU setting; *(d)* prospective cohort, retrospective record review, or controlled trial; and *(e)* identification of independent risk factors for pressure injury (multivariate analysis). Exclusion criteria included the following: *(a)* limited to pediatric patient population (age <18 years), *(b)* >25% of the study population were excluded from analysis due to loss to follow up or missing records, *(c)* prevalence or cross-sectional study, *(d)* limited to evaluation of a pressure injury risk-assessment scale, and *(e)* limited to spinal cord injury (SCI) patients (due to the specialized physiology involved in spinal cord injuries and the associated risk for pressure injury among individuals with SCI.[13] There was no language restriction.

Search Strategy

We searched the medical subject headings *pressure injury* and *intensive care units* in addition to field-restricted keywords for the following databases: CINAHL (EBSCOhost), the Cochrane Library (Wilson), Dissertations & Theses Global (ProQuest), and PubMed (National Library of Medicine). We downloaded our final results on December 17, 2016. A complete description of the search is outlined in Appendix A.

Data Extraction

Two investigators (XX and XX) identified potentially eligible studies. Among those deemed potentially eligible, XX noted whether each study met inclusion criteria for this review (or stated the reason the study did not meet criteria) and XX checked XX's categorizations. Disagreements were addressed by a third researcher, XX, and agreement was determined by consensus. In addition, one investigator (XX) extracted data pertaining to study design, population, setting, analysis, and results, and a second investigator (XX) reviewed the data for accuracy.

Quality Appraisal

In an effort to identify a quality-assessment tool for the current review, we conducted a literature search. We determined that no currently available checklists or scales fit closely with the objectives of the current review while offering adequate inter-rater reliability.

We used the available tools to guide development of our tool for assessing quality among pressure injury risk-factor studies. First, the authors of a systematic review of quality-assessment tools for observational studies concluded that available checklists and scales did not differentiate well between poor study reporting and a truly flawed study.[14] The authors recommended that instead of assigning a summative score based primarily on reporting,

quality assessment of observational risk-factor studies should be conducted by defining flaws in different domains—an approach that results in more transparent conclusions when compared with global scoring based on a checklist or summative evaluation tool. Similarly, authors of a systematic review of quality-appraisal tools for observational epidemiological studies recommended against summative scores and instead advised an approach based on evaluation of bias in particular quality domains.[15]

The quality-appraisal tool developed for the current review (see Appendix B) includes the domains identified in Sanderson and colleagues'[15] review of quality appraisal among observational studies: methods for selecting participants, methods for measuring exposure and outcome variables, design-specific sources of bias, methods to control confounding, statistical methods (excluding control of confounding), and conflict of interest. Major and moderate flaws are noted in each domain in which presence of a major flaw is a significant indicator that the flaw has substantially compromised our confidence in the study conclusions.

Although the quality-appraisal method employed in this study was focused on sources of bias in different domains, we determined that an evaluative descriptor was necessary to facilitate study classification according to the degree of actual or potential bias. Using the rubric provided in Appendix B, we employed the following evaluation based on specific sources of bias:

1. *High-quality studies* had 0 potential sources of bias with major implications for study quality and <1 potential sources of bias with moderate implications for study quality;
2. *Moderate-quality studies* had 1 potential source of bias with major implications for study quality and <1 potential sources of bias with moderate implications for study quality; or 0 potential sources of bias with major implications for study quality and 2–3 potential sources of bias with moderate implications for study quality;
3. *Low-quality studies* had 1 potential source of bias with major implications for study quality and 2–4 potential sources of bias with moderate implications for study quality, or 0 potential sources of bias with major implications for study quality and 4–7 potential sources of bias with moderate implications for study quality; and
4. *Very-low-quality studies* had 2 or more potential sources of bias with major implications for study quality, or >8 potential sources of bias with moderate implications for study quality.

Indeterminate sources of bias were items that may or may not have introduced bias; indeterminate items were noted but did not count toward the evaluative descriptor category. We sought expert input during tool development, and the final tool reflects consensus among two experts in pressure injury research and one expert in observational research.

Data Synthesis

Meta-analysis was not feasible for this review because of a high degree of clinical heterogeneity related to population, predictor variable operationalization, preventive interventions, and different thresholds for the pressure injury outcome variable (new Category 1 and greater pressure injury vs. new Category 2 and greater) according to the international National Pressure Ulcer Advisory Panel/European Pressure Ulcer Advisory Panel (NPUAP/EPUAP) classification system.[5] The purpose of the review was to identify risk factors rather than to quantify the effect size of the relationship between a given factor and pressure injury development; therefore, we conducted a narrative synthesis. We utilized the narrative synthesis method previously employed by Coleman and colleagues.[9] We recorded all potential risk factors entered into multivariate analysis and identified the factors that emerged as independent factors for pressure injury risk. For studies using stepwise regression, we included factors that were not statistically significant upon bivariate analysis if those factors were identified as independent risk factors for pressure injuries in the final model.[9] Finally, we categorized recorded risk factors and potential risk factors into domains and subdomains.

Domains were structured according to Coleman and colleagues'[11] interpretation of the NPUAP/EPUAP conceptual framework (see Figure 1). Domain 1 encompasses mechanical boundary conditions to include sources of pressure and also friction and shear, which are conceptualized as mechanical boundary conditions rather than as patient characteristics.[11] Domain 2 comprises those factors that influence the susceptibility and tolerance of the individual. Some factors have an effect on mechanical boundary conditions *and* on the susceptibly and tolerance of the individual, and therefore some overlap exists between the two major domains; for example, diabetes affects mechanical load through sensory deficits and affects individual tolerance and susceptibility through altered perfusion. We developed subdomains in relation to Coleman and colleagues'[11] theoretical schema of a proposed causal pathway for pressure ulcer development (see Figure 2), which built upon the NPAUP/EPUAP/Pan Pacific Pressure Injury Alliance (PPPIA) conceptual framework[5] and identified immobility, skin and pressure injury status, and poor perfusion as direct causal factors in pressure injury development.[11]

Results

Study Characteristics

Of 1753 abstracts reviewed, 158 were identified as potentially eligible and 18 fulfilled eligibility criteria (see Figure 3). The retained studies included 13 prospective cohort and five retrospective record reviews. A summary of the included studies is presented in Table 1.

Quality Appraisal

Two researchers conducted the quality appraisal and reached "substantial" agreement independently, as evidenced by Kappa = 0.72.[16] After inter-rater reliability was calculated, the researchers reviewed any discrepancies and came to agreement. When possible, we contacted study authors for clarification purposes.

Quality appraisal results are identified in Table 2. The included studies had between zero and two major sources of bias, and between one and six moderate sources of bias; overall, five studies were classified as high quality,[4,17–20] two were of moderate quality,[21,22] nine were of low quality,[2,23–30] and two were of very low quality[1,31] (Table 2). The methodological limitations we found were similar to other reviews of pressure injury risk-factor studies in the sense that most of the included studies (61%) were of either low quality or very low quality.[7,9] Eleven (64%) of the 17 included studies did not have adequate numbers of pressure injury events for analysis, a limitation that is reflected in some studies in the wide confidence intervals associated with reported odds ratios.

Pressure Injury Outcome Variable

Two of the 18 studies included for review did not describe criteria used to designate a pressure injury.[1,31] Two studies did not report specific pressure injury categories,[1,4] six studies designated a pressure injury as a new injury ≥Category 1,[17,23–27] eight studies included only new pressure injuries that were ≥Category 2,[2,19,21,22,28–31] and two studies included separate models for pressure injuries ≥Category 1 and ≥Category 2 (Table 1).[20,25]

Risk-Factor Domains and Subdomains

The authors of 14 studies reported all of the risk factors entered into multivariate modeling as well as those that emerged as independently predictive of pressure injury,[2,4,17,19–28,31] whereas authors of three studies reported only the variables that emerged as significant from multivariate modeling.[1,18,29] A summary of risk factors entered into the multivariate model (when available) and those that emerged as independent risk factors are summarized by study (Table 1) and by risk-factor domain (see Table 3).[9]

Domain 1: Mechanical Boundary Conditions—Mechanical boundary conditions are aspects that influence the magnitude of the mechanical load, the time duration, and also the type of loading (pressure, friction, shear; Figure 1).[5] We extended this category to include body size because of the potential for increased mechanical load due to bony prominence among underweight individuals. We also included emergent admission because emergency department gurneys have a suboptimal surface,[32] and surgical time as time in surgery confers immobility.

Body Size: One moderate-quality study[21] and one low-quality study[28] included body size in the multivariate analysis, but neither weight nor height emerged as significant upon multivariate analysis (Table 3). No study included change in weight, however, which might have been useful for assessing fluid shifts. Additionally, no study included a height/weight composite such as body mass index, which would have indicated underweight or excessive adipose tissue.

Friction and Shear: Recent developments in pressure injury research indicate that friction-induced skin injuries are not true pressure injuries, whereas shearing forces cause a decrease in regional blood flow and therefore are important in pressure injury risk.[33,34] Authors of only one study[20] entered a shear-related variable into multivariate modeling; the study,

which was of high quality, found that friction/shear (as defined by the Braden Scale)[35] was independently predictive of pressure injury development (Table 3).

Emergent Versus Scheduled Admission: We included emergent admission in Domain 1 because time in the emergency department is associated with time spent on suboptimal surfaces such as gurneys.[32] Five study authors entered admission type into their statistical model.[19,21,23,25,31] In two of those studies (33%),[23,31] emergent admission was found to be independently predictive for pressure injury development; however, the two studies were of low- and very-low quality.

Domain 1 Subdomain: Immobility—Within Domain 1, Coleman and colleagues'[11] schema depicts immobility as a direct causal factor (Figure 2). Therefore, factors associated with this subdomain are presented below.

Mental/Neurologic Status: Researchers in four studies,[22,24,26,28] including one moderate-quality study[22] and three low-quality studies,[24,26,28] entered variables related to neurologic status into multivariate analysis. No variables related to mental status emerged in multivariate analysis (Table 3).

Mobility/Activity: One high-quality study[20] and one low-quality study[24] each identified mobility and activity level, respectively, as independently predictive of pressure injuries (Table 3).

Sensory Perception: Sensory perception was entered into the statistical model of one high-quality study but did not emerge as an independent risk factor.[20]

Surgical Factors: Information pertaining to surgical factors was limited. One high-quality study[19] found that undergoing noncardiac surgery was an independent risk factor for pressure injury, whereas one low-quality study[25] entered operative time into the multivariate model, but it did not emerge as an independent risk factor (Table 3).

Turning/Repositioning and Surface: Overall, authors of six studies entered one or more turning- and/or repositioning-related variables into the statistical model[4,18,22,23,25,26]; one study entered four variables related to positioning[22] (Table 3). Results were conflicting. In their moderate-quality study, Nijs and colleagues[22] found that *more frequent* turning was an independent risk factor for pressure injury development, whereas two low-quality studies[23,25] each found that *less frequent* repositioning was independently predictive of pressure injury risk (Table 3). Nijs and colleagues speculated that perhaps high-risk patients experienced enhanced nursing vigilance in turning and repositioning.[22]

Domain 2: Susceptibility and Tolerance of the Individual—Domain 2 includes factors that influence the susceptibility and tolerance of the individual (Figure 1). Subdomains within Domain 2 are skin/pressure injury status, which includes existing and previous pressure injuries and general skin status, and poor perfusion, which encompasses conditions that alter oxygen delivery to the tissues.[11]

Body Temperature: Three studies,[18,22,28] including one of high quality, one of moderate quality, and one of low quality, included body temperature in multivariate analysis, with conflicting results. The high-quality study found that fever was an independent risk factor for pressure injury development[18]; the moderate-quality study found that fever was a protective factor[22], and in the low-quality study,[28] fever did not emerge as significant in multivariate analysis (Table 2).

Diagnosis Not Directly Related to Oxygenation and Perfusion: Renal failure and high creatinine were each determined to be independent risk factors for pressure injury development in one high-quality study[19] and one low-quality study,[2] respectively. Researchers in one high-quality[4] and one moderate-quality study[22] entered dialysis into multivariate modeling. In the moderate-quality study, dialysis was independently predictive of pressure injury development, whereas dialysis did not emerge as an independent risk factor in the high-quality study. Serum creatinine was independently predictive of pressure injury development in one low-quality study[2] (Table 3).

Laboratory Values: Researchers in six studies,[2,17,24,26–28] including one high-quality study, entered laboratory values into multivariate analysis (apart from albumin, which is discussed under "Nutrition," and blood-gas values, which are included in the oxygenation results; see Table 2). Only two laboratory values were statistically significant upon multivariate analysis: creatinine was an independent risk factor in one low-quality study,[2] and anemia emerged in one low-quality study.[26]

Length of Stay: Length of stay (LOS) independently predicted risk for pressure injury development in seven[1,20,24–26,30,31] of the 11 studies that included LOS in multivariate analysis (Table 2).[1,17,20,21,24–26,28,30,31,36] Only one study,[21] however, differentiated LOS *prior* to pressure injury development, which is important, because development of a pressure injury increases the length of a hospital stay.[37]

Medications: Among five studies that included medications other than vasopressors,[4,19,22,26,28] one moderate-quality study[22] found that sedative use was an independent risk factor for pressure injury development (Table 3).

Nutrition: In the current review, only one low-quality study determined that a nutrition-related variable (serum albumin) was independently predictive of pressure injury risk.[27] Four other studies evaluated nutrition-related variables,[20,23,26,28] but nutrition did not emerge as predictive in multivariate modeling (Table 3). Of note, one very-low-quality but frequently cited study indicated that days without nutrition was an independent risk factor for pressure injury development[31]; in that study, however, the data presented in tables and the associated odds ratio indicate the opposite: that days without nutrition was a *protective* factor. That paradoxical finding was actually replicated in the bivariate analysis conducted by Slowikowski and Funk,[4] but the authors did not enter nutrition in the multivariate analysis because they thought it might have been a spurious finding.

Severity of Illness/Health Status: Eight studies included the Acute Physiology and Chronic Health Evaluation (APACHE) score as a marker of severity of illness in their multivariate

model,[17,20,22,23,26,27,30,31] and two low-quality studies[26,30] identified the APACHE score as predictive of pressure injury risk (Table 2). The APACHE score is calculated using measurements that occur within 24 hours after admission, and the score is not repeated; therefore, the APACHE may not be a sensitive indicator of severity of illness throughout a several-day hospital course.[38] Furthermore, experts contend that the APACHE should be used primarily to provide performance comparisons between ICUs rather than to provide an assessment of an individual patient's illness severity.[38]

Among other markers of illness severity, an American Society of Anesthesiologists (ASA) Class-4 or Class-5 score was an independent risk factor for pressure injuries in one high-quality study,[19] and sequential organ failure assessments on Days 1 and 4 were also independent risk factors for pressure injuries in a moderate-quality study[21] (Table 3). Hospital and/or ICU mortality were considered in one high-quality study[17] and two moderate-quality studies,[21,28] but mortality did not emerge as statistically significant in the multivariate model.

Domain 2 Subdomain: Poor Perfusion—The subdomain of poor perfusion includes factors that alter oxygen delivery to tissues. Poor perfusion is included in Coleman and colleagues' conceptual schema as a direct causal factor in pressure injury development.[11]

Blood Pressure: Two high-quality studies included blood pressure,[17,20] and blood pressure was an independent risk factor in one of the studies.[17] Cox defined blood pressure as the total number of hours in the first 48 hours that the patient had a mean arterial pressure <60 mm Hg, and/or systolic blood pressure <90 mm Hg, and/or diastolic blood pressure <60 mm Hg; however, in that study, the mean length of stay was five days, and therefore blood pressure readings were not recorded for more than half of a typical patient's ICU stay.[20] In a another study, Cox and Roche determined that the total number of hours a patient experienced a mean arterial blood pressure of <60mmHg while on vasopressors was independently predictive of pressure injury development.[17]

Diagnosis Related to Oxygenation and/or Perfusion: Researchers in 10 studies (including four high-quality studies[4,17,19,20]) entered diagnoses related to potentially altered perfusion (including diabetes, cardiovascular disease, and peripheral vascular disease) into multivariate modeling[2,4,17,18,19,20,21,22,25,28]; the diagnoses emerged as independent risk factors in six,[2,4,17–19,22] including all four high-quality studies,[4,17,19,20] one moderate-quality study,[22] and one low-quality study[2] (Table 2). Researchers in two studies included sepsis, another condition resulting in altered tissue perfusion, in their multivariate modeling, but sepsis did not emerge as a significant risk factor.[21,28] In addition, researchers in two studies entered cigarette smoking into multivariate modeling[18,26]; smoking was an independent risk factor for pressure injury development in the high-quality study by Suriadi et al.[18]

Heart Rate and Monitoring: One low-quality study recorded heart rate and invasive monitoring and determined that neither variable was independently predictive of pressure injury development; however, the authors recorded variables only for the first 24 hours of a patient's ICU stay, despite inclusion criteria that required an ICU length of stay >72 hours.[28]

Oxygenation and Ventilation: Authors of seven studies entered oxygenation and ventilation-related variables into multivariate modeling[4,17,19,21,22,25,28]; among those, one high-quality[17] and one moderate-quality[21] study identified length of mechanical ventilation as independently predictive of pressure injury risk. Other oxygenation and ventilation-related variables did not emerge as independently predictive (Table 3); however, variable operationalization limits the generalizability of the findings: only two studies included blood-gas results, and both studies limited their data collection to the first 24 hours.[21,28] Furthermore, mechanical ventilation may be more indicative of severity of illness than oxygenation status because a patient could be stable from a respiratory standpoint but still require mechanical ventilation support due to other disease processes.

Vasopressors: Vasopressor infusion is commonly administered to critical-care patients to improve perfusion in shock states, with resulting peripheral vasoconstriction, which may confer risk for pressure injury.[20] Authors of six studies entered a vasopressor variable into multivariate analysis[2,17,20,22,26,28] and in four of those studies, including both of the high-quality studies,[17,20] vasopressor infusion emerged as independently predictive of pressure injury development[17,20,22,26] (Table 3). In their high-quality study, Cox and Roche found that patients receiving vasopressin were at increased risk for pressure injury development.[17] Variable operationalization contributed to difficulty comparing across studies. Cox[20] and Cox and Roche[17] recorded hours of administration of specific vasopressor agents and hour/dose, respectively, whereas Nijs and colleagues[22] recorded dose but not duration of vasopressor infusion and Theaker et al.[26] dichotomized norepinephrine infusion as “yes/no.”

Domain 2 Subdomain: Skin/Pressure Injury Status—The subdomain of skin and pressure injury status includes existing and previous pressure injuries and general skin status. Skin/pressure injury status is included in Coleman and colleagues’[11] conceptual schema as a direct causal factor in pressure injury development (Figure 2).

Moisture: Moisture is included in skin/pressure injury status due to its close relationship with skin condition.[39] Two studies evaluated moisture,[26,28] and it emerged as an independent risk factor for pressure injury in one moderate-quality study[28] (Table 3).

External Skin Factors: Researchers in six studies entered variables related to skin status into multivariate modeling.[4,17,22,23,26,28] The variables included external conditions (incontinence), assessment of the skin’s appearance, and edema (Table 2). Edema emerged from multivariate modeling in one low-quality study,[28] but was not independently predictive of pressure injury risk in one high-quality study,[4] one moderate-quality study,[22] and two low-quality studies.[23,26] Peripheral necrosis due to vasopressor use was not an independent predictor of pressure injury in one study.[17] A single study recorded detailed examination of the skin’s condition[28]; that low-quality study found that centralized circulation, mottled skin, and reddened skin were independent predictors of pressure injury development, whereas livid skin and hyperemic skin did not emerge from the multivariate analysis (Table 2).

Other Factors Not Included in Domains 1 and 2

Gender: Four studies included gender in the multivariate model,[1,23,27,28] and in three of the four,[1,27,28] male gender was independently predictive of pressure injury risk.

Risk-Assessment Scales: Overall, seven studies included a risk-assessment-scale total score in their multivariate analysis,[4,17,20,25,28,29,31] and in three studies (43%)[4,29,31] the total score emerged as an independent risk factor (Table 3). The total score for the Braden Scale[35] emerged in one high-quality study[4] and one low-quality study,[29] and did not emerge in two high-quality studies[17,20] and one low-quality study.[25]

Other Factors: A high-quality study found winter season was a risk factor for pressure injury development.[21] One low-quality study noted that increased nursing workload was a slightly protective factor.[1]

Discussion

Our findings reveal inconsistent results among studies, as well as marked variability in study quality, indicating that researchers should avoid overinterpretation of results from any single study. Each study was subjected to quality assessment, which will allow clinicians and researchers to take quality into consideration when evaluating results.

In the current review of pressure injury risk factors among critical-care patients, age, mobility/activity, perfusion, and vasopressor infusion frequently emerged as important factors in pressure injury development, particularly among high-quality studies. Findings for age and mobility/activity are consistent with the results from a systematic review conducted by Coleman and colleagues in an acute, rehabilitative, long-term-care population.[11] The finding that mobility and poor perfusion are important subdomains is in keeping with current theoretical knowledge, given that mobility and poor perfusion are both direct causal factors in Coleman and colleagues' conceptual model; however, results for skin and pressure injury status, which is also conceptualized as a direct causal factor, were mixed.[11]

Results for the perfusion subdomain were mixed; however, the bulk of evidence from high-quality studies favored perfusion as an important independent risk factor, whereas negative findings from lower quality studies may have reflected methodologic limitations. Perfusion is a dynamic process, particularly among critical-care patients, who are at risk for hemodynamic instability. Only one study incorporated perfusion-related measures throughout the patient's entire ICU stay[17]; other studies that included perfusion-related variables utilized cut points that presented dynamic hemodynamic processes as dichotomous variables, an approach that fails to quantify the magnitude of hypotension. Similarly, only one study recorded the duration of hypotension.[17]

Vasopressor agents are an important element influencing perfusion among ICU patients, but are difficult to study due to variability in effects on peripheral circulation related to dose delivered and receptors targeted. Among studies in the current review, only one study included the dose of the vasopressor for the entire duration of administration, and the same study was the only one to capture the potentially synergistic effects of more than one

vasopressor agent.[17] Despite methodological limitations, however, results from the current review indicate that vasopressor agents are important in pressure injury development. Among two high-quality and one moderate-quality studies that examined various vasopressor-related variables, all found that vasopressors were independent predictors.[17,20,22]

Cox and Roche[17] examined a population receiving vasopressor therapy and found increased risk among individuals receiving vasopressin, which is important because vasopressin is typically considered a second-line drug and is commonly administered along with norepinephrine for vasodilatory shock.[40] This is particularly interesting in light of a prevalence study conducted by Bly and colleagues[36] that determined that infusion of more than one vasopressor conferred risk for pressure ulcers.• Additional research is needed to elucidate the effects of individual vasopressor agents, the potentially synergistic effects of multiple agents (particularly concomitant use of norepinephrine and vasopressin), and the underlying effects of the shock state that the vasopressor agents treat.

Coleman and colleagues conceptual model indicates that skin and pressure injury status are direct causal factors in pressure injury development.[11] The conclusion that skin status is important is also supported by current clinical practice guidelines and by the broader pressure injury literature.[5] Unfortunately, however, information pertaining to skin and pressure injury status in the current review was extremely limited; only one study addressed skin status (excepting edema) throughout the hospitalization (vs. only on admission).[17] Additionally, the authors of 10 (56%) of the 18 studies in the current review excluded patients who were admitted to the ICU with a pre-existing pressure injury, which is unfortunate, because individuals with proven skin compromise are therefore not represented in more than half of the included studies.[1,17–20,23,26–29]

Although nutrition is theoretically a factor in pressure injury development, results from the current review failed to demonstrate a connection between nutrition status and pressure injury development among critical-care patients. Eachempati and colleagues' study concluded that more days without nutrition conferred risk for pressure injuries; however, careful analysis of their study shows the opposite.[31] In Table 4 on page 1681, the 33 patients with a pressure injury experienced a mean of 1.9 days without nutrition, whereas the 22 patients without a pressure injury experienced a mean of 4.3 days without nutrition. Furthermore, the reported odds ratio of 0.51 indicates a protective effect.[31] In their high-quality study, Slowikowski and Funk[4] also found that patients receiving no nutrition had a lower incidence of pressure injury, but they chose not to enter nutrition in multivariate analysis because they were concerned that it was a spurious finding, citing Eachempati and colleagues'[31] erroneous conclusion that days without nutrition conferred risk. In the future, researchers should utilize more sensitive nutrition indictors. Guidance on appropriate measurement of nutrition status among critical-care patients is available from the American Society for Parenteral and Enteral Nutrition in coordination with the Society of Critical Care Medicine.[41]

•The study by Bly et al.[36] was a prevalence study, and therefore did not meet inclusion criteria for the current review.

In addition to skin/pressure injury status and nutrition, more information is needed about the relationship between surgery and the risk for pressure injury development. A high-quality retrospective record review of 3225 surgical patients (not limited to critical care) found that multiple surgeries and total surgical time were independent risk factors for pressure injury development.[42] Only two studies in the current review included surgical factors in multivariate analysis.[19,25]

Our study was limited to critical-care patients within the ICU setting. Therefore, it is possible that we failed to include research that featured critically ill patients in other settings, or subgroup analysis of studies that featured various levels of acuity among hospitalized patients. Finally, our search strategy included databases that are primarily in the English language—CINAHL (EBSCOhost), the Cochrane Library (Wilson), Dissertations & Theses Global (ProQuest), PubMed (National Library of Medicine), and Scopus—which may have failed to identify some articles in languages other than English.

Conclusion

Results from this review of pressure injury risk factors among critical-care patients underscore the importance of avoiding overinterpretation of a single study, and the importance of taking study quality into consideration when reviewing risk factors. Age, mobility/activity, perfusion, and vasopressor infusion emerged as important risk factors for pressure injury development, whereas results for risk categories that are theoretically important, including skin and pressure injury status and nutrition, were mixed.[5] Methodological limitations across studies limit generalizability of results, and future research is needed, particularly to elucidate risk conferred by illness severity, nutrition, and skin and pressure injury status. Clinicians may consider extending maximal preventive interventions to critical-care patients who are older, experience altered mobility/activity, have altered perfusion, or receive vasopressor infusions. Future research examining the effects of poor nutrition, and especially skin and pressure injury status, is needed. In addition, research is still needed to elucidate the effects of specific perfusion related variables, including high doses of vasopressors, combinations of vasopressors, and duration of decreased oxygen delivery to tissues (hypotension and/or decreased blood oxygen content).

Acknowledgments

This publication was supported by the National Institute of Nursing Research of the National Institutes of Health under Award Number T32NR01345 and F31NR014608. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Appendix A: Database Search Strategies

Search Lexicon	
MH	Restricts the search to MeSH headings assigned to the article
TI	Keyword search for terms in the article title
tiab	Keyword search for terms in the title or abstract

Search Lexicon	
+	Medical subject heading exploded to include all narrower subject terms
“ ”	Exact phrase search
*	Wildcard - can replace any letter or, at the end of the word, multiple letters
su	ProQuest subject headings

Search Statements Employed		
Database	**Search Statement**	**Number of Results**
Medline (EBSCO)	((MH “Pressure Ulcer”) OR (TI “pressure ulcer*”)) AND ((MH “intensive care”) OR (MH “intensive care units”) OR (TI intensive care unit*) OR (TI “critical care”))	243
Medline (EBSCO)	((MH “Intensive Care Units+”) OR (MH “Critical Care+”)) AND (MH “Pressure Ulcer+”)	334
PubMed	(pssure injur*[TI] OR pressure ulcer*[TI] OR pressure sore*[TI] OR bed sore*[TI] OR bedsore*[TI] OR decubital ulcer*[TI] OR decubitus ulcer*[TI] OR ulcus decubitus[TI] OR “Pressure Ulcer”[Mesh]) AND (“Critical Care”[Mesh] OR “Intensive Care Units”[Mesh] OR “Burn Units”[Mesh] OR “Coronary Care Units”[Mesh] OR “Intensive Care Units, Pediatric”[Mesh] OR “Intensive Care Units, Neonatal”[Mesh] OR “Recovery Room”[Mesh] OR “Respiratory Care Units”[Mesh] OR “Critical Illness”[Mesh] OR “Critical Care Nursing”[Mesh] OR “Critical Care Outcomes”[Mesh] OR critical care[TI] OR Critically Ill[TI] OR critical ill*[TI] OR intensive care[TI] OR cardiovascular unit*[TI] OR coronary care[TI] OR Cardiac Care[TI] OR neurocritical care[TI] OR neurointensive care[TI] OR step-down unit*[TI] OR step down unit*[TI] OR burn unit*[TI] OR high dependency unit*[TI] OR neurosurgical unit*[TI] OR surgical intensive care[TI] OR Recovery Room*[TI] OR recovery unit*[TI] OR observation unit*[TI] OR observational unit*[TI] OR Respiratory Care[TI] OR ICU[tiab] OR ICUs[tiab] OR NICU[tiab] OR NICUs[tiab] OR CCU[tiab] OR CCUs[tiab] OR SICU[tiab] OR SICUs[tiab])	441
CINAHL (EBSCO)	((MH “Intensive Care, Neonatal+”) OR (MH “Intensive Care Units+”) OR (MH “Critical Care+”) OR (TI “intensive care”) OR (TI “critical care”)) AND ((MH “Pressure Ulcer+”) OR (TI “Pressure Ulcer”) OR (TI “Pressure ulcers”))	506
Cochrane	pressure ulcer* AND (“intensive care” unit* OR “intensive care” OR “critical care”) in Title, abstract, kw	113
Scopus	pressure ulcer* AND (“intensive care” unit* OR “intensive care” OR “critical care”) in Title, abstract, kw	926
Dissertations and Theses	su(pressure ulcer*) AND su((intensive care OR critical care))	9
Dissertations and Theses	diskw(pressure ulcer*) AND diskw((intensive care OR critical care))	8

Note. NLM subject headings: https://www.nlm.nih.gov/mesh/. With regard to database selection: Though the material indexed in Medline is also included in NLM PubMed, the search algorithms can vary between interface providers, as can post-limit features and other options, and thus can yield slightly different results sets.

Appendix B Quality Appraisal of Observational Studies of Pressure Ulcer Risk in Critical Care

Domain	Major flaws	Moderate Flaws	Indeterminate Flaws
Methods for selecting participants	(More than 25% of sample lost to follow up and missing records were exclusion criteria for the current review.)	≥15% of the population lost to follow up or missing records Restricted sampling, resulting in limited generalizability The study sampled from high-risk patients on a risk-assessment scale and then included the factors in the scale as potential predictor variables; or, very restricted sampling frame that resulted in limited generalizability	Inclusion/exclusion criteria are unclear
Statistical methods and control of confounding	Clearly incorrect statistical methods Inadequate number of events (pressure ulcers) for analysis: <10 pressure ulcers per variable included in the multivariate analysis[10,43]	Nonindependent factors are included in analysis without appropriate adjustment[10] Time-dependent covariates (e.g., blood pressure) included without appropriate adjustment[10] Selective reporting of results[9] Inappropriate strategy for model building[3] Unclear statistical reporting: • Multivariate statistical significance is only reported for variables deemed significant (for underpowered studies, it is not possible to tell which variables were close and may be significant if the study was adequately powered) • Despite the presence of missing data, the authors do not describe how missing data were handled Problematic statistical methods: • Poor model fit or no reporting of model fit • Significance tests for predictors not reported	Unclear statistical reporting
Methods for measuring exposure	Temporal ambiguity: it is possible that the predictor variable occurred *after* the pressure ulcer event.	Variable operationalization is unclear or misleading. Incomplete data for predictor variables • Despite the presence of missing data, no description of how missing data were handled; or missing data were handled inappropriately	No reporting of missing data for predictor variables despite high likelihood of missing data
Methods for measuring outcome variable	No criteria for wound designation as a pressure ulcer (e.g., NPUAP/EPUAP ≥category 1 or equivalent)	Nurses who were not wound nurses and not specially trained identified or categorized pressure ulcers.	Limited description of the outcome variable (e.g., no staging information)
Conflict of interest	Evidence of conflict of interest, with major	Evidence of conflict of interest, with minor implications for study results	Evidence of conflict of interest, with unclear implications for study results

Domain	Major flaws	Moderate Flaws	Indeterminate Flaws
	implications for study results		

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*43*Peduzzi PJ, Concato AR, Feinstein X, Holford TR. Importance of events per independent variable in proportional hazards regression analysis. II. Accuracy and precision of regression estimates. *J Clin Epidemiol*. 1996;48(12):1503–1510.

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What is already known about this topic?

- Critical care patients are exposed to unique potential risk factors for pressure injury (PI) development, such as vasopressor infusion and the effects of severe illness.
- Although studies have examined PI risk among critical care patients, there is little consensus about which factors influence PI risk in the critical care population.

What this paper adds

- Age, mobility/activity, poor perfusion, and vasopressor infusion are risk factors for pressure-injury development among critical care patients.
- Future research is needed to evaluate risk conferred by malnutrition, and skin/pressure injury status.
- Future research is also needed to further elucidate risk conferred by specific perfusion related variables including high doses of vasopressors, combinations of vasopressors, and duration of decreased oxygen delivery to tissues (hypotension and/or decreased blood oxygen content).

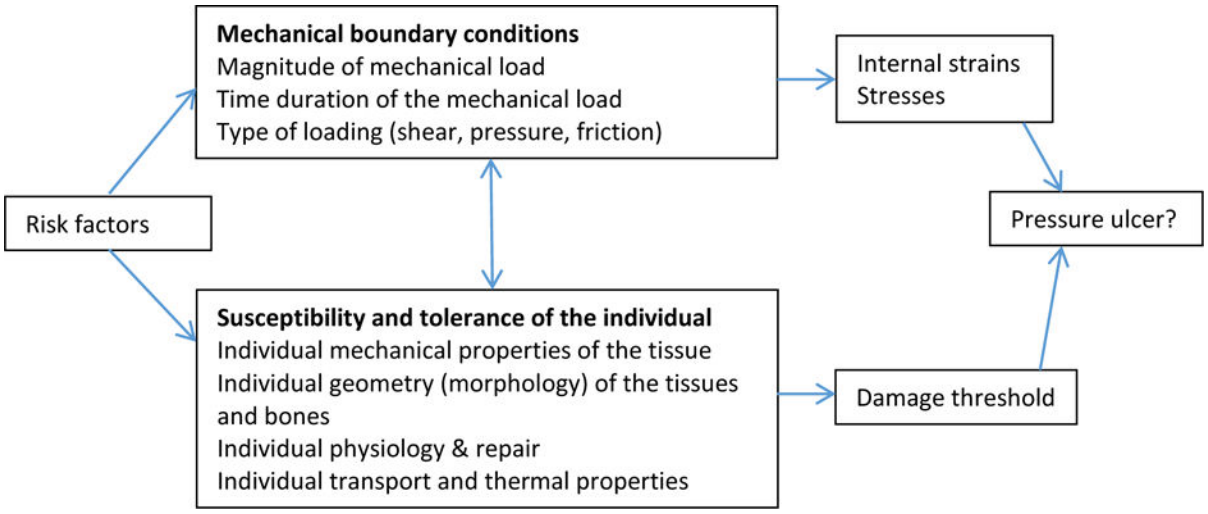

Figure 1.

Enhancement of NPUAP/EPUAP (2009) factors that influence susceptibility for pressure ulcer development (Coleman et al., 2014, p. 2229, used with permission).

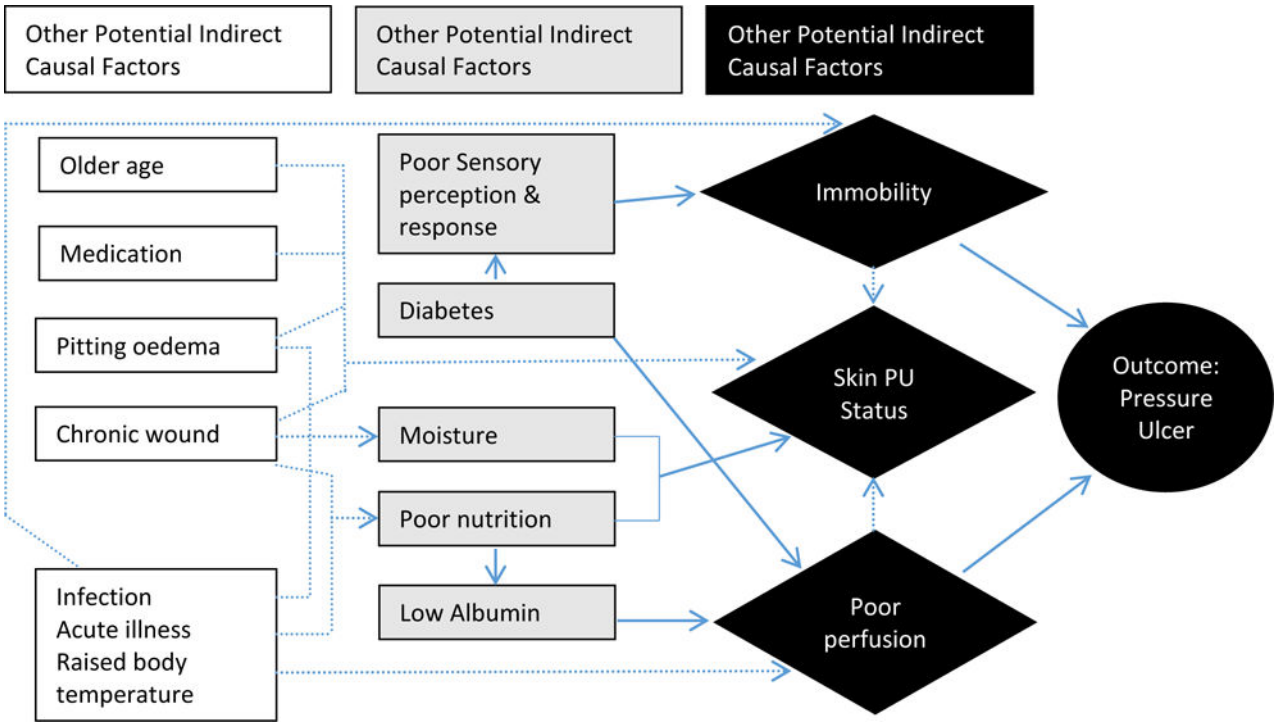

Figure 2.

Theoretical schema of proposed causal pathway for pressure ulcer development. The solid arrows show the causal relationship between the key indirect causal factors and the outcome. Interrupted arrows show the causal relationship between other potential indirect causal factors and key indirect causal factors and between direct causal factors. Interrupted arrows also demonstrate interrelationships between direct causal factors and indirect causal factors (Coleman et al, 2014, p. 2229, used with permission).[11]

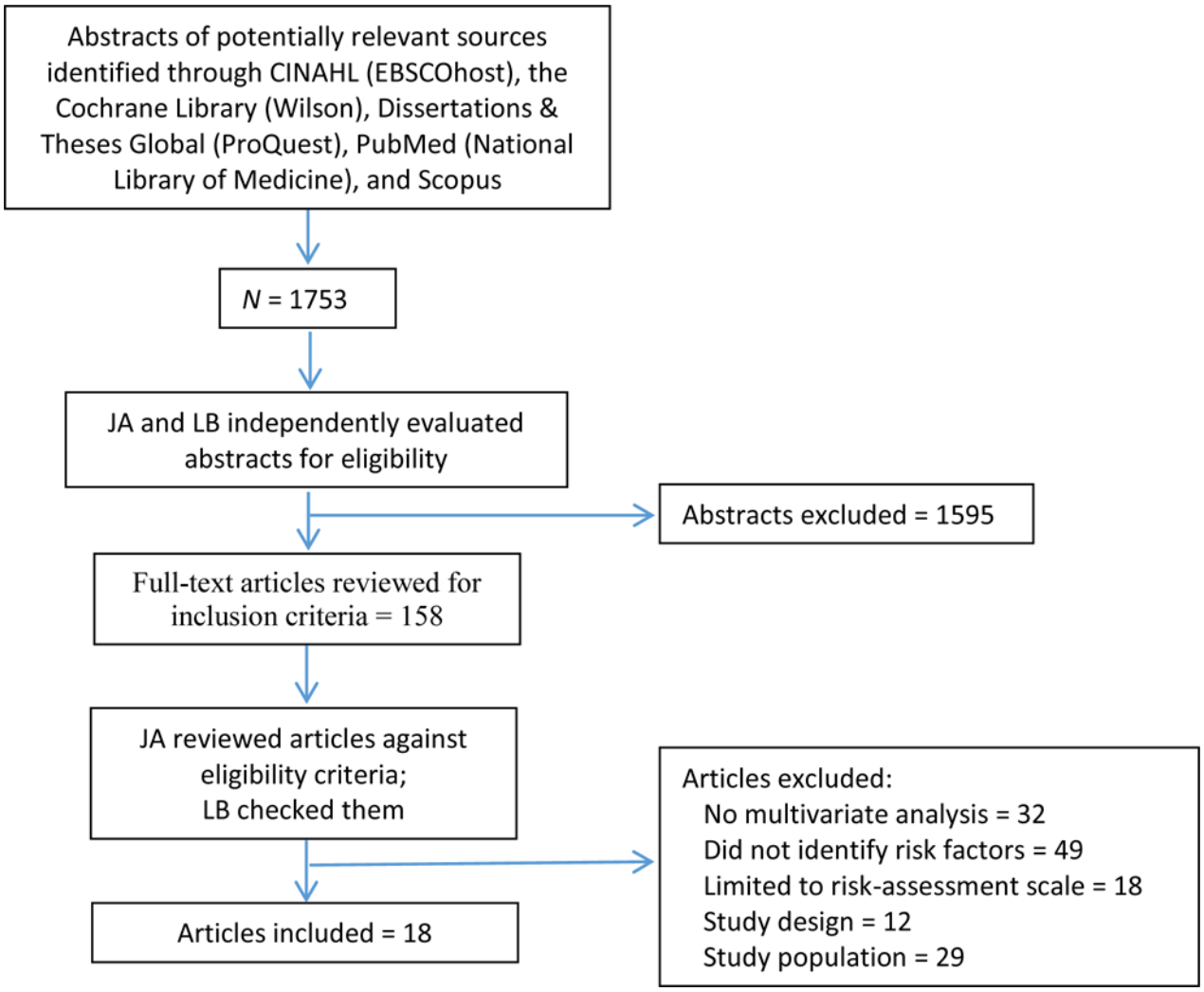

Figure 3.
Decision Process

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Table 1

Summary of Studies

Study Authors	Sample and Country	Inclusion Criteria	Design and Analysis	No. in Final Model (PI%), No. of PI and Category	Results: No. of Risk Factors (No. in Model), Model Risk-Factor Names: Odds Ration (95% Confidence Interval)	Study Quality
Compton et al.[28]	713 general ICU patients in Germany	≥72-hour stay No pressure injury upon admission	Retrospective record review Logistic regression	698 (17%), 121 Categories 2–4	32 (6) Male gender: 1.8 (NR) Moist skin: 2.4 (NR) Edematous skin: 2.2 (NR) Centralized circulation: 2.4 (NR) Mottled skin: 2.0 (NR) Reddened skin: 2.3 (NR)	MQS
Cox[11]	347 medical–surgical ICU patients in the United States	≥24-hour stay No pressure injuey upon admission Age ≥18 years	Retrospective record review Logistic regression	Model 1: 347 (18.7%), 65 ≥Category 1 Model 2: 327 (13.7%), 45 ≥Category 2	Model 1: 15 (4) Mobility: 0.439 (0.21–0.95) Age: 1.033 (1.003–1.064) Length of ICU stay: 1.008 (1.005–1.011) Cardiovascular disease: 2.952 (1.3–6.4) Model 2: 15 (4) Friction/shear: 5.715 (1.423–22.95) Length of ICU stay: 1.008 (1.004–1.012) Norepinephrine: 1.017 (1.001–1.033) Cardiovascular disease: 3.380 (1.223–9.347)	HQS
Cox & Roche[17]	306 medical, surgical, and cardiothoracic ICU patients in the United States	≥24-hour stay No pressure injury upon admission Age ≥18 Received a vasopressor during ICU stay	Retrospective record review Logistic regression	306 (13%), 41 ≥Category 1	11 (5) Cardiac arrest: 3.894 (0.998–15.118) Mechanical ventilation ≥72 hours: 23.604 (0.998–15.118) Hours of MAP less than 60 mm HG while on vasopressors: 1.096 (1.020–1.178) Vasopressin: 4.816 (1.666–13.925) Cardiac diagnosis at admission: 0.035 (0.002–0.764)	HQS
Cremasco et al.[1]	160 modical–surgical ICU patients in three ICUs in	≥24-hour stay No pressure injury upon admission	Prospective cohort Logistic regression	160 (34.4%), 55, Category not reported	NR (4) Male gender: 5.4 (1.42–22.09) Length of ICU stay: 1.120 (1.943–1.202) SAPSI score: 1.058 (1.004–1.114)	LQS
	Brazil				NAS score: 0.916 (0.855–0.980)	
Eachempati et al.[31]	Phase 2: 412 surgical ICU patients in the United States	Length of stay>7 days	Prospective cohort Logistic regression	55 (60%), 33 ≥Category 2	7 (5) Emergent admission: 36 (0.2290–0.7694) Age: –0.0131) Days in bed: 1.05 (−0.0013–0.0156) CURS day 8: 1.45 (−0.0048–−0.0833) Days without any nutrition: 0.51 (−0.1095– −0.0334)	VLQS

Study Authors	Sample and Country	Inclusion Criteria	Design and Analysis	No. in Final Model (PI%), No. of PI and Category	Results: No. of Risk Factors (No. in Model), Model Risk-Factor Names: Odds Ration (95% Confidence Interval)	Study Quality
Fife et al.[29]	186 neurologic ICU patients in the United States	No pressure injury upon admission No diagnosis of brain death on life support pending organ donation	Prospective cohort Logistic regression	186 (12%), 23 ≥Category 2	NR (2) Braden score: NR (NR) Low body mass index (BMI): NR (NR)	MQS
Frankel et al.[2]	820 surgical ICU patients in the United States	Not reported	Retrospective record review Logistic regression	820 (3%), 25 ≥Category 2	9 (4) Diabetes: 2.7 (1.1–6.4) Age: 2.9 (1.2–7.1) Creatinine: 3.7 (1.2–9.2) Spinal cord injury: 16.8 (1.5–182)	MQS
Kaitani et al.[23]	98 ICU and high-care-unit patients in Japan	Age≥20 years No pressure injury upon admisison ≥24-hour stay Unable to make major and frequent position changes independently	Prospective cohort Logistic regression	98 (11.2%), 11 Categories 1–4	6 (2) Scheduled admission: 0.04 (0–0.47) Frequency of turning: 0.45 (0.21–0.97)	LQS
Manzano et al.[21]	299 patients in nine ICUs in Spain	Mechanical ventilation Age≥18 years Nonpregnant	Prospective cohort Logistic regression	299 (15.7%), 47 ≥Category 2	16 (5) Day 1 respiratory SOFA: 1.56 (1.026–2.360) Day 4 cardiovascular SOFA: 1.33 (1.066–1.664) Age: 1.042 (1.013–1.072) Winter: 4.6 (1.99–10.59) Length of mechanical ventilation: 1.042 (1.005–1.080)	HQS
Nijs et al.[22]	520 surgical ICU patients in Belgium	Age≥16 years ≥24-hour expected stay Absence of burns	Prospective cohort Logistic regression	463 (28.9%), 134 Categories 2–4	19 (9) Dopamine <5 mcg/kg/min: 6.1 (1.9–19.5) Vascular disease: 4.5 (2.0–10.2) Dialysis: 3.8 (1.0–13.9) “Adequate prevention”: 6.0 (1.9–18.6) Frequency of turning six or more times daily or alternating mattress: 30.2 (12.2–74.8) “Turning”: 6.7 (2.7–16.4) Sedative use: 0.3 (0.1–0.7) Body temperature≤38.5: 0.2 (0.2–0.9) Sitting in chair: 0.1 (0.0–0.3)	HQS
O’Brien et al.[19]	2695 surgical and burn ICU patients in the United States	Age≥18 years ≥48-hour ICU stay Underwent a surgical procedure No pressure injury upon admission	Retrospective record review	2695 (10.7%), 288 ≥Category 2	12 (7) Existing airway: 5.28 (3.63–7.67) Low BMI: 2.7 (1.45–5.04) Noncardiac surgery: 1.84 (1.31–2.59) History of heart failure: 1.78 (1.27–2.49) History of renal failure: 1.75 (1.27–2.39) ASA class 4 or 5: 1.63 (1.19–2.29) Age: 1.02 (1.01–1.03)	HQS

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Study Authors	Sample and Country	Inclusion Criteria	Design and Analysis	No. in Final Model (PI%), No. of PI and Category	Results: No. of Risk Factors (No. in Model), Model Risk-Factor Names: Odds Ration (95% Confidence Interval)	Study Quality
Sayar et al.[24]	140 medical–surgical ICU patients in Turkey	At risk or at high risk on Waterlow pressure ulcer risk scale	Prospective cohort Logistic regression	140 (14.3%), 20 ≥Category 1	5 (2) Length of stay: 1.2 (1.1–1.3) Activity level: 0.3 (.02–0.7)	MQS
Slowikowski & Funk[4]	369 surgical ICU petients in the United States	Age≥16 years	Prospective cohort Logistic regression	369 (23.9%), 88, Category not reported	8 (3) Braden Scale score: 1.3 (1.15–1.47) Diabetes: 1.93 (1.11–3.35) Age≥70 years: 2.14 (1.27–3.62)	HQS
Suriadi et al.[18]	253 general ICU patients in Indonesia	Age≥18 years Bedfast No pressure injury upon admission ≥24-hour stay and anticipated stay≥72 hours	Prospective cohort Logistic regression	253 (28.4%), 72 ≥Category 1	NR (3) Interface pressure: 2.2 (1.6–2.9) Body temperature: 2.0 (1.7–2.5) Cigarette smoking: 1.6 (1.1–2.5)	HQS
Tayyib et al.[25]	84 general ICU patients in Saudi Arabia	Age≥18 years	Prospective cohort	84 (39.3%), 33 Categories 1–4	Model 1 Categories 1–4: 7 (3) Age: 1.254 (1.054–1.492) Longer ICU stay: 1.23 (1.014–3.309) Infrequent repositioning: 250.04 (230–11,954.16) Model 2 Categories 2–4: 3 (2) Longer ICU stay: 1.831 (1.054–1.492) Infrequent repositioning: 2.96 (1.23–7.153)	MQS
Theaker et al.[26]	286 general ICU patients in the United Kingdom	>24-hour stay No pressure injury upon admission Three or more pressure injury risk factors	Prospective cohort Logistic regression	286 (26.9%), 77 Categories 2–4	18 (5) Norepinephrine infusion: 8.11 (3.64–18) APACHE II≥13: 2.4 (1.4–7.92) Fecal incontinence: 3.27 (1.32–8.3) Anemia: 2.81 (1.24–6.34) Length of stay≥three days: 2.76 (1.06–7.05)	LQS
Ulker Efteli &Yapucu Gunes[27]	70 general ICU patients in Turkey	Age≥18 years Expected ICU stay≥7 days No pressure injury upon admission Braden Scale score<12	Prospective cohort Logistic regression	70 (33%), 23 ≥Category 1	6 (2) Female gender: 0.15 (0.03–0.71) Lower serum albumin level: 11.6 (1.92–70.4)	MQS
Yepes et al.[30]	150 ICU patients in Bolivia	Intubated On mechanical ventilation Received vasopressor	Prospective cohort Logistic regression	150 (26.7%), 40 ≥Category 2	3 (3) Presence of infection: 4.39 (6.92–18.25) Length of stay in the ICU: 1.13 (1.06–1.22) APACHE II: 1.06 (1.0–1.12)	LQS

NR = not reported

PI = pressure injury

ICU = intensive care unit

NR = not reported

MQS = moderate-quality study

HQS = high-quality study

MAP = mean arterial pressure

LQS = low-quality study

SAPSI = Simplified Acute Physiology Score

NAS = nursing activities score

VLQS = very-low-quality study

CURS = Corneil ulcer risk score

SOFA = sequential organ failure assessment

ASA = American Society of Anesthesiologists

APACHE =acute physiology and chronic health evaluation

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Table 2

Study Quality: Potential Bias

Study	Methods for Selecting Participants	Statistical Methods and Control of Confounding	Methods for Measuring Exposure	Methods for Measuring Outcome Variable	Conflict of Interest	Notes and Quality Appraisal
Compton et al.[28]	–	Major: Inadequate number of events for analysis Moderate: Unclear statistical reporting	–	Moderate: Nurses who were not specially trained identified pressure injuries	–	LQS Strength: Used an independent cohort to validate model
Cox[20]	–	Note on events for analysis: The author included a power analysis indicating there were enough events.	–	Moderate: Nurses who were not specially trained identified pressure injuries	–	HQS
Cox & Roche[17]	–	–	–	–	–	HQS
Cremasco et al.[1]	–	Major: Inadequate number of events for analysis Moderate: Unclear statistical reporting Moderate: Non-independent factors included in the analysis without appropriate adjustment	–	Major: No criteria for designation of wound as a pressure injury Moderate: Nurses who were not specially trained identified pressure injuries Moderate: Limited description of the outcome variable	–	VLQS
Eachempati et al.[31]	Moderate: Restricted sampling (included only patients with LOS>6 days) Moderate: Unclear inclusion/exclusion criteria	Major: Clearly incorrect statistical methods Moderate: Inappropriate strategy for model building	–	Major: No criteria for designation of wound as a pressure injury Moderate: Nurses who were not specially trained identified pressure injuries Moderate: Limited description of the outcome variable	–	VLQS
Fife et al.[29]	–	Major: Inadequate number of events for analysis Moderate: Unclear statistical reporting	–	Moderate: Limited description of the outcome variable	–	LQS
Frankel et al.[2]	Indeterminate: Individuals appear to have been excluded from the study but the inclusion/exclusion criteria are not defined	Major: Inadequate number of events for analysis	–	Moderate: Nurses who were not specially trained identified pressure injuries	–	LQS
Kaitani et al.[23]	–	Major: Inadequate number of events for analysis Moderate: >15% lost to follow up or missing records/inadequate data collection Moderate: Inappropriate strategy for model building	Moderate: Variable operation is unclear	–	–	LQS

Study	Methods for Selecting Participants	Statistical Methods and Control of Confounding	Methods for Measuring Exposure	Methods for Measuring Outcome Variable	Conflict of Interest	Notes and Quality Appraisal
Manzano et al.[21]	–	Major: Inadequate number of events for analysis	Indeterminate: No reporting of missing data for predictor variables despite high likelihood of missing data	–	–	MQS
Nijs et al.[22]	–	Major: Inadequate number of events for analysis Moderate: Problematic statistical methods with moderate implications for study findings	Indeterminate: Potential temporal ambiguity (it is possible that the predictor variable occurred after the pressure ulcer event)	–	–	MQS
O'Brien et al.[19]	–	–	–	Moderate: Nurses who were not specially trained identified pressure injuries	–	HQS
Sayar et al.[24]	–	Moderate: Sampled from "high-risk" patients on a risk-assessment scale and then included attributes of the same scale as predictor variables	Moderate: Non-independent factors are included in the analysis without proper adjustment Moderate: Selective reporting of results Moderate: Unclear statistical reporting	–	–	LQS
Slowikowski & Funk[4]	–	–	–	Moderate: Limited description of the outcome variable	–	HQS
Suriadi et al.[18]			Moderate: Unclear statistical reporting	–	–	HQS
Tayyib et al.[25]	–	Major: Inadequate number of events for analysis Moderate: Nonindependent factors included in the analysis without appropriate adjustment	–	Moderate: Nurses who were not specially trained identified pressure injuries	–	LQS
Theaker et al.[26]	–	Major: Inadequate number of events for analysis Moderate: >15% lost to follow up or missing records Moderate: Nonindependent factors included in the analysis without appropriate adjustment	–	Moderate: Nurses who were not specially trained identified pressure injuries Moderate: Limited description of the outcome variable	–	LQS
Ulker Efteli & Yapucu Gunes[27]	Moderate: Restricted sampling (included only patients with LOS>6 days)	Major: Inadequate number of events for analysis	–	Moderate: Nurses who were not specially trained identified pressure injuries	–	LQS

Int J Nurs Stud. Author manuscript; available in PMC 2018 June 01.

Study	Methods for Selecting Participants	Statistical Methods and Control of Confounding	Methods for Measuring Exposure	Methods for Measuring Outcome Variable	Conflict of Interest	Notes and Quality Appraisal
Yepes et al.[30]	Moderate: Restricted sampling (included only patients on mechanical ventilation and vasopressor support)	Moderate: Nonindependent factors included in the analysis without appropriate adjustment Moderate: Unclear statistical reporting	–	Moderate: Nurses who were not specially trained identified pressure injuries	–	LQS

Table 3

Summary of Evidence for Risk Factor Domains and Subdomains

Variable	Studies With Variable Significant in Multivariate Model Study Quality (Study Authors) Variable: Odds Ratio (95% Confidence Interval)	Studies With Variable Not Significant in Multivariate Model Study Quality (Study Authors) Variable
Domain 1: Mechanical Boundary Conditions		
Body size	–	MQS (Manzano et al.[21]) Body weight LQS (Compton et al.[28]) Body weight and height
Friction and shear	HQS (Cox[20]) Friction/shear: 5.715 (1.423–22.95)	–
Emergent vs. scheduled admission	LQS (Kaitani et al.[23]) Scheduled admission: 0.04 (0–0.47) VLQS (Eachempati et al.[31]) Emergent admission: 36 (0.2290–0.7694)	HQS (O'Brien et al.[19]) Emergent admission MQS (Manzano et al.[21]) Type of admission (medical vs. surgical) LQS (Tayyib et al.[25]) Emergent admission LQS (Kaitani et al.[23]) Admission type
Domain 1 Subdomain: Immobility		
Mental/neurologic status	–	MQS (Nijs et al.[22]) GCS: opens eyes MQS (Nijs et al.[22]) GCS: movement, localizes pain MQS (Nijs et al.[22]) GCS: movement, follows commands LQS (Compton et al.[28]) Minimum GCS LQS (Compton et al.[28]) Maximum GCS LQS (Sayar et al.[24]) Consciousness LQS (Sayar et al.[24]) Cooperation LQS (Theaker et al.[26]) Pain
Mobility/activity	HQS (Cox[20]) Mobility: 0.439 (0.21–0.95) LQS (Sayar et al.[24]) Activity level: 0.3 (0.2–0.7)	–
Sensory perception	–	HQS (Cox[20]) Sensory perception
Surgical factors	HQS (O'Brien et al.[19]) Noncardiac surgery: 1.84 (1.31–2.59)	LQS (Tayyib et al.[25]) Operation time
Turning/repositioning and surface	HQS (Suriadi et al.[18]) Interface pressure: 2.2 (1.6–2.9) MQS (Nijs et al.[22]) "Adequate prevention": 6.0 (1.9–18.6) MQS (Nijs et al.[22]) Frequency of turning six or more times daily or alternating mattress: 30.2 (12.2–74.8) MQS (Nijs et al.[22]) "Turning": 6.7 (2.7–16.4) MQS (Nijs et al.[22]) Sitting in chair: 0.1 (0.0–0.3) LQS (Tayyib et al.[25]) Infrequent repositioning: 2.96 (1.23–7.153) LQS (Kaitani et al.[23]) Frequency of turning: 0.45 (0.21–.0.97)	HQS (Slowikowski & Funk[4]) Not repositioned LQS (Theaker et al.[26]) Too unstable to turn
Domain 2: Susceptibility and Tolerance of the Individual		
Age	HQS (Cox[20]) Age: 1.033 (1.003–1.064) HQS (O'Brien et al.[19]) Age: 1.02 (1.01–1.03) HQS (Slowikowski & Funk[4]) Age≥70 years: 2.14 (1.27–3.62) MQS (Frankel et al.[2]) Age: 2.9 (1.2–7.1) LQS (Tayyib et al.[25]) Age: 1.254 (1.054–1.492) VLQS (Eachempati et al.[31]) Age: 1.08 (0.0026–0.0131)	MQS (Manzano et al.[21]) Age
Body temperature	HQS (Suriadi et al.[18]) Body temperature: 2.0 (1.7–2.5)	LQS (Compton et al.[28]) Maximum body temperature

Variable	Studies With Variable Significant in Multivariate Model Study Quality (Study Authors) Variable: Odds Ratio (95% Confidence Interval)	Studies With Variable Not Significant in Multivariate Model Study Quality (Study Authors) Variable
	MQS (Nijs et al.[22]) Body temperature≥38.5: 0.2 (0.2–0.9)	
Diagnosis (excepting diagnosis related to oxygenation and perfusion, included below under Subdomain: Poor Perfusion)	HQS (O'Brien et al.[19]) History of renal failure: 1.75 (1.27–2.39) LQS (Frankel et al.[2]) Spinal cord injury: 16.8 (1.5–182) LQS (Yepes et al.[30]) Presence of infection: 4.39 (6.92–18.25)	HQS (O'Brien et al.[19]) History of liver disease MQS (Manzano et al.[21]) Multiple organ failure MQS (Nijs et al.[22]) Gastrointestinal diagnosis LQS (Tayyib et al.[25]) History of kidney disease
Laboratory values (excepting values related to oxygenation and perfusion, included below under Subdomain: Poor Perfusion)	LQS (Frankel et al.[2]) Creatinine: 3.7 (1.2–9.2) LQS (Theaker et al.[26]) Anemia: 2.81 (1.24–6.34)	HQS (Cox & Roche[17]) Severe anemia LQS (Compton et al.[26]) Maximum serum potassium LQS (Compton et al.[28]) Maximum creatinine LQS (Compton et al.[28]) Maximum blood glucose LQS (Compton et al.[28]) Maximum c-reactive protein LQS (Compton et al.[28]) Minimum thromboplastin time LQS (Compton et al.[28]) Maximum serum bilirubin LQS (Ulker Efteli & Yapucu Gunes[27]) Hemoglobin LQS (Ulker Efteli & Yapucu Gunes[27]) Blood glucose LQS (Sayar et al.[24]) C-reactive protein LQS (Theaker et al.[26]) Coagulopathy
Length of stay	HQS (Cox[20]) Length of ICU stay: 1.008 (1.005–1.011) LQS (Sayar et al.[24]) Length of stay: 1.2 (1.1–1.3) LQS (Tayyib et al.[25]) Longer ICU stay: 1.831 (1.014–3.309) LQS (Yepes et al.[30]) Length of stay: 1.13 (1.06–1.22) LQS (Theaker et al.[26]) Length of stay > 3 days: 2.76 (1.08–7.05) VLQS (Cremasco et al.[1]) Length of ICU stay: 1.120 (1.943–1.202) VLQS (Eachempati et al.[31]) Days in bed: 1.05 (−0.0013–0.0156)	HQS (Cox & Roche[17]) Hospital length of stay HQS (Cox & Roche[17]) Length of stay before ICU admission HQS (Cox & Roche[17]) ICU length of stay MQS (Manzano et al.[21]) ICU length of stay MQS (Manzano et al.[21]) Pre-ICU hospital stay LQS (Compton et al.[28]) Duration of ICU stay
Medication (excepting vasopressors) and treatments	MQS (Nijs et al.[22]) Sedative use: 0.3 (0.1–0.7) MQS (Nijs et al.[22]) Dialysis: 3.8 (1.0–3.9)	HQS (O'Brien et al.[19]) Current corticosteroid use HQS (Slowikowski & Funk[4]) Orthotics HQS (Slowikowski & Funk[4]) Hemodialysis MQS (Nijs et al.[22]) Physical fixation MQS (Nijs et al.[22]) Major analgesics MQS (Nijs et al.[22]) "Floating heels" LQS (Compton et al.[28]) Sedation LQS (Compton et al.[28]) Insulin therapy LQS (Theaker et al.[26]) Current corticosteroid use
Nutrition and laboratory values related to nutrition status	LQS (Ulker Efteli & Yapucu Gunes[27]) Lower serum albumin level: 11.6 (1.92–70.4) VLQS (Eachempati et al.[31]) Days without any nutrition 0.51 (−0.1095–−0.0334)	HQS (Cox[20]) Nutrition LQS (Compton et al.[28]) Parenteral nutrition LQS (Kaitani et al.[23]) Nutrition LQS (Theaker et al.[26]) Serum albumin LQS (Theaker et al.[26]) Reduced nutritional intake
Severity of illness/health status	HQS (Cox & Roche[17]) Cardiac arrest: 3.894 (0.998–15.118) HQS (O'Brien et al.[19]) ASA class 4 or 5: 1.63 (1.19–2.23)	HQS (Cox[20]) APACHE HQS (Cox & Roche[17]) APACHE II HQS (Cox & Roche[17]) Died in ICU MQS (Manzano et al.[21]) Hospital mortality

Variable	Studies With Variable Significant in Multivariate Model Study Quality (Study Authors) Variable: Odds Ratio (95% Confidence Interval)	Studies With Variable Not Significant in Multivariate Model Study Quality (Study Authors) Variable
	MQS (Manzano et al.[21]) Day 1 respiratory SOFA: 1.56 (1.026–2.360) MQS (Manzano et al.[21]) Day 4 cardiovascular SOFA: 1.33 (1.066–1.664) LQS (Yepes et al.[30]) APACHE II: 1.06 (1.0–1.12) LQS (Theaker et al.[26]) APACHE II> 13: 2.4 (1.4–7.92) VLQS (Cremasco et al.[1]) SAPSII score: 1.058 (1.004–1.114)	MQS (Nijs et al.[22]) APACHE II LQS (Ulker Efteli & Yapucu Gunes[27]) APACHE II LQS (Compton et al.[28]) ICU mortality LQS (Compton et al.[28]) TISS LQS (Kaitani et al.[23]) APACHE II LQS (Theaker et al.[26]) Peripheral vascular disease VLQS (Eachempati et al.[31]) MODS VLQS (Eachempati et al.[31]) APACHE III
Domain 2 Subdomain: Poor Perfusion *Including Factors That Affect Oxygenation and Perfusion Status/Delivery of Oxygen to the Tissues*		
Blood pressure	HQS (Cox & Roche[17]) Hours of MAP less than 60 mm HG while on vasopressors: 1.096 (1.020–1.178)	HQS (Cox[20]) Mean arterial pressure HQS (Cox[20]) Systolic blood pressure HQS (Cox[20]) Diastolic blood pressure
Diagnosis related to oxygenation and/or perfusion (also included in global diagnosis, above)	HQS (Cox[20]) Cardiovascular disease: 2.952 (1.3–6.4) HQS (Cox & Roche[17]) Cardiac diagnosis at admission: 0.035 (0.002–0.764) HQS (O'Brien et al.[19]) History of heart failure: 1.78 (1.27–2.49) HQS (Slowikowski & Funk[4]) Diabetes: 1.93 (1.11–3.35) HQS (Suriadi et al.[18]) Cigarette smoking: 1.6 (1.1–2.5) MQS (Nijs et al.[22]) Vascular disease: 4.5 (2.0–10.2) LQS (Frankel et al.[2]) Diabetes: 2.7 (1.1–6.4)	HQS (O'Brien et al.[19]) History of diabetes MQS (Manzano et al.[21]) Septic shock MQS (Manzano et al.[21]) Acute respiratory distress syndrome LQS (Frankel et al.[2]) Vascular disease LQS (Compton et al.[28]) Sepsis LQS (Tayyib et al.[25]) History of cardiovascular disease LQS (Theaker et al.[26]) Diabetes LQS (Theaker et al.[26]) History of smoking
Heart rate and monitoring		LQS (Compton et al.[28]) Maximum heart rate LQS (Compton et al.[28]) Invasive monitoring
Oxygenation/ventilation	HQS (Cox & Roche[17]) mechanical ventilation longer than 72 hours: 23.604 (6.427–86.668) HQS (O'Brien et al.[19]) existing airway: 5.28 (3.63–7.67) MQS (Manzano et al.[21]) length of mechanical ventilation: 1.042 (1.005–1.080)	HQS (Slowikowski & Funk[4]) Ventilator support MQS (Manzano et al.[21]) Pa02/Fi02 ratio on Day 1 MQS (Nijs et al.[22]) Mechanical ventilation LQS (Compton et al.[28]) Minimum PaCO2 LQS (Compton et al.[28]) Minimum arterial pH LQS (Compton et al.[28]) Mechanical ventilation LQS (Compton et al.[28]) Cyanosis LQS (Tayyib et al.[25]) Mechanical ventilation
Vasopressor	HQS (Cox[20]) Norepinephrine: 1.017 (1.001–1.033) HQS (Cox & Roche[17]) Vasopressin infusion: 4.816 (1.666–13.925) MQS (Nijs et al.[22]) Dopamine<5 mcg/kg/min: 6.1 (1.9–19.5) LQS (Theaker et al.[26]) Norepinephrine infusion: 8.11 (3.64–18)	LQS (Compton et al.[28]) Vasopressor therapy LQS (Frankel et al.[2]) Vasopressor therapy LQS (Theaker et al.[26]) Dopamine LQS (Theaker et al.[26]) Epinephrine LQS (Theaker et al.[26]) Norepinephrine
Domain 2 Subdomain: Skin/Pressure Injury Status *Including Factors That Affect Skin and Pressure Injury Status*		
Moisture	LQS (Compton et al.[28]) Moist skin: 2.4 (NR)	LQS (Theaker et al.[26]) Moisture
Skin/external skin factors/PI status	LQS (Compton et al.[28]) Edematous skin: 2.2 (NR) LQS (Compton et al.[28]) Centralized circulation: 2.4 (NR) LQS (Compton et al.[28]) Mottled skin: 2.0 (NR) LQS (Compton et al.[28]) Reddened skin: 2.3, (NR) LQS (Theaker et al.[26]) Fecal incontinence: 3.27 (1.32–8.3)	HQS (Cox & Roche[17]) Peripheral necrosis in patients receiving vasopressors HQS (Slowikowski & Funk[4]) Edema MQS (Nijs et al.[22]) Pitting edema LQS (Compton et al.[28]) Livid skin LQS (Compton et al.[28]) Hyperemic skin LQS (Kaitani et al.[23]) Edema

Variable	Studies With Variable Significant in Multivariate Model Study Quality (Study Authors) Variable: Odds Ratio (95% Confidence Interval)	Studies With Variable Not Significant in Multivariate Model Study Quality (Study Authors) Variable
		LQS (Theaker et al.[26]) Edema
Other Factors Not Included In Domains 1 or 2		
Gender	LQS (Ulker Efteli & Yapucu Gunes[27]) Female gender:0.15 (0.03–0.71) LQS (Compton et al.[28]) Male gender: 1.8 (NR) VLQS (Cremasco et al.[1]) Male gender: 5.6 (1.42–22.09)	LQS (Kaitani et al.[23]) gender G
Risk-assessment scales	HQS (Slowikowski & Funk[4]) Braden Scale score: 1.3 (1.15–1.47) LQS (Fife et al.[29]) Braden Scale score: NR (NR) VLQS (Eachempati et al.[31]) CURS Day 8: 1.45 (−0.0048–−0.0833)	HQS (Cox[20]) Braden Scale total HQS (Cox & Roche[17]) Braden Scale at hospital admission HQS (Cox & Roche[17]) Braden Scale at ICU admission LQS (Compton et al.[28]) Waterlow score LQS (Tayyib et al.[25]) Braden Scale score
Other factors	MQS (Manzano et al.[21]) Winter admission: 4.6 (1.99–10.59) VLQS (Cremasco et al.[1]) NAS score: 0.916 (0.855–0.980)	–

Adapted from Coleman et al.[9]

HQS = high-quality study

MQS = moderate-quality study

LQS = low-quality study

VLQS = very-low-quality study

GCS = Glaslow Coma Score

APACHE = Acute Physiology and Chronic Health Evaluation

TISS = Trauma Injury Severity Score

MODS = multiple organ dysfunction syndrome

PA02/FI02 = ratio of arterial oxygen partial pressure to fractional inspired oxygen PaCO2 = carbon dioxide partial pressure

MAP = mean arterial pressure

CURS = Corneil ulcer risk score

NAS = nursing activities score

PI = pressure injury