REVIEW ARTICLE

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Outcomes for Pressure Ulcer Trials (OUTPUTs) project: review and classification of outcomes reported in pressure ulcer prevention research

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Summary

In order to overcome inconsistencies in the reporting of outcomes in clinical trials, core outcome sets (COSs) have been developed in many clinical areas and the awareness of this concept is growing steadily. The Outcomes for Pressure Ulcer Trials (OUTPUTs) project aims to improve the quality of evidence from pressure ulcer prevention trials by developing a COS. As an initial step in the COS process we aimed to identify and classify both outcomes and concepts that represent potential outcomes for future trials that have been reported in pressure ulcer prevention research. A review was conducted in 12 major databases covering the literature indexed until 2016. Outcomes and relevant concepts reported in primary studies and/or reviews on pressure ulcer prevention in adult patients were extracted as presented in the articles, and afterwards inductively grouped into outcome domains. The domains were then categorized according to the outcome domain taxonomy recently proposed by the COMET group. In total 332 studies were included and 68 outcome domains were identified, covering multiple aspects of pressure ulcer prevention. Pressure ulcer occurrence was reported in 71% of all included studies, representing the most frequent outcome, followed by costs (22% of all studies) and acceptability of intervention and comfort (18% of all studies). A plethora of different outcomes are applied in pressure ulcer prevention research and substantial variations in definitions and reporting of similar outcomes were observed. A COS for pressure ulcer prevention trials is needed to overcome the noncomparability of outcomes.

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A pressure ulcer is defined as 'localized damage to the skin and/or underlying tissue, as a result of pressure or pressure in combination with shear'. Patients whose ability to move or position themselves is impaired are especially vulnerable to the development of pressure ulcers due to prolonged tissue exposure to pressure. Pressure ulcer prevention comprises different strategies (Figure 1).

Interventions aim to reduce the magnitude and duration of mechanical load such as pressure or shear forces, or intend to enhance tissue tolerance, for example by application of skincare products.[1,2] Important efforts to establish and improve pressure ulcer prevention have been made in the past. Overall, the availability and quality of evidence to make recommendations for pressure ulcer prevention are weak.[3] Thus, further research is necessary.[4–6]

There are many clinical trials testing pressure ulcer prevention strategies. Unfortunately, there is also huge heterogeneity and inconsistency of outcomes used in pressure ulcer prevention trials. Outcomes are dependent variables measured during interventional studies and enable researchers to make statements about the effects, effectiveness and/or safety of interventions.[7] The selection of patient-relevant and valid outcomes in clinical trials is crucial for the quality of study results.[8,9] In order to generate meaningful evidence, it is also important that the study results of the same clinical area are comparable, as otherwise they cannot be summarized and pooled in systematic reviews or meta-analyses.[10]

The incomparability of outcomes restricts evidence-based knowledge and aggravates decision making for clinicians in practice. To improve this situation, the concept of 'core outcome sets' (COSs) has been introduced and is promoted in many clinical areas now. A COS represents an agreed standardized set of outcomes that should be reported as a minimum in all clinical trials of a specific area (www.comet-initiative.org).[11] Developing a COS is a multistep consensus process that defines what to measure (core outcome domain set) and the measurement methods to quantify the determined core outcomes (core outcome measurement set). To date, no COS for pressure ulcer prevention trials exists. Thus, the 'Outcomes for Pressure Ulcer Trials project' (OUTPUTs project) has set the objective to develop a COS for this field following the latest methodological standards and recommendations.[12–14] The aim is to develop a COS for the evaluation of the clinical efficacy, effectiveness and safety of pressure ulcer prevention strategies.

According to the Harmonising Outcome Measures for Eczema (HOME) roadmap,[15] a suggested starting point for developing a COS is a list of all outcome domains ('long list').[11] Within this review, outcomes and outcome domains are regarded as synonyms because both are intended to measure the 'what' of outcomes. However, differences exist of

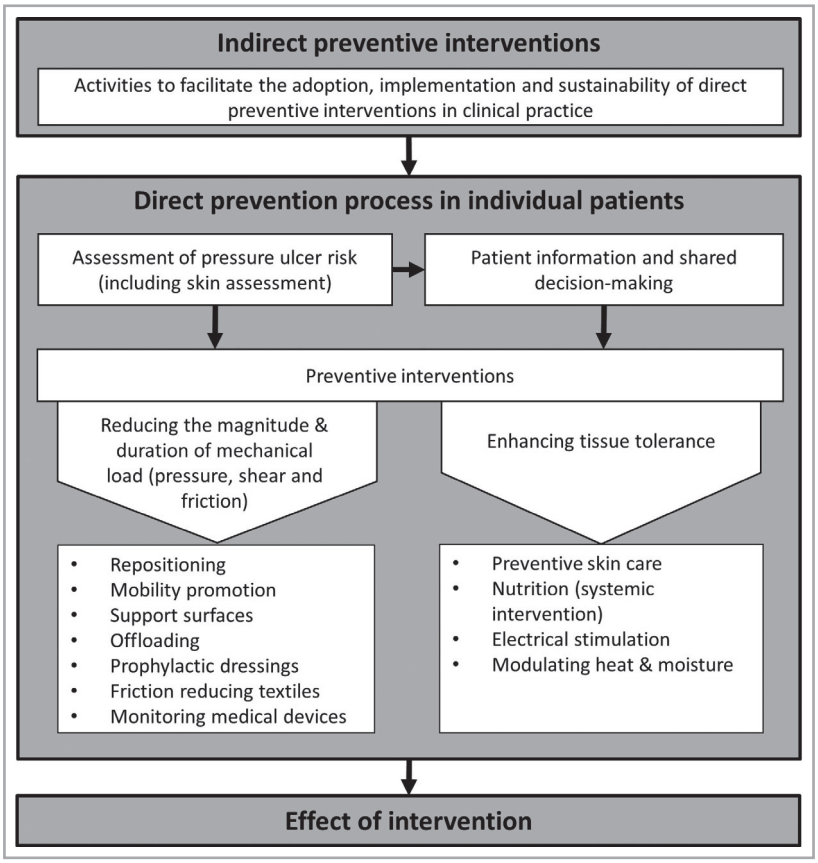

Figure 1 Conceptual scheme of pressure ulcer prevention.

how broadly or abstractly the outcome domains are defined.[16] The aim of this research was to compile as comprehensive a list of outcome domains for clinical trials as possible. We sought to identify and classify both outcomes and concepts that represent potential outcomes for future trials that have been used and/or described in previous pressure ulcer prevention research literature.

Methods

A protocol describing the steps of the OUTPUTs project to develop a COS has been published.[17] The OUTPUTs project is registered in the COMET database (http://www.comet-initiative.org/studies/details/283) and is part of the Cochrane Skin Core Outcome Set Initiative (http://cs-cousin.org/outputs).

As one first step of this project, a scoping review was conducted to identify as many potential outcomes for pressure ulcer prevention trials as possible, including patient-reported outcomes (PROs), which are defined as outcomes that are directly reported by patients. Compared with a systematic review, a scoping review has less depth, but is favourable to get an overview of a broad topic and can cover a broader conceptual range.[18,19] Unlike a systematic review this review did not aim to assess the 'weight' of evidence or appraise the methodological quality of studies, but aimed to provide a comprehensive overview of outcome domains.[19–21]

Search strategy

Systematic searches were conducted between February and August 2016 in the following electronic databases: Cochrane Wounds Group/Cochrane Skin Group/Cochrane Wounds Group Specialised Register, Cochrane Central Register of Controlled Trials, Ovid MEDLINE, Ovid Embase, EBSCO CINAHL, PsychINFO, British Nursing Index, Allied and Complementary Medicine Database, Web of Knowledge, Clinical trials.gov and the WHO International Clinical Trials Registry Platform Search Portal. Database-specific search strategies were used covering the concept of 'pressure ulcer' (example in Appendix S1; see Supporting Information). The search strategies comprised controlled terms and free-text words retrieved from existing systematic reviews on pressure ulcer prevention efficacy.[22–29] Electronic searches for evidence on PROs regarding pressure ulcer prevention were based for the most part on the same search strings used by Gorecki *et al.*[30] An update of the searches was not planned because it can be assumed that outcome saturation is reached using our comprehensive search strategy.

Eligibility criteria

The COMET Handbook recommends that the scope of a review 'should be carefully considered in the context of the COS to ensure that outcomes are included from all relevant studies without unnecessary data collection'.[11] It emphasizes, as does the Cochrane Skin Core Outcome Set Initiative, that not only clinical trials but also other study types like qualitative work should be considered.[11,14] Therefore, even though our future COS should be applicable only for clinical trials on pressure ulcer prevention, other study types were also eligible for inclusion as they could contribute additional outcomes.

In this review, controlled trials and systematic reviews investigating the efficacy, effectiveness and/or safety of pressure ulcer prevention interventions, full health economic evaluations and any kind of primary studies and systematic reviews exploring PROs related to pressure ulcers or pressure ulcer prevention were eligible. If a publication such as a position paper appeared to the reviewer as relevant for the identification of pressure ulcer prevention outcomes, this criterion took precedence over the exclusion criteria regarding the study design and it was included as well. Due to the objective of this review the eligibility assessment process was therefore carried out in an inclusive rather than exclusive way.

For feasibility reasons, papers had to be published in the English language. No restrictions were set in terms of healthcare settings or publication date, except for the primary studies on PROs, which were only taken into account when they were published after 2008, as a systematic review by Gorecki *et al.* in 2009 on PROs related to pressure ulcer and other chronic wounds already existed.[30] Studies with a target population aged < 18 years and that included healthy volunteers only were excluded. A detailed list of the inclusion and exclusion criteria is shown in Appendix S2 (see Supporting Information).

Study selection

All identified publications were imported to the Covidence platform (www.covidence.org), which was used for the study selection procedures. After removal of duplicates, the references were assessed for eligibility based on title and abstract screening, followed by full-text screening. The evaluation was performed independently by pairs of two reviewers of the project team. Discrepancies were discussed within the project team in order to reach a final decision.

Data charting and synthesis

Data on key study characteristics (author, year, country, study type, type of intervention, healthcare setting and target population) and both outcomes and concepts that present potential outcomes for clinical trials were extracted into standardized data files by means of SPSS 23 (IBM, Armonk, NY, USA). The data extraction was performed by two reviewers independently and cross-checked by a third reviewer. Cases of disagreement were resolved among the data extractors through discussion. The concepts of outcomes were extracted as presented in the studies. Based on an inductive approach, the identified potential outcomes of the literature were compiled to overarching outcome domains by two project members in cooperation and were reviewed by the whole project team. Identified outcome domains were then assigned to broader

outcome domains and core areas according to the taxonomy of Dodd *et al.*[31]

This newly developed taxonomy of Dodd *et al.* comprises 38 overall domains, allocated to the five core areas 'death', 'physiological/clinical', 'life impact', 'resource use' and 'adverse events'. Tools measuring health-related quality of life, which comprised several questions and therefore covered multiple outcome domains, were classified within each of the separate domains, as recommended by COMET and Dodd *et al.*[31,32] Outcomes were only allocated to 'global quality of life' when patients were generally asked to assess their quality of life. Specifically reported adverse events were classified within the most suitable outcome domain and marked as 'adverse event'.[31,32]

Results

Study selection

The searches identified 4498 references. After removal of duplicates and title and abstract screening, 668 full-text publications were evaluated for eligibility. Finally, 357 publications were included for data extraction (Figure 2).

Included publications

The included publications comprised 51 reviews and 281 primary studies. Twenty-five publications were identified as additional articles on a study already included. Most of the included studies were randomized controlled trials or controlled trials (n = 190). The other primary studies were identified as qualitative studies (n = 24) or full health economic evaluations (n = 21) or were allocated to the category 'other' (n = 46). The category 'other' comprised among others pre- and postimplementation studies, a series of single-case studies, a quasiexperimental study with interrupted time-series design and case–control studies. These studies were included as the reviewers assessed these publications as beneficial in the identification of pressure ulcer prevention outcomes, which took precedence over the study design.

Identified outcomes

Based on all identified outcomes in the included studies, 68 outcome domains were inductively created (Table 1). A detailed description of the extracted terms per outcome is shown in Appendix S3 (see Supporting Information). Most of the identified outcomes belonged to the outcome domain 'skin and subcutaneous tissue outcomes' according to Dodd *et al.*[31] To this broad outcome domain of Dodd *et al.* we have allocated 21 outcome domains such as 'tissue oxygenation', 'skin temperature' or 'pressure ulcer occurrence'. Pressure ulcer occurrence referring to the whole body (no. 18) was reported in 168 studies (95 clinical trials, 36 other primary studies and 37 reviews) and pressure ulcer occurrence referring to distinct body sites (no. 19) in 64 studies (51 clinical trials, seven other primary studies and six reviews). Therefore, pressure ulcer occurrence was the most frequently captured outcome overall. There was a great variety in the terminology and reporting of pressure ulcer (Appendix S3, no.18).

When reporting the frequency of pressure ulcer occurrence the included references stated among other measures the

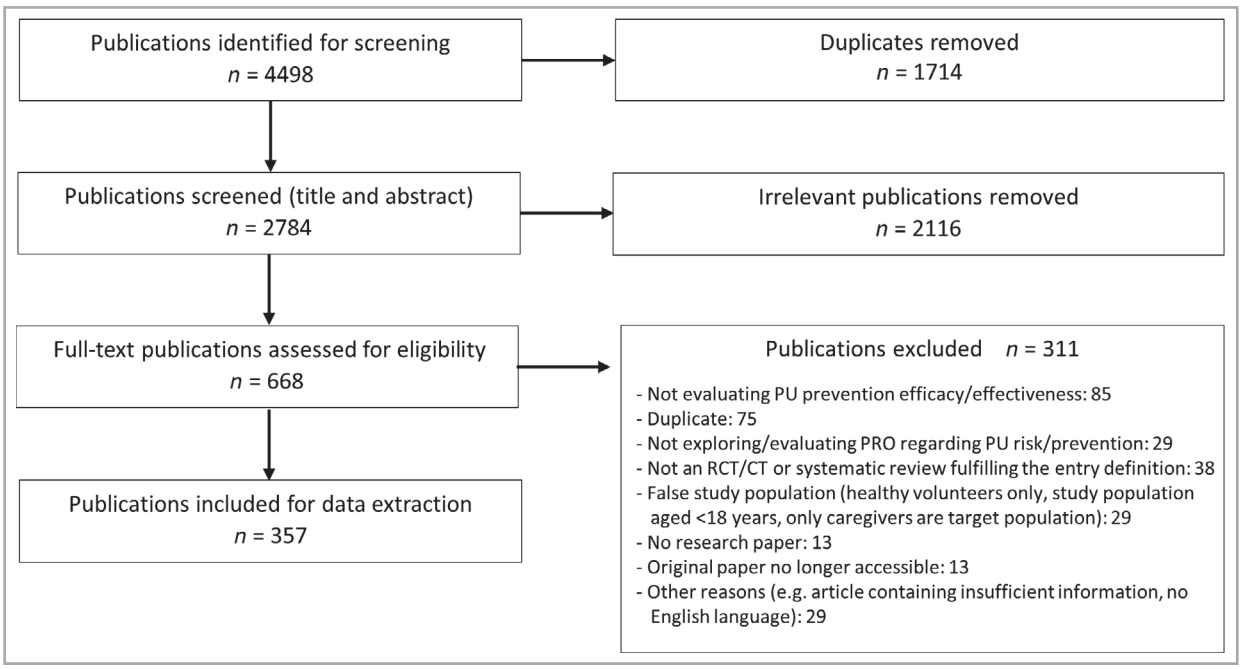

Figure 2 Flowchart of the screening and eligibility assessment process. CT, controlled trial; PRO, patient-reported outcome; PU, pressure ulcer; RCT, randomized controlled trial.

Table 1 Outcome domain long list based on the review

No.	Outcome domain (from inductive approach)	Frequency in clinical trials	Frequency in other primary studies	Frequency in reviews	Taxonomy according to Dodd *et al.*[31]	
					Outcome domain	Core area
1	Death reported as adverse event	1	/	/	1. Mortality/survival	Death
2	Fatigue	/	1	2	9. General outcomes	Physiological/clinical
3	Appetite	/	2	/	9. General outcomes	
4	Weight change	2	1	2	9. General outcomes	
5	Patient's balance	/	1	/	9. General outcomes	
6	Posture	1	1	/	9. General outcomes	
7	Patient's body perception	1	/	/	9. General outcomes	
8	Sitting tolerance	/	/	2	9. General outcomes	
9	Body displacement	/	/	1	9. General outcomes	
10	Falls reported as adverse event	1	1	2	9. General outcomes	
11	Injuries reported as adverse event	/	1	/	9. General outcomes	
12	Disorientation or confusion reported as adverse event	/	1	/	9. General outcomes	
13	Blood marker	2	/	1	14. Metabolism and nutrition outcomes	
14	Nutritional status	/	/	1	14. Metabolism and nutrition outcomes	
15	Nutritional intake	3	/	1	14. Metabolism and nutrition outcomes	
16	Adverse event regarding renal functioning	/	/	1	19. Renal and urinary outcomes	
17	Adverse events regarding respiratory tract	1	1	/	22. Respiratory, thoracic and mediastinal outcomes	
18	Pressure ulcer occurrence – whole body	95	36	37	23. Skin and subcutanous tissue outcomes	
19	Pressure ulcer occurrence – defined body sites	51	7	6	23. Skin and subcutanous tissue outcomes	
20	Pressure ulcer occurrence – device related	2	1	/	23. Skin and subcutanous tissue outcomes	
21	Pressure ulcer status (deterioration, healing, wound status)	30	6	6	23. Skin and subcutanous tissue outcomes	
22	Interface pressure	27	9	11	23. Skin and subcutanous tissue outcomes	
23	Blood perfusion	8	0	9	23. Skin and subcutanous tissue outcomes	
24	Tissue oxygenation	3	1	7	23. Skin and subcutanous tissue outcomes	
25	Transcutaneous carbon dioxide	/	/	2	23. Skin and subcutanous tissue outcomes	
26	Pressure ulcer precursor signs/skin changes	14	3	3	23. Skin and subcutanous tissue outcomes	
27	Tissue viability	/	/	1	23. Skin and subcutanous tissue outcomes	
28	Skin temperature	4	/	6	23. Skin and subcutanous tissue outcomes	
29	Body core temperature	1	/	/	23. Skin and subcutanous tissue outcomes	
30	Skin structure	3	/	1	23. Skin and subcutanous tissue outcomes	
31	Skin function	4	/	2	23. Skin and subcutanous tissue outcomes	
32	Muscle thickness	1	/	2	23. Skin and subcutanous tissue outcomes	
33	Muscle tonus	/	1	/	23. Skin and subcutanous tissue outcomes	
34	Tissue deformation	/	/	1	23. Skin and subcutanous tissue outcomes	
35	Pain associated with pressure ulcer	10	24	3	23. Skin and subcutanous tissue outcomes	
36	Pain associated with intervention	1	6	8	23. Skin and subcutanous tissue outcomes	
37	Pressure relief performance	/	1	1	23. Skin and subcutanous tissue outcomes	
38	Adverse events regarding skin and subcutaneous tissue	7	/	3	23. Skin and subcutanous tissue outcomes	

(continued)

Table 1 (continued)

No.	Outcome domain (from inductive approach)	Frequency in clinical trials	Frequency in other primary studies	Frequency in reviews	Taxonomy according to Dodd et al.[31]	
					Outcome domain	Core area
39	Autonomy and independence	1	4	1	25. Physical functioning	Life impact
40	Ability to move	11	16	1	25. Physical functioning	
41	Activities of daily living	3	12	2	25. Physical functioning	
42	Ability to be active	/	5	1	25. Physical functioning	
43	Physical functioning	3	6	1	25. Physical functioning	
44	Pressure ulcer prevention self-care	3	9	3	25. Physical functioning	
45	Handling skills	/	/	1	25. Physical functioning	
46	Sleep	3	7	/	25. Physical functioning	
47	Energy and vitality	4	5	/	25. Physical functioning	
48	Social functioning	4	14	2	26. Social functioning	
49	Role functioning	/	2	1	27. Role functioning	
50	Self-efficacy	1	6	/	28. Emotional functioning/wellbeing	
51	Willingness to change self-care	/	3	1	28. Emotional functioning/wellbeing	
52	Self-consciousness and self-esteem	/	6	/	28. Emotional functioning/wellbeing	
53	Emotional wellbeing	6	20	3	28. Emotional functional/wellbeing	
54	Privacy	/	1	/	28. Emotional functioning/wellbeing	
55	Knowledge of patient	8	5	5	29. Cognitive functioning	
56	Global quality of life	1	2	13	30. Global quality of life	
57	General health/malaise	3	8	/	31. Perceived health status	
58	Patient satisfaction with intervention	5	3	5	32. Delivery of care	
59	Acceptability of intervention and comfort	31	10	18	32. Delivery of care	
60	Adherence and compliance	8	2	1	32. Delivery of care	
61	Access to service	1	3	/	32. Delivery of care	
62	Patient participation in care	1	1	/	32. Delivery of care	
63	Resource use (nonhospital)	4	3	1	34. Economic	Resource use
64	Costs	28	27	18	34. Economic	
65	Hospital resource use	4	7	5	35. Hospital	
66	Time investment by patient	/	1	/	37. Societal/carer burden	
67	Healthcare utilization	2	/	2	37. Societal/carer burden	
68	Any adverse events/safety	15	5	12	38. Adverse events/effects	Adverse events

incidence or the prevalence of pressure ulcers, hospital-acquired pressure ulcer prevalence, the raw numbers of pressure ulcers that occurred, or the time until occurrence. There were also differences in the reported categories (e.g. including or excluding category 1, only category 3 and above). Some publications assessed the whole body, whereas others defined specific body areas for the assessment of pressure ulcer occurrence. Examples of the verbatim text describing the body areas that were considered for evaluation are 'sacrum, hips and heels', 'sacrum, buttocks and heels', 'trunk and heels' and 'trochanter' (Appendix S3, no. 19).

The second most commonly reported outcome domain was 'costs', including cost outcomes that were associated with a prevention intervention in any manner, like cost savings per year, hospital costs or direct staff costs (Appendix S3, no. 64). Cost outcomes were reported in 73 studies. 'Acceptability of intervention and comfort' was another frequent outcome domain (reported in 59 studies, no. 59). This domain represents outcomes that were reported by patients.[33] Other examples of listed PROs are 'pain associated with pressure ulcer' (no. 35), 'pain associated with intervention' (no. 36), 'emotional wellbeing' (no. 53), 'patient satisfaction with intervention' (no. 58) and 'global quality of life' (no. 56).

In order to evaluate the success of a pressure ulcer prevention intervention, trials also assessed outcomes that were considered to correlate with the development of pressure ulcer occurrence, like 'interface pressure' (no. 22), 'blood perfusion' (no. 23), 'skin function' (no. 31) or 'tissue oxygenation' (no. 24). Domains like 'nutritional intake' (no. 15) and 'nutritional status' (no. 14) are examples of intervention-specific domains, which are relevant only for trials investigating nutritional supplementation.

Types of preventive interventions

Table 2 shows the most frequent types of preventive interventions used in the included studies. The effects of support surfaces for the bed were reported most frequently (n = 93), followed by trials that evaluated the implementation of any kind of preventive guidelines or programmes, like the implementation of educational programmes or bundle-of-care interventions (n = 47). Other interventions that were also common (reported in more than 20 studies) are the application of preventive dressings and repositioning.

Discussion

As described in previous systematic reviews,[4,25,26] the reporting of pressure ulcer occurrence was heterogeneous. There were differences not only in how the occurrence of pressure ulcers was reported, but also regarding the body sites. Even when similar body areas were evaluated for the effectiveness of pressure ulcer prevention, a great variation of definitions exists (e.g. sacrum, buttocks, trochanter, trunk, pelvis). The use of the same terminology, classification systems and method to calculate pressure ulcer occurrence is important to enhance the comparison of study results.[34] The harmonization of capturing and reporting the identified core outcome domains will be a major task in future project steps, when it comes to developing the measurement methods.

Besides the occurrence of pressure ulcers, many other outcomes showed huge variation as well. For example, the indirect measure 'interface pressure' included, among others, the outcomes 'maximum interface pressure', 'mean interface pressure' and 'the average of highest four pressures'. Regarding 'blood perfusion' some studies measured the 'skin perfusion' and others the 'capillary blood flow' or 'tissue blood flow'. These examples emphasize again the difficulties that can emerge when trying to pool study results.

Our review results also indicate that there is heterogeneity between outcomes regarded as important in reviews and in primary studies. For example, 'sleep' was reported in primary studies, but not in any of the included reviews. On the other hand, some outcomes reported in the reviews were not applied in primary studies. This situation is similar in other fields. For example, a recently published review showed that 68% of dermatological trial outcomes were not included as outcomes in the corresponding Cochrane Reviews, and vice versa, 28% of outcomes defined by the reviewers were not reported in any supporting trial.[35] Similar observations have

Table 2 Types of preventive interventions reported in the included studies

Type of preventive intervention	Reported in clinical trials (n)	Reported in other primary studies (n)	Reported in reviews (n)
Support surface – bed	66	20	7
Guideline, education, programmes	23	14	10
Dressings	23	2	3
Repositioning	13	4	4
Support surface – sitting position	14	3	2
Nutrition	6	4	3
Heel offloading	6	1	3
Any intervention or pressure ulcer prevention in general	0	2	4
Mobility promotion	0	1	0
Other	39	40	15

been made in the fields of oncology[36] and preterm birth prevention.[37] This indicates that trialists and systematic reviewers differ in their opinions regarding relevant outcomes, which has the potential to result in research waste.[38] Therefore both trialists and systematic reviewers should participate as key stakeholders in the subsequent COS consensus process.

Some of the extracted outcomes seem more appropriate for trials of treatment rather than prevention interventions. For example, the outcomes 'pain associated with pressure ulcer' and 'pressure ulcer status' may appear unsuitable regarding pressure ulcer prevention, as they commonly appear in connection with ulcer treatment. However, these outcomes also fit into the concept of tertiary prevention, which describes the prevention of deterioration. This is why these outcomes were also extracted when reported in pressure ulcer prevention studies. The possible overlap between prevention and treatment outcomes was observed in other COS initiatives as well.[39–41] Therefore, one of the next steps is to further define the concept and levels of pressure ulcer prevention to be used in OUTPUTs. Furthermore, many intervention-specific outcomes were identified, such as 'weight gain' or 'nutritional status'. It must be decided whether it is more useful to develop an intervention-specific COS or a generic COS that is applicable for all types of interventions. In the latter case, intervention-specific outcomes are to be excluded.

This review included not only clinical trials and reviews, but also other study designs. The inclusion of qualitative studies is considered especially important, because they are a relevant source in identifying potential outcomes important for patients.[42] Including other evidence sources in addition to published clinical trials increases the review and data extraction workload, but in this review it allowed us to identify the following eight outcome domains that would otherwise have been missed: 'appetite', 'patient's balance', 'injuries reported as adverse event', 'disorientation/confusion reported as adverse event', 'muscle tonus', 'self-consciousness and self-esteem', 'privacy' and 'time investment by patient'. Finding an optimal balance between more sensitive or more specific literature searches for long-list creation in COS development is challenging, but we support the statement that looking at published clinical trials only is insufficient.[14,42]

The results of this review provide the basis for the next steps of the OUTPUTs initiative, whose main objective is to reduce this long list down to a consensus agreed list of essential outcome domains. Although the project group follows the latest methodological guidance, there are a number of methodological challenges in this new field, such as how best to involve patients in the development of a COS without overstraining them. Involving patients as participants in an e-Delphi survey might be difficult due to the complex question, which needs a deeper understanding of the concept of a COS. To ensure meaningful involvement of patients, it is essential to provide assistance and guidance. In addition, it is crucial that all outcome domains are presented with clear definitions, so that all participants understand their meaning and are able to rate their importance. Further, it is also not yet settled how to address the issue of timing.[14,43] Variations in time periods over which studies are conducted are challenging regarding the interpretation of trial results.[34] Timing is therefore also a factor that might be considered in sorting out the heterogeneity of trial results. Whatever form this may take, it will probably be necessary to distinguish between timing in terms of indirect outcomes of pressure (e.g. blood perfusion, tissue oxygenation, interface pressure) and direct outcomes of prevention (pressure ulcer development regarding the whole body, regarding defined body sites or being device related).

Limitations of the study are as follows. Only papers in the English language were included in this review, which may be regarded as language bias. Although the literature search was conducted in the most relevant electronic databases, there might be publications that were not identified. Qualitative studies were included to capture the views of patients and service users. Nevertheless, additional ways are needed to identify possibly missing outcomes, such as direct interviews with patients. The review was completed in 2016. Because data saturation was reached, it is unlikely that new outcomes have been introduced in the literature since then.

In conclusion, pressure ulcer occurrence is the most commonly reported outcome in pressure ulcer prevention research, but there is also a wide range of other outcomes. So far, there has not been a harmonization regarding the relevance of the single outcomes. OUTPUTs will help to prioritize and standardize the outcome selection in future pressure ulcer prevention trials.

Author Contribution

Anna Lechner: Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (equal); Project administration (equal); Visualization (equal); Writing-original draft (lead); Writing-review & editing (lead). **Jan Kottner:** Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (equal); Project administration (equal); Supervision (equal); Writing-review & editing (supporting). **Susanne Coleman:** Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (equal); Project administration (equal); Supervision (equal); Writing-review & editing (supporting). **Delia Muir:** Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (equal); Project administration (equal); Supervision (equal). **Dimitri Beeckman:** Conceptualization (equal); Methodology (equal); Supervision (equal); Writing-review & editing (supporting). **Wendy Chaboyer:** Conceptualization (equal); Methodology (equal); Supervision (equal); Writing-review & editing (supporting). **Janet Cuddigan:** Conceptualization (equal); Methodology (equal); Supervision (equal); Writing-review & editing (supporting). **Zena E. H. Moore:** Conceptualization (equal); Methodology (equal); Supervision (equal); Writing-review & editing (supporting). **Claudia Rutherford:** Conceptualization (equal); Methodology (equal); Supervision (equal); Writing-review & editing (supporting). **Jochen Schmitt:** Conceptualization (equal); Methodology (equal);

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Appendix S1 Example of the search strategy.
Appendix S2 Eligibility criteria.
Appendix S3 Extracted outcomes and corresponding outcome domains.