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Negative Pressure Wound Therapy on surgical incisions for Patients Post-Surgery

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Abbreviations

AGREE II	Appraisal of Guidelines for Research and Evaluation II
ASA	American Society of Anesthesiologists
BMI	body mass index
CABG	coronary artery bypass graft
CDC	Centers for Disease Control and Prevention
DSWI	deep sternal wound infection
EQ-5D-3L	EuroQol Group five dimensions 3-level version tool
GSV	great saphenous vein
HRQoL	health-related quality of life
ICU	intensive care unit
LOS	length of stay at the hospital
NPWT	negative pressure would therapy
RCT	randomized controlled trials
SD	standard deviation
SR	systematic review
SSI	surgical site infection
THA	total hip arthroplasty
VSS	Vancouver Scar Scale

Context and Policy Issues

Surgical site infection (SSI) is defined as an infection that occurs at the site of a surgical incision or in an organ space within 30 days of the surgery.[1] It has been estimated SSIs occur in 2% to 22% of all surgical procedures.[2] SSIs are a contributing factor to other surgical site complications such as systemic sepsis and septic embolization, all of which correlate with an extended postoperative hospital stay, and death, among others.[2,3] Surgical site complications also result in decreased patients' quality of life, increased rates of readmissions and reoperations, and pose a significant economic burden on patients and the healthcare system.[2-4]

Conventional approaches for preventing SSI include preoperative prophylactic systemic antibiotics, preoperative antiseptic shower/bath; aseptic incision site surgical preparation; and sterile and meticulous surgical technique.[5] Negative pressure wounds therapy (NPWT) has been proposed as a prophylactic measure in preventing surgical site complications.[4-7] The technology helps manage exudate and increase microvascular perfusion in high-risk surgical wounds.[7]

The precise way in which NPWT promotes the wound-healing process is unclear. However, there is evidence suggesting that the mechanism of action of NPWT involves protecting the wound from external contamination, increasing local blood flow and the production of granulation tissue, reducing lateral skin tension associated with incisions, and drawing the wound edges together.[1,4,6,7] Commercially available NPWT systems have varying suction pressure pressures, including some with -75 mmHg, -80 mm Hg, or -125 mmHg.[1] This report aims to identify and summarize evidence on the clinical- and cost-effectiveness of -125 mmHg pressure NPWT for preventing SSI and its attendant complications in patients with closed surgical incisions. An additional objective is to summarize evidence-based guidelines for the use of NPWT devices for the prevention of surgical site infections post-surgery.

Research Questions

1. What is the clinical effectiveness of negative pressure wound therapy for the prevention of surgical site infections for patients post-surgery?
2. What is the cost-effectiveness of negative pressure wound therapy for the prevention of surgical site infections for patients post-surgery?
3. What are the evidence-based guidelines regarding negative pressure wound therapy for the prevention of surgical site infections for patients post-surgery?

Key Findings

Overall, the identified evidence suggested that the -125 mmHg negative pressure wound therapy (NPWT) system is statistically significantly more effective than conventional wound dressing for preventing surgical site infections (SSI), though some studies showed no difference. However, results from a systematic review subgroup analysis indicated that the difference in SSI incidence between the NPWT and standard dressing groups reached the level of significance only in patients who had superficial SSI (Szilagyi I). Due to conflicting results from the included studies, there was no conclusive evidence indicating that a -125 mmHg negative pressure wound therapy (NPWT) system is statistically significantly more effective than conventional wound dressing for reducing the rate of reoperation and readmissions due to wound complications, or reducing the duration of postoperative stay in hospital or the intensive care unit. Evidence of limited quality suggested that at the time of discharge after surgery, patients' health-related quality of life (HRQoL) may be significantly better with NPWT than standard wound dressing. However, there was no statistically significant difference in HRQoL scores at the 6-week follow-up assessment. The difference in mortality rate between the two groups was not statistically significant, and the causes of death were not reported.

The evidence concerning non-SSI outcomes was limited in quality due to study design and methodological limitations such as open-label randomized controlled trials with unclear exclusion criteria, suboptimal randomization processes, and high patient dropout rate. Furthermore, most of the studies had inherently higher risk of systemic biases because they were non-randomized and lacked the risk-diminishing property of randomization.

The literature search for this review did not identify any relevant evidence regarding the cost-effectiveness of using a -125 mm Hg negative pressure wound therapy device; therefore, no summary can be provided.

The evidence-based guideline recommends that surgeons assess individual patients' risk factors and surgical risks and consider using negative pressure wound therapy for patients at high risk for developing surgical site occurrences, or who are undergoing a high-risk procedure, or a procedure that would have highly morbid consequences if a surgical site infection occurred. The strength of the recommendation and the specific evidence supporting it were not provided. However, the authors indicate that evidence for the guideline came from 100 publications, including systematic reviews, randomized controlled trials, and non-randomized studies.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources, including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were negative pressure wound therapy and surgical site infection. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2015 and May 26, 2020.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed, and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults (18 years or older) requiring surgery
Intervention	-125 mmHg negative pressure wound therapy devices (e.g., PREVENA)
Comparator	Q1-2: Standard dressings, other forms of dressing (e.g., moist wound healing dressings, cryocuffs), no treatment/placebo Q3: Not applicable
Outcomes	Q1: Clinical effectiveness (e.g., healing time, function, mobility or mobilization, wound healing, hospital stay, quality of life); Safety (e.g., prevention or decreased incidence of postoperative infections, adverse events [e.g., mortality, contact rashes, skin issues]) Q2: Cost-effectiveness (e.g., cost per benefit gained, quality-adjusted life years, incremental cost-effectiveness ratios) Q3: Recommendations regarding the use of negative pressure wound therapy post-surgery for the prevention of infection
Study Designs	Health Technology Assessments, Systematic Reviews, Randomized Controlled Trials, Nonrandomized Studies, Economic Evaluations, Evidence-based Guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1; they were duplicate publications or were published before 2015. The focus of this report is on -125 mmHg devices. Therefore, to proceed to the next level screening of full-text publications for eligibility, articles had to explicitly mention -125 mmHg NPWT devices (e.g., PREVENA) in the title or abstract. Systematic reviews (SRs), cost-effectiveness studies, and primary studies that did not report separate results or specific conclusions about -125 mmHg NPWT were excluded. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

One reviewer critically appraised the studies included in this report using version two of A Measurement Tool to Assess Systematic Reviews (AMSTAR 2)[8] for the SR, the Downs and

Black checklist[9] for the randomized controlled trials and non-randomized studies, and the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument[10] for the evidence-based guideline. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 548 citations were identified in the literature search. Following the screening of titles and abstracts, 505 citations were excluded, and 43 potentially relevant reports from the electronic search were retrieved for full-text review. The grey literature search did not identify additional publications of potential relevance. Of the 43 potentially relevant articles, 31 were excluded for various reasons, while 12 publications met the inclusion criteria and were included in this report. These comprised one SR,[11] three randomized controlled trials (RCTs),[2,3,12] seven non-randomized studies,[13-19] and one evidence-based guideline.[5] Appendix 1 presents the PRISMA[20] flowchart of the study selection. Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Study Design

The included SR with meta-analysis was authored by Gombert et al. and published in 2020.[11] Systematic searches for relevant literature for the SR focused on publications from 1 January 2005 to 31 December 2018 that were written in the English language. The SR included six RCTs published between 2016 to 2018, including two RCTs[2,3] selected for inclusion in this Rapid Response report. Those two RCTs are also summarized separately in this Rapid Response report because they report other outcomes in addition to SSI that were not captured in the SR.[11]

Two of the included RCTs[2,3] were single-center unblinded trials, published in 2018. One single-center, single-blind RCT[12] was published in 2017. The non-randomized studies comprised four retrospective cohort studies[13-16] two prospective cohort studies,[17,18] and one retrospective non-randomized study.[19] They were published between 2016 and 2020.

The evidence-based guideline[5] was published in 2017. It was developed by a multidisciplinary group of physicians with diverse practice experience to represent several different surgical specialties and clinical microbiology and infectious disease experts. According to the authors, the evidence for the recommendation was based on 100 publications, including SRs, RCTs, non-randomized studies, and preclinical studies, retrieved through a systematic search of Medline (PubMed), EMBASE, and the Cochrane Library from January 2000 to February 2016. Electronic searches were supplemented with searches in the references for additional potentially relevant publications. The guideline development was based on a multidisciplinary consensus meeting, and follow-up discussions via electronic mail and a follow-up teleconference over 12 weeks.[5] Available evidence was reviewed by a panel of 12 members, using the 2009 Oxford Centre for Evidence-based Medicine classification system.[21] The panelists relied on the available evidence and their experiences to formulate recommendations using a consensus

approach.[5] However, the ratings and strength of recommendations concerning the use of NPWT for closed surgical incisions were not reported.

Country of Origin

Authors from Germany and the United States of America conducted the SR.[11] One RCT by Kwon et al.[3] and two retrospective cohort studies, one each by Tyagi et ai.[13] and Curran et al.,[14] were conducted in the United States of America. One RCT by Pleger et al.[2] and one prospective cohort study by Poehnert et al.[17] were conducted in Germany. One RCT by Lee et al.,[12] one prospective cohort study by Cantero et al.,[18] and one retrospective cohort study by Nickl et al.[15] were conducted in Canada, Spain, and Austria, respectively. One retrospective study by Lo Torto et al.[16] and one case-control study by Abatangelo et al.[19] were conducted in Italy.

The lead author for the guideline[5] was from Germany. However, all the panelists reviewed and agreed upon the final manuscript. The panel members were from Denmark (1), Germany (2), Italy (1), United Kingdom (1), and the United States of America (7).

Patient Population

The SR involved a total of 733 adult patients with closed groin incisions following vascular surgery.[11] Actual patients' ages and other demographic characteristics were not specified.

Two included RCTs[2,3] were conducted in patients who underwent groin surgeries. The RCT by Kwon et al.[3] involved 119 patients undergoing elective vascular surgery involving unilateral or bilateral high-risk femoral incisions. Patients were classified as high risk if any of the following criteria were present: body mass index (BMI) >30 kg/m^2; significant pannus overlying groin skin or abnormal skin as evidenced by fungal infection; reoperative groin surgery; placement of prosthetic vascular graft; poor nutrition (BMI <18 kg/m^2, cachectic in appearance); immunosuppression (use of any immunosuppressive medications); and poorly controlled diabetes (hemoglobin A1c >8%). Eligible patients in the RCT by Pleger et al.[2] had to be undergoing vascular procedures with access to the common femoral artery with at least one of the following risk factors of wound healing: age >50 years, diabetes mellitus, renal insufficiency, malnutrition, obesity, and chronic obstructive pulmonary disease. A total of 100 patients participated in that study.[2] The median age of patients across study groups in both RCTs[2,3] varied from 65 to 71 years old. The RCT by Lee et al.[12] involved a total of 64 patients who underwent great saphenous vein (GSV) harvest for coronary artery bypass graft (CABG). Patients were eligible if they were receiving an isolated elective or semi-elective CABG and were above 18 years of age and living within one hour of the institution where the study took place.[12] The average age was 67.1 years and 68.3 years in the study and control groups, respectively.

The retrospective study by Tyagi et al.,[13] included data from 235 patients who underwent primary posterior approach total hip arthroplasty (THA). The retrospective studies by Nickl et al.,[15] and Lo Torto et al.,[16] involved patients with deep sternal wound infection (DSWI) following cardiac surgery. Nickl et al.,[15] included data from 111 obese patients (BMI > 30) whereas Lo Torto et al.,[16] used data from 78 patients who had significant risk factors for post-sternotomy complications, such as BMI≥30, people with diabetes, smokers, age ≥66 years, and the female gender. The retrospective study by Curran et al., [14] included data from 315 patients who had undergone high-risk open colorectal surgery. Patients were classified as high risk if they had one or more of the following factors: pre- or postoperative stoma, diabetes mellitus, obesity, preoperative steroid or immunosuppressant use, and a

contaminated or dirty wound. The mean age of patients across study groups in the retrospective studies[13-16] varied from 56 to 68 years old.

Both prospective cohort studies[17,18] involved patients who underwent surgical reversal of ileostomy. The study by Poehnert et al.[17] included 49 patients, whereas Cantero et al.[18] involved 60 patients. The mean age of patients across study groups in the two studies[17,18] varied from 55 to 65 years old. The retrospective non-randomized study by Abatangelo et al.[19] reviewed the clinical data of a total of 11 adult patients who had undergone an abdominoplasty after previous bariatric surgery. The study's eligibility criteria included total weight loss of > 30% after bariatric surgery while still having residual obesity, defined as BMI > 30 kg/m^2.[19] The mean age was 40.4 years in the intervention group and 49.5 years in the control group.

The target population in the guideline[5] was patients with closed surgical incisions.

Interventions and Comparators

The intervention of interest evaluated in the included SR,[11] RCTs[2,3,12] and non-randomized studies[2,3,13-19] was the NPWT system applying a suction pressure of -125 mm Hg. The device was applied after closing the incision and left in place for five to eight days,[2,3,11-14,17-19] or until the built-in battery had ended its lifespan (i.e., up to nine days).[15,16] In 10 of the studies,[2,3,11,12,14-19] the comparator comprised sterile gauzes and elastic bandages. In the study by Tyagi et al.,[13] the standard dressing was described as silver-impregnated island dressings (Aquacel). Patients were monitored daily for wound or systemic infection symptoms, and their wounds were inspected immediately after the NPWT dressing was removed. The SR[11] and one RCT[12] did not report the type of dressing used after the NPWT was removed. In each of the remaining nine studies,[2,3,13-19] subsequent wound dressing after NPWT used standard dressings similar to those used in the comparator groups. The follow-up duration ranged from 30 to 42 days for five of the six primary studies in the SR,[11] while one study in the SR[11] had four months follow-up period. For the remaining studies included in this report, the follow-up duration was 30 days in six studies[2,3,14,15,17,18], 42 days in one study,[12] and 90 days in another study.[19] Two studies did not report a follow-up period.[13,16]

The intervention of interest in the guideline[5] was commercially available closed incision negative pressure therapy, which included but was not limited to -125 mm Hg.NPWT systems.

Outcomes

Outcomes of interest reported in the included studies were SSI,[2,3,11-14,17,18] need for revision surgery due to wound complications,[2,3,13,15,16,19] postoperative length of stay at the hospital,[3,12-17] duration of stay in the intensive care unit (ICU) after surgery,[15,16] readmission due to wound complications,[3,13,14] health-related quality of life,[12,17] mobility,[12] ability for self-care,[12] wound healing,[19] quality of scars[19] as measured by the Vancouver Scar Scale (VSS), and death while on admission.[14-16] The VSS is widely used in clinical practice and research to document change in scar appearance.[22] It is scored over four domains: vascularity (0-3 points), pliability (0-5 points), pigmentation (0-2 points), and height (0-3 points) with total score of 0 to 13, where 0 represents normal on each scale and 13 the worst case.[22,23] The RCTs by Kwon et al.[3] and Pleger et al.[2] reported SSI outcomes among others that are relevant to this report. However, these RCTs[2,3] were included in the SR,[11] which pooled the SSI findings from six RCTs in meta-analyses. Therefore, to avoid double-counting and overestimation of effects, the SSI findings from the RCTs by Kwon et al.[3] and

Pleger et al.[2] are not reported separately from the effect estimate provided by the SR[11] in this Rapid Response report.

The SR[11] defined SSIs using the Szilagyi classification,[24] which has three grade levels. Grade-I refers to superficial infections restricted on the skin, grade-II describes an infiltration of the subcutaneous layer without the arterial graft participation, and grade-III represents an infection involving the arterial graft.[2] In the RCT by Lee et al.,[12] SSI was assessed using the ASEPSIS score. The studies by Poehnert et al.[17] and Cantero et al.[18] identified the presence of SSI according to the Centers for Disease Control and Prevention (CDC) criteria. The ASEPSIS score is a validated measurement tool for postoperative wound infections.[12,25] Scoring relies on multiple clinical observations and awards points for the need for Additional treatment, presence of Serous discharge, Erythema, Purulent exudate, Separation of the deep tissues, Isolation of bacteria, and the duration of inpatient Stay (ASEPSIS).[25] In the RCT,[12] ASEPSIS scores of >20, 11–20, and <10 represented infection, disturbance in healing, and no infection, respectively.[12] The CDC criteria are 1) purulent secretion, and/or 2) positive wound swab, and/or 3) clinical symptoms of inflammation or surgical diagnosis of SSI of the skin or the subcutaneous tissue within 30 days after surgery.[17] The determination criteria for SSI were not reported in studies by Tyagi et al.[13] and Curran et al.[14]

Lee et al.,[12] assessed patients' health-related quality of life (HRQoL) by the validated, 3-level version of the EuroQol Group five dimensions (EQ-5D-3L) Measure of Health Status tool. In contrast, Poehnert et al.[17] evaluated HRQoL using a tailored questionnaire covering subjective items of quality of life and well-being before and after ileostomy reversal. However, the questionnaire was not identified by name, and it was unknown if it was validated for that purpose.

The outcomes of interest in the guideline[5] were SSI and other wound healing complications such as surgical dehiscence, hematoma, seroma, and incision drainage.

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Systematic review

The included SR[11] stated the study objectives and clearly defined its populations, interventions, comparators, and outcomes. The study protocol was not published or registered, and the authors did not provide any details about the internal protocol, which they stated were followed. Thus, it was unclear if the investigators worked with a written protocol with independent verification, or if there were deviations from the protocol that could introduce risk of bias in the review. The RCTs included in the SR[11] were identified through a systematic literature search conducted in multiple databases. Two reviewers independently assessed the eligibility of primary studies for inclusion in the review, whereas data extraction was performed by one reviewer and independently checked by a second reviewer. Disagreement concerning study eligibility and data extraction were resolved by consensus involving a third reviewer. The risk of bias in the primary studies of the SR[11] was assessed using the Cochrane Collaboration tool, and a summary of the relevant characteristics of the included studies was provided in tabular form. However, a list of excluded studies was not provided, although a PRISMA flowchart illustrating the study selection process listed the reasons for the exclusions. The meta-analyses were performed

appropriately using a random-effects model for each analysis performed and combining treatment effects using Mantel-Haenszel odds ratios as the summary statistics. Heterogeneity was assessed using the Chi-Square test, and funnel plots were used to evaluate publication bias. Sensitivity analyses were conducted regardless of the heterogeneity assessment to test robustness of the results. Subgroup analyses showing the performance of NPWT and control in subpopulations of the study participants were performed based on patients' risk of complication (i.e., high-risk or normal-risk) and classification of infection outcomes (i.e., Szilagyi I, II, and III). The authors stated no financial support for the research, authorship, and publication of the SR.[11] However, all the authors were affiliated with KCI USA incorporated, the manufacturer of the PREVENA, the NPWT device that was investigated in the study.

Primary studies

All the included primary studies had well-defined objectives[2,3,12-18] or hypothesis,[19] and they described the interventions and comparators, as well as the main outcomes measures, and findings clearly. All the studies[2,3,12-19] provided inclusion criteria, including seven[3,12-14,17-19] that also defined clear exclusion criteria. One RCT[2] and two retrospective cohort studies[15,16] did not provide exclusion criteria. One RCT[3] reported that patients were randomized to either of the two study arms by a coin toss, and another RCT[2] did not give details on how patients were assigned to the study groups. Therefore, it was unclear whether randomization was adequately achieved in these studies.[2,3] None of the RCTs[2,3,12] blinded patients to the assigned treatment. Although it did not appear feasible that patients could be blinded in the studies, this does not eliminate lack of blinding as a potential source of bias in these studies. In one RCT,[12] the outcome assessor was blinded to the patients' grouping to minimize the risk of bias due to an assessor's awareness of patients' treatment allocation. In contrast, two RCTs[2,3] did not attempt to blind outcomes assessors to the assignment of treatments.

One retrospective study[13] reported statistically significant differences in some demographic and risk factors for wound complications, which were not adjusted for in the analysis. In one retrospective cohort study[18] and one retrospective non-randomized study,[19] there appeared to be differences in some risk factors and patients' characteristics such as age, ASA scores,[18] total weight loss,[19] and time since the last bariatric surgery.[19] However, in the absence of any measure of significance (e.g. p-value), it was unknown if the differences between the groups concerning these parameters were statistically significant. It was unclear if these differences impacted the reported findings of the studies.[13,18,19] The method of selecting patients whose data were used in the retrospective non-randomized study[19] was not reported, and the inclusion and exclusion criteria of the study appeared restrictive. For example, to be eligible, patients had to have a total weight loss > 30% after bariatric surgery and have residual obesity with BMI > 30 kg/m^2 and local risk factors, among others, but patients were excluded if they had severe systemic co-morbidities.[19] Furthermore, the study was based on data from a total of 11 patients, which is not likely to be representative of the entire population undergoing a similar procedure. Thus, the generalizability of the study findings in other patient groups was unclear

The statistical approaches in all the studies[2,3,12-19] were generally appropriate. However, in one RCT,[12] the analysis was not based on the intention-to-treat population because 6.25% of patients withdrew consent after surgery, and an additional 20% was lost to follow-up. Thus, the large proportion of excluded data was likely to offset the randomization effect that minimized systemic bias. Also, the analyses did not adjust for potential confounders in any of the non-randomized studies.[13-19] In three retrospective cohort studies,[14-16] data for

patients treated with NPWT were compared with data from a historical cohort that underwent similar surgical operations, with incision wound treated with standard dressings. Similarly, in one prospective cohort study,[18] prospectively collected data for the use of NPWT were compared with control group data from a historical cohort that used standard dressing. Thus, patients in the intervention groups in these four studies,[14-16,18] received treatment at different periods from their respective control groups. It was also unknown if the cases and controls in the retrospective non-randomized study[19] were recruited over the same period. Therefore, for these studies,[14-16,18,19] it was unknown if there were any changes in surgical procedure or dressing materials over time that could have influenced the reported findings. Other limitations included the use of an unnamed questionnaire with unknown validation status to assess patients' health-related quality of life,[17] subjective patient-reported outcomes,[12,17] inconsistency in reported data,[16] and not reporting actual probability values (p-values).[16,19]

The SR,[11] one retrospective cohort study,[13] and one prospective cohort study[17] reported receiving no funding support. One RCT was funded by a department of the local hospital where the study was conducted and RCT[12] was funded by KCI USA incorporated, the manufacturer of the NPWT device investigated in the study. In six studies, the authors did not specify if there was any funding support. However, they reported having no disclosure to make,[14] no conflicting interest,[3,19] or no competing financial interest[15,16,18] regarding the studies. All the RCTs[2,3,12] were single-center studies, and each of the non-randomized studies[13-19] used data from single institutions. Considering this, along with the fact that the studies did not apply standardized definitions of high-risk patients and outcome measures, the generalizability of the findings is unknown.

The guideline had a well-defined objective and stated the specific health questions to answer. The population of interest was identified. Though it appeared that the target users were surgeons and infectious disease physicians, that was not specified. Evidence was collected from literature identified through systematic literature searches in multiple electronic databases, supplemented with manual searches. The methods for formulating the recommendations were described. Recommendations considered the health benefits, side effects, and risks based on supporting evidence. However, the rating and strength of recommendations concerning NPWT for closed surgical incisions were not reported. The key recommendation was specific and unambiguous. A provided chart gives guidance on assessing options for managing different surgical incisions with NPWT, based on patients' risk and surgical risks. However, there was no input from patients and the public, the document was not externally reviewed, and the strengths and limitations of the body of evidence were unclear. Further details about the strengths and limitations are available in Table 7, Appendix 3.

Summary of Findings

Appendix 4 presents the main study findings and the authors' conclusions.

Clinical Effectiveness of -125 mm Hg Negative Pressure Wound Therapy Device for the prevention of surgical site infections for patients post-surgery

Surgical site infections

One SR,[11] three RCTs,[2,3,12] two retrospective cohort studies,[13,14] and two prospective cohort studies,[17,18] reported SSI outcomes after using NPWT on closed surgical incisions, with inconsistent findings. Of note, the SSI data from the RCTs by Kwon et al.[3] and Pleger et al.[2] were included in the meta-analysis of the SR.[11] Therefore, to avoid double-counting

and overestimation of results, the SSI findings of the RCTs[2,3] are not reported independently from the effect estimates with 95% CI provided by the SR[11] in this Rapid Response report.

Systematic review

Meta-analyses of data from six RCTs (number of patients [n] =733) in the SR[11] found that the overall risk of developing SSI in patients with closed groin incisions following vascular surgery was statistically significantly lower with NPWT than with standard dressing (OR = 3.06, 95% CI: 2.05 – 4.58; P < 0.05). Subgroup analyses involving four studies (n=568) showed that the risk was significantly lower for NPWT than standard dressing (OR = 3.09, 95% CI: 1.68 – 5.67; P < 0.0003) in patients with superficial SSI (i.e., Szilagyi grade-I SSI). However, the risk of developing Szilagyi grade-II or grade-III SSI was not statistically significantly different between treatments with NPWT and standard dressing.

Primary studies

One retrospective cohort study Curran et al.[14] found that among patients who had undergone high-risk open colorectal surgery, the SSI rate was statistically significantly lower with NPWT than with standard dressing (6.5% versus 15.1%; p = 0.05). Moreover, one prospective cohort study by Cantero et al.,[18] found that in patients who underwent elective ileostomy reversal, there were no SSIs in the NPWT group versus SSI in 9 (21%) patients who used standard dressing. The difference was statistically significant (p < 0.038).

On the contrary, one RCT by Lee et al.,[12] found that in patients who underwent GSV harvest for elective CABG, there was no statistically significant difference in SSI incidence between patients treated with NPWT and those who had standard dressing at the initial assessment or 6-week follow-up. Similarly, one retrospective cohort study[13] in patients who underwent primary THA and one prospective cohort study in patients who underwent double loop ileostomy reversal[17] did not find a statistically significant difference in the SSI incidence between patients treated with NPWT and controls.

Revision Surgeries

Two RCTs,[2,3] two retrospective cohort studies,[15,16] and one retrospective non-randomized study,[19] reported the need for reoperation due to surgical wound complications, but the results were inconsistent.

In patients who underwent elective vascular surgery, the rate of wound complications requiring reoperation was statistically significantly lower with NPWT than with conventional dressing in one RCT by Kwon et al.[3] (8.5% versus 18.3%; p = 0.05) and another RCT by Pleger et al.[2] (1.7% versus 14.1%; p = 0.022). Similarly, in one retrospective cohort study by Nickl et al.,[15] surgical revisions due to wound complications were statistically significantly lower with NPWT than conventional dressings (5.3% versus 32%, p = 0.034) in patients with BMI > 30 and DSWI following cardiac surgery. However, in one retrospective cohort study by Lo Torto et al.,[16] the difference between the NWPT and conventional dressings groups in surgical revision due to complications did not reach the level of statistical significance (3% versus 15%; p =0.1433) in high-risk patients with DSWI following cardiac surgery. The retrospective non-randomized study by Abatangelo et al.[19] also did not find a significant difference in the rates of complications requiring reoperation between the two groups.

Postoperative length of stay in hospital

Two RCTs,[3,12] four retrospective cohort studies,[13-16] and one retrospective non-randomized study[19] reported inconsistent findings on the duration of post-surgery hospital stay outcomes following the use of NPWT.

In one RCT by Lee et al.,[12] patients in the NPWT group had a statistically significantly earlier median discharge date than those in the standard dressing group (6 days versus 10 days; P = 0.008). However, one RCT by Kwon et al.[3] found no significant difference in hospitalization duration between patients treated with NPWT and those who received standard dressing. One prospective cohort study by Poehnert et al.[17] found that the median duration of hospitalization after surgery was statistically significantly shorter with NPWT than with standards dressings (5 days versus 7 days; p = 0.019). However, one retrospective cohort study by Nickl et al.[15] found no significant difference in the median duration of hospitalization between patients treated with NPWT and those who received standard dressing (14.0 days versus 19.5 days; p = 0.179). The mean duration of postoperative hospital stays across two retrospective cohort studies[13,14] and one retrospective non-randomized study[19] varied from 3.0 days to 9.2 days with NPWT and 3.1 days to 12.3 days with standard dressings. However, the difference in the duration of stay between NPWT and standard dressings groups did not reach the level of statistical significance,[13,14] or a measure of statistical difference between groups was not reported.[19]

Postoperative length of stay in ICU

Two retrospective cohort studies reported findings on the duration of ICU stay after surgery. The study by Nickl et al.[15] reported a statistically significantly lower median duration of stay in the ICU with NPWT than with standard dressings (0 [range: 0 to 5 days] versus 3.5 days [range 0 to 34 days]; p < 0.001). However, Lo Torto et al.[16] found that the mean length of postoperative stay at the ICU was not statistically significantly different between the NPWT and the standard dressing groups (3.7 days versus 4.2 days; p-value was not reported).

Readmission due to wound complications

One RCT[3] and two retrospective cohort studies[13,14] reported findings on hospital readmission due to wound complications. Kwon et al.[3] found that patients who used NWPT had a statistically significantly lower readmissions rate than those who had standard dressing (6.8% versus 16.7%; p = 0.04). Curran et al.[14] also reported that the readmissions rate with NPWT was half that of the standard dressing; however, the difference was not statistically significant (8% versus 16%; p = 0.09). Tyagi et al.[13] did not find a statistically significant difference in the overall readmission rate between the NPWT and the control groups (6.52% versus 10.49%; p = 0.43). However, the investigators found that the readmission rate among high-risk patients was statistically significantly lower in the NPWT group than the standard dressing group (4.82% versus 14.85%; p = 0.028).

Health-related quality of life

One RCT by Lee et al.[12] reported that patients' HRQoL as determined by EQ-5D-3L score was statistically significantly higher in the NPWT group than the standard dressing group at initial assessment (73 versus 59; P = 0.039) but not at the 6-week follow-up assessment. On the contrary, the prospective cohort study by Poehnert et al.,[17] reported no significant (p = 0.37) difference in overall health-related quality of life between the patients treated with NPWT and those who had standard dressings. However, patients treated with NPWT had a statistically significantly (p = 0.03) better satisfaction with the course of wound healing and indicated a lower need for help with wound care. Also, they had fewer sleep disorders and a

better ability to fulfill daily tasks. However, patients treated with standard dressings showed significantly less anxiety about the negative impact on professional performance due to their condition (p = 0.027). It must be noted that the tool used for the quality of life assessment was not identified by name, and it was unknown if it had been validated for such evaluations.

Mobility and ability for self-care

One RCT by Lee et al.[12] found that patients treated with NPWT self-reported a statistically significantly greater improvement in mobility than those treated with standard dressing at both the time of discharge (initial assessment) (P = 0.0117) and at 6-week follow-up assessment (P = 0.0123). In the same study, patients treated with NPWT self-reported a statistically significantly increased self-care ability at the initial assessment than those treated with standard dressings (P = 0.0234). However, at the 6-week follow-up assessment, the difference in self-care ability between the two groups was not statistically significant.

In-hospital mortality

Three retrospective cohort studies[14-16] reported the number of deaths during hospitalization after surgery. In the study by Curran et al.,[14] there was no mortality in the NPWT group, while four (1%) patients in the control group died during hospitalization. Nickl et al.[15] reported that no patients in the NPWT group died, and one (3.6%) patient in the standard dressing group died during hospitalization. In the study by Lo Torto et al.,[16] one patient in the NPWT group died during hospitalization, whereas no patient in the control group died before discharge. In all the three studies,[14-16] the difference was not statistically significant, and the cause of death was not reported.

Wound healing time, minor complications, and quality of scars

In one retrospective non-randomized study,[19] patients treated with NPWT had a shorter mean time to wound healing (11 days versus 23 days), a lower rate of minor local surgical wound complication (0 versus 67%), and a better quality of scars as indicated by the mean VSS scores (2 for NPWT versus 6 for controls). The difference was statistically significant in all the measurements (p < 0.05).

Cost-Effectiveness of -125 mm Hg Negative Pressure Wound Therapy Device for the prevention of surgical site infections for patients post-surgery

The literature search for this review did not identify any relevant evidence regarding the cost-effectiveness effectiveness of a -125 mm Hg NPWT device; therefore, no summary can be provided.

Guidelines for using Negative Pressure Wound Therapy for closed incisional wounds

The evidence-based guideline[5] recommends that surgeons assess the individual patient's risk factors and surgical risks and consider using NPWT for patients at high risk for developing surgical site occurrences or undergoing a high-risk procedure or a procedure that would have highly morbid consequences if an SSI occurred. The strength of the recommendation and the specific supporting evidence was not provided. However, the evidence for the guideline is based on 100 publications, including systematic reviews, RCTs, and non-randomized studies.

Limitations

The evidence in this Rapid Response report to address the clinical effectiveness of negative pressure wound therapy for the prevention of surgical site infections for patients post-surgery is based on one SR,[11] three open-label RCTs[2,3,12] (two of which were included in the SR[11]) and seven non-randomized studies[13-19] with an inherent risk for biases due to their design. Due to the limitations discussed in the critical appraisal section and Appendix 3, including but not limited to lack of rigor in the randomization process,[2,3] a high patient dropout rate,[12] unclear exclusion criteria,[2,15,16] restrictive eligibility criterial that limited generalizability,[19] and study designs with inherently higher risk of systemic biases due to lack of the risk-diminishing property of randomization,[13-18] all the primary studies[2,3,12-19] were limited in quality. It is noteworthy that all the included studies reported only numerical values as results with some providing statistical measures of significance. Thus, in the absence of a reported minimal clinically important difference for each outcome, the clinical relevance of the findings is unclear. Given the volume of available literature on NWPT devices, the literature search was limited to the past five years to feasibly provide a review within rapid timelines. However, the included SR[11] was based on a systematic literature search spanning 1 January 2005 to 31 December 2018, thus mitigating the risk of missing older literature. Furthermore, as the focus of this report is on -125 mmHg devices, articles that did not explicitly mention -125 mmHg NPWT devices (e.g., PREVENA) in the title or abstract were not selected for inclusion. Thus, the possibility of missing some potentially relevant publications due to the literature search and selection process cannot be ruled out. The SR[11] and seven of the included studies[2,3,12,14,15,17,18] had a follow-up duration of 30 to 42 days, and two retrospective cohort studies[13,16] did not report follow-up periods. Thus, there is uncertainty about the generalizability of the findings over periods beyond 42 days.

The literature search for this review did not identify any relevant evidence regarding the cost-effectiveness of a -125 mm Hg NPWT device. Thus, there is a need for studies that assess the cost-effectiveness of -125 mm Hg NPWT devices for the prevention of surgical site infections for patients post-surgery. Similarly, there was only one included guideline that provided a very broad recommendation and unclear description of facilitators and barriers to its application. There is also a need for evidence-based guidelines with more specific details and graded recommendations for using NPWT for closed incisional wounds.

Conclusions and Implications for Decision or Policy Making

One SR,[11] three RCTs,[2,3,12] four retrospective cohort studies,[13-16] and two prospective cohort studies,[17,18] assessed the clinical effectiveness of negative pressure wound therapy for the prevention of surgical site infections for patients post-surgery. Evidence from one SR[11] and two non-randomized studies[14,18] indicated that the incidence of SSI was statistically significantly lower with NPWT compared with conventional wound dressing. However, results from a subgroup analysis in the SR[11] indicated that the difference in the incidence of SSI between the NPWT and standard dressing groups reached the level of significance only in patients who had superficial SSI (Szilagyi I). On the contrary, one RCT[2,12] and two non-randomized studies[13,17] did not find a statistically significant difference in the incidence of SSIs between patients treated with NPWT and those who received conventional wound dressing. Evidence from one retrospective non-randomized study[19] suggested that the time to wound healing and quality of scars were statistically significantly shorter and better, respectively; with NPWT than standard dressing, and the rate of minor local wound complication was statistically significantly lower with NPWT.

Evidence from two RCTs[2,3] and one retrospective cohort study[15] indicated that the use of NPWT resulted in a significantly lower rate of surgical revisions due to wound complications. However, another retrospective cohort study[16] and one retrospective non-randomized study[19] did not find a statistically significant difference in surgical revision rates between NPWT and standard wound dressings.

Two RCTs,[3,12] five retrospective cohort studies,[13-17] and one retrospective non-randomized study[19] provided information about hospitalization duration after surgery. One RCT[12] and one prospective cohort study[17] found that the duration was statistically significantly shorter with NPWT than standard wound dressing. On the contrary, evidence from one RCT,[3] four retrospective cohort studies[13-16] and one retrospective non-randomized study[19] suggested no significant difference in hospitalization duration between the two groups. Furthermore, evidence from one retrospective study[15] indicated that the duration of stay in the ICU after surgery was significantly shorter with NPWT than standard wound dressing. However, another retrospective cohort study[16] found no significant difference between the two groups regarding this outcome.

One RCT[3] and two retrospective cohort studies[13,14] reported findings on hospital readmission due to wound complications. Evidence from one RCT[3] and one retrospective cohort study[13] indicated that the use of NPWT resulted in a statistically significantly lower rate of readmissions due to wound complications than standard dressing. However, one retrospective cohort study[16] did not find a statistically significant difference in readmission rates between the two groups.

Evidence from one RCT[12] suggested a statistically significantly higher EQ-5D-3L score in the NPWT group than the standard dressing group, indicating a better HRQoL in favour of NPWT. However, the advantage was limited to the assessment at discharge and not maintained at the 6-week follow-up evaluation. There was also evidence from the RCT,[12] indicating that patients treated with NPWT had statistically significantly more significant improvement in mobility and ability for self-care at the initial assessment, at least. However, one prospective cohort study[17] suggested no significant difference in overall HRQoL between the patients treated with NPWT and those who had standard dressings. The evidence from that study[17] was limited because an unidentified tool with unknown validation status was used for the quality of life assessment.

On mortality, three retrospective cohort studies[14-16] reported the number of deaths during hospitalization after surgery. Evidence from all the studies[14-16] indicated that the number of deaths during hospitalization after surgery was not statistically significant between patients treated with NWPT or those who received conventional wound dressing.

Despite some studies[12,13,17] showing no difference, overall, there is evidence indicating that the -125 mm Hg NPWT device is statistically significantly more effective than conventional wound dressing for preventing SSIs than standard wound dressings. However, a subgroup analysis in the included SR[11] indicated that the advantage of the NPWT over standard dressings in reducing SSI incidence reached the level of significance only in patients who had superficial SSI (Szilagyi I), and there was no evidence of a significant difference between the two groups in the prevention of Szilagyi Grade II and Szilagyi Grade III SSI. The other studies[12-14,17,18] did not conduct subgroup analysis. Thus, the results from the subgroup analysis in the SR[11] suggested that the lower overall rate of SSIs with NPWT than standard dressings may have been driven by outcomes from patients with superficial SSIs. It was unclear if the different surgical operations performed across the various studies

and the difference in expertise, study setting, and wound assessment methods could account for the inconsistency in the reported outcomes.

Evidence of limited quality suggested that HRQoL may be significantly better with NPWT than standard dressings at the discharge time but not at 6-week follow-up. However, the comparative clinical effectiveness of the -125 mm Hg NPWT device versus standard wound dressings in preventing or reducing surgical revision rates, duration of postoperative hospital or ICU stay, and readmission rates could not be conclusively determined due to the conflicting evidence from the studies included in this report. However, within the boundaries of the reported limitations, the evidence favoring statistically significantly lower rates of reoperations and readmissions with NPWT than with standard dressings appeared more reliable. Also, given the comparable quality of the RCTs and the similarity in quality of the nonrandomized studies that reported on these outcomes, there was more evidence suggesting no significant reduction[3,13-15,19] in the duration of postoperative hospitalization with the use of NPWT compared with standard dressings.

A key source of uncertainty in the evidence concerning non-SSI outcomes was limitation in quality due to study design and methodological limitations such as open-label randomized controlled trials with unclear exclusion criteria, suboptimal randomization processes, and high patient dropout rate. Also, most of the evidence for non-SSI outcomes came from non-randomized studies with an inherently higher risk of systemic biases due to lack of the risk-diminishing property of randomization,[13-18] comparing data from cohorts of different historical periods,[14-16,18] and significant differences in demographic and other risk factors.[13,14] Also, the generalizability of findings from the individual studies was limited because they all used data from single institutions, and there were no standardized outcome measures. The focus of this report is on -125 mmHg devices; therefore, articles that did not explicitly mention -125 mmHg NPWT devices (e.g., PREVENA) in the title or abstract were not selected for inclusion. Thus, the possibility of missing some potentially relevant publications due to the selection process cannot be ruled out.

The literature search for this review did not identify any relevant evidence regarding the cost-effectiveness effectiveness of a -125 mm Hg NPWT device.

One evidence-based guideline[5] recommends that the surgeon assess the individual patient's risk factors and surgical risks and consider using NPWT for patients at high risk for developing surgical site occurrences or undergoing a high-risk procedure or a procedure that would have highly morbid consequences if an SSI occurred. The strength of the recommendation and the specific supporting evidence were not provided. However, the authors indicate that the evidence for the guideline was derived from 100 publications, including systematic reviews, RCTs, and non-randomized studies.

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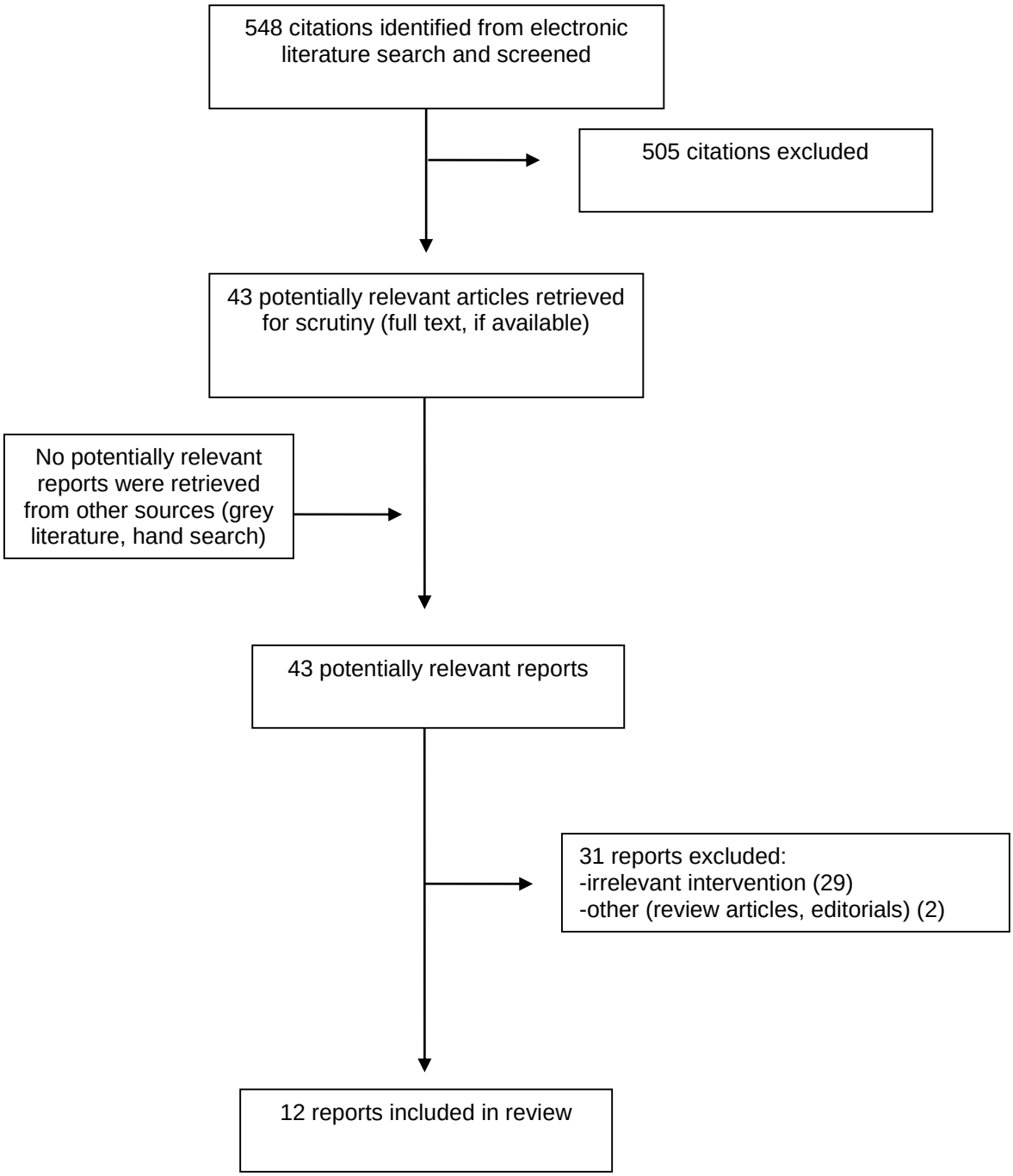
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Review and Meta-Analysis

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Gombert et al., 2020[11] Germany and the USA **Sources of funding** – No funding received	A systematic review with meta-analysis. Six RCTs were included in the systematic review, one of which was a published abstract reporting on results from the midpoint of RCT enrollment.	A total of 733 adult patients with closed groin incisions following vascular surgery Actual patients' ages were not specified.	A closed incision negative pressure dressing device applying -125 mm Hg pressure Versus Standard surgical dressings (i.e., absorbent dressings, sterile adhesive wound dressings, gauze, and conventional adhesive plaster)	• Surgical site infection Duration of follow-up ranged from 30 to 42 days in five studies, while one study had four months follow-up period.

Table 3: Characteristics of Included Primary Clinical Studies

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Kwon et al., 2018[3] **USA** **Sources of funding –** None reported	A single-centre unblinded RCT	A total of 119 patients, aged 18 years and older with closed incisions after undergoing elective vascular surgery involving unilateral or bilateral groin incisions The median (range) age of the patients was 64.6 (44 to 83) years in the NPWT group and 67.4 (41 to 84).	A closed incision negative pressure dressing attached to a suction device that applied -125 mm Hg pressure Versus Standard surgical dressings	• SSI rates • Reoperation • Readmission • Postoperative length of stay at the hospital Follow-up was 30 days
Pleger et al., 2018[2] **Germany** **Sources of funding –** Funded by the	A single-centre unblinded RCT	A total of 100 patients >50 years of age, undergoing vascular procedures The median (range) age of the patients was 71 (54 to 89)	A closed incision negative pressure dressing device with a preset negative pressure of -125 mm Hg	• Need for revision surgery Follow-up was 30 days

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Department of Vascular Surgery in a hospital, without external financial or scientific involvement.		years in the NPWT group and 66.5 (41 to 88).	Versus Standard wound dressings	
Lee et al., 2017[12] **Canada** **Sources of funding –** Funded by KCI USA Incorporated.	A single-centre, single-blind, RCT	A total of 64 patients who underwent GSV harvest for elective CABG The average age was 67.1 years in the NPWT group and 68.3 years in the control group.	A closed incision negative pressure dressing attached to a suction device that applied -125 mm Hg pressure Versus Standard surgical dressings	• SSI rates • Length of stay • Mobility • Self-care ability • HRQoL • Other self-reported measures of function Follow-up duration was 42 days (six weeks)
Tyagi et al., 2020[13] **USA** **Sources of funding –** No funding received	A retrospective single-center cohort study	A total of 235 patients who underwent primary posterior approach THA by a single surgeon The average age was 64.8 years in the NPWT group and 61.9 years in the control group.	Closed incision NPWT with a preset negative pressure of -125 mm Hg between July 2018 and January 2019 (n=92) Versus A silver-impregnated occlusive island dressing from January 2016 to January 2019. (n=143)	• SSI rates • Readmission rates • Need for reoperation • Postoperative length of stay at the hospital Duration of follow-up was not reported
Curran et al., 2019[14] **USA** **Sources of funding –** None reported. The authors indicated that they had no disclosures to make	A retrospective single-center cohort study	A total of 315 patients who had undergone high-risk open colorectal surgery High-risk referred to patients with one or more of the following factors: pre- or postoperative stoma, diabetes mellitus, obesity, preoperative steroid or immunosuppressant use and/or a	Closed incision NPWT (n=77) with a preset negative pressure of -125 mm Hg between 2014 and 2016 Versus Standard postoperative wound care between 2012 and 2014 (n=238)	• SSI rates • Readmission rates • Postoperative length of stay at the hospital • In-hospital Mortality Follow-up was until 30 days after surgery

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
		contaminated/dirty wound. The mean (SD) age was 56 (15) years in the NPWT group and 58 (16) years in the control group.		
Nickl et al., 2018[15] **Austria** **Sources of funding –** None reported. The authors stated that no competing financial interests existed	A retrospective single-center study	A total of 111 obese patients (BMI > 30) with post sternotomy DSWI following cardiac surgery The mean (SD) age was 67.3 (7.4) years in the NPWT group and 63.2 (8.9) years in the control group.	Closed incision NPWT with a preset negative pressure of -125 mm Hg between 2011 and 2016 (n=19) Versus Standard incision dressing with sterile gauzes between 2000 and 2010 (n=92)	• Need for surgical revisions, • Postoperative length of stay at the hospital • Duration of ICU stay, • In-hospital mortality Follow-up was until 30 days after surgery
Lo Torto et al., 2017[16] **Italy** **Sources of funding –** None reported. The authors declared no financial interest regarding this work.	A retrospective, single-center cohort study,	A total of 78 patients with DSWI following cardiac surgery who had major risk factors for post-sternotomy complications (BMI≥30, diabetics, smokers, age≥66 years, and female gender) The mean age was 68.1 years in the NPWT group and 64.2 years in the control group.	Closed incision NPWT with a preset negative pressure of -125 mm Hg between 2012 and 2016 (n=30) Versus Standard wound dressings, such as sterile gauzes and elastic bandages between 2008 and 2011 (n=48)	• Need for surgical revisions, • Postoperative length of stay at the hospital • Duration of ICU stay, • In-hospital mortality Duration of follow-up was not reported
Poehnert et al., 2017[17] **Germany** **Sources of funding –** No funding received	A prospective single-center cohort study	A total of 50 patients who underwent a surgical reversal of double loop ileostomy The median age of patients was 56.5 (range; 24 to 90) years in the NPWT group and 56.0 (range; 18 to 83). Mean ages of 56.3 and 55.4 years old were reported	Closed incision NPWT (n=24) with a preset negative pressure of -125 mm Hg Versus Standard postoperative wound dressings (n=26)	• Superficial SSI according to CDC criteria [a] • Postoperative length of stay at the hospital • Quality of life Follow-up was until 30 days after surgery

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
		without SD for the two groups, respectively.		
Cantero et al., 2016[18] **Spain** **Funding –** None reported. The authors disclosed that they have no financial relationships related to this article.	A prospective single-center pilot cohort study	A total of 60 patients who underwent elective ileostomy reversal The mean age was 64.7 years in the NPWT group and 60.3 years in the control group.	Closed incision NPWT with a preset negative pressure of -125 mm Hg from January and June of 2014 (n=17) Versus Standard wound dressings such as sterile gauzes and elastic bandages between 2011 and 2013 (n=43)	SSI (defined by CDC criteria) Follow-up was until 30 days after surgery
Abatangelo et al., 2018[19] **Italy** **Funding –** None reported. The authors declared that they have no conflict of interest	A retrospective non-randomized study	A total of 11 adult post-bariatric patients who had undergone an abdominoplasty The mean (SD) age was 40.4 (8.3) years in the NPWT group and 49.5 (6.7) years in the control group.	Closed incision NPWT (n=5) with a preset negative pressure of -125 mm Hg Versus Standard postoperative wound dressings (n=6)	• Wound healing time (measured as time-to-dry) • Local surgical wound complications • Length of hospital stay • Quality of scars Follow-up was until 90 days after surgery

BMI = body mass index; CABG = coronary artery bypass graft; CDC = Center of Disease Control; DSWI = Deep sternal wound infection; GSV = great saphenous vein; HRQoL = health-related quality of life; LOS = length of stay at the hospital after operation; NPWT = negative pressure wound therapy; PMF = pectoralis major flap; SD = standard deviation; SSI surgical site infection; THA = total hip arthroplasty.

[a] CDC criteria are 1) purulent secretion, and/or 2) positive wound swab, and/or 3) clinical symptoms of inflammation or surgical diagnosis of superficial SSI of the skin or the subcutaneous tissue within 30 days after surgery.[17]

Table 4: Characteristics of Included Guideline

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
Closed Incision Negative Pressure Therapy: International Multidisciplinary Consensus Recommendations – Willy et al., 2017[5]						
Intended users: Surgeons **Target population:** Patients with closed surgical incisions	Commercially available closed incision negative pressure therapy devices	• Surgical site infection • Surgical site occurrence • Dehiscence • Wound complication • Hematoma/seroma formation • Incisional drainage	The evidence for the recommendation was based on 100 publications, including systematic reviews, RCTs, case studies, caser series, non-RCT, and preclinical studies from 2000-2016 retrieved from Medline (PubMed), EMBASE and the Cochrane library. The searches were expanded using a 'snowball' system with further searches in the references of the self-researched publications.	The strength of evidence was evaluated using EbM classification system developed by the Oxford Centre for Evidence-Based Medicine	Twelve panelists made the recommendations by consensus after reviewing the publications retrieved by the systematic literature review. All panelist reviewed and agreed upon the final manuscript	NR

EbM = evidence-based medicine; RCT = randomized controlled trial; NR = not reported.

Appendix 3: Critical Appraisal of Included Publications

Table 5: Strengths and Limitations of Systematic Review and Meta-Analysis Using AMSTAR 2 [8]

Strengths	Limitations
Gombert et al., 2020[11]	
• The components of PICO were described clearly in the report. • A systematic literature search was conducted in multiple databases for relevant material published between 1 January 2005 and 31 December 2018. • Two reviewers independently assessed the eligibility of full-text articles for inclusion. Disagreements were resolved by consensus involving a third person reviewer. • One reviewer performed data extraction, which was independently checked by a second reviewer. Disagreements were resolved by the discussion between the two reviewers or involving a third reviewer. • The authors summarized the relevant characteristics of the included primary studies in tabular form. • The risk of bias in the primary studies of the SR was assessed using the Cochrane Collaboration tool for assessing the risk of bias. • The random-effects model was used to perform the meta-analyses, and weighted odds ratios and 95% CI were calculated to pool study and control groups in each publication for analysis. • Sensitivity analyses were conducted regardless of the heterogeneity assessment, and subgroup analyses were performed for high-risk or normal-risk patients and the classification of infection outcomes (i.e., Szilagyi I, II, and III). • Heterogeneity was assessed using the Chi-Square test, • Funnel plots were used to evaluate publication bias. • According to the authors, there was no financial support for the research, authorship, and publication of the article.	• The protocol for the SR and meta-analysis was not published or registered. However, the authors stated that they followed an internal protocol, details of which were not provided. • The literature searches were limited to databases and were not supplemented by checking published articles, specialized registers, or experts in the field of study and reviewing the reference list from the studies found. • A list of excluded studies was not provided, although a PRISMA flowchart illustrating the study selection process listed the reasons for the exclusions • The authors reported affiliation with KCI as consultants or employees. KCI was the manufacturer of PREVENA, which was the index intervention investigated in the systematic review.

CI = confidence intervals; PICO = population, intervention, control group and outcome; SR = systematic review

Table 6: Strengths and Limitations of Primary Studies Using the Downs and Black checklist[9]

Strengths	Limitations
Kwon et al., 2018[3]	
• Randomization reduced potential systemic bias • The study objectives and the main outcomes measures were defined. • The inclusion and exclusion criteria were provided.	• The patients were randomized to the treatment groups by a coin toss. It is unknown if adequate randomization was achieved using that method.

Strengths	Limitations
• Demographic and risk factors for wound complications between the two study groups were similar and without significant statistical differences. • The interventions of interest and main findings were described clearly. • The statistical approach to analyzing results was appropriate, and actual probability values were reported. • The authors stated that no competing financial interests existed.	• No attempt was made to blind study outcome assessors to the assignment of patients to the treatment groups. • There was no objective measure to assess wound complications, and the decision to re-open an infected wound was left to the discretion of the attending surgeon. • It was unknown if the definition of high-risk vascular groin wounds was a widely accepted standard as used in the study. Thus, it was unclear if the study population rightly represent high-risk patients as defined in other settings. • The generalizability of the findings was unknown since this was a single-center study.
Pleger et al., 2018[2]	
• Randomization reduced potential systemic bias • The study objectives, the intervention, and the main outcomes measures were defined. • The inclusion criteria were provided. • Demographic and risk factors for wound complications between the two study groups were similar and without significant statistical differences. • The statistical approach to analyzing results was appropriate. • The authors stated that no competing financial interests existed.	• Clear exclusion criteria were not provided • No attempt was made to blind outcome assessors to the assignment of patients to the treatment groups. • The generalizability of the findings is unknown since this was a single-center study.
Lee et al., 2017[12]	
• Randomization reduced potential systemic bias • The study objectives, the intervention, and the main outcomes measures were defined • The outcome assessor was blinded to the treatment grouping. • SSI and HRQoL outcomes were assessed using validated measurement tools (i.e., ASEPSIS and EQ-5D-3L, respectively). • Statistical analysis used appropriate methods • The authors declared that they had no conflict of interest.	• The study was conducted in a single institution, and the inclusion criteria restricted participation to patients living within one hour of the institution where the study took place. Thus, there is a high potential for limited generalizability of the study findings. • The skin and tissue closure technique was not standardized but was at the surgeon's discretion. • The analysis was not based on the ITT population because four (6.25%) of the 64 randomized patients were excluded from the analysis due to withdrawal of consent postoperatively. Another 12 patients (20%) lost to follow-up were excluded from the analysis. • Funding support for the RCT was provided by KCI USA incorporated, the manufacturer of PREVENA, the NPWT device that was evaluated in the study.
Tyagi et al., 2020[13]	
• The study objectives and the main outcomes measures were defined. • The inclusion and exclusion criteria were provided. • The interventions of interest and main findings were described clearly • The statistical approach to analyzing results was appropriate.	• As a non-randomized study, it lacked the risk-diminishing property of randomization and was inherently likely to have more systemic biases. • The percentage of patients classified as high risk and some demographic and risk factors for wound complications such as the proportion of males, BMI,

Strengths	Limitations
• The authors stated that there was no funding for the study.	and ASA class, were significantly different across the two study groups. • Generalizability was uncertain considering that the study used data from one institution, and a single surgeon performed all the surgeries
Curran et al., 2019[14]	
• The study objectives and the main outcomes measures were defined. • The inclusion and exclusion criteria were provided. • The interventions of interest and main findings were described clearly • The investigators used NSQIP-reviewed patient records, which captured complete events after surgery up to 30 days, including readmissions to outside institutions, and provided standardized criteria for postoperative adverse events. • The statistical approach to analyzing results was appropriate. • The authors indicated that they had no disclosures to make.	• The study had a non-randomized design with historical controls, which might result in treatment bias. • It was unknown if there were any procedural changes when NPWT was in use compared with the relatively earlier time when patients were treated with non-NPWT dressings.
Nickl et al., 2018[15]	
• The study objectives and the main outcomes measures were defined. • The inclusion criteria were provided. • Overall, there were no statistically significant differences in patient characteristics and risk factors for wound healing complications between the two groups. • The interventions of interest and main findings were described clearly. • The statistical approach to analyzing results was appropriate, and actual probability values were reported. • The authors stated that no competing financial interests existed	• The study had a non-randomized design with historical controls, which might result in treatment bias. • Clear exclusion criteria were not provided • It was unknown if there were any procedural changes when NPWT was in use (2011 to 2016) compared with the relatively earlier time when patients were treated with non-NPWT dressings (2000 and 2010).
Lo Torto et al., 2017[16]	
• The study objectives and the main outcomes measures were defined. • The inclusion criteria were provided. • The interventions of interest and main findings were described clearly. • The statistical approach to analyzing results was appropriate. • The authors stated that no competing financial interests existed	• The study had a non-randomized design with historical controls, which might result in treatment bias. • It was unknown if there were any procedural changes when NPWT was in use (2012 to 2016) compared with the relatively earlier time when patients were treated with non-NPWT dressings (2008 and 2011). • There was inadequate reporting, with p-values reported for some outcomes and not others. Also, data for postoperative hospitalization duration, including ICU stay, differed between the results and the discussion sections. • The authors reported no statistically significant differences in patient characteristics, heart surgery-

Strengths	Limitations
	related variables, and comorbidities between the two groups. However, apart from age, there was no data for independent confirmation.
Poehnert et al., 2017[17]	
• The study objectives and the main outcomes measures were defined. • The inclusion criteria and exclusion were provided. • There were no statistically significant differences in demographic data between the two investigated cohorts. • The interventions of interest and main findings were described clearly. • The statistical approach to analyzing results was appropriate, and actual probability values were reported. • There was no funding for the study, and all authors declare no conflict of interest.	• As a non-randomized study, it lacked the risk-diminishing property of randomization and was inherently likely to have more systemic biases. • Patients reported the study endpoints by telephone. Patient-reported outcomes are subjective, and it is unknown if the response could be replicated in another cohort of patients. • The use of an unidentified assessment tool with unknown validated status to evaluate patients' health-related quality of life
Cantero et al., 2016[18]	
• The study objective and the main outcomes measures were defined. • The inclusion criteria **and** were provided. • There were no significant differences in demographic variables between groups. • The interventions of interest and main findings were described clearly. • The statistical approach to analyzing results was appropriate. • There was no funding for the study, and all authors declare no conflict of interest. • The authors declare no conflict of interest.	• As a non-randomized study, it lacked the risk-diminishing property of randomization and was inherently likely to have more systemic biases. • Clear exclusion criteria were not provided • Although data from the NPWT system group were prospectively collected from January to June of 2014, the control group consisted of a historical cohort treated between 2011 to 2013. Thus, it was unknown if there were any procedural differences in the two time periods that could have impacted the reported outcomes.
Abatangelo et al., 2018[19]	
• The study hypothesis and the main outcomes measures were defined. • The inclusion and exclusion criteria and the characteristics of the patients included in the study were provided. • The interventions of interest and main findings were described clearly. • The authors declare no conflict of interest	• As a non-randomized study, the study lacked the risk-diminishing property of randomization and was inherently likely to have systemic biases. • The inclusion and exclusion criteria appeared restrictive. For instance, for patients to be eligible, they had to have a total weight loss > 30% after bariatric surgery, have residual obesity (BMI > 30 kg/m2), and local risk factors, among others, and not have severe systemic co-morbidities. Thus, the generalizability of the study findings in other patient groups was unclear. • The method of selecting patients whose data were used in the study was not reported. • It was unknown if the cases and controls were recruited over the same period. • There appeared to be differences in some patients' characteristics such as age, total weight loss, and time from previous bariatric surgery. The impact of these differences on the outcome was unclear.

Strengths	Limitations
	• Although the authors stated that they performed a sample size calculation, the calculation assumptions were not reported, and it was not specified if the study was adequately powered for all the outcomes. • P-values were not reported for some outcomes, so it was unknown if the differences between groups reached the level of statistical significance. Where p-values were stated, they were presented as <0.05 without the actual probability values, thus making it difficult to assess the magnitude of significance. • The authors did not adjust for potential confounders in the statistical analysis.

ASA = American Society of Anesthesiologists; BMI = body mass index; ICU = intensive care unit; ITT = intention-to-treat; NPWT = negative pressure would therapy; NSQIP = National Surgical Quality Improvement Program.

Table 7: Strengths and Limitations of Included Guideline Using AGREE II[10]

Item	Guideline
	Willy et al., 2017[5]
Domain 1: Scope and Purpose	
1. The overall objective(s) of the guideline is (are) specifically described.	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	Yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Yes
Domain 2: Stakeholder Involvement	
4. The guideline development group includes individuals from all relevant professional groups.	Yes
5. The views and preferences of the target population (patients, public, etc.) have been sought.	No
6. The target users of the guideline are clearly defined.	Unclear
Domain 3: Rigour of Development	
7. Systematic methods were used to search for evidence.	Yes
8. The criteria for selecting the evidence are clearly described.	Yes
9. The strengths and limitations of the body of evidence are clearly described.	Unclear
10. The methods for formulating the recommendations are clearly described.	Yes
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Yes
12. There is an explicit link between the recommendations and the supporting evidence.	Yes
13. The guideline has been externally reviewed by experts prior to its publication.	No
14. A procedure for updating the guideline is provided.	Unclear
Domain 4: Clarity of Presentation	
15. The recommendations are specific and unambiguous.	Yes
16. The different options for management of the condition or health issue are clearly presented.	Yes
17. Key recommendations are easily identifiable.	Yes
Domain 5: Applicability	
18. The guideline describes facilitators and barriers to its application.	Unclear
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	Yes
20. The potential resource implications of applying the recommendations have been considered.	Unclear
21. The guideline presents monitoring and/or auditing criteria.	Unclear
Domain 6: Editorial Independence	
22. The views of the funding body have not influenced the content of the guideline.	Yes
23. Competing interests of guideline development group members have been recorded and addressed.	Yes

AGREE II = Appraisal of Guidelines for Research and Evaluation II.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 8: Summary of Findings Included Systematic Review and Meta-Analysis

Main study findings	Authors' conclusion
Gombert et al., 2020[11]	
Surgical site infection • From six studies (n=733), the overall risk of developing SSI was statistically significantly lower in patients treated with NPWT than those treated with standard dressing (OR = 3.06, 95% CI: 2.05 – 4.58; P < 0.05) • From a subgroup analysis involving four RCTs (n=568), the risk of developing Szilagyi grade-I (superficial) SSI was significantly lower in patients treated with NPWT than those treated with standard dressing (OR = 3.09, 95% CI: 1.68 – 5.67; P < 0.0003) • From a subgroup analysis involving four RCTs (n=568), the risk of developing Szilagyi grade-II SSI (from four studies, n=568) was not statistically significantly different between patients treated with NPWT and those treated with standard dressing (OR = 1.92, 95% CI: 0.34 – 10.82; P = 0.47) • From a subgroup analysis involving four RCTs (n=568), the risk of developing Szilagyi grade-III SSI (from four studies, n=568) was not statistically significantly different between patients treated with NPWT and those treated with standard dressing (OR = 3.01, 95% CI: 0.93 – 9.77; P = 0.07)	• "For these meta-analyses, ciNPT usage demonstrated a statistically significant reduction in the incidence of SSI relative to traditional post-surgical dressings in patients undergoing vascular surgery with groin incisions. Future studies further assessing cost-effectiveness and adverse events following ciNPT use compared with traditional post-surgical dressings are required."[11](*pp283*)

CI = confidence interval; ciNPT = closed-incision negative pressure therapy; NPWT = negative pressure wound therapy; OR = odds ratio

Table 9: Summary of Findings of Included Primary Clinical Studies

Main study findings	Authors' conclusion
Kwon et al., 2018[3]	
Reoperation • The need for reoperation due to surgical wound complications within 30 days was statistically significantly lower among patients who received NWPT compared with those treated with standard dressing (5 [8.5%]) vs. 11 [18.3%]; p = 0.05]). **Readmissions** • Patients who used NWPT had a lower rate (4 [6.8%]) in readmissions for groin wound complication within 30 days than those who had standard dressing (10 [16.7%]). The difference was statistically significant (p = 0.04). **Length of stay** • There was no significant difference in LOS between patients treated with NPWT and those who received	• "Based on previous literature and this randomized controlled trial, the application of negative pressure to a closed groin incision appears to decrease the incidence of wound complications, particularly in patients at high risk for this common problem."[3] (*pp1751*)

Main study findings	Authors' conclusion
standard dressing (10.0 ± 11.5 days versus 9.1 ± 7.5 days, respectively).	
Pleger et al., 2018[2]	
Revision surgeries • One (1·7%) case in the NPWT group versus 10 (14·1%) cases in the control group. The difference was statistically significant (p = 0·022)	• "In comparison to conventional adhesive plaster, the use of ciNPT demonstrates a statistically significant reduction of postoperative WHCs in the groin on postoperative days 5–7 and 30 and revision surgeries until day 30 postoperatively in patients after several vascular surgeries."[2] (*pp82*)
Lee et al., 2017[12]	
Surgical site infection • There was no statistically significant difference between the NPWT and control groups in the incidence of SSI at initial assessment (p = 0.69) or 6-week follow-up (p = 1.0) **Length of stay** • Patients in the NPWT group had a statistically significantly earlier median (IQR) discharge date than those in the standard dressings group (6 [6 – 9] days vs 10 [7 – 13] days; p = 0.008). **Mobility** • Increased mobility was statistically significantly higher in the NPWT group than the standard dressing group at both the time of discharge (initial assessment) and 6-week follow-up assessments (p = 0.0117 and p = 0.0123, respectively). **Self-care ability** • Increased self-care ability at the discharge time (initial assessment) was statistically significantly higher in the NPWT group than the standard dressing group (p = 0.0234) but not at the 6-week follow-up assessment. **Health-related quality of life** • EQ-5D-3L score at initial assessment was statistically significantly higher in the NPWT group than the standard dressing group (73 vs. 59; p = 0.039) but not at the 6-week follow-up assessment.	• "The use of NPWT following GSV harvest is safe, well-tolerated and improves postoperative recovery with prolonged impact on mobility at 6 weeks."[12] (*pp324*)
Tyagi et al., 2020[13]	
Surgical Site Infections • SSI occurred in 1 (1%) patient in the NWPT group and 3 (2%) in the silver-impregnated occlusive dressing control group. The overall SSI rate difference between the two groups was not statistically significant (p = 0.553). • In a subgroup of high-risk patients, SSI occurred in 1 (1.2%) of those in the NWPT group versus 3 (2.97%) in the silver-impregnated occlusive dressing control	• "Our findings suggest that the use of incisional NPWT helps to reduce reoperation and readmission rates in high-risk patients after undergoing primary posterior approach THA. Given the significant costs associated with reoperations and readmissions, our data indicate that prophylactic use of NPWT in high-risk patients may be a useful adjunct to reduce complications."[13] (*pp7*)

Main study findings	Authors' conclusion
group. The difference was not statistically significant (p = 0.348). **Readmission Rate** • The readmission rate among the NPWT group was 6.52% compared with 10.49% in the occlusive dressing group. The difference was not statistically significant (p = 0.43). • In a subgroup of high-risk patients, the readmission rate was 4.82% in the NPWT group compared with 14.85% in the occlusive dressing group. The difference was statistically significant (p = 0.028). **Reoperation rates** • The reoperation rate was 4% in the NPWT group compared with 10% in the occlusive dressing group. The difference was not statistically significant (p = 0.09). • In a subgroup of high-risk patients, the reoperation rate was 1.2% among the NPWT group compared with 13.86 % in the occlusive dressing group. The difference was statistically significant (p = 0.001). **Length of Stay in Hospital** • Patients treated with NPWT had an average postoperative stay in the hospital of 3 days compared with 3.1 days for those in the occlusive dressing group. The difference was not statistically significant (p = 0.855). • In a subgroup of high-risk patients, the average duration of postoperative hospitalization was 3.02 days in the NPWT group compared with 3.22 days in the occlusive dressing group. The difference was not statistically significant (p = 0.620).	• "Further study is needed regarding the use of incisional NPWT dressings in high risk and revision hip arthroplasty cases."[13] (*pp7*)
Curran et al., 2019[14]	
Surgical site infection • The rate of SSI was statistically significantly lower with NPWT than conventional surgical wound care (6.5% vs. 15.1%; p = 0.05). **Readmissions** • The rate of unplanned readmissions was twice as high in the control group (16%) as in the NPWT group (8%). However, the difference was not statistically significant (P = 0.09). **Length of stay** • The mean postoperative length of stay was 8.7 days (SD, 7.5) with the NPWT group and 8.3 (9.5) days with the control group. **Mortality** • Four patients died in the control group while there was no mortality in the NPWT group. The difference was not statistically significant, and the cause of death was not reported.	"Negative pressure therapy was associated with decreased surgical site infection. Negative pressure therapy offers significant potential for quality improvement."[14] (*pp110*)

Main study findings	Authors' conclusion
Nickl et al., 2018[15]	
Surgical revision • One patient (5.3%) in the NPWT group needed a surgical revision due to wound complications compared with 9 (32%) in the control group. The difference was statistically significant (p = 0.034) **Length of stay at hospital/ICU** • The median duration of hospital stay was 14 days for the NPWT group and 19.5 days for the conventional dressing group. The differenced was not statistically significant (p = 0.179) • Postoperative length of stay in ICU was significantly shorter with NPWT than conventional dressing (median = 0, range: 0 to 5 days vs. median = 3.5, range 0 to 34 days; p < 0.001) **Mortality** • One (3.6%) patient in the conventional dressing group died during hospitalization, whereas no patient in the NPWT group died during hospitalization. The cause of death was not reported	• "In conclusion, we could show that Prevena was a useful additional tool in the treatment of obese patients with DSWI and subsequent PMF surgery. A lower rate of revision surgery after pectoralis major flap surgery for the treatment of deep sternal wound infection, a shorter length of stay in the ICU, and a trend toward a shorter hospitalization length were observed."[15] (*pp6*)
Lo Torto et al., 2017[16]	
Wound complications • Overall, 4 (13%) patients in the NPWT group had wound complications versus 18 (37.5%) in the control group. The difference was not significant (p-value not reported). **Surgical revision** • One (3%) patient in the NPWT group needed surgical revision compared with 7 (15%) patients in the control group. The difference was not statistically significant (p = 0.1433). **Length of stay at the hospital/ICU** • The mean (SD) duration of postoperative hospital stay until discharge were 15.5 (3.4) days and 15.8 (3.0) days for the NPWT and control groups, respectively. The difference was not significant (p-value not reported) • Patients in the NPWT group spent a mean (SD) of 3.7 (1.3) days in the ICU after the operation compared with 4.2 (2.0) days in the control group. The difference was not significant (p-value not reported) **Mortality** • One patient in the NPWT group died during hospitalization, whereas no patient in the control group died before discharge. The cause of death was not reported.	"Our results evidenced Prevena™ system's ability in improving the outcome of DSWI surgical treatment with MPMF in a high-risk patient population."[16] (*pp1335*) "We could demonstrate that Prevena™ can be a useful additional tool in the treatment of high-risked patients (obese patients BMI≥30, diabetics, smokers, age≥66 years and female gender) with DSWI and subsequent pectoralis major muscle surgery. Further study with a larger cohort of patients will be necessary to confirm our results."[16] (*pp1338*)

Main study findings	Authors' conclusion
Poehnert et al., 2017[17]	
Surgical site infections • The incidence of superficial SSI was 12.5% with an NPWT system compared with 20% with standard care. The difference was not statistically significant (P =0.051). **Length of stay at the hospital** • The postoperative median [range] duration of hospital stay was shorter with NPWT (5 [5 to 18] days) than with standard care (7 [4 to 18] days). The difference was statistically significant (p = 0.019). **Quality of life** • There was no significant difference in overall quality of life between the NPWT and standard dressings groups, although the latter point did not differ statistically significant (p = 0.37) • Patients treated with NPWT had a significantly better satisfaction with the course of wound healing (p = 0.03) and indicated a significantly lower need for help with wound care. Also, they had fewer sleep disorders and a better ability to fulfill daily tasks and to enjoy spare-time activities • However, anxiety that negatively affected professional performance was significantly less among patients in the standard dressings group (p = 0.027).	• "In conclusion, in the presented prospective observational study comparing the impact of SSD and iNPWT application on wounds after reversal of double loop ileostomy, we observed a decrease of SSSI rate and duration of hospital stay in iNPWT treated patients. This was accompanied by an increasing quality of life and, therefore, an overall better subjective value in terms of patients' satisfaction with the course of wound healing. Therefore, iNPWT wound management seems to be a reasonable therapeutic option, when administered postoperatively in a prophylactic manner in contaminated wounds."[17] (*pp1001*)
Cantero et al., 2016[18]	
• There was no incidence of SSIs in the NPWT group versus 9 (21%) in the control group. The difference was statistically significant (P < 0.038).	• "In conclusion, the NPWT system investigated was safe and easy to use and may prevent SSIs in dirty wounds, such as those from ileostomy closure."[18] (*pp 118*)
Abatangelo et al., 2018[19]	
Wound healing time • The mean (SD) time to wound healing was statistically significantly shorter with NPWT than standard dressings (11 [5] days vs. 23 [7] days; P < 0.05). **Local surgical wound complications** • The rate of minor local complications was statistically significantly lower with NPWT than with standard dressings (0 vs. 67%; P < 0.05). • One patient in the NPWT group experienced supra-fascial hematoma that required re-operation, and one patient in the standard dressing group had severe seroma that did not require reoperation. Thus, a statistically significant difference in major local complications was not observed between the two groups.	• "In conclusion, we demonstrate that ciNPT might significantly decrease the rate of minor local complications, but not of major local complications, in post-bariatric patients undergoing abdominoplasty. This strategy could represent a cost-effective adjuvant treatment in body-contouring procedures. Yet, our study represents only an initial, preliminary report, and further research is needed before routine clinical adoption of this technique as gold standard and best practice in post-bariatric body-contouring surgeries."[19] (*pp2102*)

Main study findings	Authors' conclusion
Length of hospital stay • The mean (SD) length of post-operative hospitalization was shorter for patients treated with NPWT than patients treated with standard dressings (9.2 [6.9] days vs. 12.3 [3.8] days). The level of statistical significance of the difference between the groups was not reported. **Quality of scars** • The mean (SD) VSS scores at 90-day follow-up assessment showed statistically significantly higher quality of scare with NPWT than with standard dressing (average VSS: 2 [1] for NPWT vs. 6.5 [1] for controls; P < 0.05)	

BMI = body mass index; ciNPT = closed incision negative pressure therapy; ICU = intensive care unit DSWI = Deep sternal wound infection; iNPWT = incisional negative wound pressure therapy; LOS = length of stay at the hospital; MPMF = monolateral pectoralis major muscle flap; NPWT = negative pressure would therapy; PMF = pectoralis major flap; SD = standard deviation; SSI = surgical site infection; THA = total hip arthroplasty; VSC = Vancouver Scar Scale; WHC = wound-healing complications.

Table 10: Summary of Recommendations in Included Guideline

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
Closed Incision Negative Pressure Therapy: International Multidisciplinary Consensus Recommendations – Willy et al., 2017[5]	
• "We recommend that the surgeon assess the individual patient's risk factors and surgical risks. Surgeons should consider using ciNPT for patients at high risk for developing SSOs or who are undergoing a high-risk procedure or a procedure that would have highly morbid consequences if an SSI occurred."[5] P.385 **Supporting evidence** • A majority of the 100 publications providing evidence for the development of the recommendation reported that the use of ciNPT decreased rates of SSIs, dehiscence, and hematoma/seroma formation. • "A recent meta-analysis reported a 50% reduction in the rate of SSIs in the ciNPT group compared with the control group (OR 0·564; P<0·00001)."[5] P.394	Not provided

ciNPT = closed incision negative pressure therapy; SSO = surgical site occurrence; SSI = surgical site infection.

Appendix 5: Additional References of Potential Interest

The following studies were not included because they did not have separate results or specific conclusions about -125 mmHg negative pressure wound therapy devices.

A. Systematic reviews

Cagney D, Simmons L, O'Leary DP, et al. The efficacy of prophylactic negative pressure wound therapy for closed incisions in breast surgery: a systematic review and meta-analysis. *World J Surg.* 2020 May;44(5):1526-1537.
PubMed: PM31900568

Norman G, Goh EL, Dumville JC, et al. Negative pressure wound therapy for surgical wounds healing by primary closure. *Cochrane Database Syst Rev.* 2020 May 1;5(5):Cd009261.
PubMed: PM32356396

Sexton F, Healy D, Keelan S, Alazzawi M, Naughton P. A systematic review and meta-analysis comparing the effectiveness of negative-pressure wound therapy to standard therapy in the prevention of complications after vascular surgery. *Int J Surg.* 2020 Apr;76:94-100.
PubMed: PM32142903

Shiroky J, Lillie E, Muaddi H, Sevigny M, Choi WJ, Karanicolas PJ. The impact of negative pressure wound therapy for closed surgical incisions on surgical site infection: a systematic review and meta-analysis. *Surgery*. 2020 March 3.
PubMed: PM32143842

Huang HP, Zhao WJ, Pu J, He F. Prophylactic negative pressure wound therapy for surgical site infection in obese women undergoing cesarean section: an evidence synthesis with trial sequential analysis(). *J Matern Fetal Neonatal Med*. 2019 September 25:1-8.
PubMed: PM31530067

Li Y, Wu B, Liu Y. The effect of negative pressure therapy on closed wound after the orthopedic surgery of lower limb: a meta-analysis. *Surg Innov*. 2020 Apr;27(2):165-172.
PubMed: PM31874595

Li HZ, Xu XH, Wang DW, Lin YM, Lin N, Lu HD. Negative pressure wound therapy for surgical site infections: a systematic review and meta-analysis of randomized controlled trials. *Clin Microbiol Infect*. 2019 Nov;25(11):1328-1338.
PubMed: PM31220604

Svensson-Björk R, Zarrouk M, Asciutto G, Hasselmann J, Acosta S. Meta-analysis of negative pressure wound therapy of closed groin incisions in arterial surgery. *Br J Surg*. 2019 Mar;106(4):310-318.
PubMed: PM30725478

Webster J, Liu Z, Norman G, et al. Negative pressure wound therapy for surgical wounds healing by primary closure. *Cochrane Database Syst Rev.* 2019 March 26;3(3):Cd009261.
PubMed: PM30912582

Wee IJY, Syn N, Choong A. closed incision negative pressure wound therapy in vascular surgery: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg.* 2019 Sep;58(3):446-454.
PubMed: PM31378658

Wells CI, Ratnayake CBB, Perrin J, Pandanaboyana S. Prophylactic negative pressure wound therapy in closed abdominal incisions: a meta-analysis of randomised controlled trials. *World J Surg.* 2019 Nov;43(11):2779-2788.
PubMed: PM31396673

Zwanenburg PR, Tol BT, Obdeijn MC, Lapid O, Gans SL, Boermeester MA. Meta-analysis, meta-regression, and GRADE assessment of randomized and nonrandomized studies of incisional negative pressure wound therapy versus control dressings for the prevention of postoperative wound complications. *Ann Surg.* 2019 October 4.
PubMed: PM31592899

Smid MC, Dotters-Katz SK, Grace M, et al. Prophylactic negative pressure wound therapy for obese women after cesarean delivery: a systematic review and meta-analysis. *Obstet Gynecol*. 2017 Nov;130(5):969-978.
PubMed: PM29016508

Strugala V, Martin R. Meta-Analysis of comparative trials evaluating a prophylactic single-use negative pressure wound therapy system for the prevention of surgical site complications. *Surg Infect (Larchmt).* 2017 Oct;18(7):810-819.
PubMed: PM28885895

De Vries FE, Wallert ED, Solomkin JS, et al. A systematic review and meta-analysis including GRADE qualification of the risk of surgical site infections after prophylactic negative pressure wound therapy compared with conventional dressings in clean and contaminated surgery. *Medicine (Baltimore).* 2016 Sep;95(36):e4673.
PubMed: PM27603360

B. Cost-effectiveness studies

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PubMed: PM30999239

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PubMed: PM27320010

Hyldig N, Joergensen JS, Wu C, et al. Cost-effectiveness of incisional negative pressure wound therapy compared with standard care after caesarean section in obese women: a trial-based economic evaluation. *BJOG*. 2019 Apr;126(5):619-627.
PubMed: PM30507022

Nherera LM, Trueman P, Schmoeckel M, Fatoye FA. Cost-effectiveness analysis of single-use negative pressure wound therapy dressings (sNPWT) compared to standard of care in reducing surgical site complications (SSC) in patients undergoing coronary artery bypass grafting surgery. *J Cardiothorac Surg.* 2018 October 3;13(1):103.
PubMed: PM30285811

Nherera LM, Trueman P, Karlakki SL. Cost-effectiveness analysis of single-use negative pressure wound therapy dressings (sNPWT) to reduce surgical site complications (SSC) in routine primary hip and knee replacements. *Wound Repair Regen*. 2017 May;25(3):474-482.
PubMed: PM28370637

Correction Notice

The original report published June 30, 2020, included nine studies comprising two open-label randomized controlled trials (RCTs),[2,3] six non-randomized studies,[13-18] and one evidence-based guideline.[5] Evidence from one systematic review (SR) with meta-analysis,[11] one single-blind RCT,[12] and one retrospective case-control study[19] has now been added, bringing the number of studies included in this updated version to 12.

The two RCTs[2,3] in the original publication were part of the primary studies of the SR,[11] and their surgical site infections (SSI) data were captured in the meta-analysis of the SR. Therefore, to avoid double-counting and overestimation of results, the SSI findings of the RCTs[2,3] were not reported independently from the effect estimates with 95% CI provided by the SR[11] in this updated report. The RCTs[2,3] have been retained in this version due to additional relevant outcomes not reported in the SR.[11]

The report conclusions have changed with the addition of these studies. The original report stated, “there was no conclusive evidence indicating that a -125 mm Hg negative pressure wound therapy (NPWT) system is statistically significantly more effective than conventional wound dressing for preventing surgical site infections.” This has been updated to reflect that, despite some studies showing no difference, there is evidence that the -125 mm Hg NPWT device is statistically significantly more effective than conventional wound dressings for preventing SSI than standard wound dressings. However, the overall SSI reduction benefit with NPWT may be due to outcomes from patients with superficial SSI. Also, evidence of limited quality suggested that HRQoL may be significantly better with NPWT than standard dressings at the discharge time but not at 6-week follow-up.