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Review Article

A Systematic Review and Meta-analysis of Two Negative Pressure Wound Therapy Devices to Manage Cesarean Section Incisions

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Abstract

This paper aims to evaluate whether there is a device-dependent effect on the reduction of surgical site complications in obese patients (body mass index [BMI] $\geq$ 30 kg/m^2) undergoing cesarean section (C-section). PubMed, Embase, Cochrane Library, and ClinicalTrials.gov were searched for the period, January 2011 to September 2021. English language articles describing a randomized controlled trial (RCT) that compared either a −80 or −125 mm Hg single-use negative pressure wound therapy (sNPWT) device to standard dressings in obese (BMI $\geq$ 30 kg/m^2) patients undergoing C-section were included. Conference abstracts and "terminated" RCTs with published results were deemed eligible for inclusion. The primary outcome of interest was surgical site infection (SSI), classified as composite, superficial, or deep. Secondary outcomes assessed included seroma, dehiscence, hematoma, bleeding, reoperation, readmission, blistering, and (composite) wound complications. A total of 223 titles were identified, of which 129 were screened by full-text review. Eleven RCTs encompassing 5,847 patients met the inclusion criteria and were considered eligible for further analysis (−80 mm Hg: six studies; −125 mm Hg: five studies). A statistically significant improvement in the composite SSI (odds ratio [OR]: 0.69; 95% confidence interval [CI]: 0.54–0.89) and superficial SSI (OR: 0.66; 95% CI: 0.50–0.86) outcomes was observed with the −80 mm Hg device, compared with standard dressings. The same effect on SSI outcomes was not observed with the −125 mm Hg device (composite SSI—OR: 0.91; 95% CI: 0.64–1.28; superficial SSI—OR: 1.12; 95% CI: 0.70–1.78). There were no statistically significant differences in any of the other assessed outcomes. sNPWT devices may differ in their ability to reduce composite or superficial SSI after C-section.

Keywords

- surgical site infection
- obesity
- cesarean section
- negative pressure wound therapy
- meta-analysis
- systematic review

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Key Points

- Negative pressure benefits obese patients undergoing C-section.
- Negative pressure devices may differ in performance.
- A head-to-head clinical trial is needed.

Deliveries by cesarean section (C-section) are one of the most common obstetric procedures worldwide, with rates increasing over the last 30 years.[1,2] By 2030, it is projected that 28.5% of all births will be by C-section, with an even higher rate of 33.8% in the United States.[3] Brazil has one of the highest rates, globally, at 55.8%.[4]

The rising prevalence of C-section deliveries is driven by elements of perception (i.e., it is controllable and convenient[5]) and an increase in medical risk factors, especially prepregnancy obesity (body mass index [BMI] $\geq$ 30 kg/m^2).[6] Prepregnancy obesity in the United States rose from 26.1% in 2016 to 29.0% in 2019.[7] Surgeon preference for incision types in obese patients is largely weighted towards using a Pfannenstiel incision,[8] although vertical incisions have been shown to have roughly similar postoperative wound morbidity in this population.[9]

The incidence of surgical site infection (SSI) after C-section is approximately 10% in the United States.[10] Prepregnancy obesity is an additional risk factor for SSI after C-section[11–15] and other surgical site complications (SSCs), including dehiscence, seroma, hematoma, and bleeding.[16–18]

Prophylactic negative pressure wound therapy (NPWT) has emerged as a successful intervention in patients undergoing C-section at high risk for SSI[19] and other SSCs. Single-use NPWT (sNPWT) devices are especially advantageous, as they are small, light, and highly portable.[20] The two most widely used sNPWT devices following C-section are PICO (Smith & Nephew Medical Ltd; Hull, United Kingdom; −80 mm Hg device) and PREVENA (previously KCI, an Acelity Company, now 3M; San Antonio, TX; −125 mm Hg device), which have been approved since 2010 by the U.S. Food and Drug Administration for prophylactic application after incisional closure at the time of surgery.[21]

Both consist of a single-use, battery-powered device and a foam-based or absorbent layer-based, peel-and-place dressing designed for closed surgical incisions. There have been multiple studies comparing each device against standard dressings, but none offering head-to-head comparisons of outcomes with these two devices in this indication.[22]

With the −80 mm Hg device, exudate is managed predominantly by evaporation through the dressing, therefore negating the need for a canister.[23] It is a multilayered adhesive dressing including an AIRLOCK (Smith & Nephew Medical Ltd; Hull, United Kingdom) Technology layer that delivers consistent negative pressure across the whole dressing to ensure treatment is delivered to a wider zone beyond the wound itself.[24] The device delivers continuous negative pressure at −80 mm Hg for up to 7 days.[23]

The −125 mm Hg device collects exudate in a replaceable 45-mL canister[25] and uses a reticulated polyurethane foam dressing covered with a thin film. The device delivers continuous negative pressure at −125 mm Hg for up to 7 days.[26]

Both devices are currently indicated in the United States to aid in the reduction of the incidence of postoperative seroma and, in patients at high risk for postoperative infection, superficial SSI in Class I and II wounds. The −80 mm Hg device is also additionally indicated in the United States to aid in the reduction of the incidence of dehiscence and deep SSI in Class I and II wounds.

Previous studies have shown inconsistencies in the clinical outcomes obtained with sNPWT devices, which may be in part due to differences in the sNPWT interventions used between studies. Several recent systematic literature reviews and meta-analyses[27–29] have demonstrated reductions in the incidence of SSIs by using sNPWT for the management of closed surgical incisions in patients undergoing C-section. However, most of these studies have only reported on the pooled data of the different sNPWT devices versus standard of care. Guo et al investigated different sNPWT devices as part of a secondary subgroup analysis but their study was not specifically designed to answer the question of whether differences in performance exist between sNPWT devices and confined their analysis to a single outcome (composite SSI).[28]

Therefore, the research question this study aims to answer is whether there are any differences in relation to standard care in the clinical performances of two sNPWT devices across a number of different wound complication outcomes. By answering the question, this analysis will expand on previous studies in this area by providing additional information on variables likely to influence successful wound healing in this patient population and guide future research.

Sources

This review was written in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[30] This review was not preregistered.

A search was undertaken using Embase, PubMed, Cochrane Library, and ClinicalTrials.gov to identify studies reporting on the use of either the −80 or the −125mm Hg devices. The search string/keywords can be found in the supplementary material (►**Supplementary Table S1**, available in online version). To increase the scope of the search, the search terms were left intentionally broad (e.g., no outcomes were specified).

Study Selection

English language studies published from 2011 to September 2021 were included. Two experienced data reviewers screened for relevant studies independently by examining titles and abstracts. To be included, the study must have been a randomized controlled trial (RCT) with $\geq$10 patients in each treatment arm and

report on the use of sNPWT (−80 or −125 mm Hg device) for the management of surgical site incisions in patients of any age undergoing C-section. The study must also have reported on obese patients (BMI $\geq$ 30 kg/m^2). RCTs deemed potentially relevant progressed to full-text screening. In instances of disagreement, a third reviewer made the final decision for inclusion after reading the full-text paper or conference abstract. Included RCTs compared outcomes following the use of either −80 or −125 mm Hg device versus standard care for closed surgical incisions in obstetrics (i.e., the use of standard non-NPWT dressings).

Data were extracted from included RCTs using a predefined and standardized data extraction form and checked for accuracy by a second reviewer. No automated extraction tools were used. Extracted data included descriptions of location of the RCT, the number of patients in each treatment arm, type of dressing used, treatment duration, follow-up period, and outcomes data. Outcome data were extracted based on the values reported at final assessment or follow-up. Where possible, conference abstracts were extracted in the same manner as full manuscripts. Missing or additional information from the abstract was obtained from the study's ClinicalTrials.gov registration.

The primary outcome of interest was the number of patients who had an SSI (classified as composite [overall], superficial, or deep) with either −80 or −125 mm Hg devices, compared with the standard of care. Secondary outcomes of interest were the number of patients who developed composite wound complications, dehiscence, seroma, hematoma, bleeding, or blistering. Readmission and reoperation rates were also collected.

The reviewers assessed the risk of bias for each RCT, considering the challenges of blinding clinicians and participants to sNPWT devices. Bias assessments were performed for individual RCTs using quality criteria taken from the Centre for Reviews and Dissemination guidelines[31] for the assessment of risk of bias in RCTs. Each criterion was rated for low, unclear/medium, and high risk of bias. To assess publication bias, an Egger's test was performed using the dmetar package in R 3.6.1 (R Core Team, 2019).

Overall effect estimates were calculated using the meta package in R. Formal meta-analyses were conducted when there were at least two RCTs reporting on the same outcome. The Mantel–Haenszel method was used for binary outcomes, with either a fixed effect model or a random effects model. Individual odds ratio (OR) estimates and summary estimates (including 95% confidence interval [CI]) were displayed graphically in forest plots. Heterogeneity was quantified with the I^2 statistic. The fixed effect model was used when heterogeneity was low ($I^2 < 50\%$) and random effects model when heterogeneity was high ($I^2 \geq 50\%$). Sensitivity analyses were performed by the exclusion or inclusion of terminated RCTs and using fixed effect or random effects models. $p < 0.05$ denoted statistical significance.

Results

The PRISMA flow diagram outlining the study selection at various phases of the systematic literature review is shown in ►Fig. 1.[32] In total, 223 studies were identified from the review, of which 129 were screened by full text. There was one study that appeared to meet the inclusion criteria but was excluded (i.e., "near-miss"), as it did not report the type of negative pressure device used.[33] No other "near-misses" were identified. Eleven RCTs met the inclusion criteria and were considered eligible for further analysis.

Key study characteristics are outlined in ►Table 1. Six RCTs evaluated the −80 mm Hg device,[34–39] of which two RCTs[36,39] were available as conference abstracts only. Five RCTs evaluated the −125 mm Hg device.[25,26,40–42] Two RCTs, one reporting on the −80 mm Hg device and the other on the −125 mm Hg device, were identified as "terminated".[38,41] All studies reported on either composite, superficial, or deep SSI, except Gonzalez et al who only reported overall wound complications.[36] The majority of studies stated that all patients received antibiotic prophylaxis, except for some studies where their use was not mentioned.[34,36,37] The majority (>98%) of patients in the Gillespie et al's study received antibiotic prophylaxis.[35]

In total, 5,847 patients were investigated from the collective RCTs (numbers at randomization). For the −80 mm Hg device RCTs, 1,689 patients received the intervention and 1,699 patients received standard dressings. For the −125 mm Hg device RCTs, 1,231 patients received the intervention and 1,228 patients received standard dressings.

The results of the bias assessment for the included studies can be seen in ►Fig. 2. The overall quality of the studies was deemed acceptable, with the studies at low-to-moderate risk of bias. This was consistent between both −80 and −125 mm Hg device studies. The main factor contributing to increased risk of bias among most studies was an unclear, or unavailable, intention-to-treat analysis. No studies were completely blinded due to the nature of the interventions being administered.

An overview of the meta-analysis results is shown in ►Table 2. A statistically significant improvement in the composite SSI (OR: 0.69; 95% CI: 0.54–0.89) and superficial SSI (OR: 0.66; 95% CI: 0.50–0.86) outcomes was observed with the −80 mm Hg device (►Figs. 3 and 4), compared with standard of care. The same effect on SSI outcomes was not observed with the −125 mm Hg device (composite SSI—OR: 0.91; 95% CI: 0.64–1.28; superficial SSI—OR: 1.12; 95% CI: 0.70–1.78; ►Figs. 5 and 6). There were no statistically significant improvements in deep SSI outcomes for either the −80 mm Hg device (OR: 0.84; 95% CI: 0.43–1.66) or the −125 mm Hg device (OR: 0.99; 95% CI: 0.43–2.31).

There was no statistically significant difference in the composite wound complication outcome for either −80 mm Hg (OR: 0.85; 95% CI: 0.53–1.35) or −125 mm Hg (OR: 0.89; 95% CI: 0.68–1.17) interventions, compared to standard of care. Meta-analysis of each component of the composite wound complications outcome also demonstrated no statistically significant reduction in dehiscence (−80 mm Hg device—OR: 1.01; 95% CI: 0.80–1.26; −125 mm Hg device—OR: 1.11; 95% CI: 0.65–1.90) and seroma (−80 mm Hg device—OR: 1.04; 95% CI: 0.62–1.75; −125 mm Hg device—OR: 0.82; 95% CI: 0.39–1.74). All other SSCs analyzed (hematoma, bleeding) were also not statistically significant (►Table 2;

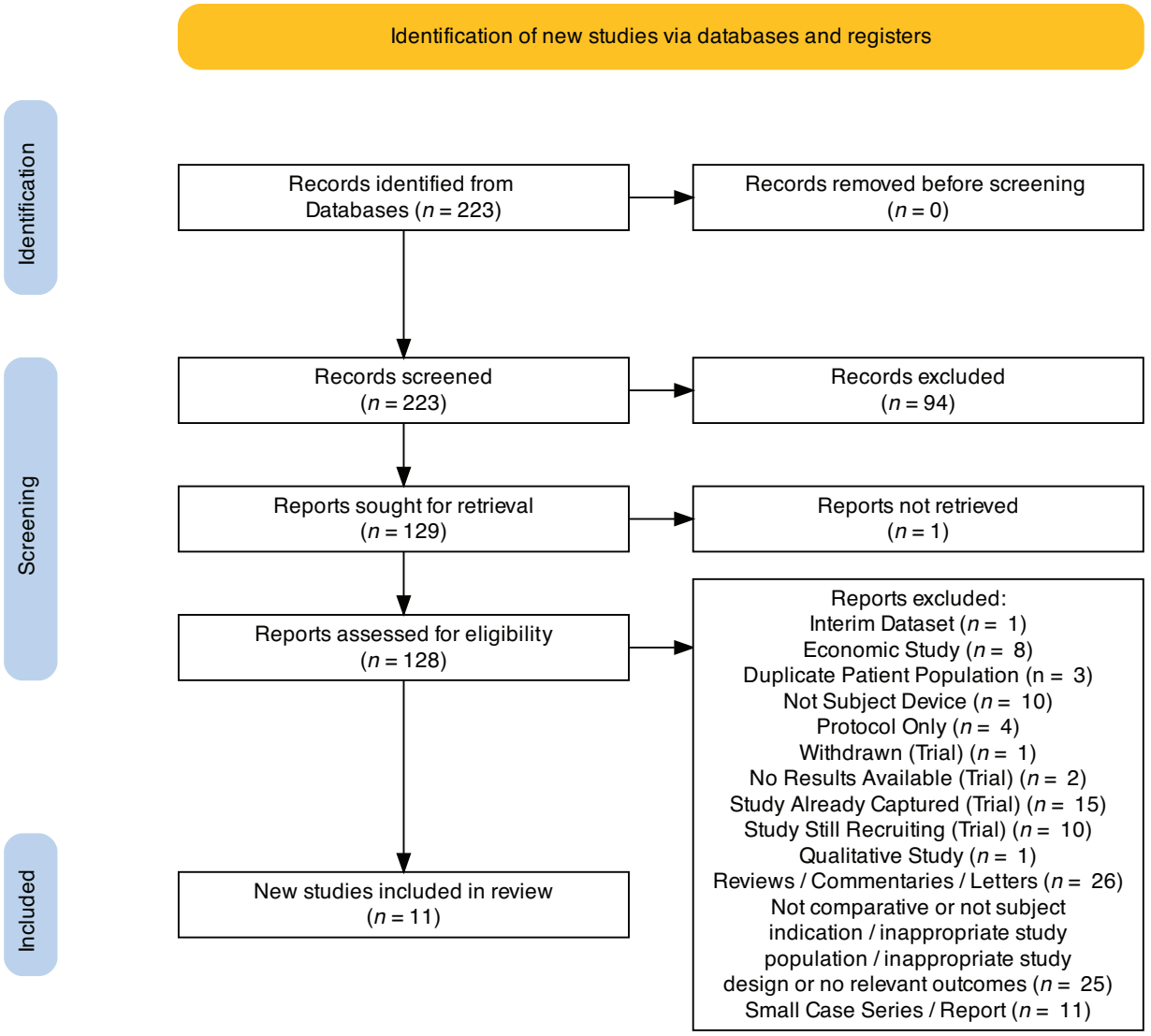

Fig. 1 PRISMA flow diagram of included studies. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

►**Supplementary Figs. S1–S16;** available in the online version). No statistical difference was observed with the readmission (−80 mm Hg device—OR: 1.68; 95% CI: 0.88–3.21; −125 mm Hg device—OR: 1.21; 95% CI: 0.59–2.46) outcome. A meta-analysis for the reoperation outcome was not possible for the −80 mm Hg device due to insufficient data. No statistical difference was observed with the −125 mm Hg device compared to standard of care for this outcome (OR: 1.00; 95% CI: 0.52–1.93).

For the blistering outcome, no statistically significant increase was identified with the use of either the −80 mm Hg device (three RCTs; 1,095 patients in the intervention group and 1,081 patients in the control group; OR: 1.42; 95% CI: 0.40–5.04) or the −125 mm Hg device (two RCTs; 867 patients in the intervention group and 860 patients in the control group; OR: 12.71; 95% CI: 0.69–235.29) compared to standard of care. One study with the −125 mm Hg device was halted due to increased blistering.[41] An additional study reported a number of blistering cases in the −125 mm Hg group compared to zero in the standard group, although the authors pooled these events with other skin reactions making it unsuitable for inclusion in this subanalysis.[25]

Statistical heterogeneity denoted by the I^2 statistic was not significant (<50%) for all outcomes, except for the −80 and −125 mm Hg devices blistering outcome subanalyses ($I^2 = 54\%$ and $I^2 = 70\%$, respectively). Sensitivity analyses were performed for the composite SSI and superficial SSI outcomes. Applying a random effects model, it was still possible to demonstrate a statistically significant reduction in composite SSI (OR: 0.70; 95% CI: 0.54–0.90) and superficial SSI (OR: 0.64; 95% CI: 0.44–0.93) for the −80 mm Hg device, but no statistically significant difference for the −125 mm Hg device when compared to standard of care. Further sensitivity analyses were performed by eliminating the terminated studies from each subanalysis to determine their impact on the results. Both the composite (OR: 0.68; 95% CI: 0.52–0.88) and superficial SSI (OR: 0.64; 95% CI: 0.48–0.85) outcomes remained statistically significant for the −80 mm Hg device, with no statistically significant difference detected with either outcome for the −125 mm Hg device.

Table 1 Characteristics of included studies

Author, year, country, BMI inclusion criteria	Relevant outcome(s) assessed[b]											Antibiotic prophylaxis used? (Y/N/NR)	BMI (kg/m^2)	Emergency C-section (frequency)	Final outcome assessment duration	Incisional dressings used	Subjects[c]	Treatment duration
	SSI (overall)	SSI (superficial)	SSI (deep)	Wound complications	Dehiscence	Seroma	Hematoma	Bleeding	Blistering	Readmission	Reoperations							
Hyldig et al 2018[37], Denmark, BMI $\geq$ 30 kg/m^2	x	x	x	–	x	–	–	–	–	–	–	NR	Median (IQR): 34.7 (31.5–38.2)	203 (47.1%)	30 days	−80 mm Hg device	432	5 days
													Median (IQR): 34.2 (31.6–38.1)	209 (47.0%)		Standard postoperative dressing	444	The dressing was left in situ for at least 24 hours
Tuuli et al 2017[39], the United States, BMI $\geq$ 30 kg/m^2	x	–	–	x	x	x	x	–	–	–	–	Y	Mean (SD): 39.2 (9.2)	Included but not reported	30 days	−80 mm Hg device	60	Removed at discharge (usually on day 4)
													Mean (SD): 40.7 (8.6)	Included but not reported		Standard wound dressing	60	The dressing was removed after 24 hours
Chaboyer et al 2014[34], Australia, BMI $\geq$ 30 kg/m^2	x	x	x	x	x	x	–	x	x	x	–	NR	Median (IQR): 35.7 (4.5)	Excluded	28 days	−80 mm Hg device	46	The dressing remained in place until day 4, unless it became soiled or dislodged, in that case a new dressing of the same type was applied
												NR	Median (IQR): 36.8 (5.8)	Excluded		Standard dressing	46	The dressing remained in place until day 4, unless it became soiled or dislodged, in that case a new dressing of the same type was applied
Gillespie et al 2021[35], Australia, BMI $\geq$ 30 kg/m^2	x	x	x	x	x	x	x	x	x	x	x	Y[d]	BMI, *n* (%): 30–34.9: 488 (48) 35–39.9: 268 (26) 40–49.9: 218 (21) ≥50: 43 (4)	Excluded	30 days	−80 mm Hg device	1,017	The dressing was left intact for 5 to 7 days
													BMI, *n* (%): 30 – 34.9: 524 (52) 35 – 39.9: 247 (24) 40 – 49.9: 211 (21) ≥50: 117 (12)	Excluded		Standard dressing	1018	The dressing was left intact for 5 to 7 days
Peterson et al 2021[a,38], the United States, BMI $\geq$ 40 kg/m^2	–	x	–	x	–	x	x	–	x	x	–	Y	Mean (SD): 49.3 (6.6)	Unscheduled: 32 (58.2%)	6 weeks	−80 mm Hg device	55	The NPWT dressing was changed once by the discharging physician on postoperative day 3 or 4 to evaluate the wound before hospital discharge. If the indicator light on the negative-pressure dressing indicated that the dressing was no longer functioning, then the initial negative-pressure dressing was changed, and wound

(*Continued*)

Table 1 (*Continued*)

Author, year, country, BMI inclusion criteria	Relevant outcome(s) assessed[b]											Antibiotic prophylaxis used? (Y/N/NR)	BMI (kg/m^2)	Emergency C-section (frequency)	Final outcome assessment duration	Incisional dressings used	Subjects[c]	Treatment duration
	SSI (overall)	SSI (superficial)	SSI (deep)	Wound complications	Dehiscence	Seroma	Hematoma	Bleeding	Blistering	Readmission	Reoperations							
																		evaluation performed before postoperative day 3. The patient was given standardized verbal and written instructions on how to remove and discard the NPWT dressing on postoperative day 7
													Mean (SD): 47.8 (6.9)	Unscheduled: 35 (63.6%)		Sterile nonadherent wound dressing, a sterile abdominal gauze pad, and a waterproof transparent adhesive dressing	55	The standard dressing was removed on postoperative day 1 and inspected daily during inpatient admission
Gonzalez et al 2020[36], the United States, BMI ≥ 30 kg/m^2	–	–	–	x	–	–	–	–	–	–	–	NR	Mean (SD): 39.9 (8.3)	NR	6 weeks	−80 mm Hg device	79	The NPWT dressing was removed on the day of hospital discharge and replaced with a second dressing. The patient removed the NPWT dressing on postoperative day 7
														NR		Standard dressing	76	28 to 48 hours
Gunatilake et al 2017[26], the United States, BMI ≥ 35 kg/m^2	x	–		x	x	x	–	–	–	–	x	Y	Mean (SD): 46.3 (7.3) Range: 35.7 – 60.8	NR	52 days	−125 mm Hg device	46	Duration of NPWT was ≥5 to ≤7 days, immediately following surgery
													Mean (SD): 46.8 (5.6) Range: 38.9 – 60.8	NR		Sterile adhesive strips, sterile gauze, and a waterproof transparent adhesive dressing	46	1 to 2 days
Hussamy et al 2019[25], United States, BMI ≥ 40 kg/m^2	x	x	x	x	x	–	–	–	–	x	x	Y	Mean (SD): 46.6 (6.0)	Urgent: 141 (64%) Emergency: 9 (4%)	60 days	−125 mm Hg device	222	Until hospital discharge or unless premature removal was indicated or requested by the primary obstetric care team
													Mean (SD): 45.8 (5.8)	Urgent: 138 (63%) Emergency: 9 (4%)		Standard dressing	219	Per hospital routine, usually day 1 postoperatively
Ruhstaller et al 2017[40], the United States, BMI ≥ 30 kg/m^2	x	–	–	x	–	–	–	–	x	–	x	Y	Median (range): 36.1 (33.2 – 41.8)	Unscheduled: 61 (100%)	4 weeks	−125 mm Hg device	67	The dressing was removed at day 3 postoperatively

Table 1 (*Continued*)

Author, year, country, BMI inclusion criteria	Relevant outcome(s) assessed[b]											Antibiotic prophylaxis used? (Y/N/NR)	BMI (kg/m^2)	Emergency C-section (frequency)	Final outcome assessment duration	Incisional dressings used	Subjects[c]	Treatment duration
	SSI (overall)	SSI (superficial)	SSI (deep)	Wound complications	Dehiscence	Seroma	Hematoma	Bleeding	Blistering	Readmission	Reoperations							
													Median (range): 35.1 (32.6 – 42.1)	Unscheduled: 57 (98%)		Sterile nonadherent wound dressing overlaid with a 4 cm × 4 cm gauze pad and surgical tape	69	Dressing was removed 24 hours after surgery
Wihbey et al 2018[42], the United States, BMI ≥ 35 kg/m^2	x	x	x	x	x	x	x	–	–	x	x	Y	Mean (SD): 44.9 (8.0)	Scheduled: 9 (12%)	30 days	−125 mm Hg device	80	Dressing was removed between postoperative days 5 and 7
													Mean (SD): 43.4 (7.0)	Scheduled: 7 (8%)		Sterile nonadherent wound dressing, a sterile gauze, and a waterproof transparent adhesive dressing	86	The dressing was removed on postoperative day 2
Tuuli et al 2020[a,41], the United States, BMI ≥ 30 kg/m^2	x	x	x	x	x	x	x	x	x	x	–	Y	Mean (SD): 39.6 (7.7)	Unscheduled: 253 (31.4%) Urgent: 90 (11.2%) Emergency: 46 (5.7%)	30 days	−125 mm Hg device	816	Removed on discharge at postoperative day 4 or 7 for patients who remained hospitalized
													Mean (SD): 39.5 (8.1)	Unscheduled: 256 (31.9%) Urgent: 96 (12.0%) Emergency: 36 (4.5%)		Standard dressing	808	Dressing was removed at 24 hours

Abbreviations: BMI, body mass index; C-section, cesarean section; IQR, interquartile range; NPWT, negative pressure wound therapy; NR, not reported; RCT, randomized controlled trial; SD, standard deviation; SSI, surgical site infection.
[a]Terminated RCT.
[b]Studies reported upon additional outcomes not relevant to this analysis.
[c]At randomization.
[d]The authors report that the majority of patients received antibiotic prophylaxis although not all patients received prophylaxis.

Fig. 2 Bias assessment of included studies. ITT, intention to treat; RCT, randomized controlled trial.

The Egger's publication bias test did not indicate the presence of funnel plot asymmetry for the −80 mm Hg device composite SSI (intercept: 0.491; 95% CI: −1.08 to 2.06; $t = 0.613$; p-value = 0.5833) and superficial SSI outcomes (intercept: −0.387; 95% CI: −3.01 to 2.24; $t = -0.289$; p-value = 0.7997). For details on the funnel plots, refer to the supplementary material (►**Supplementary Figs. S17–S36,** available in the online version).

Discussion

This systematic literature review identified a balanced number of RCTs investigating either −80 or −125 mm Hg devices for the management of surgical site incisions in patients undergoing C-section. It demonstrates a significant benefit of using sNPWT devices to reduce SSIs after C-section over standard dressings, which agrees with recent similar systematic literature reviews[27–29] as well as previous studies.[21,43] Importantly, the present study goes further to demonstrate that this significant benefit in the reduction of SSI may be device specific.

These findings agree with a previous systematic literature review and meta-analysis conducted by Guo et al in 2021, who identified a difference between the two sNPWT devices in a subgroup analysis for overall SSI.[28] The primary research question of the present study was to compare the two negative pressure devices in detail for the most clinically relevant wound complications such as SSI, seroma, hematoma, and dehiscence. This differs from the study by Guo et al who only investigated device differences as part of a secondary analysis for a single outcome and were, therefore not capable of answering this question comprehensively. Specifically, Guo et al did not evaluate SSI subtypes (superficial, deep) or any other key wound complication outcome in relation to a device subgroup analysis. The present study, therefore, provides a detailed comparison of the clinical performances of the two devices, which allows for greater understanding of what variables contribute to successful clinical outcomes in obese patients undergoing C-section. In addition, the present updated analysis provides additional relevant data not included in previous reviews, thereby providing the most comprehensive picture to date in this research area.

The main finding of this analysis, therefore, expands on prior reviews in demonstrating that using the −80 mm Hg device resulted in a significantly lower number of superficial SSIs (as well as overall SSIs) compared with standard dressings. This significant difference was not demonstrated with the −125 mm Hg device (when compared to standard of care). Various sensitivity analyses performed on these outcomes demonstrate the robustness of these findings. Although the majority of the treatment effect on SSI reduction is being driven by a reduction in superficial SSIs, this is to be expected given the low relative incidence of deep SSIs, as most studies will not be sufficiently powered to detect a statistical difference.[44] A statistically significant reduction in superficial SSI is, therefore, clinically relevant as this subtype represents the majority of SSIs.

These differences could be explained with the differing mode of action of the devices. The −80 mm Hg device has a primary mode of action of evaporation through four layers whereas the −125 mm Hg device has a foam filler and a separate exudate canister. They also operate at different

Table 2 Results of meta-analyses performed for all surgical site complication outcomes

Outcome	Device	Number of studies	Number of participants	Statistical method	I^2 statistic (%)	Effect estimate	*p*-Value
SSI (composite)	−80 mm Hg device	5	3,228	OR (M–H, fixed effect, 95% CI)	0	0.69 (0.54–0.89)	0.0043[a]
	−125 mm Hg device	5	2,411		0	0.91 (0.64–1.28)	0.5867
Superficial SSI	−80 mm Hg device	4	3,108	OR (M–H, fixed effect, 95% CI)	22	0.66 (0.50–0.86)	0.0025[a]
	−125 mm Hg device	3	1,848		0	1.12 (0.70–1.78)	0.6430
Deep SSI	−80 mm Hg device	3	2,998	OR (M–H, fixed effect, 95% CI)	0	0.84 (0.43–1.66)	0.6243
	−125 mm Hg device	3	1,848		NA	0.99 (0.43–2.31)	0.9906
Wound complications (composite)[b]	−80 mm Hg device	4	472	OR (M–H, fixed effect, 95% CI)	0	0.85 (0.53–1.35)	0.4834
	−125 mm Hg device	5	2,411		0	0.89 (0.68–1.17)	0.4017
Seroma	−80 mm Hg device	4	2,352	OR (M–H, fixed effect, 95% CI)	0	1.04 (0.62–1.75)	0.8915
	−125 mm Hg device	3	1,851		0	0.82 (0.39–1.74)	0.6072
Dehiscence	−80 mm Hg device	4	3,069	OR (M–H, fixed effect, 95% CI)	0	1.01 (0.80–1.26)	0.9444
	−125 mm Hg device	4	1,930		26.9	1.11 (0.65–1.90)	0.7074
Hematoma	−80 mm Hg device	3	2,265	OR (M–H, fixed effect, 95% CI)	0	1.94 (0.75–5.01)	0.1736
	−125 mm Hg device	2	1,769		0	0.49 (0.18–1.33)	0.1623
Bleeding	−80 mm Hg device	2	2,122	OR (M–H, fixed effect, 95% CI)	0	0.88 (0.44–1.77)	0.7207
	−125 mm Hg device	NA	NA	NA	NA	NA	NA
Reoperation	−80 mm Hg device	NA	NA	NA	NA	N/A	NA
	−125 mm Hg device	4	803	OR (M–H, fixed effect, 95% CI)	14	1.00 (0.52–1.93)	0.9914
Readmission	−80 mm Hg device	3	2,232	OR (M–H, fixed effect, 95% CI)	0	1.68 (0.88–3.21)	0.1147
	−125 mm Hg device	3	2,210		0	1.21 (0.59–2.46)	0.6008
Blistering	−80 mm Hg device	3	2,176	OR (M–H, random effect, 95% CI)	54	1.42 (0.40–5.04)	0.5922
	−125 mm Hg device	2	1,727	OR (M–H, random effect, 95% CI)	70	12.71 (0.69–235.29)	0.0878

Abbreviations: CI, confidence interval; M–H, Mantel–Haenszel; NA, not available; OR, odds ratio; SSI, surgical site infection.
[a]Denotes statistical significance.
[b]The definition of wound complications differed between included studies but generally included seroma, dehiscence, hematoma, bleeding, and blistering.

negative pressures; however, there have been no head-to-head studies to date that would have detected such a difference. Brownhill et al demonstrated that use of the −80 mm Hg device resulted in faster stimulation of reepithelialization and promotion of granulation tissue than using traditional NPWT devices, which generate negative pressure between −50 and −175 mm Hg.[45] Wilkinson et al reported that a heightened damage response in the epidermis was shown with a

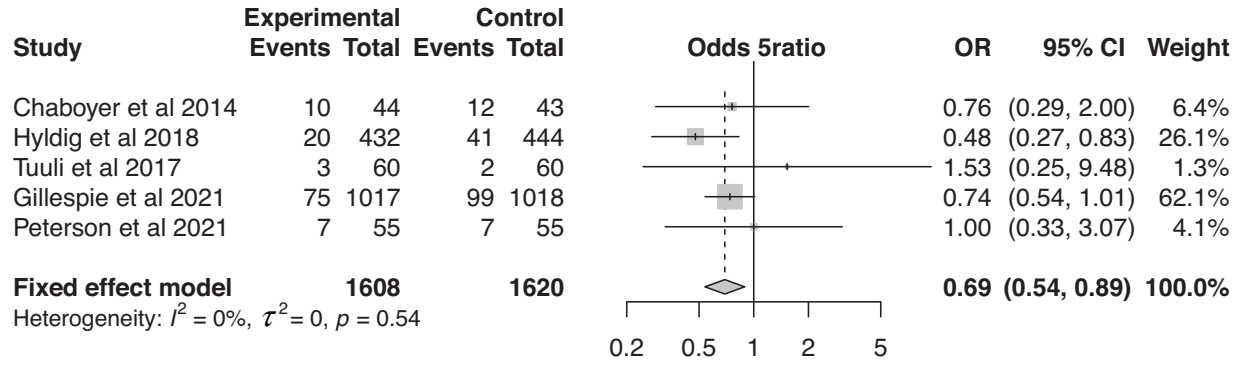

Fig. 3 Forest plot for the −80 mm Hg device; composite surgical site infection outcome. CI, confidence interval.

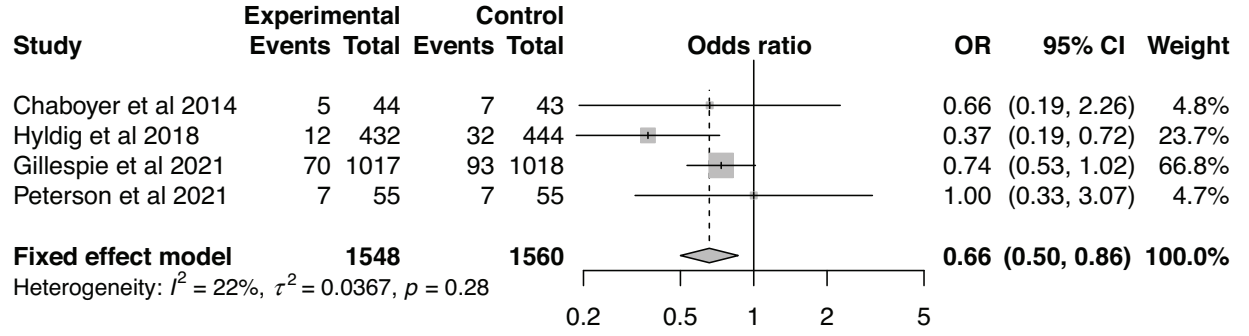

Fig. 4 Forest plot for the −80 mm Hg device; superficial surgical site infection outcome.

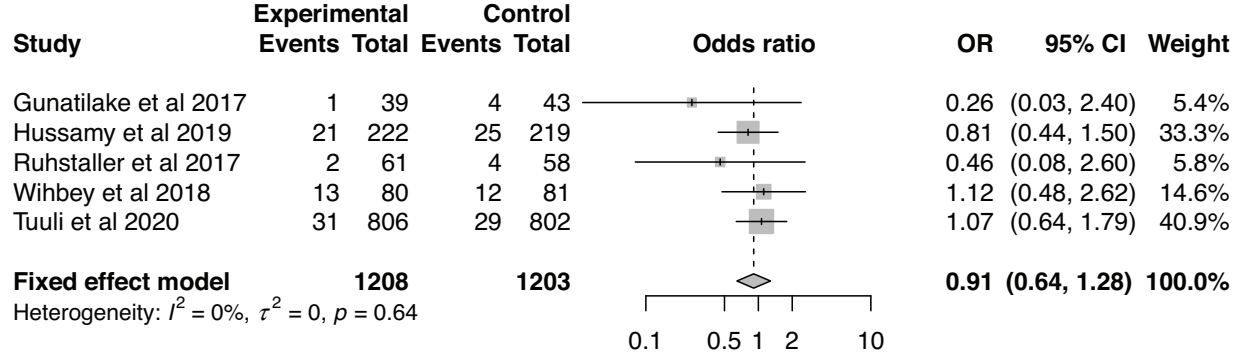

Fig. 5 Forest plot for the −125 mm Hg device; composite surgical site infection outcome.

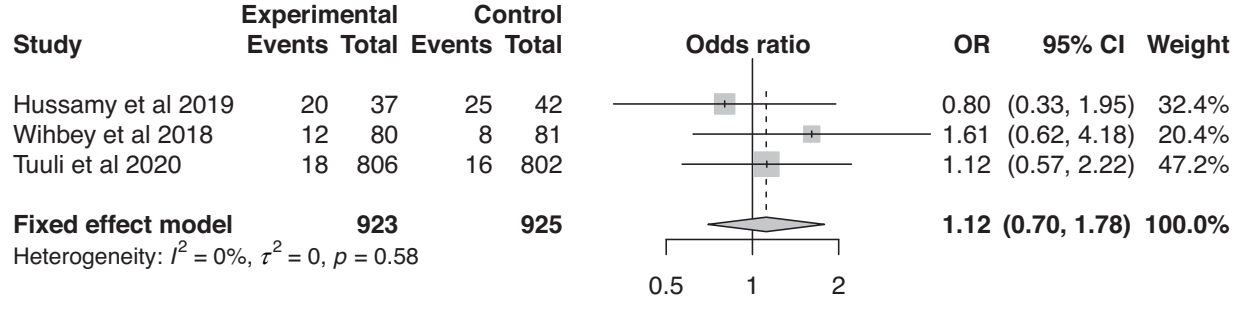

Fig. 6 Forest plot for the −125 mm Hg device; superficial surgical site infection outcome.

traditional NPWT device generating a negative pressure of −100 mm Hg compared to one of the devices in this systematic literature review which generates a pressure of −80 mm Hg.[46] This was in addition to the studies that have shown that retention of wound filler can also increase inflammatory cell influx and promote foreign body reactions.[47,48]

The reduction of SSIs is an outcome of interest to patients, clinicians, and health care systems. SSI following C-section causes pain and anxiety to new parents, and incurs a financial burden to the health care system in both community and hospital health care settings.[49] An SSI can impact the quality of life of the gestational carrier and risk to bonding with the newborn.[50] The postoperative length of stay in a hospital setting is often increased,[51] along with higher rates of readmission and in some cases postpartum mortality.[52] SSIs in C-section have been estimated to cost approximately £1,866 per infection in the United Kingdom[49] and $3,500 per infection in the United States.[53] These complications are increasingly problematic in light of the rising global prevalence of obesity,[54] which is a known contributor to postoperative SSIs; therefore, considering therapies that may reduce this and other wound complications is important.[55]

There is a substantial price difference in the cost of each sNPWT device kit, with the −80 mm Hg device being the cheaper of the two devices. Using prices from the United Kingdom as an example, the −80 mm Hg device costs between $159 and $182,[56] while the −125 mm Hg device costs between $373 and $438.[57] From a U.S. payer perspective, the −80 mm Hg device has been reported to save $637 per patient when compared to standard care, with greater savings achievable in higher risk patients such as those with a BMI $\geq$ 30 kg/m^2.[58] These findings are based on composite SSI incidence rates and so account for the disproportionate health care costs and differences in device efficacy associated with the various SSI subtypes. Clinicians should, therefore, be aware of the differences in clinical and economic outcomes obtained with various sNPWT devices and factor this into any decisions made regarding their use.

The studies included in this systematic review all had patients with a BMI $\geq$ 30 kg/m^2. These patients are particularly at risk of SSC when undergoing C-section. Increasing BMI may be correlated with an increasing incidence of SSCs. For instance, those with even higher BMIs, surpassing 40 kg/m^2, may be at increasingly higher risk compared to patients with a BMI of 30–35 kg/m^2.[16,59]

Neither the −80 nor the −125 mm Hg device demonstrated a benefit in any of the other assessed outcomes (e.g., wound complications, seroma, dehiscence), which is consistent with the Gillespie et al 2022, Guo et al, and Angarita et al reviews,[27–29] who found no difference in the pooled sNPWT data when comparing to standard care. This apparent lack of treatment effect could be because many studies are not powered to detect these complications in sufficient numbers as they occur at a relatively lower frequency than compared to SSI. Furthermore, these outcomes were not as frequently reported between studies, meaningless data were available for assessment. Further studies may or may not establish whether a statistically significant treatment effect can be obtained with these devices in other outcomes. Despite no currently identified difference in the other assessed outcomes, the use of sNPWT is justified on the basis of a reduction in SSIs alone due to the associated morbidity, mortality, and subsequent health care costs caused by this complication.

Previous studies[27–29] have noted that the incidence of blistering is higher with sNPWT dressings compared with standard dressings. In this systematic literature review, no statistically significant increase was shown in blistering with the −80 or the −125 mm Hg device. A trend toward increased incidence of blistering with both devices was identifiable, however. Stratifying the blistering outcome by sNPWT device results in insufficient data to detect a statistically significant difference and may be reflected in the moderate-to-high statistical heterogeneity observed for these subanalyses. The results of this study show that blistering is not a unique phenomenon associated with a particular type of sNPWT device but is a common issue when using this intervention more generally. The incidence of blistering should be considered in context of the clinical benefit obtained with using sNPWT, as a statistically significant reduction in the odds of developing SSIs is likely more desirable to clinicians than the occurrence of a minor, self-limiting adverse event. In terms of clinical practice, further product training for health care professionals may be required on application technique, which may help to reduce this blistering effect.[56]

Most studies were at risk of bias because of a lack of blinding; however, blinding is acknowledged to be very difficult due to the nature of these interventions. There could be variations in outcomes based on surgical approach taken (i.e., whether a Pfannenstiel or a vertical incision was made) but this was not apparent from the studies included in this systematic literature review. Additional variables between studies that may have influenced the results include the use of antibiotic prophylaxis and the proportion of pregnant patients undergoing emergency C-sections. Most studies reported the use of antibiotic prophylaxis, although some studies omitted this detail. A higher frequency of emergency C-sections would indicate a higher risk population and therefore higher baseline complication rate, making it easier to detect a statistical difference in the outcome of interest. Other notable differences between studies were the variation in follow-up times and treatment durations between each study, which will increase the degree of heterogeneity and result in wider CIs for each outcome. The length of treatment (sNPWT) duration is based on clinician's judgement and influenced by the patient's response to therapy. The sNPWT devices included in this analysis can be used for up to 7 days continuously. The employment of the more conservative random effects model was used in instances where heterogeneity was high and may account for some of this type of methodological heterogeneity. Future studies should aim to investigate the impact of these factors on the treatment effect observed with sNPWT devices.

Strict inclusion criteria focused on RCT-only data. This approach decreases heterogeneity and allows for narrower CIs in determining benefit in this patient population. However, it reduces external validity due to exclusion of observational

studies, which are subject to higher degrees of bias but can account for a wider breadth of patient populations/risk factors. Inclusion of terminated RCTs can limit the influence of publication bias but can introduce other problems, such as the over- or underestimation of treatment effects, depending on the reasons for study termination (e.g., apparent treatment benefit or lack thereof). Specifically, one −80 mm Hg device study[38] was terminated early due to slow enrollment, resulting in performance of an unplanned interim analysis that showed a lack of treatment effect. Similarly, Tuuli et al 2020 terminated their study also due to a lack of identified treatment effect and an increase in adverse event rates in the intervention arm.[41] These two studies may, therefore, have led to an underestimation of the treatment effects for both interventions, although sensitivity analyses performed to account for this by removing these terminated studies did not alter the main findings. Overall, further studies are required to fully elucidate the treatment effect across all the relevant SSC outcomes. Specifically, a head-to-head trial directly comparing −80 to −125 mm Hg devices would provide additional clarity as to whether one device should be selected over another in this patient population, particularly for SSCs other than SSI.

Conclusion

The −80 mm Hg sNPWT device significantly reduces overall and superficial SSIs after C-section in obese pregnant patients compared to standard of care, an effect not observed with the −125 mm Hg device. More studies and larger patient numbers are needed to confirm the extent of the device-specific effect and understand the benefits of sNPWT in outcomes other than SSI.

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Conflict of Interest

T.G. has a consultancy agreement with Smith & Nephew for this work and B.C. is an employee of Smith & Nephew.

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