Prophylactic negative-pressure wound therapy after cesarean is associated with reduced risk of surgical site infection: a systematic review and meta-analysis

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OBJECTIVE: The objective of the study was to assess the effect of prophylactic negative-pressure wound therapy on surgical site infections and other wound complications in women after cesarean delivery.

DATA SOURCES: We searched Ovid Medline, Embase, SCOPUS, Cochrane Database of Systematic Reviews, and ClinicalTrials.gov.

STUDY ELIGIBILITY CRITERIA: We included randomized controlled trials and observational studies comparing prophylactic negative-pressure wound therapy with standard wound dressing for cesarean delivery.

STUDY APPRAISAL AND SYNTHESIS METHODS: The primary outcome was surgical site infection after cesarean delivery. Secondary outcomes were composite wound complications, wound dehiscence, wound seroma, endometritis, and hospital readmission. Heterogeneity was assessed using Higgin's I^2. Relative risks with 95% confidence intervals were calculated using random-effects models.

RESULTS: Six randomized controlled trials and 3 cohort studies in high-risk mostly obese women met inclusion criteria and were included in the meta-analysis. Six were full-text articles, 2 published abstracts, and 1 report of trial results in ClinicalTrials.gov. Studies were also heterogeneous in the patients included and type of negative-pressure wound therapy device. The risk of surgical site infection was significantly lower with the use of prophylactic negative-pressure wound therapy compared with standard wound dressing (7 studies: pooled risk ratio, 0.45; 95% confidence interval, 0.31—0.66; adjusted risk ratio, −6.0%, 95% confidence interval, −10.0% to −3.0%; number needed to treat, 17, 95% confidence interval, 10—34). There was no evidence of significant statistical heterogeneity ($I^2 = 9.9\%$) or publication bias (Egger $P = .532$). Of the secondary outcomes, only composite wound complications were significantly reduced in patients receiving prophylactic negative-pressure wound therapy compared with standard dressing (9 studies: pooled risk ratio, 0.68, 95% confidence interval, 0.49—0.94).

CONCLUSION: Studies on the effectiveness of prophylactic negative-pressure wound therapy at cesarean delivery are heterogeneous but suggest a reduction in surgical site infection and overall wound complications. Larger definitive trials are needed to clarify the clinical utility of prophylactic negative-pressure wound therapy after cesarean delivery.

Key words: antibiotics, cesarean delivery, dehiscence, endometritis, hospital readmission, meta-analysis, prophylactic negative-pressure wound therapy, seroma, surgical site infection

Cesarean delivery is the most common major surgical procedure among women in the United States. In 2015 more than 1.2 million cesarean deliveries were performed in the United States, representing 32% of all births.[1] The overall rate of cesarean delivery has increased dramatically since 1996, although starting in 2009, this rate has been slowly decreasing, in part because of efforts to reduce non—medically indicated cesareans.[2]

Postoperative complications remain a significant and costly contributor to maternal morbidity, particularly among

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high-risk patients.[3] Obesity (body mass index [BMI] >30 kg/m^2) exacerbates the problem of surgical-site infection after cesarean delivery.[4,5] The impact of obesity has received particular attention, given the rising global levels of obesity.[6]

Modern techniques for the prevention of wound complications include proper preoperative skin preparation, antiseptic surgical techniques, prophylactic antibiotics, and sterile postoperative dressings.[7] Despite these measures, wound complications after cesarean remain common.

More recently, prophylactic negative-pressure wound therapy (NPWT) has emerged as a possible intervention for reducing surgical wound complications. This type of dressing, first approved by the Food and Drug Administration in 1995, uses negative pressure at the wound site to reduce edema, remove exudate, increase localized blood flow, stimulate granulation tissue growth, and ultimately accelerate wound healing.[8] Although most commonly utilized in the treatment of wounds, emerging research suggests that NPWT may be beneficial as prophylaxis among high-risk patients.

In 2010, 2 brands of modified, single-use, battery-powered, portable NPWT devices (Prevena; KCI USA, San Antonio, TX, and PICO; Smith & Nephew, St Petersburg, FL) were Food and Drug Administration cleared for prophylactic application after wound closure at the time of surgery.

A recent meta-analysis of randomized controlled trials investigating the use of NPWT for closed surgical incisions showed significant reductions in wound infection, seroma formation, and wound exudate compared with a standard surgical dressing.[9] However, none of the included studies reported data for cesarean deliveries. While several observational studies and pilot randomized trials (RCTs) have supported the use of NPWT to reduce wound complications after cesarean delivery, the relatively small sample sizes in these studies limit their impact on clinical practice.

The objective of this systematic review and meta-analysis was to evaluate the effectiveness of prophylactic NPWT on the rate of surgical site infections and other wound complications in women undergoing cesarean delivery compared with standard surgical dressings.

Materials and Methods

This study did not involve any patient health information or human or animal experimentation and was therefore exempt from institutional review board review. Acelity played no role in the design, analysis, or interpretation of this study.

Search strategy and study selection

This systematic review and meta-analysis were conducted based on a predefined study protocol following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis criteria.[10] A medical librarian searched the published and gray literature for records discussing cesarean delivery and prophylactic NPWT in March 2017.

The librarian (L.S.) created search strategies using a combination of key words and controlled vocabulary in Ovid Medline 1946-, Embase 1947-, Scopus 1823-, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), and Clinicaltrials.gov 1997-. If studies in Clinicaltrials.gov were reported as completed but did not provide results and a related publication was not found, the corresponding author was queried for unpublished results. The full search strategies can be found in the Appendix.

Two authors (R.K. and L.Y.) independently reviewed the search results to identify relevant studies. Titles and abstracts were screened, and articles deemed potentially relevant were retrieved for full-text review. Studies that did not involve NPWT and cesarean delivery in human subjects were excluded. Studies that investigated nonprophylactic use of NPWT or did not include outcome data relevant to wound infections or complications were also excluded. Reviews, commentaries, and case reports were also excluded.

Given that the use of prophylactic NPWT at cesarean delivery is still relatively novel, including only RCTs would likely be too restrictive and potentially introduce publication bias. Therefore, we included both RCTs and cohort studies. The bibliographies of included studies were searched for additional eligible studies. Lastly, an expert in the field (M.T.) was queried for any additional studies, which led to retrieval of a PhD thesis with interim results from an RCT.

Data extraction

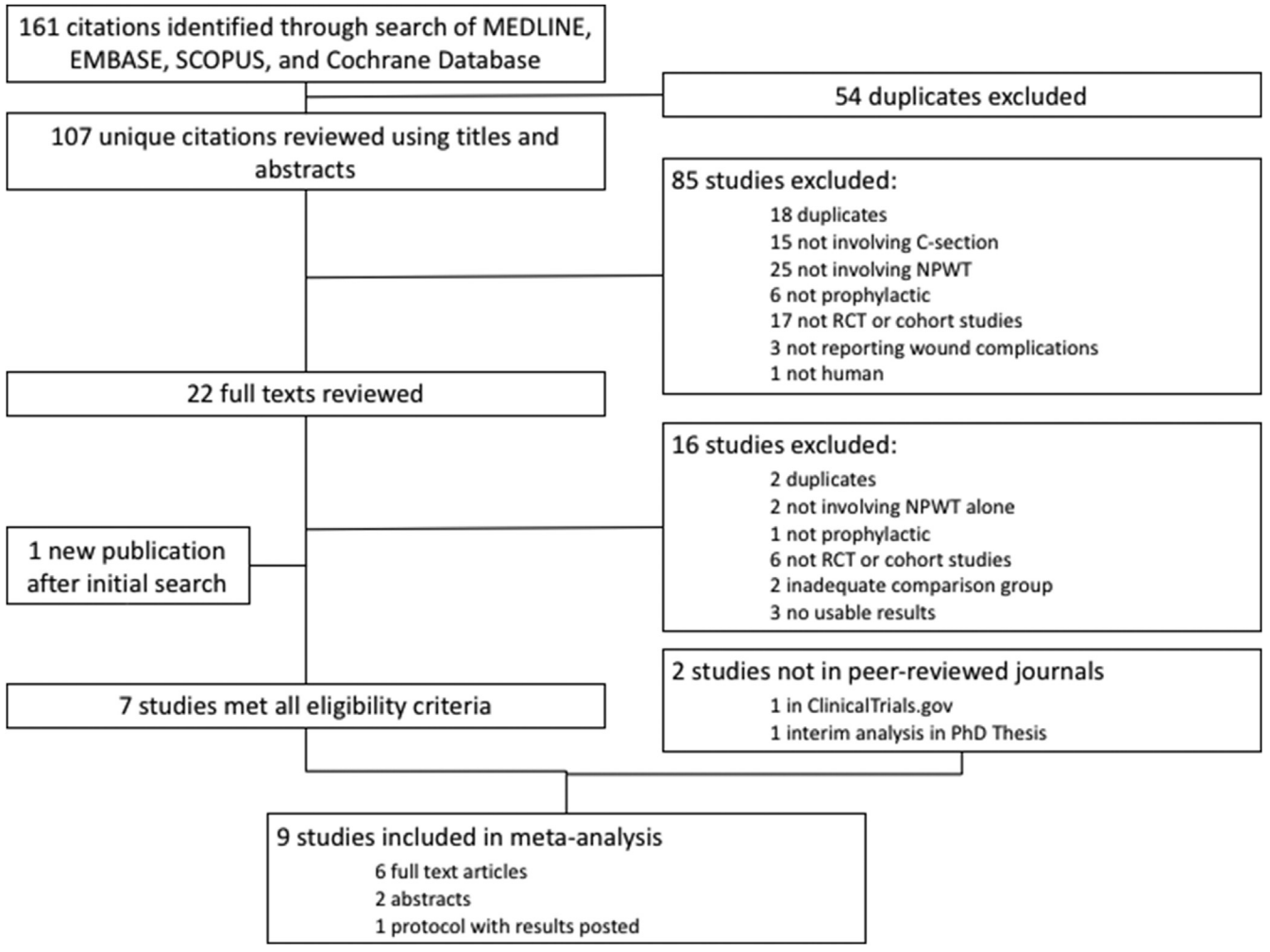
Two reviewers (R.K. and L.Y.) independently reviewed eligible articles to extract data regarding study characteristics including design and location, inclusion and exclusion criteria, number of patients, patient demographics and comorbidities, frequency of wound complications, and hospital readmissions. The type of NPWT device and length of treatment in both the intervention and control groups was collected. In case of published abstracts, the first author was contacted for additional information regarding methods, baseline demographics, unpublished results, and detailed outcome information, although no additional results were obtained from this correspondence.

The 2 reviewers assessed the quality of each study based on criteria adapted from the Cochrane Handbook.[11] Individual study quality was assessed using predefined criteria. High-quality studies were defined as randomized trials with appropriate randomization method, clear definition of outcomes, and use of intention-to-treat analysis, while low-quality studies were missing 1 or more of these attributes. Outcomes were considered clearly defined if the authors provided an adequate level of detail about the criteria and timing of outcome data collection for this metric to be reproducible. Disagreements were resolved through arbitration and discussion with a third author (M.T.).

Outcomes

The primary outcome for this analysis was surgical-site infection after cesarean. This was chosen because of its clinical significance and the biological plausibility of NPWT on its prevention.

FIGURE 1
Flow diagram for study selection



NPWT, negative-pressure wound therapy; *RCT*, randomized controlled trial.

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Secondary outcomes included dehiscence, seroma, endometritis, a composite measure for wound complications, and hospital readmission. In studies for which there were both overall complication rates and rates stratified by complication type, the overall complication rate as reported was used for the outcome of wound complications to avoid counting patients multiple times.

Statistical Analysis

All statistical analyses were performed in the METAN add-on program in STATA version 14.2 (StataCorp LP, College Station, TX). Statistical heterogeneity was assessed using the Higgin's I^2, with a value >30% considered to represent significant heterogeneity.[12] With the exception of a sensitivity analysis described in the following text, all risk estimates were reported as pooled relative risks with 95% confidence intervals (CI).

Additionally, we estimated pooled absolute risks for the primary outcome of surgical site infection in the NPWT and standard dressing groups using a meta-analysis of proportions and the associated absolute risk reduction and number needed to treat. A random-effects model[13] was used for all meta-analyses, even when statistical heterogeneity was not evident, given the likelihood of clinical heterogeneity between studies. One study also reported adjusted odds ratios for surgical site infection and overall wound complications.[14]

We conducted a sensitivity analysis to assess whether the use of the adjusted odds ratios would have an impact on the pooled estimates. Analyses were also stratified by study design, abstract vs full text, NPWT device type, and study quality to assess their impact on our estimates. All secondary analyses were prespecified. Publication bias was

TABLE 1
Characteristics of included studies

Author	Year	Country	Study design	Text form	Inclusion criteria	Exclusion criteria	Sample size, n	NPWT device used	Quality
Chaboyer et al[18]	2014	Australia	RCT	Full text	(1) Elective CD (2) Prepregnany BMI $\geq$30 kg/m^2 (3) Able to provide written informed consent	(1) Urgent or emergent CS (2) Previous participation in trial (3) Existing infection between admission and CD (4) Unable to speak or understand English	87	PICO	High
Mark et al[21]	2014	United States	RC	Full text	(1) BMI $\geq$45 kg/m^2	Not reported	69	KCl	Low
Ruhstaller et al[19]	2017	United States	RCT	Full text	(1) BMI $\geq$30 kg/m^2 (2) $\geq$4 cm dilation at time of CD	(1) Initiation of prenatal care after 23 weeks (2) Preexisting diabetes, using chronic steroids or immunosuppressants, or active cancer treatment (3) Allergy to silver (4) Scheduled CS or planned vertical skin incision	119	Prevena	High
Swift et al[22]	2015	United States	Mixed	Full text	Not reported	Not reported	319	Prevena	Low
Tuuli et al[20]	2017	United States	RCT	Abstract	(1) BMI $\geq$30 kg/m^2	(1) Nonavailability for postoperative follow-up (2) Preexisting infection at incision site (3) Bleeding disorder or anticoagulation	120	PICO	High
Villers et al[15]	2017	United States	RC	Abstract	(1) BMI $\geq$40 kg/m^2	Not reported	317	Not reported	Low
Hyldig et al[25]	2016	Denmark	RCT	PhD thesis	(1) 18 years old or older (2) Pregestational BMI $\geq$30 kg/m^2 (3) Giving birth by planned or emergent CD at 1 of 5 trial centers	(1) Non-Danish speakers	535	PICO	High

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(continued)

TABLE 1
Characteristics of included studies *(continued)*

Author	Year	Country	Study design	Text form	Inclusion criteria	Exclusion criteria	Sample size, n	NPWT device used	Quality
Gunatilake et al[23]	2017	United States	RCT	Full text	(1) Female ≥18 years old (2) Able to provide informed consent (3) CD using subcuticular skin closure within the next 42 days (4) Surgical incision able to be covered completely by PIMS (5) BMI ≥35 kg/m^2 during screening period up to 42 days before surgery (6) CDC wound classification of clean or clean contaminated (7) Willing and able to return for all scheduled and required study visits (8) Not enrolled in another study	(1) ASA class P4, P5, or P6 (2) Systemic bacterial/fungal infection at time of surgery (3) Remote-site skin infection at time of surgery (4) Life expectancy <12 months (5) Preoperatively classified to undergo CDC wound classification of contaminated or dirty infected (6) Intraoperative hemorrhage requiring transfusion, DIC, or other medical condition that makes participant high risk (7) Clinically significant condition that would impair compliance with study procedure (8) Allergy or hypersensitivity to silver or drape materials	82	Prevena	High
Stitely et al[24]	N/A	United States	RCT	Clinical Trials.gov (NCT0065 4641)	(1) 18 years old or older (2) Weight >199 pounds (3) Depth of subcutaneous tissue ≥4 cm	(1) Weight ≤199 pounds, or <4 cm subcutaneous tissue (2) Inability to give proper informed consent (3) Inability to adhere to follow-up	54	Not reported	Low

ASA, American Society of Anesthesiologists; *BMI*, body mass index; *CD*, cesarean delivery; *CDC*, Centers for Disease Control and Prevention; *DIC*, dissmninated intravascular coagulation; *NPWT*, negative-pressure wound therapy; *PIMS*, Prevena Incision Management System; *RC*, retrospective cohort; *RCT*, randomized controlled trial.

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TABLE 2
Baseline characteristics of patient populations in the included studies

Characteristic	Chaboyer	Mark	Ruhstaller	Swift	Villers	Heine	Hyldig
Age							
Intervention	30.6 (5.5)[a]	26.1 (4.2)[b]	27 (8)[a]	30.8 (6.0)[b]	—	30.35 (5.724)[b]	32 (5)[b]
Control	30.7 (5.0)	29.5 (6.6)	29 (10)	29.4 (5.8)		29.67 (4.953)	32 (5)
BMI, kg/m^2							
Intervention	35.7 (4.5)[a]	53.8 (11.1)[b]	36.1 (8.6)[a]	37.7 (9.0)[b]	48.2[c]	46.25 (7.319)[b]	34.7 (6.7)[a]
Control	36.8 (5.8)	51.3 (5.8)	35.1 (9.5)	33.6 (8.5)	44.6	46.79 (5.608)	33.9 (6.5)
Race, n, %[d]							
White	—	—	26 (21.8)	—	—	27 (29.3)	
African American			91 (76.4)			64 (69.6)	
Other			2 (1.7)			1 (1.1)	
Gestational age, wks							
Intervention	—	37.8 (2.9)[b]	39 (2)[a]	39 (2.6)[a]	—	38.08 (1.983)[b]	
Control		36.9 (3.8)	39 (2)	39 (4.3)		37.87 (1.976)	
Planned CD, %							
Intervention	100	52.4	0				52
Control	100	77.1	0				53
Comorbidities, %							
Any							
Intervention	68.1	—	—	100	—	—	
Control	69.7			100			
Diabetes							
Intervention	29.5	35	8.2	19.1	—	—	19
Control	27.9	27.1	7.0	16.3			19
Smoker							
Intervention	6.8	14.3	8.2	—	—	—	8
Control	23.3	16.7	5.2				9
Multiparous							
Intervention	—	61.9	62.3	—	—	—	
Control		70.8	60.3				
Previous CD							
Intervention	84	—	18.0	43.6	—	—	
Control	93		19.0	36.8			
Chorioamnionitis							
Intervention	—	0	16.4	15.4	10	—	
Control		4.2	12.1	2.9	1		
Surgical characteristics							
Length of surgery, min							
Intervention	—	76.3 (18.8)[b]	61 (22)[a]	64.6 (24.2)[b]	—	—	37 (15)[a]
Control		63.9 (21.6)	62 (18)	60.3 (20.1)			36 (17)

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(continued)

TABLE 2
Baseline characteristics of patient populations in the included studies *(continued)*

Characteristic	Chaboyer	Mark	Ruhstaller	Swift	Villers	Heine	Hyldig
Closed with staples, %							
Intervention	—	4.8	—	3	—	—	61
Control		85.4		12			60

Authors Tuuli and Stitely did not provide baseline characteristics. *BMI*, body mass index; *CD*, cesarean delivery; *IQR*, interquartile range.

[a] Values were reported as median (IQR); [b] Values were reported as mean (SD); [c] Values were reported as median; [d] Race was reported as a combined term for the intervention and control groups.

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assessed by visual inspection of a funnel plot and symmetry was tested statistically using the Egger's test.[15,16]

Results

Study selection

A total of 161 results were identified in the initial search and exported to EndNote. Following the removal of duplicates, a total of 107 unique citations remained. The titles and abstracts were screened for initial inclusion. Eighty-five studies were excluded for being additional duplicates (n = 18), not related to the use of prophylactic NPWT after cesarean delivery (n = 46), ineligible study designs (n = 17), not reporting appropriate outcomes (n = 3), and nonhuman subjects (n = 1).

Twenty-two remaining studies were reviewed in full text or published abstract if no full text was available. Of these, 16 studies were excluded for duplicate publication of results (n = 2), not involving prophylactic NPWT alone (n = 3), ineligible study designs (n = 6), no usable results (n = 3), and not having a valid comparison group (n = 2) (Figure 1). One cohort study comparing prophylactic NPWT with standard dressing with regard to overall wound complications was not included because the authors reported odds ratios only and did not present the necessary count data for calculating absolute and relative risks.[17]

In addition to the 6 remaining studies,[15,18-22] 2 unpublished studies reported outcomes in ClinicalTrials.gov,[23,24] one of which was published during manuscript preparation,[23] and one RCT was available as part of a published PhD thesis,[25] resulting in a total of 9 studies included in the analysis.

Study characteristics

Of the 9 studies meeting inclusion criteria, 6 studies were RCTs, while 3 were cohort studies (2 retrospective, 1 prospective with a historical control group[22]). Six studies were full-text publications, 2 were published abstracts, and 1 was presented as results in ClinicalTrials.gov. Five studies were determined to be high quality and four were low quality. Seven studies were conducted in the United States and 2 were conducted in Australia[18] and Denmark.[25]

Inclusion and exclusion criteria differed significantly across studies, with the majority including high-risk obese women above a given BMI threshold. Inclusion of scheduled or emergent cesarean deliveries in the studies was variable. Various prophylactic NPWT devices were used, with Prevena and PICO systems being the most common. Sample sizes ranged from 54 to 535 patients (Table 1).

Reporting of baseline characteristics varied across studies, with several studies lacking any information (Table 2). The most commonly reported characteristics were age and BMI, while diabetes was the most commonly reported comorbidity. Only 2 studies reported race. While the age distribution appeared similar across studies, the average BMI was highly variable, ranging from 35 to 54 kg/m^2 in the intervention groups. Other potentially important comorbidities such as smoking history, parity, cesarean history, and chorioamnionitis were reported by 4 or fewer studies. Surgical characteristics including length of surgery and closure technique were infrequently reported.

Meta-analysis results and risk of bias

The absolute risk of developing surgical site infection was 5.0% (95% CI, 2.0−7.0%) with prophylactic NPWT and 11% (95% CI, 7.0−16.0%) with standard wound dressing. Compared with standard wound dressing, prophylactic NPWT was associated with a significantly lower risk of surgical-site infection (7 studies, pooled risk ratio (RR), 0.45, 95% CI, 0.31−0.66) (Figure 2 and Table 3). The absolute risk reduction was −6.0 % (95% CI, −10.0 % to −3.0 %), with a number needed to treat of 17 (95% CI, 10−34).

There was no evidence of significant statistical heterogeneity (I^2 = 9.9%). In stratified analyses the risk estimate suggested a lower rate of surgical site infection with the use of prophylactic NPWT across the type of estimates used, study design, NPWT device, reporting as full text or abstract, and study quality, although not statistically significant in some subgroups (Table 4). There was no evidence of publication bias (Egger test P = .532) (Figure 3).

Prophylactic NPWT was associated with a statistically significant reduction in composite wound complications (9 studies, pooled RR, 0.68, 95% CI, 0.49−0.94) but not in the other secondary outcomes, including dehiscence (5 studies, pooled RR, 0.86 95% CI, 0.61−1,23), seroma (2 studies, pooled RR, 1.21, 95% CI, 0.93−1.57), endometritis (3 studies, pooled RR, 0.37, 95% CI, 0.13−1.07), or hospital readmission (2 studies, pooled RR, 0.80, 95% CI, 0.23−2.76) (Table 3).

FIGURE 2
Forest plot of prophylactic NPWT on infection after CD

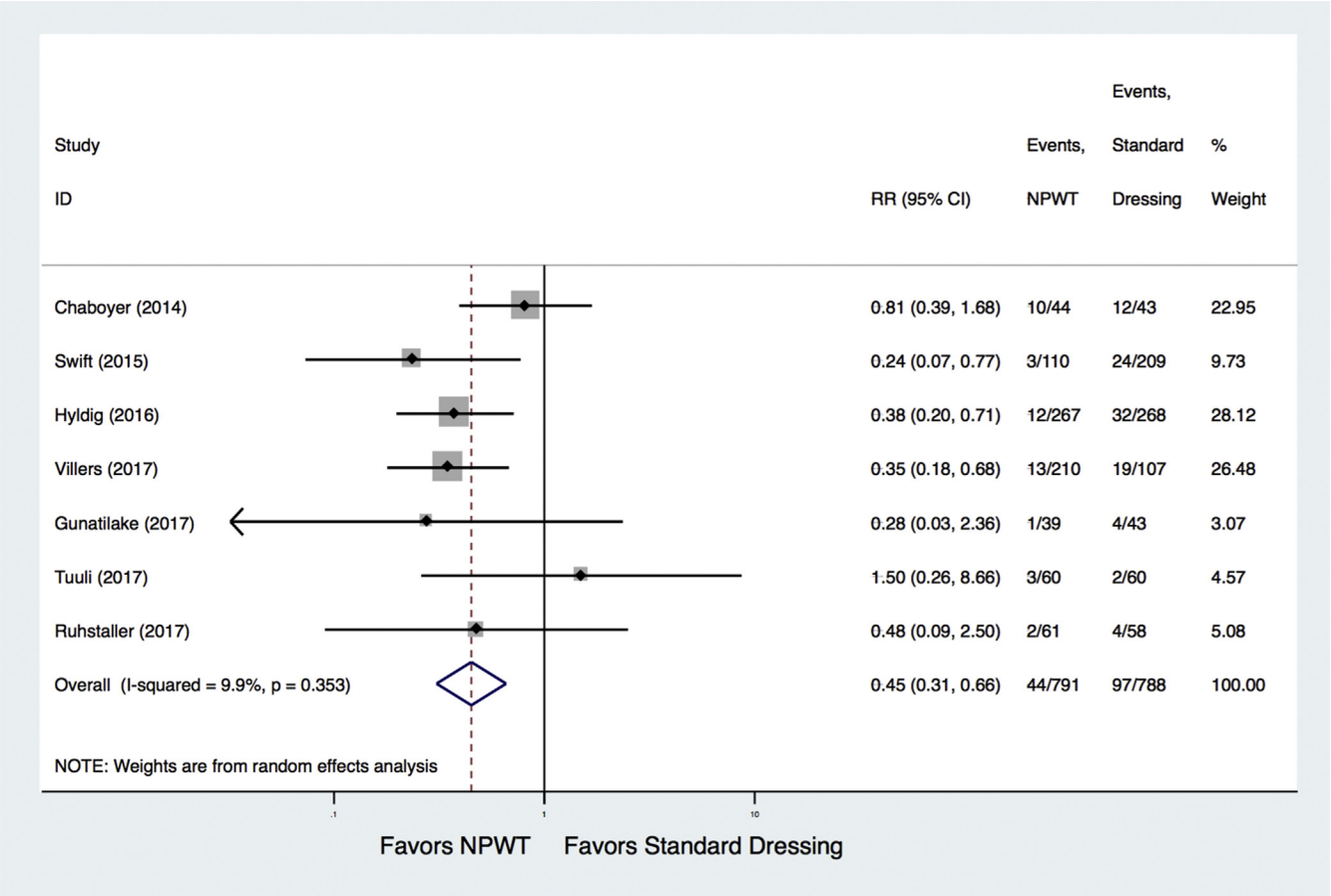

Figure shows the forest plot of the effect of prophylactic negative-pressure wound therapy on surgical-site infection after cesarean delivery.

CD, cesarean delivery; *CI*, confidence interval; *NPWT*, negative-pressure wound therapy; *RR*, relative risk.

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Comment

Main findings

We conducted this systematic review and meta-analysis to comprehensively synthesize evidence on the effectiveness of prophylactic NPWT on the risk of surgical site infections and other would complications after cesarean delivery. Studies were heterogeneous in their design, patients included, type of NPWT device, and publication type. Nonetheless, our results show that prophylactic NPWT was associated with a statistically significant 55% reduction in surgical-site infection and overall wound complications after cesarean delivery. The number needed to treat to prevent 1 surgical site infection was 17. We observed no statistically significant reduction in secondary outcomes including dehiscence, seroma, endometritis, or hospital readmission.

Clinical implications

Our findings are consistent with previous studies showing a reduction in infection rates with the use of prophylactic NPWT after non–obstetrical/gynecological surgical procedures. A meta-analysis of prophylactic NPWT after general surgical procedures found a significant reduction in surgical site infections.[9]

In contrast to our study, the authors also reported a significant reduction in seroma. Cesarean deliveries were not included in that study. Another meta-analysis of ventral hernia repair including 5 retrospective cohort studies reported a reduction in surgical-site infection and wound dehiscence with the use of prophylactic NPWT but not in the rate of seroma.[26]

A reduction in surgical-site infection with prophylactic NPWT is biologically plausible. Proposed mechanisms of prophylactic NPWT include wound shrinkage, induction of cellular stretch that promotes wound healing, removal of extracellular fluid, creation of a favorable environment for healing, and promotion of angiogenesis and neurogenesis.[27] It may also serve as a microbial barrier, increase blood flow, and improve tissue oxygenation.

TABLE 3
Pooled estimates of the effect of prophylactic NPWT on the primary and secondary outcomes

Outcome	Studies, n	Total n	Pooled RR (95% CI)	I^2, %
Surgical site infection	7	1579	0.45 (0.31–0.66)	9.9
Composite wound complications	9	1702	0.68 (0.49–0.94)	44.2
Dehiscence	5	1175	0.86 (0.61–1.23)	0
Seroma	2	437	1.21 (0.93–1.57)	0
Endometritis	3	1171	0.37 (0.13–1.07)	36.5
Hospital readmission	2	156	0.80 (0.23–2.76)	0

CI, confidence interval; *RR*, relative risk.

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Cellular deformation may also release cytokines and inflammatory factors that promote chemotaxis of other cells, including leukocytes, into the area.[8,28]

Of our secondary outcomes, only overall wound complications were significantly reduced with prophylactic NPWT. The inclusion of surgical-site infection in the composite wound complication measure likely explains this result in the absence of other significant differences in dehiscence, seroma, endometritis, and hospital readmission. However, these secondary outcomes were reported by only a subset of studies and thus may be limited by small overall sample sizes.

Additionally, composite wound complication measures are difficult to interpret because of a lack of consistent definitions across studies. Nevertheless, these results are encouraging with regard to the potential ability of prophylactic NPWT to alter patient outcomes postoperatively.

Strengths and Weaknesses

Strengths of this review include the predesigned protocol, comprehensive search strategy involving an expert librarian (L.S.), 2 investigators independently screening all articles for eligibility,

TABLE 4
Stratified analysis of the effect of prophylactic NPWT on surgical-site infection, composite wound complications, and wound dehiscence

Stratification	Surgical-site infection, pooled RR (95% CI)	I^2, %	Composite wound complications, pooled RR (95% CI)	I^2, %	Dehiscence, pooled RR (95% CI)	I^2, %
Estimates						
Unadjusted	0.45 (0.31–0.66)[b]	9.9	0.68 (0.49–0.94)[b]	44.2	0.86 (0.61–1.23)	0
Adjusted[a]	0.42 (0.28–0.63)[b]	0	—	—	—	—
Study design						
RCT	0.55 (0.35–0.87)[b]	4.8	0.82 (0.57–1.18)	38.6	0.88 (0.52–1.50)	7.2
Cohort	0.32 (0.18–0.57)[b]	0	0.45 (0.26–0.78)[b]	24.7	0.71 (0.19–2.63)	—
Device						
PICO	0.62 (0.31–1.26)	46.6	0.69 (0.54–0.90)[b]	5.8	1.08 (0.35–3.31)	21.7
Prevena	0.30 (0.12–0.71)[b]	0	0.36 (0.19–0.66)[b]	0	0.69 (0.27–1.76)	0
KCI	—	—	0.20 (0.01–3.50)	—		
Unknown	0.35 (0.18–0.68)[b]		0.90 (0.39–2.08)	78.3		
Reported form						
Full text	0.46 (0.29–0.72)[b]	8.4	0.66 (0.44–0.99)[b]	52.5	0.82 (0.57–1.19)	0
Abstract	0.57 (0.15–2.23)	57.2	0.81 (0.32–2.03)	46.5	1.96 (0.43–8.91)	0
Quality						
High	0.55 (0.35–0.87)[b]	4.8	0.67 (0.54–0.84)[b]	0.0	0.81 (0.28–2.32)	31.6
Low	0.32 (0.18–0.57)[b]	0	0.60 (0.27–1.32)	74.6	0.91 (0.32–2.60)	0

CI, confidence interval; *NPWT*, negative-pressure wound therapy; *RR*, relative risk.

[a] Denotes the adjusted odds ratio; [b] Denotes statistical significance.

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FIGURE 3
Funnel plot of prophylactic NPWT effect on SSI after CD

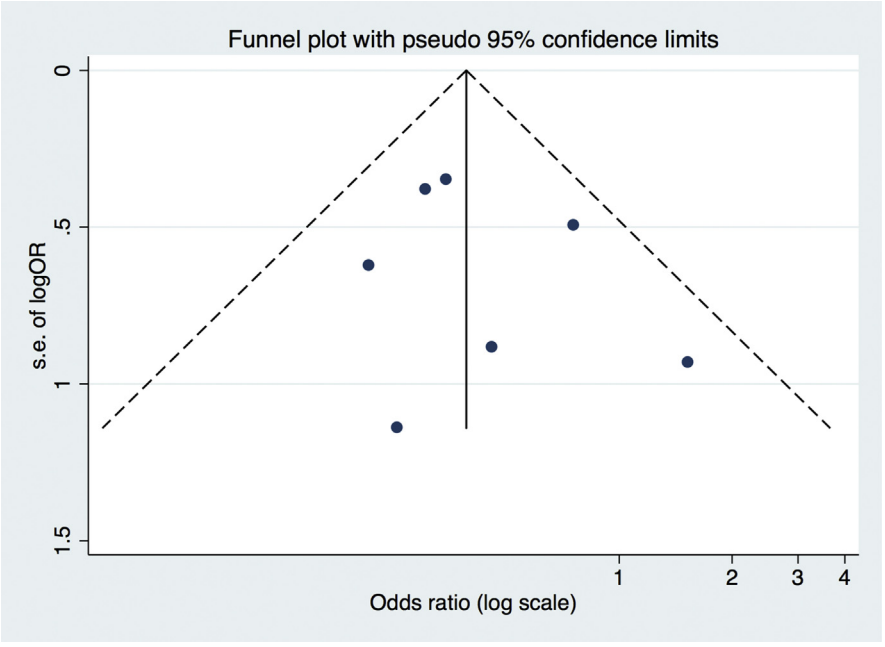

Figure shows the funnel plot of the effect of prophylactic negative-pressure wound therapy on surgical-site infection after cesarean delivery.

CD, cesarean delivery; *NPWT*, negative-pressure wound therapy; *OR*, odds ratio; *SSI*, surgical site infection.

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and extracting data to reduce bias. We used a random-effects model to pool data to take into account heterogeneity between studies, even in the absence of demonstrable statistical heterogeneity. We included published abstracts to avoid publication bias because full-text articles represented only a proportion of studies. Finally, we conducted sensitivity and stratified analyses to assess the impact of various factors on our findings.

There are limitations that should be considered. Our findings carry forward the limitations of the primary studies. The relatively small number of studies and significant variability in outcome reporting are important limitations. While the inclusion of published abstracts and unpublished studies reduced publication bias, it carries the risk of including lower quality non—peer-reviewed data. Moreover, there was significant heterogeneity between the studies included.

The inclusion of cohort studies carries a risk of confounding, especially because many potential confounders were not consistently assessed in the primary studies. However, the sensitivity analysis including adjusted estimates produced similar findings, suggesting robustness of our findings. Definitions of surgical-site infections and other wound complication were unclear in some studies.[14,21] Side effects were not consistently reported in the studies and could not be synthesized. This is important because some studies have reported high rates of side effects including skin blisters, erythema, and wound bleeding with the use of prophylactic NPWT after other types of surgical procedures.[29]

Finally, we did not include a cost-effectiveness analysis as part of the current study. Given that prophylactic NPWT devices cost between $200 and $500 USD, this is an important consideration in applying these results in a clinical setting.[30]

Since 2015, 3 cost-effectiveness analyses of prophylactic NPWT for post—cesarean delivery have been performed using various methods but with inconclusive results.[30-32] Two studies based in Australia suggested that prophylactic NPWT was cost effective in obese women undergoing cesarean delivery, although the degree of uncertainty around these estimates was high.[31,32] A US-based decision-analytic model favored the standard postoperative dressing as the most cost-effective strategy in a patient population with a surgical-site infection rate of 14% or less.[30]

On the other hand, prophylactic NPWT was potentially cost effective in populations with a higher risk of surgical-site infection. Based on this model and our pooled estimates of absolute risk, it would seem that prophylactic NPWT would not be cost effective in the patient population represented in our meta-analysis. However, as previously noted, patient characteristics were heterogeneous between studies and may not truly reflect a high-risk population as defined in these cost-effectiveness analyses.

Clinical heterogeneity may also explain why the conclusions differed between the Australian analyses predicated on a specific group of women and the US-based model that potentially involved a broader population of interest. Nevertheless, several additional studies, including those in our sample, have been conducted since the publication of these cost-effectiveness analyses, necessitating an updated assessment to incorporate these findings as well as changes in device pricing over time.

Summary and future research direction

In conclusion, the results of this meta-analysis suggest that use of prophylactic NPWT after cesarean delivery in high-risk patients is associated with a significant reduction in the risk of surgical site infection. However, because of the limited number and clinical heterogeneity between studies, further research is needed. Results of ongoing clinical trials[33,34] powered to assess effectiveness, side effects and cost-effectiveness will

help clarify the role of prophylactic NPWT after cesarean delivery. ■

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Supplemental Material Appendix

Full-search strategy

Ovid Medline

Date searched: March 6, 2017

Number of results: 25

Search terms: exp cesarean section/ OR (cesarean OR cesarian OR caesarean OR caesarian OR postcesarean OR abdominal deliveries OR C-section OR c-sections OR fetectomy OR repeated cesarotomy OR sectio caesarea).mp. AND (exp negative-pressure wound therapy/ OR NPWT.ti,ab. OR (topical negative pressure).mp. OR ([vacuum assisted OR vacuum-assisted] adj2 [closure*].mp.) OR (vacuum adj1 therap*).mp. OR ([negative pressure OR negative-pressure] adj2 (therap* OR dressing*).mp.]).

Embase

Date searched: March 6, 2017

Number of results: 54

Search terms: cesarean section/exp or cesarean OR cesarian OR caesarean OR caesarian OR postcesarean OR abdominal deliveries OR C-section OR c-sections OR fetectomy OR repeated cesarotomy OR sectio caesarea AND (vacuum assisted closure/exp OR NPWT:ti,ab OR topical negative pressure OR [(vacuum assisted OR vacuum-assisted) NEAR/2 [closure*]) OR [vacuum NEAR/1 therap*] OR [(negative pressure OR negative-pressure] NEAR/2 [therap* OR dressing*)]).

Cochrane

Date searched: March 6, 2017

Number of results from each database in Cochrane: CDSR - 4; CENTRAL - 11

Search terms: ([mh cesarean section] OR cesarean OR cesarian OR caesarean OR caesarian OR postcesarean OR abdominal deliveries OR C-section OR c-sections OR fetectomy OR repeated cesarotomy OR sectio caesarea) AND ([mh negative-pressure wound therapy] OR NPWT:ti,ab OR topical negative pressure OR [(vacuum assisted OR vacuum-assisted) NEAR/2 (closure*]) OR [vacuum NEAR/1 therap*] OR [(negative pressure OR negative-pressure] NEAR/2 (therap* OR dressing*)]).

Scopus

Date searched: March 6, 2017

Number of results: 67

Search terms: TITLE-ABS-KEY (cesarean OR cesarian OR caesarean OR caesarian OR postcesarean OR abdominal deliveries OR C-section OR c-sections OR fetectomy OR repeated cesarotomy OR sectio caesarea) AND (title-abs (NPWT) OR title-abs-key [topical negative pressure] OR title-abs-key ([vacuum assisted OR vacuum-assisted] w/2 [closure*]) OR title-abs-key [vacuum w/1 therap*] OR title-abs-key [(negative pressure OR negative-pressure) w/2 (therap* OR dressing*)]).

ClinicalTrials.gov

Date searched: March 6, 2017

Number of results: 31

Search terms: (cesarean OR cesarean OR cesarian OR caesarean OR C-section OR abdominal deliveries) AND (negative pressure wound therapy OR NPWT OR vacuum assisted closure OR vacuum therapy OR negative pressure dressing OR negative pressure therapy).