National Institute for Health and Care Excellence

FINAL

Caesarean birth

[B] Methods to reduce infectious morbidity at caesarean birth

NICE guideline NG192

Evidence review

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Final

This evidence review was developed by the National Guideline Alliance which is a part of the Royal College of Obstetricians and Gynaecologists

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Methods to reduce infectious morbidity at caesarean birth

Review question

What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

Introduction

Surgical site infection is a common complication of a caesarean birth. It may require readmission to hospital and can give rise to more severe complications such as sepsis and necrotising fasciitis.

In addition to the routine use of pre-incision antibiotic prophylaxis, a number of non-pharmacological interventions may be carried out before, during, and after surgery with the aim of reducing the risk of surgical site infection, such as the use of pre-operative skin or vaginal preparations and different types of wound dressings.

The aim of this review is to determine which of these methods are effective at reducing infections and improving women's outcomes.

Summary of the protocol

Please see Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Women having a caesarean birth (CB). This population includes women undergoing: • Emergency CB • Elective CB

Intervention	• Pre-operative washes
	• Drapes
	  ○ standard drape
	  ○ incise drape
	• Removal of body hair
	  ○ before surgery
	  ○ in the operating theatre
	  ○ no shaving
	• Use of face masks
	• Type of dressing/ wound covering
	  ○ topical/spray-on adhesive dressing (for example, Dermabond)
	  ○ different types of dressings
	  - dry absorbent dressings
	  - hydroactive dressings
	  - hydrocolloid dressing
	  - negative pressure wound therapy (NPWT) (for example, PICO dressing)
	  - honeycomb dressing (for example, Opsite)
	• Time of dressing removal

	• Pre-operative skin preparation
	  ○ alcohol scrubs
	  - iodophor based (for example, Duraprep)
	  - chlorhexidine based (for example, Chloraprep)
	  ○ aqueous scrubs
	  - iodophor based (for example, Betadine)
	  - chlorhexidine based (for example, Hibiclens)
	  ○ water
	• Vaginal preparation
	  ○ alcohol-based
	  - iodophor based (for example, Duraprep)
	  - chlorhexidine based (for example, Chloraprep)
	  ○ aqueous-based
	  - iodophor based (for example, Betadine)
	  - chlorhexidine based (for example, Savlon)
	  ○ water
	• Intra-abdominal irrigation
	  ○ saline
	  ○ aqueous iodine washes
	• Use of diathermy

Comparison	• Each treatment compared to another (within their sections) • No treatment/placebo (except for the use of drapes, where only the above comparison will be considered)
Outcome	**Critical outcomes:** • Sepsis (including for example necrotising fasciitis) • Wound infection/surgical site infection • Need for antibiotics **Important outcomes:** • Adverse skin events from techniques (for example contact dermatitis/allergy) • Endometritis • Women's experience (patient satisfaction/health related quality of life) • Readmission into hospital (up to 28 days) The relevant time period for all of these outcomes is up to 7 days post-operatively.

CB: Caesarean birth, NPWT: negative pressure wound therapy

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual (2014). Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy until 31 March 2018. From 1 April 2018, declarations of interest were recorded according to NICE's 2018 conflicts of interest policy. Those interests declared until April 2018 were reclassified according to NICE's 2018 conflicts of interest policy (see Register of Interests).

Clinical evidence

Included studies

Three systematic reviews (Eke 2016, Haas 2018, Tolcher 2018) including 18 randomised controlled trials (RCTs) were included (N=7324) (Ahmed 2017, Asad 2017, Asghania 2011, Goymen 2017, Guzman 2002, Haas 2010, Harrigil 2003, Kunkle 2015, Memon 2011, Ngai 2015, Reid 2011, Rouse 1997, Springel 2017, Starr 2005, Temizcan 2015, Tuuli 2016, Viney 2012, Yildirim 2012). In addition, 7 other RCTs were included in this systematic review (N=4258) (Chaboyer 2014, Gunatilake 2017, Hussamy 2019, Hyldig 2018, Peleg 2016, Ruhstaller 2017, Stanirowski 2016, Tuuli 2020, Wihbey 2018).

The committee also discussed the findings of a health economic analysis including clinical results published after the search for this review (Hyldig 2019) that was a follow-up publication to one of the RCTs included above (Hyldig 2018), see appendix M for more details.

Tuuli 2020 and Hussamy 2019 are studies that were published after the original search for this review and in the case of the former, during the consultation period for this guideline. They were flagged by stakeholders and due to their potential to impact on the recommendations, an additional update search specifically for the negative pressure wound therapy studies was run during the post-consultation period and these two studies were fully incorporated into the review.

Evidence was found for all interventions except pre-operative washes, drapes, removal of body hair, use of face masks, and use of diathermy.

Some of the identified trials were suitable for meta-analyses and these have been performed as appropriate. Studies were classified as low/middle and high income setting as per the classification of the Organisation of Economic Co-Operation and Development (OECD).

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of clinical studies included in the evidence review

A summary of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Participants	Intervention	Control	Outcomes
Chaboyer 2014 RCT Australia	N=87	NPWT (PICO)	Standard dressing	• Surgical site infection • Adverse skin events (bruising) • Readmission into hospital
Eke 2016 Systematic review Turkey and US	K=3 (Harrigil 2003, Temizcan 2015, Viney 2012) N=862	Intra-abdominal saline irrigation	No irrigation	• Wound infection • Endometritis

Study	Participants	Intervention	Control	Outcomes
Gunatilake 2017 RCT US	N=82	NPWT (PREVENA)	Standard dressing	• Surgical site infection • Women's experience: reported pain at rest (days 1 to 7 post-operatively, Wong-Baker Faces Scale)
Haas 2018 Cochrane systematic review Iran, Saudi Arabia, Pakistan, Turkey, US	K=11 (Ahmed 2017, Asad 2017, Asghania 2011, Goymen 2017, Guzman 2002, Haas 2010, Memon 2011, Reid 2011, Rouse 1997, Starr 2005, Yildirim 2012) N=3403	Iodophor-based aqueous vaginal preparation; chlorhexidine-based aqueous vaginal preparation	No vaginal preparation; saline vaginal wash; sterile water	• Wound infection • Endometritis
Hussamy 2019 RCT US	N=441	NPWT (PREVENA)	Standard dressing	• Surgical site infection • Need for antibiotics • Adverse skin events • Patient satisfaction (women who were satisfied with treatment) • Readmission into hospital
Hyldig 2018, Hyldig 2019 RCT Denmark	N=876	NPWT (PICO)	Standard dressing	• Surgical site infection • Endometritis • Women's experience: self-rated health status (measured with EQ-VAS)
Peleg 2016 RCT Israel	N=320	Early (6 hours) removal of wound dressing	Standard (24 hours) removal of wound dressing	• Wound infection • Patient satisfaction (women who were satisfied with treatment) • Readmission into hospital

Study	Participants	Intervention	Control	Outcomes
Ruhstaller 2017 RCT US	N=119	NPWT (PREVENA)	Standard dressing	• Wound infection • Women's experience: sharp pain at postoperative day
Stanirowski 2016 RCT Poland	N=543	Hydroactive dressing (DACC)	Standard dressing	• Surgical site infection • Need for antibiotic • Readmission into hospital
Tolcher 2018 Systematic review US	K=4 (Kunkle 2015, Ngai 2015 Springel 2017, Tuuli 2016) N=3059	Chlorhexidine-based alcohol skin preparation	Povidone-iodine with/without alcohol	• Surgical site infection • Adverse skin reaction • Endometritis • Readmission into hospital
Tuuli 2020 RCT US	N=1624	NPWT (PREVENA)	Standard dressing	• Sepsis • Surgical site infection • Adverse skin events • Women's experience: satisfaction • Readmission into hospital
Wihbey 2018 RCT US	N=166	NPWT (PREVENA)	Standard dressing	• Surgical site infection • Need for antibiotics • Adverse skin events from techniques (hematoma)

DACC: dialkylcarbamoyl chloride; EQ-VAS: EuroQol visual analogue scale; NPWT: negative pressure wound therapy; RCT: randomised controlled trial

See the full evidence tables in appendix D and the forest plots in appendix E.

Quality assessment of clinical outcomes included in the evidence review

See the clinical evidence profiles (GRADE tables) in appendix F.

Economic evidence

Included studies

Two relevant studies were identified in a literature review of published cost-effectiveness analyses on this topic: Heard 2017 and Tuffaha 2015. The studies considered the cost-effectiveness of negative pressure wound therapy (NPWT) in obese women undergoing

caesarean birth. The analyses were cost-utility analyses measuring effectiveness in terms of quality adjusted life years (QALYs).

In addition, a further economic study (Hyldig 2019) was identified that was an economic evaluation relating to one of the included clinical studies (Hyldig 2019). This Danish study was an economic evaluation undertaken alongside an RCT, which addressed the cost-utility of incisional negative pressure wound therapy compared with standard care after caesarean birth in obese women:

See the literature search strategy in appendix B and economic study selection flow chart in appendix G.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of studies included in the economic evidence review

The base case results of Heard 2017 and Tuffaha 2015 showed that NPWT was marginally more costly and more effective than standard care. The resulting ICER was AU$42,340 per QALY in Heard 2017 and AU$15,000 per QALY in Tuffaha 2015.

Probabilistic sensitivity analysis was conducted in both of these studies but results were not fully reported in Heard 2017 (probability of each intervention being cost-effective was not presented). The results in Heard 2017 indicated that NPWT was more costly and more effective in the majority of scenarios. Probabilistic sensitivity analysis in Tuffaha 2015 showed that, at a threshold of AU$50,000 per QALY, the probability of NPWT being cost-effective was 65%.

Both of these studies were deemed to be only partially applicable to the decision problem in the UK setting as they were conducted from the perspective of the Australian health care system. The studies were found to meet most of the requirements of an adequate economic evaluation [see Developing NICE guidelines: the manual (2014) appendix H]. However, some potentially serious limitations were identified in Heard 2017 with the most notable being the absence of a full set of deterministic sensitivity analysis. Tuffaha 2015 was adjudged to have only minor limitations.

A Danish study, Hyldig 2019, reported an economic evaluation undertaken alongside an RCT (Hyldig 2018). In the base case analysis, it found that NPWT was cost-effective relative to standard dressings in women with a BMI ≥30 kg/m^2 before pregnancy who had a planned or emergency caesarean birth. The point estimates suggested that NPWT dominated standard dressings although neither the differences in costs or QALYs were statistically significant at the 5% level. Probabilistic sensitivity analysis suggested there was a 92.8% probability that NPWT was cost-effective at a willingness to pay threshold of €30,000 per QALY although this may be over-estimated if the decision to extrapolate health state utility gains over 12 months is not valid. However, probabilistic sensitivity analysis also suggested a 65% probability that NPWT was cost saving relative to standard dressings. The authors reported that cost savings were driven by a sub-group of more obese women with BMI ≥35 kg/m^2. This was borne out with sub-group analysis suggesting that NPWT generated cost savings of €339 per woman in this group compared to a cost increase of €155 per woman in those with a BMI <35 kg/m^2.

Overall, the results suggest that NPWT may be cost-effective but there is uncertainty (especially with respect to obese women but with a BMI <35 kg/m^2) and the applicability to the UK context is limited.

See the economic evidence tables in appendix H and economic evidence profiles in appendix I.

Original economic analysis

Ad-hoc cost minimisation and cost-utility analyses were undertaken as a result of a published cost-effectiveness analysis (Hyldig 2019) which was not included in the clinical review due to its date of publication as it was a cost-effectiveness analysis conducted alongside one of the included clinical reviews (Hyldig 2018). It was thought economic analysis could help inform whether recommendations on NPWT could be stratified by BMI. The analysis is summarised briefly below and described in more detail in appendix J.

The absolute treatment effect of NPWT compared to standard dressing to prevent surgical site infection, following caesarean birth, was estimated for women with BMI ≥ 30 kg/m^2 to BMI < 35 kg/m^2 and BMI ≥ 35 kg/m^2. Data to inform these estimates of treatment effectiveness were based on a published cost-effectiveness analysis (Hyldig 2019) and a meta-analysis undertaken for this review.

The analysis did not find strong evidence that NPWT was cost-effective in either sub-group. However, NPWT was relatively more likely to be cost-effective in women with BMI ≥ 35 kg/m^2 and the conclusion that it was not cost-effective was somewhat borderline. When compared to standard dressing in this population, NPWT was estimated to have a mean incremental net monetary benefit of -£29 and a 30.4% chance of being cost-effective. It was also estimated to result in a mean net cost of £32 and a 28.2% chance that it would be cost saving relative to standard dressing.

In women with BMI ≥ 30 kg/m^2 to BMI < 35 kg/m^2, NPWT had a mean incremental net monetary benefit of -£74 and a 3.0% probability of being cost-effective when compared to standard dressing. NPWT was also estimated to be £77 more expensive than standard dressing in this sub-group with only a 2.2% chance of producing net cost savings.

Evidence statements

Clinical evidence statements

Comparison 1. Hydroactive dressing versus standard dressing

Critical outcomes

Sepsis

- No evidence was available for this outcome

Surgical site infection

- One randomised controlled trial (n=543) provided very low quality evidence to show that those who received a hydroactive dressing experienced a clinically important decrease in the number of surgical site infections as compared to those who received a standard dressing.

Need for antibiotics

- One randomised controlled trial (n=543) provided very low quality evidence to show that those who received a hydroactive dressing experienced a clinically important decrease in the need for antibiotics as compared to those who received a standard dressing.

Important outcomes

Adverse skin events from techniques

- No evidence was available for this outcome

Endometritis

- No evidence was available for this outcome

Women´s experience

- No evidence was available for this outcome

Readmission into hospital

- One randomised controlled trial (n=543) provided very low quality evidence to show that there was no clinically important difference in readmission into hospital between those who received hydroactive or standard dressing.

Comparison 2. Negative pressure wound therapy (NPWT) versus standard dressing

Critical outcomes

Sepsis

- One randomised controlled trial (n=1606) provided very low quality evidence to show that for women with raised BMI (≥30 kg/m^2), there was no clinically important difference in sepsis between those who received negative pressure wound therapy or standard dressing.

Wound infection/ surgical site infection

- Seven randomised controlled trials (n=3380) provided very low quality evidence to show that, for women with raised BMI (≥30 kg/m^2), those who received negative pressure wound therapy may have experienced a clinically important decrease in the number of wound infections or surgical site infections as compared to those who received standard dressing.
  - One of the five randomised controlled trials (n=876) reported its results separately by BMI (women with a BMI between 30 and 34.9 kg/m^2, and women with a BMI of 35 kg/m^2 and greater) in both subgroups the point estimate suggested there was a clinically important decrease in the number of surgical site infections for those who received negative pressure wound therapy. However, for the BMI 30-34.9 kg/m^2 subgroup, the effect was not statistically significant (see appendix M for details).

Need for antibiotics

- Two randomised controlled trials (n=602) provided very low quality evidence to show that, for women with raised BMI (≥30 kg/m^2), there was no clinically important difference in the need for antibiotics between those who received negative pressure wound therapy or standard dressing.

Important outcomes

Adverse skin events from techniques

- Four randomised controlled trials (n=2303) provided very low quality evidence to show that, for women with raised BMI (≥30 kg/m^2), there was no clinically important difference in adverse skin events between those who received negative pressure wound therapy or standard dressing.

Endometritis

- One randomised controlled trial (n=876) provided very low quality evidence to show that, for women with raised BMI (≥30 kg/m^2), there was no clinically important difference in the occurrence of endometritis between those who received negative pressure wound therapy or standard dressing.

Women's experience: reported pain score (days 1 to 7)

- One randomised controlled trial (n=89) provided low quality evidence to show that, for women with raised BMI (≥35 kg/m^2), women who received negative pressure wound therapy had a clinically important reduction in pain on days 1-7 post-operatively (score of ≥2 on the Wong Baker faces score) as compared to those who received standard dressing.

Women's experience: sharp pain at postoperative day 2

- One randomised controlled trial (n=119) provided very low quality evidence to show that, for women with raised BMI (≥30 kg/m^2), there was no clinically important difference in sharp pain score on the second postoperative day between those who received negative pressure wound therapy or standard dressing.

Women's experience: self-rated health status; measured with EQ-VAS

- One randomised controlled trial (n=876) provided low quality evidence to show that, for women with raised BMI (≥30 kg/m^2), there was no clinically important difference in self-rated health status between those who received negative pressure wound therapy or standard dressing.

Women's experience: satisfaction (0-10, higher is better)

- One randomised controlled trial (n=1604) provided low quality evidence to show that, for women with raised BMI (≥30 kg/m^2), there was no clinically important difference in satisfaction between those who received negative pressure wound therapy or standard dressing.

Women's experience: satisfaction (would use this dressing again)

- One randomised controlled trial (n=411) provided low quality evidence to show that, for women with raised BMI (≥30 kg/m^2), there was no clinically important difference in satisfaction between those who received negative pressure wound therapy or standard dressing.

Readmission into hospital

- Four randomised controlled trials (n=2297) provided very low quality evidence to show that, for women with raised BMI (≥30 kg/m^2), there was no clinically important difference in readmission into hospital between those who received negative pressure wound therapy or standard dressing.

Comparison 3. Early (6 hours) versus standard (24 hours) timing of dressing removal

Critical outcomes

Sepsis

- No evidence was available for this outcome

Wound infection

- One randomised controlled trial (n=320) provided very low quality evidence to show that there was no clinically important difference in wound infection rates between those whose dressing was removed at 6 hours or 24 hours.

Need for antibiotics

- No evidence was available for this outcome

Important outcomes

Adverse skin events from techniques

- No evidence was available for this outcome

Endometritis

- No evidence was available for this outcome

Women's experience: women who were satisfied with the intervention

- One randomised controlled trial (n=320) provided moderate quality evidence to show a clinically important increase in satisfaction with the intervention for those whose dressing was removed at 6 hours compared to those whose dressing was removed at 24 hours.

Readmission into hospital

- One randomised controlled trial (n=320) provided very low quality evidence to show that there was no clinically important difference in readmission into hospital between those whose dressing was removed at 6 or 24 hours.

Comparison 4. Chlorhexidine-based alcohol skin preparation versus iodophor-based aqueous/alcohol skin preparation

Critical outcomes

Sepsis

- No evidence was available to inform this outcome

Surgical site infection

- Four randomised controlled trials (N=3059) provided low quality evidence to show a clinically important decrease in the number of surgical site infections for those who received chlorhexidine-based alcohol skin preparation compared to those who received iodophor-based skin preparation (including alcohol and aqueous based preparations).

Iodophor-based aqueous skin preparation

- Two randomised controlled trials (N=975) provided very low quality evidence to show that there was no clinically important difference in surgical site infections between those who received chlorhexidine-based alcohol skin preparation or iodophor-based aqueous skin preparation.

Iodophor-based alcohol skin preparation

- Two randomised controlled trials (N=2084) provided low quality evidence to show a clinically important decrease in the number of surgical site infections for those who received chlorhexidine-based alcohol skin preparation as compared to those who received iodophor-based alcohol skin preparation.

Need for antibiotics

- No evidence was available for this outcome

Important outcomes

Adverse skin reaction

- Two randomised controlled trials (N=2079) provided very low quality evidence to show that there was no clinically important difference in adverse skin reactions between those who received chlorhexidine-based alcohol skin preparation or iodophor-based aqueous/alcohol skin preparation.

Iodophor-based aqueous skin preparation

- One randomised controlled trial (N=932) provided very low quality evidence to show that there was no clinically important difference in adverse skin reactions between those who received chlorhexidine-based alcohol skin preparation or iodophor-based aqueous skin preparation.

Iodophor-based alcohol skin preparation

- One randomised controlled trial (N=1147) provided very low quality evidence to show that there was no clinically important difference in adverse skin reactions between those who received chlorhexidine-based alcohol skin preparation or iodophor-based alcohol skin preparation.

Endometritis

- Two randomised controlled trials (N=2079) provided very low quality evidence to show that there was no clinically important difference in the occurrence of endometritis between those who received chlorhexidine-based alcohol skin preparation or iodophor-based aqueous/alcohol skin preparation.

Iodophor-based aqueous skin preparation

- One randomised controlled trial (N=932) provided very low quality evidence to show that there was no clinically important difference in the occurrence of endometritis between those who received chlorhexidine-based alcohol skin preparation or iodophor-based aqueous skin preparation.

Iodophor-based alcohol skin preparation

- One randomised controlled trial (N=1147) provided very low quality evidence to show that there was no clinically important difference in the occurrence of endometritis between those who received chlorhexidine-based alcohol skin preparation or iodophor-based alcohol skin preparation.

Women´s experience

- No evidence was available for this outcome

Readmission into hospital

- Two randomised controlled trials (N=2079) provided low quality evidence to show that there was no clinically important difference in readmission into hospital between those who received chlorhexidine-based alcohol skin preparation or iodophor-based aqueous/alcohol skin preparation.

Iodophor-based aqueous skin preparation

- One randomised controlled trial (N=932) provided very low quality evidence to show that there was no clinically important difference in readmission into hospital between those

who received chlorhexidine-based alcohol skin preparation or iodophor-based aqueous skin preparation.

Iodophor-based alcohol skin preparation

- One randomised controlled trial (N=1147) provided very low quality evidence to show that there was no clinically important difference in readmissions into hospital between those who received chlorhexidine-based alcohol skin preparation or iodophor-based alcohol skin preparation.

Comparison 5. Iodophor-based aqueous vaginal preparation versus no vaginal/saline vaginal preparation

Critical outcomes

Sepsis

- No evidence was available for this outcome

Wound infection

- Seven randomised controlled trials (N=2639) provided very low quality evidence to show that there was no clinically important difference in the number of wound infections between those who received iodophor-based aqueous vaginal preparation or no vaginal/saline vaginal preparation.

Need for antibiotics

- No evidence was available for this outcome

Important outcomes

Adverse skin events from techniques

- No evidence was available for this outcome

Endometritis

- Eight randomised controlled trials (N=3069) provided low quality evidence to show a clinically important decrease in the occurrence of endometritis for those who received iodophor-based aqueous vaginal preparation compared to those who received no vaginal/saline vaginal preparation.

Women with ruptured membranes

- Three randomised controlled trials (N=272) provided moderate quality evidence to show that women with ruptured membranes who received iodophor-based aqueous vaginal preparation experienced a clinically important decrease in the occurrence of endometritis compared to those who received no vaginal/saline vaginal preparation.

Women with intact membranes

- Three randomised controlled trials (N=857) provided low quality evidence to show, for women with intact membranes, that there was no clinically important difference in endometritis between those who received iodophor-based aqueous vaginal preparation or no vaginal/saline vaginal preparation.

Women with mixed/unclear rupture of membranes

- Five randomised controlled trials (N=1940) provided very low quality evidence to show that, where membrane status was not reported or included a mixed population, those who received iodophor-based aqueous vaginal preparation had a clinically important decrease

in the number of episodes of endometritis compared to those who received no vaginal/saline vaginal preparation.

Women´s experience

- No evidence was available for this outcome

Readmission into hospital

- No evidence was available for this outcome

Comparison 6. Chlorhexidine-based aqueous vaginal preparation versus no vaginal cleansing/sterile water

Critical outcomes

Sepsis

- No evidence was available for this outcome

Wound infection

- One randomised controlled trial (N=200) provided very low quality evidence to show that there was no clinically important difference in wound infections between those who received chlorhexidine-based aqueous vaginal preparation or no vaginal cleansing/sterile water.

Need for antibiotics

- No evidence was available for this outcome

Important outcomes

Adverse skin events from techniques

- No evidence was available for this outcome

Endometritis

- Two randomised controlled trials (N=214) provided moderate quality evidence to show a clinically important decrease in the number of episodes of endometritis for those who received chlorhexidine-based aqueous vaginal preparation compared to those who received no vaginal cleansing/sterile water.

Women´s experience

- No evidence was available for this outcome

Readmission into hospital

- No evidence was available for this outcome

Comparison 7. Saline intra-abdominal irrigation versus no irrigation

Critical outcomes

Sepsis

- No evidence was available for this outcome

Wound infection

- Two randomised controlled trials (N=626) provided very low quality evidence to show that there was no clinically important difference in wound infections between those who received saline intra-abdominal irrigation or no irrigation.

Need for antibiotics

- No evidence was available for this outcome

Important outcomes

Adverse skin events

- No evidence was available for this outcome

Endometritis

- Three randomised controlled trials (N=862) provided very low quality evidence to show that there was no clinically important difference in the occurrence of endometritis between those who received saline intra-abdominal irrigation or no irrigation.

Women´s experience

- No evidence was available for this outcome

Readmission into hospital

- No evidence was available for this outcome

Economic evidence statements

- One cost utility analysis undertaken in an Australian setting found that NPWT was more costly and more effective than standard care with an ICER of AU$15,000 per QALY. This analysis is partially applicable with minor limitations.
- Another cost utility analysis undertaken in an Australian setting found that NPWT was more costly and more effective than standard care with an ICER of AU$42,340 per QALY. This analysis is partially applicable with serious limitations.
- An economic evaluation performed alongside an RCT found that NPWT dominated standard dressings in women with a BMI ≥30 kg/m^2 before pregnancy who had a planned or emergency caesarean birth although differences in costs and QALYs were not statistically significant. This analysis is partially applicable with major limitations.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The aim of this review was to identify which interventions reduced infectious morbidity in women undergoing caesarean birth. The committee therefore designated 3 critical outcomes: sepsis, wound infection/surgical site infection and need for antibiotics. These outcomes were selected as the most direct indicators for the efficacy and safety of the different interventions considered to reduce infectious morbidity.

The committee identified 4 further outcomes as important: endometritis, readmission into hospital, adverse skin events from techniques or interventions, and women's experience. These outcomes were important because endometritis may occur after caesarean birth, readmission may indicate the presence of a wound-related problem, and some of the skin preparations and wound dressings may lead to adverse skin events so including this allowed the benefits and harms of the interventions to be balanced. As post-operative wound problems can have a detrimental impact on quality of life, it was also thought important to include women's experience.

The quality of the evidence

Twenty-seven RCTs (18 of which were incorporated from 3 previously published systematic reviews) were included in this review. The quality of the evidence ranged from very low to moderate as assessed by GRADE.

The main reason for downgrading the evidence was the risk of bias due to studies not reporting how randomisation was performed or concealed, or because women, investigators and assessors were aware of treatment allocation. Other reasons for downgrading the quality of the evidence included sponsorship bias, where studies were funded by the manufacturers of the intervention under investigation, or indirectness (as some studies were conducted in low or middle income countries). Additionally, studies were also downgraded because of imprecision, as the trials had few women included, and therefore the confidence intervals around the estimate for each of the outcomes were wide.

The analysis comparing efficacy of NPWT in different BMI categories was a post-hoc subgrouping of an RCT. As such there is an additional risk of bias as these subgroups did not appear to be pre-specified or stratification that occurred prior to randomisation. However, the thresholds chosen (BMI 30-34.9 and 35 kg/m^2 or above) were reasonable and therefore the likelihood they were selected to emphasise a certain outcome is limited.

Benefits and harms

Although the use of prophylactic antibiotics is standard practice for women undergoing caesarean birth, there is still a risk of infection during any surgical procedure. Infections complicate recovery after surgery, may require a protracted hospital stay or intensive monitoring, and can have an important, detrimental effect on the woman's quality of life and emotional state. The committee's priority with these recommendations was to minimise maternal morbidity through the use of specific interventions.

The committee made the recommendations about choice of skin and vaginal preparation based on the evidence in this report, which suggested that these interventions reduce the risk of surgical site infections and endometritis, respectively.

Skin preparation for the abdomen is standard practice for a caesarean birth and the evidence indicated that the use of alcohol-based chlorhexidine skin preparation of the abdomen offered an important reduction in wound/surgical site infection compared to iodine skin preparations. The committee noted that this evidence, specific to women undergoing caesarean birth, is also in keeping with the recommendations for the general surgical population, contained in the NICE guideline on the prevention and treatment of surgical site infections. However, the committee noted that there was no difference in the rates of adverse events, endometritis or readmission between alcohol-based chlorhexidine preparations and iodine preparations, and so suggested that iodine preparations could be used as an alternative if alcohol-based chlorhexidine skin preparations were not available. This hierarchy is also in line with the NICE guideline on the prevention and treatment of surgical site infections.

The evidence showed a clinically important reduction in the occurrence of endometritis when antiseptic vaginal preparation (cleansing solution) was used, as compared to no vaginal preparation, or the use of saline only. Aqueous iodine vaginal solutions were shown to result in a clinically important reduction in endometritis, as compared to no preparation/saline preparation. On subgroup analysis according to membrane status, this difference was found to be most marked for women with ruptured membranes. The data regarding aqueous chlorhexidine vaginal preparation were more limited (2 studies), but also demonstrated a clinically important reduction in endometritis with the use of this solution. Therefore the committee decided that it would be appropriate to recommend aqueous iodine solution but to state that aqueous chlorhexidine vaginal preparation could be used as an alternative solution if the woman has allergies to iodine or if an iodine preparation is not available. The evidence

for aqueous chlorhexidine vaginal preparation was not specific for women with ruptured membranes.

The evidence suggested that negative pressure wound therapy (NPWT) is likely to be effective in reducing wound infections or surgical site infections in women with body mass index (BMI) of 30 kg/m^2 or more, although the outcome is on the cusp of statistical significance.The committee discussed the evidence relevant for this intervention and noted that the studies were not robust enough to make a strong recommendation in all women with a BMI of 30 kg/m^2 or above. The main issues that the committee noted were that 2 different brands of NPWT were used across the studies and, as a result, the negative pressure that women received varied substantially. Five of the included studies (Gunatilake 2017, Hussamy 2019, Ruhstaller 2017, Tuuli 2020, Wihbey 2018) used the PREVENA negative pressure wound therapy device, applying a negative pressure of 125 mmHg, whereas 2 of the included studies in this comparison (Chaboyer 2014, Hyldig 2018) used the PICO negative pressure wound therapy device, applying a negative pressure of 80 mmHg. Furthermore, some of these studies were funded by the manufacturer of the negative pressure wound therapy device, which introduced a potential risk of bias. The experience of the committee was that, in current practice, NPWT was more commonly used for women with a BMI of 40 kg/m^2 or more, but the inclusion criteria for the studies reviewed was often lower than this. In a health economic analysis of one of the larger trials (Hyldig 2018), the trial authors reported their results separately for the group of women with a BMI 30-34.9 kg/m^2 and those with a BMI of 35 kg/m^2 or greater. The direction and point estimate of the effect was similar between the two groups. However, the relative effect was not statistically significant in the BMI 30-34.9 kg/m^2 group and the absolute effect was smaller. The results of the economic analysis differed between these groups (see below). There was some inconsistent evidence on adverse skin events occurring with NPWT. Overall there appeared to be no clinically important difference in adverse skin events between NPWT and standard dressing, however in 2 of the larger studies there were far more adverse skin events in the NPWT arm. The committee noted it was difficult to determine the severity of these events and also queried whether the inconsistent results could be due to varying monitoring strategies or inclusion criteria in terms of allergies. Finally the committee also noted the NICE medical technologies guidance (MTG43) about PICO negative pressure wound dressings for closed surgical incisions, which recommended their use for people at high risk of wound infections. Taking all of this into account, the committee agreed that there was sufficient evidence to make a weak recommendation for the use of NPWT in women with a BMI of 35 kg/m^2 and above.

Some limited evidence suggested that there were no clinically important differences in early (6 hours) as compared to standard (24 hours) removal of wound dressings, and that women were more satisfied when the dressing was removed earlier. This was consistent with the committee's experience, and the committee also noted that women included in this study were being treated in an inpatient setting, and their surgical wounds were examined prior to discharge, which would be standard care in the UK. The committee therefore considered that the methods of the study were robust. The previous guideline had recommended that dressings were removed after 24 hours so the committee amended this recommendation to state that dressings could be removed between 6 and 24 hours after the CB. The committee also made a new recommendation to advise women that the evidence showed no differences in the risk of wound infection when the dressing was removed 6 hours or 24 hours postoperatively.

There was very limited evidence on the use of different types of postoperative dressings. A single study was identified which considered two specific types of dressing. The committee acknowledged that there are many different types available, but could not recommend one dressing over another as there was not enough evidence to support the decision. However, as women may ask about different dressings, the committee made a recommendation to clarify that there was evidence to demonstrate that one type of wound dressing was better at reducing wound infections that another.

There was some evidence comparing saline intra-abdominal irrigation with no irrigation which found no difference for wound infection or endometritis, and the committee decided that it was not necessary to make any recommendations relating to this intervention.

Due to the paucity of evidence in the use of hair removal, incise drapes and diathermy, the committee were unable to make specific recommendations regarding these interventions. Instead, they noted the relevant recommendations in the NICE guideline on surgical site infections: prevention and treatment. These apply to the general population undergoing surgery, rather than specifically to women having a caesarean birth, but were in line with the committee's experience.

Cost effectiveness and resource use

The committee discussed the three relevant studies that considered the cost-effectiveness of NPWT in obese women (BMI ≥ 30 kg/m^2) having a caesarean birth.

The results of Heard 2017 and Tuffaha showed NPWT to be more effective and more costly than standard care. In both studies, the ICER result was interpreted as showing that NPWT is cost-effective (based on an Australian cost-effectiveness threshold). However, there was some uncertainty around the result in both models (largely as a result of uncertainty in the clinical evidence base). The committee also noted that these 2 studies are Australian and are therefore of limited applicability to the UK health care setting.

Hyldig 2019 found NPWT to be dominant when compared to standard dressing but neither the cost saving or QALY benefit were found to be statistically significant. Nevertheless, probabilistic sensitivity analysis suggested there was a 65% probability that NPWT was cost saving. In addition, the committee noted that any cost savings appeared to be driven by the sub-group of women with BMI ≥ 35 kg/m^2.

The results of an economic study conducted as part of a recent NICE medical technology guidance on NPWT using PICO dressings (MTG43) were also discussed by the committee. The report included a cost analysis submitted by the manufacturer which was subsequently revised by the external assessment centre (EAC). The revised EAC cost analysis showed that, in comparison to standard dressings, PICO dressings resulted in modest cost savings when considering all surgery types. However, this overall result was driven by the large cost savings seen in highly invasive surgery (such as colorectal cancer) and PICO dressings were unlikely to be cost saving when used for surgeries undertaken on healthier patients such as caesarean birth and orthopaedic surgery.

On the basis of the economic evidence, the committee considered that a weak recommendation to consider NPWT was justified in women with a BMI of 35 kg/m^2 or above. An original economic analysis undertaken for this guideline suggested that although unlikely on the balance of probabilities, NPWT might be cost saving in this population due to a reduced incidence of surgical site infections when compared to standard dressings. The committee also thought that this was reflective of NHS practice where NPWT following caesarean birth would normally be reserved for this population. The committee also considered that this analysis finding was consistent with the MTG43 view that cost savings were more likely in less healthy patients. The committee agreed that no recommendation to consider NPWT in women with a BMI ≥ 30 kg/m^2 to BMI < 35 kg/m^2 was warranted from the economic evidence presented.

The committee identified that considering the use of NPWT in women with a BMI of 35 kg/m^2 or above having a caesarean birth, will be a change of practice for many units, who currently do not use it all at or who may use it at higher BMI thresholds, and may have resource implications, particularly in areas where a higher proportion of pregnant women will meet this criterion.

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Appendices

Appendix A – Review protocols

Review protocol for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

Table 3: Review protocol for techniques to reduce infectious morbidity in caesarean birth

Field (based on PRISMA-P)	Content
Key area in the scope	Procedural aspects of caesarean birth (CB): timing of planned caesarean birth, preoperative testing and preparation, anaesthesia and surgical techniques
Draft review question from the surveillance report	Surgical techniques for CB – use of antibiotics- methods to reduce infectious morbidity at CB
Actual review question	What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a CB?
Type of review question	Intervention
Objective of the review	To identify if there are effective ways of reducing infectious morbidity at CB. Administration of prophylactic antibiotics is now standard practice, but additional methods to reduce infectious morbidity may vary between different obstetric units. The purpose of this review is to assess which of these methods are effective at reducing infectious morbidity in the mother.
Eligibility criteria – **population**/disease/condition/issue/domain	Women undergoing caesarean section include emergency and elective CB

Eligibility criteria – **intervention**(s)/exposure(s)/prognostic factor(s)	• Pre-operative washes
	• Drapes
	  ○ standard drape
	  ○ incise drape
	• Removal of body hair

Field (based on PRISMA-P)	Content
	○ before surgery ○ in the operating theatre ○ no shaving • Use of face masks • Type of dressing/wound covering ○ topical/spray-on adhesive dressing (e.g. Dermabond) ○ different types of dressings - dry absorbent dressings - hydroactive dressing - hydrocolloid dressing - negative pressure wound therapy (e.g. PICO dressing) - Honeycomb dressing (e.g. Opsite) • Time of dressing removal • Pre-operative skin preparation ○ alcohol scrubs - iodophor based (e.g. Duraprep) - chlorhexidine based (e.g. Chloraprep) ○ aqueous scrubs - iodophor based (e.g. betadine) - chlorhexidine based (e.g. Hibiclens) ○ water • Vaginal preparation ○ alcohol scrubs - iodophor based (e.g. Duraprep) - chlorhexidine based (e.g. Chloraprep) ○ aqueous scrubs - iodophor based (e.g. betadine) - chlorhexidine based (e.g. savlon) ○ water

Field (based on PRISMA-P)	Content

	• Intra-abdominal irrigation
	  ○ Saline
	  ○ Aqueous iodine washes
	• Use of diathermy

Eligibility criteria – **comparator(s)**/control or reference (gold) standard	• Each intervention compared to another (within their sections – see specified comparisons below) • No treatment/placebo • Relevant comparisons are therefore: 1. Use of pre-op wash compared to no use/placebo 2. One type of pre-op wash compared to another 3. Use of standard drape compared to incise drape 4. Removal of body hair compared to no removal 5. Removal of body hair before surgery compared to removal in the operating theatre 6. Use of face masks (by the operating team) compared to no face masks 7. Use of topical/spray-on adhesive dressing compared to non-use/placebo 8. Use of one type of topical/spray-on adhesive dressing compared to another 9. Use of any dressing compared to no dressing 10. Use of one type of dressing compared to another 11. Removal of dressing at one post-operative time, compared to removal of dressing at a different time 12. One type of skin preparation compared to no skin preparation/placebo 13. One type of skin preparation compared to another type 14. One type of vaginal preparation compared to no vaginal preparation 15. One type of vaginal preparation compared to another type

Field (based on PRISMA-P)	Content
	16. One type of abdominal irrigation compared to no abdominal irrigation 17. One type of abdominal irrigation compared to another 18. The use of diathermy compared to no use of diathermy
Outcomes and prioritisation	• The relevant time period for all of these outcomes is up to 7 days post-operative: **Critical outcomes:** • Sepsis (including e.g. necrotising fasciitis) • Wound infection/surgical site infection • Need for antibiotics **Important outcomes:** • Adverse skin events from techniques (e.g. contact dermatitis/allergy) • Endometritis • Women's experience (patient satisfaction/health related quality of life) • Readmission into hospital (up to 28 days)
Eligibility criteria – **study design**	Only published full text papers • Systematic reviews/meta-analyses of RCTs • RCTs
Other inclusion **exclusion criteria**	Exclude conference abstracts Exclude studies from low/middle income countries Exclude studies where prophylactic antibiotics have not been administered, unless no/very sparse evidence is identified
Proposed stratified, sensitivity/**sub-group analysis**, or meta-regression	Subgroup analysis will be conducted if heterogeneity is identified: • for elective versus emergency CB • ruptured membranes/intact membranes • by gestational age (<34 weeks and <28 weeks) • by stage of labour in which CB is carried out

Field (based on PRISMA-P)	Content
	• first stage (cervix <10 cm dilated) • second stage (cervix 10cm [fully] dilated) • women known to be MRSA +ve • procedures where prophylactic antibiotics were given before and after cord clamping • women with raised BMI
Selection process – duplicate screening/selection/analysis	Duplicate screening/selection/analysis will not be undertaken for this review as this question was not prioritised for it. Included and excluded studies will be cross checked with the committee and with published systematic reviews when available.
Data management (software)	If pairwise meta-analyses are undertaken, they will be performed using Cochrane Review Manager (RevMan5). 'GRADE' will be used to assess the quality of evidence for each outcome. STAR will be used for bibliographies/citations and study sifting. Microsoft Word will be used for data extraction and quality assessment/critical appraisal
Information sources – databases and dates	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques will be used. See appendix B for full strategies.
Identify if an update	No, this question was not included in the existing guideline
Author contacts	Developer: National Guideline Alliance NGA-enquiries@RCOG.ORG.UK

Field (based on PRISMA-P)	Content
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
Search strategy – for one database	For details please see appendix B
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables)
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables)
Methods for assessing bias at outcome/study level	Appraisal of methodological quality: The methodological quality of each study will be assessed using an appropriate checklist: • ROBIS for systematic reviews • Cochrane risk of bias tool for randomised studies • For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence will evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual
Methods for quantitative analysis – combining studies and exploring (in)consistency	Synthesis of data: Meta-analysis will be conducted where appropriate using Review Manager. Minimum important differences Default values will be used of: 0.8 and 1.25 relative risk for dichotomous outcomes; 0.5 times control group SD for continuous outcomes, unless more appropriate values are identified by the guideline committee or in the literature. Double sifting, data extraction and methodological quality assessment:

Field (based on PRISMA-P)	Content
	Sifting, data extraction, appraisal of methodological quality and GRADE assessment will be performed by the systematic reviewer. Quality control will be performed by the senior systematic reviewer. Dual quality assessment and data extraction will not be performed.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale/context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and chaired by Sarah Fishburn in line with section 3 of Developing NICE guidelines: the manual. Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods chapter.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for the NHS in England.
PROSPERO registration number	Not registered to PROSPERO

CB: caesarean birth; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; NGA: National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation

Appendix B – Literature search strategies

Literature search strategies for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

Review question search strategies

Note: The full searches for this review question were run on 02/10/2018 but a targeted top up search just for negative pressure wound therapy using the relevant terms from the full searches was run on 10/12/2020. This was done in response to stakeholder consultation comments regarding potentially relevant publications that had been published since the full searches were run. See the Included Studies section of this Evidence Report for more details.

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

Date of last search: 02/10/2018

#	Searches
1	exp CESAREAN SECTION/
2	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
3	or/1-2
4	SURGICAL DRAPES/
5	(drape or drapes or draping).ti,ab.
6	HAIR REMOVAL/
7	((remov$ or cut$) adj3 hair?).ti,ab.
8	shav$.ti,ab.
9	((no or avoid$ or stop$ or discourag$) adj5 (remov$ or cut$) adj3 hair?).ti,ab.
10	((no or avoid$ or stop$ or discourag$) adj5 shav$).ti,ab.
11	MASKS/
12	(face adj3 (mask? or shield? or visor?)).ti,ab.
13	facemask?.ti,ab.
14	exp BANDAGES/
15	dressing?.ti,ab.
16	(wound? adj3 cover$).ti,ab.
17	exp TISSUE ADHESIVES/
18	(tissue adj3 adhesive?).ti,ab.
19	(Bucrylate or Collodion or Fibrin Foam or Fibrin Tissue Adhesive or Karaya Gum or Cyanoacrylate? or Enbucrilate or dermabond).mp.
20	NEGATIVE-PRESSURE WOUND THERAPY/
21	(negative$ adj3 pressur$ adj3 therap$).ti,ab.
22	(vacuum? adj3 wound? adj3 clos$).ti,ab.
23	opsite.mp.
24	THERAPEUTIC IRRIGATION/
25	VAGINAL DOUCHING/
26	(therap$ adj3 (irrigat$ or lavag$)).ti,ab.
27	((alcohol$ or aqueous or water) adj3 (scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.

#	Searches
28	((skin or vagina$) adj3 (prepar$ or clean$ or scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
29	exp ANTI-INFECTIVE AGENTS, LOCAL/
30	(antiseptic? or anti-septic?).ti,ab.
31	(antiinfective? or anti-infective?).ti,ab.
32	(Acriflavine or Aminacrine or Bacitracin or Benzalkonium Compound? or Benzethonium or Bithionol or Camphor or Carbadox or Carbocysteine or Cetylpyridinium or Chlorhexidine or Clotrimazole or Dequalinium or Ethacridine or Ethanol or Furazolidone or Gentian Violet or Gramicidin or Hexachlorophene or Hexetidine or Hydrogen Peroxide or Iodine or Lysostaphin or Mafenide or Mercuric Chloride or Natamycin or Noxythiolin or Phenol or Phenylethyl Alcohol or Povidone-Iodine or Proflavine or Silver Nitrate or Silver Protein? or Silver Sulfadiazine or Sulfacetamide or Tea Tree Oil or Thymol or Triclosan or Tyrocidine or Tyrothricin or chloraprep or hibiclens or savlon).mp.
33	IODOPHORS/
34	(iodophor? or Duraprep or betadine).mp.
35	*WATER/
36	WATER/ and STERILIZATION/
37	(steril$ adj3 water?).ti,ab.
38	PERITONEAL LAVAGE/
39	((Intraabdom$ or (Intra adj3 abdom$) or periton$) adj3 (irrigat$ or lavag$)).ti,ab.
40	((saline or sodium chloride) adj3 (scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
41	DIATHERMY/
42	diatherm$.ti,ab.
43	or/4-42
44	INFECTION CONTROL/mt [Methods]
45	3 and 43
46	3 and 44
47	or/45-46
48	limit 47 to english language
49	LETTER/
50	EDITORIAL/
51	NEWS/
52	exp HISTORICAL ARTICLE/
53	ANECDOTES AS TOPIC/
54	COMMENT/
55	CASE REPORT/
56	(letter or comment*).ti.
57	or/49-56
58	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
59	57 not 58
60	ANIMALS/ not HUMANS/
61	exp ANIMALS, LABORATORY/
62	exp ANIMAL EXPERIMENTATION/
63	exp MODELS, ANIMAL/
64	exp RODENTIA/
65	(rat or rats or mouse or mice).ti.
66	or/59-65

#	Searches
67	48 not 66

Databases: Embase; and Embase Classic

Date of last search: 02/10/2018

#	Searches
1	exp CESAREAN SECTION/
2	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
3	or/1-2
4	SURGICAL DRAPE/
5	(drape or drapes or draping).ti,ab.
6	exp HAIR REMOVAL/
7	((remov$ or cut$) adj3 hair?).ti,ab.
8	shav$.ti,ab.
9	((no or avoid$ or stop$ or discourag$) adj5 (remov$ or cut$) adj3 hair?).ti,ab.
10	((no or avoid$ or stop$ or discourag$) adj5 shav$).ti,ab.
11	MASK/
12	FACE MASK/
13	(face adj3 (mask? or shield? or visor?)).ti,ab.
14	facemask?.ti,ab.
15	exp WOUND DRESSING/
16	dressing?.ti,ab.
17	(wound? adj3 cover$).ti,ab.
18	exp TISSUE ADHESIVE/
19	(tissue adj3 adhesive?).ti,ab.
20	(Bucrylate or Collodion or Fibrin Foam or Fibrin Tissue Adhesive or Karaya Gum or Cyanoacrylate? or Enbucrilate or dermabond).mp.
21	VACUUM ASSISTED CLOSURE/
22	(negative$ adj3 pressur$ adj3 therap$).ti,ab.
23	(vacuum? adj3 wound? adj3 clos$).ti,ab.
24	opsite.mp.
25	LAVAGE/
26	VAGINAL LAVAGE/
27	SKIN DECONTAMINATION/
28	(therap$ adj3 (irrigat$ or lavag$)).ti,ab.
29	((alcohol$ or aqueous or water) adj3 (scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
30	((skin or vagina$) adj3 (prepar$ or clean$ or scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
31	exp TOPICAL ANTIINFECTIVE AGENT/
32	(antiseptic? or anti-septic?).ti,ab.
33	(antiinfective? or anti-infective?).ti,ab.
34	(Acriflavine or Aminacrine or Bacitracin or Benzalkonium Compound? or Benzethonium or Bithionol or Camphor or Carbadox or Carbocysteine or Cetylpyridinium or Chlorhexidine or Clotrimazole or Dequalinium or Ethacridine or Ethanol or Furazolidone or Gentian Violet or Gramicidin or Hexachlorophene or Hexetidine or Hydrogen Peroxide or Iodine or Lysostaphin or Mafenide or Mercuric Chloride or Natamycin or Noxythiolin or Phenol or Phenylethyl Alcohol or Povidone-Iodine or Proflavine or Silver Nitrate or Silver Protein? or

#	Searches
	Silver Sulfadiazine or Sulfacetamide or Tea Tree Oil or Thymol or Triclosan or Tyrocidine or Tyrothricin or chloraprep or hibiclens or savlon).mp.
35	IODOPHOR/
36	(iodophor? or Duraprep or betadine).mp.
37	*WATER/
38	STERILE WATER/
39	(steril$ adj3 water?).ti,ab.
40	PERITONEUM LAVAGE/
41	INTRAABDOMINAL IRRIGATION/
42	((Intraabdom$ or (Intra adj3 abdom$) or periton$) adj3 (irrigat$ or lavag$)).ti,ab.
43	((saline or sodium chloride) adj3 (scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
44	DIATHERMY/
45	diatherm$.ti,ab.
46	or/4-45
47	3 and 46
48	limit 47 to english language
49	letter.pt. or LETTER/
50	note.pt.
51	editorial.pt.
52	CASE REPORT/ or CASE STUDY/
53	(letter or comment*).ti.
54	or/49-53
55	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
56	54 not 55
57	ANIMAL/ not HUMAN/
58	NONHUMAN/
59	exp ANIMAL EXPERIMENT/
60	exp EXPERIMENTAL ANIMAL/
61	ANIMAL MODEL/
62	exp RODENT/
63	(rat or rats or mouse or mice).ti.
64	or/56-63
65	48 not 64

Databases: Cochrane Central Register of Controlled Trials; and Cochrane Database of Systematic Reviews

Date of last search: 02/10/2018

#	Searches
#1	MeSH descriptor: [CESAREAN SECTION] explode all trees
#2	(cesarean* or caesarean* or “c section*” or csection* or (deliver* near/3 abdom*)):ti,ab
#3	#1 or #2
#4	MeSH descriptor: [SURGICAL DRAPES] this term only
#5	(drape or drapes or draping):ti,ab
#6	MeSH descriptor: [HAIR REMOVAL] this term only
#7	((remov* or cut*) near/3 hair*):ti,ab

#	Searches
#8	shav*:ti,ab
#9	((no or avoid* or stop* or discourag*) near/5 (remov* or cut*) near/3 hair*):ti,ab
#10	((no or avoid* or stop* or discourag*) near/5 shav*):ti,ab
#11	MeSH descriptor: [MASKS] this term only
#12	(face near/3 (mask* or shield* or visor*)):ti,ab
#13	facemask*:ti,ab
#14	MeSH descriptor: [BANDAGES] explode all trees
#15	dressing*:ti,ab
#16	(wound* near/3 cover*):ti,ab
#17	MeSH descriptor: [TISSUE ADHESIVES] explode all trees
#18	(tissue near/3 adhesive*):ti,ab
#19	(Bucrylate or Collodion or Fibrin Foam or Fibrin Tissue Adhesive or Karaya Gum or Cyanoacrylate* or Enbucrilate or dermabond).ti,ab.
#20	MeSH descriptor: [NEGATIVE-PRESSURE WOUND THERAPY] this term only
#21	(negative* near/3 pressur* near/3 therap*):ti,ab
#22	(vacuum* near/3 wound* near/3 clos*):ti,ab
#23	opsite:ti,ab
#24	MeSH descriptor: [THERAPEUTIC IRRIGATION] this term only
#25	MeSH descriptor: [VAGINAL DOUCHING] this term only
#26	(therap* near/3 (irrigat* or lavag*)):ti,ab
#27	((alcohol* or aqueous or water) near/3 (scrub* or swabb* or irrigat* or douch* or lavag* or wash or washes or washing)):ti,ab
#28	((skin or vagina*) near/3 (prepar* or clean* or scrub* or swabb* or irrigat* or douch* or lavag* or wash or washes or washing)):ti,ab
#29	MeSH descriptor: [ANTI-INFECTIVE AGENTS, LOCAL] explode all trees
#30	(antiseptic* or anti-septic*):ti,ab
#31	(antiinfective* or anti-infective*):ti,ab
#32	(Acriflavine or Aminacrine or Bacitracin or “Benzalkonium Compound*” or Benzethonium or Bithionol or Camphor or Carbadox or Carbocysteine or Cetylpyridinium or Chlorhexidine or Clotrimazole or Dequalinium or Ethacridine or Ethanol or Furazolidone or “Gentian Violet” or Gramicidin or Hexachlorophene or Hexetidine or “Hydrogen Peroxide” or Iodine or Lysostaphin or Mafenide or “Mercuric Chloride” or Natamycin or Noxythiolin or Phenol or “Phenylethyl Alcohol” or “Povidone-Iodine” or Proflavine or “Silver Nitrate” or “Silver Protein*” or “Silver Sulfadiazine” or Sulfacetamide or “Tea Tree Oil” or Thymol or Triclosan or Tyrocidine or Tyrothricin or chloraprep or hibiclens or savlon):ti,ab
#33	MeSH descriptor: [IODOPHORS] this term only
#34	(iodophor* or Duraprep or betadine):ti,ab
#35	MeSH descriptor: [WATER] this term only
#36	MeSH descriptor: [STERILIZATION] this term only
#37	#35 and #36
#38	(steril* near/3 water*):ti,ab
#39	MeSH descriptor: [PERITONEAL LAVAGE] this term only
#40	((Intraabdom* or (Intra near/3 abdom*) or periton*) near/3 (irrigat* or lavag*)):ti,ab
#41	((saline or sodium chloride) near/3 (scrub* or swabb* or irrigat* or douch* or lavag* or wash or washes or washing)):ti,ab
#42	MeSH descriptor: [DIATHERMY] this term only
#43	diatherm*:ti,ab

#	Searches
#44	#4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #37 or #38 or #39 or #40 or #41 or #42 or #43
#45	MeSH descriptor: [INFECTION CONTROL] this term only and with qualifier(s): [methods - MT]
#46	#3 and #44
#47	#3 and #45
#48	#46 or #47

Health economics search strategies

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

Date of last search: 02/10/2018

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	exp CESAREAN SECTION/
23	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
24	or/22-23
25	SURGICAL DRAPES/
26	(drape or drapes or draping).ti,ab.
27	HAIR REMOVAL/
28	((remov$ or cut$) adj3 hair?).ti,ab.
29	shav$.ti,ab.
30	((no or avoid$ or stop$ or discourag$) adj5 (remov$ or cut$) adj3 hair?).ti,ab.
31	((no or avoid$ or stop$ or discourag$) adj5 shav$).ti,ab.

#	Searches
32	MASKS/
33	(face adj3 (mask? or shield? or visor?)).ti,ab.
34	facemask?.ti,ab.
35	exp BANDAGES/
36	dressing?.ti,ab.
37	(wound? adj3 cover$).ti,ab.
38	exp TISSUE ADHESIVES/
39	(tissue adj3 adhesive?).ti,ab.
40	(Bucrylate or Collodion or Fibrin Foam or Fibrin Tissue Adhesive or Karaya Gum or Cyanoacrylate? or Enbucrilate or dermabond).mp.
41	NEGATIVE-PRESSURE WOUND THERAPY/
42	(negative$ adj3 pressur$ adj3 therap$).ti,ab.
43	(vacuum? adj3 wound? adj3 clos$).ti,ab.
44	opsite.mp.
45	THERAPEUTIC IRRIGATION/
46	VAGINAL DOUCHING/
47	(therap$ adj3 (irrigat$ or lavag$)).ti,ab.
48	((alcohol$ or aqueous or water) adj3 (scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
49	((skin or vagina$) adj3 (prepar$ or clean$ or scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
50	exp ANTI-INFECTIVE AGENTS, LOCAL/
51	(antiseptic? or anti-septic?).ti,ab.
52	(antiinfective? or anti-infective?).ti,ab.
53	(Acriflavine or Aminacrine or Bacitracin or Benzalkonium Compound? or Benzethonium or Bithionol or Camphor or Carbadox or Carbocysteine or Cetylpyridinium or Chlorhexidine or Clotrimazole or Dequalinium or Ethacridine or Ethanol or Furazolidone or Gentian Violet or Gramicidin or Hexachlorophene or Hexetidineor Hydrogen Peroxide or Iodine or Lysostaphin or Mafenide or Mercuric Chloride or Natamycin or Noxythiolin or Phenol or Phenylethyl Alcohol or Povidone-Iodine or Proflavine or Silver Nitrate or Silver Protein? or Silver Sulfadiazine or Sulfacetamide or Tea Tree Oil or Thymol or Triclosan or Tyrocidine or Tyrothricin or chloraprep or hibiclens or savlon).mp.
54	IODOPHORS/
55	(iodophor? or Duraprep or betadine).mp.
56	*WATER/
57	WATER/ and STERILIZATION/
58	(steril$ adj3 water?).ti,ab.
59	PERITONEAL LAVAGE/
60	((Intraabdom$ or (Intra adj3 abdom$) or periton$) adj3 (irrigat$ or lavag$)).ti,ab.
61	((saline or sodium chloride) adj3 (scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
62	DIATHERMY/
63	diatherm$.ti,ab.
64	or/25-63
65	INFECTION CONTROL/mt [Methods]
66	24 and 64
67	24 and 65
68	or/66-67

#	Searches
69	limit 68 to english language
70	LETTER/
71	EDITORIAL/
72	NEWS/
73	exp HISTORICAL ARTICLE/
74	ANECDOTES AS TOPIC/
75	COMMENT/
76	CASE REPORT/
77	(letter or comment*).ti.
78	or/70-77
79	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
80	78 not 79
81	ANIMALS/ not HUMANS/
82	exp ANIMALS, LABORATORY/
83	exp ANIMAL EXPERIMENTATION/
84	exp MODELS, ANIMAL/
85	exp RODENTIA/
86	(rat or rats or mouse or mice).ti.
87	or/80-86
88	69 not 87
89	21 and 88

Databases: Embase; and Embase Classic

Date of last search: 02/10/2018

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	exp CESAREAN SECTION/
19	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
20	or/18-19

#	Searches
21	SURGICAL DRAPE/
22	(drape or drapes or draping).ti,ab.
23	exp HAIR REMOVAL/
24	((remov$ or cut$) adj3 hair?).ti,ab.
25	shav$.ti,ab.
26	((no or avoid$ or stop$ or discourag$) adj5 (remov$ or cut$) adj3 hair?).ti,ab.
27	((no or avoid$ or stop$ or discourag$) adj5 shav$).ti,ab.
28	MASK/
29	FACE MASK/
30	(face adj3 (mask? or shield? or visor?)).ti,ab.
31	facemask?.ti,ab.
32	exp WOUND DRESSING/
33	dressing?.ti,ab.
34	(wound? adj3 cover$).ti,ab.
35	exp TISSUE ADHESIVE/
36	(tissue adj3 adhesive?).ti,ab.
37	(Bucrylate or Collodion or Fibrin Foam or Fibrin Tissue Adhesive or Karaya Gum or Cyanoacrylate? or Enbucrilate or dermabond).mp.
38	VACUUM ASSISTED CLOSURE/
39	(negative$ adj3 pressur$ adj3 therap$).ti,ab.
40	(vacuum? adj3 wound? adj3 clos$).ti,ab.
41	opsite.mp.
42	LAVAGE/
43	VAGINAL LAVAGE/
44	SKIN DECONTAMINATION/
45	(therap$ adj3 (irrigat$ or lavag$)).ti,ab.
46	((alcohol$ or aqueous or water) adj3 (scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
47	((skin or vagina$) adj3 (prepar$ or clean$ or scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
48	exp TOPICAL ANTIINFECTIVE AGENT/
49	(antiseptic? or anti-septic?).ti,ab.
50	(antiinfective? or anti-infective?).ti,ab.
51	(Acriflavine or Aminacrine or Bacitracin or Benzalkonium Compound? or Benzethonium or Bithionol or Camphor or Carbadox or Carbocysteine or Cetylpyridinium or Chlorhexidine or Clotrimazole or Dequalinium or Ethacridine or Ethanol or Furazolidone or Gentian Violet or Gramicidin or Hexachlorophene or Hexetidineor Hydrogen Peroxide or Iodine or Lysostaphin or Mafenide or Mercuric Chloride or Natamycin or Noxythiolin or Phenol or Phenylethyl Alcohol or Povidone-Iodine or Proflavine or Silver Nitrate or Silver Protein? or Silver Sulfadiazine or Sulfacetamide or Tea Tree Oil or Thymol or Triclosan or Tyrocidine or Tyrothricin or chloraprep or hibiclens or savlon).mp.
52	IODOPHOR/
53	(iodophor? or Duraprep or betadine).mp.
54	*WATER/
55	STERILE WATER/
56	(steril$ adj3 water?).ti,ab.
57	PERITONEUM LAVAGE/
58	INTRAABDOMINAL IRRIGATION/

#	Searches
59	((Intraabdom$ or (Intra adj3 abdom$) or periton$) adj3 (irrigat$ or lavag$)).ti,ab.
60	((saline or sodium chloride) adj3 (scrub$ or swabb$ or irrigat$ or douch$ or lavag$ or wash or washes or washing)).ti,ab.
61	DIATHERMY/
62	diatherm$.ti,ab.
63	or/21-62
64	20 and 63
65	limit 64 to english language
66	letter.pt. or LETTER/
67	note.pt.
68	editorial.pt.
69	CASE REPORT/ or CASE STUDY/
70	(letter or comment*).ti.
71	or/66-70
72	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
73	71 not 72
74	ANIMAL/ not HUMAN/
75	NONHUMAN/
76	exp ANIMAL EXPERIMENT/
77	exp EXPERIMENTAL ANIMAL/
78	ANIMAL MODEL/
79	exp RODENT/
80	(rat or rats or mouse or mice).ti.
81	or/73-80
82	65 not 81
83	17 and 82

Database: Cochrane Central Register of Controlled Trials

Date of last search: 02/10/2018

#	Searches
#1	MeSH descriptor: [ECONOMICS] this term only
#2	MeSH descriptor: [VALUE OF LIFE] this term only
#3	MeSH descriptor: [COSTS AND COST ANALYSIS] explode all trees
#4	MeSH descriptor: [ECONOMICS, HOSPITAL] explode all trees
#5	MeSH descriptor: [ECONOMICS, MEDICAL] explode all trees
#6	MeSH descriptor: [RESOURCE ALLOCATION] explode all trees
#7	MeSH descriptor: [ECONOMICS, NURSING] this term only
#8	MeSH descriptor: [ECONOMICS, PHARMACEUTICAL] this term only
#9	MeSH descriptor: [FEES AND CHARGES] explode all trees
#10	MeSH descriptor: [BUDGETS] explode all trees
#11	budget*:ti,ab
#12	cost*:ti,ab
#13	(economic* or pharmaco?economic*):ti,ab
#14	(price* or pricing*):ti,ab
#15	(financ* or fee or fees or expenditure* or saving*):ti,ab

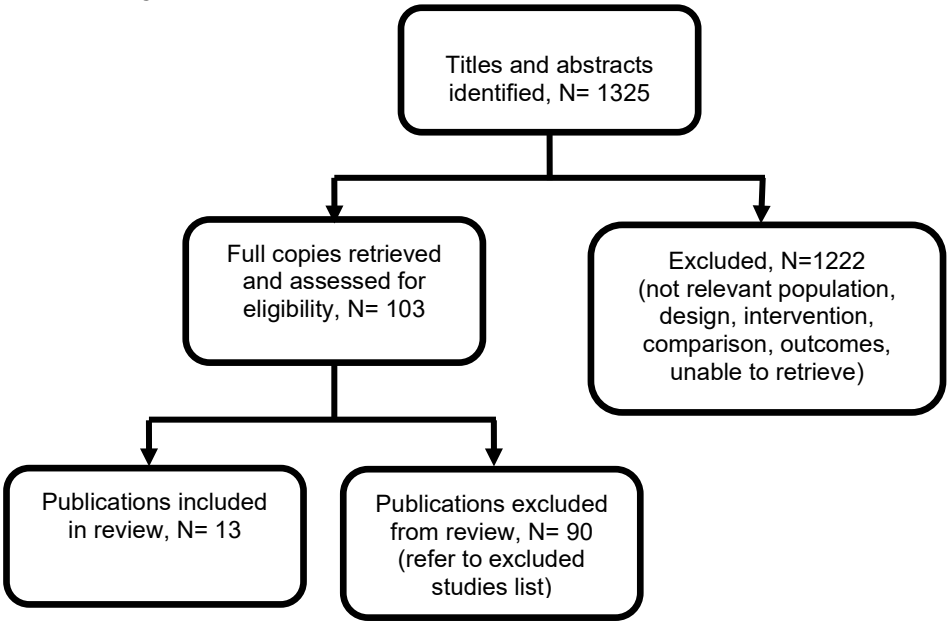
#	Searches
#16	(value near/2 (money or monetary)):ti,ab
#17	resourc* allocat*:ti,ab
#18	(fund or funds or funding* or funded):ti,ab
#19	(ration or rations or rationing* or rationed) .ti,ab.
#20	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21	MeSH descriptor: [CESAREAN SECTION] explode all trees
#22	(cesarean* or caesarean* or “c section*” or csection* or (deliver* near/3 abdom*)):ti,ab
#23	#21 or #22
#24	MeSH descriptor: [SURGICAL DRAPES] this term only
#25	(drape or drapes or draping):ti,ab
#26	MeSH descriptor: [HAIR REMOVAL] this term only
#27	((remov* or cut*) near/3 hair*):ti,ab
#28	shav*:ti,ab
#29	((no or avoid* or stop* or discourag*) near/5 (remov* or cut*) near/3 hair*):ti,ab
#30	((no or avoid* or stop* or discourag*) near/5 shav*):ti,ab
#31	MeSH descriptor: [MASKS] this term only
#32	(face near/3 (mask* or shield* or visor*)):ti,ab
#33	facemask*:ti,ab
#34	MeSH descriptor: [BANDAGES] explode all trees
#35	dressing*:ti,ab
#36	(wound* near/3 cover*):ti,ab
#37	MeSH descriptor: [TISSUE ADHESIVES] explode all trees
#38	(tissue near/3 adhesive*):ti,ab
#39	(Bucrylate or Collodion or Fibrin Foam or Fibrin Tissue Adhesive or Karaya Gum or Cyanoacrylate* or Enbucrilate or dermabond).ti,ab.
#40	MeSH descriptor: [NEGATIVE-PRESSURE WOUND THERAPY] this term only
#41	(negative* near/3 pressur* near/3 therap*):ti,ab
#42	(vacuum* near/3 wound* near/3 clos*):ti,ab
#43	opsite:ti,ab
#44	MeSH descriptor: [THERAPEUTIC IRRIGATION] this term only
#45	MeSH descriptor: [VAGINAL DOUCHING] this term only
#46	(therap* near/3 (irrigat* or lavag*)):ti,ab
#47	((alcohol* or aqueous or water) near/3 (scrub* or swabb* or irrigat* or douch* or lavag* or wash or washes or washing)):ti,ab
#48	((skin or vagina*) near/3 (prepar* or clean* or scrub* or swabb* or irrigat* or douch* or lavag* or wash or washes or washing)):ti,ab
#49	MeSH descriptor: [ANTI-INFECTIVE AGENTS, LOCAL] explode all trees
#50	(antiseptic* or anti-septic*):ti,ab
#51	(antiinfective* or anti-infective*):ti,ab
#52	(Acriflavine or Aminacrine or Bacitracin or “Benzalkonium Compound*” or Benzethonium or Bithionol or Camphor or Carbadox or Carbocysteine or Cetylpyridinium or Chlorhexidine or Clotrimazole or Dequalinium or Ethacridine or Ethanol or Furazolidone or “Gentian Violet” or Gramicidin or Hexachlorophene or Hexetidine or “Hydrogen Peroxide” or Iodine or Lysostaphin or Mafenide or “Mercuric Chloride” or Natamycin or Noxythiolin or Phenol or “Phenylethyl Alcohol” or “Povidone-Iodine” or Proflavine or “Silver Nitrate” or “Silver Protein*” or “Silver Sulfadiazine” or Sulfacetamide or “Tea Tree Oil” or Thymol or Triclosan or Tyrocidine or Tyrothricin or chloraprep or hibiclens or savlon):ti,ab

#	Searches
#53	MeSH descriptor: [IODOPHORS] this term only
#54	(iodophor* or Duraprep or betadine):ti,ab
#55	MeSH descriptor: [WATER] this term only
#56	MeSH descriptor: [STERILIZATION] this term only
#57	#55 and #56
#58	(steril* near/3 water*):ti,ab
#59	MeSH descriptor: [PERITONEAL LAVAGE] this term only
#60	((Intraabdom* or (Intra near/3 abdom*) or periton*) near/3 (irrigat* or lavag*)):ti,ab
#61	((saline or sodium chloride) near/3 (scrub* or swabb* or irrigat* or douch* or lavag* or wash or washes or washing)):ti,ab
#62	MeSH descriptor: [DIATHERMY] this term only
#63	diatherm*:ti,ab
#64	#24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #57 or #58 or #59 or #60 or #61 or #62 or #63
#65	MeSH descriptor: [INFECTION CONTROL] this term only and with qualifier(s): [methods - MT]
#66	#23 and #64
#67	#23 and #65
#68	#66 or #67
#69	#20 and #68

Appendix C – Clinical evidence study selection

Clinical study selection for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

Figure 1: Study selection flow chart



Appendix D – Clinical evidence tables

Clinical evidence tables for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

Table 4: Clinical evidence tables for methods to reduce infectious morbidity

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Chaboyer, Wendy, Anderson, Vinah, Webster, Joan, Sneddon, Anne, Thalib, Lukman, Gillespie, Brigid M., Negative Pressure Wound Therapy on Surgical Site Infections in Women Undergoing Elective Caesarean Sections: A Pilot RCT, Healthcare (Basel, Switzerland), 2, 417-28, 2014 **Ref Id** 910644 **Country/ies where the study was carried out** Australia **Study type** RCT	**Sample size** N=87 (n=44 randomised to NPWT and n=43 randomised to standard dressing) **Characteristics** <table><tr><td></td><td>NPWT (N=44)</td><td>Standard dressing (N=43)</td></tr><tr><td>Age, mean (SD)*</td><td>30.6 (5.5)</td><td>30.7 (5)</td></tr><tr><td>BMI, mean (SD)*</td><td>35.7 (4.5)</td><td>36.8 (5.8)</td></tr></table>*Assumed typo in paper, which reported median (IQR) **Inclusion criteria** Pregnant women who provided written informed consent; BMI ≥ 30kg/m2 at the first antenatal visit; booked for elective CS surgery (before the start of labour) **Exclusion criteria** Previous participation in the trial; non-English speaking without interpreter; pre-existing infection	**Interventions** All women were administered prophylactic antibiotics, although there were differences in timing (what the differences were has not been reported). NPWT group had a PICO applied at the completion of skin closure. A gauze based dressing was secured with fixation strips and continuous negative pressure of 80mmHg was administered via a tube. Standard dressing group had a Comfeel Plus dressing applied at the completion of skin closure. Both dressings were removed after	**Details** Participants were randomised and stratified by hospital in a 1:1 ratio and using a computer generated list. Allocation sequence was done using a centralised web-based randomisation program. Blinding was not feasible due to the nature of the intervention. An external contractor, blinded to treatment allocation, assessed the outcomes. Unclear whether a sample size calculation was performed. Follow-up: 28 days	**Results** Surgical site infection NPWT: 10/44 Standard dressing:12/43 Adverse skin events (bruising) NPWT: 1/44 Standard dressing:4/43 Readmission into hospital NPWT: 1/44 Standard dressing:1/43	**Limitations** Methodological limitations assessed using the Cochrane collaboration's tool for assessing risk of bias **Random sequence generation:** low risk (participants were randomised and stratified by hospital in a 1:1 ratio and using a computer generated list) **Allocation concealment:** low risk (randomisation was concealed using a centralised web-based randomisation program) Blinding of participants and personnel: high risk (not blinded) **Blinding of outcome assessment:** low risk (outcome assessors were blinded to treatment allocation) **Blinding (performance bias and detection bias):**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To assess whether negative pressure wound therapy (NPWT) is more effective than standard dressing at reducing surgical site infections in women with obesity undergoing caesarean section (CS) **Study dates** July 2012 to April 2014 **Source of funding** Office of Health and Medical Research and NHMRC Centre of Research Excellence in Nursing Interventions for Hospitalised Patients, Griffith University		4 days, unless the dressing became soiled or dislodged, in which case it was replaced with one of the same type.			moderate risk (see details above) **Incomplete outcome data:** low risk (there was a low rate of drop-outs and reasons for these were provided) **Selective reporting:** low risk (outcomes reported match with those in the study protocol https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=361982) Other sources of bias: low risk
Full citation Eke, Ahizechukwu Chigoziem, Shukr, Ghadear	**Sample size** K=3 RCTs (N=862) **Characteristics** Harrigil 2003	**Interventions** In all trials, all women were administered	**Details** A literature search was done in the Cochrane	**Results** Wound infection Harrigil 2003 Intra-abdominal irrigation:1/97	**Limitations** ROB assessed using AMSTAR checklist Total score: 13/16

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr>
<td>Hussein, Chaalan, Tina Taissir, Nashif, Sereen Khaled, Eleje, George Uchenna, Intra-abdominal saline irrigation at cesarean section: a systematic review and meta-analysis, The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 29, 1588-94, 2016

Ref Id
910726

Country/ies where the study was carried out
US and Turkey

Study type</td>
<td>
<table>
<tr><td></td><td>Intra-abdominal irrigation (N=97)</td><td>No irrigation (N=99)</td></tr>
<tr><td>Country</td><td colspan="2">US</td></tr>
<tr><td>Age, mean</td><td>28</td><td>27</td></tr>
<tr><td>BMI, mean</td><td>32.3</td><td>35.2</td></tr>
<tr><td>GA, mean</td><td>39.1</td><td>38.2</td></tr>
</table>
Viney 2012
<table>
<tr><td></td><td>Intra-abdominal irrigation (N=126)</td><td>No irrigation (N=110)</td></tr>
<tr><td>Country</td><td colspan="2">US</td></tr>
<tr><td>Age, mean</td><td>27</td><td>27</td></tr>
<tr><td>BMI, mean</td><td>35.6</td><td>35.1</td></tr>
<tr><td>GA, mean</td><td>38.5</td><td>37.9</td></tr>
</table>
Temizcan 2015
<table>
<tr><td></td><td>Intra-abdominal irrigation (N=215)</td><td>No irrigation (N=215)</td></tr>
<tr><td>Country</td><td colspan="2">Turkey</td></tr>
<tr><td>Age, mean</td><td>28</td><td>28</td></tr>
<tr><td>BMI, mean</td><td>28.5</td><td>28.2</td></tr>
<tr><td>GA, mean</td><td>38.5</td><td>38.4</td></tr>
</table>
Inclusion criteria
RCTs in which saline irrigation was used intra-operatively as compared to no treatment
</td>
<td>antibiotic prophylaxis.
Intra-abdominal irrigation group received 500 to 1000 mls of warm normal saline solution instilled into the abdominal cavity after the uterus was closed.
No irrigation group received no intervention after the cavity was closed.
No information was provided regarding sample size calculations or follow-up length.</td>
<td>Central Register of Controlled Trials, PubMed, African Journals Online (AJOL), Embase, Medline, LILACS, CINAHL, Web of Science, and Google Scholar. Authors were contacted to retrieve additional data regarding methods and/or outcomes. Two authors assessed inclusion and exclusion of the studies independently. Follow-up length was not reported.</td>
<td>No irrigation: 2/99

Temizcan 2015
Intra-abdominal irrigation: 1/215
No irrigation: 2/215

<u>Endometritis</u>
Harrigil 2003
Intra-abdominal irrigation: 9/97
No irrigation: 7/99

Viney 2012
Intra-abdominal irrigation: 8/110
No irrigation: 12/126

Temizcan 2015
Intra-abdominal irrigation:26/215
No irrigation: 28/215</td>
<td><u>The following items were not met by the study authors:</u>
• The study did not contain a specific statement that the review methods were established prior to the review
• Unclear whether data extraction was performed in duplicate
• Sources of funding for the included studies were not reported

<u>Limitations for each of the included studies assessed with the Cochrane Risk of Bias Tool</u>

<u>Harrigil 2003*</u>
Random sequence generation: unclear risk
Allocation concealment: unclear risk
Blinding of participants and personnel: high risk
Blinding of outcome assessment: low risk
Incomplete outcome data: low risk
Selective reporting: unclear risk
Other bias: low risk

<u>Viney 2012*</u>
Random sequence generation: low risk
Allocation concealment: low risk
Blinding of participants and personnel: high risk</td>
</tr>
</table>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Systematic review **Aim of the study** To assess and review the evidence about intra-abdominal saline irrigation at caesarean section (CS) **Study dates** Last search was carried out in April 2015 **Source of funding** Not reported	**Exclusion criteria** RCTs that used antibiotics or colloid solutions intra-operatively for irrigation; studies that compared intra-abdominal antibiotic irrigation with saline irrigation; quasi-randomised trials; abstracts in which no additional methodological data could be retrieved				**Blinding of outcome assessment:** high risk Incomplete outcome data: low risk **Selective reporting:** low risk Other bias: low risk <u>Temizkan 2015*</u> **Random sequence generation**: low risk **Allocation concealment:** low risk **Blinding of participants and personnel:** high risk **Blinding of outcome assessment:** low risk **Incomplete outcome data:** low risk **Selective reporting:** low risk Other bias: low risk **Other information** The data presented in this evidence table has been adapted from the original systematic review. We present the data that is relevant to the aims of this review. Individual studies were retrieved for accuracy and to check if other outcomes of interest were reported. Data extracted by the review team from the original study has been marked with an *.
Full citation Gunatilake, Ravindu P.,	**Sample size** N=92 randomised (n=46 randomised to NPWT and n=46 randomised to standard dressing);	**Interventions** Women received prophylactic	**Details** Women were randomised in a	**Results** <u>Surgical site infection</u> NPWT: 1/39	**Limitations** <u>Methodological limitations assessed using the</u>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Swamy, Geeta K., Brancazio, Leo R., Smrtka, Michael P., Thompson, Jennifer L., Gilner, Jennifer B., Gray, Beverly A., Heine, Robert Phillips, Closed-Incision Negative-Pressure Therapy in Obese Patients Undergoing Cesarean Delivery: A Randomized Controlled Trial, AJP reports, 7, e151-e157, 2017 **Ref Id** 910797 **Country/ies where the study was carried out** US **Study type** RCT **Aim of the study** To assess the effectiveness of negative pressure wound therapy (NPWT) compared to standard	N=82 included after drop-outs (n=39 in NPWT group and n=43 in standard dressing group) **Characteristics** NPWT (N=46) / Standard dressing (N=46) Age, mean (SD): 30.4 (5.7) / 29.7 (5) Gestational age, mean (SD): 38.1 (2) / 37.9 (2) Baseline BMI, mean (SD): 46.3 (7.3) / 46.8 (5.6) **Inclusion criteria** Pregnant women ≥ 18 years; able to provide informed consent; BMI ≥ 35 kg/m^2 as determined during the screening period. **Exclusion criteria** Women with a bacterial or fungal infection; chorioamnionitis; critical illness; or at high risk for anaesthesia.	antibiotics within 30 minutes before the incision (cefazolin 2 to 4 grams based on body weight). NPWT group had a PREVENA "peel-and-place" multilayer dressing over the incision. A gauze based dressing was secured with fixation strips and continuous negative pressure of 125mmHg was administered via a tube. Standard dressing group had Steri-Strips, sterile gauze, and Tegaderm applied over the incision.	1:1 fashion. Randomisation was concealed with sequentially numbered opaque envelopes. Blinding was not feasible due the nature of the intervention, however outcome assessors were blinded to treatment allocation and used a standardised checklist to assess the outcomes. Sample size calculations were conducted and, after an interim analysis, it was established that a sample size of 96 would be needed to detect differences in surgical site infections in the NPWT group and standard dressing group with 80% power.	Standard dressing: 4/43 Women's experience - reported pain at rest (post operatively [days 1 to 7], Wong-Baker Faces Scale) NPWT:20/46 Standard dressing:39/43	Cochrane collaboration's tool for assessing risk of bias **Random sequence generation:** unclear risk (randomisation method has not been reported) **Allocation concealment:** low risk (randomisation was concealed with sequentially numbered opaque envelopes) **Blinding of participants and personnel:** high risk (not blinded) **Blinding of outcome assessment:** low risk (outcome assessors were masked to treatment allocation) **Blinding (performance bias and detection bias):** moderate risk (see details above) **Incomplete outcome data:** low risk (there was a low rate of drop-outs and reasons for these were provided) **Selective reporting:** low risk (outcomes reported match with those in the study protocol, although the study protocol reported more adverse events https://clinicaltrials.gov/ct2/s

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td>dressing in women undergoing caesarean section (CS)

Study dates
2012 to 2014

Source of funding
KCI USA, Inc. (Acelity)</td><td></td><td></td><td>Follow-up: 42 ± 10 days.</td><td></td><td>how/results/NCT01450631?view=results)
Other sources of bias: high risk (trial received funding from the Prevena manufacturer, Acelity)</td></tr>
<tr><td>Full citation
Haas, D. M., Morgan, S., Contreras, K., Enders, S., Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections, Cochrane Database of Systematic Reviews, 2018, CD007892, 2018

Ref Id
910804

Country/ies where the study was carried out
Saudi Arabia, Pakistan, Iran, Turkey and USA

Study type</td><td>Sample size
K= 11 RCTs (N=3403)

Characteristics
Ahmed 2017*<table><tr><td></td><td>Vaginal preparation (N=109)</td><td>No vaginal preparation (N=109)</td></tr><tr><td>Age, mean years (SD)</td><td>28.8 (9.1)</td><td>29.2 (7.9)</td></tr><tr><td>BMI, mean (SD)</td><td>29.57 (2.9)</td><td>30.16 (3.5)</td></tr><tr><td>GA, mean weeks (SD)</td><td>38.1 (1.3)</td><td>38.4 (1.8)</td></tr><tr><td>Intact membranes at time of caesarean, N (%)</td><td>109 (100)</td><td>109 (100)</td></tr></table>Asad 2017*<table><tr><td></td><td>Vaginal preparation (N=217)</td><td>No vaginal preparation (N=217)</td></tr></table></td><td>Interventions
In all trials, all women were administered antibiotic prophylaxis.
The preparation used for vaginal cleansing varied across studies, and it was spread as follows:
Iodophor-based aqueous scrub : Asad 2017, Asghania 2011, Goymen 2017, Guzman 2002, Haas 2010, Memon 2011, Reid 2011, Starr 2005, and Yildirim 2012
Chlorhexidine-based aqueous scrub: Ahmed 2017, Rouse 1997
Most studies compared it with no vaginal cleansing,</td><td>Details
A literature search was done in the Cochrane Pregnancy and Childbirth's Trials Register, the WHO International Clinical Trials Registry Platform and reference lists were searched.
At least 3 authors reviewed eligibility of the studies, and 2 authors extracted study characteristics, quality assessments and data for eligible studies.</td><td>Results
Wound infection
Asad 2017
Iodophor-based aqueous scrub: 3/217
No vaginal preparation:8/217

Asghania 2011
Iodophor-based aqueous scrub: 10/284
No vaginal preparation: 9/284

Guzman 2002
Iodophor-based aqueous scrub: 7/80
Saline vaginal wash: 4/80

Guzman 2002 - results by ruptured vs intact membranes
Iodophor-based aqueous scrub (ruptured membranes): 6/36
Saline vaginal wash (ruptured membranes): 1/36
Iodophor-based aqueous scrub (intact membranes): 1/44</td><td>Limitations
Quality of the Cochrane Systematic review assessed using AMSTAR checklist. Total score:16/16

Limitations for each of the included studies assessed with the Cochrane Risk of Bias Tool
Ahmed 2017
Random sequence generation: low risk
Allocation concealment: unclear risk
Blinding of participants and personnel: high risk
Blinding of outcome assessment: low risk
Incomplete outcome data: low risk
Selective reporting: low risk
Other bias: low risk

Asad 2017
Random sequence generation: unclear risk
Allocation concealment: unclear risk</td></tr>
</table>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Cochrane systematic review **Aim of the study** To assess whether cleansing the vagina before caesarean section (CS) reduces the risk of maternal infections. **Study dates** Last search was carried out in July 2017 **Source of funding** Indiana University School of Medicine	Age, mean years (SD) 28.4 (4.6) 27.6 (5.9) GA, mean weeks (SD) 38.6 (1.2) 38 (1.6) Asghania 2011* Vaginal preparation (N=284) / No vaginal preparation (N=284) Age, mean years (SD) 26.8 (5.2) 26.2 (5.5) GA <37 weeks, N (%) 106 (37) 76 (26.8) Goymen 2017* Povidone - iodine vaginal preparation (N=41) / No vaginal preparation (N=40) Age, mean years (SD) 29 (5) 27 (5) GA, mean weeks (SD) 38 (1.1) 38 (0.3) Guzman 2002* Vaginal preparation (N=80) / Saline vaginal wash (N=80) Age, mean years (SD) 25.8 (6.2) 25.0 (6.9)	with the exception of comparisons to: Saline vaginal wash: Guzman 2002 Sterile water: Rouse 1997		Saline vaginal wash (intact membranes): 3/44 Haas 2010 Iodophor-based aqueous scrub: 7/155 No vaginal preparation: 10/145 Haas 2010 - *results by ruptured vs intact membranes* Iodophor-based aqueous scrub (ruptured membranes): 2/34 No vaginal preparation (ruptured membranes):5/42 Iodophor-based aqueous scrub (intact membranes): 5/121 No vaginal preparation (intact membranes): 5/103 Memon 2011 Iodophor-based aqueous scrub: 1/100 No vaginal preparation: 3/100 Starr 2005 Iodophor-based aqueous scrub: 1/142 No vaginal preparation: 2/166 Yildirim 2012 Iodophor-based aqueous scrub: 6/334 No vaginal preparation: 9/335	**Blinding of participants and personnel:** high risk **Blinding of outcome assessment:** unclear risk **Incomplete outcome data:** unclear risk **Selective reporting: low risk** **Other bias:** low risk Asghania 2011 **Random sequence generation:** high risk **Allocation concealment:** high risk **Blinding of participants and personnel:** low risk **Blinding of outcome assessment:** low risk **Incomplete outcome data:** low risk **Selective reporting:** low risk **Other bias:** high risk Goymen 2017 **Random sequence generation**: low risk **Allocation concealment:** unclear risk **Blinding of participants and personnel:** high risk **Blinding of outcome assessment:** unclear risk **Incomplete outcome data:** low risk **Selective reporting:** low risk **Other bias:** low risk Guzman 2002 **Random sequence generation:** unclear risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments

Intact membranes at time of caesarean, N (%)	44 (55)	44 (55)

Haas 2010*

	Vaginal preparation (N=155)	No vaginal preparation (N=145)
Age, mean years (SD)	26.6 (5.7)	26.8 (5.9)
BMI, mean (SD)	33.3 (6)	33.9 (7.7)
GA, mean weeks (SD)	38.2 (2.7)	38.5 (1.6)
Cervix was dilated at time of caesarean, N (%)	63 (40.6)	67 (46.2)
Intact membranes at time of caesarean, N (%)	121 (78.06)	103(71.03)

Memon 2011*

	Vaginal preparation (N=100)	No vaginal preparation (N=100)
Age, mean years (SD)	27.2 (4.96)	27.09 (4.55)
GA, mean (SD)	36.65 (2.05)	36.86 (2.46)
Cervical dilation at time of CS, N (%)	26 (26)	40 (40)

Yildirim 2012 - *results by ruptured vs intact membranes*
Iodophor-based aqueous scrub(ruptured membranes): 0/68
No vaginal preparation (ruptured membranes): 1/56
Iodophor-based aqueous scrub (intact membranes): 6/266
No vaginal preparation (intact membranes): 8/279

Ahmed 2017 - all women presented with intact membranes
Chlorhexidine-based aqueous scrub: 4/102
No vaginal preparation: 7/98

Endometritis
Asad 2017
Iodophor-based aqueous scrub: 3/217
No vaginal preparation: 19/217

Asghania 2011
Iodophor-based aqueous scrub: 1/284
No vaginal preparation: 7/284

Guzman 2002
Iodophor-based aqueous scrub: 2/80
Saline vaginal wash: 13/80
Guzman 2002 - *results by ruptured vs intact membranes*

Allocation concealment: unclear risk
Blinding of participants and personnel: low risk
Blinding of outcome assessment: low risk
Incomplete outcome data: low risk
Selective reporting: low risk
Other bias: low risk

Haas 2010
Random sequence generation: low risk
Allocation concealment: low risk
Blinding of participants and personnel: low risk
Blinding of outcome assessment: low risk
Blinding (performance bias and detection bias): low risk
Incomplete outcome data: low risk
Selective reporting: low risk
Other bias: unclear risk

Memon 2011
Random sequence generation: unclear risk
Allocation concealment: unclear risk
Blinding of participants and personnel: unclear risk
Blinding of outcome assessment: low risk
Incomplete outcome data: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Reid 2001* <table><tr><td></td><td>Vaginal preparation (N=217)</td><td>No vaginal preparation (N=213)</td></tr><tr><td>Age, mean years (SD)</td><td>26 (26)</td><td>27.5 (6.3)</td></tr></table> Rouse 1997* <table><tr><td></td><td>Vaginal preparation (N=508)</td><td>Sterile water (N=516)</td></tr><tr><td>Age, mean years (SD)</td><td>27.6 (6)</td><td>27.5 (6.3)</td></tr><tr><td>GA, mean (SD)</td><td>39 (2)</td><td>39 (2)</td></tr></table> (n.b. majority of participants had vaginal delivery. Data included represents those who underwent caesarean section only.) Starr 2005* <table><tr><td></td><td>Vaginal preparation (N=142)</td><td>No vaginal preparation (N=166)</td></tr><tr><td>Age ≥ 20 years, N (%)</td><td>126 (88.7)</td><td>147 (88.6)</td></tr><tr><td>GA <37 weeks, N (%)</td><td>16 (11.3)</td><td>30 (18.1)</td></tr></table> Yildirim 2012* <table><tr><td></td><td>Vaginal preparation (N=334)</td><td>No vaginal preparation (N=335)</td></tr></table>			Iodophor-based aqueous scrub (ruptured membranes): 1/36 Saline vaginal wash (ruptured membranes): 10/36 Iodophor-based aqueous scrub (intact membranes): 1/44 Saline vaginal wash (intact membranes): 3/44 Haas 2010 Iodophor-based aqueous scrub: 0/155 No vaginal preparation: 4/145 Haas 2010 - *results by ruptured vs intact membranes* Iodophor-based aqueous scrub (ruptured membranes): 0/34 No vaginal preparation (ruptured membranes): 2/42 Iodophor-based aqueous scrub (intact membranes): 0/121 No vaginal preparation (intact membranes): 2/103 Memon 2011 Iodophor-based aqueous scrub: 1/100 No vaginal preparation: 7/100 Reid 2001 Iodophor-based aqueous scrub: 19/217 No vaginal preparation: 16/213	**Selective reporting:** low risk **Other bias:** low risk <u>Reid 2001</u> **Random sequence generation:** low risk **Allocation concealment**: low risk **Blinding of participants and personnel:** unclear risk **Blinding of outcome assessment:** low risk **Incomplete outcome data:** low risk **Selective reporting:** high risk **Other bias:** low risk <u>Rouse 1997</u> **Random sequence generation:** low risk **Allocation concealment:** low risk **Blinding of participants and personnel:** low risk **Blinding of outcome assessment**: low risk **Incomplete outcome data:** low risk **Selective reporting: low** risk **Other bias**: low risk <u>Starr 2005</u> **Random sequence generation:** low risk **Allocation concealment:** low risk **Blinding of participants and personnel:** low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	<table><tr><td>Age, mean years (SD)</td><td>28.8 (5.4)</td><td>29 (5.4)</td></tr><tr><td>GA, mean weeks (SD)</td><td>39.05 (1.82)</td><td>38.9 (1.54)</td></tr><tr><td>Intact membranes at time of caesarean, N (%)</td><td>279 (83.2)</td><td>266 (67.46)</td></tr></table> *Indicates data extracted by the review team from the original study **Inclusion criteria** Randomised and quasi-randomised controlled trials including pregnant women who were about to receive a CS. Any type of vaginal preparation ≤ 1 hour pre-procedure were considered with any type of antiseptic solution compared to placebo or standard care. **Exclusion criteria** Randomised trials using vaginal cleansing during birth; trials not using prophylactic antibiotics; cross-over trials.			Starr 2005 Iodophor-based aqueous scrub: 10/142 No vaginal preparation: 24/166 Yildirim 2012 Iodophor-based aqueous scrub: 23/334 No vaginal preparation: 39/335 Yildirim 2012 - *results by ruptured vs intact membranes* Iodophor-based aqueous scrub (ruptured membranes): 5/68 No vaginal preparation (ruptured membranes): 12/56 Iodophor-based aqueous scrub(intact membranes):18/266 No vaginal preparation (intact membranes): 27/279 Ahmed 2017 - all women presented with intact membranes Chlorhexidine-based aqueous scrub: 3/102 No vaginal preparation: 13/98 Rouse 1997 Chlorhexidine-based aqueous scrub: 0/6 Sterile water: 0/8	**Blinding of outcome assessment:** low risk **Incomplete outcome data:** unclear risk **Selective reporting:** low risk **Other bias:** low risk Yildirim 2012 **Random sequence generation:** low risk **Allocation concealment:** low risk **Blinding of participants and personnel:** high risk **Blinding of outcome assessment:** high risk **Incomplete outcome data:** low risk **Selective reporting:** low risk **Other bias:** low risk **Other information** The data presented in this evidence table has been adapted from the Cochrane systematic review. We present the data that is relevant to the aims of this review. Individual studies were retrieved for accuracy and to check if other outcomes of interest were reported. Data extracted by the review team from the original study has been marked with an *.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Hussamy, D. J., Wortman, A. C., McIntire, D. D., Leveno, K. J., Casey, B. M., Roberts, S. W., Closed Incision Negative Pressure Therapy in Morbidly Obese Women Undergoing Cesarean Delivery: a Randomized Controlled Trial, Obstetrics and gynecology, 134, 781-789, 2019 **Ref ID** 1291275 **Country/ies where the study was carried out** US **Study type** RCT **Aim of the study** To evaluate the efficacy of incisional NPWT in preventing post-operative wound morbidity in women with class III obesity	**Sample size** N=441, (n=229 NPWT, n=219 standard wound dressing) **Characteristics** NPWT (N=229) / Standard dressing (N=219) Age, mean (SD): 29.1 (6.1) / 30.3 (6.1) BMI at delivery (SD): 46.6 (6.0) / 45.8 (5.8) Rupture of membranes (prelabour - prolonged premature rupture of membranes), N (%): 33 (7.6) / 30 (6.8) Scheduled CS, N (%): 72 (32) / 72 (33) Urgent CS, N (%): 141 (64) / 138 (63) **Inclusion criteria** BMI >40, having caesarean **Exclusion criteria** Anticoagulation therapy, HIV infection, silver or acrylic allergy	**Interventions** All women received prophylactic 2g of cefazolin within 60 minutes of skin incision, pubic hair shaving, skin preparation of 2% chlorhexidine, 70% isopropyl alcohol solution. Subcutaneous tissue was closed with 3-0 plain gut if depth was greater than 2 cm. Skin was approximate with subcuticular 4-0 Vicryl or staples. Standard dressing included reinforced adhesive skin closures as well as a gauge adhesive bandage. Dressings removed usually on postoperative day 1. The NPWT arm received the Prevena system (single use, impregnated with ionic silver, 125 mmHg continuous suction pressure) which was placed according to its protocol. Dressings	**Details** Randomised using block randomisation stratified by presence of labour, computer generated sequence. Allocation concealed but no blinding due to the nature of the interventions. Sample size calculated to have 80% power to detect 50% difference in rate of postoperative wound morbidity. Follow-up included 2 week postpartum appointment, telephone contact 30-60 days after delivery	**Results** Surgical site infection NPWT: 21/222 (20 superficial, 1 organ space) Standard dressing: 25 (25 superficial) Need for antibiotics NPWT: 33/222 Standard dressing: 39/219 Adverse skin events NPWT: 63/222 (skin maceration or bullae Standard dressing: 0/219 Patient satisfaction ("I would use this dressing again", 30-60 days post-operation) NPWT: 187/210 Standard dressing: 185/201 Readmission to hospital NPWT: 12/222 Standard dressing: 9/219	**Limitations** Methodological limitations assessed using the Cochrane collaboration's tool for assessing risk of bias **Random sequence generation:** low risk (participants randomised using a computer system) **Allocation concealment:** low risk (allocation was done concealed) **Blinding of participants and personnel:** high risk (not blinded) **Blinding of outcome assessment:** high risk (not blinded) **Blinding (performance bias and detection bias):** high risk (see details above) **Incomplete outcome data:** low risk (analyses for main outcome were ITT; there was a loss of follow up for secondary outcomes, but this is <2% and there were not significant differences between treatment arms) **Selective reporting:** low risk (outcomes reported match with those in the study protocol https://trialbulletin.com/lib/entry/ct-02289157) **Other sources of bias:** low risk

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td>undergoing caesarean

Study dates
January 2015 to July 2016

Source of funding
Study devices provided by manufacturer but with no other input</td><td></td><td>usually removed on day of discharge</td><td></td><td></td><td></td></tr>
<tr><td>Full citation
Hyldig, N., Vinter, C. A., Kruse, M., Mogensen, O., Bille, C., Sorensen, J. A., Lamont, R. F., Wu, C., Heidemann, L. N., Ibsen, M. H., Laursen, J. B., Ovesen, P. G., Rorbye, C., Tanvig, M., Joergensen, J. S., Prophylactic incisional negative pressure wound therapy reduces the risk of surgical site infection after caesarean section in obese women: a pragmatic</td><td>Sample size
N=876 (n=432 randomised to NPWT and n=444 randomised to standard dressing)

Characteristics
<table><tr><td></td><td>NPWT (N=432)</td><td>Standard dressing (N=444)</td></tr><tr><td>Age, mean (SD)</td><td>32 (5)</td><td>32 (5)</td></tr><tr><td>Prepregnancy BMI, median (IQR)</td><td>34.7 (31.5-38.2)</td><td>34.2 (31.6-38.1)</td></tr><tr><td>Rupture of membranes (prelabour - prolonged premature rupture of membranes), N (%)</td><td>33 (7.6)</td><td>30 (6.8)</td></tr><tr><td>Rupture of membranes (during labour), N (%)</td><td>22 (5.1)</td><td>34 (7.7)</td></tr></table></td><td>Interventions
All women were administered a single dose of cefuroxime IV (1.5 or 3.0 g according to standard procedures) during surgery.
NPWT group had a PICO applied immediately after skin closure. The dressing was removed after 5 days following surgery.
Standard dressing group had a standard wound dressing applied immediately after skin closure. The dressing was removed after at least 24 hours following surgery.</td><td>Details
Women were randomised using a web-based randomisation programme with a 1:1 allocation ratio and random block sizes of 4 to 6, stratified by centre and type of caesarean section. The allocation sequence was done by a third party. Blinding was not feasible due the nature of the intervention.
Sample size calculations were conducted.
It was estimated</td><td>Results
Surgical site infection
NPWT: 20/432
Standard dressing: 41/444

Endometritis
NPWT: 8/432
Standard dressing: 8/444

Women's experience: self-rated health status (EQ-VAS) [better represented by higher values]
NPWT, mean (95% CI): 83 (82-84)
Standard dressing, mean (95% CI): 82 (80-84)</td><td>Limitations
Methodological limitations assessed using the Cochrane collaboration's tool for assessing risk of bias
Random sequence generation: low risk (participants randomised using a web-based randomisation programme with a 1:1 allocation ratio and random block sizes of 4 to 6, stratified by centre and type of caesarean section)
Allocation concealment: low risk (allocation sequence generation was done by a third party)
Blinding of participants and personnel: high risk (not blinded)
Blinding of outcome assessment: high risk (not blinded)
Blinding (performance bias and detection bias):</td></tr>
</table>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
randomised clinical trial, BJOG : an international journal of obstetrics and gynaecology, 2018 **Ref Id** 910850 **Country/ies where the study was carried out** Denmark **Study type** RCT **Aim of the study** To assess whether negative pressure wound therapy (NPWT) is more effective than standard dressing at reducing surgical site infections in women with obesity undergoing caesarean section (CS) **Study dates** September 2013 to October 2016 **Source of funding**	Elective CS, N (%) 229 (52.9) 235 (53) Emergency CS, N (%) 203 (47.1) 209 (47) **Inclusion criteria** Pregnant women ≥ 18 years old; who can read and understand Danish; pre-gestational BMI ≥ 30 kg/m^2 **Exclusion criteria** Not reported		that a sample size of 870 was needed to give 80% power to detect a 50% reduction in surgical site infections in the NPWT group as compared to a 10% rate in the standard dressing group, at the 5% significance level. Follow-up: 30 days.		high risk (see details above) **Incomplete outcome data:** low risk (analyses for main outcome were ITT; there was a loss of follow up for secondary outcomes, but this is <20% and there were not significant differences between treatment arms) **Selective reporting:** low risk (outcomes reported match with those in the study protocol https://clinicaltrials.gov/ct2/show/study/NCT01890720) **Other sources of bias:** high risk (trial had an unrestricted grant from the PICO manufacturer and main author and co-authors have received funding from it (Smith & Nephew). One of the co-authors received funding from The Novo Risk Foundation)

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td>University of Southern Denmark, Odense University Hospital, the Region of Southern Denmark, Lundbeckfonden and an unrestricted grant from Smith & Nephew</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Full citation
Peleg, David, Eberstark, Esther, Warsof, Steven L., Cohen, Nadav, Ben Shachar, Inbar, Early wound dressing removal after scheduled cesarean delivery: a randomized controlled trial, American Journal of Obstetrics and Gynecology, 215, 388.e1-5, 2016

Ref Id
911172

Country/ies where the study was carried out
Israel</td><td>Sample size
N=320 (n=160 randomised to 6h removal and n=160 randomised to 24h removal)

Characteristics
<table><tr><td></td><td>Dressing removed at 6h (N=160)</td><td>Dressing removed at 24h (N=160)</td></tr><tr><td>Age, mean (SD)</td><td>32.9 (5.3)</td><td>31.6 (4.7)</td></tr><tr><td>Gestational age, mean (SD)</td><td>38 (4)</td><td>38 (4)</td></tr><tr><td>BMI at birth, mean (SD)</td><td>30.9 (6.2)</td><td>29.8 (5.5)</td></tr></table>
Inclusion criteria
Term low-risk women between 18 and 44 years old; singleton pregnancies; elective caesarean section, primary or repeat caesarean birth and failed inductions.

Exclusion criteria
Women with co-occurring pregnancy complications, such as fever, chorioamnionitis, diabetes, or PE; those who had pre laboured or</td><td>Interventions
Antibiotic prophylaxis were provided 1 hour prior to skin incision.
All CS were done in a similar manner, using a standard adhesive nonwoven wound dressing. Wound dressings were removed at 6 or 24 hours, and women could only use the bathroom for personal hygiene after these had been removed.</td><td>Details
Randomisation was performed with computer-generated blocks of 2, women were randomised to wound dressing removal at 6 or 24 hours post-surgery. Investigators were blinded to treatment allocation. Sample size calculations were conducted and, assuming a wound complication rate of 12% in the standard treatment group, a sample size calculation found that a sample of 320</td><td>Results
<u>Wound infection</u>
Wound dressing removed at 6 hours: 8/160
Wound dressing removed at 24 hours: 6/160

<u>Women's experience (N of women who were satisfied with the intervention)</u>
Wound dressing removed at 6 hours: 121/160
Wound dressing removed at 24 hours: 91/160

<u>Readmission into hospital</u>
Wound dressing removed at 6 hours: 3/160
Wound dressing removed at 24 hours: 3/160</td><td>Limitations
<u>Methodological limitations assessed using the Cochrane collaboration's tool for assessing risk of bias</u>
Random sequence generation: low risk (computer-generated blocks of 2 were used)
Allocation concealment: unclear risk (no information was provided)
Blinding of participants and personnel: high risk (not blinded)
Blinding of outcome assessment: low risk (outcome assessors were blinded to treatment allocation)
Blinding (performance bias and detection bias): moderate risk (see details above)
Incomplete outcome data: low risk (no drop-outs were reported)</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td>Study type
RCT

Aim of the study
To assess whether early wound dressing removal has an impact on wound complications

Study dates
August 2013 to January 2015

Source of funding
Ziv Medical Center</td><td>with prelabour rupture of membranes; those with more than 3 caesareans; and those with a BMI ≥35</td><td></td><td>would give 80% power to detect a doubling in wound complication rates (from 12 to 24%) in the intervention arm, at the 5% significance level.
Follow-up: 7 days</td><td></td><td>Selective reporting: low risk (outcomes reported match with those in the study protocol https://clinicaltrials.gov/ct2/show/study/NCT01867567)
Other sources of bias: low risk</td></tr>
<tr><td>Full citation
Ruhstaller, Kelly, Downes, Katheryne L., Chandrasekaran, Suchitra, Srinivas, Sindhu, Durnwald, Celeste, Prophylactic Wound Vacuum Therapy after Cesarean Section to Prevent Wound Complications in the Obese Population: A Randomized Controlled Trial</td><td>Sample size
N=136 (n=67 randomised to NPWT and n=69 randomised to standard wound care); N=119 after drop-outs (n=61 in NPWT group and n=58 in standard dressing group)

Characteristics
<table>
<tr><td></td><td>NPWT (N=61)</td><td>Standard dressing (N=58)</td></tr>
<tr><td>Age, median(IQR)</td><td>27 (24-32)</td><td>29 (24-34)</td></tr>
<tr><td>BMI, median (IQR)</td><td>36.1 (33.2-41.8)</td><td>35.1 (32.6-42.1)</td></tr>
<tr><td>GA, median(IQR)</td><td>39 (38-40)</td><td>39 (38-40)</td></tr>
</table></td><td>Interventions
94.1% of women received 2 g IV (weight < 120 kg) or 3 g IV (weight ≥ 120 kg) prior skin incision.
NPWT group received a Prevena Incision Management System placed on the closed incision. The dressing was removed after 24h following surgery.
Standard dressing group received a Telfa bandage on the closed incision.</td><td>Details
Randomisation was computer-generated.
Unclear how allocation was done. The study was open-label.
Sample size calculations were performed and it was estimated that a sample size of 1282 women would be required for 90% power to detect a 5% decrease in</td><td>Results
<u>Wound infection</u>
NPWT group: 2/61
Standard dressing group: 4/58

<u>Women's experience - sharp pain at postoperative day 2 (better indicated by lower values)</u>
NPWT group - median (IQR): 5.5 (3-8)
Standard dressing group - median (IQR): 6 (4-8)</td><td>Limitations
<u>Methodological limitations assessed using the Cochrane collaboration's tool for assessing risk of bias</u>
Random sequence generation: low risk (computer generated list)
Allocation concealment: unclear risk (no details were provided)
Blinding of participants and personnel: high risk (not blinded)
Blinding of outcome assessment: high risk (not blinded)
Blinding (performance bias and detection bias):</td></tr>
</table>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
(the ProVac Study), American Journal of Perinatology, 34, 1125-1130, 2017 **Ref Id** 915391 **Country/ies where the study was carried out** US **Study type** RCT **Aim of the study** To assess whether the use of negative pressure wound therapy (NPWT) decreases the incidence of surgical site infection in women undergoing caesarean section (CS) **Study dates** May 2014 to March 2016 **Source of funding** National Institute of Health Reproductive Epidemiology.	**Inclusion criteria** Pregnant women ≥18 year old; BMI ≥30 kg/m^2 at <22 weeks gestational age who presented in labour. **Exclusion criteria** Lack of information regarding BMI at <23 weeks; chronic steroid use; planned vertical skin incision; allergy to silver; scheduled CS.	The dressing was removed after 24h following surgery.	complications in the intervention group, at the 5% significance level. Follow-up: 4 weeks		high risk (see details above) **Incomplete outcome data:** low risk (there was a low rate of drop-outs and reasons for these were provided) **Selective reporting:** low risk (outcomes reported match with those in the study protocol https://clinicaltrials.gov/ct2/show/record/NCT02128997) **Other sources of bias:** high risk (devices were provided by Acelity, the manufacturer of Prevena) **Other information** 5.9% of women did not receive prophylactic antibiotics

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td>Study devices were provided by Acelity (manufacturer of NPWT)</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Full citation
Stanirowski, P. J., Bizoń, M., Cendrowski, K., Sawicki, W., Randomized Controlled Trial Evaluating Dialkylcarbamoyl Chloride Impregnated Dressings for the Prevention of Surgical Site Infections in Adult Women Undergoing Cesarean Section, Surgical Infections, 17, 427-435, 2016

Ref Id
911312

Country/ies where the study was carried out
Poland

Study type
RCT

Aim of the study
To assess the effectiveness of dialkylcarbamoyl</td><td>Sample size
N=543 (n=272 women allocated to the DACC group and n=271 women allocated to the standard dressing group)

Characteristics
<table><tr><th></th><th>DACC impregnated dressing (N=272)</th><th>Standard dressing (N=271)</th></tr><tr><td>Age, mean (SD)</td><td>31.2 (4.8)</td><td>30.6 (4.8)</td></tr><tr><td>Gestational age, mean (SD)</td><td>38.1 (2.4)</td><td>38 (2.5)</td></tr><tr><td>Pre-pregnancy BMI, mean (SD)</td><td>23.9 (4.5)</td><td>24.2 (4.9)</td></tr><tr><td>Elective CS, N (%)</td><td>214 (78.7)</td><td>211 (77.9)</td></tr><tr><td>Emergency CS, N (%)</td><td>58 (21.3)</td><td>60 (22.1)</td></tr></table>
Inclusion criteria
Pregnant women ≥18 years old undergoing emergency or planned CS and able to provide informed consent to participate in the study.

Exclusion criteria
Those who did not receive prophylactic antibiotics; those with skin incisions other than low transverse; women who did not receive irrigation of the wound with octenidine prior to subcutaneous tissue closure.</td><td>Interventions
Women received antibiotic prophylaxis (1g of cefazolin) up to 30 minutes before the procedure and wound irrigation with octenidine solution before the subcutaneous tissue closure. DACC impregnated dressing placed over post-caesarean wound after skin closure. The dressing was removed 48 hours after the procedure. Standard surgical dressing placed over post-caesarean wound after skin closure. The dressing was removed 48 hours after the procedure.</td><td>Details
Simple randomisation with 1:1 allocation ratio was performed using alternation of even and odd numbers. Randomisation was concealed in white sealed envelopes. Clinicians were masked to treatment allocation until skin closure. Sample size calculations were conducted and it was estimated that a sample size of 248 for each of the treatment arms was needed to give 90% power to detect a difference in surgical site infections at the 5% significance level. Expected</td><td>Results
<u>Surgical site infections</u>
DACC impregnated dressing: 5/272
Standard dressing: 14/271

<u>Need for antibiotic</u>
DACC impregnated dressing: 0/272
Standard dressing: 4/271

<u>Readmission into hospital</u>
DACC impregnated dressing: 0/272
Standard dressing: 3/271</td><td>Limitations
<u>Methodological limitations assessed using the Cochrane collaboration's tool for assessing risk of bias</u>
Random sequence generation: high risk (odd and even number were used to produce the sequence generation)
Allocation concealment: low risk (randomisation was concealed with white sealed envelopes)
Blinding of participants and personnel: high risk (participants were blinded, but personnel were not)
Blinding of outcome assessment: high risk (not blinded)
Blinding (performance bias and detection bias): high risk (see details above)
Incomplete outcome data: low risk (reasons for drop-outs were provided and accounted for <20% in each group)
Selective reporting: low risk (outcomes reported match with those in the study protocol https://clinicaltrials.gov/ct2/show/record/NCT02168023)</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td>chloride (DACC) impregnated dressings for reducing wound infections in women undergoing caesarean section (CS).

Study dates
April 2015 to June 2015

Source of funding
Medical University of Warsaw</td><td></td><td></td><td>difference was not reported.
Follow-up: not reported</td><td></td><td>Other sources of bias: low risk</td></tr>
<tr><td>Full citation
Tolcher, Mary Catherine, Whitham, Megan D., El-Nashar, Sherif A., Clark, Steven L., Chlorhexidine-Alcohol Compared with Povidone-Iodine Preoperative Skin Antisepsis for Cesarean Delivery: A Systematic Review and Meta-Analysis, American Journal of Perinatology, 2018

Ref Id</td><td>Sample size
K=4 RCTs (N=3059)

Characteristics
Kunkle 2015*<table><tr><td></td><td>Chlorhexidine - alcohol (N=27)</td><td>Povidone-iodine (N=33)</td></tr><tr><td>Country</td><td colspan="2">US</td></tr><tr><td>Age, mean (SD)</td><td>31 (4.4)</td><td>29.1 (6.5)</td></tr><tr><td>BMI, mean (SD)</td><td>31.3 (6.1)</td><td>33.2 (5.9)</td></tr></table>Ngai 2015*<table><tr><td></td><td>Chlorhexidine - alcohol (N=474)</td><td>Povidone-iodine with alcohol(N=463)</td></tr><tr><td>Country</td><td colspan="2">US</td></tr></table></td><td>Interventions
In all trials, women were administered antibiotic prophylaxis.
All studies compared chlorhexidine-alcohol to povidone-iodine.
No further details were provided.</td><td>Details
A literature search was done in MEDLINE, Embase, and clinicaltrials.gov. Authors were contacted to retrieve additional data regarding methods and/or outcomes. Two authors assessed inclusion and exclusion of the studies independently. Follow up was between 14 days (Kunkle 2015) and 30</td><td>Results
<u>Surgical site infection</u>
Kunkle 2015
Chlorhexine-alcohol:2/21
Povidone-iodine: 1/22

Ngai 2015
Chlorhexine-alcohol: 18/474
Povidone-iodine with alcohol: 19/463

Ngai 2015 - results by planned versus emergency caesarean*
Chlorhexine-alcohol (planned): 10/327
Chlorhexine-alcohol (emergency): 8/147
Povidone-iodine with alcohol (planned): 9/329
Povidone-iodine with alcohol (emergency): 10/134

Springel 2017</td><td>Limitations
<u>ROB assessed using AMSTAR checklist</u>
Total score: 12/16
The following items were not met by the study authors:
The study did not contain a specific statement that the review methods were established prior to the review
Excluded studies list was not provided, included studies not described in adequate detail
Sources of funding of the included studies were not reported</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr>
<td>911357

Country/ies where the study was carried out
US

Study type
Systematic review

Aim of the study
To assess the effectiveness of chlorhexidine alcohol compared to povidone iodine skin preparations for preventing infections in women undergoing caesarean section

Study dates
Not reported

Source of funding
Not reported</td>
<td>
<table>
<tr><td>Age, mean (SD)</td><td>30.3 (5.7)</td><td>29.9 (6)</td></tr>
<tr><td>BMI, mean (SD)</td><td>34.8 (6.6)</td><td>34.3 (6.5)</td></tr>
</table>

Springel 2017*
<table>
<tr><td></td><td>Chlorhexidine - alcohol (N=461)</td><td>Povidone-iodine(N=471)</td></tr>
<tr><td>Country</td><td colspan="2">US</td></tr>
<tr><td>Age, median (IQR)</td><td>28 (24-33)</td><td>28 (24-32)</td></tr>
<tr><td>Gestational age, median (IQR)</td><td>39 (37-39)</td><td>39 (37-39)</td></tr>
<tr><td>BMI, median (IQR)</td><td>35 (30-42)</td><td>36 (30-43)</td></tr>
</table>

Tuuli 2016*
<table>
<tr><td></td><td>Chlorhexidine - alcohol (N=572)</td><td>Povidone-iodine with alcohol (N=575)</td></tr>
<tr><td>Country</td><td colspan="2">US</td></tr>
<tr><td>Age, mean (SD)</td><td>28.3 (5.8)</td><td>28.4 (5.8)</td></tr>
<tr><td>BMI, mean (SD)</td><td>35.1 (8.9)</td><td>34.1 (8.1)</td></tr>
<tr><td>GA, mean (SD)</td><td>37.6 (2.8)</td><td>37.7 (3.1)</td></tr>
</table>
</td>
<td></td>
<td>days (Ngai 2015, Springel 2017, Tuuli 2016)</td>
<td>Chlorhexine-alcohol: 21/461
Povidone-iodine: 28/471

Tuuli 2016
Chlorhexine-alcohol: 23/572
Povidone iodine with alcohol: 42/575

Tuuli 2016 - results by planned versus emergency caesarean*
Chlorhexine-alcohol (planned): 8/334
Chlorhexine-alcohol (emergency): 15/238
Povidone iodine with alcohol (planned): 21/335
Povidone iodine with alcohol (emergency): 21/240

Tuuli 2016 - results by BMI ≥30 vs BMI <30*
Chlorhexine-alcohol (BMI ≥30): 18/402
Chlorhexine-alcohol (BMI <30): 5/170
Povidone iodine with alcohol (BMI ≥30): 30/387
Povidone iodine with alcohol (BMI <30): 12/188

<u>Adverse skin reaction</u>
Springel 2017 (type not specified)*
Chlorhexine-alcohol: 2/461
Povidone-iodine: 1/471

Tuuli 2016 (skin irritation or allergic skin reaction)*
Chlorhexine-alcohol: 2/572
Povidone iodine with alcohol: 4/575</td>
<td><u>Limitations for each of the included studies assessed with the Cochrane Risk of Bias Tool</u>
Kunkle 2015
Random sequence generation: unclear risk
Allocation concealment: unclear risk
Blinding of participants and personnel: low risk
Blinding of outcome assessment: unclear risk
Incomplete outcome data: high risk
Selective reporting: low risk
Other bias: low risk

<u>Ngai 2015</u>
Random sequence generation: low risk
Allocation concealment: low risk
Blinding of participants and personnel: low risk
Blinding of outcome assessment: unclear risk
Incomplete outcome data: low risk
Selective reporting: low risk
Other bias: low risk

<u>Springel 2017</u>
Random sequence generation: low risk
Allocation concealment: low risk
Blinding of participants and personnel: low risk
Blinding of outcome assessment: low risk</td>
</tr>
</table>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	<table><tr><td>Planned caesarean, N (%)</td><td>334 (58.4)</td><td>335 (58.3)</td></tr><tr><td>Emergency caesarean, N (%)</td><td>238 (41.6)</td><td>240 (41.7)</td></tr></table> *Indicates data extracted by the review team from the original study **Inclusion criteria** RCTs comparing chlorhexidine-alcohol with povidone-iodine in women undergoing caesarean section. **Exclusion criteria** Not reported			Endometritis* Springel 2017* Chlorhexine-alcohol: 8/461 Povidone iodine: 5/471 Tuuli 2016* Chlorhexine-alcohol: 8/572 Povidone iodine with alcohol: 11/575 Readmission into hospital* Springel 2017* Chlorhexine-alcohol: 5/461 Povidone-iodine: 9/471 Tuuli 2016* Chlorhexine-alcohol: 19/572 Povidone-iodine with alcohol: 25/575 *Indicates data extracted by the review team from the original study	**Incomplete outcome data:** low risk **Selective reporting:** unclear risk **Other bias:** low risk Tuuli 2016 **Random sequence generation:** low risk **Allocation concealment:** unclear risk **Blinding of participants and personnel:** low risk **Blinding of outcome assessment:** low risk **Incomplete outcome data:** low risk **Selective reporting: low** risk **Other bias:** low risk **Other information** The data presented in this evidence table has been adapted from the original systematic review. We present the data that is relevant to the aims of this review. Individual studies were retrieved for accuracy and to check if other outcomes of interest were reported. Data extracted by the review team from the original study has been marked with an *.
Full citation Tuuli, M. G., Liu, J., Tita, A. T. N., Longo, S., Trudell, A., Carter, E. B.,	**Sample size** N=1624 (n=816 randomised to NPWT and n=808 randomised to standard dressing). Originally intended to recruit 2850 participants but stopped prematurely (see limitations).	**Interventions** NPWT group had the Prevena device applied immediately after repair of the incision, secured	**Details** Randomised centrally, 1:1 ratio, computer generated sequence with	**Results** Sepsis NPWT dressing: 3/806 Standard dressing: 2/802	**Limitations** Methodological limitations assessed using the Cochrane collaboration's tool for assessing risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Shanks, A., Woolfolk, C., Caughey, A. B., Warren, D. K., Odibo, A. O., Colditz, G., MacOnes, G. A., Harper, L., Effect of prophylactic negative pressure wound therapy vs standard wound dressing on surgical-site infection in obese women after cesarean delivery: A randomized clinical trial, JAMA - Journal of the American Medical Association, 324, 1180-1189, 2020 **Ref Id** 1291286 **Country/ies where the study was carried out** US **Study type** RCT **Aim of the study** To determine the effect of prophylactic	**Characteristics** NPWT (N=806) / Standard dressing (N=802) Age, mean (SD): 30.2 (5.6) / 30.5 (6.1) BMI, mean (SD): 39.6 (7.7) / 39.5 (8.1) GA, mean (SD): 37.3 (3.1) / 37.4 (2.9) **Inclusion criteria** BMI 30 or more, at or beyond 23 weeks gestation, planned or unplanned caesarean birth **Exclusion criteria** Not available for post-operative follow-up, contraindication to NPWT use (e.g. pre-existing infection at incision site), bleeding disorder, therapeutic anticoagulation, or allergy to silicone or adhesive tape	with fixation adhesion strips. Negative pressure was delivered at -125mmHg. The device was removed on the day of discharge, typically on postoperative day 4 or day 7 if patients remained hospitalised. Standard dressing group had their closed incisions covered with routine postoperative wound dressing consisting of layers of gauze and adhesive tape, the dressing was removed after 24 hours.	variable blocks of 4 and 6, stratified by study site, BMI and planned or unplanned caesarean birth. No blinding. Monitored daily until discharge. Telephone follow-up at day 30.	Surgical site infection (excluding organ space) NPWT dressing: 29/806 Standard dressing: 27/808 Adverse skin events NPWT dressing: 56/806 (27 blisters, 9 bleeding, 10 erythema, 14 other) Standard dressing: 5/808 Women's experience (satisfaction score, 0-10, higher is better): Difference in medians at discharge: 0.79 (95% CI 0.25 to 1.32) NPWT vs standard Difference in medians at day 30: 0.19 (95% CI -0.01 to 0.39) NPWT vs standard Readmission to hospital (within 28 days): NPWT dressing: 2/806 Standard dressing: 0/802	**Random sequence generation:** low risk (computer-generated, block randomisation schedule) **Allocation concealment:** low risk (obtained from a secure website after eligibility locked) **Blinding of participants and personnel:** high risk (not blinded) **Blinding of outcome assessment:** high risk (not blinded) **Blinding (performance bias and detection bias):** high risk (see details above) **Incomplete outcome data:** low risk (there was a low rate of drop-outs <20%, results were ITT, and reasons for these were provided) **Selective reporting: low** risk (outcomes reported match with those in the study protocol) **Other sources of bias**: low risk (trial terminated early due to pre-planned interim analysis showing increased adverse events without difference in efficacy, however conditional power analysis at the time suggested only 11% probability of detecting a significant difference in the primary outcome if planned sample size was recruited).

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td>negative pressure wound therapy on risks of surgical-site infection and other wound complications in obese women after cesarean delivery

Study dates
February 2017 to November 2019

Source of funding
Academic but with industry donation of devices and 'supplemental' funding</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Full citation
Wihbey, Kristina A., Joyce, Ellen M., Spalding, Zachary T., Jones, Hayley J., MacKenzie, Todd A., Evans, Rebecca H., Fung, June L., Goldman, Marlene B., Erekson, Elisabeth, Prophylactic Negative Pressure Wound Therapy and</td><td>Sample size
N=166 (n=80 randomised to NPWT dressing and n=86 randomised to standard dressing)

Characteristics<table><tr><th></th><th>NPWT (N=80)</th><th>Standard dressing (N=86)</th></tr><tr><td>Age, mean (SD)</td><td>31 (6)</td><td>30.2 (5)</td></tr><tr><td>BMI, mean (SD)</td><td>44.9 (8)</td><td>43.4 (7)</td></tr><tr><td>GA ≤28, N (%)</td><td>1 (1)</td><td>3 (3)</td></tr><tr><td>GA 28-37, N (%)</td><td>21 (29)</td><td>17 (22)</td></tr></table></td><td>Interventions
Women received prophylactic antibiotics prior to skin incision. NPWT group received the Prevena (VAC) device at the time of primary skin closure. The dressing was removed after 5-7 days following surgery. Standard dressing group received a standard sterile</td><td>Details
Randomisation was done with a program, using opaque sealed envelopes for arm assignment. A permuted block randomisation schedule was created for women with BMI of 35 to 40 and BMI ≥40. Sample size calculations were conducted</td><td>Results
<u>Surgical site infection</u>
NPWT dressing: 12/80
Standard dressing:8/81

Women with BMI 40 to 50
NPWT dressing: 7/31
Standard dressing: 7/40

Women with BMI > 50
NPWT dressing: 4/19
Standard dressing: 3/15

<u>Need for antibiotics due to SSI infection</u>
NPWT dressing: 14/80
Standard dressing: 10/81</td><td>Limitations
<u>Methodological limitations assessed using the Cochrane collaboration's tool for assessing risk of bias</u>
Random sequence generation: low risk (computer-generated, permuted block randomisation schedule)
Allocation concealment: low risk (opaque sealed envelopes were used)
Blinding of participants and personnel: high risk (not blinded)</td></tr>
</table>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Wound Complication After Cesarean Delivery in Women With Class II or III Obesity: A Randomized Controlled Trial, Obstetrics and Gynecology, 132, 377-384, 2018 **Ref Id** 911409 **Country/ies where the study was carried out** US **Study type** RCT **Aim of the study** To assess whether negative pressure wound therapy (NPWT) is related with a reduced number of surgical site infections in women with obesity undergoing caesarean section (CS) **Study dates**	<table><tr><td>GA ≥37-42, N (%)</td><td>51 (70)</td><td>59 (74)</td></tr><tr><td>GA ≥ 42, N (%)</td><td>0</td><td>0</td></tr></table> **Inclusion criteria** Pregnant women ≥18 years old undergoing any type of caesarean section for birth (primary and repeat, scheduled and urgent); BMI ≥35 kg/m^2 **Exclusion criteria** Those with silver allergy, those with a skin incision that would not fit the NPWT device or standard dressing, or non-English speaking	dressing at the time of skin closure. The dressing was removed 1-2 days following surgery.	and it was determined that a sample size of 400 would be needed to give 80% power to detect a 50% decrease in surgical site infections, at the 5% significance level. Follow-up: 30 days.	Adverse skin events from techniques (hematoma) NPWT dressing: 2/80 Standard dressing: 4/81 Readmission into hospital NPWT dressing: 3/80 Standard dressing: 5/81	**Blinding of outcome assessment:** high risk (not blinded) **Blinding (performance bias and detection bias):** high risk (see details above) **Incomplete outcome data:** low risk (there was a low rate of drop-outs <20%, results were ITT, and reasons for these were provided) **Selective reporting: low** risk (outcomes reported match with those in the study protocol https://clinicaltrials.gov/ct2/show/record/NCT02390401?view=record) **Other sources of bias**: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
May 2015 to July 2017 **Source of funding** Dartmouth-Hitchcock Medical Center, Southern New Hampshire Medical Center					

Appendix E – Forest plots

Forest plots for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here, but the quality assessment for these outcomes is provided in the GRADE profiles in appendix F.

Comparison 2. Negative wound pressure therapy (NPWT) versus standard dressing

Critical outcomes

Figure 2: Wound infection/ surgical site infection

Study or Subgroup	NPWT Events	NPWT Total	Standard dressing Events	Standard dressing Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chaboyer 2014	10	44	12	43	10.1%	0.81 [0.39, 1.68]
Gunatilake 2017	1	39	4	43	3.2%	0.28 [0.03, 2.36]
Hussamy 2019	21	222	25	219	20.9%	0.83 [0.48, 1.44]
Hyldig 2018	20	432	41	444	33.5%	0.50 [0.30, 0.84]
Ruhstaller 2017	2	61	4	58	3.4%	0.48 [0.09, 2.50]
Tuuli 2020	29	806	27	808	22.4%	1.08 [0.64, 1.80]
Wihbey 2018	12	80	8	81	6.6%	1.52 [0.66, 3.52]
Total (95% CI)		**1684**		**1696**	**100.0%**	**0.79 [0.61, 1.02]**
Total events	95		121			

Heterogeneity: Chi² = 8.00, df = 6 (P = 0.24); I² = 25%
Test for overall effect: Z = 1.81 (P = 0.07)

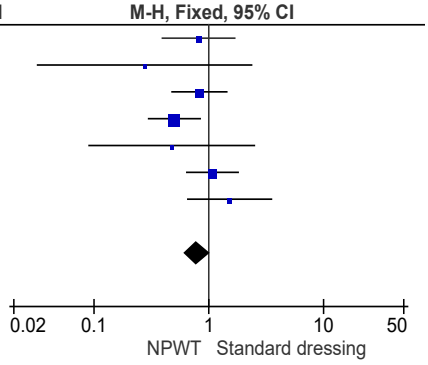
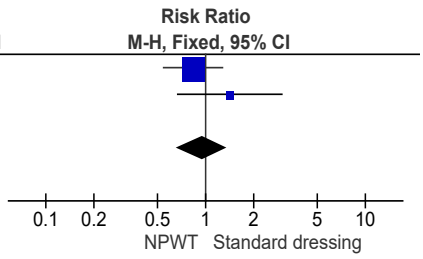


Figure 3: Need for antibiotics

Study or Subgroup	NPWT Events	NPWT Total	Standard dressing Events	Standard dressing Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hussamy 2019	33	222	39	219	79.8%	0.83 [0.55, 1.28]
Wihbey 2018	14	80	10	81	20.2%	1.42 [0.67, 3.00]
Total (95% CI)		**302**		**300**	**100.0%**	**0.95 [0.66, 1.37]**
Total events	47		49			

Heterogeneity: Chi² = 1.45, df = 1 (P = 0.23); I² = 31%
Test for overall effect: Z = 0.26 (P = 0.79)



Important outcomes

Figure 4: Adverse skin events from techniques

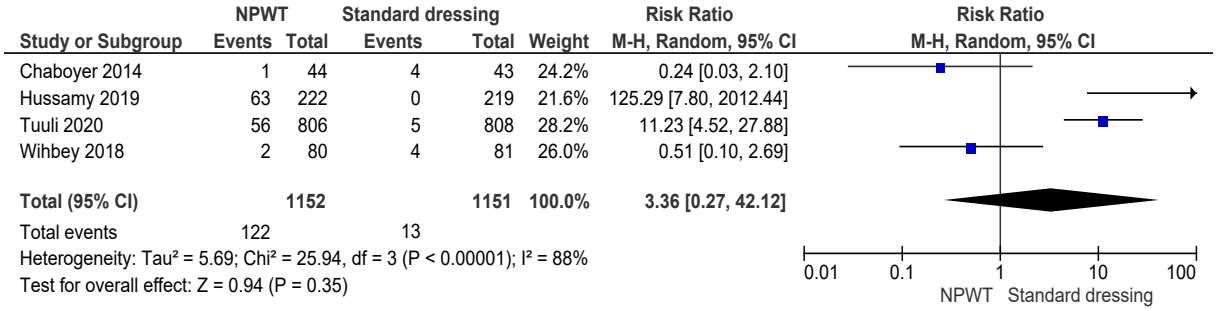
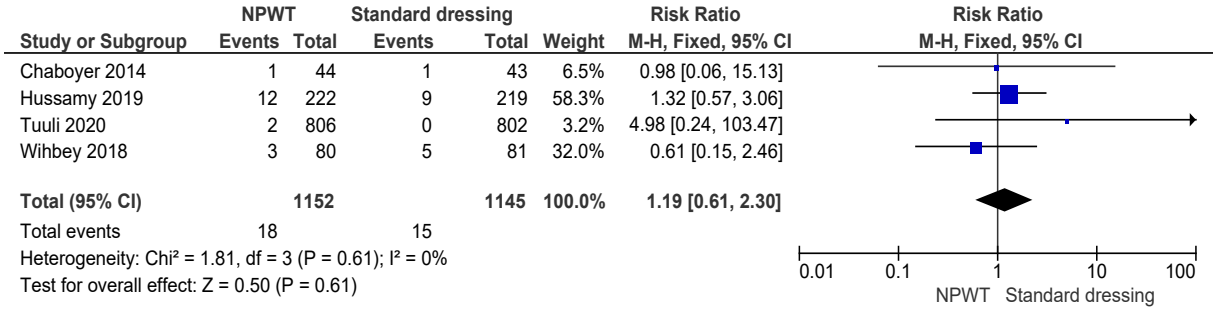


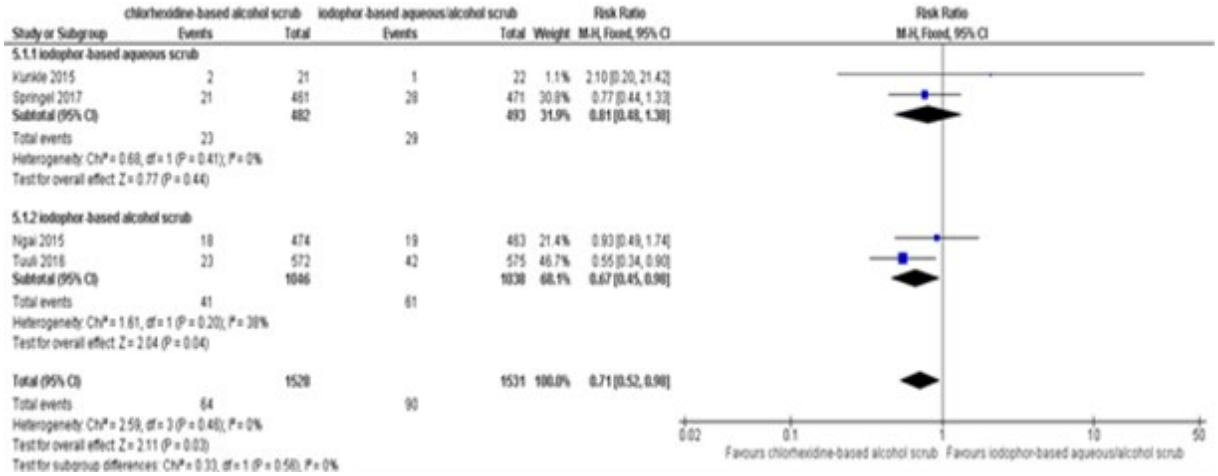
Figure 5: Readmission into hospital



Comparison 4. Chlorhexidine-based alcohol skin preparation versus iodophor-based aqueous/alcohol skin preparation

Critical outcomes

Figure 6: Surgical site infection



Important outcomes

Figure 7: Adverse skin reaction

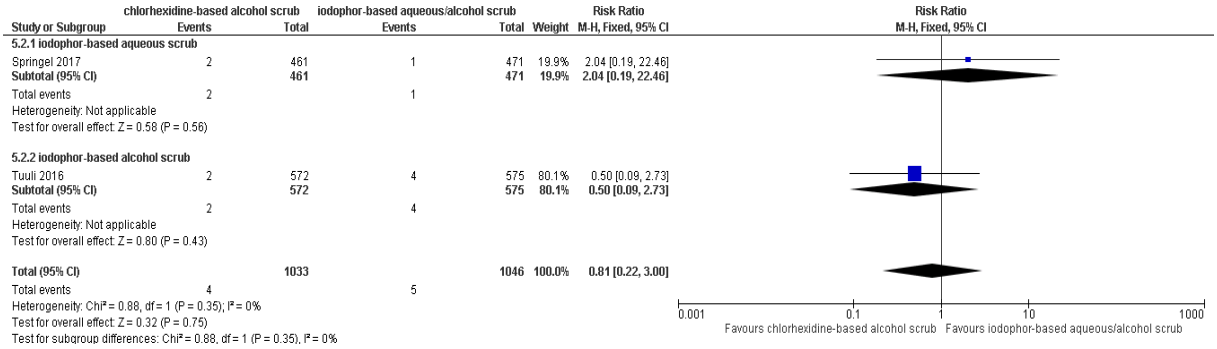


Figure 8: Endometritis

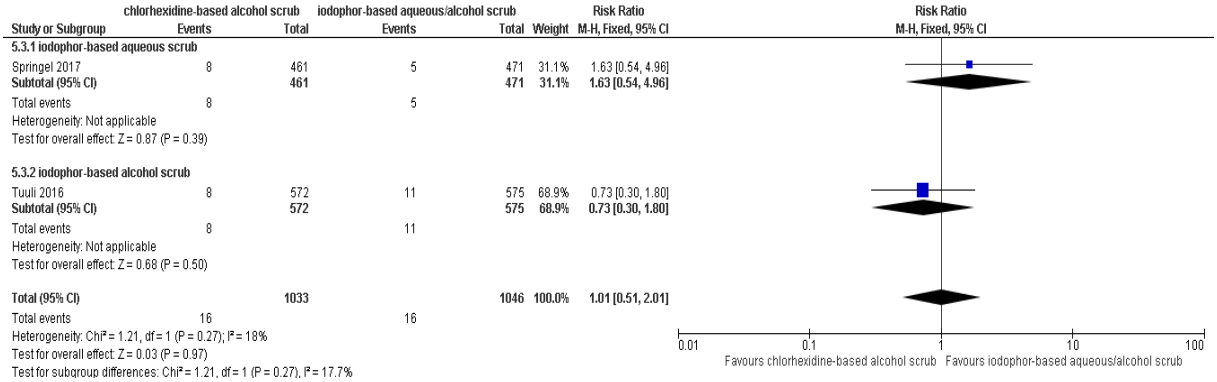
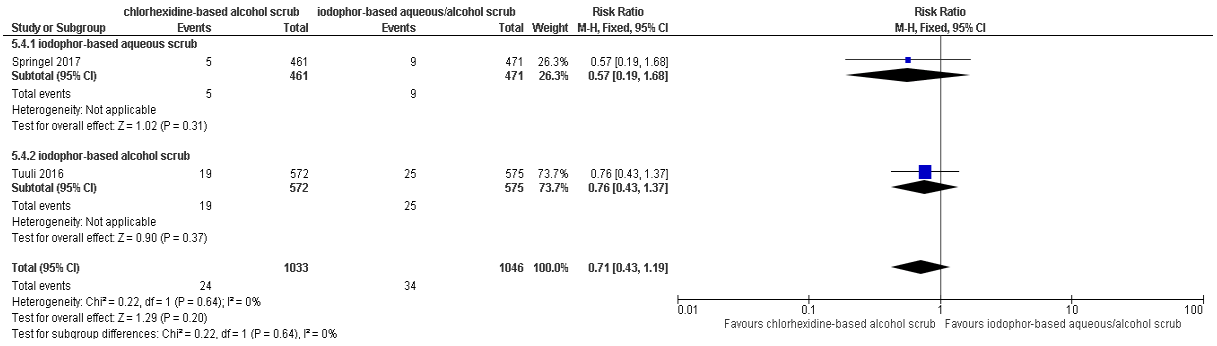


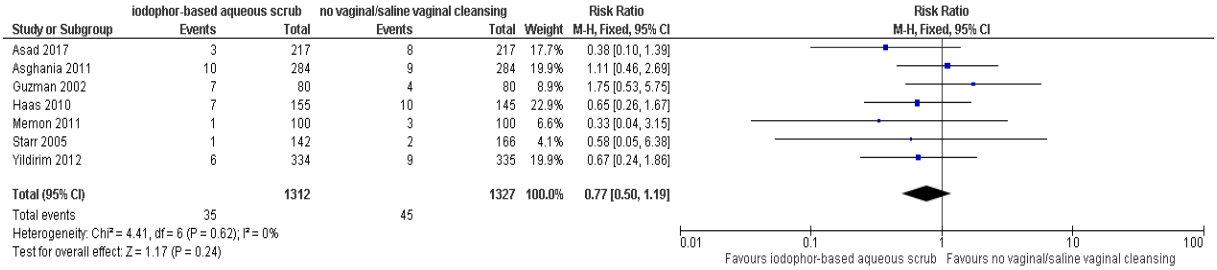
Figure 9: Readmission into hospital



Comparison 5. Iodophor-based aqueous vaginal preparation versus no vaginal/saline vaginal preparation

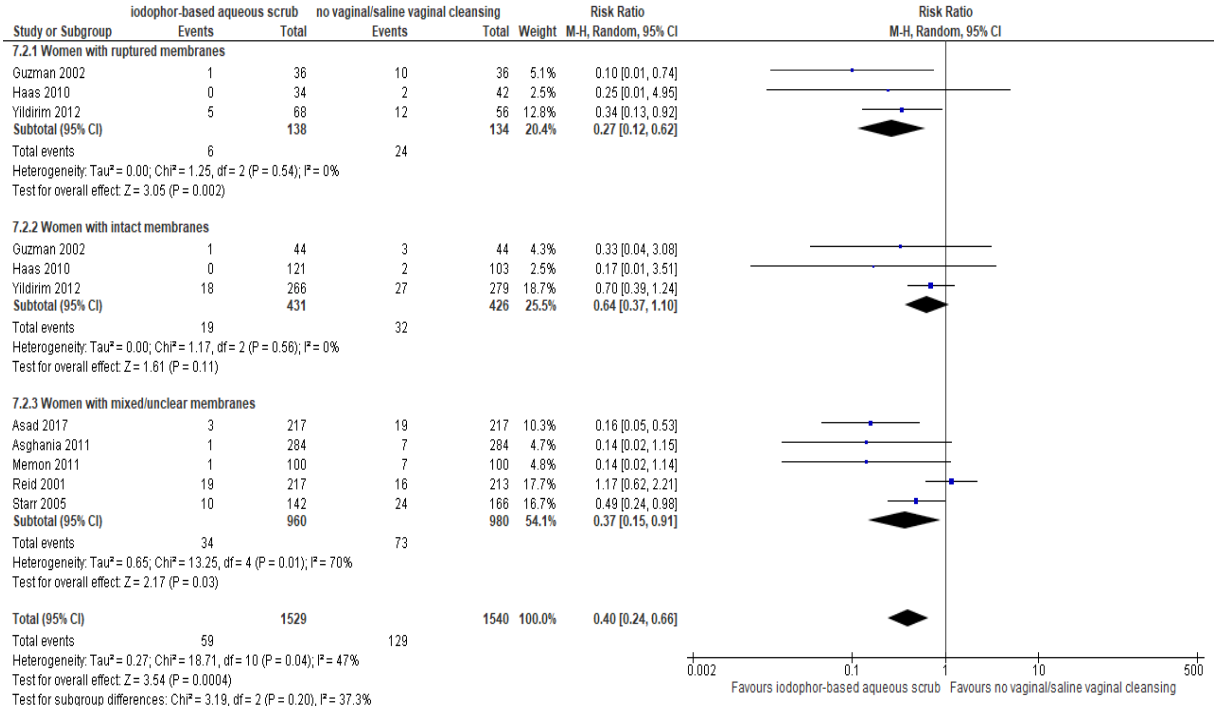
Critical outcomes

Figure 10: Wound infection



Important outcomes

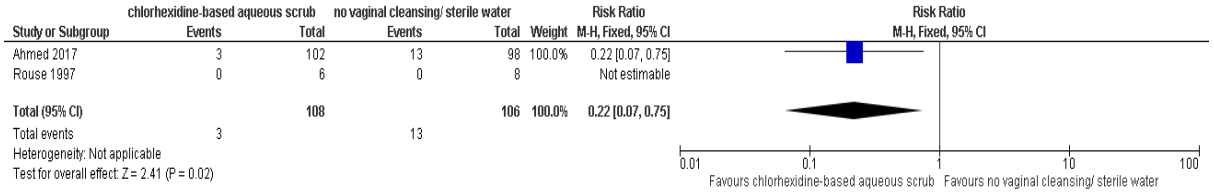
Figure 11: Endometritis



Comparison 6. Chlorhexidine-based aqueous vaginal preparation versus no vaginal cleansing/sterile water

Important outcomes

Figure 12: Endometritis



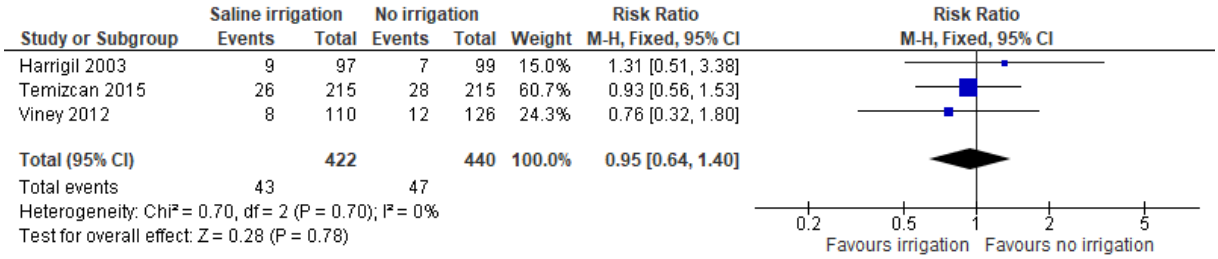
Comparison 7. Saline intra-abdominal irrigation versus no irrigation

Critical outcomes

Figure 13: Wound infection

Important outcomes

Figure 14: Endometritis



Appendix F – GRADE tables

GRADE tables for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

Table 5: Comparison 1. Hydroactive dressing versus standard dressing

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hydroactive dressing	Standard dressing	Relative (95% CI)	Absolute	Quality	Importance
Surgical site infection												
1 (Stanirowski 2016)	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	5/272 (1.8%)	14/271 (5.2%)	RR 0.36 (0.13 to 0.97)	33 fewer per 1000 (from 2 fewer to 45 fewer)	VERY LOW	CRITICAL
Need for antibiotics												
1 (Stanirowski 2016)	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	0/272 (0%)	4/271 (1.5%)	POR 0.13 (0.02 to 0.95)	13 fewer per 1000 (from 1 fewer to 14 fewer)	VERY LOW	CRITICAL
Readmission into hospital												
1 (Stanirowski 2016)	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Very serious[3]	None	0/272 (0%)	3/271 (1.1%)	POR 0.13 (0.01 to 1.29)	10 fewer per 1000 (from 11 fewer to 19 more)	VERY LOW	IMPORTANT

[1] *The quality of the evidence was downgraded by two levels due to high risk of bias in random sequence generation, and study personnel and outcome assessors were not blinded*
[2] *The quality of the evidence was downgraded by one level as the 95% CI crossed 1 default MID threshold (0.8)*
[3] *The quality of the evidence was downgraded by two levels as the 95% CI crossed 2 default MID thresholds (0.8 and 1.25)*

Table 6: Comparison 2. Negative pressure wound therapy (NPWT) versus standard dressing

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Negative pressure wound therapy	Standard dressing	Relative (95% CI)	Absolute	Quality	Importance
Sepsis												
1 (Tuuli 2020)	Randomised trials	Serious[3]	No serious inconsistency	No serious indirectness	Very serious[4]	None	3/806 (0.37%)	2/802 (0.25%)	Peto OR 1.49 (0.26 to 8.60)	1 more per 1000 (from 2 fewer to 19 more)	VERY LOW	CRITICAL
Wound infection/ surgical site infection												
7 (Chaboyer 2018, Gunatilake 2017, Hussamy 2019, Hyldig 2018, Ruhstaller 2017, Tuuli 2020, Wihbey 2018)	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	95/1684 (5.6%)	121/1696 (7.1%)	RR 0.79 (0.61 to 1.02)	15 fewer per 1000 (from 28 fewer to 1 more)	VERY LOW	CRITICAL
Need for antibiotics												
2 (Hussamy 2019, Wihbey 2018)	Randomised trials	Serious[3]	No serious inconsistency	No serious indirectness	Very serious[4]	none	47/302 (15.6%)	49/300 (16.3%)	RR 0.95 (0.66 to 1.37)	8 fewer per 1000 (from 56 fewer to 60 more)	VERY LOW	CRITICAL
Adverse skin events from techniques												
4 (Chaboyer 2018, Hussamy 2019, Tuuli 2020, Wihbey 2018)	Randomised trials	Serious[3]	Very serious inconsistency[10]	No serious indirectness	Very serious[4]	None	122/1152 (10.6%)	13/1151 (1.1%)	RR 3.36 (0.27 to 42.12)	27 more per 1000 (from 8 fewer to 464 more)	VERY LOW	IMPORTANT
Endometritis												
1 (Hyldig 2018)	Randomised trials	Very serious[5]	No serious inconsistency	No serious indirectness	Very serious[4]	None	8/432 (1.9%)	8/444 (1.8%)	RR 1.03 (0.39 to 2.71)	1 more per 1000 (from	VERY LOW	IMPORTANT

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Negative pressure wound therapy	Standard dressing	Relative (95% CI)	Absolute	Quality	Importance
										11 fewer to 31 more)		
Women's experience: reported pain (days 1 to 7)												
1 (Gunatilake 2017)	Randomised trials	Very serious[6]	No serious inconsistency	No serious indirectness	No serious imprecision	None	20/46 (43.5%)	39/43 (90.7%)	RR 0.48 (0.34 to 0.68)	472 fewer per 1000 (from 290 fewer to 599 fewer)	LOW	IMPORTANT
Women's experience: sharp pain at postoperative day (better indicated by lower values)												
1 (Gunatilake 2017)	Randomised trials	Very serious[7]	No serious inconsistency	Serious[8]	Serious[9]	None	N=61 Median=6 IQR= 4 to 8	N=58 Median=5.5 IQR= 3 to 8	p-value = 0.56	-	VERY LOW	IMPORTANT
Women's experience: self-rated health status (measured with: EQ-VAS; better indicated by higher values)												
1 (Hyldig 2018)	Randomised trials	Very serious[5]	No serious inconsistency	No serious indirectness	No serious imprecision	None	432	444	-	MD 1 higher (1.23 lower to 3.23 higher)	LOW	IMPORTANT
Women's experience: satisfaction (day 30, 0-10, better indicated by higher values)												
1 (Tuuli 2020)	Randomised trials	Very serious[5]	No serious inconsistency	No serious indirectness	No serious imprecision	None	806	802	-	MD 0.19 higher (0.01 lower to 0.39 higher)	LOW	IMPORTANT
Women's experience: "would use this dressing again" (day 30-60)												
1 (Hussamy 2019)	Randomised trials	Very serious[5]	No serious inconsistency	No serious indirectness	No serious imprecision	None	187/210 (89%)	185/201 (92%)	RR 0.97 (0.91 to 1.03)	28 fewer per 1000 (from 83 fewer to 28 more)	LOW	IMPORTANT
Readmission into hospital												
4 (Chaboyer 2018, Hussamy 2019, Tuuli 2020, Wihbey 2018)	Randomised trials	Serious[3]	No serious inconsistency	No serious indirectness	Very serious[4]	None	18/1152 (1.6%)	15/1145 (1.3%)	RR 1.19 (0.61 to 2.30)	2 more per 1000 (from 5 fewer to 17 more)	VERY LOW	IMPORTANT

[1] The quality of the evidence was downgraded by two levels due to unclear risk of bias in randomisation in one study; unclear risk of allocation concealment in one study; study participants, personnel and outcome assessors were not blinded in five studies; study received funding from the NPWT manufacturer in three studies
[2] The quality of the evidence was downgraded by one level as the 95% CI crossed 1 default MID threshold (0.8)
[3] The quality of the evidence was downgraded by one level as study participants, personnel and outcome assessors were not blinded
[4] The quality of the evidence was downgraded by two levels as the 95% CI crossed 2 default MID thresholds (0.8 and 1.25)
[5] The quality of the evidence was downgraded by two levels as study participants, personnel and outcome assessors were not blinded and the study received funding from the NPWT manufacturer
[6] The quality of the evidence was downgraded by two levels as the randomisation method was not reported; study participants, personnel and outcome assessors were not blinded and the study received funding from the NPWT manufacturer
[7] The quality of the evidence was downgraded by two levels as there was an unclear risk of bias in allocation concealment; participants, personnel and outcome assessors were not blinded and the study received funding from the NPWT manufacturer
[8] The quality of the evidence was downgraded by one level as 5.9% of women did not receive prophylactic antibiotics
[9] The quality of the evidence was downgraded by one level as imprecision was not calculable because the uncertainty around the outcome was not available
[10] The quality of the evidence was downgraded by two levels due to wide variation in point estimates and confidence intervals in the meta-analysis, I2=88%

Table 7: Comparison 3. Early (6 hours) versus standard (24 hours) timing of dressing removal

Quality assessment							Number of patients		Effect		Quality	Importance
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Early (6h) removal**	**Standard (24h) removal**	**Relative (95% CI)**	**Absolute**		
Wound infection												
1 (Peleg 2016)	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	8/160 (5%)	6/160 (3.8%)	RR 1.33 (0.47 to 3.76)	12 more per 1000 (from 20 fewer to 104 more)	VERY LOW	CRITICAL
Women's experience: women who were satisfied with the intervention												
1 (Peleg 2016)	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	121/160 (75.6%)	91/160 (56.9%)	RR 0.57 (0.41 to 0.78)	245 fewer per 1000 (from 125 fewer to 336 fewer)	MODERATE	IMPORTANT
Readmission into hospital												
1 (Peleg 2016)	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	3/160 (1.9%)	3/160 (1.9%)	RR 1 (0.20 to 4.88)	0 fewer per 1000 (from 15 fewer to 73 more)	VERY LOW	IMPORTANT

[1] The quality of the evidence was downgraded by one level as there was an unclear risk of bias in allocation concealment, and study participants and personnel were not blinded
[2] The quality of the evidence was downgraded by two levels as the 95% CI crossed 2 default MIDs (0.8 and 1.25)

Table 8: Comparison 4. Chlorhexidine-based alcohol skin preparation versus iodophor-based aqueous/alcohol skin preparation

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Chlorhexidine-based alcohol skin preparation	Iodophor-based aqueous/ alcohol skin preparation	Relative (95% CI)	Absolute	Quality	Importance
Surgical site infection												
4 (Kunkle 2015, Ngai 2015, Springel 2017, Tuuli 2016)	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	64/1528 (4.2%)	90/1531 (5.9%)	RR 0.71 (0.52 to 0.98)	17 fewer per 1000 (from 1 fewer to 28 fewer)	LOW	CRITICAL
Surgical site infection - iodophor-based aqueous skin preparation												
2 (Kunkle 2015, Springel 2017)	Randomised trials	Serious[3]	No serious inconsistency	No serious indirectness	Very serious[4]	None	23/482 (4.8%)	29/493 (5.9%)	RR 0.81 (0.48 to 1.38)	11 fewer per 1000 (from 31 fewer to 22 more)	VERY LOW	CRITICAL
Surgical site infection - iodophor-based alcohol skin preparation												
2 (Ngai 2015, Tuuli 2016)	Randomised trials	Serious[5]	No serious inconsistency	No serious indirectness	Serious[2]	None	41/1046 (3.9%)	61/1038 (5.9%)	RR 0.67 (0.45 to 0.98)	19 fewer per 1000 (from 1 fewer to 32 fewer)	LOW	CRITICAL
Adverse skin reaction												
2 (Springel 2017, Tuuli 2016)	Randomised trials	Serious[6]	No serious inconsistency	No serious indirectness	Very serious[4]	None	4/1033 (0.39%)	5/1046 (0.48%)	POR 0.81 (0.22 to 2.99)	1 fewer per 1000 (from 4 fewer to 10 more)	VERY LOW	IMPORTANT
Adverse skin reaction - iodophor-based aqueous skin preparation												
1 (Springel 2017)	Randomised trials	Serious[7]	No serious inconsistency	No serious indirectness	Very serious[4]	None	2/461 (0.43%)	1/471 (0.21%)	POR 1.99 (0.21 to 19.21)	2 more per 1000 (from 2 fewer to 39 more)	VERY LOW	IMPORTANT
Adverse skin reaction - iodophor-based alcohol skin preparation												
1 (Tuuli 2016)	Randomised trials	Serious[8]	No serious inconsistency	No serious indirectness	Very serious[4]	None	2/572 (0.35%)	4/575 (0.7%)	POR 0.51 (0.10 to 2.56)	3 fewer per 1000 (from 6	VERY LOW	IMPORTANT

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Chlorhexidine-based alcohol skin preparation	Iodophor-based aqueous/ alcohol skin preparation	Relative (95% CI)	Absolute	Quality	Importance
										fewer to 11 more)		
Endometritis												
2 (Springel 2017, Tuuli 2016)	Randomised trials	Serious[6]	No serious inconsistency	No serious indirectness	Very serious[4]	None	16/1033 (1.5%)	16/1046 (1.5%)	RR 1.01 (0.51 to 2.01)	0 more per 1000 (from 7 fewer to 15 more)	VERY LOW	IMPORTANT
Endometritis - iodophor-based aqueous skin preparation												
1 (Springel 2017)	Randomised trials	Serious[7]	No serious inconsistency	No serious indirectness	Very serious[4]	None	8/461 (1.7%)	5/471 (1.1%)	RR 1.63 (0.54 to 4.96)	7 more per 1000 (from 5 fewer to 42 more)	VERY LOW	IMPORTANT
Endometritis - iodophor-based alcohol skin preparation												
1 (Tuuli 2016)	Randomised trials	Serious[8]	No serious inconsistency	No serious indirectness	Very serious[4]	None	8/572 (1.4%)	11/575 (1.9%)	RR 0.73 (0.30 to 1.80)	5 fewer per 1000 (from 13 fewer to 15 more)	VERY LOW	IMPORTANT
Readmission into hospital												
2 (Springel 2017, Tuuli 2016)	Randomised trials	Serious[6]	No serious inconsistency	No serious indirectness	Serious[2]	None	24/1033 (2.3%)	34/1046 (3.3%)	RR 0.71 (0.43 to 1.19)	9 fewer per 1000 (from 19 fewer to 6 more)	LOW	IMPORTANT
Readmission into hospital - iodophor-based aqueous skin preparation												
1 (Springel 2017)	Randomised trials	Serious[7]	No serious inconsistency	No serious indirectness	Very serious[4]	None	5/461 (1.1%)	9/471 (1.9%)	RR 0.57 (0.19 to 1.68)	8 fewer per 1000 (from 15 fewer to 13 more)	VERY LOW	IMPORTANT
Readmission into hospital - iodophor-based alcohol skin preparation												
1 (Tuuli 2016)	Randomised trials	Serious[6]	No serious inconsistency	No serious indirectness	Very serious[4]	None	19/572 (3.3%)	25/575 (4.3%)	RR 0.76 (0.43 to 1.37)	10 fewer per 1000 (from 25 fewer to 16 more)	VERY LOW	IMPORTANT

[1] The quality of the evidence was downgraded by one level due to an unclear risk of bias in random sequence generation in one study; unclear allocation concealment in two studies; unclear blinding of outcome assessors in two studies; high risk of incomplete outcome data in one study and unclear risk of selective reporting in one study

[2] *The quality of the evidence was downgraded by one level as the 95% CI crossed 1 default MID threshold (0.8)*
[3] *The quality of the evidence was downgraded by one level due to an unclear risk of bias in random sequence generation, allocation concealment, blinding of outcome assessors and high risk of incomplete outcome data in one study, and unclear risk of selective reporting in one study*
[4] *The quality of the evidence was downgraded by two levels as the 95% CI crossed 2 default MID thresholds (0.8 and 1.25)*
[5] *The quality of the evidence was downgraded by one level due to an unclear risk of blinding of outcome assessors in one study and unclear risk of allocation concealment in one study*
[6] *The quality of the evidence was downgraded by one level due to an unclear risk of selective reporting in one study, and unclear risk of allocation concealment in one study*
[7] *The quality of the evidence was downgraded by one level due to an unclear risk of selective reporting*
[8] *The quality of the evidence was downgraded by one level due to an unclear risk of allocation concealment*

Table 9: Comparison 5. Iodophor-based aqueous vaginal preparation versus no vaginal/saline vaginal preparation

Quality assessment							Number of patients		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Iodophor-based aqueous vaginal preparation	No vaginal preparation/ saline vaginal cleansing	Relative (95% CI)	Absolute		
Wound infection												
7 (Asad 2017, Asghania 2011, Guzman 2002, Haas 2010, Memon 2011, Starr 2005, Yildrim 2012)	Randomised trials	Serious[1]	No serious inconsistency	Serious[2]	Serious[3]	None	35/1312 (2.7%)	45/1327 (3.4%)	RR 0.77 (0.50 to 1.19)	8 fewer per 1000 (from 17 fewer to 6 more)	VERY LOW	CRITICAL
Endometritis												
8 (Asad 2017, Asghania 2011, Guzman 2002, Haas 2010, Memon 2011, Reid	Randomised trials	Serious[4]	No serious inconsistency	Serious[2]	No serious imprecision	None	59/1529 (3.9%)	129/1540 (8.4%)	RR 0.40 (0.24 to 0.66)	50 fewer per 1000 (from 28 fewer to 64 fewer)	LOW	IMPORTANT

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Iodophor-based aqueous vaginal preparation	No vaginal preparation/ saline vaginal cleansing	Relative (95% CI)	Absolute	Quality	Importance
2001, Starr 2005, Yildrim 2012)												
Endometritis - Women with ruptured membranes												
3 (Guzman 2002, Haas 2010, Yildrim 2012)	Randomised trials	Serious[5]	No serious inconsistency	No serious indirectness	No serious imprecision	None	6/138 (4.3%)	24/134 (17.9%)	RR 0.27 (0.12 to 0.62)	131 fewer per 1000 (from 68 fewer to 158 fewer)	MODERATE	IMPORTANT
Endometritis - Women with intact membranes												
3 (Guzman 2002, Haas 2010, Yildrim 2012)	Randomised trials	Serious[5]	No serious inconsistency	No serious indirectness	Serious[3]	None	19/431 (4.4%)	32/426 (7.5%)	RR 0.64 (0.37 to 1.10)	27 fewer per 1000 (from 47 fewer to 8 more)	LOW	IMPORTANT
Endometritis - Women with mixed/unclear membranes												
5 (Asad 2017, Asghania 2011, Memon 2011, Reid 2001, Starr 2005)	Randomised trials	Serious[6]	Serious[7]	Serious[8]	Serious[9]	None	34/960 (3.5%)	73/980 (7.4%)	RR 0.37 (0.15 to 0.91)	47 fewer per 1000 (from 7 fewer to 63 fewer)	VERY LOW	IMPORTANT

[1] The quality of the evidence was downgraded by one level due to an unclear risk of bias in random sequence generation in three studies; unclear risk of allocation concealment in three studies; participants and personnel were not blinded in two studies; unclear risk of outcome assessment in one study; a high risk of random sequence generation in one study; a high risk of allocation concealment in one study; a high risk of other bias in one study and unclear risk of other bias in one study
[2] The quality of the evidence was downgraded by one level as four of the studies were conducted in low or middle income countries (Pakistan, Iran, and Turkey)
[3] The quality of the evidence was downgraded by one level as the 95% CI crossed 1 default MID threshold (0.8)
[4] The quality of the evidence was downgraded by one level due to an unclear risk of bias in random sequence generation in three studies; unclear risk of allocation concealment in three studies; participants and personnel were not blinded in three studies; unclear risk of blinding of outcome assessors in one study; high risk of random sequence

generation in one study; high risk of allocation concealment in one study; high risk of selective reporting in one study; high risk of other bias in one study and unclear risk of other bias in one study

[5] The quality of the evidence was downgraded by one level due to an unclear risk of bias in random sequence generation in one study; unclear risk of allocation concealment in one study; unclear risk of other bias in one study; study participants and personnel were not blinded in one study; unclear whether the outcome assessors were blinded in one study

[6] The quality of the evidence was downgraded by one level due to an unclear risk of bias in random sequence generation in two studies; unclear risk of allocation concealment in two studies; participants and personnel were not blinded in two studies; outcome assessors were not blinded in one study; unclear risk of incomplete outcome data in two studies; high risk of random sequence generation in one study; high risk of allocation concealment in one study; high risk of other bias in one study and high risk of selective reporting in one study

[7] The quality of the evidence was downgraded by one level as $I^2 > 70\%$

[8] The quality of the evidence was downgraded by one level as three of the studies were conducted in low or middle income countries (Iran, Pakistan)

[9] The quality of the evidence was downgraded by one level as the 95% CI crossed 1 default MID threshold (0.8)

Table 10: Comparison 6. Chlorhexidine-based aqueous vaginal preparation versus no vaginal cleansing/sterile water

Quality assessment							Number of patients		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Chlorhexidine-based aqueous vaginal preparation	No vaginal cleansing/ sterile water	Relative (95% CI)	Absolute		
Wound infection												
1 (Ahmed 2017)	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Very serious[2]	None	4/102 (3.9%)	7/98 (7.1%)	RR 0.55 (0.17 to 1.82)	32 fewer per 1000 (from 59 fewer to 59 more)	VERY LOW	CRITICAL
Endometritis												
2 (Ahmed 2017, Rouse 1997)	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	None	3/108 (2.8%)	13/106 (12.3%)	RR 0.22 (0.07 to 0.75)	96 fewer per 1000 (from 31 fewer to 114 fewer)	MODERATE	IMPORTANT

[1] The quality of the evidence was downgraded by one level due to an unclear risk of bias in allocation concealment and study participants and personnel were not blinded

[2] The quality of the evidence was downgraded by two levels as the 95% CI crossed 2 default MID thresholds (0.8 and 1.25)

Table 11: Comparison 7. Saline intra-abdominal irrigation versus no irrigation

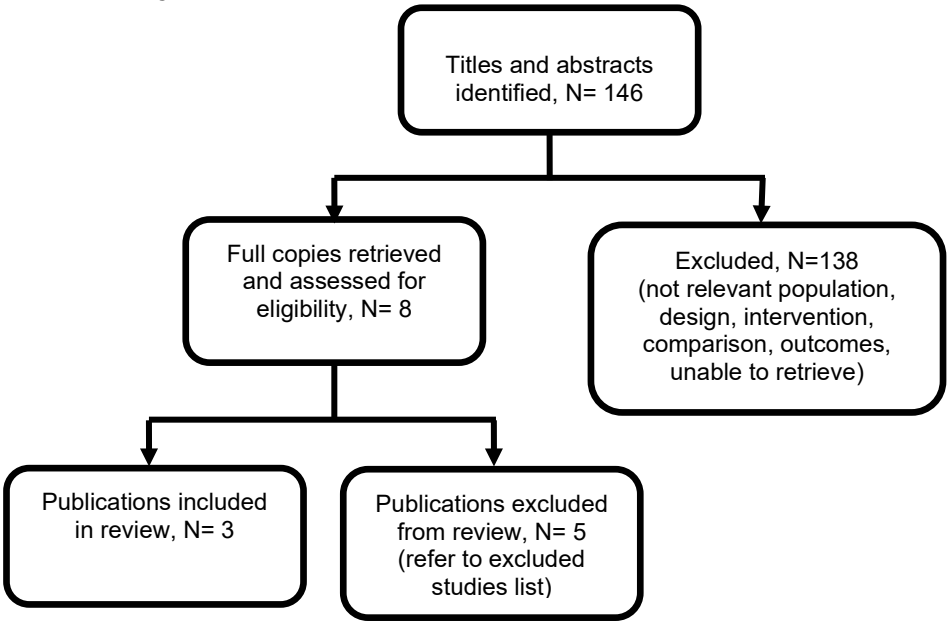
Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Saline intra-abdominal irrigation	No irrigation	Relative (95% CI)	Absolute	Quality	Importance
Wound infection												
2 (Harrigil 2003, Temizcan 2015)	Randomised trials	Serious[1]	No serious inconsistency	Serious[2]	Very serious[3]	None	2/312 (0.64%)	4/314 (1.3%)	RR 0.51 (0.09 to 2.73)	6 fewer per 1000 (from 12 fewer to 22 more)	VERY LOW	CRITICAL
Endometritis												
3 (Harrigil 2003, Temizcan 2015, Viney 2012)	Randomised trials	Serious[4]	No serious inconsistency	Serious[2]	Very serious[3]	None	43/422 (10.2%)	47/440 (10.7%)	RR 0.95 (0.64 to 1.40)	5 fewer per 1000 (from 38 fewer to 43 more)	VERY LOW	IMPORTANT

[1] The quality of the evidence was downgraded by one level due to an unclear risk of random sequence generation in one study; unclear risk of allocation concealment in one study; study participants and personnel were not blinded in two studies and there was an unclear risk of selective reporting in one study
[2] The quality of the evidence was downgraded by one level as one of the studies was conducted in a middle income country (Turkey)
[3] The quality of the evidence was downgraded by two levels as the 95% CI crossed 2 default MID thresholds (0.8 and 1.25)
[4] The quality of the evidence was downgraded by one level due to an unclear risk of bias in random sequence generation in one study; unclear risk of allocation concealment in one study; study participants and personnel were not blinded in three studies; outcome assessors were not blinded in one study and an unclear risk of selective reporting in one study

Appendix G – Economic evidence study selection

Economic evidence study selection for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

Figure 15: Study selection flow chart



Appendix H – Economic evidence tables

Economic evidence tables for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

Table 12: Economic evidence tables for methods to reduce infectious morbidity

Study details	Treatment strategies	Study population, design and data sources	Results	Comments
Author & year: Heard et al. 2017 **Country:** Australia **Type of economic analysis:** Cost Utility Analysis (CUA) **Source of funding:** Pilot study was funded by the Office of Health and Medical Research, Queensland Health, the National Health and Medical Research Council Centre of Research	**Intervention in detail:** Negative pressure wound therapy (NPWT) using PICO™ dressings. (Smith and Nephew, UK) **Comparator in detail:** Standard care consisting of Comfeel Plus® dressing (Coloplast, Denmark). Allocated dressings were applied by the operating obstetrician and their surgical assistant following wound closure.	**Population characteristics:** Obese women (BMI >30 kg/m^2) who have undergone a caesarean section. **Modelling approach:** Economic evaluation conducted alongside a pilot randomised controlled trial at one Australian hospital. **Source of base-line and effectiveness data:** The economic analysis was based on data from the pilot randomised controlled trial. The trial included 44 women in the NPWT arm and 43 women in the standard care arm. The incidence of surgical site infections (SSIs) was the primary clinical output in the clinical trial. **Source of cost data:** Resource use in hospital was based on data collected by direct observation or chart audit as part of the trial. Resource	**Mean cost per patient** • Standard care: AU$5,754 • NPWT: AU$5,887 • Difference: AU$133 **Mean QALYs per patient:** • Standard care: 0.066 QALYs • NPWT: 0.069 QALYs • Difference: 0.0031 QALYs **ICER:** AU$42,340 per QALY **Subgroup analysis:** Not conducted. **Deterministic sensitivity analysis:** A full set of deterministic sensitivity analyses does not appear to have been conducted. However, one alternative scenario is considered in which only post-discharge QALYs are	**Perspective:** Public health care provider perspective in Australia. **Currency:** Australian dollars (AU$) **Cost year:** 2014 **Time horizon:** Four weeks post discharge **Discounting:** Not conducted due to short time horizon. **Applicability:** The study was deemed to be only *partially applicable* to the UK because it considered

Study details	Treatment strategies	Study population, design and data sources	Results	Comments
Excellence in Nursing and a Gold Coast University Hospital Private Practice grant. Heard received funding from The University of Queensland under the UQ Summer Research Scholarship program.		use post-discharge was estimated using data collected during the weekly post-discharge telephone follow-ups with patients. Unit cost data were mostly based on data from databases of price schedules appropriate to the setting. The cost of NPWT was based on the list price from the manufacturer. The cost of dressings used in standard care was based on a hospital estimate. **Source of QoL data:** Health related QoL data were collected using the SF-12 survey, which was administered at baseline (prior to surgery) and at each of the weekly post-discharge follow-ups.	considered (ignoring QALY differences during the hospitalisation period). The ICER result (AU$49,736 per QALY) was found to be similar to the base case estimate. The authors report that the uncertainty around the point estimate was also similar to the uncertainty around the base case result. Therefore the inclusion or exclusion of the period of hospitalisation does not seem to be influential in determining the results of the analysis. **Probabilistic sensitivity analysis:** Probabilistic sensitivity analysis appears to have been conducted. However it is not clear which variables were included or how the values were varied. The PSA results were presented using a cost-effectiveness plane only. The majority of points were found to lie in the NE quadrant of the cost-effectiveness plane indicating that NPWT was more effective and more costly in most modelled scenarios. The proportion of points below the threshold of AU$50,000 per QALY (which the authors report is commonly accepted in Australia) is not presented. However, the threshold line is included on the cost-effectiveness plane and it appears	the perspective of the Australian health care system. **Limitations:** Whilst the study meets most of the requirements of an adequate economic evaluation (see Developing NICE guidelines: appendix H), some *potentially serious* limitations were noted. In particular, uncertainty was not explored as fully as it could have been due to a lack of deterministic sensitivity analysis. It is also unclear whether parameter uncertainty was fully captured in the PSA due to the limited details provided. **Other comments:** One of the authors reported a potential conflict as they had provided health economic advice to Coloplast Denmark under a small commercial research

Study details	Treatment strategies	Study population, design and data sources	Results	Comments
			that NPWT is cost-effective in around 50% of simulations.	contract that was paid to her Institution.
Author & year: Tuffaha et al. 2015 **Country:** Australia **Type of economic analysis:** Cost Utility Analysis (CUA) **Source of funding:** Lead author was supported by a National Health and Medical Research Council PhD scholarship through the Centre for Research Excellence in Nursing Interventions for Hospitalised Patients. Authors report that there were no potential conflicts of interest.	**Intervention in detail:** Negative pressure wound therapy (NPWT) using PICO™ dressings. (Smith and Nephew, UK) **Comparator in detail:** Standard care using hydrocolloid dressing (Comfeel plus®, Coloplast, Denmark) Treatment before wound dressings are applied would be the same in both groups i.e. they would receive the same antibiotic prophylaxis before surgery and would be operated using the same technique in the same setting.	**Population characteristics:** Hypothetical cohort of obese women (BMI ≥30 kg/m^2 before pregnancy) with an average age of 32 years old who underwent an elective caesarean section. **Modelling approach:** Decision tree conducted using TreeAge Pro 2013. **Source of base-line and effectiveness data:** Parameters were obtained from a systematic review of literature. Expert opinion was used when data was unavailable. Data from a recent pilot study conducted by the authors group was also incorporated by combining the results with the evidence already available. The pilot study included 92 obese women undergoing elective caesarean section who were randomised to receive NPWT or standard dressings. Baseline risk of SSI was estimated from the incidence of SSI in the control arm of the pilot trial in combination with four observational studies reporting SSI in obese women undergoing CS.	**Mean cost per patient** • Standard care: AU$570 • NPWT: AU$600 • Difference: AU$30 **Mean QALYs per patient:** • Standard care: 0.446 QALYs • NPWT: 0.448 QALYs • Difference: 0.002 QALYs **ICER:** AU$15,000 per QALY ICER value is not reported in study (results are reported using net monetary benefit) and has been estimated based on incremental cost and QALY values. **Subgroup analysis:** Not conducted. **Deterministic sensitivity analysis:** Deterministic sensitivity analysis was conducted, with variations in NPWT price, willingness to pay threshold, RR and technology lifetime explored. Results were presented using incremental net monetary benefit using a threshold of AU$50,000 per	**Perspective:** State Department of Health in Queensland, Australia (third party payer perspective) **Currency:** Australian dollars (AU$) **Cost year:** 2014 **Time horizon:** 6 months **Discounting:** Not conducted due to short time horizon. **Applicability:** The study was deemed to be only *partially applicable* to the UK because it considered the perspective of the Australian health care system. **Limitations:**

Study details	Treatment strategies	Study population, design and data sources	Results	Comments
		The relative effectiveness of NPWT in reducing SSIs was based on the RR estimated in the pilot study in combination with the RR from another RCT (Masden 2012). Masden considered a different population (high risk with co-morbidities undergoing a range of procedures). Data was combined using a Bayesian approach under which the RR from Masden et al. (i.e., prior information) was updated with the RR from the pilot trial resulting in an updated (i.e., posterior) RR. The probability for deep/organ SSI, death from deep/organ SSI and death from superficial SSIs was estimated from published studies. **Source of cost data:** The cost of NPWT PICO dressings and standard dressing were based on current market prices. Staff time costs to apply each dressing were estimated by combining staff time estimates (10 minutes for NPWT and 2 minutes for standard dressing) with the average hourly wage. The cost of treating superficial SSIs was obtained from a published study and included the cost of a general practitioner visit, 7 days of oral antibiotics and the cost of a test and/or swab. The cost of managing deep/organ SSIs was estimated from the 2009-2010	QALY. The incremental net monetary benefit was found to be positive in the vast majority of scenarios (indicating that NPWT is cost-effective. However the incremental net monetary benefit was found to be negative in one scenario (indicating standard care is cost-effective), in which the RR from the pilot trial alone was applied. **Probabilistic sensitivity analysis:** Probabilistic sensitivity analysis was conducted. It was found that NPWT had a 65% probability of being cost-effective at a willingness to pay threshold of AU$50,000 per QALY. **Value of information analysis:** Value of information analysis was also conducted. The expected value of perfect information (EVPI) for adopting NPWT was estimated to be AU$76 per patient. This results in a total of AU$2.7million for the population expected to benefit from NPWT over the next 10 years (35,000 people). The parameter with the highest value of information was the RR of SSI with NPWT. The results of the value of information analysis also showed that the optimal sample size of a future clinical trial was 200 patients in each arm.	The study was found to meet most of the requirements of an adequate economic evaluation (see Developing NICE guidelines: appendix H), and was adjudged to have only minor limitations. However, it should be noted that there is a lack of robust clinical evidence in this area which leads to uncertainty around the cost-effectiveness estimates **Other comments:**

Study details	Treatment strategies	Study population, design and data sources	Results	Comments
		Australian Refined Diagnosis Related Groups, item T61 (postoperative and posttrauma infection). This includes the cost of hospitalization, tests and/or swabs, and intravenous antibiotics for 7-14 days. Costs obtained in other price years were inflated to 2014 prices. **Source of QoL data:** The utilities in the model were based on EQ-5D-3L scores using preference weights for the Australian population. Utility scores for women undergoing caesarean section were based on a published study (Clemens 2014). Disutility values for the development of superficial and deep/organ SSIs were based on another published study (Lipsky 2012). It was assumed that the disutility duration would be 1 week for superficial SSIs and 2 weeks for deep/organ SSIs.		
Author & year: Hyldig et al. 2019 **Country:** Denmark **Type of economic analysis:** Cost Utility Analysis (CUA)	**Intervention in detail:** Incisional negative pressure wound therapy (iNPWT) using PICO™ dressings. (Smith and Nephew, UK) **Comparator in detail:**	**Population characteristics:** Women with a BMI ≥30 kg/m^2 before pregnancy) who had a planned or emergency caesarean birth. **Modelling approach:** Economic evaluation alongside an RCT **Source of base-line and effectiveness data:**	**Mean cost per patient** • Standard dressing: €5,841 • NPWT: €5,794 • Difference: -€47 (95% CI: -€425 to €330) **Mean QALYs per patient:** • Standard care: 0.856 QALYs • NPWT: 0.863 QALYs • Difference: 0.007 QALYs (95% CI: -0.008 to 0.022)	**Perspective:** Danish healthcare perspective **Currency:** Euro (€) Costs were obtained in DKK and converted to

Study details	Treatment strategies	Study population, design and data sources	Results	Comments
Source of funding: The RCT was funded by the University of Southern Denmark, Odense University Hospital, the Region of Southern Denmark, Lundbeckfonden, and a grant from the iNPWT device manufacturer Smith & Nephew. Several authors received funding or honoraria from Smith and Nephew	Standard postoperative dressings for prevention of SSI after caesarean birth	Estimates of incremental effectiveness and costs were derived from the intervention and control arms in the study. **Source of cost data:** Micro costing was used to provide a cost for each study participant. The costing consisted of 4 components: 1. Hospital costs 2. Contacts with general practitioners 3. Antibiotic treatment 4. Postoperative dressing Resource use data was obtained from the Danish national databases and unit costs were obtained from the cost database. The cost of NPWT PICO dressings was based on the device cost and the additional time needed to apply the dressing which was estimated at 8 minutes. **Source of QoL data:** The utilities in the model were estimated using the EQ-5D-5L instrument which was sent to all study participants 30 days after their caesarean birth. The EQ-5D index values were based on the Danish crosswalk value sets for the EQ-5D-5L questionnaire	**ICER:** NPWT dominates. **Subgroup analysis:** <u>Women with a BMI ≥30 kg/m^2 and BMI <35 kg/m^2</u> **Mean cost per patient** • Standard dressing: €5,481 • NPWT: €5,636 • Difference: €155 (95% CI: €146 to €456) **Mean QALYs per patient:** • Standard care: 0.854 QALYs • NPWT: 0.860 QALYs • Difference: 0.006 QALYs (95% CI: 0.015 to 0.026) **ICER:** €29,005 <u>Women with a BMI ≥35 kg/m^2</u> **Mean cost per patient** • Standard dressing: €6,296 • NPWT: €5,957 • Difference: -€339 (95% CI: -€1,069 to -€391) **Mean QALYs per patient:** • Standard care: 0.858 QALYs • NPWT: 0.867 QALYs	Euros (€1 = DKK 7.46 and €1 = US$1.11). **Cost year:** 2015 **Time horizon:** 6 months **Discounting:** Not conducted due to short time horizon for costs and benefits. **Applicability:** The study was deemed to be only *partially applicable* to the UK because it considered the perspective of the Danish health care system. **Limitations:** The study was found to meet most of the requirements of an adequate economic evaluation (see Developing NICE guidelines: appendix H), but was adjudged to have major limitations. Sub-group

Study details	Treatment strategies	Study population, design and data sources	Results	Comments
			• Difference: 0.008 QALYs (95% CI: 0.015 to 0.031) **ICER:** NPWT dominates **Deterministic sensitivity analysis:** A number of scenario analyses were run to explore different time horizons for costs and QALYs and to assess the implications of excluding a patient outlier and missing data. However, these did not lead to substantially different results with iNPWT remaining dominant or having low ICERs. **Probabilistic sensitivity analysis:** Probabilistic sensitivity analysis was conducted. For the base case analysis it found that NPWT had a 92.8% probability of being cost-effective at a willingness to pay threshold of €30,000 per QALY and a 65.4% probability of being cost saving.	analysis was not presented in the paper that reported the results of the RCT and therefore there is some concern that the analysis may reflect 'data mining' although the sub-group analysis undertaken is reasonable from a clinical perspective. Extrapolating health state utilities for a period of 12 months could lead to over estimation of QALY gains. There are also some limitations with respect to the way that missing data is handled. Finally, the study was partly funded by the manufacturer and therefore conflicts of interest may exist. **Other comments:** This study was also reviewed for NICE medical technology guidance (MTG43)

Appendix I – Economic evidence profiles

Economic evidence profiles for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women undergoing CS?

Table 13: Economic evidence profiles for methods to reduce infectious morbidity

Study	Population	Comparators	Costs	Effects	Incr costs	Incr effects	ICER	Uncertainty	Applicability and limitations
Heard 2017	Obese women (BMI >30 kg/m2) who have undergone a caesarean section.	Standard care	AU$5,754	0.066 QALYs	Reference			A full set of deterministic sensitivity analyses was not conducted. However, one alternative scenario is considered in which only post-discharge QALYs are considered. The result was found to be similar to the base case indicating that the parameter is not influential in determining results. Probabilistic sensitivity analysis was conducted. However, it is not clear which variables were included or how the values were varied. PSA results were presented using a cost-effectiveness plane only. The majority of points were found to lie in the NE quadrant of the cost-effectiveness plane indicating that NPWT was more effective and more costly in most modelled scenarios.	The study was deemed to be only partially applicable to the UK because it considered the perspective of the Australian health care system. Some potentially serious limitations were noted. In particular, uncertainty was not explored as fully as it could have been due to a lack of deterministic sensitivity analysis. It is also unclear whether parameter uncertainty was fully captured in the PSA due to the limited details provided.
		NPWT	AU$5,887	0.069 QALYs	AU$133	0.0031 QALYs	AU$42,340 per QALY		
	Comments:								

Study	Population	Comparators	Costs	Effects	Incr costs	Incr effects	ICER	Uncertainty	Applicability and limitations
Tuffaha 2015	Obese women (BMI >30 kg/m2) who have undergone a caesarean section.	Standard care	AU$570	0.446 QALYs	Reference			Deterministic sensitivity analysis was conducted, with variations in NPWT price, willingness to pay threshold, RR and technology lifetime explored. NPWT was only found to not be cost-effective in one scenario in which an alternative RR for SSIs with NPWT was applied. Probabilistic sensitivity analysis was also conducted. It was found that NPWT had a 65% probability of being cost-effective at a willingness to pay threshold of AU$50,000 per QALY.	The study was deemed to be only partially applicable to the UK because it considered the perspective of the Australian health care system. The study was adjudged to have only minor limitations. However, it should be noted that there is a lack of robust clinical evidence in this area which leads to uncertainty around the cost-effectiveness estimates
		NPWT	AU$600	0.448 QALYs	AU$30	0.002 QALYs	AU$15,000 per QALY		
	Comments: ICER value is not reported in study (results are reported using net monetary benefit). ICER value above has been estimated based on incremental cost and QALY values reported in the study.								
Hyldig 2019	Obese women (BMI >30 kg/m2) who have undergone a caesarean section.	Standard care	€5,841	0.856 QALYs	Reference			Deterministic sensitivity analysis was conducted to explore different scenarios with respect to costs and QALYs and to assess the implications of missing data. NPWT remained either dominant or with a low ICER	The study was deemed to be only partially applicable to the UK because it considered the perspective of the Danish health care system.

Study	Population	Comparators	Costs	Effects	Incr costs	Incr effects	ICER	Uncertainty	Applicability and limitations
								Probabilistic sensitivity analysis found that NPWT had a 92.8% probability of being cost-effective at a willingness to pay threshold of €30,000 per QALY.	The study was adjudged to have only major limitations.
		NPWT	€5,794	0.863 QALYs	-€47	0.007 QALYs	Dominant		
	Comments: ICER value is not reported in study (results are reported using net monetary benefit). ICER value above has been estimated based on incremental cost and QALY values reported in the study.								

Appendix J – Economic analysis

Economic evidence analysis for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

Cost-minimisation analysis of NPWT compared to standard dressing in women with having a caesarean birth

An ad-hoc cost-minimisation and cost-utility analysis was undertaken for this guideline in order to give the committee a clearer understanding of the contribution of different BMI categories in the NHS context. The committee considered this of particular relevance to UK practice where most clinicians reserve the use of NPWT for those women with BMI ≥ 35 kg/m^2.

The data used in the ad-hoc analysis are shown in Table 14.

Table 14: Data inputs for ad-hoc analysis of costs on NPWT by BMI sub-group

Variable	Value	Source
Incremental costs of NPWT[a]	£136	NICE (MTG43)
Cost of surgical site infection	£4,192	Jenks (2014)[b]
Baseline risk (BMI ≥ 30 to BMI < 35)	0.067 (α=16; β=223)	Hyldig (2019)[c]
Baseline risk (BMI ≥ 35)	0.122 (α=23; β=166)	Hyldig (2019)[c]
Relative risk	0.79 (95% CI 0.61 to 1.02)	Figure 2[d]
QALY gain from averted SSI	0.008	NG125[e]

(a) Incremental cost relative to standard dressing
(b) Updated to 2018/19 price year using the NHS Cost Inflation Index (https://kar.kent.ac.uk/79286/11/UCFinalFeb20.pdf)
(c) See Figure 19 in Appendix M
(d) Meta-analysis of studies included in the clinical review
(e) Data on health state utilities from the NICE guideline on Surgical Site Infection (NG125 - https://www.nice.org.uk/guidance/ng125/evidence/health-economic-model-report-pdf-6727106989) was used to estimate the QALY gain from an averted SSI based on assumptions of the time taken to return to baseline utility after surgery in patients with and without SSI

i. Cost-minimisation analysis

A probabilistic sensitivity analysis (PSA) with 10,000 simulations was undertaken for each sub-group (BMI ≥ 30 kg/m^2 to BMI < 35 kg/m^2; BMI ≥ 35 kg/m^2). The baseline risk was sampled using a Beta distribution and relative risk was sampled using a log-normal distribution. For women with a BMI ≥ 30 kg/m^2 to BMI < 35 kg/m^2 NPWT led to a mean net increase in costs of £77 when compared to standard dressing. The PSA suggested that there was only a 2.2% chance that NPWT was cost saving relative to standard dressing. In the sub-group of women with a BMI ≥ 35 kg/m^2 the ad-hoc analysis suggested that NPWT resulted in a £32 increase in mean net costs and had a 28.2% probability of being cheaper than standard dressing. The estimated probability distribution for the increase in costs with NPWT relative to standard dressing for each of the sub-groups is given in Figure 16 and Figure 17 respectively.

Figure 16: Probability distribution for net increase in costs with NPWT relative to standard dressing in women with a BMI ≥ 30 kg/m² to BMI < 35 kg/m²

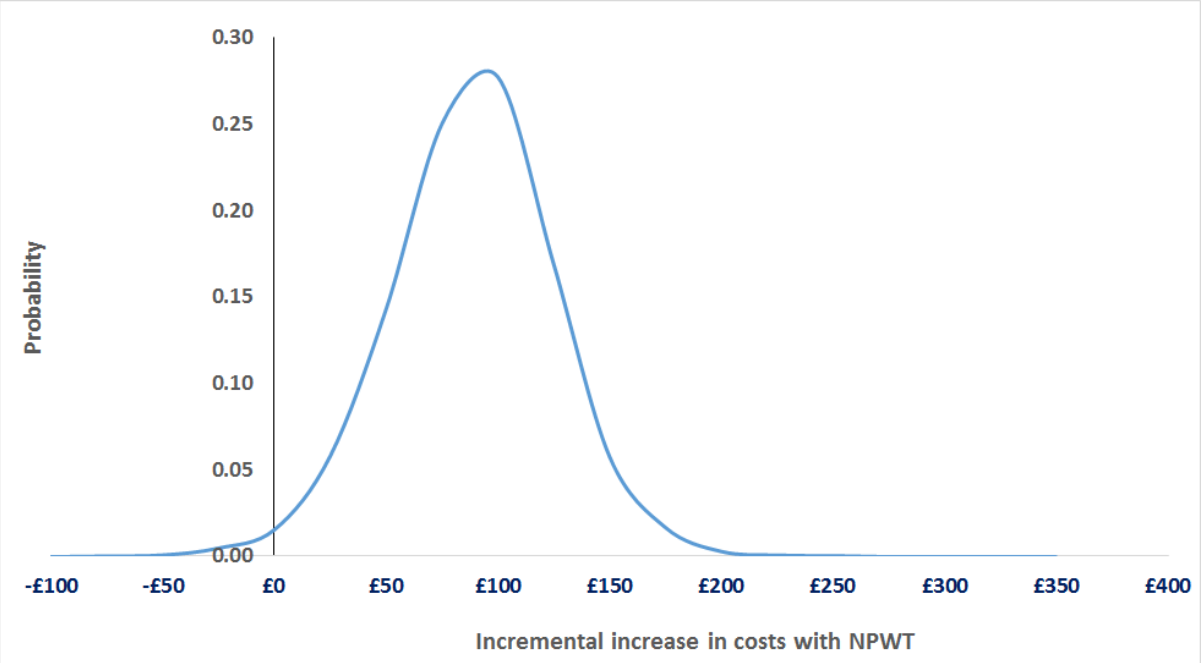
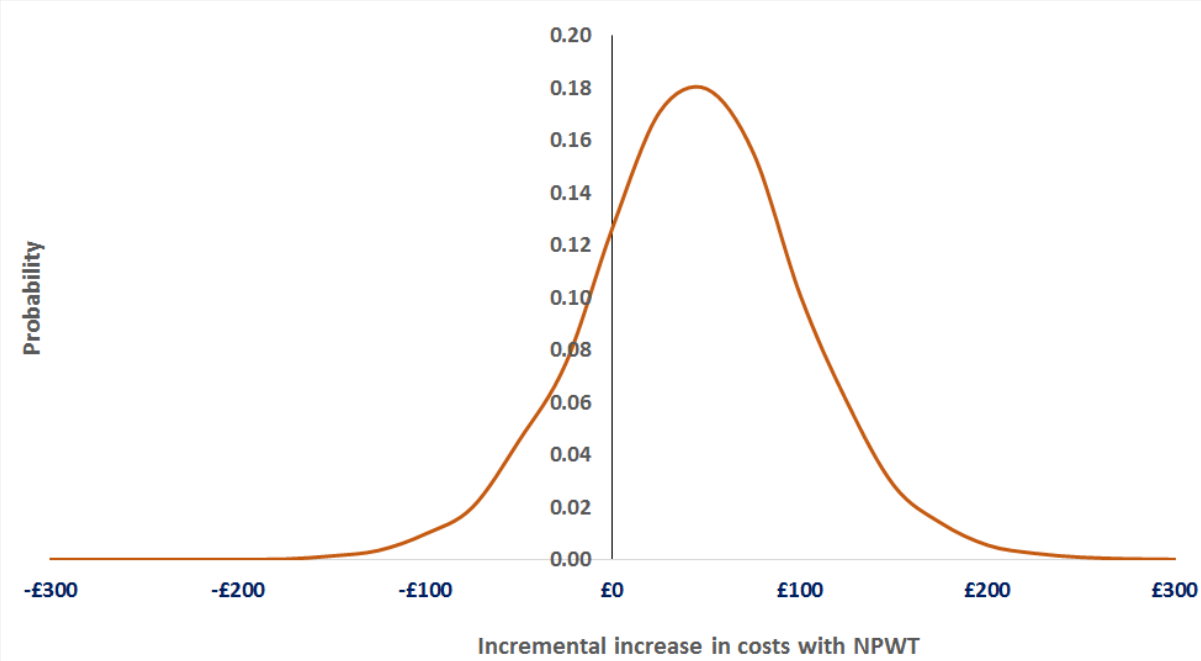


Figure 17: Probability distribution for net increase in costs with NPWT relative to standard dressing in women with a BMI ≥ 35 kg/m²



ii. Cost-utility analysis

A PSA was undertaken for each of the sub-groups (BMI ≥ 30 kg/m² to BMI < 35 kg/m²; BMI ≥ 35 kg/m²) and the results are summarised in Table 15 and the cost-effectiveness analysis curves in Figure 18 and Figure 19.

Table 15: Summary results of cost-utility analysis of NPWT compared to standard dressing

Sub-group	Mean incremental net monetary benefit	Probability cost-effective [a]
BMI ≥ 30 to BMI < 35	-£74	3.0%
BMI ≥ 35	-£29	30.4%

(a) Based on a cost-effectiveness threshold of £20,000 per QALY

Figure 18: Cost-effectiveness acceptability curve for NPWT compared to standard dressing in women with BMI ≥ 30 kg/m² to BMI < 35 kg/m²

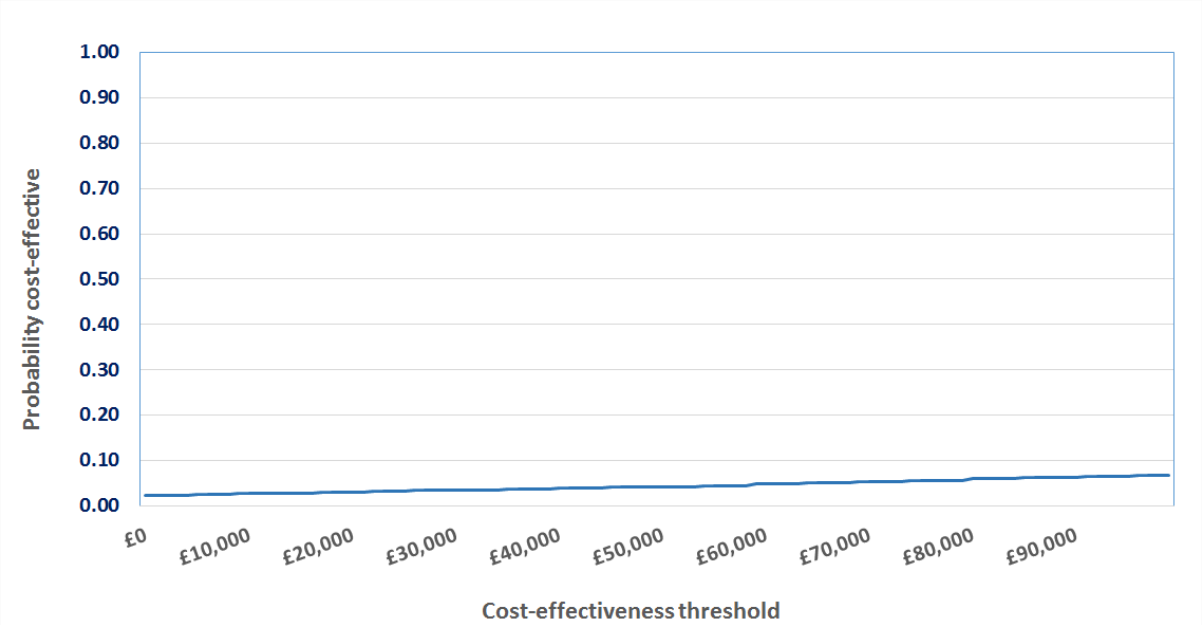
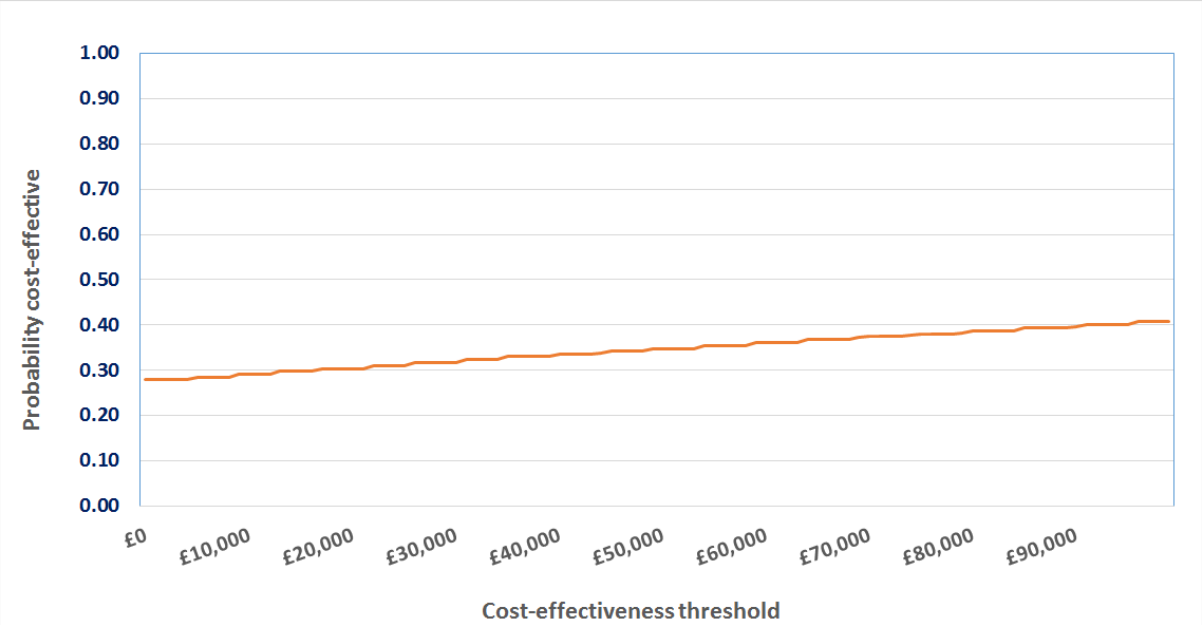


Figure 19: Cost-effectiveness acceptability curve for NPWT compared to standard dressing in women with BMI ≥ 35 kg/m²



The committee were aware that that a NICE medical technology guidance (MTG43) considered Hyldig 2019 a weak publication, based on the method for eliciting QALYs and concerns around missing data for costs in the base case analysis. However, these limitations were not relevant to the findings of the ad-hoc analysis undertaken.

Appendix K – Excluded studies

Excluded clinical and economic studies for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women having a caesarean birth?

Clinical studies:

Table 16: Excluded studies and reasons for their exclusion

Study	Reason for Exclusion
Chlorhexidine vaginal wipes prior to elective cesarean section: does it reduce infectious morbidity? A randomized trial, Journal of Maternal-Fetal & Neonatal Medicine, 1-4, 2016	Included in Haas 2018
Abdallah, A. A., Evaluation of the risk of postcesarean endometritis with preoperative vaginal preparation with povidone-iodine: A randomized controlled study, Middle East Fertility Society Journal, 20, 246-250, 2015	This paper has been retracted by the journal
Agbunag, R., Preoperative vaginal preparation with povidone-iodine decreases the risk of post-cesarean endometritis, American Journal of Obstetrics and Gynecology, 184, S182, 2001	Abstract
Ahmed, Magdy R., Aref, Nisreen K., Sayed Ahmed, Waleed A., Arain, Farzana R., Chlorhexidine vaginal wipes prior to elective cesarean section: does it reduce infectious morbidity? A randomized trial, The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 30, 1484-1487, 2017	Included in Haas 2018
Anonymous,, Should negative pressure wound therapy be used at the time of caesarean in obese women?, BJOG: An International Journal of Obstetrics and Gynaecology, 126, 636, 2019	Commentary
Asad, S., Batool Mazhar, S., Khalid Butt, N., Habiba, U., Vaginal cleansing prior to caesarean section and postoperative infectious morbidity, BJOG: An International Journal of Obstetrics and Gynaecology, 124, 45, 2017	Included in Haas 2018
Asghania,M., Mirblouk,F., Shakiba,M., Faraji,R., Preoperative vaginal preparation with povidone-iodine on post-caesarean infectious morbidity, Journal of Obstetrics and Gynaecology, 31, 400-403, 2011	Included in Haas 2018
Aslan Cetin, Berna, Aydogan Mathyk, Begum, Barut, Sibel, Koroglu, Nadiye, Zindar, Yelda, Konal, Merve, Atis Aydin, Alev, The impact of subcutaneous irrigation on wound complications after cesarean sections: A prospective randomised study, European journal of obstetrics, gynecology, and reproductive biology, 227, 67-70, 2018	Study was conducted in a low/middle income country (Turkey)
Atkinson, J. A., McKenna, K. T., Barnett, A. G., McGrath, D. J., Rudd, M., A randomized, controlled	Intervention not considered in the protocol (paper tape)

Study	Reason for Exclusion
trial to determine the efficacy of paper tape in preventing hypertrophic scar formation in surgical incisions that traverse Langer's skin tension lines, Plastic and reconstructive surgery, 116, 1648â□□56; discussion 1657â□□8, 2005	
Ausbeck, E. B., Impact of skin preparation type on postcesarean infection in the setting of adjunctive azithromycin prophylaxis, American Journal of Obstetrics and Gynecology, 218, S524-S525, 2018	Abstract
Bennett, K., Kellett, W., Braun, S., Spetalnick, B., Huff, B., Slaughter, J., Carroll, M., Silver ion-eluting dressings for prevention of post cesarean wound infection: A randomized, controlled trial, American Journal of Obstetrics and Gynecology, 208 (1 SUPPL.1), S337, 2013	Abstract
Bolte, M., Walker, T., Implementation of a bundled approach to reduce surgical site infections with caesarean sections in a rural NSW Referral Hospital. The highs and lows of the project at the half way mark, Infection, Disease and Health, 23, S12, 2018	Study design - non-randomised
Brown, T. R., Ehrlich, C. E., Stehman, F. B., Golichowski, A. M., Madura, J. A., Eitzen, H. E., A clinical evaluation of chlorhexidine gluconate spray as compared with iodophor scrub for preoperative skin preparation, Surgery, gynecology & obstetrics, 158, 363-6, 1984	Trial focused on general surgery, with cases of C-section, but the results were not reported separately for C-section
Caissutti, Claudia, Saccone, Gabriele, Zullo, Fabrizio, Quist-Nelson, Johanna, Felder, Laura, Ciardulli, Andrea, Berghella, Vincenzo, Vaginal Cleansing Before Cesarean Delivery: A Systematic Review and Meta-analysis, Obstetrics and Gynecology, 130, 527-538, 2017	Most of the included studies overlap with those included in Haas 2018, with the exception of 6 studies, which were either developed in a low/middle income country or used antibiotics for vaginal cleansing before CS
Connery, S., Louis, J., Downes, K. L., Odibo, L., Raitano, O., Yankowitz, J., A prospective randomized study assessing cesarean wound infections comparing silver dressings to gauze dressings, Obstetrics and Gynecology, 131, 34S-35S, 2018	Abstract
Cordtz, T., Schouenborg, L., Laursen, K., Daugaard, H. O., Buur, K., Munk Christensen, B., Sederberg-Olsen, J., Lindhard, A., Baldur, B., Engdahl, E., The effect of incisional plastic drapes and redisinfection of operation site on wound infection following caesarean section, The Journal of hospital infection, 13, 267-72, 1989	Compared the use of drape versus no drape
Dahlke,J.D., Mendez-Figueroa,H., Rouse,D.J., Berghella,V., Baxter,J.K., Chauhan,S.P., Evidence-based surgery for cesarean delivery: An updated systematic review, American Journal of Obstetrics and Gynecology, 209, 294-306, 2013	Other interventions than the ones considered in the protocol have been included
Dashow,E.E., Read,J.A., Coleman,F.H., Randomized comparison of five irrigation solutions at cesarean section, Obstetrics and Gynecology, 68, 473-478, 1986	Study compared different types of antibiotics with no treatment
De Jonge, S. W., Boldingh, Q. J. J., Solomkin, J. S., Allegranzi, B., Egger, M., Dellinger, E. P.,	Systematic review focused on general surgery

Study	Reason for Exclusion
Boermeester, M. A., Systematic review and meta-analysis of randomized controlled trials evaluating prophylactic intra-operative wound irrigation for the prevention of surgical site infections, Surgical Infections, 18, 508-519, 2017	
Elbohoty, A. E., Gomaa, M. F., Abdelaleim, M., Abd-El-Gawad, M., Elmarakby, M., Diathermy versus scalpel in transverse abdominal incision in women undergoing repeated cesarean section: a randomized controlled trial, Journal of Obstetrics and Gynaecology Research, 41, 1541â□□1546, 2015	Study developed in a low/middle income country (Egypt)
Fahmi, M. N., Hadiati, D. R., Widad, S., Comparison of skin preparation with alcohol-chlorhexidine versus alcohol-povidone iodine on surgical site infection following caesarean section, Journal of Obstetrics and Gynaecology Research, 43, 38, 2017	Abstract
Givens, Vanessa A., Lipscomb, Gary H., Meyer, Norman L., A randomized trial of postoperative wound irrigation with local anesthetic for pain after cesarean delivery, American Journal of Obstetrics and Gynecology, 186, 1188-91, 2002	Intervention was subcutaneous rather than intra-abdominal irrigation
Göymen, A., Å□imÅŸek, Y., Özdurak, HÄ°, Özkaplan, Å□E, Akpak, Y. K., Özdamar, Ö, Oral, S., Effect of vaginal cleansing on postoperative factors in elective caesarean sections: a prospective, randomised controlled trial, Journal of maternal-fetal & neonatal medicine, 30, 442â□□445, 2017	Included in Haas 2018
Gungorduk, K., Asicioglu, O., Celikkol, O., Ark, C., Tekirdag, A. I., Does saline irrigation reduce the wound infection in caesarean delivery?, Journal of Obstetrics & Gynaecology, 30, 662-6, 2010	Intervention was subcutaneous rather than intra-abdominal irrigation
Guzman,M.A., Prien,S.D., Blann,D.W., Post-cesarean related infection and vaginal preparation with povidone-iodine revisited, Primary Care Update for Ob/Gyns, 9, -209, 2002	Included in Haas 2018
Haas, David M., Pazouki, Fatemeh, Smith, Ronda R., Fry, Amy M., Podzielinski, Iwona, Al-Darei, Sarah M., Golichowski, Alan M., Vaginal cleansing before cesarean delivery to reduce postoperative infectious morbidity: a randomized, controlled trial, American Journal of Obstetrics and Gynecology, 202, 310.e1-6, 2010	Included in Haas 2018
Hadiati, Diah R., Hakimi, Mohammad, Nurdiati, Detty S., Ota, Erika, Skin preparation for preventing infection following caesarean section, Cochrane Database of Systematic Reviews, 2014	The included studies in this review had either irrelevant interventions or outcomes. Cordtz 1989 and Ward 2001 compared the use of drape versus no drape; Magann 1993 compared povidone iodine with PCMX, which is not a relevant intervention. Pello 1990 does not have any relevant outcome; Lorenz 1989 did not use drape in the control group, and Kunkle 2014 was included in Tolcher 2018 as a full text
Harrigill, Keith M., Miller, Hugh S., Haynes, Deborah E., The effect of intraabdominal irrigation	Included in Eke 2016

Study	Reason for Exclusion
at cesarean delivery on maternal morbidity: a randomized trial, Obstetrics and Gynecology, 101, 80-5, 2003	
Hodgetts Morton, V., Wilson, A., Hewitt, C., Weckesser, A., Farmer, N., Lissauer, D., Hardy, P., Morris, R. K., Chlorhexidine vaginal preparation versus standard treatment at caesarean section to reduce endometritis and prevent sepsis-a feasibility study protocol (the PREPS trial), Pilot and feasibility studies, 4, 84, 2018	Study protocol
Huang, Huaping, Li, Guirong, Wang, Haiyan, He, Mei, Optimal skin antiseptic agents for prevention of surgical site infection in cesarean section: a meta-analysis with trial sequential analysis, The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 31, 3267-3274, 2018	Observational studies have also been included
Hussamy, D. J., Wortman, A. C., McIntire, D. D., Leveno, K. J., Casey, B. M., Roberts, S. W., A randomized trial of closed incision negative pressure therapy in morbidly obese women undergoing cesarean delivery, American Journal of Obstetrics and Gynecology, 218, S35, 2018	Abstract
Hyldig, N., Vinter, C. A., Kruse, M., Mogensen, O., Bille, C., Sorensen, J. A., Lamont, R. F., Wu, C., Heidemann, L. N., Ibsen, M. H., Laursen, J. B., Ovesen, P. G., Rorbye, C., Tanvig, M., Joergensen, J. S., Prophylactic incisional negative pressure wound therapy reduces the risk of surgical site infection after caesarean section in obese women: a pragmatic randomised clinical trial, BJOG : an international journal of obstetrics and gynaecology, 126, 628-635, 2019	Duplicate
Hyldig, Nana, Moller, Soren, Joergensen, Jan Stener, Bille, Camilla, Clinical Evaluation of Scar Quality Following the Use of Prophylactic Negative Pressure Wound Therapy in Obese Women Undergoing Cesarean Delivery: A Trial-Based Scar Evaluation, Annals of plastic surgery, 85, e59-e65, 2020	Post hoc additional single centre analysis, overall quality of life already reported in main study
Iqbal, P., ruparelia, B. A., Robson, P., Johnson, I. R., Collins, M. F., Clinical evaluation of the use of povidone-iodine powder in caesarean section wounds, Journal of Obstetrics and Gynaecology, 10, 41-42, 1989	Not a randomised trial
Keblawi, H. A., Dawley, B. L., Does saline irrigation in peritoneal cavity at the time of a non-scheduled cesarean section reduce maternal morbidity, American Journal of Obstetrics and Gynecology, 195, S96, 2006	Abstract
Kesani, V., Talasila, S., Chlorhexidine-alcohol versus povidone-iodinealcohol for surgical-site antisepsis in caesarean section, BJOG: An	Abstract

Study	Reason for Exclusion
International Journal of Obstetrics and Gynaecology, 125, 147-148, 2018	
Kovavisarach, Ekachai, Jirasettasiri, Phuntip, Randomised controlled trial of perineal shaving versus hair cutting in parturients on admission in labor, Journal of the Medical Association of Thailand = Chotmaihet thangphaet, 88, 1167-71, 2005	Women undergoing C- section were excluded
Kremer, P. A., McMullen, K., Russo, A. J., Babcock, H., Warren, D., What a difference a day makes: Removing post-operative dressing on day 2, American Journal of Infection Control, 42, S128-S129, 2014	Abstract
Kunkle, Cynelle M., Marchan, Jennifer, Safadi, Sara, Whitman, Stephanie, Chmait, Ramen H., Chlorhexidine gluconate versus povidone iodine at cesarean delivery: a randomized controlled trial, The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 28, 573-7, 2015	Included in Tolcher 2018
Lee,N., Martensson,L.B., Homer,C., Webster,J., Gibbons,K., Stapleton,H., Santos,N.D., Beckmann,M., Gao,Y., Kildea,S., Impact on Caesarean section rates following injections of sterile water (ICARIS): A multicentre randomised controlled trial, BMC Pregnancy and Childbirth, 13 , 2013. Article Number, -, 2013	Study protocol
Liu, Z., Dumville, J. C., Norman, G., Westby, M. J., Blazeby, J., McFarlane, E., Welton, N. J., O'Connor, L., Cawthorne, J., George, R. P., Crosbie, E. J., Rithalia, A. D., Cheng, H. Y., Intraoperative interventions for preventing surgical site infection: An overview of Cochrane Reviews, Cochrane Database of Systematic Reviews, 2018, CD012653, 2018	Systematic review focused on general surgery
Lorenz, R. P., Botti, J. J., Appelbaum, P. C., Bennett, N., Skin preparation methods before cesarean section. A comparative study, The Journal of reproductive medicine, 33, 202-4, 1988	Compared the use of drape versus no drape
Magann, E. F., Dodson, M. K., Ray, M. A., Harris, R. L., Martin, J. N., Jr., Morrison, J. C., Preoperative skin preparation and intraoperative pelvic irrigation: impact on post-cesarean endometritis and wound infection, Obstetrics and Gynecology, 81, 922-5, 1993	PCMX was used in the intervention group
Mahomed, K., Ibiebele, I., Buchanan, J., Povidone-Iodine wound irrigation prior to skin closure at caesarean section to prevent surgical site infection: A randomised controlled trial, BJOG: An International Journal of Obstetrics and Gynaecology, 123, 146-147, 2016	Abstract
Mahomed, K., Ibiebele, I., Buchanan, J., The Betadine trial - Antiseptic wound irrigation prior to skin closure at caesarean section to prevent surgical site infection: A randomised controlled trial,	This paper looks at wound irrigation at time of skin closure, which is not a relevant intervention

Study	Reason for Exclusion
Australian and New Zealand Journal of Obstetrics and Gynaecology, 56, 301-306, 2016	
Maiwald, Matthias, Skin Preparation for Prevention of Surgical Site Infection After Cesarean Delivery: A Randomized Controlled Trial, Obstetrics and Gynecology, 129, 750-751, 2017	Response letter
Maneepitaksanit, R., Ubolsaard, S., A randomized trial of surgical scrubbing with a brush compared to antiseptic soap alone in elective cesarean section, Chon buri hospital journal, 28, 17â□□23, 2003	Study developed in low/middle income country (Thailand)
Martin, E. K., Beckmann, M. M., Barnsbee, L. N., Halton, K. A., Merollini, K. M. D., Graves, N., Best practice perioperative strategies and surgical techniques for preventing caesarean section surgical site infections: a systematic review of reviews and meta-analyses, BJOG: An International Journal of Obstetrics and Gynaecology, 125, 956-964, 2018	No relevant interventions have been included
Martin, E., Beckmann, M., Merollini, K., Halton, K., Graves, N., An infection prevention bundle to reduce the risk of surgical site infection at caesarean section: Recommendations from a systematic review, Australian and New Zealand Journal of Obstetrics and Gynaecology, 57, 7, 2017	Other interventions than the ones included in the protocol have been included
Memon, Shahneela, Qazi, Roshan Ara, Bibi, Seema, Parveen, Naheed, Effect of preoperative vaginal cleansing with an antiseptic solution to reduce post caesarean infectious morbidity, JPMA. The Journal of the Pakistan Medical Association, 61, 1179-83, 2011	Included in Haas 2018
Murray, C., Marchan, J., Safadi, S., Opper, N., Yedigarova, L., Chmait, R., Efficacy of chlorhexidine gluconate versus povidone iodine for skin disinfection at cesarean section: A randomized controlled trial, American Journal of Obstetrics and Gynecology, 206, S152, 2012	Abstract
Najafian, Aida, Fallahi, Soghra, Khorgoei, Tahereh, Ghahiri, Ataollah, Alavi, Azin, Rajaei, Minoo, Eftekhaari, Tasnim Eqbal, Role of soap and water in the treatment of wound dehiscence compared to normal saline plus povidone-iodine: A randomized clinical trial, Journal of education and health promotion, 4, 86, 2015	Trial focused on general surgery, with cases of C-section, but the results were not reported separately for C-section
Nct,, Prospective Study on Cesarean Wound Outcomes, Https://clinicaltrials.gov/show/nct01927211, 2013	This study has not been published
Nct,, Prevention of Wound Complications After Cesarean Delivery in Obese Women Utilizing Negative Pressure Wound Therapy, Https://clinicaltrials.gov/show/nct00654641, 2008	This study has not been published
Nct,, PROphylactic Wound VACuum Therapy to Decrease Rates of Cesarean Section in the Obese Population, Https://clinicaltrials.gov/show/nct02128997, 2014	This study has not been published
Nct,, Silver Impregnated Dressings to Reduce Wound Complications in Obese Patients at	This study has not been published

Study	Reason for Exclusion
Cesarean Section, Https://clinicaltrials.gov/show/nct01528696, 2012	
Nct,, Topical Silver for Prevention of Wound Infection After Cesarean Delivery, Https://clinicaltrials.gov/show/nct01169064, 2010	This study has not been published
Nesrallah, M., Cole, P., Kiley, K., The effect of timing of removal of wound dressing on surgical site infection rate after cesarean delivery, Obstetrics and Gynecology, 129, 148S-149S, 2017	Abstract
Ngai, I., Govindappagari, S., Van Arsdale, A., Judge, N. E., Neto, N., Bernstein, J., Garry, D., Skin preparation in cesarean birth for prevention of surgical site infection (SSI): A prospective randomized clinical trial, American Journal of Obstetrics and Gynecology, 212, S424, 2015	Abstract
Ngai, Ivan M., Van Arsdale, Anne, Govindappagari, Shravya, Judge, Nancy E., Neto, Nicole K., Bernstein, Jeffrey, Bernstein, Peter S., Garry, David J., Skin Preparation for Prevention of Surgical Site Infection After Cesarean Delivery: A Randomized Controlled Trial, Obstetrics and Gynecology, 126, 1251-7, 2015	Included in Tolcher 2018
Norman, G., Atkinson, R. A., Smith, T. A., Rowlands, C., Rithalia, A. D., Crosbie, E. J., Dumville, J. C., Intracavity lavage and wound irrigation for prevention of surgical site infection, Cochrane Database of Systematic Reviews, 2017	Any type of surgical procedure was included
Norman, G., Goh, E. L., Dumville, J. C., Shi, C., Liu, Z., Chiverton, L., Stankiewicz, M., Reid, A., Negative pressure wound therapy for surgical wounds healing by primary closure, The Cochrane database of systematic reviews, 6, CD009261, 2020	Cochrane review - references checked and included where appropriate
Reid, G. C., Hartmann, K. E., MacMahon, M. J., Can postpartum infectious morbidity be decreased by vaginal preparation with povidone iodine prior to cesarean delivery?, American Journal of Obstetrics and Gynecology, 182, S96, 2000	Included in Haas 2018
Reid,V.C., Hartmann,K.E., MCMahon,M., Fry,E.P., Vaginal preparation with povidone iodine and postcesarean infectious morbidity: a randomized controlled trial, Obstetrics and Gynecology, 97, 147-152, 2001	Included in Haas 2018
Robins, K., Wilson, R., Watkins, E. J., Columb, M. O., Lyons, G., Chlorhexidine spray versus single use sachets for skin preparation before regional nerve blockade for elective caesarean section: an effectiveness, time and cost study, International Journal of Obstetric Anesthesia, 14, 189-92, 2005	No relevant outcomes were reported
Roeckner, J., Sanchez-Ramos, L., Comparative effectiveness of skin preparations for the prevention of wound infection and endometritis following cesarean delivery: A systematic review and network meta-analysis, American Journal of Obstetrics and Gynecology, 216, S519, 2017	Abstract
Rouse,D.J., Hauth,J.C., Andrews,W.W., Mills,B.B., Maher,J.E., Chlorhexidine vaginal irrigation for the	Included in Haas 2018

Study	Reason for Exclusion
prevention of peripartal infection: a placebo-controlled randomized clinical trial, American Journal of Obstetrics and Gynecology, 176, 617-622, 1997	
Rudd,E.G., Long,W.H., Dillon,M.B., Febrile morbidity following cefamandole nafate intrauterine irrigation during cesarean section, American Journal of Obstetrics and Gynecology, 141, 12-16, 1981	Intrauterine rather than intra-abdominal irrigation was used
Ruhstaller, K., Downes, K. L., Chandrasekaran, S., Srinivas, S., Durnwald, C., Prophylactic Wound Vacuum Therapy after Cesarean Section to Prevent Wound Complications in the Obese Population: a Randomized Controlled Trial (the ProVac Study), American Journal of Perinatology, (no pagination), 2017	Duplicate
Ruhstaller, K., Downes, K., Chandrasekaran, S., Elovitz, M., Srinivas, S., Durnwald, C., PROphylactic wound VACuum therapy after cesarean section to prevent wound complications in the obese population: A randomized controlled trial (The ProVac Study), American Journal of Obstetrics and Gynecology, 216 (1 Supplement 1), S34, 2017	Abstract
Sanchez-Ramos, L., Roeckner, J., Kaunitz, A. M., Comparative effectiveness of antiseptic formulations for the surgical preparation of the vagina prior to cesarean delivery. A systematic review and network meta-analysis, American Journal of Obstetrics and Gynecology, 218, S499, 2018	Abstract
Sargin, M. A., Yassa, M., Turunc, M., Karadogan, F. O., Aydin, S., Tug, N., Abdominal irrigation during cesarean section: Is it beneficial for the control of postoperative pain and gastrointestinal disturbance? A randomized controlled, double-blind trial, International Journal of Clinical and Experimental Medicine, 9, 3416-3424, 2016	Study conducted in a low/middle income country (Turkey)
Smid, Marcela C., Dotters-Katz, Sarah K., Grace, Matthew, Wright, Sarah T., Villers, Margaret S., Hardy-Fairbanks, Abbey, Stamilio, David M., Prophylactic Negative Pressure Wound Therapy for Obese Women After Cesarean Delivery: A Systematic Review and Meta-analysis, Obstetrics and Gynecology, 130, 969-978, 2017	The majority of the studies included as part of the randomised trials were abstracts that are currently available in full text
Springel, E. H., Wang, X. Y., Sarfoh, V. M., Stetzer, B. P., Weight, S. A., Mercer, B. M., A randomized open-label controlled trial of chlorhexidine-alcohol vs povidone-iodine for cesarean antisepsis: the CAPICA trial, American Journal of Obstetrics & Gynecology, 07, 07, 2017	Included in Tolcher 2018
Starr, Rosally V., Zurawski, Jill, Ismail, Mahmoud, Preoperative vaginal preparation with povidone-iodine and the risk of postcesarean endometritis, Obstetrics and Gynecology, 105, 1024-9, 2005	Included in Haas 2018
Stout, M. J., Martin, S., Cahill, A. G., Macones, G. A., Tuuli, M. G., Impact of chlorhexidine-alcohol	Abstract

Study	Reason for Exclusion
versus iodine-alcohol skin antisepsis on methicillin-resistant staphylococcus aureus infection after cesarean, American Journal of Obstetrics and Gynecology, 214, S119, 2016	
Strugala, Vicki, Martin, Robin, Meta-Analysis of Comparative Trials Evaluating a Prophylactic Single-Use Negative Pressure Wound Therapy System for the Prevention of Surgical Site Complications, Surgical Infections, 18, 810-819, 2017	Other surgical procedures than c section have been included
Swift, Sara H., Zimmerman, M. Bridget, Hardy-Fairbanks, Abbey J., Effect of Single-Use Negative Pressure Wound Therapy on Postcesarean Infections and Wound Complications for High-Risk Patients, The Journal of reproductive medicine, 60, 211-8, 2015	Not a randomised trial
Temizkan, O., AsÄ±cÄ±oglu, O., Güngördük, K., AsÄ±cÄ±oglu, B., Yalcin, P., Ayhan, I., The effect of peritoneal cavity saline irrigation at cesarean delivery on maternal morbidity and gastrointestinal system outcomes, Journal of maternal-fetal & neonatal medicine, 29, 651â□□655, 2016	Included in Eke 2016
Tuuli, M. G., Liu, J., Stout, M. J., Martin, S., Cahill, A. G., Colditz, G., Macones, G. A., Chlorhexidine-alcohol compared with iodine-alcohol for preventing surgical-site infection at cesarean: A randomized controlled trial, American Journal of Obstetrics and Gynecology, 214, S3-S4, 2016	Abstract
Tuuli, M. G., Martin, S., Stout, M. J., Steiner, H. L., Harper, L. M., Longo, S., Cahill, A. G., Tita, A. T., Macones, G. A., Pilot randomized trial of prophylactic negative pressure wound therapy in obese women after cesarean delivery, American Journal of Obstetrics and Gynecology, 216, S245, 2017	Abstract
Tuuli, M. G., Woolfolk, C., Stout, M. J., Temming, L., Cahill, A. G., Macones, G. A., Does the relative efficacy of chlorhexidine-alcohol versus iodine-alcohol antisepsis differ between unscheduled and scheduled cesareans?, American Journal of Obstetrics and Gynecology, 214, S120, 2016	Abstract
Tuuli, Methodius G., Liu, Jingxia, Stout, Molly J., Martin, Shannon, Cahill, Alison G., Odibo, Anthony O., Colditz, Graham A., Macones, George A., A Randomized Trial Comparing Skin Antiseptic Agents at Cesarean Delivery, The New England journal of medicine, 374, 647-55, 2016	Included in Tolcher 2018
Villers, M. S., Hopkins, M. K., Harris, B. S., Brancazio, L. R., Grotegut, C. A., Heine, R. P., Negative pressure wound therapy reduces cesarean delivery surgical site infections in morbidly obese women, American Journal of Obstetrics and Gynecology, 216, S207, 2017	Abstract
Viney, Reagan, Isaacs, Christine, Chelmow, David, Intra-abdominal irrigation at cesarean delivery: a randomized controlled trial, Obstetrics and Gynecology, 119, 1106-11, 2012	Included in Eke 2016

Study	Reason for Exclusion
Ward, H. R., Jennings, O. G., Potgieter, P., Lombard, C. J., Do plastic adhesive drapes prevent post caesarean wound infection?, Journal of Hospital Infection, 47, 230-4, 2001	Compared the use of drape versus no drape
Wihbey, K. A., Joyce, E. M., Spalding, Z. T., Jones, H. J., MacKenzie, T. A., Evans, R. H., Fung, J. L., Goldman, M. B., Erekson, E., Prophylactic Negative Pressure Wound Therapy and Wound Complication after Cesarean Delivery in Women with Class II or III Obesity: a Randomized Controlled Trial, Obstetrics and Gynecology, 132, 377â□□384, 2018	Duplicate
Yildirim, G., Güngördük, K., AsicioÄŸlu, O., Basaran, T., Temizkan, O., Davas, I., Gulkilik, A., Does vaginal preparation with povidone-iodine prior to caesarean delivery reduce the risk of endometritis? A randomized controlled trial, Journal of maternal-fetal & neonatal medicine, 25, 2316â□□2321, 2012	Included in Haas 2018
Yu, L., Kronen, R. J., Simon, L. E., Stoll, C. R. T., Colditz, G. A., Tuuli, M. G., Prophylactic negative-pressure wound therapy after cesarean is associated with reduced risk of surgical site infection: a systematic review and meta-analysis, American Journal of Obstetrics and Gynecology, 218, 200, 2018	Systematic review - references checked
Yu, Lulu, Kronen, Ryan J., Simon, Laura E., Stoll, Carolyn R. T., Colditz, Graham A., Tuuli, Methodius G., Prophylactic negative-pressure wound therapy after cesarean is associated with reduced risk of surgical site infection: a systematic review and meta-analysis, American Journal of Obstetrics and Gynecology, 218, 200-210.e1, 2018	Observational studies were included and meta-analysed with the randomised trials

Economic studies

Table 17: Excluded studies and reasons for their exclusion

Study	Reason for Exclusion
Bennett K, Kellett W, Braun S, Spetalnick B, Huff B, Slaughter J, Carroll M. Silver ion-eluting dressings for prevention of post cesarean wound infection: a randomized, controlled trial. American Journal of Obstetrics & Gynecology 208(1): S337 2013	Available as abstract only
DeNoble A, Hughes B, Villers M. Cost analysis of negative pressure wound therapy in morbidly obese women at the time of caesarean. American Journal of Obstetrics and Gynecology 217(6): 723 2017	Available as abstract only
Echebiri N, McDoom M, Aalto M, Fauntleroy J, Nagappan N, Barnabei V. Prophylactic use of negative pressure wound therapy after cesarean delivery. Obstet Gynecol 125(2):299-307 2015	Not cost-utility analysis. Cost study considering US perspective.

Study	Reason for Exclusion
Hyldig N, Bille C, Kruse M, Bøgeskov RA, Jørgensen JS. Intervention for postpartum infections following caesarean section. 2012	Available as abstract only
Skeith AE, Tuuli M, Caughey AB. Cost-effectiveness analysis of vaginal preparation with antiseptic solution for cesarean infection prophylaxis. American Journal of Obstetrics & Gynecology 218(1):S340-S341 2018	Available as abstract only

Appendix L – Research recommendations

Research recommendations for review question: What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women undergoing CS?

No research recommendations were made for this review question.

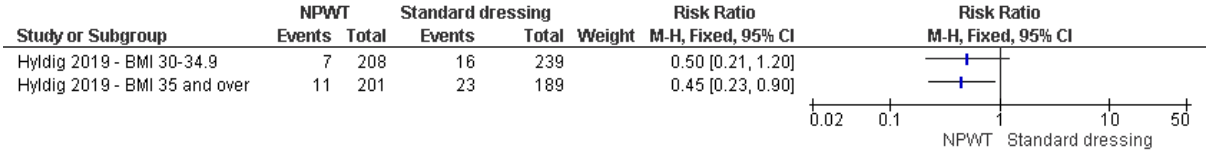
Appendix M – BMI subgrouping of NPWT

Hyldig 2019

Hyldig 2019 is a within trial cost effectiveness analysis that was published after the search date for this review. While the study was not fully included in the review due to its date of publication, the committee briefly discussed its findings as it was a publication including further information on a study that was included in the review (Hyldig 2018), answered a possible research recommendation and helped inform whether recommendations could be stratified by BMI.

Additional evidence from Hyldig 2019, in terms of effect of NPWT versus standard dressing on surgical site infections, is presented in the forest plot below (Figure 20). These relative effects would be expected to translate to an absolute effect of 33 fewer per 1000 treated (95% CI from 53 fewer to 13 more) in the BMI 30-34.9 kg/m^2 group and 67 fewer per 1000 treated (95% CI from 12 fewer to 94 fewer) in the BMI 35 kg/m^2 and over group.

Figure 20: Wound infection/ Surgical site infections, Hyldig 2019, stratified by BMI



The overall meta-analysed outcome was considered very low quality evidence (see appendix F). The additional Hyldig 2019 evidence should be considered of similar quality. The estimate for the BMI 30-34.9 kg/m^2 subgroup is also seriously imprecise and both outcomes are from a post-hoc analysis of an RCT.