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Narice, B.F., Almeida, J.R., Farrell, T. et al. (1 more author) (2021) Impact of changing gloves during cesarean section on postoperative infective complications : a systematic review and meta-analysis. Acta Obstetricia et Gynecologica Scandinavica, 100 (9). pp. 1581-1594. ISSN 0001-6349

https://doi.org/10.1111/aogs.14161

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## SYSTEMATIC REVIEW



# Impact of changing gloves during cesarean section on postoperative infective complications: A systematic review and meta-analysis

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## Abstract

**Introduction:** The cesarean section rate around the world, currently estimated at 21.1%, continues to increase. Women who undergo a cesarean section sustain a seven- to ten-fold greater risk of infective morbidity compared with those who de-liver vaginally.

**Material and methods:** We aimed to assess the impact of changing gloves intraoperatively on post-cesarean section infective morbidity (PROSPERO CRD42018110529). MEDLINE, Scopus, Web of Science, CINAHL, WHO Global Index Medicus, and Cochrane Central were searched for randomized controlled trials until June 2020. Published randomized controlled trials that evaluated the effects of glove changing during cesarean section on infective complications were considered eligible for the review. Two reviewers independently selected studies, assessed the risk of bias, and extracted data about interventions and adverse maternal outcomes. Dichotomous variables were presented and included in the meta-analyses as risk ratios (RR) with 95% confidence intervals (CI). The quality of evidence was assessed using the GRADE approach in alignment with the recommendations from the Cochrane Review Group.

**Results:** We identified seven randomized controlled trials reporting data over 1948 women. Changing gloves during a cesarean section was associated with a statistically significantly lower incidence of wound infective complications (RR 0.41, 95% CI 0.26–0.65, p < 0.0001; GRADE moderate quality evidence). This intervention seemed to be effective only if performed after delivery of the placenta. No significant difference was seen in the incidence of endometritis (RR 0.96, 95% CI 0.78–1.20, p = 0.74; GRADE moderate quality evidence) and/or febrile morbidity (RR 0.73, 95% CI 0.30–1.81, p = 0.50; GRADE moderate quality evidence), regardless of the timing of the intervention.

Abbreviations: CI, confidence interval; CS, cesarean section; 1<sup>2</sup>, heterogeneity index; RCT, randomized controlled trial; RR, risk ratio; SSI, surgical site infection.

Brenda F Narice and Joana R Almeida contributed equally to this paper.

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AOGS Acta Obstetricia et Gynecologica

**Conclusions:** Changing gloves after delivery of the placenta during a cesarean section is associated with a significant reduction in the incidence of post-surgical wound complications compared with keeping the same gloves throughout the whole surgery. However, an adequately powered study to assess the limitations and cost-effectiveness of the intervention is needed before this recommendation can be translated into current clinical practice.

#### KEYWORDS

cesarean section, changing gloves, endometritis, infection, postoperative morbidity

## 1 | INTRODUCTION

Cesarean sections (CS) and its concomitant postoperative complications continue to grow. In 2015, CS represented 21.1% of all the deliveries worldwide with cases being disproportionally higher in Latin America and Oceania.<sup>1.2</sup> CS is generally a safe procedure but is still a major laparotomy, which carries intra- and postoperative risks among which infection remains a leading cause of maternal morbidity and mortality.<sup>3</sup>

Infection is seven to ten times more likely after CS than after vaginal delivery, especially as an emergency procedure.<sup>1</sup> Surgical site infections (SSI) are one of the commonest infective complications with an estimated incidence of 3%–15%<sup>4,5</sup> and are associated with adverse maternal outcomes, poorer maternal-newborn bonding, longer hospitalization times and higher costs.<sup>6</sup>

Broad-spectrum prophylactic antibiotics during CS reduce wound infection and serious complications by at least 60%-70%.<sup>7-10</sup> However, its indiscriminate use has resulted in multi-resistant organisms and intractable wound infections. No other measure on its own has led to substantial SSI reduction, perhaps because of limited insight into the exact pathophysiology of wound infections.<sup>11-15</sup>

Significant amounts of non-staphylococcal bacteria were cultured from the dorsal aspect of surgeons' gloves after delivery by CS, which may derive from contact with the vaginal wall or the endocervical canal.<sup>16</sup> Based on these findings, the contaminated gloves were proposed to seed the pelvic cavity and layers of the abdominal wall with vaginal bacteria when reintroduced into the endometrial cavity during CS and coming in contact with the highly vascularized endometrial placental bed.<sup>16,17</sup> Therefore, small randomized controlled trials (RCTs) in the mid-1990s tested whether changing gloves intraoperatively might reduce infection after CS. However, no clinical consensus was reached because the studies lacked power.<sup>18-20</sup> A series of new studies re-explored this practice, reviving interest in this simple yet potentially effective intervention.<sup>17,21</sup>

This systematic review and meta-analysis aims to comprehensively evaluate the strength of the available evidence to determine whether changing gloves during CS reduces the risk of postoperative infections in the hope of informing future research and guiding clinical practice.

#### Key message

Implementing glove changing practices during cesarean sections can significantly reduce postoperative surgical site infections.

# 2 | MATERIAL AND METHODS

#### 2.1 | Protocol, search strategies, and sources

The protocol for this systematic review was based on PRISMA guidelines, and registered a priori in PROSPERO in 2018 (CRD42018110529).

We systematically searched MEDLINE, Scopus, Web of Science, CINAHL, WHO Global Index Medicus, and Cochrane Central for RCTs on the effects of changing gloves intraoperatively in postoperative infectious morbidity from inception until June 2020 with no language restriction.

In addition to the aforementioned searches of electronic databases, we also hand-checked all reference lists of identified trials and other relevant articles. We contacted trial authors where there was insufficient information regarding the outcomes or other relevant methodological aspects of the trial.<sup>22</sup>

Our strategy search consisted of a relevant combination of Medical Subject Headings (MeSH), core search terms and synonyms for cesarean section, gloves, and infection (Appendix S1).

#### 2.2 | Eligibility criteria and study selection

All RCTs or quasi-RCTs in which at least one arm assessed the impact of intraoperatively changing gloves on infection were considered for inclusion. RCTs that evaluated glove change in surgeries other than CS or that did not specifically analyze and report on postoperative complications were excluded. No observational studies, anecdotal evidence, or animal studies were included.

All studies assessing pregnant women undergoing CS were considered for inclusion regardless of age, country of origin, body mass index, CS category of urgency, indication for surgery, and/or preexistent comorbidities.

Although an effort was made to obtain the full text of all shortlisted studies, abstracts and conferences, procedures with enough information for analysis were also considered for inclusion to minimize the risk of publication bias.

## 2.3 | Data collection and outcomes

Two authors (BFN and JRA) independently extracted data from the included trials using a standardized data extraction form. The eligibility and quality of each study was assessed independently by these two investigators. In case of disagreement, a consensus was reached by a third investigator (PM).

The primary outcome was defined as the incidence of wound infective complications understood as per the Centers for Disease Control and Prevention definition of superficial and deep SSIs, i.e. postoperative infections involving the skin, subcutaneous tissue, and deep soft tissues of the incision (fascial and muscle layers).<sup>23-25</sup> The report of this outcome varied across studies and included a wide spectrum of presentations such as wound infection, serous drainage, induration, pus, and gaping (Table 1). For secondary outcomes, we included clinical endometritis (we accepted any definition of endometritis understood as raised temperature and uterine tenderness) and febrile morbidity (defined as persistent raised temperature without a clear focus of infection; Table 1).

Further subgroup analysis was performed based on the timing of the intervention, that is, whether gloves had been changed after delivery of the baby but before delivery of the placenta, or after delivery of the placenta but before closing the abdominal wall.

### 2.4 | Risk of bias

Two review authors (BFN, JRA) independently assessed the risk of bias of the included trials using the Cochrane Risk of bias tool.<sup>26</sup> We evaluated random sequence generation (selection bias); allocation concealment (selection bias); blinding of participants or personnel (performance bias); blinding of outcome assessment (detection bias); completeness of outcome data (attrition bias); selective reporting (reporting bias); and other potential sources of bias. We resolved any differences in opinion by discussion. Where disagreement persisted, we consulted a third party (PM). Poorly reported trials were judged as unclear risk of bias. This analysis proved essential to aid interpretation of overall findings, identify potential sources of heterogeneity across studies, and guide the grading and strength of the body of evidence available.

# 2.5 | Measures of effect

Processing of data from the included trials was carried out according to the *Cochrane Handbook for Systematic Reviews of Interventions*.<sup>26</sup> The outcomes were quantitatively analyzed using Review MANAGER 5 (Cochrane Collaboration) and MEDCALC<sup>®</sup>. For all outcomes, we calculated risk ratio (RR) with 95% confidence intervals (CI).

## 2.6 | Dealing with missing data

As far as possible, we analyzed data on an intention-to-treat basis, meaning that the analysis of patients was according to the groups to which they were originally randomized. However, if data were missing, we used the numbers as reported by the authors.

## 2.7 | Sensitivity analysis

We planned to perform sensitivity analyses to determine the effects of including or excluding trials at a high risk of bias. However, given the limited number of studies, such an approach was not always feasible.

# 2.8 | Assessment of heterogeneity and subgroup analysis

Trial heterogeneity indices ( $l^2$ ) were interpreted as low (<30%), moderate (30%–60%), or high (>60%). When noticed to be high, we attempted to perform subgroup analyses to assess whether timing of the intervention, for example, could account for some of the heterogeneity seen across studies. We used a random effect model to combine trials with similar interventions and report means of the observed effect. We favored a random effect over a fixed effect model based on the assumption that estimates of effect are likely to vary across studies not only because of sampling variability but also through a true difference in the intervention effect.<sup>27</sup> We did not choose the meta-analysis model based on the trial heterogeneity test.<sup>28</sup>

### 2.9 | Assessment of publication bias

For the evaluation of potential publication bias and small-study effect in our meta-analysis, we employed funnel plots, which were first assessed visually and subsequently with the Egger's test using MEDCALC<sup>®</sup> (version 19.6.4). For funnel plots with fewer than ten studies, we interpreted the results with caution, being aware that they may not detect publication bias (type II error due to small number of studies).<sup>29</sup> Symmetric funnel plots were considered indicative of low risk of significant publication bias, whereas asymmetric plots suggested significant publication bias.



#### TABLE 1 Characteristics of included studies

Study	Author	Publication year	Study design	Country	Study period	Sample size	Inclusion criteria
1	Atkinson W, et al <sup>24</sup>	1996	RCT	USA (single center, Alabama University Hospital)	May 1993 to December 1994	Total participants <i>n</i> = 643 *Spontaneous removal of placenta (SROP) <i>n</i> = 320 *Manual removal of placenta (MROP) <i>n</i> = 323	ELCS/ EMCS
2	Turrentine M, et al <sup>22</sup>	1996	RCT	USA (single center, Hermann Hospital, Houston)	September 1994 to August 1995	Total (all with MROP) n = 228	Women in labor undergoing CS
3	Cernadas M, et al <sup>23</sup>	1998	RCT	USA (single center, St Peter's Medical Center)	October 1995 to March 1996	Total <i>n</i> = 108 *Expressed removal of placenta (EROP) <i>n</i> = 55 *MROP <i>n</i> = 53	ELCS/ EMCS
4	Szatámary FP, et al <sup>32</sup> (only published as an abstract)	2004	RCT	Hungary (data about number of centers not provided)	Data not available	Total participants n = 241	CS
5	Ventolini G, et al <sup>35</sup> (only published as an abstract)	2004	RCT	USA (single center, Wright State University)	Data not available	Total participants n = 92	CS
6	Devoor A, et al <sup>8</sup>	2014	RCT	India (data about number of centers not provided but assumed to be single- contered as others for the	Data not available	Total participants <i>n</i> = 150	CS with intact membranes or rupture of membranes

centered as ethics for the

study was obtained in

one institution)

membranes

<4 h, <3 cm



	Preoperative and intrapartum infection				
Exclusion criteria	prophylaxis	Intervention	Comparison	Outcomes	Follow-up
Women requiring cesarean hysterectomy or evidence of intrapartum chorioamnionitis	Surgical preparation with 1% povidone- iodine solution and iodophor-isopropyl alcohol, surgeons scrubbed with iodine or chlorhexidine solution, prophylactic antibiotics (first-generation cephalosporin)	Glove change before SROP <i>n</i> = 164 or MROP <i>n</i> = 161	No glove change and SROP n = 156 or MROP n = 162	Primary end point: endometritis defined as 38°C ± uterine tenderness or foul- smelling lochia in the absence of other source of sepsis	No data
Intra-amniotic infection Prophylactic postpartum antibiotics	Standard abdominal preparation and aseptic surgical technique Prophylactic antibiotics after clamping the umbilical cord Placenta manually removed and uterus exteriorized in all CS	Glove change before MROP n = 113	No glove change and MROP n = 115	Primary end point: endometritis defined as oral temperature ≥38°C twice at least 6 h apart and 24 h after delivery, uterine tenderness and peripheral leukocytosis (≥15 000 cells/mL) in the absence of other source of sepsis	Up to 2 weeks of discharge post-CS
Multiple pregnancies Pre-existing maternal infective condition other than chorioamnionitis (UTI/respiratory tract infection)	Surgical preparation with iodophor detergent (0.75% iodine) solution, and painted with 1% povidone-iodine topical solution	Glove change before EROP <i>n</i> = 28 or MROP <i>n</i> = 27	No glove change before EROP <i>n</i> = 27 or MROP <i>n</i> = 26	Primary end point: (1) postpartum febrile morbidity defined as temperature ≥38°C after the first 24 h post-CS (2) endometritis diagnosed with temperature ≥38°C 24 h after CS and significant uterine tenderness in the absence of another source of sepsis (3) Length of febrile episode (from temperature ≥38°C)	Until patients' discharge
	Similar between two groups	Change gloves after SROP n = 151	No glove change +MROP and perioperative antibiotics n = 90	Primary end point: endometritis	Data not available
SROM, morbidly obese women, ≥3 VE, prepregnancy diabetes	Data not available	Glove change after delivery of placenta <i>n</i> = 46	No glove change n = 46	Primary end point: (1) wound infection, (2) serosanguineous drainage from wound infection	Data not available
Morbid obesity (BMI >30 kg/m²), rupture of membranes >4 h, pre- pregnancy diabetes, immunocompromised status	Intraoperative antibiotics after cord clamping	Glove change after delivery of the baby (by whole operating team) n = 50 Glove change after delivery of the placenta (by whole operating team) $n=50$	No glove change n = 50	Primary end point: (1) febrile morbidity defined as ≥38.2°C twice at least 6 h apart and 24 h after CS (2) wound infection defined as the presence of cellulitis, purulent discharge from incision site or fluctuant tender and erythematous incision margins (3) foul- smelling lochia	



#### TABLE 1 (Continued)

NARICE	ΕT	AL.

Study	Author	Publication year	Study design	Country	Study period	Sample size	Inclusion criteria
7	Scrafford J, et al <sup>25</sup>	2018	RCT	USA (single center, HealthPartners Regions Hospital, St Paul, Minnesota)	August 2015 to November 2016	Total number of participants n = 486	CS

Abbreviations: BMI, body mass index; ELCS, elective cesarean section; EMCS, emergency cesarean section; EROP, expressed delivery of placenta; MROP, manual removal of placenta; RCT, randomized controlled trial; SROM, spontaneous rupture of membranes; SROP, spontaneous removal of placenta; VE, vaginal examination.

The asymmetry of the data was quantitatively assessed with the Egger's regression test (normalized effect estimate against precision)<sup>30</sup> with low p values deemed indicative of potential publication bias.

## 2.10 | GRADE/ Summary of Findings tables

We employed the Quality assessment Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to determine the certainty of the evidence related to the primary and secondary outcomes and inform future clinical recommendations.<sup>31</sup> We used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias). We justified all decisions to downgrade the certainty of studies using footnotes. A "Summary of findings" table was prepared accordingly using the GRADEpro software (GRADEpro GDT 2015).

# 3 | RESULTS

# 3.1 | General characteristics of the studies included

The database search yielded a total of 104 studies, 35 of which were excluded for duplication (Appendix S1). One further study was retrieved from searching references and gray literature to give a total of 70 articles. The titles and abstracts of these papers were assessed against the eligibility criteria, and 61 further studies were excluded for not addressing the outcome of interest (n = 45), not being RCTs

(*n* = 13) or being published partially as commentaries (*n* = 3). The remaining nine papers were read in depth, three of which were only available as abstracts.<sup>32-34</sup> Several attempts were made to contact the authors of these studies without success. One of the abstracts was excluded because there were insufficient data for analysis.<sup>33</sup> For outcomes in which abstracts were included, sensitivity analysis with and without these studies was planned in view of the limited information available. However, such analysis was not always possible. A further study was also excluded for not being an RCT.<sup>16</sup> Overall, seven primary research papers were included in the systematic review with outcome data from a total of 1948 women. The literature search strategy is illustrated in Figure 1.

The timing of the intervention varied across studies. In three RCTs, the gloves were changed immediately before delivery of the placenta (n = 979),<sup>18-20</sup> in another three studies they were changed after delivery of the placenta (n = 819).<sup>21,32,34</sup> Only one study compared glove change before and after delivery of the placenta (n = 150)<sup>17</sup> as a three-arm trial. For this study in particular, data were first analyzed based on intervention, i.e. glove change (n = 100) versus control (n = 50) regardless of the timing of glove changing before proceeding to subgroup analysis.

Some studies also randomized patients based on the method to remove the placenta including manual, expressed, and/or spontaneous removal of the placenta (Table 1).

#### 3.2 | Methodological quality assessment

Methodological information was not available for the two abstracted studies included in the review, which were automatically deemed at unclear risk of bias.<sup>32,34</sup>



Exclusion criteria	Preoperative and intrapartum infection prophylaxis	Intervention	Comparison	Outcomes	Follow-up
Multiple pregnancies and emergency procedures	Preoperative antibiotics, chlorhexidine skin preparation, hair clipping. Vaginal preparation and surgical technique at the discretion of the attending surgeon	Change of gloves prior to abdominal closure -closure of the perineum and/or fascia n = 236	No glove change n = 250	Primary end point: (1) wound-related complications understood as hematoma, seroma, gaping >1 cm, wound infection or any abnormality of the wound) Secondary end points: (2) febrile morbidity defined as ≥38° prior to hospital discharge, (3) cellulitis, (4) endometritis, (5) infectious complications defined as the occurrence of at least outcomes 1, 3 or 4)	Up to 8 weeks post-CS

Four studies described the randomization process,<sup>18-21</sup> out of which three specified the concealment allocation.<sup>19-21</sup> The method of randomization and allocation was unclear in the remaining studies. Only one study blinded outcomes to the investigators,<sup>19</sup> and one to the patients but not the surgeons.<sup>21</sup>

All studies offered similar concurrent treatment to intervention and control groups except for the trial by Cernadas et al in which the preoperative preparation of the patient, perioperative administration of antibiotics, and surgical technique were left to the discretion of the surgeon.<sup>19</sup>

Four studies<sup>18-21</sup> provided sample size calculation with target samples being achieved in three of these studies except for Cernadas et al.<sup>19</sup> With the exception of the two abstracted studies,<sup>32,34</sup> all remaining studies defined clear and measurable outcomes though not necessarily standardized definitions. Follow up and intention-to-treat, on the other hand, was only reported in three of the studies.<sup>18,19,21</sup>

Each study tried to adjust for potential confounding factors including patient's age, body mass index, parity, gestational age at time of delivery, indication of CS, presence of labor, rupture of membranes, concomitant preoperative preparation—antibiotics/scrubbing, number of vaginal examinations, and insertion of intrauterine fetal devices. However, not all studies addressed the same variables and when they did they were not always equally distributed across studies.

Overall, two studies<sup>20,21</sup> were classified as high methodological quality, two as of moderate quality,<sup>18,19</sup> and the remaining three as of low quality<sup>17,32,34</sup> (Figure 2; Table S2).

When the studies included in the review were assessed with GRADEpro,<sup>31</sup> the recommendations derived from our review were graded of moderate quality (Table S3).

#### 3.3 | Publication bias

The funnel plots for the primary and secondary outcomes were rather symmetrical, suggesting low evidence of publication bias (Figure 3). This visual assessment was further supported by the Egger's regression test, which was not significant for any of the outcomes assessed (wound infective complication, p = 0.73; endometritis, p = 0.72; febrile morbidity, p = 0.45).

#### 3.4 | Synthesis of the results

# 3.4.1 | Primary outcome: Wound infective complications

Four studies<sup>17,19,21,34</sup> compared the incidence of wound infective complications when changing gloves. Information from a total of 836 women was included for this outcome, of whom 52.27% (*n* = 437) were in the glove changing groups and 47.73% (*n* = 399) in the control groups. Wound infective complications were significantly lower in the glove changing groups (RR 0.41, 95% CI 0.26-0.65, *p* < 0.0001). Further subgroup analysis showed that changing the gloves after delivery of placenta (RR 0.39, 95% CI 0.24–0.63, *p* < 0.0002)<sup>17,21,34</sup> but not before (RR 0.62, 95% CI 0.15–2.49, *p* = 0.5)<sup>17,19</sup> was associated with a lower incidence of wound infective complications.

Heterogeneity across all studies was noted to be low as suggested by a heterogeneity index  $l^2 = 0\%$  (Figure 4A). Even when the subgroup analysis suggested greater heterogeneity among trials in which the intervention was carried out before but not after

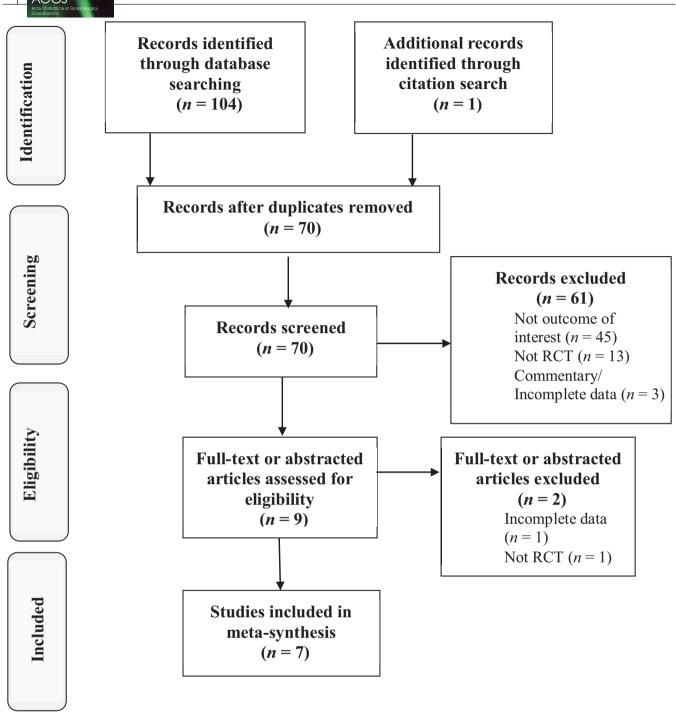


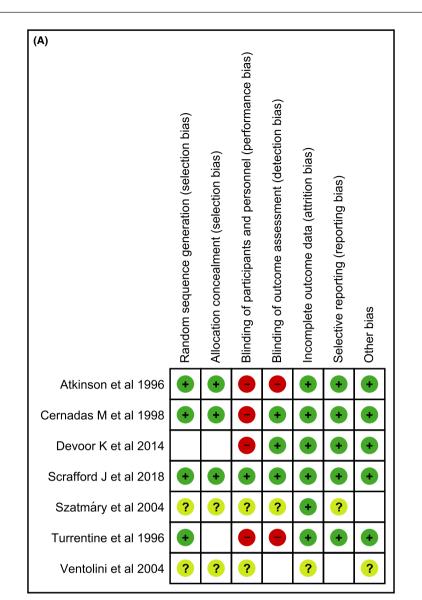
FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow chart showing the methodology for the selection of studies

delivery of the placenta, heterogeneity was still low ( $I^2 = 17\%$ ) (Figure 4B).

# 3.4.2 | Secondary outcome (1): Endometritis

Five studies, which collectively assessed a total of 1706 women, reported on the incidence of endometritis after changing gloves during a CS compared with routine care.<sup>18–21,32</sup> Just over half of the participants were allocated to the intervention group (51.58%, n = 880), whereas 48.42% of the women were in the control group (n = 826). Changing gloves intraoperatively was not associated with a significant change in the incidence of endometritis (RR 0.96, 95% CI 0.78–1.20, p = 0.74) (Figure 5A).

Three of these studies assessed glove changing before removing the placenta,<sup>18–20</sup> whereas the remaining two evaluated the impact of the intervention after delivery of the placenta.<sup>21,32</sup> Further subgroup analysis based on the timing of the intervention, however, did not seem to statistically affect the incidence of endometritis (Figure 5B).



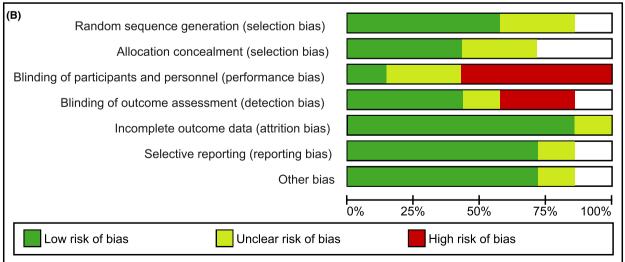


FIGURE 2 (A) Risk of bias graph for the studies included in this systematic review, (B) overall bias risk assessment suggests relatively high risk of performance and detection biases due to limited blinding in the studies selected [Color figure can be viewed at wileyonlinelibrary. com]

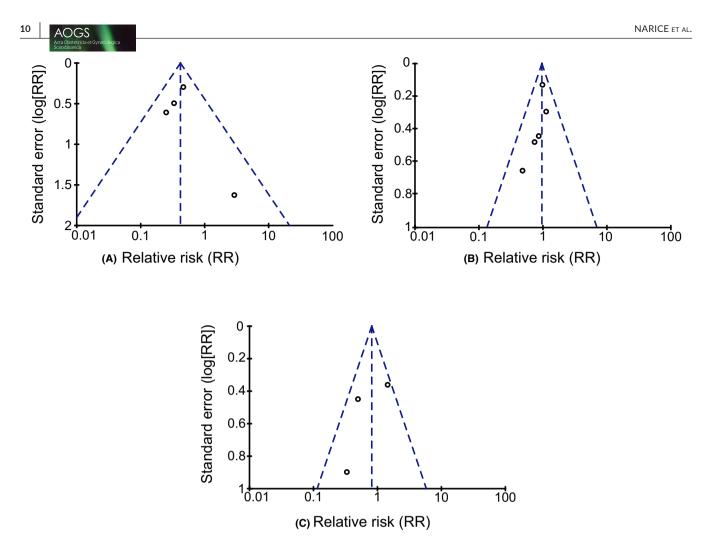


FIGURE 3 Funnel plots for the meta-analysis of included studies for the main outcome (A) wound infective complication, and the secondary outcomes (B) endometritis and (C) febrile morbidity. The triangle lines represent the regions in which 95% of the data points (normalized effect estimate against precision –standard error) would lie in the absence of publication bias [Color figure can be viewed at wileyonlinelibrary.com]

Similarly to the primary outcome, the heterogeneity across studies for endometritis was low ( $l^2 = 0\%$ ).

#### 3.4.3 | Secondary outcome (2): Febrile morbidity

Three studies compared the incidence of febrile morbidity in 744 women based on whether gloves were changed during the CS or not.<sup>17,19,21</sup> The distribution of participants between the intervention and control groups was similar (intervention: 52.55%, n = 391; control: 47.45%, n = 353).

No statistically significant differences were identified on postoperative febrile morbidity regardless of whether the gloves were changed before and/or after delivery of the placenta (RR 0.73, 95% Cl 0.30–1.81, p = 0.50) (Figure 6A and B).

Contrary to the other outcomes, heterogeneity across studies for febrile morbidity was deemed moderate ( $I^2 = 58\%$ ), which resolved when studies were grouped by timing of the intervention (Figure 6B).

#### 4 | DISCUSSION

Infective complications after CS continue to be a frequent cause of postoperative morbidity, which not only adversely affects the physical and emotional well-being of the new mothers and their families but also places a heavy financial burden on strained healthcare systems.<sup>35</sup> Specifically for the National Health Service, reducing CS-related SSI could lower the cost of managing postoperative infections by up to £4000 per case with shorter hospitalization times and decreased need for antibiotics.<sup>36,37</sup> Therefore, cost-effective interventions that are easy to perform are urgently needed as an attempt to counteract these complications. Our systematic review suggests that minimal but key changes to current clinical practice may play an instrumental role in this global effort.

WHO has previously assessed the effectiveness of doublegloving, the criteria for changing gloves during an operation, and the types of gloves to be used to prevent SSI.<sup>38</sup> However, to the best of our knowledge, our review is the first to systematically evaluate the effects of changing gloves at different stages of CS on postoperative infective complications. We have shown that

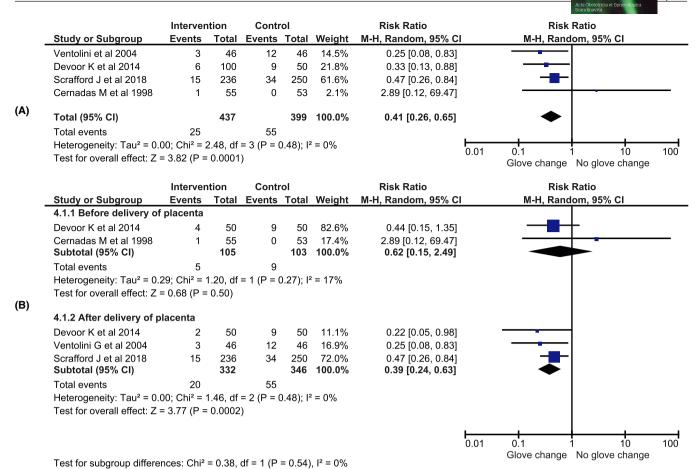


FIGURE 4 (A) Forest plot showing the relationship of changing gloves during a CS and wound infective complications, (B) subgroup analysis by timing of changing gloves. Values show the risk ratio (95% CI) of wound complications using a random effect model [Color figure

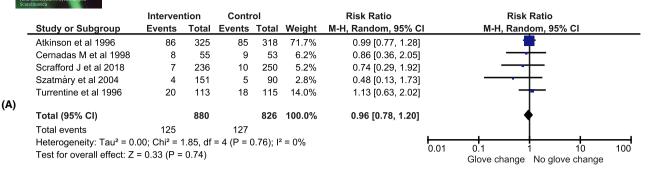
changing gloves intraoperatively significantly decreases the incidence of wound infective complications, but it does not affect the incidence of endometritis or febrile morbidity. We have also highlighted that timing of the intervention plays a major role. Whereas no benefits have been found for changing gloves before delivery of the placenta, it may prove effective for reduction of wound infection if performed after delivery of the placenta and before closing the abdominal wall. This finding is consistent with previous studies that evaluated infection prevention bundles for CS and found that changing gloves intraoperatively after delivery of the placenta when assessed in conjunction with other interventions such as chlorhexidine preparation, perioperative antibiotics, and removal of placenta by gentle traction might reduce the incidence of SSI.<sup>8,39</sup> Other specialties like Urology and Colorectal, however, have not found any statistically significant differences in postoperative infective complications after changing gloves, which we think may be due to intrinsic differences in the surgical nature of CS compared with other operations.<sup>4,21</sup>

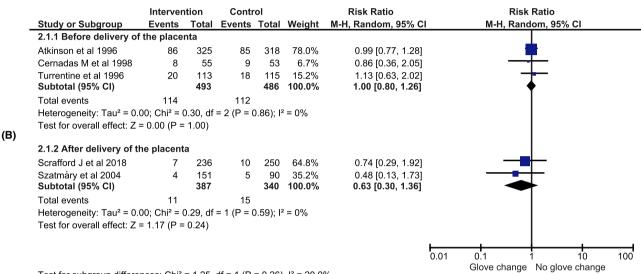
can be viewed at wileyonlinelibrary.com]

Even though the pathophysiology of SSI following CS remains to be fully elucidated, we hypothesized that changing gloves intraoperatively may be more effective to contain infection at a local rather than at a systemic level because it reduces contamination of the wound with commensal flora from the vagina during surgery. Postoperative low-grade febrile episodes, on the other hand, are not necessarily infective in nature and might represent a physiological response to surgery.<sup>40</sup> This would explain why changing gloves during CS may not be as effective at reducing postoperative fever as it is for wound complications. Endometritis may also be less affected by intraoperative changing of gloves because its strongest risk factors tend to occur in the antenatal period and during labor (vaginal dysbiosis, prolonged rupture of membranes, multiple vaginal examinations).<sup>41</sup> Therefore, interventions that are carried out during delivery such as intraoperative changing of gloves may have missed the window of opportunity.

The strength of our study relies on the relevance on the topic as well as on the robustness of the methodology employed to conduct the systematic review and subsequent meta-analysis. We thoroughly and systematically searched a wide range of electronic databases, references, and gray literature with clearly defined inclusion criteria against a peer-reviewed published protocol in PROSPERO.

However, we also recognize a series of limitations to our review. Certain end points of interest such as wound complications and endometritis were defined differently across studies, which may have affected comparability (Table 1). Similarly, in some studies, the





Test for subgroup differences:  $Chi^2 = 1.25$ , df = 1 (P = 0.26), l<sup>2</sup> = 20.0%

**FIGURE 5** (A) Forest plot showing the relationship of changing gloves during a CS and endometritis, (B) subgroup analysis by timing of changing gloves. Values show the risk ratio (95% CI) of endometritis using a random effect model [Color figure can be viewed at wileyonlinelibrary.com]

intervention was combined with different modes of placental delivery, which is likely to have affected the outcome.<sup>18-20</sup> McCurdy et al reported that expressed removal of the placenta could be responsible for a significant reduction in post-CS endometritis compared with manual placental delivery (3% vs 23%, respectively; p < 0.05).<sup>42</sup>

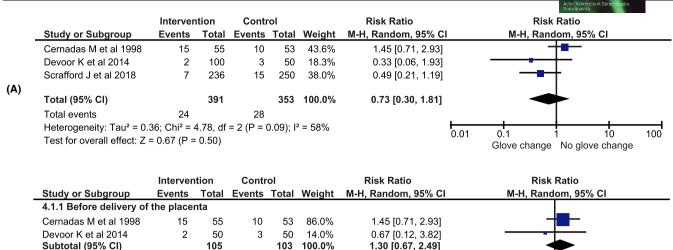
In order to minimize the risk of publication bias, we attempted to consider all available data including small studies, which were published only in their abstracted form. Even though our analyses suggested low risk of publication bias, we understand that the small number of studies available for each outcome of interest may have resulted in underpowered funnel plots to detect publication bias. Additionally, the inclusion of gray literature came at the expense of increasing other sources of systematic error because some key methodological information was missing in the abstracted studies. Moreover, as the included studies spanned many decades, not all of them met the minimum reporting criteria set by the CONSORT (Consolidating Standards of Reporting Trials) statement,<sup>43</sup> which significantly affected the methodological quality assessment. Most studies did not blind participants, operators and assessors, which increased the risk of performance and detection biases. Furthermore, not all studies reported on whether potential confounding factors such as rupture of membranes and number of vaginal examinations had been addressed or provided information about intention-to-treat and loss to follow up.

Interestingly, none of the studies assessed whether changing gloves intraoperatively prolonged surgical time, and only Scrafford et al. acknowledged that changing gloves immediately after delivering the placenta could pose safety concerns.<sup>21</sup>

Therefore, although our systematic review strongly suggests that changing gloves after delivery of the placenta may prove useful to reduce wound complications after CS, a formal health economics evaluation and a comprehensive study of potential barriers to implementing this intervention in the clinical setting are still needed.

# 5 | CONCLUSION

Changing gloves after delivery of the placenta during a CS may be associated with a significant reduction in the incidence of infective wound complications. Nonetheless, before this intervention can be



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(B)

Subtotal (95% CI)

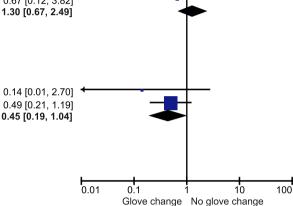
Test for overall effect: Z = 0.78 (P = 0.44)

4.1.2 After delivery of the placenta

Total events

Devoor K et al 2014 0 50 3 50 8.2% Scrafford J et al 2018 236 250 7 15 91.8% Subtotal (95% CI) 286 300 100.0% Total events 18 Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.64, df = 1 (P = 0.42); l<sup>2</sup> = 0% Test for overall effect: Z = 1.88 (P = 0.06)

17 Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.65, df = 1 (P = 0.42); l<sup>2</sup> = 0%



Test for subgroup differences:  $Chi^2 = 3.84$ , df = 1 (P = 0.05), l<sup>2</sup> = 74.0%

FIGURE 6 (A) Forest plot showing the relationship of changing gloves during a CS and febrile morbidity, (B) subgroup analysis by timing of changing gloves. Values show the risk ratio (95% CI) of wound complications using a random effect models [Color figure can be viewed at wileyonlinelibrary.com]

recommended as routine clinical practice, we believe a high-quality. adequately powered, multicenter RCT with a validated SSI definition as primary outcome should be conducted to evaluate the costeffectiveness and acceptability of the intervention in the clinical setting.

#### CONFLICT OF INTEREST

None.

#### AUTHOR CONTRIBUTIONS

BFN and JRA contributed to project development, data collection and analysis, and writing the manuscript (equal work); TF contributed to project conception and manuscript revision; and PM contributed to project conception and development, analysis, and manuscript revision.

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Narice BF, Almeida JR, Farrell T, Madhuvrata P. Impact of changing gloves during cesarean section on postoperative infective complications: A systematic review and meta-analysis. *Acta Obstet Gynecol Scand*. 2021;00:1–14. https://doi.org/10.1111/aogs.14161