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Risk factors for surgical site infection (SSI) in patients undergoing hysterectomy: A meta-analysis and network analysis

Short title: Risk factors for SSI after hysterectomy

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Abstract

Background: Surgical site infections (SSI) after hysterectomy constitute significant postoperative complications, affecting patient recovery and healthcare costs. Despite known risk factors, comprehensive quantitative reviews synthesising these risks are needed.

Method: The current study conducted a quantitative systematic review with meta-analysis and network analysis to identify and summarise risk factors for SSI following hysterectomy. After searching in Pubmed, Medline, Embase, Web of Science, and Cochrane Central Register of Controlled Trials and screened with PRISMA procedure, 14 retrospective observational studies were identified, encompassing 2,887 SSI positive and 150,106 negative cases post-hysterectomy, under 11 risk factors. Meta-analysis was restricted to factors with sufficient data synchronisation, including blood transfusion, tumour presence, obesity, diabetes, and tobacco use.

Findings: Blood transfusion emerged as the largest risk factor (OR = 2.55), followed by tumour presence (OR = 2.23), obesity (OR = 1.79), diabetes (OR = 1.70), and tobacco use (OR = 1.43). The ORs varied by incision type. Network analysis revealed that vaginal and laparoscopic hysterectomies had significantly lower SSI risk (59% and 55%, respectively) compared to abdominal hysterectomies.

Interpretations: The study establishes blood transfusion, tumour presence, obesity, diabetes, and tobacco use as significant risk factors for SSI after hysterectomy, with variations in risk evident across different incision types. The findings also suggest vaginal and laparoscopic hysterectomies as preferable alternatives to abdominal hysterectomy in mitigating SSI risk. Future research should aim for more granular data to untangle the interplay between comorbidities and further elucidate the differential risk across SSI types.

Keywords: Hysterectomy; Surgical Site Infections; Risk Factors; Meta-analysis; Network Analysis

Introduction

Hysterectomy is an optional treatment for leiomyoma, endometriosis, abnormal bleeding, benign ovarian neoplasms, pelvic organ prolapse, and gynecologic cancer [1]. Epidemiological research estimated that the lifetime prevalence of hysterectomy surgery is approximately 2.36 ‰ in Germany, 1.43‰ in the US [2,3], 0.8‰ in China [4], and 0.42 ‰ in the UK [2] among the female population, depending on waitlist queuing time of different regions [2]. Among patients who had hysterectomies, 2.1% are estimated to develop surgical site infections (SSI) worldwide [5], which has been one of the most common complications after hysterectomy surgery [6]. Considering these figures were estimated based on the whole female population, the number of individuals potentially requiring hysterectomy is substantial.

The risk factors of hysterectomy SSI were evident in different reports, yet the results were diverse between different studies. Accordingly, one of the most recent studies suggested that the risk factors include age, body mass index (BMI), smoking, and diabetes [7]. One study from Spain only considered obesity and inadequate prophylaxis as meaningful indicators [8], whereas another study from the UK also suggested that the operative time should be considered an independent risk factor [9]. The evidence seemed diverse, isolated and lack of quantitative power. Consequently, the current study aims to summarise the results of risk factors of hysterectomy SSI through a quantitative approach.

Method

Study Registration

The protocol of the current study was registered and reviewed by the PROSPERO International Prospective Register of Systematic Reviews (No. CRD42023411668). The protocol is available at: https://www.crd.york.ac.uk/PROSPERO/export_details_pdf.php

Search Strategy

The data was extracted from published empirical study reports retrieved from the databases, including Pubmed (central), Medline (Ovid), Embase (Ovid), Web of Science, and Cochrane Central Register of Controlled Trials. The search terms followed the standard PICO guideline (population, intervention, comparator, outcome) and were adapted according to Medical Subject Headings (MeSH) terms [10]. The search was conducted upon the completion of study registration.

Eligibility criteria

The inclusion criteria were 1) population: female participants who had post-hysterectomy SSI incisions; 2) intervention: hysterectomy surgeries; 3) comparators: the number of participants who had or had not post-hysterectomy SSI incisions; 4) outcomes: the number of participants exposed and not exposed to the risk factors of SSI incisions. The exclusion criteria were 1) non-English studies and 2) studies that provided insufficient data.

Study screening and data extraction

The report articles were retrieved in RIS format and managed with Endnote (Bld13966, EndNote X9.3.3, 2023). The screening process followed the PRISMA guidelines [11]. Two independent reviewers conducted the screening process. Initially, they removed all duplicate articles. Then, articles that did not meet the inclusion criteria were excluded. For those that met the criteria, full-text papers were procured. Any discrepancies between the reviewers were resolved through discussion. Data from the selected articles was subsequently extracted.

Risk of bias assessment

Two reviewers independently scored the studies using the Newcastle-Ottawa quality assessment (NOS) [12,13]. NOS is a validated, easy-to-use scale containing 8 items organised into three dimensions: selection, comparability, and

exposure/outcome, which has been endorsed for use in systematic reviews of non-randomised studies by The Cochrane Collaboration [13]. Studies rated 0-2 as poor quality, 3-5 as fair quality, and 6–9 as good/high quality.

Data synthesis

Data synthesis requires at least four sets of data according to the general conduct suggested by the Cochrane Handbook [14]. The effect size of each identified risk factor will be pooled in a quantitative meta-analysis using STATA v18. The risk factors were expected to be reported as binary data about whether or not the patients were exposed to the risk factor and were infected. Consequently, odds ratios (ORs) would be calculated as the effect size with the following formula:

$$OR = \frac{a}{b} \div \frac{c}{d}$$

Where *a* represents cases exposed to the risk factor and infected, *b* represents those exposed but not infected, *c* represents unexposed but infected, and *d* represents unexposed and uninfected cases. And the LogOR is the natural log of the OR.

Statistical Analysis Plan

The meta-analysis was conducted with STATA v18. Only risk factors reported in over 4 datasets were synthesised into meta-analysis. A random effect model meta-analysis with the restricted maximum likelihood method was used to evaluate the pooled ORs (LogORs). The heterogeneity was also assessed with the random effects model, where heterogeneity I^2 is considered moderate when $I^2 > 50\%$ and high when $I^2 > 75\%$ [14]. Sensitivity analysis was conducted using the Leave-one-out approach by omitting one dataset each time and evaluating the pooled effect sizes. Egger's test and funnel plots were used to assess potential publication bias.

The pooled effect sizes were also entered into subgroup analysis based on the incision types (superficial, deep, organ space) with available datasets. BMI was entered into the meta-regression analysis with pooled effect sizes of diabetes to explore the relationship between obesity and diabetes and its influence on SSI risk prediction.

Finally, a Bayesian network model was conducted with R and WinBugs to determine the risk of SSI between three surgery types (abdominal, vaginal, and laparoscopic). The Bayesian network model offers a probabilistic graphical

framework that represents and analyses the probabilistic relationships among binominal variables [15]. The model fit of the Bayesian network was evaluated with the Deviance Information Criterion (DIC), where a lower DIC indicates a better-fitting model.

Results

Systematic review

Initially, searching the keywords in PubMed, Medline (Ovid), Embase (Ovid), Web of Science, and the Cochrane Central Register of Controlled Trials produced 3821 records. Fourteen studies met the inclusion criteria after screening based on the PRISMA guidelines. The PRISMA procedure is shown in Figure 1.

Figure 1 The PRISMA Flow

All identified studies were retrospective observations to record the case numbers of SSI incisions after hysterectomy surgeries with or without the occurrence of each risk factor. In total, 152993 female patients (age: 47.53±8.29) who underwent hysterectomy were included in the current 14 studies, of whom 2887 had SSI incisions in different types, and 150106 had no SSI incisions taken as controls. The details of all studies are described in Table 1.

Table 1 Study SummaryTable 2 Study Summary

Author & Year	Sample Origin	N	SSI +	Age (±SD)	Surgery Method	Age RF	Anti-microbial	Blood Loss	Blood Transfusion	BMI	Diabetes	Obesity	Surgery Duration	Tobacco Use	Tumour	Wound Cleanness
Molina-Cabrillana 2008	2000-2004 Hospital Universitario Materno-Infantil de Canarias, Sapin	1540	72	54.00 (±12.90)	abdominal & vaginal	Age >60	Y/N	NR	NR	NR	Y/N	Y/N	≥P75	NR	Y/N	Clean-contaminated vs Contaminated /dirty
Olsen 2009	2003-2005 CDC Prevention Epicenter Program hospitals, USA	820	66	51.70 (±17.78)	abdominal & vaginal	Mean	NR	NR	NR	Mean	Y/N	N	Mean	Y/N	Y/N	NR
Lake 2013	2005-2009 ACS-NSQIP, USA	13822	375	NR	abdominal & vaginal & laparoscopic	Age >80	NR	NR	Y/N	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	≥P75	Y/N	Y/N	Clean vs Clean-contaminated vs Contaminated vs Dirty
Savage 2013	2007-2010 University of Iowa Hospitals and Clinics, USA	1104	126	54.53 (±13.66)	abdominal	Mean	Mean	NR	Median	BMI≥30 (Obesity)	Y/N	Y/N	Mean	NR	Y/N	NR
Coleman 2014	1999-2012 Johns Hopkins Medical Institution, USA	77	17	42.56 (±5.93)	abdominal & vaginal & laparoscopic	Mean	NR	>250ml; ≥451ml	Y/N	Median	Y/N	BMI≥30 (Obesity)	NR	Y/N	NR	NR
Mahdi 2014	2005-2011 ACS-NSQIP, USA	28366	296	NR	laparoscopic	Age >60, 70 & 80	NR	NR	>4 units of packed red blood cells	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	>60 min, 180 min	Y/N	NR	NR
Pop-Vicas 2014	2012-2015 University of Wisconsin Hospitals, USA	1531	52	58.27 (±12.31)	abdominal & vaginal & laparoscopic	Mean	Y/N	Median*	NR	NR	NR	NR	Mean	Y/N	Y/N	NR

Uppal 2015	2012-2015 MSQC, USA	21358	441	48.10 (±11.70)	abdominal & vaginal & laparoscopic	Median	Y/N	Median	NR	BMI≥30 (Obesity)	NR	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Morgan 2016	2012-2014 MSQC, USA	16548	315	NR	abdominal	Age >50	NR	Mean	Y/N	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Tuomi 2016	2007-2013 Helsinki University Hospital, Finland	1164	94	67.46 (±10.23)	abdominal & vaginal & laparoscopic	Mean	NR	Median	NR	Mean	Y/N	NR	Mean	Y/N	NR	NR
Till 2017	2012-2015 MSQC, USA	18255	329	NR	abdominal & vaginal & laparoscopic	Age >65	NR	≥250ml	NR	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Brown 2019	2012-2014 ACS-NSQIP, USA	46755	445	45.95 (±1.51)	laparoscopic	Mean	NR	NR	Y/N	Mean	Y/N	NR	Mean	Y/N	NR	Clean vs Clean-contaminated vs Contaminated vs Dirty
Tsuzuki 2021	2014-2018 Teine Keijinkai Hospital, Japan	1559	71	48.28 (±11.39)	laparoscopic	Mean	NA	NR	Y/N	Mean	Y/N	NR	Mean	Y/N	NR	NR
Wang 2022	2012-2022 Two Grade A Tertiary Hospitals, China	94	188	47.70 (±10.87)	abdominal	Age >50	Y/N	≥500ml	NR	Mean	Y/N	NR	>180 min	NR	Y/N	Clinicians determined Class II vs Class III
Overall		152993	2887	47.53 (±8.29)												

Note. The content under each risk factor was how these studies presented their data. The detailed case numbers are in Table 3; SSI+ refers to SSI-positive cases; ACS-NSQIP refers to the American College of Surgeons National Surgical Quality Improvement Program; MSQC refers to the Michigan Surgical Quality Collaborative; NR refers to not reported; NA refers to not applicable; Y/N refers to reported in Yes or No; Median*: the median reported in this study did not include IQR to estimate its variance; P75 refers to the 75th percentile.

Among these studies, seven only reported infection cases in mixed three incision types (superficial, deep or organ space) [8,16-21], two only reported in mixed two incision places (deep or organ space) [22,23], one study reported each incision types separately [24] and one study reported superficial and organ space incisions separately [25], one study reported superficial incision independently but mixed deep or organ space incisions [26], one study reported deep incision independently but mixed superficial or deep incisions [5], one study reported only organ space incisions [27]. Since it requires at least four datasets to conduct meta-analyses [14], the studies reported cases in independent incision types were combined into three mixed incision types (superficial, deep or organ space) to synthesise with those only reported the mixed incision types. The NOS risk of bias assessment rated three studies scored 6 [8,19,24], seven scored 7 [5,16-18,21,23,27], two scored 8 [20,25], and the other two scored 9 [22,26]. All 14 studies are ranked as good/high quality and were included in the following review.

Among the 14 studies, there were 11 risk factors identified in total, including age, antimicrobial, blood loss, blood transfusion, BMI, diabetes (both type I or type II), obesity, surgery duration, tobacco use, tumour, and wound cleanness. However, antimicrobial and blood loss were reported in less than four datasets. Wound cleanness and age were reported in different classification standards. Only 5 factors reported in more than 4 datasets are available for quantitative analysis, including blood transfusion, diabetes, obesity, tobacco use, and tumour. Age, high BMI, and surgery duration reported continued data and thus could not be directly synthesised.

Meta-analyses

The identified risk factors with sufficient datasets were entered into meta-analyses respectively. As shown in Table 2, pooled effect sizes revealed significant overall logORs of blood transfusion (logOR = .94, OR = 2.55, p <.001), obesity (logOR = .58, OR = 1.79, p <.001), diabetes (logOR = .53, OR = 1.70, p <.001), tobacco use (logOR = .36, OR = 1.43, p <.001), but not tumour (logOR = .30, OR = 1.36, p =.362), as the risk factors for SSI infections. However, after removing each dataset one at a time, leave-one-out sensitivity analysis on all risk factors suggested no changes except for tumour, where one dataset changed the results [8]. Further analysis with publication bias suggested no publication bias in all factors. However, as shown in Figure 2A, the funnel plot suggested three outlier datasets [8,20,24]. One borderline dataset was decided to be kept [20], and the other two were excluded from the analysis [8,24].

Table 2 Summary of Meta-analyses

	Case Number				Meta-analysis					Heterogeneity Test			Leave-one-out Sensitivity		Egger's Publication Bias			
Risk Factor	RF+ SSI+	RF+ SSI-	RF- SSI+	RF- SSI-	LogOR	OR	SE	z	p	I^2	Q (df)	p	Lowest LogOR	Highest LogOR	β	SE	z	p
Blood Transfusion	39	998	1075	62830	.94	2.55	.17	5.57	<.001	0.00%	.17 (3)	.983	.88	.96	.09	1.08	.08	.934
Tumour	226	3924	769	44733	.80	2.23	.09	8.80	<.001	0.00%	1.34 (4)	.850	.70	.86	.05	.81	.06	.950
Obesity	720	28717	531	36398	.58	1.79	.12	5.07	<.001	67.56%	11.58 (4)	.020	.54	.66	1.79	7.60	1.12	.263
Diabetes	229	5330	1314	62893	.53	1.70	.15	3.50	<.001	64.07%	21.13 (7)	<.001	.44	.64	-1.21	.89	-1.35	.178
Tobacco Use	340	13645	938	54500	.36	1.43	.07	5.54	<.001	0.00%	5.78 (5)	.330	.32	.43	.76	.73	.91	.363

Note. The presenting data of the tumour was after exclusions of outliers. RF+ refers to exposure to the risk factor, RF- refers to no exposure to the risk factor, SSI+ refers to SSI incision positive, and SSI- refers to SSI incision negative.

Figure 2 The Funnel Plots

After exclusion, data from the tumour was entered into meta-analysis again and reported a significant pooled effect size predicting SSI infections (logOR = .80, OR = 2.23, p <.001), and, as shown in Figure 2B, there were no outliers. As shown in Figure 3A, 3B, and 3C, the estimation of heterogeneity suggested that the chance of inconsistent distribution of the pooled logORs was not significant in blood transfusion datasets (I^2 = 0%, $Q_{(3)}$ = .17, p = .983), tumour (I^2 = 0%, $Q_{(4)}$ = 1.34, p = .850) or tobacco use (I^2 = 0%, $Q_{(5)}$ = 5.78, p = .330). However, Figure 3D and Figure 4E suggested significant moderate heterogeneity in obesity (I^2 = 67.56%, $Q_{(4)}$ = 11.58, p <.001) and diabetes datasets (I^2 = 64.07%, $Q_{(7)}$ = 21.13, p <.001). These results suggested that blood transfusion, tumour, tobacco use, obesity, and diabetes were significant risk factors predicting post-hysterectomy SSI. Patients who underwent blood transfusion had a 155% increased likelihood of experiencing post-hysterectomy SSI. Similarly, individuals with tumours had a 123% increased risk, obese individuals 79%, diabetics 70%, and tobacco users 43%.

Figure 3 The Forest Plots for Each Risk Factor

Note. RF+ refers to cases exposed to the risk factor; RF- refers to cases not exposed to the risk factor; SSI+ refers to SSI positive cases; SSI- refers to SSI negative cases;

Subgroup analysis between studies reporting different incision types (mixed superficial or deep or organ space vs. mixed deep or organ space) was conducted among tobacco use and diabetes, for they obtained more than 4 datasets under each subgroup. The difference was whether they included superficial incisions. Table 3 shows a significant group difference in pooled ORs between mixed superficial & deep & organ space cases and mixed deep or organ space among tobacco use, $Q_{(1)} = 11.59$, $p < .001$, but not among diabetes, $Q_{(1)} = .71$, $p = .400$.The impact of tobacco use on the risk of SSI varied significantly depending on the type of SSI. While tobacco use was associated with a 143% increased risk for combined superficial, deep, and organ space SSIs, this risk escalated to a 272% increase when considering only deep and organ space SSIs. This suggests that the influence of smoking may be more pronounced for deep and organ space infections than superficial ones. Given the observed discrepancy in risk between the combined three types of SSIs and the combined two types (deep or organ space) for tobacco use, it is plausible that other risk factors might also exhibit differential effects across various SSI categories.

Figure 4 Tobacco Use Subgroup Forest Plot between SSI Types

Continuous BMI data was incorporated into a meta-regression analysis alongside the ORs of diabetes to evaluate the relationship between obesity and diabetes. Given the absence of group differences or heterogeneity discrepancies across SSI types in the effect sizes associated with diabetes, datasets from both SSI types (though not originating from identical studies) were incorporated into the meta-regression. The results suggested that BMI did not significantly predict the ORs of diabetes (β = .001, SE = .08, t = .02, p = .989). While this does not suggest that BMI (or obesity) is not correlated with the incidence of diabetes, it does affirm that high BMI did not affect the outcomes in this particular analysis.

Bayesian Network Analysis

The infected and non-infected case numbers under each surgery method (abdominal, vaginal, laparoscopic) were analysed with a Bayesian network model to determine whether vaginal and laparoscopic surgeries had a lower SSI risk than abdominal surgeries. The Bayesian network model exhibited a DIC of 111.5. Compared to abdominal surgeries, vaginal surgeries reduced the risk of developing SSI by 59% (logOR = -.90, OR = .41, 95%CI [0.33, 0.67]) and laparoscopic surgeries by 55% (logOR = -.80, OR = .45, 95%CI [0.37, 0.67]). However, the latter two did not distinguish from each other (logOR = -.1, OR = .9, 95%CI [0.72, 1.21]). These results suggest that conducting the hysterectomy with the vaginal or laparoscopic methods is respectively safer than the abdominal method in terms of SSI risk.

Discussion

The current study conducted a quantitative systematic review with meta-analysis and network analysis to summarise the evidence of risk factors of SSI incisions after hysterectomy surgeries. To our knowledge, this is the first quantitative review of the topic. In total, 14 retrospective observations studies were identified with 2887 SSI positive and 150106 negative cases under 11 risk factors, including age, antimicrobial, blood loss, blood transfusion, high BMI, diabetes, obesity, surgery duration, tobacco use, tumour, and wound cleanness. However, only 5 were available for meta-analysis synchronisation. Among which, blood transfusion, tumour, obesity, diabetes, and tobacco use were factors that significantly increased the risk of SSI. The estimated ORs also seemed to vary between different incision types (superficial, deep, or organ space). Apart from risk factors, Bayesian network analysis also suggested that conducting vaginal or laparoscopic hysterectomies induced a significantly lower risk of SSI infection than abdominal surgeries. The details of the quantitative analysis are discussed as follows.

The largest risk factor of SSI incision is blood transfusion (OR = 2.55), with a 155% increased likelihood of SSI incisions. Blood transfusion has always been identified as a major source of post-surgical infections [28,29]. Administrative errors, such as bacterial contamination in platelet products, are believed responsible for infections induced by blood transfusion [28]. These issues are related to the healthcare service environment and beyond the current paper's discussion. Instead, the need for blood transfusion deserves further elaboration from the patients' site. For example, obese patients are found to bleed more, where blood loss was reported to be positively correlated with BMI [30,31]. This is because obese patients have larger surface areas of subcutaneous fat, resulting in more tissue fluid for drainage, blood loss, and a further

reduction in haematocrit. Consequently, it is reasonable to presume that part of the blood transfusion OR was potentially attributed to obesity. However, the current study could not provide evidence to support this hypothesis by estimating the quantitative relationship between blood transfusion and BMI because only two studies reported both blood transfusion and continuous BMI data [22,23]. These are not sufficient to provide a valid meta-regression analysis. Apart from obesity, severe abnormal uterine bleeding and cancer-related anaemia are also important reasons that patients require extra blood transfusion. However, none of the included studies attempted to isolate these factors, nor did they report preoperative haemoglobin. Consequently, we could not address whether blood transfusion was an independent factor or it was attributed to other factors such as obesity, severe abnormal uterine bleeding, cancer-related anaemia, preoperative haemoglobin or whether its estimated ORs were inflated. Future studies should consider reporting more comprehensive data to precisely estimate the ORs for blood transfusion as the SSI incision risk factor.

Likewise, one may argue that obesity and diabetes are comorbid, where obesity-induced insulin resistance is one of the major sources of type 2 diabetes [32]. This might explain the moderate heterogeneity of the ORs in obesity (OR = 1.79, I^2 = 67.56%) and diabetes (OR = 1.70, I^2 = 64.07%). This is, in fact, a methodological issue, where all studies directly counted the case number that was exposed and not exposed to the specific risk factors, but none attempted to distinguish whether the case was exposed to multiple risk factors. That is, one might suffer from obesity or diabetes or both, and the case would be counted in each risk factor respectively when they suffer from both. Consequently, the estimated ORs were not solely attributed to one risk factor and might be overestimated. Hypothetically, in the current case, the heterogeneity of the ORs in obesity and diabetes was moderate because some studies included more

patients suffering from both obesity and diabetes and reported higher ORs than those with fewer such patients. As a result, although both obesity and diabetes are significant risk factors, their estimated ORs should be considered cautiously and require further clarification in future studies by reporting cases separately.

To further address this issue, the current study conducted a meta-regression analysis to investigate whether BMI predicts the ORs of diabetes. The analysis found no significant relationship between continuous BMI values and the ORs of diabetes. Notably, the absence of a significant predictive relationship between BMI and the OR for diabetes does not imply that these two factors were unrelated or that obesity does not influence the estimation of OR for diabetes. On the one hand, the absence of a significant predictive relationship might arise from including both type I and type II diabetes in the studies, with type I diabetes having less direct relevance to obesity. On the other hand, the estimation of ORs may still have been elevated due to the repeated counting of cases exposed to multiple risk factors. Instead, this result might be interpreted as the pathologies of obesity and diabetes are relatively independent in the context of SSI risk.

Apart from obesity and diabetes, the second-largest risk factor was tumour (OR = 2.23), with a 123% increased likelihood of SSI incisions. The immune system in patients afflicted with malignant tumours was generally compromised [33]. This impairment in the primary immune function directly results from the tumour's pervasive influence on the natural defence mechanisms. Furthermore, the standard therapeutic interventions for tumours, including surgery, chemotherapy, and radiotherapy, also contribute to the weakened immune state [34].

Tobacco use was the last risk factor (OR = 1.43), with a 43% increased likelihood of SSI incisions. Nicotine and carbon monoxide, two primary agents produced in tobacco use, contribute to the constriction of peripheral blood vessels. This vasoconstriction reduces the oxygen supply to tissues, vital for cellular function and healing processes [35]. Consequently, this oxygen deficit can precipitate the formation of microthrombi, which are small clots that can impair blood flow and further hinder tissue repair and regeneration.

However, the estimated ORs of tobacco use seemed to vary between incision types. A subgroup comparison was conducted between studies that reported all mixed SSI incisions and those that only reported deep or organ space incisions for tobacco use and diabetes, where only these two risk factors were reported repeatedly in distinguishing between SSI incision types. Significant subgroup differences were observed exclusively in the context of tobacco use. Specifically, tobacco use was associated with a 43% increased risk for superficial, deep, or organ space SSIs. This risk escalated to a 172% increase when focusing solely on deep or organ space SSIs. The pronounced impact of tobacco use appears more substantial in increasing the risk of deep or organ space infections compared to superficial ones. This discrepancy may also be attributed to tobacco-induced vasoconstriction. The vascular system supporting superficial cells, such as those in the skin, is more prosperous than the vasculature of deep and organ space cells. Consequently, cells in deeper tissues and organ spaces are more vulnerable to oxygen supply alterations exacerbated by tobacco use. However, this was merely a hypothetical explanation without solid evidence, which requires further investigation.

Finally, the current Bayesian model revealed a significant reduction in SSI incision risk with vaginal and laparoscopic hysterectomies compared to the abdominal

approach, with decreases of 59% and 55% respectively. This is the first quantitative evidence of their superiority in reducing SSI incidence. Abdominal hysterectomy, though designed to prevent bladder damage by opening the peritoneal reflection and mobilising the bladder, increases postoperative infection risks due to larger incisions and greater abdominal exposure [36]. In contrast, laparoscopic methods, utilising smaller incisions and camera systems, minimise air exposure and use electrocoagulation for cutting and hemostasis, thereby reducing pelvic-abdominal disturbances and promoting a stable internal environment [37]. While total laparoscopic hysterectomy demands high skill levels, vaginal hysterectomy offers a simpler approach to uterine manipulation, albeit with a slight increase in urinary system infection risks from metal cannula introduction [38]. Although each technique has distinct risk-benefit profiles, the current results provided straightforward evidence of SSI incision risk, comparing the techniques to reference individual patient needs and surgical goals.

There are four limitations in the current study. First, the included studies did not differentiate cases based on the number of risk factors present, counting each instance for all identified risks. This approach likely inflated the ORs, particularly for comorbid conditions like patients with severe abnormal uterine bleeding or cancer-related anaemia and obesity and diabetes. Second, there was no distinction between Type I and Type II diabetes in the studies, potentially contributing to moderate heterogeneity in the pooled OR estimates. Therefore, the estimated ORs for obesity and diabetes as risk factors for SSIs should be interpreted cautiously. Thirdly, since none of the studies isolated patients with severe abnormal uterine bleeding, suffered from cancer-related anaemia, or reported pre-operative HbA1, it is unclear whether these factors also inflated the estimation ORs for blood transfusion, and thus, they

should be interpreted cautiously as well. Lastly, few studies specified the types of SSI incisions (superficial, deep, or organ space). Given that our analysis indicates variation in tobacco use ORs across different SSI types, it is crucial to ascertain if similar variations apply to other risk factors. Addressing these issues in future research, with more detailed data reporting, is essential for a clearer understanding of the risk factors for SSIs. Future studies should report more comprehensive data to address these limitations.

In summary, the current study conducted a quantitative systematic review with meta-analysis and network analysis of the risk factors of SSI incisions after hysterectomy surgeries. In total, 11 risk factors were mentioned, whereas only blood transfusion, tumour, obesity, diabetes, and tobacco use had sufficient data to be entered into meta-analysis and yield statistical significance. With limited available data, the ORs of tobacco use seemed to vary between different SSI incision types, suggesting potential diversity in other risk factors. Finally, a Bayesian network model compared the risk of SSI incisions between vaginal and laparoscopic and abdominal hysterectomy approaches. This approach offers valuable insights into the varying risks associated with each surgical method.

Conflict of Interest: The authors declare that they have no conflict of interest

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Data Sharing: All relevant data are within the manuscript and its Supporting information files.

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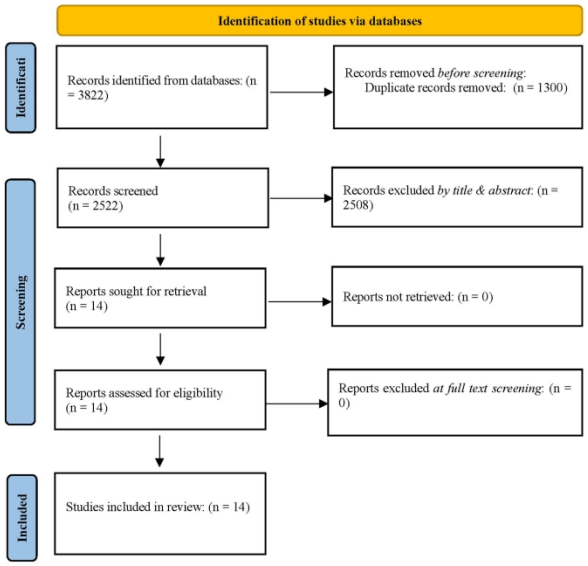
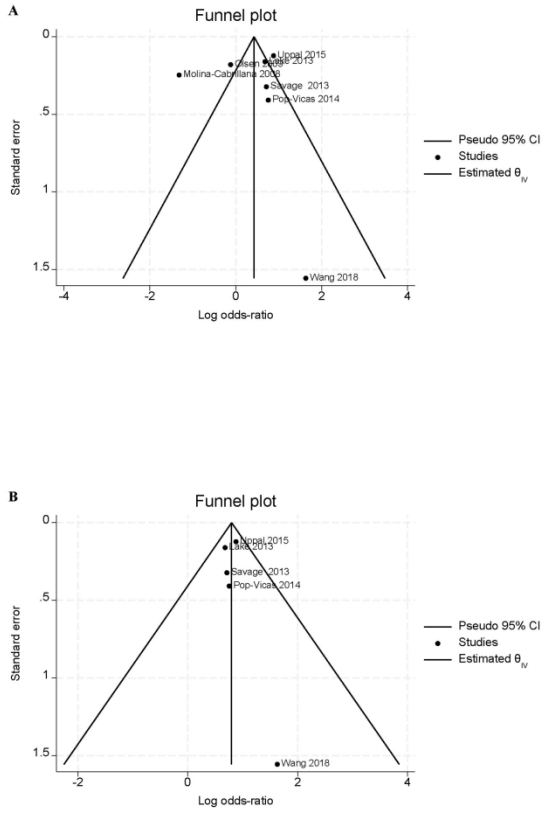
Figure 1 The PRISMA Flow



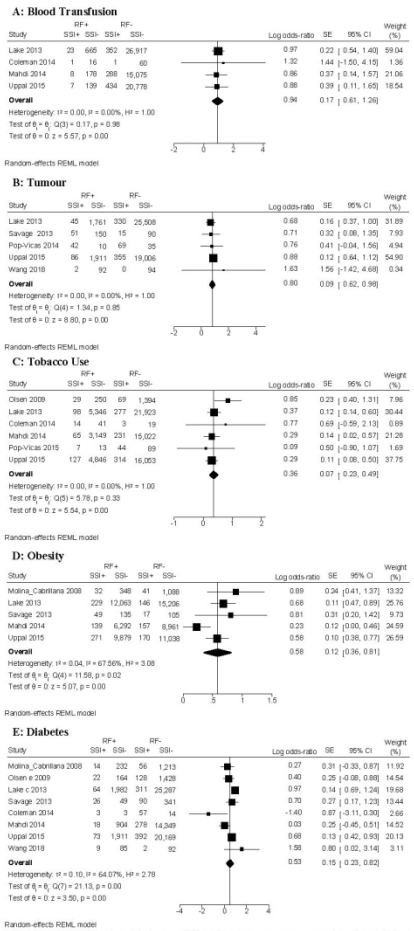
209x297mm (300 x 300 DPI)

Figure 2 The Funnel Plots



210x294mm (300 x 300 DPI)

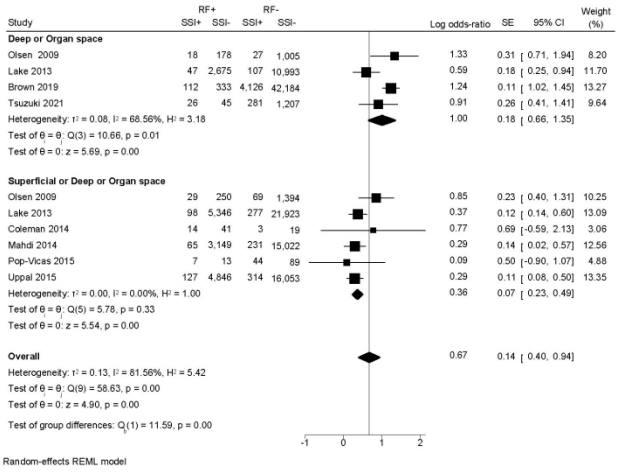
Figure 3 The Forest Plots for Each Risk Factor



Note. RF+ refers to cases exposed to the risk factor; RF- refers to cases not exposed to the risk factor; SSI+ refers to SSI positive cases; SSI- refers to SSI negative cases;

210x297mm (200 x 200 DPI)

Figure 1 Tobacco Use Subgroup Forest Plot between SSI Types



297x210mm (200 x 200 DPI)

Contents

Search Terms

Pubmed (Central) Search Strategy

Framework Item	Target	Search term
Population	Patients who have undergone hysterectomy (no restriction to age)	hysterectomy mesh term: #1
Intervention	Hysterectomy (No restriction on the surgery type, e.g. laparoscopy)	hysterectomy mesh term: #1
Comparator	RCT, case-control, cross-sectional or longitudinal design	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term: #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
Outcome	Risk of infection	Infection mesh term: #10

step	code	results
#1	(((((((hysterectomy) OR (hysterectomies)) OR (hysterectomy, Vaginal)) OR (hysterectomies, Vaginal)) OR (vaginal hysterectomies)) OR (vaginal hysterectomy)) OR (Colpohysterectomy)) OR (Colpohysterectomies))	53,350
#2	((Clinical Trials, Randomized) OR (Trials, Randomized Clinical)) OR (Controlled Clinical Trials, Randomized)	742,997
#3	(((((((((((((((((((((((Cross Sectional Studies) OR (Cross-Sectional Study)) OR (Studies, Cross-Sectional)) OR (Study, Cross-Sectional)) OR (Surveys, Disease Frequency)) OR (Disease Frequency Survey)) OR (Survey, Disease Frequency)) OR (Analysis, Cross-Sectional)) OR (Analyses, Cross-Sectional)) OR (Analysis, Cross Sectional)) OR (Cross-Sectional Analyses)) OR (Cross-Sectional Analysis)) OR (Cross Sectional Analysis)) OR (Analyses, Cross Sectional)) OR (Cross Sectional Analyses)) OR (Cross-Sectional Survey)) OR (Cross Sectional Survey)) OR (Cross-Sectional Surveys)) OR (Survey, Cross-Sectional)) OR (Surveys, Cross-Sectional)) OR (Disease Frequency Surveys)) OR (Prevalence Studies)) OR (Prevalence Study)) OR (Studies, Prevalence)) OR (Study, Prevalence)	1,122,672
#4	(((((((((((((((((((((((((((((Longitudinal Study) OR (Studies, Longitudinal)) OR (Study, Longitudinal)) OR (Tuskegee Syphilis Study)) OR (Syphilis Studies, Tuskegee)) OR (Syphilis Study, Tuskegee)) OR (Tuskegee Syphilis Studies)) OR (Jackson Heart Study)) OR (Heart Studies, Jackson)) OR (Heart Study, Jackson)) OR (Jackson Heart Studies)) OR (Studies, Jackson Heart)) OR (California Teachers Study)) OR (California Teachers Studies)) OR (Studies, California Teachers)) OR (Study, California Teachers)) OR (Teachers Studies, California)) OR (Teachers Study, California)) OR (Bogalusa Heart Study)) OR (Bogalusa Heart Studies)) OR (Heart Studies, Bogalusa)) OR (Heart Study, Bogalusa)) OR (Studies, Bogalusa Heart)) OR (Study, Bogalusa Heart)) OR (Framingham Heart Study)) OR (Framingham Heart Studies)) OR (Heart Studies, Framingham)) OR (Heart Study, Framingham)) OR (Longitudinal Survey)) OR (Longitudinal Surveys)) OR (Survey, Longitudinal)) OR (Surveys, Longitudinal)	339,768
#5	(((((((((((((((((((((((((((((((((((((Case-Control Study) OR (Studies, Case-Control)) OR (Study, Case-Control)) OR (Case-Comparison Studies)) OR (Case Comparison Studies)) OR (Case-Comparison Study)) OR (Studies, Case-Comparison)) OR (Study, Case-Comparison)) OR (Case-Compeer Studies)) OR (Studies, Case-Compeer)) OR (Case-Referrent Studies)) OR (Case Referrent Studies)) OR (Case-Referrent Study)) OR (Studies, Case-Referrent)) OR (Study, Case-Referrent)) OR (Case-Referent Studies)) OR (Case Referent Studies)) OR (Case-Referent Study)) OR (Studies, Case-Referent)) OR (Study, Case-Referent)) OR (Case-Base Studies)) OR (Case Base Studies)) OR (Studies, Case-Base)) OR (Case Control Studies)) OR (Case Control Study)) OR (Studies, Case Control)) OR (Study, Case Control)) OR (Nested Case-Control Studies)) OR (Case-Control Studies, Nested)) OR (Case-Control Study, Nested)) OR (Nested Case Control Studies)) OR (Nested Case-Control Study)) OR (Studies, Nested Case-Control)) OR (Study, Nested Case-Control)) OR (Matched Case-Control Studies)) OR (Case-Control Studies,	1,589,628

	Matched)) OR (Case-Control Study, Matched)) OR (Matched Case Control Studies)) OR (Matched Case-Control Study)) OR (Studies, Matched Case-Control)) OR (Study, Matched Case-Control)	
#6	((Prospective Study) OR (Studies, Prospective)) OR (Study, Prospective)	904,417
#7	((((((((((((((((((((((((((((((Cohort Study) OR (Studies, Cohort)) OR (Study, Cohort)) OR (Concurrent Studies)) OR (Studies, Concurrent)) OR (Concurrent Study)) OR (Study, Concurrent)) OR (Closed Cohort Studies)) OR (Cohort Studies, Closed)) OR (Closed Cohort Study)) OR (Cohort Study, Closed)) OR (Study, Closed Cohort)) OR (Studies, Closed Cohort)) OR (Birth Cohort Studies)) OR (Birth Cohort Study)) OR (Cohort Studies, Birth)) OR (Cohort Study, Birth)) OR (Studies, Birth Cohort)) OR (Study, Birth Cohort)) OR (Analysis, Cohort)) OR (Analyses, Cohort)) OR (Cohort Analyses)) OR (Cohort Analysis)) OR (Historical Cohort Studies)) OR (Cohort Studies, Historical)) OR (Cohort Study, Historical)) OR (Historical Cohort Study)) OR (Study, Historical Cohort)) OR (Studies, Historical Cohort)) OR (Incidence Studies)) OR (Incidence Study)) OR (Studies, Incidence)) OR (Study, Incidence)	3,150,416
#8	Observational Study	205,618
#9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	4,994,412
#10	((((Infection and Infestation) OR (Infestation and Infection)) OR (Infections and Infestations)) OR (Infestations and Infections)) OR (Infection)	4003846
#11	#1 AND #9 AND #10	1,758
#12	The year 2000 - Current	1,198
#13	English	1,096

The results are hyperlinked in each column

Medline (Ovid) Search Strategy

Framework Item	Target	Search term
Population	Patients who have undergone hysterectomy (no restriction to age)	Hysterectomy mesh term with Medline code
Intervention	Hysterectomy (No restriction on the surgery type, e.g. laparoscopy)	Hysterectomy mesh term with Medline code
Comparator	RCT, case-control, cross-sectional or longitudinal design	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term with Medline code
Outcome	Risk of infection	Infection mesh term with Medline code

	Term searched	Results
Group 1	Population	
1	hysterectomy. ti,ab,mp.	52599
2	hysterectomies. ti,ab,mp.	3423
3	hysterectomy, Vaginal. ti,ab,mp.	3235
4	hysterectomies, Vaginal. ti,ab,mp.	9
5	vaginal hysterectomies. ti,ab,mp.	437
6	vaginal hysterectomy. ti,ab,mp.	3593
7	Colpohysterectomy. ti,ab,mp.	84
8	Colpohysterectomies. ti,ab,mp.	8
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	53278
Group 2	Intervention	
10	hysterectomy. ti,ab,mp.	52599
11	hysterectomies. ti,ab,mp.	3423
12	hysterectomy, Vaginal. ti,ab,mp.	3235
13	hysterectomies, Vaginal. ti,ab,mp.	9
14	vaginal hysterectomies. ti,ab,mp.	437
15	vaginal hysterectomy. ti,ab,mp.	3593
16	Colpohysterectomy. ti,ab,mp.	84
17	Colpohysterectomies. ti,ab,mp.	8
18	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	53278
Group 3	Comparator	
19	Cross-sectional. ti,ab,mp.	632818
20	Longitudinal. ti,ab,mp.	377935
21	Prospective study. ti,ab,mp.	159216
22	Cohort study. ti,ab,mp.	274386
23	Observational study. ti,ab,mp.	199248
24	Randomized control study. ti,ab,mp.	937
25	Case-Control Studies. ti,ab,mp.	338463
26	19 or 21 or 22 or 23 or 24 or 25	1494518
Group 4	Outcome	
27	Infections. ti,ab,mp.	1470008
28	"Infection and Infestation". ti,ab,mp.	86
29	"Infestation and Infection". ti,ab,mp.	51
30	"Infections and Infestations". ti,ab,mp.	311

31	"Infestations and Infections". ti,ab,mp.	28
32	Infection. ti,ab,mp.	1418735
33	27 or 28 or 29 or 30 or 31 or 32	2279134
Combined	9 and 18 and 26 and 33	407
Limited to English only	9 and 18 and 26 and 33	384
The year 2000 to present	9 and 18 and 26 and 33	337

Results link:

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=5SYIqKO2Gpep7EBCDrAGLmKZrFtVAMXrv0wx7zAaFQsQRH5DCIC4ESMKrqhH2tOv1

Embase (Ovid) Search Strategy

Framework Item	Target	Search term
Population	Patients who have undergone hysterectomy (no restriction to age)	Hysterectomy mesh term with Embase code
Intervention	Hysterectomy (No restriction on the surgery type, e.g. laparoscopy)	Hysterectomy mesh term with Embase code
Comparator	RCT, case-control, cross-sectional or longitudinal design	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term with Embase code
Outcome	Risk of infection	Infection mesh term with Embase code

	Term searched	Results
Group 1	Population	
1	hysterectomy. ti,ab,mp.	93767
2	hysterectomies. ti,ab,mp.	6284
3	hysterectomy, Vaginal. ti,ab,mp.	392
4	trachelectomy. ti,ab,mp.	19
5	hysterectomies, Vaginal. ti,ab,mp.	758
6	vaginal hysterectomies. ti,ab,mp.	8954
7	vaginal hysterectomy. ti,ab,mp.	83
8	Colpohysterectomy. ti,ab,mp.	5
9	Colpohysterectomies. ti,ab,mp.	94170
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	93767
Group 2	Intervention	
11	hysterectomy. ti,ab,mp.	93767
12	hysterectomies. ti,ab,mp.	6284
13	hysterectomy, Vaginal. ti,ab,mp.	392
14	trachelectomy. ti,ab,mp.	19
15	hysterectomies, Vaginal. ti,ab,mp.	758
16	vaginal hysterectomies. ti,ab,mp.	8954
17	vaginal hysterectomy. ti,ab,mp.	83
18	Colpohysterectomy. ti,ab,mp.	5
19	Colpohysterectomies. ti,ab,mp.	94170
20	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	93767
Group 3	Comparator	
21	Cross-sectional. ti,ab,mp.	765496
22	Longitudinal. ti,ab,mp.	475332
23	Prospective study. ti,ab,mp.	899849
24	Cohort study. ti,ab,mp.	405571
25	Observational study. ti,ab,mp.	342074
26	Randomized control study. ti,ab,mp.	1628
27	Case-Control Studies. ti,ab,mp.	27610
28	21 or 22 or 23 or 24 or 25 or 26 or 27	2146419
Group 4	Outcome	
29	Infections. ti,ab,mp.	835857
30	"Infection and Infestation". ti,ab,mp.	107

31	"Infestation and Infection". ti,ab,mp.	55
32	"Infections and Infestations". ti,ab,mp.	807
33	"Infestations and Infections". ti,ab,mp.	49
34	Infection. ti,ab,mp.	2763568
35	29 or 30 or 31 or 32 or 33 or 34	2991465
Combined	10 and 20 and 28 and 35	1510
Limited to English only	10 and 20 and 28 and 35	1468
The year 2000 to present	10 and 20 and 28 and 35	1419

Results link:

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=79TCxxCp1oN0adXj9ZUf4UzOGz44m8xhcwT9pEsrMoJkpSIjfY4IktYO5RKZbvU7

Web of Science Search Strategy

Framework Item	Target	Search term
Population	Patients who have undergone hysterectomy (no restriction to age)	Hysterectomy mesh term with the web of science code: #1
Intervention	Hysterectomy (No restriction on the surgery type, e.g. laparoscopy)	Hysterectomy mesh term with the web of science code: #1
Comparator	RCT, case-control, cross-sectional or longitudinal design	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh terms with the web of science code: #2, #3, #4, #5, #6, #7, #8
Outcome	Risk of infection	Infection mesh term with the web of science code: #10

step	code	results
#1	TS= (hysterectomy* OR hysterectomies* OR hysterectomy, vaginal* OR hysterectomies, vaginal OR vaginal hysterectomies* OR vaginal hysterectomy* OR colpohysterectomy* OR colpohysterectomies*)	40974
#2	TS= (Clinical Trials, Randomized* OR Trials, Randomized Clinical* OR Controlled Clinical Trials, Randomized*)	357993
#3	TS= (Longitudinal Study* OR Studies, Longitudinal* OR Study, Longitudinal* OR Tuskegee Syphilis Study* OR Syphilis Studies, Tuskegee* OR Syphilis Study, Tuskegee* OR Tuskegee Syphilis Studies* OR Jackson Heart Study* OR Heart Studies, Jackson* OR Heart Study, Jackson* OR Jackson Heart Studies* OR Studies, Jackson Heart* OR California Teachers Study* OR California Teachers Studies* OR Studies, California Teachers* OR Study, California Teachers* OR Teachers Studies, California* OR Teachers Study, California* OR Bogalusa Heart Study* OR Bogalusa Heart Studies* OR Heart Studies, Bogalusa* OR Heart Study, Bogalusa* OR Studies, Bogalusa Heart* OR Study, Bogalusa Heart* OR Framingham Heart Study* OR Framingham Heart Studies* OR Heart Studies, Framingham* OR Heart Study, Framingham* OR Longitudinal Survey* OR Longitudinal Surveys* OR Survey, Longitudinal* OR Surveys, Longitudinal*)	389252
#4	TS= (Case-Control Study* OR Studies, Case-Control* OR Study, Case-Control* OR Case-Comparison Studies* OR Case Comparison Studies* OR Case-Comparison Study* OR Studies, Case-Comparison* OR Study, Case-Comparison* OR Case-Compeer Studies* OR Studies, Case-Compeer* OR Case-Referrent Studies* OR Case Referrent Studies* OR Case-Referrent Study* OR Studies, Case-Referrent* OR Study, Case-Referrent* OR Case-Referent Studies* OR Case Referent Studies* OR Case-Referent Study* OR Studies, Case-Referent* OR Study, Case-Referent* OR Case-Base Studies* OR Case Base Studies* OR Studies, Case-Base* OR Case Control Studies* OR Case Control Study* OR Studies, Case Control* OR Study, Case Control* OR Nested Case-Control Studies* OR Case-Control Studies, Nested* OR Case-Control Study, Nested* OR Nested Case Control Studies* OR Nested Case-Control Study* OR Studies, Nested Case-Control* OR Study, Nested Case-Control* OR Matched Case-Control Studies* OR Case-Control Studies, Matched* OR Case-Control Study, Matched* OR Matched Case Control Studies* OR Matched Case-Control Study* OR Studies, Matched Case-Control* OR Study, Matched Case-Control*)	742023
#5	TS= (Cross Sectional Studies* OR Cross-Sectional Study * OR Studies, Cross-Sectional * OR Study, Cross-Sectional * OR Surveys, Disease Frequency * OR Disease Frequency Survey * OR Survey, Disease Frequency * OR Analysis, Cross-Sectional * OR Analyses, Cross-Sectional * OR Analysis, Cross Sectional * OR Cross-Sectional Analyses * OR Cross-Sectional Analysis * OR Cross Sectional Analysis	1164085

	* OR Analyses, Cross Sectional * OR Cross Sectional Analyses * OR Cross-Sectional Survey * OR Cross Sectional Survey * OR Cross-Sectional Surveys * OR Survey, Cross-Sectional * OR Surveys, Cross-Sectional * OR Disease Frequency Surveys * OR Prevalence Studies * OR Prevalence Study * OR Studies, Prevalence * OR Study, Prevalence*)	
#6	TS= (Prospective Study* OR Studies, Prospective* OR Study, Prospective*)	721432
#7	TS= (Cohort Study* OR Studies, Cohort * OR Study, Cohort * OR Concurrent Studies * OR Studies, Concurrent * OR Concurrent Study * OR Study, Concurrent * OR Closed Cohort Studies * OR Cohort Studies, Closed * OR Closed Cohort Study * OR Cohort Study, Closed * OR Study, Closed Cohort * OR Studies, Closed Cohort * OR Birth Cohort Studies * OR Birth Cohort Study * OR Cohort Studies, Birth * OR Cohort Study, Birth * OR Studies, Birth Cohort * OR Study, Birth Cohort * OR Analysis, Cohort * OR Analyses, Cohort * OR Cohort Analyses * OR Cohort Analysis * OR Historical Cohort Studies * OR Cohort Studies, Historical * OR Cohort Study, Historical * OR Historical Cohort Study * OR Study, Historical Cohort * OR Studies, Historical Cohort * OR Incidence Studies * OR Incidence Study * OR Studies, Incidence * OR Study, Incidence*)	1333108
#8	TS= (Observational study *)	234254
#9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	3887063
#10	TS= (Infections* OR Infection and Infestation * OR Infestation and Infection * OR Infections and Infestations * OR Infestations and Infections * OR Infection *)	1895911
#11	#1 AND #9 AND #10	853
#12	The year 2000 – current; English	726

The results are hyperlinked in each column

Cochrane Library Search Strategy

Framework Item	Target	Search term
Population	Patients who have undergone hysterectomy (no restriction to age)	Hysterectomy Cochrane search manager Hysterectomy with Cochrane code based on mesh term: #1
Intervention	Hysterectomy (No restriction on the surgery type, e.g. laparoscopy)	Hysterectomy with Cochrane code based on mesh term
Comparator	RCT, case-control, cross-sectional or longitudinal design	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study with Cochrane code based on mesh term:
Outcome	Risk of infection	Hysterectomy with Cochrane code based on mesh term

step	code	results
#1	(hysterectomy):ti,ab,kw OR (hysterectomies):ti,ab,kw OR (hysterectomy,Vaginal):ti,ab,kw OR (hysterectomies,Vaginal):ti,ab,kw OR (vaginal hysterectomies):ti,ab,kw OR (vaginal hysterectomy):ti,ab,kw OR (Colpohysterectomy):ti,ab,kw OR (Colpohysterectomies):ti,ab,kw	8202
#2	(Clinical Trials, Randomized):ti,ab,kw OR (Trials, Randomized Clinical):ti,ab,kw OR (Controlled Clinical Trials, Randomized):ti,ab,kw	154945
#3	(Longitudinal Study):ti,ab,kw OR (Studies, Longitudinal):ti,ab,kw OR (Study, Longitudinal):ti,ab,kw OR (Tuskegee Syphilis Study):ti,ab,kw OR (Syphilis Studies, Tuskegee):ti,ab,kw OR (Syphilis Study, Tuskegee):ti,ab,kw OR (Tuskegee Syphilis Studies):ti,ab,kw OR (Jackson Heart Study):ti,ab,kw OR (Heart Studies, Jackson):ti,ab,kw OR (Heart Study, Jackson):ti,ab,kw OR (Jackson Heart Studies):ti,ab,kw OR (Studies, Jackson Heart):ti,ab,kw OR (California Teachers Study):ti,ab,kw OR (California Teachers Studies):ti,ab,kw OR (Studies, California Teachers):ti,ab,kw OR (Study, California Teachers):ti,ab,kw OR (Teachers Studies, California):ti,ab,kw OR (Teachers Study, California):ti,ab,kw OR (Bogalusa Heart Study):ti,ab,kw OR (Bogalusa Heart Studies):ti,ab,kw OR (Heart Studies, Bogalusa):ti,ab,kw OR (Heart Study, Bogalusa):ti,ab,kw OR (Studies, Bogalusa Heart):ti,ab,kw OR (Study, Bogalusa Heart):ti,ab,kw OR (Framingham Heart Study):ti,ab,kw OR (Framingham Heart Studies):ti,ab,kw OR (Heart Studies, Framingham):ti,ab,kw OR (Heart Study, Framingham):ti,ab,kw OR (Longitudinal Survey):ti,ab,kw OR (Longitudinal Surveys):ti,ab,kw OR (Survey, Longitudinal):ti,ab,kw OR (Surveys, Longitudinal):ti,ab,kw	23544
#4	(Case-Control Study):ti,ab,kw OR (Studies, Case-Control):ti,ab,kw OR (Study, Case-Control):ti,ab,kw OR (Case-Comparison Studies):ti,ab,kw OR (Case Comparison Studies):ti,ab,kw OR (Case-Comparison Study):ti,ab,kw OR (Studies, Case-Comparison):ti,ab,kw OR (Study, Case-Comparison):ti,ab,kw OR (Case-Compeer Studies):ti,ab,kw OR (Studies, Case-Compeer):ti,ab,kw OR (Case-Referrent Studies):ti,ab,kw OR (Case Referrent Studies):ti,ab,kw OR (Case-Referrent Study):ti,ab,kw OR (Studies, Case-Referrent):ti,ab,kw OR (Study, Case-Referrent):ti,ab,kw OR (Case-Referent Studies):ti,ab,kw OR (Case Referent Studies):ti,ab,kw OR (Case-Referent Study):ti,ab,kw OR (Studies, Case-Referent):ti,ab,kw OR (Study, Case-Referent):ti,ab,kw OR (Case-Base Studies):ti,ab,kw OR (Case Base Studies):ti,ab,kw OR (Studies, Case-Base):ti,ab,kw OR (Case Control Studies):ti,ab,kw OR (Case Control Study):ti,ab,kw OR (Studies, Case Control):ti,ab,kw OR (Study, Case Control):ti,ab,kw OR (Nested Case-Control Studies):ti,ab,kw OR (Case-Control Studies, Nested):ti,ab,kw OR (Case-Control Study, Nested):ti,ab,kw OR (Nested Case Control Studies):ti,ab,kw OR (Nested Case-Control Study):ti,ab,kw OR (Studies, Nested Case-Control):ti,ab,kw OR (Study, Nested Case-Control):ti,ab,kw OR (Matched Case-Control Studies):ti,ab,kw OR (Case-Control	33557

	Studies, Matched):ti,ab,kw OR (Case-Control Study, Matched):ti,ab,kw OR (Matched Case Control Studies):ti,ab,kw OR (Matched Case-Control Study):ti,ab,kw OR (Studies, Matched Case-Control):ti,ab,kw OR (Study, Matched Case-Control):ti,ab,kw	
#5	(Cross Sectional Studies):ti,ab,kw OR (Cross-Sectional Study):ti,ab,kw OR (Studies, Cross-Sectional):ti,ab,kw OR (Study, Cross-Sectional):ti,ab,kw OR (Surveys, Disease Frequency):ti,ab,kw OR (Disease Frequency Survey):ti,ab,kw OR (Survey, Disease Frequency):ti,ab,kw OR (Analysis, Cross-Sectional):ti,ab,kw OR (Analyses, Cross-Sectional):ti,ab,kw OR (Analysis, Cross Sectional):ti,ab,kw OR (Cross-Sectional Analyses):ti,ab,kw OR (Cross-Sectional Analysis):ti,ab,kw OR (Cross Sectional Analysis):ti,ab,kw OR (Analyses, Cross Sectional):ti,ab,kw OR (Cross Sectional Analyses):ti,ab,kw OR (Cross-Sectional Survey):ti,ab,kw OR (Cross Sectional Survey):ti,ab,kw OR (Cross-Sectional Surveys):ti,ab,kw OR (Survey, Cross-Sectional):ti,ab,kw OR (Surveys, Cross-Sectional):ti,ab,kw OR (Disease Frequency Surveys):ti,ab,kw OR (Prevalence Studies):ti,ab,kw OR (Prevalence Study):ti,ab,kw OR (Studies, Prevalence):ti,ab,kw OR (Study, Prevalence):ti,ab,kw	54133
#6	(Prospective Study):ti,ab,kw OR (Studies, Prospective):ti,ab,kw OR (Study, Prospective):ti,ab,kw	233446
#7	(Cohort Study):ti,ab,kw OR (Studies, Cohort):ti,ab,kw OR (Study, Cohort):ti,ab,kw OR (Concurrent Studies):ti,ab,kw OR (Studies, Concurrent):ti,ab,kw OR (Concurrent Study):ti,ab,kw OR (Study, Concurrent):ti,ab,kw OR (Closed Cohort Studies):ti,ab,kw OR (Cohort Studies, Closed):ti,ab,kw OR (Closed Cohort Study):ti,ab,kw OR (Cohort Study, Closed):ti,ab,kw OR (Study, Closed Cohort):ti,ab,kw OR (Studies, Closed Cohort):ti,ab,kw OR (Birth Cohort Studies):ti,ab,kw OR (Birth Cohort Study):ti,ab,kw OR (Cohort Studies, Birth):ti,ab,kw OR (Cohort Study, Birth):ti,ab,kw OR (Studies, Birth Cohort):ti,ab,kw OR (Study, Birth Cohort):ti,ab,kw OR (Analysis, Cohort):ti,ab,kw OR (Analyses, Cohort):ti,ab,kw OR (Cohort Analyses):ti,ab,kw OR (Cohort Analysis):ti,ab,kw OR (Historical Cohort Studies):ti,ab,kw OR (Cohort Studies, Historical):ti,ab,kw OR (Cohort Study, Historical):ti,ab,kw OR (Historical Cohort Study):ti,ab,kw OR (Study, Historical Cohort):ti,ab,kw OR (Studies, Historical Cohort):ti,ab,kw OR (Incidence Studies):ti,ab,kw OR (Incidence Study):ti,ab,kw OR (Studies, Incidence):ti,ab,kw OR (Study, Incidence):ti,ab,kw	184886
#8	(Observational Study):ti,ab,kw	20328
#9	(Infection and Infestation):ti,ab,kw OR (Infection and Infestation):ti,ab,kw OR (Infections and Infestations):ti,ab,kw OR (Infestations and Infections):ti,ab,kw OR (Infection):ti,ab,kw	102985
#10	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	552677
#11	#1 AND #9 AND #10	382
#12	Trials	377
#13	The year 2000 – current; English	243

Risk of Bias Assessment

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (CASE CONTROL STUDIES)

Selection

1) Is the case definition adequate?

a) yes, with independent validation □

b) yes, e.g. record linkage or based on self-reports

c) no description

2) Representativeness of the cases

a) consecutive or obviously representative series of cases □

b) potential for selection biases or not stated

3) Selection of Controls

a) community controls □

b) hospital controls

c) no description

4) Definition of Controls

a) no history of disease (endpoint) □

b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis

a) study controls for _____ (Select the most important factor.) □

b) study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure

a) secure record (e.g. surgical records) □

b) structured interview where blind to case/control status □

c) interview not blinded to case/control status

d) written self-report or medical record only

e) no description

2) Same method of ascertainment for cases and controls

a) yes □

b) no

3) Non-response rate

a) same rate for both groups □

b) non-respondents described

c) rate different and no designation

Table 1 Risk of Bias Assessment with NOS Case-control Study Scale

Author & Year	Selection				Comparability	Exposure			Total score
Olsen 2009	1	1	1	0	2	1	1	0	6
Lake 2013	1	1	1	1	2	1	1	1	9
Savage 2013	1	1	1	0	2	1	1	0	7
Pop-Vicas 2014	0	1	1	0	2	0	1	1	6
Morgan 2016	1	1	1	0	2	0	1	1	7
Wang 2022	1	1	1	0	2	1	1	0	7

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (COHORT STUDIES)

Selection

1) Representativeness of the exposed cohort

a) truly representative of the average _____ (describe) in the community □

b) somewhat representative of the average _____ in the community □

c) selected group of users e.g. nurses, volunteers

d) no description of the derivation of the cohort

2) Selection of the non-exposed cohort

a) drawn from the same community as the exposed cohort □

b) drawn from a different source

c) no description of the derivation of the non-exposed cohort

3) Ascertainment of exposure

a) secure record (e.g. surgical records) □

b) structured interview □

c) written self-report

d) no description

4) Demonstration that outcome of interest was not present at start of study

a) yes □

b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for _____ (select the most important factor) □

b) study controls for any additional factor □ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome

a) independent blind assessment □

b) record linkage □

c) self-report

d) no description

2) Was follow-up long enough for outcomes to occur

a) yes (select an adequate follow-up period for outcome of interest) □

b) no

3) Adequacy of follow-up of cohorts

a) complete follow-up - all subjects accounted for □

b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) □

c) follow up rate < ____% (select an adequate %) and no description of those lost

d) no statement

Table 2 Risk of Bias Assessment with NOS Cohort Study Scale

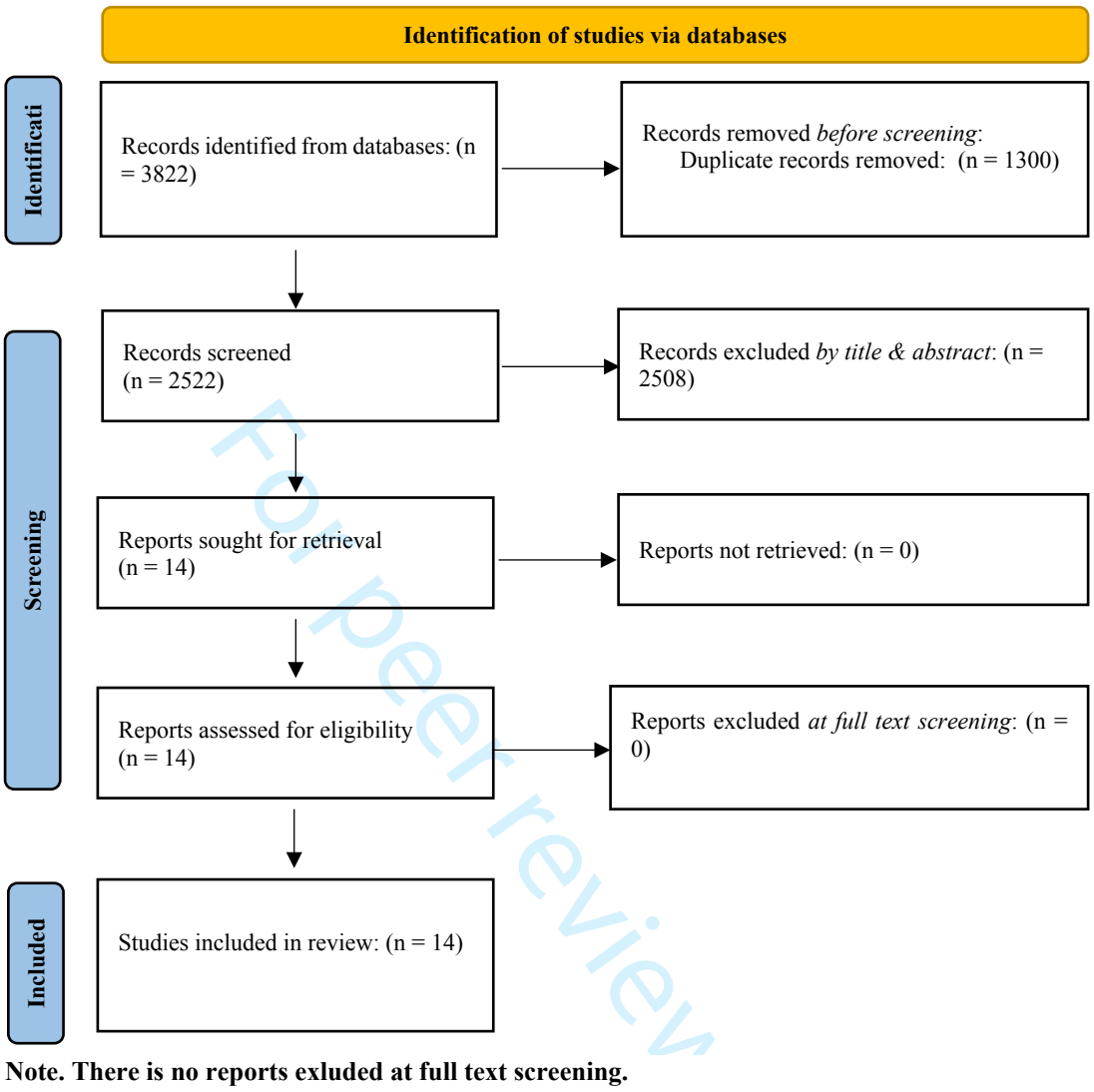
Author & Year	Selection				Comparability	Exposure			Total score
Molina-Cabrillana 2008	0	1	1	0	2	1	1	0	6
Coleman 2014	1	1	1	0	2	1	0	1	7
Mahdi 2014	1	1	1	0	2	1	1	0	7
Uppal 2015	1	1	1	0	2	1	1	1	8
Tuomi 2016	1	1	1	0	2	1	1	1	8
Till 2017	1	1	1	0	2	0	1	1	7
Brown 2019	1	1	1	1	2	1	1	1	9
Tsuzuki 2021	1	1	1	0	2	1	1	0	7

Table 3 Study Summary

Author & Year	Selection				Comparability	Exposure			Total score
Molina-Cabrillana 2008#	0	1	1	0	2	1	1	0	6
Olsen 2009*	1	1	1	0	2	1	1	0	6
Lake 2013*	1	1	1	1	2	1	1	1	9
Savage 2013*	1	1	1	0	2	1	1	0	7
Coleman 2014#	1	1	1	0	2	1	0	1	7
Mahdi 2014#	1	1	1	0	2	1	1	0	7
Pop-Vicas 2014*	0	1	1	0	2	0	1	1	6
Uppal 2015#	1	1	1	0	2	1	1	1	8
Morgan 2016*	1	1	1	0	2	0	1	1	7
Tuomi 2016#	1	1	1	0	2	1	1	1	8
Till 2017#	1	1	1	0	2	0	1	1	7
Brown 2019#	1	1	1	1	2	1	1	1	9
Tsuzuki 2021#	1	1	1	0	2	1	1	0	7
Wang 2022*	1	1	1	0	2	1	1	0	7

Note. *means this study was assessed through the items for case-control studies. # means this study was assessed through the items for cohort studies.

PRISMA Flow



Note. There is no reports exluded at full text screening.

BMJ Open

Risk factors for surgical site infection (SSI) in patients undergoing hysterectomy: A systematic review, meta-analysis and network analysis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-093072.R1
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Date Submitted by the Author:	04-Dec-2024
Complete List of Authors:	liu, yin; West China Women's and Children's Hospital, Nosocomial Infection Management Department; Sichuan University West China Second University Hospital Key Laboratory of Birth Defects and Related Diseases of Women and Children liu, yihao; University of Exeter, School of Psychology, Faculty of Health and Life Sciences yang, zhan; West China Women's and Children's Hospital, Medical Department; Sichuan Children's Hospital (Sichuan Children's Medical Center), Medical Department; Sichuan University West China Second University Hospital Key Laboratory of Birth Defects and Related Diseases of Women and Children wu, jinlin; West China Women's and Children's Hospital, medical department li, juan; West China Women's and Children's Hospital, Nosocomial Infection Management Department
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Obstetrics and gynaecology
Keywords:	Risk Factors, Network Meta-Analysis, Meta-Analysis

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Risk factors for surgical site infection (SSI) in patients undergoing hysterectomy: A systematic review, meta-analysis and network analysis

Abstract

Objective: Surgical site infections (SSI) after hysterectomy constitute significant postoperative complications, affecting patient recovery and healthcare costs. We conducted a systematic review of risk factors for SSI in patients undergoing hysterectomy.

Design: The current study conducted a systematic review with meta-analysis and network analysis to identify and summarise risk factors for SSI following hysterectomy.

Data sources: Pubmed, Medline, Embase, Web of Science, and Cochrane Central Register of Controlled Trials were searched through 1 November 2023.

Eligibility criteria: The inclusion criteria were 1) population: female participants who had post-hysterectomy SSI; 2) intervention: hysterectomy surgeries; 3) comparators: the number of participants who had or had not post-hysterectomy SSI; 4) outcomes: the number of participants exposed and not exposed to the risk factors of SSI. The exclusion criteria were 1) non-English studies and 2) studies that provided insufficient data.

Data extraction and synthesis: Two reviewers conducted the screening process independently. Initially, removed all duplicate articles. Then, articles that did not meet the inclusion criteria were excluded. For those that met the criteria, full-text papers were procured. Any discrepancies between the reviewers were resolved through discussion. Data from the selected articles was subsequently extracted.

Results: Blood transfusion emerged as the largest risk factor (OR = 2.55, 95%CI [0.61, 1.26]), followed by tumour presence (OR = 2.23, 95%CI [0.62, 0.98]), obesity (OR = 1.79, 95%CI [0.36, 0.81]), diabetes (OR = 1.70, 95%CI [0.23, 0.82]), and tobacco use (OR = 1.43, 95%CI [0.23, 0.49]). The ORs varied by incision type. Network analysis revealed that vaginal and laparoscopic hysterectomies had significantly lower SSI risk (59% and 55%, respectively) compared to abdominal hysterectomies.

Conclusion: The study establishes blood transfusion, tumour presence,

obesity, diabetes, and tobacco use as significant risk factors for SSI after hysterectomy, with variations in risk evident across different incision types. The findings also suggest vaginal and laparoscopic hysterectomies as preferable alternatives to abdominal hysterectomy in mitigating SSI risk. Future research should aim for more granular data to untangle the interplay between comorbidities and further elucidate the differential risk across SSI types.

Keywords: Hysterectomy; Surgical Site Infections; Risk Factors; Meta-analysis; Network Analysis

Strengths and limitations of this study

1. The current systematic review synthesised evidence on odds ratios of risk factors for post-hysterectomy SSI and applied Bayesian network analysis to compare SSI risks among three commonly used hysterectomy approaches.

2. The current systematic review included 152993 patients who underwent hysterectomy, including 2887 who had post-hysterectomy SSI.

3. The major limitation was that we found the case numbers exposed to each risk factor were counted respectively, such that the odds ratios were not solely attributed to a single risk factor and might be overestimated.

Introduction

Hysterectomy is a very common procedure in which the uterus is surgically removed, and it is an optional treatment for leiomyoma, endometriosis, abnormal bleeding, benign ovarian neoplasms, pelvic organ prolapse, and gynecologic cancer [1]. Epidemiological research estimated that the lifetime prevalence of hysterectomy surgery is approximately 236/100,0000 in Germany, 143/100,0000 in the US [2,3], 80/100,0000 in China [4], and 42/100,0000 in the UK [2] among the female population, depending on waitlist queuing time of different regions [2]. Among patients who had hysterectomies, 2.1% are estimated to develop surgical site infections (SSI) worldwide [5], which has been one of the most common complications after hysterectomy surgery [6]. According to CDC, SSI is an infection that develops in the portion of the body where the operation was performed. It might be superficial, affecting simply the skin, or more serious, involving tissues beneath the skin, organs, or implanted material. The currently accepted risk factors of hysterectomy SSI are age, body mass index (BMI), smoking, and diabetes [7]. However, many studies have shown different results, one study from Spain only considered obesity and inadequate prophylaxis as meaningful indicators [8], whereas another study from the UK also suggested that the operative time should be considered an independent risk factor [9]. The evidence from current research appears to be diverse, isolated, and lacking in quantitative power. Consequently, the current study aims to summarise the results of risk factors of hysterectomy SSI through a quantitative approach.

Method

Study Registration

The protocol of the current study was registered and reviewed by the PROSPERO International Prospective Register of Systematic Reviews (No. CRD42023411668). The protocol is available at: https://www.crd.york.ac.uk/PROSPERO/export_details_pdf.php

The Patient and Public Involvement statement

None

Search Strategy

The data was extracted from published empirical study reports retrieved from the databases, including Pubmed (central), Medline (Ovid), Embase (Ovid), Web of Science, and Cochrane Central Register of Controlled Trials. The search terms followed the standard PICO guideline (population, intervention, comparator, outcome) and were adapted according to Medical Subject Headings (MeSH) terms [10]. The search was conducted upon the completion of study registration.

Eligibility criteria

The inclusion criteria were 1) population: female participants who had post-hysterectomy SSI; 2) intervention: hysterectomy surgeries; 3) comparators: the number of participants who had or had not post-hysterectomy SSI; 4) outcomes: SSI. The exclusion criteria were 1) non-English studies and 2) studies that provided insufficient data.

Study screening and data extraction

The report articles were retrieved in RIS format and managed with Endnote (Bld13966, EndNote X9.3.3, 2023). The screening process followed the PRISMA guidelines [11]. Tworeviewers conducted the screening process independently. Initially, they removed all duplicate articles. Then, articles that did not meet the inclusion criteria were excluded. For those that met the criteria, full-text papers were procured. Any discrepancies between the reviewers were resolved through discussion. Data from the selected articles was subsequently extracted.

Risk of bias assessment

Two reviewers independently scored the studies using the Newcastle-Ottawa quality assessment (NOS) [12,13]. NOS is a validated, easy-to-use scale containing 8

items organised into three dimensions: selection, comparability, and exposure/outcome, which has been endorsed for use in systematic reviews of non-randomised studies by The Cochrane Collaboration [13]. Studies rated 0-2 as poor quality, 3-5 as fair quality, and 6–9 as good/high quality.

Data synthesis

Data synthesis requires at least four sets of data according to the general conduct suggested by the Cochrane Handbook [14]. The effect size of each identified risk factor will be pooled in a quantitative meta-analysis using STATA v18. The risk factors were expected to be reported as binary data about whether or not the patients were exposed to the risk factor and were infected. Consequently, odds ratios (ORs) would be calculated as the effect size with the following formula:

$$OR = \frac{a}{b} \div \frac{c}{d}$$

Where *a* represents cases exposed to the risk factor and infected, *b* represents those exposed but not infected, *c* represents unexposed but infected, and *d* represents unexposed and uninfected cases. And the LogOR is the natural log of the OR.

Statistical Analysis Plan

The meta-analysis was conducted with STATA v18. Only risk factors reported in over 4 datasets were synthesised into meta-analysis. A random effect model meta-analysis with the restricted maximum likelihood method was used to evaluate the pooled ORs (LogORs). The heterogeneity was also assessed with the random effects model, where heterogeneity I^2 is considered moderate when $I^2 > 50\%$ and high when $I^2 > 75\%$ [14]. Sensitivity analysis was conducted using the Leave-one-out approach by omitting one dataset each time and evaluating the pooled effect sizes. Egger's test and funnel plots were used to assess potential publication bias.

The pooled effect sizes were also entered into subgroup analysis based on the SSI types (superficial, deep, organ space) with available datasets. BMI was entered into the meta-regression analysis with pooled effect sizes of diabetes to explore the relationship between obesity and diabetes and its influence on SSI risk prediction.

Finally, a Bayesian network model was conducted with R and WinBugs to determine the risk of SSI between three surgery types (abdominal, vaginal, and laparoscopic). The Bayesian network model offers a probabilistic graphical

framework that represents and analyses the probabilistic relationships among binominal variables [15]. The model fit of the Bayesian network was evaluated with the Deviance Information Criterion (DIC), where a lower DIC indicates a better-fitting model.

Results

Systematic review

Initially, searching the keywords in PubMed, Medline (Ovid), Embase (Ovid), Web of Science, and the Cochrane Central Register of Controlled Trials produced 3821 records. Fourteen studies met the inclusion criteria after screening based on the PRISMA guidelines. The PRISMA procedure is shown in Figure 1.

Figure 1 The PRISMA Flow

All identified studies were retrospective observations to record the case numbers of SSI after hysterectomy surgeries with or without the occurrence of each risk factor. In total, 152993 female patients (age: 47.53±8.29) who underwent hysterectomy were included in the current 14 studies, of whom 2887 had SSI in different types, and 150106 had no SSI taken as controls. The details of all studies are described in Table 1 (More detailed information can be found at supplymentary material 1).

Table 1 Study Summary

Author & Year	Sample Origin	Surgery Method	Blood Transfusion	Diabetes	Obesity	Tobacco Use	Tumour
Molina-Cabrillana 2008	2000-2004 Hospital Universitario Materno-Infantil de Canarias, Sapin	abdominal & vaginal	NR	Y/N	Y/N	NR	Y/N
Olsen 2009	2003-2005 CDC Prevention Epicenter Program hospitals, USA	abdominal & vaginal	NR	Y/N	NR	Y/N	Y/N
Lake 2013	2005-2009 ACS-NSQIP, USA	abdominal & vaginal & laparoscopic	Y/N	Y/N	BMI≥30 (Obesity)	Y/N	Y/N
Savage 2013	2007-2010 University of Iowa Hospitals and Clinics, USA	abdominal	Median	Y/N	Y/N	NR	Y/N
Coleman 2014	1999-2012 Johns Hopkins Medical Institution, USA	abdominal & vaginal & laparoscopic	Y/N	Y/N	BMI≥30 (Obesity)	Y/N	NR
Mahdi 2014	2005-2011 ACS-NSQIP, USA	laparoscopic	>4 units of packed red blood cells	Y/N	BMI≥30 (Obesity)	Y/N	NR
Pop-Vicas 2014	2012-2015 University of Wisconsin Hospitals, USA	abdominal & vaginal & laparoscopic	NR	NR	NR	Y/N	Y/N
Uppal 2015	2012-2015 MSQC, USA	abdominal & vaginal & laparoscopic	NR	NR	BMI≥30 (Obesity)	Y/N	Y/N
Morgan 2016	2012-2014 MSQC, USA	abdominal	Y/N	Y/N	BMI≥30 (Obesity)	Y/N	Y/N
Tuomi 2016	2007-2013 Helsinki University Hospital, Finland	abdominal & vaginal & laparoscopic	NR	Y/N	NR	Y/N	NR
Till 2017	2012-2015 MSQC, USA	abdominal & vaginal & laparoscopic	NR	Y/N	BMI≥30 (Obesity)	Y/N	Y/N
Brown 2019	2012-2014 ACS-NSQIP, USA	laparoscopic	Y/N	Y/N	NR	Y/N	NR
Tsuzuki 2021	2014-2018 Teine Keijinkai Hospital, Japan	laparoscopic	Y/N	Y/N	NR	Y/N	NR

bmjopen-2024-093072 on 4 June 2025. Downloaded from

Wang 2022	2012-2022 Two Grade A Tertiary Hospitals, China	abdominal	NR	Y/N	NR	NR	Y/N

Note. The content under each risk factor was how these studies presented their data. The detailed case numbers are in supplymentary material 1; ACS-NSQIP refers to the American College of Surgeons National Surgical Quality Improvement Program; MSQC refers to the Michigan Surgical Quality Collaborative; NR refers to not reported; NA refers to not applicable; Y/N refers to reported in Yes or No.

Among these studies, seven only reported infection cases in mixed three SSI types (superficial, deep or organ space) [8,16-21], two only reported in mixed two SSI (deep or organ space) [22,23], one study reported each SSI types separately [24] and one study reported superficial and organ space SSIs separately [25], one study reported superficial SSI independently but mixed deep or organ space SSIs [26], one study reported deep SSI independently but mixed superficial or deep SSIs [5], one study reported only organ space SSIs [27]. Since it requires at least four datasets to conduct meta-analyses [14], the studies reported cases in independent SSI types were combined into three mixed SSI types (superficial, deep or organ space) to synthesise with those only reported the mixed SSI types. The NOS risk of bias assessment rated three studies scored 6 [8,19,24], seven scored 7 [5,16-18,21,23,27], two scored 8 [20,25], and the other two scored 9 [22,26]. All 14 studies are ranked as good/high quality and were included in the following review.

Among the 14 studies, there were 11 risk factors identified in total, including age, antimicrobial, blood loss, blood transfusion, BMI, diabetes (both type I or type II), obesity, surgery duration, tobacco use, tumour, and wound cleanness. However, antimicrobial and blood loss were reported in less than four datasets. Wound cleanness and age were reported in different classification standards. Only 5 factors reported in more than 4 datasets are available for quantitative analysis, including blood transfusion, diabetes, obesity, tobacco use, and tumour. Age, high BMI, and surgery duration reported continued data and thus could not be directly synthesised.

Meta-analyses

The identified risk factors with sufficient datasets were entered into meta-analyses respectively. As shown in Table 2, pooled effect sizes revealed significant overall logORs of blood transfusion (logOR = .94, OR = 2.55, p <.001, 95%CI [0.[illegible].26]), obesity (logOR = .58, OR = 1.79, p <.001, 95%CI [0.36, 0.81]), diabetes (logOR = .53, OR = 1.70, p <.001, 95%CI [0.23, 0.82]), tobacco use (logOR = .36, OR = 1.43, p <.001, 95%CI [0.23, 0.49]), but not tumour (logOR = .30, OR = 1.36, p =.362, 95%CI [0.62, 0.98]) to the risk factors for SSI infections. However, after removing each dataset one at a time, leave-one-out sensitivity analysis on all risk factors suggested no changes except for tumour, where one dataset changed the results [8]. Further analysis with publication bias suggested no publication bias in all factors. However, as shown in Figure 2A, the funnel plot suggested three outlier datasets [8,20,24]. One border dataset was decided to be kept [20], and the other two were excluded from the analysis [8,24].

Table 2 Summary of Meta-analyses

Risk Factor	Meta-analysis		Heterogeneity Test		Leave-one-out Sensitivity		Egger's Publication Bias
	OR	p	I^2	p	lowest LogOR	Highest LogOR	p
Blood Transfusion	2.55	<.001	0.00%	.983	.88	.9[illegible]	.934
Tumour	2.23	<.001	0.00%	.850	.70	.8[illegible]	.950
Obesity	1.79	<.001	67.56%	.020	.54	.6[illegible]	.263
Diabetes	1.70	<.001	64.07%	<.001	.44	.5[illegible]	.178
Tobacco Use	1.43	<.001	0.00%	.330	.32	.4[illegible]	.363

Note. The presenting data of the tumour was after exclusions of outliers. RF+ refers to exposure to the risk factor, RF- refers to no exposure to the risk factor, SSI+ refers to SSI positive, and SSI- refers to SSI negative.

Figure 2 The Funnel Plots

After exclusion, data from the tumour was entered into meta-analysis again and reported a significant pooled effect size predicting SSI infections (logOR = .80, OR = 2.23, p <.001), and, as shown in Figure 2B, there were no outliers. As shown in Figure 3A, 3B, and 3C, the estimation of heterogeneity suggested that the chance of inconsistent distribution of the pooled logORs was not significant in blood transfusion datasets (I^2 = 0%, $Q_{(3)}$ = .17, p = .983), tumour (I^2 = 0%, $Q_{(4)}$ = 1.34, p = .850) or tobacco use (I^2 = 0%, $Q_{(5)}$ = 5.78, p = .330). However, Figure 3D and Figure 3E suggested significant moderate heterogeneity in obesity (I^2 = 67.56%, $Q_{(4)}$ = 11.58, p <.001) and diabetes datasets (I^2 = 64.07%, $Q_{(7)}$ = 21.13, p <.001). These results suggested that blood transfusion, tumour, tobacco use, obesity, and diabetes were significant risk factors predicting post-hysterectomy SSI. Patients who underwent blood transfusion had a 155% increased likelihood of experiencing post-hysterectomy SSI. Similarly, individuals with tumours had a 123% increased risk, obese individuals 79%, diabetics 70%, and tobacco users 43%.

Figure 3 The Forest Plots for Each Risk Factor

Subgroup analysis between studies reporting different SSI types (mixed superficial or deep or organ space vs. mixed deep or organ space) was conducted among tobacco use and diabetes, for they obtained more than 4 datasets under each subgroup. The difference was whether they included superficial SSI. A significant group difference in pooled ORs between mixed superficial & deep & organ space cases and mixed deep or organ space among tobacco use, $Q_{(1)}$ = 11.59, p <.001, but not among diabetes, $Q_{(1)}$ = .71, p = .400.The impact of tobacco use on the risk of SSI varied significantly depending on the type of SSI, see supplymentary material Table 2. As shown in Figure 4, while tobacco use was associated with a 143% increased risk for combined superficial, deep, and organ space SSIs, this risk escalated to a 272% increase when considering only deep and organ space SSIs. This suggests that the influence of smoking may be more pronounced for deep and organ space infections than superficial ones. Given the observed discrepancy in risk between the combined

three types of SSIs and the combined two types (deep or organ space) for tobacco use, it is plausible that other risk factors might also exhibit differential effects across various SSI categories.

Figure 4 Tobacco Use Subgroup Forest Plot between SSI Types

Continuous BMI data was incorporated into a meta-regression analysis alongside the ORs of diabetes to evaluate the relationship between obesity and diabetes. Given the absence of group differences or heterogeneity discrepancies across SSI types in the effect sizes associated with diabetes, datasets from both SSI types (though not originating from identical studies) were incorporated into the meta-regression. The results suggested that BMI did not significantly predict the ORs of diabetes (β = .001, SE = .08, t = .02, p = .989). While this does not suggest that BMI (or obesity) is not correlated with the incidence of diabetes, it does affirm that high BMI did not affect the outcomes in this particular analysis.

Bayesian Network Analysis

The infected and non-infected case numbers under each surgery method (abdominal, vaginal, laparoscopic) were analysed with a Bayesian network model to determine whether vaginal and laparoscopic surgeries had a lower SSI risk than abdominal surgeries, see Figure 5. The Bayesian network model exhibited a DIC of 111.5. Compared to abdominal surgeries, vaginal surgeries reduced the risk of developing SSI by 59% (logOR = -.90, OR = .41, 95%CI [0.33, 0.67]) and laparoscopic surgeries by 55% (logOR = -.80, OR = .45, 95%CI [0.37, 0.67]). However, the latter two did not distinguish from each other (logOR = -.1, OR = .9, 95%CI [0.72, 1.21]). These results suggest that conducting the hysterectomy with the vaginal or laparoscopic methods is respectively safer than the abdominal method in terms of SSI risk.

Figure 5 Bayesian network analysis

Discussion

The current study conducted a systematic review with meta-analysis and network analysis to summarise the evidence of risk factors of SSI after hysterectomy surgeries. To our knowledge, this is the first quantitative review of the topic. In total, 14 retrospective observations studies were identified with 2887 SSI positive and 150106 negative cases under 11 risk factors, including age, antimicrobial, blood loss, blood transfusion, high BMI, diabetes, obesity, surgery duration, tobacco use, tumour, and wound cleanness. However, only 5 were available for meta-analysis synchronisation. Among which, blood transfusion, tumour, obesity, diabetes, and tobacco use were factors that significantly increased the risk of SSI. The estimated ORs also seemed to vary between different SSI types (superficial, deep, or organ space). Apart from risk factors, Bayesian network analysis also suggested that conducting vaginal or laparoscopic hysterectomies induced a significantly lower risk of SSI infection than abdominal surgeries. The details of the quantitative analysis are discussed as follows.

The largest risk factor of SSI is blood transfusion (OR = 2.55), with a 155% increased likelihood of SSI. Blood transfusion has always been identified as a major source of post-surgical infections [28,29]. Administrative errors, such as bacterial contamination in platelet products, are believed responsible for infections induced by blood transfusion [28]. These issues are related to the healthcare service environment and beyond the current paper's discussion. Instead, the need for blood transfusion deserves further elaboration from the patients' site. For example, blood loss was reported to be positively correlated with BMI [30,31]. Apart from obesity, severe abnormal uterine bleeding and cancer-related anaemia are also important reasons that patients require extra blood transfusion. However, none of the included studies attempted to isolate these factors, nor did they report preoperative haemoglobin. Consequently, we could not address whether blood transfusion was an independent factor or it was attributed to other factors such as obesity, severe abnormal uterine bleeding, cancer-related anaemia, preoperative haemoglobin or whether its estimated ORs were inflated. Future studies should consider reporting more comprehensive data to precisely estimate the ORs for blood transfusion as the SSI risk factor.

Likewise, one may argue that obesity and diabetes are comorbid, where obesity-induced insulin resistance is one of the major sources of type 2 diabetes [32]. This might explain the moderate heterogeneity of the ORs in obesity (OR = 1.79, I^2 = 67.56%)

and diabetes (OR = 1.70, I^2 = 64.07%). This is, in fact, a methodological issue, where all studies directly counted the case number that was exposed and not exposed to the specific risk factors, but none attempted to distinguish whether the case was exposed to multiple risk factors. That is, one might suffer from obesity or diabetes or both, and the case would be counted in each risk factor respectively when they suffer from both. Consequently, the estimated ORs were not solely attributed to one risk factor and might be overestimated. Hypothetically, in the current case, the heterogeneity of the ORs in obesity and diabetes was moderate because some studies included more patients suffering from both obesity and diabetes and reported higher ORs than those with fewer such patients. As a result, although both obesity and diabetes are significant risk factors, their estimated ORs should be considered cautiously and require further clarification in future studies by reporting cases separately.

To further address this issue, the current study conducted a meta-regression analysis to investigate whether BMI predicts the ORs of diabetes. The analysis found no significant relationship between continuous BMI values and the ORs of diabetes. Notably, the absence of a significant predictive relationship between BMI and the OR for diabetes does not imply that these two factors were unrelated or that obesity does not influence the estimation of OR for diabetes. On the one hand, the absence of a significant predictive relationship might arise from including both type I and type II diabetes in the studies, with type I diabetes having less direct relevance to obesity. On the other hand, the estimation of ORs may still have been elevated due to the repeated counting of cases exposed to multiple risk factors. Instead, this result might be interpreted as the pathologies of obesity and diabetes are relatively independent in the context of SSI risk.

Apart from obesity and diabetes, the second-largest risk factor was tumour (OR = 2.23), with a 123% increased likelihood of SSI. The immune system in patients afflicted with malignant tumours was generally compromised [33]. This impairment in the primary immune function directly results from the tumour's pervasive influence on the natural defence mechanisms. Furthermore, the standard therapeutic interventions for tumours, including surgery, chemotherapy, and radiotherapy, also contribute to the weakened immune state [34].

Tobacco use was the last risk factor (OR = 1.43), with a 43% increased likelihood of SSI. Nicotine and carbon monoxide, two primary agents produced in tobacco use, contribute to the constriction of peripheral blood vessels. This vasoconstriction reduces the oxygen supply to tissues, vital for cellular function and healing processes [35]. Consequently, this oxygen deficit can precipitate the formation of microthrombi, which are small clots that can impair blood flow and further hinder tissue repair and regeneration.

However, the estimated ORs of tobacco use seemed to vary between SSI types. A subgroup comparison was conducted between studies that reported all mixed SSI and those that only reported deep or organ space SSI for tobacco use and diabetes, where only these two risk factors were reported repeatedly in distinguishing between SSI types. Significant subgroup differences were observed exclusively in the context of tobacco use. Specifically, tobacco use was associated with a 43% increased risk for superficial, deep, or organ space SSIs. This risk escalated to a 172% increase when focusing solely on deep or organ space SSIs. The pronounced impact of tobacco use appears more substantial in increasing the risk of deep or organ space infections compared to superficial ones. This discrepancy may also be attributed to tobacco-induced vasoconstriction. The vascular system supporting superficial cells, such as those in the skin, is more prosperous than the vasculature of deep and organ space cells. Consequently, cells in deeper tissues and organ spaces are more vulnerable to oxygen supply alterations exacerbated by tobacco use. However, this was merely a hypothetical explanation without solid evidence, which requires further investigation.

Finally, the current Bayesian model revealed a significant reduction in SSI risk with vaginal and laparoscopic hysterectomies compared to the abdominal approach, with decreases of 59% and 55% respectively. Abdominal hysterectomy, though designed to prevent bladder damage by opening the peritoneal reflection and mobilising the bladder, increases postoperative infection risks due to larger incisions and greater abdominal exposure [36]. In contrast, laparoscopic methods, utilising smaller incisions and camera systems, minimise air exposure and use electrocoagulation for cutting and hemostasis, thereby reducing pelvic-abdominal disturbances and promoting a stable internal environment [37]. While total laparoscopic hysterectomy demands high skill levels, vaginal hysterectomy offers a simpler approach to uterine manipulation, albeit with a slight increase in urinary system

infection risks from metal cannula introduction [38]. Although each technique has distinct risk-benefit profiles, the current results provided straightforward evidence of SSI risk, comparing the techniques to reference individual patient needs and surgical goals.

There are five limitations in the current study. First, some procedures performed in conjunction with hysterectomy can also affect SSI, but this was not explored in this paper. Second, the included studies did not differentiate cases based on the number of risk factors present, counting each instance for all identified risks. This approach likely inflated the ORs, particularly for comorbid conditions like patients with severe abnormal uterine bleeding or cancer-related anaemia and obesity and diabetes. Thirdly, there was no distinction between Type I and Type II diabetes in the studies, potentially contributing to moderate heterogeneity in the pooled OR estimates. Therefore, the estimated ORs for obesity and diabetes as risk factors for SSIs should be interpreted cautiously. Then, since none of the studies isolated patients with severe abnormal uterine bleeding, suffered from cancer-related anaemia, or reported pre-operative HbA1, it is unclear whether these factors also inflated the estimation ORs for blood transfusion, and thus, they should be interpreted cautiously as well. Lastly, few studies specified the types of SSI (superficial, deep, or organ space). Given that our analysis indicates variation in tobacco use ORs across different SSI types, it is crucial to ascertain if similar variations apply to other risk factors. Addressing these issues in future research, with more detailed data reporting, is essential for a clearer understanding of the risk factors for SSIs. Future studies should report more comprehensive data to address these limitations.

In summary, the current study conducted a systematic review with meta-analysis and network analysis of the risk factors of SSI after hysterectomy surgeries. In total, 11 risk factors were mentioned, whereas only blood transfusion, tumour, obesity, diabetes, and tobacco use had sufficient data to be entered into meta-analysis and yield statistical significance. With limited available data, the ORs of tobacco use seemed to vary between different SSI types, suggesting potential diversity in other risk factors. Finally, a Bayesian network model compared the risk of SSI between vaginal and laparoscopic and abdominal hysterectomy approaches. This approach offers valuable insights into the varying risks associated with each surgical method.

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Figure 1 The PRISMA Flow

Figure 2 The Funnel Plots

Figure 3 The Forest Plots for Each Risk Factor

Figure 4 Tobacco Use Subgroup Forest Plot between SSI Types

Figure 5 Bayesian network analysis

Figure 1 The PRISMA Flow

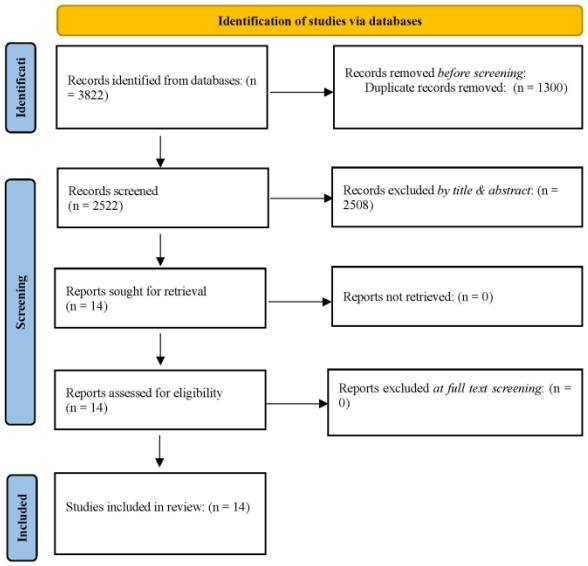

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Figure 2 The Funnel Plots

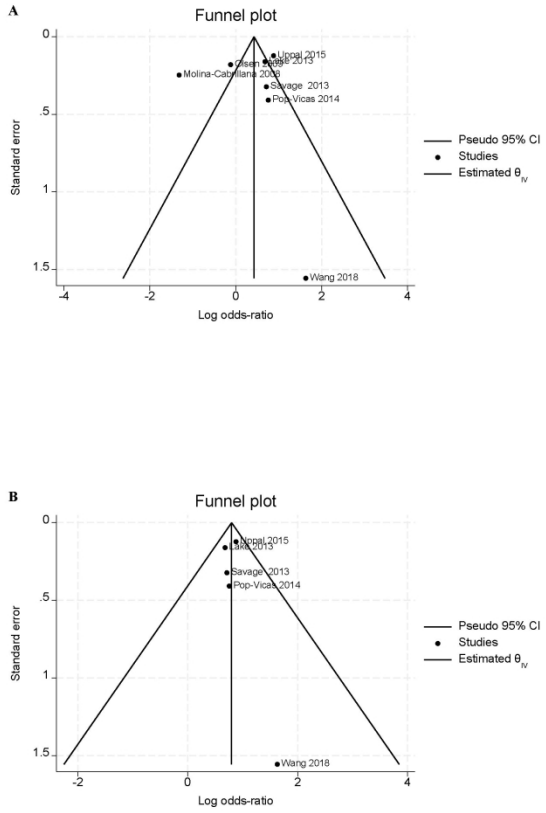

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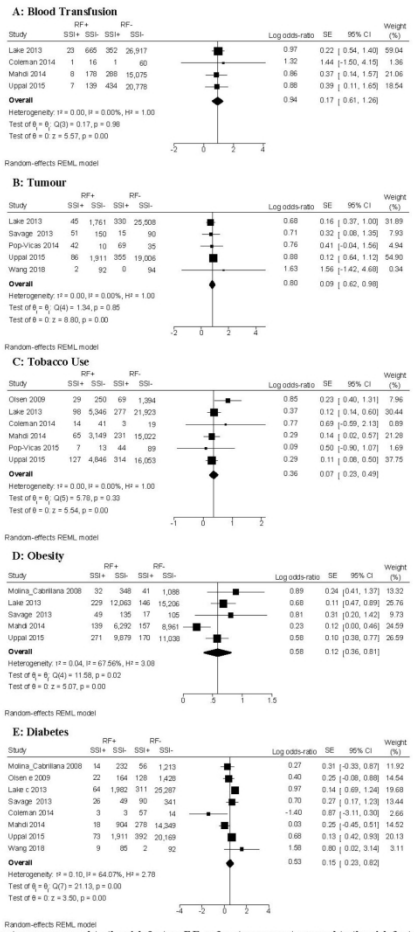
Figure 3 The Forest Plots for Each Risk Factor



Note. RF+ refers to cases exposed to the risk factor; RF- refers to cases not exposed to the risk factor; SSI+ refers to SSI positive cases; SSI- refers to SSI negative cases;

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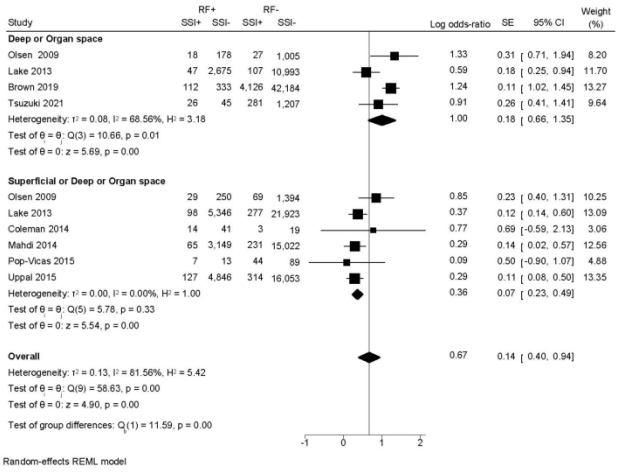
Figure 1 Tobacco Use Subgroup Forest Plot between SSI Types



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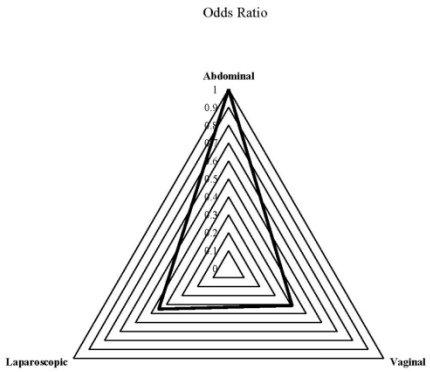

297x210mm (300 x 300 DPI)

Contents

Search Terms

Pubmed (Central) Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeries SSI (no restriction to age)	hysterectomy surgeriesmesh term: #1
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term: #1
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term: #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
Outcome	SSI	Infection mesh term: #10

step	code	results
#1	(((((((hysterectomy) OR (hysterectomies)) OR (hysterectomy, Vaginal)) OR (hysterectomies, Vaginal)) OR (vaginal hysterectomies)) OR (vaginal hysterectomy)) OR (Colpohysterectomy)) OR (Colpohysterectomies))	53,350
#2	((Clinical Trials, Randomized) OR (Trials, Randomized Clinical)) OR (Controlled Clinical Trials, Randomized)	742,997
#3	((((((((((((((((((((((((Cross Sectional Studies) OR (Cross-Sectional Study)) OR (Studies, Cross-Sectional)) OR (Study, Cross-Sectional)) OR (Surveys, Disease Frequency)) OR (Disease Frequency Survey)) OR (Survey, Disease Frequency)) OR (Analysis, Cross-Sectional)) OR (Analyses, Cross-Sectional)) OR (Analysis, Cross Sectional)) OR (Cross-Sectional Analyses)) OR (Cross-Sectional Analysis)) OR (Cross Sectional Analysis)) OR (Analyses, Cross Sectional)) OR (Cross Sectional Analyses)) OR (Cross-Sectional Survey)) OR (Cross Sectional Survey)) OR (Cross-Sectional Surveys)) OR (Survey, Cross-Sectional)) OR (Surveys, Cross-Sectional)) OR (Disease Frequency Surveys)) OR (Prevalence Studies)) OR (Prevalence Study)) OR (Studies, Prevalence)) OR (Study, Prevalence)	1,122,672
#4	((((((((((((((((((((((((((((((Longitudinal Study) OR (Studies, Longitudinal)) OR (Study, Longitudinal)) OR (Tuskegee Syphilis Study)) OR (Syphilis Studies, Tuskegee)) OR (Syphilis Study, Tuskegee)) OR (Tuskegee Syphilis Studies)) OR (Jackson Heart Study)) OR (Heart Studies, Jackson)) OR (Heart Study, Jackson)) OR (Jackson Heart Studies)) OR (Studies, Jackson Heart)) OR (California Teachers Study)) OR (California Teachers Studies)) OR (Studies, California Teachers)) OR (Study, California Teachers)) OR (Teachers Studies, California)) OR (Teachers Study, California)) OR (Bogalusa Heart Study)) OR (Bogalusa Heart Studies)) OR (Heart Studies, Bogalusa)) OR (Heart Study, Bogalusa)) OR (Studies, Bogalusa Heart)) OR (Study, Bogalusa Heart)) OR (Framingham Heart Study)) OR (Framingham Heart Studies)) OR (Heart Studies, Framingham)) OR (Heart Study, Framingham)) OR (Longitudinal Survey)) OR (Longitudinal Surveys)) OR (Survey, Longitudinal)) OR (Surveys, Longitudinal)	339,768
#5	((((((((((((((((((((((((((((((((((((((Case-Control Study) OR (Studies, Case-Control)) OR (Study, Case-Control)) OR (Case-Comparison Studies)) OR (Case Comparison Studies)) OR (Case-Comparison Study)) OR (Studies, Case-Comparison)) OR (Study, Case-Comparison)) OR (Case-Compeer Studies)) OR (Studies, Case-Compeer)) OR (Case-Referrent Studies)) OR (Case Referrent Studies)) OR (Case-Referrent Study)) OR (Studies, Case-Referrent)) OR (Study, Case-Referrent)) OR (Case-Referent Studies)) OR (Case Referent Studies)) OR (Case-Referent Study)) OR (Studies, Case-Referent)) OR (Study, Case-Referent)) OR (Case-Base Studies)) OR (Case Base Studies)) OR (Studies, Case-Base)) OR (Case Control Studies)) OR (Case Control Study)) OR (Studies, Case Control)) OR (Study, Case Control)) OR (Nested Case-Control Studies)) OR (Case-Control Studies, Nested)) OR (Case-Control Study, Nested)) OR (Nested Case Control Studies)) OR (Nested Case-Control Study)) OR (Studies, Nested Case-Control)) OR (Study, Nested Case-Control)) OR (Matched Case-Control Studies)) OR (Case-Control Studies,	1,589,628

	Matched)) OR (Case-Control Study, Matched)) OR (Matched Case Control Studies)) OR (Matched Case-Control Study)) OR (Studies, Matched Case-Control)) OR (Study, Matched Case-Control)	
#6	((Prospective Study) OR (Studies, Prospective)) OR (Study, Prospective)	904,417
#7	((((((((((((((((((((((((((((Cohort Study) OR (Studies, Cohort)) OR (Study, Cohort)) OR (Concurrent Studies)) OR (Studies, Concurrent)) OR (Concurrent Study)) OR (Study, Concurrent)) OR (Closed Cohort Studies)) OR (Cohort Studies, Closed)) OR (Closed Cohort Study)) OR (Cohort Study, Closed)) OR (Study, Closed Cohort)) OR (Studies, Closed Cohort)) OR (Birth Cohort Studies)) OR (Birth Cohort Study)) OR (Cohort Studies, Birth)) OR (Cohort Study, Birth)) OR (Studies, Birth Cohort)) OR (Study, Birth Cohort)) OR (Analysis, Cohort)) OR (Analyses, Cohort)) OR (Cohort Analyses)) OR (Cohort Analysis)) OR (Historical Cohort Studies)) OR (Cohort Studies, Historical)) OR (Cohort Study, Historical)) OR (Historical Cohort Study)) OR (Study, Historical Cohort)) OR (Studies, Historical Cohort)) OR (Incidence Studies)) OR (Incidence Study)) OR (Studies, Incidence)) OR (Study, Incidence)	3,150,416
#8	Observational Study	205,618
#9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	4,994,412
#10	((((Infection and Infestation) OR (Infestation and Infection)) OR (Infections and Infestations)) OR (Infestations and Infections)) OR (Infection)	4003846
#11	#1 AND #9 AND #10	1,758
#12	The year 2000 - Current	1,198
#13	English	1,096

The results are hyperlinked in each column

Medline (Ovid) Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesmesh term with Medline code
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term with Medline code
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term with Medline code
Outcome	SSI	Infection mesh term with Medline code

	Term searched	Results
Group 1	Population	
1	hysterectomy. ti,ab,mp.	52599
2	hysterectomies. ti,ab,mp.	3423
3	hysterectomy, Vaginal. ti,ab,mp.	3235
4	hysterectomies, Vaginal. ti,ab,mp.	9
5	vaginal hysterectomies. ti,ab,mp.	437
6	vaginal hysterectomy. ti,ab,mp.	3593
7	Colpohysterectomy. ti,ab,mp.	84
8	Colpohysterectomies. ti,ab,mp.	8
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	53278
Group 2	Intervention	
10	hysterectomy. ti,ab,mp.	52599
11	hysterectomies. ti,ab,mp.	3423
12	hysterectomy, Vaginal. ti,ab,mp.	3235
13	hysterectomies, Vaginal. ti,ab,mp.	9
14	vaginal hysterectomies. ti,ab,mp.	437
15	vaginal hysterectomy. ti,ab,mp.	3593
16	Colpohysterectomy. ti,ab,mp.	84
17	Colpohysterectomies. ti,ab,mp.	8
18	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	53278
Group 3	Comparator	
19	Cross-sectional. ti,ab,mp.	632818
20	Longitudinal. ti,ab,mp.	377935
21	Prospective study. ti,ab,mp.	159216
22	Cohort study. ti,ab,mp.	274386
23	Observational study. ti,ab,mp.	199248
24	Randomized control study. ti,ab,mp.	937
25	Case-Control Studies. ti,ab,mp.	338463
26	19 or 21 or 22 or 23 or 24 or 25	1494518
Group 4	Outcome	
27	Infections. ti,ab,mp.	1470008
28	"Infection and Infestation". ti,ab,mp.	86
29	"Infestation and Infection". ti,ab,mp.	51
30	"Infections and Infestations". ti,ab,mp.	311

31	"Infestations and Infections". ti,ab,mp.	28
32	Infection. ti,ab,mp.	1418735
33	27 or 28 or 29 or 30 or 31 or 32	2279134
Combined	9 and 18 and 26 and 33	407
Limited to English only	9 and 18 and 26 and 33	384
The year 2000 to present	9 and 18 and 26 and 33	337

Results link:

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=5SYIqKO2Gpep7EBCDrAGLmKZrFtVAMXrv0wx7zAaFQsQRH5DCIC4ESMKrqhH2tOv1

Embase (Ovid) Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesmesh term with Embase code
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term with Embase code
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term with Embase code
Outcome	SSI	Infection mesh term with Embase code

	Term searched	Results
Group 1	Population	
1	hysterectomy. ti,ab,mp.	93767
2	hysterectomies. ti,ab,mp.	6284
3	hysterectomy, Vaginal. ti,ab,mp.	392
4	trachelectomy. ti,ab,mp.	19
5	hysterectomies, Vaginal. ti,ab,mp.	758
6	vaginal hysterectomies. ti,ab,mp.	8954
7	vaginal hysterectomy. ti,ab,mp.	83
8	Colpohysterectomy. ti,ab,mp.	5
9	Colpohysterectomies. ti,ab,mp.	94170
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	93767
Group 2	Intervention	
11	hysterectomy. ti,ab,mp.	93767
12	hysterectomies. ti,ab,mp.	6284
13	hysterectomy, Vaginal. ti,ab,mp.	392
14	trachelectomy. ti,ab,mp.	19
15	hysterectomies, Vaginal. ti,ab,mp.	758
16	vaginal hysterectomies. ti,ab,mp.	8954
17	vaginal hysterectomy. ti,ab,mp.	83
18	Colpohysterectomy. ti,ab,mp.	5
19	Colpohysterectomies. ti,ab,mp.	94170
20	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	93767
Group 3	Comparator	
21	Cross-sectional. ti,ab,mp.	765496
22	Longitudinal. ti,ab,mp.	475332
23	Prospective study. ti,ab,mp.	899849
24	Cohort study. ti,ab,mp.	405571
25	Observational study. ti,ab,mp.	342074
26	Randomized control study. ti,ab,mp.	1628
27	Case-Control Studies. ti,ab,mp.	27610
28	21 or 22 or 23 or 24 or 25 or 26 or 27	2146419
Group 4	Outcome	
29	Infections. ti,ab,mp.	835857
30	"Infection and Infestation". ti,ab,mp.	107

31	"Infestation and Infection". ti,ab,mp.	55
32	"Infections and Infestations". ti,ab,mp.	807
33	"Infestations and Infections". ti,ab,mp.	49
34	Infection. ti,ab,mp.	2763568
35	29 or 30 or 31 or 32 or 33 or 34	2991465
Combined	10 and 20 and 28 and 35	1510
Limited to English only	10 and 20 and 28 and 35	1468
The year 2000 to present	10 and 20 and 28 and 35	1419

Results link:

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=79TCxxCp1oN0adXj9ZUf4UzOGz44m8xhcwT9pEsrMoJkpSIjfY4IktYO5RKZbvU7

Web of Science Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesmesh term with the web of science code: #1
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term with the web of science code: #1
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh terms with the web of science code: #2, #3, #4, #5, #6, #7, #8
Outcome	SSI	Infection mesh term with the web of science code: #10

step	code	results
#1	TS= (hysterectomy* OR hysterectomies* OR hysterectomy, vaginal* OR hysterectomies, vaginal OR vaginal hysterectomies* OR vaginal hysterectomy* OR colpohysterectomy* OR colpohysterectomies*)	40974
#2	TS= (Clinical Trials, Randomized* OR Trials, Randomized Clinical* OR Controlled Clinical Trials, Randomized*)	357993
#3	TS= (Longitudinal Study* OR Studies, Longitudinal* OR Study, Longitudinal* OR Tuskegee Syphilis Study* OR Syphilis Studies, Tuskegee* OR Syphilis Study, Tuskegee* OR Tuskegee Syphilis Studies* OR Jackson Heart Study* OR Heart Studies, Jackson* OR Heart Study, Jackson* OR Jackson Heart Studies* OR Studies, Jackson Heart* OR California Teachers Study* OR California Teachers Studies* OR Studies, California Teachers* OR Study, California Teachers* OR Teachers Studies, California* OR Teachers Study, California* OR Bogalusa Heart Study* OR Bogalusa Heart Studies* OR Heart Studies, Bogalusa* OR Heart Study, Bogalusa* OR Studies, Bogalusa Heart* OR Study, Bogalusa Heart* OR Framingham Heart Study* OR Framingham Heart Studies* OR Heart Studies, Framingham* OR Heart Study, Framingham* OR Longitudinal Survey* OR Longitudinal Surveys* OR Survey, Longitudinal* OR Surveys, Longitudinal*)	389252
#4	TS= (Case-Control Study* OR Studies, Case-Control* OR Study, Case-Control* OR Case-Comparison Studies* OR Case Comparison Studies* OR Case-Comparison Study* OR Studies, Case-Comparison* OR Study, Case-Comparison* OR Case-Compeer Studies* OR Studies, Case-Compeer* OR Case-Referrent Studies* OR Case Referrent Studies* OR Case-Referrent Study* OR Studies, Case-Referrent* OR Study, Case-Referrent* OR Case-Referent Studies* OR Case Referent Studies* OR Case-Referent Study* OR Studies, Case-Referent* OR Study, Case-Referent* OR Case-Base Studies* OR Case Base Studies* OR Studies, Case-Base* OR Case Control Studies* OR Case Control Study* OR Studies, Case Control* OR Study, Case Control* OR Nested Case-Control Studies* OR Case-Control Studies, Nested* OR Case-Control Study, Nested* OR Nested Case Control Studies* OR Nested Case-Control Study* OR Studies, Nested Case-Control* OR Study, Nested Case-Control* OR Matched Case-Control Studies* OR Case-Control Studies, Matched* OR Case-Control Study, Matched* OR Matched Case Control Studies* OR Matched Case-Control Study* OR Studies, Matched Case-Control* OR Study, Matched Case-Control*)	742023
#5	TS= (Cross Sectional Studies* OR Cross-Sectional Study * OR Studies, Cross-Sectional * OR Study, Cross-Sectional * OR Surveys, Disease Frequency * OR Disease Frequency Survey * OR Survey, Disease Frequency * OR Analysis, Cross-Sectional * OR Analyses, Cross-Sectional * OR Analysis, Cross Sectional * OR Cross-Sectional Analyses * OR Cross-Sectional Analysis * OR Cross Sectional Analysis	1164085

	* OR Analyses, Cross Sectional * OR Cross Sectional Analyses * OR Cross-Sectional Survey * OR Cross Sectional Survey * OR Cross-Sectional Surveys * OR Survey, Cross-Sectional * OR Surveys, Cross-Sectional * OR Disease Frequency Surveys * OR Prevalence Studies * OR Prevalence Study * OR Studies, Prevalence * OR Study, Prevalence*)	
#6	TS= (Prospective Study* OR Studies, Prospective* OR Study, Prospective*)	721432
#7	TS= (Cohort Study* OR Studies, Cohort * OR Study, Cohort * OR Concurrent Studies * OR Studies, Concurrent * OR Concurrent Study * OR Study, Concurrent * OR Closed Cohort Studies * OR Cohort Studies, Closed * OR Closed Cohort Study * OR Cohort Study, Closed * OR Study, Closed Cohort * OR Studies, Closed Cohort * OR Birth Cohort Studies * OR Birth Cohort Study * OR Cohort Studies, Birth * OR Cohort Study, Birth * OR Studies, Birth Cohort * OR Study, Birth Cohort * OR Analysis, Cohort * OR Analyses, Cohort * OR Cohort Analyses * OR Cohort Analysis * OR Historical Cohort Studies * OR Cohort Studies, Historical * OR Cohort Study, Historical * OR Historical Cohort Study * OR Study, Historical Cohort * OR Studies, Historical Cohort * OR Incidence Studies * OR Incidence Study * OR Studies, Incidence * OR Study, Incidence*)	1333108
#8	TS= (Observational study *)	234254
#9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	3887063
#10	TS= (Infections* OR Infection and Infestation * OR Infestation and Infection * OR Infections and Infestations * OR Infestations and Infections * OR Infection *)	1895911
#11	#1 AND #9 AND #10	853
#12	The year 2000 – current; English	726

The results are hyperlinked in each column

Cochrane Library Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesCochrane search manager hysterectomy surgerieswith Cochrane code based on mesh term: #1
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgerieswith Cochrane code based on mesh term
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study with Cochrane code based on mesh term:
Outcome	SSI	hysterectomy surgerieswith Cochrane code based on mesh term

step	code	results
#1	(hysterectomy):ti,ab,kw OR (hysterectomies):ti,ab,kw OR (hysterectomy,Vaginal):ti,ab,kw OR (hysterectomies,Vaginal):ti,ab,kw OR (vaginal hysterectomies):ti,ab,kw OR (vaginal hysterectomy):ti,ab,kw OR (Colpohysterectomy):ti,ab,kw OR (Colpohysterectomies):ti,ab,kw	8202
#2	(Clinical Trials, Randomized):ti,ab,kw OR (Trials, Randomized Clinical):ti,ab,kw OR (Controlled Clinical Trials, Randomized):ti,ab,kw	154945
#3	(Longitudinal Study):ti,ab,kw OR (Studies, Longitudinal):ti,ab,kw OR (Study, Longitudinal):ti,ab,kw OR (Tuskegee Syphilis Study):ti,ab,kw OR (Syphilis Studies, Tuskegee):ti,ab,kw OR (Syphilis Study, Tuskegee):ti,ab,kw OR (Tuskegee Syphilis Studies):ti,ab,kw OR (Jackson Heart Study):ti,ab,kw OR (Heart Studies, Jackson):ti,ab,kw OR (Heart Study, Jackson):ti,ab,kw OR (Jackson Heart Studies):ti,ab,kw OR (Studies, Jackson Heart):ti,ab,kw OR (California Teachers Study):ti,ab,kw OR (California Teachers Studies):ti,ab,kw OR (Studies, California Teachers):ti,ab,kw OR (Study, California Teachers):ti,ab,kw OR (Teachers Studies, California):ti,ab,kw OR (Teachers Study, California):ti,ab,kw OR (Bogalusa Heart Study):ti,ab,kw OR (Bogalusa Heart Studies):ti,ab,kw OR (Heart Studies, Bogalusa):ti,ab,kw OR (Heart Study, Bogalusa):ti,ab,kw OR (Studies, Bogalusa Heart):ti,ab,kw OR (Study, Bogalusa Heart):ti,ab,kw OR (Framingham Heart Study):ti,ab,kw OR (Framingham Heart Studies):ti,ab,kw OR (Heart Studies, Framingham):ti,ab,kw OR (Heart Study, Framingham):ti,ab,kw OR (Longitudinal Survey):ti,ab,kw OR (Longitudinal Surveys):ti,ab,kw OR (Survey, Longitudinal):ti,ab,kw OR (Surveys, Longitudinal):ti,ab,kw	23544
#4	(Case-Control Study):ti,ab,kw OR (Studies, Case-Control):ti,ab,kw OR (Study, Case-Control):ti,ab,kw OR (Case-Comparison Studies):ti,ab,kw OR (Case Comparison Studies):ti,ab,kw OR (Case-Comparison Study):ti,ab,kw OR (Studies, Case-Comparison):ti,ab,kw OR (Study, Case-Comparison):ti,ab,kw OR (Case-Compeer Studies):ti,ab,kw OR (Studies, Case-Compeer):ti,ab,kw OR (Case-Referrent Studies):ti,ab,kw OR (Case Referrent Studies):ti,ab,kw OR (Case-Referrent Study):ti,ab,kw OR (Studies, Case-Referrent):ti,ab,kw OR (Study, Case-Referrent):ti,ab,kw OR (Case-Referent Studies):ti,ab,kw OR (Case Referent Studies):ti,ab,kw OR (Case-Referent Study):ti,ab,kw OR (Studies, Case-Referent):ti,ab,kw OR (Study, Case-Referent):ti,ab,kw OR (Case-Base Studies):ti,ab,kw OR (Case Base Studies):ti,ab,kw OR (Studies, Case-Base):ti,ab,kw OR (Case Control Studies):ti,ab,kw OR (Case Control Study):ti,ab,kw OR (Studies, Case Control):ti,ab,kw OR (Study, Case Control):ti,ab,kw OR (Nested Case-Control Studies):ti,ab,kw OR (Case-Control Studies, Nested):ti,ab,kw OR (Case-Control Study, Nested):ti,ab,kw OR (Nested Case Control Studies):ti,ab,kw OR (Nested Case-Control Study):ti,ab,kw OR (Studies, Nested Case-Control):ti,ab,kw OR (Study, Nested Case-Control):ti,ab,kw OR (Matched Case-Control Studies):ti,ab,kw OR (Case-Control	33557

	Studies, Matched):ti,ab,kw OR (Case-Control Study, Matched):ti,ab,kw OR (Matched Case Control Studies):ti,ab,kw OR (Matched Case-Control Study):ti,ab,kw OR (Studies, Matched Case-Control):ti,ab,kw OR (Study, Matched Case-Control):ti,ab,kw	
#5	(Cross Sectional Studies):ti,ab,kw OR (Cross-Sectional Study):ti,ab,kw OR (Studies, Cross-Sectional):ti,ab,kw OR (Study, Cross-Sectional):ti,ab,kw OR (Surveys, Disease Frequency):ti,ab,kw OR (Disease Frequency Survey):ti,ab,kw OR (Survey, Disease Frequency):ti,ab,kw OR (Analysis, Cross-Sectional):ti,ab,kw OR (Analyses, Cross-Sectional):ti,ab,kw OR (Analysis, Cross Sectional):ti,ab,kw OR (Cross-Sectional Analyses):ti,ab,kw OR (Cross-Sectional Analysis):ti,ab,kw OR (Cross Sectional Analysis):ti,ab,kw OR (Analyses, Cross Sectional):ti,ab,kw OR (Cross Sectional Analyses):ti,ab,kw OR (Cross-Sectional Survey):ti,ab,kw OR (Cross Sectional Survey):ti,ab,kw OR (Cross-Sectional Surveys):ti,ab,kw OR (Survey, Cross-Sectional):ti,ab,kw OR (Surveys, Cross-Sectional):ti,ab,kw OR (Disease Frequency Surveys):ti,ab,kw OR (Prevalence Studies):ti,ab,kw OR (Prevalence Study):ti,ab,kw OR (Studies, Prevalence):ti,ab,kw OR (Study, Prevalence):ti,ab,kw	54133
#6	(Prospective Study):ti,ab,kw OR (Studies, Prospective):ti,ab,kw OR (Study, Prospective):ti,ab,kw	233446
#7	(Cohort Study):ti,ab,kw OR (Studies, Cohort):ti,ab,kw OR (Study, Cohort):ti,ab,kw OR (Concurrent Studies):ti,ab,kw OR (Studies, Concurrent):ti,ab,kw OR (Concurrent Study):ti,ab,kw OR (Study, Concurrent):ti,ab,kw OR (Closed Cohort Studies):ti,ab,kw OR (Cohort Studies, Closed):ti,ab,kw OR (Closed Cohort Study):ti,ab,kw OR (Cohort Study, Closed):ti,ab,kw OR (Study, Closed Cohort):ti,ab,kw OR (Studies, Closed Cohort):ti,ab,kw OR (Birth Cohort Studies):ti,ab,kw OR (Birth Cohort Study):ti,ab,kw OR (Cohort Studies, Birth):ti,ab,kw OR (Cohort Study, Birth):ti,ab,kw OR (Studies, Birth Cohort):ti,ab,kw OR (Study, Birth Cohort):ti,ab,kw OR (Analysis, Cohort):ti,ab,kw OR (Analyses, Cohort):ti,ab,kw OR (Cohort Analyses):ti,ab,kw OR (Cohort Analysis):ti,ab,kw OR (Historical Cohort Studies):ti,ab,kw OR (Cohort Studies, Historical):ti,ab,kw OR (Cohort Study, Historical):ti,ab,kw OR (Historical Cohort Study):ti,ab,kw OR (Study, Historical Cohort):ti,ab,kw OR (Studies, Historical Cohort):ti,ab,kw OR (Incidence Studies):ti,ab,kw OR (Incidence Study):ti,ab,kw OR (Studies, Incidence):ti,ab,kw OR (Study, Incidence):ti,ab,kw	184886
#8	(Observational Study):ti,ab,kw	20328
#9	(Infection and Infestation):ti,ab,kw OR (Infection and Infestation):ti,ab,kw OR (Infections and Infestations):ti,ab,kw OR (Infestations and Infections):ti,ab,kw OR (Infection):ti,ab,kw	102985
#10	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	552677
#11	#1 AND #9 AND #10	382
#12	Trials	377
#13	The year 2000 – current; English	243

Risk of Bias Assessment

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (CASE CONTROL STUDIES)

Selection

1) Is the case definition adequate?

a) yes, with independent validation □

b) yes, e.g. record linkage or based on self-reports

c) no description

2) Representativeness of the cases

a) consecutive or obviously representative series of cases □

b) potential for selection biases or not stated

3) Selection of Controls

a) community controls □

b) hospital controls

c) no description

4) Definition of Controls

a) no history of disease (endpoint) □

b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis

a) study controls for _____ (Select the most important factor.) □

b) study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure

a) secure record (e.g. surgical records) □

b) structured interview where blind to case/control status □

c) interview not blinded to case/control status

d) written self-report or medical record only

e) no description

2) Same method of ascertainment for cases and controls

a) yes □

b) no

3) Non-response rate

a) same rate for both groups □

b) non-respondents described

c) rate different and no designation

Table 1 Risk of Bias Assessment with NOS Case-control Study Scale

Author & Year	Selection				Comparability	Exposure			Total score
Olsen 2009	1	1	1	0	2	1	1	0	6
Lake 2013	1	1	1	1	2	1	1	1	9
Savage 2013	1	1	1	0	2	1	1	0	7
Pop-Vicas 2014	0	1	1	0	2	0	1	1	6
Morgan 2016	1	1	1	0	2	0	1	1	7
Wang 2022	1	1	1	0	2	1	1	0	7

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (COHORT STUDIES)

Selection

1) Representativeness of the exposed cohort

a) truly representative of the average _____ (describe) in the community □

b) somewhat representative of the average _____ in the community □

c) selected group of users e.g. nurses, volunteers

d) no description of the derivation of the cohort

2) Selection of the non-exposed cohort

a) drawn from the same community as the exposed cohort □

b) drawn from a different source

c) no description of the derivation of the non-exposed cohort

3) Ascertainment of exposure

a) secure record (e.g. surgical records) □

b) structured interview □

c) written self-report

d) no description

4) Demonstration that outcome of interest was not present at start of study

a) yes □

b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for _____ (select the most important factor) □

b) study controls for any additional factor □ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome

a) independent blind assessment □

b) record linkage □

c) self-report

d) no description

2) Was follow-up long enough for outcomes to occur

a) yes (select an adequate follow-up period for outcome of interest) □

b) no

3) Adequacy of follow-up of cohorts

a) complete follow-up - all subjects accounted for □

b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) □

c) follow up rate < ____% (select an adequate %) and no description of those lost

d) no statement

Table 2 Risk of Bias Assessment with NOS Cohort Study Scale

Author & Year	Selection				Comparability	Exposure			Total score
Molina-Cabrillana 2008	0	1	1	0	2	1	1	0	6
Coleman 2014	1	1	1	0	2	1	0	1	7
Mahdi 2014	1	1	1	0	2	1	1	0	7
Uppal 2015	1	1	1	0	2	1	1	1	8
Tuomi 2016	1	1	1	0	2	1	1	1	8
Till 2017	1	1	1	0	2	0	1	1	7
Brown 2019	1	1	1	1	2	1	1	1	9
Tsuzuki 2021	1	1	1	0	2	1	1	0	7

Table 3 Study Summary

Author & Year	Selection				Comparability	Exposure			Total score
Molina-Cabrillana 2008#	0	1	1	0	2	1	1	0	6
Olsen 2009*	1	1	1	0	2	1	1	0	6
Lake 2013*	1	1	1	1	2	1	1	1	9
Savage 2013*	1	1	1	0	2	1	1	0	7
Coleman 2014#	1	1	1	0	2	1	0	1	7
Mahdi 2014#	1	1	1	0	2	1	1	0	7
Pop-Vicas 2014*	0	1	1	0	2	0	1	1	6
Uppal 2015#	1	1	1	0	2	1	1	1	8
Morgan 2016*	1	1	1	0	2	0	1	1	7
Tuomi 2016#	1	1	1	0	2	1	1	1	8
Till 2017#	1	1	1	0	2	0	1	1	7
Brown 2019#	1	1	1	1	2	1	1	1	9
Tsuzuki 2021#	1	1	1	0	2	1	1	0	7
Wang 2022*	1	1	1	0	2	1	1	0	7

Note. *means this study was assessed through the items for case-control studies. # means this study was assessed through the items for cohort studies.

Table 3 Study Summary

Author & Year	Sample Origin	N	SSI +	Age (±SD)	Surgery Method	Age RF	Anti-microbial	Blood Loss	Blood Transfusion	BMI	Diabetes	Obesity	Surgery Duration	Tobacco Use	Tumour	Wound Cleanness
Molina-Cabrillana 2008	2000-2004 Hospital Universitario Materno-Infantil de Canarias, Sapin	1540	72	54.00 (±12.90)	abdominal & vaginal	Age >60	Y/N	NR	NR	NR	Y/N	Y/N	≥P75	NR	Y/N	Clean-contaminated vs Contaminated /dirty
Olsen 2009	2003-2005 CDC Prevention Epicenter Program hospitals, USA	820	66	51.70 (±17.78)	abdominal & vaginal	Mean	NR	NR	NR	Mean	Y/N	NR	Mean	Y/N	Y/N	NR
Lake 2013	2005-2009 ACS-NSQIP, USA	13822	375	NR	abdominal & vaginal & laparoscopic	Age >80	NR	NR	Y/N	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	≥P75	Y/N	Y/N	Clean vs Clean-contaminated Contaminated vs Dirty
Savage 2013	2007-2010 University of Iowa Hospitals and Clinics, USA	1104	126	54.53 (±13.66)	abdominal	Mean	Mean	NR	Median	BMI≥30 (Obesity)	Y/N	Y/N	Mean	NR	Y/N	NR
Coleman 2014	1999-2012 Johns Hopkins Medical Institution, USA	77	17	42.56 (±5.93)	abdominal & vaginal & laparoscopic	Mean	NR	>250ml; ≥451ml	Y/N	Median	Y/N	BMI≥30 (Obesity)	NR	Y/N	NR	NR
Mahdi 2014	2005-2011 ACS-NSQIP, USA	28366	296	NR	laparoscopic	Age >60, 70 & 80	NR	NR	>4 units of packed red blood cells	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	>60 min, 180 min	Y/N	NR	NR
Pop-Vicas 2014	2012-2015 University of Wisconsin Hospitals, USA	1531	52	58.27 (±12.31)	abdominal & vaginal & laparoscopic	Mean	Y/N	Median*	NR	NR	NR	NR	Mean	Y/N	Y/N	NR

Uppal 2015	2012-2015 MSQC, USA	21358	441	48.10 (±11.70)	abdominal & vaginal & laparoscopic	Median	Y/N	Median	NR	BMI≥30 (Obesity)	NR	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Morgan 2016	2012-2014 MSQC, USA	16548	315	NR	abdominal	Age >50	NR	Mean	Y/N	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Tuomi 2016	2007-2013 Helsinki University Hospital, Finland	1164	94	67.46 (±10.23)	abdominal & vaginal & laparoscopic	Mean	NR	Median	NR	Mean	Y/N	NR	Mean	Y/N	NR	NR
Till 2017	2012-2015 MSQC, USA	18255	329	NR	abdominal & vaginal & laparoscopic	Age >65	NR	≥250ml	NR	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Brown 2019	2012-2014 ACS-NSQIP, USA	46755	445	45.95 (±1.51)	laparoscopic	Mean	NR	NR	Y/N	Mean	Y/N	NR	Mean	Y/N	NR	Clean vs Clean-contaminated vs Contaminated vs Dirty
Tsuzuki 2021	2014-2018 Teine Keijinkai Hospital, Japan	1559	71	48.28 (±11.39)	laparoscopic	Mean	NA	NR	Y/N	Mean	Y/N	NR	Mean	Y/N	NR	NR
Wang 2022	2012-2022 Two Grade A Tertiary Hospitals, China	94	188	47.70 (±10.87)	abdominal	Age >50	Y/N	≥500ml	NR	Mean	Y/N	NR	>180 min	NR	Y/N	Clinicians determined Class II vs Class III
Overall		152993	2887	47.53 (±8.29)												

Note. The content under each risk factor was how these studies presented their data. The detailed case numbers are in Table 3; SSI+ refers to SSI-positive cases; ACS-NSQIP refers to the American College of Surgeons National Surgical Quality Improvement Program; MSQC refers to the Michigan Surgical Quality Collaborative; NR refers to not reported; NA refers to not applicable; Y/N refers to reported in Yes or No; Median*: the median reported in this study did not include IQR to estimate its variance; P75 refers to the 75th percentil

Table 2 Subgroup Analyses Between Different SSI Types

	Superficial & Deep & Organ Space						Deep & Organ Space						Group Difference	
Risk Factors	**LogOR**	**I^2**	**OR**	**SE**	**z**	**p**	**LogOR**	**I^2**	**OR**	**SE**	**z**	**p**	**Q (df)**	**p**
Tobacco Use	0.36	0.00%	1.43	0.07	5.78	<.001	1	68.56%	2.72	.18	5.69	.001	11.59 (1)	<.001
Diabetes	0.53	64.07%	1.70	0.15	2.5	<.001	0.27	61.95%	1.31	.25	1.06	.290	.71 (1)	.400

Note. Only Tobacco Use and Diabetes retrieved more than 4 datasets reporting Deep or Organ Space SSI types. The individual SSI types, such as Superficial, Deep, or Organ Space, were reported in less than 4 sets. This is to demonstrate that ORs of risk factors might differ between SSI types.

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Risk factors for surgical site infection (SSI) in patients undergoing hysterectomy: A systematic review, meta-analysis and network analysis

Abstract

Objective: Surgical site infections (SSI) after hysterectomy constitute significant postoperative complications, affecting patient recovery and healthcare costs. We conducted a systematic review of risk factors for SSI in patients undergoing hysterectomy.

Design: The current study conducted a systematic review with meta-analysis and network analysis to identify and summarise risk factors for SSI following hysterectomy.

Data sources: Pubmed, Medline, Embase, Web of Science, and Cochrane Central Register of Controlled Trials were searched through 1 November 2023.

Eligibility criteria: The inclusion criteria were 1) population: female participants who had post-hysterectomy SSI; 2) intervention: hysterectomy surgeries; 3) comparators: the number of participants who had or had not post-hysterectomy SSI; 4) outcomes: the number of participants exposed and not exposed to the risk factors of SSI. The exclusion criteria were 1) non-English studies and 2) studies that provided insufficient data.

Data extraction and synthesis: Two reviewers conducted the screening process independently. Articles that did not meet the inclusion criteria were excluded. For those that met the criteria, full-text papers were procured. Any discrepancies between the reviewers were resolved through discussion.The meta-analysis synthesised risk factors reported ≥ 4 datasets via random-effects models, assessing heterogeneity, sensitivity (leave-one-out), publication bias (Egger's test/funnel plots), and subgroup analyses (incision types). A Bayesian network evaluated SSI risk across surgical types, validated by DIC.

Results: Blood transfusion emerged as the largest risk factor (OR = 2.55, 95%CI [1.84, 3.56]), followed by tumour presence (OR = 2.23, 95%CI [1.86, 2.66]), obesity (OR = 1.79, 95%CI [1.43, 2.23]), diabetes (OR = 1.70, 95%CI [1.26, 2.29]), and tobacco use (OR = 1.43, 95%CI [1.26, 1.63]). The ORs varied by incision type.

Network analysis revealed that vaginal and laparoscopic hysterectomies had significantly lower SSI risk (59% and 55%, respectively) compared to abdominal hysterectomies.

Conclusion: The study establishes blood transfusion, tumour presence, obesity, diabetes, and tobacco use as significant risk factors for SSI after hysterectomy, with variations in risk evident across different incision types. The findings also suggest vaginal and laparoscopic hysterectomies as preferable alternatives to abdominal hysterectomy in mitigating SSI risk. Future research should aim for more granular data to untangle the interplay between comorbidities and further elucidate the differential risk across SSI types.

Keywords: Hysterectomy; Surgical Site Infections; Risk Factors; Meta-analysis; Network Analysis

Strengths and limitations of this study

1. The current systematic review synthesised evidence on odds ratios of risk factors for post-hysterectomy SSI and applied Bayesian network analysis to compare SSI risks among three commonly used hysterectomy approaches.

2. The current systematic review included 152993 patients who underwent hysterectomy, including 2887 who had post-hysterectomy SSI.

3. The major limitation was that we found the case numbers exposed to each risk factor were counted respectively, such that the odds ratios were not solely attributed to a single risk factor and might be overestimated.

Introduction

Hysterectomy is a very common procedure in which the uterus is surgically removed, and it is an optional treatment for leiomyoma, endometriosis, abnormal bleeding, benign ovarian neoplasms, pelvic organ prolapse, and gynecologic cancer [1]. Epidemiological research estimated that the lifetime prevalence of hysterectomy surgery is approximately 236/100,0000 in Germany, 143/100,0000 in the US [2 3], 80/100,0000 in China [4], and 42/100,0000 in the UK [2] among the female population, depending on waitlist queuing time of different regions [2]. Among patients who had hysterectomies, 2.1% are estimated to develop surgical site infections (SSI) worldwide [5], which has been one of the most common complications after hysterectomy surgery [6]. According to Centers for Disease Control and Prevention (CDC), SSI is an infection that develops in the portion of the body where the operation was performed. It might be superficial, affecting simply the skin, or more serious, involving tissues beneath the skin, organs, or implanted material. The currently accepted risk factors of hysterectomy SSI are age, body mass index (BMI), smoking, and diabetes [7]. However, many studies have shown different results, one study from Spain only considered obesity and inadequate prophylaxis as meaningful indicators [8], whereas another study from the UK also suggested that the operative time should be considered an independent risk factor [9]. The evidence from current research appears to be diverse, isolated, and lacking in quantitative power. One study analyzed the risk factors for SSI after obstetric and gynecological surgery; in fact, the types of obstetric and gynecological surgeries are varied; for example, breast-conserving surgeries are cleansing surgeries, and breast reconstruction may use silicone implants, so the factors affecting SSI for these surgeries may be different than for hysterectomies [10].

Consequently, the current study aims to summarise the results of risk factors of hysterectomy SSI through a quantitative approach.

Method

Study Registration

The protocol of the current study was registered and reviewed by the PROSPERO International Prospective Register of Systematic Reviews (No. CRD42023411668). The protocol is available at: https://www.crd.york.ac.uk/PROSPERO/export_details_pdf.php

The Patient and Public Involvement statement

None

Search Strategy

The data was extracted from published empirical study reports retrieved from the databases, including Pubmed (central), Medline (Ovid), Embase (Ovid), Web of Science, and Cochrane Central Register of Controlled Trials. The search terms followed the standard PICO guideline (population, intervention, comparator, outcome) and were adapted according to Medical Subject Headings (MeSH) terms [11]. The search was conducted upon the completion of study registration.

Eligibility criteria

The inclusion criteria were 1) population: female participants who had post-hysterectomy SSI; 2) intervention: hysterectomy surgeries; 3) comparators: the number of participants who had or had not post-hysterectomy SSI; 4) outcomes: SSI. The exclusion criteria were 1) non-English studies and 2) studies that provided insufficient data.

Study screening and data extraction

The report articles were retrieved in RIS format and managed with Endnote (Bld13966, EndNote X9.3.3, 2023). The screening process followed the PRISMA guidelines [12]. Two reviewers conducted the screening process independently. Initially, they removed all duplicate articles. Then, articles that did not meet the inclusion criteria were excluded. For those that met the criteria, full-text papers were procured. Any discrepancies between the reviewers were resolved through discussion. Data from the selected articles was subsequently extracted.

Risk of bias assessment

Two reviewers independently scored the studies using the Newcastle-Ottawa quality assessment (NOS) [13 14]. NOS is a validated, easy-to-use scale containing 8

items organised into three dimensions: selection, comparability, and exposure/outcome, which has been endorsed for use in systematic reviews of non-randomised studies by The Cochrane Collaboration [14]. Studies rated 0-2 as poor quality, 3-5 as fair quality, and 6–9 as good/high quality.

Data synthesis

Data synthesis requires at least four sets of data according to the general conduct suggested by the Cochrane Handbook [15]. The effect size of each identified risk factor will be pooled in a quantitative meta-analysis using STATA v18. The risk factors were expected to be reported as binary data about whether or not the patients were exposed to the risk factor and were infected. Consequently, odds ratios (ORs) would be calculated as the effect size with the following formula:

$$OR = \frac{a}{b} \div \frac{c}{d}$$

Where *a* represents cases exposed to the risk factor and infected, *b* represents those exposed but not infected, *c* represents unexposed but infected, and *d* represents unexposed and uninfected cases. And the LogOR is the natural log of the OR.

Statistical Analysis Plan

The meta-analysis was conducted with STATA v18. Only risk factors reported in over 4 datasets were synthesised into meta-analysis. A random effect model meta-analysis with the restricted maximum likelihood method was used to evaluate the pooled ORs (LogORs). The heterogeneity was also assessed with the random effects model, where heterogeneity I^2 is considered moderate when $I^2 > 50\%$ and high when $I^2 > 75\%$ [15]. Sensitivity analysis was conducted using the Leave-one-out approach by omitting one dataset each time and evaluating the pooled effect sizes. Egger's test and funnel plots were used to assess potential publication bias.

The pooled effect sizes were also entered into subgroup analysis based on the SSI types (superficial, deep, organ space) with available datasets. BMI was entered into the meta-regression analysis with pooled effect sizes of diabetes to explore the relationship between obesity and diabetes and its influence on SSI risk prediction.

Finally, a Bayesian network model was conducted with R and WinBugs to determine the risk of SSI between three surgery types (abdominal, vaginal, and laparoscopic). The model structure defined SSI risk (binomial variable: infected/non-

infected) as the child node conditional on the surgical approach (categorical variable: abdominal, vaginal, laparoscopic). The Bayesian network model offers a probabilistic graphical framework that represents and analyses the probabilistic relationships among binominal variables [16]. The model fit of the Bayesian network was evaluated with the Deviance Information Criterion (DIC), where a lower DIC indicates a better-fitting model.

Results

Systematic review

Initially, searching the keywords in PubMed, Medline (Ovid), Embase (Ovid), Web of Science, and the Cochrane Central Register of Controlled Trials produced 3821 records. Fourteen studies met the inclusion criteria after screening based on the PRISMA guidelines. The PRISMA procedure is shown in Figure 1.

Figure 1 The PRISMA Flow

All identified studies were retrospective observations to record the case numbers of SSI after hysterectomy surgeries with or without the occurrence of each risk factor. In total, 152993 female patients (age: 47.53±8.29) who underwent hysterectomy were included in the current 14 studies, of whom 2887 had SSI in different types, and 150106 had no SSI taken as controls. The details of all studies are described in Table 1 (More detailed information can be found at supplymentary material 1).

Table 1 Study Summary

Author & Year	Sample Origin	Surgery Method	Blood Transfusion	Diabetes	Obesity	Tobacco Use	Tumour
Molina-Cabrillana 2008	2000-2004 Hospital Universitario Materno-Infantil de Canarias, Sapin	abdominal & vaginal	NR	Y/N	Y/N	NR	Y/N
Olsen 2009	2003-2005 CDC Prevention Epicenter Program hospitals, USA	abdominal & vaginal	NR	Y/N	NR	Y/N	Y/N
Lake 2013	2005-2009 ACS-NSQIP, USA	abdominal & vaginal & laparoscopic	Y/N	Y/N	BMI≥30 (Obesity)	Y/N	Y/N
Savage 2013	2007-2010 University of Iowa Hospitals and Clinics, USA	abdominal	Median	Y/N	Y/N	NR	Y/N
Coleman 2014	1999-2012 Johns Hopkins Medical Institution, USA	abdominal & vaginal & laparoscopic	Y/N	Y/N	BMI≥30 (Obesity)	Y/N	NR
Mahdi 2014	2005-2011 ACS-NSQIP, USA	laparoscopic	>4 units of packed red blood cells	Y/N	BMI≥30 (Obesity)	Y/N	NR
Pop-Vicas 2014	2012-2015 University of Wisconsin Hospitals, USA	abdominal & vaginal & laparoscopic	NR	NR	NR	Y/N	Y/N
Uppal 2015	2012-2015 MSQC, USA	abdominal & vaginal & laparoscopic	NR	NR	BMI≥30 (Obesity)	Y/N	Y/N
Morgan 2016	2012-2014 MSQC, USA	abdominal	Y/N	Y/N	BMI≥30 (Obesity)	Y/N	Y/N
Tuomi 2016	2007-2013 Helsinki University Hospital, Finland	abdominal & vaginal & laparoscopic	NR	Y/N	NR	Y/N	NR
Till 2017	2012-2015 MSQC, USA	abdominal & vaginal & laparoscopic	NR	Y/N	BMI≥30 (Obesity)	Y/N	Y/N
Brown 2019	2012-2014 ACS-NSQIP, USA	laparoscopic	Y/N	Y/N	NR	Y/N	NR
Tsuzuki 2021	2014-2018 Teine Keijinkai Hospital, Japan	laparoscopic	Y/N	Y/N	NR	Y/N	NR

Wang 2022	2012-2022 Two Grade A Tertiary Hospitals, China	abdominal	NR	Y/N	NR	NR	Y/N

Note. The content under each risk factor was how these studies presented their data. The detailed case numbers are in supplymentary material 1; ACS-NSQIP refers to the American College of Surgeons National Surgical Quality Improvement Program; MSQC refers to the Michigan Surgical Quality Collaborative; NR refers to not reported; NA refers to not applicable; Y/N refers to reported in Yes or No.

Among these studies, seven only reported infection cases in mixed three SSI types (superficial, deep or organ space) [8 17-22], two only reported in mixed two SSI (deep or organ space) [23 24], one study reported each SSI types separately [25] and one study reported superficial and organ space SSIs separately [26], one study reported superficial SSI independently but mixed deep or organ space SSIs [27], one study reported deep SSI independently but mixed superficial or deep SSIs [5], one study reported only organ space SSIs [28]. Since it requires at least four datasets to conduct meta-analyses [15], the studies reported cases in independent SSI types were combined into three mixed SSI types (superficial, deep or organ space) to synthesise with those only reported the mixed SSI types. The NOS risk of bias assessment rated three studies scored 6 [8 20 25], seven scored 7 [5 17-19 22 24 28], two scored 8 [21 26], and the other two scored 9 [23 27]. All 14 studies are ranked as good/high quality and were included in the following review.

Among the 14 studies, there were 11 risk factors identified in total, including age, antimicrobial, blood loss, blood transfusion, BMI, diabetes (both type I or type II), obesity, surgery duration, tobacco use, tumour, and wound cleanness. However, antimicrobial and blood loss were reported in less than four datasets. Wound cleanness and age were reported in different classification standards. Only 5 factors reported in more than 4 datasets are available for quantitative analysis, including blood transfusion, diabetes, obesity, tobacco use, and tumour. Age, high BMI, and surgery duration reported continued data and thus could not be directly synthesised.

Meta-analyses

The identified risk factors with sufficient datasets were entered into meta-analyses respectively. As shown in Table 2, pooled effect sizes revealed significant overall logORs of blood transfusion (OR = 2.55, 95%CI [1.84, 3.56], p <.001), obesity (OR = 1.79, 95%CI [1.43, 2.23], p <.001), diabetes (OR = 1.70, 95%CI [1.26, 2.29], p <.001), tobacco use (OR = 1.43, 95%CI [1.26, 1.63], p <.001), but not tumour (OR = 1.35, p =.362), as the risk factors for SSI infections. However, after removing each dataset one at a time, leave-one-out sensitivity analysis on all risk factors suggested no changes except for tumour (OR = 2.33, 95%CI [1.86, 2.66], p <.001), where one dataset changed the results [8]. Further analysis with publication bias suggested no publication bias in all factors. However, as shown in Figure 2A, the funnel plot suggested three outlier datasets [8 21 25]. One border dataset was decided to

be kept [21], and the other two were excluded from the analysis [8 25].

Table 2 Summary of Meta-analyses

	Risk Factor	Blood Transfusion	Tumour	Obesity	Diabetes	Tobacco Use
Case Number	RF+ SSI+	39	226	720	229	340
	RF+ SSI-	998	3924	28717	5330	13645
	RF- SSI+	1075	769	531	1314	938
	RF- SSI-	62830	44733	36398	62893	54500
Meta-analysis	LogOR	0.94	0.8	0.58	0.53	0.36
	OR	2.55	2.23	1.79	1.7	1.43
	SE	0.17	0.09	0.12	0.15	0.07
	z	5.57	8.8	5.07	3.5	5.54
	p	<.001	<.001	<.001	<.001	<.001
Heterogeneity Test	I^2	0.00%	0.00%	67.56%	64.07%	0.00%
	$Q_{(df)}$	.17 (3)	1.34 (4)	11.58 (4)	21.13 (7)	5.78 (5)
	p	0.983	0.85	0.02	<.001	0.33
Leave-one-out Sensitivity	lowest LogOR	0.88	0.7	0.54	0.44	0.32
	Highest LogOR	0.96	0.86	0.66	0.64	0.43
Egger's Publication Bias	β	0.09	0.05	1.79	-1.21	0.76
	SE	1.08	0.81	7.6	0.89	0.73
	z	0.08	0.06	1.12	-1.35	0.91
	p	0.934	0.95	0.263	0.178	0.363

Note. The presenting data of the tumour was after exclusions of outliers. RF+ refers to exposure to the risk factor, RF- refers to no exposure to the risk factor, SSI+ refers to SSI positive, and SSI- refers to SSI negative, OR refers to Odds ratio, I^2 refers to Heterogeneity index, p refers to p-value.

Figure 2 The Funnel Plots

After exclusion, data from the tumour was entered into meta-analysis again and reported a significant pooled effect size predicting SSI infections (logOR = .80, OR = 2.23, p <.001), and, as shown in Figure 2B, there were no outliers. As shown in Figure 3A, 3B, and 3C, the estimation of heterogeneity suggested that the chance of inconsistent distribution of the pooled logORs was not significant in blood transfusion datasets (I^2 = 0%, $Q_{(3)}$ = .17, p = .983), tumour (I^2 = 0%, $Q_{(4)}$ = 1.34, p = .850) or tobacco use (I^2 = 0%, $Q_{(5)}$ = 5.78, p = .330). However, Figure 3D and Figure 3E suggested significant moderate heterogeneity in obesity (I^2 = 67.56%, $Q_{(4)}$ = 11.58, p <.001) and diabetes datasets (I^2 = 64.07%, $Q_{(7)}$ = 21.13, p <.001). These results suggested that blood transfusion, tumour, tobacco use, obesity, and diabetes were significant risk factors predicting post-hysterectomy SSI. Patients who underwent blood transfusion had a 155% increased likelihood of experiencing post-hysterectomy SSI. Similarly, individuals with tumours had a 123% increased risk, obese individuals 79%, diabetics 70%, and tobacco users 43%.

Figure 3 The Forest Plots for Each Risk Factor

Subgroup analysis between studies reporting different SSI types (mixed superficial or deep or organ space vs. mixed deep or organ space) was conducted among tobacco use and diabetes, for they obtained more than 4 datasets under each subgroup. The difference was whether they included superficial SSI. A significant group difference in pooled ORs between mixed superficial & deep & organ space cases and mixed deep or organ space among tobacco use, $Q_{(1)}$ = 11.59, p <.001, but not among diabetes, $Q_{(1)}$ = .71, p = .400.The impact of tobacco use on the risk of SSI varied significantly depending on the type of SSI, see supplymentary material Table 2. As shown in Figure 4, while tobacco use was associated with a 143% increased risk for combined superficial, deep, and organ space SSIs, this risk escalated to a 272% increase when considering only deep and organ space SSIs. This suggests that the influence of smoking may be more pronounced for deep and organ space infections than superficial ones. Given the observed discrepancy in risk between the combined three types of SSIs and the combined two types (deep or organ space) for tobacco use,

it is plausible that other risk factors might also exhibit differential effects across various SSI categories.

Figure 4 Tobacco Use Subgroup Forest Plot between SSI Types

Continuous BMI data was incorporated into a meta-regression analysis alongside the ORs of diabetes to evaluate the relationship between obesity and diabetes. Given the absence of group differences or heterogeneity discrepancies across SSI types in the effect sizes associated with diabetes, datasets from both SSI types (though not originating from identical studies) were incorporated into the meta-regression. The results suggested that BMI did not significantly predict the ORs of diabetes (β = .001, SE = .08, t = .02, p = .989). While this does not suggest that BMI (or obesity) is not correlated with the incidence of diabetes, it does affirm that high BMI did not affect the outcomes in this particular analysis.

Bayesian Network Analysis

The infected and non-infected case numbers under each surgery method (abdominal, vaginal, laparoscopic) were analysed with a Bayesian network model to determine whether vaginal and laparoscopic surgeries had a lower SSI risk than abdominal surgeries, see Figure 5. The Bayesian network model exhibited a DIC of 111.5. Compared to abdominal surgeries, vaginal surgeries reduced the risk of developing SSI by 59% (OR = .41, 95%CI [0.33, 0.67]) and laparoscopic surgeries by 55% (OR = .45, 95%CI [0.37, 0.67]). However, the latter two did not distinguish from each other (OR = .9, 95%CI [0.72, 1.21]). These results suggest that conducting the hysterectomy with the vaginal or laparoscopic methods is respectively safer than the abdominal method in terms of SSI risk.

Figure 5 Bayesian network analysis

Discussion

The current study conducted a systematic review with meta-analysis and network analysis to summarise the evidence of risk factors of SSI after hysterectomy surgeries. To our knowledge, this is the first quantitative review of the topic. In total, 14 retrospective observations studies were identified with 2887 SSI positive and 150106 negative cases under 11 risk factors, including age, antimicrobial, blood loss, blood transfusion, high BMI, diabetes, obesity, surgery duration, tobacco use, tumour, and wound cleanness. However, only 5 were available for meta-analysis synchronisation. Among which, blood transfusion, tumour, obesity, diabetes, and tobacco use were factors that significantly increased the risk of SSI. The estimated ORs also seemed to vary between different SSI types (superficial, deep, or organ space). Apart from risk factors, Bayesian network analysis also suggested that conducting vaginal or laparoscopic hysterectomies induced a significantly lower risk of SSI infection than abdominal surgeries. The details of the quantitative analysis are discussed as follows.

The largest risk factor of SSI is blood transfusion (OR = 2.55), with a 155% increased likelihood of SSI. Blood transfusion has always been identified as a major source of post-surgical infections [29] [30]. Administrative errors, such as bacterial contamination in platelet products, are believed responsible for infections induced by blood transfusion [29]. These issues are related to the healthcare service environment and beyond the current paper's discussion. Instead, the need for blood transfusion deserves further elaboration from the patients' site. For example, blood loss was reported to be positively correlated with BMI [31] [32]. Apart from obesity, severe abnormal uterine bleeding and cancer-related anaemia are also important reasons that patients require extra blood transfusion. However, none of the included studies attempted to isolate these factors, nor did they report preoperative haemoglobin. Consequently, we could not address whether blood transfusion was an independent factor or it was attributed to other factors such as obesity, severe abnormal uterine bleeding, cancer-related anaemia, preoperative haemoglobin or whether its estimated ORs were inflated. Future studies should consider reporting more comprehensive data to precisely estimate the ORs for blood transfusion as the SSI risk factor.

Likewise, one may argue that obesity and diabetes are comorbid, where obesity-induced insulin resistance is one of the major sources of type 2 diabetes [33]. This might explain the moderate heterogeneity of the ORs in obesity (OR = 1.79, I^2 = 67.56%)

and diabetes (OR = 1.70, I^2 = 64.07%). This is, in fact, a methodological issue, where all studies directly counted the case number that was exposed and not exposed to the specific risk factors, but none attempted to distinguish whether the case was exposed to multiple risk factors. That is, one might suffer from obesity or diabetes or both, and the case would be counted in each risk factor respectively when they suffer from both. Consequently, the estimated ORs were not solely attributed to one risk factor and might be overestimated. Hypothetically, in the current case, the heterogeneity of the ORs in obesity and diabetes was moderate because some studies included more patients suffering from both obesity and diabetes and reported higher ORs than those with fewer such patients. As a result, although both obesity and diabetes are significant risk factors, their estimated ORs should be considered cautiously and require further clarification in future studies by reporting cases separately.

To further address this issue, the current study conducted a meta-regression analysis to investigate whether BMI predicts the ORs of diabetes. The analysis found no significant relationship between continuous BMI values and the ORs of diabetes. Notably, the absence of a significant predictive relationship between BMI and the OR for diabetes does not imply that these two factors were unrelated or that obesity does not influence the estimation of OR for diabetes. On the one hand, the absence of a significant predictive relationship might arise from including both type I and type II diabetes in the studies, with type I diabetes having less direct relevance to obesity. On the other hand, the estimation of ORs may still have been elevated due to the repeated counting of cases exposed to multiple risk factors. Instead, this result might be interpreted as the pathologies of obesity and diabetes are relatively independent in the context of SSI risk.

Apart from obesity and diabetes, the second-largest risk factor was tumour (OR = 2.23), with a 123% increased likelihood of SSI. The immune system in patients afflicted with malignant tumours was generally compromised [34]. This impairment in the primary immune function directly results from the tumour's pervasive influence on the natural defence mechanisms. Furthermore, the standard therapeutic interventions for tumours, including surgery, chemotherapy, and radiotherapy, also contribute to the weakened immune state [35].

Tobacco use was the last risk factor (OR = 1.43), with a 43% increased likelihood of SSI. Nicotine and carbon monoxide, two primary agents produced in tobacco use, contribute to the constriction of peripheral blood vessels. This vasoconstriction reduces the oxygen supply to tissues, vital for cellular function and healing processes [36]. Consequently, this oxygen deficit can precipitate the formation of microthrombi, which are small clots that can impair blood flow and further hinder tissue repair and regeneration.

However, the estimated ORs of tobacco use seemed to vary between SSI types. A subgroup comparison was conducted between studies that reported all mixed SSI and those that only reported deep or organ space SSI for tobacco use and diabetes, where only these two risk factors were reported repeatedly in distinguishing between SSI types. Significant subgroup differences were observed exclusively in the context of tobacco use. Specifically, tobacco use was associated with a 43% increased risk for superficial, deep, or organ space SSIs. This risk escalated to a 172% increase when focusing solely on deep or organ space SSIs. The pronounced impact of tobacco use appears more substantial in increasing the risk of deep or organ space infections compared to superficial ones. This discrepancy may also be attributed to tobacco-induced vasoconstriction. The vascular system supporting superficial cells, such as those in the skin, is more prosperous than the vasculature of deep and organ space cells. Consequently, cells in deeper tissues and organ spaces are more vulnerable to oxygen supply alterations exacerbated by tobacco use. However, this was merely a hypothetical explanation without solid evidence, which requires further investigation.

Finally, the current Bayesian model revealed a significant reduction in SSI risk with vaginal and laparoscopic hysterectomies compared to the abdominal approach, with decreases of 59% and 55% respectively. Abdominal hysterectomy, though designed to prevent bladder damage by opening the peritoneal reflection and mobilising the bladder, increases postoperative infection risks due to larger incisions and greater abdominal exposure [37]. In contrast, laparoscopic methods, utilising smaller incisions and camera systems, minimise air exposure and use electrocoagulation for cutting and hemostasis, thereby reducing pelvic-abdominal disturbances and promoting a stable internal environment [38]. While total laparoscopic hysterectomy demands high skill levels, vaginal hysterectomy offers a simpler approach to uterine manipulation, albeit with a slight increase in urinary system

infection risks from metal cannula introduction [39]. Although each technique has distinct risk-benefit profiles, the current results provided straightforward evidence of SSI risk, comparing the techniques to reference individual patient needs and surgical goals.

There are five limitations in the current study. First, some procedures performed in conjunction with hysterectomy can also affect SSI, but this was not explored in this paper. Second, the included studies did not differentiate cases based on the number of risk factors present, counting each instance for all identified risks. This approach likely inflated the ORs, particularly for comorbid conditions like patients with severe abnormal uterine bleeding or cancer-related anaemia and obesity and diabetes. Thirdly, there was no distinction between Type I and Type II diabetes in the studies, potentially contributing to moderate heterogeneity in the pooled OR estimates. Therefore, the estimated ORs for obesity and diabetes as risk factors for SSIs should be interpreted cautiously. Then, since none of the studies isolated patients with severe abnormal uterine bleeding, suffered from cancer-related anaemia, or reported pre-operative HbA1, it is unclear whether these factors also inflated the estimation ORs for blood transfusion, and thus, they should be interpreted cautiously as well. Lastly, few studies specified the types of SSI (superficial, deep, or organ space). Given that our analysis indicates variation in tobacco use ORs across different SSI types, it is crucial to ascertain if similar variations apply to other risk factors. Addressing these issues in future research, with more detailed data reporting, is essential for a clearer understanding of the risk factors for SSIs. Future studies should report more comprehensive data to address these limitations.

In summary, the current study conducted a systematic review with meta-analysis and network analysis of the risk factors of SSI after hysterectomy surgeries. In total, 11 risk factors were mentioned, whereas only blood transfusion, tumour, obesity, diabetes, and tobacco use had sufficient data to be entered into meta-analysis and yield statistical significance. With limited available data, the ORs of tobacco use seemed to vary between different SSI types, suggesting potential diversity in other risk factors. Finally, a Bayesian network model compared the risk of SSI between vaginal and laparoscopic and abdominal hysterectomy approaches. This approach offers valuable insights into the varying risks associated with each surgical method.

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YL and ZY contributed to the conception of the work; YL, ZY, JL W and J L were the independent investigators to conducted the study's review, quality assessment, and data extraction. YL and YH L completed the data analysis, and drafted the manuscript. Finally, ZY and YH L gave final approval for the publish version; and ZY agreed to be responsible for all aspects of the work and to ensure that problems relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Figure 1 The PRISMA Flow

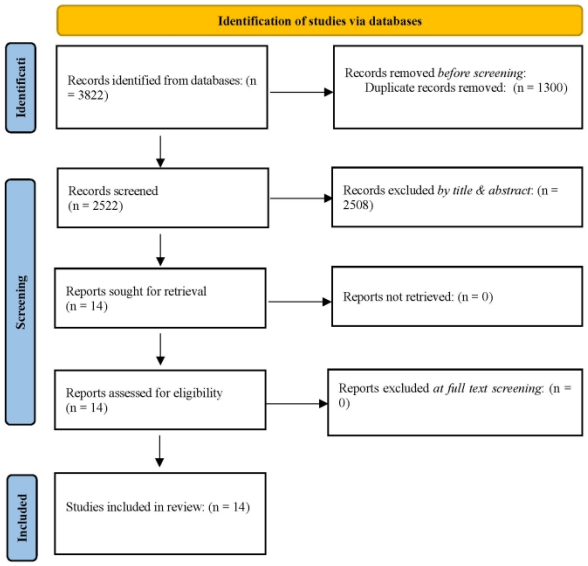
Figure 2 The Funnel Plots

Figure 3 The Forest Plots for Each Risk Factor

Figure 4 Tobacco Use Subgroup Forest Plot between SSI Types

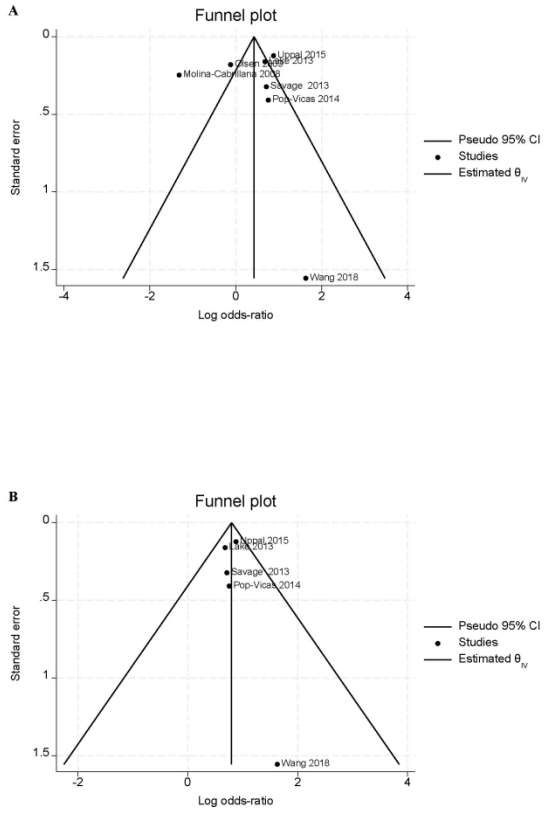
Figure 5 Bayesian network analysis

Figure 1 The PRISMA Flow



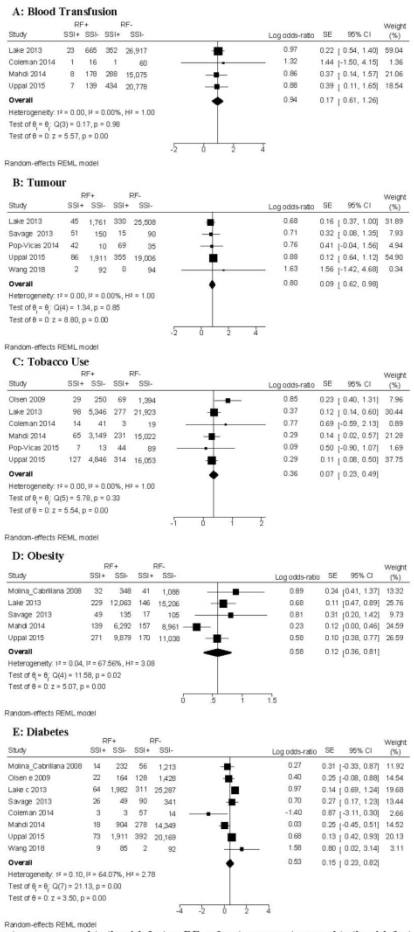
210x297mm (300 x 301 DPI)

Figure 2 The Funnel Plots



210x297mm (302 x 300 DPI)

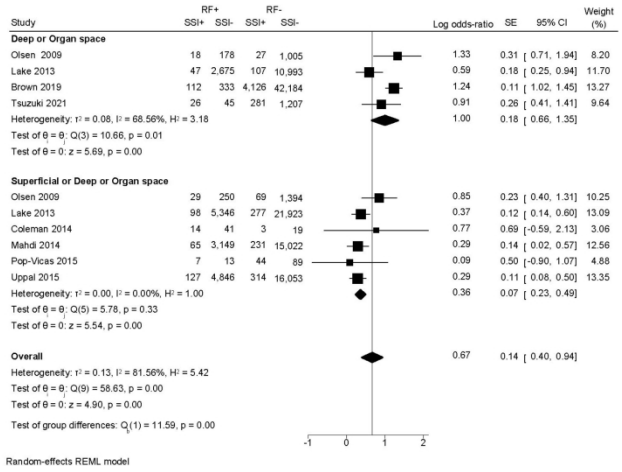
Figure 3 The Forest Plots for Each Risk Factor



Note. RF+ refers to cases exposed to the risk factor; RF- refers to cases not exposed to the risk factor; SSI+ refers to SSI positive cases; SSI- refers to SSI negative cases;

210x297mm (300 x 300 DPI)

Figure 1 Tobacco Use Subgroup Forest Plot between SSI Types



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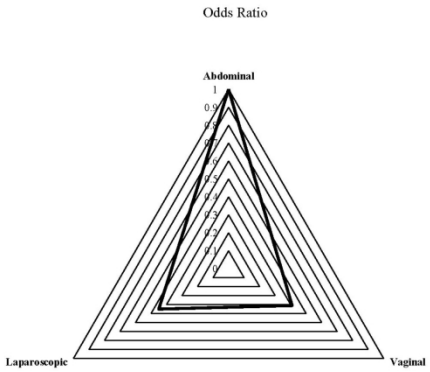

297x210mm (300 x 300 DPI)

Contents

Search Terms

Pubmed (Central) Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeries SSI (no restriction to age)	hysterectomy surgeriesmesh term: #1
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term: #1
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term: #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
Outcome	SSI	Infection mesh term: #10

step	code	results
#1	(((((((hysterectomy) OR (hysterectomies)) OR (hysterectomy, Vaginal)) OR (hysterectomies, Vaginal)) OR (vaginal hysterectomies)) OR (vaginal hysterectomy)) OR (Colpohysterectomy)) OR (Colpohysterectomies))	53,350
#2	((Clinical Trials, Randomized) OR (Trials, Randomized Clinical)) OR (Controlled Clinical Trials, Randomized)	742,997
#3	((((((((((((((((((((((((Cross Sectional Studies) OR (Cross-Sectional Study)) OR (Studies, Cross-Sectional)) OR (Study, Cross-Sectional)) OR (Surveys, Disease Frequency)) OR (Disease Frequency Survey)) OR (Survey, Disease Frequency)) OR (Analysis, Cross-Sectional)) OR (Analyses, Cross-Sectional)) OR (Analysis, Cross Sectional)) OR (Cross-Sectional Analyses)) OR (Cross-Sectional Analysis)) OR (Cross Sectional Analysis)) OR (Analyses, Cross Sectional)) OR (Cross Sectional Analyses)) OR (Cross-Sectional Survey)) OR (Cross Sectional Survey)) OR (Cross-Sectional Surveys)) OR (Survey, Cross-Sectional)) OR (Surveys, Cross-Sectional)) OR (Disease Frequency Surveys)) OR (Prevalence Studies)) OR (Prevalence Study)) OR (Studies, Prevalence)) OR (Study, Prevalence)	1,122,672
#4	((((((((((((((((((((((((((((((Longitudinal Study) OR (Studies, Longitudinal)) OR (Study, Longitudinal)) OR (Tuskegee Syphilis Study)) OR (Syphilis Studies, Tuskegee)) OR (Syphilis Study, Tuskegee)) OR (Tuskegee Syphilis Studies)) OR (Jackson Heart Study)) OR (Heart Studies, Jackson)) OR (Heart Study, Jackson)) OR (Jackson Heart Studies)) OR (Studies, Jackson Heart)) OR (California Teachers Study)) OR (California Teachers Studies)) OR (Studies, California Teachers)) OR (Study, California Teachers)) OR (Teachers Studies, California)) OR (Teachers Study, California)) OR (Bogalusa Heart Study)) OR (Bogalusa Heart Studies)) OR (Heart Studies, Bogalusa)) OR (Heart Study, Bogalusa)) OR (Studies, Bogalusa Heart)) OR (Study, Bogalusa Heart)) OR (Framingham Heart Study)) OR (Framingham Heart Studies)) OR (Heart Studies, Framingham)) OR (Heart Study, Framingham)) OR (Longitudinal Survey)) OR (Longitudinal Surveys)) OR (Survey, Longitudinal)) OR (Surveys, Longitudinal)	339,768
#5	((((((((((((((((((((((((((((((((((((((Case-Control Study) OR (Studies, Case-Control)) OR (Study, Case-Control)) OR (Case-Comparison Studies)) OR (Case Comparison Studies)) OR (Case-Comparison Study)) OR (Studies, Case-Comparison)) OR (Study, Case-Comparison)) OR (Case-Compeer Studies)) OR (Studies, Case-Compeer)) OR (Case-Referrent Studies)) OR (Case Referrent Studies)) OR (Case-Referrent Study)) OR (Studies, Case-Referrent)) OR (Study, Case-Referrent)) OR (Case-Referent Studies)) OR (Case Referent Studies)) OR (Case-Referent Study)) OR (Studies, Case-Referent)) OR (Study, Case-Referent)) OR (Case-Base Studies)) OR (Case Base Studies)) OR (Studies, Case-Base)) OR (Case Control Studies)) OR (Case Control Study)) OR (Studies, Case Control)) OR (Study, Case Control)) OR (Nested Case-Control Studies)) OR (Case-Control Studies, Nested)) OR (Case-Control Study, Nested)) OR (Nested Case Control Studies)) OR (Nested Case-Control Study)) OR (Studies, Nested Case-Control)) OR (Study, Nested Case-Control)) OR (Matched Case-Control Studies)) OR (Case-Control Studies,	1,589,628

	Matched)) OR (Case-Control Study, Matched)) OR (Matched Case Control Studies)) OR (Matched Case-Control Study)) OR (Studies, Matched Case-Control)) OR (Study, Matched Case-Control)	
#6	((Prospective Study) OR (Studies, Prospective)) OR (Study, Prospective)	904,417
#7	((((((((((((((((((((((((((((((Cohort Study) OR (Studies, Cohort)) OR (Study, Cohort)) OR (Concurrent Studies)) OR (Studies, Concurrent)) OR (Concurrent Study)) OR (Study, Concurrent)) OR (Closed Cohort Studies)) OR (Cohort Studies, Closed)) OR (Closed Cohort Study)) OR (Cohort Study, Closed)) OR (Study, Closed Cohort)) OR (Studies, Closed Cohort)) OR (Birth Cohort Studies)) OR (Birth Cohort Study)) OR (Cohort Studies, Birth)) OR (Cohort Study, Birth)) OR (Studies, Birth Cohort)) OR (Study, Birth Cohort)) OR (Analysis, Cohort)) OR (Analyses, Cohort)) OR (Cohort Analyses)) OR (Cohort Analysis)) OR (Historical Cohort Studies)) OR (Cohort Studies, Historical)) OR (Cohort Study, Historical)) OR (Historical Cohort Study)) OR (Study, Historical Cohort)) OR (Studies, Historical Cohort)) OR (Incidence Studies)) OR (Incidence Study)) OR (Studies, Incidence)) OR (Study, Incidence)	3,150,416
#8	Observational Study	205,618
#9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	4,994,412
#10	((((Infection and Infestation) OR (Infestation and Infection)) OR (Infections and Infestations)) OR (Infestations and Infections)) OR (Infection)	4003846
#11	#1 AND #9 AND #10	1,758
#12	The year 2000 - Current	1,198
#13	English	1,096

The results are hyperlinked in each column

Medline (Ovid) Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesmesh term with Medline code
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term with Medline code
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term with Medline code
Outcome	SSI	Infection mesh term with Medline code

	Term searched	Results
Group 1	Population	
1	hysterectomy. ti,ab,mp.	52599
2	hysterectomies. ti,ab,mp.	3423
3	hysterectomy, Vaginal. ti,ab,mp.	3235
4	hysterectomies, Vaginal. ti,ab,mp.	9
5	vaginal hysterectomies. ti,ab,mp.	437
6	vaginal hysterectomy. ti,ab,mp.	3593
7	Colpohysterectomy. ti,ab,mp.	84
8	Colpohysterectomies. ti,ab,mp.	8
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	53278
Group 2	Intervention	
10	hysterectomy. ti,ab,mp.	52599
11	hysterectomies. ti,ab,mp.	3423
12	hysterectomy, Vaginal. ti,ab,mp.	3235
13	hysterectomies, Vaginal. ti,ab,mp.	9
14	vaginal hysterectomies. ti,ab,mp.	437
15	vaginal hysterectomy. ti,ab,mp.	3593
16	Colpohysterectomy. ti,ab,mp.	84
17	Colpohysterectomies. ti,ab,mp.	8
18	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	53278
Group 3	Comparator	
19	Cross-sectional. ti,ab,mp.	632818
20	Longitudinal. ti,ab,mp.	377935
21	Prospective study. ti,ab,mp.	159216
22	Cohort study. ti,ab,mp.	274386
23	Observational study. ti,ab,mp.	199248
24	Randomized control study. ti,ab,mp.	937
25	Case-Control Studies. ti,ab,mp.	338463
26	19 or 21 or 22 or 23 or 24 or 25	1494518
Group 4	Outcome	
27	Infections. ti,ab,mp.	1470008
28	"Infection and Infestation". ti,ab,mp.	86
29	"Infestation and Infection". ti,ab,mp.	51
30	"Infections and Infestations". ti,ab,mp.	311

31	"Infestations and Infections". ti,ab,mp.	28
32	Infection. ti,ab,mp.	1418735
33	27 or 28 or 29 or 30 or 31 or 32	2279134
Combined	9 and 18 and 26 and 33	407
Limited to English only	9 and 18 and 26 and 33	384
The year 2000 to present	9 and 18 and 26 and 33	337

Results link:

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=5SYIqKO2Gpep7EBCDrAGLmKZrFtVAMXrv0wx7zAaFQsQRH5DCIC4ESMKrqhH2tOv1

Embase (Ovid) Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesmesh term with Embase code
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term with Embase code
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term with Embase code
Outcome	SSI	Infection mesh term with Embase code

	Term searched	Results
Group 1	Population	
1	hysterectomy. ti,ab,mp.	93767
2	hysterectomies. ti,ab,mp.	6284
3	hysterectomy, Vaginal. ti,ab,mp.	392
4	trachelectomy. ti,ab,mp.	19
5	hysterectomies, Vaginal. ti,ab,mp.	758
6	vaginal hysterectomies. ti,ab,mp.	8954
7	vaginal hysterectomy. ti,ab,mp.	83
8	Colpohysterectomy. ti,ab,mp.	5
9	Colpohysterectomies. ti,ab,mp.	94170
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	93767
Group 2	Intervention	
11	hysterectomy. ti,ab,mp.	93767
12	hysterectomies. ti,ab,mp.	6284
13	hysterectomy, Vaginal. ti,ab,mp.	392
14	trachelectomy. ti,ab,mp.	19
15	hysterectomies, Vaginal. ti,ab,mp.	758
16	vaginal hysterectomies. ti,ab,mp.	8954
17	vaginal hysterectomy. ti,ab,mp.	83
18	Colpohysterectomy. ti,ab,mp.	5
19	Colpohysterectomies. ti,ab,mp.	94170
20	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	93767
Group 3	Comparator	
21	Cross-sectional. ti,ab,mp.	765496
22	Longitudinal. ti,ab,mp.	475332
23	Prospective study. ti,ab,mp.	899849
24	Cohort study. ti,ab,mp.	405571
25	Observational study. ti,ab,mp.	342074
26	Randomized control study. ti,ab,mp.	1628
27	Case-Control Studies. ti,ab,mp.	27610
28	21 or 22 or 23 or 24 or 25 or 26 or 27	2146419
Group 4	Outcome	
29	Infections. ti,ab,mp.	835857
30	"Infection and Infestation". ti,ab,mp.	107

31	"Infestation and Infection". ti,ab,mp.	55
32	"Infections and Infestations". ti,ab,mp.	807
33	"Infestations and Infections". ti,ab,mp.	49
34	Infection. ti,ab,mp.	2763568
35	29 or 30 or 31 or 32 or 33 or 34	2991465
Combined	10 and 20 and 28 and 35	1510
Limited to English only	10 and 20 and 28 and 35	1468
The year 2000 to present	10 and 20 and 28 and 35	1419

Results link:

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=79TCxxCp1oN0adXj9ZUf4UzOGz44m8xhcwT9pEsrMoJkpSIjfY4IktYO5RKZbvU7

Web of Science Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesmesh term with the web of science code: #1
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term with the web of science code: #1
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh terms with the web of science code: #2, #3, #4, #5, #6, #7, #8
Outcome	SSI	Infection mesh term with the web of science code: #10

step	code	results
#1	TS= (hysterectomy* OR hysterectomies* OR hysterectomy, vaginal* OR hysterectomies, vaginal OR vaginal hysterectomies* OR vaginal hysterectomy* OR colpohysterectomy* OR colpohysterectomies*)	40974
#2	TS= (Clinical Trials, Randomized* OR Trials, Randomized Clinical* OR Controlled Clinical Trials, Randomized*)	357993
#3	TS= (Longitudinal Study* OR Studies, Longitudinal* OR Study, Longitudinal* OR Tuskegee Syphilis Study* OR Syphilis Studies, Tuskegee* OR Syphilis Study, Tuskegee* OR Tuskegee Syphilis Studies* OR Jackson Heart Study* OR Heart Studies, Jackson* OR Heart Study, Jackson* OR Jackson Heart Studies* OR Studies, Jackson Heart* OR California Teachers Study* OR California Teachers Studies* OR Studies, California Teachers* OR Study, California Teachers* OR Teachers Studies, California* OR Teachers Study, California* OR Bogalusa Heart Study* OR Bogalusa Heart Studies* OR Heart Studies, Bogalusa* OR Heart Study, Bogalusa* OR Studies, Bogalusa Heart* OR Study, Bogalusa Heart* OR Framingham Heart Study* OR Framingham Heart Studies* OR Heart Studies, Framingham* OR Heart Study, Framingham* OR Longitudinal Survey* OR Longitudinal Surveys* OR Survey, Longitudinal* OR Surveys, Longitudinal*)	389252
#4	TS= (Case-Control Study* OR Studies, Case-Control* OR Study, Case-Control* OR Case-Comparison Studies* OR Case Comparison Studies* OR Case-Comparison Study* OR Studies, Case-Comparison* OR Study, Case-Comparison* OR Case-Compeer Studies* OR Studies, Case-Compeer* OR Case-Referrent Studies* OR Case Referrent Studies* OR Case-Referrent Study* OR Studies, Case-Referrent* OR Study, Case-Referrent* OR Case-Referent Studies* OR Case Referent Studies* OR Case-Referent Study* OR Studies, Case-Referent* OR Study, Case-Referent* OR Case-Base Studies* OR Case Base Studies* OR Studies, Case-Base* OR Case Control Studies* OR Case Control Study* OR Studies, Case Control* OR Study, Case Control* OR Nested Case-Control Studies* OR Case-Control Studies, Nested* OR Case-Control Study, Nested* OR Nested Case Control Studies* OR Nested Case-Control Study* OR Studies, Nested Case-Control* OR Study, Nested Case-Control* OR Matched Case-Control Studies* OR Case-Control Studies, Matched* OR Case-Control Study, Matched* OR Matched Case Control Studies* OR Matched Case-Control Study* OR Studies, Matched Case-Control* OR Study, Matched Case-Control*)	742023
#5	TS= (Cross Sectional Studies* OR Cross-Sectional Study * OR Studies, Cross-Sectional * OR Study, Cross-Sectional * OR Surveys, Disease Frequency * OR Disease Frequency Survey * OR Survey, Disease Frequency * OR Analysis, Cross-Sectional * OR Analyses, Cross-Sectional * OR Analysis, Cross Sectional * OR Cross-Sectional Analyses * OR Cross-Sectional Analysis * OR Cross Sectional Analysis	1164085

	* OR Analyses, Cross Sectional * OR Cross Sectional Analyses * OR Cross-Sectional Survey * OR Cross Sectional Survey * OR Cross-Sectional Surveys * OR Survey, Cross-Sectional * OR Surveys, Cross-Sectional * OR Disease Frequency Surveys * OR Prevalence Studies * OR Prevalence Study * OR Studies, Prevalence * OR Study, Prevalence*)	
#6	TS= (Prospective Study* OR Studies, Prospective* OR Study, Prospective*)	721432
#7	TS= (Cohort Study* OR Studies, Cohort * OR Study, Cohort * OR Concurrent Studies * OR Studies, Concurrent * OR Concurrent Study * OR Study, Concurrent * OR Closed Cohort Studies * OR Cohort Studies, Closed * OR Closed Cohort Study * OR Cohort Study, Closed * OR Study, Closed Cohort * OR Studies, Closed Cohort * OR Birth Cohort Studies * OR Birth Cohort Study * OR Cohort Studies, Birth * OR Cohort Study, Birth * OR Studies, Birth Cohort * OR Study, Birth Cohort * OR Analysis, Cohort * OR Analyses, Cohort * OR Cohort Analyses * OR Cohort Analysis * OR Historical Cohort Studies * OR Cohort Studies, Historical * OR Cohort Study, Historical * OR Historical Cohort Study * OR Study, Historical Cohort * OR Studies, Historical Cohort * OR Incidence Studies * OR Incidence Study * OR Studies, Incidence * OR Study, Incidence*)	1333108
#8	TS= (Observational study *)	234254
#9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	3887063
#10	TS= (Infections* OR Infection and Infestation * OR Infestation and Infection * OR Infections and Infestations * OR Infestations and Infections * OR Infection *)	1895911
#11	#1 AND #9 AND #10	853
#12	The year 2000 – current; English	726

The results are hyperlinked in each column

Cochrane Library Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesCochrane search manager hysterectomy surgerieswith Cochrane code based on mesh term: #1
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgerieswith Cochrane code based on mesh term
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study with Cochrane code based on mesh term:
Outcome	SSI	hysterectomy surgerieswith Cochrane code based on mesh term

step	code	results
#1	(hysterectomy):ti,ab,kw OR (hysterectomies):ti,ab,kw OR (hysterectomy,Vaginal):ti,ab,kw OR (hysterectomies,Vaginal):ti,ab,kw OR (vaginal hysterectomies):ti,ab,kw OR (vaginal hysterectomy):ti,ab,kw OR (Colpohysterectomy):ti,ab,kw OR (Colpohysterectomies):ti,ab,kw	8202
#2	(Clinical Trials, Randomized):ti,ab,kw OR (Trials, Randomized Clinical):ti,ab,kw OR (Controlled Clinical Trials, Randomized):ti,ab,kw	154945
#3	(Longitudinal Study):ti,ab,kw OR (Studies, Longitudinal):ti,ab,kw OR (Study, Longitudinal):ti,ab,kw OR (Tuskegee Syphilis Study):ti,ab,kw OR (Syphilis Studies, Tuskegee):ti,ab,kw OR (Syphilis Study, Tuskegee):ti,ab,kw OR (Tuskegee Syphilis Studies):ti,ab,kw OR (Jackson Heart Study):ti,ab,kw OR (Heart Studies, Jackson):ti,ab,kw OR (Heart Study, Jackson):ti,ab,kw OR (Jackson Heart Studies):ti,ab,kw OR (Studies, Jackson Heart):ti,ab,kw OR (California Teachers Study):ti,ab,kw OR (California Teachers Studies):ti,ab,kw OR (Studies, California Teachers):ti,ab,kw OR (Study, California Teachers):ti,ab,kw OR (Teachers Studies, California):ti,ab,kw OR (Teachers Study, California):ti,ab,kw OR (Bogalusa Heart Study):ti,ab,kw OR (Bogalusa Heart Studies):ti,ab,kw OR (Heart Studies, Bogalusa):ti,ab,kw OR (Heart Study, Bogalusa):ti,ab,kw OR (Studies, Bogalusa Heart):ti,ab,kw OR (Study, Bogalusa Heart):ti,ab,kw OR (Framingham Heart Study):ti,ab,kw OR (Framingham Heart Studies):ti,ab,kw OR (Heart Studies, Framingham):ti,ab,kw OR (Heart Study, Framingham):ti,ab,kw OR (Longitudinal Survey):ti,ab,kw OR (Longitudinal Surveys):ti,ab,kw OR (Survey, Longitudinal):ti,ab,kw OR (Surveys, Longitudinal):ti,ab,kw	23544
#4	(Case-Control Study):ti,ab,kw OR (Studies, Case-Control):ti,ab,kw OR (Study, Case-Control):ti,ab,kw OR (Case-Comparison Studies):ti,ab,kw OR (Case Comparison Studies):ti,ab,kw OR (Case-Comparison Study):ti,ab,kw OR (Studies, Case-Comparison):ti,ab,kw OR (Study, Case-Comparison):ti,ab,kw OR (Case-Compeer Studies):ti,ab,kw OR (Studies, Case-Compeer):ti,ab,kw OR (Case-Referrent Studies):ti,ab,kw OR (Case Referrent Studies):ti,ab,kw OR (Case-Referrent Study):ti,ab,kw OR (Studies, Case-Referrent):ti,ab,kw OR (Study, Case-Referrent):ti,ab,kw OR (Case-Referent Studies):ti,ab,kw OR (Case Referent Studies):ti,ab,kw OR (Case-Referent Study):ti,ab,kw OR (Studies, Case-Referent):ti,ab,kw OR (Study, Case-Referent):ti,ab,kw OR (Case-Base Studies):ti,ab,kw OR (Case Base Studies):ti,ab,kw OR (Studies, Case-Base):ti,ab,kw OR (Case Control Studies):ti,ab,kw OR (Case Control Study):ti,ab,kw OR (Studies, Case Control):ti,ab,kw OR (Study, Case Control):ti,ab,kw OR (Nested Case-Control Studies):ti,ab,kw OR (Case-Control Studies, Nested):ti,ab,kw OR (Case-Control Study, Nested):ti,ab,kw OR (Nested Case Control Studies):ti,ab,kw OR (Nested Case-Control Study):ti,ab,kw OR (Studies, Nested Case-Control):ti,ab,kw OR (Study, Nested Case-Control):ti,ab,kw OR (Matched Case-Control Studies):ti,ab,kw OR (Case-Control	33557

	Studies, Matched):ti,ab,kw OR (Case-Control Study, Matched):ti,ab,kw OR (Matched Case Control Studies):ti,ab,kw OR (Matched Case-Control Study):ti,ab,kw OR (Studies, Matched Case-Control):ti,ab,kw OR (Study, Matched Case-Control):ti,ab,kw	
#5	(Cross Sectional Studies):ti,ab,kw OR (Cross-Sectional Study):ti,ab,kw OR (Studies, Cross-Sectional):ti,ab,kw OR (Study, Cross-Sectional):ti,ab,kw OR (Surveys, Disease Frequency):ti,ab,kw OR (Disease Frequency Survey):ti,ab,kw OR (Survey, Disease Frequency):ti,ab,kw OR (Analysis, Cross-Sectional):ti,ab,kw OR (Analyses, Cross-Sectional):ti,ab,kw OR (Analysis, Cross Sectional):ti,ab,kw OR (Cross-Sectional Analyses):ti,ab,kw OR (Cross-Sectional Analysis):ti,ab,kw OR (Cross Sectional Analysis):ti,ab,kw OR (Analyses, Cross Sectional):ti,ab,kw OR (Cross Sectional Analyses):ti,ab,kw OR (Cross-Sectional Survey):ti,ab,kw OR (Cross Sectional Survey):ti,ab,kw OR (Cross-Sectional Surveys):ti,ab,kw OR (Survey, Cross-Sectional):ti,ab,kw OR (Surveys, Cross-Sectional):ti,ab,kw OR (Disease Frequency Surveys):ti,ab,kw OR (Prevalence Studies):ti,ab,kw OR (Prevalence Study):ti,ab,kw OR (Studies, Prevalence):ti,ab,kw OR (Study, Prevalence):ti,ab,kw	54133
#6	(Prospective Study):ti,ab,kw OR (Studies, Prospective):ti,ab,kw OR (Study, Prospective):ti,ab,kw	233446
#7	(Cohort Study):ti,ab,kw OR (Studies, Cohort):ti,ab,kw OR (Study, Cohort):ti,ab,kw OR (Concurrent Studies):ti,ab,kw OR (Studies, Concurrent):ti,ab,kw OR (Concurrent Study):ti,ab,kw OR (Study, Concurrent):ti,ab,kw OR (Closed Cohort Studies):ti,ab,kw OR (Cohort Studies, Closed):ti,ab,kw OR (Closed Cohort Study):ti,ab,kw OR (Cohort Study, Closed):ti,ab,kw OR (Study, Closed Cohort):ti,ab,kw OR (Studies, Closed Cohort):ti,ab,kw OR (Birth Cohort Studies):ti,ab,kw OR (Birth Cohort Study):ti,ab,kw OR (Cohort Studies, Birth):ti,ab,kw OR (Cohort Study, Birth):ti,ab,kw OR (Studies, Birth Cohort):ti,ab,kw OR (Study, Birth Cohort):ti,ab,kw OR (Analysis, Cohort):ti,ab,kw OR (Analyses, Cohort):ti,ab,kw OR (Cohort Analyses):ti,ab,kw OR (Cohort Analysis):ti,ab,kw OR (Historical Cohort Studies):ti,ab,kw OR (Cohort Studies, Historical):ti,ab,kw OR (Cohort Study, Historical):ti,ab,kw OR (Historical Cohort Study):ti,ab,kw OR (Study, Historical Cohort):ti,ab,kw OR (Studies, Historical Cohort):ti,ab,kw OR (Incidence Studies):ti,ab,kw OR (Incidence Study):ti,ab,kw OR (Studies, Incidence):ti,ab,kw OR (Study, Incidence):ti,ab,kw	184886
#8	(Observational Study):ti,ab,kw	20328
#9	(Infection and Infestation):ti,ab,kw OR (Infection and Infestation):ti,ab,kw OR (Infections and Infestations):ti,ab,kw OR (Infestations and Infections):ti,ab,kw OR (Infection):ti,ab,kw	102985
#10	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	552677
#11	#1 AND #9 AND #10	382
#12	Trials	377
#13	The year 2000 – current; English	243

Risk of Bias Assessment

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (CASE CONTROL STUDIES)

Selection

1) Is the case definition adequate?

a) yes, with independent validation □

b) yes, e.g. record linkage or based on self-reports

c) no description

2) Representativeness of the cases

a) consecutive or obviously representative series of cases □

b) potential for selection biases or not stated

3) Selection of Controls

a) community controls □

b) hospital controls

c) no description

4) Definition of Controls

a) no history of disease (endpoint) □

b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis

a) study controls for _____ (Select the most important factor.) □

b) study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure

a) secure record (e.g. surgical records) □

b) structured interview where blind to case/control status □

c) interview not blinded to case/control status

d) written self-report or medical record only

e) no description

2) Same method of ascertainment for cases and controls

a) yes □

b) no

3) Non-response rate

a) same rate for both groups □

b) non-respondents described

c) rate different and no designation

Table 1 Risk of Bias Assessment with NOS Case-control Study Scale

Author & Year	Selection				Comparability	Exposure			Total score
Olsen 2009	1	1	1	0	2	1	1	0	6
Lake 2013	1	1	1	1	2	1	1	1	9
Savage 2013	1	1	1	0	2	1	1	0	7
Pop-Vicas 2014	0	1	1	0	2	0	1	1	6
Morgan 2016	1	1	1	0	2	0	1	1	7
Wang 2022	1	1	1	0	2	1	1	0	7

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (COHORT STUDIES)

Selection

1) Representativeness of the exposed cohort

a) truly representative of the average _____ (describe) in the community □

b) somewhat representative of the average _____ in the community □

c) selected group of users e.g. nurses, volunteers

d) no description of the derivation of the cohort

2) Selection of the non-exposed cohort

a) drawn from the same community as the exposed cohort □

b) drawn from a different source

c) no description of the derivation of the non-exposed cohort

3) Ascertainment of exposure

a) secure record (e.g. surgical records) □

b) structured interview □

c) written self-report

d) no description

4) Demonstration that outcome of interest was not present at start of study

a) yes □

b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for _____ (select the most important factor) □

b) study controls for any additional factor □ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome

a) independent blind assessment □

b) record linkage □

c) self-report

d) no description

2) Was follow-up long enough for outcomes to occur

a) yes (select an adequate follow-up period for outcome of interest) □

b) no

3) Adequacy of follow-up of cohorts

a) complete follow-up - all subjects accounted for □

b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) □

c) follow up rate < ____% (select an adequate %) and no description of those lost

d) no statement

Table 2 Risk of Bias Assessment with NOS Cohort Study Scale

Author & Year	Selection				Comparability	Exposure			Total score
Molina-Cabrillana 2008	0	1	1	0	2	1	1	0	6
Coleman 2014	1	1	1	0	2	1	0	1	7
Mahdi 2014	1	1	1	0	2	1	1	0	7
Uppal 2015	1	1	1	0	2	1	1	1	8
Tuomi 2016	1	1	1	0	2	1	1	1	8
Till 2017	1	1	1	0	2	0	1	1	7
Brown 2019	1	1	1	1	2	1	1	1	9
Tsuzuki 2021	1	1	1	0	2	1	1	0	7

Table 3 Study Summary

Author & Year	Selection				Comparability	Exposure			Total score
Molina-Cabrillana 2008#	0	1	1	0	2	1	1	0	6
Olsen 2009*	1	1	1	0	2	1	1	0	6
Lake 2013*	1	1	1	1	2	1	1	1	9
Savage 2013*	1	1	1	0	2	1	1	0	7
Coleman 2014#	1	1	1	0	2	1	0	1	7
Mahdi 2014#	1	1	1	0	2	1	1	0	7
Pop-Vicas 2014*	0	1	1	0	2	0	1	1	6
Uppal 2015#	1	1	1	0	2	1	1	1	8
Morgan 2016*	1	1	1	0	2	0	1	1	7
Tuomi 2016#	1	1	1	0	2	1	1	1	8
Till 2017#	1	1	1	0	2	0	1	1	7
Brown 2019#	1	1	1	1	2	1	1	1	9
Tsuzuki 2021#	1	1	1	0	2	1	1	0	7
Wang 2022*	1	1	1	0	2	1	1	0	7

Note. *means this study was assessed through the items for case-control studies. # means this study was assessed through the items for cohort studies.

Table 3 Study Summary

Author & Year	Sample Origin	N	SSI +	Age (±SD)	Surgery Method	Age RF	Anti-microbial	Blood Loss	Blood Transfusion	BMI	Diabetes	Obesity	Surgery Duration	Tobacco Use	Tumour	Wound Cleanness
Molina-Cabrillana 2008	2000-2004 Hospital Universitario Materno-Infantil de Canarias, Sapin	1540	72	54.00 (±12.90)	abdominal & vaginal	Age >60	Y/N	NR	NR	NR	Y/N	Y/N	≥P75	NR	Y/N	Clean-contaminated vs Contaminated /dirty
Olsen 2009	2003-2005 CDC Prevention Epicenter Program hospitals, USA	820	66	51.70 (±17.78)	abdominal & vaginal	Mean	NR	NR	NR	Mean	Y/N	NR	Mean	Y/N	Y/N	NR
Lake 2013	2005-2009 ACS-NSQIP, USA	13822	375	NR	abdominal & vaginal & laparoscopic	Age >80	NR	NR	Y/N	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	≥P75	Y/N	Y/N	Clean vs Clean-contaminated Contaminated vs Dirty
Savage 2013	2007-2010 University of Iowa Hospitals and Clinics, USA	1104	126	54.53 (±13.66)	abdominal	Mean	Mean	NR	Median	BMI≥30 (Obesity)	Y/N	Y/N	Mean	NR	Y/N	NR
Coleman 2014	1999-2012 Johns Hopkins Medical Institution, USA	77	17	42.56 (±5.93)	abdominal & vaginal & laparoscopic	Mean	NR	>250ml; ≥451ml	Y/N	Median	Y/N	BMI≥30 (Obesity)	NR	Y/N	NR	NR
Mahdi 2014	2005-2011 ACS-NSQIP, USA	28366	296	NR	laparoscopic	Age >60, 70 & 80	NR	NR	>4 units of packed red blood cells	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	>60 min, 180 min	Y/N	NR	NR
Pop-Vicas 2014	2012-2015 University of Wisconsin Hospitals, USA	1531	52	58.27 (±12.31)	abdominal & vaginal & laparoscopic	Mean	Y/N	Median*	NR	NR	NR	NR	Mean	Y/N	Y/N	NR

Uppal 2015	2012-2015 MSQC, USA	21358	441	48.10 (±11.70)	abdominal & vaginal & laparoscopic	Median	Y/N	Median	NR	BMI≥30 (Obesity)	NR	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Morgan 2016	2012-2014 MSQC, USA	16548	315	NR	abdominal	Age >50	NR	Mean	Y/N	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Tuomi 2016	2007-2013 Helsinki University Hospital, Finland	1164	94	67.46 (±10.23)	abdominal & vaginal & laparoscopic	Mean	NR	Median	NR	Mean	Y/N	NR	Mean	Y/N	NR	NR
Till 2017	2012-2015 MSQC, USA	18255	329	NR	abdominal & vaginal & laparoscopic	Age >65	NR	≥250ml	NR	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Brown 2019	2012-2014 ACS-NSQIP, USA	46755	445	45.95 (±1.51)	laparoscopic	Mean	NR	NR	Y/N	Mean	Y/N	NR	Mean	Y/N	NR	Clean vs Clean-contaminated vs Contaminated vs Dirty
Tsuzuki 2021	2014-2018 Teine Keijinkai Hospital, Japan	1559	71	48.28 (±11.39)	laparoscopic	Mean	NA	NR	Y/N	Mean	Y/N	NR	Mean	Y/N	NR	NR
Wang 2022	2012-2022 Two Grade A Tertiary Hospitals, China	94	188	47.70 (±10.87)	abdominal	Age >50	Y/N	≥500ml	NR	Mean	Y/N	NR	>180 min	NR	Y/N	Clinicians determined Class II vs Class III
Overall		152993	2887	47.53 (±8.29)												

Note. The content under each risk factor was how these studies presented their data. The detailed case numbers are in Table 3; SSI+ refers to SSI-positive cases; ACS-NSQIP refers to the American College of Surgeons National Surgical Quality Improvement Program; MSQC refers to the Michigan Surgical Quality Collaborative; NR refers to not reported; NA refers to not applicable; Y/N refers to reported in Yes or No; Median*: the median reported in this study did not include IQR to estimate its variance; P75 refers to the 75th percentil

Table 2 Subgroup Analyses Between Different SSI Types

	Superficial & Deep & Organ Space						Deep & Organ Space						Group Difference	
Risk Factors	**LogOR**	**I^2**	**OR**	**SE**	**z**	**p**	**LogOR**	**I^2**	**OR**	**SE**	**z**	**p**	**Q (df)**	**p**
Tobacco Use	0.36	0.00%	1.43	0.07	5.78	<.001	1	68.56%	2.72	.18	5.69	.001	11.59 (1)	<.001
Diabetes	0.53	64.07%	1.70	0.15	2.5	<.001	0.27	61.95%	1.31	.25	1.06	.290	.71 (1)	.400

Note. Only Tobacco Use and Diabetes retrieved more than 4 datasets reporting Deep or Organ Space SSI types. The individual SSI types, such as Superficial, Deep, or Organ Space, were reported in less than 4 sets. This is to demonstrate that ORs of risk factors might differ between SSI types.

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Risk factors for surgical site infection (SSI) in patients undergoing hysterectomy: A systematic review and meta-analysis

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Primary Subject Heading:	Surgery
Secondary Subject Heading:	Obstetrics and gynaecology
Keywords:	Risk Factors, Meta-Analysis, Systematic Review

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Risk factors for surgical site infection (SSI) in patients undergoing hysterectomy: A systematic review and meta-analysis

Abstract

Objective: Surgical site infections (SSI) after hysterectomy constitute significant postoperative complications, affecting patient recovery and healthcare costs. We conducted a systematic review of risk factors for SSI in patients undergoing hysterectomy.

Design: The current study conducted a systematic review with meta-analysis to identify and summarise risk factors for SSI following hysterectomy.

Data sources: Pubmed, Medline, Embase, Web of Science, and Cochrane Central Register of Controlled Trials were searched through 1 November 2023.

Eligibility criteria: The inclusion criteria were 1) population: female participants who had post-hysterectomy SSI; 2) intervention: hysterectomy surgeries; 3) comparators: the number of participants who had or had not post-hysterectomy SSI; 4) outcomes: the number of participants exposed and not exposed to the risk factors of SSI. The exclusion criteria were 1) non-English studies and 2) studies that provided insufficient data.

Data extraction and synthesis: Two reviewers conducted the screening process independently. Articles that did not meet the inclusion criteria were excluded. For those that met the criteria, full-text papers were procured. Any discrepancies between the reviewers were resolved through discussion.The meta-analysis synthesised risk factors reported ≥ 4 datasets via random-effects models, assessing heterogeneity, sensitivity (leave-one-out), publication bias (Egger's test/funnel plots), and subgroup analyses (incision types).

Results: Blood transfusion emerged as the largest risk factor (OR = 2.55, 95%CI [1.84, 3.56]), followed by tumour presence (OR = 2.23, 95%CI [1.86, 2.66]), obesity (OR = 1.79, 95%CI [1.43, 2.23]), diabetes (OR = 1.70, 95%CI [1.26, 2.29]), and tobacco use (OR = 1.43, 95%CI [1.26, 1.63]). The ORs varied by incision type.

Conclusion: The study establishes blood transfusion, tumour presence, obesity, diabetes, and tobacco use as significant risk factors for SSI after

hysterectomy, with variations in risk evident across different incision types. The findings also suggest vaginal and laparoscopic hysterectomies as preferable alternatives to abdominal hysterectomy in mitigating SSI risk. Future research should aim for more granular data to untangle the interplay between comorbidities and further elucidate the differential risk across SSI types.

Keywords: Hysterectomy; Surgical Site Infections; Risk Factors; Meta-analysis

Strengths and limitations of this study

1. The current systematic review synthesised evidence on odds ratios of risk factors for post-hysterectomy SSI.

2. The current systematic review included 152993 patients who underwent hysterectomy, including 2887 who had post-hysterectomy SSI.

3. The major limitation was that we found the case numbers exposed to each risk factor were counted respectively, such that the odds ratios were not solely attributed to a single risk factor and might be overestimated.

Introduction

Hysterectomy is a very common procedure in which the uterus is surgically removed, and it is an optional treatment for leiomyoma, endometriosis, abnormal bleeding, benign ovarian neoplasms, pelvic organ prolapse, and gynecologic cancer [1]. Epidemiological research estimated that the lifetime prevalence of hysterectomy surgery is approximately 236/100,0000 in Germany, 143/100,0000 in the US [2 3], 80/100,0000 in China [4], and 42/100,0000 in the UK [2] among the female population, depending on waitlist queuing time of different regions [2]. Among patients who had hysterectomies, 2.1% are estimated to develop surgical site infections (SSI) worldwide [5], which has been one of the most common complications after hysterectomy surgery [6]. According to Centers for Disease Control and Prevention (CDC), SSI is an infection that develops in the portion of the body where the operation was performed. It might be superficial, affecting simply the skin, or more serious, involving tissues beneath the skin, organs, or implanted material. The currently accepted risk factors of hysterectomy SSI are age, body mass index (BMI), smoking, and diabetes [7]. However, many studies have shown different results, one study from Spain only considered obesity and inadequate prophylaxis as meaningful indicators [8], whereas another study from the UK also suggested that the operative time should be considered an independent risk factor [9]. The evidence from current research appears to be diverse, isolated, and lacking in quantitative power. One study analyzed the risk factors for SSI after obstetric and gynecological surgery; in fact, the types of obstetric and gynecological surgeries are varied; for example, breast-conserving surgeries are cleansing surgeries, and breast reconstruction may use silicone implants, so the factors affecting SSI for these surgeries may be different than for hysterectomies [10].

Consequently, the current study aims to summarise the results of risk factors of hysterectomy SSI through a quantitative approach.

Method

Study Registration

The protocol of the current study was registered and reviewed by the PROSPERO International Prospective Register of Systematic Reviews (No. CRD42023411668). The protocol is available at: https://www.crd.york.ac.uk/PROSPERO/export_details_pdf.php

The Patient and Public Involvement statement

None

Search Strategy

The data was extracted from published empirical study reports retrieved from the databases, including Pubmed (central), Medline (Ovid), Embase (Ovid), Web of Science, and Cochrane Central Register of Controlled Trials. The search terms followed the standard PICO guideline (population, intervention, comparator, outcome) and were adapted according to Medical Subject Headings (MeSH) terms [11]. The search was conducted upon the completion of study registration.

Eligibility criteria

The inclusion criteria were 1) population: women undergoing hysterectomy; 2) intervention: hysterectomy surgeries; 3) comparators: the number of participants who had or had not post-hysterectomy SSI; 4) outcomes: SSI. The exclusion criteria were 1) non-English studies and 2) studies that provided insufficient data.

Study screening and data extraction

The report articles were retrieved in RIS format and managed with Endnote (Bld13966, EndNote X9.3.3, 2023). The screening process followed the PRISMA guidelines [12]. Two reviewers conducted the screening process independently. Initially, they removed all duplicate articles. Then, articles that did not meet the inclusion criteria were excluded. For those that met the criteria, full-text papers were procured. Any discrepancies between the reviewers were resolved through discussion. Data from the selected articles was subsequently extracted.

Risk of bias assessment

Two reviewers independently scored the studies using the Newcastle-Ottawa quality assessment (NOS) [13 14]. NOS is a validated, easy-to-use scale containing 8 items organised into three dimensions: selection, comparability, and

exposure/outcome, which has been endorsed for use in systematic reviews of non-randomised studies by The Cochrane Collaboration [14]. Studies rated 0-2 as poor quality, 3-5 as fair quality, and 6–9 as good/high quality.

Data synthesis

Data synthesis requires at least four sets of data according to the general conduct suggested by the Cochrane Handbook [15]. The effect size of each identified risk factor will be pooled in a quantitative meta-analysis using STATA v18. The risk factors were expected to be reported as binary data about whether or not the patients were exposed to the risk factor and were infected. Consequently, odds ratios (ORs) would be calculated as the effect size with the following formula:

$$OR = \frac{a}{b} \div \frac{c}{d}$$

Where *a* represents cases exposed to the risk factor and infected, *b* represents those exposed but not infected, *c* represents unexposed but infected, and *d* represents unexposed and uninfected cases. And the LogOR is the natural log of the OR.

Statistical Analysis Plan

The meta-analysis was conducted with STATA v18. Only risk factors reported in over 4 datasets were synthesised into meta-analysis. A random effect model meta-analysis with the restricted maximum likelihood method was used to evaluate the pooled ORs (LogORs). The heterogeneity was also assessed with the random effects model, where heterogeneity I^2 is considered moderate when $I^2 > 50\%$ and high when $I^2 > 75\%$ [15]. Sensitivity analysis was conducted using the Leave-one-out approach by omitting one dataset each time and evaluating the pooled effect sizes. Egger's test and funnel plots were used to assess potential publication bias.

The pooled effect sizes were also entered into subgroup analysis based on the SSI types (superficial, deep, organ space) with available datasets. BMI was entered into the meta-regression analysis with pooled effect sizes of diabetes to explore the relationship between obesity and diabetes and its influence on SSI risk prediction.

Results

Systematic review

Initially, searching the keywords in PubMed, Medline (Ovid), Embase (Ovid), Web of Science, and the Cochrane Central Register of Controlled Trials produced 3821 records. Fourteen studies met the inclusion criteria after screening based on the PRISMA guidelines. The PRISMA procedure is shown in Figure 1.

Figure 1 The PRISMA Flow

All identified studies were retrospective observations to record the case numbers of SSI after hysterectomy surgeries with or without the occurrence of each risk factor. In total, 152993 female patients (age: 47.53±8.29) who underwent hysterectomy were included in the current 14 studies, of whom 2887 had SSI in different types, and 150106 had no SSI taken as controls. The details of all studies are described in Table 1 (More detailed information can be found at supplymentary material 1).

Table 1 Study Summary

Author & Year	Sample Origin	Study Design	Surgery Method	Blood Transfusion	Diabetes	Obesity	Tobacco Use	Tumour
Molina-Cabrillana 2008	2000-2004 Hospital Universitario Materno-Infantil de Canarias, Sapin	Cohort Study	abdominal & vaginal	NR	Y/N	N	NR	Y/N
Olsen 2009	2003-2005 CDC Prevention Epicenter Program hospitals, USA	Case-control Study	abdominal & vaginal	NR	Y/N	NR	Y/N	Y/N
Lake 2013	2005-2009 ACS-NSQIP, USA	Case-control Study	abdominal & vaginal & laparoscopic	Y/N	Y/N	BMI≥30 (Obesity)	Y/N	Y/N
Savage 2013	2007-2010 University of Iowa Hospitals and Clinics, USA	Case-control Study	abdominal	Median	Y/N	N	NR	Y/N
Coleman 2014	1999-2012 Johns Hopkins Medical Institution, USA	Cohort Study	abdominal & vaginal & laparoscopic	Y/N	Y/N	BMI≥30 (Obesity)	Y/N	NR
Mahdi 2014	2005-2011 ACS-NSQIP, USA	Cohort Study	laparoscopic	>4 units of packed red blood cells	Y/N	BMI≥30 (Obesity)	Y/N	NR
Pop-Vicas 2014	2012-2015 University of Wisconsin Hospitals, USA	Case-control Study	abdominal & vaginal & laparoscopic	NR	NR	NR	Y/N	Y/N
Uppal 2015	2012-2015 MSQC, USA	Cohort Study	abdominal & vaginal & laparoscopic	NR	NR	BMI≥30 (Obesity)	Y/N	Y/N
Morgan 2016	2012-2014 MSQC, USA	Case-control Study	abdominal	Y/N	Y/N	BMI≥30 (Obesity)	Y/N	Y/N
Tuomi 2016	2007-2013 Helsinki University Hospital, Finland	Cohort Study	abdominal & vaginal & laparoscopic	NR	Y/N	NR	Y/N	NR
Till 2017	2012-2015 MSQC, USA	Cohort Study	abdominal & vaginal & laparoscopic	NR	Y/N	BMI≥30 (Obesity)	Y/N	Y/N
Brown 2019	2012-2014 ACS-NSQIP, USA	Cohort Study	laparoscopic	Y/N	Y/N	NR	Y/N	NR
Tsuzuki 2021	2014-2018 Teine Keijinkai Hospital, Japan	Cohort Study	laparoscopic	Y/N	Y/N	NR	Y/N	NR

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Wang 2022	2012-2022 Two Grade A Tertiary Hospitals, China	Case-control Study	abdominal	NR	Y/N	NR	NR	Y/N

Note. The content under each risk factor was how these studies presented their data. The detailed case numbers are in supplymentary material 1; ACS-NSQIP refers to the American College of Surgeons National Surgical Quality Improvement Program; MSQC refers to the Michigan Surgical Quality Collaborative; NR refers to not reported; NA refers to not applicable; Y/N refers to reported in Yes or No.

Among these studies, seven only reported infection cases in mixed three SSI types (superficial, deep or organ space) [8 17-22], two only reported in mixed two SSI (deep or organ space) [23 24], one study reported each SSI types separately [25] and one study reported superficial and organ space SSIs separately [26], one study reported superficial SSI independently but mixed deep or organ space SSIs [27], one study reported deep SSI independently but mixed superficial or deep SSIs [5], one study reported only organ space SSIs [28]. Since it requires at least four datasets to conduct meta-analyses [15], the studies reported cases in independent SSI types were combined into three mixed SSI types (superficial, deep or organ space) to synthesise with those only reported the mixed SSI types. The NOS risk of bias assessment rated three studies scored 6 [8 20 25], seven scored 7 [5 17-19 22 24 28], two scored 8 [21 26], and the other two scored 9 [23 27]. All 14 studies are ranked as good/high quality and were included in the following review.

Among the 14 studies, there were 11 risk factors identified in total, including age, antimicrobial, blood loss, blood transfusion, BMI, diabetes (both type I or type II), obesity, surgery duration, tobacco use, tumour, and wound cleanness. However, antimicrobial and blood loss were reported in less than four datasets. Wound cleanness and age were reported in different classification standards. Only 5 factors reported in more than 4 datasets are available for quantitative analysis, including blood transfusion, diabetes, obesity, tobacco use, and tumour. Age, high BMI, and surgery duration reported continued data and thus could not be directly synthesised.

Meta-analyses

The identified risk factors with sufficient datasets were entered into meta-analyses respectively. As shown in Table 2, pooled effect sizes revealed significant overall logORs of blood transfusion (OR = 2.55, 95%CI [1.84, 3.56], p <.001), obesity (OR = 1.79, 95%CI [1.43, 2.23], p <.001), diabetes (OR = 1.70, 95%CI [1.26, 2.29], p <.001), tobacco use (OR = 1.43, 95%CI [1.26, 1.63], p <.001), but not tumour (OR = 1.35, p =.362), as the risk factors for SSI infections. However, after removing each dataset one at a time, leave-one-out sensitivity analysis on all risk factors suggested no changes except for tumour (OR = 2.33, 95%CI [1.86, 2.66], p <.001), where one dataset changed the results [8]. Further analysis with publication bias suggested no publication bias in all factors. However, as shown in Figure 2A, the funnel plot suggested three outlier datasets [8 21 25]. One border dataset was decided to

be kept [21], and the other two were excluded from the analysis [8 25].

Table 2 Summary of Meta-analyses

	Risk Factor	Blood Transfusion	Tumour	Obesity	Diabetes	Tobacco Use
Case Number	RF+ SSI+	39	226	720	229	340
	RF+ SSI-	998	3924	28717	5330	13645
	RF- SSI+	1075	769	531	1314	938
	RF- SSI-	62830	44733	36398	62893	54500
Meta-analysis	LogOR	0.94	0.8	0.58	0.53	0.36
	OR	2.55	2.23	1.79	1.7	1.43
	SE	0.17	0.09	0.12	0.15	0.07
	z	5.57	8.8	5.07	3.5	5.54
	p	<.001	<.001	<.001	<.001	<.001
Heterogeneity Test	I^2	0.00%	0.00%	67.56%	64.07%	0.00%
	$Q_{(df)}$	.17 (3)	1.34 (4)	11.58 (4)	21.13 (7)	5.78 (5)
	p	0.983	0.85	0.02	<.001	0.33
Leave-one-out Sensitivity	lowest LogOR	0.88	0.7	0.54	0.44	0.32
	Highest LogOR	0.96	0.86	0.66	0.64	0.43
Egger's Publication Bias	β	0.09	0.05	1.79	-1.21	0.76
	SE	1.08	0.81	7.6	0.89	0.73
	z	0.08	0.06	1.12	-1.35	0.91
	p	0.934	0.95	0.263	0.178	0.363

Note. The presenting data of the tumour was after exclusions of outliers. RF+ refers to exposure to the risk factor, RF- refers to no exposure to the risk factor, SSI+ refers to SSI positive, and SSI- refers to SSI negative, OR refers to Odds ratio, I^2 refers to Heterogeneity index, p refers to p-value.

Figure 2 The Funnel Plots

After exclusion, data from the tumour was entered into meta-analysis again and reported a significant pooled effect size predicting SSI infections (logOR = .80, OR = 2.23, p <.001), and, as shown in Figure 2B, there were no outliers. As shown in Figure 3A, 3B, and 3C, the estimation of heterogeneity suggested that the chance of inconsistent distribution of the pooled logORs was not significant in blood transfusion datasets (I^2 = 0%, $Q_{(3)}$ = .17, p = .983), tumour (I^2 = 0%, $Q_{(4)}$ = 1.34, p = .850) or tobacco use (I^2 = 0%, $Q_{(5)}$ = 5.78, p = .330). However, Figure 3D and Figure 3E suggested significant moderate heterogeneity in obesity (I^2 = 67.56%, $Q_{(4)}$ = 11.58, p <.001) and diabetes datasets (I^2 = 64.07%, $Q_{(7)}$ = 21.13, p <.001). These results suggested that blood transfusion, tumour, tobacco use, obesity, and diabetes were significant risk factors predicting post-hysterectomy SSI. Patients who underwent blood transfusion had a 155% increased likelihood of experiencing post-hysterectomy SSI. Similarly, individuals with tumours had a 123% increased risk, obese individuals 79%, diabetics 70%, and tobacco users 43%.

Figure 3 The Forest Plots for Each Risk Factor

Subgroup analysis between studies reporting different SSI types (mixed superficial or deep or organ space vs. mixed deep or organ space) was conducted among tobacco use and diabetes, for they obtained more than 4 datasets under each subgroup. The difference was whether they included superficial SSI. A significant group difference in pooled ORs between mixed superficial & deep & organ space cases and mixed deep or organ space among tobacco use, $Q_{(1)}$ = 11.59, p <.001, but not among diabetes, $Q_{(1)}$ = .71, p = .400.The impact of tobacco use on the risk of SSI varied significantly depending on the type of SSI, see supplymentary material Table 2. As shown in Figure 4, while tobacco use was associated with a 143% increased risk for combined superficial, deep, and organ space SSIs, this risk escalated to a 272% increase when considering only deep and organ space SSIs. This suggests that the influence of smoking may be more pronounced for deep and organ space infections than superficial ones. Given the observed discrepancy in risk between the combined three types of SSIs and the combined two types (deep or organ space) for tobacco use,

it is plausible that other risk factors might also exhibit differential effects across various SSI categories.

Figure 4 Tobacco Use Subgroup Forest Plot between SSI Types

Continuous BMI data was incorporated into a meta-regression analysis alongside the ORs of diabetes to evaluate the relationship between obesity and diabetes. Given the absence of group differences or heterogeneity discrepancies across SSI types in the effect sizes associated with diabetes, datasets from both SSI types (though not originating from identical studies) were incorporated into the meta-regression. The results suggested that BMI did not significantly predict the ORs of diabetes ($\beta = .001$, SE = .08, $t = .02$, $p = .989$). While this does not suggest that BMI (or obesity) is not correlated with the incidence of diabetes, it does affirm that high BMI did not affect the outcomes in this particular analysis.

Discussion

The current study conducted a systematic review with meta-analysis to summarise the evidence of risk factors of SSI after hysterectomy surgeries. To our knowledge, this is the first quantitative review of the topic. In total, 14 retrospective observations studies were identified with 2887 SSI positive and 150106 negative cases under 11 risk factors, including age, antimicrobial, blood loss, blood transfusion, high BMI, diabetes, obesity, surgery duration, tobacco use, tumour, and wound cleanness. However, only 5 were available for meta-analysis synchronisation. Among which, blood transfusion, tumour, obesity, diabetes, and tobacco use were factors that significantly increased the risk of SSI. The estimated ORs also seemed to vary between different SSI types (superficial, deep, or organ space). The details of the quantitative analysis are discussed as follows.

The largest risk factor of SSI is blood transfusion (OR = 2.55), with a 155% increased likelihood of SSI. Blood transfusion has always been identified as a major source of post-surgical infections [29] [30]. Administrative errors, such as bacterial contamination in platelet products, are believed responsible for infections induced by blood transfusion [29]. These issues are related to the healthcare service environment and beyond the current paper's discussion. Instead, the need for blood transfusion deserves further elaboration from the patients' site. For example, blood loss was reported to be positively correlated with BMI [31] [32]. Apart from obesity, severe abnormal uterine bleeding and cancer-related anaemia are also important reasons that patients require extra blood transfusion. However, none of the included studies attempted to isolate these factors, nor did they report preoperative haemoglobin. Consequently, we could not address whether blood transfusion was an independent factor or it was attributed to other factors such as obesity, severe abnormal uterine bleeding, cancer-related anaemia, preoperative haemoglobin or whether its estimated ORs were inflated. Future studies should consider reporting more comprehensive data to precisely estimate the ORs for blood transfusion as the SSI risk factor.

Likewise, one may argue that obesity and diabetes are comorbid, where obesity-induced insulin resistance is one of the major sources of type 2 diabetes [33]. This might explain the moderate heterogeneity of the ORs in obesity (OR = 1.79, I^2 = 67.56%) and diabetes (OR = 1.70, I^2 = 64.07%). This is, in fact, a methodological issue, where all studies directly counted the case number that was exposed and not exposed to the

specific risk factors, but none attempted to distinguish whether the case was exposed to multiple risk factors. That is, one might suffer from obesity or diabetes or both, and the case would be counted in each risk factor respectively when they suffer from both. Consequently, the estimated ORs were not solely attributed to one risk factor and might be overestimated. Hypothetically, in the current case, the heterogeneity of the ORs in obesity and diabetes was moderate because some studies included more patients suffering from both obesity and diabetes and reported higher ORs than those with fewer such patients. As a result, although both obesity and diabetes are significant risk factors, their estimated ORs should be considered cautiously and require further clarification in future studies by reporting cases separately.

To further address this issue, the current study conducted a meta-regression analysis to investigate whether BMI predicts the ORs of diabetes. The analysis found no significant relationship between continuous BMI values and the ORs of diabetes. Notably, the absence of a significant predictive relationship between BMI and the OR for diabetes does not imply that these two factors were unrelated or that obesity does not influence the estimation of OR for diabetes. On the one hand, the absence of a significant predictive relationship might arise from including both type I and type II diabetes in the studies, with type I diabetes having less direct relevance to obesity. On the other hand, the estimation of ORs may still have been elevated due to the repeated counting of cases exposed to multiple risk factors. Instead, this result might be interpreted as the pathologies of obesity and diabetes are relatively independent in the context of SSI risk.

Apart from obesity and diabetes, the second-largest risk factor was tumour (OR = 2.23), with a 123% increased likelihood of SSI. The immune system in patients afflicted with malignant tumours was generally compromised [34]. This impairment in the primary immune function directly results from the tumour's pervasive influence on the natural defence mechanisms. Furthermore, the standard therapeutic interventions for tumours, including surgery, chemotherapy, and radiotherapy, also contribute to the weakened immune state [35].

Tobacco use was the last risk factor (OR = 1.43), with a 43% increased likelihood of SSI. Nicotine and carbon monoxide, two primary agents produced in tobacco use, contribute to the constriction of peripheral blood vessels. This

vasoconstriction reduces the oxygen supply to tissues, vital for cellular function and healing processes [36]. Consequently, this oxygen deficit can precipitate the formation of microthrombi, which are small clots that can impair blood flow and further hinder tissue repair and regeneration.

However, the estimated ORs of tobacco use seemed to vary between SSI types. A subgroup comparison was conducted between studies that reported all mixed SSI and those that only reported deep or organ space SSI for tobacco use and diabetes, where only these two risk factors were reported repeatedly in distinguishing between SSI types. Significant subgroup differences were observed exclusively in the context of tobacco use. Specifically, tobacco use was associated with a 43% increased risk for superficial, deep, or organ space SSIs. This risk escalated to a 172% increase when focusing solely on deep or organ space SSIs. The pronounced impact of tobacco use appears more substantial in increasing the risk of deep or organ space infections compared to superficial ones. This discrepancy may also be attributed to tobacco-induced vasoconstriction. The vascular system supporting superficial cells, such as those in the skin, is more prosperous than the vasculature of deep and organ space cells. Consequently, cells in deeper tissues and organ spaces are more vulnerable to oxygen supply alterations exacerbated by tobacco use. However, this was merely a hypothetical explanation without solid evidence, which requires further investigation.

There are five limitations in the current study. First, some procedures performed in conjunction with hysterectomy can also affect SSI, but this was not explored in this paper. Second, the included studies did not differentiate cases based on the number of risk factors present, counting each instance for all identified risks. This approach likely inflated the ORs, particularly for comorbid conditions like patients with severe abnormal uterine bleeding or cancer-related anaemia and obesity and diabetes. Thirdly, there was no distinction between Type I and Type II diabetes in the studies, potentially contributing to moderate heterogeneity in the pooled OR estimates. Therefore, the estimated ORs for obesity and diabetes as risk factors for SSIs should be interpreted cautiously. Then, since none of the studies isolated patients with severe abnormal uterine bleeding, suffered from cancer-related anaemia, or reported pre-operative HbA1, it is unclear whether these factors also inflated the estimation ORs for blood transfusion, and thus, they should be interpreted cautiously as well. Lastly, few studies specified the types of SSI (superficial, deep, or organ space). Given that

our analysis indicates variation in tobacco use ORs across different SSI types, it is crucial to ascertain if similar variations apply to other risk factors. Addressing these issues in future research, with more detailed data reporting, is essential for a clearer understanding of the risk factors for SSIs. Future studies should report more comprehensive data to address these limitations.

In summary, the current study conducted a systematic review with meta-analysis of the risk factors of SSI after hysterectomy surgeries. In total, 11 risk factors were mentioned, whereas only blood transfusion, tumour, obesity, diabetes, and tobacco use had sufficient data to be entered into meta-analysis and yield statistical significance. With limited available data, the ORs of tobacco use seemed to vary between different SSI types, suggesting potential diversity in other risk factors. This approach offers valuable insights into the varying risks associated with each surgical method.

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YL and ZY contributed to the conception of the work; YL, ZY, JL W and J L were the independent investigators to conducted the study's review, quality assessment, and data extraction. YL and YH L completed the data analysis, and drafted the manuscript. Finally, ZY and YH L gave final approval for the publish version; and ZY agreed to be responsible for all aspects of the work and to ensure that problems relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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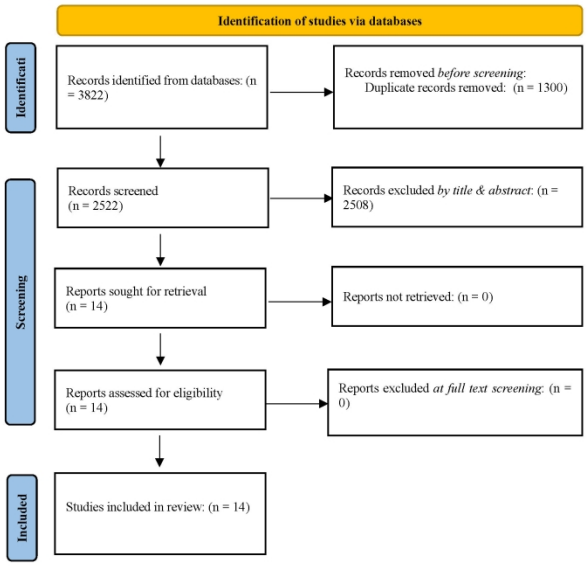
Figure 1 The PRISMA Flow

Figure 2 The Funnel Plots

Figure 3 The Forest Plots for Each Risk Factor

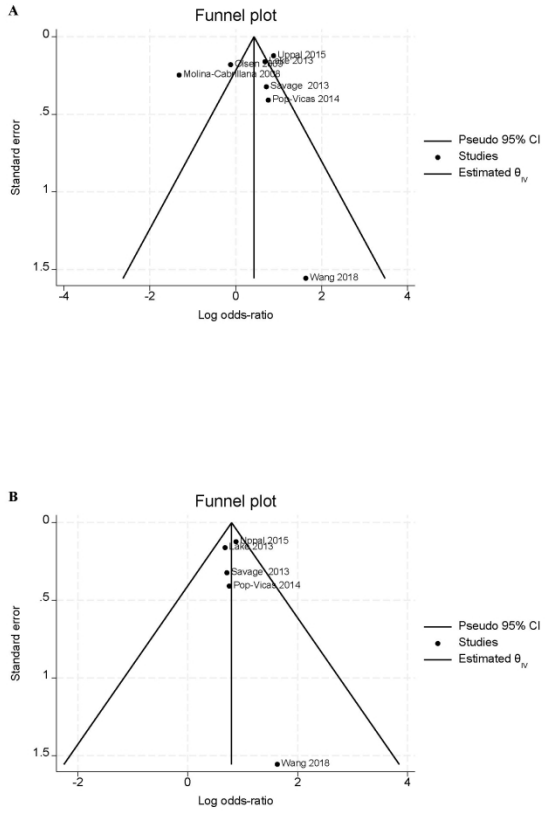
Figure 4 Tobacco Use Subgroup Forest Plot between SSI Types

Figure 1 The PRISMA Flow



210x297mm (300 x 301 DPI)

Figure 2 The Funnel Plots



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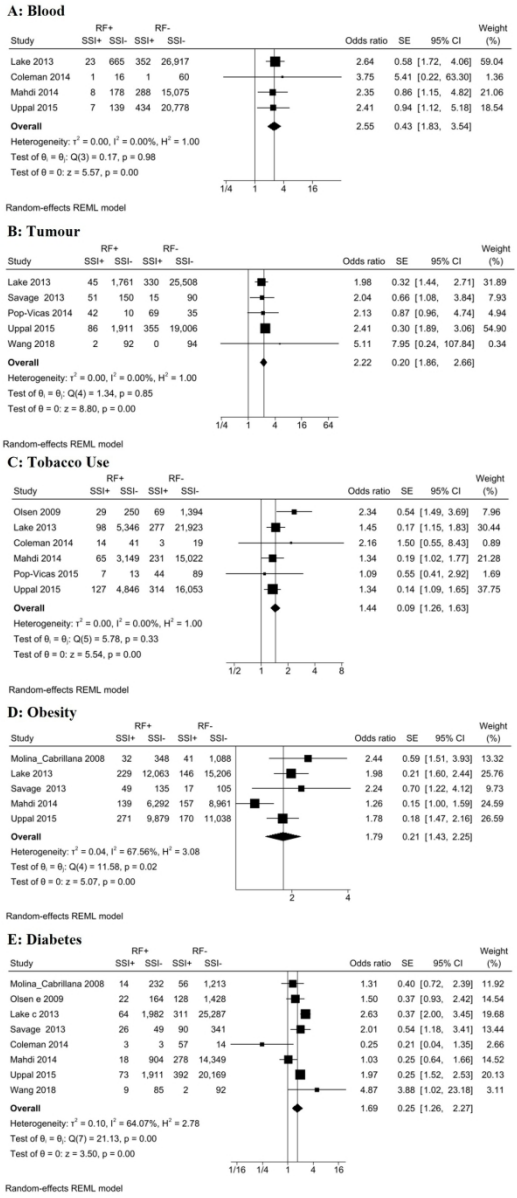

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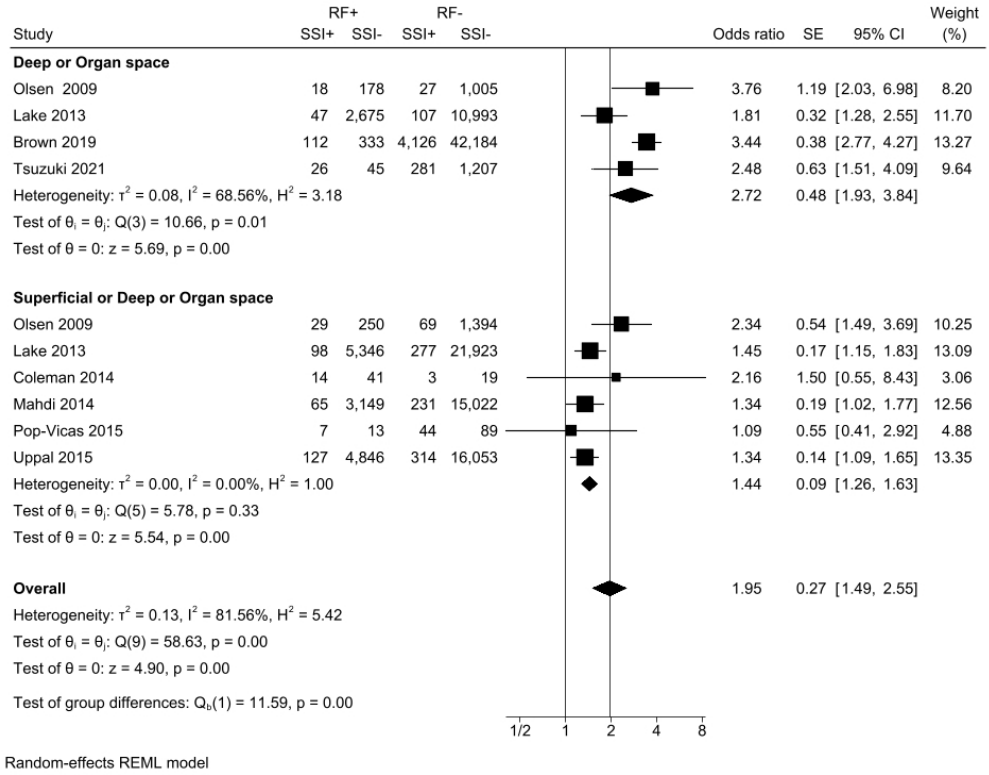

248x194mm (96 x 96 DPI)

Contents

Search Terms

Pubmed (Central) Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeries SSI (no restriction to age)	hysterectomy surgeriesmesh term: #1
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term: #1
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term: #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
Outcome	SSI	Infection mesh term: #10

step	code	results
#1	(((((((hysterectomy) OR (hysterectomies)) OR (hysterectomy, Vaginal)) OR (hysterectomies, Vaginal)) OR (vaginal hysterectomies)) OR (vaginal hysterectomy)) OR (Colpohysterectomy)) OR (Colpohysterectomies))	53,350
#2	((Clinical Trials, Randomized) OR (Trials, Randomized Clinical)) OR (Controlled Clinical Trials, Randomized)	742,997
#3	((((((((((((((((((((((((Cross Sectional Studies) OR (Cross-Sectional Study)) OR (Studies, Cross-Sectional)) OR (Study, Cross-Sectional)) OR (Surveys, Disease Frequency)) OR (Disease Frequency Survey)) OR (Survey, Disease Frequency)) OR (Analysis, Cross-Sectional)) OR (Analyses, Cross-Sectional)) OR (Analysis, Cross Sectional)) OR (Cross-Sectional Analyses)) OR (Cross-Sectional Analysis)) OR (Cross Sectional Analysis)) OR (Analyses, Cross Sectional)) OR (Cross Sectional Analyses)) OR (Cross-Sectional Survey)) OR (Cross Sectional Survey)) OR (Cross-Sectional Surveys)) OR (Survey, Cross-Sectional)) OR (Surveys, Cross-Sectional)) OR (Disease Frequency Surveys)) OR (Prevalence Studies)) OR (Prevalence Study)) OR (Studies, Prevalence)) OR (Study, Prevalence)	1,122,672
#4	((((((((((((((((((((((((((((((Longitudinal Study) OR (Studies, Longitudinal)) OR (Study, Longitudinal)) OR (Tuskegee Syphilis Study)) OR (Syphilis Studies, Tuskegee)) OR (Syphilis Study, Tuskegee)) OR (Tuskegee Syphilis Studies)) OR (Jackson Heart Study)) OR (Heart Studies, Jackson)) OR (Heart Study, Jackson)) OR (Jackson Heart Studies)) OR (Studies, Jackson Heart)) OR (California Teachers Study)) OR (California Teachers Studies)) OR (Studies, California Teachers)) OR (Study, California Teachers)) OR (Teachers Studies, California)) OR (Teachers Study, California)) OR (Bogalusa Heart Study)) OR (Bogalusa Heart Studies)) OR (Heart Studies, Bogalusa)) OR (Heart Study, Bogalusa)) OR (Studies, Bogalusa Heart)) OR (Study, Bogalusa Heart)) OR (Framingham Heart Study)) OR (Framingham Heart Studies)) OR (Heart Studies, Framingham)) OR (Heart Study, Framingham)) OR (Longitudinal Survey)) OR (Longitudinal Surveys)) OR (Survey, Longitudinal)) OR (Surveys, Longitudinal)	339,768
#5	((((((((((((((((((((((((((((((((((((((Case-Control Study) OR (Studies, Case-Control)) OR (Study, Case-Control)) OR (Case-Comparison Studies)) OR (Case Comparison Studies)) OR (Case-Comparison Study)) OR (Studies, Case-Comparison)) OR (Study, Case-Comparison)) OR (Case-Compeer Studies)) OR (Studies, Case-Compeer)) OR (Case-Referrent Studies)) OR (Case Referrent Studies)) OR (Case-Referrent Study)) OR (Studies, Case-Referrent)) OR (Study, Case-Referrent)) OR (Case-Referent Studies)) OR (Case Referent Studies)) OR (Case-Referent Study)) OR (Studies, Case-Referent)) OR (Study, Case-Referent)) OR (Case-Base Studies)) OR (Case Base Studies)) OR (Studies, Case-Base)) OR (Case Control Studies)) OR (Case Control Study)) OR (Studies, Case Control)) OR (Study, Case Control)) OR (Nested Case-Control Studies)) OR (Case-Control Studies, Nested)) OR (Case-Control Study, Nested)) OR (Nested Case Control Studies)) OR (Nested Case-Control Study)) OR (Studies, Nested Case-Control)) OR (Study, Nested Case-Control)) OR (Matched Case-Control Studies)) OR (Case-Control Studies,	1,589,628

	Matched)) OR (Case-Control Study, Matched)) OR (Matched Case Control Studies)) OR (Matched Case-Control Study)) OR (Studies, Matched Case-Control)) OR (Study, Matched Case-Control)	
#6	((Prospective Study) OR (Studies, Prospective)) OR (Study, Prospective)	904,417
#7	((((((((((((((((((((((((((((((Cohort Study) OR (Studies, Cohort)) OR (Study, Cohort)) OR (Concurrent Studies)) OR (Studies, Concurrent)) OR (Concurrent Study)) OR (Study, Concurrent)) OR (Closed Cohort Studies)) OR (Cohort Studies, Closed)) OR (Closed Cohort Study)) OR (Cohort Study, Closed)) OR (Study, Closed Cohort)) OR (Studies, Closed Cohort)) OR (Birth Cohort Studies)) OR (Birth Cohort Study)) OR (Cohort Studies, Birth)) OR (Cohort Study, Birth)) OR (Studies, Birth Cohort)) OR (Study, Birth Cohort)) OR (Analysis, Cohort)) OR (Analyses, Cohort)) OR (Cohort Analyses)) OR (Cohort Analysis)) OR (Historical Cohort Studies)) OR (Cohort Studies, Historical)) OR (Cohort Study, Historical)) OR (Historical Cohort Study)) OR (Study, Historical Cohort)) OR (Studies, Historical Cohort)) OR (Incidence Studies)) OR (Incidence Study)) OR (Studies, Incidence)) OR (Study, Incidence)	3,150,416
#8	Observational Study	205,618
#9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	4,994,412
#10	((((Infection and Infestation) OR (Infestation and Infection)) OR (Infections and Infestations)) OR (Infestations and Infections)) OR (Infection)	4003846
#11	#1 AND #9 AND #10	1,758
#12	The year 2000 - Current	1,198
#13	English	1,096

The results are hyperlinked in each column

Medline (Ovid) Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesmesh term with Medline code
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term with Medline code
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term with Medline code
Outcome	SSI	Infection mesh term with Medline code

	Term searched	Results
Group 1	Population	
1	hysterectomy. ti,ab,mp.	52599
2	hysterectomies. ti,ab,mp.	3423
3	hysterectomy, Vaginal. ti,ab,mp.	3235
4	hysterectomies, Vaginal. ti,ab,mp.	9
5	vaginal hysterectomies. ti,ab,mp.	437
6	vaginal hysterectomy. ti,ab,mp.	3593
7	Colpohysterectomy. ti,ab,mp.	84
8	Colpohysterectomies. ti,ab,mp.	8
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	53278
Group 2	Intervention	
10	hysterectomy. ti,ab,mp.	52599
11	hysterectomies. ti,ab,mp.	3423
12	hysterectomy, Vaginal. ti,ab,mp.	3235
13	hysterectomies, Vaginal. ti,ab,mp.	9
14	vaginal hysterectomies. ti,ab,mp.	437
15	vaginal hysterectomy. ti,ab,mp.	3593
16	Colpohysterectomy. ti,ab,mp.	84
17	Colpohysterectomies. ti,ab,mp.	8
18	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	53278
Group 3	Comparator	
19	Cross-sectional. ti,ab,mp.	632818
20	Longitudinal. ti,ab,mp.	377935
21	Prospective study. ti,ab,mp.	159216
22	Cohort study. ti,ab,mp.	274386
23	Observational study. ti,ab,mp.	199248
24	Randomized control study. ti,ab,mp.	937
25	Case-Control Studies. ti,ab,mp.	338463
26	19 or 21 or 22 or 23 or 24 or 25	1494518
Group 4	Outcome	
27	Infections. ti,ab,mp.	1470008
28	"Infection and Infestation". ti,ab,mp.	86
29	"Infestation and Infection". ti,ab,mp.	51
30	"Infections and Infestations". ti,ab,mp.	311

31	"Infestations and Infections". ti,ab,mp.	28
32	Infection. ti,ab,mp.	1418735
33	27 or 28 or 29 or 30 or 31 or 32	2279134
Combined	9 and 18 and 26 and 33	407
Limited to English only	9 and 18 and 26 and 33	384
The year 2000 to present	9 and 18 and 26 and 33	337

Results link:

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=5SYIqKO2Gpep7EBCDrAGLmKZrFtVAMXrv0wx7zAaFQsQRH5DCIC4ESMKrqhH2tOv1

Embase (Ovid) Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesmesh term with Embase code
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term with Embase code
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh term with Embase code
Outcome	SSI	Infection mesh term with Embase code

	Term searched	Results
Group 1	Population	
1	hysterectomy. ti,ab,mp.	93767
2	hysterectomies. ti,ab,mp.	6284
3	hysterectomy, Vaginal. ti,ab,mp.	392
4	trachelectomy. ti,ab,mp.	19
5	hysterectomies, Vaginal. ti,ab,mp.	758
6	vaginal hysterectomies. ti,ab,mp.	8954
7	vaginal hysterectomy. ti,ab,mp.	83
8	Colpohysterectomy. ti,ab,mp.	5
9	Colpohysterectomies. ti,ab,mp.	94170
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	93767
Group 2	Intervention	
11	hysterectomy. ti,ab,mp.	93767
12	hysterectomies. ti,ab,mp.	6284
13	hysterectomy, Vaginal. ti,ab,mp.	392
14	trachelectomy. ti,ab,mp.	19
15	hysterectomies, Vaginal. ti,ab,mp.	758
16	vaginal hysterectomies. ti,ab,mp.	8954
17	vaginal hysterectomy. ti,ab,mp.	83
18	Colpohysterectomy. ti,ab,mp.	5
19	Colpohysterectomies. ti,ab,mp.	94170
20	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	93767
Group 3	Comparator	
21	Cross-sectional. ti,ab,mp.	765496
22	Longitudinal. ti,ab,mp.	475332
23	Prospective study. ti,ab,mp.	899849
24	Cohort study. ti,ab,mp.	405571
25	Observational study. ti,ab,mp.	342074
26	Randomized control study. ti,ab,mp.	1628
27	Case-Control Studies. ti,ab,mp.	27610
28	21 or 22 or 23 or 24 or 25 or 26 or 27	2146419
Group 4	Outcome	
29	Infections. ti,ab,mp.	835857
30	"Infection and Infestation". ti,ab,mp.	107

31	"Infestation and Infection". ti,ab,mp.	55
32	"Infections and Infestations". ti,ab,mp.	807
33	"Infestations and Infections". ti,ab,mp.	49
34	Infection. ti,ab,mp.	2763568
35	29 or 30 or 31 or 32 or 33 or 34	2991465
Combined	10 and 20 and 28 and 35	1510
Limited to English only	10 and 20 and 28 and 35	1468
The year 2000 to present	10 and 20 and 28 and 35	1419

Results link:

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=79TCxxCp1oN0adXj9ZUf4UzOGz44m8xhcwT9pEsrMoJkpSIjfY4IktYO5RKZbvU7

Web of Science Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesmesh term with the web of science code: #1
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgeriesmesh term with the web of science code: #1
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study mesh terms with the web of science code: #2, #3, #4, #5, #6, #7, #8
Outcome	SSI	Infection mesh term with the web of science code: #10

step	code	results
#1	TS= (hysterectomy* OR hysterectomies* OR hysterectomy, vaginal* OR hysterectomies, vaginal OR vaginal hysterectomies* OR vaginal hysterectomy* OR colpohysterectomy* OR colpohysterectomies*)	40974
#2	TS= (Clinical Trials, Randomized* OR Trials, Randomized Clinical* OR Controlled Clinical Trials, Randomized*)	357993
#3	TS= (Longitudinal Study* OR Studies, Longitudinal* OR Study, Longitudinal* OR Tuskegee Syphilis Study* OR Syphilis Studies, Tuskegee* OR Syphilis Study, Tuskegee* OR Tuskegee Syphilis Studies* OR Jackson Heart Study* OR Heart Studies, Jackson* OR Heart Study, Jackson* OR Jackson Heart Studies* OR Studies, Jackson Heart* OR California Teachers Study* OR California Teachers Studies* OR Studies, California Teachers* OR Study, California Teachers* OR Teachers Studies, California* OR Teachers Study, California* OR Bogalusa Heart Study* OR Bogalusa Heart Studies* OR Heart Studies, Bogalusa* OR Heart Study, Bogalusa* OR Studies, Bogalusa Heart* OR Study, Bogalusa Heart* OR Framingham Heart Study* OR Framingham Heart Studies* OR Heart Studies, Framingham* OR Heart Study, Framingham* OR Longitudinal Survey* OR Longitudinal Surveys* OR Survey, Longitudinal* OR Surveys, Longitudinal*)	389252
#4	TS= (Case-Control Study* OR Studies, Case-Control* OR Study, Case-Control* OR Case-Comparison Studies* OR Case Comparison Studies* OR Case-Comparison Study* OR Studies, Case-Comparison* OR Study, Case-Comparison* OR Case-Compeer Studies* OR Studies, Case-Compeer* OR Case-Referrent Studies* OR Case Referrent Studies* OR Case-Referrent Study* OR Studies, Case-Referrent* OR Study, Case-Referrent* OR Case-Referent Studies* OR Case Referent Studies* OR Case-Referent Study* OR Studies, Case-Referent* OR Study, Case-Referent* OR Case-Base Studies* OR Case Base Studies* OR Studies, Case-Base* OR Case Control Studies* OR Case Control Study* OR Studies, Case Control* OR Study, Case Control* OR Nested Case-Control Studies* OR Case-Control Studies, Nested* OR Case-Control Study, Nested* OR Nested Case Control Studies* OR Nested Case-Control Study* OR Studies, Nested Case-Control* OR Study, Nested Case-Control* OR Matched Case-Control Studies* OR Case-Control Studies, Matched* OR Case-Control Study, Matched* OR Matched Case Control Studies* OR Matched Case-Control Study* OR Studies, Matched Case-Control* OR Study, Matched Case-Control*)	742023
#5	TS= (Cross Sectional Studies* OR Cross-Sectional Study * OR Studies, Cross-Sectional * OR Study, Cross-Sectional * OR Surveys, Disease Frequency * OR Disease Frequency Survey * OR Survey, Disease Frequency * OR Analysis, Cross-Sectional * OR Analyses, Cross-Sectional * OR Analysis, Cross Sectional * OR Cross-Sectional Analyses * OR Cross-Sectional Analysis * OR Cross Sectional Analysis	1164085

	* OR Analyses, Cross Sectional * OR Cross Sectional Analyses * OR Cross-Sectional Survey * OR Cross Sectional Survey * OR Cross-Sectional Surveys * OR Survey, Cross-Sectional * OR Surveys, Cross-Sectional * OR Disease Frequency Surveys * OR Prevalence Studies * OR Prevalence Study * OR Studies, Prevalence * OR Study, Prevalence*)	
#6	TS= (Prospective Study* OR Studies, Prospective* OR Study, Prospective*)	721432
#7	TS= (Cohort Study* OR Studies, Cohort * OR Study, Cohort * OR Concurrent Studies * OR Studies, Concurrent * OR Concurrent Study * OR Study, Concurrent * OR Closed Cohort Studies * OR Cohort Studies, Closed * OR Closed Cohort Study * OR Cohort Study, Closed * OR Study, Closed Cohort * OR Studies, Closed Cohort * OR Birth Cohort Studies * OR Birth Cohort Study * OR Cohort Studies, Birth * OR Cohort Study, Birth * OR Studies, Birth Cohort * OR Study, Birth Cohort * OR Analysis, Cohort * OR Analyses, Cohort * OR Cohort Analyses * OR Cohort Analysis * OR Historical Cohort Studies * OR Cohort Studies, Historical * OR Cohort Study, Historical * OR Historical Cohort Study * OR Study, Historical Cohort * OR Studies, Historical Cohort * OR Incidence Studies * OR Incidence Study * OR Studies, Incidence * OR Study, Incidence*)	1333108
#8	TS= (Observational study *)	234254
#9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	3887063
#10	TS= (Infections* OR Infection and Infestation * OR Infestation and Infection * OR Infections and Infestations * OR Infestations and Infections * OR Infection *)	1895911
#11	#1 AND #9 AND #10	853
#12	The year 2000 – current; English	726

The results are hyperlinked in each column

Cochrane Library Search Strategy

Framework Item	Target	Search term
Population	female participants who had post-hysterectomy surgeriesSSI(no restriction to age)	hysterectomy surgeriesCochrane search manager hysterectomy surgerieswith Cochrane code based on mesh term: #1
Intervention	hysterectomy surgeries(No restriction on the surgery type, e.g. laparoscopy)	hysterectomy surgerieswith Cochrane code based on mesh term
Comparator	the number of participants who had or had not post-hysterectomy SSI	RCT, case-control, cross-sectional, longitudinal, observational, cohort and prospective study with Cochrane code based on mesh term:
Outcome	SSI	hysterectomy surgerieswith Cochrane code based on mesh term

step	code	results
#1	(hysterectomy):ti,ab,kw OR (hysterectomies):ti,ab,kw OR (hysterectomy,Vaginal):ti,ab,kw OR (hysterectomies,Vaginal):ti,ab,kw OR (vaginal hysterectomies):ti,ab,kw OR (vaginal hysterectomy):ti,ab,kw OR (Colpohysterectomy):ti,ab,kw OR (Colpohysterectomies):ti,ab,kw	8202
#2	(Clinical Trials, Randomized):ti,ab,kw OR (Trials, Randomized Clinical):ti,ab,kw OR (Controlled Clinical Trials, Randomized):ti,ab,kw	154945
#3	(Longitudinal Study):ti,ab,kw OR (Studies, Longitudinal):ti,ab,kw OR (Study, Longitudinal):ti,ab,kw OR (Tuskegee Syphilis Study):ti,ab,kw OR (Syphilis Studies, Tuskegee):ti,ab,kw OR (Syphilis Study, Tuskegee):ti,ab,kw OR (Tuskegee Syphilis Studies):ti,ab,kw OR (Jackson Heart Study):ti,ab,kw OR (Heart Studies, Jackson):ti,ab,kw OR (Heart Study, Jackson):ti,ab,kw OR (Jackson Heart Studies):ti,ab,kw OR (Studies, Jackson Heart):ti,ab,kw OR (California Teachers Study):ti,ab,kw OR (California Teachers Studies):ti,ab,kw OR (Studies, California Teachers):ti,ab,kw OR (Study, California Teachers):ti,ab,kw OR (Teachers Studies, California):ti,ab,kw OR (Teachers Study, California):ti,ab,kw OR (Bogalusa Heart Study):ti,ab,kw OR (Bogalusa Heart Studies):ti,ab,kw OR (Heart Studies, Bogalusa):ti,ab,kw OR (Heart Study, Bogalusa):ti,ab,kw OR (Studies, Bogalusa Heart):ti,ab,kw OR (Study, Bogalusa Heart):ti,ab,kw OR (Framingham Heart Study):ti,ab,kw OR (Framingham Heart Studies):ti,ab,kw OR (Heart Studies, Framingham):ti,ab,kw OR (Heart Study, Framingham):ti,ab,kw OR (Longitudinal Survey):ti,ab,kw OR (Longitudinal Surveys):ti,ab,kw OR (Survey, Longitudinal):ti,ab,kw OR (Surveys, Longitudinal):ti,ab,kw	23544
#4	(Case-Control Study):ti,ab,kw OR (Studies, Case-Control):ti,ab,kw OR (Study, Case-Control):ti,ab,kw OR (Case-Comparison Studies):ti,ab,kw OR (Case Comparison Studies):ti,ab,kw OR (Case-Comparison Study):ti,ab,kw OR (Studies, Case-Comparison):ti,ab,kw OR (Study, Case-Comparison):ti,ab,kw OR (Case-Compeer Studies):ti,ab,kw OR (Studies, Case-Compeer):ti,ab,kw OR (Case-Referrent Studies):ti,ab,kw OR (Case Referrent Studies):ti,ab,kw OR (Case-Referrent Study):ti,ab,kw OR (Studies, Case-Referrent):ti,ab,kw OR (Study, Case-Referrent):ti,ab,kw OR (Case-Referent Studies):ti,ab,kw OR (Case Referent Studies):ti,ab,kw OR (Case-Referent Study):ti,ab,kw OR (Studies, Case-Referent):ti,ab,kw OR (Study, Case-Referent):ti,ab,kw OR (Case-Base Studies):ti,ab,kw OR (Case Base Studies):ti,ab,kw OR (Studies, Case-Base):ti,ab,kw OR (Case Control Studies):ti,ab,kw OR (Case Control Study):ti,ab,kw OR (Studies, Case Control):ti,ab,kw OR (Study, Case Control):ti,ab,kw OR (Nested Case-Control Studies):ti,ab,kw OR (Case-Control Studies, Nested):ti,ab,kw OR (Case-Control Study, Nested):ti,ab,kw OR (Nested Case Control Studies):ti,ab,kw OR (Nested Case-Control Study):ti,ab,kw OR (Studies, Nested Case-Control):ti,ab,kw OR (Study, Nested Case-Control):ti,ab,kw OR (Matched Case-Control Studies):ti,ab,kw OR (Case-Control	33557

	Studies, Matched):ti,ab,kw OR (Case-Control Study, Matched):ti,ab,kw OR (Matched Case Control Studies):ti,ab,kw OR (Matched Case-Control Study):ti,ab,kw OR (Studies, Matched Case-Control):ti,ab,kw OR (Study, Matched Case-Control):ti,ab,kw	
#5	(Cross Sectional Studies):ti,ab,kw OR (Cross-Sectional Study):ti,ab,kw OR (Studies, Cross-Sectional):ti,ab,kw OR (Study, Cross-Sectional):ti,ab,kw OR (Surveys, Disease Frequency):ti,ab,kw OR (Disease Frequency Survey):ti,ab,kw OR (Survey, Disease Frequency):ti,ab,kw OR (Analysis, Cross-Sectional):ti,ab,kw OR (Analyses, Cross-Sectional):ti,ab,kw OR (Analysis, Cross Sectional):ti,ab,kw OR (Cross-Sectional Analyses):ti,ab,kw OR (Cross-Sectional Analysis):ti,ab,kw OR (Cross Sectional Analysis):ti,ab,kw OR (Analyses, Cross Sectional):ti,ab,kw OR (Cross Sectional Analyses):ti,ab,kw OR (Cross-Sectional Survey):ti,ab,kw OR (Cross Sectional Survey):ti,ab,kw OR (Cross-Sectional Surveys):ti,ab,kw OR (Survey, Cross-Sectional):ti,ab,kw OR (Surveys, Cross-Sectional):ti,ab,kw OR (Disease Frequency Surveys):ti,ab,kw OR (Prevalence Studies):ti,ab,kw OR (Prevalence Study):ti,ab,kw OR (Studies, Prevalence):ti,ab,kw OR (Study, Prevalence):ti,ab,kw	54133
#6	(Prospective Study):ti,ab,kw OR (Studies, Prospective):ti,ab,kw OR (Study, Prospective):ti,ab,kw	233446
#7	(Cohort Study):ti,ab,kw OR (Studies, Cohort):ti,ab,kw OR (Study, Cohort):ti,ab,kw OR (Concurrent Studies):ti,ab,kw OR (Studies, Concurrent):ti,ab,kw OR (Concurrent Study):ti,ab,kw OR (Study, Concurrent):ti,ab,kw OR (Closed Cohort Studies):ti,ab,kw OR (Cohort Studies, Closed):ti,ab,kw OR (Closed Cohort Study):ti,ab,kw OR (Cohort Study, Closed):ti,ab,kw OR (Study, Closed Cohort):ti,ab,kw OR (Studies, Closed Cohort):ti,ab,kw OR (Birth Cohort Studies):ti,ab,kw OR (Birth Cohort Study):ti,ab,kw OR (Cohort Studies, Birth):ti,ab,kw OR (Cohort Study, Birth):ti,ab,kw OR (Studies, Birth Cohort):ti,ab,kw OR (Study, Birth Cohort):ti,ab,kw OR (Analysis, Cohort):ti,ab,kw OR (Analyses, Cohort):ti,ab,kw OR (Cohort Analyses):ti,ab,kw OR (Cohort Analysis):ti,ab,kw OR (Historical Cohort Studies):ti,ab,kw OR (Cohort Studies, Historical):ti,ab,kw OR (Cohort Study, Historical):ti,ab,kw OR (Historical Cohort Study):ti,ab,kw OR (Study, Historical Cohort):ti,ab,kw OR (Studies, Historical Cohort):ti,ab,kw OR (Incidence Studies):ti,ab,kw OR (Incidence Study):ti,ab,kw OR (Studies, Incidence):ti,ab,kw OR (Study, Incidence):ti,ab,kw	184886
#8	(Observational Study):ti,ab,kw	20328
#9	(Infection and Infestation):ti,ab,kw OR (Infection and Infestation):ti,ab,kw OR (Infections and Infestations):ti,ab,kw OR (Infestations and Infections):ti,ab,kw OR (Infection):ti,ab,kw	102985
#10	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	552677
#11	#1 AND #9 AND #10	382
#12	Trials	377
#13	The year 2000 – current; English	243

Risk of Bias Assessment

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (CASE CONTROL STUDIES)

Selection

1) Is the case definition adequate?

a) yes, with independent validation □

b) yes, e.g. record linkage or based on self-reports

c) no description

2) Representativeness of the cases

a) consecutive or obviously representative series of cases □

b) potential for selection biases or not stated

3) Selection of Controls

a) community controls □

b) hospital controls

c) no description

4) Definition of Controls

a) no history of disease (endpoint) □

b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis

a) study controls for _____ (Select the most important factor.) □

b) study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure

a) secure record (e.g. surgical records) □

b) structured interview where blind to case/control status □

c) interview not blinded to case/control status

d) written self-report or medical record only

e) no description

2) Same method of ascertainment for cases and controls

a) yes □

b) no

3) Non-response rate

a) same rate for both groups □

b) non-respondents described

c) rate different and no designation

Table 1 Risk of Bias Assessment with NOS Case-control Study Scale

Author & Year	Selection				Comparability	Exposure			Total score
Olsen 2009	1	1	1	0	2	1	1	0	6
Lake 2013	1	1	1	1	2	1	1	1	9
Savage 2013	1	1	1	0	2	1	1	0	7
Pop-Vicas 2014	0	1	1	0	2	0	1	1	6
Morgan 2016	1	1	1	0	2	0	1	1	7
Wang 2022	1	1	1	0	2	1	1	0	7

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (COHORT STUDIES)

Selection

1) Representativeness of the exposed cohort

a) truly representative of the average _____ (describe) in the community □

b) somewhat representative of the average _____ in the community □

c) selected group of users e.g. nurses, volunteers

d) no description of the derivation of the cohort

2) Selection of the non-exposed cohort

a) drawn from the same community as the exposed cohort □

b) drawn from a different source

c) no description of the derivation of the non-exposed cohort

3) Ascertainment of exposure

a) secure record (e.g. surgical records) □

b) structured interview □

c) written self-report

d) no description

4) Demonstration that outcome of interest was not present at start of study

a) yes □

b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for _____ (select the most important factor) □

b) study controls for any additional factor □ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome

a) independent blind assessment □

b) record linkage □

c) self-report

d) no description

2) Was follow-up long enough for outcomes to occur

a) yes (select an adequate follow-up period for outcome of interest) □

b) no

3) Adequacy of follow-up of cohorts

a) complete follow-up - all subjects accounted for □

b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) □

c) follow up rate < ____% (select an adequate %) and no description of those lost

d) no statement

Table 2 Risk of Bias Assessment with NOS Cohort Study Scale

Author & Year	Selection				Comparability	Exposure			Total score
Molina-Cabrillana 2008	0	1	1	0	2	1	1	0	6
Coleman 2014	1	1	1	0	2	1	0	1	7
Mahdi 2014	1	1	1	0	2	1	1	0	7
Uppal 2015	1	1	1	0	2	1	1	1	8
Tuomi 2016	1	1	1	0	2	1	1	1	8
Till 2017	1	1	1	0	2	0	1	1	7
Brown 2019	1	1	1	1	2	1	1	1	9
Tsuzuki 2021	1	1	1	0	2	1	1	0	7

Table 3 Study Summary

Author & Year	Selection				Comparability	Exposure			Total score
Molina-Cabrillana 2008#	0	1	1	0	2	1	1	0	6
Olsen 2009*	1	1	1	0	2	1	1	0	6
Lake 2013*	1	1	1	1	2	1	1	1	9
Savage 2013*	1	1	1	0	2	1	1	0	7
Coleman 2014#	1	1	1	0	2	1	0	1	7
Mahdi 2014#	1	1	1	0	2	1	1	0	7
Pop-Vicas 2014*	0	1	1	0	2	0	1	1	6
Uppal 2015#	1	1	1	0	2	1	1	1	8
Morgan 2016*	1	1	1	0	2	0	1	1	7
Tuomi 2016#	1	1	1	0	2	1	1	1	8
Till 2017#	1	1	1	0	2	0	1	1	7
Brown 2019#	1	1	1	1	2	1	1	1	9
Tsuzuki 2021#	1	1	1	0	2	1	1	0	7
Wang 2022*	1	1	1	0	2	1	1	0	7

Note. *means this study was assessed through the items for case-control studies. # means this study was assessed through the items for cohort studies.

Table 3 Study Summary

Author & Year	Sample Origin	N	SSI +	Age (±SD)	Surgery Method	Age RF	Anti-microbial	Blood Loss	Blood Transfusion	BMI	Diabetes	Obesity	Surgery Duration	Tobacco Use	Tumour	Wound Cleanness
Molina-Cabrillana 2008	2000-2004 Hospital Universitario Materno-Infantil de Canarias, Sapin	1540	72	54.00 (±12.90)	abdominal & vaginal	Age >60	Y/N	NR	NR	NR	Y/N	Y/N	≥P75	NR	Y/N	Clean-contaminated vs Contaminated /dirty
Olsen 2009	2003-2005 CDC Prevention Epicenter Program hospitals, USA	820	66	51.70 (±17.78)	abdominal & vaginal	Mean	NR	NR	NR	Mean	Y/N	NR	Mean	Y/N	Y/N	NR
Lake 2013	2005-2009 ACS-NSQIP, USA	13822	375	NR	abdominal & vaginal & laparoscopic	Age >80	NR	NR	Y/N	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	≥P75	Y/N	Y/N	Clean vs Clean-contaminated Contaminated vs Dirty
Savage 2013	2007-2010 University of Iowa Hospitals and Clinics, USA	1104	126	54.53 (±13.66)	abdominal	Mean	Mean	NR	Median	BMI≥30 (Obesity)	Y/N	Y/N	Mean	NR	Y/N	NR
Coleman 2014	1999-2012 Johns Hopkins Medical Institution, USA	77	17	42.56 (±5.93)	abdominal & vaginal & laparoscopic	Mean	NR	>250ml; ≥451ml	Y/N	Median	Y/N	BMI≥30 (Obesity)	NR	Y/N	NR	NR
Mahdi 2014	2005-2011 ACS-NSQIP, USA	28366	296	NR	laparoscopic	Age >60, 70 & 80	NR	NR	>4 units of packed red blood cells	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	>60 min, 180 min	Y/N	NR	NR
Pop-Vicas 2014	2012-2015 University of Wisconsin Hospitals, USA	1531	52	58.27 (±12.31)	abdominal & vaginal & laparoscopic	Mean	Y/N	Median*	NR	NR	NR	NR	Mean	Y/N	Y/N	NR

Uppal 2015	2012-2015 MSQC, USA	21358	441	48.10 (±11.70)	abdominal & vaginal & laparoscopic	Median	Y/N	Median	NR	BMI≥30 (Obesity)	NR	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Morgan 2016	2012-2014 MSQC, USA	16548	315	NR	abdominal	Age >50	NR	Mean	Y/N	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Tuomi 2016	2007-2013 Helsinki University Hospital, Finland	1164	94	67.46 (±10.23)	abdominal & vaginal & laparoscopic	Mean	NR	Median	NR	Mean	Y/N	NR	Mean	Y/N	NR	NR
Till 2017	2012-2015 MSQC, USA	18255	329	NR	abdominal & vaginal & laparoscopic	Age >65	NR	≥250ml	NR	BMI≥30 (Obesity)	Y/N	BMI≥30 (Obesity)	Mean	Y/N	Y/N	NR
Brown 2019	2012-2014 ACS-NSQIP, USA	46755	445	45.95 (±1.51)	laparoscopic	Mean	NR	NR	Y/N	Mean	Y/N	NR	Mean	Y/N	NR	Clean vs Clean-contaminated vs Contaminated vs Dirty
Tsuzuki 2021	2014-2018 Teine Keijinkai Hospital, Japan	1559	71	48.28 (±11.39)	laparoscopic	Mean	NA	NR	Y/N	Mean	Y/N	NR	Mean	Y/N	NR	NR
Wang 2022	2012-2022 Two Grade A Tertiary Hospitals, China	94	188	47.70 (±10.87)	abdominal	Age >50	Y/N	≥500ml	NR	Mean	Y/N	NR	>180 min	NR	Y/N	Clinicians determined Class II vs Class III
Overall		152993	2887	47.53 (±8.29)												

Note. The content under each risk factor was how these studies presented their data. The detailed case numbers are in Table 3; SSI+ refers to SSI-positive cases; ACS-NSQIP refers to the American College of Surgeons National Surgical Quality Improvement Program; MSQC refers to the Michigan Surgical Quality Collaborative; NR refers to not reported; NA refers to not applicable; Y/N refers to reported in Yes or No; Median*: the median reported in this study did not include IQR to estimate its variance; P75 refers to the 75th percentil

Table 2 Subgroup Analyses Between Different SSI Types

	Superficial & Deep & Organ Space						Deep & Organ Space						Group Difference	
Risk Factors	**LogOR**	**I^2**	**OR**	**SE**	**z**	**p**	**LogOR**	**I^2**	**OR**	**SE**	**z**	**p**	**Q (df)**	**p**
Tobacco Use	0.36	0.00%	1.43	0.07	5.78	<.001	1	68.56%	2.72	.11	5.69	.001	11.59 (1)	<.001
Diabetes	0.53	64.07%	1.70	0.15	2.5	<.001	0.27	61.95%	1.31	.22	1.06	.290	.71 (1)	.400

Note. Only Tobacco Use and Diabetes retrieved more than 4 datasets reporting Deep or Organ Space SSI types. The individual SSI types, such as Superficial, Deep, or Organ Space, were reported in less than 4 sets. This is to demonstrate that ORs of risk factors might differ between SSI types.