

Systematic Review

# Risk Factors for Surgical Site Infection in Patients Undergoing Breast Surgery: A Systematic Review and Meta-Analysis

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## Abstract

**Background:** Surgical site infection (SSI) following breast surgery remain a significant clinical challenge, with reported incidence rates ranging from 1% to 35%. Despite advancements in surgical techniques, SSIs contribute to prolonged hospitalization, increased mortality, and substantial healthcare costs. This research applied a quantitative systematic review and meta-analysis to identify and summarize risk factors for SSIs following breast surgery. **Methods:** Relevant literature from PubMed, Medline, Embase, Web of Science, and the Cochrane Central Register of Controlled Trials published between January 1, 2004, and December 25, 2023, was searched and screened using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) procedure. The effect sizes for each identified risk factor were calculated using STATA v18 and RevMan 5.3. Heterogeneity was tested using the Q-test, and sensitivity analysis was performed using the leave-one-out method, in which one dataset was removed at a time to evaluate changes in the pooled effect sizes. A funnel plot was employed to evaluate potential publication bias. **Results:** 12 studies were identified, including 2412 SSI-positive and 166,794 SSI-negative cases undergoing breast surgery. 22 potential risk factors were identified, and those reported in  $\geq 3$  studies were analyzed. Mastectomy emerged as the strongest risk factor (odds ratio [OR] = 2.61,  $p < 0.001$ ), followed by diabetes (OR = 2.49,  $p < 0.001$ ), body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> (OR = 2.08,  $p < 0.001$ ), American Society of Anesthesiologists (ASA) score  $\geq 3$  (OR = 1.99,  $p < 0.001$ ), and smoking (OR = 1.38,  $p < 0.001$ ). **Conclusions:** Patients who underwent mastectomy demonstrated 2.61 times higher odds of developing SSI post-breast surgery (OR = 2.61). Similarly, diabetes was associated with more than twice the odds of developing SSIs (OR = 2.49), BMI  $\geq 25$  kg/m<sup>2</sup> with twofold increase in odds (OR = 2.08), ASA score  $\geq 3$  with 99% higher odds (OR = 1.99), and smoking with a 38% increased odds (OR = 1.38). This study highlights the importance of closely monitoring surgical incisions in patients with a history of smoking, high ASA scores, or those who have undergone mastectomy. BMI and diabetes may affect each other; therefore, future studies should provide detailed reporting on the number of patients with these correlated factors. **Registration:** The study has been registered on <https://www.crd.york.ac.uk/prospero/> (registration number: CRD42023492359).

**Keywords:** breast surgery; SSI; risk factors; meta-analysis

## 1. Introduction

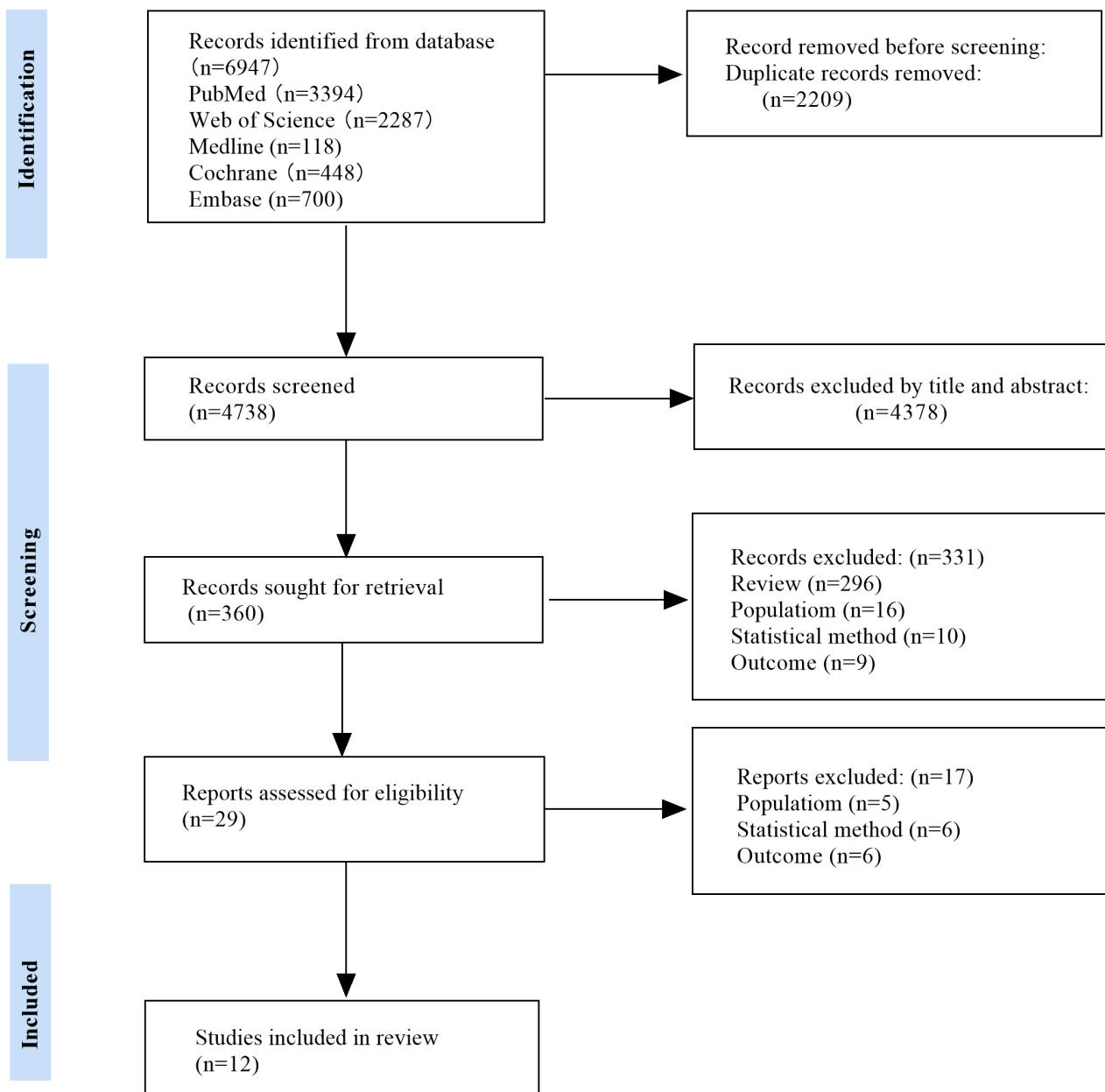
Breast surgery is a broad concept that encompasses various surgical procedures. Common breast surgeries include mastectomy, breast reconstruction, breast reduction, and breast augmentation, among others. The frequency of mammoplasty surgeries has increased significantly in recent years, driven by medical advancements and a growing desire for aesthetic enhancement, particularly in the United States [1]. Breast surgery is generally considered a safe procedure [2]; however, the incidence of surgical site infections (SSIs) remains high, ranging between 1% to 35% [3]. SSI is one of the most common complications of breast surgery. It has been shown that SSIs prolong hospital stays, lead to reoperations and readmissions, and can even increase mortality. SSIs also result in a substantial financial

burden, with additional costs arising from medical staff, investigations, and treatment [4].

The risk factors for SSIs following breast surgery have been reported in various studies; however, the results differ across these studies. There are various risk factors for SSI following breast surgery, including age [5], tobacco use [6], diabetes [7], obesity [8], flap necrosis [9], medical staff [10], malignancy [5], mastectomy [11], prior radiotherapy or chemotherapy [12,13], inappropriate use of antibiotics [14], prolonged postoperative drainage [15], and immediate reconstructive surgery [16].

The existing literature primarily relies on observational studies with small sample sizes, characterized by wide methodological variations and varying conclusions. In addition, many risk factors lack reliable quantitative syn-





**Fig. 1. PRISMA flowchart.** Note: Population: studies that included male patients or patients undergoing non-breast surgery were excluded. Outcomes: the primary outcome of the study was surgery site infections (SSIs). Studies that did not provide effect estimates (RR/OR) with 95% CIs were excluded. Statistical methods: studies that did not perform multivariate analysis after identifying significant indicators in univariate analysis ( $p < 0.05$ ) were excluded. SSI, surgical site infection; RR, relative risk; OR, odds ratio; CI, confidence interval; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

theses. This meta-analysis provides updated and more comprehensive data to support the prediction and prevention of SSIs after breast surgery by pooling high-quality evidence, utilizing standardized definitions, and quantifying pooled effect sizes of risk factors in 169,206 patients. The aim is to provide clinicians actionable insights for risk stratification and prevention.

## 2. Methods

### 2.1 Search Strategy

The data was extracted from published empirical studies retrieved the databases, including PubMed (Central), Medline (Ovid), Embase (Ovid), Web of Science, and the Cochrane Library. The search terms followed the standard PICO (population, intervention, comparison, outcome) guideline and were adapted according to Medical Subject Headings (MeSH) terms [17]. A detailed search

**Table 1. Study summary.**

Author, year	Vilar-Compte <i>et al.</i> , 2004 [18]	Olsen <i>et al.</i> , 2008 [19]	Nguyen <i>et al.</i> , 2012 [20]	Davis <i>et al.</i> , 2013 [21]	Chung <i>et al.</i> , 2015 [22]	Olsen <i>et al.</i> , 2016 [23]	Parikh <i>et al.</i> , 2016 [24]	Struik <i>et al.</i> , 2018 [29]	Kraenzlin <i>et al.</i> , 2022 [25]	Rothe <i>et al.</i> , 2022 [26]	Zhang <i>et al.</i> , 2022 [27]	Chin <i>et al.</i> , 2023 [28]
Sample origin	2000 INCan, USA	1998–2002 Barnes-Jewish Hospital, USA	2005–2009 ACS-NSQIP, USA	2005–2009 ACS-NSQIP, USA	2005–2012 ACS-NSQIP, USA	2004–2011 Commercial claims data, USA	2010–2014 NHSN, USA	2013–2016 Franciscus Gasthuis, NL	2016–2018 Medical center, USA	2011–2018 University hospital, Germany	2012–2021 CAMS, China	2016–2020 Sahlgrenska University Hospital, Sweden
N	230	325	9315	38,739	2899	7115	110,987	230	490	240	4793	958
SSI	76	57	330	891	143	595	630	23	66	62	34	100
BMI (kg/m <sup>2</sup> )	≥27	NR	≥25	≥25	NR	≥25	NR	NR	NR	≥25	NR	≥30
Previous RT/CH	Y/N	Y/N	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mastectomy	Y/N	Y/N	NR	NR	NR	NR	NR	NR	Y/N	NR	>1500 g	Y/N
Length of drain stay (days)	>19	NR	NR	NR	NR	NR	NR	>3	Mean	NR	NR	NR
2nd drain insertion	Y/N	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Implant	NR	Y/N	NR	NR	NR	Y/N	NR	NR	NR	NR	NR	NR
Antibiotic	NR	dosing	NR	NR	NR	NR	NR	NR	NR	NR	Y/N	NR
Transfusion	NR	Y/N	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Smoking	NR	Y/N	NR	Y/N	Y/N	Y/N	NR	NR	NR	NR	NR	NR
Anesthetic	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Alcohol consumption	NR	NR	Y/N	NR	NR	NR	NR	NR	NR	NR	NR	NR
ASA	NR	NR	≥3	≥3	NR	NR	≥3	NR	NR	NR	NR	NR
Flap failure	NR	NR	Y/N	NR	NR	NR	NR	NR	NR	NR	NR	NR
Operative time	NR	NR	≥6 h	≥2 h	NR	NR	≥53 min	NR	NR	NR	NR	NR
Diabetes	NR	NR	NR	Y/N	NR	Y/N	NR	NR	NR	NR	NR	Y/N
Hypertension	NR	NR	NR	NR	Y/N	Y/N	NR	NR	NR	NR	NR	NR
Age	NR	NR	NR	NR	NR	NR	Y/N	NR	Mean	NR	Mean	NR
ASC	NR	NR	NR	NR	NR	NR	Y/N	NR	NR	NR	NR	NR
Dressing change	NR	NR	NR	NR	NR	NR	NR	≤48 h	NR	NR	NR	NR
Seroma	NR	NR	NR	NR	NR	NR	NR	NR	Y/N	NR	NR	Y/N
Axillary incision	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	Y/N	NR

Note: The content under each risk factor reflects how the data were presented in the original studies. The detailed case numbers are provided in Table 3. “Sample Origin” refers to the geographic or institutional source of the study population. “N” refers to the total sample size. “SSI” refers to the number of patients with surgical site infections. BMI, body mass index; RT/CH, radiotherapy/chemotherapy; ASA, American Society of Anesthesiologists; ASC, ambulatory surgery center; NR, not reported; NA, not applicable; Y/N, reported in Yes/No; NSQIP, National Surgical Quality Improvement Program; NHSN, National Healthcare Safety Network; CAMS, Collaborative Assessment and Management of Suicidality; INCan, Instituto Nacional de Cancerología.

methodology is provided in **Supplementary File 1**. The search was conducted upon the completion of study registration and was finalized on December 25, 2023.

## 2.2 Eligibility Criteria

The inclusion criteria were as follows: (1) Population: female participants who developed SSI after various breast surgeries; (2) Intervention: breast surgeries; (3) Comparators: participants who did or did not develop SSI after various breast surgeries; (4) Outcomes: occurrence of SSI. The exclusion criteria were as follows: (1) Non-English studies; (2) Studies that did not provide the odds ratios (ORs) or relative risks (RRs) with 95% confidence intervals (CIs); (3) Studies that did not meet the National Healthcare Safety Network's definition of Breast Surgery SSI Criteria.

## 2.3 Study Screening and Data Extraction

The studies were retrieved in RIS format (.ris) and managed with EndNote X9.3.3 (Clarivate Analytics, Philadelphia, PA, USA). The screening process followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. 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 studies that met the criteria, full-text papers were obtained. Any discrepancies between the reviewers were resolved through discussion and consensus. Data extraction was done independently by two reviewers. The extraction included patient demographic characteristics, type of surgery, SSI diagnostic criteria, risk factors, OR or RR, and 95% CIs.

## 2.4 Risk of Bias Assessment

Two reviewers independently scored the studies using the Cochrane Risk of Bias Tool (ROB-2) and Newcastle-Ottawa Scale (NOS) for quality assessment. NOS was used for observational studies, and the ROB-2 was used for randomized controlled trials (RCTs). Any disagreements between reviewers were resolved through discussion, and if necessary, third-party adjudication was employed.

## 2.5 Data Synthesis

The effect size of each identified risk factor was calculated using STATA v18 (Stata Corporation, College Station, TX, USA) and RevMan 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark). Only risk factors reported in at least 3 datasets were synthesized for the meta-analysis. A significance level of  $\alpha = 0.05$  (two-tailed) was used for all hypothesis tests. Pooled ORs with 95% CIs were calculated. The 95% CIs reflect the precision of the estimated effect. Results were considered statistically significant when  $p < 0.05$ . Heterogeneity was tested by the Q-test and  $I^2$  statistics (moderate heterogeneity:  $I^2 > 50\%$ ; high heterogeneity:  $I^2 > 75\%$ ). Mantel-Haenszel random-effects models were applied when substantial heterogeneity was

detected ( $I^2 > 50\%$  or Q-test  $p < 0.10$ ); otherwise, fixed-effects models were used. Sensitivity analysis was 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.

## 3. Results

### 3.1 Study Selection and Evaluation

A search of keywords in PubMed, Medline (Ovid), Embase (Ovid), Web of Science, and the Cochrane Library yielded 6947 records. After screening based on the PRISMA guidelines, 12 studies met the inclusion criteria. The PRISMA flowchart is shown in Fig. 1.

A total of 12 articles were included, including 5 case-control study [18–22], 6 retrospective cohort studies [23–28], and 1 RCT [29]. A total of 169,206 female patients who underwent breast surgery were included in the current analysis across 12 studies. Among them, 2412 had SSI-incisions of various types, and 166,794 with no SSI-incisions were included as controls. The details of all studies are described in Table 1 (Ref. [18–29]).

Among these studies, only 1 reported each incision type separately [28]. The remaining 11 studies reported infection cases as a combination of three incision types (superficial, deep, or organ space). The studies reporting cases with independent incision types were combined into the mixed incision category to align with those reporting mixed incision types for synthesis. As shown in Table 2 (Ref. [18–28]), the NOS risk of bias assessment rated 2 studies with a score of 6 [20,23], 7 studies with a score of 7 [18,19,21,22,24,25,28], and the remaining 2 with a score of 8 [26,27]. The only RCT article was assessed using ROB-2 and was considered to have a low-risk of bias [29]. The process is detailed in **Supplementary File 1**. All 12 studies were included in the following review.

Among the 12 studies, a total of 22 risk factors were identified, including body mass index (BMI), previous radiotherapy/chemotherapy (RT/CH), mastectomy, length of drain stay, second drain insertion, implant, antibiotic use, transfusion, smoking, anesthetic type, alcohol consumption, American Society of Anesthesiologists (ASA) classification, flap failure, operative time, diabetes, hypertension, age, ambulatory surgery center (ASC), dressing change, seroma, and axillary incision. However, only 2 factors, BMI and mastectomy, were reported in 5 datasets. 4 factors-length of drain stay, ASA, operation time, and age were reported in 3 datasets. The remaining factors were reported in only 1 or 2 datasets. Only factors reported in 3 or more datasets were selected for analysis in this study.

### 3.2 Meta-Analyses

A total of 8 risk factors had sufficient data subsets. Age, length of drain stay, and operative time reported continuous data and could not be directly synthesized. Lastly, mastectomy, diabetes,  $ASA \geq 3$ ,  $BMI \geq 25 \text{ kg/m}^2$ , and

**Table 2. Risk of bias assessment with NOS.**

Author, year	Selection				Comparability	Exposure			Total score
Vilar-Compte <i>et al.</i> , 2004* [18]	1	1	1	1	1	1	1	0	7
Olsen, 2008 <i>et al.</i> * [19]	1	1	1	0	2	1	1	0	7
Nguyen <i>et al.</i> , 2012* [20]	1	1	0	0	1	1	1	1	6
Davis <i>et al.</i> , 2013* [21]	1	1	0	0	2	1	1	1	7
Chung <i>et al.</i> , 2015* [22]	1	1	1	0	2	1	1	0	7
Olsen <i>et al.</i> , 2016# [23]	0	1	1	0	2	1	1	0	6
Parikh <i>et al.</i> , 2016# [24]	1	1	1	0	2	1	0	1	7
Kraenzlin <i>et al.</i> , 2022# [25]	1	1	1	0	2	1	1	0	7
Rothe <i>et al.</i> , 2022# [26]	1	1	1	0	2	1	1	1	8
Zhang <i>et al.</i> , 2022# [27]	1	1	1	0	2	1	1	1	8
Chin <i>et al.</i> , 2023# [28]	1	1	1	0	2	1	1	0	7

Note. \* indicates the study was assessed using the criteria for case-control studies. #; indicates the study was assessed using the criteria for cohort studies. NOS, Newcastle-Ottawa Scale.

**Table 3. Summary of meta-analyses.**

Risk factor	Case number				Meta-analysis			Heterogeneity test			Egger's publication bias
	RF+ SSI+	RF+ SSI-	RF- SSI+	RF- SSI-	OR (95% CI)	Z	p	I <sup>2</sup>	df	p	p
BMI ≥25 kg/m <sup>2</sup>	1071	30,239	714	23,694	1.96 (1.61, 2.40)	6.63	<0.00001	51%	5	0.07	0.20
Mastectomy	196	726	88	979	3.70 (1.79, 7.65)	3.53	0.0004	76%	3	0.006	0.04
Smoking	281	1404	6450	41,838	1.53 (1.21, 1.93)	3.55	0.0004	52%	3	0.10	0.15
ASA ≥3	706	33,813	1151	123,613	1.99 (1.74, 2.27)	10.11	<0.00001	43%	2	0.17	0.30
Diabetes	260	4789	1186	40,577	2.20 (1.70, 2.84)	6.03	<0.00001	56%	2	0.10	0.12

Note. RF+ refers to exposure to the risk factor, RF- refers to no exposure to the risk factor, SSI+ refers to patients with a positive SSI incision, and SSI- refers to patients with a negative SSI incision.

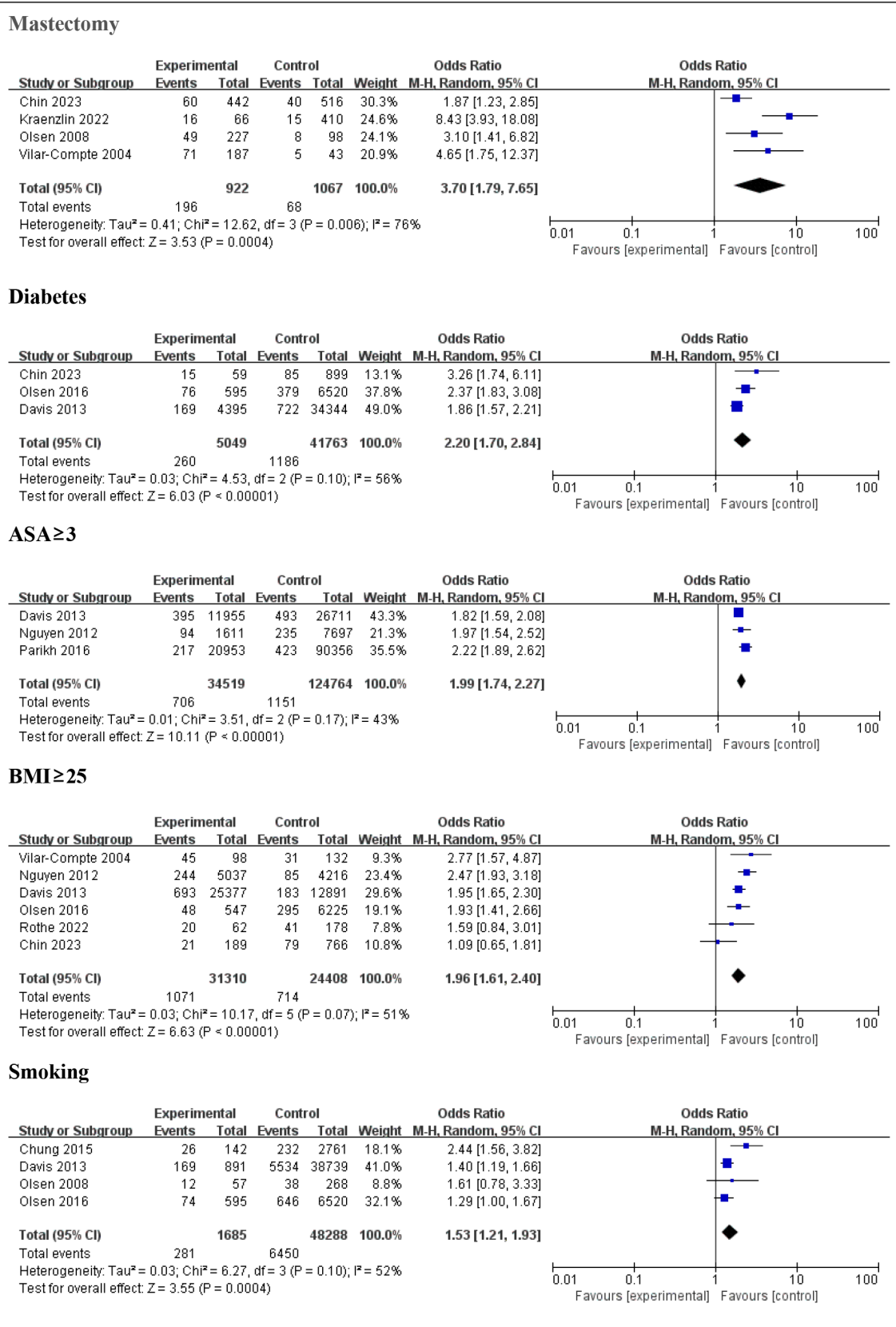
smoking were included separately in the Meta-analysis. As shown in Fig. 2 and Table 3, pooled effect sizes revealed significant overall risk factors for SSIs: mastectomy (OR = 3.70,  $p < 0.001$ ), diabetes (OR = 2.20,  $p < 0.001$ ), ASA ≥3 (OR = 1.99,  $p < 0.001$ ), BMI ≥25 kg/m<sup>2</sup> (OR = 1.96,  $p < 0.001$ ), and smoking (OR = 1.53,  $p < 0.001$ ).

However, BMI ≥25 kg/m<sup>2</sup> ( $I^2 = 51%$ ), mastectomy ( $I^2 = 76%$ ), smoking ( $I^2 = 52%$ ), and diabetes ( $I^2 = 56%$ ) all showed  $I^2$  values greater than 50%, indicating significant heterogeneity. The combination of the funnel plot and Egger's test results suggested the presence of publication bias. Therefore, a sensitivity analysis was conducted. As shown in Fig. 3, the funnel plot shows an outlier dataset for each of the 4 factors. The heterogeneity of mastectomy was significantly reduced after removing Kraenzlin *et al.*, 2022 [25]. Davis *et al.*, 2013 [21] in the diabetes group, Chin *et al.*, 2023 [28] in the BMI group, and Chung *et al.*, 2015 [22] in the smoking group were the main contributors to heterogeneity. The meta-analysis was rerun after removing the literature that contributed to the heterogeneity. These results suggested that mastectomy (OR = 2.61,  $p < 0.001$ ), diabetes (OR = 2.49,  $p < 0.001$ ), BMI ≥25 kg/m<sup>2</sup> (OR = 2.08,  $p < 0.001$ ), ASA ≥3 (OR = 1.99,  $p < 0.001$ ), and smoking (OR = 1.38,  $p < 0.001$ ) were significant risk factors predicting post-breast surgery SSIs, as shown in Fig. 4.

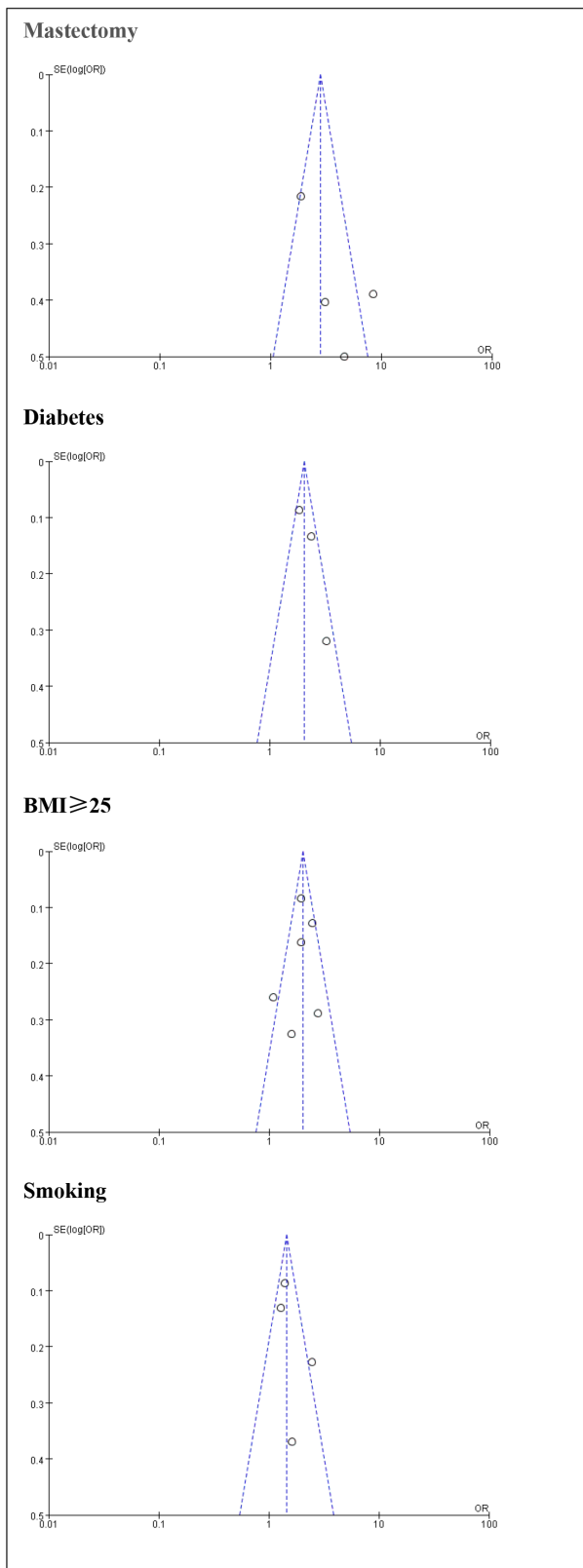
## 4. Discussion

The current study used a quantitative systematic review and meta-analysis to summarize the data for risk variables for SSI incisions following breast surgery. In total, 12 studies were identified with 2412 SSI-positive cases and 166,794 SSI-negative cases, under 22 identified risk factors. These factors included BMI, previous RT/CH, mastectomy, length of drain stay, second drain insertion, implant, antibiotic use, transfusion, smoking, anesthetic use, alcohol consumption, ASA score, flap failure, operative time, diabetes, hypertension, age, ASC, dressing change, seroma, and axillary incision. However, only 5 could be synthesized for the meta-analysis. Of these, mastectomy (OR = 2.61,  $p < 0.001$ ), diabetes (OR = 2.49,  $p < 0.001$ ), BMI ≥25 kg/m<sup>2</sup> (OR = 2.08,  $p < 0.001$ ), ASA ≥3 (OR = 1.99,  $p < 0.001$ ), and smoking (OR = 1.38,  $p < 0.001$ ) were factors that significantly increased the risk of SSI.

The largest risk factor for SSI incisions is mastectomy (OR = 2.61), which demonstrates 2.61 times higher odds of developing SSI [30]. Some articles have shown that mastectomy is one of the risk factors for postoperative SSI when compared to breast-conserving surgery (BCS) [31,32]. Compared to BCS, mastectomy involves extensive tissue removal and a larger surgical wound, which can



**Fig. 2. Forest plots for each risk factor.** This figure displays the forest plots for the identified risk factors, showing the pooled effect sizes for each factor associated with SSIs after breast surgery. ASA, American Society of Anesthesiologists; BMI, body mass index; OR, odds ratio; CI, confidence interval; SSI, surgical site infection; M-H, Mantel-Haenszel.



**Fig. 3. Funnel plots for each risk factor.**

disrupt the vascular supply, create a more hypoxic environment in the tissue, and increase the risk of bacterial colonization. However, this does not imply that BCS should al-

ways be prioritized in clinical practice. Clinicians should focus on the patient's individual condition and requirements. After mastectomy, the patient's surgical incision should be closely monitored, and measures to prevent incision infection should be implemented.

Diabetes is the second significant risk factor for SSI. Elevated blood glucose levels promote bacterial adhesion and biofilm formation, exacerbating infection risks. It could be argued that BMI and diabetes are linked, as obesity-induced insulin resistance is one of the leading causes of type 2 diabetes [33]. This may explain the variability of the ORs in BMI  $\geq 25$  (OR = 2.08) and diabetes (OR = 2.49). The datasets included in the analysis were reported separately for only 2 exposure factors, diabetes and BMI  $\geq 25$  kg/m<sup>2</sup>. However, we were unable to obtain the specific number of patients with diabetes and BMI  $\geq 25$  kg/m<sup>2</sup>, as well as those without diabetes and BMI  $\geq 25$  kg/m<sup>2</sup>. Therefore, although the ORs for diabetes and BMI were derived in this study, it is prudent to consider that the values may be somewhat biased due to the lack of detailed data on the overlap between these factors. It is suggested that future studies should report the number of patients with similar correlations in greater detail to provide more accurate and reliable estimates.

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 the inclusion of 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 have been inflated due to the repeated counting of cases exposed to multiple risk factors. Instead, this result might suggest that the pathological mechanisms of obesity and diabetes operate relatively independently in the context of SSI risk, rather than one being a direct predictor of the other.

Apart from diabetes and BMI  $\geq 25$  kg/m<sup>2</sup>, the third-largest risk factor was ASA  $\geq 3$  (OR = 1.99,  $p < 0.001$ ), with a 99% higher odds of SSI incisions. The ASA Physical Status Classification System categorizes patients based on their overall health status and their risk associated with surgery. The purpose of ASA grading is to evaluate a patient's ability to tolerate the risks associated with surgery and anesthesia by evaluating their overall health status and comorbid conditions. Based on the scoring rules, it can be assumed that a higher score indicates lower overall physical fitness, making patients with high scores more prone to postoperative surgical incision infections. One study has shown a clear and strong relationship between ASA classifi-

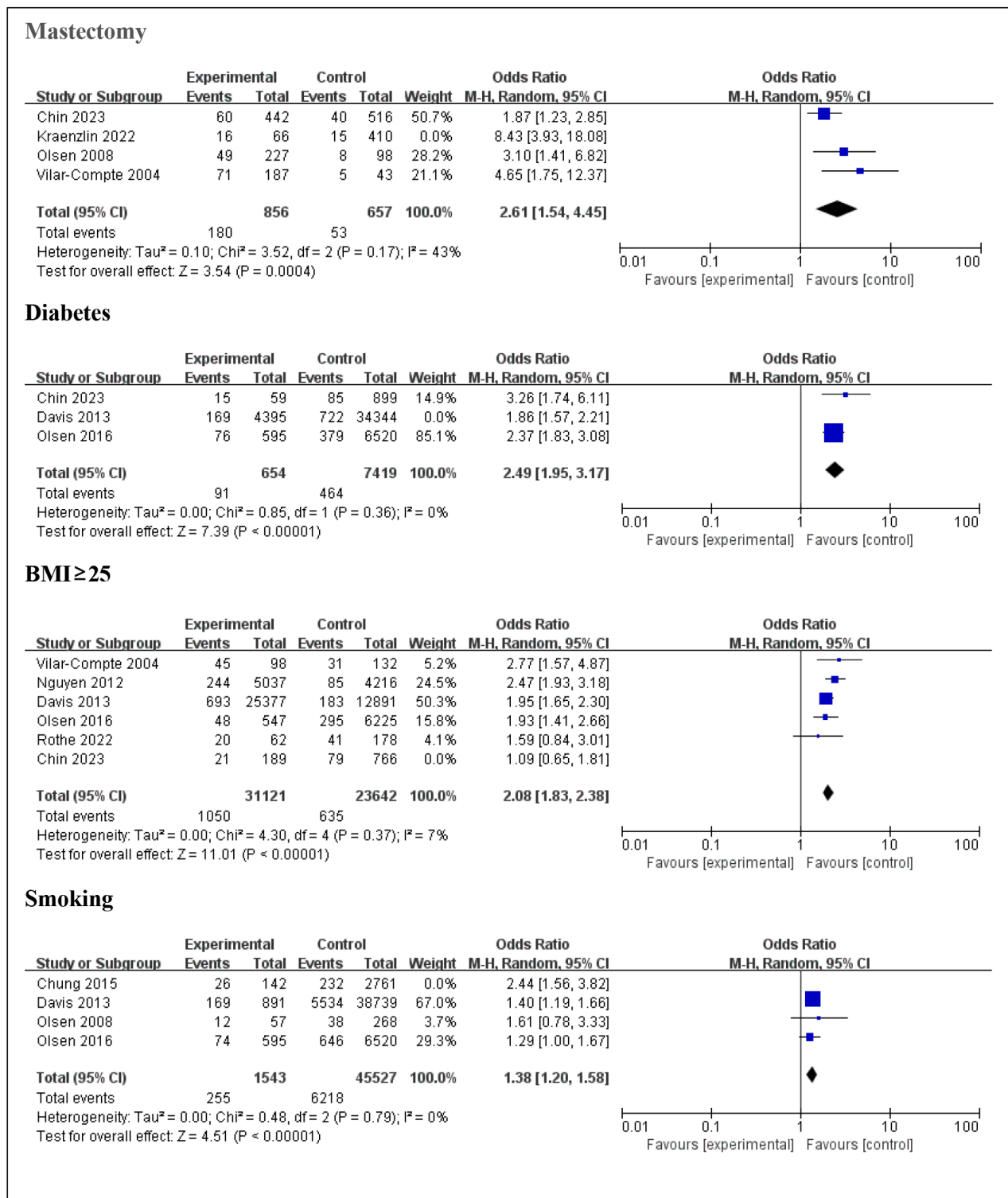


Fig. 4. Forest plot for each risk factor after reducing heterogeneity.

cation and postoperative complications, as well as all-cause mortality [34]. A possible reason is that patients with ASA  $\geq 3$  often have comorbidities (e.g., cardiovascular disease, renal dysfunction) that reduce physiological reserve, delay recovery, and increasing susceptibility to infections.

Smoking was the last risk factor (OR = 1.38,  $p < 0.001$ ), with a 38% higher odds of SSI incisions. Nicotine in tobacco can weaken the immune response and reduce the body's defense against pathogens [35]. Smoking reduces the oxygenation capacity of the erythrocytes [36], affect-

ing the oxygenation of wound tissue and preventing proper wound healing. Additionally, nicotine can cause a contraction of the capillary blood vessels, impairing the blood supply around the wound and providing conditions for bacterial reproduction [37]. Smoke also stimulates the respiratory tract to produce more secretions, increasing coughing, which may lead to surgical site dehiscence, further increasing the risk of lung infections [38].

To account for multiple comparisons across risk factors, we applied the Benjamini-Hochberg false discovery rate (FDR) correction. After adjusting for multiple comparisons using the FDR correction, the significance threshold for each test was adjusted to  $q = 0.05/5 = 0.01$  and all identified risk factors remained statistically significant, confirming that mastectomy, diabetes, BMI  $\geq 25$  kg/m<sup>2</sup>, ASA  $\geq 3$ , and smoking are predictors of SSI. There are four limitations in this study. First, types of breast surgeries (e.g., simple mastectomies, therapeutic mammoplasties, and reconstructions with implants or autologous tissue) can also affect SSI, but this was not explored in this paper. Second, few studies specified the types of SSI (superficial, deep, or organ space), and the dataset was not sufficiently large for us to analyze in subgroups; therefore, we did not perform subgroup analyses. Future research should provide more comprehensive data to address these limitations. Third, 11 of the 12 studies included in this review were conducted in the US or Europe, limiting the global applicability of the findings. The economic situation, clinical practices, and healthcare facilities in different regions influence SSI risk factors. Antibiotic prophylaxis protocols vary globally: the US emphasizes the avoidance of antibiotic misuse, the United Kingdom clarifies that routine antibiotic prophylaxis is not required for clean incisions, and China limits prophylactic drug use to less than 30% for benign breast surgery. In addition, differences in BMI distribution, prevalence of diabetes, and prevalence of smoking in different regions may further confound risk estimates. For example, obesity rates are much higher in the US than in China, which may have led to an overestimation of the risk OR for BMI  $\geq 25$  kg/m<sup>2</sup> in this study. Fourth, the studies included in this article span nearly two decades (2004–2023). With rapid advances in clinical medicine, significant progress has been made in breast surgery techniques and antimicrobial practices. For example, the 2017 update of the Centers for Disease Control and Prevention (CDC) Guideline for the Prevention of Surgical Site Infections refined recommendations for the timing and dosage of preoperative antibiotics, while the adoption of minimally invasive surgeries has further reduced the incidence of SSIs. However, our meta-analysis did not adjust for temporal trends, which may confound historical and contemporary risk estimates. Additionally, the insufficient stratification of the data from the included studies precludes an in-depth exploration of these trends.

## 5. Conclusions

This meta-analysis identified 5 significant risk factors for SSI after breast surgery, with mastectomy being most strongly associated with SSI. The factors that significantly increased the risk of SSI included mastectomy, diabetes, BMI  $\geq 25$  kg/m<sup>2</sup>, ASA  $\geq 3$ , and smoking. Clinicians should prioritize preoperative optimization, including glycemic control and smoking cessation programs for diabetic patients. In obese patients (BMI  $\geq 25$  kg/m<sup>2</sup>), wound monitoring and wound care should be enhanced. Patients with high ASA scores ( $\geq 3$ ) require preoperative evaluation. Where feasible, BCS should be prioritized over mastectomy to minimize tissue trauma. It is also recommended that future studies provide more detailed information, such as the categorization of the three types of SSIs.

## Availability of Data and Materials

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

## Author Contributions

YL and ZY designed the research study, and drafted the protocol documents for registration. YL, ZY and HZ were the independent investigators to conducted the study's review, quality assessment, and data extraction. YL and ZY completed the data analysis, DW interpretation of data for the work, and YL drafted the manuscript. Finally, ZY and DW revised the draft. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

Not applicable.

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## Conflict of Interest

The authors declare no conflict of interest.

## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.31083/CEOG37161>.

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