



# Prediction models of surgical site infection after gastrointestinal surgery: a nationwide prospective cohort study

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**Objective:** This study aimed to construct and validate a clinical prediction model for surgical site infection (SSI) risk 30 days after gastrointestinal surgery.

**Materials and methods:** This multicentre study involving 57 units conducted a 30-day postoperative follow-up of 17 353 patients who underwent gastrointestinal surgery at the unit from 1 March 2021 to 28 February 2022. The authors collected a series of hospitalisation data, including demographic data, preoperative preparation, intraoperative procedures and postoperative care. The main outcome variable was SSI, defined according to the Centres for Disease Control and Prevention guidelines. This study used the least absolute shrinkage and selection operator (LASSO) algorithm to screen predictive variables and construct a prediction model. The receiver operating characteristic curve, calibration and clinical decision curves were used to evaluate the prediction performance of the prediction model.

**Results:** Overall, 17 353 patients were included in this study, and the incidence of SSI was 1.6%. The univariate analysis combined with LASSO analysis showed that 20 variables, namely, chronic liver disease, chronic kidney disease, steroid use, smoking history, C-reactive protein, blood urea nitrogen, creatinine, albumin, blood glucose, bowel preparation, surgical antibiotic prophylaxis, appendix surgery, colon surgery, approach, incision type, colostomy/ileostomy at the start of the surgery, colostomy/ileostomy at the end of the surgery, length of incision, surgical duration and blood loss were identified as predictors of SSI occurrence (P < 0.05). The area under the curve values of the model in the train and test groups were 0.7778 and 0.7868, respectively. The calibration curve and Hosmer–Lemeshow test results demonstrated that the model-predicted and actual risks were in good agreement, and the model forecast accuracy was high.

**Conclusions:** The risk assessment system constructed in this study has good differentiation, calibration and clinical benefits and can be used as a reference tool for predicting SSI risk in patients.

Keywords: calibration curve, gastrointestinal surgery, prediction model, ROC, surgical-site infection

#### Introduction

Surgical site infection (SSI) is defined by the Centres for Disease Control and Prevention (CDC) as a surgery-related infection that occurs at or near the surgical incision within 30 days of surgery<sup>[1]</sup>. Infection can involve the skin at the site of the incision (superficial

incision SSI), underlying tissues and muscles (deep incision SSI) or spread further into organs and/or spaces between organs (organ/space SSI). SSIs are among the most common nosocomial infections, accounting for ~20% of all hospital-acquired infections<sup>[2]</sup>. As a serious postoperative complication, SSI can lead to prolonged hospital stay, delayed wound healing, impaired tissue

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repair and flap necrosis, resulting in graft failure<sup>[3,4]</sup>. SSIs pose a significant financial burden on the healthcare sector because of their complex and variable nature, resulting in prolonged patient stays, readmissions, the need for multiple investigations and treatment options, ICU bed requirements and the cost of wound care materials<sup>[5]</sup>.

Additionally, many microorganisms exist in the gastrointestinal area; therefore, in the classification of surgical incisions, gastrointestinal surgical incisions are categorised into grade 2 or above incisions<sup>[6]</sup>. SSI rates are generally higher in gastrointestinal surgery than in other types of surgery<sup>[7,8]</sup>. Guidelines have recommended an increased coverage of gram-negative *Bacilli* and *Enterococci* for antibiotic prophylaxis in cases of gastrointestinal surgery<sup>[9]</sup>. However, the factors affecting the risk of SSI, including preoperative and postoperative antibiotic prophylaxis and preoperative skin preparation, require further investigation.

Therefore, based on the assessment results, conducting a risk assessment for patients undergoing gastrointestinal surgery and implementing early prevention for high-risk patients are important. Currently, the development of clinical prediction models is the most common method for screening high-risk groups for complications. The United Kingdom, Japan and other countries have raised concerns about SSI risk factors in appendectomy and gastric surgery<sup>[10–12]</sup>. Related studies have found that kidney function, incision length and surgical duration can predict SSI discovery<sup>[10,11]</sup>. However, the limitations of these models are the small sample size, incomplete collection of assessment variables and exclusion of small intestine resections. Particularly, in China<sup>[13]</sup>, the scale of relevant studies is small and a large gap still exists in multicentre monitoring and prevention strategies for SSI after gastrointestinal surgery.

Therefore, this study aimed to explore the factors influencing the risk of SSI occurrence and to construct a clinical prediction model to provide convenient tools and evaluation methods for the prevention and early intervention of SSI.

# **Materials and methods**

# Study design

This was an observational, multicentre, prospective cohort study. The recruitment principle of this experiment was that the participating centre should be a tertiary hospital with a fixed team to ensure stable data entry. Additionally, the participating centres should provide at least 20 cases. After recruiting participants from the centre, it was found that the 57 hospitals included were distributed throughout the country (Supplementary Table 1, Supplemental Digital Content 1, http://links.lww.com/JS9/B151). The selected study participants were patients who underwent gastrointestinal surgery in each hospital between 1 March 2021 and 28 February 2022. The inclusion criteria were as follows: (1) gastrointestinal surgery, such as stomach, small intestine, appendix, colon and rectal surgery; and (2) age greater than or equal to 16 years during operation. All nonabdominal surgeries and surgeries involving mesh implants were excluded. Serious missing data, such as the lack of key outcome indicators, namely, the occurrence of SSI and those with a missing data ratio of more than 50%, were excluded. The Ethics Committee of Jinling Hospital provided ethical approval for this study on 15 May 2020, and the study protocol was registered in the ClinicalTrials. gov Registry before enrolment. Overall, 17 353 surgical patients

#### **HIGHLIGHTS**

- This study is a nationwide multicentre study involving 17 353 patients after gastrointestinal surgery from 57 hospitals.
- LASSO analysis was used to screen perioperative variables and reduce the complexity of the model, ultimately resulting in a stable model containing 20 predictive factors.
- The optimisation model was validated to have good predictive performance and clinical benefits, with internal and external validation AUC values of 0.7778 and 0.7868, respectively. This prediction model can be used to reduce the incidence of surgical site infection after gastrointestinal surgery.

(10 678 males and 6675 females) were enrolled in this study, and all patients provided written informed consent before study participation.

#### Data collection

Our research team developed a secure web application called Chinese SSI surveillance (CSSIS, http://ssi.meddb.cn/login\_index. do/), which is convenient for multiple units to establish and manage online patient information databases. According to the CSSIS procedure, we collected data, including demographics (age, sex, smoking history and BMI), preoperative blood biochemical parameters, evaluation scores [American Society of Anaesthesiologists (ASA) score, total bilirubin, blood glucose, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, blood urea nitrogen (BUN), white blood cell count, haemoglobin, platelet count and C-reactive protein], comorbidities (diabetes mellitus, hypertension, chronic liver diseases, chronic kidney diseases, chronic heart diseases and tuberculosis), immunosuppressors (corticoids and other immunosuppressors), preoperative preparation (hair removal, bowel preparation and surgical antibiotic prophylaxis) and surgical information (type, urgency, approach, incision type, length of incision, colostomy/ ileostomy at start or end of surgery, surgical duration and blood loss). There were 41 variables, including the outcome indicators of SSI occurrence, within 30 days postoperatively.

Before enrolment, the research team organised a kick-off meeting on data entry and database utilisation to ensure the quality of data collection. Additionally, we unified the definitions and classifications of the relevant variables at the meetings. Bowel preparation was categorised as no/mechanical bowel preparation (MBP) only/oral antibiotic bowel preparation (OABP) only/the combination MBP and OABP, the approach of surgery as laparoscopic or robotic/open surgery and the incision type as clean/clean-contaminated/contaminated/dirty-infected, according to the WHO guidelines for the prevention of SSI<sup>[14]</sup>. The trained researchers in each unit informed the patients of the purpose of the study, the information collected and its use before enrolment, and they signed an informed consent form. Data consistency was verified through random cheques by staff at the participating institutions, followed by a final review by the first author for data quality assurance. All methods were performed in accordance with the relevant guidelines (Strengthening the Reporting of Cohort Studies in Surgery [STROCSS])<sup>[15]</sup>. Supplemental Digital Content 2, http://links.lww.com/JS9/B152.

#### Data analysis

The research group collected 20 976 pieces of data from 57 units. Based on the inclusion and exclusion criteria, the first author deleted cases of minors, nonabdominal surgery cases, those containing implants, and those with serious data loss, leaving 17 353 cases (Fig. 1). The data were analysed and visualised using the R software's 'DataExplorer' package. Subsequently, the data quality of the 40 dependent variables was assessed, and outliers and erroneous records were removed. The proportion of missing variables was low. Variables with missing values were multiinterpolated using the 'mice' package in R (version 4.3.0) to obtain five low-bias output datasets (Supplementary Fig. 1, Supplemental Digital Content 3, http://links.lww.com/JS9/B153 and 2, Supplemental Digital Content 4, http://links.lww.com/JS9/ B154). Additionally, a density map was constructed independently, which indicated a good fit for the distribution. A complete dataset was randomly selected for further analysis.

Univariate analysis was performed on variable data. Measurement data with a normal distribution were described as means and SD, and comparisons between groups were performed using the t-test. Furthermore, measurement data with a nonnormal distribution were described as median and quartile (Q1 and Q3), and comparisons between groups were performed using the Mann–Whitney U test. Count data were expressed as frequency or percentage, and the  $\chi^2$  test was used for comparison between groups. Thirteen dependent variables with no significant differences were excluded. The remaining data were randomly

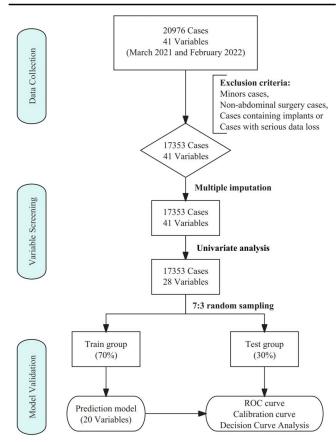


Figure 1. Flow chart of the cohort study and data analysis.

categorised into train (70%) and test (30%) groups, with the train group used for model fitting. The model was validated internally and externally in the train and test groups, respectively. First, the remaining 27 variables were used to directly conduct logistic regression to establish the prediction model and calculate the odds ratios and regression coefficients. To effectively reduce model complexity due to the large number of remaining 27 variables after univariate analysis, variables were selected based on the least absolute shrinkage and selection operator (LASSO) regression method, and an optimised model was constructed, which was internally verified using the bootstrap repeated sampling method (1000 times). We used the R version 4.3.0 software to construct the regression model (R Foundation for Statistical Computing).

#### Model validation

For the model's prediction performance, we evaluated the discrimination, calibration and clinical benefits. Discrimination refers to a model's ability to correctly classify a population into patients/nonpatients, distinguish between individuals at low or high risk, or predict whether a patient will survive or die. The receiver operating characteristic (ROC) curve and area under the curve (AUC) were used to evaluate model discrimination. The closer the AUC value was to 1, the better the model discrimination. It is generally believed that an AUC or C-Statistic less than 0.6, 0.6–0.75, and greater than 0.75 indicate low, medium and high discrimination, respectively. The degree of calibration refers to the consistency between the probability of the outcome occurring and the probability predicted by the model, also known as consistency and goodness of fit. The degree of calibration reflected the accuracy of the absolute risk prediction of the model. A calibration curve was used to directly examine the relationship between the predicted and real probabilities. The Hosmer-Lemeshow test was used to further assess the calibration. When the P-value was <0.05, a difference was found between the predicted and true values of the model. Decision curve analysis (DCA) was used to compare the net benefits of the intervention according to the model with those of the default approach (full and no intervention) to fully evaluate the model's advantages. This study was conducted following the STROCSS criteria<sup>[16]</sup>.

#### **Results**

The initial survey included 20 976 patients from 57 hospitals (Fig. 1). Overall, 3623 cases were excluded because of underage (996 cases), nonabdominal surgery (778 cases), implants (727 cases), or significant data loss (1122 cases).

After 30 days of postoperative follow-up, the patients were categorised into the SSI (1.6%) and the non-SSI (98.4%) groups according to the CDC guidelines (Table 1). Hair removal was performed in ~87% of patients, followed by surgical antibiotic prophylaxis in approximately half, and emergency surgery in approximately one-fourth. Univariate analysis revealed 27 statistically significant variables between the SSI and non-SSI groups. Age, ASA, hypertension, chronic liver disease, chronic kidney disease, steroid use, smoking history, haemoglobin, C-reactive protein, blood urea nitrogen, creatinine, albumin, blood glucose, bowel preparation, surgical antibiotic prophylaxis, stomach surgery, small intestine surgery, appendix surgery, colon surgery, rectal surgery, approach, incision type, colostomy/ileostomy at

Table 1
Univariate analysis of SSI incidence.

Variables	Total (n = 17 353)	Non-SSI group ( <i>n</i> = 17 077)	SSI group ( <i>n</i> = 276)	P
Sex (%)				0.088
Male	10 678 (62)	10 494 (61)	184 (67)	
Female	6675 (38)	6583 (39)	92 (33)	
Age (Mean $\pm$ SD), years	$55.16 \pm 16.80$	$55.08 \pm 16.80$	$60.35 \pm 15.40$	< 0.001
BMI (Mean ± SD), kg/m <sup>2</sup>	$23.46 \pm 4.40$	23.47 ± 4.41	23.25 ± 3.63	0.833
ASA, n (%)		· -		< 0.001
1	5819 (34)	5726 (34)	93 (34)	
2	8762 (50)	8644 (51)	118 (43)	
3	2388 (14)	2327 (14)	61 (22)	
4	207 (1)	203 (1)	4 (1)	
5	177 (1)	177 (1)	0 (0)	
Diabetes mellitus (%)	(.)	(.)	- (-)	0.051
No	15 927 (92)	15 683 (92)	244 (88)	0.001
Yes	1426 (8)	1394 (8)	32 (12)	
Hypertension (%)	1420 (0)	1004 (0)	02 (12)	0.004
No	13 802 (80)	13 602 (80)	200 (72)	0.001
Yes	3551 (20)	3475 (20)	76 (28)	
Chronic liver disease (%)	3331 (20)	3473 (20)	70 (20)	< 0.001
. ,	17 009 (00)	16 843 (99)	255 (02)	< 0.001
No Yes	17 098 (99) 255 (1)	234 (1)	255 (92) 21 (8)	
	255 (1)	234 (1)	21 (0)	.0.001
Chronic kidney disease (%)	17 167 (00)	10,000,(00)	001 (05)	< 0.001
No	17 167 (99)	16 906 (99)	261 (95)	
Yes	186 (1)	171 (1)	15 (5)	
Chronic heart disease (%)	10 700 (07)	4.0 5.00 (0.7)	000 (05)	0.21
No	16 796 (97)	16 533 (97)	263 (95)	
Yes	557 (3)	544 (3)	13 (5)	
Tuberculosis (%)				0.376
No	17 271 (100)	16 997 (100)	274 (99)	
Yes	82 (0)	80 (0)	2 (1)	
Steroid use (%)				0.043
No	17 270 (100)	16 998 (100)	272 (99)	
Yes	83 (0)	79 (0)	4 (1)	
Immunosuppressors (%)				0.719
No	17 232 (99)	16 958 (99)	274 (99)	
Yes	121 (1)	119 (1)	2 (1)	
Smoking history (%)				0.039
None	15 409 (89)	15 177 (89)	232 (84)	
Former	1327 (8)	1298 (8)	29 (11)	
Current	617 (4)	602 (4)	15 (5)	
Haemoglobin (Mean $\pm$ SD)	$125.54 \pm 22.76$	$125.60 \pm 22.72$	$121.48 \pm 24.33$	0.001
White blood cell count, Median (Q1, Q3)	6.51 (5.08, 9)	6.51 (5.08, 9)	6.5 (5.09, 9.35)	0.918
Platelet count, Median (Q1, Q3)	225 (183, 271)	225 (183, 271)	223.5 (178.75, 282.5)	0.548
C-reactive protein, Median (Q1, Q3), mg/l	16.27 (6.84, 30.96)	16.20 (6.81, 30.84)	23.45 (9.92, 41.57)	< 0.001
Total bilirubin, Median (Q1, Q3), µmol/l	12.4 (8.8, 17.3)	12.4 (8.8, 17.3)	12.5 (8.84, 18.25)	0.515
ALT (Mean $\pm$ SD), U/I	$23.73 \pm 25.90$	$23.69 \pm 25.88$	$26.08 \pm 26.47$	0.792
AST (Mean ± SD), U/I	$24.40 \pm 21.11$	$24.34 \pm 21.03$	$27.70 \pm 25.27$	0.166
Blood urea nitrogen, Median (Q1, Q3), mmol/l	5.1 (4.2, 6.3)	5.1 (4.19, 6.3)	5.8 (4.42, 7.3)	< 0.001
Creatinine (Mean $\pm$ SD), $\mu$ mol/l	$68.72 \pm 35.20$	$68.60 \pm 35.13$	$76.21 \pm 38.58$	< 0.001
Albumin (Mean $\pm$ SD, g/l)	40.1 (36.5, 43.6)	40.2 (36.6, 43.6)	37.8 (32.88, 41.11)	< 0.001
Blood glucose, Median (Q1, Q3), mmol/l	5.42 (4.87, 6.23)	5.42 (4.87, 6.21)	5.7 (4.9, 6.88)	< 0.001
Hair removal (%)	3.42 (4.07, 0.23)	3.42 (4.07, 0.21)	3.7 (4.9, 0.00)	0.326
No	2193 (13)	2164 (13)	29 (11)	0.320
	, ,	, ,	, ,	
Yes	15160 (87)	14913 (87)	247 (89)	0.004
Bowel preparation (%)	0050 (40)	7000 (47)	00 (00)	< 0.001
No	8059 (46)	7960 (47)	99 (36)	
MBP only	8672 (50)	8502 (50)	170 (62)	
OABP only	61 (0)	56 (0)	5 (2)	
MBP and OABP	561 (3)	559 (3)	2 (1)	
Surgical antibiotic prophylaxis (%)				< 0.001
No	8696 (50)	8589 (50)	169 (61)	
Yes	8657 (50)	8488 (50)	107 (39)	
Stomach surgery (%)				< 0.001

## Table 1

#### (Continued)

Variables	Total (n = 17 353)	Non-SSI group (n = 17 077)	SSI group ( <i>n</i> = 276)	P
No	12 435 (72)	12 208 (71)	227 (82)	
Yes	4918 (28)	4869 (29)	49 (18)	
Small intestine surgery (%)				< 0.001
No	14 392 (83)	14 202 (83)	190 (69)	
Yes	2961 (17)	2875 (17)	86 (31)	
Appendix surgery (%)				< 0.001
No	12 818 (74)	12 566 (74)	252 (91)	
Yes	4535 (26)	4511 (26)	24 (9)	
Colon surgery (%)				< 0.001
No	13 149 (76)	12 980 (76)	169 (61)	
Yes	4204 (24)	4097 (24)	107 (39)	
Rectal surgery (%)				0.017
No	14 633 (84)	14 415 (84)	218 (79)	
Yes	2720 (16)	2662 (16)	58 (21)	
Urgency of surgery (%)				0.161
Selective	13 512 (78)	13 287 (78)	225 (82)	
Emergency	3841 (22)	3790 (22)	51 (18)	
Approach (%)				< 0.001
Laparoscopic or robotic	13 292 (77)	13 165 (77)	127 (46)	
Open	4061 (23)	3912 (23)	149 (54)	
Incision type (%)				< 0.001
Clean	7 (0)	7 (0)	0 (0)	
Clean-contaminated	12 102 (70)	11 955 (70)	147 (53)	
Contaminated	4943 (28)	4827 (28)	116 (42)	
Dirty-infected	301 (2)	288 (2)	13 (5)	
Colostomy/ileostomy at start of surgery				< 0.001
No	16 882 (97)	16 629 (97)	253 (92)	
Yes	471 (3)	448 (3)	23 (8)	
Colostomy/ileostomy at end of surgery				< 0.001
No	15 894 (92)	15 693 (92)	201 (73)	
Yes	1459 (8)	1384 (8)	75 (27)	
Length of incision, Median (Q1, Q3), cm	5 (2, 9)	5 (2, 9)	10 (5, 15)	< 0.001
Surgical duration, Median (Q1, Q3), days	140 (80, 193)	140 (80, 190)	155.75 (120, 230)	< 0.001
Blood loss, Median (Q1, Q3), ml	28 (10, 58.5)	25 (10, 54.08)	50 (20, 100)	< 0.001

ASA, American society of anesthesiologists physical status classification system; MBP, mechanical bowel preparation; OABP, oral antibiotic bowel preparation.

start of surgery, colostomy/ileostomy at end of surgery, length of incision, surgical duration and blood loss were associated with an increased risk of SSI (P < 0.05). These 27 variables were considered potential predictive factors of SSI.

SSI was used as the dependent variable, and 27 statistically significant variables in the univariate analysis were used as independent variables. Data from the train group were subjected to multivariate logistic regression analysis. The results showed that chronic liver disease [OR (odds ratio): 5.962, P < 0.001], C-reactive protein (OR: 1.005, P = 0.001), albumin (OR: 0.957, P < 0.001), surgical antibiotic prophylaxis (OR: 1.429, P = 0.024), colon surgery (OR: 1.625, P = 0.025), approach (OR: 2.047, P = 0.001), incision type (OR: 1.631, P = 0.001), colostomy/ileostomy at the start of surgery (OR: 2.071, P = 0.017), and colostomy/ileostomy at the end of surgery (OR: 2.026, P < 0.001) were independent risk factors for SSI (Table 2).

LASSO regression was used to filter and select prediction variables, and multiple logistic regression was used to establish the prediction model. The LASSO is a variable selection method based on the penalty for the train group data. The small coefficients were directly compressed to 0 by compressing the original

coefficients. The variables corresponding to these coefficients were considered insignificant and were discarded, ensuring the best-fit error while reducing model complexity. Therefore, based on the LASSO and multivariate logistic regression, 20 nonzero coefficient variables, including chronic liver disease, chronic kidney disease, steroid use, smoking history, C-reactive protein, blood urea nitrogen, creatinine, albumin, blood glucose, bowel preparation, surgical antibiotic prophylaxis, appendix surgery, colon surgery, approach, incision type, colostomy/ileostomy at start of surgery, colostomy/ileostomy at end of surgery, length of incision, surgical duration and blood loss were identified as independent predictors (Table 3). Chronic liver disease, approach, colon surgery, appendix surgery, colostomy/ileostomy at the start of surgery, and colostomy/ileostomy at the end of surgery had high coefficients in the model, which significantly impacted the incidence of SSI. A nomogram constructed based on the overall model is shown in Figure 2.

A model can be evaluated based on the following three aspects: discrimination, calibration and clinical benefits. In the ROC analysis, the AUC value of the model without screened variables in the train and test groups was 0.6236 (95% CI: 0.584–0.6632)

and 0.5808 (95% CI: 0.518–0.6436), respectively (Fig. 3). In contrast, the internal and external validation results of the model optimised using LASSO analysis showed that the AUC value of the participants was 0.7868 (95% CI: 0.7345–0.8392) and 0.7778 (95% CI: 0.7215–0.8340), respectively.

Therefore, this study also used the Hosmer–Lemeshow Goodness of fit test to evaluate the calibration of the optimisation model, and its results demonstrated that the predicted risk of the model was in good agreement with the actual risk (train group:  $\chi^2 = 9.026984$ , P = 0.5635; test group:  $\chi^2 = 11.047789$ , P = 0.8997). The calibration curve also showed that the model's prediction accuracy was relatively high (Fig. 4), which satisfied the scientific requirements and rigour of the model construction process. Additionally, the DCA indicated that the net benefits of the intervention based on the optimised model were better than those of the default methods (full and no intervention) (Fig. 5). This proves that the model has certain benefits for clinical applications.

# **Discussion**

SSI is a severe postoperative complication that increases the risk of readmission and mortality<sup>[17]</sup>. Based on data collected by the CSSIS, we established the largest SSI monitoring study in China. The latest data on the incidence of SSI in gastrointestinal surgery and the predictive factors for SSI risk were determined.

Table 2
Odds ratios of 27 variables and logistic regression model for SSI risk.

Variables	Regression coefficient	P	Odds ratio (95% CI)
Age	0.008	0.175	1.008 (0.997-1.019)
ASA	-0.081	0.401	0.922 (0.763-1.114)
Hypertension	-0.02	0.916	0.981 (0.683-1.409)
Chronic liver disease	1.785	< 0.001	5.962 (3.26-10.904)
Chronic kidney disease	0.498	0.253	1.646 (0.700-3.871)
Steroid use	0.249	0.694	1.283 (0.371-4.428)
Smoking history	0.083	0.562	1.087 (0.82-1.439)
Haemoglobin	0.002	0.509	1.002 (0.996-1.009)
C-reactive protein	0.005	0.001	1.005 (1.002-1.008)
Blood urea nitrogen	-0.005	0.458	0.995 (0.981-1.009)
Creatinine	0.002	0.102	1.002 (1.000-1.005)
Albumin	-0.044	< 0.001	0.957 (0.934-0.981)
Blood glucose	0.02	0.188	1.020 (0.990-1.051)
Hair removal	-0.069	0.547	0.933 (0.745-1.169)
Surgical antibiotic prophylaxis	-0.357	0.024	0.700 (0.549-0.916)
Stomach surgery	-0.286	0.284	0.751 (0.445-1.268)
Small intestine surgery	0.066	0.752	1.068 (0.711-1.605)
Appendix surgery	-0.186	0.557	0.831 (0.447-1.543)
Colon surgery	0.485	0.025	1.625 (1.062-2.486)
Rectal surgery	0.353	0.157	1.424 (0.873-2.321)
Approach	0.716	0.001	2.047 (1.323-3.165)
Incision type	0.489	0.001	1.631 (1.234-2.155)
Colostomy/ileostomy at start of surgery	0.728	0.017	2.071 (1.139–3.765)
Colostomy/ileostomy at end of surgery	0.706	< 0.001	2.026 (1.385–2.965)
Length of incision	0.028	0.082	1.029 (0.996-1.062)
Surgical duration	0.001	0.194	1.001 (0.999–1.003)
Blood loss	0.001	0.024	1.001 (1.000–1.001)

The latest CDC data demonstrate that the incidence rate of SSI in the United States was ~1.9% from 2006 to 2009<sup>[1]</sup>, which was slightly higher than that reported in this study. However, after worldwide attention and prevention of postoperative complications, the incidence rate of SSI has considerably improved. Recently, minimally invasive surgeries, including laparoscopic or robotic surgeries, have gradually become the standard treatment for many gastrointestinal surgeries. Consistent with many previous studies<sup>[18,19]</sup>, surgical approaches can affect the risk of SSI, and this study included open surgery as an important independent risk factor for the occurrence of SSI. However, prolonged surgical duration may increase the risk of SSI in patients. Although the factors influencing the surgical duration are yet to be determined, appropriate surgical planning to reduce the surgical duration may help reduce the risk of SSI after gastrointestinal surgery.

After selection and optimisation using univariate and LASSO analysis, respectively, the prediction model included 20 variables associated with SSI risk. In 2021, a study by the American Association of Anaesthesiologists showed that the ASA score of patients was related to the incidence rate of SSI and mortality postoperatively; however, the data were limited. Our study used LASSO analysis optimisation to exclude ASA as a less important influencing factor. In this model, comorbidities, including chronic kidney and liver diseases, increased the risk of SSI. Previous studies have demonstrated that chronic liver and kidney diseases are independent risk factors for SSI<sup>[10,13]</sup>. Indicators related to renal function, such as blood urea nitrogen and creatinine, can also serve as factors for predicting the risk of SSI and can more accurately predict the risk of SSI in patients with different levels of renal function. In contrast, diabetes was excluded as a predictor of complications, and preoperative blood glucose levels were positively correlated with the risk of SSI postoperatively. In this model, hyperglycaemia negatively affected the occurrence of postoperative SSI. Therefore, the CDC guidelines<sup>[1]</sup> recommend that patients with and without diabetes implement perioperative blood glucose control, and the blood glucose target level is

Table 3

The regression coefficient of the clinical prediction model.

Variables	Coefficients	95% CI	P
Chronic liver disease	1.7658	(1.1338-2.3394)	< 0.001
Chronic kidney disease	0.5087	(0.3974-0.7182)	0.042
Steroid use	0.1937	(0.0651-0.2732)	0.037
Smoking history	0.1108	(0.0329 - 0.2753)	0.043
C-reactive protein	0.0046	(0.0015-0.0075)	0.002
Blood urea nitrogen	0.0050	(0.0031-0.0179)	0.016
Creatinine	0.0022	(0.0007 - 0.0047)	0.009
Albumin	-0.0426	(-0.0649 - 0.0202)	< 0.001
Blood glucose	0.0198	(0.0075-0.0442)	0.017
Bowel preparation	-0.0123	(-0.0339 - 0.0059)	0.015
Surgical antibiotic prophylaxis	-0.3438	(-0.6542 - 0.0382)	0.028
Appendix surgery	-0.3825	(-0.6365-0.0540)	0.012
Colon surgery	0.3976	(0.0602-0.7360)	0.021
Approach	0.6673	(0.2429-1,0887)	0.002
Incision type	0.4654	(0.1865 - 0.7387)	< 0.001
Colostomy/ileostomy at start of surgery	0.7724	(0.1616-1.3273)	0.009
Colostomy/ileostomy at end of surgery	0.8032	(0.4333 - 1.1605)	< 0.001
Length of incision	0.0338	(0.0021-0.0648)	0.035
Surgical duration	0.0017	(0.0010-0.0034)	0.024
Blood loss	0.0005	(0.0001-0.0009)	0.042

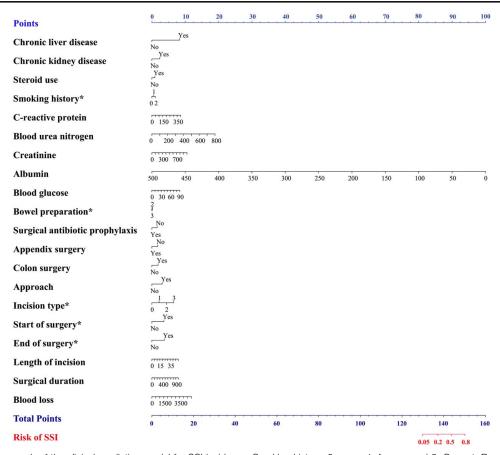


Figure 2. Nomogram graph of the clinical prediction model for SSI incidence. Smoking history: 0, none; 1, former; and 2, Current. Bowel preparation: 0, no preparation; 1, MBP only; 2, OABP only; and 3, MBP and OABP. Incision type: 0, clean wound; 1, clean-contaminated wound; 2, contaminated wound; and 3, infected wound.

<200 mg/dl. Low serum albumin levels increased the risk of SSI postoperatively, which is consistent with previous findings<sup>[13]</sup>.

In previous studies, insufficient randomised controlled trial evidence was found to evaluate the advantages and disadvantages of surgical antibiotic prophylaxis for SSI prevention<sup>[20,21]</sup>. However, the effect of surgical antibiotic prophylaxis on SSI remains unclear. In this model, surgical antibiotic prophylaxis was classified as a negative regulator that slightly reduced the risk of SSI. The CDC also recommends surgical antibiotic prophylaxis according to its guidelines<sup>[1]</sup>. However, no clear evidence exists regarding the strategy and timing of antibiotic use for SSI<sup>[22]</sup>.

This model suggests that colon surgery has the highest risk of SSI among gastrointestinal surgeries. Previous studies have also reported that the incidence of colorectal surgery and SSI is four times higher than that of other abdominal surgeries<sup>[7]</sup>. The high incidence of SSI in colorectal surgery is mainly related to the following four factors: the type of surgery defined as clean contamination or contamination<sup>[23]</sup>, the median age of patients (over 65 years old), the incidence of colorectal surgical complications (postoperative bleeding and anastomotic leakage, among others), and tumours as the main cause of treatment. Therefore, SSI prevention should be emphasised in patients undergoing colorectal surgery; however, its prevention strategy needs further research. Previous studies have found that preoperative MBP combined with oral antibiotics (OA) diminishes the effectiveness of SSI by reducing

the colonic bacterial burden and contact with infectious substances during intestinal anastomosis. Previous studies have not yet reached a consensus on the use of MBP alone; however, it has been demonstrated that combined preoperative bowel preparation (MBP and OA) is associated with a significant reduction in the incidence of incision SSI<sup>[24]</sup>. Our study further showed that combined preoperative bowel preparation (MBP and OA) was more effective in reducing the risk of SSI than MBP or OA alone. The research mentioned above indicates that it is appropriate to use routine combined bowel preparations (MBP and OA) as standard care for patients undergoing colorectal surgery. Therefore, it is best to incorporate this into the hospital best-practice models.

The CDC classifies surgical incisions into the following four categories: 1) clean wounds; 2) clean-contaminated wounds; 3) contaminated wounds; and 4) infected wounds<sup>[1]</sup>. Notably, the effect of incision grade on SSI has been demonstrated in numerous studies<sup>[25,26]</sup>. This model also revealed that the presence of a colostomy/ileostomy before and after surgery had adverse effects on SSI occurrence. Particularly, preoperative colostomy/ileostomy had a greater effect on the incidence of SSI than post-operative colostomy/ileostomy.

Although there is currently an increased national awareness of the risk factors for SSI, previous studies have yielded mixed results and lack high-quality evidence, which has hindered the establishment of optimal care strategies<sup>[27,28]</sup>. The CSSIS participating units are

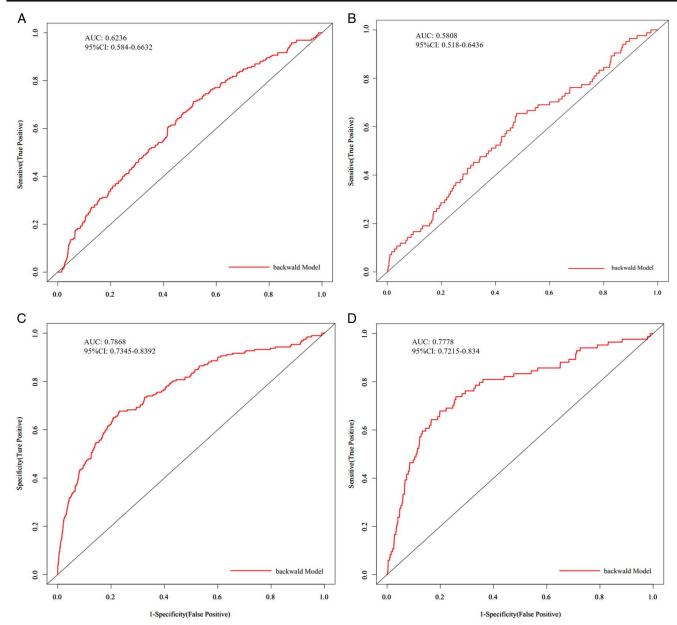


Figure 3. ROC curves of two prediction models in the train and test group. The abscissa of the ROC curve is 1- specificity, and the ordinate is sensitivity. It means that the abscissa and ordinate are false and true positive, respectively. The larger the area under the curve, the better the model differentiation. A, B, The ROC curve of the unoptimised model in the train (A) and test (B) groups. C, D, The ROC curves of the model optimised using LASSO analysis in the train (C) and test (D) groups.

distributed across the country, making it the first large-scale national multicentre SSI surveillance network in China to provide high-quality representative samples of potential predictive factors for this study. LASSO analysis was used to screen the variables in this study owing to various clinical variables in the patient data. Compared to other models established solely using logistic regression<sup>[2]</sup>, this optimised model is less complex and helps physicians develop personalised treatment plans to minimise the risk of SSI in patients undergoing gastrointestinal surgery. This study had some limitations. First, our analysis lacked some important variables, such as the surgeons' experience and strategies for surgical antibiotic prophylaxis, which may have affected the occurrence of SSI. Second, ~5.3% (1122/20976) of the patients were excluded due to loss to follow-up or

missing data exceeding 50%. Some of the enroled patients had missing data (<50%), and it was necessary to strengthen the follow-up of patient data. Therefore, this study has not stopped updating clinical data and is expected to continue tracking and reporting to the Chinese Surgical Site Infection Surveillance Project. Based on the continued tracking of SSI risk factors, monitoring important variables, such as surgical antibiotic prophylaxis strategy and time, is added to explore medical strategies for preventing and treating SSI.

#### Conclusion

This study analysed 17 535 gastrointestinal surgeries from 57 units to obtain a model for predicting SSI risk. This model covers

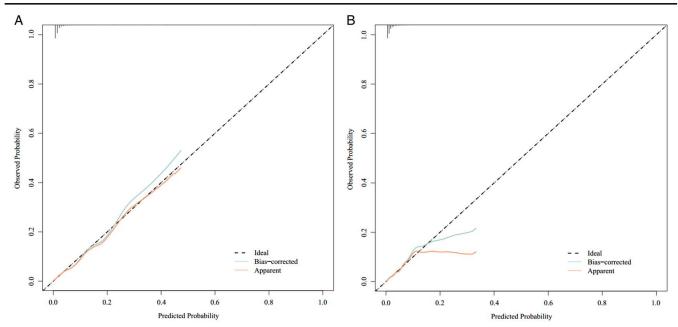


Figure 4. Calibration curve of the optimised model verified internally and externally. The abscissa and ordinate are the prediction and observation probabilities, respectively. The X-axis is the outcome possibility predicted using the model, while the Y-axis is the observed value, and the calculation is repeated 1000 times, where bias-corrected is the correction curve, and the green line ideal is the ideal curve. The closer the correction curve is to the ideal curve, the better the model's prediction ability. A, B, The calibration curves of the model optimised using LASSO analysis in the train (A) and test (B) groups.

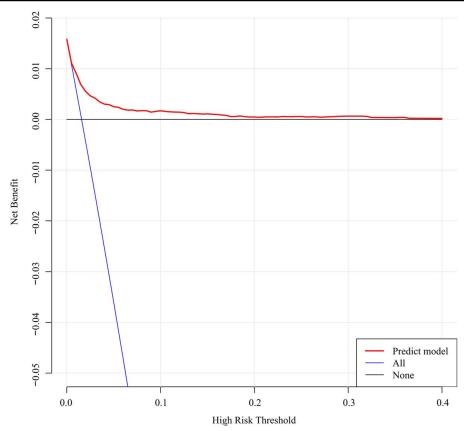


Figure 5. Decision curve analysis. Compare the net benefits of intervention based on the optimisation model (red) with the net benefits of full intervention (blue) and no intervention (black).

20 predictive factors, including baseline patient characteristics and perioperative management, with sufficient predictive accuracy and clinical benefits for postoperative SSI risk in patients undergoing gastrointestinal surgery. Clinicians can strengthen SSI prevention and health measures for patients with chronic liver and kidney disease, colon surgery, open surgery and colostomy/ ileostomy at the beginning of the surgery, which can reduce the risk of experiencing SSI. Our nomograms integrated into an online risk calculator can assist in clinical trial design and decision-making. These models could be further tested and updated as new clinical trial data become available.

# **Ethical approval**

The Ethics Committee of Jinling Hospital provided ethical approval for this study (No. 2020NZKY-010-01) on 15 May 2020, and the study protocol was registered in the ClinicalTrials. gov Registry (ChiCTR2100043706) before enrolment.

#### Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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# **Author contribution**

J.R., X.W., and Y.Y.: study conception and design, data collection. All units involved in CSSIS project (Supplementary Table 1). Y.Y. and X.Z.: statistical analysis; Y.Y., J.R., and X.W.: manuscript draft. All Authors commented the study and approved the final manuscript.

#### **Conflicts of interest disclosure**

The authors declare no conflicts of interest.

# Research registration unique identifying number (UIN)

The study protocol registered on the ClinicalTrials.gov Registry (ChiCTR2100043706) before enrolment commenced (https://www.chictr.org.cn/showproj.html?proj=122424).

#### Guarantor

Jianan Ren and Xiuwen Wu.

#### **Data availability statement**

The study protocol registered on the ClinicalTrials.gov Registry (ChiCTR2100043706) before enrolment commenced.

# Provenance and peer review

Not commissioned, externally peer-reviewed.

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