MIDLINE INCISIONAL HERNIA PROPHYLAXIS AND HERNIA RISK PREDICTION MODEL

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ABSTRACT

Incisional hernia (IH), which occurs in 5% to 30% of abdominal incisions, could cause severe complications and impaired quality of life. Therefore, treatment and management of hernia, including prophylaxis, efficacy, and identification of a high-risk population, are important. This study was conducted regarding these objectives.

First, the treatment efficacy of the prophylactic mesh technique was investigated by conducting a systematic review and network meta-analysis (NMA). Relative treatment efficacy and adverse events were simultaneously assessed using a risk-benefit analysis (RBA). The most suitable mesh technique was identified accordingly. Twenty randomized controlled trials (RCTs) were included in NMA. Pooled risk ratios (RRs) [95% confidence interval (CI)] of IH occurrence were 0.24 (0.12, 0.46), 0.32 (0.16, 0.66), 0.58 (0.23, 1.47), and 0.58 (0.32, 1.06) for onlay (OM), retrorectus (RM), pre-peritoneal (PM), and intra-peritoneal (IM) versus primary suture closure (PSC), respectively. From RBA, RM was preferred to OM for IH prophylaxis considering both benefits and complication risks.

Second, a multicenter RCT protocol was developed in the ideal situation to evaluate mesh's efficacy in patients undergoing emergency abdominal surgery, in which the risk of IH is high, and the efficacy of prophylactic mesh is unknown. However, only 11.1% of the estimated sample size was recruited since the commencement of enrollment.

Third, the existing hernia prediction model was externally validated and updated in Thai patients who underwent abdominal surgery from 2010 to 2021. From a systematic review, an IH prediction model named *Penn hernia risk calculator* was selected for validation. Only fair discrimination performance was observed in Ramathibodi data (C-statistic = 0.645). By model revising of coefficients and adding new predictor variables, C-statistic was improved to 0.733 with a good calibration (observed/expected ratio = 0.968).

This study provides a wide range of knowledge about incisional hernia, including hernia prophylaxis and risk prediction models. Evidence from NMA and RBA, RM was suggested for hernia prevention. The RCT, conducted regarding the developed protocol, will fill the knowledge gap in IH prevention. The revised *Penn hernia risk calculator* could be deployed for routine clinical practice. High-risk patients would be identified and targeted for additional hernia prophylaxis procedures. As a result, adherence to hernia prophylaxis could be increased.

KEY WORDS: ABDOMINAL SURGERY/ INCISIONAL HERNIA/ PROPHYLAXIS/ MESH-AUGMENTED FASCIA CLOSURE/ PREDICTION MODEL

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LIST OF ABBREVIATIONS

ASA	American Society of Anesthesiologists
AT	As-treated
BMI	Body mass index
CEA	Cost-effectiveness analysis
CDC	Center of Disease Control
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CRF	Case record form
C-statistics	Concordance statistics
CSH	Composite seroma and hematoma
DMA	Direct meta-analysis
DMU	Data management unit
DSMB	Data safety and monitoring board
EHS	European Hernia Society
FD	Fascial dehiscence
FMI	Fraction of missing information
ICD	International statistical Classification of Disease and related health problem
ICER	Incremental cost effectiveness ratio
IH	Incisional hernia
IM	Intra-peritoneal mesh
IQR	Interquartile range
IRB	Institutional review board
IRBR	Incremental risk benefit ratio
IV	Instrumental variable
MA	Meta-analysis
MAR	Missing at random

LIST OF ABBREVIATIONS (Cont.)

MD	Mean difference
ML	Machine learning
NMA	Network meta-analysis
NMB	Net monetary benefit
NNH	Number needed to harm
NNT	Number needed to treat
O/E	Observed/Expected
OM	Onlay mesh
OR	Odds ratio
PCA	Patient-control anesthesia
PM	Pre-peritoneal mesh
PP	Per-protocol
PPV	Positive predictive value
PRB	Probability of being risk-beneficial
PSC	Primary suture closure
RBA	Risk benefit analysis
RCT	Randomized controlled trial
RD	Risk difference
RM	Retrorectus mesh
RoB	Risk of bias
ROC	Receiver operating characteristic
RR	Risk ratio
RVI	Relative variance increase
SD	Standard deviation
SE	Standard error
SL	Suture length
SSI	Surgical site infection
SUCRA	Surface under the cumulative ranking

LIST OF ABBREVIATIONS (Cont.)

VHR	Ventral hernia repair
WL	Wound length

PART I
HERNIA PREVENTION

CHAPTER I
BACKGROUND AND RATIONALE OF HERNIA PREVENTION

1.1 BACKGROUND

Hernia means rupture in the Latin word, is a protrusion of the internal organ through the wall of the cavity where it is contained.[1] The European hernia society (EHS) has classified abdominal hernia into two major types, i.e., primary and incisional hernia (IH).[2] The primary hernia occurs spontaneously, whereas the IH occurs at the surgical incision after surgery.

The IH may cause by impaired fascia healing, which is a complex process consisting of hemostasis, inflammatory, proliferative, and maturation phases. Every wound must progress through all these processes where many cells work in concert with cytokines. However, many negative factors (e.g., infection,[3, 4] obesity,[3-5] smoking,[4, 5] malnutrition,[4] and diabetes[6]) can delay wound healing. If delayed healing occurred at a laparotomy wound, this could lead to an IH occurrence (Figure 1.1).

1.2 PATHOGENESIS OF INCISIONAL HERNIA

All wounds, including fascial wounds, follow a predictable pattern of healing following processes as previously mentioned; any factor that impedes normal healing will result in wound failure. Prolonged inflammatory phase, as is seen with surgical site infection, will delay the progression into the proliferative phase and imposes fascial wound on the risk of dehiscence and IH.[3, 4]

The proliferative phase starts around day 4 and takes approximately 1 week to complete the process.[7] Tissue continuity is re-established, and fibroblasts and

endothelial cells are recruited into the wound area by chemotaxis.[7] By infiltration of fibroblasts, collagen and proteoglycan synthesis begins. Because collagen is a significant component of the extra-cellular matrix, factors that impair collagen synthesis (e.g., nutrition deficiencies, smoking, etc.) will cause the failure of wound healing.[4, 5] A higher risk of hernia formation is observed in patients with extra-cellular matrix disorders e.g., Ehlers-Danlos syndrome,[8] aneurysmal diseases.[9, 10]

Although there are many types of collagen, only collagen types I and III are involved in the wound healing process.[7] The maturation phase, which is characterized by the reorganization of the matrix, involves the deposition of new collagen and the breaking down of previously synthesized one by matrix metalloproteinases. Collagen type III, which deposits early in the wound, will be replaced by mature collagen type I. Researches linked collagen and proteinase metabolism to hernia formation[11, 12], which found that incremental collagen type III/I ratio and matrix metalloproteinases activity were observed in hernia tissues.

Early wound failure (i.e., fascial dehiscence) is also an important risk of subsequent IH. The study of Pollock and Evans[13] in 1989 demonstrated that most of the IHs were predetermined by dehiscence, which occurred within 1 month after laparotomy. During the early period of healing, wound strength depends totally on sutures, thus a surgical technique is a critical factor that affects IH formation.

1.3 MAGNITUDE OF THE PROBLEM

Operations were performed on approximately 234 million cases per year globally.[14] Almost 14 million operations were gastrointestinal tract diseases,[15] of which were accessed via an abdominal incision. IH could occur after abdominal surgery about 5% to 20%, and even as high as 30% in high-risk patients.[16]

IH can be asymptomatic, however, serious complications could happen. If internal organs were trapped in the hernia sac, organ strangulation would be inevitable. A long-standing IH can progress to be a huge sac and lead to a condition known as the loss of domain. Treatment and management of his condition are challenged because reducing the hernia content back into the relatively small intra-abdominal space is very complicated.

Once IH is repaired either open or laparoscopic approach, a recurrence is predicted at about 7.3% to 21.1%.[17-20] During 2007-2011, around 470,000 IH repair cases were performed in the United States.[21] Significant monetary use for reconstruction of the abdominal wall defect has been estimated. The median cost for inpatient IH repair was 10,845$ in the US during 2008-2015.[22] One case of IH repair could cost approximately 6,451€ in France (2011), and the implementation of the hernia prevention techniques could save the national cost of around 4 million Euros.[23]

1.4 INCISIONAL HERNIA PREVENTION

Several interventions have been studied and applied in an attempt to prevent hernia occurrence. Apart from risk optimization, improving the fascial closure technique is another key strategy to achieve this goal. For instance, the continuous suture was associated with lower rates of IH when compared with interrupted sutures.[24] Rapidly absorbable sutures may cause a higher risk of hernia but slowly absorbable sutures did not when compared with non-absorbable material.[25] The advantages of the slowly absorbable suture over the non-absorbable suture were associated with less wound pain and wound sinus formation.[25] Therefore, continuous closure with slowly absorbable materials should be recommended as a standard technique for abdominal wall closure in the European Hernia Society guideline.[26]

Adding a small tissue bite technique to continuous suturing could reduce IH from 18% to 5.6% referencing to Millbourn et al.[27] This technique can be performed by placing stitches at less than 10 mm from the wound edge and including only the aponeurosis. In addition, the suture length (SL) to wound length (WL) ratio of lower than 4 is associated with a higher IH incidence with an odds ratio (OR) of 3.73 (95% confidence interval (CI): 1.36, 10.26).[27] Deerenberg et al. used smaller bite closure than Millbourn's group by placing stitches at 5 mm from the wound edge and intersuture spacing of 5 mm; SL to WL ratio of higher than 4 could be ensured, and the IH rate was decreased from 21% to 13%.[28] Nevertheless, IH is still a significant problem.

Mesh implantation, introduced by Lichtenstein in the 1980s as a key component of tension-free hernia repair,[29] resulted in low hernia recurrence and became a standard practice of inguinal hernia surgery.[30, 31] Subsequently, meshes are routinely

used in all fields of abdominal wall reconstruction. Because of the proven benefit of mesh placement in many situations, mesh-augmented fascia closure was introduced as a prophylactic intervention to prevent IH occurrence after abdominal surgery. Results from previous meta-analyses (MA) indicated that the immediate mesh placement in a surgical wound could result in 70% to 86% reduction of hernia risk.[32-37] In addition, cost-utility analysis has indicated the benefit of prophylactic mesh augmentation.[38]

1.5 RATIONALE OF THE STUDY

Even though the benefits of prophylactic mesh placement were confirmed in many meta-analyses,[32-37] no proper mesh positioning has been recommended. There are 15 randomized clinical trials (RCTs) that assessed the efficacy of mesh reinforcement on IH occurrence.[39-53] All studies indicated the efficacy of mesh in IH prevention with risk ratio (RR) of 0.06-0.89. In most of the studies[39-48, 50-53] compared mesh reinforcement with primary suture closure (PSC). Mesh positions, studied in those RCTs, included onlay (OM),[40, 46, 47, 51] retrorectus (RM),[41, 43, 48, 53] preperitoneal (PM),[42, 44, 45] and intraperitoneal mesh (IM) placement[39, 50, 52] (Figure 1.2). Only Jairam et al.'s RCT[49] composed of 3 intervention arms (OM versus RM versus PSC); however, OM versus RM comparison was designed to test for equivalence but failed to confirm that. Significant difference between the benefits of OM and RM was not indicated in this trial.

RCT is the best design for comparing interventions, although conducting multi-arm study is burdensome since there are more than 2 candidate mesh positions for IH prophylaxis. Estimated sample size would be large when being compared among efficacious interventions. Considering resources and budget, RCT might not be a possible option. Therefore, network meta-analysis (NMA), which allows indirect comparison among interventions and ranking them,[54] were applied in this study to identify the best mesh position for hernia prophylaxis in terms of benefits and risks. This knowledge was further used to develop an RCT protocol for studying a population whose mesh efficacy has yet to be investigated.

Among 15 available RCTs[39-53] assessing prophylactic mesh efficacy, Some RCTs studied the treatment effect in a specific type of surgery, including bariatric

surgery[39, 41, 44, 45] and aneurysm repair.[43, 46, 48, 49] However, only 4 studies reported the proportion of performed urgency/emergency surgery which ranged from 1.9% to 53%.[47, 48, 50, 53] While many elective procedures are performed via minimally invasive approach, an open incision is still useful in urgency/emergency setting. Regarding Basta et al.'s study,[5] both emergency operation and open approach were significant IH risk factors. IH incidence was 15.8% in emergency surgery versus 2.2% in elective surgery.[5] After emergency laparotomy, 17%-33% IH incidence has been reported,[55-58] and incidence could be as high as 54.3% if the operation was performed due to peritonitis.[59] In urgencies/emergencies, all negative factors could affect fascia healing simultaneously. Patients might be at a higher risk of a low perfusion state. Most of the comorbidities are unable to be optimized before surgery. In addition, most of the urgency/emergency abdominal operations would face some degree of bacterial contamination, which may cause SSI and IH subsequently.[60] Therefore, IH prevention is essential in this particular group of patients. Unfortunately, there are only 2 retrospective studies comparing mesh augmentation to conventional fascial closure in emergency conditions in which the effectiveness of prophylactic mesh was confirmed without a significant increase in risks.[56, 57] Given the lack of strong evidence of prophylactic mesh's benefits and risks in this population, RCT is required to fill this gap of knowledge. The RCT protocol of the ongoing trial targeted urgency/emergency patients was proposed in this study.

This study would indicate the best mesh technique used in IH prevention and develop a trial protocol that would close the gap of knowledge. Altogether, this study would globally and locally impact clinical practice.

1.6 RESEARCH QUESTION

- What is the best mesh technique for IH prevention in patients undergoing abdominal surgery via midline incision?
- What should the trial protocol be to fill the gap of knowledge in IH prevention in an ideal situation?

1.7 RESEARCH OBJECTIVES

- To compare IH occurrence and complication rates among prophylactic mesh techniques
- To identify the best mesh technique for IH prevention
- To develop a trial protocol to fill the knowledge gap in an ideal situation

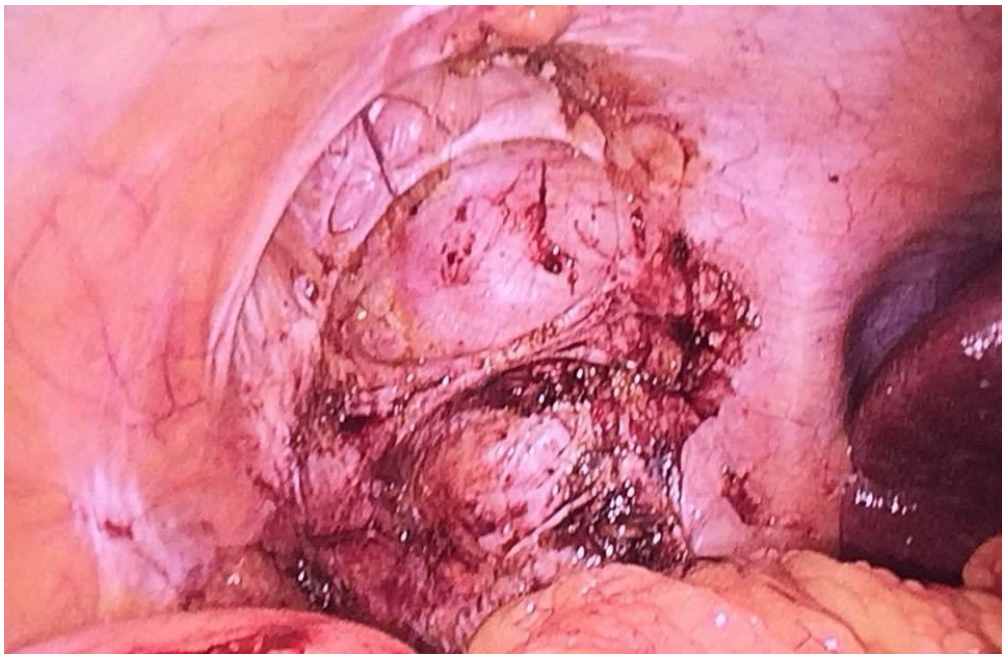


Figure 1.1 Intraperitoneal view of incisional hernia

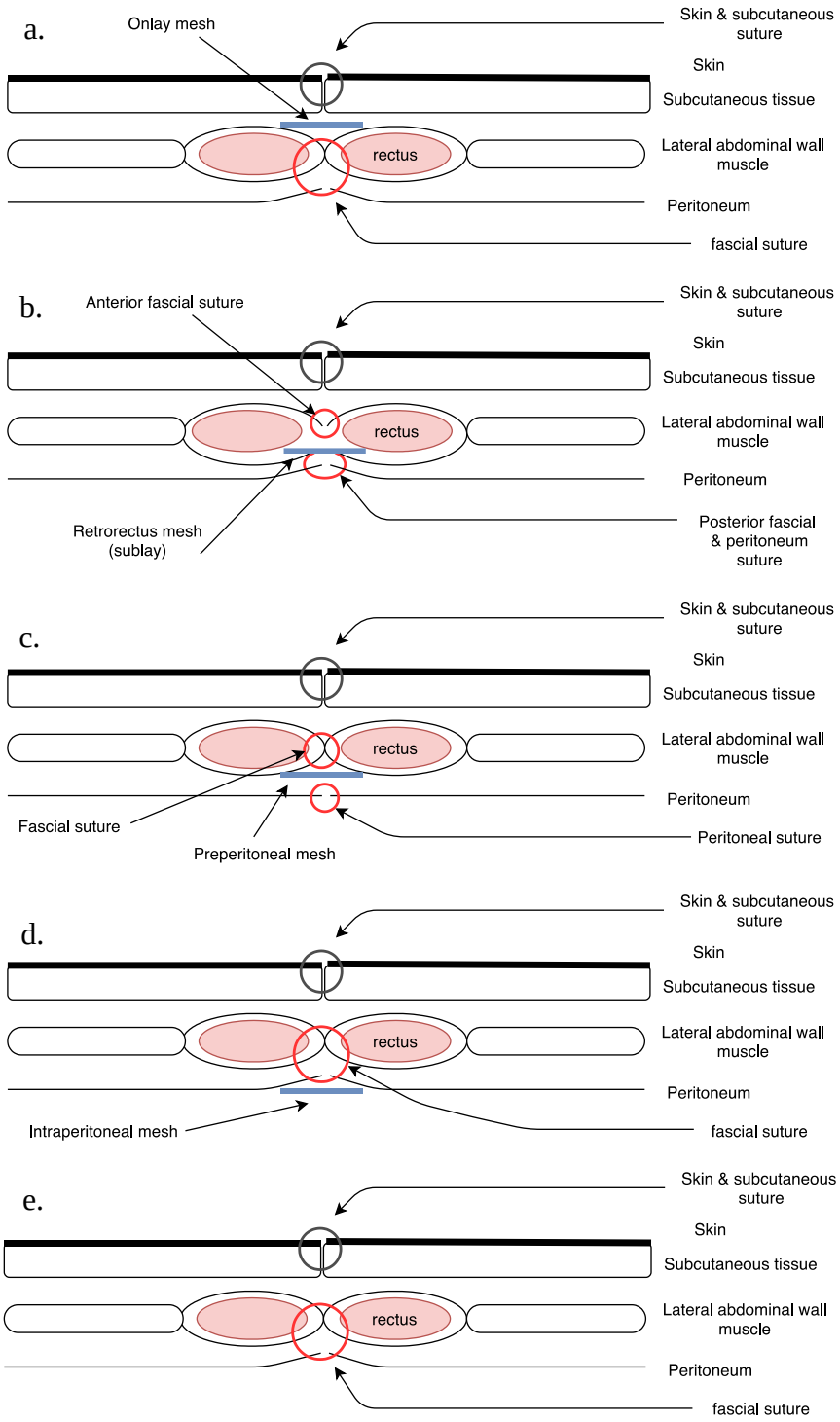


Figure 1.2 Diagram demonstrates fascial closure technique a) onlay mesh b) retrorectus mesh c) preperitoneal mesh d) intraperitoneal mesh and e) primary suture closure.

CHAPTER II
MESH POSITION FOR INCISIONAL HERNIA PROPHYLAXIS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

All previous meta-analyses have confirmed the efficacy of prophylactic mesh in IH prevention;[32-37] however, an appropriate mesh position remains unanswered. Therefore, we conducted a systematic review and NMA to find the most suitable technique in terms of both benefits and risks. Review protocol followed PRISMA guideline[61] and was registered at PROSPERO (CRD42019145939).

2.1 METHODS

2.1.1 Search strategy and studies selection

Scopus and Medline (via PubMed) were our primary databases. Searching included all studies up to December 2019 without language limitation. Our search terms were constructed based on keywords as follows: midline laparotomy, mesh, prophylaxis, incisional hernia, wound infection, and seroma. The keywords and their synonyms were combined to become a search string for use in search engines (Table 2.1). RCTs conducted in adults who underwent surgery via mainly median abdominal incision were eligible if they compared at least one pair of primary fascia closure techniques, i.e., OM, RM, PM, IM, and PSC. The primary outcome was IH, whereas secondary outcomes included wound infection, seroma, hematoma, fascial dehiscence, chronic pain, abdominal closure time, and mesh removal rates. Cochrane Central databases, ClinicalTrials.gov, and all reference lists of included studies were also thoroughly checked for potentially eligible studies.

2.1.2 Data extraction and risk of bias assessment

Two reviewers extracted data and assessed the risk of bias independently using pre-specified data extraction form (Appendix A). The extracted data included sample size, percentage of midline incisions, mean age, sex, body mass index, comorbidities, smoking status, physical status, history of previous surgery, type of surgery, wound classification, mesh type, mesh fixation, and mean follow-up time. Outcome data were extracted as a cross-tabulated format with their interventions. The Revised Cochrane risk-of-bias tool for RCT[62] was used to assess the risk of bias (RoB) of each study. Any disagreement was solved by consensus between two reviewers or by the third reviewer's judgment.

2.1.3 Statistical analysis

Both direct and network meta-analyses (DMAs and NMAs) were performed in this study. STATA version 16 was used for all analyses.

For DMAs, pooled effect sizes (RR or mean difference (MD)) were estimated using a random-effect model if heterogeneity was indicated by the Cochrane Q test p-value of less than 0.1 or I^2 of more than 25%. The fix-effect model was used instead if there was no evidence of heterogeneity. Meta-regression was performed by fitting each study-level co-variable one by one to explore the source of heterogeneity. Publication bias was assessed using both Egger's test and funnel plot. P-value of less than 0.05 or asymmetry on this plot suggested further exploration by a contour-enhanced funnel plot.

For NMAs, we started with coding for each intervention. Networks of the interventions were constructed separately for each outcome. Multivariate meta-analysis was used for pooling the relative treatment effect (i.e., lnRRs or risk difference (RD)). Treatment contrasts for each pair of interventions were estimated. The surface under the cumulative ranking curve (SUCRA) was used for ranking all interventions in terms of being the best in lowering each outcome (i.e., IH, wound infection, seroma, hematoma, and dehiscence). SUCRAs of benefit (lowering IH occurrence) of each intervention were plotted against SUCRAs of risks (i.e., wound infection, seroma, and hematoma) for risk-benefit assessment. By using a design-by-treatment model, the consistency assumption was examined. Publication bias was checked by a comparison-adjusted

funnel plot. The number needed to treat (NNT), or harm (NNH) was also calculated from pooled RDs according to each outcome.

2.2 RESULTS

2.2.1 Characteristics of included studies

Twenty studies[39-53, 63-67] were eligible after screening from 4,833 studies, which were identified from databases (Figure 2.1). A total of 2,716 subjects were included. The mean age ranged from 36.5 to 74.3 years. The percentage of male sex ranged from 20.3% to 92.1%. The follow-up period ranged from 1 to 61.7 months. Four eligible RCTs[39, 41, 44, 45] were specific to open bariatric surgery, whereas 5 studies[43, 46, 48, 49, 65] were conducted in aortic aneurysm subjects. The rest of the studies included colorectal or nonspecific abdominal surgery (Table 2.2). However, rates of emergency/urgency operation were reported in only 4 studies,[47, 48, 50, 53] ranging from 1.9% to 53%.

Among 20 RCTs, 15 studies involved nonabsorbable mesh.[40-44, 47-52, 64-67] Three absorbable mesh[39, 53, 63], and two biological mesh studies[45, 46] were the rest. OM, RM, PM, and IM were compared to PSC in 7, 4, 3, and 4 studies, respectively. There were two studies[49, 65] consisted of 3 intervention arms, which included OM, RM, and PSC. IH was the primary outcome in 15 studies. Wound infection, seroma, hematoma, and fascial dehiscence were reported in 15, 15, 9, and 11 studies, respectively (Table 2.2). Unfortunately, sparse data of chronic pain (N = 5) and abdominal wall closure time (N = 2) precluded separate pooling for each mesh intervention. Mesh removal rates were reported in 5 studies. RoB was judged as raising some concern in the majority of studies. In other words, only 4 and 1 studies were at low and high RoB, respectively (Figure 2.2).

2.2.2 Direct meta-analysis

All mesh techniques had demonstrated efficacy for IH prevention. Pooled RRs (95%CI) of IH occurrence of OM, RM, PM, and IM versus PSC were 0.25 (0.12, 0.50), 0.33 (0.16, 0.68), 0.43 (0.12, 1.59), and 0.61 (0.42, 0.88), respectively (Figure

2.3). For other outcomes including wound infection, seroma, hematoma, and dehiscence, most of the treatment effects did not indicate a significant difference between mesh placement and PSC, except seroma occurrence, which was higher in OM when compared with PSC [RR (95% CI: 2.13 (1.42, 3.18)], see Figure 2.4, Figure 2.5, Figure 2.6, and Figure 2.7.

Due to insufficient data for separate pooling, we combined all mesh techniques and compared them with PSC for chronic pain. This analysis resulted in a pooled RR (95% CI) of 1.48 (0.96, 2.29), which was not significant (Figure 2.8). Abdominal wall closure time was reported in only 2 studies[48, 53] of RM versus PSC. RM spent 11.27 (95% CI: 3.56, 18.98) minutes longer than PSC, which was unconvincing to be clinically significant (Figure 2.9). The pooled rate of mesh removal (95% CI) was 3.7% (2.3%, 5.2%).

Moderate heterogeneity, which was indicated by I^2 of 39.4% to 56.2%, was observed from a pooling of IH outcomes. Heterogeneity ranged from 0% to 64.5% in other outcomes (Table 2.3). We explored the source of heterogeneity by fitting co-variables, i.e., age, percentage of male, and type of operation, once at a time in meta-regression. However, only the heterogeneity of the IH outcome of IM versus PSC and the dehiscence outcome of OM versus PSC can be explained by these co-variables (Table 2.4).

Asymmetrical funnel plots were observed for the pooling of IH outcome of RM versus PSC and PM versus PSC corresponding with Egger's test p-values of 0.006 and 0.049, respectively (Figure 2.10 and Table 2.3). Subsequently, contour-enhanced funnel plots were constructed for these comparisons. The plot indicated the publication bias of RM versus PSC comparison, whereas heterogeneity could be a cause of asymmetry of PM versus PSC (Figure 2.11). None of the other outcome comparisons resulted in an asymmetrical funnel plot (Figure 2.12, Figure 2.13, Figure 2.14, Figure 2.15, and Figure 2.16)

2.2.3 Network meta-analysis

Extracted data were provided in Table 2.5. Network configurations were displayed in Figure 2.17. The efficacy of IH prevention was demonstrated in all mesh techniques, but only the effects of OM and RM reached statistical significance. Pooled

RRs (95% CI) were 0.24 (0.12, 0.46), 0.32 (0.16, 0.66), 0.58 (0.23, 1.47), and 0.58 (0.32, 1.06) for OM, RM, PM, and IM versus PSC, respectively. Most of the comparisons between mesh techniques did not result in significant RR, except OM versus IM [RR (95% CI): 0.41 (0.17, 0.98)]. All mesh techniques demonstrated a trend of increasing risk of wound infection and hematoma, but these were not statistically significant. OM caused a significantly higher risk of seroma than PSC with the pooled RR (95% CI) of 2.21 (1.44, 3.39). Other mesh techniques also increased the risk of seroma, but none of them were significant. Even though all mesh placements, except for RM, could prevent fascial dehiscence, their pooled effects were not statistically significant (Table 2.6). OM, RM, IM, and PM yielded NNTs of 4, 5, 8, and 10 for hernia prevention, respectively (Table 2.7). The first rank indicated by SUCRA belonged to OM for IH prophylaxis. The second, third, and fourth ranks were RM, PM, and IM, respectively. Nevertheless, RM was better than OM regarding wound infection and seroma (Table 2.8 and Figure 2.18). OM, IM, and PM could prevent fascial dehiscence with NNTs of 54, 147, and 400, respectively, but this effect was not observed in RM (Table 2.7).

No inconsistency, in any network, was detected by a global test. Comparison-adjusted funnel plots displayed asymmetry for IH, but not for other outcomes (Figure 2.19). A sensitivity analysis was performed, excluding studies that showed variance higher than the 75th percentile. Results were robust with pooled RRs (95% CI) of 0.28 (0.15, 0.52), 0.41 (0.22, 0.78), 0.66 (0.26, 1.65), and 0.65 (0.35, 1.19) for OM, RM, PM, and IM, respectively.

2.2.4 Sensitivity analysis

After the exclusion of biologic/absorbable mesh studies, PM became the best ranked for IH prophylaxis. Pooled RRs (95% CI) of 0.25 (0.13, 0.50), 0.34 (0.15, 0.78), 0.19 (0.04, 0.91), and 0.47 (0.22, 1.01) belonged to OM, RM, PM, and IM versus PSC, respectively (Table 2.9). Nevertheless, the estimated treatment effect of PM versus PSC was imprecise because the comparison consisted of only 2 studies. Moreover, these studies came from the same institute in which the estimate might be a reflection of the institutional effect.

Results did not be substantially altered by the exclusion of studies that mixed midline and non-midline incisions. Pooled RRs (95% CI) of OM, RM, PM, and

IM versus PSC were 0.24 (0.12, 0.49), 0.32 (0.15, 0.67), 0.56 (0.21, 1.50), and 0.65 (0.31, 1.34), respectively (Table 2.10). OM, followed by RM, was the best rank for IH prophylaxis even though the study rated as high RoB was excluded (Table 2.11).

2.3 DISCUSSION

NMA was performed to compare mesh-augmented fascial closure techniques and PSC using data from 20 RCTs. This study is the first MA comparing among each other mesh positioning. Results from NMA indicated that only OM and RM significantly lowered IH occurrence compared with PSC. From OM versus RM comparison, OM was better than RM for IH prevention but the effect size was not statistically significant.

Findings from this study contradicted previous evidence of IH repair. When mesh is used in IH treatment, RM is associated with lower hernia recurrence.[68, 69] However, OM yielded lower hernia occurrence than RM when performed in prophylaxis indication. This astonishing result still required explanation from a further study.

Most of the mesh techniques seemed to increase wound complication rates; however, results were not statistically significant except in seroma outcomes. A significantly higher rate of seroma was observed in OM when compared with RM and PSC. Differences in tissue plane dissection (i.e., subcutaneous plane in OM and retromuscular plane in RM) might be a reason for this finding. Even though OM better prevented IH than RM, RM would be a better option considering safety. Therefore, which mesh technique (i.e., OM or RM) is the most suitable for IH prevention is still debatable.

Wound infection rates were not significantly increased by any mesh placement. Again, OM was associated with a 32% higher rate of infection compared with RM; however, it was not significant. Withal, RM should be better selected in a contaminated environment. Results from this study should be interpreted with caution because only a few included RCTs had a substantial number of contaminated wounds. RCT investigating the effect of prophylactic mesh in a contaminated environment is required.

Fascial dehiscence leads to IH. Even though a trend of dehiscence reduction was observed from OM, PM, and IM, no mesh technique demonstrated significant dehiscence prevention in this study. We have defined dehiscence per the original studies' definition which was not clear whether it occurred at superficial or fascial levels. This would leave some questions in interpretation.

Chronic pain is also important but is not always reported in studies. As a result, we could not investigate the effect of mesh in chronic pain outcomes stratified by mesh position. Mesh was not significantly associated with chronic pain in DMA. We can investigate the timeliness of closure only in RM in which RM required approximately 11 minutes more than PSC (unlikely to have clinically meaningful). Due to data limitations, we could not assess for other rare adverse events (e.g., fistula, wound sinus, and mesh migration).

Sensitivity analyses were also performed in this study by excluding studies that were characterized as follows: involving absorbable/biologic mesh use, mixing midline and non-midline incisions, and having high RoB. Results of hernia prevention were robust, especially in OM and RM.

Nowadays, open laparotomy is less frequently performed in the elective setting, whereas it is still a standard approach for urgency/emergency operations. According to our systematic review, evidence of prophylactic mesh efficacy is lack in patients undergoing urgency/emergency surgery. A meta-analysis of prophylactic mesh in emergency surgery,[70] which included only 2 non-RCTs,[56, 57] also concluded that better evidence is required.

Even though this study is the only study that compared available mesh positioning. Some limitation is inevitable. First, some comparisons (i.e., PM versus PSC and IM versus PSC) consisted of few studies which would make PM and IM's effect size imprecise. When new studies of PM and IM are available, this NMA should be updated. Second, heterogeneities were even observed but cannot be adjusted in meta-regression due to the scarcity of covariate data or agreement in reporting. Finally, publication bias was suggested in some analyses which might undermine the certainty of synthesized evidence.

2.4 CONCLUSION

OM and RM were efficacious in IH prophylaxis for patients undergoing midline laparotomy. However, it is still difficult to conclude which technique should be recommended considering both benefits and risks. Additional analysis technique is required to make a conclusion.

Due to a limit number of included studies, this NMA needs update when more trials are published. Regarding systematic review, evidence of prophylactic mesh in urgency/emergency surgery is lacking, and this gap should be filled by further RCT.

Table 2.1 Search terms and strategies

Database	Search term
Medline (via PubMed)	(((open OR abdominal) AND surgery) OR laparotomies) AND ((mesh* OR prosthe* OR bioprosthe* OR endoprosthe*) AND (prophyla*OR prevent*)) AND (((incision* OR postoperative OR ventral) AND hernia*) OR seromas OR (“wound infection” OR “surgical site infection” OR “mesh infection”))
Scopus	(((open OR abdomen) AND surgery) OR laparotomy) AND (((TITLE-ABS-KEY(mesh) OR TITLE-ABS-KEY(*prosthe*)) AND (prophyla* OR prevent*)) AND ((TITLE-ABS-KEY(“incision* hernia*”) OR TITLE-ABS-KEY(“postoperative hernia*) OR TITLE-ABS-KEY(“ventral hernia*)) OR seroma* OR ("wound infection" OR "surgical site infection" OR "mesh infection")) AND ((LIMIT-TO(DOCTYPE, “ar”) OR LIMIT-TO(DOCTYPE, “re”) OR LIMIT-TO(DOCTYPE, “cp”))

Table 2.2 Characteristics of included studies

Study	Mesh positioning technique	Mesh type	% Midline incision	Surgery type	Age (Mean±SD)	% Male	BMI (Mean±SD)	Outcomes
Pans (1998)	Intraperitoneal	Polyglactin	100	Bariatric	36.5	24.7	43.8	Hernia, Wound infection
Peña (2003)	Onlay	Polypropylene	73	General	64.3±10.3	67	NR	Hernia, Wound infection, Seroma, Hematoma, Chronic pain
Strzelczyk (2006)	Retrorectus	Polypropylene	100	Bariatric	39.1	63.5	46.5	Hernia, Seroma, Dehiscence
Portilla (2008)	Onlay	Polyglycolic	86.7	Colorectal	64±17.3	55.9	NR	Wound infection, Seroma, Hematoma, Dehiscence
El-khadrawy (2009)	Preperitoneal	Polypropylene	100	General	47.7±14.8	45	NR	Hernia, Wound infection, Seroma, Hematoma, Dehiscence, Chronic pain
Bevis (2010)	Retrorectus	Polypropylene	100	Aneurysm	73±7.5	91	NR	Hernia, Wound infection, Seroma
Abo-ryia (2013)	Preperitoneal	Polypropylene	100	Bariatric	37.7	20.3	51.8	Hernia, Wound infection, Seroma, Dehiscence
Sarr (2014)	Preperitoneal	Porcine intestinal submucosa	100	Bariatric	44.9	20.5	48.2	Hernia, Wound infection, Seroma, Dehiscence, Chronic pain
Bali (2015)	Onlay	Bovine pericardium	100	Aneurysm	74.3±5.8	90	NR	Hernia, Seroma
García-ureña (2015)	Onlay	Polypropylene	100	Colorectal	63.5	59.8	NR	Hernia, Wound infection, Seroma, Dehiscence
Muysoms (2016)	Retrorectus	Polypropylene	100	Aneurysm	72	92.1	NR	Hernia, Wound infection, Seroma, Hematoma, Dehiscence, Chronic pain

Table 2.2 Characteristics of included studies (Cont.)

Study	Mesh positioning technique	Mesh type	% Midline incision	Surgery type	Age (Mean±SD)	% Male	BMI (Mean±SD)	Outcomes
Jairam (2017) [Timmermans (2015)]	Onlay & Retrorectus	Polypropylene	100	Aneurysm	64.5±11.2	60.8	30.6±5.3	Hernia, Wound infection, Seroma, Hematoma, Dehiscence
Glauser (2019) [Brosi (2018)]	Intraperitoneal	Polyester	100	General	62.5	42	25.4	Hernia, Wound infection, Seroma, Hematoma, Dehiscence
Caro-tarrago (2019) [Caro-tarrago (2014)]	Onlay	Polypropylene	100	General	65.8	56.3	NR	Hernia, Wound infection, Seroma, Hematoma
Kohler (2019)	Intraperitoneal	Polyvinylidene fluoride	40.7	General	64.2±11.1	68	27.1	Hernia, Wound infection, Hematoma, Chronic pain
Pizza (2019)	Retrorectus	Gore® Bio-A®	100	General	57±16.5	50	27.5±5.3	Hernia, Wound infection, Seroma, Hematoma, Dehiscence
Lima (2019)	Onlay	Polypropylene	100	General	63.3	57.4	25.5	Wound infection, Seroma, Hematoma, Dehiscence

NR not reported

Table 2.3 Heterogeneity and publication bias assessments for direct meta-analyses

DMA	Incisional hernia		Wound infection		Seroma		Hematoma		Dehiscence	
	I^2 (%)	Egger's test p-value	I^2 (%)	Egger's test p-value	I^2 (%)	Egger's test p-value	I^2 (%)	Egger's test p-value	I^2 (%)	Egger's test p-value
OM vs PSC	50.4	0.061	59.8	0.855	20.4	0.213	23.9	0.179	51.8	0.089
RM vs PSC	48.9	0.006	0	0.133	0	0.408	19.4	0.979	0	0.373
PM vs PSC	56.2	0.049	64.5	0.021	37.6	0.090	N/A	N/A	0.9	0.189
IM vs PSC	39.4	0.408	0	0.161	N/A	N/A	0	0.940	N/A	N/A

DMA, direct meta-analysis; IM, intraperitoneal mesh; N/A, not available; OM, onlay mesh; PM, preperitoneal mesh; PSC, primary suture closure; and RM, retrorectus mesh

Table 2.4 Heterogeneity exploration by adjusting of covariables in meta-regression

Outcome/Comparison	Adjusting covariable							
	None		Age		Percent male		Type of operation*	
	Number of studies	I^2 (%)	Number of studies	I^2 (%)	Number of studies	I^2 (%)	Number of studies	I^2 (%)
Incisional hernia								
OM vs PSC	5	50.4	5	41.7	5	62.6	5	40.2
RM vs PSC	5	48.9	5	60.4	5	55.7	5	65.4
PM vs PSC	3	56.2	3	53.8	3	74.8	3	74.6
IM vs PSC	3	39.4	3	0	3	0	3	0
Wound infection								
OM vs PSC	6	59.8	6	67.5	6	67.8	6	36.2
PM vs PSC	3	64.5	3	81.2	3	64.8	3	64.1
Seroma								
PM vs PSC	3	37.6	3	65.4	3	67.2	3	67.1
Dehiscence								
OM vs PSC	4	51.8	4	44.9	4	0	4	30.9

* Type of operation was defined as follows: aneurysm repair, bariatric surgery, and other abdominal operations

IM, intraperitoneal mesh; OM, onlay mesh; PM, preperitoneal mesh; PSC, primary suture closure; and RM, retrorectus mesh

Table 2.5 Summary data used in network meta-analysis by comparisons and outcomes

Author (Year)	Intervention	Incisional hernia		Wound infection		Seroma		Hematoma		Dehiscence	
		N	Event (n)	N	Event (n)	N	Event (n)	N	Event (n)	N	Event (n)
Peña (2003)	OM	44	0	44	1	44	1	44	3		
	PSC	44	5	44	1	44	3	44	2		
Portilla (2008)	OM			71	3	71	8	71	0	71	1
	PSC			72	2	72	5	72	2	72	4
Caro-tarrago (2014)	OM			80	5	80	23	80	1		
	PSC			80	6	80	9	80	3		
Bali (2015)	OM	20	0			20	2				
	PSC	20	6			20	1				
García-ureña (2015)	OM	53	6	53	10	53	7			53	2
	PSC	54	17	54	18	54	7			54	2
Caro-tarrago (2019)	OM	80	4								
	PSC	80	37								
Lima (2019)	OM			63	13	63	12	63	1	63	0
	PSC			52	4	52	3	52	1	52	7
Strzelczyk (2006)	RM	36	0			36	5			36	0
	PSC	38	8			38	4			38	0
Bevis (2010)	RM	37	5	40	2	40	2				
	PSC	43	16	45	2	45	0				
Muysoms (2016)	RM	56	0	56	1	56	2	56	2	56	1
	PSC	58	16	58	3	58	0	58	0	58	0
Pizza (2019)	RM	45	3	50	3	50	2	50	1	50	0
	PSC	47	11	50	3	50	3	50	2	50	0
Ei-khadrawy (2009)	PM	20	1	20	2	20	4			20	1
	PSC	20	3	20	4	20	3			20	3
Abo-ryia (2013)	PM	32	1	32	5	32	6			32	1
	PSC	32	9	32	5	32	5			32	2
Sarr (2014)	PM	185	32	185	22	185	9			185	4
	PSC	195	38	195	7	195	1			195	2
Pans (1998)	IM	144	33	144	5						
	PSC	144	41	144	4						
Brosi (2018)	IM			131	4	131	2	131	3	131	2
	PSC			136	1	136	2	136	3	136	3

Table 2.5 Summary data used in network meta-analysis by comparisons and outcomes (Cont.)

Author (Year)	Intervention	Incisional hernia		Wound infection		Seroma		Hematoma		Dehiscence	
		N	Event (n)	N	Event (n)	N	Event (n)	N	Event (n)	N	Event (n)
Glauser (2019)	IM	95	26								
	PSC	88	46								
Kohler (2019)	IM	69	5	61	7			69	1		
	PSC	81	15	69	10			81	1		
Timmermans (2015)	OM			188	27	188	34	188	11	188	6
	RM			185	16	185	13	185	9	185	9
	PSC			107	4	107	5	107	1	107	1
Jairam (2017)	OM	188	25								
	RM	185	34								
	PSC	107	33								

IM, intraperitoneal mesh; OM, onlay mesh; PM, preperitoneal mesh; PSC, primary suture closure; and RM, retrorectus mesh

Table 2.6 Estimation of risk ratios for each comparison and outcome in network meta-analyses

Intervention	Comparator	Incisional hernia	Wound infection	Seroma	Hematoma	Dehiscence
OM	PSC	**0.24 (0.12, 0.46)**	1.32 (0.69, 2.52)	**2.21 (1.44, 3.39)**	1.19 (0.48, 2.94)	0.64 (0.20, 2.04)
	RM	0.73 (0.34, 1.57)	1.38 (0.54, 3.50)	**2.05 (1.01, 4.15)**	1.04 (0.47, 2.31)	0.44 (0.11, 1.72)
	PM	0.41 (0.14, 1.15)	0.91 (0.29, 2.81)	1.30 (0.51, 3.36)	N/A	0.76 (0.14, 4.22)
	IM	**0.41 (0.17, 0.98)**	1.09 (0.33, 3.54)	2.13 (0.28,15.99)	1.11 (0.21, 5.75)	0.92 (0.09,9.47)
RM	PSC	**0.32 (0.16, 0.66)**	0.96 (0.40, 2.29)	1.08 (0.56, 2.07)	1.14 (0.41, 3.22)	1.44 (0.38, 5.46)
	OM	1.37 (0.64, 2.96)	0.72 (0.29, 1.84)	**0.49 (0.24, 0.99)**	0.96 (0.43, 2.13)	2.25 (0.58, 8.71)
	PM	0.56 (0.20, 1.58)	0.66 (0.18, 2.35)	0.64 (0.23, 1.74)	N/A	1.71 (0.25,11.54)
	IM	0.56 (0.23, 1.38)	0.79 (0.21, 2.95)	1.04 (0.13, 8.27)	1.07 (0.19, 5.95)	2.07 (0.18,23.33)
PM	PSC	0.58 (0.23, 1.47)	1.46 (0.58, 3.65)	1.70 (0.75, 3.85)	N/A	0.84 (0.23, 3.13)
	OM	2.47 (0.87, 7.01)	1.10 (0.36, 3.41)	0.77 (0.30, 1.98)	N/A	1.32 (0.24, 7.32)
	RM	1.79 (0.63, 5.09)	1.52 (0.43, 5.41)	1.57 (0.57, 4.31)	N/A	0.59 (0.09, 3.96)
	IM	1.00 (0.34, 2.95)	1.20 (0.30, 4.71)	1.64 (0.19,13.81)	N/A	1.21 (0.11,13.51)
IM	PSC	0.58 (0.32, 1.06)	1.22 (0.45, 3.30)	1.04 (0.14, 7.44)	1.07 (0.27, 4.22)	0.69 (0.09, 5.21)
	OM	**2.47 (1.03, 5.93)**	0.92 (0.28, 3.00)	0.47 (0.06, 3.53)	0.90 (0.17, 4.66)	1.08 (0.11, 11.12)
	RM	1.79 (0.73, 4.43)	1.27 (0.34, 4.76)	0.96 (0.12, 7.66)	0.94 (0.17, 5.22)	0.48 (0.04, 5.42)
	PM	1.00 (0.34, 2.95)	0.84 (0.21, 3.30)	0.61 (0.07, 5.17)	N/A	0.82 (0.07, 9.16)

IM, intraperitoneal mesh; N/A, not available; OM, onlay mesh; PM, preperitoneal mesh; PSC, primary suture closure; and RM, Retrorectus mesh

Table 2.7 Pooled risk difference of interventions versus primary suture closure along with the number needed to treat/harm

Outcomes	Effect sizes	Interventions			
		OM	**RM**	**PM**	**IM**
Incisional hernia	RD	-0.2374	-0.2015	-0.1036	-0.1310
	(95% CI)	(-0.3238, -0.1510)	(-0.2885, -0.1144)	(-0.2230, 0.0158)	(-0.2407, -0.0214)
	NNT	4	5	10	8
	(95% CI)	(3, 7)	(4, 9)	(NNT 5, NNH 63)	(4, 47)
Wound infection	RD	0.0268	-0.0012	0.0556	0.0102
	(95% CI)	(-0.0123, 0.0659)	(-0.0459, 0.0436)	(-0.0164, 0.1276)	(-0.0343, 0.0546)
	NNH	37	833[a]	18	98
	(95% CI)	(NNT 81, NNH 15)	(NNT 22, NNH 23)	(NNT 61, NNH 8)	(NNT 29, NNH 18)
Seroma	RD	0.0738	0.0163	0.0425	0.0006
	(95% CI)	(0.0264, 0.1212)	(-0.0305, 0.0630)	(-0.0289, 0.1139)	(-0.0786, 0.0797)
	NNH	14	61	24	1,667
	(95% CI)	(38, 8)	(NNT 33, NNH 16)	(NNT 35, NNH 9)	(NNT 13, NNH 13)
Hematoma	RD	0.0024	0.0168	N/A	0.0015
	(95% CI)	(-0.0255, 0.0304)	(-0.0194, 0.0531)		(-0.0354, 0.0384)
	NNH	417	60	N/A	667
	(95% CI)	(NNT 39, NNH 33)	(NNT 52, NNH 19)		(NNT 28, NNH 26)
Dehiscence	RD	-0.0184	0.0108	-0.0025	-0.0068
	(95% CI)	(-0.0585, 0.0218)	(-0.0205, 0.0422)	(-0.0521, 0.0471)	(-0.0633, 0.0498)
	NNT	54	93[b]	400	147
	(95% CI)	(NNT 17, NNH 46)	(NNT 49, NNH 24)	(NNT 19, NNH 21)	(NNT 16, NNH 20)

[a] number needed to treat (NNT)

[b] number needed to harm (NNH)

IM, intraperitoneal mesh; N/A, not available; OM, onlay mesh; PM, preperitoneal mesh; RD, risk difference; and RM, retrorectus mesh.

Table 2.8 SUCRA and probability of being the best treatment in lowering each outcome

Intervention	Incisional hernia		Wound infection		Seroma		Hematoma		Dehiscence	
	SUCRA	**Pr**	**SUCRA**	**Pr**	**SUCRA**	**Pr**	**SUCRA**	**Pr**	**SUCRA**	**Pr**
OM	**92.5**	**74.6**	37.1	6.2	14.1	0.0	42.5	15.6	**70.8**	**33.8**
RM	74.7	20.8	66.1	40.5	68.1	26.6	45.9	21.3	24.7	4.4
PM	39.6	3.1	33.6	11.1	33.6	5.0	N/A	N/A	54.1	23.2
IM	38.9	1.5	44.3	20.7	59.3	41.2	51.4	34.8	57.7	35.4
PSC	4.2	0.0	**68.8**	**21.5**	**74.9**	**27.2**	**60.3**	**28.3**	42.7	3.2

IM, intraperitoneal mesh; N/A, not available; OM, onlay mesh; PM, preperitoneal mesh; Pr, probability of being the best treatment; PSC, primary suture closure; RM, retrorectus mesh; and SUCRA, surface under the cumulative ranking curve

Table 2.9 Mixed relative treatment comparisons of incisional hernia outcome between fascial closure techniques considering only the nonabsorbable mesh studies

intervention	**PSC**	1.4 (0.0)				
	OM	0.25 (0.13, 0.50)	75.7 (28.3)			
	RM	0.34 (0.15, 0.78)	1.36 (0.60, 3.05)	55.5 (8.8)		
	PM	0.19 (0.04, 0.91)	0.74 (0.13, 4.18)	0.54 (0.09, 3.27)	79.9 (60.4)	
	IM	0.47 (0.22, 1.01)	1.88 (0.69, 5.13)	1.39 (0.47, 4.13)	2.56 (0.44, 14.95)	37.5 (2.5)
comparator		**PSC**	**OM**	**RM**	**PM**	**IM**

Values off diagonal line are RRs (95%CI). In diagonal line are SUCRAs, whereas the probability of being the best treatment is shown in parentheses. IM, intraperitoneal mesh; OM, onlay mesh; PM, preperitoneal mesh; PSC, primary suture closure; and RM, retrorectus mesh

Table 2.10 Mixed relative treatment comparisons of incisional hernia outcome between fascial closure techniques excluding the studies that mixed midline and non-midline incisions

intervention	**PSC**	6.2 (0.0)				
	OM	0.24 (0.12, 0.49)	90.6 (69.1)			
	RM	0.32 (0.15, 0.67)	1.32 (0.58, 3.00)	75.4 (24.3)		
	PM	0.56 (0.21, 1.50)	2.33 (0.76, 7.11)	1.76 (0.59, 5.29)	43.0 (4.9)	
	IM	0.65 (0.31, 1.34)	2.68 (0.98, 7.33)	2.03 (0.72, 5.74)	1.15 (0.34, 3.91)	34.8 (1.7)
comparator		**PSC**	**OM**	**RM**	**PM**	**IM**

Values off diagonal line are RRs (95%CI). In diagonal line are SUCRAs, whereas the probability of being the best treatment is shown in parentheses. IM, intraperitoneal mesh; OM, onlay mesh; PM, preperitoneal mesh; PSC, primary suture closure; and RM, retrorectus mesh

Table 2.11 Mixed relative treatment comparisons of incisional hernia outcome between fascial closure techniques excluding the studies that rated as high risk of bias

intervention	**PSC**	7.8 (0.0)				
	OM	0.25 (0.13, 0.45)	94.3 (79.1)			
	RM	0.34 (0.18, 0.66)	1.39 (0.69, 2.79)	76.1 (18.9)		
	PM	0.79 (0.35, 1.78)	3.21 (1.20, 8.59)	2.31 (0.85, 6.28)	26.9 (0.7)	
	IM	0.59 (0.34, 1.01)	2.40 (1.08, 5.31)	1.72 (0.76, 3.92)	0.75 (0.28, 1.96)	44.8 (1.3)
comparator		**PSC**	**OM**	**RM**	**PM**	**IM**

Values off diagonal line are RRs (95%CI). In diagonal line are SUCRAs, whereas the probability of being the best treatment is shown in parentheses. IM, intraperitoneal mesh; OM, onlay mesh; PM, preperitoneal mesh; PSC, primary suture closure; and RM, retrorectus mesh

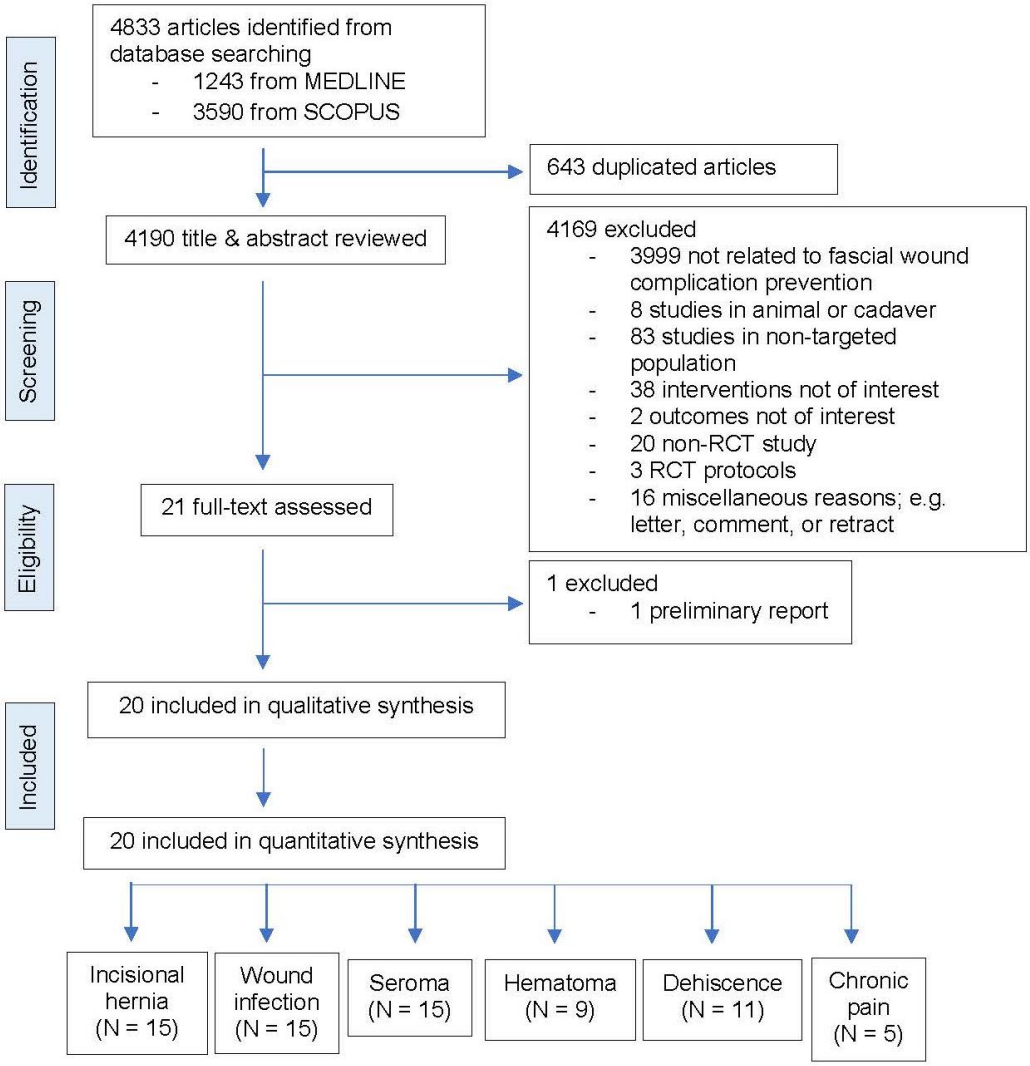


Figure 2.1 PRISMA flow diagram of included studies

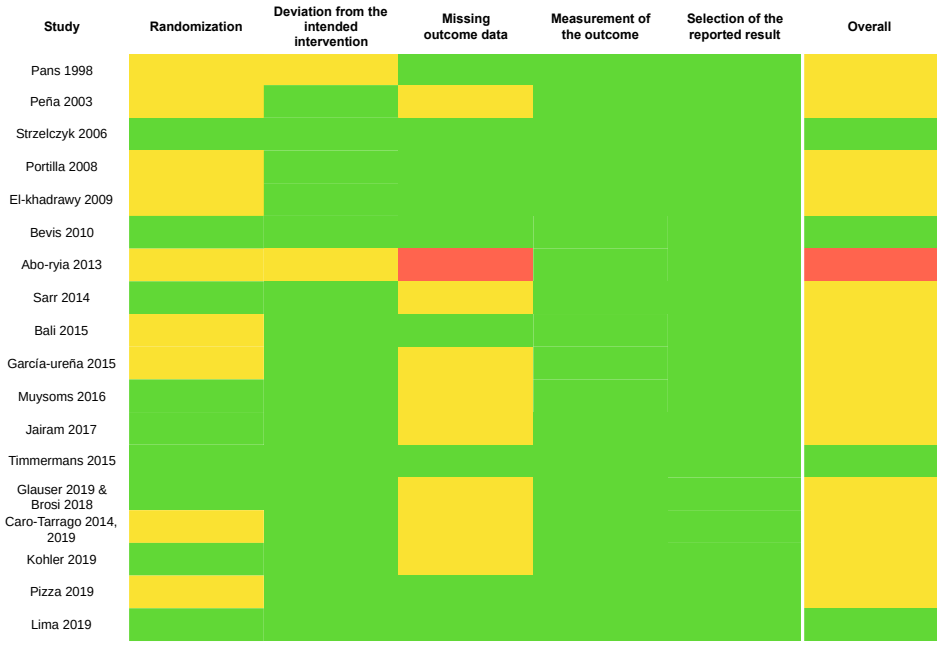
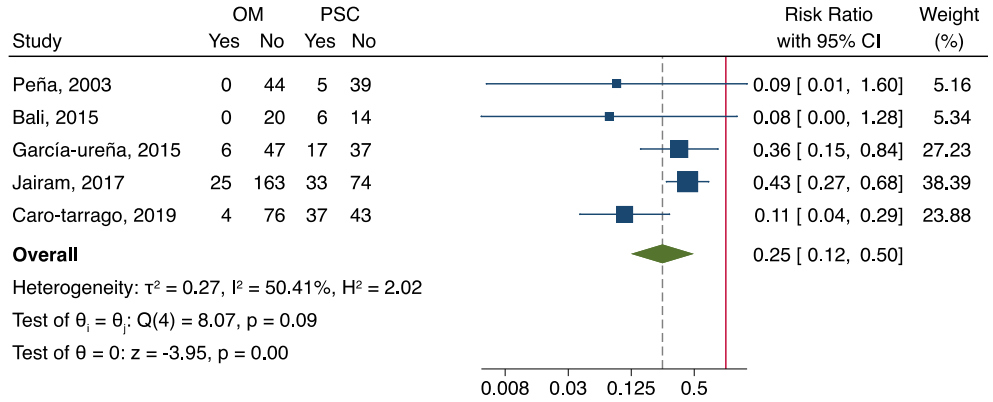


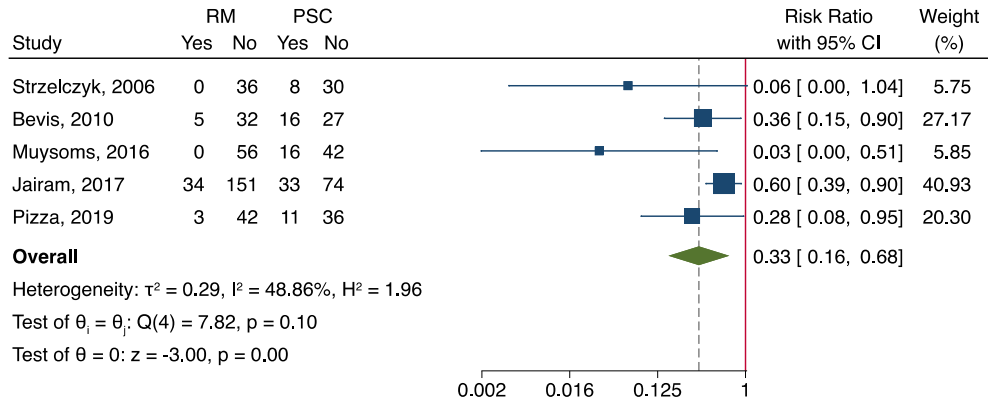
Figure 2.2 Risk of bias of the included studies assessed by the Cochrane Risk-of-Bias tool version 2

a) OM versus PSC



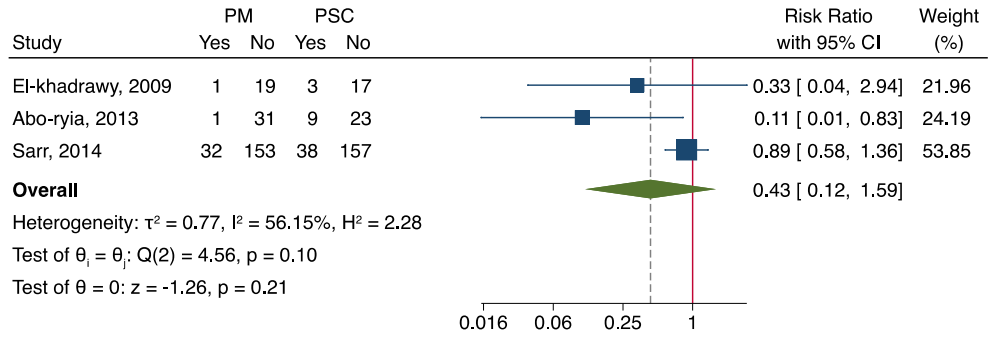
Random-effects DerSimonian-Laird model

b) RM versus PSC



Random-effects DerSimonian-Laird model

c) PM versus PSC



Random-effects DerSimonian-Laird model

Figure 2.3 Forest plots of hernia occurrence comparing between: a) onlay mesh (OM) and primary suture closure (PSC) b) retrorectus mesh (RM) and PSC c) preperitoneal mesh (PM) and PSC d) intraperitoneal mesh (IM) and PSC

d) IM versus PSC

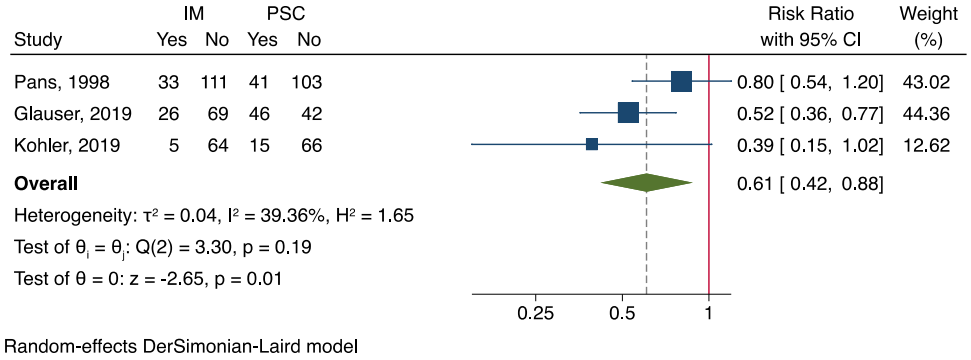
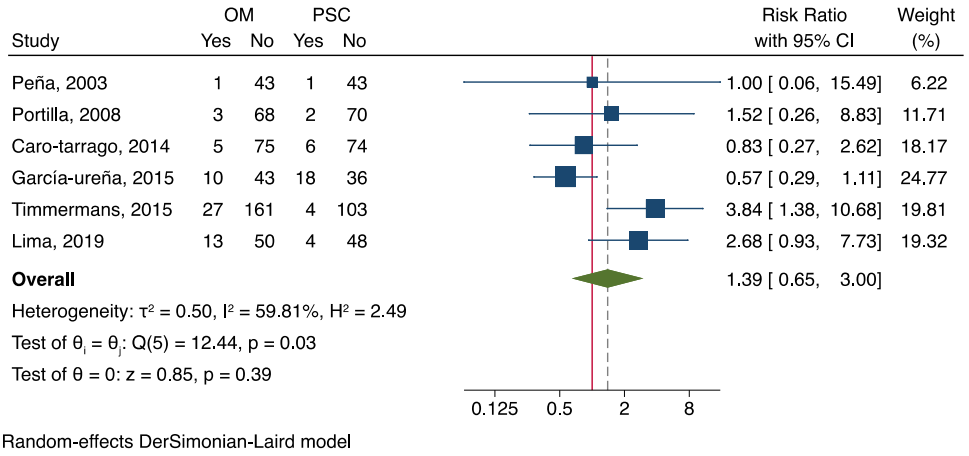
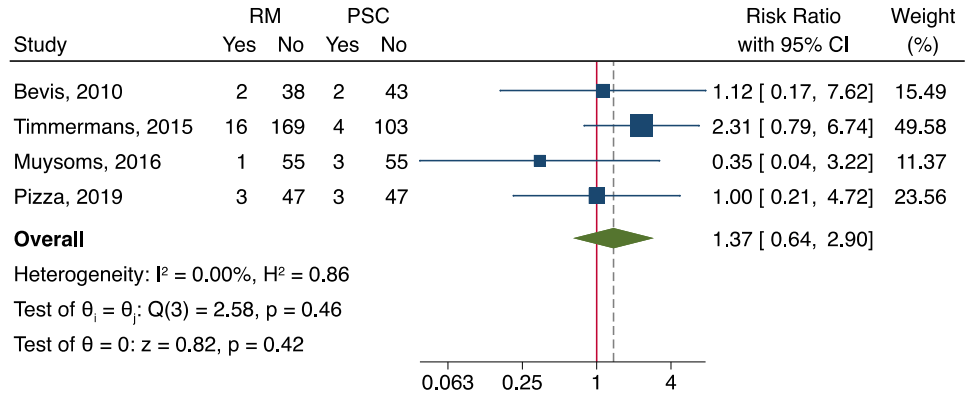


Figure 2.3 Forest plots of hernia occurrence comparing between: a) onlay mesh (OM) and primary suture closure (PSC) b) retrorectus mesh (RM) and PSC c) preperitoneal mesh (PM) and PSC d) intraperitoneal mesh (IM) and PSC (Cont.)

a) OM versus PSC



b) RM versus PSC



c) PM versus PSC

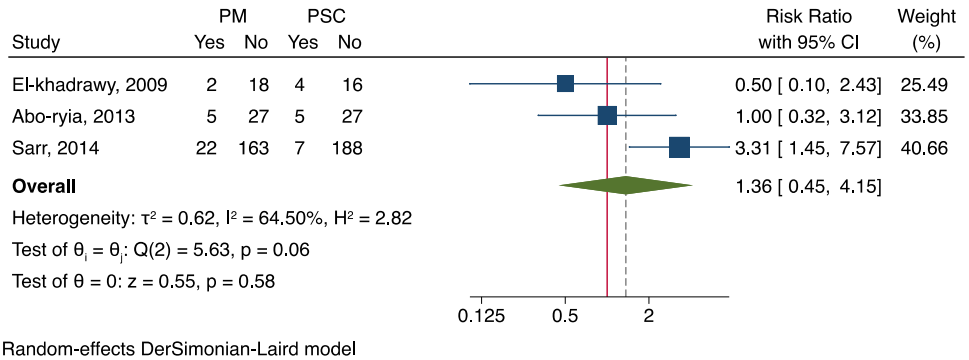


Figure 2.4 Forest plots of wound infection outcome comparing between: a) onlay mesh (OM) and primary suture closure (PSC) b) retrorectus mesh (RM) and PSC c) preperitoneal mesh (PM) and PSC d) intraperitoneal mesh (IM) and PSC

d) IM versus PSC

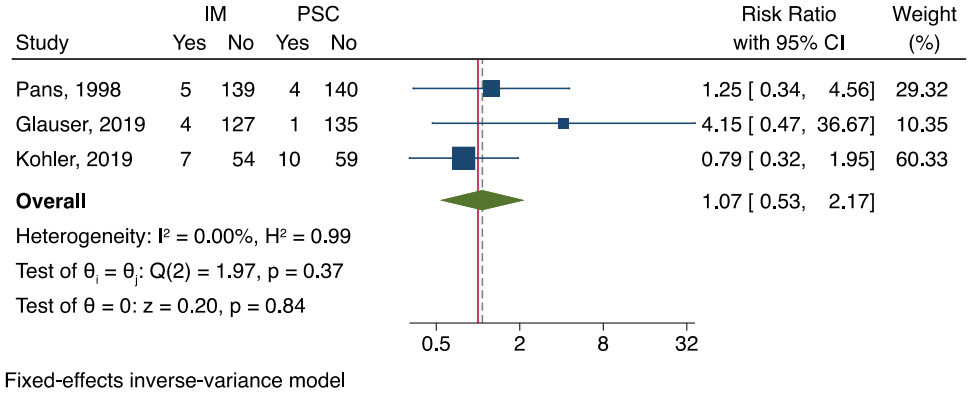
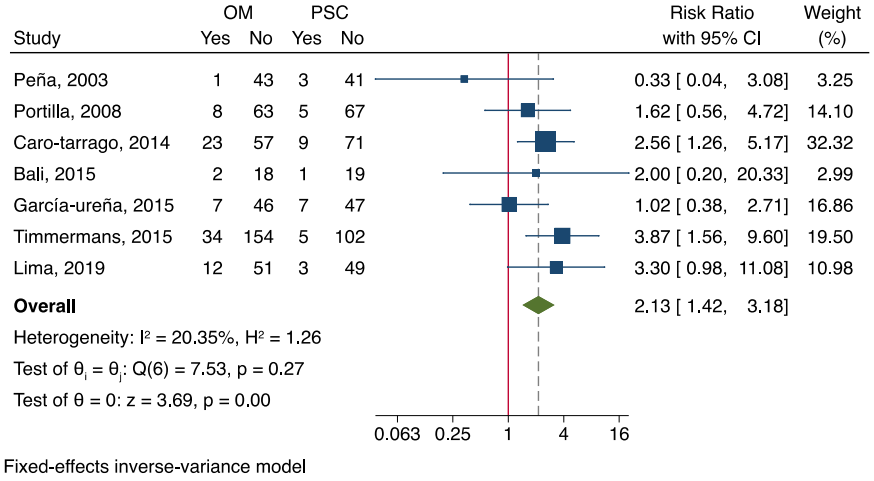


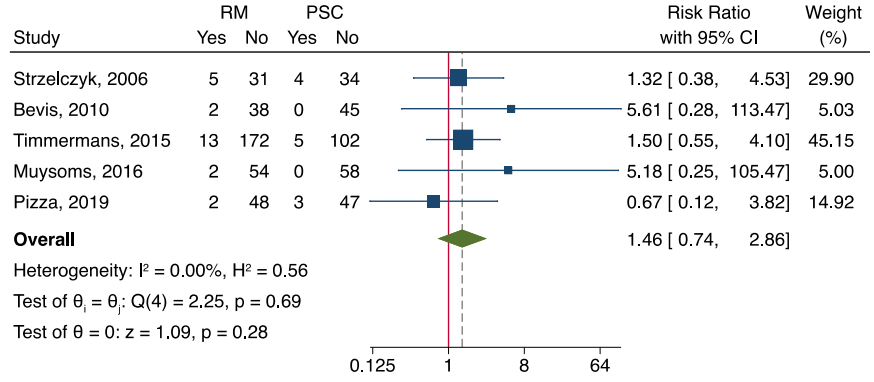
Figure 2.4 Forest plots of wound infection outcome comparing between: a) onlay mesh (OM) and primary suture closure (PSC) b) retrorectus mesh (RM) and PSC c) preperitoneal mesh (PM) and PSC d) intraperitoneal mesh (IM) and PSC (Cont.)

a) OM versus PSC



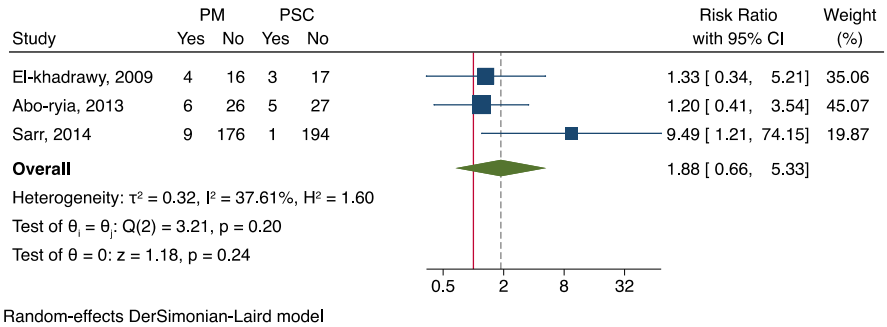
Fixed-effects inverse-variance model

b) RM versus PSC



Fixed-effects inverse-variance model

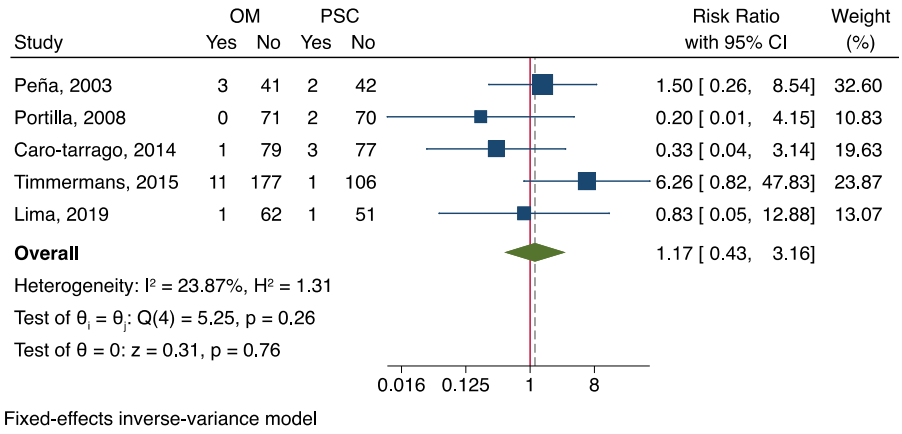
c) PM versus PSC



Random-effects DerSimonian-Laird model

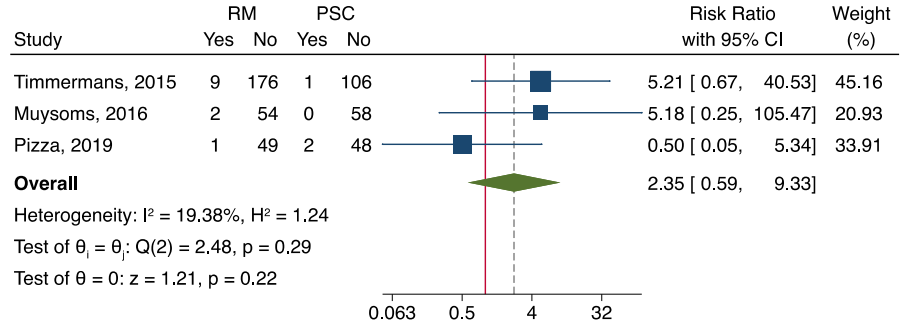
Figure 2.5 Forest plots of seroma outcome comparing between: a) onlay mesh (OM) and primary suture closure (PSC) b) retrorectus mesh (RM) and PSC c) preperitoneal mesh (PM) and PSC.

a) OM versus PSC



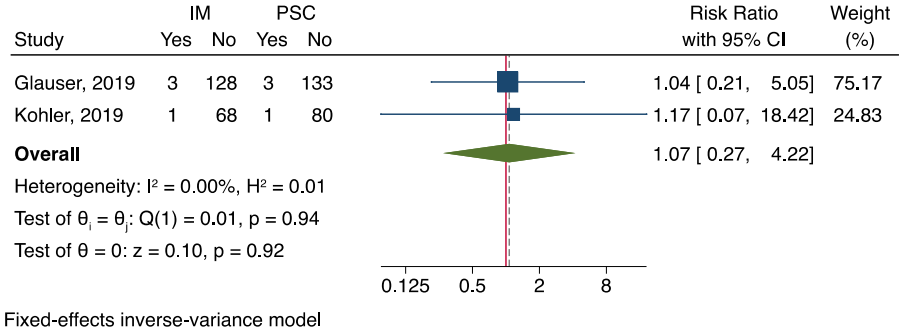
Fixed-effects inverse-variance model

b) RM versus PSC



Fixed-effects inverse-variance model

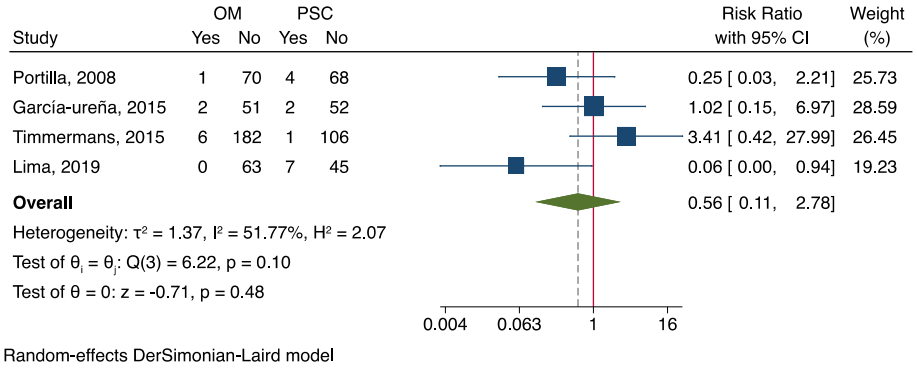
c) IM versus PSC



Fixed-effects inverse-variance model

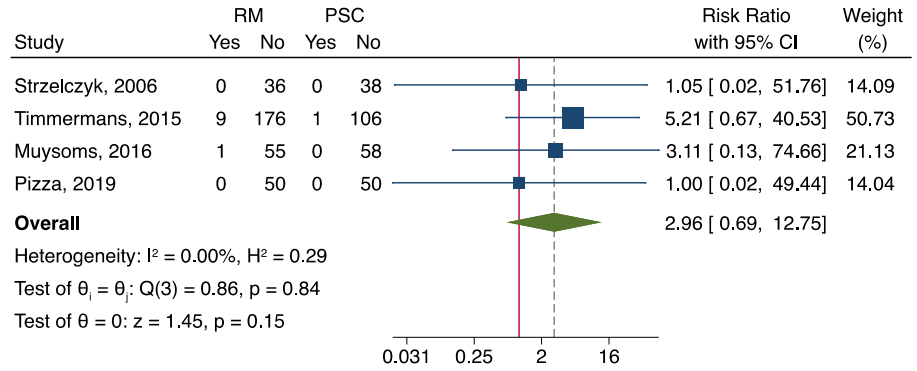
Figure 2.6 Forest plots of hematoma outcome comparing between: a) onlay mesh (OM) and primary suture closure (PSC) b) retrorectus mesh (RM) and PSC c) intraperitoneal mesh (IM) and PSC.

a) OM versus PSC



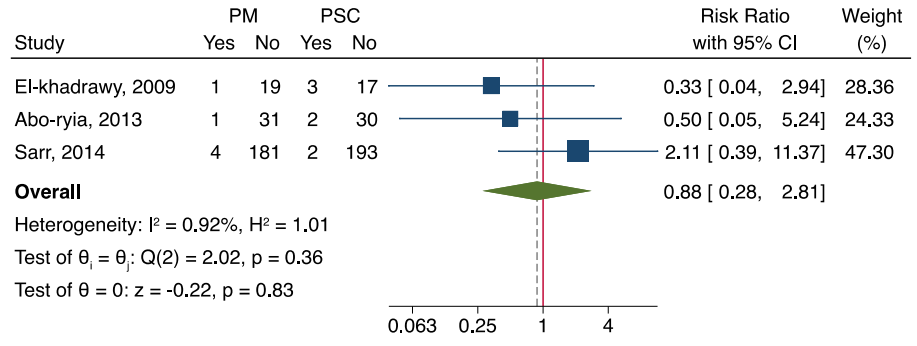
Random-effects DerSimonian-Laird model

b) RM versus PSC



Fixed-effects inverse-variance model

c) PM versus PSC



Fixed-effects inverse-variance model

Figure 2.7 Forest plots of dehiscence outcome comparing between: a) onlay mesh (OM) and primary suture closure (PSC) b) retrorectus mesh (RM) and PSC c) preperitoneal mesh (PM) and PSC.

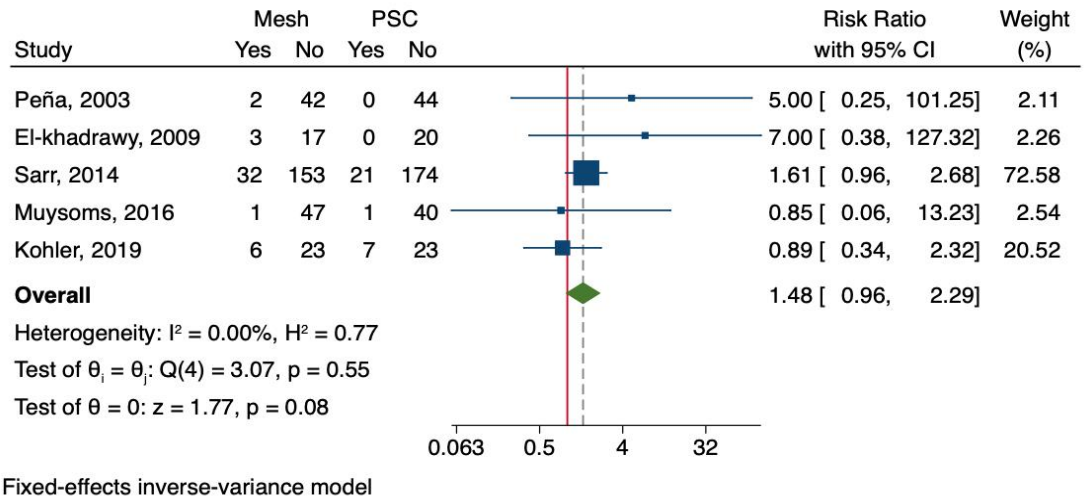


Figure 2.8 Forest plot of chronic pain outcome comparing between mesh placement and primary suture closure

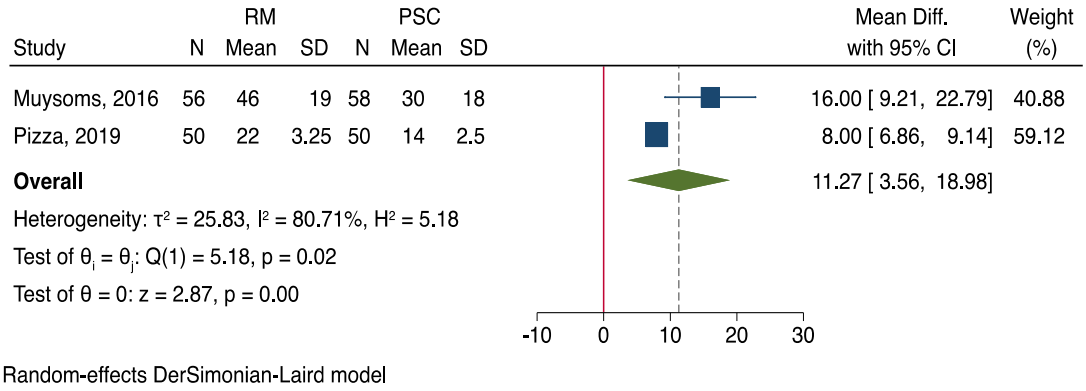


Figure 2.9 Forest plot of abdominal wall closure time comparing between mesh placement and primary suture closure. Only data from retrorectus mesh versus primary suture closure were available for pooling

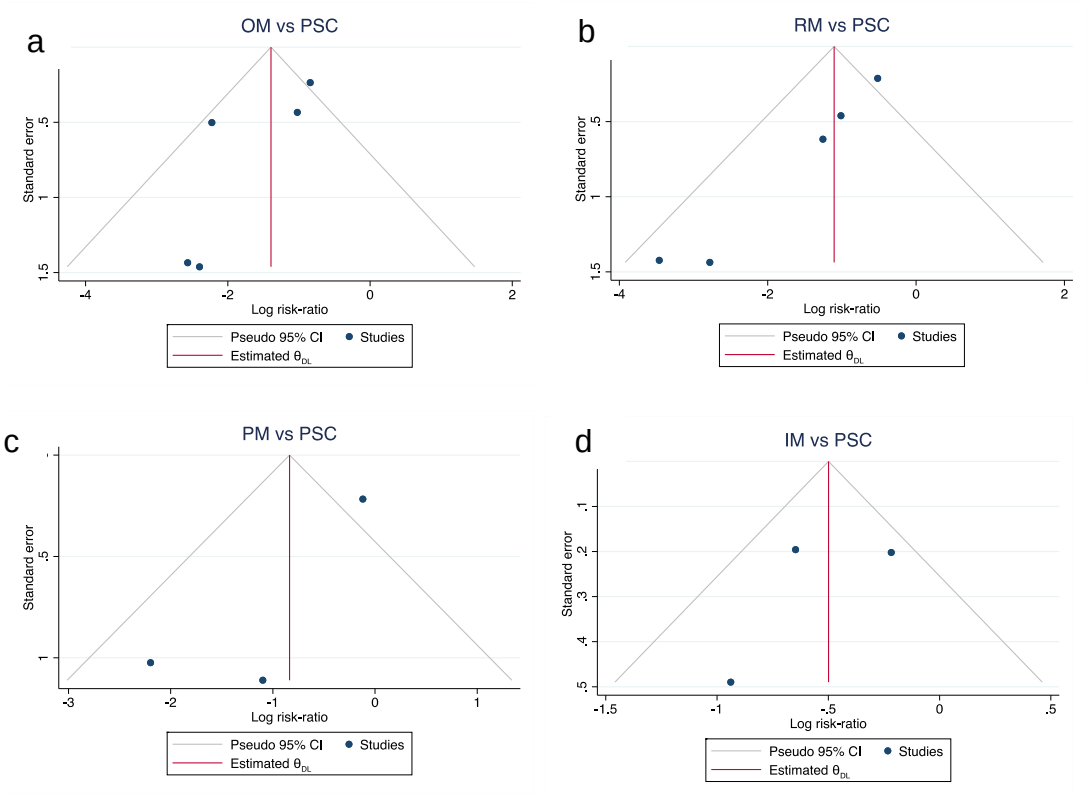


Figure 2.10 Funnel plots for hernia outcome of: a) onlay mesh (OM) vs primary suture closure (PSC) b) retrorectus mesh (RM) vs PSC c) preperitoneal mesh (PM) vs PSC d) intraperitoneal mesh (IM) vs PSC

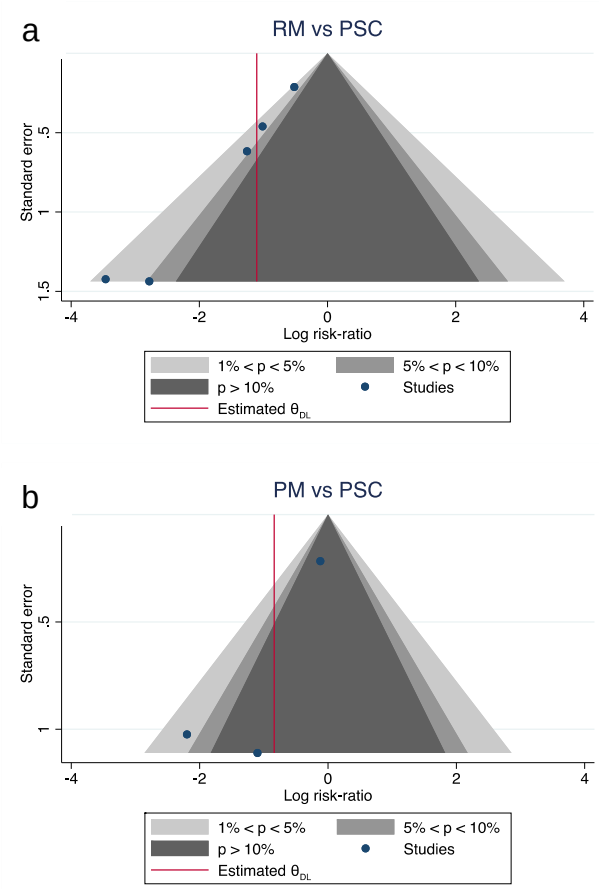


Figure 2.11 Contour-enhanced funnel plots for hernia outcome of: a) retrorectus mesh (RM) vs primary suture closure (PSC) b) preperitoneal mesh (PM) vs PSC

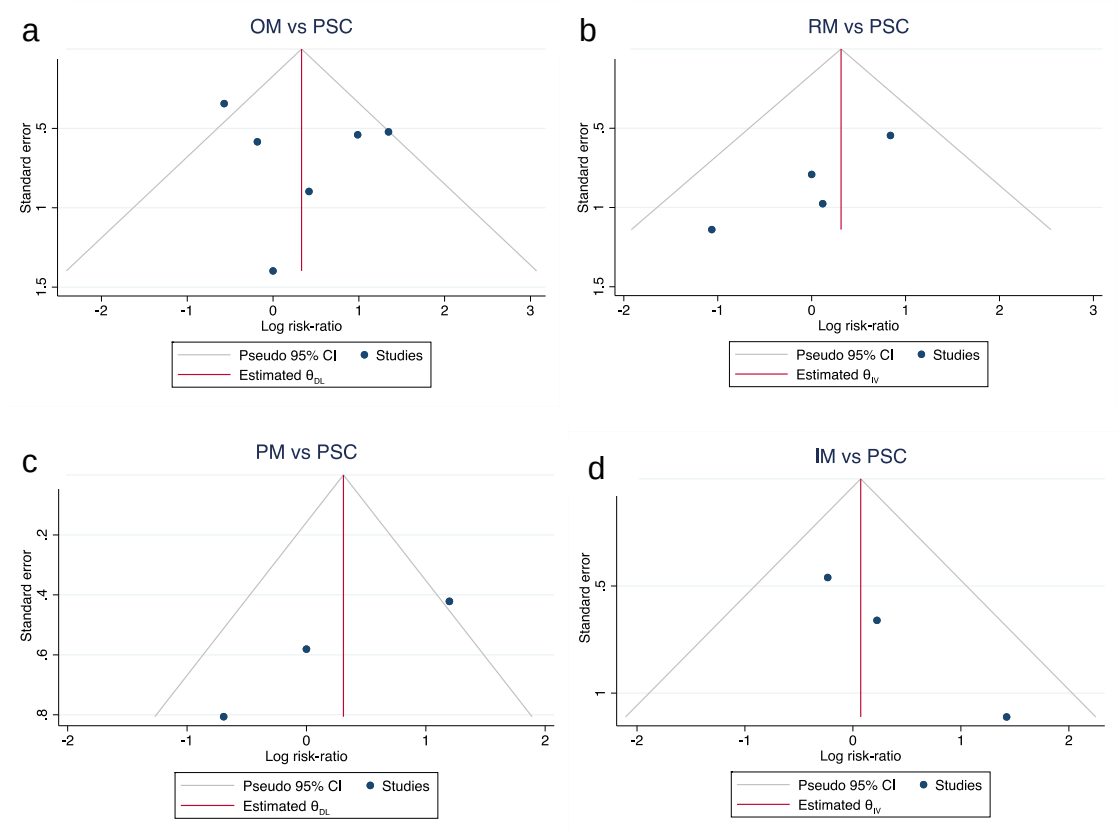


Figure 2.12 Funnel plots for wound infection outcome of: a) onlay mesh (OM) vs primary suture closure (PSC) b) retrorectus mesh (RM) vs PSC c) preperitoneal mesh (PM) vs PSC d) intraperitoneal mesh (IM) vs PSC

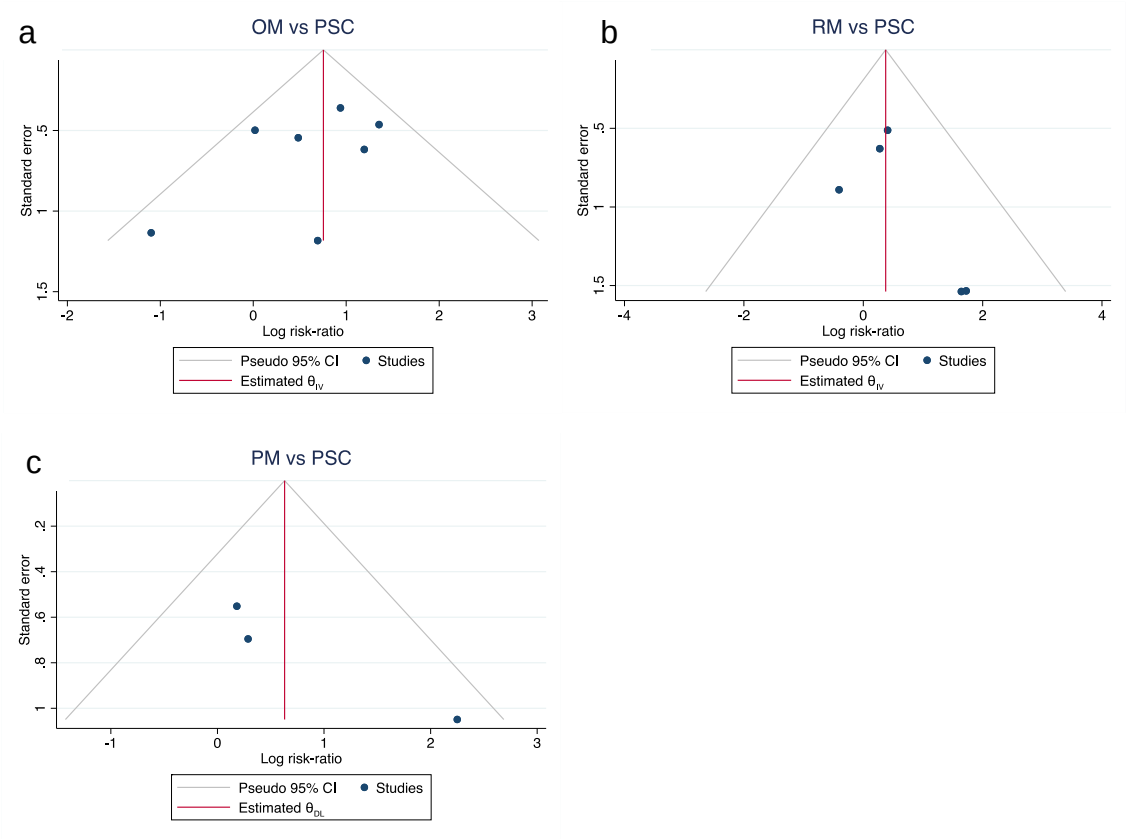


Figure 2.13 Funnel plots for seroma outcome of: a) onlay mesh (OM) vs primary suture closure (PSC) b) retrorectus mesh (RM) vs PSC c) preperitoneal mesh (PM) vs PSC

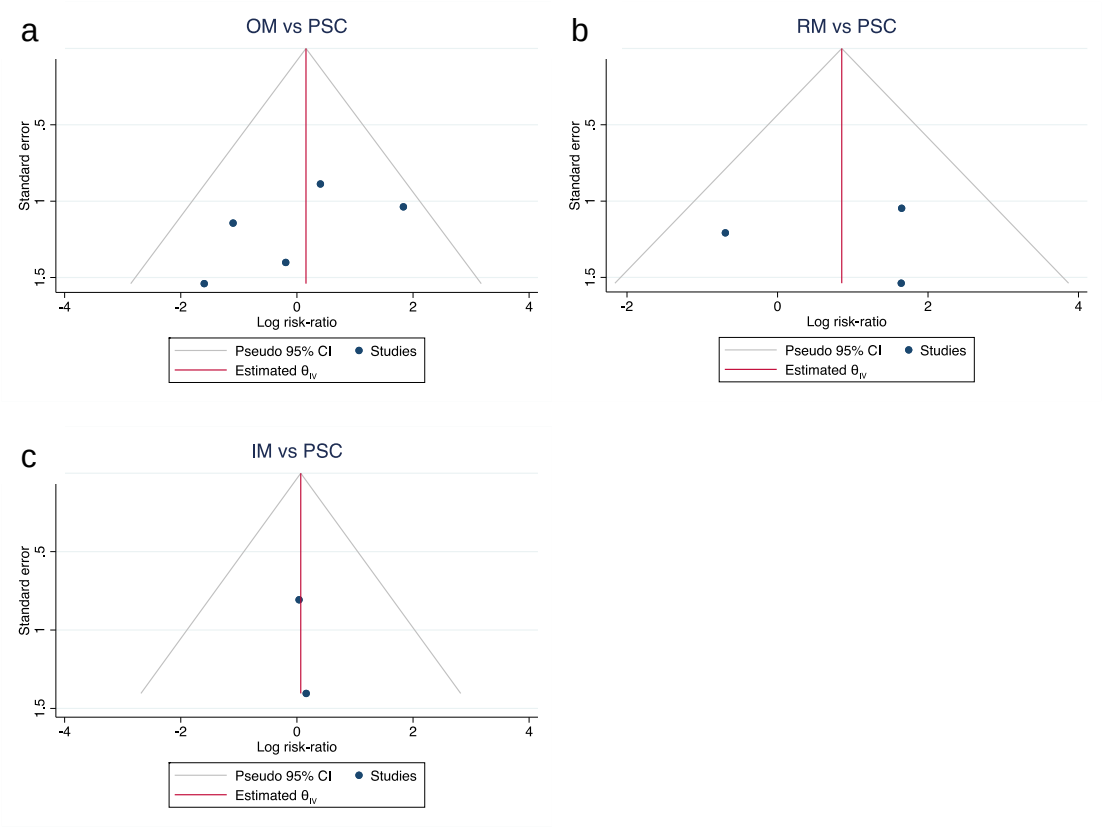


Figure 2.14 Funnel plots for hematoma outcome of: a) onlay mesh (OM) vs primary suture closure (PSC) b) retrorectus mesh (RM) vs PSC c) intraperitoneal mesh (IM) vs PSC

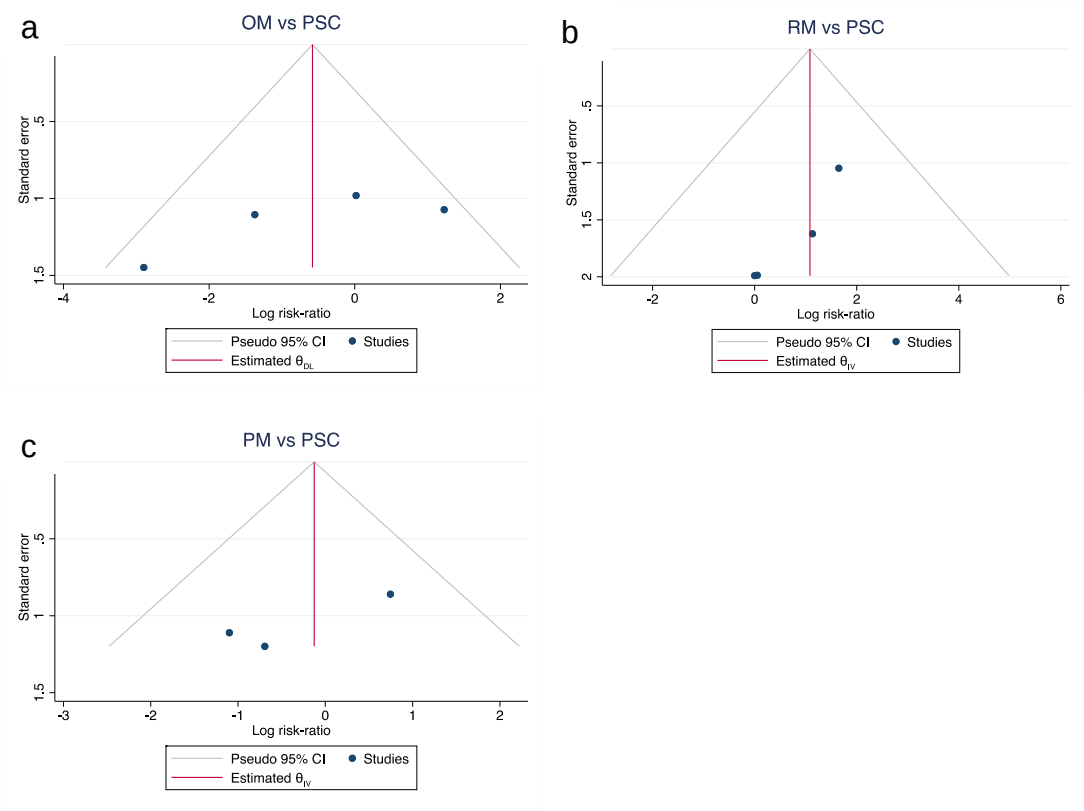


Figure 2.15 Funnel plots for dehiscence outcome of: a) onlay mesh (OM) vs primary suture closure (PSC) b) retrorectus mesh (RM) vs PSC c) preperitoneal mesh (PM) vs PSC

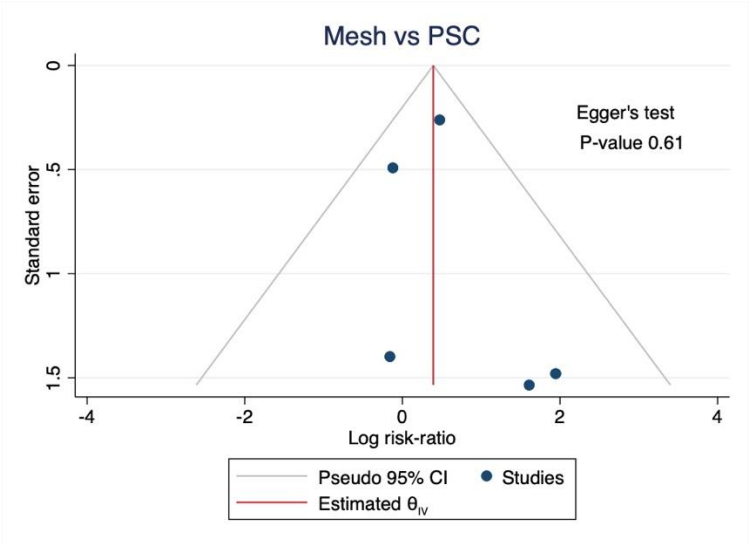


Figure 2.16 Funnel plot for chronic pain outcome of mesh placement versus primary suture closure

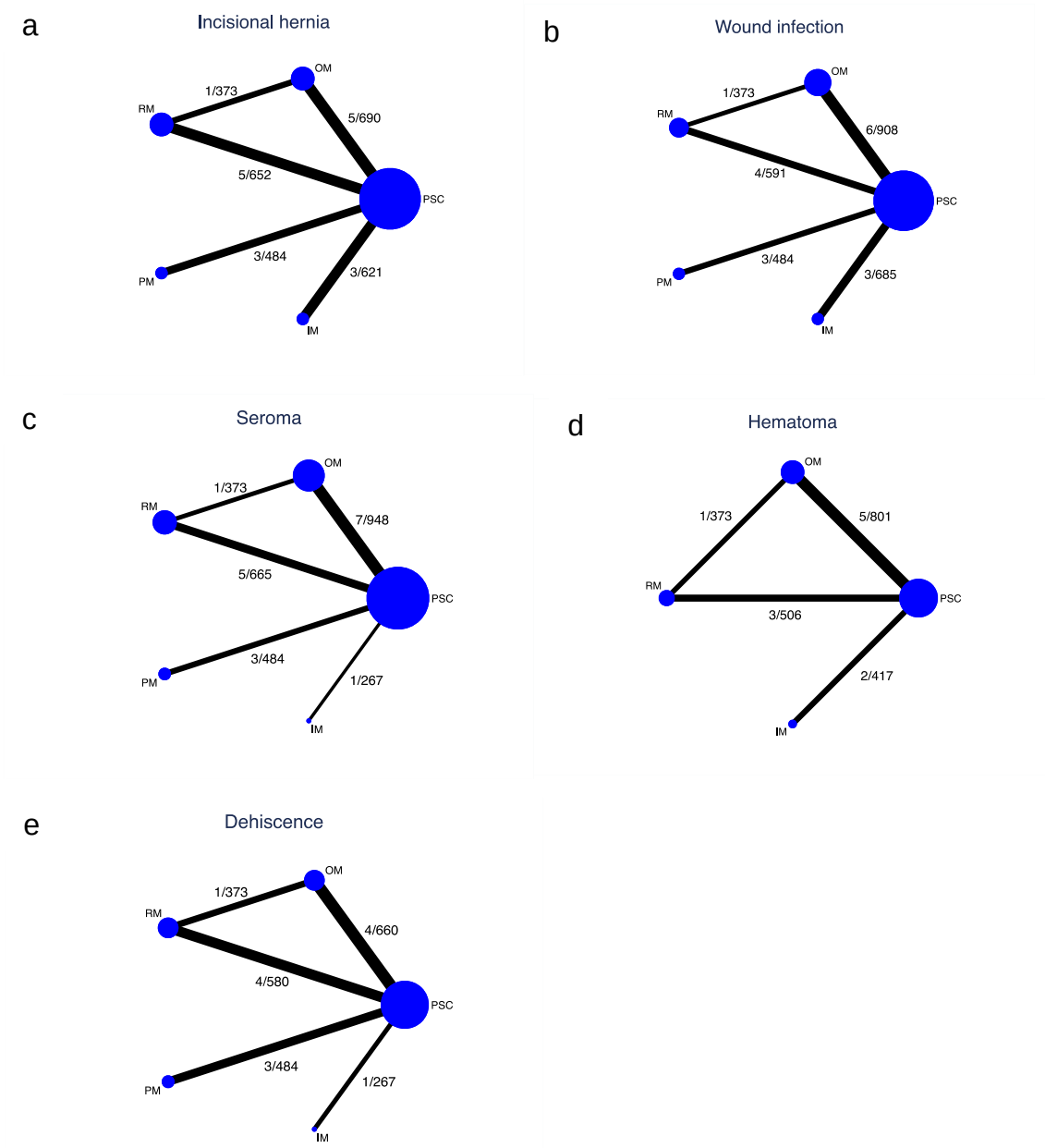


Figure 2.17 Network configurations of different fascia closure techniques a) incisional hernia b) wound infection c) seroma d) hematoma e) dehiscence. Size of nodes was weighted by numbers of studies. Size of edges was weighted by numbers of subjects in each comparison. Each number on plots represents numbers of studies and subjects contributing to the corresponding comparison. (IM intraperitoneal mesh, OM onlay mesh, PM preperitoneal mesh, PSC primary suture closure, and RM retrorectus mesh)

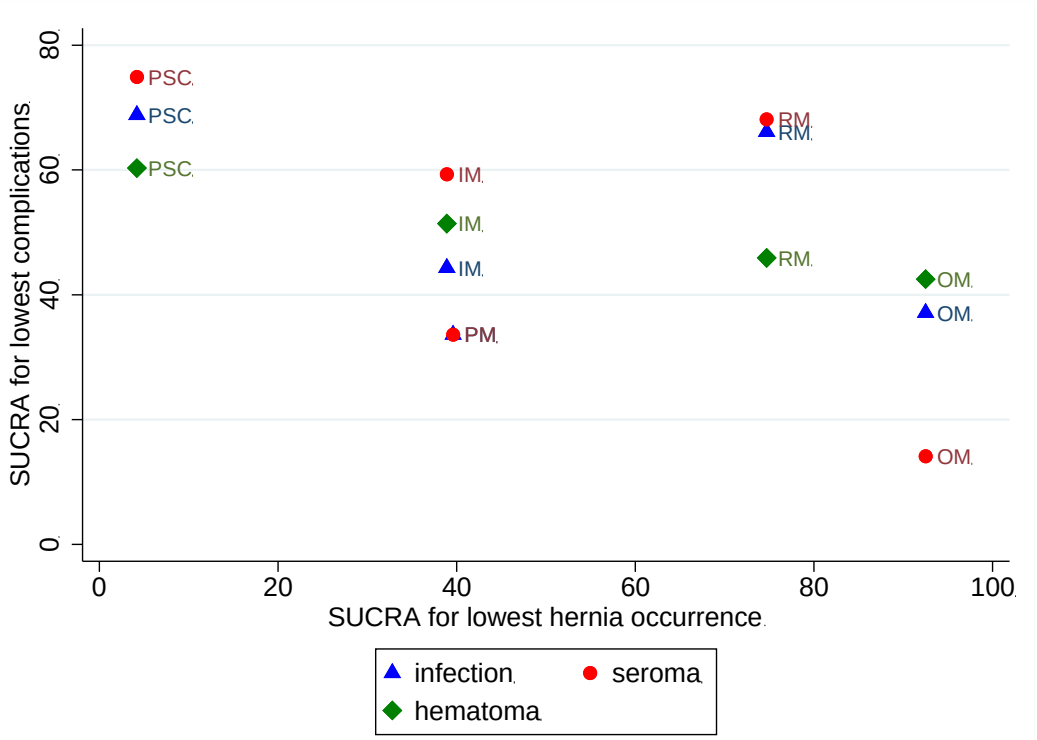


Figure 2.18 Scatter plots of SUCRA values for lowering hernia occurrence versus lowering complications, including wound infection, seroma, and hematoma. Interventions that fall on the area of the right upper corner are associated with both higher preventive effects and lower complications. (IM intraperitoneal mesh, OM onlay mesh, PM preperitoneal mesh, PSC primary suture closure, and RM retrorectus mesh)

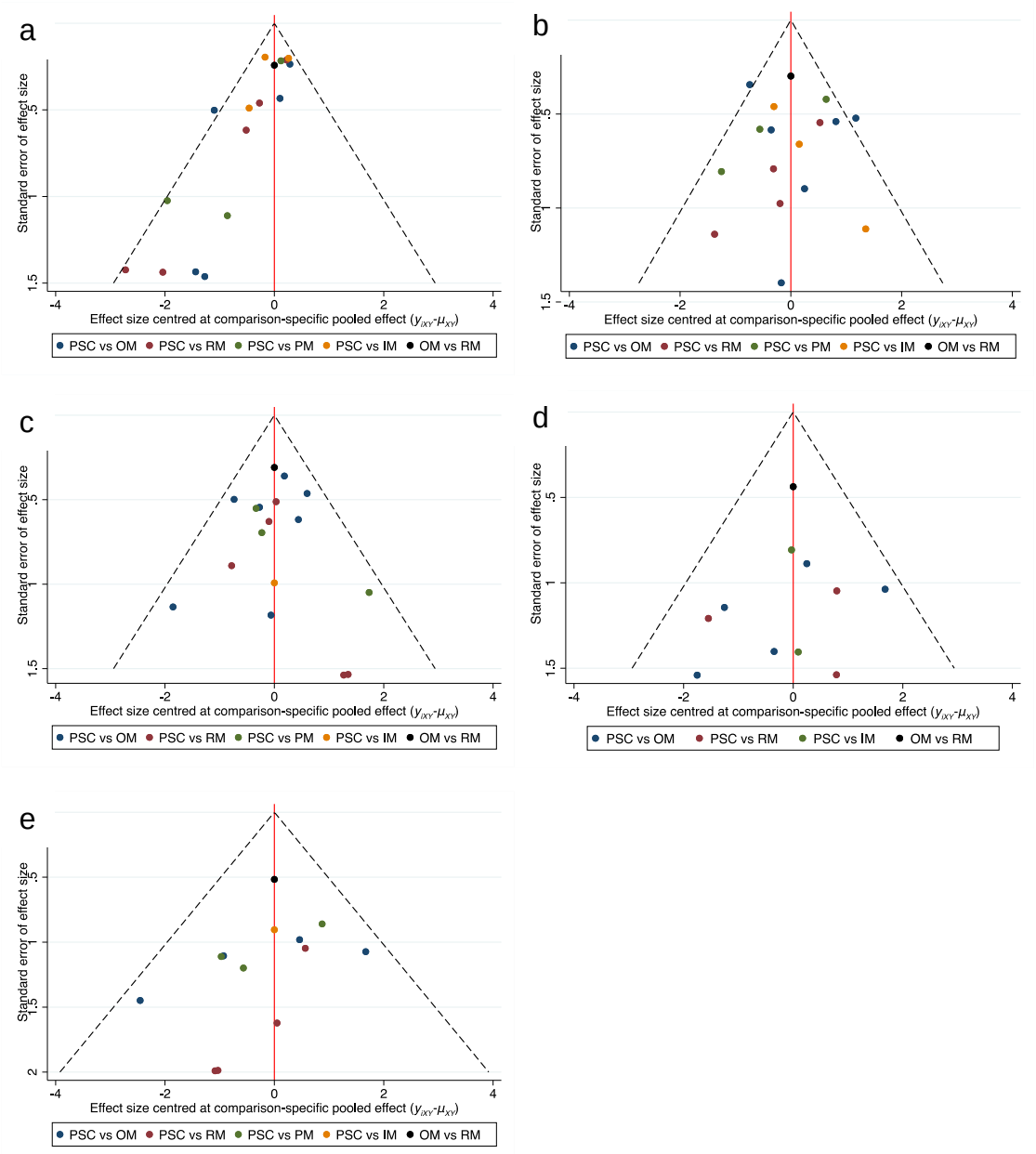


Figure 2.19 Comparison-adjusted funnel plot for a) incisional hernia b) wound infection c) seroma d) hematoma and e) dehiscence. IM, intraperitoneal mesh; OM, onlay mesh; PM, preperitoneal mesh; PSC, primary suture closure; and RM, retrorectus mesh

CHAPTER III
RISK-BENEFIT ASSESSMENT OF MESH-AUGMENTED FASCIA CLOSURE FOR INCISIONAL HERNIA PREVENTION

Findings in chapter 2 indicated that OM was superior to RM in IH prevention. However, OM might carry higher risks of seroma and hematoma than RM. Consequently, a recommendation for a mesh technique for IH prophylaxis cannot be made without additional analysis. Risk-benefit assessment (RBA) in this study was performed to compare the benefits and risks in each mesh technique, and the recommended technique could be appreciated accordingly.

3.1 METHODS

RBA shares the same concept of the cost-effectiveness analysis (CEA). In CEA, incremental benefit (Δbenefit) is compared with incremental cost (Δcost). Instead of Δcost, incremental risk (Δrisk) is used in RBA.[71] When IH occurrence represented benefits and wound complications (i.e., SSI, seroma, and hematoma) represented risks in this study, Δbenefits, and Δrisks were obtained from pooled RDs of each outcome of mesh techniques versus PSC in NMA (Table 3.1).

To facilitate result interpretation, seroma and hematoma were combined into a composite outcome. SSI was considered separately. Incremental risk-benefit ratios (IRBRs) were computed afterward using the following equation:

$$IRBR = \frac{\Delta risk}{\Delta benefit} = \frac{RD_{wound}}{RD_{IH}} \quad \ldots (1)$$

Where RD_{wound} = RD of wound complication which can be SSI (RD_{SSI}) or composite seroma and hematoma (CSH) outcome (RD_{CSH}), and RD_{IH} = RD of IH occurrence.

Therefore, both OM and RM had 2 IRBRs each regarding RD_{wound} (i.e., RD_{SSI} or RD_{CSH}) used in the equation (1). Because both mesh techniques can effectively prevent IH, RD_{IH} inevitably had negative signs from subtracting IH risk of PSC from the

mesh technique. When IRBRs of OM and RM were compared, a higher value (i.e., a negative value closer to zero) represented more benefits compared to the associated risk.

By using RDs and their associated standard errors (SEs), a Monte-Carlo simulation with 1000 replications was performed. This procedure provided 2 benefits: 1) 95% CI can be obtained for each IRBR 2) Simulated IRBRs can be compared with the acceptability threshold (i.e., acceptable risk of the adverse event), then the probability of being risk-beneficial (PRB), or the chance of IRBR lower than the threshold, can be computed at each threshold level. In this study, thresholds of 0.05, 0.1, 0.2, and 0.3 were arbitrarily set as references to facilitate data visualization.

Results from Monte-Carlo simulation were plotted on a risk-benefit plane in which the x-axis and y-axis represented Δbenefit and Δrisk, respectively. The left lower quadrant represented where the mesh procedure was superior to PSC, whereas PSC was superior to the mesh procedure if coordinates fell in the right upper quadrant. Lines depicting acceptability thresholds of 0.05, 0.1, 0.2, and 0.3 were also drawn on the same plane. The number of coordinates located below those lines indicated PRB at the corresponding threshold levels. PRBs were also plotted against varying threshold levels in the risk-benefit acceptability curve. Results of OM and RM were plotted in the same risk-benefit plane and acceptability curve for comparison. STATA version 16 was used in all analyses.

3.2 RESULTS

Both OM and RM significantly reduced IH occurrence with RDs (95% CI) of -0.237 (-0.324, -0.151) and -0.201 (-0.289, -0.114), respectively. Better IH prevention could be expected from OM. On the other hand, RM seemed to be safer than OM in terms of SSI and CSH, see Table 3.1. OM significantly increased CSH risk with RD (95% CI) of 0.090 (0.052, 0.128).

When RD_{SSI} was plugged into equation (1), OM and RM yielded IRBRs (95% CI) of -0.118 (-0.124, -0.112) and 0.006 (-0.002, 0.013) relative to PSC, respectively. These findings mean RM is more risk-beneficial than OM. When results from a Monte-Carlo simulation were plotted on the risk-benefit plane (Figure 3.1a), more coordinates from RM fell below the threshold lines than OM, corresponded with

the risk-benefit acceptability curve that indicated higher PRB from RM than OM in every threshold level (Figure 3.1b). For instance, PRBs of RM and OM were 0.70 versus 0.24 and 0.82 versus 0.44 at the threshold levels of 0.05 and 0.1, respectively.

When RD_{CSH} was Δrisk in equation (1), OM was evidently less risk-beneficial than RM [IRBRs (95% CI): -0.388 (-0.395, -0.381) versus -0.105 (-0.111, -0.100), respectively]. Figure 3.2a demonstrates that OM was unlikely to be risk-beneficial because too many coordinates were located above the threshold lines. From the risk-benefit acceptability curve (Figure 3.2b), RM yielded PRBs of 0.50 and 0.87 at the threshold levels of 0.1 and 0.2, respectively. PRB of OM was not considerably higher than zero until reaching the threshold level of 0.2.

3.3 DISCUSSION

NMA suggested OM and RM as candidates for IH prevention due to their significant effect sizes. Nevertheless, the recommended technique was controversial, especially when considering the risks. Results from this RBA suggested that RM was beneficial when risks of SSI and CSH were considered while OM was not.

Even though a single benefit (i.e., IH occurrence) was evaluated in this study, it was compared with 2 adverse outcomes (i.e., SSI and CSH). As a result, 2 IRBRs were obtained for each mesh procedure and might suggest the opposite direction. Fortunately, both IRBRs calculated from RD_{SSI} and RD_{CSH} suggested that RM was superior to OM. To avoid misfortune, adverse events should be combined into a single composite outcome, likewise benefit endpoints. Thus, only one IRBR would be obtained for each procedure. All adverse outcomes at surgical incision could be combined into one composite outcome called surgical site occurrence.[72] However, the composite outcome comes with drawbacks. It is difficult to understand or even misleading interpretations. Moreover, each outcome to be combined should have the same level of importance.[73] In this study, we considered SSI separately and combined seroma with hematoma. While SSI is seriously concerned in surgery involving foreign body implantation, seroma and hematoma are common and could be managed expectantly.

Clean, clean-contaminated, contaminated, and dirty wounds carried SSI risks of 1%-5%, 3%-11%, 10%-17%, and > 27%, respectively.[74] In modern surgery,

these rates were reduced to 2.3%, 4.8%, 6.1%, and 7.3%, respectively.[75] Given that most of the included RCTs involved clean and clean-contaminated incisions, the SSI threshold level of 0.05 should be a proper reference. Because seroma is frequently found after abdominal wall surgery,[76] the CSH threshold level of 0.2 seemed appropriate. At these threshold levels of SSI and CSH, RM was much more risk-beneficial than OM. Because SSI risk of the included RCTs was relatively low, results from this RBA should be extrapolated with caution in a more contaminated operation (e.g., in emergency settings).

RM required some technical expertise that might not be familiar to all surgical specialists. Moreover, dissection in the retrorectus plane for RM placement will cause adhesion in that plane and would preclude retrorectus hernia repair if IH occurred afterward. Albeit these drawbacks cannot be assessed in RBA framework, they should be acknowledged and weighted against RM's benefits.

This study provided procedures comparison objectively. PRB is also comprehensive and could guide decision-making. However, there are some limitations. This RBA is the secondary analysis of NMA which included a small number of RCTs that limited the precision of the estimated effect sizes. In addition, rare adverse events were not included in the analysis due to the unavailability of data. However, such rare events (e.g., fistula, wound sinus, and mesh migration) are unlikely to affect RBA results.

3.4 CONCLUSION

OM and RM were suggested by NMA to be used for IH prevention considering the benefits of lowering IH occurrence. However, OM was unlikely to be risk-beneficial when SSI and CSH were considered. Thus, RM should be recommended as a mesh technique of choice used for prophylactic purposes.

Table 3.1 Pooled risk differences and 95% confidence intervals with standard error of the risk difference

Outcomes	Comparisons	RD (95% CI)	SE
IH	OM vs PSC	-0.237 (-0.324, -0.151)	0.044
	RM vs PSC	-0.201 (-0.289, -0.114)	0.044
SSI	OM vs PSC	0.027 (-0.012, 0.066)	0.020
	RM vs PSC	-0.001 (-0.046, 0.044)	0.023
CSH	OM vs PSC	0.090 (0.052, 0.128)	0.019
	RM vs PSC	0.020 (-0.012, 0.051)	0.016

CSH, composite seroma/hematoma; IH, incisional hernia; OM, onlay mesh; PSC, primary suture closure; RD, risk difference; RM, retrorectus mesh; SE, standard error of risk difference; SSI, surgical site infection

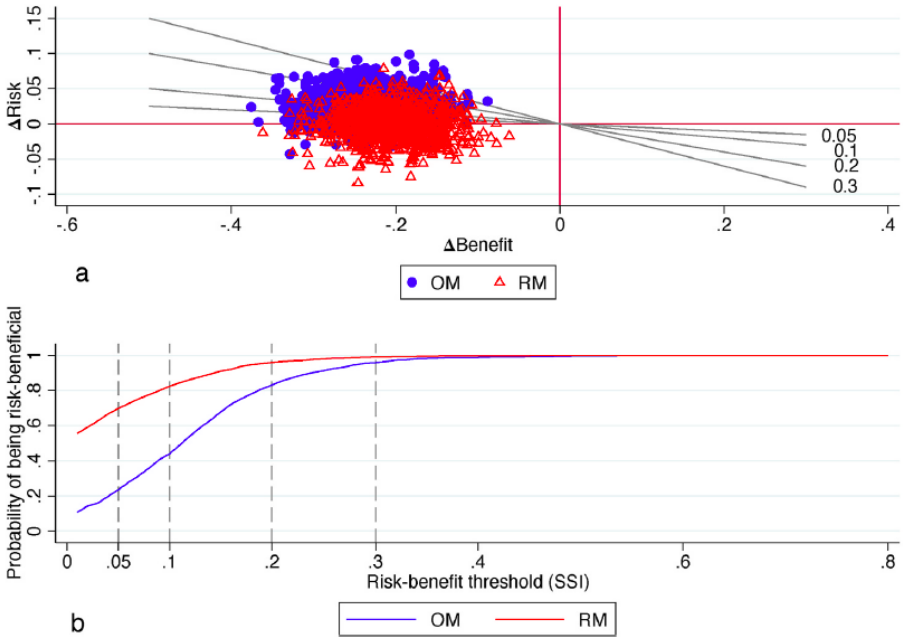


Figure 3.1 Risk-benefit analysis of onlay and retrorectus mesh, considering surgical site infection (SSI) as a risk a) scatter plot of simulated △benefits and △risks on the risk-benefit plane along with reference acceptability thresholds of 0.05, 0.1, 0.2, and 0.3. The left lower quadrant of the plane represents the area where mesh procedures dominate primary suture closure b) risk-benefit acceptability curve (OM onlay mesh, RM retrorectus mesh).

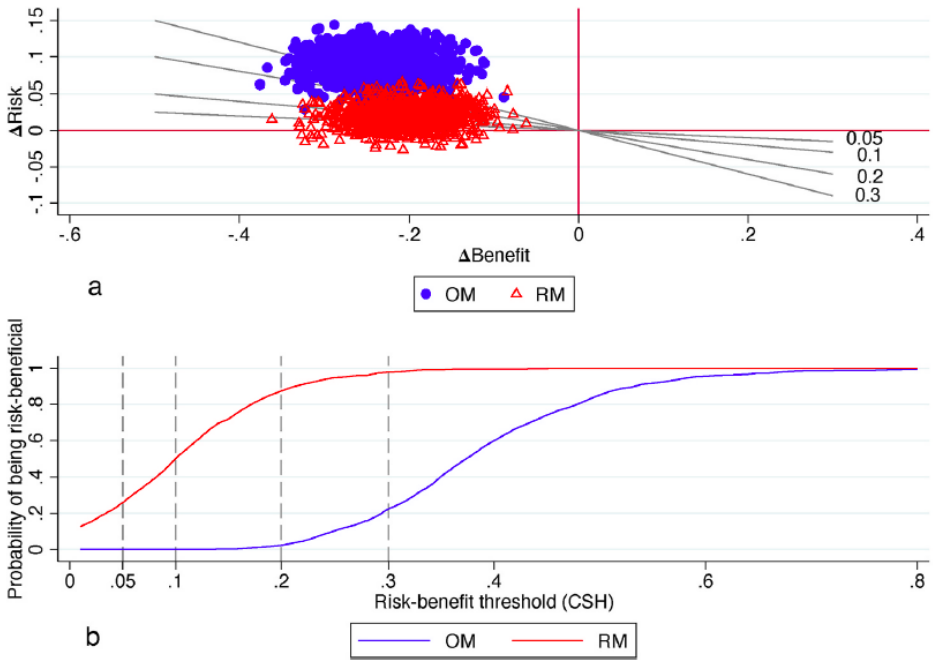


Figure 3.2 Risk-benefit analysis of onlay and retrorectus mesh, considering composite seroma/hematoma (CSH) as a risk a) scatter plot of simulated △benefits and △risks on the risk-benefit plane along with reference acceptability thresholds of 0.05, 0.1, 0.2, and 0.3. The left lower quadrant of the plane represents the area where mesh procedures dominate primary suture closure b) risk-benefit acceptability curve (OM onlay mesh, RM retrorectus mesh).

CHAPTER IV
PROTOCOL OF RANDOMIZED CONTROLLED TRIAL FOR PROPHYLACTIC MESH-AUGMENTED FASCIA CLOSURE IN URGENCY/EMERGENCY MIDLINE LAPAROTOMY

4.1 RELEVANT INFORMATION

4.1.1 Incidence of incisional hernia after emergency/urgency laparotomy

The incidence of incisional hernia after emergency/urgency laparotomy was 16%- 54%.[5, 55-59] From Ramathibodi databases year 2019, 7% of emergency laparotomies developed IH. Therefore, pooled incidence (95%CI) was 24% (16%, 31%). If the study of Moussavian et al.,[59] which reported the highest rate of IH occurrence (54%), was excluded, the pooled incidence was 19% (13%, 24%).

4.1.2 Synthetic mesh placement in a contaminated environment

Surgeons are reluctant to apply a synthetic mesh in the contaminated area because a foreign material, left in such an environment, can increase the risk of infection. Most evidence of mesh placement in the contaminated field came from studies of hernia repair. Choi et al.[77] have reported that ventral hernia repair (VHR) using mesh in clean-contaminated and contaminated cases significantly increased the risk of surgical site infection (SSI) compared with clean cases. From this study, the odds ratio (OR) of combined superficial and deep SSI was calculated. In a clean-contaminated environment, mesh placement yielded OR (95%CI) of 1.36 (1.14, 1.63) when compared to no mesh.

However, this dogma has been challenged in many studies. Carbonell et al.[78] reported SSI rates of 7.1% and 19% after VHR using polypropylene mesh in clean-contaminated and contaminated cases, respectively. These SSI rates were comparable to those usually observed in other contaminated operations.[79] Moreover, no correlation

between mesh removal and SSI was detected in this study. Emile et al.[80] reported no difference in SSI rates between mesh and non-mesh repair in incarcerated and strangulated ventral hernia. Recently, Birollini et al.[81] found that rates of SSI after contaminated mesh repair did not significantly differ from mesh repair in a clean environment (15% versus 10%, respectively). Moreover, a high success rate of conservative management without mesh removal has been observed in some studies.[82, 83] Perhaps, new generation synthetic meshes, engineered to be macroporous, were responsible for acceptable SSI outcomes.[84]

Few studies of prophylactic mesh have been conducted in an emergency setting, in which contamination is likely. Two retrospective studies[56, 57] evaluated the effectiveness of mesh on midline IH prophylaxis. They found that mesh can be safely placed even in peritonitis. Prophylactic mesh yielded 82.1% - 88.8% of IH risk reduction while did not significantly increase the risk of SSI. Contrary, the study of Lima et al.,[67] testing the efficacy of OM on fascial dehiscence prevention, reported significantly higher SSI rates in OM than PSC (20.6% versus 7.7%, P-value 0.05). In summary, mesh placement is effective in lowering hernia occurrence and recurrence; however, whether mesh substantially increases SSI rate in a contaminated environment is still controversial.

4.2 STUDY DESIGN

This study is a multicenter randomized controlled trial, which was conducted from January 2021 to December 2024. Six study centers were included, i.e., Ramathibodi, Vajira, Bhumibol Adulyadej, Hatyai, Maharaj Nakorn Ratchasima, and Surin. This study was approved by the ethical committee of the Faculty of Medicine Ramathibodi hospital and all other study centers. The protocol was registered at Thai Clinical Trial Registry (TCTR20200924002).

4.3 STUDY SUBJECTS

All patients who were admitted to the emergency department or surgical wards due to urgent GI conditions are invited to participate in this study. Eligibility is checked as follows.

4.3.1 Inclusion criteria

4.3.1.1. Age ≥ 18 years

4.3.1.2. Operation is performed within 24 hours after admission with the indication of suspected GI pathology

4.3.1.3. Midline abdominal incision with the incision length of at least 1/4 of the distance from the xiphoid process to the pubic symphysis

4.3.1.4. Having an American Society of Anesthesiologist (ASA) physical status class I-IV

4.3.1.5. Not having the following conditions

- septic shock (hemodynamic instability)
- metastasis cancer (stage IV) before or during the operation
- a dirty surgical wound, which involves severe contamination of fecal material and frank pus (surgical wound class IV)
- massive devitalized bowel ischemia

4.3.1.6. No potential for second-look operation and no planned definite or revisionary surgery via a midline incision

4.3.1.7. Not a secondary fascial closure

4.3.1.8. No existence of incisional hernia and no history of incisional hernia repair

4.3.1.9. Not a pregnant woman nor suspected pregnancy

4.3.1.10. No connective tissue disorders

4.3.1.11. No current immunosuppressive use

4.3.1.12. No allergy to polypropylene

4.3.2 Exclusion criterion

4.3.2.1. Become pregnant after the index operation

4.3.2.2. Newly diagnosed connective tissue disorder after the index operation

4.3.2.3. Newly administered immunosuppressive agent after the index operation

4.4 RANDOMIZATION

Participants were randomly allocated to either RM or PSC of the fascia with a ratio of 1:1. Stratified block randomization is applied with varying block sizes to be 4 to 8, and study centers are considered as strata. The allocation sequence was kept confidential at the data management unit (DMU) in the clinical epidemiology and biostatistics department of Ramathibodi hospital. Treatment allocation is concealed in sequentially numbered, opaque, and sealed envelopes. Both the allocation sequence and the opaque envelopes were created by a statistician not involved in the trial. All envelopes were distributed to each study center.

At a surgical ward or an emergency room, eligible patients are invited to participate after receiving adequate pain control. Surgeons provide information about the trial, and the information sheet is provided as a companion (Appendix B). All patients have at least 15 minutes to decide whether she/he would participate in this trial. Informed consent (Appendix C) is signed by all participants and witnesses. The concealment would be broken in the operative theatre just before fascial closure if all inclusion criteria were met. Study flow is demonstrated in Figure 4.1.

4.5 BLINDING

Surgeons are unable to be blinded to whether patients receive RM or PSC. However, the intervention is assigned just before fascial closure to prevent unequal delivery of co-interventions between the 2 groups. Patients, outcome assessors, and data analysts are blinded.

4.6 INTERVENTIONS AND CO-INTERVENTIONS

4.6.1 Interventions

The operation is conducted under general anesthesia. Abdominal skin is scrubbed and painted with an antiseptic solution. Surgery is performed via a midline incision, and linea alba is slit open. The procedure is carried out according to the causal pathology. The abdominal cavity is decontaminated with at least 3 L of normal saline before termination.

For the RM group, the retrorectus plane is dissected on all sides to achieve a 4-cm distance from the incision edge. Posterior rectus sheath and peritoneum are closed using a running stitch of 3-0 polyglactin 910 suture. A light-weight polypropylene mesh is placed in the retrorectus plane aimed to overlap the fascial incision by 3 cm on all sides. The mesh is fixed to posterior rectus fascia with 3-0 polypropylene suture at all four corners and the mid of the long side of the mesh strip. The 2nd piece of mesh would be placed if using a single mesh was unable to reinforce the length of the fascial incision; however, the 2nd piece of mesh would overlap the first one for at least 2 cm stitched to the first mesh with 3-0 polypropylene suture. The anterior rectus sheath is closed by small tissue bite continuous stitches (i.e., approximately 5-8 mm bites and 5-mm intersuture spacing), using 2-0 monofilament polydioxanone suture (PDS). If needed, a 2nd PDS would be used by overlapping the first suture for at least 2 cm. Subcutaneous space is toileted with at least 1 L of normal saline. The skin incision is closed or left open, depending on a surgeons' decision.

For the PSC group, linea alba is approximated by small tissue bite continuous stitches, which is the same as previously described. None of the drains are placed in the incision in both group.

4.6.2 Intervention training

Surgeons and surgical residents, who participate in this trial, must be trained in the RM and PSC technique. A video clip of the intervention is also be provided for each center. At least 5 cases of RM augmentation are required for each site before the start of patient enrollment.

4.6.3 Co-interventions

Antibiotics were administered to all participants in intravenous form and switched to oral form after afebrile for 24 -48 hours. The entire course of antibiotics was at least 7 days. Antibiotic of choice was judged according to the suspected pathogens and the allergic status of the participants. Antibiotic is changed after the pathogen susceptibility report is available.

Participants received 0.5 mg/kg of intravenous pethidine or 0.05 mg/kg of intravenous morphine every 4 hours as standard pain control. Additional doses would be given as needed to achieve adequate pain relief. This pain control was set for the first 24 hours and was adjusted on the following days depending on the pain level of the patient. Patient-controlled analgesia (PCA) or epidural analgesia is another option for pain relief. The oral diet would be advanced if bowel sound was present, or there was no evidence of intestinal distension. Oral analgesia (i.e., paracetamol 500 mg) was added after resuming oral intake.

4.7 VARIABLES AND MEASUREMENTS

4.7.1 Primary endpoint

IH occurrence, our primary outcome, is defined as a fascial gap in the area of a previous incision detectable by clinical examination or imaging. Follow-up time was set to be 24 months. Participants were assessed for IH occurrence at 1, 3, 2, 12, 18, and 24 months after the index operation. If the uncertainty of IH occurrence by clinical examination existed, participants would be further evaluated with ultrasound. Uncertain ultrasound results will shift to a CT scan. Participants are reminded of a follow-up visit by telephone to minimize loss to follow-up.

4.7.2 Secondary endpoints

4.7.2.1 Wound infection

Wound infection includes superficial and deep surgical site infection (SSI) according to the diagnostic criteria from the center of disease control (CDC)[85] as follows:

Superficial SSI

Infection occurs within 30 days after the operation *and* infection involves only skin or subcutaneous tissue of the incision *and* at least *one* of the following:

- Purulent drainage, with or without laboratory confirmation, from the superficial incision.
- Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
- At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat , *and* superficial incision is deliberately opened by surgeons *unless* incision is culture-negative.
- Diagnosis of superficial incisional SSI by the surgeon or attending physician.

Deep SSI

Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if the implant is in place and the infection appears to be related to the operation *and* infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision *and* at least *one* of the following:

- Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
- A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38˚C), localized pain, or tenderness unless the site is culture-negative.
- An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
- Diagnosis of a deep incisional SSI by a surgeon or attending physician.

4.7.2.2 Seroma

Seroma is defined as a fluid collection or serous fluid leakage in the incision area. The diagnosis could be made by physical examination and confirmed with ultrasound.

4.7.2.3 Hematoma

Hematoma is defined as the accumulation of a blood clot in the area of the incision, which can be detected by physical examination, and needs evacuation.

4.7.2.4 Burst abdomen

This condition is defined as a gap in fascial wound combined with skin and subcutaneous tissue dehiscence, which occurs within 30 days after the index surgery.

4.7.2.5 Acute postoperative pain

Pain intensity is measured with 10-cm visual analog scale (VAS) at postoperative day 1 and day 3.

4.7.2.6 Chronic pain

Participants are asked whether he/she experienced any pain or discomfort in the area of the incision. Data are collected at 3, 6, 12, 18, and 24 months after index operation.

4.7.2.7 Enterocutaneous fistula and wound sinus

Enterocutaneous fistula is diagnosed when there is continuity between GI mucosa and skin, causing GI content leakage. Wound sinus is defined as a chronic sinus tract at the incision with or without serous discharge.

4.7.2.8 Abdominal wall closure time

This outcome is defined as the time from the starting of abdominal wall closure to completing skin approximation. Abdominal wall closure time is recorded in minutes.

4.7.2.9 Length of hospital stay

This outcome is recorded in days from the operation date until the discharge date.

4.7.2.10 Mesh removal rate (from any reason)

4.7.2.11 Cost

Direct medical (e.g., operation, hospital admission, medication), direct non-medical (e.g., transportation, informal care), and indirect costs (e.g., income lost) were collected in Thai Baht at admission, follow-up, and any visit related to surgical wound complications.

4.7.3 Co-variables

Data of the following co-variables were collected: age, gender, body mass index (BMI), ASA classification, co-morbidities (i.e., diabetes, malnutrition, chronic obstructive pulmonary disease), smoking status, pathological cause of the operation, operative procedure, wound classification, incision length, and the length of suture used for fascial closure.

4.8 DATA COLLECTION

4.8.1 Case record form

Case record forms (CRFs), see Appendix D, were prepared by the DMU at Department of Clinical Epidemiology, Ramathibodi hospital. CRFs were then distributed to all study centers.

4.8.2 Training

A meeting among researchers was scheduled before subject recruitment. The objectives, the research protocol, the process, and the CRF were clarified and discussed at the meeting. Research assistants were trained in data collection and query, whereas doctors were trained and guided about the eligible criteria, information sheet, informed consent form, and clinical outcome assessment. Trainings were conducted every 6 months.

4.8.3 Non-participation

To compare with the subjects who participate in the study, patients who decided not to participate would be asked to retrieve their demographic and clinical data for further analysis.

4.8.4 Data flow and monitoring

Research assistants retrieved demographic and related clinical data from participants and medical records. Information about the operation was collected from operative notes. Primary and secondary outcomes were assessed by investigators or research assistants at the surgical ward and outpatient clinic.

Participants were scheduled to follow up at approximately 1 month, 3, 6, 12, 18, and 24 months after surgery. The outcomes, including hernia occurrence, SSI, seroma, and chronic pain, were assessed at an outpatient surgery clinic according to the follow-up protocol (Table 4.1) and documented by investigators.

Completeness of CRFs was daily checked by the research assistants and investigators. All problems on data recording and queries were solved at each study site. All CRFs and patients' log sheets were delivered to the central DMU at Ramathibodi Hospital. CRFs were inspected by the principal investigator before the process of data entry. Data quality and research progression were also monitored by the data manager. Patients' flow and trial activity is demonstrated in Figure 4.2 and Figure 4.3, respectively.

During the trial, site monitoring was conducted every 6 months. All trial activities, including enrollment and consent process, protocol adherence, and data collection were audited. Completeness of eligibility and consent forms was checked weekly. The following key performance indices were monthly reported to a committee.

- Screening rate = Number of screened patients/Number of emergency and urgency exploratory laparotomy patients
- Eligibility rate = Number of eligible patients/Number of screened patients
- Rate of completion of informed consent = Number of patients whose informed consent was obtained/Number of eligible patients
- Number of enrolled participants
- Number of protocol violations

4.8.5 Databases and data entry

Databases were constructed using EpiData version 3.1. The databases contain the eligible criteria, demographic and related clinical data, operative data, and

all study outcomes. Interactive quality control is set within the databases to control data entry.

Before data entry, all CRFs were approved by the principal investigator. Unclear, missing, or non-sensible data are compared with medical records. Double data entry was performed with 2 independent staff for further data validation. Any discrepancy in data validation was compared with the original CRF. Data consistency checking was also performed. The databases are checked and cleaned every month. All paper and electronic documents are kept in a safe location. By using a password, only the principal investigator and an authorized person could access the databases. The databases were automatically real-time backed up at the DMU server to prevent data loss.

4.8.6 Data safety and monitoring board (DSMB)

DSMB was set and consisted of a surgeon, epidemiologist, and biostatistician who did not involve in the study. This board's role was to monitor the study process, audit data validity and integrity, and observe an unexpected serious adverse event (Figure 4.3).

4.9 SAMPLE SIZE ESTIMATION

According to our systematic review, 69.7% (49.5%, 90.0%) of IH risk was lowered by RM. By this evidence, we believe that RM could reduce IH incidence by at least 50% approximately. The pooled incidence of IH was 7.1% after RM augmentation or 7.4% regardless of mesh technique. Incidence of IH in emergency/urgency patients was approximately 19% from our pooling, see section 4.1.1. Thus, estimated IH incidence after RM augmentation could be 9.5%, which is still higher than pooled IH incidence (7.4%) after prophylactic nonabsorbable mesh placement. The type I error and the power of the test were set as 0.05 and 0.80, respectively. The randomization ratio was 1:1 (RM: PSC). Therefore, the total number of subjects was 424. A loss to follow-up rate of 10% was added to the subject pool; thus, we have to recruit 470 participants. Because emergency/urgency gastrointestinal conditions are relatively

common, we expect the recruitment rate of 30-40 cases/month. Thus, the recruitment period would be around 18-24 months. See Table 4.2 for sample size calibration.

4.10 DATA ANALYSIS

4.10.1 Statistical analysis

Mean and standard deviation (SD) were used to describe continuous data. Categorical data were presented as frequency and percentage. The balance of co-variables between the two intervention groups was tested using independent student t-test and chi-square/Fisher's exact test for continuous and categorical data, respectively.

Categorical outcome variables, including primary endpoint, were compared between groups using chi-square or Fisher's exact test, whereas independent t-test would be used for continuous outcome variables. The relative intervention effect was estimated using RR or MD along with 95% CI depending on the types of outcomes. In case of an imbalance of co-variables, an adjustment would be performed using multivariate regression.

4.10.2 Protocol violation

Protocol violation dealt with four analyses: intention-to-treat (ITT), per-protocol (PP), and as-treated (AT). Each analysis has its benefits and limitations. In ITT analysis, participants are analyzed in their allocated group, regardless of what treatment they actually received. ITT analysis preserves randomization, but it could result in bias to null if protocol violation is critical. Contrastingly, PP considered only participants who have adhered to the trial protocol, therefore those patients who have not adhered well will be excluded.

AT would consider both ITT and PP together, i.e., initially random allocation and the actual received intervention. The counterfactual approach[86] would be applied to estimate the relative treatment efficacy for AT approach. The concept is that an instrumental variable (IV)[87] regression will be applied to estimate the probability of receiving treatment, then adjusts by this probability while estimating the treatment effect. The randomly assigned treatment was selected as IV, whereas the actual received

treatment was the endogenous variable in the bivariate probit or multivariate logistic model. Randomization can be preserved in this analysis technique, while treatment contamination is adjusted.[88]

All analyses were performed using STATA version 17. Statistical significance was considered when P-value < 0.05.

4.10.3 Imputation

All missing data will be checked with CRFs or medical records. Telephone interview was used to retrieve some missing co-variables. If such procedures could not solve the problem, missing data would be assumed missing at random (MAR), and data imputation will be performed. The missing data would be regressed on complete data using linear truncated/interval or logistic regression with 10 imputations for continuous and categorical data, respectively. Missing data would be imputed accordingly. The fraction of missing information (FMI) and relative variance increase (RVI) were used as assessment tools for imputation performance.

4.10.4 Interim analysis

Interim analysis was planned and will be conducted by the DSMB when the number of subjects reached 30% and 60% of the total sample size. Considering the harm of mesh placement, the rate of SSI would be compared between 2 interventions. The analysis would be adjusted by O'Brien and Fleming's method to prevent inflation of the type I error.[89] If the difference in the rate of SSI reached a statistically significant level, enrollment would be terminated.

4.10.5 Cost-effectiveness analysis (CEA)

Analyses would be performed from societal and provider perspectives. All data were retrieved from each participant; thus, no economic model was needed for analysis. The time horizon was one year, so no discounting would be applied to costs. Costs were included with direct medical, direct non-medical, and indirect costs. Costs, occurring from the treatment of complications, were included in direct medical costs. Both Δeffectiveness and Δcost were calculated by subtracting the incidence of IH and

the cost of RM with PSC. The incremental cost-effectiveness ratio (ICER) was calculated by dividing *Δ*cost by *Δ*effectiveness as the following equation:

$$ICER = \frac{\Delta cost}{\Delta effectiveness}$$

The replications of 1000 Monte-Carlo simulation were performed to estimate ICER. Simulated ICERs were plotted on the cost-effectiveness plane and compared with the different levels of the willingness-to-pay threshold. By plotting the probability of being cost-effectiveness against each threshold level, the cost-effectiveness acceptability curve was constructed accordingly. At each threshold level, the net monetary benefit (NMB) was computed as follows:

$$NMB = Rx\Delta effectiveness - \Delta cost$$

where R = the willingness-to-pay thresholds

One-way sensitivity analyses was performed by varying variables once at a time. Results of the sensitivity analyses are demonstrated in the tornado diagram.

4.11 ETHIC CONSIDERATION

This study was conducted concerning the Helsinki declaration principles and medical research involving human subjects act. Before the subject recruitment, the study protocol was submitted to the ethical committee of all study centers. The first subject was recruited after approval from IRB. The ethical principles from the Belmont report were applied in this study as follows:

4.11.1 Respect for persons

The study's aim, risks and benefits, and detail of each surgical procedure are informed to the eligible patient along with the information sheet (Appendix B). Any question from the eligible patients was welcome. The eligible patients were allowed for at least 15 minutes to decide whether to participate. The consent form (Appendix C) was signed by the patient (or representative) if he/she decided to participate. The right to withdraw from the study at any time was reserved for all participants without any influence on the treatment.

If the patient decided not to participate, the surgical procedure would be selected according to share decision-making between the patient and doctor. However, baseline characteristics of non-participant were recorded after receiving permission from the patient, so no vulnerable subject was recruited in this study.

Participant identification is protected. By using the study ID, neither the name nor hospital number of participants appears in the CRFs. The patient's log sheet, which contains participant identification and contact information, can be accessed only by the principal investigator and the permitted research assistant. The document is kept in the safe-locked cabinet, and the electronic database is protected using the password. Only the principal investigator and the database manager have the access to these databases. After 5 years, all CRFs will be destroyed by shredding. None of the participant identification will be appreared in reports and publications from this study.

4.11.2 Beneficence and non-maleficence

The minimal increment of the risk of infection, seroma, hematoma, and postoperative pain might be observed in the RM group when compared with the PSC group; however, no significant difference has been reported in our meta-analysis. If the study hypothesis was true, the risk of IH occurrence in the RM would be lower than the PSC group. Therefore, the study risk could be considered "more than minimal risk without direct benefit to the subject but benefits to the science". However, participants receive physical examination and investigation might increase the chance of early IH detection during the follow up visit.

All complications, if occurred, would be treated according to the standard guideline. Any unexpected complications that might be associated with the study procedure were reported to the DSMB.

4.11.3 Justice

The studied procedure is randomly assigned to the participant. The same standard co-interventions were provided for participants regardless of their allocated procedure. The participant would receive 200 THB per visit as compensation for their time loss and travel cost. This study's results would bring advantages to all emergency/urgency laparotomy patients who are the same population as the participant.

4.12 BUDGET

The total budget was 1,078,015 Baht in total. Details are provided in Table 4.3.

4.13 PRELIMINARY RESULTS OF THE ENROLLMENT

Enrollment had been started since January 1, 2021. Among 6 centers, 3 of them (Vajira, Hatyai, and Bhumibol Adulyadej Hospital) were actively recruiting participants. Fifty-two participants (11.1% of estimated sample size) were enrolled; 41, 5, and 6 participants were from Vajira, Hatyai, and Bhumibol Adulyadej Hospital, respectively. Mean age (SD) was 57.9 (14.8) years and 63.5% of participants were male. Mean BMI (SD) was 23.4 (4.6) kg/m^2. Prevalence of diabetes and COPD was 19.6% and 3.9%, respectively. Participants were classified as having ASA class I, II, III, IV in 15.4%, 48.1%, 34.6%, and 1.9%, respectively. Most of the participants have never smoked or quit smoking more than 6 months before the operation (55.3% and 14.9%). Mean preoperative albumin level (SD) was 3.8 (0.6) g/dL. Missing data were observed for diabetes, COPD, smoking status, and albumin level in 1.9%, 1.9%, 9.6%, and 9.6%, respectively. Most of the participants (61.4%) were classified as having nutrition status class B (i.e., moderate malnutrition) using the nutrition alert form. Prevalence of severe malnutrition was 18.2%. Nutritional status was not assessed using nutrition alert form in eight participants (15.4%), especially in participants from Bhumibol Adulyadej Hospital (six from eight participants) because nutritional alert form and classification were not routinely used in this institute.

Benign perforation, benign obstruction, cancer, and inflammation were the leading causes of emergency/urgency operation; 48.1%, 34.6%, 7.7%, and 5.8%, respectively. Frequently performed procedures are listed as follows: local repair of perforation (46.2%), adhesiolysis (23.1%), small intestinal resection (13.5%), large intestinal resection (7.7%), and gallbladder and biliary tract surgery (3.9%). Incisional wounds were classified as clean-contaminated, contaminated, and clean in 61.5%, 30.8%, and 7.7% of participants, respectively. Mean incisional length (SD) was 15.3 (3.8) cm.

Length of the follow-up ranged from 1 to 18 months. Due to the severity of comorbid disease and surgical complications, two participants died after 1 month. Thus, 50 participants were left to be followed for 1 month. Our research assistants contacted all participants by telephone call to remind their appointment, but some participants could not be contacted or did not attend follow-up. According to our follow-up protocol, 52, 47, 45, 37, and 18 participants should visit 1-, 3-, 6-, 12-, and 18-month follow-up, respectively. Until now, none of the participants reached 24-month follow-up. Unfortunately, only 66.7% to 88.5% of participants attended each follow-up appointment, see Table 4.4.

4.14 DISCUSSION

Even though evidence of prophylactic mesh efficacy has been confirmed, no study focuses on emergency/urgency patients. Regarding systematic review in Chapter 2, this trial would be the first study in this particular population. RM's efficacy in IH prevention is less than OM but has less wound-related complications. Therefore, RM is the intervention of interest selected by balancing between benefits and risks, see Chapter 3. PSC with small-bites continuous technique is a comparator following abdominal wall closure recommendation.[26]

This RCT has several strengths. First, the sample size is relatively large compared to previously published trial[40-44, 47, 48, 50-52] Second, all outcomes were blindly assessed and analyzed to minimize bias. Third, the primary outcome (i.e., IH) would be assessed for 24 months corresponding with the recommendation from European Hernia Society.[26] Finally, an economic evaluation would be performed alongside a clinical outcome assessment to inform policymakers.

Some challenges are acknowledged. Results could be affected by surgeons' experience. However, surgeons involved in this trial were trained for both RM and PSC to standardize closure techniques. Protocol violation could be anticipated but ITT was selected to be the primary analysis, whereas AS and PP would be performed as sensitivity analysis. Intervention adherence would also be assessed using IV regression, in which the benefit of randomization would be maintained.

The enrollment was started since January 2021. However, the enrollment rate was poor. Subsequently, all surgical procedures were affected by COVID-19 pandemic which consumed most of the healthcare resources. Therefore, hospital beds and intensive care units were overwhelmed by COVID-19 patients. In addition, a significant number of healthcare personnel were shifted to COVID-19 section. As a result, care delivered to surgical patients was less optimal. This situation directly affected participant enrollment. Surgeons were unwilling to enroll patients to receive intervention which might be associated with additional risks. Even though COVID-19 infection is not an exclusion criterion, no investigator enrolled patients with COVID-19 infection because of the limited ability of post-operative care and assessment in these patients. In some situations, non-operative management was preferred if it was feasible and safe. Altogether, a poor enrollment rate was inevitable.

Another reason for poor enrollment rate is that this trial involves emergency surgery, which increases the risk of SSI. Applying foreign material (i.e., synthetic mesh) in this situation, though many studies[56, 57, 80, 81] demonstrated safe mesh use in a contaminated surgical environment, contradicts long-standing dogma of avoiding foreign material in such an environment. Therefore, only a limited number of surgeons in each center participated in this study. Moreover, some eligible patients missed trial enrollment given the intense workloads on the nightshifts and the nature of emergency conditions that require time management. As such, high enrollment rate is difficult to achieve. This RCT was designed to be a multicenter study considering this inconvenient situation. However, until now, only some centers actively enroll participants. Most of the time, enrollment occurred at Vajira hospital, the principal investigator's institute. To overcome this problem, more centers must be persuaded to participate in this trial. Affirmatively, it would significantly increase the cost of conducting the study.

Table 4.1 Time table of the clinical outcome measurement

Outcome	PO D1,3	Within 1 MO	3 MO	6 MO	12 MO	18 MO	24 MO
IH			✓	✓	✓	✓	✓
Wound infection	✓	✓	✓	✓	✓		
Seroma		✓	✓				
Burst abdomen	✓	✓					
Hematoma	✓						
Enterocutaneous fistula and wound sinus		✓	✓	✓	✓	✓	✓
Acute pain	✓						
Chronic pain			✓	✓	✓	✓	✓

MO, month; PO D, post-operative day

Table 4.2 Sample size calculation

Control group event rate	Intervention group event rate	% risk reduction	α	power	ratio	Total sample size
0.19	0.095	50	0.05	0.8	1:1	424
0.19	0.114	40	0.05	0.8	1:1	700
0.19	0.133	30	0.05	0.8	1:1	1,308

Table 4.3 Estimated budget

Activity	Unit	No. of Units	Unit cost (THB)	Total (THB)
1. Study-related costs				
1.1 Creating the protocol	Protocol	1	No charge	-
1.2 Creating the CRF	CRF	1	No charge	-
1.3 Document preparation	Case	470	10	4,700
1.4 IRB/Ethics committee	Site	6	No charge	-
1.5 Investigator fee (exclude Ramathibodi and Vajira)	site	4	10,000	40,000
1.6 Manager fee	Person	1	No charge	-
1.7 Statistical plan				
1.7.1 consultation	Person	1	No charge	-
1.7.2 report	Report	1	No charge	-
1.8 Manuscript				
1.8.1 writing	Manuscript	1	No charge	-
1.8.2 English proving & editing	Manuscript	1	No charge	-
1.8.3 submission fee	Manuscript	1	40,000	40,000
			Total	84,700
2.Participant-related costs				
2.1 Research assistant fee	Case	470	500	235,000
2.2 Telephone call (3 times/case)	Case	470 x 3	1.50	2,115
2.3 Mesh	Mesh	260	570	148,200
2.4 Anesthesia fee	Case	235	400	94,000
2.5 Ultrasound	Case	470	No charge	-

Table 4.3 Estimated budget (Cont.)

Activity	Unit	No. of Units	Unit cost (THB)	Total (THB)
2.6 Compensation for follow-up visit	Case	470 x 5	200	470,000
			Total	949,315
3. Data-related costs				
3.1 Data entry (double)	Record	470 x 2	No charge	-
3.2 Data cleaning	Record	470	No charge	-
3.3 Database programing	Person	1	No charge	-
3.4 Generation & Review of tables	Person	1	No charge	-
			Total	-
4. Site-related costs				
4.1 Initiating (exclude Ramathibodi and Vajira)	Site	4	1,000	4,000
4.2 Training (twice a year)	Site	6 x 2 x 2	1,000	24,000
4.3 Investigator meeting (online)	Site	6	No charge	-
4.4 Monitoring (twice a year) (exclude Ramathibodi and Vajira)	Visit	4 x 2 x 2	1,000	16,000
4.5 Closing	site	6	No charge	-
			Total	44,000
			Grand Total	1,078,015

Table 4.4 Total number of participants at each follow-up period and the percentage of participants attending follow-up visit

Follow-up period, Months	Total participants, N	Visiting participants, N (%)
1	52	46 (88.5)
3	47	41 (87.2)
6	45	33 (73.3)
12	37	30 (81.1)
18	18	12 (66.7)
24	0	0

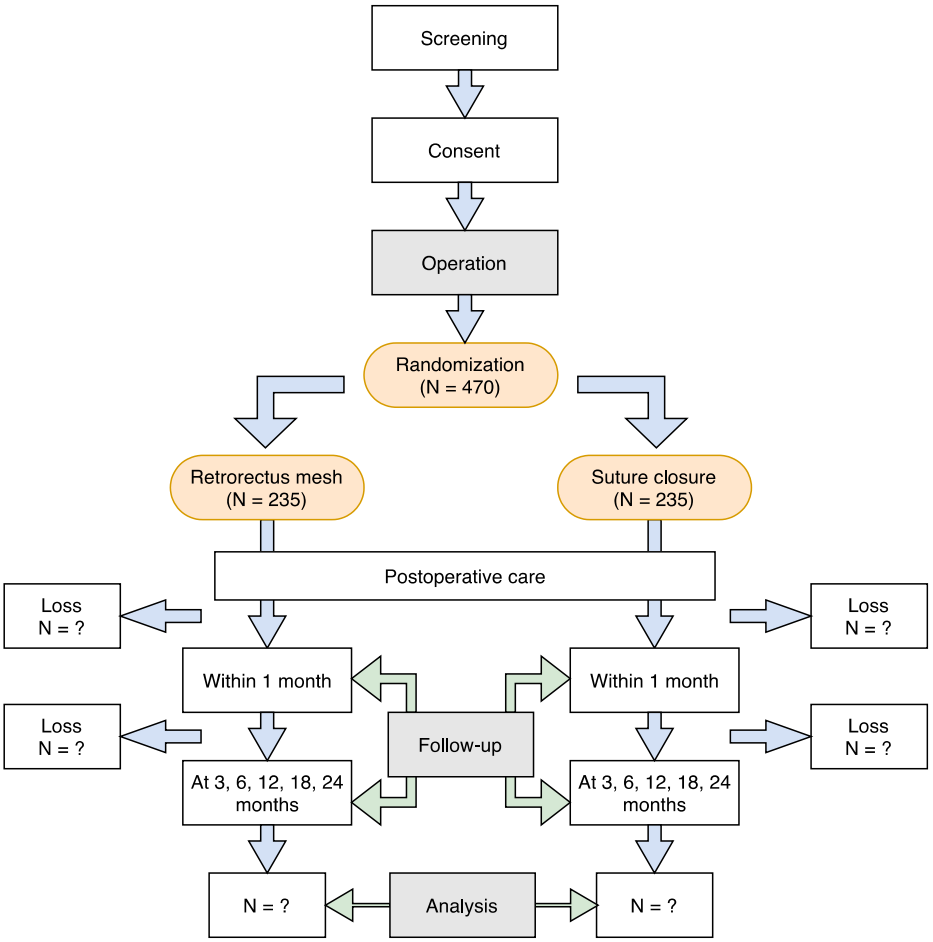


Figure 4.1 Study flow diagram

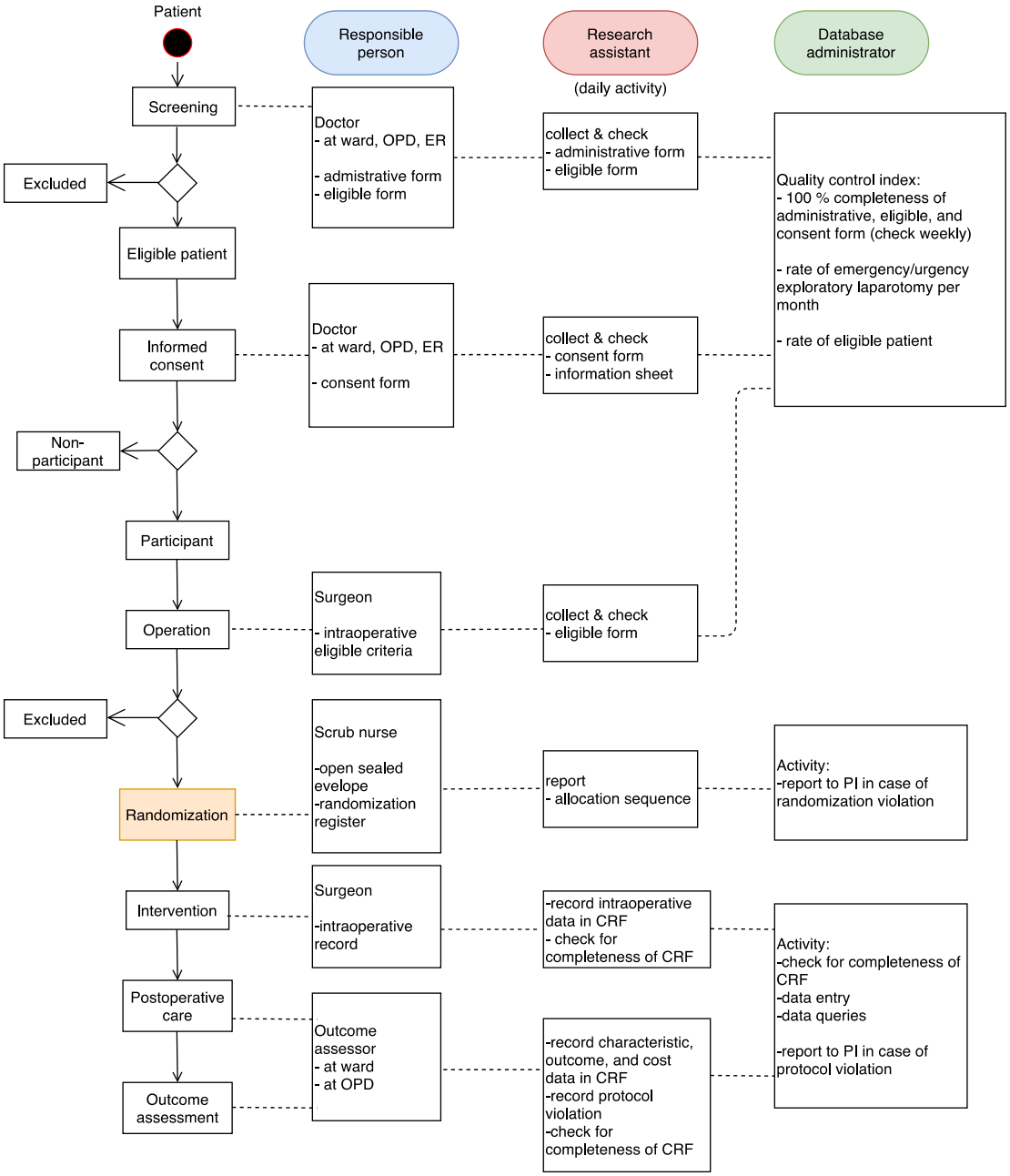


Figure 4.2 Patients' flow diagram

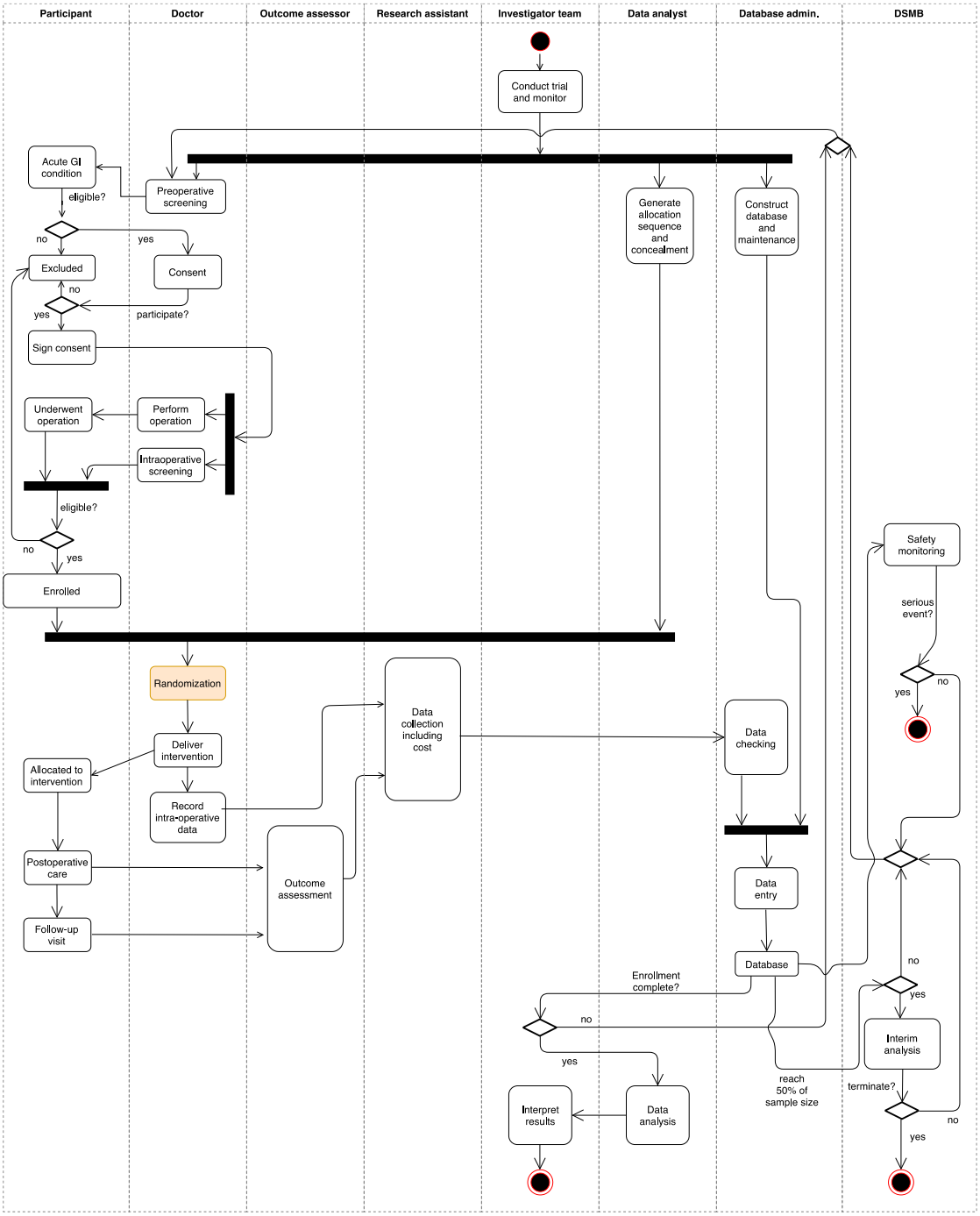


Figure 4.3 Trial activity

PART II
HERNIA PREDICTION

CHAPTER V
RATIONALE AND SYSTEMATIC REVIEW OF HERNIA PREDICTION MODEL

Even if prophylactic mesh shows benefits in the prevention of IH, it is still expensive and its accessibility is still limited particularly where resources are limited. Therefore, identifying individualized patients who are at high risk of IH occurrence should be useful. By applying a risk prediction model, mesh intervention could be allocated to patients, who are likely to gain benefits from IH prophylaxis.

5.1 SYSTEMATIC REVIEW

A systematic review was conducted to identify existed IH prediction model. Models were reviewed and their model performance and prediction variables were extracted. Since IH might be predetermined by fascial dehiscence (FD),[13] FD prediction models were also included in the review to identify predictor variables that could be added during IH prediction model revision. Review protocol followed PRISMA guideline[61] and was registered at PROSPERO (CRD42021282463).

5.1.1 Review methods

Searching was performed in Scopus, Medline (via PubMed), and Web of Science from inception to September 2021. Terms used for identifying studies constructed from the following keywords: incisional hernia, dehiscence, prediction model, receiver operating characteristic (ROC) curve, concordance statistic (C-statistic), sensitivity, specificity, derivation, and validation (Table 5.1). No language

limitation was applied. Studies would be eligible if they studied IH or FD prediction models in adult patients undergoing any abdominal operation, derived or validated models which consisted of more than one predictor variable, and reported at least one of the following model performances: C-statistic, sensitivity, specificity, predictive values (positive and negative), and observed/expected (O/E) outcome ratio. Models that predicted hernia recurrence after IH or parastomal hernia repair or hernia occurrence after open abdomen closure were excluded.

Studies' title, the first author's name, year of publication, study design, study phase (i.e., derivation or validation), model's name (if any), model derivation method (i.e., conventional statistic model or machine learning (ML)), the number of patients and events (i.e., IH or FD), demographic data and patients' characteristics were extracted.

Predictor variables and model's discrimination performances with 95% CI were extracted. When there was no reported 95% CI of C-statistics, it would be calculated from Hanley and McNeil's method.[90] If calibration performance (e.g., O/E ratio) was reported, it would also be retrieved.

RoB of each study was evaluated using PROBAST tool.[91] This tool evaluates 4 domains as follows: participants, predictors, outcome, and analysis. Each study was assessed as high, low, and unclear RoB. Screening for eligible studies, data extraction, and RoB assessment were performed by 2 independent reviewers.

5.1.2 Review results

Seven IH prediction models were identified from 7 studies.[5, 92-97] Five of them were developed by the research team of University of Pennsylvania.[5, 94-97] All studies were derivation-internal-validation phase. No external-validation study was eligible (Figure 5.1). The mean age ranged from 45.3 to 60.7 years; male was 26.6% to 93.9% (Table 5.2). BMI was reported in 3/7 studies which ranged from 28.2 to 56.8 kg/m^2. Follow-up time ranged from 6 to 57.9 months. RoB assessment was omitted in one study[96] due to the unavailability of full-text. The rest were judged as having a high risk of bias, especially in the participants and data analysis domains (Table 5.3).

Four models[5, 92, 93, 95] were developed to predict IH occurrence after a general abdominal operation, whereas IH occurrence after bariatric,[94] colorectal,[96] and

gynecologic surgery[97] was specifically predicted by one model each. Equations of IH prediction models are shown in Table 5.4. Their C-statistics are displayed in Figure 5.2.

Veljkovic et al.'s model[92] came from logistic regression using data from 603 patients. Four predictor variables (i.e., BMI, SSI, suture length to incision length ratio, and time to suture removal) were used to construct this model. Its C-statistic (95% CI) was 0.92 (0.88, 0.96). This model was developed for IH prediction in midline laparotomy patients.

The well-known IH prediction model named HERNIA score was developed by Goodenough et al. using Cox regression. The model was derived from and internally validated in data from 428 and 197 patients, respectively. BMI, COPD, and surgical approach were included in the model which yielded C-statistic (95% CI) of 0.77 (0.68, 0.86) in the internal-validation sample.

Among models from University of Pennsylvania, 2 models[5, 95] were developed for general abdominal surgery. Fischer et al.'s model[95] was developed for only elective open surgery, whereas Basta et al.'s model named *Penn hernia risk calculator*[5] is more general. The *Penn hernia risk calculator* is the most recent model from the University of Pennsylvania's research group which was deployed as a mobile application. Its C-statistic (95% CI) was 0.83 (0.81, 0.85) in the combined derivation-validation cohort. This model consists of sixteen prediction variables.

All existing IH prediction models were reported of having good calibration performance. Predictor variables used in each IH prediction model were listed in Table 5.5. Predictor variables from 3 identified FD prediction models were also listed in the same table.

5.2 CONCLUSION FROM SYSTEMATIC REVIEW

After a careful review of the candidate prediction models, *Penn Hernia Risk Calculator*[5] might be the most suitable model to adopt for our practice in terms of model performance and predictor variables. However, risk prediction model's performance usually drops from what was originally reported. Embracing any risk prediction model in a new clinical setting, and so it requires validation or even revision.[98, 99] Therefore, *Penn Hernia Risk Calculator*[5] was selected by this study for external validation and

revision using the Ramathibodi surgery dataset. This study derived IH risk prediction model that could be used in Thai setting

5.3 RESEARCH QUESTION

How about the performance of IH prediction tool in Thai patients undergoing abdominal surgery? Is revision required?

5.4 RESEARCH OBJECTIVE

To validate the existing IH prediction tool and revised it if needed.

Table 5.1 Search terms

Database	Search term
Scopus	TITLE-ABS-KEY (((((((incision*) OR (postoperative)) OR (ventral)) OR (scar)) AND (hernia*)) OR (((dehiscence) OR (eviscerat*)) OR ("burst abdomen"))) AND (((((predict*) OR (prognos*)) OR (risk)) OR (stratif*)) AND (((model) OR (score)) OR (index)))) AND ((((((((("receiver operating characteristic") OR (roc)) OR (auc)) OR (auroc)) OR ("concordance statistic")) OR ("c-statistic")) OR (accuracy)) OR (sensitivity)) OR (specificity)) OR (((validat*) OR (deriv*)) OR (develop*)))) AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re"))
Medline (PubMed)	(((((((incision*) OR (postoperative)) OR (ventral)) OR (scar)) AND (hernia*)) OR (((Dehiscence) OR (eviscerat*)) OR ("burst abdomen"))) AND (((((Predict*) OR (prognos*)) OR (risk)) OR (stratif*)) AND (((model) OR (score)) OR (index)))) AND ((((((((("receiver operating characteristic") OR (ROC)) OR (AUC)) OR (AUROC)) OR ("concordance statistic")) OR ("c-statistic")) OR (accuracy)) OR (sensitivity)) OR (specificity)) OR (((validat*) OR (deriv*)) OR (develop*)))
Web of Science	(((((((incision*) OR (postoperative)) OR (ventral)) OR (scar)) AND (hernia*)) OR (((Dehiscence) OR (eviscerat*)) OR ("burst abdomen"))) AND (((((Predict*) OR (prognos*)) OR (risk)) OR (stratif*)) AND (((model) OR (score)) OR (index)))) AND ((((((((("receiver operating characteristic") OR (ROC)) OR (AUC)) OR (AUROC)) OR ("concordance statistic")) OR ("c-statistic")) OR (accuracy)) OR (sensitivity)) OR (specificity)) OR (((validat*) OR (deriv*)) OR (develop*)))

Table 5.2 Characteristics of the included studies

Study	Population	Incision (approach)	Data source	Study design	Phase	Patients (n)	Events (n)	Age, year (mean)	Sex, male (%)	BMI, kg/m^2 (mean)	Follow-up, month
Veljkovic, 2010	Mixed abdominal surgery	Open	Prospective data	Cohort	Derivation	603	81	59	53.7	n/a	> 6
Goodenough, 2015 (HERNIAscore)	Mixed abdominal surgery	Open/Lap	Prospective data	Cohort	Derivation Internal-validation	428 197	70 23	60.7 n/a	93.9 n/a	28.2 n/a	41 41
Basta, 2016	Bariatric	Open/Lap	Medical records	Cohort	Derivation	2,161	52	45.3	26.6	56.8	28.3
Fischer, 2016	Mixed abdominal surgery	Open	Medical records	Cohort	Derivation	12,373	436	55.9	33.4	n/a	32.2±26.6
Lanni, 2016[a]	Colectomy	Open/Lap	Medical records	Cohort	Derivation	30,865	1,698	n/a	n/a	n/a	30
Tecce, 2017	Hysterectomy	Open	Medical records	Cohort	Derivation	2,145	76	52.6	n/a	n/a	n/a
Basta, 2019 (Penn risk calculator)	Mixed abdominal surgery	Open/Lap	Medical records	Cohort	Mixed derivation and internal-validation	29,739 19,799/9,940[b]	1,127	52.6	36.6	30.1	57.9

BMI, body mass index; FD, fascial dehiscence; IH, incisional hernia; Lap, Laparoscopic surgery; n/a, not available; NSQIP, National Surgical Quality Improvement Program; VAMC, Veteran Affairs Medical Centre

[a] No full-text available, [b] Derivation/Internal-validation

Table 5.3 Risk of bias of the included studies

PROBAST		Incisional hernia						
		Veljkovic	Goodenough	Basta	Fischer	Lanni	Tecce	Basta
Domain	Signal question	2010	2015	2016	2016	2016*	2017	2019
Participants	Were appropriate data sources used?	Y	Y	N	N		N	N
	Were all inclusions and exclusions of participants appropriate?	Y	Y	Y	Y		Y	Y
	Summary domain 1	+	+	-	-		-	-
Predictors	Were predictors defined and assessed in a similar way for all participants?	PY	PY	PY	PY		PY	PY
	Were predictor assessments made without knowledge of outcome data?	PY	Y	Y	Y		Y	Y
	Are all predictors available at the time the model is intended to be used?	Y	Y	Y	Y		Y	Y
	Summary domain 2	+	+	+	+		+	+
Outcome	Was the outcome determined appropriately?	NI	Y	PY	PY		PY	PY
	Was a pre-specified or standard outcome definition used?	NI	Y	Y	Y		Y	Y
	Were predictors excluded from the outcome definition?	Y	Y	Y	Y		Y	Y
	Was the outcome defined and determined in a similar way for all participants?	PY	N	NI	NI		NI	NI
	Was the outcome determined without knowledge of predictor information?	NI	NI	Y	Y		Y	Y
	Was the time interval between predictor assessment and outcome determination appropriate?	N	PY	Y	Y		Y	Y
	Summary domain 3	-	-	?	?		?	?

Table 5.3 Risk of bias of the included studies (Cont.)

PROBAST		Incisional hernia						
Domain	Signal question	Veljkovic 2010	Goodenough 2015	Basta 2016	Fischer 2016	Lanni 2016*	Tecce 2017	Basta 2019
Analysis	Were there a reasonable number of participants with the outcome?	N	N	N	Y		N	Y
	Were continuous and categorical predictors handled appropriately?	N	N	PN	PN		PN	PN
	Were all enrolled participants included in the analysis?	N	NI	Y	Y		Y	Y
	Were participants with missing data handled appropriately?	N	PN	NI	NI		NI	N
	Was selection of predictors based on univariable analysis avoided?	N	N	N	N		N	N
	Were complexities in the data accounted for appropriately?	Y	Y	Y	Y		Y	Y
	Were relevant model performance measures evaluated appropriately?	N	N	N	N		N	N
	Were model overfitting and optimism in model performance accounted for?	N	N	Y	Y		Y	PN
	Do predictors and their assigned weights in the final model correspond to the results from multivariable analysis?	N	Y	Y	Y		Y	Y
	Summary domain 4	-	-	-	-		-	-
	Overall	high	high	high	high		high	high

* No available full-text

Table 5.4 Risk score equations

Study	Equation
Veljkovic, 2010	Score = 32*(Suture incision ratio < 4.2) + 30*(SSI CDC 2 or 3) + 9*(Time to suture removal > 16 d) + 2*(BMI > 24 kg/m^2)
Goodenough, 2015	Score = 4*(Laparotomy) + 3*(HAL) + 1*(COPD) + 1*(BMI ≥ 25 kg/m^2)
Basta, 2016	Score = 5*(Open bariatric approach) + 2*(Malnutrition) + 2*(History of abdominal surgery) + 2*(BMI ≥ 60 kg/m^2) + 1*(Age 45-65)
Fischer, 2016	Score = 3*(Hispanic or Native American) + 2*(White) – 1*(Asian) + 3*(Concurrent ostomy/fistula takedown) + 1*(Concurrent ostomy creation) + 2*(Recent chemotherapy) + 2*(Obesity) – 1*(Normal weight) + 2*(Bariatric procedure) + 2*(Proctectomy) + 1*(Partial colectomy) + 1*(Small bowel resection) + 2*(History of alcohol abuse) + 2*(History of smoking) + 2*(History of liver disease) + 1*(Acute inflammatory process) + 1*(History of surgical wound complication) + 1*(Malnutrition) + 1*(Age > 45 yr) – 1*(Benign gynecologic mass)
Tecce, 2017	Score = 2*(Vertical incision) + 1*(Ascites) + 1*(Gynecologic malignancy) + 1*(BMI > 30 kg/m^2) + 1*(Acute inflammatory process) + 1*(Anemia) + 1*(Smoking history) + 1*(Concurrent GI procedure)
Basta, 2019	Score = 4*(Emergency laparotomy) + 2*(History of abdominal surgery) + 2*(Emergent vascular procedure) + 2*(Caucasian) + 1*(Indication: SBO) + 1*(Smoker) + 1*(2+ Elixhauser comorbidities) + 1*(Open approach) + 1*(BMI > 30 kg/m^2) – 2*(BMI 18-25 kg/m^2) – 4*(BMI < 18 kg/m^2) + 1*(Chronic liver disease) + 1*(History of cancer) + 1*(History of chemotherapy/XRT) + 1*(Concurrent fistula/ostomy procedure) + 1*(ASA/Anticoagulant use) + 1*(Chronic pulmonary disease) – 2*(Laparoscopic hysterectomy)

Table 5.5 Included prediction variables in each prediction model

Predictor variable	Study									
	Fascial dehiscence			Incisional hernia						
	Webster, 2003	Ramshorst, 2010	Cole, 2021	Veljkovic, 2010	Goodenough, 2015	Basta, 2016	Fischer, 2016	Lanni, 2016[a]	Tecce, 2017	Basta, 2019
Age		◉#	◉			◉#	◉#			
Sex		◉	◉							
Ethnicity							◉	◉		◉
BMI			◉	◉#	◉#	◉#	◉#	◉#	◉#	◉#
ASA status			◉							
2+ Elixhauser Comorbidity										◉
Chronic obstructive pulmonary disease	◉	◉	◉		◉					◉
Smoking			◉				◉		◉	◉
Coughing		◉								
Cerebrovascular accident	◉									
Ascites		◉							◉	
Jaundice		◉								
Anemia		◉							◉	
Hypertension			◉							
Cancer								◉		◉
Chemotherapy							◉			◉
Malnutrition						◉	◉			
Chronic liver disease							◉			
Alcohol abuse							◉			
Antiplatelet/anticoagulant										◉
Steroid			◉							
Prior hernia								◉		
History of abdominal surgery						◉				◉
Emergency operation	◉	◉	◉							◉
Open surgery					◉	◉		◉		◉
Midline incision									◉	
Hand-assisted laparoscopy					◉					
Organ of surgery		◉					◉			
Concurrent fistula/ostomy							◉			◉
Concurrent gastrointestinal procedure									◉	
Emergent vascular procedure										◉
Laparoscopic hysterectomy										◉

Table 5.5 Included prediction variables in each prediction model (Cont.)

Predictor variable	Study									
	Fascial dehiscence			Incisional hernia						
	Webster, 2003	Ramshorst, 2010	Cole, 2021	Veljkovic, 2010	Goodenough, 2015	Basta, 2016	Fischer, 2016	Lanni, 2016[a]	Tecce, 2017	Basta, 2019
Small bowel obstruction										◉
Gynecologic pathology							◉		◉	
Acute inflammation							◉		◉	
Operative time	◉#		◉							
Suture length: Incision length				◉#						
Surgeon's experience	◉									
Wound class	◉		◉							
Reoperation	◉									
Time to stitch removal				◉#						
SSI	◉	◉	◉	◉						
Wound complication							◉			
Pneumonia	◉									
Failure to wean	◉									
Any complication	◉									
Sodium			◉							
Creatinine			◉							
Hematocrit			◉							

ASA, American Society of Anesthesiologists; BMI, body mass index; SSI, surgical site infection

Used in categorized form, [a] Full-text not available – not all predictors reported

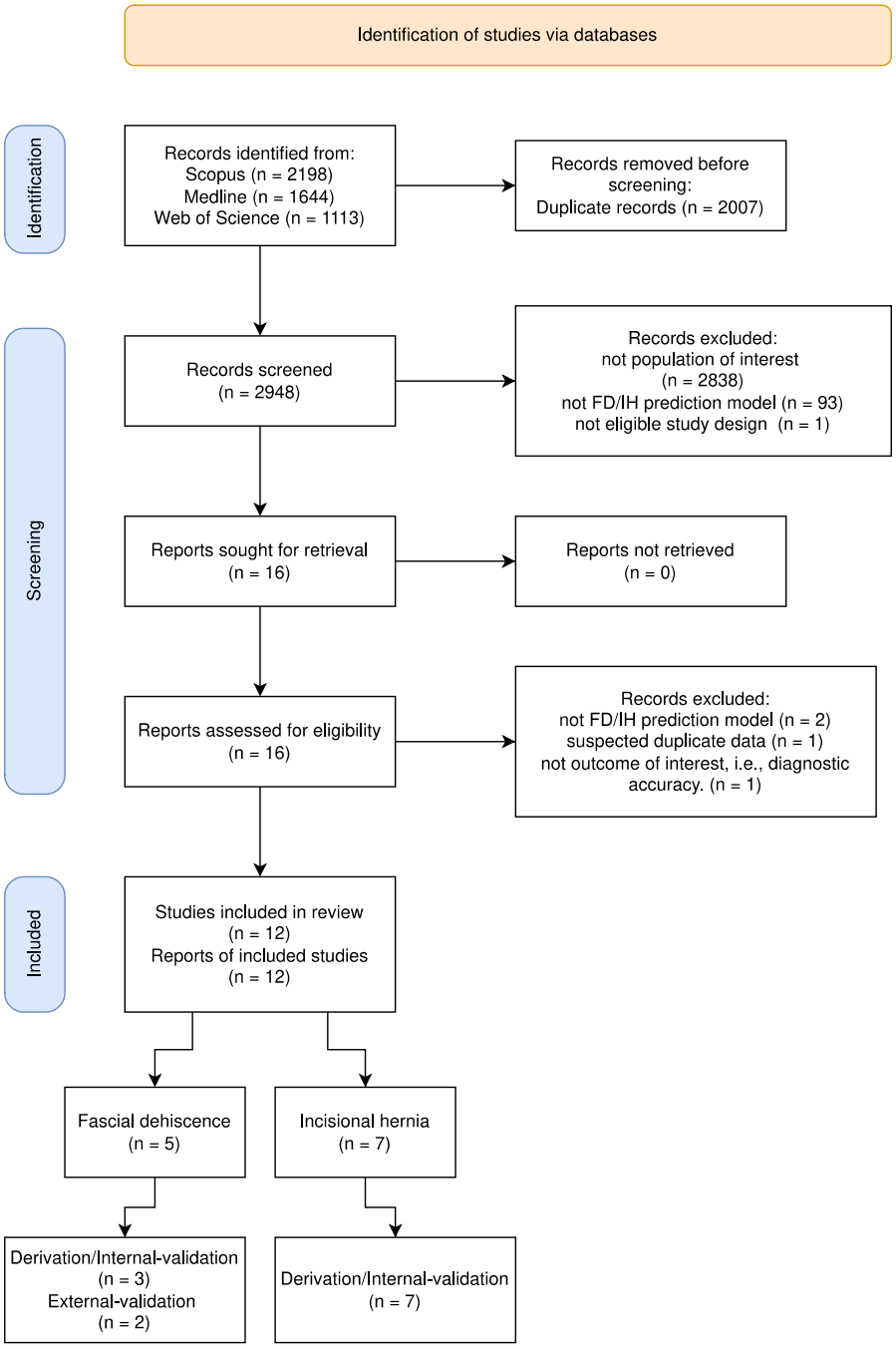


Figure 5.1 PRISMA flow of study selection

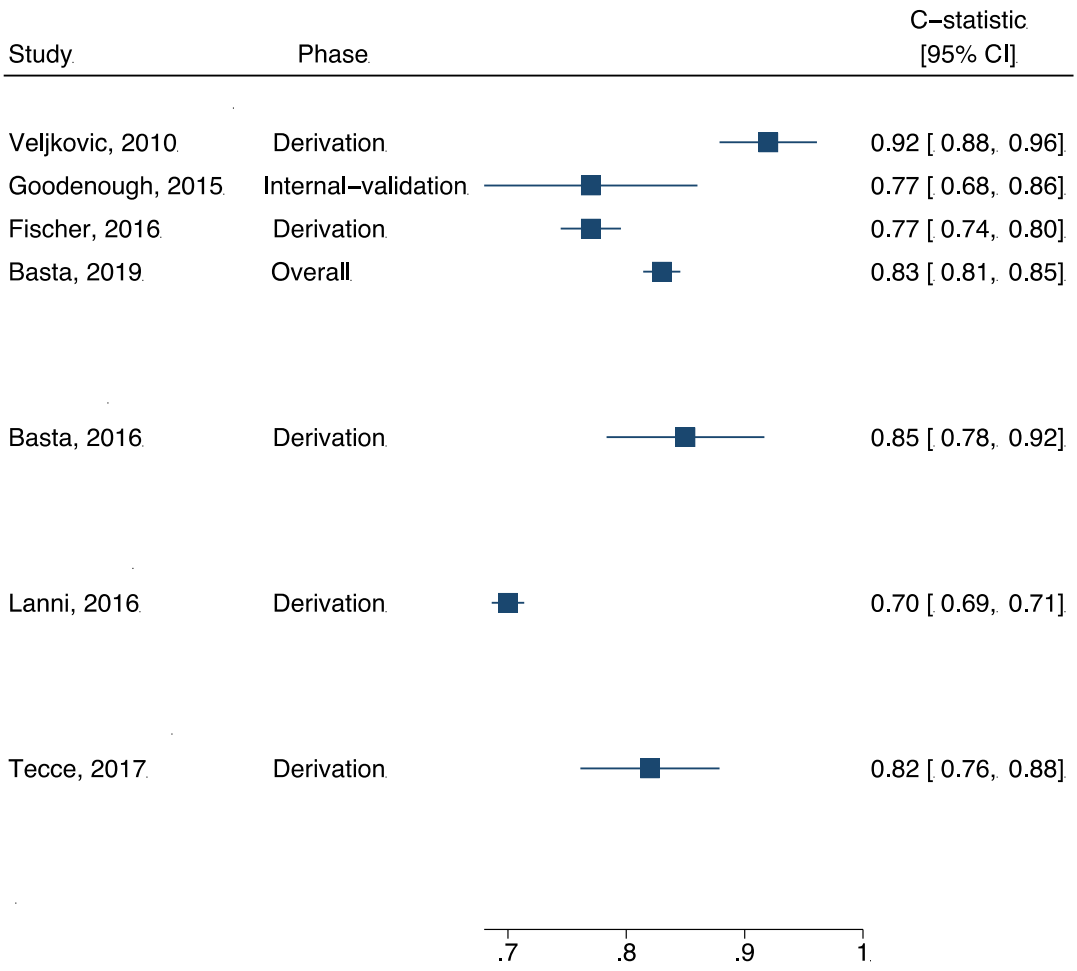


Figure 5.2 Incisional hernia prediction models' C-statistics

CHAPTER VI
EXTERNAL VALIDATION AND REVISION OF THE INCISIONAL HERNIA PREDICTION MODEL

Even though RM was efficacious for IH prevention, applying mesh-augmented fascia closure in all abdominal operated patients might not be cost-effective. Therefore, IH risk prediction model is required to target patients who are at high risk of IH occurrence and could be benefited from prophylactic strategy. Mesh's cost-effectiveness could be enhanced accordingly.

According to our review, *Penn hernia risk calculator*[5] was selected for further external validation based on its performance and included predictor variables.

6.1 METHODS

6.1.1 Study design and population

A retrospective cohort study was conducted on patients who underwent abdominal surgery in Ramathibodi Hospital from January 2010 to August 2021. The International Statistical Classification of Diseases and Related Health Problems (ICD) codes for the procedure (ICD-9-CM) related to the abdominal operation were used to identify target patients (Figure 6.1). Then, demographic, diagnosis (ICD-10), operative, hospital visit, hospital admission, laboratory, medication, and billing data were linked using an encrypted patient identification number. Patients would be eligible if they met the following criteria: age ≥ 18 years old, not pregnant nor in the postpartum period, and underwent intra-abdominal surgery. Incisional hernia diagnosed before or at the index operation was an exclusion criterion. Records that related to iatrogenic injury or post-operative complications were also excluded (Figure 6.1). Characteristics of our data were compared with the Penn cohort which included 29,739 abdominal operated patients from January 2005 to June 2016.

6.1.2 Retrieved data

Sixteen predictor variables were included in the Penn model and listed as follows: race, BMI, smoking status, COPD, chronic liver disease, cancer, the Elixhauser comorbidity score, history of chemotherapy/radiation therapy, antiplatelet/anticoagulant use, previous abdominal surgery, open approach, emergency surgery, emergency vascular surgery, laparoscopic hysterectomy, concurrent ostomy procedure, and small bowel obstruction. Race was not applied because only Thai nationals were included. The Elixhauser comorbidity score was absent because it is not routinely used in Thai practice. Therefore, only 14 predictor variables were retrieved. We decided to perform the complete case analysis. As a result, records that contained missing data on the mentioned variables were excluded.

Other variables which might be associated with IH were retrieved and later considered in the revision step. These variables included age, sex, the American Society of Anesthesiologists (ASA) physical status classification, comorbidity, immunosuppressive medication, wound classification, ostomy reversal, surgical procedure, intra-operative pathology, transfusion, intensive care unit admission, post-operative complications (i.e., SSI, wound complication, pneumonia). IH occurrence after the index operation was the outcome of interest identified by diagnosis (ICD-10: K43.0, K43.1, K43.2, K43.6, K43.7, and K43.9) and repair surgery (ICD-9-CM: 53.5, 53.6). Databases and modes of identification used for data retrieval were listed in Table 6.1. By rule-based decision, doubtful data were sought and verified with medical records. If this procedure could not clarify those data, they would be replaced with a missing value.

6.1.3 Statistical analysis

Data were described as mean and SD or median and interquartile range (IQR) depending on whether they were normally distributed or not. Otherwise, frequency and percentage were used. Because variables in the article on the *Penn hernia risk calculator* were described in the categorical form, chi-square test was used to compare between Ramathibodi and Penn cohorts. The Penn IH prediction model was validated and revised in Ramathibodi data by fitting logistic regression which had IH

occurrence as an outcome. Validation and revision were performed in the following step.[99]

Step 1: Model performance

The Penn hernia prediction score was computed using β-coefficients (Score A) and weighted scores (Score B) as originally proposed. Score A and B were as follows:

$$\begin{aligned}\text{Score A} = &- 1.61 \text{ x (BMI } < 18) - 0.65 \text{ x (BMI } 18-25) + 0.35 \text{ x (BMI } > 30) \\ &+ 0.50 \text{ x (Smoking)} + 0.22 \text{ x (COPD)} + 0.31 \text{ x (Cirrhosis)} \\ &+ 0.29 \text{ x (Cancer)} + 0.29 \text{ x (Chemotherapy or RT)} \\ &+ 0.25 \text{ x (Antiplatelet or Anticoagulant)} + 1.54 \text{ x (Emergency)} \\ &+ 0.35 \text{ x (Open surgery)} + 0.25 \text{ x (Ostomy)} \\ &+ 0.85 \text{ x (Previous surgery)} + 0.51 \text{ x (SBO)}\end{aligned}$$

$$\begin{aligned}\text{Score B} = &- 4 \text{ x (BMI } < 18) - 2 \text{ x (BMI } 18-25) + 1 \text{ x (BMI } > 30) \\ &+ 1 \text{ x (Smoking)} + 1 \text{ x (COPD)} + 1 \text{ x (Cirrhosis)} + 1 \text{ x (Cancer)} \\ &+ 1 \text{ x (Chemotherapy or RT)} + 1 \text{ x (Antiplatelet or Anticoagulant)} \\ &+ 4 \text{ x (Emergency)} + 1 \text{ x (Open surgery)} + 1 \text{ x (Ostomy)} \\ &+ 2 \text{ x (Previous surgery)} + 1 \text{ x (SBO)}\end{aligned}$$

Then, scores were regressed on the IH outcome in the following equation.

Model 1.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score A]}$$

Model 1.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score B]}$$

Step 2: Model revision

Each original predictor variable was added to the model from step 1. Only significant variables remained in the models.

Model 2.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score A]} + \sum_i b_i x_i$$

Model 2.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score B]} + \sum_i b_i x_i$$

Step 3: Model update

Predictor variables significantly associated with IH occurrence in the Ramathibodi cohort but not included in the original models (i.e., step 1 models) were added in this step.

Model 3.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score A]} + \sum_i b_i z_i$$

Model 3.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score B]} + \sum_i b_i z_i$$

Step 4: Model update

All original predictor variables were included and regressed on the IH outcome. However, new β-coefficients were estimated based on Ramathibodi data.

$$\begin{aligned}\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = {} & b_0 - b_1 \text{ x (BMI } < 18) - b_2 \text{ x (BMI } 18-25) + b_3 \text{ x (BMI } > 30) \\ & + b_4 \text{ x (Smoking)} + b_5 \text{ x (COPD)} + b_6 \text{ x (Cirrhosis)} \\ & + b_7 \text{ x (Cancer)} - b_8 \text{ x (Chemotherapy or RT)} \\ & + b_9 \text{ x (Antiplatele or Anticoagulant)} + b_{10} \text{ x (Emergency)} \\ & + b_{11} \text{ x (Open surgery)} + b_{12} \text{ x (Ostomy)} \\ & + b_{13} \text{ x (Previous surgery)} - b_{14} \text{ x (SBO)}\end{aligned}$$

Step 5: Model update

From step 4, only significant predictor variables remained in the equation.

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \sum_i b_i x_i$$

Where x_i = significant predictors

Step 6: Model update

The predictor variables in step 3 and 5 were fitted simultaneously; however, only significant ones were retained in the equation.

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \sum_i b_i x_i + \sum_i b_i z_i$$

Where x_i = significant predictors from step 5

Step 7: Model update

From step 6, only pre-operative and intra-operative predictors were retained.

Each model from steps 1 to 7 was assessed for its discrimination and calibration performance. C-statistic (i.e., area under the receiver operating characteristic curve) was used to assess discrimination performance, whereas calibration performance was assessed by Hosmer-Lemeshow goodness-of-fit chi-square tests of O/E outcome ratio and the O/E plot. Then, the best model was selected based on performance, and a composite risk score was constructed using the model's coefficients. By using 25^{th}, 50^{th}, and 75^{th} percentiles of the distribution, the new composite risk score was categorized into 4 levels of IH risk (i.e., very low, low, moderate, moderate-high). At each cut-off, sensitivity, specificity, positive predictive values (PPVs), and likelihood ratios were estimated. We considered significance at p-value < 0.05. STATA version 17 was used in statistical analysis.

6.2 RESULTS

From 423,704 records in the Ramathibodi surgery database (January 2010 - August 2021), 18,358 records underwent abdominal operation and 16,731 of them met

our eligibility criteria. However, only 12,155 records (11,617 patients) had complete data and were used in this analysis (Figure 6.1). The median follow-up time (IQR) was 23.4 (6.3 – 52) months. The mean age (SD) was 57 (16.1) years, and 38.4% of them were male. Frequently performed procedures in this database included biliary (41.5%), gastrointestinal (24%), colorectal (19.5%), and gynecologic procedures (10.2%).

Ramathibodi cohort substantially differed from the Penn cohort in terms of patients' characteristics (Table 6.2). More than half of the patients in Ramathibodi cohort had BMI in normal range, whereas approximately one quarter of the Penn cohort had a normal BMI. COPD and smoking prevalence were extremely low in Ramathibodi cohort when compared with Penn cohort (1.7% versus 27.2% and 0.2% versus 29.0%, respectively). Prevalence of hypertension and diabetes were also higher in the Penn than Ramathibodi cohort; 49.6% versus 31.3% and 19.2% and 12.0%, respectively. Contrary, Ramathibodi cohort had a significantly higher prevalence of cancer (31.7%) and chemotherapy/radiotherapy (16.1%) than the Penn cohort (22.3% and 4.4%, respectively). A higher prevalence of previous abdominal surgery was observed in the Penn cohort (12.7% versus 5.4%). While rates of surgery performed via open approach were similar, the emergency surgery rate was 2.4-fold higher in Ramathibodi than Penn cohort (28.3% versus 11.8%). IH incidence was substantially lower in Ramathibodi than Penn cohort (1.5% versus 3.8%).

The original *Penn hernia risk calculator* consists of 16 predictor variables but only 14 variables were used in validation in Ramathibodi cohort. Laparoscopic hysterectomy and emergency vascular surgery patients in Ramathibodi cohort had no IH occurrence. Thus, the coefficients of these 2 variables were not used in the model. Only 12 predictor variables remained. Among these variables, BMI, chronic liver disease, antiplatelet/anticoagulant use, open surgery, concurrent ostomy, and previous abdominal surgery (6 predictor variables) were significantly associated with IH occurrence (Table 6.3). Of these 6 variables, similar coefficients of open surgery and previous abdominal surgery in Ramathibodi and the Penn data were observed; 0.36 versus 0.35 and 0.82 versus 0.85, respectively. Coefficients of the rest variables (i.e., BMI, chronic liver disease, antiplatelet/anticoagulant use, and concurrent ostomy) substantially differed between the 2 datasets.

Validation and revision were performed in steps. Equations were constructed from each step and both discrimination and calibration performance were assessed by C-statistic and O/E ratio, respectively (Table 6.4). In steps 1 to 3, models were constructed by both variable coefficients and weighted scores. Steps 4 to 7 resulted in only 1 model per step.

Step 1:

Model 1.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 4.52\ +\ 0.48\ \text{x [Score A]}$$

Model 1.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 4.55\ +\ 0.19\ \text{x [Score B]}$$

Step 2:

Model 2.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 4.54\ +\ 0.47\ \text{x [Score A]} + 1.08\ \text{x (Cirrhosis)}$$

Model 2.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 4.50\ +\ 0.30\ \text{x [Score B]} + 0.87\ \text{x (Cirrhosis)} - 0.89\ \text{x (Emergency)}$$

Step 3:

Model 3.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 5.84\ +\ 0.41\ \text{x [Score A]} + 1.14\ \text{x (Age } 45-65) + 1.64\ \text{x (Age} > 65) + 0.96\ \text{x (SSI)} + 0.74\ \text{x (Immunosuppression)} + 1.89\ \text{x (Ostomy reversal)}$$

Model 3.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 5.84\ +\ 0.16\ \text{x [Score B]} + 1.13\ \text{x (Age } 45-65)$$
$$+\ 1.61\ \text{x (Age } >\ 65) +\ 0.94\ \text{x (SSI)}$$
$$+\ 0.73\ \text{x (Immunosuppression)} +\ 1.91\ \text{x (Ostomy reversal)}$$

Step 4:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -4.57 -\ 0.52\ \text{x (BMI } <\ 18) -\ 0.60\ \text{x (BMI } 18-25)$$
$$+\ 0.52\ \text{x (BMI } >\ 30) +\ 0.96\ \text{x (Smoking)} +\ 0.38\ \text{x (COPD)}$$
$$+\ 1.13\ \text{x (Cirrhosis)}$$
$$+\ 0.30\ \text{x (Cancer)} -\ 0.18\ \text{x (Chemotherapy or RT)}$$
$$+\ 0.58\ \text{x (Antiplatele or Anticoagulant)} +\ 0.27\ \text{x (Emergency)}$$
$$+\ 0.36\ \text{x (Open surgery)} +\ 0.52\ \text{x (Ostomy)}$$
$$+\ 0.82\ \text{x (Previous surgery)} -\ 0.02\ \text{x (SBO)}$$

Step 5:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -4.49 -\ 0.48\ \text{x (BMI } <\ 18) -\ 0.58\ \text{x (BMI } 18-25)$$
$$+\ 0.52\ \text{x (BMI } >\ 30) +\ 1.13\ \text{x (Cirrhosis)}$$
$$+\ 0.62\ \text{x (Antiplatelet or Anticoagulant)} +\ 0.49\ \text{x (Open surgery)}$$
$$+\ 0.81\ \text{x (Previous surgery)} +\ 0.56\ \text{x (Ostomy)}$$

Step 6:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -5.72 -\ 0.37\ \text{x (BMI } <\ 18) -\ 0.56\ \text{x (BMI } 18-25)$$
$$+\ 0.63\ \text{x (BMI } >\ 30) +\ 1.09\ \text{x (Age } 45-65)$$
$$+\ 1.61\ \text{x (Age } >\ 65) +\ 0.93\ \text{x (Cirrhosis)}$$
$$+\ 0.69\ \text{x (Immunosuppression)} +\ 0.46\ \text{x (Open surgery)}$$
$$+\ 1.96\ \text{x (Ostomy reversal)} +\ 0.50\ \text{x (Transfusion)} +\ 0.96\ \text{x (SSI)}$$

The original models (step 1) demonstrated fair discrimination performance in both weighted score and coefficient models. C-statistics (95% CI) were 0.645 (0.607, 0.683) and 0.634 (0.595, 0.674), respectively. Better performance of weighted score models was also observed in steps 2 and 3. Coefficient adjustment in steps 2, 4, and 5, which still focused on original predictors, could improve C-statistics (95% CI) to 0.679 (0.641, 0.717), 0.692 (0.655, 0.729), and 0.689 (0.652, 0.726), respectively.

Substantial improvement was observed when new variables were added to the model. Additional predictors, obtained from a systematic review (section 5.2) and clinical knowledge, would be included in the original model if they were significantly associated with IH occurrence in univariate analysis. These new predictor variables along with their coefficients are displayed in Table 6.5. Only significant variables in the multivariate equation (i.e., age, immunosuppressive medication, ostomy reversal, and SSI) were kept in the step 3 model. This model yielded a C-statistic (95% CI) of 0.729 (0.693, 0.765). In step 6, variables that were considered to add in step 3 and that remained in step 5 were fitted together in the equation. By stepwise elimination, age, BMI, cirrhosis, immunosuppressive medication, open surgery, ostomy reversal, transfusion, and SSI remained in the model. Step 6's C-statistic was 0.743 (0.707, 0.778). Good model calibration was observed from each step with the O/E ratios ranging from 0.967 to 1.031.

Prediction model can predict a patient's prognosis but it would be more advantageous if it could also guide treatment allocation. When mesh-augmented fascia closure, which can be delivered in the operation room, can effectively prevent IH, the model that includes only pre-operative and intra-operative but not post-operative predictors would be beneficial. Therefore, we decided to remove SSI from the step 6 model. Only pre-operative and intra-operative predictors were retained in the step 7 model as described below.

Step 7:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -5.71 - 0.39 \text{ x (BMI } < 18) - 0.57 \text{ x (BMI } 18-25)$$
$$+ 0.64 \text{ x (BMI } > 30) + 1.11 \text{ x (Age } 45-65)$$
$$+ 1.63 \text{ x (Age } > 65) + 0.92 \text{ x (Cirrhosis)}$$
$$+ 0.74 \text{ x (Immunosuppression)} + 0.50 \text{ x (Open surgery)}$$
$$+ 2.06 \text{ x (Ostomy reversal)} + 0.60 \text{ x (Transfusion)}$$

C-statistic (95% CI) of 0.733 (0.698, 0.768) and the O/E ratio (95% CI) of 0.968 (0.848, 1.088) were indicated (Table 6.4 and Figure 6.2). Coefficients and their 95% CIs are described in Table 6.6. The risk scores computed from this final model ranged from -6.28 to 1.38, which were stratified into very low, low, moderate, and moderate-high by the cut-off of -5.17, -4.60, and -4.07 (i.e., 25th, 50th, and 75th percentiles). Table 6.7 presents sensitivity, specificity, PPVs, and likelihood ratios according to each stratum. At the cut-off of -4.07, sensitivity and specificity were 58.4% and 74.1%, respectively. Because of the low incidence of IH in Ramathibodi dataset, PPVs were low in all strata. Patients who later developed IH were 2.26 times more likely to have a risk score ≥ -4.07 compared with patients who did not experience IH.

6.3 DISCUSSION

We performed a systematic review to identify existing IH prediction models and selected a model for further validation. Seven models[5, 92-97] were reviewed, in which 4 of them[5, 92, 93, 95] were derived for patients undergoing a general abdominal operation.

Among 4 models for general abdominal surgery, the best discrimination performance belonged to the Veljkovic et al.'s model[92] (C-statistic = 0.92). However, it is questionable whether the time to suture removal or complete epithelialization affects fascia healing and should be presented in the IH prediction model. This variable was also unavailable in Ramathibodi's data. In addition, follow-up time in Veljkovic et al.'s study was too short. Therefore, this model was not selected for validation.

HERNIAscore,[93] which yielded a C-statistic of 0.77, was constructed from 3 predictor variables. One of them is a surgical approach which has 3 categories

including total laparoscopy, hand-assisted laparoscopy, and open surgery. Given that hand-assisted laparoscopy is almost replaced by total laparoscopy, this model might be considered out of date. Both Veljkovic et al.'s model and HERNIAscore derived from a small number of patients (603 and 428 patients, respectively).

Fischer et al.[95] from University of Pennsylvania developed IH prediction model that was specific to elective open abdominal surgery. Its C-statistic was also 0.77. A few years later, this model was replaced by a newer version named *Penn hernia risk calculator*.[5] This new model derived from data from 19,799 patients, aimed for both elective and emergency surgery, was not limited to open approach, and yielded a C-statistic of 0.84 in the derivation cohort.

Considering that a prediction model usually performs less well outside the derivation population, it should be validated or even revised before using in a new setting.[99] Among 4 models for general abdominal surgery, only HERNIAscore has been externally validated and revised in Cherla et al.'s study[100] (this study was not eligible in our systematic review due to outcome reporting). In our study, *Penn hernia risk calculator* was selected for validation and revision according to its performance and availability of predictor variables' data in Ramathibodi database.

We started with validation of the *Penn hernia risk calculator,* then derived a new model finally. Our approach followed recommendations in the Moons et al.'s article.[99] Only fair discrimination performance was observed when *Penn hernia risk calculator* was applied to Ramathibodi data (step 1 C-statistic = 0.645). Performance discrepancy could be explained by the difference in characteristics between Ramathibodi and the Penn cohort which was obvious when both cohorts were compared with each other. In addition, a markedly lower IH incidence was observed in Ramathibodi data. These findings suggested model revision. Model performance was improved with C-statistics ranging from 0.679 to 0.692 by model revision using only original predictor variables. However, only six of 14 original predictors were significantly associated with IH occurrence in Ramathibodi cohort (step 5). Emergency surgery which had the strongest association with the IH occurrence was eliminated from the model in this step.

Further improvement was achieved by adding new predictor variables into the model (steps 3 and 6). Three more original predictors were eliminated and 4 new

predictors were included in step 6 to achieve acceptable discrimination and calibration performance (C-statistic = 0.743, O/E ratio = 0.967). Among predictors included in step 6, only SSI was the post-operative factor. When SSI was removed in step 7, we arrived at the final model with a little lower C-statistic (0.733) and higher calibration (O/E ratio = 0.968), but could guide adding a preventive procedure (e.g., mesh-augmented fascia closure) right during surgery. In the end, our updated model substantially differed from the original Penn model.

Even though the efficacy of prophylactic mesh in hernia prevention was indicated in many trials. Surgeons are still reluctant to adopt mesh-augmented fascial closure in their practice. Prediction model that could inform patients' risk of hernia occurrence might increase the adoption rate by suggesting patients at high IH risk who would benefit from prophylactic mesh.

Prediction model could be further improved in a way that might increase surgeons' adoption rate of prophylactic mesh by applying a counterfactual approach. Whether treatment effect has been confirmed in the clinical trial or not, it is the population-level effect which can significantly differ from an individual effect. In other words, individual patients that have different pattern of risk factors respond to treatment differently. The counterfactual prediction model considering treatment level (i.e., receiving or not receiving treatment) and other covariates in the model allow clinicians to estimate treatment effect for individual.[101, 102] This approach supports a personalized medicine paradigm and has been applied in other medical fields.[102-104] If prophylactic mesh was considered in the prediction model, surgeons would easily estimate benefits of mesh use in each patient and decide whether to implant mesh or not. This counterfactual prediction model will be a future work because more data from patients who received mesh placement must be collected. Given that few patients underwent mesh-augmented fascial closure, multicenter data collection is necessary.

Strengths of this study are that IH prediction models were systematically reviewed and the most promising model was selected for further validation. The validation and revision steps were also performed systematically. Additional predictors came from a thorough review of IH and FD prediction models. However, there were some limitations that we acknowledged. First, we did not include race and the Elixhauser comorbidity score in the model due to the unavailability of data. In addition,

emergency vascular surgery and laparoscopic hysterectomy were not associated with IH. These variables were omitted from the model because their coefficients cannot be estimated. Therefore, only 12 out of 14 original predictors were used. Second, we performed complete case analysis. A significant number of patients were excluded (4,576 records) because of BMI missing, and this might cause some bias.

6.4 CONCLUSION

Among IH prediction models, *Penn hernia risk calculator* was selected for validation and revision in this study. Even though the performance of the model was not satisfactory at the beginning, a new model with an acceptable performance can be derived from a systematic approach. This new model consists of only pre-operative and intra-operative factors. Therefore, it could help identify patients at high IH risk and suggests intra-operative IH prophylaxis to those patients. Given that prophylactic procedures including mesh-augmented fascia closure are efficacious, applying this tool in clinical practice could enhance the efficacy and cost-effectiveness of IH prophylactic measures.

Table 6.1 List of databases and mode of identification used for data retrieval

Variable	Database	Mode of identification
Age	Demographic	Date of surgery – Date of birth (in years)
Sex	Demographic	As recorded in database
BMI	Hospital visit	Average, 365 days before to 90 days after the index record
Smoking	Demographic	As recorded in database
ASA class	Operative	As recorded in database
COPD	Diagnosis	ICD-10: J44.0, J44.1, J44.8, J44.9 Diagnosed surgery date
Chronic liver diseases	Diagnosis	ICD-10: K70.3, K74.3, K74.4, K74.5, K74.6 Diagnosed before surgery date
CKD	Diagnosis	ICD-10: N18, N19 Diagnosed before surgery date
Diabetes	Diagnosis	ICD-10: E10, E11, E12, E13 Diagnosed before surgery date
Antiplatelet/Anticoagulant	Medication	Keyword: Aspirin, Clopidogrel, Heparin, warfarin, Clexane, Fraxiparine, Enoxaparin, etc. From admission to 90 days after surgery date
Immunosuppressive medication	Medication	Keyword: Prednisolone, Ciclosporin, Mycophenolate, Tacrolimus, etc. From admission to 90 days after surgery date
Chemotherapy	Diagnosis	ICD-10: Z51.1, Z92.6, Z08.2 Diagnosed in 365 days after surgery date
Radiotherapy	Diagnosis	ICD-10: Z51.0 Diagnosed in 365 days after surgery date
Previous abdominal surgery	Operative	ICD-9-CM listed in Figure 5.2 Performed before the index record
Emergency surgery	Operative	As recorded in database
Open surgery	Operative	Not recorded as laparoscopic surgery in database
Ostomy	Operative	ICD-9-CM: 46.1x, 46.2x
Ostomy reversal	Operative	ICD-9-CM: 46.5x
Colorectal surgery	Operative	ICD-9-CM: 45.03, 45.4x, 45.52, 45.7x, 45.8x, 45.92 – 45.95, 46.63, 46.64, 46.75, 46.76, 46.94, 48.0, 48.1, 48.3x – 48.9x
Small intestinal resection	Operative	ICD-9-CM: 45.6x

Table 6.1 List of databases and mode of identification used for data retrieval (Cont.)

Variable	Database	Mode of identification
Emergency vascular surgery	Operative	ICD-9-CM: 38.04, 38.06, 38.14, 38.16, 38.44, 38.46 + "emergency"
Laparoscopic hysterectomy	Operative	ICD-9-CM: 68.3, 68.4, 68.6, 68.9 + "laparoscopic surgery"
Wound class	Operative	As recorded in database
Cancer	Operative	Keyword: Malignant neoplasm, neoplasm, carcinoma, sarcoma
Small bowel obstruction	Operative	ICD-10: K56.1-K56.6
SSI	Diagnosis	ICD-10: T81.4 Diagnosed in 365 days after surgery date
Pneumonia	Diagnosis	ICD-10: E10, E11, E12, E13 Diagnosed in 90 days after surgery date
Transfusion	Billing	As recorded in database
ICU stay	Operative	As recorded in database (refer to)

ASA, American society of anesthesiologists; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; SSI, surgical site infection

Table 6.2 Summary characteristics for Ramathibodi and Penn cohorts

Predictors, n (%)	Penn cohort (N = 29,739)	Ramathibodi cohort (N = 12,155)	P-value
Incisional hernia	1,127 (3.8)	178 (1.5)	< 0.001
Race, Caucasian	18,702 (62.8)	NA	
Age, years			
< 45	8,837 (29.7)	2,887 (23.8)	< 0.001
45 – 65	13,895 (46.7)	5,168 (42.5)	
> 65	7,007 (23.5)	4,100 (33.7)	
Sex, male	10,894 (36.6)	4,667 (38.4)	0.001
BMI, kg/m^2			
< 18	1,103 (3.7)	662 (5.5)	< 0.001
18 – 25	8,021 (26.9)	6,811 (56.0)	
> 25 – 30	9,928 (33.4)	3,451 (28.4)	
> 30	10,687 (35.9)	1,231 (10.1)	
Smoker	8,102 (27.2)	27 (0.2)	< 0.001
COPD	8,632 (29.0)	207 (1.7)	< 0.001
Hypertension	14,776 (49.6)	3,798 (31.3)	< 0.001
Diabetes	5,720 (19.2)	1,463 (12.0)	< 0.001
Cirrhosis	NA	206 (1.7)	NA
2+ Elixhauser comorbidity score	18,711 (62.9)	NA	NA
Cancer	6,654 (22.3)	3,853 (31.7)	< 0.001
Chemotherapy/Radiotherapy	1,306 (4.4)	1,954 (16.1)	< 0.001
Antiplatelet/Anticoagulant	3,016 (10.1)	1,572 (12.9)	< 0.001
Emergency surgery	3,523 (11.8)	3,434 (28.3)	< 0.001
Open surgery	11,628 (39.1)	5,431 (44.7)	< 0.001
Concurrent Ostomy	NA	753 (6.2)	NA
Ostomy reversal	NA	56 (0.5)	NA
Small bowel resection	NA	416 (3.4)	NA
Large bowel surgery			
Partial colectomy	NA	1,902 (15.7)	NA
Proctectomy	NA	288 (2.4)	NA
Emergency vascular procedure	354 (1.2)	2 (0.02)	< 0.001
Laparoscopic hysterectomy	2,446 (8.2)	92 (0.8)	< 0.001
History of abdominal surgery	3,781 (12.7)	652 (5.4)	< 0.001
Small bowel obstruction	3,561 (11.9)	508 (4.2)	< 0.001
Wound complication	NA	660 (5.4)	NA

BMI, body mass index; COPD, chronic obstructive pulmonary disease; NA, not available

Table 6.3 Estimation of Penn model predictor coefficients based on Ramathibodi surgical cohort data

Variables, n (%)	Ramathibodi data						Penn IH prediction model			
	IH		Univariate		Multivariate					
	Yes N = 178	No N = 11,977	Coef (95% CI)	p-value	Coef (95% CI)	p-value	% IH	Coef (95% CI)	OR (95% CI)	Score
Caucasian										
Yes							4.5	0.67 (0.49, 0.84)	1.95 (1.63, 2.32)	2
No							2.7	0	1	0
BMI, kg/m^2										
< 18	9 (1.4)	653 (98.6)	-0.27 (-0.97, 0.44)	0.458	-0.52 (-1.23, 0.20)	0.154	1.8	-1.61 (-2.21, -0.99)	0.20 (0.11, 0.37)	-4
18-25	74 (1.1)	6,737 (98.9)	-0.49 (-0.84, -0.15)	0.005	-0.60 (-0.94, -0.25)	0.001	2.9	-0.65 (-0.87, -0.45)	0.52 (0.42, 0.64)	-2
25-30	61 (1.8)	3,390 (98.2)	0		0		-	0	1	0
> 30	34 (2.8)	1,197 (97.2)	0.46 (0.03, 0.88)	0.035	0.52 (0.10, 0.95)	0.017	5.1	0.35 (0.16, 0.54)	1.42 (1.17, 1.72)	1
Smoker										
Yes	1 (3.7)	26 (96.3)	0.95 (-1.05, 2.96)	0.350	0.96 (-1.06, 2.97)	0.353	6.7	0.50 (0.34, 0.66)	1.65 (1.40, 1.94)	1
No	177 (1.5)	11,951 (98.5)	0		0		2.7	0	1	0
COPD										
Yes	6 (2.9)	201 (97.1)	0.71 (-0.11, 1.54)	0.09	0.38 (-0.46, 1.23)	0.378	6.3	0.22 (0.05, 0.38)	1.24 (1.05, 1.46)	1
No	172 (1.4)	11,776 (98.6)	0		0		2.8	0	1	0
Chronic liver disease										
Yes	10 (4.9)	196 (95.2)	1.27 (0.62, 1.93)	< 0.001	1.13 (0.46, 1.80)	0.001	NA	0.31 (0.11, 0.50)	1.36 (1.12, 1.65)	1
No	168 (1.4)	11,781 (98.6)	0		0		NA	0	1	0

Table 6.3 Estimation of Penn model predictor coefficients based on Ramathibodi surgical cohort data (Cont.)

Variables, n (%)	Ramathibodi data						Penn IH prediction model			
	IH		Univariate		Multivariate					
	Yes N = 178	No N = 11,977	Coef (95% CI)	p-value	Coef (95% CI)	p-value	% IH	Coef (95% CI)	OR (95% CI)	Score
2+ Elixhauser score										
Yes							5.1	0.41 (0.17, 0.65)	1.51 (1.18, 1.91)	1
No							1.6	0	1	0
Cancer										
Yes	71 (1.8)	3,782 (98.2)	0.36 (0.06, 0.67)	0.019	0.30 (-0.09, 0.69)	0.127	5.7	0.29 (0.10, 0.47)	1.34 (1.11, 1.60)	1
No	107 (1.3)	8,195 (98.7)	0		0		3.2	0	1	0
Chemo/RT										
Yes	35 (1.8)	1,919 (98.2)	0.25 (-0.12, 0.62)	0.190	-0.18 (-0.61, 0.26)	0.427	9.6	0.29 (0.01, 0.57)	1.33 (1.01, 1.76)	1
No	143 (1.4)	10,058 (98.6)	0		0		3.5	0	1	0
Antiplatelet /anticoagulant										
Yes	43 (2.7)	1,529 (97.3)	0.78 (0.43, 1.13)	< 0.001	0.58 (0.21, 0.94)	0.002	8.2	0.25 (0.04, 0.31)	1.28 (1.04, 1.36)	1
No	135 (1.3)	10,488 (98.7)	0		0		3.3	0	1	0
Emergency surgery										
Yes	62 (1.8)	3,372 (98.2)	0.31 (-0.001, 0.62)	0.050	0.27 (-0.10, 0.63)	0.155	15.8	1.54 (1.36, 1.71)	4.65 (3.90, 5.55)	4
No	116 (1.3)	8,605 (98.7)	0		0		2.2	0	1	0
Open surgery										
Yes	101 (1.9)	5,330 (98.1)	0.49 (0.19, 0.79)	0.001	0.36 (0.02, 0.70)	0.039	6.3	0.35 (0.17, 0.54)	1.42 (1.18, 1.72)	1

Table 6.3 Estimation of Penn model predictor coefficients based on Ramathibodi surgical cohort data (Cont.)

Variables, n (%)	Ramathibodi data						Penn IH prediction model			
	IH		Univariate		Multivariate					
	Yes N = 178	No N = 11,977	Coef (95% CI)	p-value	Coef (95% CI)	p-value	% IH	Coef (95% CI)	OR (95% CI)	Score
No	77 (1.2)	6,647 (98.9)	0		0		2.2	0	1	0
Ostomy										
Yes	21 (2.8)	732 (97.2)	0.72 (0.26, 1.18)	0.002	0.52 (0.03, 1.02)	0.039	NA	0.25 (0.02, 0.46)	1.28 (1.02, 1.59)	1
No	157 (1.4)	11,245 (98.6)	0		0		NA	0	1	0
Emergency vascular surgery										
Yes	0 (0)	2 (100)	NA	NA	NA	NA	11.9	0.79 (0.33, 1.25)	2.21 (1.39, 3.50)	2
No	178 (1.5)	11,975 (98.5)	NA		NA		3.7	0	1	0
Laparoscopic hysterectomy										
Yes	0 (0)	92 (100)	NA	NA	NA	NA	0.8	-0.58 (-1.11, -0.05)	0.56 (0.33, 0.95)	-2
No	178 (1.5)	11,885 (98.5)	NA		NA		4.1	0	1	0
History of abdominal surgery										
Yes	23 (3.5)	629 (96.5)	0.98 (0.54, 1.43)	< 0.001	0.82 (0.34, 1.29)	0.001	11.1	0.85 (0.67, 1.03)	2.33 (1.95, 2.79)	2
No	155 (1.4)	11,348 (98.7)	0		0		2.7	0	1	0
Small bowel obstruction										
Yes	10 (2.0)	498 (98.0)	0.32 (-0.33, 0.96)	0.336	-0.02 (-0.71, 0.67)	0.954	10.7	0.51 (0.32, 0.69)	1.66 (1.38, 2.00)	1
No	168 (1.4)	11,479 (98.6)	0		0		2.8	0	1	0

BMI, body mass index; Chemo/RT, chemotherapy or radiation therapy; CI, confidence interval; Coef, coefficient; COPD, chronic obstructive pulmonary disease; IH, incisional hernia; NA, not available; OR, odds ratio

Table 6.4 Penn model performance validation in the Ramathibodi cohort data

Step	Model	C-statistic (95% CI)	O/E (95% CI)
1	Coefficient	0.634 (0.595, 0.674)	1.031 (0.930, 1.132)
	Weighted score	0.645 (0.607, 0.683)	1.021 (0.897, 1.145)
2	Coefficient	0.646 (0.607, 0.684)	1.026 (0.919, 1.134)
	Weighted score	0.679 (0.641, 0.717)	1.006 (0.906, 1.106)
3	Coefficient	0.727 (0.691, 0.763)	0.984 (0.847, 1.120)
	Weighted score	0.729 (0.693, 0.765)	0.984 (0.894, 1.074)
4		0.692 (0.655, 0.729)	0.978 (0.875, 1.081)
5		0.689 (0.652, 0.726)	0.995 (0.891, 1.100)
6		0.743 (0.707, 0.778)	0.967 (0.861, 1.072)
7		0.733 (0.698, 0.768)	0.968 (0.848, 1.088)

CI, confidence interval; O/E, the observed/expected outcome ratio

Table 6.5 Additional predictor variables significantly associated with incisional hernia occurrence in Ramathibodi surgical cohort data

Variables	Univariate analysis	
	Coefficient (95% CI)	p-value
Age, years		
< 45	0	
45 - 65	1.18 (0.56, 1.79)	< 0.001
> 65	1.76 (1.16, 2.36)	< 0.001
ASA classification		
Class 1	0	
Class 2	-0.28 (-0.71, 0.16)	0.215
Class 3 - 5	0.70 (0.34, 1.05)	< 0.001
Diabetes	0.83 (0.48, 1.18)	< 0.001
Immunosuppressive drug	0.99 (0.53, 1.45)	< 0.001
Small bowel resection	1.12 (0.61, 1.63)	< 0.001
Colorectal procedure	0.60 (0.28, 0.92)	< 0.001
Ostomy reversal	2.12 (1.26, 2.98)	< 0.001
Wound classification		
Clean and Clean-contaminated	0	
Contaminated and Dirty	0.65 (0.06, 1.24)	0.032
Wound complication	1.45 (1.07, 1.84)	< 0.001
Surgical site infection	1.35 (0.93, 1.77)	< 0.001
Transfusion	0.88 (0.56, 1.19)	< 0.001
ICU stay	0.85 (0.52, 1.19)	< 0.001

ASA, American Society of Anesthesiologist; CI, confidence interval; ICU, intensive care unit

Table 6.6 Final validation step multivariable predictor coefficients and 95% confidence intervals

Variables	Coefficient (95% CI)	p-value
Age, years		
< 45	0	
45 - 65	1.11 (0.49, 1.73)	< 0.001
> 65	1.63 (1.03, 2.24)	< 0.001
BMI, kg/m^2		
< 18	-0.39 (-1.11, 0.33)	0.285
18 – 24.9	-0.57 (-0.91, -0.22)	0.001
25 – 29.9	0	
> 30	0.64 (0.21, 1.07)	0.004
Cirrhosis	0.92 (0.25, 1.59)	0.007
Immunosuppressive drug	0.74 (0.27, 1.22)	0.002
Open surgery	0.50 (0.19, 0.81)	0.002
Ostomy reversal	2.06 (1.18, 2.95)	< 0.001
Transfusion	0.60 (0.26, 0.93)	< 0.001
Constant term	-5.17 (-6.35, -5.07)	< 0.001

BMI, body mass index; CI, confidence interval

Table 6.7 Revised Ramathibodi incisional hernia risk classification score using only pre- and intra-operative predictor variables

Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	LR (+)
-6.28	100 (97.9, 100)	5.9 (5.5, 6.3)	1.6 (1.3, 1.8)	1.06 (1.06, 1.07)
-5.17	97.2 (93.6, 99.1)	19.9 (19.2, 20.6)	1.8 (1.5, 2.1)	1.21 (1.18, 1.25)
-4.60	77.5 (70.7, 83.4)	55.6 (54.7, 56.5)	2.5 (2.1, 3.0)	1.75 (1.61, 1.89)
-4.07	58.4 (50.8, 65.8)	74.1 (73.3, 74.9)	3.3 (2.7, 3.9)	2.26 (1.99, 2.57)

LR, likelihood; PPV, positive predictive value; 95% confidence intervals are shown in parentheses

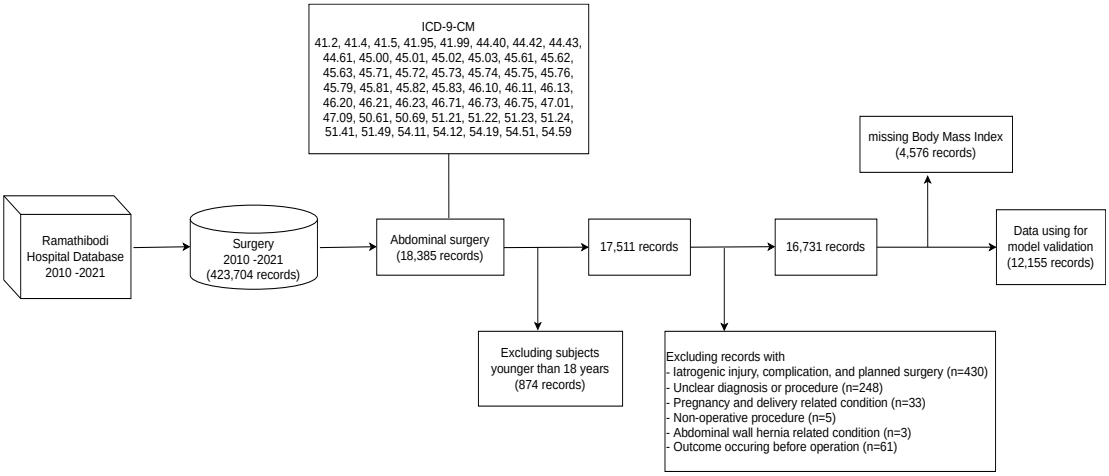


Figure 6.1 Ramathibodi surgical data extraction

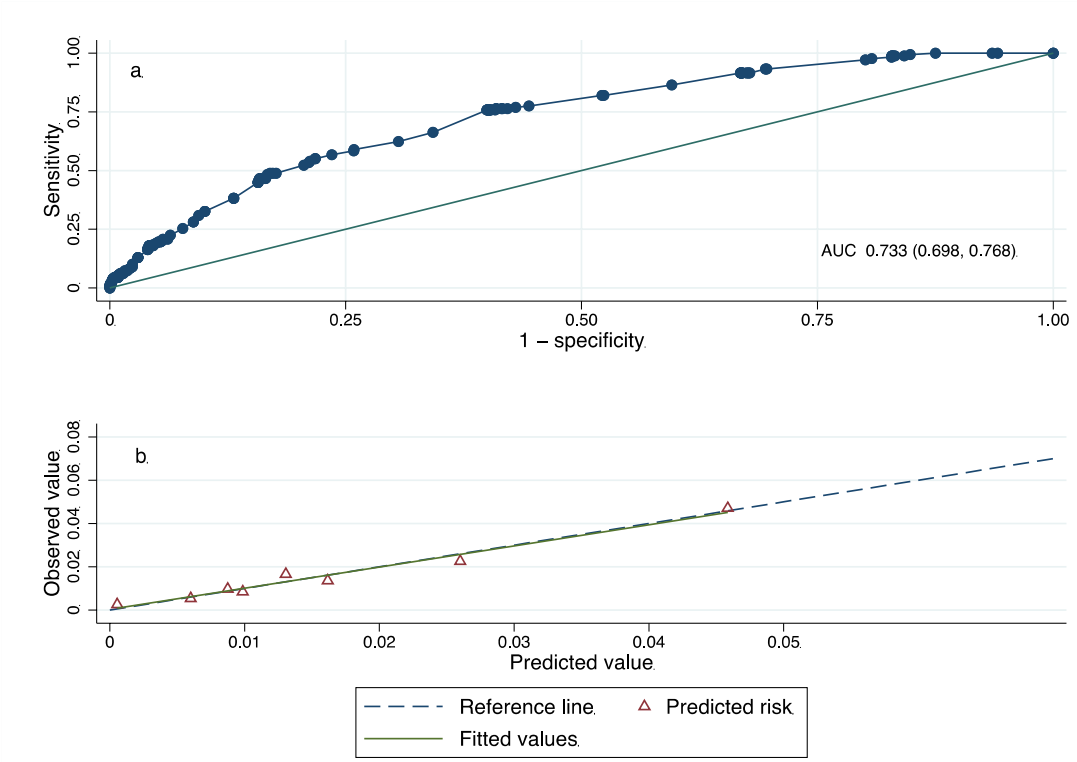


Figure 6.2 Revised incisional hernia prediction model performance for abdominal surgery a) Receiver operating characteristic curve b) Calibration plot

CHAPTER VII
SUMMARY

This study aimed to fill gaps of knowledge in IH prevention and prediction. We believe that prevention and prediction are just different faces of the same coin. IH prediction model would be worth its existence if there is an effective IH preventive strategy. Without effective intervention, knowing the patient's prognosis is not much useful. On the other hand, IH prediction models using in clinical practice could increase the efficacy and cost-effectiveness of prophylactic interventions by targeting patients at high risk of IH development.

We conducted a systematic review and found that fascia-enhanced mesh placement is efficacious in IH prevention However, which techniques should be recommended is still pending. If RCT could be conducted to compare all available mesh techniques, it would be the strongest evidence. Unfortunately, that RCT will be a multi-arm trial. Even though only a pair of mesh techniques are selected to compare in 2 parallel arms RCT, due to a small difference between techniques' efficacy, that RCT will have to enroll a large number of participants and would consume a significant budget and time. Instead of RCT, NMA can compare multiple treatment options by borrowing information via a common comparator. As a result, we decided to conduct NMA to answer this question. Results indicated that only OM and RM significantly reduced IH occurrence. OM was more efficacious than RM but no significant difference in efficacy was indicated between these 2 techniques. OM seems to have more SSI risk than RM but this finding was also not significant. Only seroma was observed more frequently in OM than RM significantly. Because superior benefits came along with higher risks, pinpointing the best technique to recommend was still difficult. That was when RBA played an important role.

RBA allows us to compare interventions by simultaneously considering benefits and risks. The concept of RBA is analogous to cost-effectiveness analysis frequently used in health technology assessment. Instead of the incremental cost, incremental risk is considered with the incremental benefit. Our analysis indicated that

RM was more beneficial (i.e., reducing IH occurrence) than OM at the same level of incremental risk (i.e., SSI and CSH). These results might conclude that RM should be the recommended technique considering mesh-augmented hernia prophylaxis.

Another gap of knowledge is that the evidence of mesh-augmented hernia prophylaxis is lack in urgency/emergency operated patients in whom open midline incision is still popular. This population should gain benefits from IH prevention. Therefore, we designed an RCT protocol to examine mesh's efficacy in this setting. It is a multicenter RCT comparing RM with PSC and requires 470 participants to be enrolled. Since enrollment had been started, the recruitment rate was poor due to COVID-19 situation.

As mentioned earlier, another aspect that we would like to study was IH prediction model. Our goal was to find a high-performance prediction model and then subsequently validate and revise it to use in our practice. Systematic review was conducted to identify existing IH prediction models. Among these models, *Penn hernia risk calculator* was selected for further validation and revision. When the original model was applied in the Ramathibodi dataset, just fair discrimination performance was achieved. However, the model's performance was improved to an acceptable level after revision. Model revision led to a new model which substantially differed from the original version. This model included only pre-operative and intra-operative predictor variables as follows: age, BMI, cirrhotic status, immunosuppressive medication, open surgery, ostomy reversal, and transfusion. Hence, this model could guide intra-operatively whether patients have high IH risk and should receive prophylactic intervention. Better patient selection could enhance the intervention's efficacy.

In summary, outputs from this study are listed as follows: 1) RM should be recommended as a meh-augmented hernia prophylaxis, 2) an ideal RCT protocol was developed and enrollment is ongoing, 3) the IH prediction model with an acceptable performance was derived and ready for use in our setting. These findings would affect global guideline updates and benefit surgical practice, especially for Thai patients.

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APPENDICES

APPENDIX A

DATA EXTRACTION FORM FOR NETWORK META-ANALYSIS

Reviewer: ☐ **Amarit** ☐ **Suphakarn** **Study ID:** _____

General Characteristic of study

Title				
1st Author name				
Corresponding	Name:		Email:	
Country				
Journal				
Year				
Population	☐ 1. General ☐ 3. AAA ☐ 5. Bariatric ☐ 2. High-risk ☐ 4. AAA & Obese ☐ 6. Colorectal			
Intervention/Comparator				
Mesh position		Mesh type		
		☐ 1. Non-absorbable	☐ 2. Absorbable	☐ 3. Biologic
☐ 1. Onlay		☐ 11	☐ 21	☐ 31
☐ 2. Sublay		☐ 12	☐ 22	☐ 32
☐ 3. Pre-peritoneal		☐ 13	☐ 23	☐ 33
☐ 4. Intra-peritoneal		☐ 14	☐ 24	☐ 34
Primary suture		☐ 0		
Mesh	If Non-absorbable major polymer =?	☐ 1. Polypropylene ☐ 3. PTFE ☐ 2. Polyester ☐ 4. PVDF		
	If Absorbable	☐ 1. Vicryl ☐ 3. TIGR ☐ 2. Phasix ☐ 4. BIO-A		
	If Biologic – Species	☐ 1. Human ☐ 2. Porcine ☐ 3. Bovine ☐ 4. Equine		
	If Biologic – Tissue	☐ 1. Dermis ☐ 2. Intestinal submucosa ☐ 3. Pericardium		
	If Biologic – Processing	☐ 1. Crosslinked ☐ 2. Non-crosslinked		
Fixation	☐ 1. Suture ☐ 2. Glue ☐ 3. Combined ☐ 4. No-fixation			
Outcome	▷▷▷		If YES…	

Incisional hernia	☐ 1. YES ☐ 2. NO	☐ 1. Freq ☐ 2. RR ☐ 3. HR	
		Imaging?	☐ 1. YES ☐ 2. NO ☐ 3. UNCLEAR
Kaplan-Meier curve	☐ 1. YES ☐ 2. NO	With risk table? ☐ 1. YES ☐ 2. NO	
Wound infection (Superficial & Deep)	☐ 1. YES ☐ 2. NO	☐ 1. Freq ☐ 2. RR	
Seroma	☐ 1. YES ☐ 2. NO	☐ 1. Freq ☐ 2. RR	
Hematoma	☐ 1. YES ☐ 2. NO	☐ 1. Freq ☐ 2. RR	
Dehiscence/Evisceration	☐ 1. YES ☐ 2. NO	☐ 1. Freq ☐ 2. RR	
Chronic pain at _____ mo.	☐ 1. YES ☐ 2. NO	☐ 1. Freq ☐ 2. RR	
		tool	
		criteria	
Pain score at 24 hr. (VAS)	☐ 1. YES ☐ 2. NO		
Mesh removal	☐ 1. YES ☐ 2. NO		
Follow up (mo.)	☐ MEAN (SD) _____ ☐ MEDIAN (IR) _____ ☐ Range _____	Planned period of FU: _____ mo.	
Loss to follow up	_____(number)/_____(total)= _____ %		
Analysis	☐ 1. ITT ☐ 2. PP		

Characteristic of subject

characteristics	Intervention						total	
	Arm 1: _____		Arm 2: _____		Arm 3: _____			
N								
Age Mean, SD (95%CI, range – pls specify) *or* Age group 1._____ No., % 2._____ No., % 3._____ No., % 4._____ No., %								
Sex, Male No., %								
BMI Mean, SD (95%CI, range – pls specify) *or* BMI group 1._____ No., % 2._____ No., % 3._____ No., % 4._____ No., % 5._____ No., %								
ASA status I: No., % II: No., % III: No., % IV: No., % V: No., %								
DM: No., %								
COPD: No., %								
Smoking: No., %								
Malignancy: No., %								
Emergency Sx: No., %								
Previous midline laparotomy No., %								
Wound contamination Clean								

No., % Clean-contaminated No., % Contaminated No., % Dirty No., %								
Wound drain: No., %								

Outcome data (frequency)

Outcomes	Arm 1: _____			Arm 2: _____			Arm 3: _____		
	N	YES	NO	N	YES	NO	N	YES	NO
Incisional hernia									
Wound infection (superficial + deep)									
Seroma									
Hematoma									
Dehiscence/ Evisceration									
Chronic pain									

Outcome data (summary statistics)

Outcomes	Arm 1: _____			Arm 2: _____			Arm 3: _____		
	RR	95%CI		RR	95%CI		RR	95%CI	
		LL	UL		LL	UL		LL	UL
Incisional hernia									
Incisional hernia (HR)									
Wound infection									
Seroma									
Hematoma									
Dehiscence/ Evisceration									
Chronic pain									

Continuous outcomes

	Arm 1: _____			Arm 2: _____			Arm 3: _____		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Acute pain (VAS)									

Mesh removal rate

intervention	Removal rate	
	total	n
Arm 1: _____		
Arm 2: _____		
Arm 3: _____		

APPENDIX B
PATIENT INFORMATION SHEET

เอกสารชี้แจงข้อมูลแก่ผู้เข้าร่วมโครงการวิจัย

(Research Subject Information sheet)

ชื่อโครงการวิจัย การใช้ตาข่ายสังเคราะห์ในแผลผ่าตัดเพื่อป้องกันไส้เลื่อนที่แผลกึ่งกลางท้องอันเนื่องมาจากการผ่าตัดฉุกเฉินหรือกึ่งฉุกเฉินของโรคระบบทางเดินอาหาร

ผู้สนับสนุนการวิจัย *ทุนส่งเสริมการวิจัย คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช*

<u>แพทย์ผู้ทำวิจัยหลัก</u>
ชื่อ นายแพทย์อมฤต ตาลเสวต
ที่อยู่ ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช
เบอร์โทรศัพท์ 0891268484

เรียน ผู้เข้าร่วมโครงการวิจัยทุกท่าน

ท่านได้รับการเชิญชวนให้เข้าร่วมในโครงการวิจัยนี้ เนื่องจากท่านเป็นผู้ป่วยที่จำเป็นต้องเข้ารับการผ่าตัดฉุกเฉินหรือกึ่งฉุกเฉินจากโรคหรือภาวะทางระบบทางเดินอาหาร และอายุมากกว่า 18 ปีบริบูรณ์ แต่ก่อนที่ท่านจะตกลงใจเข้าร่วมหรือไม่ โปรดอ่านข้อความในเอกสารนี้ทั้งหมด เพื่อให้ทราบว่า เหตุใดท่านจึงได้รับเชิญให้เข้าร่วมในโครงการวิจัยนี้ โครงการวิจัยนี้ทำเพื่ออะไร หากท่านเข้าร่วมโครงการวิจัยนี้ท่านจะต้องทำอะไรบ้าง รวมทั้งข้อดีและข้อเสียที่อาจจะเกิดขึ้นในระหว่างการวิจัย

ในเอกสารนี้ อาจมีข้อความที่ท่านอ่านแล้วยังไม่เข้าใจ โปรดสอบถามผู้วิจัยหรือผู้ช่วยผู้วิจัยที่ทำโครงการนี้เพื่อให้อธิบายจนกว่าท่านจะเข้าใจ การเข้าร่วมในโครงการวิจัยครั้งนี้จะต้องเป็นความสมัครใจของท่าน ไม่มีการบังคับหรือชักจูง ถึงแม้ท่านจะไม่เข้าร่วมในโครงการวิจัย ท่านก็

จะได้รับการรักษาพยาบาลตามปกติ การไม่เข้าร่วมหรือถอนตัวจากโครงการวิจัยนี้ จะไม่มีผลกระทบต่อการได้รับบริการ การรักษาพยาบาลหรือผลประโยชน์ที่พึงจะได้รับของท่านแต่อย่างใด

โปรดอย่าลงลายมือชื่อของท่านในเอกสารนี้จนกว่าท่านจะแน่ใจว่ามีความประสงค์จะเข้าร่วมในโครงการวิจัยนี้ คำว่า“ ท่าน ”ในเอกสารนี้ หมายถึงผู้เข้าร่วมโครงการวิจัยในฐานะเป็นอาสาสมัครในโครงการวิจัยนี้ หากท่านเป็นผู้แทนโดยชอบธรรมตามกฎหมายของผู้ที่จะเข้าร่วมในโครงการวิจัย และลงนามแทนในเอกสารนี้ โปรดเข้าใจว่า “ท่าน” ในเอกสารนี้หมายถึงผู้เข้าร่วมในโครงการวิจัยเท่านั้น

<u>ที่มาของการศึกษา</u>

ภาวะไส้เลื่อนที่เกิดขึ้นบริเวณแผลผ่าตัดเป็นภาวะที่พบได้บ่อยหลังผ่าตัดช่องท้อง พบราว 5%-20% ตามที่มีรายงาน เมื่อเกิดไส้เลื่อนขึ้นแล้วอาจจะก่อให้เกิดอาการปวดจุกบริเวณไส้เลื่อน เกิดความไม่สวยงาม รวมถึงมีโอกาสเกิดไส้เลื่อนติดค้างเป็นเหตุให้มีการเน่าตายของอวัยวะภายในที่มาติดอยู่ ดังนั้นเมื่อเกิดไส้เลื่อนจึงควรที่จะได้รับการผ่าตัดแก้ไข ทว่าแม้จะทำการผ่าตัดเพื่อแก้ไขแล้วก็ยังมีโอกาสที่จะเกิดไส้เลื่อนซ้ำอีกราว 20% ดังนั้นการป้องกันไม่ให้เกิดไส้เลื่อนเสียตั้งแต่ในการผ่าตัดครั้งแรกจึงเป็นเป้าหมายที่สำคัญ

ปัจจุบันพบว่าการวางตาข่ายสังเคราะห์ในบริเวณแผลผ่าตัดจะช่วยลดโอกาสเกิดไส้เลื่อนที่แผลผ่าตัดได้ดี อย่างไรก็ตามในกลุ่มผู้ป่วยที่ได้รับการผ่าตัดช่องท้องฉุกเฉินซึ่งถือว่าเป็นกลุ่มเสี่ยงกลับยังไม่มีการศึกษาถึงผลของการใช้ตาข่ายสังเคราะห์ป้องกันไส้เลื่อน

<u>วัตถุประสงค์ของการศึกษา</u>

วัตถุประสงค์ของการวิจัยนี้ เพื่อเปรียบเทียบผลการป้องกันการเกิดไส้เลื่อนที่แผลตามหลังการผ่าตัด, ภาวะแทรกซ้อนที่แผลผ่าตัด, และประเมินความคุ้มค่าทางเศรษฐศาสตร์ ของการใช้ตาข่ายสังเคราะห์เทียบกับการไม่ใส่ตาข่ายสังเคราะห์

<u>หากท่านตัดสินใจเข้าร่วมการวิจัยแล้ว</u>

ท่านจะได้รับการซักประวัติ ตรวจร่างกาย เก็บเลือดรวมถึงการตรวจทางรังสีวิทยาเพื่อเตรียมท่านสำหรับการผ่าตัดตามมาตรฐานทั่วไป และได้รับคำแนะนำต่างๆ ที่เกี่ยวข้องกับการผ่าตัด ภาวะแทรกซ้อนที่อาจเกิดขึ้นได้จากการดมยาสลบ และการผ่าตัด

ในห้องผ่าตัด ท่านจะได้รับคำแนะนำก่อนการดมยาสลบจากทีมวิสัญญีแพทย์ ท่านจะได้รับการเตรียมการดมสลบ ซึ่งภายหลังที่ท่านได้รับยาดมสลบ ศัลยแพทย์จะเริ่มการผ่าตัดเพื่อรักษา

โรคที่ท่านเป็น เมื่อการผ่าตัดใกล้เสร็จสิ้นและไม่มีข้อบ่งห้าม ท่านจะถูกสุ่มให้ได้รับการเย็บปิดผนังหน้าท้องบริเวณแผลผ่าตัดด้วยวิธีการอย่างใดอย่างหนึ่งดังต่อไปนี้ 1. เย็บปิดแผลด้วยวิธีมาตรฐาน 2. เสริมตาข่ายสังเคราะห์เข้าไปในระดับผนังหน้าท้อง (ในแผลผ่าตัด ไม่ใช่ภายนอกแผล) ส่วนผิวหนังที่แผลผ่าตัดจะได้รับการเย็บปิดหรือเปิดแผลเพื่อทำความสะอาดตามความเหมาะสมเป็นกรณีไป

หลังการผ่าตัดเสร็จสิ้น ท่านจะได้รับการดูแลหลังผ่าตัดตามมาตรฐานวิชาชีพเหมือนกัน เช่นการให้ยาปฏิชีวนะ การให้ยาควบคุมอาการปวด รวมถึงการนัดการติดตามอาการ

ท่านจะได้รับการประเมินอาการต่าง ๆโดยแพทย์ ค่าใช้จ่ายต่าง ๆ ที่เกิดขึ้นระหว่างการรักษาพยาบาลในครั้งนี้ของท่านและผู้ที่ดูแลจะถูกสอบถามเพื่อการวิเคราะห์ความคุ้มค่าในแง่เศรษฐศาสตร์ของการใช้ตาข่ายสังเคราะห์

ในการติดตามอาการหลังผ่าตัด ท่านจะได้รับการนัด 6 ครั้ง ในการนัดครั้งแรกเป็นการนัดประเมินซึ่งร่วมไปกับการติดตามอาการหลังผ่าตัด คือหลังผ่าตัดภายใน 1 เดือน และครั้งต่อมาที่ 3, 6, 12, 18, และ 24 เดือนหลังผ่าตัด ท่านจะได้รับการประเมินแผลผ่าตัด อาการปวด และภาวะแทรกซ้อนที่อาจพบได้ เช่น การคั่งของน้ำเหลือง แผลผ่าตัดติดเชื้อ เป็นต้น นอกจากนี้การประเมินเรื่องไส้เลื่อนที่แผลผ่าตัดโดยเฉพาะ ท่านอาจจะได้รับการตรวจอัลตร้าซาวด์เพิ่มเติม

เพื่อให้งานวิจัยนี้ประสบความสำเร็จ ผู้ทำวิจัยใคร่ขอความร่วมมือจากท่านปฏิบัติตามคำแนะนำและมาติดตามอาการตามนัดทุกครั้ง โดยที่ก่อนถึงวันนั้นจะมีโทรศัพท์ไปยังท่านเพื่อเตือนความจำ หากไม่สามารถมาติดตามอาการตามที่กำหนดได้ ใคร่ขอความกรุณาแจ้งมายังผู้ประสานงานทุกครั้ง

<u>จะมีผู้ร่วมวิจัย/อาสาสมัครนี้ทั้งสิ้นประมาณ</u>.

โครงการวิจัยนี้ จะมีอาสาสมัครทั้งสิ้น 470 คน โดยเป็นผู้ได้รับการเย็บแผลบริเวณผนังหน้าท้องตามแบบมาตรฐานจำนวน 235 คน และผู้ที่ได้รับการวางตาข่ายสังเคราะห์ในชั้นผนังหน้าท้อง 235 คน โดยจะเก็บข้อมูลที่คณะแพทยศาสตร์ วชิรพยาบาล, คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี, , โรงพยาบาลภูมิพลอดุลยเดช, โรงพยาบาลหาดใหญ่, โรงพยาบาลมหาราชนครราชสีมา, และโรงพยาบาลสุรินทร์

<u>ความเสี่ยงที่อาจเกิดขึ้นเมื่อเข้าร่วมการวิจัย</u>

การเย็บปิดแผลโดยเสริมตาข่ายสังเคราะห์ เป็นการปฏิบัติที่ในแนวทางใหม่ที่เชื่อว่าจะลดโอกาสเกิดไส้เลื่อนตามหลังที่แผลผ่าตัด อย่างไรก็ตาม แม้จากการวิจัยต่าง ๆ จะไม่ได้บ่งชี้ว่าโอกาสเกิดภาวะแทรกซ้อนมีมากไปกว่าการเย็บแผลปกติอย่างมีนัยสำคัญ แต่ก็มีความเป็นไปได้ที่จะ

มีโอกาสเกิดการติดเชื้อที่แผลผ่าตัด, เกิดการคั่งของเลือดและน้ำเหลืองบริเวณแผล สูงกว่าการเย็บแผลตามมาตรฐาน และอาจจะมีโอกาสเจ็บเรื้อรังที่แผลมากกว่าในผู้ป่วยกลุ่มที่วางตาข่ายสังเคราะห์ ซึ่งเป็นสิ่งที่การวิจัยนี้กำลังหาคำตอบทั้งในแง่ประสิทธิภาพในการป้องกันไส้เลื่อนและภาวะแทรกซ้อน โดยผู้วิจัยมีการป้องกันโดยเลือกผู้ป่วยที่มีความเสี่ยงต่อภาวะแทรกซ้อนต่ำเข้าร่วมโครงการ มีกระบวนการเตรียมผู้ป่วยก่อนการผ่าตัดตามมาตรฐาน การให้ยาแก้ปวดหลังผ่าตัด การให้ยาปฏิชีวนะเพื่อป้องกันการติดเชื้อ และหากเกิดภาวะแทรกซ้อนดังกล่าว ผู้วิจัยก็จะดำเนินการรักษาภาวะนั้น ๆ ตามแนวทางเฉพาะของแต่ละภาวะตามแนวทางมาตรฐานวิชาชีพ

<u>ความเสี่ยงที่ไม่ทราบแน่นอน</u>

ท่านอาจเกิดอาการข้างเคียง หรือความไม่สบาย นอกเหนือจากที่ได้แสดงในเอกสารฉบับนี้ ซึ่งอาการข้างเคียงเหล่านี้เป็นอาการที่ไม่เคยพบมาก่อน เพื่อความปลอดภัยของท่าน ควรแจ้งผู้ทำวิจัยให้ทราบทันทีเมื่อเกิดความผิดปกติใดๆ เกิดขึ้น

หากท่านมีข้อสงสัยใดๆ เกี่ยวกับความเสี่ยงที่อาจได้รับจากการเข้าร่วมในโครงการวิจัย ท่านสามารถสอบถามจากผู้ทำวิจัยได้ตลอดเวลา

หากมีการค้นพบข้อมูลใหม่ ๆ ที่อาจมีผลต่อความปลอดภัยของท่านในระหว่างที่ท่านเข้าร่วมในโครงการวิจัย ผู้ทำวิจัยจะแจ้งให้ท่านทราบทันที เพื่อให้ท่านตัดสินใจว่าจะอยู่ในโครงการวิจัยต่อไปหรือจะขอถอนตัวออกจากการวิจัย

<u>การพบแพทย์นอกตารางนัดหมายในกรณีที่เกิดอาการข้างเคียง</u>

หากมีอาการข้างเคียงใดๆ ที่เกิดกับท่าน ขอให้ท่านรีบมาพบแพทย์ที่สถานพยาบาลทันที ถึงแม้ว่าจะอยู่นอกตารางการนัดหมาย เพื่อแพทย์จะได้ประเมินอาการข้างเคียงของท่าน และให้การรักษาที่เหมาะสมทันที หากอาการดังกล่าวเป็นผลจากการเข้าร่วมโครงการวิจัย ท่านจะไม่เสียค่าใช้จ่าย

<u>ประโยชน์ที่อาจได้รับ</u>

ข้อมูลของการวิจัยสามารถพัฒนาแนวทางการดูแลผู้ป่วยที่ต้องรับการผ่าตัดฉุกเฉินหรือกึ่งฉุกเฉินต่อไปในอนาคต โดยผู้เข้าร่วมวิจัยจะได้รับประโยชน์ในการตรวจอัลตร้าซาวด์ที่แผลผ่าตัดเพื่อสังเกตภาวะไส้เลื่อนที่แผลผ่าตัด เป็นประโยชน์ในการเฝ้าระวังและการรักษาไส้เลื่อนอย่างทันถ่วงที

<u>วิธีการและรูปแบบการรักษาอื่นๆ ซึ่งมีอยู่สำหรับอาสาสมัคร</u>

ท่านสามารถที่จะไม่เข้าร่วมการวิจัยครั้งนี้ โดยท่านก็ยังได้รับการผ่าตัดรักษาโรคที่ท่านเป็นโดยแพทย์เจ้าของไข้ ตามมาตรฐานทางวิชาชีพเช่นเดิม อย่างไรก็ตามการเย็บปิดแผลผ่าตัดจะเป็นการเย็บปิดตามมาตรฐานโดยไม่มีการใส่ตาข่ายสังเคราะห์

<u>ข้อปฏิบัติของท่านขณะที่ร่วมในโครงการวิจัย</u>

ขอให้ท่านปฏิบัติดังนี้

- ขอให้ท่านให้ข้อมูลทางการแพทย์ของท่านทั้งในอดีต และปัจจุบัน แก่ผู้ทำวิจัยด้วยความสัตย์จริง
- ขอให้ท่านแจ้งให้ผู้ทำวิจัยทราบความผิดปกติที่เกิดขึ้นระหว่างที่ท่านร่วมในโครงการวิจัย
- ขอให้ท่านแจ้งให้ผู้ทำวิจัยเกี่ยวกับข้อมูลในการสัมภาษณ์ และประเมินผลหลังผ่าตัดอย่างครบถ้วน
- ขอให้ท่านมาติดตามอาการตามแพทย์นัดทุกครั้ง

<u>การเก็บข้อมูลเป็นความลับ</u>

หากมีข้อมูลเพิ่มเติมทั้งด้านประโยชน์และโทษที่เกี่ยวข้องกับการวิจัยนี้ ผู้วิจัยจะแจ้งให้ทราบโดยรวดเร็วและไม่ปิดบัง

ข้อมูลส่วนตัวของผู้ร่วมวิจัย/อาสาสมัคร จะถูกเก็บรักษาไว้เป็นความลับและจะไม่เปิดเผยต่อสาธารณะเป็นรายบุคคล แต่จะรายงานผลการวิจัยเป็นข้อมูลส่วนรวม ข้อมูลของผู้ร่วมวิจัย/อาสาสมัครเป็นรายบุคคลอาจมีคณะบุคคลบางกลุ่มเข้ามาตรวจสอบได้ เช่น ผู้ให้ทุนวิจัย ผู้กำกับดูแลการวิจัย สถาบันหรือองค์กรของรัฐที่มีหน้าที่ตรวจสอบ รวมถึงคณะกรรมการจริยธรรมการวิจัยในคน เป็นต้น โดยไม่ละเมิดสิทธิของผู้ร่วมวิจัย/อาสาสมัครในการรักษาความลับเกินขอบเขตที่กฎหมายอนุญาตไว้

ข้อมูลของการวิจัย จะเก็บรักษาในคอมพิวเตอร์ส่วนบุคคล ที่เข้าถึงได้เฉพาะหัวหน้าโครงการวิจัย ส่วนเอกสารจากการสัมภาษณ์ จะเก็บรักษาในที่ปลอดภัย ในระยะเวลา 5 ปี หลังสิ้นสุดโครงการวิจัย

หากมีอาการข้างเคียงใด ๆ เกิดขึ้นกับท่าน ขอให้ท่านรีบมาพบแพทย์ที่สถานพยาบาลทันที ถึงแม้ว่าจะอยู่นอกตารางการนัดหมาย เพื่อแพทย์จะได้ประเมินอาการข้างเคียงของท่าน และ

ให้การรักษาที่เหมาะสมทันที หากอาการดังกล่าวเป็นผลจากการเข้าร่วมในโครงการวิจัย ท่านจะไม่เสียค่าใช้จ่าย

<u>อันตรายที่อาจเกิดขึ้นจากการเข้าร่วมในโครงการวิจัยและความรับผิดชอบของผู้ทำวิจัย/ผู้สนับสนุนการวิจัย</u>

ท่านจะได้รับการช่วยเหลือหรือดูแลรักษาการบาดเจ็บ/เจ็บป่วยอันเนื่องมาจากการวิจัยตามมาตรฐานทางการแพทย์ โดยผู้รับผิดชอบค่าใช้จ่ายในการรักษาคือผู้ทำวิจัย / ผู้สนับสนุนการวิจัย

ในกรณีที่ท่านต้องการข้อมูลเพิ่มเติมที่เกี่ยวข้องกับโครงการวิจัย ท่านสามารถติดต่อกับผู้ทำวิจัยคือ นพ.อมฤต ตาลเศวต (ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์วชิรพยาบาล เบอร์โทร 022443282 หรือ 0891268484) ได้ตลอด 24 ชั่วโมง

<u>ค่าใช้จ่ายของท่านในการเข้าร่วมการวิจัย</u>

ค่าใช้จ่ายที่ผู่ร่วมวิจัย/อาสาสมัครจะต้องรับผิดชอบเอง คือค่าใช้จ่ายในการรักษาโรคที่ท่านไม่สามารถเบิกได้ตามสิทธิ แต่ตาข่ายสังเคราะห์และการตรวจติดตามด้วยอัลตร้าซาวด์จะได้รับการสนับสนุนจากงบในการวิจัย โดยที่ท่านไม่ต้องเสียค่าใช้จ่ายในส่วนนี้

<u>ค่าตอบแทนสำหรับผู้เข้าร่วมวิจัย (ถ้ามี)</u>

ท่านจะไม่ได้รับเงินค่าตอบแทนจากการเข้าร่วมในการวิจัย แต่ท่านจะได้รับค่าเดินทางและเงินชดเชยการสูญเสียรายได้ หรือความไม่สะดวก ไม่สบาย ในการมาพบแพทย์ในการติดตามอาการครั้งที่ 2-6 ครั้งละ 200 บาท (สองร้อยบาทถ้วน) รวมทั้งหมด 5 ครั้ง

<u>การประกันภัยเพื่อคุ้มครองผู้เข้าร่วมวิจัย (ถ้ามี)</u>

โครงการวิจัยนี้ไม่มีการประกันภัยเพื่อคุ้มครองผู้เข้าร่วมวิจัย

<u>การเข้าร่วมและการสิ้นสุดการเข้าร่วมโครงการวิจัย</u>

การเข้าร่วมในโครงการวิจัยครั้งนี้เป็นไปโดยความสมัครใจ หากท่านไม่สมัครใจจะเข้าร่วมการศึกษาแล้ว ท่านสามารถถอนตัวได้ตลอดเวลา การขอถอนตัวออกจากโครงการวิจัยจะไม่มีผลต่อการดูแลรักษาโรคของท่านแต่อย่างใด

นอกจากนี้ผู้ทำวิจัยอาจถอนท่านออกจากการเข้าร่วมการวิจัย เพื่อเหตุผลด้านความปลอดภัยของท่าน หรือเมื่อผู้สนับสนุนการวิจัยยุติการดำเนินงานวิจัย หรือ ในกรณีดังต่อไปนี้

- ท่านไม่สามารถปฏิบัติตามคำแนะนำของผู้ทำวิจัย
- ท่านได้รับการผ่าตัดซ้ำในบริเวณแผลผ่าตัดเดิม อันเป็นมาจากสาเหตุอื่นๆ นอกเหนือจากการผ่าตัดเพื่อแก้ไขภาวะแทรกซ้อนที่แผล
- ท่านตั้งครรภ์ระหว่างที่เข้าร่วมโครงการวิจัย
- ท่านเกิดอาการข้างเคียงที่รุนแรง
- ท่านได้รับการวินิจฉัยว่าเป็นโรคของเนื้อเยื่อเกี่ยวพัน หรือได้รับยากดภูมิคุ้มกันระหว่างที่ร่วมโครงการ

<u>การปกป้องรักษาข้อมูลความลับของอาสาสมัคร</u>

หากมีข้อมูลเพิ่มเติมทั้งด้านประโยชน์และโทษที่เกี่ยวข้องกับการวิจัยนี้ ผู้วิจัยจะแจ้งให้ทราบโดยรวดเร็วและไม่ปิดบัง

ข้อมูลส่วนตัวของผู้ร่วมวิจัย/อาสาสมัคร จะถูกเก็บรักษาไว้เป็นความลับและจะไม่เปิดเผยต่อสาธารณะเป็นรายบุคคล แต่จะรายงานผลการวิจัยเป็นข้อมูลส่วนรวม กรณีเป็นการวิจัยทางคลินิกผลการวิจัยในภาพรวมนี้อาจดูได้จากเว็บไซต์ (https://www.thaiclinicaltrials.org/) ข้อมูลของผู้ร่วมวิจัย/อาสาสมัครเป็นรายบุคคลอาจมีคณะบุคคลบางกลุ่มเข้ามาตรวจสอบได้ เช่น ผู้ให้ทุนวิจัย ผู้กำกับดูแลการวิจัย สถาบันหรือองค์กรของรัฐที่มีหน้าที่ตรวจสอบ รวมถึงคณะกรรมการจริยธรรมการวิจัยในคน เป็นต้น โดยไม่ละเมิดสิทธิของผู้ร่วมวิจัย/อาสาสมัครในการรักษาความลับเกินขอบเขตที่กฎหมายอนุญาตไว้

<u>การจัดการกับตัวอย่างชีวภาพที่เหลือ</u>

โครงการวิจัยนี้ไม่มีการเก็บตัวอย่างชีวภาพของอาสาสมัคร

<u>สิทธิ์ของผู้เข้าร่วมในโครงการวิจัย</u>

ในฐานะที่ท่านเป็นผู้เข้าร่วมในโครงการวิจัย ท่านจะมีสิทธิ์ดังต่อไปนี้

1. ท่านจะได้รับทราบถึงลักษณะและวัตถุประสงค์ของการวิจัยในครั้งนี้
2. ท่านจะได้รับการอธิบายเกี่ยวกับระเบียบวิธีการของการวิจัยทางการแพทย์ รวมทั้งยาและอุปกรณ์ที่ใช้ในการวิจัยครั้งนี้
3. ท่านจะได้รับการอธิบายถึงความเสี่ยงและความไม่สบายที่จะได้รับจากการวิจัย

4. ท่านจะได้รับการอธิบายถึงประโยชน์ที่ท่านอาจจะได้รับจากการวิจัย
5. ท่านจะได้รับการเปิดเผยถึงทางเลือกในการรักษาด้วยวิธีอื่น ยา หรืออุปกรณ์ซึ่งมีผลดีต่อท่านรวมทั้งประโยชน์และความเสี่ยงที่ท่านอาจได้รับ
6. ท่านจะได้รับทราบแนวทางในการรักษา ในกรณีที่พบโรคแทรกซ้อนภายหลังการเข้าร่วมในโครงการวิจัย
7. ท่านจะมีโอกาสได้ซักถามเกี่ยวกับงานวิจัยหรือขั้นตอนที่เกี่ยวข้องกับงานวิจัย
8. ท่านจะได้รับทราบว่าการยินยอมเข้าร่วมในโครงการวิจัยนี้ ท่านสามารถขอถอนตัวจากโครงการเมื่อไรก็ได้ โดยผู้เข้าร่วมในโครงการวิจัยสามารถขอถอนตัวจากโครงการโดยไม่ได้รับผลกระทบใด ๆ ทั้งสิ้น
9. ท่านจะได้รับเอกสารข้อมูลคำอธิบายสำหรับผู้เข้าร่วมในโครงการวิจัยและสำเนาเอกสารใบยินยอมที่มีทั้งลายเซ็นและวันที่
10. ท่านมีสิทธิ์ในการตัดสินใจว่าจะเข้าร่วมในโครงการวิจัยหรือไม่ก็ได้ โดยปราศจากการใช้อิทธิพลบังคับข่มขู่ หรือการหลอกลวง

หากท่านไม่ได้รับการปฏิบัติตามที่ปรากฏในเอกสารชี้แจงข้อมูลแก่ผู้เข้าร่วมโครงการวิจัย หรือท่านไม่ได้รับการชดเชยอันควรต่อการบาดเจ็บหรือเจ็บป่วยที่เกิดขึ้นโดยตรงจากการวิจัย ท่านสามารถร้องเรียนได้ที่ สำนักงานคณะกรรมการพิจารณาจริยธรรมการวิจัย คณะแพทยศาสตร์วชิรพยาบาล

เบอร์โทร ๐-๒๒๔๔-๓๕๒๒ หรือ ๐-๒๖๖๘-๗๐๘๘

ขอขอบคุณในการร่วมมือของท่านมา ณ ที่นี้

<u>หมายเหตุ</u>: ผู้เข้าร่วมโครงการวิจัยจะได้รับเอกสารชี้แจงและหนังสือยินยอมที่มีข้อความเดียวกันกับที่นักวิจัยเก็บไว้ และได้ลงลายมือชื่อของผู้เข้าร่วมโครงการวิจัย ผู้ให้คำอธิบายเพื่อขอความร่วมมือให้เข้าร่วมโครงการวิจัย และวันที่ที่ลงชื่อเก็บไว้เป็นส่วนตัว 1 ชุด

APPENDIX C
CONSENT FORM

หนังสือแสดงเจตนายินยอมเข้าร่วมการวิจัยโดยได้รับการบอกกล่าวและเต็มใจ (อายุตั้งแต่ ๑๘ ปีขึ้นไป)

วันที่.....เดือน.....พ.ศ

ข้าพเจ้า.....อายุ.....ปี อาศัยอยู่บ้านเลขที่.....
ถนน.....ตำบล.....อำเภอ.....
จังหวัด.....รหัสไปรษณีย์.....โทรศัพท์.....

ขอแสดงเจตนายินยอมเข้าร่วมโครงการวิจัย**เรื่อง การใช้ตาข่ายสังเคราะห์ในแผลผ่าตัดเพื่อป้องกันไส้เลื่อนที่แผลกึ่งกลางท้องอันเนื่องมาจากการผ่าตัดฉุกเฉินหรือกึ่งฉุกเฉินของโรคระบบทางเดินอาหาร** โดยข้าพเจ้าได้รับทราบรายละเอียดเกี่ยวกับที่มาและจุดมุ่งหมายในการทำวิจัยรายละเอียดขั้นตอนต่าง ๆ ที่จะต้องปฏิบัติหรือได้รับการปฏิบัติ ประโยชน์ที่คาดว่าจะได้รับของการวิจัยและความเสี่ยงที่อาจจะเกิดขึ้นจากการเข้าร่วมการวิจัย รวมทั้งแนวทางป้องกันและแก้ไขหากเกิดอันตรายขึ้น ค่าตอบแทนที่จะได้รับ ค่าใช้จ่ายที่ข้าพเจ้าจะต้องรับผิดชอบจ่ายเอง โดยได้อ่านข้อความที่มีรายละเอียดอยู่ในเอกสารชี้แจงผู้เข้าร่วมการวิจัยโดยตลอด อีกทั้งยังได้รับคำอธิบายและตอบข้อสงสัยจากผู้ช่วยวิจัยหรือหัวหน้าโครงการวิจัยเป็นที่เรียบร้อยแล้ว โดยที่ไม่มีสิ่งใดปิดบังซ่อนเร้น

ข้าพเจ้าจึงสมัครใจเข้าร่วมในโครงการวิจัยนี้ :

ข้าพเจ้าได้ทราบถึงสิทธิที่ข้าพเจ้าจะได้รับข้อมูลเพิ่มเติมทั้งทางด้านประโยชน์และโทษจากการเข้าร่วมการวิจัย และสามารถถอนตัวหรืองดเข้าร่วมการวิจัยได้ทุกเมื่อ โดยจะไม่มีผลกระทบต่อการบริการและการรักษาพยาบาลที่ข้าพเจ้าจะได้รับต่อไปในอนาคต และยินยอมให้ผู้วิจัยใช้ข้อมูลส่วนตัวที่ได้รับจากการวิจัย แต่จะไม่เผยแพร่ต่อสาธารณะเป็นรายบุคคล โดยจะนำเสนอเป็นข้อมูลโดยรวมจากการวิจัยเท่านั้น

หากมีอาการผิดปกติ รู้สึกไม่สบายกาย หรือมีผลกระทบต่อจิตใจของข้าพเจ้าเกิดขึ้นระหว่างการวิจัย ข้าพเจ้าจะแจ้งผู้วิจัยโดยเร็วที่สุด

หากข้าพเจ้ามีข้อข้องใจเกี่ยวกับขั้นตอนของการวิจัย หรือหากเกิดผลข้างเคียงที่ไม่พึงประสงค์จากการวิจัยขึ้นกับข้าพเจ้าข้าพเจ้า จะสามารถติดต่อกับ อาจารย์ น.พ.อมฤต ตาลเสวต เบอร์โทรศัพท์ 089-1268484 ได้ตลอด 24 ชั่วโมง

หากข้าพเจ้า ได้รับการปฏิบัติไม่ตรงตามที่ได้ระบุไว้ในเอกสารชี้แจงผู้เข้าร่วมการวิจัย ข้าพเจ้าจะสามารถติดต่อกับประธานคณะกรรมการจริยธรรมการวิจัยในคนหรือผู้แทน ได้ที่สำนักงานคณะกรรมการพิจารณาจริยธรรมการวิจัยคณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช หมายเลขโทรศัพท์

เบอร์โทร 02-244-3840 หรือโทรสาร 02-244-3843 ข้าพเจ้าเข้าใจข้อความเอกสารชี้แจงผู้เข้าร่วมการวิจัย และหนังสือแสดงเจตนายินยอมนี้โดยตลอดแล้ว จึงลงลายมือชื่อไว้

ลงชื่อ.....ผู้เข้าร่วมการวิจัย/ผู้แทนโดยชอบธรรม/วันที่.....

(.....)

ลงชื่อ.....ผู้ให้ข้อมูลและขอความยินยอม/หัวหน้าโครงการวิจัย/วันที่.....

(.....)

ในกรณีผู้เข้าร่วมการวิจัยไม่สามารถอ่านหนังสือได้ ผู้ที่อ่านข้อความทั้งหมดแทนผู้เข้าร่วมวิจัย คือ ..... จึงได้ลงลายมือชื่อไว้เป็นพยาน

ลงชื่อ.....พยาน/วันที่.....

(.....)

ข้าพเจ้าไม่สามารถอ่าน เขียนหนังสือได้แต่มีผู้อ่านข้อความในแบบคำยินยอมนี้ให้แก่ข้าพเจ้าฟังจนเข้าใจดี ข้าพเจ้าจึงพิมพ์ลายนิ้วมือขวาของข้าพเจ้าในแบบคำยินยอมนี้ด้วยความเต็มใจ

พิมพ์ลายนิ้วมือขวา

ลงชื่อ.....พยาน/วันที่.....

(.....)

ลงชื่อ.....พยาน/วันที่.....

(.....)

ของ นาย / นาง / นางสาว.....(ผู้เข้าร่วมวิจัย)

APPENDIX D

CASE RECORD FORM FOR RANDOMIZED CONTROLLED TRIAL

Site	Patient No.
ID	□□ – □□□

Sign _____

Date of Screening □□/□□/25□□ (DD/MM/YYYY)

กรุณาทำเครื่องหมายถูก (✓) ในช่อง

(1) เกณฑ์คัดเลือกก่อนเข้าผ่าตัด

		ถูกต้อง	ไม่ถูกต้อง
1.1.	อายุ ≥ 18 ปี		
1.2.	ต้องผ่าตัดภายใน 24 ชม. หลังจากมีข้อบ่งชี้ เนื่องจากพยาธิสภาพของทางเดินอาหาร		
1.3.	ผ่าตัดผ่าน midline incision ซึ่งยาวอย่างน้อย 1/4 ของระยะจาก xyphoid ถึง pubis		
1.4.	ไม่ใช่ผู้ป่วยตามระดับ American Society of Anesthesiologist (ASA) physical status class 5 (Moribund)		
1.5.	ไม่อยู่ในภาวะช็อคจากการติดเชื้อ (Septic shock)		
1.6.	ไม่ใช่ secondary closure (จาก open abdomen, temporary closure, fascial dehiscence)		
1.7.	ไม่ถูกวินิจฉัยว่าเป็นมะเร็งในระยะแพร่กระจายหรือ unresectable อยู่ก่อน		
1.8.	ไม่ใช่ mesenteric ischemia		
1.9.	ไม่มี incisional hernia อยู่ก่อน หรือเคยผ่าตัด incisional hernia repair		
1.10.	ไม่อยู่ระหว่างตั้งครรภ์ หรือคาดว่าจะตั้งครรภ์ในระยะเวลา 2 ปีหลังผ่าตัด		
1.11.	ไม่มีภาวะ connective tissue disorder		
1.12.	ไม่อยู่ระหว่างการใช้ยา immunosuppressive		
1.13.	ไม่มีประวัติแพ้ polypropylene		
1.14.	ยินยอมติดตามการรักษาเป็นเวลา 2 ปี		

(ต้องตอบ “ถูกต้อง” ทุกข้อจึงจะผ่านเข้าสู่ขั้นตอนต่อไปได้)

(2) มี consent form แสดงความยินยอมเข้าร่วมวิจัยหรือไม่ ☐ มี ☐ ไม่มี

(3) เกณฑ์คัดเลือกระหว่างผ่าตัด

		ถูกต้อง	ไม่ถูกต้อง
3.1.	ไม่ใช่แผล dirty surgical wound (severe fecal and frank pus contamination)		
3.2.	ไม่มีภาวะเน่าตายของอวัยวะในช่องท้องเป็นอย่างมาก (bowel necrosis)		
3.3.	ไม่พบว่ามีมะเร็งแพร่กระจายในช่องท้อง (peritoneal metastasis) หรือเป็น incomplete resection (R2)		
3.4.	ไม่มีแผน re-operation/second-look ผ่านแผล midline ภายในระยะเวลา 2 ปี หลังผ่าตัด		

** ผ่านเกณฑ์คัดเลือก**ทั้งก่อน (1) และระหว่าง (3)** การผ่าตัดและมี **consent form (2)** ☐ ใช่ ☐ ไม่ใช่

Baseline sign_____

Site Patient No.

ID ☐☐ – ☐☐☐

Date of Admission ☐☐/☐☐/25☐☐ (DD/MM/YYYY)

วันเกิด ☐☐/☐☐/☐☐☐☐ (DD/MM/YYYY: พ.ศ.)

เพศ ☐ 1. หญิง ☐ 2. ชาย

น้ำหนัก ☐☐☐.☐ kg (999.9 not available)

ส่วนสูง ☐☐☐.☐ cm (999.9 not available)

ASA status ☐ 1. Class 1 ☐ 2. Class 2

☐ 3. Class 3 ☐ 4. Class 4 ☐ 9. Not available

เบาหวาน ☐ 1. Yes ☐ 2. No ☐ 9. Not available

COPD ☐ 1. Yes ☐ 2. No ☐ 9. Not available

การสูบบุหรี่ ☐ 1. ไม่สูบ ☐ 2. เคยสูบ หยุดมามากกว่า 6 เดือนแล้ว

☐ 3. ยังสูบอยู่ ☐ 9. Not available

เคยผ่าตัดช่องท้อง (แผล midline) มาก่อน ☐ 1. Yes ☐ 2. No ☐ 9. Not available

ระดับ Albumin ก่อนผ่าตัด ☐☐.☐ g/dL (99.9 not available)

Nutrition status

NAF (perioperative period) ☐ 1. A ☐ 2. B ☐ 3. C ☐ 9. Not available

Intra-operative data sign _____

Site Patient No.

ID □□ – □□□

Date of Operation □□/□□/25□□ (DD/MM/YYYY)

ลำดับของ Randomization (sequence number) □□□

Random ได้ □ 1. Suture □ 2. Retrorectus mesh

Pathology □ 1. Cancer □ 2. Benign obstruction □ 3. Benign perforation
□ 4. Inflammation □ 5. GI hemorrhage □ 6. Ischemia
□ 7. Others

Operation □ 1. Small intestinal resection □ 2. Large intestinal resection
□ 3. Gastric resection □ 4. Anastomosis of hollow viscus
□ 5. Local repair of perforation □ 6. Appendectomy
□ 7. Gallbladder and biliary tract surgery □ 8. Another solid organ surgery
□ 9. Adhesiolysis □ 10. Hemostasis for bleeding ulcer
□ 11. Intra-abdominal drainage □ 12. Others

Wound classification □ 1. Clean □ 2. Clean-contaminated □ 3. Contaminated

การปิดแผล □ 1. เย็บปิด □ 2. เปิดแผล

ความยาวของแผล fascia □□□ cm

ความยาวของ PDS loop 2-0 ที่ใช้ □□□ cm

จำนวน mesh □ แผ่น (0 = ไม่ใช้ (suture))

เวลาเข้าห้องผ่าตัด □□.□□ (0-23 นาฬิกา)

เวลาลง incision □□.□□ (0-23 นาฬิกา)

เวลาเริ่มปิด abdominal wall □□.□□ (0-23 นาฬิกา)

เวลาที่ปิด abdominal wall เสร็จ □□.□□ (0-23 นาฬิกา)

เวลาเสร็จขั้นตอน anesthesia □□.□□ (0-23 นาฬิกา)

Post-op Day 1, 3 sign _____

Site Patient No.

ID □□ – □□□ Date □□/□□/25□□ (DD/MM/YYYY)

Post-op day: □ day 1 □ day 3

Pain score (1-10; 1 = น้อยที่สุด, 10 = มากที่สุด, 99 = ไม่สามารถประเมินได้) □□

ขนาดของ Opioid (mg) ที่ใช้รวมทั้งหมด	ใน 24 ชั่วโมง	ใน 72 ชั่วโมง
1. Morphine	□□□.□	□□□.□
2. Pethidine	□□□.□	□□□.□
3. Fentanyl (microgram)	□□□.□	□□□.□

Summary on discharge sign_____

Site Patient No.

ID □□ – □□□

Date of Discharge □□/□□/25□□ (DD/MM/YYYY)

ส่วนที่ 1 Clinical outcome and Medications

COMPLICATION	มี/ไม่มี		ถ้า มี – วันที่พบ (DD/MM/YYYY)
Incisional hernia	□ 1. Yes	□ 2. No	□□/□□/25□□
Superficial SSI (ไม่เกิน 30 วัน)	□ 1. Yes	□ 2. No	□□/□□/25□□
Deep SSI (ไม่เกิน 1 ปี)	□ 1. Yes	□ 2. No	□□/□□/25□□
Burst abdomen (ไม่เกิน 30 วัน)	□ 1. Yes	□ 2. No	□□/□□/25□□
Seroma (ไม่เกิน 3 เดือน)	□ 1. Yes	□ 2. No	□□/□□/25□□
Hematoma (ไม่เกิน 1 สัปดาห์)	□ 1. Yes	□ 2. No	□□/□□/25□□
Enterocutaneous fistula (ไม่เกิน 1 ปี)	□ 1. Yes	□ 2. No	□□/□□/25□□
Wound sinus (ไม่เกิน 1 ปี)	□ 1. Yes	□ 2. No	□□/□□/25□□

Duration of IV antibiotic ☐☐ วัน

Type of antibiotic (ตอบได้มากกว่า 1 ช่อง)

Cephalosporin ☐ Cefazolin ☐ Cefoxitin ☐ Cefotaxime ☐ Ceftriaxone ☐ Other Cephalosporins

Quinolone ☐ Ciprofloxacin ☐ Levofloxacin ☐ Other Quinolones

☐ Metronidazole

ส่วนที่ 2 การผ่าตัดซ้ำใน admission เดียวกัน

2.1 มีการผ่าตัดซ้ำ ใน admission เดียวกันนี้หรือไม่ ☐ 1. มี (ไปข้อ 2.2)

☐ 2. ไม่มี (ไม่ต้องตอบข้อต่อไป)

2.2 ถ้ามีการผ่าตัดซ้ำ

วันที่ (DD/MM/YYYY)	เกี่ยวข้องกับภาวะแทรกซ้อนของแผล?	ต้องเอา mesh ออก?
☐☐/☐☐/25☐☐	☐ 1. Yes ☐ 2. No	☐ 1. Yes ☐ 2. No ☐ 9. Not applicable
☐☐/☐☐/25☐☐	☐ 1. Yes ☐ 2. No	☐ 1. Yes ☐ 2. No ☐ 9. Not applicable
☐☐/☐☐/25☐☐	☐ 1. Yes ☐ 2. No	☐ 1. Yes ☐ 2. No ☐ 9. Not applicable

ส่วนที่ 3 การตรวจทางรังสีวิทยาเนื่องจากสงสัยภาวะแทรกซ้อนของแผลผ่าตัด

วันที่ (DD/MM/YYYY)	US or CT?
☐☐/☐☐/25☐☐	☐ 1. US ☐ 2. CT
☐☐/☐☐/25☐☐	☐ 1. US ☐ 2. CT
☐☐/☐☐/25☐☐	☐ 1. US ☐ 2. CT

*ภาวะแทรกซ้อนของแผล ได้แก่ SSI, Burst abdomen, Seroma, Hematoma, Fistula

ส่วนที่ 4 Cost

ต้นทุนทางตรงที่ไม่ใช่การแพทย์		จำนวนหน่วย	ราคา (บาท)/หน่วย	ราคารวม (บาท)
ค่าเดินทางของผู้ป่วย				☐☐☐☐
ค่าเดินทางของผู้มาเฝ้า		☐☐☐ วัน	☐☐☐	☐☐☐☐
ค่าอาหารส่วนที่เพิ่มขึ้นของผู้มาเฝ้า		☐☐☐ วัน	☐☐☐	☐☐☐☐
ค่าที่พักของผู้มาเฝ้า		☐☐☐ คืน	☐☐☐☐	☐☐☐☐☐
ค่าจ้างผู้ดูแลพิเศษ	☐ มี ☐ ไม่มี	☐☐☐ วัน	☐☐☐☐	☐☐☐☐☐

ต้นทุนทางอ้อม		จำนวนหน่วย	ราคา (บาท)/ หน่วย	ราคารวม (บาท)
ค่าสูญเสียรายได้ของผู้ป่วย	☐ มี ☐ ไม่มี	☐☐☐ วัน	☐☐☐☐	☐☐☐☐☐
ค่าสูญเสียรายได้ของผู้ดูแล	☐ มี ☐ ไม่มี	☐☐☐ วัน	☐☐☐☐	☐☐☐☐☐

Outcome assessment (OPD 1 mo) sign_____

Site Patient No.

ID ☐☐ – ☐☐☐ Date of Follow-up ☐☐/☐☐/25☐☐ (DD/MM/YYYY)

ส่วนที่ 1 Follow-up

Visit	Outcome
Superficial SSI	☐ 1. Yes ☐ 2. No
Deep SSI	☐ 1. Yes ☐ 2. No
Seroma	☐ 1. Yes ☐ 2. No
Burst abdomen	☐ 1. Yes ☐ 2. No
Fistula	☐ 1. Yes ☐ 2. No

ส่วนที่ 2 การนัดตรวจทางรังสีวิทยา (ถ้าหากมี)

วันที่นัด ☐☐/☐☐/25☐☐ (DD/MM/YYYY)

Imaging ☐ 1. US ☐ 2. CT

นัดเนื่องจากสงสัยภาวะแทรกซ้อนที่แผลผ่าตัด ☐ 1. ใช่ ☐ 2. ไม่ใช่

Outcome assessment (OPD 3 mo) sign_____

Site Patient No.

ID ☐☐ – ☐☐☐ Date of Follow-up ☐☐/☐☐/25☐☐ (DD/MM/YYYY)

ส่วนที่ 1 Follow-up

Visit	Outcome
Incisional hernia	☐ 1. Yes ☐ 2. No
Superficial SSI	☐ 1. Yes ☐ 2. No
Deep SSI	☐ 1. Yes ☐ 2. No
Seroma	☐ 1. Yes ☐ 2. No

Fistula	☐ 1. Yes ☐ 2. No
Wound sinus	☐ 1. Yes ☐ 2. No
Chronic pain	☐ 1. รบกวนชีวิตประจำวัน ☐ 2. เจ็บเล็กน้อย ☐ 3. ไม่มี

ส่วนที่ 2 การนัดตรวจทางรังสีวิทยา (ถ้าหากมี)

วันที่นัด ☐☐/☐☐/25☐☐ (DD/MM/YYYY)

Imaging ☐ 1. US ☐ 2. CT

นัดเนื่องจากสงสัยภาวะแทรกซ้อนที่แผลผ่าตัด ☐ 1. ใช่ ☐ 2. ไม่ใช่

Outcome assessment (OPD 6, 12 mo) sign_____

Site Patient No.

ID ☐☐ – ☐☐☐ Date of Follow-up ☐☐/☐☐/25☐☐ (DD/MM/YYYY)

Follow-up: ☐ 6 mo. ☐ 12 mo.

ส่วนที่ 1 Follow-up

Visit	Outcome
Incisional hernia	☐ 1. Yes ☐ 2. No
Deep SSI	☐ 1. Yes ☐ 2. No
Fistula	☐ 1. Yes ☐ 2. No
Wound sinus	☐ 1. Yes ☐ 2. No
Chronic pain	☐ 1. รบกวนชีวิตประจำวัน ☐ 2. เจ็บเล็กน้อย ☐ 3. ไม่มี

ส่วนที่ 2 การนัดตรวจทางรังสีวิทยา (ถ้าหากมี)

วันที่นัด ☐☐/☐☐/25☐☐ (DD/MM/YYYY)

Imaging ☐ 1. US ☐ 2. CT

นัดเนื่องจากสงสัยภาวะแทรกซ้อนที่แผลผ่าตัด ☐ 1. ใช่ ☐ 2. ไม่ใช่

Outcome assessment (OPD 18, 24 mo) sign_____

Site Patient No.

ID ☐☐ – ☐☐☐ Date of Follow-up ☐☐/☐☐/25☐☐ (DD/MM/YYYY)

Follow-up: ☐ 18 mo. ☐ 24 mo.

ส่วนที่ 1 Follow-up

Visit	Outcome
Incisional hernia	☐ 1. Yes ☐ 2. No
Chronic pain	☐ 1. รบกวนชีวิตประจำวัน ☐ 2. เจ็บเล็กน้อย ☐ 3. ไม่มี

ส่วนที่ 2 การนัดตรวจทางรังสีวิทยา (ถ้าหากมี)

วันที่นัด ☐☐/☐☐/25☐☐ (DD/MM/YYYY)

Imaging ☐ 1. US ☐ 2. CT

นัดเนื่องจากสงสัยภาวะแทรกซ้อนที่แผลผ่าตัด ☐ 1. ใช่ ☐ 2. ไม่ใช่

Outcome assessment (นอก protocol) sign_____

Site Patient No.

ID ☐☐ – ☐☐☐ Date of Follow-up ☐☐/☐☐/25☐☐ (DD/MM/YYYY)

ส่วนที่ 1 Follow-up

Complication	พบ complication?	
Incisional hernia	☐ 1. Yes	☐ 2. No
Superficial SSI (ไม่เกิน 30 วันหลังผ่าตัด)	☐ 1. Yes	☐ 2. No
Deep SSI (ไม่เกิน 1 ปีหลังผ่าตัด)	☐ 1. Yes	☐ 2. No
Seroma (ไม่เกิน 3 เดือนหลังผ่าตัด)	☐ 1. Yes	☐ 2. No
Burst abdomen (ไม่เกิน 30 วันหลังผ่าตัด)	☐ 1. Yes	☐ 2. No
Fistula (ไม่เกิน 1 ปีหลังผ่าตัด)	☐ 1. Yes	☐ 2. No
Wound sinus (ไม่เกิน 1 ปีหลังผ่าตัด)	☐ 1. Yes	☐ 2. No

ส่วนที่ 2 การนัดตรวจทางรังสีวิทยา (ถ้าหากมี)

วันที่นัด □□/□□/25□□ (DD/MM/YYYY)

Imaging □ 1. US □ 2. CT

นัดเนื่องจากสงสัยภาวะแทรกซ้อนที่แผลผ่าตัด □ 1. ใช่ □ 2. ไม่ใช่

ส่วนที่ 3 Cost* (สำหรับทุกการติดตามที่ OPD)

3.1 ค่าใช้จ่ายที่เกิดขึ้นที่ OPD

ต้นทุนทางตรงที่ไม่ใช่การแพทย์		จำนวนหน่วย	ราคา (บาท)/หน่วย	ราคารวม (บาท)
ค่าเดินทาง				□□□□
ค่าที่พัก		□□□ วัน	□□□□	□□□□□
ค่าอาหารส่วนที่เพิ่มขึ้น		□□□ วัน	□□□	□□□□
ค่าจ้างผู้ดูแลพิเศษ	□ มี □ ไม่มี	□□□ วัน	□□□□	□□□□□
ต้นทุนทางอ้อม		**จำนวนหน่วย**	**ราคา (บาท)/หน่วย**	**ราคารวม (บาท)**
ค่าสูญเสียรายได้ของผู้ป่วย	□ มี □ ไม่มี	□□□ วัน	□□□□	□□□□□
ค่าสูญเสียรายได้ของผู้ดูแล	□ มี □ ไม่มี	□□□ วัน	□□□□	□□□□□

3.2 ค่าใช้จ่ายระหว่างที่อยู่ที่บ้าน

ต้นทุนทางตรงการแพทย์		จำนวนหน่วย	ราคา (บาท)/หน่วย	ราคารวม (บาท)
ค่าทำแผล	□ มี □ ไม่มี	□□□ วัน	□□□□	□□□□□
ค่ายาที่ซื้อเอง (antibiotic + pain killer)	□ มี □ ไม่มี	□□□ ครั้ง	□□□□	□□□□
ต้นทุนทางตรงที่ไม่ใช่การแพทย์		**จำนวนหน่วย**	**ราคา (บาท)/หน่วย**	**ราคารวม (บาท)**
ค่าเดินทางไปทำแผล		□□□ วัน	□□□□	□□□□□
ค่าจ้างผู้ดูแลพิเศษ	□ มี □ ไม่มี	□□□ วัน	□□□□	□□□□□
ต้นทุนทางอ้อม		**จำนวนหน่วย**	**ราคา (บาท)/หน่วย**	**ราคารวม (บาท)**
ค่าสูญเสียรายได้ของผู้ป่วย	□ มี □ ไม่มี	□□□ วัน	□□□□	□□□□□
ค่าสูญเสียรายได้ของผู้ดูแล	□ มี □ ไม่มี	□□□ วัน	□□□□	□□□□□

Re-admission sign_____

Site Patient No.

ID □□ – □□□ Date of Admission□□/□□/25□□ (DD/MM/YYYY)

Date of Discharge□□/□□/25□□ (DD/MM/YYYY)

ส่วนที่ 1 (clinical)

เป็นการ re-admission แบบ? □ 1. Elective □ 2. Emergency

Re-admission ครั้งนี้เกี่ยวกับภาวะแทรกซ้อนของแผลผ่าตัดหรือไม่

□ 1. เกี่ยวข้อง

□ 2. ไม่เกี่ยวข้อง

หาก re-admission เกี่ยวข้องกับภาวะแทรกซ้อนของแผลผ่าตัด สาเหตุคือ

Complication	พบ complication?
Incisional hernia	□ 1. Yes □ 2. No
Burst abdomen	□ 1. Yes □ 2. No
Superficial SSI	□ 1. Yes □ 2. No
Deep SSI	□ 1. Yes □ 2. No
Seroma	□ 1. Yes □ 2. No
Chronic pain	□ 1. Yes □ 2. No
Outcome อื่นๆ	□ 1. Fistula □ 2. Wound sinus □ 3. None

มีการผ่าตัดเกิดขึ้นใน admission นี้ หรือไม่ □ 1. มี □ 2. ไม่มี

หากมีการผ่าตัด ต้องเอา mesh ออกหรือไม่ □ 1. เอาออก □ 2. ไม่ได้เอาออก

การตรวจทางรังสีวิทยาเนื่องจากสงสัยภาวะแทรกซ้อนของแผลผ่าตัด

วันที่ (DD/MM/YYYY)	US or CT?
□□/□□/25□□	□ 1. US □ 2. CT
□□/□□/25□□	□ 1. US □ 2. CT
□□/□□/25□□	□ 1. US □ 2. CT

ส่วนที่ 2 Cost เฉพาะเมื่อ readmission เกี่ยวข้องกับภาวะแทรกซ้อนของแผลผ่าตัด

ต้นทุนทางตรงที่ไม่ใช่การแพทย์		จำนวนหน่วย	ราคา (บาท)/หน่วย	ราคารวม (บาท)
ค่าเดินทางของผู้ป่วย				□□□

ค่าเดินทางของผู้มาเฝ้า		□□□ วัน	□□□	□□□□
ค่าอาหารส่วนที่เพิ่มขึ้นของผู้มาเฝ้า		□□□ วัน	□□□	□□□□
ค่าที่พักของผู้มาเฝ้า		□□□ คืน	□□□□	□□□□□
ค่าจ้างผู้ดูแลพิเศษ	□ มี □ ไม่มี	□□□ วัน	□□□□	□□□□□
ต้นทุนทางอ้อม		จำนวนหน่วย	ราคา (บาท)/ หน่วย	ราคารวม (บาท)
ค่าสูญเสียรายได้ของผู้ป่วย	□ มี □ ไม่มี	□□□ วัน	□□□□	□□□□□
ค่าสูญเสียรายได้ของผู้ดูแล	□ มี □ ไม่มี	□□□ วัน	□□□□	□□□□□

Direct medical cost (นอน รพ. ครั้งแรก) sign_____

Site Patient No.

ID □□ – □□□ Date of admission □□/□□/25□□ (DD/MM/YYYY)

ต้นทุนทางตรงการแพทย์		จำนวนหน่วย	ราคา (บาท)/ หน่วย	ราคารวม (บาท)
ค่าบริการผ่าตัด				□□□□□
ค่าบริการวิสัญญี				□□□□□
ค่าเรียกเก็บอย่างอื่นที่เกิดขึ้น**ในหอผู้ป่วย** (ไม่รวมค่ายา และค่าตรวจทางรังสีวิทยา)				□□□□□□
ค่า antibiotic IV 1. 2. 3. 4.		□□□ vial □□□ vial □□□ vial □□□ vial	□□□□ □□□□ □□□□ □□□□	□□□□□
ค่า antibiotic PO 1. 2. 3.		□□□tab/cap □□□tab/cap □□□tab/cap	□□□□ □□□□ □□□□	□□□□□
ค่ายาอื่นระหว่างนอน รพ.				□□□□□
ค่ายากลับบ้าน (antibiotic + pain killer)				□□□□□

ค่าตรวจทางรังสีวิทยา **เนื่องจากภาวะแทรกซ้อนของแผล** 1. Ultrasound 2. CT	□ ทำ □ไม่ทำ □ ทำ □ไม่ทำ	□□ครั้ง □□ ครั้ง	□□□□□ □□□□□	□□□□□□
ค่าใช้จ่ายทั้งหมดในห้องผ่าตัดเนื่องจาก**การผ่าตัดซ้ำเพราะภาวะแทรกซ้อนจากแผล**	□ มีการผ่าตัดซ้ำ □ไม่มีการผ่าตัดซ้ำ			□□□□□□

Direct medical cost (OPD follow-up) sign_____

(เฉพาะนัดที่เกี่ยวกับงานวิจัย)

Site Patient No.

ID □□ – □□□ Date □□/□□/25□□ (DD/MM/YYYY)

Follow-up: □ 1 mo. □ 3 mo. □ 6 mo. □ 12 mo.
□ 18 mo. □ 24 mo. □ นอก protocol

ต้นทุนทางตรงการแพทย์		จำนวนหน่วย	ราคา (บาท)/หน่วย	ราคารวม (บาท)
ค่าเรียกเก็บการบริการผู้ป่วยนอก				□□□□
ค่ายากลับบ้าน (antibiotic + pain killer)				□□□□
ค่าตรวจทางรังสีวิทยา **เนื่องจากภาวะแทรกซ้อนของแผล** 1. Ultrasound 2. CT	□ ทำ □ ไม่ทำ □ ทำ □ ไม่ทำ	□□□ ครั้ง □□□ ครั้ง	□□□□□ □□□□□	□□□□□□

Direct medical cost (Re-admission) sign_____

Site Patient No.

ID □□ – □□□ Date of Admission□□/□□/25□□ (DD/MM/YYYY)

ต้นทุนทางตรงการแพทย์		จำนวนหน่วย	ราคา (บาท)/ หน่วย	ราคารวม (บาท)
ค่าใช้จ่ายที่เกิดขึ้นทั้งหมดในห้องผ่าตัด รวมค่าบริการวิสัญญี				□□□□□□
ค่าเรียกเก็บอย่างอื่นที่เกิดขึ้น **ในหอผู้ป่วย** (ไม่รวมค่ายา และค่าตรวจทางรังสีวิทยา)				□□□□□□
ค่า antibiotic IV 1. 2. 3. 4.		□□□ vial □□□ vial □□□ vial □□□ vial	□□□□ □□□□ □□□□ □□□□	□□□□□
ค่า antibiotic PO 1. 2. 3.		□□□tab/cap □□□tab/cap □□□tab/cap	□□□□ □□□□ □□□□	□□□□□
ค่ายาอื่นระหว่างนอน รพ.				□□□□□
ค่ายากลับบ้าน (antibiotic + pain killer)				□□□□□
ค่าตรวจทางรังสีวิทยา **เนื่องจากภาวะแทรกซ้อนของแผล** 1. Ultrasound 2. CT	□ ทำ □ ไม่ทำ □ ทำ □ ไม่ทำ	□□□ ครั้ง □□□ ครั้ง	□□□□□ □□□□□	□□□□□□

BIOGRAPHY

NAME	Amarit Tansawet
DATE OF BIRTH	August 12, 1980
PLACE OF BIRTH	Bangkok, Thailand
INSTITUTION ATTENDED	Chulalongkorn University, 1997 – 2003 Doctor of Medicine
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