Systematic review and/or Meta-analysis

INTERNATIONAL JOURNAL OF SURGERY

OPEN

What is the ideal mesh location for incisional hernia prevention during elective laparotomy? A network meta-analysis of randomized trials

Alberto Aiolfi, MD, FACS, FEBS (UGI)[a,*], Davide Bona, MD[a], Fabio Gambero, MD[a], Andrea Sozzi, MD[a], Gianluca Bonitta, MSc[a], Emanuele Rausa, MD[c], Piero G. Bruni, MD[b], Marta Cavalli, MD[b], Giampiero Campanelli, MD[b]

Background: Incisional hernia (IH) represents an important complication after surgery. Prophylactic mesh reinforcement (PMR) with different mesh locations [onlay (OL), retromuscular (RM), preperitoneal (PP), and intraperitoneal (IP)] has been described to possibly reduce the risk of postoperative IH. However, data reporting the 'ideal' mesh location are sparse. The aim of this study was to evaluate the optimal mesh location for IH prevention during elective laparotomy.

Methods: Systematic review and network meta-analysis of randomized controlled trials (RCTs). OL, RM, PP, IP, and no mesh (NM) were compared. The primary aim was postoperative IH. Risk ratio (RR) and weighted mean difference (WMD) were used as pooled effect size measures, whereas 95% credible intervals (CrI) were used to assess relative inference.

Results: Fourteen RCTs (2332 patients) were included. Overall, 1052 (45.1%) had no mesh (NM) while 1280 (54.9%) underwent PMR stratified in IP ($n = 344$ pts), PP ($n = 52$ pts), RM ($n = 463$ pts), and OL ($n = 421$ pts) placement. Follow-up ranged from 12 months to 67 months. RM (RR = 0.34; 95% CrI: 0.10–0.81) and OL (RR = 0.15; 95% CrI: 0.044–0.35) were associated with significantly reduced IH RR compared to NM. A tendency toward reduced IH RR was noticed for PP versus NM (RR = 0.16; 95% CrI: 0.018–1.01), while no differences were found for IP versus NM (RR = 0.59; 95% CrI: 0.19–1.81). Seroma, hematoma, surgical site infection, 90-day mortality, operative time and hospital length of stay were comparable among treatments.

Conclusions: RM or OL mesh placement seems associated with reduced IH RR compared to NM. PP location appears promising; however, future studies are warranted to corroborate this preliminary indication.

Keywords: incisional hernia prevention, network meta-analysis, onlay, prophylactic mesh placement, retromuscular

Introduction

Incisional hernia (IH) represents an important complication after abdominal surgery, with a reported incidence of up to 30–40% in high-risk subjects[1–8]. IH can impair patients' quality of life, diminish function, impact body image, cause chronic pain, and possibly result in life-threatening complications such as bowel incarceration and obstruction[9,10]. In an attempt to prevent the occurrence of postoperative IH, prophylactic mesh reinforcement (PMR) to buttress the abdominal wall closure has been advocated. However, criticism regarding presumed higher complication rates, longer operative time, and increased costs has been raised[11–13]. Furthermore, different mesh locations (onlay, OL; retromuscular, RM; preperitoneal, PP; and intraperitoneal, IP) have been described[14] with dissimilar outcomes and significant data heterogeneity. These contributed to limit the reputation and widespread utilization of PMR during elective laparotomy.

HIGHLIGHTS

- Incisional hernia (IH) represents an important complication after surgery. Prophylactic mesh reinforcement has been advocated to possibly reduce the postoperative IH risk.
- Different mesh locations such as onlay (OL), retromuscular (RM), preperitoneal (PP), and intraperitoneal (IP) have been described and are currently used.
- RM (RR = 0.34; 95% CrI: 0.10–0.81) and OL (RR = 0.15; 95% CrI: 0.044–0.35) location was associated with a significantly reduced IH risk compared to no mesh (NM).
- A tendency toward reduced IH risk was noticed for PP versus NM (RR = 0.16; 95% CrI: 0.018–1.01), while no differences were found for IP versus NM (RR = 0.59; 95% CrI: 0.19–1.81).
- Seroma, hematoma, surgical site infection, 90-day mortality, operative time, and hospital length of stay were comparable among treatments.

[a]Division of General Surgery, Department of Biomedical Science for Health, University of Milan, [b]Department of Surgery, University of Insubria, Istituto Clinico Sant'Ambrogio, Milan and [c]General Surgery 1, Papa Giovanni XXIII Hospital, Bergamo, Italy

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Via Luigi Giuseppe Faravelli n.16, Milan 20149, Italy. Tel.: +39 02 8350 0010; fax: +39 02 8350 0012. E-mail: alberto.aiolfi86@gmail.com (A. Aiolfi).

International Journal of Surgery (2023) 109:1373–1381

Received 13 September 2022; Accepted 26 January 2023

Published online 10 April 2023

http://dx.doi.org/10.1097/JS9.0000000000000250

Previous systematic reviews and pairwise analyses have been published on this topic[15–22]. Results seem to support PMR during abdominal wall closure with encouraging data and a tendency toward reduced postoperative IH risk. However, because of the significant heterogeneity, the debate is still ongoing, while robust evidence concerning the 'ideal' mesh location for IH prevention during elective laparotomy is lacking.

Hence, the purpose of the present network meta-analysis was to perform an updated, comprehensive, and stratified evaluation according to different mesh locations for IH prevention in the setting of randomized controlled trials (RCTs).

Materials and methods

A systematic review was performed according to the guidelines from the preferred reporting items for systematic reviews and network meta-analyses (PRISMA-NMA)[23], Supplemental Digital Content 1, http://links.lww.com/JS9/A278. Institutional review board approval was not required. MEDLINE, Scopus, Web of Science, Cochrane Central Library, and ClinicalTrials.gov were used[24]. The last date of the search was 30th April 2022. A combination of the following MeSH terms (Medical Subject Headings) was used: 'Incisional', 'Hernia', 'Mesh', 'Prosthetic material', 'Augmentation', 'Closure', 'Prevention', and 'Elective' (Appendix 1). Titles, abstracts, and references were evaluated. The PROSPERO study protocol was CRD42022328691.

Eligibility criteria

Inclusion criteria: RCTs evaluating the use of PMR for the prevention of IH among adult patients undergoing elective midline laparotomy; English written; minimum 12 months follow-up; when two or more papers were published by the same institution, study group, or using the same dataset, articles with the longest follow-up or the largest sample size; in case of duplicate studies with accumulating numbers of patients only the most complete reports were included for quantitative analysis. Exclusion criteria: not English written; not clearly described surgical technique and mesh location; no clear outcome distinction between PMR versus primary suture closure (PSC); articles with less than 10 patients per study arm; urgent/emergent repair in more than 20% of the patient population.

Data extraction

The following data were collected: authors, year of publication, country, study design, number of patients, sex, age, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status, comorbidities, surgical indication, mesh type (synthetic/biologic), anatomic mesh location (onlay: mesh placement on top of anterior fascia, retromuscular: retromuscular mesh placement, preperitoneal: behind all of the abdominal wall muscles and in front of the peritoneum, intraperitoneal: intraperitoneal position)[14], mesh fixation technique (suture fixation, fibrin glue, no fixation), PSC techniques (running vs. interrupted sutures) and postoperative outcomes. All data were computed independently by four investigators (A.A., F.G., M.C., and E.R.) and compared at the end of the reviewing process. A fifth author (G.C.) clarified discrepancies.

Quality assessment

Three authors (A.A., F.G., and A.S.) independently assessed the methodologic quality of the selected trials by using the Cochrane risk of bias tool[25]. This tool evaluates the following criteria: method of randomization; allocation concealment; baseline comparability of study groups; and blinding and completeness of follow-up. Trials were graded as follows: A = adequate, B = unclear, and C = inadequate on each criterion. Thus, each RCT was graded as having a low, moderate, or high risk of bias. Disagreements were solved by discussion.

Outcomes of interest

The primary outcome was the incidence of postoperative IH defined as clinical, instrumental (ultrasound or computed tomography scan), reoperation, or combined assessment, at minimum 12 months follow-up. Secondary outcomes included postoperative wound-related complications such as seroma, hematoma, surgical site infections (SSI), operative time (OT) (min), and hospital length of stay (HLOS) (days). Hematoma was defined as any clinically diagnosed surgical site hematoma. Seroma was defined clinically as a localized fluid-filled sac that appeared on the operative site. SSI was defined as the presence of clinically diagnosed erythema, purulent secretion, or purulent secretion with fever.

Statistical analysis

We performed a fully Bayesian arm-based random effect network meta-analysis[26,27]. An ordinary consistency model was adopted with the binomial/log model[28]. We used risk ratio (RR) as a pooled effect size measure for categorical outcomes and weighted mean difference (WMD) for continuous outcomes. For RR on the log scale, we considered the prior information[29]. In particular, we assigned a Normal with zero mean and scale 4; we assigned Normal with zero mean and scale 100 as a vague prior distribution, and we used it as prior distribution in prior sensitivity analysis. For the between-study variability (τ), we used an informative half-normal prior with zero mean and a scale of 0.5[30]. Sensitivity analysis regarding the choice of the prior distribution for τ was considered[31]. Statistical heterogeneity was evaluated (I^2 index): value of 25% or smaller was defined as low heterogeneity, value between 50 and 75% as moderate heterogeneity, and 75% or larger as high heterogeneity[32]. In the case of moderate-high heterogeneity, meta-regression analysis was used in an attempt to determine the main factors affecting heterogeneity. The inference was performed using mean and relative 95% credible intervals (CrI) based on draws from the marginal posterior distribution in the Monte Carlo Markov chain (MCMC), simulating 300 000 iterations after a burn-in period of 30 000 iterations. We consider the estimated parameter statistically significant when its 95% CrI encompasses a null hypothesis value[33,34]. The plot of leverage values versus the square root of the residual deviance was used to identify potential outliers. The transitivity assumption was considered, and descriptive statistics were generated to compare the distributions of baseline participant characteristics across studies and treatment comparisons. To assess local inconsistencies, we used the node-splitting method[35] but it was not possible to conduct a formal assessment of the consistency of the direct and indirect evidence where the evidence network included open loops. We plotted rank

probabilities against the possible ranks for all competing treatments. The treatment ranking probability was computed with the gemtc R package. The ranking probability indicates which approach is the best in dependence on a given outcome. The confidence in estimates of the outcome was assessed using Confidence in Network Meta-Analysis (CINeMA)[36]. Statistical analyses were carried out using JAGS and R-Cran 3.4.3 (Distributed Statistical Computing; Vienna, Austria)[37].

Results

Systematic review

The selection process flowchart is reported in Figure 1. Overall, 3954 publications were acknowledged, and 2018 titles were screened after duplicates were removed. Afterward, 347 abstracts were reviewed, and 26 full-text articles were found relevant. After evaluation, 14 RCTs met the inclusion–exclusion criteria and were incorporated into the quantitative analysis (Table 1). The quality of the studies is depicted in Supplementary Figure 1, Supplemental Digital Content 2, http://links.lww.com/JS9/A279. Few studies specified the experience of the operating surgeons, the method of randomization ($n = 10$), and details regarding the power analysis ($n = 8$) (Supplementary Table 1, Supplemental Digital Content 3, http://links.lww.com/JS9/A280).

Overall, 2332 patients were included. Of those, 1052 (45.1%) had no mesh (NM) while 1280 (54.9%) underwent PMR stratified in IP ($n = 344$ pts), PP ($n = 52$ pts), RM ($n = 463$ pts), and OL ($n = 421$ pts) placement. There were no significant imbalances in baseline characteristics. The age of the patient population ranged from 18 to 75 years, the BMI ranged from 23.5 to 51 kg/m^2, and 52.9% were females. Indications for surgery were abdominal aortic aneurysm (4 studies), obesity (4 studies), colorectal surgery for cancer (1 study), or a mixture of abdominal procedures (5 studies) (Table 1). Most of the studies reported outcomes for polypropylene mesh ($n = 10$)[3–7,39–42,44], two studies reported outcomes for biologic mesh[8,38,] while one study described the use of polyglactin mesh[2]. For the NM group, 10 studies described the mass closure technique, while seven specified the adoption of the suture length (SL) to wound length (WL), 4 : 1 ratio. Five trials[5,7,39,42,43] specified the utilization of a long-stitch closure technique with 10 mm stitch intervals and a 10 mm distance from the wound edge. The continuous nonabsorbable suture was adopted in five studies[3,5–7,38,] while slowly absorbable continuous suture was used in eight studies[4,8,39–44]. Only one study reported outcomes for interrupted absorbable suture closure[2]. Duration of follow-up ranged from 12 months to 67 months.

Seven studies reported data for postoperative chronic pain; however, results were described heterogeneously with institutional scales[3,5,38,40] or using the Visual Analogue Scale[41–43]. One trial reported data for patient quality of life assessment[41,] while none described the analysis of costs or the postoperative abdominal wall function assessment.

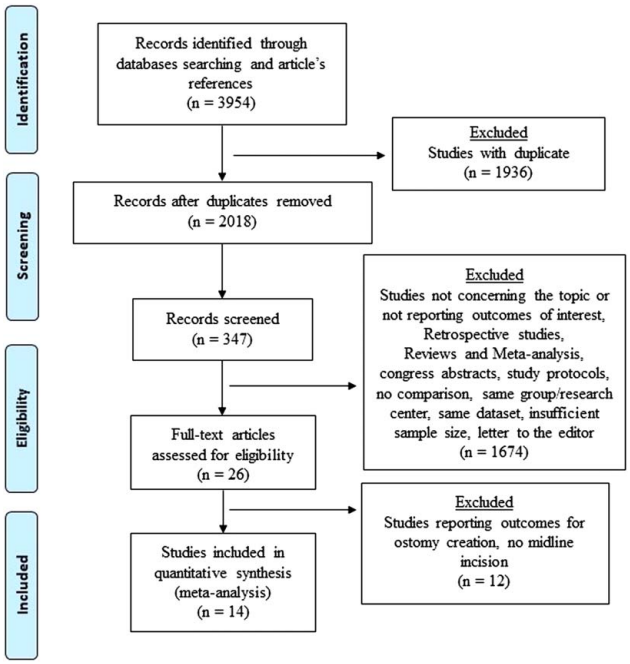

Figure 1. The Preferred Reporting Items for Systematic Reviews and Network Meta-Analyses checklist (PRISMA-NMA) diagram.

Meta-analysis

Primary outcome

IH was reported in all studies (2332 patients)[2–8,38–44] with significantly reduced RR for RM versus NM (RR = 0.34; 95% CrI: 0.10–0.81) and OL versus NM (RR = 0.15; 95% CrI: 0.044–0.35) (Fig. 2). No significant differences were found comparing PP versus NM (RR = 0.16; 95% CrI: 0.018–1.01) and IP versus NM (RR = 0.59; 95% CrI: 0.19–1.81). The global heterogeneity was moderate ($I^2 = 39.2\%$), while the prior sensitivity analysis yielded robust results for all treatment comparisons. The treatment ranking plot showed that OL (15%) and RM (22%) had the lowest probability for IH recurrence, followed by PP (46.7%), IP (70%), and NM (95%) (Fig. 3A).

Secondary outcomes

The pooled network analysis for seroma (10 studies, 1740 patients)[3,5,7,8,38–41,43,44], hematoma (7 studies, 1300 patients)[3,39–44], SSI (13 studies, 2258 patients)[2,3,5–8,38–44], and 90-day mortality (9 studies, 1438 patients)[5,6,8,39–44] does not show significant differences among treatment groups with a moderately related heterogeneity ($I^2 < 50\%$). Again, no significant differences were found for operative time (8 studies)[6,8,39–44] and hospital length of stay (6 studies)[4,7,39–42]. Despite the lack of statistical significance, the treatment ranking plot showed that NM had the lowest probability for postoperative seroma (24%) and hematoma (36%), while PP placement had the lowest probability for SSI (29%) (Fig. 3 B–D). Descriptive statistics and the League table are depicted in Table 2 and Table 3, respectively. Meta-regression analysis results showed that age, gender, BMI, and surgical indication did not influence heterogeneity for IH, seroma, SSI, and operative time. The node split analysis does not show evidence of inconsistence. The Leverage plots do not show evidence of study outliers into this network meta-analysis. For all outcomes, there was no evidence of non-MCMC convergence using the diagnostic tools described in the statistical analysis section. The assessments of confidence in the estimates using CINeMA show moderate to

Table 1

Demographic and clinical characteristics of patients undergoing prophylactic mesh reinforcement (PMR) versus primary suture closure (PSC).

Author, year, country	Study period	Indications for surgery	Treatment	Number of patients	Mesh type	Mesh location	Mesh fixation	PSC technique	Age (years) (mean ± SD)	BMI (kg/m^2) (mean ± SD)	Follow-up (months)
Pans *et al.*, 1998, Belgium[2]	1990–1993	Morbid obesity	PMR	144	Polyglactin	IP	Not fixed	Interrupted sutures	36.6 ± 0.9	43.8	29
			PSC	144				(polyglactin)	36.4 ± 0.9	43.7	31
Gutiérrez de la Peña *et al.*, 2003, Spain[3]	2002	High-risk patients	PMR	44	Polypropylene	OL	Separate stitches of absorbable material with a single crown	Continuous suture (nonabsorbable monofilament)	nr	nr	36
			PSC						nr	nr	36
Strzelczyk *et al.*, 2006, Poland[4]	1999–2001	Morbid obesity	PMR	36	Polypropylene	RM	Interrupted sutures	Continuous suture	39.4 ± 12.3	46.2 ± 7.1	28
			PSC	38				mass closure (PDS)	38.9 ± 11.8	46.8 ± 7.6	28
El-Khadrawy *et al.*, 2009, Egypt[5]	2000–2002	High-risk patients	PMR	20	Polypropylene	PP	Four cardinal stitches	Continuous suture	47.8 ± 13.8	nr	37
			PSC	20				(polypropylene)	47.6 ± 14.1	nr	36
Bevis *et al.*, 2010, UK[6]	2003–2007	AAA	PMR	37	Polypropylene	RM	Four tacking sutures (polypropylene 2.0)	Continuous suture	74	nr	30
			PSC					Mass closure (nonabsorbable) (4 : 1 ratio)	72	nr	20
Abo-ryia *et al.*, 2013, Egypt[7]	2004–2006	Morbid obesity	PMR	32	Polypropylene	PP	Interrupted stitches	Continuous suture	38.5 ± 10.8	52.2 ± 9.1	48
			PSC	32				Mass closure (Prolene)	36.9 ± 11.3	51.4 ± 10.5	49
Bali *et al.*, 2014, Greece[8]	2007–2009	AAA	PMR	20	Bovine pericardium	OL	Bilateral running nonabsorbable sutures	Continuous suture	74.3 ± 5.8	25.4 (median)	36
			PSC	20				Mass closure (PDS) (4 : 1 ratio)	74.3 ± 5.8	24.4 (median)	36
Sarr *et al.*, 2014, USA[38]	2014	Morbid obesity	PMR	185	Biological (Surgisis Gold)	RM	Transmural sutures	Continuous suture	44.6 ± 10.6	48.2 ± 8.2	24
			PSC	195				(Nylon 0-1-2; polypropylene, PDS)	45.1 ± 12.1	48.2 ± 7.7	24
Garcia-Ureña *et al.*, 2015, Spain[39]	2009–2011	Age > 18 years operated on any colorectal disease	PMR	53	Polypropylene	OL	Interrupted sutures (PDS 3.0)	Continuous suture (poly-4-hydroxybutyrate) (4 : 1 ratio)	65.6 ± 13.3	nr	24
			PSC	54					61.46 ± 15.6	nr	24
Muysoms *et al.*, 2016 – PRIMAAT trial, Belgium[40]	2009–2013	AAA	PMR	56	Polypropylene	RM	Interrupted sutures (Polyglactin 3.0)	Continuous suture (PDS) (4 : 1 ratio)	72 ± 7.4	25 ± 3.7	24
			PSC	58					72 ± 8.4	26 ± 3.7	24
Jairam *et al.*, 2017 (Timmermans *et al.*, 2015) – PRIMA trial, Germany, Austria, Netherlands[41]	2009–2012	AAA (150) or BMI > 27 (330)	PMR	185	Polypropylene	RM	Fibrin sealant	Continuous suture	64.4 ± 10.4	30.8 ± 5.2	23
			PMR	188		OL		PDS (4 : 1 ratio)	64.2 ± 12.3	30.8 ± 5.9	23
			PSC	107					65.2 ± 10.5	29.8 ± 4.4	23
Kohler *et al.*, 2018 – PROPHMESH trial, Switzerland[42]	2011–2014	Presence of at least 2 of BMI > 25, neoplastic disease, male sex, history of laparotomy	PMR	69	Double-layered polypropylene-polyvinylidene fluoride	IP	Interrupted stitches	Continuous suture (PDS loop)	64.2 ± 11.1	27.6 ± 4.6	30
			PSC	81					64.2 ± 11.1	26.7 ± 4.8	30
Glauser *et al.*, 2019, Switzerland[43]	2008–2018	nr	PMR	131	Parietex dual-layer composite mesh	IP	Mesh strips fixed in the midline with the PDS loop	Continuous suture (mass closure) PDS (4 : 1 ratio)	64.1	25.8	60
			PSC	136					65.1	26.6	60
Caro-Tarrago *et al.*, 2019, Spain[44]	2009–2017	ASA <4 in people who needed median laparotomy	PMR	80	Polypropylene	OL	Interrupted polyglactin 2.0 stitches	Continuous suture PDS (4 : 1 ratio)	64.3 ± 14.3	nr	15
			PSC	80					67.3 ± 11.1	nr	12

AAA, abdominal aortic aneurism; IP, intraperitoneal; nr, not reported; OL, onlay; PDS, polydioxanone; PP, preperitoneal; RM, retromuscular.

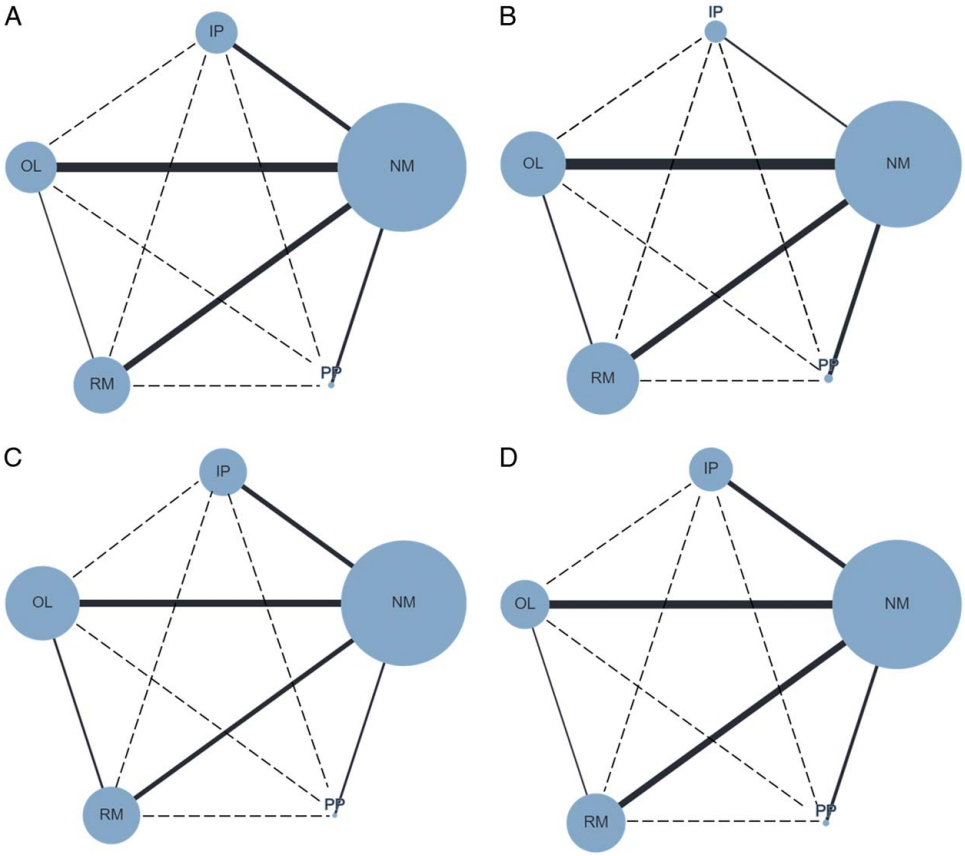

Figure 2. Network geometry. Nodes size reflects the sample size, and edges width reflects the number of studies for specific pairwise comparison. The solid line indicates direct comparisons, while the dotted line indicates indirect comparisons performed with the network methodology; (A) Incisional hernia; (B) seroma; (C) hematoma; and (D) surgical site infection. IP, intraperitoneal; NM, no mesh; OL, onlay; PP, preperitoneal; RM, retromuscular.

very low confidence, essentially due to study limitation, imprecision, and inconsistency.

Discussion

This network analysis shows that OL and RM mesh placement seem associated with a significantly reduced postoperative IH RR risk compared to NM. PP seems associated with a tendency toward reduced risk compared to NM, while no differences were found for IP versus NM. Short-term complications, operative time, and HLOS seem comparable among different mesh locations.

IH is a common complication after open abdominal surgery, with an estimated frequency of 30–40% in high-risk patients[1–5]. IH can generate social and financial burdens for patients, the economic system, and social healthcare organizations with impact on the subject's quality of life[45–48]. IH prevention is of paramount importance and a matter of debate. The use of small bites (short-stitch technique) and protocols for the SL : WL, 4 : 1 ratio have been proposed after midline laparotomy in an attempt to reduce the risk of IH[49], but its prevalence remains significant. The utilization of PMR has been proposed with the intent to further reduce the postoperative IH risk; however, its true effect and indications are discussed. The European Hernia Society (EHS) Guidelines Development Group sustained that PMR seems to reduce the incidence of IH in high-risk patients[50]. However, the quality of this evidence was poor because based on observational studies with important selection bias and limited follow-up. Moreover, heterogeneous mesh location contributed to the growing skepticism toward PMR while conclusive evidence regarding the 'ideal' mesh location is evanishing.

In an attempt to condense this heterogeneity and decrease preoperative selection bias, we focused on RCTs with a 1-year minimum follow-up. The diagnosis of IH was both clinical and radiologic, thus possibly minimizing any potential postoperative reporting bias. The cumulative prevalence of IH was 27.6% for NM, 18.6% for IP, 15.3% for RM, 8.06% for OL, and 3.8% for PP. The quantitative analysis suggests that, compared to NM, RM (RR = 0.34; 95% CrI: 0.10–0.81) and OL (RR = 0.15; 95% CrI: 0.04–0.35) seem associated with a significantly reduced IH RR. This corroborates what was recently suggested in the PRIMA trial, where the authors reported a considerably reduced IH for RM (18%) and OL (13%) placement versus NM (30%)[41]. Related heterogeneity was moderate ($I^2 = 39.2\%$); therefore, a cautionary interpretation remains advisable. Meta-regression analysis adjusted for age, gender, BMI, and surgical indication failed to justify this heterogeneity. Therefore, demographics, comorbidities, surgical indications, surgeon proficiency, hospital volume, mesh type (synthetic vs. biologic), fixation techniques, and detection/publication bias may hypothetically explain this heterogeneity. Notably, the comparison of PP versus NM (RR = 0.16) seems to suggest a potential clinical tendency toward

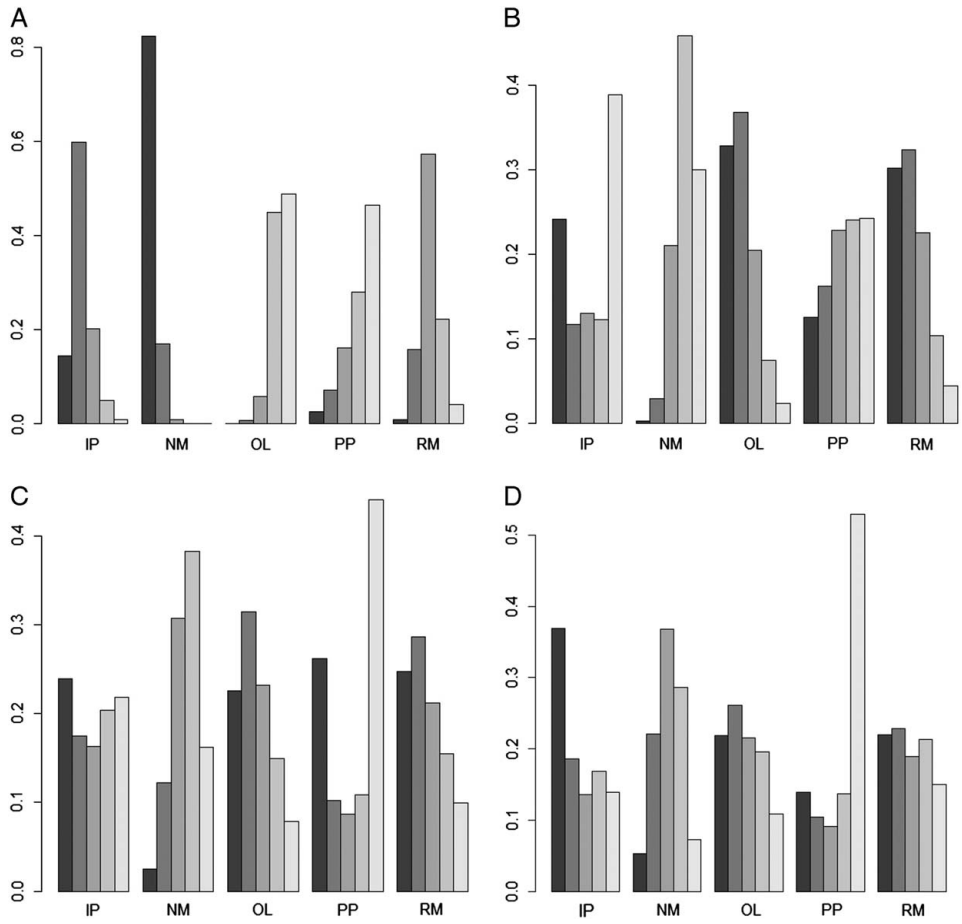

Figure 3. The ranking plot applied to the five surgical treatments illustrates the empirical probability that each treatment is ranked first through fifth (left to right). The abscissa axis shows the different treatments. The ordinate axis shows the probability (%) of ranking better (higher rankings associated with smaller outcomes values); (A) incisional hernia; (B) seroma; (C) hematoma; and (D) surgical site infection. IP, intraperitoneal; NM, no mesh; OL, onlay; PP, preperitoneal; RM, retromuscular.

a reduced IH risk. However, the upper 95% CrI barely encompasses the null hypothesis, thus making the result not significant. This may be attributable to the narrow patient population in this arm comparison ($n = 104$); therefore, further studies with a specific focus on PP location are warranted to endorse this initial suggestion. The treatment ranking plot showed that OL and RM had the lowest probability for IH recurrence. Notably, the long-term effect (> 5 years) of PMR is still not demarcated. Even if all the included studies reported outcomes for follow-up longer than 12 months, it is ascertained that a large effect size in the short term may potentially overemphasize the tangible benefits of a treatment and may not automatically correlate with results in the

Table 2

Descriptive statistics stratified according to different treatments.

IP	NM	OL	PP	RM	
		Categorical variables			
18.6 (7.2–22.9)	27.6 (11–46)	8.1 (0–12.7)	3.8 (3.1–5)	15.3 (0–18)	Incisional hernia
1.5 (1.5–1.5)	4.82 (0–15.6)	17.1 (2.3–29)	19.2 (18.7–20)	5.6 (3.6–7)	Seroma
2 (1.4–2.3)	2.5 (0.9–4.7)	4.8 (1.2–6.8)	5 (5–5)	4.5 (3.6–4.9)	Hematoma
5.8 (3.0–15.9)	8.8 (0.7–3.3)	15.8 (2.3–25)	13.5 (10–15.6)	9.5 (1.7–11.9)	SSI
1.5 (1.4–1.6)	8.1 (1.5–22.4)	13.49 (3.8–18)	5 (5–5)	6.8 (1.8–8.1)	90-day mortality
		Continuous variables			
54.9 (9–102)	56.5 (10–109)	44.4 (27.5–65.8)	nr	37.9 (22.5–62)	OT (minutes)
1.3 (1.33–1.33)	6.6 (2–11)	5.12 (2.5–8.3)	3.6 (3.4–3.4)	4.73 (2–7)	HLOS (days)

Values are presented as percentages (range) for categorical variables and as mean (range) for continuous variables.

HLOS, hospital length of stay; IP, intraperitoneal; NM, no mesh; nr, not reported; OL, onlay; OT, operative time; PP, preperitoneal; RM, retromuscular; SSI, surgical site infection.

Table 3

League table. Each row represents a specific outcome.

					I^2 (%)	
		Categorical variables				
IP	1.68 (0.55–5.29)	0.26 (0.045–0.96)	0.2691 (0.02–2.43)	0.57 (0.11–2.27)	39.2	Incisional hernia
0.59 (0.19–1.81)	NM	0.15 (0.044–0.35)	0.16 (0.02–1.01)	0.34 (0.10–0.81)		
3.87 (1.04–22.18)	6.59 (2.87–22.91)	OL	1.07 (0.11–10.7)	2.21 (0.66–8.60)		
3.72 (0.41–41.65)	6.23 (0.96–54.48)	0.94 (0.05–9.13)	PP	2.09 (0.22–21.04)		
1.74 (0.44–9.34)	2.96 (1.23–9.76)	0.45 (0.12–1.5)	0.48 (0.05–4.56)	RM		
IP	0.86 (0.07–10.19)	1.79 (0.11–24.02)	1.06 (0.06–18.65)	1.73 (0.11–30.98)	23.9	Seroma
1.17 (0.10–15.04)	NM	2.11 (0.78–4.86)	1.24 (0.30–5.30)	1.98 (0.68–8.38)		
0.56 (0.04–8.78)	0.47 (0.21–1.28)	OL	0.59 (0.12–3.54)	0.93 (0.30–4.96)		
0.94 (0.05–17.52)	0.81 (0.19–3.36)	1.7 (0.28–8.59)	PP	1.60 (0.28–12.76)		
0.58 (0.03–8.81)	0.50 (0.12–1.48)	1.07 (0.20–3.27)	0.63 (0.08–3.57)	RM		
IP	0.82 (0.13–4.92)	1.22 (0.12–10.36)	0.71 (0.02–25.77)	1.23 (0.12–12.06)	0.0	Hematoma
1.21 (0.20–7.43)	NM	1.48 (0.39–4.94)	0.87 (0.03–19.55)	1.49 (0.34–6.32)		
0.82 (0.09–7.97)	0.68 (0.20–2.54)	OL	0.59 (0.02–17.46)	0.99 (0.23–5.00)		
1.41 (0.04–59.67	1.15 (0.05–31.01)	1.69 (0.06–54.94)	PP	1.70 (0.05–60.81)		
0.82 (0.08–8.50)	0.67 (0.16–2.91)	1.00 (0.1999–4.34)	0.59 (0.02–17.91)	RM		
IP	0.85 (0.28–2.21)	0.93 (0.24–2.96)	0.62 (0.107–3.04)	0.90 (0.21–3.08)	42.1	SSI
1.17 (0.45–3.52)	NM	1.09 (0.52–2.19)	0.733 (0.19–2.65)	1.05 (0.44–2.39)		
1.08 (0.34–4.17)	0.92 (0.46–1.93)	OL	0.67 (0.15–2.99)	0.97 (0.36–2.61)		
1.60 (0.33–9.33)	1.36 (0.38–5.26)	1.48 (0.33–6.75)	PP	1.44 (0.30–6.95)		
1.11 (0.32–4.6)	0.95 (0.42–2.24)	1.03 (0.38–2.77)	0.69 (0.14–3.28)	RM		
IP	1.34 (0.30–6.52)	1.23 (0.243–6.88)	1.13 (0.03–32.75)	0.59 (0.11–3.54)	0.0	90-day mortality
0.74 (0.15–3.28)	NM	0.91 (0.47–1.84)	0.84 (0.03–15.86)	0.44 (0.20–1.03)		
0.81 (0.14–4.10)	1.1 (0.54–2.10)	OL	0.92 (0.03–18.62)	0.48 (0.20–1.20)		
0.89 (0.03–29.68)	1.18 (0.06–29.58)	1.08 (0.05–29.26)	PP	0.53 (0.03–14.53)		
1.68 (0.28–8.95)	2.28 (0.97–4.88)	2.08 (0.83–4.90)	1.9 (0.07–39.4)	RM		
		Continuous variables				
IP	4.98 (– 11.29 to 21.18)	0.95 (– 19.02 to 20.09)	– 9.07 (– 29.54 to 11.36)		86	OTa (min)
– 4.98 (– 21.18 to 11.29)	NM	– 4.02 (– 15.36 to 6.54)	– 14.07 (– 26.41 to – 1.53)			
– 0.95 (– 20.09 to 19.02)	4.02 (– 6.54 to 15.36)	OL	– 10.03 (– 25.9 to 6.71)			
9.07 (– 11.36 to 29.54)	14.07 (1.53 to 26.41)	10.03 (– 6.71 to 25.9)	RM			
IP	2.37 (– 54.11 to 57.83)	– 0.31 (– 61.9 to 62.07)	2.04 (– 62.38 to 67.21)	– 0.82 (– 69.99 to 69.15)	0.0	HLOSa(days)
– 2.37 (– 57.83 to 54.11)	NM	– 2.25 (– 28.53 to 23.61)	– 0.12 (– 34.13 to 33.86)	– 3.06 (– 44.56 to 39.86)		
0.31 (– 62.07 to 61.9)	2.24 (– 23.61 to 28.53)	OL	2.25 (– 40.67 to 44.91)	– 0.81 (– 49.06 to 49.51)		
– 2.04 (– 67.21 to 62.38)	0.12 (– 33.86 to 34.13)	– 2.25 (– 44.91 to 40.67)	PP	– 2.48 (– 57.03 to 50.95)		
0.82 (– 69.15 to 69.99)	3.06 (– 39.86 to 44.56)	0.81 (– 49.51 to 49.06)	2.48 (– 50.95 to 57.03)	RM		

Values in each column represent the relative effect of the referral treatment (bold) with the comparator. I^2, heterogeneity.
Values are expressed as risk ratio (RR) and 95% credible intervals (95% CrI).
HLOS, hospital length of stay; IP, intraperitoneal; NM, no mesh; OL, onlay; OT, operative time; PP, preperitoneal; RM, retromuscular; SSI, surgical site infection.
aWeighted mean differences.

long run. Therefore, studies with long-term data analysis are warranted.

Postoperative seroma RR was comparable among all treatment arms. The cumulative frequency of postoperative seroma was 4.8%, 1.5%, 19.2%, 5.6%, and 17.4% for NM, IP, PP, RM, and OL (Table 2). Point estimation for IP (RR = 1.2), PP (RR = 1.24), RM (RR = 1.98), and OL (RR = 2.11) versus NM seem to suggest a trend toward increased risk for postoperative seroma formation; however, the results were not significant. This seems equivalent to what was reported by Payne *et al.*[15] and Wang *et al.*[18]. that stated a trend toward higher risk for seroma after PMR conceivably related to the extended lateral dissection for adequate mesh allocation and wound overlap. Related heterogeneity was moderate ($I^2 = 36\%$). This may be attributable to patient comorbidities, surgeon experience, techniques for mesh fixation, and drain use. Interestingly, the treatment ranking plot defined OL as the treatment with the highest probability of seroma. Finally, no significant differences were found for postoperative hematoma, SSI, HLOS, and OT with a related moderate-high heterogeneity. Again, interpretation of these results should be cautious, being theoretically influenced by multifaceted elements such as comorbidities, BMI, ASA grade, surgical indications, smoking status, antibiotic therapy, lack of standardized reporting, hospital practices, implementation of enhanced recovery after surgery protocols, and surgeons' capability.

Opponents of PMR may argue that longer operative times and increased healthcare costs related to consumable materials do not justify PMR. Because lacking well-defined financial data, a robust cost analysis was impracticable. However, the present study shows comparable operative time and HLOS among all treatments. Therefore, as argued in previous studies, it may be presumed that the reduced postoperative IH RR with concomitant diminution of outpatient visits, hospital readmissions, and the need for reoperation may potentially minimize the related economic burden[51]. Future well-detailed trials focused on cost analysis are warranted to deeply

appraise this issue. Surgeons' performance with different levels of training, learning curve, and experience might have impacted patient outcomes and can be the source of bias. It has been shown that these operator-related factors and surgeon proficiency are of utmost importance for the determination of operative time, intraoperative blood loss, and overall complications[52]. In the present analysis, only a few of included studies described the operating surgeon's proficiency and expertise; therefore, results should be cautiously appraised. Finally, methods for randomization, power analysis, blinding of assessors, and trial design were not clearly defined in all RCTs; therefore, conclusions should be prudently inferred.

There are several limitations to the current analysis. First, although the groups were balanced, the accuracy of our results can be tempered by differences in surgical indications, comorbidities, and techniques. Second, even though only RCTs were included in our analyses, the quality of evidence remained moderate, in part, due to no blinding of patients and/or surgeons, limited power in some trials, and different methods for randomization. Third, the restricted follow-up may have caused a global overestimation of the true mesh benefit. Fourth, all but one study was performed in European countries. Fifth, as operations were performed by expert surgeons in referral centers, results may not be generalizable. Lastly, chronic pain, quality of life, patient's satisfaction, and cost-effectiveness were marginally or not evaluated in the considered studies; therefore, a robust analysis was not practicable.

Conclusions

RM or OL mesh placement during midline elective laparotomy is desirable and seems associated with reduced IH RR compared to NM. PP location appears promising; however, future studies are warranted to corroborate this preliminary indication.

Ethical approval

Ethical approval was not required because this study retrieved and synthesized data from previously published studies.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

A.A., F.G., A.S., and P.G.B.: literature search; A.A., D.B., and G. C.: study design; A.A., F.G., A.S., and E.R.: data collection; A.A., G.B., and D.B.: analyzed the data; A.A., D.B., and G.C.: interpreted the data; A.A., G.B., and D.B.: wrote the manuscript. All authors critically reviewed the manuscript.

Conflicts of interest disclosure

The authors have no related conflicts of interest to declare.

Research registration unique identifying number (UIN)

1. Name of the registry: PROSPERO.
2. Unique identifying number or registration ID: CRD42022328691.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=328691

Guarantor

Alberto Aiolfi, MD, FACS, Department of General Surgery, IRCCS Ospedale Galeazzi – Sant'Ambrogio University of Milan, Italy. E-mail: alberto.aiolfi86@gmail.com

Data availability statement

All data generated or analyzed during this study are included in this article (and/or) its supplementary material files. Further inquiries can be directed to the corresponding author.

Acknowledgments

None

References

[1] Diener MK, Voss S, Jensen K, *et al*. Elective midline laparotomy closure: the INLINE systematic review and meta-analysis. Ann Surg 2010;251:843–56.
[2] Pans A, Elen P, Dewé W, *et al*. Long-term results of polyglactin mesh for the prevention of incisional hernias in obese patients. World J Surg 1998;22:479–82.
[3] Gutiérrez de la Peña C, Medina Achirica C, Domínguez- Adame E, *et al*. Primary closure of laparotomies with high risk of incisional hernia using prosthetic material: analysis of usefulness. Hernia 2003;7:134–6.
[4] Strzelczyk JM, Szymański D, Nowicki ME, *et al*. Randomized clinical trial of postoperative hernia prophylaxis in open bariatric surgery. Br J Surg 2006;93:1347–50.
[5] El-Khadrawy OH, Moussa G, Mansour O, *et al*. , Prophylactic prosthetic reinforcement of midline abdominal incisions in high-risk patients. Hernia 2009;13:267–74.
[6] Bevis PM, Windhaber RA, Lear PA, *et al*. Randomized clinical trial of mesh versus sutured wound closure after open abdominal aortic aneurysm surgery. Br J Surg 2010;97:1497–502.
[7] Abo-ryia MH, El- Khadrawy OH, Abd-Allah HS. Prophylactic preperitoneal mesh placement in open bariatric surgery: a guard against incisional hernia development. Obes Surg 2013;23:1571–4.
[8] Bali C, Papakostas J, Georgiou G, *et al*. A comparative study of sutured versus bovine pericardium mesh abdominal closure after open abdominal aortic aneurysm repair. Hernia 2015;19:267–71.
[9] van Ramshorst GH, Eker HH, Hop WC, *et al*. Impact of incisional hernia on health-related quality of life and body image: a prospective cohort study. Am J Surg 2012;204:144–50.
[10] van Ramshorst GH, Eker HH, van der Voet JA, *et al*. Long-term outcome study in patients with abdominal wound dehiscence: a comparative study on quality of life, body image, and incisional hernia. J Gastrointest Surg 2013;17:1477–84.
[11] Holihan JL, Alawadi Z, Martindale RG, *et al*. Adverse events after ventral hernia repair: the vicious cycle of complications. J Am Coll Surg 2015;221:478–85.
[12] Fischer JP, Basta MN, Mirzabeigi MN, *et al*. A risk model and cost analysis of incisional hernia after elective, abdominal surgery based upon 12,373 cases: the case for targeted prophylactic intervention. Ann Surg 2016;263:1010–7.

[13] Bhangu A, Fitzgerald JE, Singh P, *et al*. Systematic review and meta-analysis of prophylactic mesh placement for prevention of incisional hernia following midline laparotomy. Hernia 2013;17:445–55.

[14] Parker SG, Halligan S, Liang MK, *et al*. International classification of abdominal wall planes (ICAP) to describe mesh insertion for ventral hernia repair. Br J Surg 2020;107:209–17.

[15] Payne R, Aldwinckle J, Ward S. Meta-analysis of randomised trials comparing the use of prophylactic mesh to standard midline closure in the reduction of incisional herniae. Hernia 2017;21:843–53.

[16] Borab ZM, Shakir S, Lanni MA, *et al*. Does prophylactic mesh placement in elective, midline laparotomy reduce the incidence of incisional hernia? A systematic review and meta-analysis. Surgery 2017;161:1149–63.

[17] Timmermans L, de Goede B, Eker HH, *et al*. Meta-analysis of primary mesh augmentation as prophylactic measure to prevent incisional hernia. Dig Surg 2013;30:401–9.

[18] Wang XC, Zhang D, Yang ZX, *et al*. Mesh reinforcement for the prevention of incisional hernia formation: a systematic review and meta-analysis of randomized controlled trials. J Surg Res 2017;209: 17–29.

[19] Ahmed J, Hasnain N, Fatima I, *et al*. Prophylactic mesh placement for the prevention of incisional hernia in high-risk patients after abdominal surgery: a systematic review and meta-analysis. Cureus 2020;12:e10491.

[20] Jairam AP, López-Cano M, Garcia-Alamino JM, *et al*. Prevention of incisional hernia after midline laparotomy with prophylactic mesh reinforcement: a meta-analysis and trial sequential analysis. BJS Open 2020;4:357–68.

[21] Olavarria OA, Dhanani NH, Bernardi K, *et al*. Prophylactic mesh reinforcement for prevention of midline incisional hernias: a publication bias adjusted meta-analysis. Ann Surg 2023;277:e162–9.

[22] Aiolfi A, Cavalli M, Gambero F, *et al*. Prophylactic mesh reinforcement for midline incisional hernia prevention: systematic review and updated meta-analysis of randomized controlled trials. Hernia 2022. [Epub ahead of print]. http://doi: 10.1007/s10029-022-02660-4

[23] Liberati A, Altman DG, Tetzlaff J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009;339:b2700.

[24] Goossen K, Tenckhoff S, Probst P, *et al*. Optimal literature search for systematic reviews in surgery. Langenbecks Arch Surg 2018;403:119–29.

[25] Higgins JP, Altman DG, Gotzsche PC, *et al*. Cochrane Bias Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.

[26] Der Simonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.

[27] Borenstein M, Hedges LV, Higgins JP, *et al*. A basic introduction to fixed-effect and random-effects models for meta-analysis. Res Synth Methods 2010;1:97–111.

[28] Aiolfi A, Tornese S, Bonitta G, *et al*. Roux-en-Y gastric bypass: systematic review and Bayesian network meta-analysis comparing open, laparoscopic, and robotic approach. Surg Obes Relat Dis 2019;15:985–94.

[29] Kass RE, Wasserman L. A reference Bayesian test for nested hypotheses and its relationship to the Schwarz criterion. J Am Statist Assoc 1995;90 : 928–34.

[30] Friede T, Röver C, Wandel S, *et al*. Meta-analysis of few small studies in orphan diseases. Res Synth Methods 2017;8:79–91.

[31] Turner RM, Davey J, Clarke MJ, *et al*. Predicting the extent of heterogeneity in meta-analysis, using empirical data from the Cochrane database of systematic reviews. Int J Epidemiol 2012;41:818–27.

[32] Higgins JP, Thompson SG, Deeks JJ, *et al*. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.

[33] Smith BJ. boa: an R package for MCMC output convergence assessment and posterior inference. J Stat Softw 2007;21:1–37.

[34] Aiolfi A, Bona D, Riva CG, *et al*. Systematic review and Bayesian network meta-analysis comparing laparoscopic Heller myotomy, pneumatic dilatation, and peroral endoscopic myotomy for esophageal achalasia. J Laparoendosc Adv Surg Tech 2020;30:147–55.

[35] Dias S, Welton NJ, Caldwell DM, *et al*. Checking consistency in mixed treatment comparison meta-analysis. Stat Med 2010;29:932–44.

[36] Salanti G, Del Giovane C, Chaimani A, *et al*. Evaluating the quality of evidence from a network meta-analysis. PLoS One 2014;9:e99682.

[37] Core Team R. R: A Language and Environment for Statistical Computing R Foundation for Statistical Computing 2010.

[38] Sarr MG, Hutcher NE, Snyder S, *et al*. A prospective, randomized, multicenter trial of Surgisis Gold, a biologic prosthetic, as a sublay reinforcement of the fascial closure after open bariatric surgery. Surgery 2014;156:902–8.

[39] García-Ureña MA, López-Monclús J, Hernando LA, *et al*. Randomized controlled trial of the use of a large-pore polypropylene mesh to prevent incisional hernia in colorectal surgery. Ann Surg 2015;261:876–81.

[40] Muysoms FE, Detry O, Vierendeels T, *et al*. Prevention of incisional hernias by prophylactic mesh-augmented reinforcement of midline laparotomies for abdominal aortic aneurysm treatment: a randomized controlled trial. Ann Surg 2016;263:638–45.

[41] Jairam AP, Timmermans L, Eker HH, *et al*. PRIMA Trialist Group. Prevention of incisional hernia with prophylactic onlay and sublay mesh reinforcement versus primary suture only in midline laparotomies (PRIMA): 2-year follow-up of a multicentre, double-blind, randomised controlled trial. Lancet 2017;390:567–76.

[42] Kohler A, Lavanchy JL, Lenoir U, *et al*. Effectiveness of prophylactic intraperitoneal mesh implantation for prevention of incisional hernia in patients undergoing open abdominal surgery: a randomized clinical trial. JAMA Surg 2019;154:109–15.

[43] Glauser PM, Brosi P, Speich B, *et al*. Prophylactic intraperitoneal onlay mesh following midline laparotomy-long-term results of a randomized controlled trial. World J Surg 2019;43:1669–75.

[44] Caro-Tarrago A, Olona C, Millán M, *et al*. Long-term results of a prospective randomized trial of midline laparotomy closure with onlay mesh. Hernia 2019;23:335–40.

[45] Loh C, Tan L, Wijerathne S, *et al*. Open versus laparoscopic intraperitoneal on-lay mesh repair: a comparison of outcomes in small ventral hernia. Asian J Surg 2022;46:712–7.

[46] Akalin C, Karagulle OO. The effects of onlay titanium-coated mesh on recurrence, foreign body sensation and chronic pain after ventral hernia repair. Asian J Surg 2021;44:1158–65.

[47] Kesicioglu T, Yildirim K, Yuruker S, *et al*. Three-year outcome after anterior component separation repair of giant ventral hernias: a retrospective analysis of the original technique without mesh. Asian J Surg 2022;45:1117–21.

[48] Cavalli M, Aiolfi A, Bruni PG, *et al*. Prevalence and risk factors for diastasis recti abdominis: a review and proposal of a new anatomical variation. Hernia 2021;25:883–90.

[49] Deerenberg EB, Harlaar JJ, Steyerberg EW, *et al*. Small bites versus large bites for closure of abdominal midline incisions (STITCH): a double- blind, multicentre, randomised controlled trial. Lancet 2015;386:1254–60.

[50] Muysoms FE, Antoniou SA, Bury K, *et al*. European Hernia Society. European Hernia Society guidelines on the closure of abdominal wall incisions. Hernia 2015;19:1–24.

[51] Gillion JF, Sanders D, Miserez M, *et al*. The economic burden of incisional ventral hernia repair: a multicentric cost analysis. Hernia 2016;20: 819–30.

[52] Aiolfi A, Cavalli M, Ferraro SD, *et al*. Treatment of inguinal hernia: systematic review and updated network meta-analysis of randomized controlled trials. Ann Surg 2021;274:954–61.