REVIEW

Efficacy of commercially available adhesion barriers in abdominal surgery: a systematic review of randomised controlled trials

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Keywords: Surgery, Gynaecology, Adhesion prevention, Laparotomy, Minimal access surgery

Abstract

Introduction

Postoperative peritoneal adhesions remain an almost inevitable consequence of abdominopelvic surgery, causing small bowel obstruction, infertility, chronic pain, and significant healthcare costs. Numerous adhesion prevention agents have been introduced, yet their comparative efficacy and safety remain uncertain.

Methodology

This systematic review was conducted in accordance with PRISMA guidelines. Electronic databases including PubMed, Web of Science, and Google Scholar were searched up to August 2025. Randomised controlled trials (RCTs) and controlled clinical studies evaluating adhesion prevention agents in abdominal or pelvic surgery were included. Data extraction focused on study characteristics, interventions, adhesion-related outcomes, complications, and follow-up.

Results

Ten eligible trials were analysed. Hyaluronic acid/carboxymethylcellulose (HA/CMC) gels and membranes demonstrated consistent reductions in adhesion severity and extent, with Guardix-sol, Guardix-SG, and TCD-11091 showing the most favourable outcomes. Starch-based polysaccharides (4DryField PH) achieved up to an 85% reduction in adhesion scores at second-look laparoscopy and were associated with improved fertility and pain outcomes, though safety concerns were reported in pediatric and retrospective cohorts. Collagen membranes (COVA+), thermosensitive gels (Mediclore, Actamax), and fibrin sealants (Adhexil) showed promising early results but require larger confirmatory studies. Conversely, icodextrin (Adept) and spray powders such as Sepraspray yielded inconsistent benefit. Safety was generally acceptable, though with powders occasionally correlated with higher complication rates.

Conclusion

Evidence supports the selective use of HA/CMC-based gels and starch-derived barriers for adhesion prevention in high-risk surgical contexts. However, heterogeneity across trials, short follow-up, and lack of standardised adhesion scoring limit definitive recommendations. Adhesion barriers should be considered as adjuncts to meticulous surgical technique rather than substitutes. Future directions include bioactive, multifunctional platforms (Janus hydrogels, plasma-activated solutions, metabolic modulators, phytochemicals) and robust RCTs incorporating fertility, obstruction, pain, and cost-effectiveness as patient-centred endpoints.

Introduction

A significant challenge in oncological surgeries is due to development of postoperative adhesion and its related complications. Many cancer sufferers require multiple surgeries either while reconstruction and reverting to near-normal anatomy after their primary debilitating surgeries or during surgeries for recurrent lesions. Also, many benign general and gynaecological surgeries require reoperation. The difficulties are not only faced by surgeons and gynaecologists, but also the patients in form of chronic pain, bowel obstruction and infertility. For ages many adhesion prevention strategies have been tried, studied and commercialised. Every one of them has their pluses and minuses. Many of these agents have an effect on postoperative healing, inflammation and recovery. By preventing adhesion, they also have potential of cutting down healthcare expenses, the number of hospital visits, and long-term quality of life. Here in this systematic review we set our objective to compile the major evidence backing these adhesion barriers and also narrate all the relevant knowledge a surgeon must know during pre-operative, intra-operative and post-operative periods to prevent adhesions after a neatly performed surgery.

Methodology

Search strategy

We searched a few of the major databases (ie. PubMed, Web of Science, Google scholar) following the Preferred

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https://orcid.org/0009-0003-5477-8723
Received: 03-11-2025 Accepted: 25-07-2026
DOI: https://doi.org/10.4038/sljs.v44i2.9301

Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to identify studies which assessed the efficacy and safety of the available adhesion prevention barriers. The search covered literature from 2017 to 2025 and tried to ensure that our comprehensive review is up-to-date and practical, which can be used in daily surgical practice.

We chose careful keywords and Medical Subject Headings (MeSH) terms to align with our objective. Our search strategy was the following: ("adhesion prevention" OR "anti-adhesion" OR "barrier agents" OR "oxidised regenerated cellulose" OR "Seprafilm" OR "Interceed" OR "Adept" OR "hyaluronic acid" OR "icodextrin" OR "humidified carbon dioxide" OR " Sprayshield" OR "PEG-based Liquid Barrier" OR "Hyalobarrier" OR "4DryField PH" OR "Janus hydrogel" OR "T-5224 Hydrogel" OR "Guardix") AND ("abdominal surgery" OR "laparotomy" OR "laparoscopy") AND ("randomised controlled trial" OR "clinical trial" OR "RCT"). To enhance the scope of our search, we also reviewed the references of many retrieved articles, meta-analyses, and review articles.

Eligibility criteria

Inclusion criteria:
-Randomised Controlled Trials (RCTs) and Clinical Trials
-Patients undergoing abdominal or pelvic surgery
-Intervention includes adhesion prevention strategies (barriers, gels, CO_2 insufflation, etc.)
-Reported outcomes related to adhesions, bowel obstruction, infertility, or reoperation

Exclusion criteria:
-Non-randomised studies
-Animal studies
-Language other than English
-Case reports, Case series, Editorials

All selected studies were published in English in peer-reviewed journals. We excluded grey literature, cell line and animal studies in the data extraction. However, we have included the recent knowledge that we have gathered from animal studies to give the readers a future direction of research.

Data extraction

Two reviewers independently screened titles and abstracts, performed full-text screening, and extracted data using a standardised Excel sheet. Disagreements were resolved through discussion or by a third reviewer. We conducted a preliminary screening of articles by assessing titles and abstracts to determine their relevance based on predefined criteria, categorising them as "Included", "maybe" or "excluded". This stage was crucial to narrow down the focus to the most pertinent studies.

Thereafter, the articles classified as "included" and "maybe" were studied for a full-text screening for eligibility of inclusion in this review. We used Rayyan AI for this thorough process of screening. We utilised a custom-designed data extraction form developed in Microsoft Excel. This form was meticulously completed, and it included fields for extracting data on study characteristics like – Material used in experimental group, control group, comparator group, Lead author, Year of publication, Objective, Trial design, Major finding, p-value and Conclusion.

This systematic approach ensured that our data extraction process was comprehensive and consistent, even though labour-intensive. It laid a robust foundation for subsequent analysis and narrative synthesis.

Data analysis and synthesis

Methodologies and outcomes were diverse across the studies we compiled, which led us to a qualitative approach for data analysis and synthesis. In the process, we identified and systematically compiled the safety effectiveness, specific surgical context and situations where different adhesion barriers perform well, pros and cons of each adhesion barrier, and aspects other than adhesion barriers that matter in preventing postoperative adhesions.

Results

Study selection process

The study selection process began with identifying 101 studies from database searches (PubMed, Web of Science and Google Scholar), with 13 duplicates removed before screening using Rayyan AI. A total of 81 records were screened based only on title and abstract, leading to the exclusion of 69 studies that didn't align with our inclusion criteria. The remaining 12 reports were assessed for eligibility with a full-text screening. Ultimately, 10 records were included in our review. This rigorous process ensured that only the most relevant and high-quality studies were selected for our systematic analysis. The study selection process is given in the PRISMA flowchart (Figure 1).

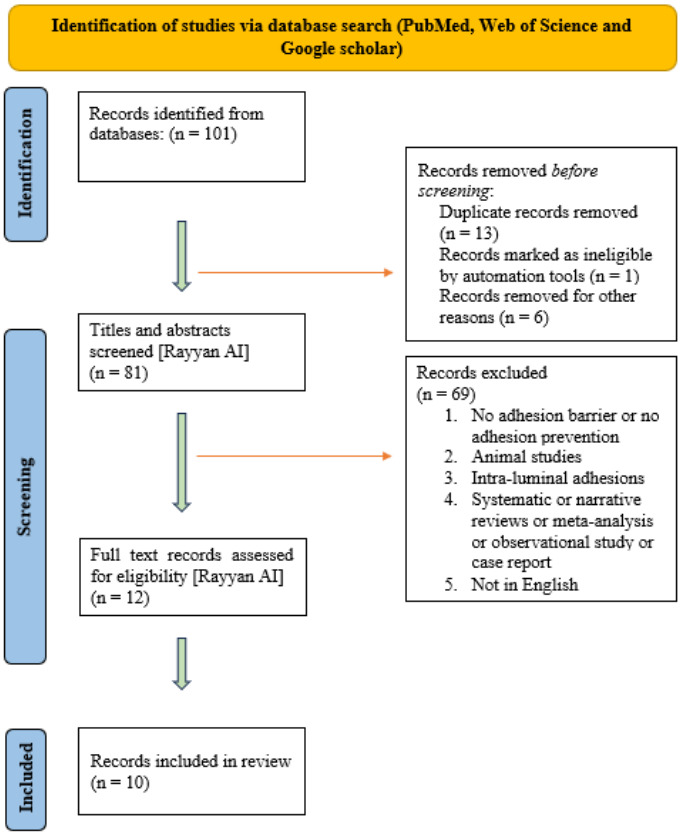

Figure 1: PRISMA recommended flow diagram for systematic reviews

Characteristics of the selected studies

Our selected studies represent a wide range of methodologies, objectives and final outcomes related to adhesion prevention strategies in abdominal and pelvic surgeries. These included general, oncological and gynaecological surgeries; clinical trials with different modes of blinding, including different adhesion barriers, such as Icodextrin, Seprafilm, SprayShield, Guardix, Interceed and 4DryField, among others. Few studies focused on safety, while a few focused mainly on efficacy. The quality of evidence varied across studies, and marketing bodies sponsored many. However, we sought to collect only the highest-quality evidence using relatively strict exclusion criteria. A summary table is synthesised in Table 1.

Discussion

The majority of evaluated interventions demonstrate some efficacy in reducing postoperative adhesion formation, though the magnitude of benefit varies considerably. Hyaluronic acid (HA)- and carboxymethylcellulose (CMC)–based agents, particularly Guardix-sol, Guardix-SG, and TCD-11091, consistently showed reduced adhesion severity at second-look surgery and a lower incidence of adhesive small bowel obstruction. In gynecologic settings, HA gels such as HYAcorp Endogel were superior to Mechanical ovarian suspension in reducing adhesions, suggesting clinical relevance in fertility-preserving procedures.

In contrast, Adept (icodextrin 4%) failed to outperform Ringer's lactate in large multicenter studies, despite earlier smaller trials suggesting efficacy. Hyalobarrier had no measurable impact on ovarian function or reproductive outcomes, highlighting a disconnect between biochemical plausibility and meaningful clinical endpoints. Powder formulations such as HA/CMC powder produced inconsistent results and, in some cases, were linked to higher complication rates. Safety outcomes were heterogeneous. HA/CMC-based gels and TCD-11091 were generally well tolerated, with no increase in adverse events. Conversely, particulate powders such as 4DryField raised concerns: while some studies showed substantial reductions in adhesion scores, pediatric and retrospective reports described higher complication rates. Similarly, HA/CMC powders were linked to adverse outcomes, suggesting that delivery form and distribution play a key role in safety. Importantly, none of the evaluated barriers impaired anastomotic healing, though most trials were underpowered to assess rare complications.

Table 1: Summary of key trials evaluating adhesion barriers

Sr No	Material used in experimental group	Material used in control group	Material used in comparator group	Lead Author & Year of Publication	Objective	Trial design	Major findings	p-value	Conclusion
1	Mediclore (CGBio Inc., Seongnam-si, Korea), a poloxame-r based thermo-sensitive so–l gel	No treatment	Adept (Icodextrin 4%)	Young Im Kim, Maria Lee 2020	To explore the efficacy of applying Mediclore during abdomino-pelvic surgery to prevent adhesions	Single-center, randomized, controlled, single-blind trial	Visceral slide test showed significantly lower incidence of abdominal adhesion formation in the experimental group compared to the control group (7.9% vs. 21.1%) [1]	p= 0.040	Use of a thermo-sensitive sol gel agent was safe and effective to prevent abdominal adhesions
2	Hyaluronic acid gel (HYAcorp Endogel)	Ovarian suspension	N/A	Shahla Chaichian 2022	To compare the effect of ovarian suspension and hyaluronic acid gel to prevent re-adhesions after laparoscopic endometrioma surgery	Double-blind randomized clinical trial	Postsurgical ultrasonography showed that ovarian soft markers, including < 1/3 ovarian adhesions (minimal adhesions) in 80.5% of ovaries of the Endogel group and 35.5% of the ovarian suspension group with higher ovarian mobility in the Endogel group (65% vs. 22%) [2]	p =<0.001	Hyaluronic acid gel can be more effective than ovarian suspension in preventing ovarian adhesions after laparoscopic treatment of endometriosis
3	Guardix-SG (poloxame-r based antiadhesive agent)	No treatment	N/A	Sung Geun Kim 2019	To investigate its efficacy in preventing abdominal adhesions in gastric cancer patients undergoing gastrectomy	Single-blind multi-center randomized clinical trial	The cumulative incidence of small bowel obstruction was significantly lower in the Guardix group compared to that seen in the control group (4.7% vs 8.6% at 6 months and 7.3% vs 20% at 1 year) [3]	p = 0.007	The incidence of intestinal obstruction i the Guardix-SG group was significantly lower than that of the control group Additionally, Guardix-SG was safe to use in terms postoperative complication
4	Guardix (carboxymethyl cellulose solution)	No treatment	Seprafilm (sodium hyaluronate-based bioresorbable membrane)	Woon Kee Lee 2019	To assess whether the use of sodium hyaluronate-based bioresorbable membrane (Seprafilm) and liquid-based hyaluronic acid and carboxymethyl cellulose solution (Guardix) reduce postoperative small bowel small bowel	Single center prospective randomized study	Small bowel obstruction developed in 9 patients (5.8%) in the Guardix group and 9 patients (7.1%) in the Seprafilm group and 19 patients (11.4%) in the control group. Seprafilm	p = 0.036	No significant difference in the incidence of small bow obstruction after colorectal surgery was detected between the Seprafilm an Guardix groups,

					undergoing colorectal surgery.		group had significantly lower obstruction rate as compared to control group (P = 0.036). Guardix group had a tendency toward lower obstruction rate but was not found to be statistically significant (p = 0.055) as compared to the control group [4]		despite the slightly lower overall incidence in the Seprafilm group than in the Guardix group (5.8% vs. 7.1%)
5	HA/CMC (Guardix-sol, Hanmi Medicare, Seoul, Korea)	No treatment	N/A	Tae Nam Kim 2018	To assess the effectiveness of hyaluronic acid/ carboxymethylcellulose (HA/CMC) in preventing adhesive bowel obstruction after laparoscopic radical cystectomy	Single-blinded, randomized controlled trial	None of the patients who received HA/CMC instillation experienced postoperative adhesive bowel obstructions, compared with 15.79% patients in the control group [5]	p = 0.025	HA/CMC instillation during laparoscopic radical cystectomy may reduce the incidence of postoperative adhesive bowel obstruction without adverse effects
6	TCD-11091 (Terumo Corporation, Tokyo, Japan)	No treatment	N/A	Takeshi Suto 2017	To confirm the efficacy and safety of TCD-11091 as aninhibitory effect of postoperative adhesion formation in patients who underwent laparotomy with ileostomy.	Prospective, multicenter, randomized single-blind study	The incidence of adhesions observed at the second-look surgery was significantly lower in the TCD-11091 group (52.7 versus 90.7%) [6]	p < 0.001	Use of TCD-11091 was safe and associated with significantly lower incidence of adhesion and severity of adhesions compared with non-treatment procedure
7	4DryField	No treatment	N/A	Michaela Klinke 2024	To assess its effectiveness of 4DryField in reducing bleeding and adhesions in children	Single-blinded, randomized controlled trial	4DryField did not affect the re-adhesion rate. Children in the treatment group had significantly more complications (47% vs. 15%), more often fever, and higher CRP levels. [7]	p = 0.002	4DryField did not show potential in reducing adhesion formation, but it was associated with significantly more complication in pediatric patients. Future prospective studies are needed to evaluate the safety and effectiveness of 4DryField in children.

8	4DryField	No treatment	N/A	Nicole Ziegler 2021	To assess its effectiveness of 4DryField in reducing adhesion severity and extent in first surgery and second look laparoscopies	Retrospective, controlled study	The statistical comparison of the two groups shows that median adhesion severity and extent both were significantly higher in the first surgery in the 4DF group. This indicates unfavourable starting conditions for the 4DF group since detached adhesions are predilection sites for adhesion (re)formation. Nevertheless, the outcome at second surgery was superior in the 4DF group with both adhesion severity and extent being significantly lower than in the control group [8]	$p < 0.001$	Adhesion extent and severity were significantly reduced by 4DF also when comparing the adhesion scores of the second surgeries
9	4DryField	No treatment	N/A	Nicole Ziegler 2021	To analyze the inflammation markers (CRP, leukocyte count, and body temperature) in patients who underwent laparoscopic adhesiolysis with or without adhesion prophylaxis	Retrospective comparative analysis	The maximum post-operative CRP level was significantly elevated in the 4DF group (87% vs. 29%) whereas leukocyte concentration and body temperature did not differ between groups. In second-look surgeries performed for other diagnoses 1–56 weeks after the first interventions, no remnants of 4DF or any peritoneal inflammatory reactions were observed [9]	$p < 0.001$	The starch-based polysaccharide 4DF can be considered safe and does not induce inflammatory reactions of clinical significance
10	4DryField	Normal Saline	N/A	Bernhard Krämer 2021	To assess its effectiveness of 4DryField in reducing adhesion severity and extent in first surgery	Prospective, randomized, controlled clinical trial	Severity and extent of adhesions were significantly reduced by 85%	$p = 0.004$	Adhesion formation could be reduced significantly

					and second look laparoscopies		in the 4DryField PH group compared to the control group (mean total adhesion score 2.2 vs. 14.2; p = 0.004). Incidence of adhesion formation based on the number of affected sites was significantly reduced by 53% in the intervention vs. control group (mean 1.1 vs. 2.3 sites; p = 0.004) [10]		by 85% by application of the adhesion barrier 4DryField PH

Interpretation of the available data is constrained by significant heterogeneity across studies. Variations in surgical indication, operative approach, outcome measures (clinical obstruction vs. second-look scoring vs. imaging), and follow-up duration limit comparability. Many studies were small, single-centre, and lacked blinding. Fertility-related outcomes, critical in gynecologic surgery, were seldom reported beyond surrogate adhesion scoring. Cost-effectiveness data were almost entirely absent, preventing a robust assessment of real-world utility.

Recent high-quality evidence reinforces the effectiveness of certain starch-based and HA-based barriers. A randomised controlled trial in women undergoing surgery for deep infiltrating endometriosis demonstrated that 4DryField PH led to an 85% reduction in adhesion severity and extent at second-look laparoscopy (mean score: 2.2 vs. 14.2; p=0.004) and 53% reduction in incidence of affected sites (mean 1.1 vs. 2.3; p=0.004). Over 12-month follow-up, the intervention group also saw higher pregnancy rates and improvement in pelvic pain scores, directly tying adhesion prevention to reproductive and symptomatic outcomes. [10, 11]

Now our goal in this review is to systematically narrate a small part of these preventive measures, ie. The adhesion barriers. An ideal barrier should be –

- Resorbable and self-eliminating
- Effective to act as a mechanical barrier during critical healing phase (5-7 days)
- Biocompatible (No foreign body reaction, inflammation, carcinogenesis)
- Surgically easy to handle (should conform to irregular surface, should not require complex preparation, non-adhesive to surgical instruments)
- Hemostatic compatibility
- Should not induce bacterial growth
- Cost effective and stable at room temperature

A few considerations for case selection:

1. Diffuse peritoneal trauma: Adept is simple and cheap but it mainly prevents reformation and not de-novo formation. [14, 15]
2. Targeted, irregular surfaces (like pelvic laparoscopic surgeries): Hyalobarrier / Oxiplex-AP / A-Part Gel / Mediclore / TCD-11091 are easier to use in laparoscopy than classic HA sheets. [1, 6, 16, 17]
3. Wide raw oozing areas: 4DryField PH can help in hemostasis and gel barrier when it's hard to achieve a dry bed for Interceed/Seprafilm. [8, 9, 10, 18]
4. Coated meshes are not ideal adhesion barriers: Omega-3 coatings (C-QUR) are mesh adjuncts and not substitutes for a dedicated adhesion barrier. [19]
5. Aim should be meticulous hemostasis before placing sheet barriers. Interceed or Seprafilm require a dry field. If persistent ooze is expected, powders (4DryField) or gels or sprays are preferred.
6. One should avoid wrapping fresh anastomoses with sheets. Sheets are kept away from suture lines.
7. Minimal effective amount to be used as thick clumps of gel or powder can paradoxically impair healing or obscure vision.

8. For laparoscopic use gels, powders, and sprays are usually better for ease of handling. [12, 20]

Future directions

While many researches are already published that brings us promise to a bright future of adhesion prevention, they still are in animal models and cell-lines and human subjects have yet to participate in many newer generation adhesion barriers.

1) Janus hydrogels and other asymmetry barriers [21, 22, 23, 24, 25, 26, 27]

A new generation of Janus hydrogels/patches is engineered so the tissue-facing side adheres (for fixation in a wet field) while the free side is ultra–anti-fouling. Zwitterionic or protein-repellent chemistries on the "outside" layer blunt fibrin/protein deposition and cellular bridging; the "inside" layer can be mildly bioadhesive to resist displacement. In rodent cecal-abrasion models, Janus patches reduced peritoneal adhesions versus single-phase gels and commercial HA controls. Materials used include PVA/PAA hybrids and zwitterionic surfaces. These designs also dovetail with immunomodulation (e.g., macrophage phenotype steering) embedded in the adhesive layer. It could land clinically in open or lap cases with irregular geometry where sheets slip and pure gels migrate.

2) Metabolic reprogramming to calm the injury response (AICAR/AMPK axis) [28]

AICAR, an AMPK agonist, limits adhesion formation in rats by reducing oxidative stress and inflammatory signaling, while accelerating mesothelial repair—the layer that decides whether fibrin is lysed or scaffolded into adhesions. Beyond AICAR, other AMPK activators (metformin analogs; A-769662) are natural candidates.

3) Cold plasma biology in a bottle: Plasma-Activated Solution (PAS/PAM) [29]

Irrigation with plasma-activated media/solution delivers short-lived reactive nitrogen/oxygen species that appear to restore eNOS signaling, temper oxidative damage, and down-shift pro-adhesive cytokines from peritoneal fibroblasts and mesothelial cells—attenuating EMT (mesothelial-to-mesenchymal transition). Recent in-vivo work shows PAS reduced adhesions via RNS-mediated pathways; in vitro, PAM suppresses pro-adhesive ECM programs. Safety windows and standardized generators/chemistries will decide clinical uptake.

4) Phytochemicals and small-molecule anti-fibrotics (Ligustrazine, Berberine) [30, 31]

Ligustrazine (tetramethylpyrazine) curbs adhesions in rodent models by dampening inflammation, reducing EMT, and promoting mesothelial repair; nano-formulations are being explored to improve residence time. Berberine shows dual effects on primary adhesion formation and re-formation, with decreases in inflammatory mediators and collagen deposition. Optimizing local delivery (gel/film) could mitigate systemic effects.

5) Smarter polymers and architectures (PLCL, GMHA, zwitterions, PCBAA) [32, 33, 34]

PLCL (poly-L-lactide-co-ε-caprolactone) films and electrospun membranes provide tunable degradation and elasticity; composite or gelatinized PLCL membranes outperformed PDLLA comparators in rats and can be loaded with pro-fibrinolytic cues. GMHA (glycidyl-methacrylated hyaluronic acid) enables photo-crosslinked HA gels with tunable stiffness and residence time; softer GMHA gels favor gentle tissue conformity and can be doped with drugs/biologics. Zwitterionic polymers (e.g., PCBAA/poly-carboxybetaine acrylamide) show near-zero protein adsorption; abdominal wall coatings with PCBAA markedly reduced fibroblast invasion and adhesions in vivo. These chemistries are expected to appear as outer layers of Janus barriers or sprayable films.

6) Bioactive, on-demand, and sprayable systems

Sprayable PEG networks, HA-based double networks, and in situ gelling systems that can be delivered laparoscopically are advancing to solve coverage on complex topography and to minimize OR time. The next step is triggerable release (pH/ROS-responsive) of antioxidants or anti-fibrotics during the 3–7 day adhesion window.

Conclusion

Postoperative adhesions remain a near-universal consequence of abdominopelvic surgery, carrying profound implications for morbidity, fertility, reoperation, and healthcare costs. This systematic review highlights that while no single intervention has proven universally effective, several adhesion barriers—particularly hyaluronic acid/ carboxymethyl cellulose gels, sprayable PEG-based hydrogels, and starch-based polysaccharides such as 4 DryField—demonstrate consistent benefits in reducing the extent and severity of adhesion. Importantly, adhesion barriers should be regarded as adjuncts rather than substitutes for meticulous surgical technique, optimised perioperative care, and prehabilitation.

Future advances are likely to emerge from bioactive, multifunctional platforms—such as Janus hydrogels, metabolic reprogramming with AICAR, plasma-activated solutions, and phytochemical agents—that target both the mechanical and molecular drivers of adhesion formation.

In clinical practice today, surgeons should consider adhesion prevention strategies, balancing evidence of efficacy, safety, availability, and cost. Continued multicenter randomised controlled trials with standardised, patient-centred outcomes—including fertility, chronic pain, and quality of life—are urgently needed to establish robust guidelines.

Limitation

Many trials were sponsored by the marketing bodies which may influence outcomes. Also due to heterogenecity across trials, a formal meta-analysis could not be performed.

Author contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Nilanjan Ghosh

Acquisition, analysis, or interpretation of data: Nilanjan Ghosh, Jayeeta Roy

Drafting of the manuscript: Nilanjan Ghosh

Critical review of the manuscript for important intellectual content: Jayeeta Roy

Conflicts of interest

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work.

Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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