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[Intervention Review]

Barrier agents for adhesion prevention after gynaecological surgery

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ABSTRACT

Background

Pelvic adhesions can form as a result of inflammation, endometriosis or surgical trauma. During pelvic surgery, strategies to reduce pelvic adhesion formation include placing barrier agents such as oxidised regenerated cellulose, polytetrafluoroethylene or fibrin sheets between the pelvic structures.

Objectives

To evaluate the effects of barrier agents used during pelvic surgery on rates of pain, live birth and postoperative adhesions in women of reproductive age.

Search methods

We searched the following databases in February 2015: the Menstrual Disorders and Subfertility Group (MDSG) Specialised Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, PsycINFO, the Cochrane Central Register of Controlled Trials (CENTRAL) and trial registries. We handsearched relevant journals, conference proceedings and grey literature sources and we contacted pharmaceutical companies for information.

Selection criteria

Randomised controlled trials (RCTs) of the use of barrier agents compared with other barrier agents, placebo or no treatment for the prevention of adhesions in women undergoing gynaecological surgery.

Data collection and analysis

Two review authors independently assessed trials for eligibility and risk of bias and extracted the data. We calculated odds ratios (ORs) or mean differences (MD) with 95% confidence intervals (CIs) using a fixed effect model. The overall quality of the evidence was assessed using GRADE (Grades of Recommendation, Assessment, Development and Evaluation) methods.

Main results

Eighteen RCTs (1262 women) were included. Six RCTs randomised women; the remainder randomised pelvic organs. Laparoscopy (eight RCTs) and laparotomy (10 RCTs) were the primary surgical techniques. Indications for surgery included myomectomy (six RCTs), ovarian surgery (five RCTs), pelvic adhesions (five RCTs), endometriosis (one RCT) and mixed (one RCT). The sole indication for surgery in three of the RCTs was infertility. Twelve RCTs reported commercial funding; the rest did not state their source of funding.

No studies reported either of our primary outcomes of pelvic pain and live birth.

Barrier agents for adhesion prevention after gynaecological surgery (Review)

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Oxidised regenerated cellulose (Interceed) versus no treatment at laparoscopy or laparotomy (13 RCTs)

At second-look laparoscopy oxidised regenerated cellulose at laparoscopy was associated with reduced incidence of de novo adhesions (OR 0.50, 95% CI 0.30 to 0.83, three RCTs, 360 participants, $I^2 = 75\%$, very low-quality evidence) and of re-formed adhesions (OR 0.17, 95% CI 0.07 to 0.41, three RCTs, 100 participants, $I^2 = 36\%$, low quality evidence).

At second-look laparoscopy no evidence was found of any difference between the groups in the incidence of de novo adhesions after laparotomy (OR 0.72, 95% CI 0.42 to 1.25, one RCT, 271 participants, $I^2 = 41\%$, low-quality evidence). However, the incidence of re-formed adhesions was lower in the intervention group (OR 0.38, 95% CI 0.27 to 0.55, six RCTs, 554 participants, moderate-quality evidence).

Expanded polytetrafluoroethylene (Gore-Tex) versus no treatment at gynaecological surgery (one RCT)

The evidence suggested that at second-look laparoscopy expanded polytetrafluoroethylene was associated with a reduction in new adhesion formation (OR 0.17, 95% CI 0.03 to 0.94, one RCT, 42 participants, low-quality evidence).

Expanded polytetrafluoroethylene (Gore-Tex) versus oxidised regenerated cellulose (Interceed) at gynaecological surgery (two RCTs)

One RCT found no difference between the groups at second-look laparoscopy in the incidence of de novo adhesions (OR 0.93, 95% CI 0.26 to 3.41, 38 participants, very low-quality evidence). A second RCT suggested that the expanded polytetrafluoroethylene group had a lower adhesion score (out of 11) (MD -3.79, 95% CI -5.12 to -2.46, 62 participants, very low-quality evidence) and a lower risk of re-formed adhesions (OR 0.13, 95% CI 0.02 to 0.80, 23 participants, very low-quality evidence). This last finding was sensitive to choice of effect estimate and no longer suggested a difference between the groups when a risk ratio was calculated (RR 0.36, 95% CI 0.13 to 1.01).

Sodium hyaluronate and carboxymethylcellulose (Septrafilm) versus no treatment at gynaecological surgery (one RCT)

Sodium hyaluronate and carboxymethylcellulose was associated with a lower adhesion score (out of 4) at second-look laparoscopy (MD 0.49, 95% CI 0.53 to 0.45, one RCT, 127 participants, moderate-quality evidence).

Fibrin sheet versus no treatment at laparoscopic myomectomy (one RCT)

There was no evidence of a difference between the groups in the incidence of de novo adhesions at second-look laparoscopy (OR 1.20, 95% CI 0.42 to 3.41, one RCT, 62 participants) or in adhesion score (out of 4) (MD 0.14, 95% CI -0.67 to 0.39, one RCT, 48 participants, low-quality evidence).

Fourteen of the 18 RCTs reported adverse events. No events directly attributed to adhesion agents were reported.

Authors' conclusions

We found no evidence on the effects of barrier agents used during pelvic surgery on either pain or fertility outcomes in women of reproductive age.

Low quality evidence suggests that oxidised regenerated cellulose (Interceed), expanded polytetrafluoroethylene (Gore-Tex) and sodium hyaluronate with carboxymethylcellulose (Septrafilm) may all be more effective than no treatment in reducing the incidence of adhesion formation following pelvic surgery. There is no conclusive evidence on the relative effectiveness of these interventions. There is no evidence to suggest that fibrin sheet is more effective than no treatment. No adverse events directly attributed to the adhesion agents were reported. The quality of the evidence ranged from very low to moderate. The most common limitations were imprecision and poor reporting of study methods. Most studies were commercially funded, and publication bias could not be ruled out.

PLAIN LANGUAGE SUMMARY

Barrier agents for adhesion prevention after gynaecological surgery

Review question

This review of trials assessed the effects of barriers agents on pelvic pain, live birth and adhesion formation after pelvic surgery.

Background

A common problem following surgery or infection is the occurrence of adhesions, where two normally separate surfaces stick together. Pelvic adhesions are commonly associated with infection, endometriosis or surgical trauma. During pelvic surgery, strategies to reduce pelvic adhesion formation include placing a synthetic physical barrier between the pelvic structures.

Study characteristics

We included 18 randomised controlled trials (RCTs) of 1262 women undergoing gynaecological surgery. They assessed different types of barrier agents for preventing adhesions and compared them with each other or with no treatment. The data are current to February 2015. Twelve RCTs reported commercial funding; the other studies did not state their source of funding.

Key results

We found no evidence on the effects of barrier agents used during pelvic surgery on either pain or fertility outcomes in women of reproductive age.

Low-quality evidence suggested that oxidised regenerated cellulose (Interceed), expanded polytetrafluoroethylene (Gore-Tex) and sodium hyaluronate with carboxymethylcellulose (Seprafilm) may all be more effective than no treatment in reducing the risk of adhesions following pelvic surgery. There was no conclusive evidence on the relative effectiveness of these interventions. There was no evidence that fibrin sheet was more effective than no treatment. No adverse events directly attributed to the adhesion agents were reported.

Quality of the evidence

The quality of the evidence ranged from very low to moderate. The most common limitations were imprecision and poor reporting of study methods. Most studies were commercially funded, and publication bias could not be ruled out.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Oxidised regenerated cellulose (Interceed) vs no treatment at laparoscopy for adhesion prevention after gynaecological surgery

Oxidised regenerated cellulose vs no treatment at laparoscopy for adhesion prevention after gynaecological surgery

Population: women having gynaecological surgery

Settings: surgical

Intervention: oxidised regenerated cellulose (Interceed) vs no treatment at laparoscopy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No treatment	Oxidised regenerated cellulose				
Incidence of adhesions—de novo Incidence of adhesions at second-look laparoscopy	333 per 1000	200 per 1000 (130 to 290)	OR 0.5 (0.3 to 0.83)	360 (3 studies)	⊕⊕⊕⊖ Very low ^{a,b,c}	
Incidence of adhesions—re-formation (or mixture) Incidence of adhesions at second-look laparoscopy	700 per 1000	284 per 1000 (140 to 489)	OR 0.17 (0.07 to 0.41)	100 (3 studies)	⊕⊕⊕⊖ Low ^{a,c}	

*The basis for the **assumed risk** is the median control group risk across studies. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

^aMethods not clearly described; high risk of attrition bias in one study.

^bSerious inconsistency; $I^2 = 75\%$.

^cPotential for publication bias unclear.

Summary of findings 2. Oxidised regenerated cellulose (Interceed) vs no treatment at laparotomy for adhesion prevention after gynaecological surgery

Oxidised regenerated cellulose (interceed) vs no treatment at laparotomy for adhesion prevention after gynaecological surgery

Population: women having gynaecological surgery

Settings: surgical

Intervention: oxidised regenerated cellulose vs no treatment at laparotomy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No treatment	Oxidised regenerated cellulose				
Incidence of adhesions—de novo Incidence at second-look laparoscopy	282 per 1000	220 per 1000 (141 to 329)	OR 0.72 (0.42 to 1.25)	271 (1 study)	⊕⊕⊕⊖ Low ^{a,b,c}	
Incidence of adhesions—re-formation (or mixture) Incidence at second-look laparoscopy	746 per 1000	528 per 1000 (443 to 618)	OR 0.38 (0.27 to 0.55)	554 (6 studies)	⊕⊕⊕⊖ Moderate ^{a,b}	

*The basis for the **assumed risk** is the median control group risk across studies. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

^aInadequate description of methods; high risk of attrition bias in one study.

^bPotential for publication bias unclear.

^cSerious imprecision: confidence intervals compatible with no effect or clinically meaningful benefit from intervention.

Summary of findings 3. Expanded polytetrafluoroethylene (Gore-Tex) vs no treatment for adhesion prevention after gynaecological surgery

Expanded polytetrafluoroethylene (Gore-Tex) vs no treatment for adhesion prevention after gynaecological surgery

Population: women having gynaecological surgery
Settings: surgical
Intervention: expanded polytetrafluoroethylene vs no treatment

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No treatment	Expanded polytetrafluoroethylene				
Incidence of adhesions—de novo Incidence at second-look laparoscopy	905 per 1000	666 per 1000 (322 to 892)	OR 0.17 (0.03 to 0.94)	42 (1 study)	⊕⊕⊕⊖ Low ^{a,b}	

*The basis for the **assumed risk** is the mean control group risk. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

^aSerious imprecision: single small study (n = 42); findings compatible with benefit from the intervention or no clinically meaningful effect.

^bMethods not described in sufficient detail.

Summary of findings 4. Expanded polytetrafluoroethylene (Gore-Tex) vs oxidised regenerated cellulose (Interceed) for adhesion prevention after gynaecological surgery

Expanded polytetrafluoroethylene (Gore-Tex) vs oxidised regenerated cellulose (Interceed) for adhesion prevention after gynaecological surgery

Population: women having gynaecological surgery
Settings: surgical
Intervention: expanded polytetrafluoroethylene vs oxidised regenerated cellulose

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				

	Oxidised regenerated cellulose	Expanded polytetrafluoroethylene				
Adhesion score Non-validated score out of 11 at SLL	Mean adhesion score was -3.79 lower (5.12 to 2.46 lower) in the expanded polytetrafluoroethylene group			58 (1 study)	⊕⊕⊕⊕ Very low ^{a,b,c}	
Incidence of adhesions—de novo Incidence at second-look laparoscopy	455 per 1000	437 per 1000 (178 to 740)	OR 0.93 (0.26 to 3.41)	38 (1 study)	⊕⊕⊕⊕ Very low ^{a,b}	
Incidence of adhesions—re-formation (or mixture) Incidence at second-look laparoscopy	750 per 1000	281 per 1000 (57 to 706)	OR 0.13 (0.02 to 0.8)	23 (1 study)	⊕⊕⊕⊕ Very low ^{a,d,e}	Confidence interval crossed the line of no effect when a risk ratio rather than an odds ratio was calculated (RR 0.36, 95% CI 0.13 to 1.01)

*The basis for the **assumed risk** is the mean control group risk across studies. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

^aMethods not described in sufficient detail.

^bVery serious imprecision: low event rate, findings compatible with clinically meaningful benefit in either group, or with no effect.

^cNon-validated score used.

^dNot blinded.

^eSerious imprecision: low event rate. Findings sensitive to choice of effect estimate.

Summary of findings 5. Sodium hyaluronate and carboxymethylcellulose (Seprafilm) vs no treatment for adhesion prevention after gynaecological surgery

Sodium hyaluronate and carboxymethylcellulose vs no treatment for adhesion prevention after gynaecological surgery

Patient or population: patients with adhesion prevention after gynaecological surgery

Settings: surgical

Intervention: sodium hyaluronate and carboxymethylcellulose vs no treatment

Outcomes	Illustrative comparative risks* (95% CI)	Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Sodium hyaluronate and carboxymethylcellulose vs no treatment				
Adhesion score Non-validated score out of 4 at second-look laparoscopy	Mean adhesion score was 0.49 lower (0.53 to 0.45 lower) in the intervention group		127 (1 study)	⊕⊕⊕⊖ Moderate ^a	

*The basis for the **assumed risk** is the mean control group risk across studies. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

^aStudy did not use a validated scoring method for adhesion assessment. Study was also unclear regarding selective reporting bias.

Summary of findings 6. Fibrin sheet vs no treatment at laparoscopic myomectomy for adhesion prevention after gynaecological surgery

Fibrin sheet vs no treatment at laparoscopic myomectomy for adhesion prevention after gynaecological surgery

Patient or population: patients with adhesion prevention after gynaecological surgery

Settings: surgical

Intervention: fibrin sheet vs no treatment at laparoscopic myomectomy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No treatment	Fibrin sheet				
Adhesion score Non-validated score out of 4 at second-look laparoscopy	Mean adhesion score was 0.14 lower (0.67 lower to 0.39 higher) in the intervention group			62 (1 study)	⊕⊕⊕⊖ Low ^{a,b,c}	

Incidence of adhesions per participant Incidence at at second-look laparoscopy	625 per 1000	667 per 1000 (412 to 850)	OR 1.2 (0.42 to 3.41)	62 (1 study)	⊕⊕⊕⊕ Very low ^{a,d}
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*The basis for the **assumed risk** is the mean control group risk across studies.. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

^aMethods not described in adequate detail.

^bImprecision, with relatively few participants and wide confidence intervals.

^cNon-validated scoring method used.

^dVery serious imprecision: low event rate, findings compatible with clinically meaningful benefit in either group, or with no effect.

BACKGROUND

Description of the condition

Pelvic adhesions can form as the result of pelvic inflammation, endometriosis or surgical trauma. The incidence of pelvic adhesions at second-look laparoscopy in the initial few weeks after surgery has been reported to be between 50% and 100% (diZerega 1994). The consequences of adhesion formation include subfertility, development of chronic abdominal pain and dyspareunia (difficult or painful sexual intercourse) (SRS 2007). A recent study demonstrated that in women with a known reason for small bowel obstruction, adhesions were the single most common cause (Ten Broek 2013).

Cutting, surgical denudation, ischaemia, desiccation or abrasion can cause peritoneal trauma during surgery. The subsequent healing mechanism in the peritoneal cavity occurs through a combination of mesothelial regeneration and fibrosis, resulting in adhesion formation between damaged serosal surfaces (diZerega 1990).

Minimally invasive techniques such as laparoscopy reduce the risk of de novo (new) adhesion formation but do not eliminate it entirely. Studies included within this review therefore assessed both laparoscopy and laparotomy.

Description of the intervention

Several barrier agents with different characteristics are commercially available. Oxidised regenerated cellulose (Interceed) was the first tested synthetic mechanical barrier agent to cover traumatised peritoneum in the pelvis. It is applied over raw tissue surfaces at the last stage of surgery after haemostasis has been achieved, and is designed to form a gelatinous protective coat within eight hours of application. Following this, it is broken down into its monosaccharide constituents and is designed to be absorbed within two weeks. Concerns with the use of oxidised regenerated cellulose include migration and the need for meticulous haemostasis. Use of oxidised regenerated cellulose in the presence of bleeding may promote fibrin deposition at sites of incomplete haemostasis, resulting in adhesion formation rather than prevention.

Another commercially available barrier agent is expanded polytetrafluoroethylene surgical membrane (Gore-Tex). This inert and permanent barrier acts by preventing cellular growth. However, it must be sutured to remain in place, and this may increase the incidence of adhesions while prolonging operating time. Much debate is ongoing regarding the need to remove expanded polytetrafluoroethylene after peritoneal healing is complete. This debate stems from studies investigating expanded polytetrafluoroethylene in vascular and pericardial grafts, which found no significant long-term adverse effects when the barrier was not removed (Jacobs 1996). In addition, a prospective multi-centre observational study investigating the long-term use of expanded polytetrafluoroethylene without removal reported only one case of postoperative infection, which did not require removal of the membrane (Hurst 1998).

Other products include sodium hyaluronate with carboxymethylcellulose (Seprafilm), an adhesion barrier agent composed of chemically derived sodium hyaluronate and carboxymethylcellulose. It is designed to be absorbed from the

peritoneal cavity within seven days and completely excreted from the body within 28 days (Diamond 1996). Sodium hyaluronate with carboxymethylcellulose consists of chemically modified hyaluronic acid and carboxymethylcellulose. It separates denuded planes of tissue for up to seven days before it is absorbed. As with oxidised regenerated cellulose, migration is the cause of some concern; however no evidence suggests that its effectiveness is altered by the presence of blood. Although evidence for its use in gynaecological surgery is limited, sodium hyaluronate with carboxymethylcellulose has been widely studied in the context of colorectal surgery. Formation of adhesions and incidence of small bowel obstruction were reduced in five RCTs investigating its use in various colorectal and general surgical procedures (Ten Broek 2013).

Fibrin sheet is a sheet-type fibrin sealant with a solid layer of human fibrinogen, thrombin and aprotinin coating the active surface of equine collagen stained with riboflavin (Mais 1995a; Pellicino 2003).

Fluid and pharmacological methods used to prevent adhesion formation are investigated in another Cochrane review (Ahmad 2014).

How the intervention might work

Theoretically, inert physical materials that are able to prevent mechanical contact between serosal surfaces for longer than three days have the potential to be helpful in preventing adhesion formation. This would allow independent healing of each traumatised peritoneal surface. Some barrier agents (e.g. expanded polytetrafluoroethylene) need to be sutured into place, requiring extra operating time, especially during laparoscopic procedures.

Why it is important to do this review

This review is concerned with the effectiveness of barrier agents placed in the peritoneal cavity for preventing adhesions and/or improving fertility. Pharmacological adjuncts are reviewed elsewhere. Women present with the secondary effects of adhesions, including dyspareunia, subfertility, bowel obstruction and chronic pelvic pain. These problems can greatly impact on quality of life and may necessitate further surgery. No clinical consensus or guidance is available regarding the most effective antiadhesion agent. Assessment of the evidence on effectiveness of barrier agents is therefore important.

OBJECTIVES

To evaluate the effects of barrier agents used during pelvic surgery on rates of pain, live birth and postoperative adhesions in women of reproductive age.

METHODS

Criteria for considering studies for this review

Types of studies

We included published or unpublished randomised controlled trials (RCTs) in which either women or pelvic structures were the unit of randomisation. Non-randomised studies (e.g. studies with evidence of inadequate sequence generation such as alternate days or participant numbers) were excluded, as they are associated with high risk of bias. No cross-over trials were identified.

Types of participants

Women undergoing pelvic surgery for infertility or for other indications. Studies investigating adhesion prevention in non-gynaecological specialties were excluded. Types of surgery performed could include either open or laparoscopic procedures.

Types of interventions

Trials comparing physical barrier agents (oxidised regenerated cellulose, expanded polytetrafluoroethylene, sodium hyaluronate with carboxymethylcellulose, fibrin sheet) used during pelvic surgery versus any other physical barrier agent or placebo or no treatment were included.

Studies of fibrin glue and Sepracoat (Genzyme Corporation) were excluded, as these are not physical barrier agents.

Types of outcome measures

Primary outcomes

1. Pelvic pain (improvement/worsening/no change in pain at second-look laparoscopy (SLL)), as measured by validated pain scales, for example, visual analogue pain scale (VAS) scores, the McGill Pain Questionnaire (MPQ), a pain improvement rating scale, general pain experience or a gynaecological pain questionnaire.
2. Live birth rate.

Secondary outcomes

1. Adhesion score, recorded on whichever scale the study authors used, but with preference given to the modified American Fertility Society (mAFS) score.
2. Number of participants with adhesions at SLL.
3. Clinical pregnancy rate (pregnancy confirmed on ultrasound scan).
4. Miscarriage rate, defined as loss of pregnancy before 24 weeks of gestation.
5. Ectopic pregnancy rate.
6. Number of participants with improvement in quality of life (QoL) at SLL, recorded on whichever scale was chosen by study authors.
7. Adverse events

Live birth rate and clinical pregnancy rate are relevant when studies have specifically investigated use of the barrier agent in procedures performed to improve fertility. This does not apply to some studies.

Articles that met the inclusion criteria but did not report any of the outcomes considered within this review were also included within the qualitative analysis.

Search methods for identification of studies

We searched for all published and unpublished RCTs comparing the use of barrier agents versus any other active intervention or placebo/no treatment without language restriction. Searches were designed and conducted by the Trials Search Co-ordinator for the Menstrual Disorders and Subfertility Group.

Electronic searches

We searched the Menstrual Disorders and Subfertility Group (MDSG) Specialised Register of Controlled Trials, the Central Register of Controlled Trials (CENTRAL) and the electronic databases MEDLINE, EMBASE, the Cumulative Index to Nursing and Allied Health Literature (CINAHL) and PsycINFO. These searches were conducted by the Trials Search Co-ordinator for the Menstrual Disorders and Subfertility Subgroup.

Other electronic searches included trial registers for the US National Institutes of Health, the World Health Organization (WHO) international trial registry platform, the Database of Abstracts of Reviews of Effects (DARE), OpenGrey, PubMed and Google Scholar.

The last search was conducted in February 2015.

Searching other resources

We also searched the citation lists of trial registers, relevant publications, review articles and included studies. We handsearched reference lists of articles retrieved by the search and contacted experts in the field to request additional data. We handsearched relevant journals and conference abstracts that were not covered in the MDSG register, in liaison with the Trials Search Co-ordinator. Retrievals were screened by two review authors.

Data collection and analysis

Selection of studies

After an initial screen of titles and abstracts identified by the search, we retrieved the full text of all potentially eligible studies. Two review authors (HO'F, GA) independently examined these full-text articles for compliance with inclusion criteria. Disagreements as to study eligibility were resolved by discussion or by consultation with a third review author. Review authors corresponded with study investigators to clarify study eligibility (e.g. with respect to participant eligibility criteria and allocation method).

Data extraction and management

Two review authors independently extracted data from eligible studies using a data extraction form that was designed and pilot tested by the review authors. Disagreements were resolved by discussion or by consultation with a third review author. Data extracted included study characteristics and outcome data. When studies were followed by multiple publications, the main trial report was used as the reference, and additional details were derived from secondary papers. We corresponded with study investigators to ask for further data on methods and/or results, as required.

Assessment of risk of bias in included studies

Each included trial was assessed for the following criteria using the Cochrane risk of bias assessment tool: sequence generation; allocation concealment; blinding of participants, personnel and outcome assessors; completeness of outcome data; selective outcome reporting; and other potential sources of bias (Higgins 2011). Conclusions were presented in the 'Risk of bias' table and were incorporated into the interpretation of review findings by means of sensitivity analyses. Two review authors (GA and HO'F) independently performed all assessments of the quality of clinical trials. All discrepancies were resolved by AW.

In view of the difficulty involved in detecting and correcting for publication bias and other reporting biases, the review authors aimed to minimise the potential impact by ensuring a comprehensive search for eligible studies and by remaining alert for duplication of data. If 10 or more studies were included in an analysis, a funnel plot was used to explore the possibility of small-study effects (a tendency for estimates of the intervention effect to suggest that it is more beneficial in smaller studies).

Care was taken to search for within-study reporting bias, as seen in trials failing to report obvious outcomes (e.g. pregnancy rate, major complications) or reporting them in insufficient detail.

Measures of treatment effect

Results of dichotomous variables were presented as Mantel-Haenszel odds ratios (ORs) with 95% confidence intervals (CIs), and results of continuous variables are presented as mean differences (MDs).

We reversed the direction of effects of individual studies, when required, to ensure consistency across trials. We treated ordinal data as continuous outcomes. We presented 95% confidence intervals for all outcomes. When data used to calculate ORs or MDs were not available, we planned to utilise the most detailed numerical data available, which might facilitate similar analyses of included studies. We compared the magnitude and direction of effects reported by studies versus how they are presented in the review, taking account of legitimate differences.

Unit of analysis issues

For within-participant designs, 'effective sample sizes' were calculated to allow for statistical synthesis, that is, for a trial randomly assigning ovaries within each participant rather than randomly assigning participants, numbers were calculated to simulate as nearly as possible the odds ratio and the confidence interval as if the study design had randomly assigned participants, not ovaries. This was achieved as follows.

1. We calculated the odds ratio and the 95% CI for the matched design.
2. We constrained the control rate in the hypothetical parallel design to make it equal to that observed in the matched design.
3. We constrained group sizes for the parallel design to make them equal to each other.
4. Based on the two constraints above, we calculated the numbers of 'successes' and 'failures' in each group to reproduce as nearly as possible the OR (95% CI) of the matched design.

As a result of this type of reanalysis of data, studies with within-participant design that may have previously demonstrated significance may no longer do so.

Several studies of within-participant design comparing oxidised regenerated cellulose versus no treatment were presented and analysed wrongly as having a parallel design. We recognised that failure to account for pairing and failure to take account of doubling of the sample size by using ovaries instead of participants as the unit of randomisation may have yielded spurious results. For these studies, the least favourable outcome for oxidised regenerated cellulose that was compatible with the reported results was

assumed. We attempted to obtain correct results tables from study authors but were unsuccessful.

Dealing with missing data

Data were analysed on an intention-to-treat (ITT) basis as far as possible, and attempts were made to obtain missing data from the original investigators. When data for primary outcomes could not be obtained, we planned to undertake imputation of individual values. For secondary outcomes, only available data were analysed.

If studies reported sufficient detail to calculate mean differences but no information on associated standard deviation (SD), we assumed that the outcome had a standard deviation equal to the highest SD from other studies within the same analysis.

Assessment of heterogeneity

Clinical and methodological characteristics of individual studies were considered to ensure that any pooling was clinically meaningful. The I^2 statistic was calculated to assess statistical heterogeneity. An I^2 measurement over 50% was taken to indicate substantial heterogeneity.

Assessment of reporting biases

In view of the difficulty involved in detecting and correcting for publication bias and other reporting biases, the study authors aimed to minimise their potential impact by ensuring a comprehensive search for eligible studies and by remaining alert for duplication of data. In consideration of the difficulty of detecting and correcting publication bias and other reporting bias, we aimed to minimise the impact by ensuring that a robust and comprehensive search was performed. We planned to create a funnel plot if 10 or more studies were included in a meta-analysis, to assess the risk of reporting bias.

Data synthesis

Statistical analysis was performed in accordance with the guidelines developed by The Cochrane Collaboration. Data from the primary studies were combined in RevMan using the fixed-effect model. We planned to report standardised mean differences if similar outcomes were reported on different scales. An increase in the OR, the SMD or the MD was indicated to the right of the central line of the forest plot, and a decrease was indicated to the left of the central line. Whether this favoured treatment or no treatment depended on the outcome analysed, but the axes were labelled accordingly. Analyses were stratified by type of barrier agent, type of surgery and type of control.

Subgroup analysis and investigation of heterogeneity

If we had detected substantial heterogeneity, we planned to explore possible explanations in sensitivity analyses. We planned to take any statistical heterogeneity into account when interpreting the results, especially if any variation in the direction of effect was evident.

Sensitivity analysis

Sensitivity analyses were conducted for the primary outcomes to determine whether the conclusions were robust to arbitrary decisions made regarding eligibility of studies and analysis. These

analyses included consideration of whether review conclusions differed if:

1. eligibility was restricted to studies without high risk of bias;
2. a random-effects model had been adopted; or
3. relative risk had been used as the summary effects measure.

Results of the sensitivity analysis are reported in the risk of bias of included studies subsection of the Results section.

Overall quality of the body of evidence: 'Summary of findings' table

We prepared 'Summary of findings' tables using GRADEPRO software. These tables evaluate the overall quality of the body of evidence for the main review outcomes (pelvic pain, live birth rate, improvement or worsening of adhesion scores, incidence and severity of adhesions) using GRADE (Grades of Recommendation, Assessment, Development and Evaluation)

criteria (study limitations (i.e. risk of bias), consistency of effect, imprecision, indirectness and publication bias). Judgements about evidence quality (high, moderate or low) have been justified, documented and incorporated into reporting of results for each outcome.

RESULTS

Description of studies

Results of the search

Twenty-six studies were potentially eligible and were retrieved in full text. Eighteen studies met our inclusion criteria, and eight studies were excluded. See study tables under [Characteristics of included studies](#). The reasons why studies were excluded are detailed in the [Characteristics of excluded studies](#) tables. One new study was identified and was included within the meta-analysis in this update ([Tinelli 2011](#)). See [Figure 1](#)

Figure 1. Study flow diagram.

Included studies

Trial design and setting

Number of studies: We identified a total of 18 randomised controlled trials that met the inclusion criteria (1262 participants).

Multi-centre trials: Nine trials were multi-centre studies ([Azziz 1993](#); [Diamond 1996](#); [Franklin 1995](#); [Haney 1995](#); [Myomectomy ASG 1995](#); [Nordic APSG 1995](#); [Sekiba 1992](#); [Takeuchi 2005](#); [Tinelli 2011](#)).

Design: In six parallel-group trials, the unit of randomisation was the participant ([Diamond 1996](#); [Mais 1995a](#); [Mais 1995b](#); [Takeuchi 2005](#); [Tinelli 2011](#) [Wallweiner 1998](#)). The remainder were within-participant trials in which the unit of randomisation was the ovary, uterine sites or the pelvic sidewall. One study ([Takeuchi 2005](#)) was a multi-arm trial comparing fibrin gel and a fibrin sheet versus control. Comparison of the fibrin sheet arm versus the control arm was included in this review.

Support/sponsorship: Twelve trials stated sponsorship. Seven trials were sponsored by Johnson & Johnson ([Azziz 1993](#); [Franklin 1995](#); [Li 1994](#); [Nordic APSG 1995](#); [Saravolos 1996](#); [Sekiba 1992](#); [van Geldorp 1994](#)), one trial was sponsored by Genzyme ([Diamond 1996](#)) and a further two trials were sponsored by manufacturers of expanded polytetrafluoroethylene ([Haney 1995](#); [Myomectomy ASG 1995](#)). One trial received additional sponsorship from the Medical Research Council (MRC) in Canada ([Greenblatt 1993](#)). Another trial received support from Johnson & Johnson after the study was completed to help with the analysis, but the final content of the paper was under the sole control of the principal investigator ([Keckstein 1996](#)).

Participants

Primary indications for surgery: Myomectomy was the indication in five trials ([Diamond 1996](#); [Mais 1995b](#); [Myomectomy ASG 1995](#); [Takeuchi 2005](#); [Tinelli 2011](#)), and ovarian surgery was the indication in four trials ([Greenblatt 1993](#); [Keckstein 1996](#); [Saravolos 1996](#); [van Geldorp 1994](#)). Three trials were restricted to women undergoing adhesiolysis for infertility ([Azziz 1993](#); [Nordic APSG 1995](#); [Sekiba 1992](#)). Participants also underwent adhesiolysis in [Li 1994](#), although the indications were subgrouped into infertility or pelvic pain. The indication for the [Haney 1995](#) trial was also pelvic adhesions, although the primary reason for surgery was not exclusively infertility, and this trial was not subgrouped. In the remaining trials, the indications were endometriosis ([Mais 1995a](#); [Wallweiner 1998](#)) and bilateral ovarian disease ([Franklin 1995](#)).

Type of surgery: Laparotomy was performed in eight trials ([Azziz 1993](#); [Diamond 1996](#); [Franklin 1995](#); [Li 1994](#); [Myomectomy ASG 1995](#); [Nordic APSG 1995](#); [Sekiba 1992](#); [van Geldorp 1994](#)), and laparoscopy was performed in the remainder. [Tinelli 2011](#) performed both laparoscopy and laparotomy.

Suturing: Oxidised regenerated cellulose was occasionally sutured into place ([Keckstein 1996](#); [Li 1994](#); [Sekiba 1992](#)), whereas expanded polytetrafluoroethylene was always sutured into place.

Adjuvants to surgery: One trial compared oxidised regenerated cellulose versus no treatment; hydrocortisone was also instilled in both treatment and control groups ([Li 1994](#)).

Microsurgical techniques: In three trials, it was noted that microsurgery was performed ([Azziz 1993](#); [Li 1994](#); [Nordic APSG 1995](#)).

Interventions

- Thirteen RCTs compared oxidised regenerated cellulose was compared with no treatment - six at laparoscopy ([Mais 1995b](#); [Saravolos 1996](#); [Tinelli 2011](#); [Keckstein 1996](#); [Mais 1995a](#); [Wallweiner 1998](#)), and seven at laparotomy ([Azziz 1993](#); [Li 1994](#); [Nordic APSG 1995](#); [Sekiba 1992](#); [Franklin 1995](#); [van Geldorp 1994](#); [Tinelli 2011](#)).
- Two RCTs compared expanded polytetrafluoroethylene versus oxidised regenerated cellulose ([Haney 1995](#); [Korell 1994](#))
- One RCT compared expanded polytetrafluoroethylene versus no treatment ([Myomectomy ASG 1995](#))
- One RCT compared sodium hyaluronate with carboxymethylcellulose versus no treatment ([Diamond 1996](#)).
- One RCT compared fibrin sheet versus no treatment at laparoscopic myomectomy ([Takeuchi 2005](#)).

Timing of second-look laparoscopy (SLL): Only two studies stated a mean time after laparoscopy ([Diamond 1996](#)—23 days; [Haney 1995](#)—30 days). Large variation was noted in timing of the SLL both within and between studies. Only three studies performed all SLL procedures within six weeks ([Greenblatt 1993](#); [Haney 1995](#); [Myomectomy ASG 1995](#)). Only four further studies performed SLL after eight weeks ([Keckstein 1996](#); [Mais 1995a](#); [Mais 1995b](#); [Wallweiner 1998](#)). Remaining studies performed SLL after 10 days to 16 weeks.

[Tinelli 2011](#) did not routinely perform SLL but instructed participants to have any further surgery completed within a six-year period. Adhesions were assessed at the second surgery. Timing of the second surgery varied between 2.3 and 2.5 years.

Studied outcomes

Primary outcomes

Pelvic pain: No trials reported this outcome.

Live birth rate: No trials reported this outcome.

Secondary outcomes

Adhesion score: Only one study reported mean adhesion score as an outcome ([Haney 1995](#)).

Number of participants with adhesions at SLL: Eight trials reported the incidence of de novo adhesions as an outcome ([Diamond 1996](#); [Greenblatt 1993](#); [Korell 1994](#); [Mais 1995b](#); [Myomectomy ASG 1995](#); [Saravolos 1996](#); [Takeuchi 2005](#); [Tinelli 2011](#)). Ten trials reported the incidence of re-formation adhesions as an outcome ([Azziz 1993](#); [Franklin 1995](#); [Haney 1995](#); [Keckstein 1996](#); [Li 1994](#); [Mais 1995a](#); [Nordic APSG 1995](#); [Sekiba 1992](#); [van Geldorp 1994](#); [Wallweiner 1998](#)).

Clinical pregnancy rate: No trials reported on this outcome.

Miscarriage rate: No trials reported on this outcome.

Ectopic pregnancy rate: No trials reported on this outcome.

Quality of life: No trials reported on this outcome.

Adverse effects: 13 studies reported adverse effects as an outcome (Azziz 1993; Diamond 1996; Franklin 1995; Haney 1995; Keckstein 1996; Mais 1995a; Mais 1995b; Myomectomy ASG 1995; Nordic APSG 1995; Saravelos 1996; Takeuchi 2005; Tinelli 2011; van Geldorp 1994). In the remaining studies, the absence of adverse effects was not stated.

Excluded studies

Eight studies were excluded. In seven studies the agent used was not a barrier agent, and one study (To 1992) did not investigate use of a barrier agent during a gynaecological procedure.

Risk of bias in included studies

See Figure 2 and Figure 3 for a summary diagram.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Azziz 1993	?	?	?	-	?	+
Diamond 1996	+	+	+	+	?	+
Franklin 1995	?	?	+	+	?	+
Greenblatt 1993	?	?	?	+	?	-
Haney 1995	?	?	-	?	?	+
Keckstein 1996	?	?	?	-	?	+
Korell 1994	?	?	?	?	?	+
Li 1994	?	?	?	+	-	+
Mais 1995a	+	?	?	?	?	+
Mais 1995b	+	?	?	?	?	+
Myomectomy ASG 1995	+	?	?	+	?	+
Nordic APSG 1995	?	?	?	?	-	+

Figure 3. (Continued)

Nordic APSG 1995	?	?	?	?	-	+
Saravelos 1996	?	?	?	?	?	+
Sekiba 1992	?	?	?	?	?	+
Takeuchi 2005	?	?	?	?	?	+
Tinelli 2011	+	?	?	-	?	+
van Geldorp 1994	?	?	?	?	?	+
Wallweiner 1998	?	?	?	?	?	+

Allocation

Sequence generation

Thirteen studies were rated as having unclear risk of bias. Twelve did not detail the randomly assigned component despite stating that they were randomised studies (Azziz 1993; Franklin 1995; Greenblatt 1993; Haney 1995; Korell 1994; Li 1994; Nordic APSG 1995; Saravelos 1996; Sekiba 1992; Takeuchi 2005; van Geldorp 1994; Wallweiner 1998). One study used coin toss (Keckstein 1996). Five studies were deemed to have low risk of bias for sequence generation (Diamond 1996; Mais 1995a; Mais 1995b; Myomectomy ASG 1995; Tinelli 2011).

Timing of randomisation: All studies performed random assignment during or at the end of surgery.

Concealment of allocation

One study was deemed to have low risk of bias for selection bias (Diamond 1996). The remaining 12 studies were deemed to have unclear risk of selection bias. Although eight of these studies used sealed envelopes, investigators did not detail the methods used to develop and monitor the allocation process with sealed envelopes (Azziz 1993; Franklin 1995; Haney 1995; Mais 1995a; Mais 1995b; Nordic APSG 1995; Saravelos 1996; Sekiba 1992).

Blinding

One study was rated as high risk, 15 as unclear risk and two as low risk.

Blinding of observers at second-look laparoscopy: 13 studies concealed randomisation at second-look laparoscopy, three studies did not discuss blinding (Haney 1995; Myomectomy ASG 1995; van Geldorp 1994) and two studies did not use blinding (Azziz 1993; Takeuchi 2005).

Incomplete outcome data

Three studies were rated as high risk, 10 as unclear risk and five as low risk.

Dropouts: Azziz 1993 reported a large number of dropouts. A total of 198 participants were randomly assigned, but 64 were excluded from analysis because of inadequate documentation in 23, surgical technique and evaluation inconsistent with the protocol in 36, concurrent therapy in conflict with the protocol in three and participant refusal to undergo second-look laparoscopy in two (Wiseman 1999), demonstrating high risk of bias. Keckstein 1996 also reported a large number of dropouts, with eight of 25 participants not returning for SLL. No reason was given for this.

Tinelli 2011 reported participants undergoing a second surgical procedure within six years of initial surgery: 546 of 694 participants underwent a second surgery. In contrast to other trials, a second-look laparoscopy at a specified time interval was not performed on all participants, leading to the exclusion of 148 participants from the results; this may increase the risk of bias.

Withdrawals and intention-to-treat analysis: Withdrawals were stated in ten studies (Azziz 1993; Diamond 1996; Greenblatt 1993; Haney 1995; Keckstein 1996; Li 1994; Myomectomy ASG 1995; Saravelos 1996; Takeuchi 2005; Tinelli 2011; and were not stated in three studies (Franklin 1995; Nordic APSG 1995; Sekiba 1992); in five studies, no dropouts were reported (Mais 1995a; Mais 1995b; Takeuchi 2005; van Geldorp 1994; Wallweiner 1998). No studies with dropouts performed an intention-to-treat analysis. A total of six participants from all studies were reported to have been unable to undergo second-look laparoscopy because of pregnancy.

Selective reporting

Publication bias

Two studies were rated as high risk (Li 1994; Nordic APSG 1995), and the other 17 studies were rated as unclear risk. The Nordic study (Nordic APSG 1995) reported larger numbers of participants

randomly assigned in meeting abstracts before the study was fully published in a journal. The explanation for this discrepancy was that some participants who did not meet inclusion criteria were recruited and were not included in the final analysis (personal communication, Wiseman 1999). In the United Kingdom, centres other than Sheffield (Li 1994) were randomly assigning participants in a study of oxidised regenerated cellulose versus no treatment in the early 1990s (personal communication, A Watson), but the data have never been published. Attempts to identify these data by contacting the investigators and the sponsoring company (Ethicon, Bridgewater, New Jersey, USA) have proved fruitless thus far. In the study reported by van Geldorp 1994, another centre was recruiting participants (investigator: Trimbos-Kemper, Netherlands), but the results have been reported only briefly in a review (Wiseman 1999). Data regarding the use of oxidised regenerated cellulose must be interpreted with caution because of the high risk of bias.

Additional information was sought from some study authors; at the time of this writing, six replies had been received (Azziz 1993; Franklin 1995; Keckstein 1996; Myomectomy ASG 1995; Saravelos 1996; van Geldorp 1994).

Haney 1995 reported statistically significant reductions in the adhesion score, but it is not clear whether these analyses took account of the within-participant design. It should be noted that the incidence of adhesions in the oxidised regenerated cellulose arm of the trial is greater than would be expected from the RCTs of oxidised regenerated cellulose versus no barrier agent. As it was not clear from the publication whether the surgeon was unblinded at the time of the second-look laparoscopy, this result should be treated with some caution.

Other potential sources of bias

Statistical analysis: Of the 10 studies using a within-participant design and reporting adhesion formation, only three presented and analysed matched data appropriately (Azziz 1993; Saravelos 1996; Sekiba 1992). Appropriate data were extracted from the reports of two others (Franklin 1995; Haney 1995), which were incorrectly analysed in the original. See Methods section for a full description. One further study (Greenblatt 1993) failed to present comparative data and was excluded from all analyses.

Effects of interventions

See: **Summary of findings for the main comparison** Oxidised regenerated cellulose (Interceed) vs no treatment at laparoscopy for adhesion prevention after gynaecological surgery; **Summary of findings 2** Oxidised regenerated cellulose (Interceed) vs no treatment at laparotomy for adhesion prevention after gynaecological surgery; **Summary of findings 3** Expanded polytetrafluoroethylene (Gore-Tex) vs no treatment for adhesion prevention after gynaecological surgery; **Summary of findings 4** Expanded polytetrafluoroethylene (Gore-Tex) vs oxidised regenerated cellulose (Interceed) for adhesion

prevention after gynaecological surgery; **Summary of findings 5** Sodium hyaluronate and carboxymethylcellulose (Seprafilm) vs no treatment for adhesion prevention after gynaecological surgery; **Summary of findings 6** Fibrin sheet vs no treatment at laparoscopic myomectomy for adhesion prevention after gynaecological surgery

No studies reported either of our primary outcomes outcomes (pelvic pain and live birth).

1. Oxidised regenerated cellulose versus no treatment at laparoscopy

(Analysis 1.1)

Primary outcomes

1.1 Pelvic pain

Not assessed by any study.

1.2 Live birth rate

Not assessed by any study.

Secondary outcomes

1.3 Adhesion score

Not assessed by any study.

1.4 Number of participants with adhesions at SLL

Six trials reported this outcome. Three reported de novo adhesion formation (Mais 1995b; Saravelos 1996; Tinelli 2011), three reported re-formation of adhesions following adhesiolysis (Keckstein 1996; Mais 1995a; Wallweiner 1998) (Keckstein reported both de novo and re-formation adhesions) and one did not report adhesion formation (Greenblatt 1993).

Use of oxidised regenerated cellulose was associated with a reduced incidence of adhesions when compared with no treatment at second-look laparoscopy in both de novo adhesions (OR 0.50, 95% CI 0.30 to 0.83, three trials, 360 participants, $I^2 = 75\%$, very low quality) and re-formation adhesions (OR 0.16, 95% CI 0.07 to 0.41, three trials, 100 participants, $I^2 = 36\%$, low quality).

No clear explanation was provided for the high heterogeneity in this analysis ($I^2 = 75\%$). However, it is possible that the small number of participants within the included studies may partially account for it. Differences in operative procedure were observed between the studies, as were differences in wrapping and use of oxidised regenerated cellulose (Saravelos 1996). It is unclear, however, whether these differences can account for the very high level of heterogeneity observed in these studies.

See Figure 4.

Figure 4. Forest plot of comparison: 1 Oxidised regenerated cellulose (Interceed) vs no treatment at laparoscopy, outcome: 1.1 Incidence of adhesions.

1.5 Clinical pregnancy rate

Not assessed by any study.

1.6 Miscarriage rate

Not assessed by any study.

1.7 Ectopic pregnancy rate

Not assessed by any study.

1.8 Quality of life (QoL)

Not assessed by any study.

1.9 Adverse outcomes

[Tinelli 2011](#) reported the incidence of fever within 48 hours as 6.5% to 12.5% of cases; this was likely to be secondary to surgery rather than to use of the barrier agent. Otherwise, no adverse outcomes were identified among the 216 participants receiving the intervention across the five studies ([Keckstein 1996](#); [Mais 1995a](#); [Mais 1995b](#); [Saravolos 1996](#); [Tinelli 2011](#)).

2. Oxidised regenerated cellulose versus no treatment at laparotomy

(Analysis 2.1)

Primary outcomes

2.1 Pelvic pain

Not assessed by any study.

2.2 Live birth rate

Not assessed by any study.

Secondary outcomes

2.3 Adhesion score

Not assessed by any study.

2.4 Number of participants with adhesions at SLL

Six trials reported on re-formation of adhesions following laparotomy for adhesiolysis ([Azziz 1993](#); [Li 1994](#); [Nordic APSG 1995](#); [Sekiba 1992](#)) and ovarian surgery ([Franklin 1995](#); [van Geldorp 1994](#)). [Tinelli 2011](#) found no evidence of a difference in the formation of de novo adhesions following laparotomy (OR 0.72, 95% CI 0.42 to 1.25, one trial, 271 participants, $I^2 = 41\%$, low-quality evidence). Use of oxidised regenerated cellulose resulted in a reduction in the incidence of re-formation adhesions compared with no treatment (OR 0.38, 95% CI 0.27 to 0.55, six trials, 554 participants, moderate-quality evidence).

See [Figure 5](#).

Figure 5. Forest plot of comparison: 2 Oxidised regenerated cellulose (Interceed) vs no treatment at laparotomy, outcome: 2.1 Incidence of adhesions.

2.5 Clinical pregnancy rate

Not assessed by any study.

2.6 Miscarriage rate

Not assessed by any study.

2.7 Ectopic pregnancy rate

Not assessed by any study.

2.8 Quality of life (QoL)

Not assessed by any study.

2.9 Adverse outcomes

In [Azziz 1993](#), three adverse events occurred (atelectasis, postoperative ileus, fever and abdominal pain), and in [van Geldorp 1994](#), a decrease in haemoglobin was reported. These adverse effects are related to the surgery rather than to the barrier agent. Otherwise, adverse outcomes related to the agent were identified among 225 participants receiving the intervention across five studies ([Azziz 1993](#); [Franklin 1995](#); [Nordic APSG 1995](#); [Tinelli 2011](#); [van Geldorp 1994](#)). Two studies did not report on adverse outcomes ([Li 1994](#); [Sekiba 1992](#)).

3. Expanded polytetrafluoroethylene versus no treatment

(Analysis 3.1)

Primary outcomes

3.1 Pelvic pain

Not assessed by any study.

3.2 Live birth rate

Not assessed by any study.

Secondary outcomes

3.3 Adhesion score

Not assessed by any study.

3.4 Number of participants with adhesions at SLL

Only one trial reported this comparison and described a reduction in new adhesion formation in women undergoing myomectomy at laparotomy ([Myomectomy ASG 1995](#)). Use of expanded polytetrafluoroethylene was associated with a reduction in new adhesion formation (OR 0.17, 95% CI 0.03 to 0.94, one trial, 42 participants, low-quality evidence). This result was obtained by assuming the outcome least favourable to expanded polytetrafluoroethylene that was compatible with reported results. See [Figure 6](#).

Figure 6. Forest plot of comparison: 3 Expanded polytetrafluoroethylene (Gore-Tex) vs no treatment, outcome: 3.1 Incidence of adhesions. **3.5 Clinical pregnancy rate**

Not assessed by any study.

3.6 Miscarriage rate

Not assessed by any study.

3.7 Ectopic pregnancy rate

Not assessed by any study.

3.8 Quality of life (QoL)

Not assessed by any study.

3.9 Adverse outcomes

No adverse outcomes were reported for 21 participants receiving the intervention in one trial ([Myomectomy ASG 1995](#)).

4. Expanded polytetrafluoroethylene versus oxidised regenerated cellulose**Primary outcomes****4.1 Pelvic pain**

Not assessed by any study.

4.2 Live birth rate

Not assessed by any study.

Secondary outcomes**4.3 Adhesion score**

Evidence was found of a reduced mean adhesion score at SLL with the use of expanded polytetrafluoroethylene in comparison with oxidised regenerated cellulose (mean difference -3.79, 95% CI -5.12 to -2.46, one study, 62 participants, very low-quality evidence). See [Figure 7](#)

Figure 7. Forest plot of comparison: 4 Expanded polytetrafluoroethylene (Gore-Tex) vs oxidised regenerated cellulose (Interceed), outcome: 4.1 Mean adhesion score (non-validated score). **4.4 Number of participants with adhesions at SLL**

One trial reported no evidence of a difference in the formation of de novo adhesions following myomectomy at laparoscopy ([Korell 1994](#)) (OR 0.93, 95% CI 0.26 to 3.4, one trial, 38 participants, very low-quality evidence).

One trial reported this comparison for a reduction in re-formation adhesions in women undergoing adhesiolysis at laparotomy ([Haney 1995](#)). Use of expanded polytetrafluoroethylene was associated with a reduction in adhesion re-formation (OR 0.13, 95% CI 0.02 to 0.80, one trial, 23 participants, very low-quality evidence).

4.5 Clinical pregnancy rate

Not assessed by any study.

4.6 Miscarriage rate

Not assessed by any study.

4.7 Ectopic pregnancy rate

Not assessed by any study.

4.8 Quality of life (QoL)

Not assessed by any study.

4.9 Adverse outcomes

Participants in [Haney 1995](#) experienced no adverse effects (three were treated with expanded polytetrafluoroethylene during surgery; nine were treated with oxidised regenerated cellulose).

One study ([Korell 1994](#)) did not report whether adverse outcomes occurred.

5. Sodium hyaluronate and carboxymethylcellulose versus no treatment

([Analysis 5.1](#))

Primary outcomes

5.1 Pelvic pain

Not assessed by any study.

5.2 Live birth rate

Not assessed by any study.

Secondary outcomes

5.3 Adhesion score

[Diamond 1996](#) reported a reduced adhesion severity score with use of sodium hyaluronate with carboxymethylcellulose in comparison with no treatment, using a non-validated scoring method out of four (MD 0.49, 95% CI 0.53 to 0.45, one trial, 127 participants, moderate-quality evidence) ([Analysis 5.1](#)).

5.4 Number of participants with adhesions at SLL

Not assessed by any study.

5.5 Clinical pregnancy rate

Not assessed by any study.

5.6 Miscarriage rate

Not assessed by any study.

5.7 Ectopic pregnancy rate

Not assessed by any study.

5.8 Quality of life (QoL)

Not assessed by any study.

5.9 Adverse outcomes

No adverse outcomes were reported in the 59 participants undergoing the intervention in one trial ([Diamond 1996](#)).

6. Fibrin sheet versus no treatment

([Analysis 6.1](#) and [Analysis 6.2](#))

Primary outcomes

6.1 Pelvic pain

Not assessed by any study.

6.2 Live birth rate

Not assessed by any study.

Secondary outcomes

6.3 Adhesion score

One study assessed fibrin sheet versus no treatment at laparoscopic myomectomy. The study authors reported no difference in adhesion grading, using a non-validated scoring method out of four (MD 0.14, 95% CI -0.67 to 0.39, one trial, 48 participants, low-quality evidence).

6.4 Number of participants with adhesions at SLL

Only one study assessed fibrin sheet versus no treatment at laparoscopic myomectomy ([Takeuchi 2005](#)). Study authors reported the frequency and severity of postoperative adhesions. No evidence was found of differences between groups in the incidence of postoperative adhesions per participant (OR 1.20, 95% CI 0.42 to 3.41, one study, 62 participants, very low-quality evidence).

6.5 Clinical pregnancy rate

Not assessed by any study.

6.6 Miscarriage rate

Not assessed by any study.

6.7 Ectopic pregnancy rate

Not assessed by any study.

6.8 Quality of life (QoL)

Not assessed by any study.

6.9 Adverse outcomes

Participants in [Takeuchi 2005](#) experienced no adverse effects (30 were treated with fibrin sheet during surgery).

Other analyses

Sensitivity analyses

Three studies reported an unclear randomisation procedure ([Greenblatt 1993](#); [Haney 1995](#); [Wallweiner 1998](#)) (although additional information has been requested). Excluding these studies from the analyses did not substantially affect the findings.

One study ([Azziz 1993](#)) reported a large number of dropouts (64/198), but excluding this study from the analyses did not affect the findings.

In other sensitivity analyses, use of a random-effects model, or of risk ratio rather than odds ratio, did not substantially change our findings for any outcomes, except that in the comparison of expanded polytetrafluoroethylene versus oxidised regenerated cellulose ([Analysis 4.2](#)), the confidence interval crossed the line of no effect when a risk ratio rather than an odds ratio was calculated (RR 0.36, 95% CI 0.13 to 1.01).

Publication bias

Insufficient studies were included in any analysis to permit construction of a funnel plot, so we were unable to formally assess publication bias.

DISCUSSION

Summary of main results

The review identified no studies that reported our primary outcomes of pelvic pain and live birth rate.

There was evidence of a reduction in the incidence of re-formation adhesions with the use of oxidised regenerated cellulose at both laparoscopy (low-quality evidence) and laparotomy (moderate-quality evidence), along with a reduction in de novo adhesion formation at laparoscopy (very low-quality evidence).

One study demonstrated that use of expanded polytetrafluoroethylene was associated with a reduction in de novo adhesions at laparoscopy (low-quality evidence). A single, small-scale, unblinded, commercially funded study compared the use of expanded polytetrafluoroethylene versus oxidised regenerated cellulose and demonstrated a reduction in re-formation adhesions with expanded polytetrafluoroethylene in comparison with oxidised regenerated cellulose (very low-quality evidence). A study of similar size found no difference for de novo adhesions (very low-quality evidence).

A single study demonstrated a reduction in adhesion formation after laparoscopy with the use of sodium hyaluronate with carboxymethylcellulose (moderate-quality evidence).

A single small-scale study found no benefit for fibrin sheets for the incidence of adhesions (very low-quality evidence).

Overall completeness and applicability of evidence

Most gynaecological surgery is associated with a risk of pelvic adhesions. The clinical consequences of adhesions include pain, subfertility and small-bowel obstruction, as well as complications of subsequent surgery. Minimally invasive techniques such as laparoscopy reduce the risk of de novo adhesion formation but do not eliminate it entirely. Studies included within this review therefore assessed both laparoscopy and laparotomy.

This review assessed the effectiveness of barrier agents in reducing adhesions following conservative gynaecological surgery. As noted above, pharmacological and fluid agents are assessed in a separate Cochrane review.

Unfortunately, no studies in this review reported pregnancy or pelvic pain as a primary outcome but instead focused on extent of adhesion formation by incidence or by score. However, only five studies investigated the use of barrier agents in women seeking treatment to improve fertility. None of these studies reported adverse outcomes attributable to the use of a barrier agent.

Quality of the evidence

The included studies were at unclear risk of bias in most domains. The most common limitation was failure to report sufficient details of study methods. Studies were at high risk of bias related to attrition rates (three studies), selective reporting (two studies) and lack of blinding (one study). Reporting of adverse effects was inadequate. We were unable to formally assess the risk of publication bias. However, we note that 12 studies reported sponsorship, 11 of which were sponsored by companies that manufactured adhesion agents. Furthermore, evidence suggests that unpublished data may exist regarding oxidised regenerated

cellulose. Specifically, centres in the United Kingdom were known to be randomly assigning participants for a study in 1990 (personal communication, AW), although only results from Sheffield were identified by our search ([Li 1994](#)). Evidence of duplicate publication of data may contribute to increasing the risk of publication bias ([Haney 1995](#)).

Clinical heterogeneity between studies was observed, with differences in surgical technique and variable timing of second-look laparoscopy ranging from 23 days to 2.5 years. Considerable statistical heterogeneity was observed in the comparison of oxidised regenerated cellulose versus no treatment at laparoscopy ($I^2 = 75\%$), for which no clear explanation was provided.

The overall quality of the evidence was graded using GRADE methods. The quality ranged from very low to moderate but was low or very low for most comparisons. The main limitations were imprecision and poor reporting of study methods. See [Summary of findings for the main comparison](#), [Summary of findings 2](#), [Summary of findings 3](#), [Summary of findings 4](#), [Summary of findings 5](#) and [Summary of findings 6](#).

Potential biases in the review process

The review authors made every effort to identify all studies that should be considered for inclusion. Since the time of the previous review, necessary details required for inclusion in Cochrane reviews have increased substantially. Although all previously included studies were reassessed for bias, some information was required from the study authors themselves, and attempts were made to contact them.

Duplicate publication of data and existence of unreported data create a risk of bias. This is reflected in the GRADE rating of very low for oxidised regenerated cellulose versus no comparison at laparoscopy. This was often difficult to establish because the data were presented as abstracts at meetings (often by different study authors). For example, [Haney 1995](#) had four abstract publications, and [Keckstein 1996](#) had two abstract publications.

Agreements and disagreements with other studies or reviews

A review published in 2010 ([Pados 2010](#)) concludes that the "evidence is not adequate for definite conclusions to be drawn, either in terms of efficacy or in terms of safety" with regards to antiadhesion agents in gynaecological surgery. This is consistent with the findings of this review, which has found very little evidence on clinically relevant endpoints. Furthermore, the generally low GRADE evidence quality ratings given to most of the outcomes in this review show how, on our assessment, considerable uncertainty remains regarding use of these agents for improving patient outcomes.

The guidelines of the Society of Obstetricians and Gynaecologists of Canada on use of adhesion agents in gynaecological surgery are consistent with the notion that evidence on the effects of barrier agents on long-term clinical outcomes such as chronic pelvic pain and infertility is insufficient ([Robertson 2010](#)). These guidelines also state: "Oxidized regenerated cellulose (Interceed) adhesion barrier is associated with a reduced incidence of pelvic adhesion formation at both laparoscopy and laparotomy when complete haemostasis is achieved." This information is consistent with that reported in this review, which found that oxidised regenerated cellulose decreased

the incidence of re-formation adhesions at both laparoscopy and laparotomy and decreased the incidence of de novo adhesions at laparotomy. However, this review determined that the quality of evidence obtained ranged from very low to moderate.

The guidelines of the Society of Obstetricians and Gynaecologists of Canada also state: "Polytetrafluoroethylene (Gore-Tex) barrier is more effective than no barrier or oxidized regenerated cellulose in preventing adhesion formation" (Robertson 2010). This again is partially consistent with our conclusions, as we identified only one study that showed benefit with the use of expanded polytetrafluoroethylene versus no treatment. However, we rated the quality of the evidence as low. We also found one trial that showed superiority of expanded polytetrafluoroethylene over oxidised regenerated cellulose for the incidence of re-formation adhesions. We deemed this evidence to be of very low quality, as it was a very small, unblinded, privately funded study. Furthermore, no benefit was seen in a study of similar sized that compared use of these agents in de novo adhesions. This is consistent with the findings of Robertson 2010, who counselled caution when interpreting the result.

Finally, Robertson 2010 state: "Chemically modified sodium hyaluronate/carboxymethylcellulose (Seprafilm) is effective in preventing adhesion formation, especially following myomectomies," although researchers warned that these results should be interpreted with caution on the basis of comments provided in the previous version of this review. Our updated review also agrees with this conclusion.

AUTHORS' CONCLUSIONS

Implications for practice

We found no evidence on the effects of barrier agents used during pelvic surgery on either pain or fertility outcomes in women of reproductive age.

Low quality evidence suggests that oxidised regenerated cellulose (Interceed), expanded polytetrafluoroethylene (Gore-Tex) and sodium hyaluronate with carboxymethylcellulose (Seprafilm) may all be more effective than no treatment in reducing the incidence of adhesion formation following pelvic surgery. There is no conclusive evidence on the relative effectiveness of these interventions. There is no evidence to suggest that fibrin sheet is more effective than no treatment. No adverse events directly attributed to the adhesion agents were reported. The quality of the evidence ranged from very low to moderate. The most common limitations were imprecision and poor reporting of study methods. Most studies were commercially funded, and publication bias could not be ruled out.

Implications for research

Further high-quality studies with improved blinding of surgeons/ outcome assessment, reduced selective reporting and use of intention-to-treat analyses are required. Research should focus on the effects of barrier agents on clinical outcomes, with emphasis on fertility outcomes in women trying to conceive. Future studies should include women as the unit of randomisation, live birth and pain as primary outcomes and earlier second-look laparoscopy (within four to six weeks).

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REFERENCES

References to studies included in this review

Azziz 1993 {published data only}

Azziz R, Cohen S, Curole D, Diamond M, Franklin R, Haney A, et al. Microsurgery alone or with Interceed absorbable adhesion barrier for pelvic side wall adhesion re-formation. INTERCEED (TC7) Adhesion Barrier Study Group II. *Surgery Gynecology & Obstetrics* 1993;**177**(2):135-9.

Azziz R, Cohen S, Franklin R, Haney F, Russell L, Patton G, et al. Prevention of postsurgical adhesions by INTERCEED (TC7), an absorbable adhesion barrier: a prospective, randomized multicenter clinical study. INTERCEED (TC7) Adhesion Barrier Study Group. *Fertility & Sterility* 1989;**51**:933-8.

Malinak L. Interceed (TC7) as an adjuvant for adhesion reduction: clinical studies. *Treatment of Surgical Adhesions*. New York: Wiley-Liss Inc, 1990:193-206.

Diamond 1996 {published data only}

Diamond MP. Reduction of adhesions after uterine myomectomy by Seprafilm* membrane (HAL-F): a blinded, prospective, randomised, multicenter clinical study. The Seprafilm Adhesion Study Group. *Fertility & Sterility* 1996;**66**(6):904-10.

Franklin 1995 {published data only}

Franklin R, Jansen R, Larsson B, Malinak L, Rosenberg S, Webster B. A multicentre clinical evaluation of Interceed (TC7) absorbable adhesion barrier in the treatment of ovarian defects. *Fertility & Sterility* 1993;**31**:S31 (0-063).

* Franklin RR, Diamond M, Malinak R, Larsson B, Jansen R, Rosenberg S, et al. Reduction of ovarian adhesions by the use of Interceed. Ovarian Adhesion Study Group. *Obstetrics & Gynecology* 1995;**86**(3):335-40.

Greenblatt 1993 {published data only}

Greenblatt EM, Casper RF. Adhesion formation after laparoscopic ovarian cautery for polycystic ovarian syndrome: lack of correlation with pregnancy rate. *Fertility & Sterility* 1993;**60**(5):766-70.

Haney 1995 {published data only}

Haney A, Hesla J, Hurst B, Kettel L, Murphy A, Rock J, et al. Expanded polytetrafluoroethylene (Gore-Tex Surgical Membrane) is superior to oxidized regenerated cellulose (Interceed TC7) in preventing adhesions. *Fertility & Sterility* 1995;**63**(5):1021-6.

Haney A, Hesla J, Hurst B, Kettel L, Murphy A, Rock J, et al. Prevention of pelvic side wall adhesion reformation using surgical barriers: expanded polytetrafluoroethylene (Gore-Tex Surgical Membrane) is superior to oxidized regenerated cellulose (Interceed TC7). The Adhesion Barrier Study Group. *Fertility & Sterility* 1994;**S210**(abstract):265.

Haney A, Hesla J, Hurst B, Kettel M, Murphy A, Rock J, et al. Prevention of pelvic side wall adhesion reformation using surgical barriers: expanded polytetrafluoroethylene (Gore-Tex Surgical Membrane) is superior to oxidized regenerated

cellulose (Interceed TC7). The Adhesion Barrier Study Group. *Fertility & Sterility* 1994;**S210**(abstract):265.

March C, Boyers S, Franklin R, Haney A, Hurst D, Lotze E, et al. Prevention of adhesion formation/reformation with Gore-Tex Surgical Membrane. In: Diamond M, diZerega G, Linsky C, Reid RL editor(s). *Gynecologic Surgery and Adhesion Prevention*. New York: Wiley-Liss Inc, 1993:253-9.

Schlaff W, Hurst B, Kettel M, Murphy A, Franklin R, Lotze E, et al. Prevention of pelvic side wall adhesions using barrier methods: e-PTFE (Gore-Tex Surgical Membrane) and oxidized regenerated cellulose (Interceed, TC7): preliminary report. The Adhesion Barriers Study Group. *Fertility & Sterility* 1992;**S27**(abstract):58.

Keckstein 1996 {published data only}

Keckstein J, Karageorgieva E, Sasse V, Roth A, Tuttlies F, Ulrich U. Reduction of postoperative adhesion formation after laparoscopic ovarian cystectomy. *International Journal of Gynecology & Obstetrics* 1994;**46**(Suppl 1):9.

* Keckstein J, Ulrich U, Sasse V, Roth A, Tuttlies F, Karageorgieva E. Reduction of postoperative adhesion formation after laparoscopic ovarian cystectomy. *Human Reproduction* 1996;**11**(3):579-82.

Korell 1994 {published data only}

Korell M. Reduction of adhesion by INTERCEED Barrier and Gortex Surgical Membrane after laparoscopic myomectomy. Presented at "Möglichkeiten der Adhasionsprophylaxe," Munich, Germany., Munich, April 1994.

Li 1994 {published data only}

Li TC, Cooke ID. The value of an absorbable adhesion barrier, Interceed, in the prevention of adhesion reformation following microsurgical adhesiolysis. *British Journal of Obstetrics & Gynaecology* 1994;**101**(4):335-9.

Mais 1995a {published data only}

Mais V, Ajossa S, Marongiu D, Peiretti R, Guerriero S, Melis G. Reduction of adhesion reformation after laparoscopic endometriosis surgery: a randomised trial with an oxidized regenerated cellulose absorbable barrier. *Obstetrics & Gynecology* 1995;**86**(4 Pt 1):512-5.

Mais 1995b {published data only}

Mais V, Ajossa S, Piras B, Guerriero S, Marongiu D, Melis G. Prevention of de-novo adhesion formation after laparoscopic myomectomy: a randomized trial to evaluate the effectiveness of an oxidized regenerated cellulose absorbable barrier. *Human Reproduction* 1995;**10**(12):3133-5. Also presented as an abstract at 3rd International Congress on Pelvic Surgery 1996.

Myomectomy ASG 1995 {published data only}

Franklin R, Haney A, Kettel L, Eberhardt L, Murphy A, Rock J, et al. An expanded polytetrafluoroethylene barrier (Gore-Tex Surgical Membrane) reduces post-myomectomy adhesion formation. The Myomectomy Adhesion Multicenter Study Group. *Fertility & Sterility* 1995;**63**(3):491-3.

Tulandi T, Murphy A, Rock J, Franklin R, Rowe G, Lotze E. Effects of Gore-Tex Surgical Membrane on post-myomectomy adhesions. *Human Reproduction* 1993;**Abstracts of the 9th Annual Meeting of the ESHRE**:1993-1997.

Tulandi T, Rowe G, Rock J, Murphy A, Lotze E, Kettel L, et al. Effects of expanded polytetrafluoroethylene Gore-Tex Surgical Membrane on postmyomectomy adhesion. The Myomectomy Adhesion Study Group. *Fertility & Sterility* 1994;**S210(abstract)**:226.

Nordic APSG 1995 {published data only}

Larsson B. Clinical experiences with corticosteroids, 70% Dextran and Interceed TC7 as adjuvant therapy for postoperative adhesion prevention in fertility surgery. Which one is effective?. *Acta Obstetrica et Gynecologica Scandinavica* 1994;SP97.

Larsson B, Berg A, Bryman I, Thorburn J, Hogset K, Laatikainen T, et al. The efficacy of Interceed (TC7) for prevention of reformation of postoperative adhesions on ovaries, fallopian tubes, and fimbriae in microsurgical operations for fertility: a multicenter study. Nordic Adhesion Prevention Study Group. *Fertility & Sterility* 1995;**63**(4):709-14.

Larsson B, Bryman I, Thorburn J, Hogset K, Laatikainen T, Martikainen H, et al. Beneficial effect of Interceed TC7 as adjuvant therapy in prevention of postoperative adhesions on ovaries and oviducts in microsurgical operations for fertility. *Fertility & Sterility* 1993;**Suppl**:172.

Saravelos 1996 {published data only}

Saravelos H, Li T-C. Post-operative adhesions after laparoscopic electrosurgical treatment for polycystic ovarian syndrome with the application of Interceed to one ovary: a prospective randomised controlled study. *Human Reproduction* 1996;**11**(5):992-7.

Sekiba 1992 {published data only}

Sekiba K. Use of Interceed (TC7) absorbable adhesion barrier to reduce postoperative adhesion formation in infertility and endometriosis surgery. In: Diamond M, diZerega G, Linsky C, Reid R editor(s). *Gynaecologic Surgery and Adhesion Prevention*. New York: Wiley-Liss Inc, 1993:221-33.

Sekiba K, Yoshida N, Fukaya T, Ono T, Mizunuma H, Osada H, et al. The use of Interceed (TC7) absorbable adhesion barrier to reduce postoperative adhesion reformation in infertility and endometriosis surgery. The Obstetrics and Gynecology Adhesion Prevention Committee. *Obstetrics & Gynecology* 1992;**79**(4):518-22.

Takeuchi 2005 {published data only}

Takeuchi H, Kitade M, Kikuchi I, Shimanuki H, Kumakri J, Kmoshita K. Adhesion prevention effects of fibrin ceilings after laparoscopic myomectomy as determined by second look laparoscopy: a prospective randomised, controlled study. *Journal of Reproductive Medicine* 2005;**50**(8):571-7.

Tinelli 2011 {published data only}

Tinelli A, Malvas A, Guido M, Tsin DA, Hudelist G, Hurst B, et al. Adhesion formation after intracapsular myomectomy with or without adhesion barrier. *Fertility & Sterility* 2011;**95**(5):1780-5.

van Geldorp 1994 {published data only}

Wiseman D, van Geldorp H, Marks M, Diamond M. The effects of Interceed (TC7) absorbable adhesion barrier on the development of adhesions in patients with endometriosis. In: Nehzat C editor(s). *Endometriosis: Advanced Management and Surgical Techniques*. New York: Springer Verlag, 1995:200a-e.

van Geldorp H. Interceed absorbable adhesion barrier reduces the formation of postsurgical adhesions after ovarian surgery. *Fertility & Sterility* 1994;**P273**:213-4.

Wallweiner 1998 {published data only}

Wallweiner D, Meyer A, Bastert G. Adhesion formation of the parietal and visceral peritoneum: an explanation for the controversy on the use of autologous and alloplastic barriers?. *Fertility & Sterility* 1998;**69**(1):132-7.

References to studies excluded from this review

Diamond 1998 {published data only}

Diamond MP. Reduction of de novo postsurgical adhesions by intraoperative precoating with Sepracoat (HAL-C) solution: a prospective, randomized, blinded, placebo-controlled multicenter study. The Sepracoat Adhesion Study Group. *Fertility & Sterility* 1998;**69**(6):1067-74.

Dunn 2002 {published data only}

Dunn R, Johns D, Ferland R. A pilot, blinded evaluation of the adhesion barrier system. *Human Reproduction Abstracts* 2002;**17**(Abstract book 1):577.

Korrell 1998 {published data only}

* Korrell M, von Obernitz N, Hepp H. Incidence of adhesions after endoscopic myomectomy—Interceed TC7 versus intergel. Abstract from 7th Congress of the European Society for Gynaecological Endoscopy. 1998:52.

Korrell 2000a {published data only}

Korrell M, Obernitz NV, Hepp H. Incidence of adhesions after endoscopic myomectomy—Interceed TC7 versus intergel. 9th Congress of the European Society for Gynaecological Endoscopy. 2000:5.

Korrell 2000b {published data only}

Korrell M, Obernitz NV, Hepp H. Incidence of adhesions after endoscopic myomectomy—Interceed TC7 versus intergel. XV1 FIGO World Congress of O&G. 2000:25.

Reid 1993 {published data only}

* Reid R, Spence J, Tulandi T, Yuzpe A. Clinical experience of Interceed (TC7) absorbable adhesion barrier and heparin. *Fertility & Sterility* 1993;**S153**:160.

Reid 1997 {published data only}

Reid RL, Hahn PM, Spence JEH, Tulandi T, Yuzpe AA, Wiseman DM. A randomised clinical trial of oxidised regenerated cellulose adhesion barrier (Interceed, TC7) alone or in combination with heparin. *Fertility & Sterility* 1997;**67**(1):23-9.

To 1992 {unpublished data only}

To WK, Ho FC, Tang G. INTERCEED study: a preliminary report on immediate post-operative response in cesarean section patients. Presented at 2nd International Symposium on Adhesion Prevention, Palm Beach, Florida, January 1992.

Additional references
Ahmad 2014

Ahmad G, Mackie FL, Iles DA, O'Flynn H, Dias S, Metwally M, et al. Fluid and pharmacological agents for adhesion prevention after gynaecological surgery. *Cochrane Database of Systematic Reviews* 2014, Issue 7. [DOI: [10.1002/14651858.CD001298.pub4](https://doi.org/10.1002/14651858.CD001298.pub4)]

diZerega 1990

diZerega GS. The peritoneum and its response to surgical injury. *Progress in Clinical & Biological Research* 1990;**358**:1-11.

diZerega 1994

diZerega GS. Contemporary adhesion prevention. *Fertility & Sterility* 1994;**61**(2):219-35.

Higgins 2011

Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration 2011. www.cochrane-handbook.org.

Hurst 1998

Hurst BS. Permanent implantation of expanded polytetrafluoroethylene is safe for pelvic surgery. *Human Reproduction* 1999;**14**(4):925-7.

Jacobs 1996

Jacobs J, Iyer R, Weston J, Amato J, Elliott M, Leval M, et al. Expanded PTFE membrane to prevent cardiac injury during resectionectomy for congenital heart disease. *The Annals of Thoracic Surgery* 1996;**62**(6):1778-82.

Pados 2010

Pados G, Venetis CA, Almaloglou K, Tarlatzis BC. Prevention of intra-peritoneal adhesions in gynaecological surgery: theory and evidence. *Reproductive BioMedicine Online* September 2010;**21**(3):290-303.

Pellicino 2003

Pellicino M, Bramante S, Cirillo D. Effectiveness of auto-cross linked hyaluronic acid gel after laparoscopic myomectomy in infertile patients: a prospective randomised controlled study. *Fertility & Sterility* 2003;**80**:441-4.

Robertson 2010

Robertson D, Lefebvre G, Leyland N, Wolfman W, Allaire C, Awadalla A, et al. Adhesion prevention in gynaecological surgery. *Journal of Obstetrics and Gynaecology Canada* 2010 June;**32**(6):598-608.

SRS 2007

Practice Committee of the American Society for Reproductive Medicine: Society of Reproductive Surgeons. Pathogenesis, consequences and control of peritoneal adhesions in gynecologic surgery. *Fertility & Sterility* 2007;**88**:21-6.

Ten Broek 2013

ten Broek RP, Stommel MW, Strik C, van Laarhoven CJ, Keus F, van Goor H. Burden of adhesions in abdominal and pelvic surgery: systematic review and meta-analysis. *BMJ* 2013 October;**3**:347.

Wiseman 1999

Wiseman DM, Trout JR, Franklin RR, Diamond MP. Metaanalysis of safety and efficacy of an absorbable adhesion barrier (INTERCEED TC7) in laparotomy. *Journal of Reproductive Medicine* 1999;**44**(4):325-31.

References to other published versions of this review
Farquhar 1999

Farquhar C, Vandekerckhove P, Watson A, Vail A, Wiseman D. Barrier agents for preventing adhesions after surgery for preventing subfertility. *Cochrane Database of Systematic Reviews* 1999, Issue 2. [DOI: [10.1002/14651858.CD000475](https://doi.org/10.1002/14651858.CD000475)]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES
Characteristics of included studies [ordered by study ID]

Azziz 1993

Methods	Unit of randomisation: pelvic sidewall Method of randomisation: sealed envelopes, computer generated Time of randomisation: at completion of surgery Blinding: second-look laparoscopy performed by same surgeon
Participants	Patients undergoing pelvic adhesiolysis by laparotomy

Azziz 1993 (Continued)

N = 134 (268 pelvic sidewalls). Dropouts: 64 participants were excluded for surgical procedures and/or evaluations inconsistent with the protocol (39), with inadequate documentation (23) and for not returning for second-look laparoscopy (2)
Some participants underwent additional surgical procedures (salpingostomy, myomectomy, tubal anastomosis, endometriosis treatment)
Indication for surgery: infertility
Preexisting adhesions: yes
Cause of adhesions not stated (endometriosis included)
Microsurgery: yes

Age, years: > 18 (not further specified)

Location: multi-centre trial at 13 centres in North America
Timing and duration: 1986 to 1989

Interventions	Oxidised regenerated cellulose on pelvic sidewall vs uncovered opposite sidewall Other adjuvants used: none
Outcomes	Adhesions at second-look laparoscopy: at 10 days to 14 weeks 1. Incidence (per pelvic sidewall) 2. Extent: area, area differential, % improvement 3. Area: measured (not specified) 4. Severity: graded as filmy or severe Adverse effects No pregnancy outcomes Other outcomes Adhesions at second-look laparoscopy 1. Incidence: matched pair analysis 2. Incidence (per organ) 3. Incidence according to use of sutures 4. Incidence according to presence of endometriosis 5. Severity according to type of initial adhesion
Notes	Trial supported by manufacturers of Interceed (Johnson & Johnson, Inc.) Additional information provided by first study author Documented with photographs and drawings Reports of an earlier trial with a smaller sample size were published in 1989 and 1990 (see references)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	"A sealed envelope was opened which randomly assigned adnexal side to which Interceed was placed"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"The observer at laparoscopy was the same surgeon who performed the original laparotomy although he or she did not refer to their original notes"

Azziz 1993 (Continued)

Incomplete outcome data (attrition bias) All outcomes	High risk	Dropouts: 64 participants were excluded for surgical procedures and/or evaluations inconsistent with the protocol (39), inadequate documentation (23) and not returning for second-look laparoscopy (2)
Selective reporting (reporting bias)	Unclear risk	Data presented as numbers of cases and percentages; no data conversion. P values stated for outcomes. No omission of outcomes and no subsets of data. However, no prepublished protocol for reference purposes
Other bias	Low risk	No other bias identified

Diamond 1996

Methods	Unit of randomisation: women Method of randomisation: computer generated Timing of randomisation: end of surgery Blinding: surgeon unaware of randomisation at second-look laparoscopy Multi-centre trial
Participants	Women undergoing uterine myomectomy at laparotomy with at least 1 posterior uterine incision ≥ 1 cm. Similar baseline characteristics, including age, size and number of myomas and number of uterine incisions (n = 127) Microsurgery: no Dropouts: 6 (withdrew or excluded because of new medications) Age, years: 34 Location: USA (19 centres) Timing: 1993 to 1995 Preexisting adhesions Cause of adhesions not stated
Interventions	Sodium hyaluronate and carboxymethylcellulose vs no treatment
Outcomes	Adhesion formation at the time of second-look laparoscopy (mean days 23, range 7 to 70) Outcomes included number of adhesion sites, severity score and surface area of uterine adhesions No pregnancy outcomes reported
Notes	Power calculations: not stated Documented by video Multi-centre trial Sponsored by Genzyme No intention-to-treat analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"At each centre each enrolled patient was assigned consecutively a study number that corresponded to an identically numbered sealed study envelope, which determined the patient's treatment assignment via a computer derived randomisation list. After completion of myomectomy, patients were randomised at each centre into two groups"
Allocation concealment (selection bias)	Low risk	"At each centre each enrolled patient was assigned consecutively a study number that corresponded to an identically numbered sealed study envelope, which determined the patient's treatment assignment via a computer derived randomisation list. After completion of myomectomy, patients were randomised at each centre into two groups"

Diamond 1996 (Continued)

Blinding (performance bias and detection bias) All outcomes	Low risk	Second-look laparoscopy recorded on videotape for later evaluation by a surgeon who was unaware of participants' treatment status
Incomplete outcome data (attrition bias) All outcomes	Low risk	6 participants withdrawn (out of 127)
Selective reporting (reporting bias)	Unclear risk	Data presented graphically and as percentages. P values stated for outcomes. No omission of outcomes and no subsets of data. Although this was an infertility study, no pregnancy outcomes stated
Other bias	Low risk	No other bias identified

Franklin 1995

Methods	Unit of randomisation: ovary Method of randomisation: blocks of 2 with sealed envelopes Timing of randomisation: during surgery Blinding: yes 57 participants randomly assigned 2 exclusions 55 participants (110 ovaries) analysed Trial supported by manufacturers of Interceed (Johnson & Johnson Medical, Inc.)
Participants	Patients undergoing bilateral ovarian surgery by laparotomy (n = 55) Dropouts not stated Indication for surgery: bilateral ovarian disease (adhesions 37; tubal occlusion 7; PID history 4; endometriosis 5; other 2); not exclusively participants with infertility Preexisting adhesions: some (39/55) Cause of adhesions not stated (endometriosis included) Microsurgery at surgeon's discretion Age, mean, years: 29.9 (range 22-41) Location: 6 centres (Houston, Texas; Detroit, Michigan; Richmond, Virginia; Grand Rapids, Michigan—USA; Sydney—Australia; Danderyd—Sweden) Timing and duration: 1990-1993
Interventions	Oxidised regenerated cellulose on ovary vs uncovered opposite ovary Other adjuvants used: none Second-look laparoscopy <ol style="list-style-type: none"> 1. Timing: 10 to 98 days after initial surgery 2. Surgeon unaware: not stated 3. Adhesiolysis: yes
Outcomes	Adhesions at second-look laparoscopy: second or third week <ol style="list-style-type: none"> 1. Incidence (per pelvic sidewall) 2. Extent: area, area differential, % improvement 3. Severity 4. Area: measured with laparoscopic probe

Franklin 1995 (Continued)

5. Severity: graded (0 to 3): 0 = no adhesions; 1 = filmy adhesions; 2 = organised adhesions; 3 = cohesive adhesions

Pregnancy outcomes: nil

Adverse effects

Other outcomes

Adhesions at second-look laparoscopy

1. Incidence: matched pair analysis

2. Incidence according to diagnosis

3. Extent according to diagnosis: area differential

4. Extent according to time interval to second-look laparoscopy: area differential

5. Severity: grade differential

Notes

Power calculations: nil

Preliminary report of this trial published as abstract in 1993 (see references)

Documentation: video

Sponsored by Johnson & Johnson

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Before beginning the study, a treatment randomisation scheme was generated. Patients were randomised in blocks of two to provide balance with respect to the left and right ovaries. Randomised treatment assignments were placed in sealed envelope for each patient thereby blinding the surgeon to the treatment assignment during surgery"
Allocation concealment (selection bias)	Unclear risk	"Before beginning the study, a treatment randomisation scheme was generated. Patients were randomised in blocks of two to provide balance with respect to the left and right ovaries. Randomised treatment assignments were placed in sealed envelope for each patient thereby blinding the surgeon to the treatment assignment during surgery"
Blinding (performance bias and detection bias) All outcomes	Low risk	"Before beginning the study, a treatment randomisation scheme was generated. Patients were randomised in blocks of two to provide balance with respect to the left and right ovaries. Randomised treatment assignments were placed in sealed envelope for each patient thereby blinding the surgeon to the treatment assignment during surgery"
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 exclusions (out of 57 participants): 1 due to complete lysis of adhesions, and the second due to severe adhesions of pelvic wall at SLL
Selective reporting (reporting bias)	Unclear risk	Data presented as numbers of cases; no data conversion. P values stated for outcomes. No omission of outcomes and no subsets of data. No prepublished protocol identified
Other bias	Low risk	No other bias identified

Greenblatt 1993
Methods

Unit of randomisation: ovary

Method of randomisation: not stated

Greenblatt 1993 (Continued)

	Time of randomisation: at completion of surgery Blinding: surgeon at second-look laparoscopy unaware of side that was treated
Participants	<p>Patients undergoing bilateral ovarian cautery by laparoscopy N = 8; 1 exclusion, 7 participants, 14 ovaries Indication for surgery: infertility due to clomiphene-resistant PCOS Preexisting adhesions: no Microsurgery: no</p> <p>Age, mean, years: 26.6 Duration of infertility, mean, years: 3.2 (range 1.5 to 5) Tubal status: normal HSG and laparoscopy Ovulatory status: BBT and serum progesterone Semen analysis: done but results not stated</p> <p>Location: Canada Timing and duration: not stated</p>
Interventions	<p>Oxidised regenerated cellulose on ovary vs uncovered opposite ovary</p> <p>Other adjuvants used: none</p> <p>Second-look laparoscopy</p> <ol style="list-style-type: none"> 1. Timing: 3 to 4 weeks after initial surgery 2. Surgeon unaware: yes 3. Adhesiolysis: yes
Outcomes	<p>Adhesions at second-look laparoscopy at 3 to 4 weeks</p> <ol style="list-style-type: none"> 1. Incidence (per ovary) 2. Adhesion score 3. Scoring: revised AFS classification (Fertility and Sterility 1988;49:944-55) <p>Adverse effects Pregnancy outcomes stated but not by intervention, as unit of randomisation was ovaries</p>
Notes	<p>Power calculation: nil Documentation: video Sponsored by MRC Canada (Interceed provided by Johnson & Johnson) No intention-to-treat analysis</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Interceed was applied to one ovary, selected randomly"
Allocation concealment (selection bias)	Unclear risk	"Interceed was applied to one ovary, selected randomly"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Method of blinding not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 exclusion due to technical difficulty in applying oxidised regenerated cellulose

Greenblatt 1993 (Continued)

Selective reporting (reporting bias)	Unclear risk	Data presented as numbers of cases and percentages. P values stated for significant outcomes. No omission of outcomes and no subsets of data. No pre-published protocol identified
Other bias	High risk	Study used within-participant design for reporting adhesion formation. However, study was unclear on the presentation and analysis of matched data, and no comparative data were presented. As such, we were unable to extract appropriate data from the study

Haney 1995

Methods	Unit of randomisation: pelvic sidewall Method of randomisation: computerised randomisation table—sealed envelopes Timing of randomisation: at completion of surgery Blinding: not clear whether surgeon was aware of randomisation at second-look laparoscopy
Participants	Patients undergoing pelvic adhesiolysis and reconstructive pelvic surgery by laparotomy N = 29; 32 participants randomly assigned but 3 excluded (failed second-look laparoscopy) 29 participants (58 pelvic sidewalls) analysed Surgical procedures, in addition to adhesiolysis: salpingostomy, fimbrioplasty, ovarian cystectomy or endometriosis surgery Indication for surgery: not stated whether exclusively for infertility Preexisting adhesions: yes Cause of adhesions: previous surgery 27; PID history 5 (endometriosis included) Microsurgery performed at surgeon's discretion Age, years, range: 18-40 (mean not stated) Location: USA (Durham, North Carolina; Atlanta, Georgia; Denver, Colorado; San Diego, California; Houston, Texas) Timing and duration: 1991 to 1993
Interventions	Expanded polytetrafluoroethylene on pelvic sidewall vs oxidised regenerated cellulose on opposite pelvic sidewall Other adjuvants used: antibiotics Second-look laparoscopy 1. Timing: 1 to 6 weeks after initial surgery (mean 30 days) 2. Surgeon unaware: not stated 3. Adhesiolysis: yes
Outcomes	Adhesions at second-look laparoscopy 1. Incidence 2. Extent: area, area differential, % improvement 3. Adhesion score 4. Area: measured (not specified) Scoring (0 to 11) according to (1) extent: 0 = no adhesions; 1 = < 25%; 2 = 25% to 50%; 3 = 50% to 75%; 4 = > 75%; (2) type: 0 = none; 1 = filmy, transparent, avascular; 2 = opaque, transparent, avascular; 3 = opaque, capillaries present; 4 = opaque, large vessels; (3) tenacity: 0 = none; 1 = adhesions essentially fell apart; 2 = adhesions lysed with traction; 3 = adhesions required sharp dissection Adverse effects Pregnancy outcomes: nil

Haney 1995 (Continued)

Notes	<p>Power calculations: nil</p> <p>Sponsorship: trial supported by manufacturers of Gore-Tex (Gore and Associates Inc., Flagstaff, Arizona, USA)</p> <p>Documentation of adhesions: no video or photographic records stated</p> <p>Preliminary report of this trial published as abstract in 1992 and in 1994 (see references)</p> <p>? Duplicate publication of preliminary data in March 1993: further information awaited</p>
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"A randomization envelope was opened to reveal which side wall was to be covered"
Allocation concealment (selection bias)	Unclear risk	"A randomization envelope was opened to reveal which side wall was to be covered"
Blinding (performance bias and detection bias) All outcomes	High risk	Non-blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropouts: 32 participants randomly assigned but 3 excluded (failed second-look laparoscopy) 29 participants (58 pelvic sidewalls) analysed
Selective reporting (reporting bias)	Unclear risk	Data presented as scores and graphically presented. P values stated for outcomes. No omission of outcomes and no subsets of data. However, no prepublished protocol identified
Other bias	Low risk	No other bias identified

Keckstein 1996

Methods	<p>Unit of randomisation: ovary</p> <p>Method of randomisation: toss of a coin</p> <p>Time of randomisation: at completion of surgery</p> <p>Blinding: surgeon at second-look laparoscopy not aware of allocation</p>
Participants	<p>Patients undergoing bilateral ovarian cystectomy by laparoscopy (n = 25)</p> <p>14 participants with bilateral endometriomas, 6 with ovarian cysts and endometriosis and 5 with ovarian cysts only</p> <p>Dropouts: 8, not stated why</p> <p>Some participants also underwent adhesiolysis and removal of endometriosis</p> <p>Indication for surgery: ovarian cysts; not specifically participants with infertility</p> <p>Preexisting adhesions: some (but participants with dense adhesions excluded)</p> <p>Cause of adhesions: not stated (endometriosis included)</p> <p>Microsurgery: no</p> <p>Timing not stated</p> <p>Country: Germany (1 centre)</p>
Interventions	<p>Oxidised regenerated cellulose on ovary vs uncovered opposite ovary</p> <p>Other adjuvants used: none</p>

Keckstein 1996 (Continued)

Suturing: 9 of 17 in the oxidised regenerated cellulose group; 3 of 17 in the non-oxidised regenerated cellulose group

Second-look laparoscopy

1. Timing: 8 to 30 weeks after initial surgery
2. Surgeon unaware: not stated
3. Adhesiolysis: not stated

Outcomes	<p>Adhesions at second-look laparoscopy: 8 to 30 weeks</p> <ol style="list-style-type: none"> 1. Incidence (per ovary) of de novo adhesions 2. Severity: graded as filmy, vascular or dense 3. Area: estimated % of ovarian surface <p>Adverse effects Pregnancy data nil</p>
Notes	<p>Power calculations: nil Analysis sponsored by Johnson & Johnson only after study was completed First presented as abstract in 1994 No photographic or video documentation No intention-to-treat analysis</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"The random assignment of one ovary for wrapping with Interceed was revealed to the surgeon after a coin toss"
Allocation concealment (selection bias)	Unclear risk	"The random assignment of one ovary for wrapping with Interceed was revealed to the surgeon after a coin toss"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear from study
Incomplete outcome data (attrition bias) All outcomes	High risk	8 dropouts (n = 25). No reasons stated as to why participants did not return for SLL
Selective reporting (reporting bias)	Unclear risk	Data presented as numbers of cases and percentages, as well as graphically. P values stated for significant outcomes. No omission of outcomes and no subsets of data. However, no prepublished protocol identified
Other bias	Low risk	No other bias identified

Korell 1994

Methods	<p>Unit of randomisation: participant Method of randomisation: unknown Time of randomisation: unknown Blinding: unknown</p>
Participants	<p>Patients undergoing myomectomy by laparoscopy N = 38</p>

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Korell 1994 (Continued)

	Dropouts: not known Myomectomy details unknown Indication for surgery: fibroids Preexisting adhesions: no Microsurgery: no Age, mean, SD: unknown Location: Germany Timing and duration: unknown
Interventions	Oxidised regenerated cellulose applied to myomectomy incision(s) vs Gortex applied to myomectomy site(s) Other adjuvants used: none Second-look laparoscopy 1. Timing: unknown 2. Surgeon unaware: unknown 3. Adhesiolysis: unknown
Outcomes	Adhesions at second-look laparoscopy 1. Incidence (per participant) 2. Severity: graded as none, mild and severe Adverse effects: unknown Pregnancy: unknown
Notes	Power calculations: not stated Documentation not stated No source of funding stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated within study
Allocation concealment (selection bias)	Unclear risk	Not stated within study
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of whether withdrawals or dropouts occurred during the study
Selective reporting (reporting bias)	Unclear risk	Data presented as numbers of cases and percentages. P values stated for significant outcomes. No omission of outcomes and no subsets of data. However, no unpublished protocol identified
Other bias	Low risk	No other bias identified

Li 1994

Methods	Unit of randomisation: pelvic sidewall Method of randomisation: computer-generated random numbers Time of randomisation: at completion of surgery Blinding: assessor unaware of which sidewall was treated 28 participants randomly assigned 1 exclusion (declined second-look laparoscopy) 27 participants (54 pelvic sidewalls) analysed Trial supported by manufacturers of Interceed (Johnson & Johnson Medical, Ltd., UK)
Participants	Patients undergoing adhesiolysis by laparotomy (n = 28; 54 pelvic sidewalls, 1 withdrawal) Indication for surgery: infertility 21; chronic pelvic pain 6 Preexisting adhesions: yes Cause of adhesions: endometriosis 9; PID 10; previous surgery 5; uncertain 3 Microsurgery: yes Age, years, mean: 30.4 (SD 4.5) No details on participants with infertility Location: UK Timing and duration: 1989 to 1992
Interventions	Oxidised regenerated cellulose on pelvic sidewall vs uncovered opposite sidewall (oxidised regenerated cellulose sutured in 3 cases) Other adjuvants used: intraperitoneal hydrocortisone in Intralipid Second-look laparoscopy 1. Timing: 3 to 14 weeks after initial surgery 2. Surgeon unaware: yes 3. Adhesiolysis: not stated
Outcomes	Adhesions at second-look laparoscopy: 3 to 14 weeks after initial surgery 1. Incidence (per pelvic sidewall) 2. Extent: area, area differential, % improvement 3. Severity 4. Area: measured (not specified) Adverse effects Pregnancy outcomes: not stated
Notes	Documented with photographs and drawings at initial surgery and with video recording at second-look laparoscopy Sponsored by Johnson & Johnson Video at second-look laparoscopy No power calculations No intention-to-treat analysis
Risk of bias	
Bias	Authors' judgement Support for judgement

Li 1994 (Continued)

Random sequence generation (selection bias)	Unclear risk	"The assignment of the test side for each woman was carried out before the study and was randomised blocks of two to provide balance"
Allocation concealment (selection bias)	Unclear risk	"A sealed envelope was then opened revealing which of the side walls was to receive Interceed"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"The assessor was unaware of which side of the pelvis was the treatment side"
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 exclusion (declined second-look laparoscopy)
Selective reporting (reporting bias)	High risk	<p>Data presented as numbers of cases as well as graphically. P values stated for significant outcomes. No omission of outcomes and no subsets of data. Unclear whether power calculation performed</p> <p>Furthermore, despite 21 participants undergoing adhesiolysis for infertility, no pregnancy outcomes stated</p> <p>It should also be noted that centres other than Sheffield (Li 1994) were randomly assigning participants around the UK for a study of oxidised regenerated cellulose and no treatment in the early 1990s (personal communication, A Watson). However, data have never been published</p>
Other bias	Low risk	No other bias identified

Mais 1995a

Methods	Unit of randomisation: participant Method of randomisation: random number table—numbered sealed envelopes Time of randomisation: at completion of surgery Blinding: yes 32 participants No exclusions stated No source of funding stated
Participants	Patients undergoing pelvic adhesiolysis and endometriosis treatment by laparoscopy (n = 32) Dropouts: nil Endometriosis treatment consisted of coagulation or resection of implants and endometriomas, followed by a 3-month course of GnRH agonist Indication for surgery: not stated; not specifically participants with infertility Preexisting adhesions: yes Cause of adhesions: endometriosis (stage IV) Microsurgery: no Age, years, mean (SD): treatment group 30.1 (6.5); controls 29.3 (6.2) Location: Italy Timing and duration: January 1993 to June 1994
Interventions	Oxidised regenerated cellulose on ovaries and de-peritonealised areas vs surgery only Other adjuvants used: none

Mais 1995a (Continued)

	Second-look laparoscopy 1. Timing: 12 to 14 weeks after initial surgery 2. Surgeon unaware: yes 3. Adhesiolysis: not stated
Outcomes	Adhesions at second-look laparoscopy 12 to 14 weeks later 1. Incidence (per participant) Adverse effects Pregnancy outcomes: nil
Notes	Power calculation done Documentation: video Sponsorship: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned (using numbered sealed envelopes) to undergo surgery alone or surgery with an oxidised regenerated cellulose barrier. Treatment or control assignment was obtained by using a table of random digits. The envelope seal was broken in the operation room after completion of all operative procedures and before removal of laparoscopic ports
Allocation concealment (selection bias)	Unclear risk	Participants were randomly assigned (using numbered sealed envelopes) to undergo surgery alone or surgery with an oxidised regenerated cellulose barrier. Treatment or control assignment was obtained by using a table of random digits. The envelope seal was broken in the operation room after completion of all operative procedures and before removal of laparoscopic ports
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Investigator performing second-look laparoscopy blinded to treatment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of whether withdrawals or dropouts occurred during the study
Selective reporting (reporting bias)	Unclear risk	Data reported in incidences/percentages. No range or CI reported. P values reported only for significant results. No conversion of data or subsets
Other bias	Low risk	No other bias identified

Mais 1995b

Methods	Unit of randomisation: participant Method of randomisation: random number table—numbered sealed envelopes Time of randomisation: at completion of surgery Blinding: double
Participants	Patients undergoing myomectomy by laparoscopy N = 50 Dropouts: nil

Mais 1995b (Continued)

Myomectomy consisted of removal of 1 to 4 myomas; largest was 3 to 6 cm

Indication for surgery: fibroids; not specifically participants with infertility

Preexisting adhesions: no

Microsurgery: no

Age, years, mean (SD): treatment group 34.1 (5.7); controls 33.2 (5.5)

Location: Italy

Timing and duration: January 1993 to June 1994

Interventions	<p>Oxidised regenerated cellulose on myomectomy incision(s) vs uncovered myomectomy site(s)</p> <p>Other adjuvants used: none</p> <p>Second-look laparoscopy</p> <ol style="list-style-type: none"> 1. Timing: 12 to 14 weeks after initial surgery 2. Surgeon unaware: yes 3. Adhesiolysis: not stated
Outcomes	<p>Adhesions at second-look laparoscopy 12 to 14 weeks later</p> <ol style="list-style-type: none"> 1. Incidence (per participant) 2. Severity: graded as filmy and avascular, dense and/or vascular or cohesive <p>Adverse effects</p> <p>Pregnancy: not stated</p>
Notes	<p>Power calculations: nil</p> <p>Documentation: not stated</p> <p>No source of funding stated</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned (using numbered sealed envelopes) to undergo surgery alone or surgery with an oxidised regenerated cellulose barrier. Treatment or control assignment was obtained by using a table of random digits. The envelope seal was broken in the operation room after completion of all operative procedures and before removal of laparoscopic ports
Allocation concealment (selection bias)	Unclear risk	Participants were randomly assigned (using numbered sealed envelopes) to undergo surgery alone or surgery with an oxidised regenerated cellulose barrier. Treatment or control assignment was obtained by using a table of random digits. The envelope seal was broken in the operation room after completion of all operative procedures and before removal of laparoscopic ports
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Investigator performing second-look laparoscopy blinded to treatment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of whether withdrawals or dropouts occurred during the study
Selective reporting (reporting bias)	Unclear risk	Data reported in incidences/percentages. No range or CI reported. P values reported only for significant results. No conversion of data or subsets

Mais 1995b (Continued)

Other bias	Low risk	No other bias identified
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Myomectomy ASG 1995

Methods	Unit of randomisation: myomectomy site Method of randomisation: computerised randomisation table—sealed envelopes Timing of randomisation: at completion of surgery Blinding: not stated whether surgeon was aware of randomisation at second-look laparoscopy
Participants	Patients undergoing myomectomy (2 or more) by laparotomy N = 28 1 exclusion (declined second-look laparoscopy) 27 participants (54 myomectomy sites) analysed All had 2 myomectomy incisions of similar length and > 2 cm apart located on the fundus and the posterior uterine wall Indication for surgery: fibroids; not exclusively participants with infertility Microsurgery: no Preexisting adhesions: no Age, years, range: 18 to 43 Location: USA (Durham, North Carolina; Houston, Texas; Atlanta, Georgia; San Diego, California) and 1 in Canada (Montreal) Timing and duration: 1991 to 1993
Interventions	Expanded polytetrafluoroethylene over myomectomy site vs uncovered myomectomy site Other adjuvants used: antibiotics Second-look laparoscopy 1. Timing: 2 to 6 weeks after initial surgery (mean 25 days) 2. Surgeon unaware: not stated 3. Adhesiolysis: yes
Outcomes	Adhesions at second-look laparoscopy: 2 to 6 weeks after initial surgery 1. Incidence (per myomectomy site) 2. Extent: area 3. Adhesion score 4. Area: measured (not specified) Scoring (0 to 11) according to (1) extent: 0 = no adhesions; 1 = < 25%; 2 = 25% to 50%; 3 = 50% to 75%; 4 = > 75%; (2) type: 0 = none; 1 = filmy, transparent, avascular; 2 = opaque, transparent, avascular; 3 = opaque, capillaries present; 4 = opaque, large vessels; (3) tenacity: 0 = none; 1 = adhesions essentially fell apart; 2 = adhesions lysed with traction; 3 = adhesions required sharp dissection Adverse effects Pregnancy outcomes: nil
Notes	Documented with diagrams, photographs and videotapes Sponsored by Gore-Tex Surgical Membrane Multi-centre trial Power calculations: nil Preliminary reports of this trial published as abstracts 1993 and 1994 No intention-to-treat analysis

Myomectomy ASG 1995 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was done using a computerized randomisation table; random assignment was placed in a sealed envelope
Allocation concealment (selection bias)	Unclear risk	Randomisation was done using a computerized randomisation table; random assignment was placed in a sealed envelope
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear from text whether blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	One participant withdrew from study before SLL
Selective reporting (reporting bias)	Unclear risk	Data presented as incidence of adhesions with CI and adhesion score as means $\pm$ SEM. P values reported. No omissions or subsets of data. However, no pre-published protocol identified
Other bias	Low risk	No other bias identified

Nordic APSG 1995

Methods	Unit of randomisation: adnexae Method of randomisation: sealed envelopes Timing of randomisation: at completion of surgery Blinding: yes 66 participants (132 ovaries) No exclusions stated Trial supported by manufacturers of Interceed (Johnson & Johnson, Stockholm, Sweden)
Participants	Patients undergoing adhesiolysis by laparotomy N = 66 (14 more were erroneously entered, as they did not meet entry criteria of preexisting adhesions) Indication for surgery: infertility Preexisting adhesions: yes Cause of adhesions not stated (endometriosis excluded) Microsurgery: yes Age not stated No details on infertility status (duration of infertility, tubal status, ovulatory status, semen analysis) Location: Scandinavia, Sweden (Stockholm, Linköping, Göteborg, Gävle, Umeå and Skövde): 1 in Finland (Oulu), 1 in Denmark (Aalborg) Timing and duration: 1991 to 1993
Interventions	Oxidised regenerated cellulose on ovary and fallopian tube vs uncovered opposite side Other adjuvants used: none Second-look laparoscopy 1. Timing: 4 to 10 weeks after initial surgery 2. Surgeon unaware: not stated

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Nordic APSG 1995 (Continued)

3. Adhesiolysis: not stated

Outcomes	<p>Outcomes analysed in review</p> <p>Adhesions at second-look laparoscopy</p> <p>1. Incidence (per ovary)</p> <p>Scoring (0 to 4) at oviducts, fimbriae, ovaries (max score = 24): 0 = no adhesions; 1 = minimal adhesions; 2 = mild adhesions: 1 or 2 simple thin strands less than cm in width; 3 = moderate adhesions: more than 2 adhesions of type 2 or at least 1 solid adhesion; 4 = severe adhesion: more than type 3</p> <p>Adverse effects</p> <p>Pregnancy outcomes: nil</p> <p>Other outcomes</p> <p>Adhesions at second-look laparoscopy</p> <p>1. Incidence (per tube and per fimbria)</p> <p>2. Adhesion score (aggregate and per organ: ovary, tube and fimbriae)</p>
Notes	<p>Power calculations: nil</p> <p>Sponsored by Johnson & Johnson</p> <p>Multi-centre trial</p> <p>Duplicate publication with Larsson 93 (but different numbers)</p> <p>Preliminary reports of this trial published as abstracts in 1993 and 1994 (see references)</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"A sealed envelope disclosed assignment of which side was to be treated with the adjuvant therapy"
Allocation concealment (selection bias)	Unclear risk	"A sealed envelope disclosed assignment of which side was to be treated with the adjuvant therapy"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not stated in text
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of whether withdrawals or dropouts occurred during the study
Selective reporting (reporting bias)	High risk	Data presented in graphical form, as well as in tables as means $\pm$ SEMs. P values reported in table. Data reported for adhesions on ovaries, fallopian tubes, fimbriae. Data reported elsewhere with different sample size. Despite being an infertility study, pregnancy outcomes not stated
Other bias	Low risk	No other bias identified

Saravelos 1996

Methods	<p>Unit of randomisation: ovaries</p> <p>Method of randomisation: computer generated in opaque envelopes</p>
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Saravelos 1996 (Continued)

	Timing of randomisation: unclear Blinding: double
Participants	Women (n = 21) undergoing treatment for polycystic ovarian syndrome by ovarian electrocautery 7 dropouts: 4 pregnant, 2 withdrew, 1 had such dense adhesions at laparoscopy of both ovaries that no assessment could be made Preexisting adhesions: nil Mean age, years: 28 No other cause for infertility found Timing: 1994 to 1995 Country: UK (1 centre)
Interventions	Oxidised regenerated cellulose vs no treatment
Outcomes	Adhesion formation 1. Incidence 2. Extent 3. Severity Further adhesiolysis Timing of second-look laparoscopy: 2 to 11 weeks Pregnancy: outcomes given but ovaries randomly assigned, not participants
Notes	Supported by Johnson & Johnson Video taken Power calculations: nil No intention-to-treat analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"A sealed envelope disclosed the assignment of which side was to be treated with Interceed"
Allocation concealment (selection bias)	Unclear risk	"A sealed envelope disclosed the assignment of which side was to be treated with Interceed"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not stated in study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	1 participant excluded, as underwent ovarian drilling. 4 withdrew because of pregnancy, 2 withdrew because of personal choice (n = 21)
Selective reporting (reporting bias)	Unclear risk	Data reported as incidences and percentages. No data conversion. No P values reported
Other bias	Low risk	No other bias identified

Sekiba 1992

Methods	Unit of randomisation: pelvic sidewall
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Sekiba 1992 (Continued)

	<p>Method of randomisation: sealed envelopes</p> <p>Time of randomisation: at completion of surgery</p> <p>Blinding: double</p> <p>63 participants (126 pelvic sidewalls)</p> <p>No exclusions stated</p> <p>Trial supported by manufacturers of Interceed (Johnson & Johnson Medical, KK, Tokyo, Japan)</p>
Participants	<p>Participants undergoing adhesiolysis by laparotomy</p> <p>N = 63; dropouts: not stated</p> <p>Indication for surgery: infertility, known presence of bilateral sidewall adhesions</p> <p>Preexisting adhesions: yes</p> <p>Cause of adhesions: severe endometriosis 28; previous surgery 15; PID 9; no obvious cause 19</p> <p>Microsurgery: no</p> <p>Country: Japan</p> <p>Timing and duration: not stated</p>
Interventions	<p>Oxidised regenerated cellulose on pelvic sidewall vs uncovered opposite sidewall</p> <p>Other adjuvants used: none</p> <p>Second-look laparoscopy</p> <ol style="list-style-type: none"> 1. Timing: 10 days to 14 weeks after initial surgery 2. Surgeon unaware: yes 3. Adhesiolysis: not stated
Outcomes	<p>Adhesions at second-look laparoscopy at 10 days to 14 weeks</p> <ol style="list-style-type: none"> 1. Incidence (per pelvic sidewall) 2. Extent: area, area differential, % improvement 3. Area: measured with sterile ruler 4. Incidence according to size of de-peritonealised area 5. Incidence according to presence or absence of endometriosis 6. Incidence according to use of sutures 7. Extent (% improvement) according to size of de-peritonealised area 8. Extent (% improvement) according to presence or absence of endometriosis 9. Extent (% improvement) according to use of sutures <p>Pregnancy outcomes: nil</p>
Notes	<p>Documented with photographs and drawings</p> <p>No power calculations</p> <p>Duplicate publication</p> <p>Supported by Johnson & Johnson</p> <p>Multi-centre trial</p> <p>Trial also published elsewhere in 1993 (see references)</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"The pelvic sidewall to be covered was determined randomly using sealed envelopes"

Sekiba 1992 (Continued)

Allocation concealment (selection bias)	Unclear risk	"The pelvic sidewall to be covered was determined randomly using sealed envelopes"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear from text whether blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of whether withdrawals or dropouts occurred during the study
Selective reporting (reporting bias)	Unclear risk	Data presented in graphical form for some outcomes. P values stated for significant outcomes. No data subsets reported. No pregnancy outcomes reported despite being an infertility study
Other bias	Low risk	No other bias identified

Takeuchi 2005

Methods	Unit of randomisation: participant Method of randomisation: computer generated Time of randomisation: before surgery Blinding: absent
Participants	Women (n = 146) undergoing laparoscopic myomectomy; 69 in control group, 68 in fibrin gel group and 68 in fibrin sheet group 2 became pregnant, 23 other surgical procedures, 29 women with fibroid < 5 cm were excluded Preexisting adhesions: nil Mean age: no statistically significant difference Timing: 2001 to 2002 Country: multi-centric
Interventions	Fibrin sheet placed on site of myomectomy wound vs uncovered wound Other adjuvants used: none Second-look laparoscopy 1. Timing: between 13 and 19 weeks after initial surgery 2. Surgeon unaware: yes 3. Adhesiolysis: in participants who had adhesions present at second-look laparoscopy
Outcomes	Adhesions at second-look laparoscopy at 13 to 16 weeks 1. Incidence (adhesion formation per participant) 2. Adverse effects
Notes	Documentation of adhesions unclear No power calculations Support funding: unclear Multi-centre trial

Risk of bias

Bias	Authors' judgement	Support for judgement
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Takeuchi 2005 (Continued)

Random sequence generation (selection bias)	Unclear risk	"Randomisation was performed according to a computer generated list"
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not stated in text
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	"SLL was planned for 146 patients," "23 patients who underwent other surgical procedures (prior to SLL) were excluded," "29 patients in whom the maximum myoma diameter was < 5 cm were excluded," "2 women SLL was cancelled because they became pregnant." "Consequently, 91 patients who underwent (surgery) alone were evaluated"
Selective reporting (reporting bias)	Unclear risk	Data reported as incidences and percentages. P values reported only for significant outcomes. No subsets of data. No prepublished protocol identified. mAFS score done, but no standard deviations reported (review authors unable to extract standard deviations from data published in study paper because of the way they had been presented)
Other bias	Low risk	No other bias identified

Tinelli 2011

Methods	Unit of randomisation: 546 participants Time of randomisation: at completion of surgery Blinding: single Method of randomisation: Block randomisation was used to ensure balance in the numbers of participants in the 4 treatment arms. A statistician generated the entire randomisation sequence list in advance, and allocations were sequentially numbered from beginning to end Exclusion criteria for the investigation: previous uterine or pelvic surgery; previous abdominal general surgery; presurgical treatment with GnRH analogues; gynaecological malignancy; pregnancy; use of any instillation such as 32% dextran-70, corticosteroids, anticoagulants or non-steroidal anti-inflammatory drugs; haematological or coagulation disorders; presence of ongoing pelvic infection
Participants	546 participants underwent surgery Type of surgery: laparoscopic or abdominal single or multiple intracapsular myomectomy Reasons for surgery: pelvic pain, menorrhagia and growth of fibroids, as verified by ultrasound. Some women requested myomectomy because of infertility Mean age between groups, years: 28.9 to 30.2 Timing of second-look surgery between groups, years: 2.3 to 2.6 Dates: January 2003 to June 2009
Interventions	Participants were subdivided into groups for laparoscopic or abdominal surgery. Participants underwent single or multiple intracapsular myomectomy. Participants were randomly assigned to placement of oxidised regenerated cellulose absorbable adhesion barrier to the uterine incision or to control without barriers

Tinelli 2011 (Continued)

Outcomes	Primary and secondary outcomes of the analysis: presence and severity of adhesions for 4 groups: laparotomy with barrier, laparotomy without barrier, laparoscopy with barrier and laparoscopy without barrier	
Notes	Funding: no external source stated Power calculation: stated	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"After completion of reconstructive uterine surgery, subjects were assigned to the treatment in a 1:1 ratio using a randomization list with random permuted blocks, length of 4"
Allocation concealment (selection bias)	Unclear risk	"After completion of reconstructive uterine surgery, subjects were assigned to the treatment in a 1:1 ratio using a randomization list with random permuted blocks, length of 4" Did not state methods of allocation concealment in the text
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"The second surgical team to assess adhesions was blinded to the initial surgical approach and the use (or not) of the ORC adhesion barrier" Does not state method used to ensure blinding of outcome assessment by second surgical team. Unsure whether steps were taken so that surgeons who initially implanted the adhesion barrier were not the same as those who undertook subsequent surgery
Incomplete outcome data (attrition bias) All outcomes	High risk	"Of the 694 enrolled patients, 546 (78%) were available for assessment of adhesions during a subsequent operation" Adhesions were assessed at second surgery only if the participant had undergone subsequent surgery over the 6 years. Arguably, study data may be skewed by not including the 21% of participants who did not require subsequent surgery. Reasons for subsequent surgery include "laparotomy for cesarean section, laparotomy or laparoscopy for ovarian cysts, recurrent fibroids, appendectomy, cholecystectomy, extrauterine pregnancy and infertility"
Selective reporting (reporting bias)	Unclear risk	Data reported as incidences and percentages. P values reported only for significant outcomes. No differences identified between methods and reported results. However, no prepublication protocol identified for reference purposes
Other bias	Low risk	No other bias identified

van Geldorp 1994

Methods	Unit of randomisation: ovary Method of randomisation: computer generated by telephone Time of randomisation: at completion of surgery Blinding: not stated	
Participants	Patients undergoing bilateral ovarian surgery by laparotomy N = 20 participants (40 ovaries) No dropouts	

van Geldorp 1994 (Continued)

Surgery consisted of adhesiolysis, ovarian cystectomy and removal of endometriosis

Indication for surgery: not stated; not specifically participants with infertility

Preexisting adhesions: yes

Cause of adhesions: endometriosis 14; others not stated

Microsurgery: no

Age, years, mean: 31 (range 22 to 38)

Location: University Hospital, Rotterdam, The Netherlands

Timing and duration not stated

Interventions	<p>Oxidised regenerated cellulose on ovary vs uncovered opposite ovary</p> <p>Other adjuvants used: not stated</p> <p>Second-look laparoscopy</p> <ol style="list-style-type: none"> 1. Timing: 4 to 8 weeks after initial surgery 2. Surgeon unaware: not stated 3. Adhesiolysis: not stated
Outcomes	<p>Adhesions at second-look laparoscopy</p> <ol style="list-style-type: none"> 1. Incidence (per ovary) 2. Severity 3. Area: measured (not specified) 4. Severity: graded as filmy, vascular or dense 5. Extent: area, area differential, % improvement <p>Other outcomes</p> <p>Adhesions at second-look laparoscopy</p> <ol style="list-style-type: none"> 1. Incidence in participants with endometriomas 2. Severity in participants with endometriomas
Notes	<p>Trial supported by Johnson & Johnson</p> <p>Documentation: not stated</p> <p>Power calculations: not stated</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	At the end of the procedure and after haemostasis was achieved, 1 ovary was chosen on a random basis
Allocation concealment (selection bias)	Unclear risk	At the end of the procedure and after haemostasis was achieved, 1 ovary was chosen on a random basis
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear, as not stated in text
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of whether withdrawals or dropouts occurred during the study

van Geldorp 1994 (Continued)

Selective reporting (reporting bias)	Unclear risk	Data reported as mean area $\pm$ SEM. P values reported for significant outcomes. No subsets of data. No prepublication protocol for reference purposes
Other bias	Low risk	No other bias identified

Wallweiner 1998

Methods	Unit of randomisation: participant Method of randomisation: not stated Time of randomisation: at completion of surgery Blinding: yes
Participants	Women (n = 40) undergoing initial treatment for endometriosis by laparoscopy-vaporisation of peritoneal deposits, excision of endometrioma, reconstructive surgery and adhesiolysis No dropouts Mean age, years: 27 Preexisting adhesions: yes Cause of adhesions: endometriosis Microsurgery: no Location: Germany Timing: not stated 7 dropouts: 4 pregnant, 2 withdrew and 1 had such dense adhesions at laparoscopy of both ovaries that no assessment could be made Preexisting adhesions: nil Mean age, years: 28 No other cause for infertility found Timing: 1994 to 1995 Country: UK (1 centre)
Interventions	Oxidised regenerated cellulose applied to all injured visceral peritoneal surfaces of ovary, tubes and uterus vs no treatment Other adjuvants used: none Second-look laparoscopy 1. Timing: 3 to 6 months after initial surgery 2. Surgeon unaware: yes 3. Adhesiolysis: nil
Outcomes	Adhesions at second-look laparoscopy: 3 to 6 months later 1. Incidence (per participant) 2. Severity according to scoring system 3. Surface area 4. Extent: area, area differential, % improvement 5. Incidence in participants with endometriomas 6. Severity in participants with endometriomas Adverse outcomes: unknown Pregnancy: not stated
Notes	Power calculations: nil

Barrier agents for adhesion prevention after gynaecological surgery (Review)

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Wallweiner 1998 *(Continued)*

Sponsorship: not stated

Documentation: video

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear method of randomisation
Allocation concealment (selection bias)	Unclear risk	Not stated in text
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not stated in text
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of whether withdrawals or dropouts occurred during the study
Selective reporting (reporting bias)	Unclear risk	Data reported as numbers in a dichotomous score. P values stated. No conversion or subsets of data. No prepublication protocol for reference purposes
Other bias	Low risk	No other bias identified

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Diamond 1998	Excluded, as trial intervention was a solution—not a barrier
Dunn 2002	Excluded, as trial intervention was a solution—not a barrier
Korrell 1998	Excluded, as trial intervention was a solution—not a barrier
Korrell 2000a	Excluded, as trial intervention was a solution—not a barrier
Korrell 2000b	Excluded, as trial intervention was a solution—not a barrier
Reid 1993	Not an intervention that was sought by the objectives of the review
Reid 1997	Not an intervention that was sought by the objectives of the review
To 1992	Excluded, as no outcomes of interest to this review (fever and need for antibiotics)

DATA AND ANALYSES

Comparison 1. Oxidised regenerated cellulose (Interceed) vs no treatment at laparoscopy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of adhesions	6		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 De novo	3	360	Odds Ratio (M-H, Fixed, 95% CI)	0.50 [0.30, 0.83]
1.2 Reformation (or mixture)	3	100	Odds Ratio (M-H, Fixed, 95% CI)	0.17 [0.07, 0.41]

Analysis 1.1. Comparison 1 Oxidised regenerated cellulose (Interceed) vs no treatment at laparoscopy, Outcome 1 Incidence of adhesions.

Comparison 2. Oxidised regenerated cellulose (Interceed) vs no treatment at laparotomy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of adhesions	7		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 De novo	1	271	Odds Ratio (M-H, Fixed, 95% CI)	0.72 [0.42, 1.25]
1.2 Reformation (or mixture)	6	554	Odds Ratio (M-H, Fixed, 95% CI)	0.38 [0.27, 0.55]

Analysis 2.1. Comparison 2 Oxidised regenerated cellulose (Interceed) vs no treatment at laparotomy, Outcome 1 Incidence of adhesions.

Comparison 3. Expanded polytetrafluoroethylene (Gore-Tex) vs no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of adhesions	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 De novo	1	42	Odds Ratio (M-H, Fixed, 95% CI)	0.17 [0.03, 0.94]

Analysis 3.1. Comparison 3 Expanded polytetrafluoroethylene (Gore-Tex) vs no treatment, Outcome 1 Incidence of adhesions.

Comparison 4. Expanded polytetrafluoroethylene (Gore-Tex) vs oxidised regenerated cellulose (Interceed)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean adhesion score (non-validated score)	1	58	Mean Difference (IV, Fixed, 95% CI)	-3.79 [-5.12, -2.46]
2 Incidence of adhesions	2		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 De novo	1	38	Odds Ratio (M-H, Fixed, 95% CI)	0.93 [0.26, 3.41]
2.2 Re-formation (or mixture)	1	23	Odds Ratio (M-H, Fixed, 95% CI)	0.13 [0.02, 0.80]

Analysis 4.1. Comparison 4 Expanded polytetrafluoroethylene (Gore-Tex) vs oxidised regenerated cellulose (Interceed), Outcome 1 Mean adhesion score (non-validated score).

Analysis 4.2. Comparison 4 Expanded polytetrafluoroethylene (Gore-Tex) vs oxidised regenerated cellulose (Interceed), Outcome 2 Incidence of adhesions.

Comparison 5. Sodium hyaluronate and carboxymethylcellulose (Septrafilm) vs no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean adhesion score (non-validated score)	1	127	Mean Difference (IV, Fixed, 95% CI)	-0.49 [-0.53, -0.45]

Analysis 5.1. Comparison 5 Sodium hyaluronate and carboxymethylcellulose (Septrafilm) vs no treatment, Outcome 1 Mean adhesion score (non-validated score).

Comparison 6. Fibrin sheet vs no treatment at laparoscopic myomectomy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean adhesion score (non-validated score)	1	60	Mean Difference (IV, Fixed, 95% CI)	-0.14 [-0.67, 0.39]
2 Incidence of de novo adhesions per participant	1	62	Odds Ratio (M-H, Fixed, 95% CI)	1.2 [0.42, 3.41]

Analysis 6.1. Comparison 6 Fibrin sheet vs no treatment at laparoscopic myomectomy, Outcome 1 Mean adhesion score (non-validated score).

Analysis 6.2. Comparison 6 Fibrin sheet vs no treatment at laparoscopic myomectomy, Outcome 2 Incidence of de novo adhesions per participant.

APPENDICES

Appendix 1. MDSG search strategy

Menstrual disorders and subfertility (MDSG) specialised register search for CF333 25.06.12. Search was updated on 28 April 2014 and 16 February 2015.

Keywords CONTAINS "adhesion" or "adhesions" or "adhesions outcome" or "gynecologic surgical procedure" or "surgery-gynaecological" or "surgical complications" or "*Surgical-Procedures,-Laparoscopic" or "post-operative adhesions" or "post operative complications" or "cell adhesion molecules" or "laparoscopic" or "laparoscopy" or "laparotomy" or "myomectomy" or "mini-laparoscopy" or "mini-laparotomy" or "minilaparotomic myomectomy" or "minilaparotomy" or "cystectomy" or "hysterectomy" or "uterine artery embolization" or "UAE" or "pelvic adhesions" or "ovarian adhesions" or "ovarian cystectomy" or "endometrial ablation" or "endometrial adhesions" or "endometrioma" or "electrosurgery" or "electroresection" or "laparotomy" or "*Laser Surgery" or "salpingectomy" or "*Salpingostomy-" or "salpingotomy" or Title CONTAINS "adhesion" or "adhesions" or "adhesions outcome" or "surgical complications" or "*Surgical-Procedures,-Laparoscopic" or "post-operative adhesions" or "endometrial adhesions" or "pelvic adhesions"

AND

Keywords CONTAINS "Barrier Membrane" or "Gore-Tex" or "interceed" or "Polytetrafluoroethylene" or "Seprafilm" or "surgical membrane" or "dextran" or "adhesion barrier" or "adhesion barriers" or "adhesion prevention" or "adhesions outcome" or "surgical membrane" or "Oxiplex" or "SprayGel" or "adept" or "intercoat gel" or "sepracoat" or "adhesiolysis" or "polyethylene glycol" or "hydrogel" or "intergel" or "adhesions" or "adhesion" or "adhesiolysis" or Title CONTAINS "Barrier Membrane" or "Gore-Tex" or "interceed" or "Polytetrafluoroethylene" or "Seprafilm" or "surgical membrane" or "dextran" or "adhesion barrier" or "adhesion barriers" or "adhesion prevention" or "adhesions outcome" or "surgical membrane" or "Oxiplex" or "SprayGel" or "adept" or "intercoat gel" or "sepracoat" or "adhesiolysis" or "polyethylene glycol" or "hydrogel" or "intergel" or "adhesions" or "adhesion" or "adhesiolysis"

Appendix 2. MEDLINE search strategy

Search was on 25 June 2012, and updated on 28 April 2014 and 16 February 2015.

- 1 exp gynecologic surgical procedures/ or exp endometrial ablation techniques/ or exp hysterectomy/ or exp hysteroscopy/ or exp ovariectomy/ or exp salpingostomy/ or exp uterine artery embolization/ (63631)
- 2 (gyn\$ adj3 surg\$).tw. (7456)
- 3 exp cystoscopy/ (6182)
- 4 exp laparoscopy/ or exp ureteroscopy/ (69992)
- 5 laparoscop\$.tw. (81663)
- 6 (hysterectom\$ or cystoscop\$ or hysteroscop\$).tw. (37269)
- 7 endometrial ablation technique\$.tw. (38)
- 8 (ovariectom\$ or salpingostom\$).tw. (23185)
- 9 (ovar\$ adj2 surg\$).tw. (1527)
- 10 (uterine artery embolization or UAE).tw. (2683)
- 11 (pelv\$ adj5 surg\$).tw. (6767)
- 12 (ovar\$ adj5 cystect\$).tw. (441)
- 13 endometrioma\$.tw. (1493)
- 14 exp endometriosis/ (16563)

15 endometriosis.tw. (15749)
 16 fallopian\$.tw. (7901)
 17 exp Tissue Adhesions/ (10212)
 18 Adhesion\$.tw. (150768)
 19 myomectomy\$.tw. (2199)
 20 (ovar\$ adj2 defect\$).tw. (155)
 21 (ovar\$ adj2 cauter\$).tw. (31)
 22 microsurg\$.tw. (18648)
 23 adhesiolysis.tw. (980)
 24 electrosurg\$.tw. (2679)
 25 or/1-24 (382480)
 26 Interceed.tw. (115)
 27 tc7.tw. (248)
 28 exp polytetrafluoroethylene/ or exp proplast/ (9963)
 29 (polytetrafluoroethylene\$ or proplast\$).tw. (6529)
 30 (gore-tex or goretex).tw. (1815)
 31 (fibrin adj2 sheet\$).tw. (58)
 32 (surg\$ adj2 membrane\$).tw. (513)
 33 exp Cellulose, Oxidized/ (604)
 34 (Cellulose adj2 Oxidiz\$).tw. (510)
 35 (Cellulose adj2 Oxidis\$).tw. (47)
 36 70% dextran\$.tw. (13)
 37 (fibrin adj2 ceiling\$).tw. (0)
 38 barrier\$.tw. (161077)
 39 seprafilm\$.tw. (172)
 40 exp Membranes, Artificial/ (79577)
 41 (Artificial adj2 Membrane\$).tw. (2274)
 42 (surg\$ adj2 membrane\$).tw. (513)
 43 or/26-42 (252402)
 44 25 and 43 (7311)
 45 randomized controlled trial.pt. (371712)
 46 controlled clinical trial.pt. (88218)
 47 randomized.ab. (291593)
 48 placebo.tw. (157458)
 49 clinical trials as topic.sh. (169504)
 50 randomly.ab. (211409)
 51 trial.ti. (125395)
 52 (crossover or cross-over or cross over).tw. (60390)
 53 or/45-52 (918392)
 54 (animals not (humans and animals)).sh. (3836647)
 55 53 not 54 (846210)
 56 44 and 55 (275)
 57 (201206\$ or 201207\$ or 201208\$ or 201209\$ or 201210\$ or 201211\$ or 201212\$).ed. (690215)
 58 (2013\$ or 2014\$).ed. (1261715)
 59 (2013\$ or 2014\$).dp. (1311568)
 60 57 or 58 or 59 (2436277)
 61 56 and 60 (37)

Appendix 3. EMBASE search strategy

Search was on 25 June 2012, and updated on 28 April 2014 and 16 February 2015.

1 exp gynecologic surgery/ or exp pelvis surgery/ or exp uterine tube surgery/ or exp uterus surgery/ (131623)
 2 exp endometrium ablation/ (1783)
 3 exp hysterectomy/ or exp abdominal hysterectomy/ or exp vaginal hysterectomy/ or exp radical hysterectomy/ (45823)
 4 exp hysteroscopy/ (7502)
 5 exp ovariectomy/ (25394)
 6 exp salpingoplasty/ or exp salpingostomy/ (794)
 7 exp uterine artery embolization/ (1962)
 8 (gyn\$ adj3 surg\$).tw. (10032)
 9 exp cystoscopy/ (13431)
 10 exp laparoscopy/ (97153)

11 laparoscop\$.tw. (112851)
 12 (hysterectom\$ or cystoscop\$ or hysteroscop\$).tw. (50481)
 13 endometrial ablation technique\$.tw. (69)
 14 (ovariectom\$ or salpingostom\$).tw. (23821)
 15 (ovar\$ adj2 surg\$).tw. (2032)
 16 (uterine artery embolization or UAE).tw. (3817)
 17 (pelv\$ adj5 surg\$).tw. (9689)
 18 (ovar\$ adj5 cystect\$).tw. (741)
 19 endometrioma\$.tw. (2179)
 20 exp endometriosis/ (24479)
 21 endometriosis.tw. (20781)
 22 fallopian\$.tw. (8741)
 23 Adhesion\$.tw. (173518)
 24 myomectomy\$.tw. (3351)
 25 (ovar\$ adj2 defect\$).tw. (173)
 26 (ovar\$ adj2 cauter\$).tw. (39)
 27 microsurg\$.tw. (21219)
 28 adhesiolysis.tw. (1545)
 29 electrosurg\$.tw. (3197)
 30 or/1-29 (503733)
 31 exp oxidized regenerated cellulose/ (910)
 32 oxidized regenerated cellulose.tw. (250)
 33 Interceed.tw. (175)
 34 tc7.tw. (258)
 35 exp politef/ (14362)
 36 (polytetrafluoroethylene\$ or proplast\$).tw. (7006)
 37 (gore-tex or goretex).tw. (2340)
 38 (fibrin adj2 sheet\$).tw. (72)
 39 (surg\$ adj2 membrane\$).tw. (557)
 40 (Cellulose adj2 Oxidiz\$).tw. (586)
 41 (Cellulose adj2 Oxidis\$).tw. (57)
 42 70% dextran\$.tw. (12)
 43 (fibrin adj2 ceiling\$).tw. (0)
 44 barrier\$.tw. (182620)
 45 seprafilm\$.tw. (243)
 46 exp artificial membrane/ (64707)
 47 (Artificial adj2 Membrane\$).tw. (2441)
 48 (surg\$ adj2 membrane\$).tw. (557)
 49 exp tissue adhesive/ (13349)
 50 tissue adhesive\$.tw. (1570)
 51 or/31-50 (277315)
 52 30 and 51 (10255)
 53 Clinical Trial/ (830152)
 54 Randomized Controlled Trial/ (339988)
 55 exp randomization/ (61743)
 56 Single Blind Procedure/ (18122)
 57 Double Blind Procedure/ (112709)
 58 Crossover Procedure/ (38578)
 59 Placebo/ (237586)
 60 Randomized controlled trial\$.tw. (96717)
 61 Rct.tw. (13563)
 62 random allocation.tw. (1291)
 63 randomly allocated.tw. (19910)
 64 allocated randomly.tw. (1905)
 65 (allocated adj2 random).tw. (709)
 66 Single blind\$.tw. (14030)
 67 Double blind\$.tw. (138819)
 68 ((treble or triple) adj blind\$).tw. (358)
 69 placebo\$.tw. (194692)
 70 prospective study/ (247120)
 71 or/53-70 (1345024)
 72 case study/ (25459)

73 case report.tw. (255290)
74 abstract report/ or letter/ (885822)
75 or/72-74 (1161053)
76 71 not 75 (1307692)
77 52 and 76 (699)
78 (201206\$ or 201207\$ or 201208\$ or 201209\$ or 201210\$ or 201211\$ or 201212\$).em. (155774)
79 (2013\$ or 2014\$).em. (2104988)
80 (2013\$ or 2014\$).dp. (244153)
81 78 or 79 or 80 (2261481)
82 77 and 81 (92)

Appendix 4. CENTRAL search strategy

Search was on 25 June 2012, and updated on 28 April 2014 and 16 February 2015.

1 exp gynecologic surgical procedures/ or exp endometrial ablation techniques/ or exp hysterectomy/ or exp hysteroscopy/ or exp ovariectomy/ or exp salpingostomy/ or exp uterine artery embolization/ (3154)
2 (gyn\$ adj3 surg\$).tw. (1373)
3 exp cystoscopy/ (194)
4 exp laparoscopy/ or exp ureteroscopy/ (3340)
5 laparoscop\$.tw. (5707)
6 (hysterectom\$ or cystoscop\$ or hysteroscop\$).tw. (3109)
7 endometrial ablation technique\$.tw. (3)
8 (ovariectom\$ or salpingostom\$).tw. (130)
9 (ovar\$ adj2 surg\$).tw. (121)
10 (uterine artery embolization or UAE).tw. (267)
11 (pelv\$ adj5 surg\$).tw. (410)
12 (ovar\$ adj5 cystect\$).tw. (37)
13 endometrioma\$.tw. (77)
14 exp endometriosis/ (452)
15 endometriosis.tw. (784)
16 fallopian\$.tw. (266)
17 exp Tissue Adhesions/ (236)
18 Adhesion\$.tw. (2431)
19 myomectomy\$.tw. (213)
20 (ovar\$ adj2 defect\$).tw. (5)
21 (ovar\$ adj2 cauter\$).tw. (7)
22 microsurg\$.tw. (294)
23 adhesiolysis.tw. (58)
24 electrosurg\$.tw. (163)
25 or/1-24 (14783)
26 Interceed.tw. (28)
27 tc7.tw. (22)
28 exp polytetrafluoroethylene/ or exp proplast/ (409)
29 (polytetrafluoroethylene\$ or proplast\$).tw. (362)
30 (gore-tex or goretex).tw. (81)
31 (fibrin adj2 sheet\$).tw. (3)
32 (surg\$ adj2 membrane\$).tw. (94)
33 exp Cellulose, Oxidized/ (37)
34 (Cellulose adj2 Oxidiz\$).tw. (43)
35 (Cellulose adj2 Oxidis\$).tw. (6)
36 70% dextran\$.tw. (5)
37 (fibrin adj2 ceiling\$).tw. (0)
38 barrier\$.tw. (3662)
39 seprafilm\$.tw. (19)
40 exp Membranes, Artificial/ (922)
41 (Artificial adj2 Membrane\$).tw. (47)
42 (surg\$ adj2 membrane\$).tw. (94)
43 or/26-42 (5014)
44 25 and 43 (185)
45 limit 44 to yr="2012 -Current" (8)

Appendix 5. PsycINFO search strategy

Search was on 25 June 2012, and updated on 28 April 2014 and 16 February 2015.

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1 exp Postsurgical Complications/ (638)
2 Adhesion$.tw. (2076)
3 adhesiolysis.tw. (13)
4 exp Cell Adhesion Molecules/ (434)
5 or/1-4 (2749)
6 Interceed.tw. (0)
7 (polytetrafluoroethylene$ or proplast$).tw. (7)
8 (gore-tex or goretex).tw. (3)
9 (fibrin adj2 sheet$).tw. (0)
10 (surg$ adj2 membrane$).tw. (1)
11 (Cellulose adj2 Oxidiz$).tw. (1)
12 dextran$.tw. (372)
13 barrier$.tw. (39714)
14 (Artificial adj2 Membrane$).tw. (17)
15 antiadhesi$.tw. (3)
16 or/6-15 (40073)
17 5 and 16 (125)
18 limit 17 to yr="2012 -Current" (37)
19 random.tw. (40288)
20 control.tw. (312789)
21 double-blind.tw. (17774)
22 clinical trials/ (7486)
23 placebo/ (3743)
24 exp Treatment/ (576342)
25 or/19-24 (879728)
26 18 and 25 (5)

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WHAT'S NEW

Date	Event	Description
19 March 2015	New search has been performed	Review updated. One new study (Tinelli 2011) included
19 March 2015	New citation required but conclusions have not changed	We made no change to our conclusions at this update

HISTORY

Protocol first published: Issue 3, 1996

Review first published: Issue 1, 1999

Date	Event	Description
2 June 2008	Amended	Converted to new review format
20 December 2007	New citation required and conclusions have changed	Substantive amendments made
20 December 2007	New search has been performed	Review updated

CONTRIBUTIONS OF AUTHORS

Contributors to the original review and to the 2007 update included CF, AW, JD, AV, PV and DW.

In the 2015 update, contributions of the review authors included the following.

Gaity Ahmad (GA)

Main review author of the 2015 update; undertook search, screened search results, organised retrieval of papers, screened papers against inclusion criteria, extracted data from papers, managed and interpreted data and supervised HO'F throughout the process.

Helena O'Flynn (HO'F)

Co-review author of the 2015 update; organised retrieval of papers, screened papers against inclusion criteria, extracted data from papers and managed and interpreted data.

Andrew Watson (AW)

Supervised all stages of the 2015 review update.

Akshay Hindocha (AH)

Aided HO'F and GA in managing and interpreting data.

DECLARATIONS OF INTEREST

Previous review author David Wiseman was a past employee of Ethicon Limited (manufacturer of oxidised regenerated cellulose) and is now a consultant to several companies, including Ethicon.

SOURCES OF SUPPORT

Internal sources

- University of Auckland, New Zealand.

External sources

- Yorkshire Regional Health Authority—Research & Development Unit, Other.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The analysis method has been changed from Peto ORs to Mantel-Haenszel ORs.

The outcomes of "improvement of adhesion score at SLL" and "worsening of adhesion score at SLL/mean adhesion score at SLL" have been combined in the text for ease of presentation. This has not affected the analysis or the conclusions of this review.

INDEX TERMS

Medical Subject Headings (MeSH)

Cellulose, Oxidized [*therapeutic use]; Cervix Uteri [surgery]; Fibrin [administration & dosage]; Hyaluronic Acid [administration & dosage]; Infertility, Female [*surgery]; Pain, Postoperative [prevention & control]; Pelvis [surgery]; Polytetrafluoroethylene [*administration & dosage]; Postoperative Complications [*prevention & control]; Randomized Controlled Trials as Topic; Second-Look Surgery; Tissue Adhesions [prevention & control]; Viscosupplements [administration & dosage]

MeSH check words

Female; Humans