Epidemiology of adhesions: the burden

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Until recently the epidemiology of adhesion-related disease was unclear and lack of awareness of the clinical impact and extent of the problem has been cited as the greatest impediment to reducing adhesion formation. The clinical consequences and burden of disease are reviewed.

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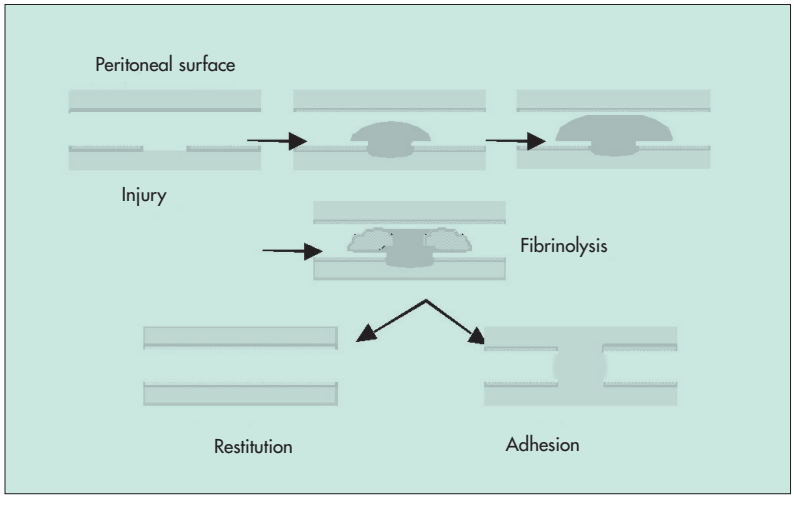
Postoperative adhesions are a major cause of morbidity and expense, an occasional cause of mortality and a potentially debilitating cause of chronic pain. They are associated with reduced quality of life, are an important complicating factor in reoperative surgery and impact negatively on clinical outcomes in patients undergoing surgery. While they are an everyday problem in clinical and surgical practice, most clinicians (including most surgeons) lack full awareness about adhesions because:

- Adhesive complications occur unpredictably up to decades after surgery
- They are often treated by physicians or specialists other than the initial operating surgeon
- The aetiology of adhesion formation remains incompletely understood
- The clinical consequences and associated impact have until recently been largely unknown.

Figure 1. Pathogenesis of adhesions. From Holmdahl (1999).



PATHOGENESIS

Adhesions are abnormal attachments between tissues and organs. Abrasion and other trauma leads to disruption of the mesothelium and fibrin is then deposited at the damaged surfaces by bleeding and post-traumatic inflammation, developing a bridge between opposing surfaces. Locally generated fibrinolytic factors are released which may degrade all or part of this fibrin bridge but surgery, infection and hypoxia dramatically diminish fibrinolytic activity – in this case, fibroblasts and other cells may migrate across the bridge remnants, transforming it into an adhesion (*Figure 1*).

The process of postoperative adhesion formation begins during surgery and while the severity and extent may change over weeks and months, the incidence of an adhesion, i.e. whether it develops at all, is determined within the first 5 days following peritoneal trauma.

Adhesions can be classified as congenital or acquired. The development of acquired adhesions is a generalized phenomenon in response to trauma to the delicate peritoneum. This peritoneal trauma causes inflammation. Infection (appendicitis, diverticulitis, pelvic inflammatory disease, regional enteritis, ulcerative colitis, tuberculosis), chemical irritation (spillage of dermoid cyst contents) and endometriosis (Holmdahl and Risberg, 1997; Diamond and Freeman, 2001) are all clinical events known to trigger adhesion formation. Surgical trauma causing adhesions includes exposure to infection or to intestinal contents, ischaemia, irritation from foreign materials such as sutures, gauze particles or glove dusting powder, abrasion (even very gentle wiping with a wet cotton gauze swab; H Ellis, unpublished data, 1996), desiccation, overheating by lamps or irrigation fluid.

Since many of these traumas are a routine reason for, or part of surgery, it is not surprising that the formation of postoperative adhesions ranges from common to nearly universal and that adhesions can form as a result of any surgery at any site.

RISK FACTORS FOR ADHESION DEVELOPMENT

Adhesions can occur at sites that have had no previous adhesion (de novo) or at sites of adhesiolysis (reformation). Furthermore, de novo adhesions can form at the site of surgery or at sites remote from the surgical site.

However, there is an important paradox in that the current method of managing adhesions – adhesiolysis – is complicated by further traumatic disruption and a high rate of adhesion reformation (85%), regardless of the method of adhesiolysis or the type of adhesion (Diamond and Freeman, 2001). Studies indicate that, compared with unaffected peritoneal tissue, adhesive tissue contains higher levels of growth factors, suggesting the greater likelihood of adhesion reformation. Since these factors depress fibrinolytic activity and induce tissue fibrosis, it is not surprising that reformed adhesions tend to be more dense and more severe than de novo adhesions (van der Krabben et al, 2000).

Previous laparotomy represents a major risk factor for adhesion development. Menzies and Ellis (1990) found that 93% of patients undergoing laparotomy develop adhesions attributable to earlier open surgery. More recently, Beck et al (2000) reported adhesions in 83% of patients who had previously undergone surgery compared with only 7% of patients undergoing initial surgery. Each additional laparotomy introduces de novo adhesions and encourages adhesion reformation. Of patients who had previously undergone surgery, 46% showed grade 3 (extensive, thick, vascular) or grade 4 (dense, bowel at risk of injury) adhesions compared with only 1% of patients undergoing initial surgery (Beck et al, 2000), suggesting that primary prevention may well be better than cure.

CLINICAL CONSEQUENCES OF POSTOPERATIVE ADHESIONS

Although it is not possible to identify which adhesions will create complications, logic and clinical observation (Menzies and Ellis, 1990; Menzies, 1993) indicate that those involving key organs and tissues, e.g. the small intestine or the uterus and adnexa, are the most likely to be symptomatic. Although the majority of postoperative adhesions are largely silent, the morbidity associated with adhesions generates significant complications for patients and a significant burden for health-care professionals.

Small bowel obstruction

Postoperative adhesions are the leading cause of intestinal obstruction in the western world (Menzies, 1993), producing more than 40% of all intestinal (Menzies, 1993) and up to 75% of small bowel obstructions (SBO) (Menzies, 1992). It is now recognized that all individuals who have undergone surgery involving the opening of the peritoneal cavity face a lifetime risk of SBO secondary to adhesion formation (Wilson et al, 1999). The mortality rate attributable to surgical treatment of adhesional obstruction has been estimated to be almost 10% (Menzies et al, 2001). Furthermore, this work has shown that in an average UK district general hospital adhesional SBO accounts for at least 10 extra emergency laparotomies, at least 2 additional days of theatre time per annum, and almost the equivalent of one bed occupied every day of the year (Menzies et al, 2001).

Infertility

Infertility represents a major morbidity that may occur as a result of adhesions associated with endometriosis, pelvic inflammatory disease, peritoneal infections or surgery (Diamond and Freeman, 2001). Postoperative adhesions occur in 60–90% of women who have undergone major gynaecological surgery (Monk et al, 1994; Liakakos et al, 2001) and account for 20–40% of cases of infertility (Mishell and Davajan, 1991; Diamond and Freeman, 2001). Consequently they are the second most common cause of female infertility.

Infertility may occur through intrauterine adhesions, but more commonly results from derangement of the normal tubo-ovarian relationship, thus preventing ovum capture and transport. Even grade 1 (thin, filmy, avascular) adhesions have the potential to distort this relationship (Diamond and Freeman, 2001). Only in recent years has the importance of endotubal health for fertility become apparent and many surgeons do not fully recognize the important consequences of what are otherwise considered to be relatively 'minor' adhesions.

Pain

Chronic pelvic pain as a result of adhesions has been a matter of discussion and debate as to the extent of the causative relationship. However, in an analysis of 12 studies (diZerega, 1997) including a total of nearly

1000 patients suffering from chronic pelvic pain, adhesions were the most common pathology, found in about 40% of cases.

The efficacy of surgery for the control of adhesion-related pain remains a subject of contention. A study in 2003 investigating the efficacy of laparoscopic adhesiolysis *vs* diagnostic laparoscopy reported significant pain relief in patients who underwent adhesiolysis. However, this reduction in pain did not differ from that in controls with the same symptoms, pain scores, and frequency and severity of adhesions who underwent diagnostic laparoscopy alone (Swank et al, 2003). The authors postulated that such reductions in pain may be, in part, a result of patients' emotional and mental attitudes to their health and to good doctor–patient relationships.

Re-operative complications

In addition to this morbidity and workload, post-surgical adhesions waste surgical time and operating theatre resources and increase the difficulty and risk of surgical re-entry (van der Krabben et al, 2000; Swank et al, 2003). Thus even if a patient has 'silent adhesions' there are considerable risks if they undergo surgery.

Enterotomy: In patients undergoing open adhesiolysis there is a 19% risk of inadvertent enterotomy (van der Krabben et al, 2000) with associated risk of postoperative complications including bowel obstruction, anastomotic leaks, wound dehiscence, sepsis and pneumonia, requiring longer hospital stays and admission to intensive care. The majority of injuries arise when dissecting adhesions between adherent intestinal loops. Pelvic adhesions are a greater risk. Subsequent work has shown the risk of bowel injury during laparoscopic adhesiolysis as between 10 and 25% (Swank et al, 2003).

Tissue damage to underlying structures has been shown to be the commonest cause of successful surgical negligence suits (Pownall, 1999) and in a study of misadventure data following laparoscopic surgery, while injury to the common bile duct was the most frequent, perforation of the small bowel or colon was the second most common injury and two thirds of injuries were initially missed and not recognized until after conclusion of the surgical procedure (Ferriman, 2000).

Increased surgical time: Two research groups have assessed the impact of previous open surgery on abdominal opening times and adhesiolysis. Both studies reported that previous laparotomy and the presence of adhesions significantly increased overall time in surgery by over 15 minutes (Beck et al, 2000; Coleman et al, 2000). Coleman et al (2000) found that post-surgical adhesions prolonged incision times by approximately 3 minutes and resulted in additional median division-of-adhesion times of 15 minutes.

EPIDEMIOLOGY OF ADHESION-RELATED READMISSIONS

Until recently the full extent of the burden of adhesion-related disease was unclear and lack of awareness of the clinical significance and frequency of adhesion formation has been cited as the greatest impediment to reducing adhesion formation (Diamond, 1988).

The unpredictable nature and time course of complications resulting from adhesions has made the epidemiological assessment of adhesive disease difficult to study. Initial research by Ellis (1983) used a retrospective review of case notes in a hospital to establish that post-surgical adhesions are the leading cause of intestinal obstruction. Adhesive intestinal obstruction in the UK accounted for 0.9% of all admissions and 3.3% of 4502 major laparotomies in a 24-year (1964–1988) study of 28 297 adult surgical admissions (Menzies and Ellis, 1990; Menzies, 1992). However, it was not until the publication of the Surgical and Clinical Adhesions Research (SCAR) study in 1999 that the burden and epidemiology of adhesions was well understood.

The SCAR study

The Scottish NHS Medical Record Linkage Database is a unique and robust tool for epidemiological research and was used by the SCAR study panel to allow 10-year follow up of nearly 30 000 patients undergoing surgery in 1986 (Ellis et al, 1999). This landmark study established the epidemiology of adhesions after open gynaecological and general surgery (lower and upper abdominal surgery) and the associated workload and cost burden.

The SCAR study identified that up to one in three patients (34.7%) were readmitted at least twice for adhesion-related problems or further unrelated surgery potentially complicated by adhesions over a 10-year period. Of those patients readmitted, 41.4% were readmitted between two and five times in the 10 years and 4.8% experienced six or more readmissions.

This research also indicated that open lower abdominal surgery procedures on the colon and rectum in general surgery (Parker et al, 2001), and fallopian tubes and ovaries in gynaecological surgery (Lower et al, 2000), were at most risk of adhesion-related readmissions.

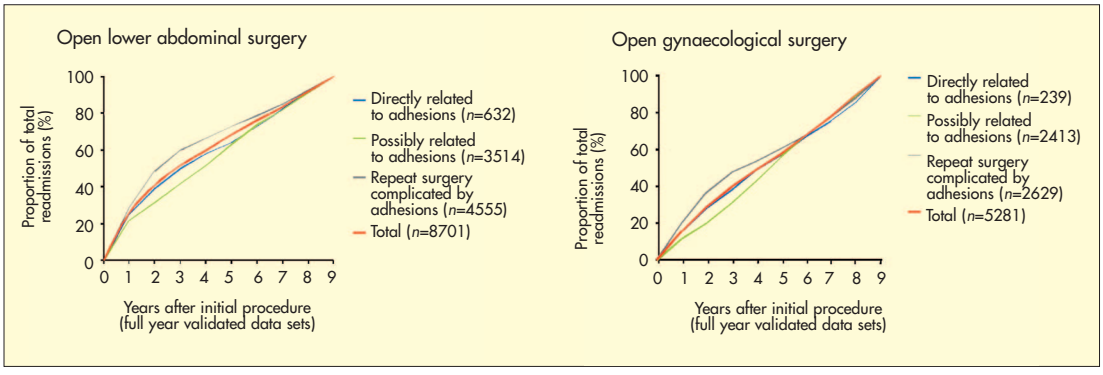


Figure 2. Timing of adhesion-related readmissions. From Lower et al (2000), Parker et al (2001).

Most adhesion-related readmissions occurred within the first year of surgery but thereafter readmissions continued steadily over the 10-year period of study with little sign of diminishing (*Figure 2*). The analysis did not investigate the effect of mortality and thus the individual risk of an adhesion-related readmission was underestimated.

In the 10 years following initial open lower abdominal surgery 7.3% of all readmissions were for events directly related to adhesions, including adhesiolysis with or without SBO, gynaecological adhesiolysis and adhesions treated non-operatively (Parker et al, 2001). This risk varied depending on the site of surgery, with rectal procedures associated with the highest risk (*Table 1*).

As part of the SCAR research, the prevalence of adhesion-related readmissions during 1994 was also assessed and the data compared with admissions for common surgical procedures from 1994 Scottish Health Statistics (the last available year of validated data at the time of the study). The data revealed that the number of admissions directly related to adhesions was similar to the numbers of admissions for appendix operations, hip replacements and coronary artery bypass grafts, indicating the extremely high prevalence and large impact of adhesion-related complications – something that had been completely unknown until this work (*Figure 3*) (Ellis et al, 1999).

The SCAR study was immediately heralded as being a landmark study, identifying the first detailed epidemiology of adhesion-related readmissions in an entire population and providing '…a cornerstone in delineating the problem' (Holmdahl, 1999).

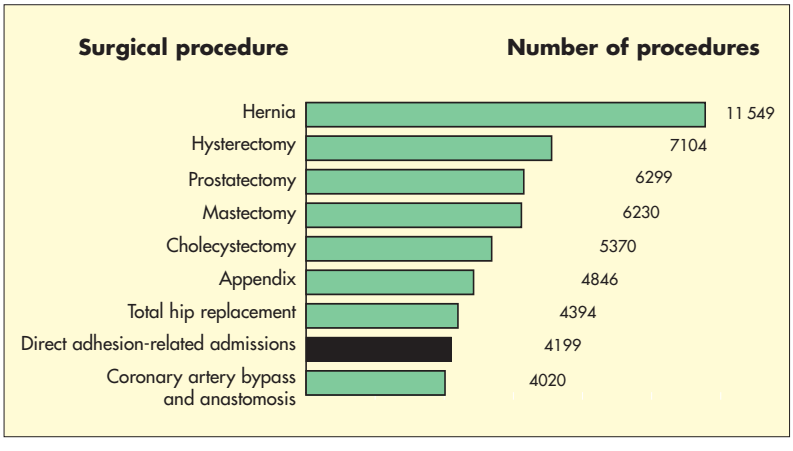
However, surgical practice has changed since the original study was initiated. The impact of therapeutic laparoscopic surgery, particularly in gynaecology, was not assessed in SCAR, because it was in its infancy and predominantly diagnostic in 1986. In addition the SCAR study did not address the risk to the patient of adhesions, but looked at the overall burden and workload. Patients who had undergone previous surgery were excluded, allowing assessment only of so-called 'virgin abdomens'. This eliminated the impact of pre-existing adhesions from previous surgery and in so doing may have underestimated the true impact of adhesions following abdominopelvic surgery.

TABLE 1.
Burden of adhesions

Site of initial surgery	Percentage of total readmissions
Rectum	8.8
Colon	7.1
Appendix	6.8
Small intestine	7.6
Abdominal wall	7.1
Ovaries	7.1
Fallopian tubes	4.9
Uterus	4.0

From Lower et al (2000), Parker et al (2001)

Figure 3. Relative importance of adhesion-related complications. From Ellis et al (1999).



SCAR-2

For these reasons, the SCAR-2 study was established to reassess the burden of adhesions following initial open surgery in 1996, focusing on gynaecological and lower abdominal surgery. The study also aimed, for the first time, to address the burden of adhesion-related events following laparoscopic surgery and compare it with that following open surgery. To determine whether these burdens had changed over time, the study compared incident surgery cohorts for the years 1996, 1997 and 1998. Importantly, unlike the original SCAR study, SCAR-2 also incorporated a direct evaluation of the risk – as well as the burden – of an adhesion-related readmission over time. SCAR-2 also examined the effects of previous surgery on adhesion-related events (Lower et al, 2004; Parker et al, 2004).

SCAR-2 colorectal epidemiology: The colorectal sub-analysis of the SCAR-2 (Parker et al, 2004) study showed a consistency between the three colorectal yearly cohorts in terms of the numbers of patients being readmitted for adhesion-related problems. Patients undergoing initial open colon and rectal surgery represented 37–38% of patients in the open lower abdominal surgery cohorts.

Rates of readmission following colorectal surgery were high and were highest within the first year. The rates of adhesion-related readmission episodes as opposed to the rates of patients readmitting were higher, suggesting that many patients were readmitted more than once within the first year for adhesion-related complications. The relative risk of a readmission episode directly or possibly related to adhesions following initial colorectal surgery in 1996 rose from 12.4% in year 1 to 29.7% in year 4, reflecting the high incidence of adhesion-related complications (*Figure 4*).

When patients who had undergone surgery within the previous 5 years were excluded from analysis, as expected, lower rates of readmission and readmission episodes were observed; rates were lower still when patients who had undergone surgery within the previous 15 years were excluded (*Figure 4*). The data reflect the substantial impact of previous surgery in increasing the risk of adhesion-related readmissions and complications, and highlight the considerable burden of adhesion-related events following colorectal surgery.

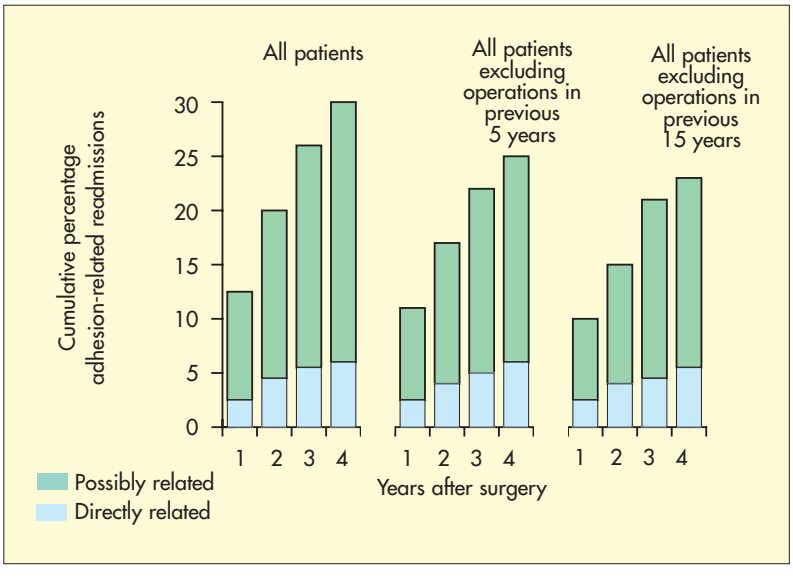
SCAR-2 gynaecological epidemiology: Adhesion-related readmission rates following open and laparoscopic gynaecological surgery were assessed. Patients undergoing initial open gynaecological procedures were categorized into groups undergoing surgery on the ovaries, fallopian tubes and uterus. As surgical coding for laparoscopic procedures is not as advanced as that for open surgery, patients undergoing gynaecological laparoscopy were categorized into low-, medium- and high-risk procedures – low risk equating to tubal sterilizations, high risk including adhesiolysis and ovarian cyst drainage procedures, with medium risk encompassing all other therapeutic and diagnostic laparoscopies (including other tubal procedures) that the SCAR-2 panel considered could be adhesiogenic procedures (Lower et al, 2004).

As with the SCAR-2 colorectal surgery findings, adhesion-related readmissions following gynaecological surgery were very similar in the three study year cohorts, indicating that little improvement in the rate of adhesion-related readmissions was achieved and showing that adhesions continue to have a significant and ongoing impact (*Figure 5*).

In the 1996 cohort, more than 7% of patients undergoing open gynaecological surgery were readmitted within 2 years for an event directly or possibly related to adhesions. However, of even more concern was the finding that 16.4% of patients undergoing high-risk laparoscopy were also readmitted within 2 years and this pattern was repeated in the three study cohorts (*Figure 5*).

The SCAR-2 study confirmed that open ovarian surgery and laparoscopic adhesiolysis are associated with the highest risks of adhesion-related readmissions. In considering the overall burden and impact of adhesions, however, one

Figure 4. Readmission episodes following abdominal surgery in 1996–97. From Parker et al (2004).



must take into account the incidence of high-, medium- and low-risk procedures. For example, open surgery on the ovaries (high risk) was associated with a 1 in 50 risk of a readmission directly related to adhesions, compared with a 1 in 120 risk associated with open procedures on the fallopian tubes (medium risk) and a 1 in 170 risk associated with open procedures on the uterus (low risk). However, given that open uterine procedures were performed nine times more frequently than procedures on the ovaries and fallopian tubes combined, low-risk open uterine surgery probably represents a greater overall burden in terms of adhesion-related events. This highlights the importance of adhesion-avoidance measures even during lower-risk procedures.

It has been suggested that laparoscopy is less adhesiogenic than laparotomy (Kavic, 2002); however, data from SCAR-2 show that the risks of adhesion-related readmissions associated with medium-risk (therapeutic and diagnostic) and high-risk (adhesiolytic) laparoscopic gynaecological procedures may be higher than those attributable to the most common open surgical procedures, such as open uterine surgery. Indeed around 40% of laparoscopic gynaecology cases had at least a comparable risk of adhesion-related readmission to laparotomy. Laparoscopic colorectal surgery is not yet as widespread as gynaecological laparoscopy but it may be surmised that it may not be less adhesiogenic than open colorectal surgery.

SCAR-2 implications: Data from both the colorectal and gynaecological surgery subgroups of the SCAR-2 study have shown no change in the rates of adhesion-related readmissions between 1996 and 1999. This indicates that the burden of adhesions has not been reduced, despite advances in surgical techniques since the original epidemiology was identified from the SCAR study in patients undergoing surgery in 1986 (Ellis et al, 1999; Lower et al, 2000; Parker et al, 2001). Adhesion-related complications are exerting a considerable and increasing impact on health-care resources and yet they still remain a largely unacknowledged problem and one that is not being adequately addressed.

THE COST BURDEN OF ADHESIONS

The SCAR study showed that in 1994 treatment costs for adhesion-related surgical procedures were over £6 million, representing 2% of Scottish expenditure on hospital and community sector services in 1994 (Parker, 1999). A subsequent cost-effectiveness model developed by Wilson and co-workers (2002), based on the SCAR data, predicted that the direct annual cost of adhesion-related readmissions for the UK as a whole within the first year after initial surgery would be in excess of £24.2 million, rising to £95.2 million in the tenth year after surgery. On a cumulative year-on-year basis direct costs of adhesion-related readmissions resulting from lower abdominal surgery for a 10-year period would then be more than £569 million.

Medicolegal litigation resulting from complications secondary to postoperative adhesion formation is adding to the economic costs to health authorities and the clinician's burden (Ellis, 2001).

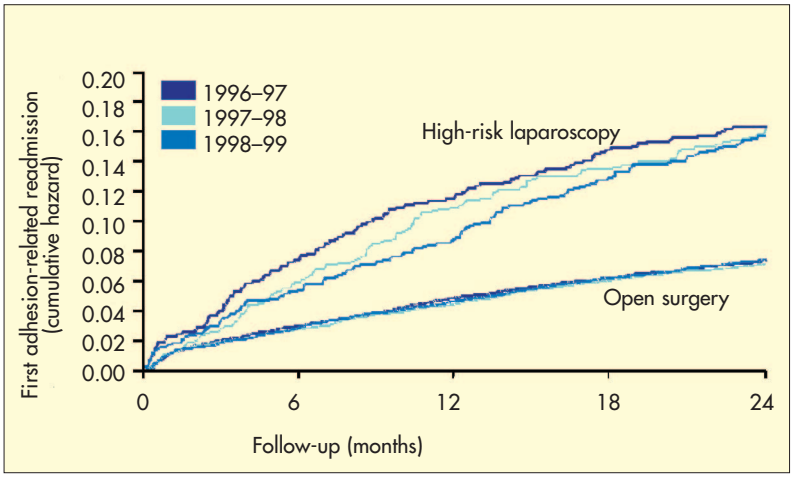
CONCLUSIONS

The natural history of adhesions has important consequences:

- For individual patients (lifelong risk of small bowel obstruction, infertility, chronic abdominal and/or pelvic pain, reoperative complications)
- For surgeons (increased workload, poor surgical outcomes, prolonged and complicated surgical procedures, postoperative complications, medicolegal risks)
- For health systems (impact on surgical throughput and theatre time, increased bed stays, and significant costs).

Since 1999 evidence regarding the epidemiological and economic burden of adhesions and their risk to patients has expanded considerably and it is clear from recent work by SCAR-2 that there has been little change in the epidemiology of adhesions even with advances in surgical techniques, including the advent of laparoscopic surgery. It is surely time for more focussed action and consideration of the routine use of the newer anti-adhesion agents in surgery known to carry a high risk of adhesion-related problems. HM

Figure 5. Risk of adhesion-related readmission for gynaecological surgery conducted in 1996, 1997 and 1998. From Lower et al (2004).



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Conflict of interest: Mr Parker has been involved in adhesions research for over 10 years as a member of the SCAR, SCAR-2 and SCAR-3 study panels. During this time he has been in receipt of research funding from Genzyme, ML Laboratories and Shire Pharmaceuticals. He has received honoraria from Genzyme, ML Laboratories, Britannia Pharmaceuticals, Baxter Healthcare and Shire Pharmaceuticals for attendance at meetings and participation in workshops on adhesion prevention strategies and studies. He is a member of the editorial panel of Adhesions News and Views.

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KEY POINTS

- Adhesions are a widespread problem and develop following any type of surgery – open or laparoscopic.
- Adhesions are a risk for patients and surgeons causing small bowel obstruction, infertility, chronic abdominal and/or pelvic pain, and reoperative complications including enterotomy, and extended theatre and hospital stay times.
- Adhesive complications occur unpredictably up to decades after surgery.
- Advances in surgery have had no impact on the burden of disease and without urgent action the serious morbidity and significant costs will grow.