**Draft Comparative Effectiveness Review**

**Number xx**

# Comparative Effectiveness of Surgical Options for Inguinal Hernia

**Prepared for:**
Agency for Healthcare Research and Quality
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# Preface

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We welcome comments on this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to epc@ahrq.hhs.gov.

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# Structured Abstract

**Objectives.** To review comprehensively the evidence to inform key decisions in the management of inguinal hernia in adults and pediatric patients. These questions included whether to repair a pain-free hernia or "wait-and-see"; whether to repair a painful hernia using an open or laparoscopic approach. If an open approach, which procedure; if a laparoscopic approach, which procedure; which type of mesh to use; which mesh fixation method (if any) to use; how prior experience with laparoscopic repair may be related to the risk of hernia recurrence; for pediatric hernia, whether to surgically explore a possible contralateral hernia or "wait-and-see"; and for pediatric hernia, whether to repair using an open or laparoscopic approach.

**Data Sources.** MEDLINE, PreMEDLINE, EMBASE, Cochrane Library, and reference lists. The last search date was May 13, 2011.

**Review Methods.** We refined the topic with Key Informants, and finalized the protocol with Technical Expert Panel members. Study inclusion criteria were determined a priori, as well as the risk of bias items. Study information was extracted into tables regarding general information, patient enrollment criteria, baseline characteristics, risk of bias items, and data. Meta-analysis was performed where appropriate, and the strength of evidence was rated for major comparisons and outcomes. Applicability was discussed by focusing on the population, interventions and settings of the included studies, separately for each clinical question.

**Results.** We included 207 publications describing 141 unique studies: 113 were RCTs, two were registries, and 26 had other designs included only for the laparoscopic surgical experience question. The evidence was international; only 11% of the studies were conducted exclusively in the U.S. The risk of bias was moderate for most outcomes in the RCTs, but high in the registries. For painless hernia, evidence was sufficient to permit the conclusion that quality of life at one year is better after surgery than watchful waiting. For painful primary hernias in adults, the risk of recurrence is lower after open surgery than after laparoscopy, whereas for recurrent hernia, this risk is lower after laparoscopic repair. Other outcomes, including short-term recovery and long-term pain, favored laparoscopic repair over open repair. Different open repair procedures generally yielded similar results, and transabdominal preperitoneal repair had the same or better outcomes than other laparoscopic procedures. Different meshes and different fixation approaches often show similar results. Many studies have reported that surgical experience lowers the risk of recurrence after laparoscopic repair, but the data were reported haphazardly and do not permit any estimate of the length of the learning curve. For pediatric hernia, no studies have compared surgical exploration for a contralateral hernia to watchful waiting, but comparing laparoscopy vs. open, outcomes generally favored laparoscopy.

**Conclusions.** This evidence review can be used by patients, families, and providers to improve decision-making about inguinal hernia. The applicability of our findings is limited to the types of populations, procedures, and settings in the included studies. The typical patient was a middle-aged man of average weight with primary unilateral inguinal hernia.

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# Comparative Effectiveness of Surgical Options for Inguinal Hernia

## *Executive Summary*

## Background

An inguinal hernia is a protrusion of abdominal contents into the inguinal canal through an abdominal wall defect. The lifetime rate of inguinal hernia is 25 percent in males and 2 percent in females.[1] The risk of inguinal hernia increases with age, and the annual incidence is around 50 percent in males by the age of 75.[2] Approximately 10 percent of cases are bilateral.[3] Recurrence occurs in approximately 1 percent to 5 percent of cases.[4] In children, the incidence ranges from 0.8 percent to 4.4 percent.[5] It is 10 times more common in boys and also more common in infants born before 32 weeks gestation (13% prevalence) and infants weighing less than 1,000 grams at birth (30% prevalence).[5]

Surgical repair of hernias is the most commonly performed general surgical procedure in the United States.[6] In 2003, an estimated 770,000 surgical repairs of inguinal hernia were performed.[6] These repairs are typically performed on an outpatient basis (87% in 1996).[6] Such a large volume of procedures suggests that even modest improvements in patient outcomes would have a substantial impact on population health.[7]

The primary goals of surgery include preventing recurrence of the hernia, returning the patient to normal activities quickly, and minimizing postsurgical discomfort and the adverse effects of surgery. The various surgeries present different constellations of benefits and risks, which presents some clinical uncertainty in the choice among approaches. Balancing these factors is a difficult yet critical process in an effort to make the best possible medical decisions.

Surgical procedures for inguinal hernia repair generally fall into three categories: open repair without the use of mesh (i.e., sutured), open repair with a mesh, and laparoscopic repair with a mesh. Within each of these categories, several specific procedures have been employed. Until the 1980s, open suture repair was the standard; however, the resulting tension along the suture line yielded relatively high rates of recurrence and patient discomfort. Nonsutured “tension-free” surgical mesh gained in popularity, and many specific open procedures were used. One author estimated that in 2003, 93 percent of groin hernia repairs involved the use of a mesh, and of these, about three-fourths of these repairs involved either a Lichtenstein repair or mesh plug.[6] Lichtenstein repair involves suturing the mesh in front of the hernia defect. Mesh plug repair involves a pre-shaped mesh plug being introduced into the hernia weakness during open surgery and a piece of flat mesh being positioned on top of the hernia defect. The near universal adoption of mesh means that the most important questions about hernia repair involve various mesh procedures.

In terms of settings, most hernia surgeries are performed not in specialized hernia centers, but rather by general surgeons who also perform many other types of surgeries.[8] It is generally recognized that the laparoscopic surgical repair of inguinal hernia is a highly specialized skill, and patients receiving care from more-experienced surgeons may be better than patients receiving care from less-experienced surgeons. The evidence review will specifically examine evidence on the association between laparoscopic surgical experience and hernia recurrence (see Key Questions below). The most commonly performed laparoscopic repair procedures are

transabdominal preperitoneal repair and totally extraperitoneal repair. Transabdominal preperitoneal repair involves entering the peritoneal cavity to place a mesh through an incision over likely hernia sites. Totally extraperitoneal (TEP) technique does not involve entering the peritoneal cavity, and a mesh is used to seal the hernia from the outside of the peritoneum.

Given the clinical uncertainty, a systematic review of the existing evidence on comparative effectiveness will help inform important medical decisions about surgical options for inguinal hernia. The findings of the review may impact clinical decisions by patients and surgeons, treatment recommendations by professional societies, purchasing decisions by hospitals, and coverage decisions by payers.

# Objectives

We sought to summarize thoroughly the evidence pertaining to nine Key Questions (listed below and presented graphically in Figure A):

**Among adults with *pain-free* primary inguinal hernias:**

Key Question 1. Does hernia repair differ from watchful waiting in patient-oriented effectiveness outcomes and/or adverse events?

**Among adults with painful inguinal hernias without incarceration/strangulation:**

Key Question 2. Does open hernia repair with a mesh differ from laparoscopic hernia repair with a mesh in patient-oriented effectiveness outcomes and/or adverse events?

a. For primary hernias?
b. For bilateral hernias?
c. For recurrent hernias?

Key Question 3. Do different open mesh-based repair procedures (e.g., Lichtenstein repair, mesh plug) differ in patient-oriented effectiveness outcomes and/or adverse events?

Key Question 4. Do different laparoscopic mesh-based repair procedures (e.g., transabdominal preperitoneal repair, totally extraperitoneal repair) differ in patient-oriented effectiveness outcomes and/or adverse events?

Key Question 5. Do different mesh products differ in patient-oriented effectiveness outcomes and/or adverse events?

Key Question 6. Do different mesh-fixation methods (e.g., no fixation, sutures, glue) differ in patient-oriented effectiveness outcomes and/or adverse events?

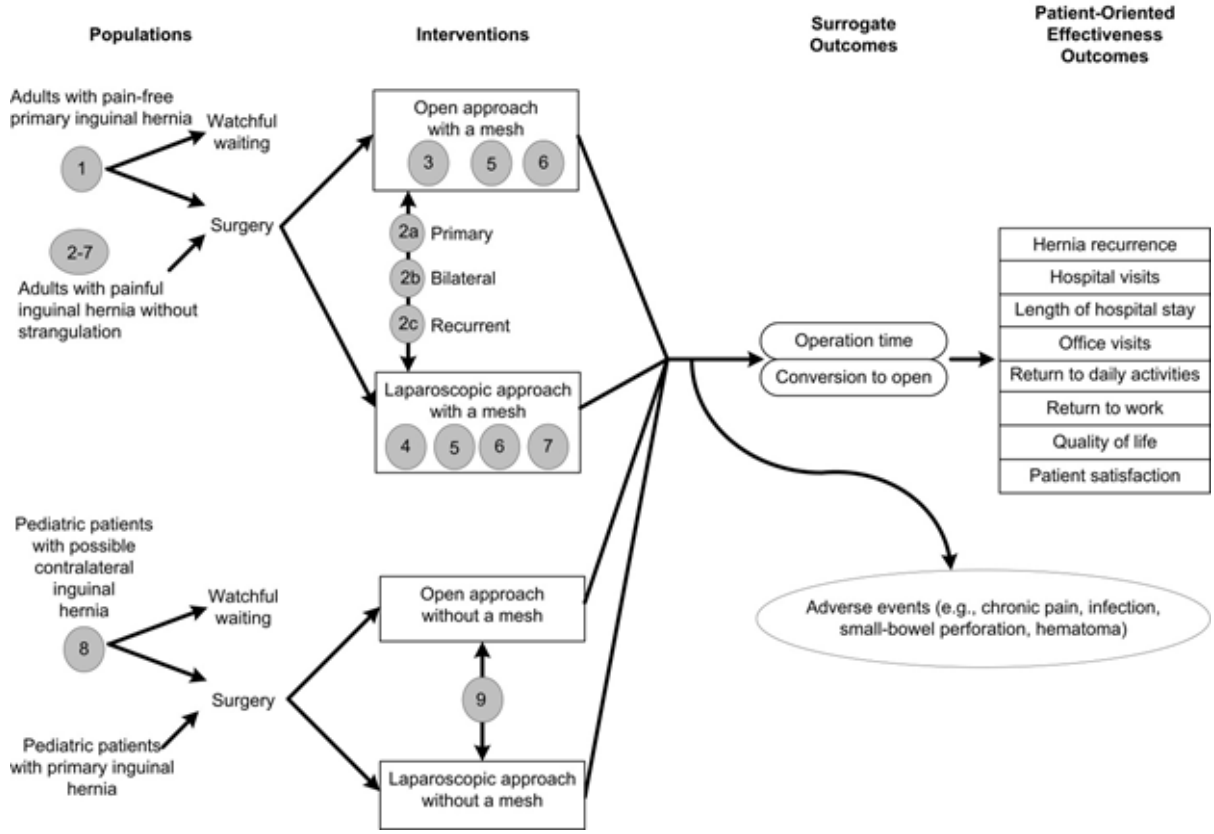
Key Question 7. For each type of laparoscopic mesh repair, what is the association between surgical experience and hernia recurrence?

**Among *pediatric* patients (age 21 years or younger):**

Key Question 8. For a possible contralateral hernia, does same-operation repair/exploration differ from watchful waiting in patient-oriented effectiveness outcomes and/or adverse events?

Key Question 9. Does open hernia repair without a mesh differ from laparoscopic hernia repair without a mesh in patient-oriented effectiveness outcomes and/or adverse events?

**Figure A. Analytic Framework**




# Methods

We developed and refined the topic in collaboration in late 2010 with five Key Informants: two hernia surgeons, two individuals from payer organizations, and one individual from a mesh manufacturer. We finalized the review protocol in the spring of 2011 based on input from four Technical Experts: three hernia surgeons, and a product specialist from a mesh manufacturer.

Literature searches were performed by Information Professionals within the Evidence-Based Practice Center Information Center, and followed established guidelines and procedures as identified by the Director of Health Technology Assessment/ Evidence-Based Practice Center Information Center. We searched the following: MEDLINE, PreMEDLINE, EMBASE, the Cochrane Library, including the Central Register of Controlled Trials, the Cochrane Database of Methodology Reviews, and the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, Health Technology Assessment Database, and the United Kingdom National Health Service Economic Evaluation Database. No limits on language were applied by the searchers, and search dates were established as January 1st 1990 to 2011. The date of the last search was May 13th, 2011.

For inclusion in the review, we selected only full articles published in English. For questions comparing interventions (i.e., all Key Questions except Key Question 7 on surgical experience), the study must have either randomized patients to treatments or used an analytic method to address selection bias, such as intentional baseline matching on multiple characteristics, propensity scoring, or other analytic approach. Studies could be prospective or retrospective, but retrospective studies must have used consecutive enrollment (or enrollment of a random sample

of eligible participants). The treatments being compared must have been administered during the same time period, so that any observed difference between treatment outcomes were not attributable to differential time frames. To be included for a given Key Question, the study must have provided data for which at least 85 percent of the patients had the condition specified in the Key Question. Criteria for reported data included data on at least one of the included outcomes for at least one of the Key Questions, outcome data must not have relied on retrospective recall, at least 6 months followup for hernia recurrence, quality of life, and patient satisfaction, and at least 10 patients with the condition of interest who represented at least 50 percent of eligible enrolled patients.

From each included study, we extracted all important information. This included author, publication year, country, study design, number of centers, dates of patient enrollment, type of setting, length of followup, funding source, which Key Question(s) the study addressed, all authors' reported patient enrollment criteria, specific procedure, specific mesh (if applicable), fixation method (if applicable), number of surgeons, surgeons' prior experience with the repair procedures performed, surgical setting (i.e., specialized hernia center or general surgery), type of anesthesia, methods of followup for data collection, and all reported baseline characteristics. We also extracted the numerical data necessary for us to compute an effect size (such as an odds ratio or standardized mean difference) and its standard error for all included outcomes for each study.

We assessed the risk-of-bias (i.e., internal validity) separately for each outcome and each time point of each study using 15 risk-of-bias items (e.g., randomization, concealment of allocation, blinding of outcome assessors, whether the surgeons had similar prior experience performing the study procedures; some studies involved one surgeon performing different procedures, whereas other studies assigned surgeons to procedures). Based on these items, each datapoint from each study was assigned a risk-of-bias category of Low, Moderate, or High. This was performed in duplicate, with disagreements resolved by consensus.

Within each treatment comparison, we examined all of the included outcomes from all of the relevant studies. The outcomes were divided into eight categories: hernia recurrence, hospital-related, including the length of hospital stay and subsequent hospital/office visits, the time to return to daily activities, the time to return to work, quality of life, patient satisfaction, pain including visual analog scale scores and the rates of chronic pain, and other adverse events not involving pain.

We performed meta-analysis wherever appropriate and possible. This decision depended on the judged clinical homogeneity of the different study populations, cointerventions, and outcomes, as well as whether studies reported the outcome in the same way. In the choice of effect size metrics, for hernia recurrence we used the relative risk because of its ease of interpretation and also because some studies only reported an adjusted relative risk. Thus, only a relative risk meta-analysis could include all of the studies. For all continuous outcomes we used the weighted mean difference, which is on the same scale as the measured outcome. For adverse events and pain reported dichotomously, we analyzed odds ratios.

To aid interpretation, for each outcome in the review we set the smallest difference between groups that can still be considered clinically significant (minimum clinically significant difference). For example, for the outcome of hernia recurrence we defined the minimum clinically significant difference as 3 percentage points (e.g., 1% vs. 4% for two separate treatments). This definition aids interpretation in two main ways: 1) to determine whether a

statistically significant difference is important and 2) to determine whether a statistically nonsignificant difference is small enough to exclude the possibility of an important difference.

If meta-analysis was deemed appropriate and possible for a given comparison and a given outcome, we performed DerSimonian and Laird random-effects meta-analysis using Comprehensive Meta-Analysis software (Biostat Inc., Englewood, NJ). To measure heterogeneity, we used both $I^2$ and tau. If there was substantial heterogeneity, and there were 10 or more studies of the same patient outcome of the same treatment comparison, we conducted meta-regressions using a variety of predictors (e.g., whether the study used concealment of allocation).

For major comparisons and outcomes, we rated the strength of evidence using the Evidence-Based Practice Center system described by Owens et al. This system includes four core domains (risk-of-bias, consistency, precision, and directness) as well as four optional domains (large magnitude of effect, all plausible confounders would reduce the effect, publication bias, and dose-response association). The directness domain does not encompass applicability, which is considered outside of the evidence rating system. The various domains were considered together using transparent rules to rate the evidence for the outcome as High, Moderate, Low, or Insufficient. We performed strength-of-evidence rating for all Key Questions except Key Question 7, which did not involve comparing treatments, but rather an assessment of the relationship between surgical experience and hernia recurrence.

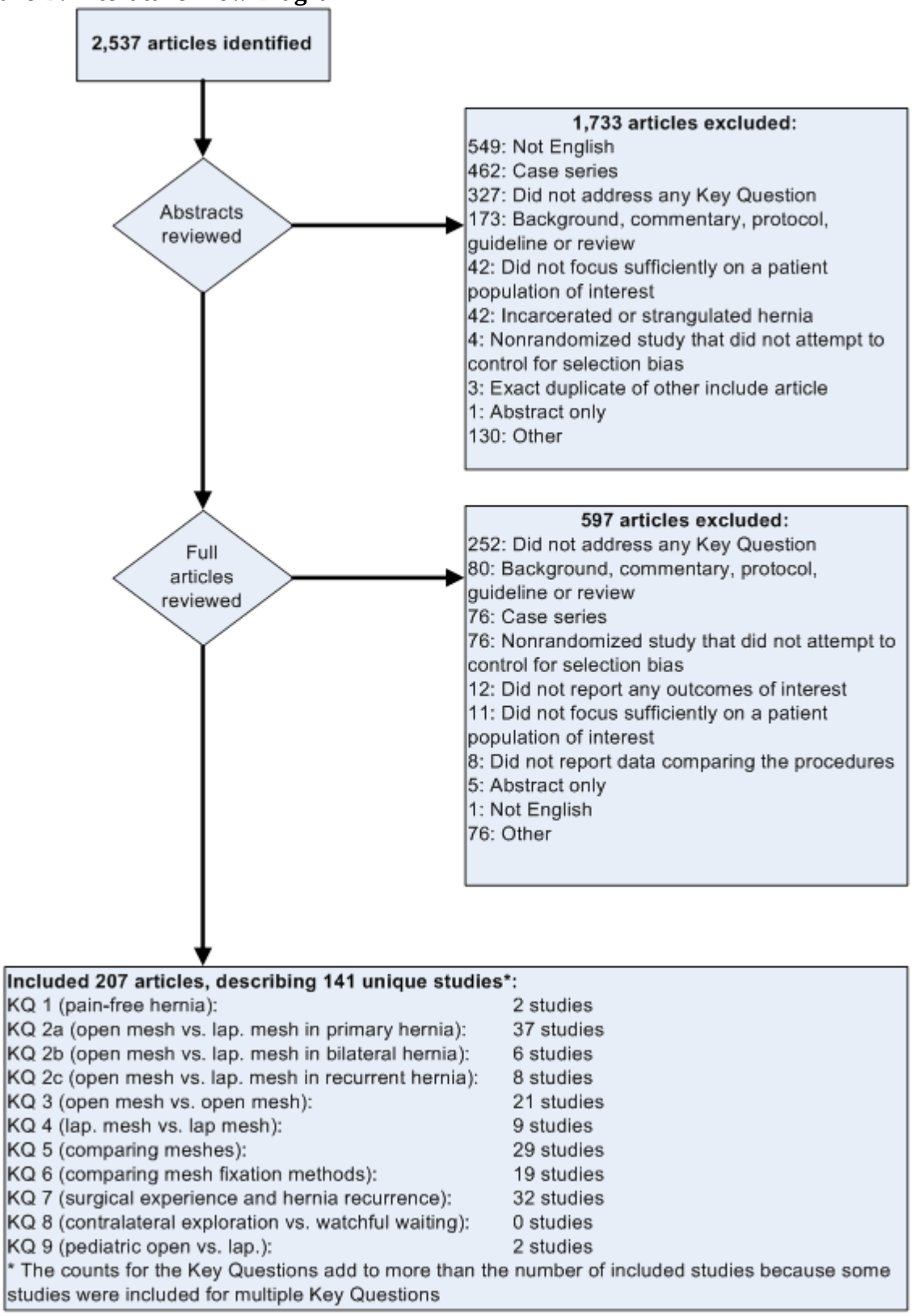
To assess applicability, we first abstracted data from each included study on factors that may affect the applicability of the study. Using the PICOTS approach as a guide, we primarily focused on three categories most relevant to inguinal hernia repair: 1) Population (demographic characteristics, comorbidity or general physical fitness, and types of hernia); 2) Intervention and comparators (inguinal repair procedure being compared, time frames of the procedure being performed, co-interventions, and experience of the surgical team); and 3) Setting (geographic and clinical factors). Based on a review of the data abstracted, we narratively summarized any patterns reflected from these factors that may potentially affect the applicability of the evidence. We made no attempt to generate any rating or score for the applicability of the evidence. Our narrative summaries were intended to draw stakeholders' attention to potential applicability issues embedded in the evidence.

# Results

Searches identified 2,537 potentially relevant articles and we excluded 1,337 of these at the abstract level (Figure B). At the full-article level we excluded another 597 articles, typically due to irrelevance to any of our Key Questions (252 publications), background/review/ commentary/protocol articles (80 publications), case series design (76 publications), or nonrandomized designs without any attempt to control for selection bias (76 publications). There remained 207 publications describing 141 unique studies that we included in our review. The largest number of studies addressed Key Question 2a (37 studies), which compared open mesh repair to laparoscopic mesh repair in patients with primary inguinal hernia. Other large evidence bases were found for Key Question 3 (comparing different procedures for open mesh repair, 21 studies), Key Question 5 (comparing meshes, 29 studies), and Key Question 7 (the association between laparoscopic hernia repair and hernia recurrence, 32 studies). No studies were identified for Key Question 8 (comparing surgical exploration vs. watchful waiting for pediatric contralateral inguinal hernia). Sixteen studies were included for multiple Key Questions

(e.g., two studies were each included for four Key Questions), because they included three or more groups or reported subgroup analyses.

**Figure B. Literature Flow Diagram**



**Key Question 1 (repair vs. watchful waiting for pain-free hernia)**

Two studies met inclusion criteria: one compared watchful waiting to Lichtenstein repair, and the other compared watchful waiting to "tension-free mesh repair" (which may have been Lichtenstein repair). Both studies were considered Moderate risk-of-bias.

For this Key Question, we considered the following outcomes to be major: long-term quality of life which was reported as "overall change in health status in previous 12 months", long-term pain, and acute hernia/strangulation. The evidence was sufficient to permit a conclusion for one of these outcomes: long-term quality of life, for which the results favored repair over watchful waiting.

**Key Question 2a (open vs. laparoscopic repair, primary hernia)**

Thirty-seven studies met inclusion criteria. Regarding specific surgical procedures, the most commonly compared procedures were transabdominal preperitoneal repair vs. Lichtenstein (14 studies), totally extraperitoneal repair vs. Lichtenstein (14 studies), transabdominal preperitoneal repair vs. mesh plug (three studies), totally extraperitoneal repair vs. mesh plug (three studies), and transabdominal preperitoneal repair / totally extraperitoneal repair vs. Lichtenstein (three studies). All but two studies (which were registry studies) were considered Moderate risk-of-bias.

For this Key Question, we considered the following outcomes to be major: hernia recurrence, length of hospital stay, return to daily activities, return to work, quality of life, patient satisfaction, long-term pain, epigastric vessel injury, small bowel injury, small bowel obstruction, urinary retention, hematoma, wound infection. The evidence was sufficient to permit the following conclusions:

- Five outcomes favored laparoscopy (return to daily activities, return to work, long-term pain, hematoma, and wound infection)
- Two outcomes favored open surgery (hernia recurrence and epigastric vessel injury)
- One outcome indicated approximate equivalence (length of stay)

**Key Question 2b (open vs. laparoscopic repair, bilateral hernia)**

Six studies met inclusion criteria. Three studies compared totally extraperitoneal repair to the Stoppa procedure, two compared transabdominal preperitoneal repair to Lichtenstein, and the Danish registry compared transabdominal preperitoneal repair / totally extraperitoneal repair to Lichtenstein (authors combined data on transabdominal preperitoneal repair and totally extraperitoneal repair procedures). All but one study (which was a registry study) were considered Moderate risk-of-bias.

For this Key Question, we considered as major the same outcomes as for Key Question 2a. The only outcome for which evidence was sufficient to permit a conclusion was return to work: bilateral hernia patients return to work sooner if they receive laparoscopic repair.

**Key Question 2c (open vs. laparoscopic repair, recurrent hernia)**

Eight studies met inclusion criteria. The open mesh procedure was Lichtenstein in six studies and the Stoppa procedure in the other two studies. For the laparoscopic mesh procedure, two studies performed transabdominal preperitoneal repair, two performed totally extraperitoneal repair, one performed both and reported data separately, and the other three performed both transabdominal preperitoneal repair and totally extraperitoneal repair and combined the data. All but two studies (which were registry studies) were considered Moderate risk-of-bias.

For this Key Question, we considered as major the same outcomes as for Key Question 2a. The evidence permitted conclusions for three outcomes, all of which favored laparoscopic repair

over open repair: hernia recurrence (lower rates after laparoscopy), return to daily activities (faster after laparoscopy), and long-term pain (lower rates after laparoscopy).

**Key Question 3 (comparing different types of open mesh repair)**

Twenty-one studies met inclusion criteria. For this Key Question, we considered the following comparisons to be major: Lichtenstein vs. mesh plug (seven studies), Lichtenstein vs. Prolene Hernia System (five studies), Lichtenstein vs. open preperitoneal mesh (three studies), mesh plug vs. Prolene Hernia (two studies), and Lichtenstein vs. Kugel patch (two studies). Most studies were considered Moderate risk of bias, except for the registry study, which was considered High risk of bias.

For each comparison, we considered the following outcomes to be major: hernia recurrence, length of hospital stay, return to daily activities, return to work, short-term pain, intermediate-term pain, seroma, urinary retention, hematoma, wound infection. Evidence was sufficient to permit the following conclusions:

- For Lichtenstein vs. mesh plug, recurrence rates are similar, but return to work and rates of seroma favor Lichtenstein
- For Lichtenstein vs. Prolene Hernia System, similar outcomes for short-term pain
- For Lichtenstein vs. open preperitoneal mesh, similar outcomes for short-term pain
- For mesh plug vs. Prolene Hernia System, similar outcomes for short-term pain
- For Lichtenstein vs. Kugel mesh, similar outcomes for short-term pain and intermediate-term pain

**Key Question 4 (comparing different types of laparoscopic mesh repair)**

Nine studies met inclusion criteria. For this Key Question, we considered two comparisons to be major: transabdominal preperitoneal repair vs. totally extraperitoneal repair, and transabdominal preperitoneal repair vs. Intraperitoneal onlay mesh. Most studies were considered Moderate risk of bias.

For each comparison, we considered the following outcomes to be major: hernia recurrence, length of hospital stay, return to daily activities, return to work, short-term pain, intermediate-term pain, urinary retention, hematoma, wound infection. Evidence was sufficient to permit the following conclusions

- For transabdominal preperitoneal repair vs. totally extraperitoneal repair, return to work favors transabdominal preperitoneal repair, and short-term pain data suggest equivalence.
- For transabdominal preperitoneal repair vs. Intraperitoneal onlay mesh, recurrence and length of stay data favor transabdominal preperitoneal repair

**Key Question 5 (comparing meshes)**

Twenty-nine studies met inclusion criteria. For this Key Question, we considered seven comparisons to be major: standard polypropylene vs. low-weight polypropylene (four studies), standard polypropylene vs. combination materials (15 studies), standard polypropylene vs. coated polypropylene (four studies), standard polypropylene vs. 3D PHS (two studies), standard polypropylene vs. porcine (two studies), combination materials vs. porcine (one study), and low-weight polypropylene vs. combination materials (one study). Most outcomes were considered Moderate risk of bias.

For this Key Question, we considered the following outcomes to be major: hernia recurrence, quality of life, patient satisfaction, long-term pain, feeling of a foreign body, infection, and bleeding. Standard polypropylene mesh had similar rates of recurrence as combination materials. Three types of meshes (standard polypropylene, low-weight polypropylene, and combination

materials) had approximately equivalent rates of long-term pain. Long-term pain was also similar between standard polypropylene and porcine.

**Key Question 6 (comparing fixation approaches)**

Nineteen studies met inclusion criteria. For this Key Question, we considered five comparisons to be major: tacks or staples vs. no fixation (six studies), fibrin glue vs. staples (four studies), sutures vs. tacks (three studies), sutures vs. glue (four studies), and absorbable sutures (short or long term) vs. nonabsorbable sutures (one study). Most studies were considered Moderate risk of bias.

For this Key Question, we considered as major the same outcomes as for Key Question 5. We found approximate equivalence in recurrence rates for glue vs. staples. Also, long-term pain was approximately equivalent between glue and staples.

**Key Question 7 (surgical experience and hernia recurrence)**

Thirty-two studies met inclusion criteria. Sixteen involved only totally extraperitoneal repair; 12 involved only transabdominal preperitoneal repair; one reported separate data on totally extraperitoneal repair and transabdominal preperitoneal repair; and three provided combined data on transabdominal preperitoneal repair and totally extraperitoneal repair. Most studies failed to report data that factored out the length of followup (patients treated earlier in the series may have had higher recurrence rates simply because they were followed longer). Some studies reported changing important procedural aspects over time, such as the size of the mesh (which typically involved the use of larger meshes in later time periods), making it difficult to pinpoint the true impact of expertise.

Among studies comparing an early set to later set(s) of repairs, the size of the early set varied from a low of 10 repairs to a high of 825 repairs. It was unclear how authors chose their cutpoints. The reporting differences mean that one cannot use the data to estimate the length of the learning curve for totally extraperitoneal repair or transabdominal preperitoneal repair in the context of hernia repair. Most studies reported results in the expected direction: lower recurrence rates with increased experience. This was also true when examined more specifically for totally extraperitoneal repair (11/17 studies) and transabdominal preperitoneal repair (11/13 studies).

**Key Question 8 (exploration vs. watchful waiting for pediatric hernia)**

No studies met inclusion criteria.

**Key Question 9 (open vs. laparoscopic for pediatric hernia)**

Two studies met inclusion criteria. Regarding patient age criteria, one study enrolled patients aged 4 months to16 years, the other study enrolled patients aged 3 months to 9 years. Both studies were considered Moderate risk-of-bias.

For this Key Question, we considered the following outcomes to be major: hernia recurrence, length of hospital stay, return to daily activities, patient/parent satisfaction. The evidence was sufficient to permit the conclusions that length of stay, long-term patient satisfaction, and long-term cosmesis each favor laparoscopy, and return to daily activities data suggest equivalence.

# Discussion

The typical adult in the included studies was a man in his mid-50s of average weight suffering from a primary unilateral hernia. About a quarter of the men worked in physically strenuous jobs; for these men, a durable repair is relatively important in order to prevent a

recurrence. Our review can inform numerous treatment decisions faced by these men. These treatment decisions include:

- Whether to undergo surgery in the first place, or wait
- Whether to choose open surgery or laparoscopic surgery
- Which type of open surgery
- Which type of laparoscopic surgery
- Choosing among meshes or fixation approaches
- Consideration of expertise with laparoscopic hernia repair

The evidence-based conclusions listed in the previous section are only applicable to the types of patients enrolled in the studies underlying those conclusions. For example, for Key Questions 2-7, the large majority of enrolled patients were middle-aged men, therefore the conclusions do not apply to women or to men of other ages. Similarly, for Key Question 9 on pediatric hernia open vs. laparoscopic repair, both studies excluded cases less than 3 months old, and so the conclusions do not apply to patients younger than 3 months old.

One limitation of this review is that we only included studies published in English. In an attempt to address this issue, we summarized the abstracts from non-English literature that may have potentially been included for each Key Question. Another limitation of this review is that for many outcomes, the evidence was inconclusive due to low precision. In general, the included studies were well-conducted, but small. We maximized the power of the data by conducting meta-analyses wherever appropriate and possible. Nevertheless, the data often precluded conclusions, because they suggested contradictory conclusions (i.e., that the evidence could favor option A or option B by a clinically significant amount). A third limitation is that no studies met our inclusion criteria for Key Question 8 on pediatric contralateral hernia. No studies have compared surgical exploration with watchful waiting in this population. Therefore, we described informally some of the existing research in this area, such as the percentage of pediatric patients with a unilateral inguinal hernia who have a contralateral patent processus vaginalis (which is a risk factor for inguinal hernia).

# Future Research Needs

Much of the existing literature on inguinal hernia has been conducted outside the United States. The differences in healthcare systems and practice patterns between the United States and other regions may potentially have an impact on the applicability of the evidence from the perspectives of the United States stakeholders. Future United States studies should define the unique needs of the United States population, describe how its needs may differ from those of Europeans (who comprise the majority of patients in studies conducted outside the United States), and target research to these unique areas. Surgical registry may help to define unique needs, but existing registries may be inadequate because they are voluntary.

A large registry may also help address a widespread problem we encountered in our evidence review: low precision. Many randomized trials have investigated important questions, but their modest size limits the usefulness of the data. Rare events, such as hernia recurrence, require much larger sample sizes in order to permit clear inferences. Registry data require sophisticated analytic techniques, such as propensity scores or instrumental variables, in order to reduce selection bias. The registries that we assessed (e.g., Swedish Hernia Registry) were quite large (e.g., 143,000 hernias), but authors did not utilize these techniques, so it was difficult to determine the potential impact of selection bias.

Another key focus of future research should be on recurrence rates in the *very long-term*. The typical patient was middle-aged, so he likely has a few decades of life ahead. Studies have not generally reported recurrence rates past 5-10 years, but conceivably patients and clinicians would be interested in much longer timeframes (e.g., 30 years). Projection factors have been proposed (e.g., to estimate the 25-year recurrence rates, multiply the one-year rate by 5), however they have not been tested empirically. We also encourage greater focus on outcomes that matter most to patients, such as chronic pain, long-term quality of life, satisfaction, and the feeling of a foreign body. These outcomes may be associated with the type of mesh or mesh fixation methods, but our evidence review neither revealed nor ruled out key components, due to low precision. Specific recommendations for future research addressing the Key Questions appear in the main document.

# Introduction

An inguinal hernia is a protrusion of abdominal contents into the inguinal canal through an abdominal wall defect. A direct inguinal hernia protrudes through the deep inguinal ring, whereas an indirect inguinal hernia protrudes through the internal inguinal ring and may descend through the inguinal canal. Direct hernias typically develop only in adulthood and are more likely to recur than indirect hernias.[9] If the hernia is severe enough to restrict blood supply to the intestine, it is termed a strangulated hernia, and immediate corrective surgery is necessary. Most inguinal hernias, however, are less dangerous, and elective surgery is often performed to correct the defect. Symptoms include abdominal pain and a lump in the groin area, which is most easily palpable during a cough. Some inguinal hernias, however, are asymptomatic.[10]

The lifetime rate of inguinal hernia is 25 percent in males and 2 percent in females.[1] The risk of inguinal hernia increases with age, and the annual incidence is around 50 percent in men by the age of 75.[2] Approximately two-thirds of inguinal hernias are indirect, and one-third are direct.[1] Approximately 10 percent of cases are bilateral.[3] Recurrence occurs in approximately 1 percent to 5 percent of cases.[4]

In children, the incidence ranges from 0.8 percent to 4.4 percent.[5] It is 10 times more common in boys and also more common in infants born before 32 weeks gestation (13% prevalence) and infants weighing less than 1,000 grams at birth (30% prevalence).[5] As in adults, about 10 percent of cases involve bilateral hernia.[11]

Numerous classification systems have been proposed for groin hernias.[12] One commonly used system was introduced by Nyhus in 1993.[13] This system employs several clinical factors including direct/indirect, degree of enlargement of the internal inguinal ring, and degree of posterior wall weakness. Specifically, it comprises six types of increasing severity: 1) indirect inguinal hernia with a normal internal ring; 2) indirect inguinal hernia with an enlarged internal ring; 3a) direct inguinal hernia; 3b) indirect inguinal hernia causing posterior wall weakness; 3c) femoral hernia; and 4) recurrent hernia.[13] (This review will not involve femoral hernias due to the different patient populations and pertinent treatments.) Stoppa[14] proposed that aggravating factors such as obesity or abdominal distension should upgrade the patient by one Nyhus level.[14] Higher severity generally means a higher risk of recurrence, and an appropriate classification may support the management approach.

Surgical repair of hernias is the most commonly performed general surgical procedure in the United States.[6] In 2003, an estimated 770,000 surgical repairs of inguinal hernia were performed.[6] These repairs are typically performed on an outpatient basis (87% in 1996).[6] This large volume of procedures suggests that even modest improvements in patient outcomes would have a substantial impact on population health.[7]

The primary goals of surgery include preventing recurrence of the hernia, returning the patient to normal activities quickly, and minimizing postsurgical discomfort and the adverse effects of surgery. The various surgeries present different constellations of benefits and risks, which presents some clinical uncertainty in the choice among approaches. Balancing these factors is a difficult yet critical process in an effort to make the best possible medical decisions.

Some patients with inguinal hernias may not be in pain or limited in any way by the hernia. For these patients, surgery may not be necessary. One of the Key Questions (KQs) in the evidence review will be a comparison between surgical and nonsurgical approaches to the management of pain-free inguinal hernias.

Surgical procedures for inguinal hernia repair generally fall into three categories: open repair without the use of mesh (i.e., sutured), open repair with a mesh, and laparoscopic repair with a mesh. Within each of these categories, several specific procedures have been employed. Until the 1980s, open suture repair was the standard; however, the resulting tension along the suture line yielded relatively high rates of recurrence and patient discomfort. Nonsutured "tension-free" surgical mesh gained in popularity, and many specific open procedures were used. One author estimated that in 2003, 93 percent of groin hernia repairs involved the use of a mesh, and of these, about three-fourths of these repairs involved either a Lichtenstein repair or mesh plug.[6] Lichtenstein repair involves suturing the mesh in front of the hernia defect. Mesh plug repair involves a pre-shaped mesh plug is introduced into the hernia weakness during open surgery and a piece of flat mesh is positioned on top of the hernia defect. The near universal adoption of mesh means that the most important questions about hernia repair involve various mesh procedures. A glossary of several other open repair procedures, as well as laparoscopic procedures, appears after the Reference section.

Almost all surgical procedures in adults involved the use of a synthetic mesh to cover the defect. However, mesh is not recommended for use in pediatric inguinal hernia due to concerns about the risk of inflammatory reactions, damage to the vas deferens and/or testes, and infertility.[5]

More recently, two laparoscopic approaches using a mesh—transabdominal preperitoneal repair (TAPP) and totally extraperitoneal repair (TEP)—have seen increased use.[15] Transabdominal preperitoneal repair involves entering the peritoneal cavity to place a mesh through an incision over likely hernia sites. Totally extraperitoneal (TEP) technique does not involve entering the peritoneal cavity, and a mesh is used to seal the hernia from the outside of the peritoneum. Laparoscopic approaches have the potential for shortening recovery time and reducing some postoperative morbidities.[16] They also may be associated with longer operation times and a relatively long learning curve. TEP was introduced after TAPP due to concerns about a possible increased risk of internal organ damage within the peritoneum.

Previous research has shown that the repair of a recurrent inguinal hernia is subject to a greater risk of additional recurrence.[17] Further, bilateral inguinal hernia is subject to a greater recurrence risk than unilateral inguinal hernia.[18] These increased risks may be due to certain anatomical difficulties that complicate the surgical approach in these types of patients.[19] Some clinicians have suggested that laparoscopic approaches are better suited to recurrent and bilateral hernias, and in Key Question 2 (see below) we delineate separate comparisons for primary, bilateral, and recurrent hernia.

Specific aspects about mesh repair that may influence outcomes are the type of mesh (e.g., polypropylene or other material), whether mesh fixation is used, and if so, whether fixation is accomplished with sutures or glue. These mesh-specific issues are covered by specific Key Questions (see Key Questions below).

Different procedures often require different methods for anesthesia. Some forms of open mesh repair can be performed with local anesthesia, whereas laparoscopic techniques such as TAPP often require general anesthesia.[8] Two key postsurgical morbidities are surgical site infection[20] and chronic pain.[21] Sanabria et al.[20] found that without prophylactic antibiotics, surgical site infections occurred in 2.9 percent of patients having undergone mesh repair, as compared to only 1.4 percent among those who received prophylactic antibiotics. Regarding chronic pain, Nienjuis et al.[21] estimated that pain lasting beyond 3 months postoperatively occurs in 11 percent of patients undergoing mesh repair.

In terms of settings, most hernia surgeries are performed not in specialized hernia centers, but rather by general surgeons who also perform many other types of surgeries.[8] It is generally recognized that the surgical repair of inguinal hernia is a highly specialized skill, and patients receiving care from more-experienced surgeons may be better than patients receiving care from less-experienced surgeons. The evidence review will specifically examine evidence on the association between surgical experience and hernia recurrence (see Key Questions below). Also regarding setting, most inguinal hernia repairs are conducted in an outpatient setting.[6] Rutkow, 2003[6] stated: "In 1996, numbers from the combined surveys showed that 87% of inguinal hernias were completed on an outpatient basis. In view of changing market forces it must be assumed that the percentage is even higher in 2003."

Given the clinical uncertainty, a systematic review of the existing evidence on comparative effectiveness will help inform important medical decisions about surgical options for inguinal hernia. The findings of the review may impact clinical decisions by patients and surgeons, treatment recommendations by professional societies, purchasing decisions by hospitals, and coverage decisions by payers.

# Methods

## Topic development and refinement

Development and refinement of the topic occurred between 6/16/2010 and 10/15/2010. This process involved a review of this clinical area, devising an initial analytic framework and list of Key Questions, obtaining the input of five Key Informants, revising the Key Questions and scope based on feedback received, and posting for public comment. The Key Informants included one surgeon with expertise in adult hernia surgery, another surgeon with expertise in pediatric hernia surgery, two individuals from payer organizations, and one individual from a mesh manufacturer.

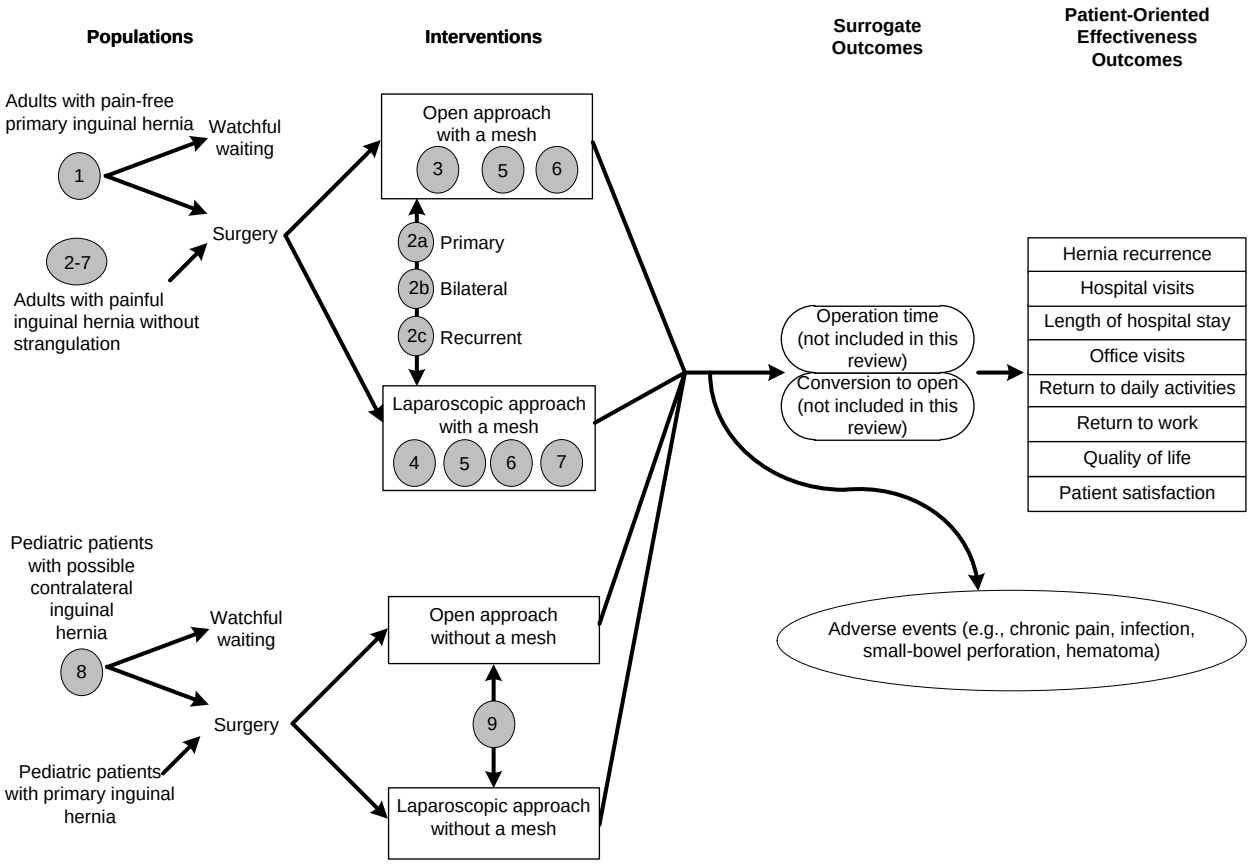
Finalization of the protocol occurred between 10/15/2010 and 4/8/2011. This involved input from the Technical Expert Panel, which was comprised of four individuals: one was a surgeon from the U.S. with expertise in adult hernia surgery who had also been a Key Informant; another was a surgeon from the U.K. who also had expertise in adult hernia surgery; the third was a surgeon who had expertise in pediatric hernia surgery and who had not been a Key Informant; and the fourth was a product specialist from a mesh manufacturer.

## Analytic framework

Figure 1 is an analytic framework that depicts the events that individuals experience while undergoing treatment for inguinal hernia. Throughout the figure, numbered circles indicate Key Questions addressed in this report. The left side of the framework lists the four patient populations: 1) adults with pain-free primary inguinal hernia; 2) adults with painful inguinal hernia without strangulation; and 3) pediatric patients with possible contralateral inguinal hernia, and 4) pediatric patients with inguinal hernia (the last two populations can be overlapping). To the right of these are the various intervention options, including watchful waiting as well as several surgical options. The surgical options are categorized based on whether the approach is open or laparoscopic and whether a mesh is used. Post-intervention outcomes are divided into three categories: surrogate outcomes (operation time and conversion to open, neither of which were included in this report), patient-oriented effectiveness outcomes (hernia recurrence, length of hospital stay, hospital visits, office visits, return to daily activities, return to work, quality of

life, and patient satisfaction), and adverse events (including such events as chronic pain, infection, small bowel perforation, hematoma, etc.).

**Figure 1. Analytic Framework**




## Key questions

This report addressed nine Key Questions, which are listed below. Most questions refer to "patient-oriented effectiveness outcomes." These include hernia recurrence, hospital visits, length of hospital stay, office visits, return to daily activities, return to work, quality of life, and patient satisfaction. We also examined adverse events, including rates of long-term pain.

**Among adults with *pain-free* primary inguinal hernias:**

Key Question 1. Does hernia repair differ from watchful waiting in patient-oriented effectiveness outcomes and/or adverse events?

**Among adults with painful inguinal hernias without incarceration/strangulation:**

Key Question 2. Does open hernia repair with a mesh differ from laparoscopic hernia repair with a mesh in patient-oriented effectiveness outcomes and/or adverse events?

a. For primary hernias?
b. For bilateral hernias?
c. For recurrent hernias?

Key Question 3. Do different open mesh-based repair procedures (e.g., Lichtenstein repair, mesh plug) differ in patient-oriented effectiveness outcomes and/or adverse events?

Key Question 4. Do different laparoscopic mesh-based repair procedures (e.g., transabdominal preperitoneal repair, totally extraperitoneal repair) differ in patient-oriented effectiveness outcomes and/or adverse events?

Key Question 5. Do different mesh products differ in patient-oriented effectiveness outcomes and/or adverse events?

Key Question 6. Do different mesh-fixation methods (e.g., no fixation, sutures, glue) differ in patient-oriented effectiveness outcomes and/or adverse events?

Key Question 7. For each type of laparoscopic mesh repair, what is the association between surgical experience and hernia recurrence?

**Among *pediatric* patients (age 21 years or younger):**

Key Question 8. For a possible contralateral hernia, does same-operation repair/exploration differ from watchful waiting in patient-oriented effectiveness outcomes and/or adverse events?

Key Question 9. Does open hernia repair without a mesh differ from laparoscopic hernia repair without a mesh in patient-oriented effectiveness outcomes and/or adverse events?

## Search strategy

Literature searches were performed by Information Professionals within the EPC Information Center, and followed established guidelines and procedures as identified by the Director of Health Technology Assessment/EPC Information Center. Below is an overview of the search process; specific search strategies are listed in Appendix A.

Consistent with our evidence-based searching protocol, for all Key Questions the following databases were searched on the OVID SP platform, utilizing the one search and de-duplication features: MEDLINE, PreMEDLINE, and EMBASE. The Cochrane Library, including the Central Register of Controlled Trials, the Cochrane Database of Methodology Reviews, and the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, Health Technology Assessment Database, and the U.K. National Health Service Economic Evaluation Database, were also searched for unique reviews, trials, economic analyses, and technology assessments.

Search terms were identified by: 1) reviewing relevant systematic reviews on similar topics that are identified by members of the research staff, 2) reviewing how other relevant studies are indexed, their subject heading terms, and their keywords, and 3) reviewing MeSH and EMTREE indexes for relevant and appropriate terms. After reviewing these, a combination of subject headings and keywords were identified. Search strategies were developed using these terms. Once developed, search strategies were reviewed by senior research analyst(s) and the Director of the Health Technology Assessment/EPC Information Center. No limits on language were applied by the search, and search dates were established as January 1st 1990 to 2011 (studies published before 1990 likely describe procedures no longer being used commonly or outcomes that are not likely to be predictive of current outcomes). A study design filter was applied to retrieve systematic reviews and clinical trials. The date of the last search was May 13th, 2011. We also examined reference lists for additional possible articles. Searches will be updated during the peer review period, and any additional studies will be incorporated into the final report.

Literature search results were initially reviewed by the Information Professional. Using the key questions and inclusion/exclusion criteria identified by senior research analyst(s), the Information Professional assessed relevancy and retrieved results. Feedback from the senior research analyst(s) and the Director of the Health Technology Assessment/EPC Information Center – including details regarding gaps in the search strategy, as well as articles [identified by the senior research analyst(s)] not retrieved by the searches – was integrated into the search strategy using key terms and subject headings. The updated strategy was re-run in all identified databases. Additional results were scanned and relevancy was assessed by the Information Professional. New results were downloaded and forwarded to senior research analyst(s) for review. Hand searches of reference lists in identified articles were also reviewed for possible inclusion.

As a check on the accuracy of abstract screening inclusion/exclusion, we randomly selected 10% of the articles excluded at the abstract level for re-screening by a second person. None of the articles were subsequently selected for inclusion.

## Study selection

The inclusion criteria are listed below in separate categories pertaining to 1) publication type, 2) study design, 3) patient characteristics, 4) treatment characteristics, and 5) data.

**Publication criteria**

1. Publication must have been a full article; abstracts alone were not included because they do not include sufficient details about experimental methods to permit an evaluation of study design and conduct and they also may only contain a subset of the measured outcomes.[22,23]
2. To capture the most relevant data, we included studies published on or after January 1, 1990. Studies published before 1990 likely describe procedures no longer being used commonly or outcomes that are not likely to be predictive of current outcomes.
3. To avoid double-counting of patients, when several reports of overlapping patients are available, only outcome data from the report with the largest number of patients were included. We included the data when a smaller report provides data on an outcome that was not provided by the largest report. Multiple publications of the same study (e.g., publications reporting subgroups, other outcomes, or longer followup) were identified by examining author affiliations, study designs, enrollment criteria, and enrollment dates.
4. Studies must have been published in English. Moher et al. have demonstrated that exclusion of non–English-language studies from meta-analyses has little impact on the conclusions drawn.[24] Juni et al. found that non-English studies typically were of lower methodological quality and that excluding them had little effect on effect-size estimates in the majority of meta-analyses they examined.[25] Although we recognize that in some situations exclusion of non-English studies could lead to bias, we believe that the few instances in which this may occur do not justify the time and cost typically necessary for translation of studies to identify those of acceptable quality for inclusion in our review.[24,25] Due to the prevalence of non–English-language studies of inguinal hernia repair, however, we examined the English abstracts of these studies in an attempt to assess the degree of bias resulting from their exclusion.

**Study design criteria**

5. For questions comparing interventions (i.e., all Key Questions except Key Question 7 on surgical experience), the study must have either randomized patients to treatments or used an analytic method to address selection bias, such as intentional baseline matching on multiple characteristics, propensity scoring, or other analytic approach. Studies with large differences at baseline between groups (regardless of whether they were randomized), or that entailed confounding by indication, were excluded. Studies comparing meshes or mesh-fixation methods must not have confounded results by differences in surgical procedures for inserting the mesh. For Key Question 7 on surgical experience, a control group was not required; however, the study must have provided data on the relation between surgical experience and outcomes. The definition of surgical experience must have been specific to laparoscopic mesh hernia repair, not simply a measure of general experience such as surgeon age.
6. Studies could be prospective or retrospective, but retrospective studies must have used consecutive enrollment (or enrollment of a random sample of eligible participants).
7. The treatments being compared must have been administered during the same time period, so that any observed difference between treatment outcomes were not attributable to differential time frames.

**Patient criteria**

8. To be included for a given Key Question, the study must have provided data for which at least 85 percent of the patients had the condition specified in the Key Question. For example, for Key Question 2a, we only included data points for which at least 85 percent of the patients were adults with painful primary inguinal hernia without incarceration/strangulation.
9. We used a flexible definition of "adulthood," defining "adults" as anyone aged 18 years or older and we defined the "pediatric population" as anyone aged 21 years or younger. This means that studies enrolling those aged 18–20 years could have been included as either an adult study or a pediatric study, depending on the average age of those enrolled.

**Treatment criteria**

10. The study must have provided sufficient information about the treatments for one to determine that the data address one of the Key Questions.
11. The study must not have described a specialized and novel hernia repair that has not been widely practiced by other surgeons. This is to maintain the focus of the report on the most common types of repair.
12. The hernia repair must not have been performed simultaneously with another operation (e.g., prostatectomy). Surgical complications of combined operations make it difficult to isolate aspects of the hernia repair itself.

**Data criteria**

13. The study must have reported data on at least one of the included outcomes for at least one of the Key Questions.
14. Outcome data must not have relied on retrospective recall (e.g., in an interview long after the procedure had been performed) because such outcomes may not accurately reflect patients' experiences.
15. For some outcomes in the adult population, we included data points at least 6 months after treatment (hernia recurrence, quality of life, and patient satisfaction). For all other outcomes (and in the pediatric population), there was no minimum followup.

16. We included data points capturing at least 10 patients with the condition of interest who represented at least 50 percent of eligible enrolled patients.

As a check on the accuracy of full-article inclusion/exclusion, we randomly selected 10% of the articles excluded at the full article for re-screening by a second person. None of the articles were subsequently selected for inclusion.

## Data extraction and management

We extracted study information into spreadsheets in Microsoft Excel.™ These included:

- **General study characteristics.** Author, publication year, country, study design, number of centers, dates of patient enrollment, type of setting, length of followup, funding source, which Key Question(s) the study addressed
- **Patient enrollment criteria.** All authors' reported patient enrollment criteria
- **Treatment characteristics.** Specific procedure, specific mesh (if applicable), fixation method (if applicable), number of surgeons, surgeons' prior experience with the repair procedures performed, surgical setting (i.e., specialized hernia center or general surgery), type of anesthesia, methods of followup for data collection
- **Baseline characteristics.** Number of enrolled patients, age, sex, comorbidities, hernia type(s), pre-surgical pain level, pre-surgical quality-of-life scores, pre-surgical functional activity scores, unilateral/bilateral, primary/recurrent, and any other reported important patient characteristics at baseline.
- **Risk of bias items.** See the next section.
- **Data.** We extracted the numerical data necessary for us to compute an effect size (such as an odds ratio or standardized mean difference) and its standard error for all included outcomes for each study. These may include means, standard deviations, counts, proportions, results of authors' statistical tests, or other statistical details, depending on what was reported. If the study did not report sufficient information to permit computation of an effect size, we extracted what was reported. We randomly selected 10% of the extracted datapoints to be extracted again by a second person, and disagreements were resolved by consensus.

## Individual study risk-of-bias assessment

We assessed the risk-of-bias (i.e., internal validity) separately for each outcome and each time point of each study. The reason for outcome specificity is that some subjective outcomes are more susceptible to bias than other outcomes. The reason for time-point specificity is that longer followup often results in attrition or right-censoring, which may yield patients who are somewhat different than the full set of enrolled patients and also may introduce a systematic difference between the groups being compared.

For all studies with control groups (regardless of whether patients were randomly assigned to groups), we assessed risk-of-bias using the items below. All but one of these items were selected from a pool of items typically used by this EPC for technology assessments. The seventh item was devised specifically for this project because of the importance of prior surgical experience in hernia repair. Each of these items was answered as "Yes," "No," or "Not reported."

1. Were patients randomly assigned to the study's groups?
2. Was there concealment of group allocation?
3. For nonrandomized trials, did the study employ any other methods to enhance group comparability?

4. Was the process of assigning patients to groups made independently from physician and patient preference?
5. Was the comparison of interest prospectively planned?
6. Were the two groups treated concurrently?
7. For questions comparing two procedures, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study? (not relevant to Key Question 1 because it does not involve comparing procedures)
8. If patients received ancillary treatment(s), was there a ≤5% difference between groups in the proportion of patients receiving each specific ancillary treatment?
9. Did patients in different study groups have similar levels of performance on the outcome of interest at the time they were assigned to groups?
10. Were the study groups comparable for all other important factors at the time they were assigned to groups?
11. Were those who assessed the patient's outcomes blinded to the group to which the patients were assigned?
12. Was the outcome measure of interest objective and was it objectively measured?
13. Was there ≤15% difference in the length of followup for the two groups?
14. Did ≥85% of enrolled patients provide data at the time point of interest?
15. Was there a ≤15% difference between groups in the percentage of patients provided data at the time point of interest?

We categorized the risk of bias for each outcome/timepoint in each study as "Low," "Medium," or "High" risk-of-bias using the following method:

- In order to be considered low risk-of-bias, the study must meet the following conditions:
  - Randomized (item 1).
  - Concealment of allocation (item 2) OR blinded outcome assessors (item 11) OR both.
  - Good baseline comparability for both outcome (item 9) and other patient characteristics (item 10).
  - Good baseline comparability on surgeons' number of prior operations performing the compared procedures (item 7).
  - If NOT blinded outcome assessors (item 11) (or NR blinded outcome assessors), then the outcome was objective (item 12).
  - ≤15 percent difference in length of followup between groups (item 13).
  - ≥85 percent of enrolled patients provided data to this time point (item 14).
  - ≤15 percent difference in data provision rates to this time point (item 15).
- In order to be considered high risk-of-bias, the study must meet AT LEAST TWO of the following conditions:
  - Process of assigning patients to groups NOT made independently from physician and patient preference (item 4)
  - Not good baseline comparability for either the outcome (item 9) or other patient characteristics (item 10)
  - Retrospective (item 5)
  - Difference in ancillary treatments ≥5 percent (item 8)
  - Not a blinded outcome assessor (item 11) AND a subjective outcome (item 12)
- In order to be considered Medium risk-of-bias, the study neither met the conditions for low risk-of-bias nor the conditions for high risk-of-bias.

## Data synthesis

For each Key Question, we determined the specific treatment comparisons that were made by the included studies. A study with more than two groups would contribute to more than two comparisons and possibly more than one Key Question. We considered each treatment comparison separately. When choosing among multiple comparisons within a study to be entered into an overall analysis, we prioritized the more common procedures (e.g., Lichtenstein, TEP).

Within each treatment comparison, we examined all of the included outcomes from all of the relevant studies. The outcomes were divided into eight categories: hernia recurrence (RC), hospital-related, including the length of hospital stay and subsequent hospital/office visits (HOSP), the time to return to daily activities (RTDA), the time to return to work (RTW), quality of life (QOL), patient satisfaction (SFN), pain including visual analog scale scores and the rates of chronic pain (PAIN), and other adverse events not involving pain (ADV). QOL was measured using the Short Form (SF)-36 health survey by most of the studies included in this report. The SF-36 covers eight health concepts and is a measure of health status. The SF-36 is comprised of eight scaled scores and a single item score that provides an indication of perceived change in health. Other outcomes such as RTDA, RTW, and long term pain were reported separately from QOL by these studies.

Within each category, the data were reported in different ways. For example, some studies reported the hazard ratio for hernia recurrence (with its 95% confidence interval [CI]) across the entire followup period, others reported the two groups' recurrence rates at a specific timepoint (e.g., x% and y% recurrence rates at one year after surgery), and other reported the two groups recurrence rates at median followup (e.g., x% and y% recurrence rates with a median followup of 17 months and a range of followup from eight months to 35 months). Within each category, we judged which studies were combinable based on the specific outcomes and methods of reporting.

Regarding timepoints, we used three categories: short-term (defined as one month or less after surgery), intermediate-term (defined as between one month and six months after surgery), and long-term (defined as six or more months after surgery). When a study reported multiple timepoints of the same outcome within the category, and we had to decide which timepoint to include in a meta-analysis with other studies, we chose the latest timepoint within that category.

We performed meta-analysis wherever appropriate and possible. This decision depended on the judged clinical homogeneity of the different study populations, cointerventions, and outcomes, as well as what is reported by those studies. For some outcomes (length of stay, return to daily activities, return to work, and Pain (measured in VAS) score), many studies did not report standard deviations (SDs) or other measures of dispersion that could be used to calculate standard deviations. To enable inclusion of these studies in meta-analysis we estimated the SDs by pooling the SDs of studies that did report them for these outcomes. Forest plots for all meta-analyses appear in the Figures section.

In the choice of effect size metrics, for hernia recurrence we used the relative risk, because of its ease of interpretation and also because some studies only reported an adjusted relative risk, thus only a relative risk meta-analysis could include all of the studies. For all continuous outcomes, we used the weighted mean difference, which is on the same scale as the measured outcome. For adverse events and pain reported dichotomously, we analyzed odds ratios.

To aid interpretation, for each outcome in the review, we set the smallest difference between groups that can still be considered clinically significant (minimum clinically significant difference or MCSD). This definition aids interpretation in two main ways: 1) to determine whether a statistically significant difference is important and 2) to determine whether a

statistically nonsignificant difference is small enough to exclude the possibility of an important difference. After hernia repair, a key outcome is hernia recurrence. For this outcome, we define the MCSD as 3 percentage points (e.g., 1% vs. 4% for two separate treatments). This was based on statements in two multicenter trials (the U.S. Department of Veterans Affairs trial[26] and the Medical Research Council trial)[27] that such a difference is clinically meaningful. For other anticipated outcomes, we used the following approaches concerning the definitions of minimum clinical significance:

- Length of hospital stay, return to daily activities (RTDA), return to work (RTW): one-day difference between groups. For RTDA and RTW, this had been defined as one week in the review protocol, but the review team decided to change it to one day upon finding that the typical RTDA after inguinal hernia surgery is about 10 days and the typical RTW is about 14 days. On that scale, a week is clearly too large to be considered the "minimum" clinically significant difference, so we changed it to one day. This was outline in a review protocol amendment dated 8/9/2011.
- Number of hospital visits/number of office visits: Twenty percent difference between groups (e.g., means of 5 visits and 4 visits).
- Quality of life: 5 percent of the range of the scale (e.g., 5 points on the SF-36, which ranges from 0–100).
- Patient satisfaction: A one-level change (this outcome is typically measured on an ordinal scale representing various levels of satisfaction)
- Pain: If reported as a continuous measure, 20 percent of the range of the scale (e.g., two points on the VAS, which typically ranges from 0–10).[28] If reported as a dichotomous measure, we defined the MCSD as an odds ratio of 1.25. This means that if the confidence limits of the odds ratio were fully within the range of 0.80 to 1.25, a conclusion of equivalence may be appropriate. The FDA uses this same range when setting criteria for concluding bioequivalence.[29]
- Other adverse events: We defined the MCSD in the same way that we did for dichotomous pain.

If meta-analysis was deemed appropriate and possible for a given comparison and a given outcome, we performed DerSimonian and Laird random-effects meta-analysis[30] using Comprehensive Meta-Analysis (CMA) software (Biostat Inc., Englewood, NJ). To measure heterogeneity, we used both $I^2$ and tau. Both are used because $I^2$ can increase simply by increasing the numbers of patients in the studies (whereas tau is a more direct measure of heterogeneity),[31] but tau is more difficult to interpret because its scale is different for different effect sizes. We defined substantial heterogeneity as a value of tau greater than the MCSD for that outcome. If this occurred, and there were 10 or more studies of the same patient outcome of the same treatment comparison, we conducted meta-regressions using the permutation test[32] in Stata software (Stata Corporation, College Station, TX). Where possible, we investigated up to 10 covariates in these meta-regressions (percentage of patients with bilateral hernia, percentage of patients with recurrent hernia, mean age, percent of laparoscopic patients undergoing TEP, percentage of open patients undergoing Lichtenstein, percentage of centers in university or specialist settings, concealment of allocation, similar levels of prior surgical experience, outcome rater blinding, and length of followup).

## Strength of evidence rating

We used the system described by Owens et al., 2009[33] to rate the strength of the evidence (SOE) for the major outcomes for each Key Question. This system includes four core domains (risk-of-bias, consistency, precision, and directness) as well as four optional domains (large magnitude of effect, all plausible confounders would reduce the effect, publication bias, and dose-response association). The directness domain does not encompass applicability, which is considered outside of the evidence rating system (we discuss our applicability methods in the next section). The various domains were considered together to rate the evidence for the outcome as High, Moderate, Low, or Insufficient. The rating was done by two independent analysts, and disagreements were resolved by consensus. Owens et al., 2009[33] defined the four ratings as:

- High = ”High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.”
- Moderate = ”Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.”
- Low = ”Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.”
- Insufficient = ”Evidence either is unavailable or does not permit a conclusion.”

The strength-of-evidence system requires one to choose the major outcomes that will receive an SOE rating. We carefully considered each Key Question and chose the following outcomes to receive SOE ratings:

- Key Question 1 (surgery vs. watchful waiting): Quality of life, long-term pain, hernia strangulation or incarceration
- Key Question 2 (open vs. laparoscopic surgery): Hernia recurrence, length of hospital stay, return to daily activities, return to work, quality of life, patient satisfaction, long-term pain, epigastric vessel injury, small bowel injury, small bowel obstruction, urinary retention, hematoma, wound infection
- Key Question 3 (comparing different types of open surgery): Hernia recurrence, length of hospital stay, return to daily activities, return to work, short-term pain, intermediate-term pain, seroma, urinary retention, hematoma, wound infection
- Key Question 4 (comparing different types of laparoscopic surgery): Hernia recurrence, length of hospital stay, return to daily activities, return to work, short-term pain, intermediate-term pain, urinary retention, hematoma, wound infection
- Key Question 5 (comparing different meshes): Hernia recurrence, quality of life, patient satisfaction, long-term pain, feeling of a foreign body, infection, bleeding
- Key Question 6 (comparing different mesh fixation approaches): Same as for Key Question 5
- Key Question 7 (association between surgical experience and recurrence): SOE was not rated because no rating system yet exists for evidence on association
- Key Question 8 (comparing different types of open surgery): SOE was not rated because no studies met inclusion criteria
- Key Question 9 (pediatric open vs. laparoscopic surgery): Hernia recurrence, length of hospital stay, return to daily activities, patient/parent satisfaction

We used the following approach to combine the SOE components and determine a rating (High, Moderate, Low, or Insufficient) for a given outcome of a given treatment comparison.

We first determined whether the combined evidence on that outcome was sufficiently precise to permit a conclusion about the direction of the effect (either favors treatment A, favors treatment B, or indicates approximate equivalence by ruling out the MCSD). If not, then the rating was Insufficient (abbreviated INSUFF in our SOE tables). If it was sufficiently precise, then we assigned point values to the four core domains as follows: Risk of bias +2/+1/0 for low/moderate/high; Consistency +1/0/0 for consistent/inconsistent/unknown; Directness +1/0 for direct/indirect; and Precision +1/0 for precise/imprecise. For the additional domains, we sometimes added 1 for a large magnitude of effect, and we sometimes subtracted 1 for potential publication bias or selective outcome reporting (e.g., if a third or fewer of the studies included for that comparison had actually reported that outcome). The other two additional domains (all plausible confounders would reduce the effect, and dose-response association), were not relevant to any of our Key Questions. We added the points for the various domains, and 5+ indicated an SOE rating of High; 4 points indicated an SOE rating of Moderate; 3 points indicated an SOE rating of Low; and 2 or fewer points indicated an SOE rating of Insufficient.

## Applicability assessment

For this evidence report, we assessed the applicability of evidence for each Key Question. As defined in the AHRQ EHCP Methods Guide for Comparative Effectiveness Reviews of Medical Interventions, applicability is "the extent to which the effects observed in published studies are likely to reflect the expected results when a specific intervention is applied to the population of interest under "real-world" conditions."[34] Applicability depends on context and cannot be assessed with a universal rating system.[34] Thus far, no system has been developed for rating the applicability of a body of evidence for inguinal hernia repair.

Assessment of the applicability of a body of evidence is a complex task and involves addressing a series of methodological questions. These questions include:

- What are the population of interest and the "real world" conditions relevant to the stakeholders of this evidence report? From whose perspectives should the applicability of the evidence be evaluated? This evidence review potentially serves multiple stakeholders, such as policy makers, clinicians, and patients and families. Different stakeholders may have different population of interest and different applicability issues for consideration.
- What factors may affect the applicability of a study? What factors need to be considered in the assessment of applicability? While the PICOS (i.e., population, intervention, comparator, outcome, and setting) approach may be used to identify these factors,[34] some of the factors may have already been considered, at least in part, in the study inclusion/exclusion process.
- How would the impact of each of these factors be judged or graded? The answer to this question is not always straightforward. For example, it is difficult to judge the exact degree by which the findings of a study that only included patients of 55 years of age or older apply to the younger population. The judgment is often made on a subjective basis.
- How would the impacts of these various factors be synthesized to reach a general conclusion about the applicability of an individual study? Studies included in evidence reviews may report different applicability-related data (e.g., different types of comorbidities) or report the same types of data (e.g., duration of hernia) in different ways (e.g., reported as longer or less than 6 weeks vs. in average years). No validated instrument is currently available for accommodating these differences to reach a general conclusion about the applicability of a study.

- When the evidence consists of multiple studies, how would the applicabilities of different studies be synthesized to reach a general conclusion about the applicability of the evidence? We did not identify any validated instrument for this type of synthesis.

Given these unresolved methodological issues, we chose a practical approach to assessing the applicability of evidence for this evidence review. The goal of our assessment is to provide useful information to concerned stakeholders in making judgment on whether the evidence is applicable to the population or conditions of their interest.

We first abstracted data from each included study on factors that may affect the applicability of the study. We primarily focused on factors in three areas that are most relevant to the inguinal hernia repair topic:

- Population: demographic characteristics (e.g., age, sex, race, and ethnicity), comorbidity or general physical fitness (e.g., chronic cough, cardiovascular conditions, pulmonary functions, BMI, activity assessment scale [AAS], and physical component summary [PCS]), and types of hernia (e.g., primary vs. recurrent, unilateral vs. bilateral, reducible vs. irreducible, and hernia duration)
- Intervention and comparators: inguinal repair procedure being compared, periods of the procedure being performed, co-interventions (e.g., type of anesthesia and perioperative use of antibiotics), and experience of the surgical team
- Setting: geographic (e.g., the United States, Canada, or European countries) and clinical (e.g., academic medical centers vs. community hospitals) settings

Based on a review of the data abstracted, we narratively summarized any patterns reflected from these factors that may potentially affect the applicability of the evidence. We made no attempt to generate any rating or score for the applicability of the evidence, due to the methodological issues previously discussed. Our narrative summaries were intended to raise stakeholders' attention to potential applicability issues embedded in the evidence.

## Peer review and public commentary

As part of a newly instituted process at AHRQ, the draft report was reviewed prior to peer review by the Task Order Office (TOO) and an AHRQ Associate Editor (a senior member of a sister EPC). The revised draft report was then sent to invited peer reviewers and was simultaneously uploaded to the AHRQ Web site where it was available for public comment for 28 days. All reviewer comments (both invited and from the public) will be collated and individually addressed. The EPC responses to all comments will be documented in a disposition of comment document which will be posted on the Effective Health Care website about three months after web publication of the evidence report. The authors of the report had final discretion as to how the report was revised based on the reviewer comments, with oversight by the TOO and Associate Editor.

# Results

## Overall Description of Included Studies

Searches identified 2,537 potentially relevant articles and we excluded 1,337 of these at the abstract level. A large number of these exclusions (549) were because the study was not published in English. We had employed this exclusion solely for practical purposes, and an important issue is whether including non-English studies would have influenced any of the

conclusions of our review. Thus, below, in the summary of each Key Question, we discuss the non-English abstracts that may have been included for that Key Question.

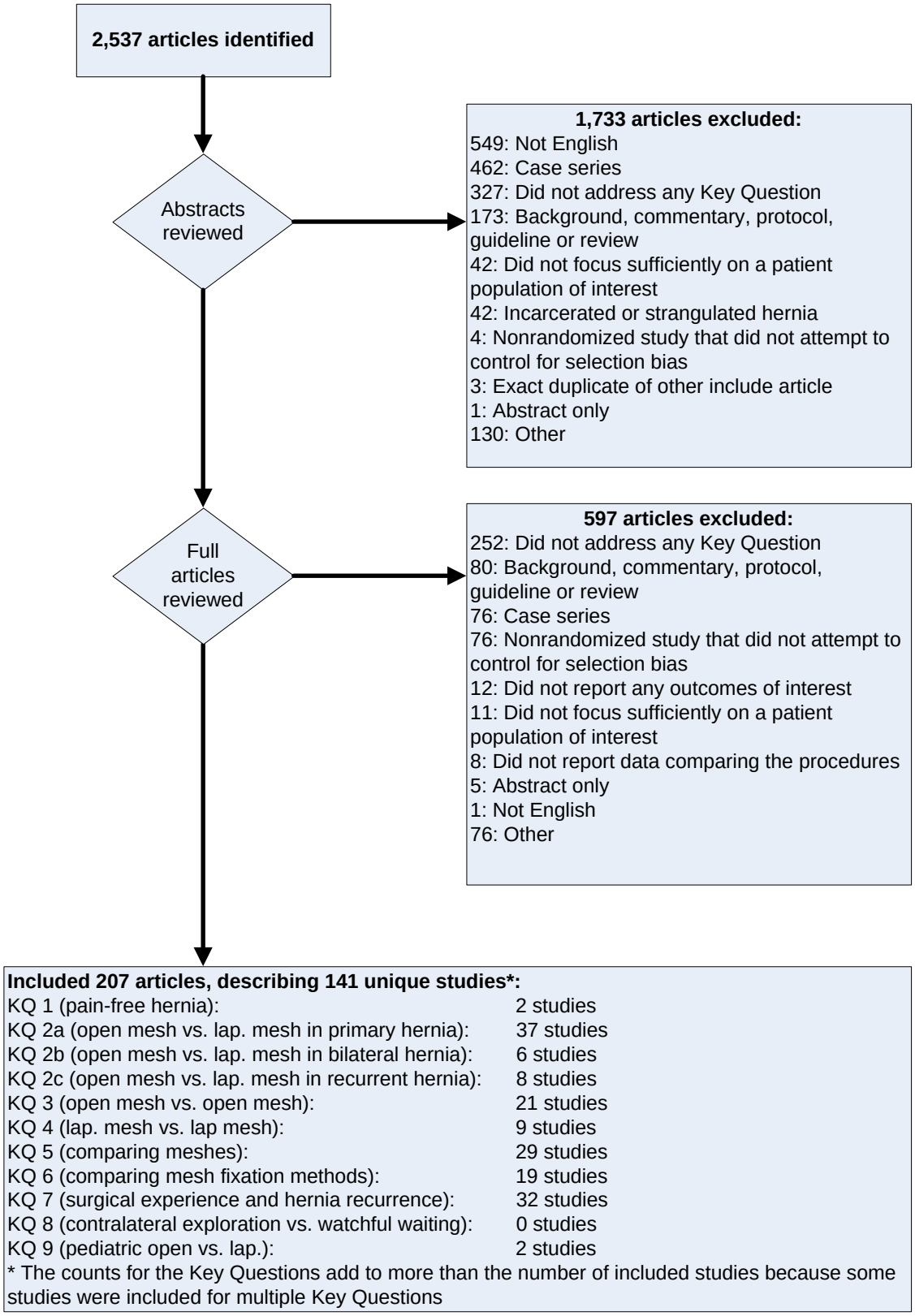
At the full-article level, we excluded another 597 articles, typically due to irrelevance to any of our Key Questions (252 publications), background/review/commentary/protocol articles (80 publications), uncontrolled design (76 publications), or nonrandomized designs without any attempt to control for selection bias (76 publications). An alphabetized list of these 597 exclusions, along with the reason for exclusion, appears in Appendix B.

There remained 207 publications describing 141 unique studies that we included in our review. Multiple publications of a given study typically involved reporting additional outcomes not reported in the original publication, or longer followup timepoints, or subgroup analyses, or additional clarification of study methods; all such publications were included, and in evidence tables we grouped together all of the study's citations. The largest number of studies addressed Key Question 2a (37 studies), which compared open mesh repair to laparoscopic mesh repair in patients with primary inguinal hernia. Other large evidence bases were found for Key Question 3 (comparing different procedures for open mesh repair, 21 studies), Key Question 5 (comparing meshes, 29 studies), and Key Question 7 (the association between laparoscopic hernia repair and hernia recurrence, 32 studies). No studies were identified for Key Question 8 (comparing surgical exploration vs. watchful waiting for pediatric contralateral inguinal hernia). Sixteen studies were included for multiple Key Questions (e.g., two studies were each included for four Key Questions), because they included three or more groups or reported subgroup analyses. A list of the included studies, along with marks identifying which studies addressed which questions, appears in Table 19 in Appendix C.

Only 15 of 141 studies (11%) were conducted exclusively in the United States. An additional 19 studies (13%) were conducted in the UK, Australia, Canada, U.S./U.K., or U.S./Canada. The remaining 107 studies (76%) were conducted in other countries, most prominently Germany (13 studies or 9%), Italy (11 studies or 8%), and Turkey (11 studies or 8%).

Eleven sections follow, one for each Key Question (Key Question 2 is actually three questions: 2a, 2b, and 2c). Each section is structured in the same manner: 1) an overview of study characteristics for the studies included for that Key Question; 2) a discussion of risk of bias of those particular studies; 3) a summary of findings (including summaries of relevant meta-analyses); 4) a discussion of the applicability of those studies; and 5) and a summary (which includes a list of our conclusions for that Key Question, a strength-of-evidence table, and a discussion of excluded non-English abstracts). All figures displaying meta-analyses are listed in the Figures section, which appears after the References. All evidence tables are in Appendix C, sorted by Key Question (i.e., all of the Key Question 1 tables appear first, then all of the Key Question 2a tables, etc.).

**Figure 2. Literature Flow Diagram**



## Key Question 1. Pain-free hernia: Does hernia repair differ from watchful waiting in patient-oriented effectiveness outcomes and/or adverse events?

### Study Characteristics

General information about the two studies included for this Key Question appears in Table 20 of Appendix C. One study was conducted in U.S. and Canada and the other in the UK. The North American study was an RCT with more than three centers and the UK study was a single-center RCT. Both studies compared mesh repair with watchful waiting. The RCTs each enrolled 720 patients and 157 patients, respectively. In the multi-center study, surgeries were performed between 1999 and 2004 at three university hospitals and two community clinics.[10,35-40] This study was funded by AHRQ and the American College of Surgeons, and the lead author disclosed financial ties with a manufacturer of a mesh plug. The other single-center study conducted at a university hospital did not report the date range of the surgeries or source of funding.[41]

Patient enrollment criteria appear in Table 21 (hernia-related criteria), Table 22 (demographic and medical criteria), and Table 23 (other criteria) of Appendix C. Enrollment criteria varied widely among both studies. The hernia-related study exclusion criteria in the studies include irreducible hernia (one study), incarcerated hernia (both studies), and femoral hernia (both studies). Regarding patient age criteria, the two studies enrolled patients aged >18 and >55, respectively. In addition, one study excluded patients unfit for general anesthesia or those with anesthesia risk scores of 3 or 4 or more; the other study excluded patients with infection and all female patients.

Treatment details appear in Table 24 of Appendix C. In one study, mesh repair was performed by the standardized Lichtenstein open tension-free repair as described by Amid[42] under local or general anesthesia. The other study did not report the detail of the "tension-free mesh repair" procedure. Neither of the studies reported the actual number of prior laparoscopic hernia repairs the surgeons had performed. Instead, studies either didn't mention their prior experience, or simply said the surgeon had general experience in hernia repair.

All reported baseline patient characteristics in the studies included for this Key Question appear in Table 25 of Appendix C. The mean age of the patients ranged from 57.5 to 71.9 years; most patients were male with primary hernias. One study reported medical comorbidities including congestive cardiac failure, prior myocardial infarction, hypertension, chronic obstructive pulmonary disease, chronic cough, prostatism, and diabetes.

### Risk of Bias

Our risk-of-bias assessments for both studies appear in Table 26 of Appendix C. One RCT was categorized as Moderate risk-of-bias for all reported outcomes and the other as either Low (for the outcomes of recurrence, healthcare utilization, adverse events) or Moderate-risk-of-bias (for pain and QOL). Many reasons underlie the Moderate rating for the two studies that addressed this Key Question. Common reasons involved concealment of allocation (either not performed or not reported), use of subjective outcome measures (pain and QOL), and the blinding of outcome assessors (either not performed or not reported).

### Findings

All included data for this Key Question appear in Table 27 of Appendix C.

### Quality of life

One study reported the QOL data on an intention-to-treat basis using the SF-36 instrument.[41] At six months, the surgical group fared better than the watchful waiting group on "general health" and "overall change in health status in the previous 12 months" (mean group difference 5.8, 95% CI: 0.1 to 11.5; mean group difference 9.4, 95% CI: 3.6 to 15.1, respectively). At 12 months, the surgical group still fared better than the watchful waiting group on "overall change in health status in the previous 12 months" (mean group difference, 7.3; 95% CI, 0.4 to 14.3; p=0.039). There were no statistically significant differences on other SF-36 items at both 6 and 12 months.

### Long-term pain

The two studies reviewed for Key Question 1 used different measures for comparing long-term pain (>6 months after surgery). One study reported group differences at 2 years for pain interfering with activities among the intention-to-treat patients. On intention-to-treat analysis, percentage of patients with pain interfering among the surgical group was 2.2% compared to 5.1% in the watchful waiting group. Although the finding of the study showed a trend in favor of surgical repair compared to watchful waiting (OR=0.42, 95% CI: 0.17 to 1.04), this difference was statistically insignificant .[10,35-40] The second study compared the Pain (measured in VAS) scores at rest and at movement between the two groups.[41] They reported no statistically significant difference in mean Pain (measured in VAS) scores at rest (difference in means=-1.5, 95% CI: -4.8 to 1.8) and at movement (difference in means=-1.5 95% CI: -6.1 to 2.3) at 12 months. The low precision precludes any conclusion for this outcome.

### Adverse events

We conducted meta-analyses of types of events (acute hernia and strangulation) (Figure 2). For these two events, the evidence was inconclusive.

## Applicability

Two studies are included for review for Key Question 1. We evaluated the studies to identify factors that may potentially affect the applicability of the evidence. As described in the *Methods* section, the goal of the evaluation is to raise stakeholders' attention to potential applicability issues embedded in the evidence rather than generating a rating or score for the applicability.

Among the two studies, the Fitzgibbons study compared watchful waiting with the Lichtenstein procedure,[10,35-40] while the O'Dwyer study compared watchful waiting with "tension-free mesh repair."[41] The findings of the studies may not apply to the comparison between other hernia repair procedures (e.g., TAPP or TEP) and watchful waiting. Meanwhile, both studies were published in 2006 and may not necessarily reflect the comparative performance of the procedures that are performed at the current time. Neither of the two studies discussed surgeons' prior experience for the surgeries being studied. Therefore, it is unclear whether there are any applicability issues related to the surgeons' level of experience.

Both the Fitzgibbons and O'Dwyer studies excluded patients with incarcerated, strangulated, or femoral hernia. Therefore, the findings of the studies may have an applicability issue for these patients. The two studies also used other enrollment criteria to exclude certain types of patients. For example, the O'Dwyer study did not include patients younger than 55 years of age, and the Fitzgibbons study did not include female patients. Other patient enrollment criteria used in the two studies are provided in Table 21and Table 22. It is unclear how these enrollment criteria and patients characteristics may affect the applicability of the evidence.

The Fitzgibbons study was conducted in five medical centers in North America (four in the U.S. and one in Canada). Three of the centers are affiliated with a university and the other two are community medical centers. The O'Dwyer study was conducted in a university hospital in the United Kingdom. Based on the data reported, it is unclear if the geographic or clinical settings of the two studies have any implication in determining the applicability of the evidence. Detailed information on geographic and clinical settings of the two studies is provided in Table 20.

## Summary of Key Question 1

A summary of the comparisons and outcomes we examined in this Key Question is provided in Table 1 below. The evidence was sufficient to permit a conclusion for one outcome:

- Quality of life at six months and one year was greater for patients who had received mesh repair than for those who were on watchful waiting.

Our ratings of the strength of evidence for this outcome also appear in the table. The factors influencing our assessment of the strength of evidence include the following: the study was at Moderate risk of bias for pain (see the pertinent section above); the consistency is unknown; the outcome is directly important to clinicians and patients; the results are imprecise. We examined the studies that had been excluded for being non-English, and none of them would have been included for this Key Question.

**Table 1. Key Question 1: Strength of evidence ratings**

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| Mesh repair vs. watchful waiting | Acute Hernia/ strangulation | 2 | MOD | C | D | I<br>OR 0.77<br>(0.06 to 10.8) | ? | INSUFF |
| Mesh repair vs. watchful waiting | Long-term pain at rest (measured in VAS at two years after trial entry) | 1 | MOD | U | D | I<br>Diff in means -1.5<br>(-4.8 to 1.8) | ? | INSUFF |
| Mesh repair vs. watchful waiting | Long-term pain during movement (measured in VAS at two years after trial entry) | 1 | MOD | U | D | I<br>Diff in means -1.5<br>(-6.1 to 2.3) | ? | INSUFF |
| Mesh repair vs. watchful waiting | Long-term pain interfering with activities (intention-to-treat) (measured in VAS at two years after trial entry) | 1 | MOD | U | D | I<br>OR 0.42<br>(0.17 to 1.04) | ? | INSUFF |
| Mesh repair vs. watchful waiting | Quality of life at 1 year (measured as overall change in health status in previous 12 ,months using the SF-36) | 1 | MOD | U | D | P<br>(reported 95% CI, difference in means 7.3, [0.4 to 14.3]) | Mesh plug repair | LOW |

**Table Note:**
**For consistency,** C=consistent, I=inconsistent, U=unknown consistency because there was only one study.
**For directness,** D=direct and I=indirect.
**For precision,** P=precise and I=imprecise.
**For the column labeled "Evidence favors,"** ? denotes inconclusive evidence, and EQ denotes approximate equivalence. SOE=strength of evidence.
**Other abbreviations:** OR=odds ratio, Diff=difference

In the Summary of Key Question 1, we looked through the list of non-English articles excluded for being non-English and found none relevant to this Key Question.

## Key Question 2a. Does open hernia repair with a mesh differ from laparoscopic hernia repair with a mesh in patient-oriented effectiveness outcomes and/or adverse events? Primary hernias

### Study Characteristics

General information about the 37 studies included for this Key Question appears in Table 28 of Appendix C. Seven were conducted in Turkey; five in Sweden; three each in Germany Finland, and the U.S.; two each in China, the Netherlands, and the UK; and the rest in other countries. Nineteen were single-center randomized trials; four were two-center randomized trials; seven were RCTs with >3 centers; two were country-wide registry studies (one in Sweden and one in Denmark); and the remaining five were RCTs that did not report the number of centers.

Regarding specific surgical procedures, the most commonly compared procedures were TAPP vs. Lichtenstein (14 studies), TEP vs. Lichtenstein (14 studies), TAPP vs. mesh plug (three studies), TEP vs. mesh plug (three studies), and TAPP/TEP vs. Lichtenstein (three studies). The RCTs enrolled between 38 and 2,164 patients each; the Swedish registry included 142,578 hernias; and the Danish registry included 67,306 hernias. The dates of patient enrollment were reported by 31/37 studies. The average length of the enrollment period was 1.9 years (range six months to 14 years). Studies were typically conducted in the mid-1990s and early 2000s.

Thirteen studies were conducted at university hospitals; 13 more were conducted at general and non-university hospitals; five included some university hospitals as well as some non-university hospitals; the remaining six did not report the type(s) of hospitals. Funding for the study was not reported by 25 studies; government funding was reported in six studies; university funding was reported in two studies; two did not report the funding source but did state they had no manufacturer ties; two did report partial manufacturer funding (and one of these stated that the manufacturer had no role in the design, conduct, or analysis of the study).

Patient enrollment criteria appear in Table 29 (hernia-related criteria), Table 30 (demographic and medical criteria), and Table 31 (other criteria) of Appendix C. Enrollment criteria varied widely among the 37 studies. The most commonly used hernia-related exclusions were recurrent hernia (19 studies), bilateral hernia (18 studies), and incarcerated hernia (16 studies). Others were femoral hernia (excluded by six studies), “emergency” hernia (excluded by five studies), and scrotal hernia (excluded by four studies). Overall, the studies paint an extraordinarily diverse portrait of the types of hernias deemed relevant to the studies, even though, by virtue of inclusion, they all compared open repair of inguinal hernia to laparoscopic repair of inguinal hernia.

Regarding patient age criteria, 29 of the 37 studies (78%) stated that they included any adults or required age >18. Twenty-two (59%) excluded those unfit for general anesthesia or those with anesthesia risk scores of 3 or 4 or more, and 16 studies excluded those who had undergone a prior surgery in the lower abdomen. Fifteen studies excluded all females, eight excluded pregnant women, and seven excluded those with coagulation disorders. As with the hernia-related exclusions, there was large variability in how studies selected patients for inclusion.

Treatment details appear in Table 32 of Appendix C. Laparoscopic treatments were TAPP for 13 studies, TEP for 15 studies, and both TAPP and TEP in the remaining nine studies. Laparoscopic repair invariably used general anesthesia, and the use of staples was the norm (with some surgeons stapling selectively). Mesh sizes varied widely, from smaller meshes at 7 x 10 cm to larger, 15 x 15 cm meshes; the typical mesh size was between these extremes, such as 10 x 14 cm. None of the studies reported the actual number of prior laparoscopic hernia repairs the surgeons had performed. Instead, studies either didn't mention their prior experience, or simply said surgeons had general laparoscopic skills that were not specific to hernia repair. Five of the 37 studies stated that "all surgeons had performed at least *X* prior procedures" of the type performed in the study (with *X* values of 5, 10, 10, 25, and 100 in the five studies).

Open hernia repairs were mostly Lichtenstein, and meshes were typically secured with sutures. The type of anesthesia was highly variable, with seven studies reporting general anesthesia for all patients, another five only using local or regional anesthesia, and seven others reporting that any type of anesthesia could be used depending on the preference of the patient or surgeon or anesthesiologist. Mesh sizes were variable, with the smallest mesh 6 x 8 cm, and the largest mesh15 x 15 cm, and the most typical size 7 x 12cm.

All reported baseline patient characteristics in the studies included for this Key Question appear in Table 33 of Appendix C. A summary of the most commonly reported baseline characteristics in studies included for Key Questions 2 through 7 appears in Table 2 below (we considered these Key Questions together because they addressed similar populations). The typical patient was a man in his mid-50s with a Body Mass Index (BMI) of 25 (which corresponds to 170 pounds in a male of average height). About a quarter of these men worked in physically strenuous jobs such as manual labor (among the 25 studies reporting this characteristic). This characteristic may be important in the context of hernia surgery because the persistence of symptoms is more likely to delay one's return to physical work than to more sedentary work. In the typical study, most patients had a primary unilateral hernia; slightly over half had an indirect hernia; slightly over half had a right-side hernia.

**Table 2. Summary of Baseline Characteristics**

| Characteristic | Number of studies from Key Questions 2-7 reporting this characteristic | Median | IQR |
|---|---|---|---|
| % male | 100 | 97% males | 92%-100% |
| Age | 126 | 54 years old | 49.5-57 |
| Body mass index | 35 | 25 | 24.7-25.5 |
| % physically strenuous job | 20 | 26% | 21%-43% |
| % primary | 106 | 99% | 88%-100% |
| % unilateral | 94 | 94% | 76%-100% |
| % indirect | 55 | 56% | 48%-66% |
| % right-side | 36 | 53% | 47%-58% |

**Table Note:**
IQR – Interquartile range

## Risk of Bias

Our risk-of-bias assessments for the 37 studies appear in Table 34 of Appendix C. The 35 RCTs were all categorized as Moderate risk-of-bias for all of their reported outcomes, and the two registry studies that were both categorized as High risk-of-bias. The latter two were retrospective and non-randomized studies that had no concealment of allocation, outcomes assessed with knowledge of treatment, and potentially other differences between the compared groups that may have influenced the registry findings.

Many reasons underlie the Moderate rating for the 35 RCTs. A common reason was that the surgeons may have had much more experience performing the study's open hernia repair procedures than the study's laparoscopic hernia repair procedures. This difference in prior experience could potentially explain differences in patient outcomes among those who received open vs. laparoscopic repair. Only three of the 35 RCTs stated that the surgeons were highly experienced with both types of repair used in the study. Most studies did not report prior experience with the procedures being compared, and a few studies made clear that the surgeons' prior experience was much greater with open repair. Two other common reasons involved concealment of allocation (either not performed or not reported by 18 studies) and the blinding of outcome assessors (either not performed or not reported for over 90% of the studies' datapoints).

## Findings

All included data for this Key Question appear in Table 35 of Appendix C.

### Hernia recurrence

We performed a meta-analysis of all 29 studies reporting this outcome, and found that recurrence was more likely after laparoscopic surgery than after open surgery (summary relative risk 1.43, 95% CI: 1.13 to 1.80) (Figure 4 upper panel). We had defined the MCSD as a three-percentage-point difference between groups. To aid interpretation, we calculated the overall rate of recurrence in the open repair groups, which was 2.56%. Multiplying a 1.80 relative risk by this rate yields a corresponding rate of 4.61% for laparoscopy. The difference between these rates is only 2.05%, which is less than our predefined MCSD of three percentage points. This implies that the difference between open and laparoscopy, while statistically significant, is not substantial.

### Length of hospital stay

Twenty-five of the 37 studies reported an outcome in this category, and 17 of these could be included in a meta-analysis of the length of stay in days (the other eight only reported dichotomous data, e.g., the percentage of patients who had a one-day stay). The meta-analysis (Figure 5 upper panel) found that length of stay was shorter after laparoscopic surgery than after open surgery (summary difference in means -0.33 days, 95% CI: -0.52 to -0.14). This is only about an eight-hour difference (e.g., a third of a day), which is less than what we defined as the MCSD (one day; see Methods section).

### Return to daily activities

Nineteen of the 37 studies reported an outcome in this category, and 15 of these could be included in a meta-analysis of number of days before returning to normal daily activities. The other four could not be included because the authors only reported dichotomous data, or did not report numbers of patients, or reported only specific activities (such as the length of

postoperative time before being able to urinate), or used a functional index scale rather than a length of time to return to activity. The meta-analysis (Figure 6 upper panel) found that RTDA was shorter after laparoscopic surgery than after open surgery (summary weighted mean difference in days of -3.9, 95% CI: -5.6 to -2.2). This is larger than what we defined as the MCSD for this outcome (one day).

The meta-analysis found substantial heterogeneity and had at least 10 studies, so we performed meta-regressions in an attempt to explain differences among studies. We investigated numerous covariates (percentage of patients with bilateral hernia, percentage of patients with recurrent hernia, mean age, percentage of laparoscopic patients undergoing TEP, percentage of open patients undergoing Lichtenstein, percentage of centers in university or specialist settings, concealment of allocation, outcome rater blinded), but none of them were statistically significantly associated with the difference between open and laparoscopic repair. Despite differences in the measured size of the effect, the overall direction of the effect consistently favored laparoscopy.

### Return to work

Twenty of 37 studies reported RTW data, and 19 of them were combined in a meta-analysis (the other did not report the Ns). The meta-analysis (Figure 7 upper panel) indicated shorter time-to-return-to-work after laparoscopic repair (summary difference in days -4.6 days, 95% CI: -6.1 to -3.1). This is larger than what we defined as the MCSD for this outcome (one day).

The meta-analysis found substantial heterogeneity and had at least 10 studies, so we performed meta-regressions in an attempt to explain differences among studies. We investigated numerous covariates (percentage of patients with bilateral hernia, percentage of patients with recurrent hernia, mean age, percentage of laparoscopic patients undergoing TEP, percentage of open patients undergoing Lichtenstein, percentage of centers in university or specialist settings, concealment of allocation, similar levels of prior surgical experience, outcome rater blinded), but none of them were statistically significantly associated with the difference between open and laparoscopic repair. Despite differences in the measured size of the effect, the overall direction of the effect consistently favored laparoscopy.

### Quality of life

Only one study reported long-term QOL data, and results suggested equivalence (on the 0-1 scale of Quality Adjusted Life Years (QALYs), the two-year difference in QALYs was only 0.014, 95% CI: -0.014 to 0.041).

### Patient Satisfaction

Three studies reported long-term data on this outcome, but they each reported it in a different way:

- One study reported degree of satisfaction on a VAS 0-100 scale, with medians of 100 for the laparoscopic group and 98 for the open group. This was reported as not statistically significantly different, but a confidence interval was neither reported nor calculable, so it is unclear whether the results indicate equivalence.
- A second study reported the percentages of patients who were “completely satisfied”/“satisfied”/“unsatisfied” (91/7/1 for the laparoscopic group vs. 75/20/5 for the open group). The study also reported the percentage of patients who said they would have this procedure again, which was 98% for the laparoscopic group vs. 86% for the open group. The study did not perform statistical tests on these outcomes, but we did (chi

square tests), and both measures showed statistically significantly greater satisfaction in the laparoscopic group.

- A third study asked four pertinent questions 1) whether recovery was faster than expected:, 59% laparoscopy patients vs. 45% open patients; 2) satisfaction with operation scars: 82% laparoscopy patients vs. 71% open patients 3) whether they would recommend that operation to others: 91% laparoscopy patients vs. 91% open patients and 4) whether they could describe life as "much better": 62% laparoscopy patients vs. 61% open patients. Authors did not report any statistical tests on these data, but our tests found that one of the four measures, satisfaction with operation scars, showed a statistically significant difference (82% vs. 71%), whereas the others were not statistically significant.

### Long-term pain

All 13 studies reporting long-term pain (>6 months after surgery) were included in a meta-analysis (Figure 8 upper panel). This analysis found a lower rate of long-term pain after laparoscopic surgery than after open surgery (OR=0.61, 95% CI: 0.48 to 0.78). This indicates a clinically significant difference in rates. The severity of pain, however, may not have differed substantially. Only one of the 13 studies measured the degree of pain severity in the long term (using a 150 millimeter visual analog scale). This study found that at two years, the between-group difference in pain at rest was no more than 3.5 millimeters, which corresponds to only 2.3% of the scale range.

The meta-analysis found substantial heterogeneity and had at least 10 studies, so we performed meta-regressions in an attempt to explain differences among studies. We investigated numerous covariates (percentage of patients with bilateral hernia, percentage of patients with recurrent hernia, mean age, percentage of laparoscopic patients undergoing TEP, percentage of open patients undergoing Lichtenstein, percentage of centers in university or specialist settings, concealment of allocation, similar levels of prior surgical experience, length of followup), but none of them were statistically significantly associated with the difference between open and laparoscopic repair. Despite differences in the measured size of the effect, the overall direction of the effect consistently favored laparoscopy.

### Adverse events

We conducted meta-analyses of six types of events (epigastric vessel injury reported by nine studies [Figure 9 upper panel], hematoma reported by 24 studies [Figure 10 upper panel], small bowel injury reported by four studies [Figure 11], small bowel obstruction reported by seven studies [Figure 12], urinary retention reported by 20 studies [Figure 13 upper panel], and wound infection reported by 17 studies [Figure 14 upper panel]). A clear direction of effect was found for three events: epigastric vessel injury (higher rates with laparoscopic repair, OR=2.0, 95% CI: 1.02 to 3.93), hematoma (lower rates with laparoscopic repair, OR=0.70, 95% CI: 0.54 to 0.89), and wound infection (lower rates with laparoscopic repair, OR=0.50, 95% CI: 0.34 to 0.73). For the other three events, the evidence was inconclusive because it was consistent with effects in either direction.

For urinary retention, the meta-analysis found substantial heterogeneity and had at least 10 studies, so we performed meta-regressions in an attempt to explain differences among studies. We investigated numerous covariates (percentage of patients with bilateral hernia, percentage of patients with recurrent hernia, mean age, percentage of laparoscopic patients undergoing TEP, percentage of open patients undergoing Lichtenstein, percentage of centers in university or specialist settings, concealment of allocation, similar levels of prior surgical experience,

outcome rater blinded), but none of them were statistically significantly associated with the difference between open and laparoscopic repair.

## Applicability

Thirty-seven studies are included for review for Key Question 2a. We evaluated these studies to identify factors that may potentially affect the applicability of the evidence. As described in the *Methods* section, the goal of the evaluation is to draw stakeholders' attention to potential applicability issues embedded in the evidence rather than generating a rating or score for the applicability.

The thirty-seven studies reviewed for Key Question 2a compared various mesh-based open surgeries with laparoscopic procedures. Table 28 provides a detailed description of the procedures being compared in the studies. The two interventions being compared in the meta-analyses—i.e., open vs. laparoscopic surgery—included different procedures (e.g., the Lichtenstein method, the mesh plug method, TEP, and TAPP). The findings from the meta-analyses (e.g., effect sizes) might not apply to comparisons of specific procedures (e.g., the Lichtenstein method vs. TEP, or the mesh plug method vs. TEP). Meanwhile, in 34 of the 37 studies reviewed for Key Question 2a, the surgeries were performed in the 1990s or early 2000s. This body of evidence may not necessarily reflect the comparative performance of the procedures that are performed at the current time.

Twenty-one of the 37 studies reviewed for Key Question 2a provided information on surgeons' prior experience for the surgeries being compared.[26,27,43-87] Surgeons' level of experience was reported as "experienced," "highly experienced," "with moderate experience," or by the number of prior cases. When the term "experienced" was used, the meaning of the term was rarely defined (e.g., by the number of prior cases or years of practice). Sixteen of the 37 studies reviewed did not report data on surgeons' experience at all. Given the limitation in data reported, we were unable to judge what implication surgeons' experience may have in the applicability of the evidence. Table 32 provides additional detail on the hernia repair procedures performed in the studies, including data on surgeons' experiences.

Patient enrollment criteria and reported baseline characteristics varied significantly across the 37 studies. Almost half of the studies reviewed excluded female patients or patients unfit for general anesthesia. Some studies excluded patients with bilateral or incarcerated hernia. Based on the data reported, we did not identify any clear patterns in the patient characteristics of the studies that indicate significant impact on the applicability of the evidence. Detailed patient enrollment criteria and baseline characteristics of these studies are provided in Table 29 and Table 30.

Except for three studies,[26,47,74-79,81] all of the other 34 studies were performed outside of the United States, primarily in European countries. The differences in healthcare systems and practice patterns between the U.S. and Europe may potentially have an impact on the applicability of the evidence from the perspectives of the US stakeholders. The clinical settings where the 37 studies were conducted varied significantly, ranging from outpatient surgical clinics, community hospitals, and academic medical centers. Based on the data reported, it is unclear how the clinical settings of the studies might affect the applicability of the evidence. Detailed information on geographic and clinical settings of the 37 studies is provided in Table 28.

## Summary of Key Question 2a

A summary of the comparisons and outcomes we examined in this Key Question is in Table 3 below. Of the 11 outcomes, the evidence was sufficient to permit a conclusion for eight outcomes:

- Five outcomes favored laparoscopy (return to daily activities, return to work, long-term pain, hematoma, and wound infection)
- Two outcomes favored open surgery (hernia recurrence and epigastric vessel injury)
- One outcome indicated approximate equivalence (length of stay)

Our ratings of the strength of evidence for these outcomes also appear in the table. Studies were typically at moderate risk of bias (see the pertinent section above); some inconsistencies were found for some outcomes based on effect sizes on opposite sides of a null effect; all of these outcomes are directly important to clinicians and patients; some imprecision was found for some outcomes that precluded conclusions. Two outcomes were judged to have a large magnitude of effect (return to daily activities and return to work, both of which indicated advantages of laparoscopy in excess of two days and possibly as much as six days). Three of the adverse events were judged to potentially be associated with publication bias, specifically in the form of selective outcome reporting (for example, only four of 37 studies reported rates of small bowel injury, and the authors' choice to report that data may have been influenced by the nature of the findings).

Questions about the relative importance of these outcomes need to be considered carefully. Some may believe the advantages of laparoscopic repair (faster recovery and lower rates of minor complications) may outweigh the disadvantages (higher rates of recurrence and epigastric vessel injury), whereas others may believe that its disadvantages outweigh the advantages.

**Table 3. Key Question 2a: Strength of evidence ratings**

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| Lap. vs. open | Hernia recurrence | 29 | MOD | I | D | P (RR 1.1 to 1.8) | Open | LOW |
| Lap. vs. open | Length of stay (days) | 25 | MOD | I | D | P (Diff. -0.52 to -0.14) | EQ | LOW |
| Lap. vs. open | RTDA (days) | 19 | MOD | C | D | P (Diff. -5.6 to -2.2) | Lap. | HIGH* |
| Lap. vs. open | RTW (days) | 20 | MOD | C | D | P (Diff. -6.1 to -3.1) | Lap. | HIGH* |
| Lap. vs. open | Quality of life (QALYs) | 1 | MOD | U | D | P (QALY difference -0.0135 to 0.0405) | EQ | INSUFF[@] |
| Lap. vs. open | Patient satisfaction | 3 | MOD | I | D | I (CI not calculable) | ? | INSUFF[@] |
| Lap. vs. open | Long-term pain (% of patients) | 13 | MOD | C | D | P (OR 0.48 to 78) | Lap. | MOD |
| Lap. vs. open | Epigastric vessel injury | 8 | MOD | C | D | P (OR 1.02 to 3.93) | Open | LOW[@] |
| Lap. vs. open | Hematoma | 24 | MOD | I | D | P (OR 0.54 to 0.89) | Lap. | LOW |
| Lap. vs. open | Small bowel injury | 4 | MOD | I | D | I OR (0.11 to 4.6) | ? | INSUFF[@] |
| Lap. vs. open | Small bowel obstruction | 7 | MOD | C | D | I (OR 0.58 to 8.0) | ? | INSUFF[@] |
| Lap. vs. open | Urinary retention | 20 | MOD | I | D | I OR (0.84 to 1.86) | ? | INSUFF |
| Lap. vs. open | Wound infection | 17 | MOD | C | D | P (OR 0.34 to 0.73) | Lap. | MOD |

**Table Note:**
**For risk of bias,** MOD.=Moderate. For consistency, C=consistent, I=inconsistent, U=unknown consistency because there was only one study.
**For directness,** D=direct, I=indirect. For precision P=precise, I=imprecise.
**For the column labeled "Evidence favors,"** ? denotes inconclusive evidence, and EQ denotes approximate equivalence. SOE=strength of evidence.
**For the column labeled SOE rating,** INSUFF=insufficient, * indicates that the SOE was upgraded due to a large magnitude of effect, and [@] indicates that the SOE was downgraded due to publication bias or selective outcome reporting.
**Other abbreviations:** NA=not applicable, OR=odds ratio, RR=relative risk, RTDA=Return to activities of daily living, RTW=Return to work

Nine non-English studies may potentially have met the inclusion criteria for this Key Question if we had not required that studies be published in English.[88-96] Three of these were clearly randomized trials, and the other six may have been randomized (the abstract was unclear on this point).We summarize the results as follows:

- One RCT[91] (comparing laparoscopic IPOM with open mesh plug) found lower rates of hematoma, wound infection, and short-term pain after IPOM, as well as faster recovery after IPOM. These results are consistent with the conclusions of our review.
- Another RCT[89] (comparing TAPP with Lichtenstein) did not find faster recovery or less pain after TAPP, and also did not find lower rates of hematoma after TAPP. These results are not consistent with the conclusions of our review. No recurrences were observed, but authors did find three contralateral hernias during TAPP and no such hernias during Lichtenstein.
- A third RCT[90] (comparing TAPP with "open mesh herniorrhaphy") found shorter hospital stay and return to daily activities after TAPP, and no difference in overall complication rates (specific complications were not delineated in the abstract of the study). Overall consistency with our review is unclear. No hernia recurrences were observed in the one-year followup period.
- One study[88] (possibly randomized, comparing TEP to Lichtenstein) found higher complication rates in the TEP group, and no TEP advantages regarding patient satisfaction. Specific complications were not reported in the abstract, so consistency with our review is unclear.
- One study[92] (possibly randomized, comparing TEP to Lichtenstein) found that TEP patients had faster recovery and lower rates of long term pain (consistent with our findings), and found no differences in recurrence or complication rates.
- One study[93] (possibly randomized, comparing TEP to "open tension free operation (OTF) using the onlay flat mesh technique") found less short-term pain after TEP.
- One study[94] (possibly randomized, comparing "laparoscopic surgery (intraabdominal preperitoneal repair)" to "open surgery (tension free repair)" only reported short-term surrogate outcomes such as fasting plasma glucose and C-reactive protein, which were not outcomes of interest in our review.
- One study[96] (possibly randomized, comparing "laparoscopic approach" to a set of open procedures ["Bassini, Shouldice, Lichtenstein"]) found laparoscopic advantages regarding "shorter hospitalization, lower morbidity and rapid socioprofessional reintegration." Consistency with our review is mixed.
- One study[97] (possibly randomized, comparing TEP to Stoppa) found one-year recurrence rates of 2.2% and 0% (respectively), three-year recurrence rates of 3.6% and 5.2% (respectively), and four-year recurrence rates of 7.4% and 10.5% (respectively). The longer-term rates, which favor laparoscopy, are opposite of our review's findings that long-term recurrence rates favor open surgery for primary hernia.

## Key Question 2b. Does open hernia repair with a mesh differ from laparoscopic hernia repair with a mesh in patient-oriented effectiveness outcomes and/or adverse events? Bilateral hernias

### Study Characteristics

General information about the six studies included for this Key Question appears in Table 36 of Appendix C. Each was conducted in a different country (Denmark, France, Italy, Switzerland, Turkey, and the UK). Three were single-center randomized trials, one was a two-center RCT, one was an RCT that did not report the number of centers, and the last was the Danish registry that was also included for Key Question 2a. Three studies compared TEP to the Stoppa procedure, two compared TAPP to Lichtenstein, and the Danish registry compared TAPP/TEP to Lichtenstein (authors combined data on TAPP and TEP procedures). Three of these six studies were also included for Key Question 2a on primary hernia; they were included for this question also because they reported subgroup analyses specifically for those with bilateral hernia.

Patient enrollment in the RCTs ranged from 43 to 403, and patients were enrolled in the same timeframe as the studies included for Key Question 2a (the mid-1990s to early 2000s). Four of the five RCTs were conducted in university hospitals (the fifth did not report the type of hospital). Funding source was unreported in three of the six studies; two involved government funding, and one RCT was supported by a manufacturer (Ethicon Endo-Surgery).

Patient enrollment criteria appear in Table 37 (hernia-related criteria), Table 38 (demographic and medical criteria), and Table 39 (other criteria) of Appendix C. Generally, their criteria were similar to the studies included for Key Question 2a, with the obvious exception that no studies excluded bilateral hernia. Three studies excluded giant scrotal hernia, two excluded femoral hernia, two excluded incarcerated hernia, and one excluded recurrent hernia. Four included any adults, whereas the other two set more specific age boundaries. Five excluded those unfit for general anesthesia, three excluded those with prior lower abdominal surgery, and only one specifically excluded women.

Treatment details appear in Table 40 of Appendix C. For laparoscopic repair, three studies performed TAPP and three performed TEP; either procedure typically involved general anesthesia. Meshes were typically stapled, and for bilateral hernias, two studies used two meshes in each patients (one on each side), one used a single large (30 x 10cm) “bikini” mesh, one reported that either one large or two regular-sized meshes were used, and two studies did not report information about meshes. The open procedure was Lichtenstein in three studies and Stoppa in three studies; the Stoppa procedure involves a single large mesh to cover both hernia defects.

Baseline patient characteristics appear in Table 41 of Appendix C, and these were similar to patients included for Key Question 2a (other than the fact that Key Question 2b patients had bilateral hernia). See the pertinent section in Key Question 2a for an overview.

### Risk of Bias

Our risk of bias assessments for the six studies appear in Table 42 of Appendix C. The five RCTs were all categorized as Moderate risk-of-bias for all of their outcomes, and the Danish registry study was categorized as High risk of bias. The reasons for this latter category assignment were mentioned above in Key Question 2a (non-random assignment, retrospectivity, lack of concealment of allocation, outcomes assessed with knowledge of treatment, and potential selection bias). Reasons for assigning a Moderate category to the five RCTs were the same as

those discussed in Key Question 2a: possible differences in prior surgical expertise, lack of concealment of allocation (either not done or not reported in three of six studies), and lack of outcome assessor blinding (clearly not done in two studies, and unreported in the other four studies).

## Findings

All included data for this Key Question appear in Table 43 of Appendix C.

### Hernia recurrence

We performed a meta-analysis of all three studies reporting this outcome specifically for bilateral hernia, and found that the evidence was inconclusive (summary relative risk 1.07, 95% CI: 0.19 to 6.06) (Figure 4 middle panel). This is inconclusive because the evidence is simultaneously consistent with a large advantage of laparoscopy (recurrence one-fifth as likely with laparoscopy) but also with a large advantage of open repair (recurrence six times more likely with laparoscopy). The length of followup was one year in two studies, and a range from 0-3 years in the third study.

### Length of hospital stay

Four of the six studies reported an outcome in this category, and all of them could be included in a meta-analysis. (Figure 5 middle panel). This meta-analysis was inconclusive (summary weighted mean difference in days -1.7, 95% CI: -4.1 to +0.6).

### Return to daily activities

Both studies reporting this outcome were meta-analyzed, but the resulting estimate was too variable to be conclusive (summary difference in days -9.0, 95% CI: -20.7 to +2.8) (Figure 6 middle panel).

### Return to work

Only one of the six studies reported data on this outcome, and the authors reported a much shorter RTW after laparoscopy (median 16 days) than after open surgery (median 30 days) ($p<0.05$).

### Quality of life

None of the studies reported QOL data.

### Patient Satisfaction

None of the studies reported patient satisfaction data.

### Long-term pain

None of the studies reported long-term pain data.

### Adverse events

Of the six adverse events we considered major outcomes (see list in Methods section), only three were reported by any of the six studies (hematoma, urinary retention, and wound infection, each reported by two studies). We conducted meta-analyses of these three events, (middle panels of Figure 10, Figure 13, and Figure 14, respectively), but for all three the evidence was inconclusive because it was consistent with effects in either direction.

## Applicability

Six studies are included for review for Key Question 2b. We evaluated these studies to identify factors that may potentially affect the applicability of the evidence. As described in the *Methods* section, the goal of the evaluation is to raise stakeholders' awareness of potential applicability issues embedded in the evidence rather than to generate a rating or score for the applicability.

These six studies reviewed for Key Question 2b compared two mesh-based open surgeries—the Stoppa and the Lichtenstein methods—with two laparoscopic procedures— TAPP and TEP— for repairing bilateral hernias. Table 36 provides a detailed description of the procedures being compared in the studies. The two interventions being compared in the meta-analyses—i.e., open vs. laparoscopic surgery—included all four different procedures. The findings of the meta-analyses (e.g., effect sizes) might not apply to comparisons of specific procedures (e.g., the Lichtenstein method vs. TAPP, or the Stoppa method vs. TEP). Meanwhile, in one of the four studies, the surgeries were performed between 2003 and 2007.[98] In the other five studies, the surgeries were performed in the 1990s. This body of evidence may not necessarily reflect the comparative performance of the procedures that are performed at the current time.

One of the six studies reviewed for Key Question 2b provided information on surgeons' prior experience for the surgeries being studied.[48-51] This study reported that the surgeon had a prior experience of 50 cases with TEP. Another study reported the annual numbers of cases performed by hospital departments.[18,99-103] The other four studies reviewed did not report data on the surgeons' level of experience. Given limited data, we were unable to judge what implication surgeons' experience may have in the applicability of the evidence. Table 40 provides additional detail on the hernia repair procedures performed in the studies, including any available data on surgeons' experience.

Patient enrollment criteria and reported baseline characteristics varied significantly across the six studies. For example, some studies excluded patients with prior lower abdominal surgeries, while others studies excluded patients unfit for general anesthesia. Based on the data reported, we did not identify any clear patterns in the patient characteristics of the studies that indicate significant impact on the applicability of the evidence. Detailed patient enrollment criteria and baseline characteristics of these studies are provided in Table 37 and Table 38.

All six studies were performed outside of the United States, primarily in European countries. The differences in healthcare systems and practice patterns between the U.S. and Europe may potentially have impact on the applicability of the evidence from the perspectives of the U.S. stakeholders. Four of the five RCTs were conducted in university hospitals (the fifth did not report the type of hospital). The only non-RCT study involved 76 centers in Denmark and reported that 76 percent of the surgeries were performed in hospital departments and the other 24 percent occurred in private clinics. Based on the data reported, it is unclear how the clinical settings of the studies might affect the applicability of the evidence. Detailed information on geographic and clinical settings of the six studies is provided in Table 36.

## Summary of Key Question 2b

A summary of the comparisons and outcomes we examined in this Key Question is in Table 4 below. The evidence was insufficient to permit conclusions for only one outcome: that bilateral hernia patients return to work sooner if they receive laparoscopic repair. This was rated as Low strength of evidence because only one of the six included studies reported information on return to work (therefore consistency with other studies could not be determined). For other

outcomes, the primary reason for the grade of Insufficient was a lack of precision. For example, for hernia recurrence, the direction of the effect could favor laparoscopy with an odds ratio of about 0.2, or it could favor open surgery with an odds ratio of over 6.

**Table 4. Key Question 2b: Strength of evidence ratings**

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| Lap. vs. open | Hernia recurrence | 3 | MOD. | I | D | I (RR 0.19 to 6.06) | ? | INSUFF |
| Lap. vs. open | Length of stay (days) | 4 | MOD. | C | D | I (-4.1 to +0.6) | ? | INSUFF |
| Lap. vs. open | RTDA (days) | 2 | MOD. | C | D | I (-20.7 to +2.8) | ? | INSUFF[@] |
| Lap. vs. open | RTW (days) | 1 | MOD. | U | D | P (CI not reported, but p<0.05) | Lap. | LOW*[@] |
| Lap. vs. open | Quality of life (QALYs) | 0 | NA | NA | NA | NA | ? | INSUFF |
| Lap. vs. open | Patient satisfaction | 0 | NA | NA | NA | NA | ? | INSUFF |
| Lap. vs. open | Long-term pain (% of patients) | 0 | NA | NA | NA | NA | ? | INSUFF |
| Lap. vs. open | Epigastric vessel injury | 0 | NA | NA | NA | NA | ? | INSUFF |
| Lap. vs. open | Hematoma | 2 | MOD. | I | D | I (OR 0.074 to 2.56) | ? | INSUFF[@] |
| Lap. vs. open | Small bowel injury | 0 | NA | NA | NA | NA | ? | INSUFF |
| Lap. vs. open | Small bowel obstruction | 0 | NA | NA | NA | NA | ? | INSUFF |
| Lap. vs. open | Urinary retention | 2 | MOD. | I | D | I (OR 0.017 to 73.2) | ? | INSUFF[@] |
| Lap. vs. open | Wound infection | 2 | MOD. | C | D | I (OR 0.019 to 1.41) | ? | INSUFF[@] |

**Table Note:**
**For risk of bias,** MOD.=Moderate. For consistency, C=consistent, I=inconsistent, U=unknown consistency because there was only one study.
**For directness,** D=direct, I=indirect. For precision P=precise, I=imprecise.
**For the column labeled "Evidence favors,"** ? denotes inconclusive evidence, and EQ denotes approximate equivalence. SOE=strength of evidence.
**For the column labeled SOE rating,** INSUFF=insufficient, * indicates that the SOE was upgraded due to a large magnitude of effect, and
[@] indicates that the SOE was downgraded due to publication bias or selective outcome reporting.
**Other abbreviations:** NA=not applicable, OR=odds ratio, RR=relative risk; RTDA=Return to activities of daily living; RTW=Return to work

One excluded non-English article compared open and laparoscopic repair for bilateral hernia.[95] The specific comparison was TEP vs. Stoppa, and the abstract gave conflicting statements about whether patients were randomly assigned to groups. Because the numbers of patients in the two groups were quite different (43 and 74), it seems unlikely that random assignment was used. Given the possibility of selection bias (assuming the authors employed no analytic controls such as propensity scores), the article would not have met our inclusion criteria for this question.

## Key Question 2c. Does open hernia repair with a mesh differ from laparoscopic hernia repair with a mesh in patient-oriented effectiveness outcomes and/or adverse events? Recurrent hernias

### Study Characteristics

General information about the eight studies included for this Key Question appears in Table 44 of Appendix C. Two were from Sweden, and the others were from six different countries (Denmark, The Netherlands, France, Greece, Finland, and the U.S.). Four were single-center RCTs, two were multicenter RCTs, and two were registry studies (Sweden and Denmark, the same registries mentioned above). The open mesh procedure was Lichtenstein in six studies and the Stoppa procedure in the other two studies. For the laparoscopic mesh procedure, two studies performed TAPP, two performed TEP, one performed both and reported data separately, and the other three performed both TAPP and TEP and combined the data. Four of these eight studies were also included for Key Question 2a on primary hernia; they were included for this question also because they reported subgroup analyses specifically for those with recurrent hernia.

Patient enrollment in the six RCTs ranged from 50 to 2,164. Patients were enrolled in the same timeframe as the studies included for Key Question 2a (the mid-1990s to early 2000s). Four studies were conducted at general and non-university hospitals, two were conducted at university hospitals, and two included some university hospitals as well as some non-university hospitals. Five studies mentioned funding source: three were government-funded, one was hospital-funded, and one was partially funded by a manufacturer that was not involved in study design and analysis.

Patient enrollment criteria appear in Table 45 (hernia-related criteria), Table 46 (demographic and medical criteria), and Table 47 (other criteria) of Appendix C. Two studies excluded bilateral hernia, two excluded strangulated hernia, two excluded incarcerated hernia, and two excluded giant scrotal hernia (some studies excluded one or more of these hernia types). Four included any adults, whereas the other four set more specific age boundaries. Five excluded those unfit for general anesthesia, three excluded those with prior lower abdominal surgery, three excluded those whose prior hernia operation employed a mesh, three specifically excluded women, and three excluded those with coagulation disorders.

Treatment details appear in Table 48 of Appendix C. For laparoscopic repair, four studies used both TAPP and TEP, two exclusively performed TAPP, and two exclusively performed TEP. As in previous Key Questions, general anesthesia and mesh stapling were the norm, and a variety of mesh sizes were used. For open repair, six studies used Lichtenstein and two performed Stoppa repairs.

Baseline patient characteristics appear in Table 49 of Appendix C, and these were similar to patients included for Key Question 2a (other than the fact that Key Question 2c patients had recurrent hernia). See the pertinent section in Key Question 2a for an overview.

## Risk of Bias

Our risk of bias assessments for the eight studies appear in Table 50 of Appendix C. The six RCTs were all categorized as Moderate risk-of-bias for all of their outcomes, and the two registry studies was categorized as High risk of bias. The reasons for these latter category assignments were mentioned above in Key Question 2a (non-random assignment, retrospectivity, lack of concealment of allocation, outcomes assessed with knowledge of treatment, and potential selection bias). Reasons for assigning a Moderate category to the six RCTs were the same as those discussed in Key Question 2a: possible differences in prior surgical expertise, lack of concealment of allocation (either not done or not reported in two of six RCTs), and lack of outcome assessor blinding (clearly not done in one RCT, and unreported in three other RCTs).

## Findings

All included data for this Key Question appear in Table 51 of Appendix C.

### Hernia recurrence

Given that this question addresses patients who are undergoing surgery for hernia recurrence, this outcome is technically hernia *re*-recurrence. Seven of the eight studies reported data on this outcome. A meta-analysis of these data favored laparoscopic repair over open repair (summary relative risk 0.82, 95% CI: 0.70 to 96) (Figure 4 lower panel). The length of followup varied widely across the studies, with one study following patients from 0-3 years and another followed patients for an average of 5.3 years. As with Key Question 2a on primary hernia, we had defined the MCSD for hernia recurrence as three percentage points. To aid interpretation of the summary relative risk of 0.82, we calculated the overall rate of re-recurrence in the open repair groups, which was 12.5%. Applying a relative risk of 0.82 to this rate yields a laparoscopic re-recurrence rate of 10.2%; applying it to the lower bound of RR=0.70 yields a lower percentage of 8.7%; applying it to the upper bound of RR=0.96 yields an upper bound of 12.0%. Thus the difference in percentages could be as high as 3.8% (12.5% to 8.7%), which is higher than our MCSD of three percentage points. Thus, it is unclear whether the advantage of laparoscopy for preventing re-recurrence can be considered clinically significant.

### Length of hospital stay

Five of the eight studies reported an outcome in this category, and three of these could be included in a meta-analysis (Figure 5 lower panel) (the other two reported the length-of-stay data only dichotomously). This meta-analysis was inconclusive (summary weighted mean difference -1.3 days, 95% CI: -2.8 to +0.33).

### Return to daily activities

Two of three studies reporting this outcome were meta-analyzed (the third used a functional index scale instead of reporting the amount of time). The meta-analysis (Figure 6 lower panel) indicated an advantage of laparoscopic repair (summary weighted mean difference in days -7.4 days, 95% CI: -11.4 to -3.4).

### Return to work

Two of three studies reporting this outcome were meta-analyzed (the third did not report the Ns). The meta-analysis (Figure 7 lower panel) did not indicate a clear direction of effect (summary weighted mean difference -6.4 days, 95% CI: -13.2 to +0.34).

### Quality of life

None of the studies reported QOL data.

### Patient Satisfaction

None of the studies reported patient satisfaction data.

### Long-term pain

Three studies reported long-term pain data, and two were meta-analyzed (Figure 8 lower panel) (the third did not report the Ns). This meta-analysis indicated lower rates of long-term pain after laparoscopy (OR=0.24, 95% CI: 0.08 to 0.74). This indicates a clinically significant difference in rates. The severity of pain is unclear, however, because none of the three studies measured long-term pain on a continuous scale.

### Adverse events

Of the six adverse events we considered major outcomes (see list in Methods section), four were reported by any of the six studies (epigastric vessel injury reported by two studies, hematoma reported by one study, urinary retention reported by three studies, and wound infection reported by three studies). We conducted meta-analyses of these four events (lower panels of Figure 9, Figure 10, Figure 13, and Figure 14, respectively), but for all four the evidence was inconclusive because it was consistent with effects in either direction.

## Applicability

Eight studies are included for review for Key Question 2c. We evaluated these studies to identify factors that may potentially affect the applicability of the evidence. As described in the *Methods* section, the goal of the evaluation is to raise stakeholders' attention to potential applicability issues embedded in the evidence rather than generating a rating or score for the applicability.

The eight studies reviewed for Key Question 2c compared mesh-based open surgeries—including the Stoppa and the Lichtenstein methods—with laparoscopic procedures—including TAPP and TEP—for repairing recurrent hernias. Table 44 provides a detailed description of the procedures being compared in the studies. The two interventions being compared in the meta-analyses—i.e., open vs. laparoscopic surgery—included different procedures (e.g., the Lichtenstein method and the Stoppa method, TEP, and TAPP). The findings from the meta-analyses (e.g., effect sizes) might not apply to comparisons of specific procedures (e.g., the Lichtenstein method vs. TEP, or the mesh plug method vs. TEP). Meanwhile, in eight studies reviewed for Key Question 2c, the surgeries were performed in the 1990s or early 2000s. This body of evidence may not necessarily reflect the comparative performance of the procedures that are performed at the current time.

Five of the eight studies reviewed for Key Question 2c discussed surgeons' prior experience for the surgeries being compared.[17,18,26,48-51,74-79,99-104] The surgeons in the studies include experts with "special training," residents, or those having more than 25 or 50 prior cases. Three studies reviewed did not discuss surgeons' prior experiences. Given the data reported, we were unable to judge what implication surgeons' experience may have in the applicability of the overall

evidence. Table 48 provides additional detail on the hernia repair procedures performed in the studies, including data on surgeons' experiences.

Patient enrollment criteria and reported baseline characteristics varied significantly across the eight studies. For example, some studies excluded patients with an ASA score >3 or patients with prior lower abdominal surgeries. Some other studies excluded patients unfit for general anesthesia. Based on the data reported, we did not identify any clear patterns in the patient characteristics of the studies that indicate significant impact on the applicability of the evidence. Detailed patient enrollment criteria and baseline characteristics of these studies are provided in Table 45 and Table 46.

Except for one study,[26,74-79] all other seven studies were performed outside of the U.S.—all in European countries. The differences in healthcare systems and practice patterns between the U.S. and Europe may potentially impact the applicability of the evidence from the perspectives of the U.S. stakeholders. The clinical settings where the eight studies were conducted varied significantly, ranging, ranging from general surgery clinics, non-teaching hospitals, to university hospitals. Based on the data reported, it is unclear how the clinical settings of the studies might affect the applicability of the evidence. Detailed information on geographic and clinical settings of the eight studies is provided in Table 44.

## Summary of Key Question 2c

A summary of the comparisons and outcomes we examined in this Key Question is in Table 5 below. The evidence permitted conclusions for three outcomes, all of which favored laparoscopic repair over open repair: hernia recurrence (lower rates after laparoscopy), return to daily activities (faster after laparoscopy), and long-term pain (lower rates after laparoscopy). This section contains no discussion of excluded non-English articles because none of those abstracts addressed recurrent hernia for open vs. laparoscopic repair.

**Table 5. Key Question 2c: Strength of evidence ratings**

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| Lap. vs. open | Hernia recurrence | 7 | MOD. | I | D | P (RR 0.70 to 0.96) | Lap. | LOW |
| Lap. vs. open | Length of stay (days) | 5 | MOD. | C | D | I (-2.8 to +0.33) | ? | INSUFF |
| Lap. vs. open | RTDA (days) | 3 | MOD. | C | D | P (-11.4 to -3.4) | Lap. | HIGH* |
| Lap. vs. open | RTW (days) | 3 | MOD. | C | D | I (-13.2 to +0.34) | ? | INSUFF |
| Lap. vs. open | Quality of life (QALYs) | 0 | NA | NA | NA | NA | ? | INSUFF |
| Lap. vs. open | Patient satisfaction | 0 | NA | NA | NA | NA | ? | INSUFF |
| Lap. vs. open | Long-term pain (% of patients) | 3 | MOD. | C | D | P (OR 0.08 to 0.74 | Lap. | MOD |
| Lap. vs. open | Epigastric vessel injury | 2 | MOD. | I | D | I (OR 0.15 to 2.48) | ? | INSUFF[@] |
| Lap. vs. open | Hematoma | 1 | MOD. | U | D | I (OR 0.62 to 6.51) | ? | INSUFF[@] |
| Lap. vs. open | Small bowel injury | 0 | NA | NA | NA | NA | ? | INSUFF |
| Lap. vs. open | Small bowel obstruction | 0 | NA | NA | NA | NA | ? | INSUFF |
| Lap. vs. open | Urinary retention | 3 | MOD. | I | D | I (OR 0.27 to 1.70) | ? | INSUFF |
| Lap. vs. open | Wound infection | 3 | MOD. | C | D | I (OR 0.05 to 1.38) | ? | INSUFF |

**Table Note:**
**For risk of bias,** MOD.=Moderate.
**For consistency,** C=consistent, I=inconsistent, U=unknown consistency because there was only one study.
**For directness,** D=direct, I=indirect. For precision P=precise, I=imprecise.
**For the column labeled "Evidence favors,"** ? denotes inconclusive evidence, and EQ denotes approximate equivalence. SOE=strength of evidence.
**For the column labeled SOE rating,** INSUFF=insufficient, * indicates that the SOE was upgraded due to a large magnitude of effect, and
[@] indicates that the SOE was downgraded due to publication bias or selective outcome reporting.
**Other abbreviations:** NA=not applicable, OR=odds ratio, RR=relative risk, RTDA=Return to activities of daily living, RTW=Return to work

## Key Question 3. Do different open mesh-based repair procedures (e.g., Lichtenstein repair, mesh plug) differ in patient-oriented effectiveness outcomes and/or adverse events?

### Study Characteristics

General information about the 21 studies included for this Key Question appears in Table 52 of Appendix C. Five studies were conducted in Turkey; four in the UK; three in Sweden; two in the Netherlands; one each in the U.S., Poland, Finland, Greece, Egypt, and one was conducted both in U.S. and UK. Fourteen studies were single-center RCTs; two were two-center RCTs; two were three-center RCTs; one was country-wide registry study in Sweden; and the remaining two were RCTs that did not report the number of centers.

Regarding specific surgical procedures, the most commonly compared procedures were Lichtenstein vs. mesh plug (seven studies), Lichtenstein vs. Prolene Hernia System (PHS) (five studies), Lichtenstein vs. the open peritoneal mesh (OPM) technique (three studies), Mesh plug vs. PHS (two studies), and Lichtenstein vs. Kugel (two studies). The RCTs enrolled between 26 and 597 patients each; and the Swedish registry included 142,578 hernias repaired in that country. The dates of patient enrollment were reported by 14/21 studies. The average length of the enrollment period was 3.5 years (range nine months to 14 years). Studies were typically conducted between 2000 and 2010.

Eighteen studies were conducted at university hospitals; two included some university hospitals as well as some non-university hospitals; the remaining did not report the type(s) of hospitals. Funding for the study was not reported by 14 studies; government funding was reported in one study; university funding was reported in two studies; two did not report the funding source but did state they had no manufacturer ties; two reported partial manufacturer funding.

Patient enrollment criteria appear in Table 53 (hernia-related criteria), Table 54 (demographic and medical criteria), and Table 55 (other criteria) of Appendix C. Enrollment criteria varied widely among the 21 studies. The most commonly used hernia-related exclusions were recurrent hernia (13 studies), bilateral hernia (11 studies), “emergency” hernia (10 studies, femoral hernia (nine studies), and incarcerated hernia (nine studies). Others were irreducible hernia (excluded by five studies), scrotal hernia (excluded by three studies), and asymptomatic hernia (excluded by one study). One study included only bilateral hernia. Overall, the studies paint an extraordinarily diverse portrait of the types of hernias deemed relevant to the studies, even though, by virtue of inclusion, they all compared open repair of inguinal hernia to laparoscopic repair of inguinal hernia.

Regarding patient age criteria, 15 of the 21 studies (71%) stated that they included any adults or required age >18. Three (14%) excluded those unfit for general anesthesia or those with anesthesia risk scores of 3 or 4 or more, and three studies excluded those who had undergone a prior surgery in the lower abdomen. Five studies excluded all females, two excluded pregnant women, and two excluded those with coagulation disorders. As with the hernia-related exclusions, there was large variability in how studies selected patients for inclusion.

Treatment details appear in Table 56 of Appendix C. All reported baseline patient characteristics in the studies included for this Key Question appear in Table 57 of Appendix C.

## Risk of Bias

Our risk-of-bias assessments for the 21 studies appear in Table 58 of Appendix C. The 20 RCTs were categorized as Moderate or low risk-of-bias for their reported outcomes, and the one registry study that was categorized as High risk-of-bias.

The reasons for this latter category assignment were mentioned above in Key Question 2a (non-random assignment, retrospectivity, lack of concealment of allocation, outcomes assessed with knowledge of treatment, and potential selection bias). Common reasons for assigning a Moderate category to the RCTs were the same as those discussed in Key Question 2a: possible differences in prior surgical expertise, lack of concealment of allocation, and lack of outcome assessor blinding.

## Findings

All included data for this Key Question appear in Table 59 of Appendix C. To address this Key Question, multiple comparisons involving different surgical procedures were performed. Summarized below are findings for the comparisons for which two or more studies had reported data on at least one outcome of interest.

### Lichtenstein vs. Mesh plug (seven studies)

**Hernia recurrence**

We performed a meta-analysis of three studies reporting this outcome (Figure 15), and identified a summary relative risk of 1.07 (95% CI: 0.33 to 3.42). We defined the MCSD as a three-percentage-point difference between groups, so to aid interpretation; we calculated the overall rate of recurrence in the Lichtenstein group, which was 1.07%. Multiplying a 3.42 relative risk with this rate yielded a corresponding rate of 3.67% for low-weight PP mesh group. The difference between these rates is only 2.59%, which is less than our predefined MCSD of three percentage points. This suggests approximate equivalence in recurrence rates.

**Length of hospital stay**

None of the studies of this comparison reported this outcome.

**Return to daily activities**

Two studies reported this outcome, and were included in a meta-analysis of number of days before returning to normal daily activities (Figure 16). The meta-analysis was inconclusive (summary difference in means:-4.38 days, 95% CI: -13.17 to 4.41).

**Return to work**

Two studies reported return-to-work data, and were combined in a meta-analysis. The meta-analysis (Figure 17) indicated shorter time-to-return-to-work after Lichtenstein repair (summary difference in means: -4.0, 95% CI: -6.97 to -1.02). This is larger than what we defined as the MCSD for this outcome (one day).

**Short-term pain**

Four studies reporting short-term pain on VAS (<1 month after surgery) were included in a meta-analysis. (Figure 18). The meta-analysis was inconclusive (summary difference in means: -1.48, 95% CI: -3.36 to 0.39 points on a 0-10 scale).

**Intermediate-term pain**

None of the studies of this comparison reported this outcome.

**Adverse events**

We conducted meta-analyses of four types of adverse events (seroma reported by three studies, hematoma reported by five studies, wound infection reported by five studies, and urinary retention reported by two studies)(Figure 19, Figure 20, Figure 21, and Figure 22, respectively). A clear direction of effect was found for one event: seroma (lower rates with Lichtenstein repair, OR=0.39, 95% CI: 0.16 to 0.94). For the other three events, the evidence was inconclusive.

## Lichtenstein vs. PHS (five studies)

**Hernia recurrence**

We performed a meta-analysis of four studies reporting this outcome (Figure 23), and found a summary RR=2.92, 95% CI: 0.57 to 15). We had defined the MCSD as a three-percentage-point difference between groups, so to aid interpretation; we calculated the overall rate of recurrence in the Lichtenstein repair groups, which was 0.9%. Multiplying a 15 relative risk to this rate yield a corresponding rate of 13.5% for PHS. The difference between these rates is over 12 percentage points, which is greater than our predefined MCSD of three percentage points. Thus, the evidence is too imprecise to permit a conclusion.

**Length of hospital stay**

One study found equivalence for this outcome (difference in means -0.03 days, 95% CI: -0.29 to 0.23).

**Return to daily activities**

None of the studies of this comparison reported this outcome.

**Return to work**

Two studies reported RTW data, and were combined in a meta-analysis. (Figure 24). The meta-analysis was inconclusive (summary difference in means -4.57 days, 95% CI: -15.74 to 6.6).

**Short-term pain**

Two studies reporting short-term pain using VAS (≤1 month after surgery) were included in a meta-analysis (Figure 25). We found equivalence comparing Lichtenstein to PHS (summary difference in means: -0.03, 95% CI: -0.37 to 0.31, points on a 0-10 scale).

**Intermediate-term pain**

Two studies reporting short-term pain using VAS (>1 month but ≤6 months after surgery) were included in a meta-analysis (Figure 26). The meta-analysis was inconclusive (summary difference in means: -1.03, 95% CI: -2.4 to 0.33, points on a 0-10 scale).

**Adverse events**

We conducted meta-analyses of two types of adverse events (hematoma reported by two studies and wound infection reported by three studies) (Figure 27 and Figure 28, respectively). The evidence was inconclusive for both events.

## Lichtenstein vs. OPM (three studies)

**Hernia recurrence**

None of the studies of this comparison reported this outcome.

**Length of hospital stay**

One study reported an outcome in this category, and the evidence was inconclusive (difference in means -0.4, 95% CI: -1.03 to 0.23).

**Return to daily activities**

One study reported an outcome in this category, and the evidence was inconclusive (difference in means -0.16, 95% CI: -1.87 to 1.55).

**Return to work**

One study reported an outcome in this category, and the evidence was inconclusive (difference in means -0.88, 95% CI: -2.66 to 0.9).

**Short-term pain**

One study reporting short-term pain using VAS (≤1 month after surgery) was evaluated and found equivalence comparing Lichtenstein to OPM (difference in means -0.27, 95% CI: -1.35 to 0.81, points on a 0-10 scale).

**Intermediate-term pain**

None of the studies of this comparison reported this outcome.

**Adverse events**

One study reported hematoma (0 events in the Lichtenstein vs. 1 event in the OPM group) and another reported wound infection (1 event the Lichtenstein vs. 1 event in the OPM group). The evidence was inconclusive for both events.

## Mesh plug vs. PHS (two studies)

**Hernia recurrence**

One study reported recurrence (1 recurrence in mesh plug vs. 0 in the PHS group), and the evidence was inconclusive.

**Length of hospital stay**

None of the studies of this comparison reported this outcome.

**Return to daily activities**

None of the studies of this comparison reported this outcome.

**Return to work**

None of the studies of this comparison reported this outcome.

**Short-term pain**

Two studies reporting short-term pain using VAS (≤1 month after surgery) were evaluated using meta-analysis (Figure 29) and found equivalence comparing mesh plug to PHS (difference in means -0.07, 95% CI: -0.41 to 0.27, points on a 0-10 scale).

**Intermediate-term pain**

None of the studies of this comparison reported this outcome.

**Adverse events**

One study reported hematoma and wound infection. The evidence was inconclusive for both events.

### Lichtenstein vs. Kugel (two studies)

**Hernia recurrence**

One study reported data on recurrence (1 recurrence in Lichtenstein group vs. 0 in the Kugel group), and the evidence was inconclusive.

**Length of hospital stay**

None of the studies of this comparison reported this outcome.

**Return to daily activities**

None of the studies of this comparison reported this outcome.

**Return to work**

None of the studies of this comparison reported this outcome.

**Short-term pain**

One study reporting short-term pain using VAS (≤1 month after surgery) was evaluated and found equivalence comparing Lichtenstein to Kugel (difference in means: -0.3, 95% CI: -0.91 to 0.31, points on a 0-10 scale).

**Intermediate-term pain**

One study reporting intermediate-term pain using VAS (>1 month but ≤6 months after surgery) was evaluated and found equivalence comparing Lichtenstein to Kugel (difference in means: -0.6, 95% CI: -1.21 to 0.01, points on a 0-10 scale).

**Adverse events**

One study reported hematoma, seroma, and wound infection. The evidence was inconclusive for all three events.

## Applicability

Twenty-one studies are included for review for Key Question 3. We evaluated these studies to identify factors that may potentially affect the applicability of the evidence. As described in the *Methods* section, the goal of the evaluation is to raise stakeholders' attention to potential applicability issues embedded in the evidence rather than generating a rating or score for the applicability.

The twenty-one studies reviewed for Key Question 3 compared various open mesh-based procedures for hernia repair, including Lichtenstein, mesh plug (using the Perfix or Proloop device), Trabucco (using the Hertra device), "preperitoneal mesh," "plug," PHS, Kugel, Nyhus, "open properitoneal mesh," Stoppa, and Read-Rives methods. Lichtenstein and mesh plug are the most commonly compared procedures in these studies. Table 52 provides a detailed description of the procedures being compared in the studies. For Key Question 3, we

summarized the findings separately by each comparison of surgical procedures, because the evidence for one set of comparisons does not apply to a different set of comparisons.

Fourteen of the twenty-one studies reviewed for Key Question 3 reported the date range of the surgeries being performed. In these studies, the majority of the surgeries were performed in 1990s and early 2000s. The other seven studies reviewed for Key Question 3 did not report a date range of surgeries being performed. This body of evidence for Key Question 3 may not necessarily reflect the comparative performance of the procedures that are performed at the current time.

Most of the studies included for review for Key Question 3 did not report the surgeons' prior experiences for the procedures being compared. Only two studies reported these data. One study primarily depended on "surgeons in training," and the other one used "highly experienced" surgeons.[46,57] No study reported the number of prior cases or years of practice of the surgeons. Given the limitation in the data reported, we were unable to judge what implication surgeons' experience may have in the applicability of the evidence. Table 56 provides additional detail on the surgical procedures compared in the studies, including data on surgeons' experiences.

Patient enrollment criteria and reported baseline characteristics varied significantly across the 21 studies. While most studies included all adult patients, several studies only included patients older than 30 or 40 years of age.[46,105,106] Many studies excluded patients with recurrent, bilateral, incarcerated, strangulated, or femoral hernia. Five studies excluded all female patients.[46,105,107-109] Based on the data reported, we did not identify any clear patterns in the patient characteristics of the studies that indicate significant impact on the applicability of the evidence. Detailed patient enrollment criteria and baseline characteristics of these studies are provided in Table 61 and Table 62.

Except for two studies,[109,110] all other studies were performed outside of the U.S.—thirteen studies from European countries, five studies from Turkey, and one study from Egypt. The differences in healthcare systems and practice patterns between the U.S. and other regions may potentially have an impact on the applicability of the evidence from the perspectives of the U.S. stakeholders. Except for three studies[46,111-119] all other 18 studies were performed in university hospitals. The evidence for Key Question 3 is potentially more applicable to academic clinical settings. Detailed information on geographic and clinical settings of the 21 studies is provided in Table 52.

## Summary of Key Question 3

A summary of the comparisons and outcomes we examined in this Key Question is provided in Table 6 below. Of the 31 outcomes, the evidence was sufficient to permit a conclusion for eight outcomes:

- Two outcomes favored Lichtenstein compared to mesh plug (return to work and seroma)
- One outcome indicated approximate equivalence comparing Lichtenstein to mesh plug (recurrence)
- One outcomes indicated approximate equivalence comparing Lichtenstein to PHS (short-term pain)
- One outcome indicated approximate equivalence comparing Lichtenstein to OPM (short-term pain)
- One outcome indicated approximate equivalence comparing mesh plug to PHS (short-term pain)

- Two outcomes indicated approximate equivalence comparing Lichtenstein to Kugel (short-term pain, intermediate-term pain).

Our ratings of the strength of evidence for these outcomes also appear in Table 6. Most studies were at moderate risk of bias (see the pertinent section above); some inconsistencies were found for some outcomes based on effect sizes on opposite sides of a null effect; all of these outcomes are directly important to clinicians and patients; some imprecision was found for some outcomes that precluded conclusions. Three outcomes (return to daily activity, return to work, urinary retention) for the Lichtenstein vs. mesh plug comparison were judged to potentially be associated with publication bias, specifically in the form of selective outcome reporting (for example, only two of seven studies reported these outcomes, and the authors' choice to report that data may have been influenced by the nature of the findings). Likewise, length of stay for the Lichtenstein vs. PHS comparison was judged to potentially be associated with publication bias, also in the form of selective outcome reporting (only one of five studies reported this outcome).

**Table 6. Key Question 3: Strength of evidence ratings**

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| Lichtenstein vs. Mesh plug | Recurrence | 3 | MOD | C | D | P<br>*RR 1.07*<br>*(0.33 to 3.42)* | EQ | MOD |
| Lichtenstein vs. Mesh plug | Return to daily activities (days) | 2 | MOD | I | D | I<br>*Diff in means -4.38*<br>*(-13.17 to 4.41)* | ? | INSUFF[@] |
| Lichtenstein vs. Mesh plug | Return to work (days) | 2 | MOD | C | D | P<br>*Diff in means -4*<br>*(-6.97 to -1.02)* | Lichtenstein | LOW[@] |
| Lichtenstein vs. Mesh plug | Short-term pain (measured in VAS) | 4 | MOD | I | D | I<br>*Diff in means-1.48*<br>*(-3.36 to 0.39)* | ? | INSUFF |
| Lichtenstein vs. Mesh plug | Seroma | 3 | MOD | C | D | P<br>*OR 0.39*<br>*(0.16 to 0.94)* | Lichtenstein | MOD |
| Lichtenstein vs. Mesh plug | Hematoma | 5 | MOD | C | D | I<br>*OR 0.8*<br>*(0.47 to 1.37)* | ? | INSUFF[@] |
| Lichtenstein vs. Mesh plug | Wound infection | 5 | MOD | C | D | I<br>*OR 1.55*<br>*(0.79 to 3.05)* | ? | INSUFF |
| Lichtenstein vs. Mesh plug | Urinary retention | 2 | MOD | C | D | I<br>*OR 2.17*<br>*(0.36 to 13.1)* | ? | INSUFF[@] |
| Lichtenstein vs. PHS | Recurrence | 4 | MOD | C | D | I<br>*RR 2.92*<br>*(0.57 to 15)* | ? | INSUFF |
| Lichtenstein vs. PHS | Length of stay (days) | 1 | MOD | U | D | P<br>*Diff in means -0.03*<br>*(-0.29 to 0.23)* | EQ | INSUFF[@] |
| Lichtenstein vs. PHS | Return to work (days) | 2 | MOD | I | D | I<br>Diff in means-4.57<br>(-15.74 to 6.6) | ? | INSUFF |

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| Lichtenstein vs. PHS | Short-term pain (measured in VAS) | 2 | MOD | C | D | P<br>*Diff in means -0.03*<br>*(-0.37 to 0.31)* | EQ | MOD |
| Lichtenstein vs. PHS | Intermediate-term pain (measured in VAS) | 2 | MOD | I | D | I<br>*Diff means -1.03*<br>*(-2.4 to 0.33)* | ? | INSUFF |
| Lichtenstein vs. PHS | Hematoma | 2 | MOD | C | D | I<br>*OR 0.49*<br>*(0.21 to 1.14)* | ? | INSUFF |
| Lichtenstein vs. PHS | Wound infection | 3 | MOD | C | D | I<br>*OR 0.99*<br>*(0.48 to 2.06)* | ? | INSUFF |
| Lichtenstein vs. OPM | Length of stay (days) | 1 | MOD | U | D | I<br>*Diff in means -0.4*<br>*(-1.03 to 0.23)* | ? | INSUFF |
| Lichtenstein vs. OPM | Return to daily activities (days) | 1 | MOD | U | D | I<br>*Diff in means -0.16*<br>*(-1.87 to 1.55)* | ? | INSUFF |
| Lichtenstein vs. OPM | Return to work (days) | 1 | MOD | U | D | I<br>*Diff in means -0.88*<br>*(-2.66 to 0.9)* | ? | INSUFF |
| Lichtenstein vs. OPM | Short-term pain (measured in VAS) | 1 | MOD | U | D | P<br>*Diff in means -0.27*<br>*(-1.35 to 0.81)* | EQ | LOW |
| Lichtenstein vs. OPM | Hematoma | 1 | MOD | U | D | I<br>*OR 0.32*<br>*(0.01 to 8.23)* | ? | INSUFF |
| Lichtenstein vs. OPM | Wound infection | 1 | MOD | U | D | I<br>*OR 1*<br>*(0.06 to 16.93)* | ? | INSUFF |
| Mesh plug vs. PHS | Recurrence | 1 | MOD | U | D | I<br>*RR 2.87*<br>*(0.12 to 69.76)* | ? | INSUFF |
| Mesh plug vs. PHS | Short-term pain (measured in VAS) | 2 | MOD | C | D | P<br>*Diff in means -0.07*<br>*(-0.41 to 0.27)* | EQ | MOD |

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| Mesh plug vs. PHS | Hematoma | 1 | MOD | U | D | I<br>*OR 0.83*<br>*(0.39 to 1.75)* | ? | INSUFF |
| Mesh plug vs. PHS | Wound infection | 1 | MOD | U | D | I<br>*OR 6.36*<br>*(0.76 to 53.48)* | ? | INSUFF |
| Lichtenstein vs. Kugel | Recurrence | 1 | MOD | U | D | I<br>*RR 3*<br>*(0.12 to 72.41)* | ? | INSUFF |
| Lichtenstein vs. Kugel | Short-term pain (measured in VAS) | 1 | MOD | U | D | P<br>*Diff in means -0.3*<br>*(-0.91 to 0.31)* | EQ | LOW |
| Lichtenstein vs. Kugel | Intermediate-term pain (measured in VAS) | 1 | MOD | U | D | P<br>*Diff in means -0.6*<br>*(-1.21 to 0.01)* | EQ | LOW |
| Lichtenstein vs. Kugel | Hematoma | 1 | MOD | U | D | I<br>*OR 0.33*<br>*(0.01 to 8.21)* | ? | INSUFF |
| Lichtenstein vs. Kugel | Seroma | 1 | MOD | U | D | I<br>*OR 0.33*<br>*(0.01 to 8.21)* | ? | INSUFF |
| Lichtenstein vs. Kugel | Wound infection | 1 | MOD | U | D | I<br>*OR 0.33*<br>*(0.01 to 8.21)* | ? | INSUFF |

**Table Note:**
**For consistency,** C=consistent, I=inconsistent, U=unknown consistency because there was only one study.
**For directness,** D=direct and I=indirect. For precision, P=precise and I=imprecise.
**For the column labeled "Evidence favors,"** ? denotes inconclusive evidence, and EQ denotes approximate equivalence. SOE=strength of evidence,
[@] indicates that the SOE was downgraded due to publication bias or selective outcome reporting.
**Other abbreviations:** OR=odds ratio, RR=relative risk, Diff=difference

Six non-English studies may potentially have met the inclusion criteria for this Key Question if we had not required that studies be published in English.[120-125] Four of these were clearly RCTs, one non-RCT, and one may have been randomized (the abstract was unclear on this point).We summarize the results as follows:

- One study[120] (possibly randomized, comparing Lichtenstein to PHS) stated that authors assessed length of stay, return to daily activities, and pain. However, the findings were not reported in the abstract.
- One non-RCT[121] (comparing PHS to Lichtenstein) found no complications and reported patient satisfaction after Lichtenstein and PHS.
- One RCT[122] (comparing Trabucco vs. plug-and-patch vs. Lichtenstein) reported a higher incidence of postoperative hematoma in the Lichtenstein group. On the contrary, none of our included studies directly compared any of these procedures with each other.
- One RCT[123] (comparing PHS to mesh plug) reported that more patients in the mesh plug group complained of numbness than those in the PHS group. However, numbness was not reported by the two included studies in our review that compared PHS to mesh plug.
- One RCT[126] (comparing peritoneal mesh graft with Lichtenstein in patients with recurrent hernia) found one re-recurrence in the mesh group and three re-recurrences in the Lichtenstein group at long-term follow-up (1 to 4 years).
- One RCT[125] (comparing Lichtenstein to mesh plug) reported there were no recurrences in both groups.

## Key Question 4. Do different laparoscopic mesh-based repair procedures (e.g., transabdominal preperitoneal repair, totally extraperitoneal repair) differ in patient-oriented effectiveness outcomes and/or adverse events?

### Study Characteristics

General information about the nine studies included for this Key Question appears in Table 60 in Appendix C. Two studies were each conducted in China and Austria; and the rest were each conducted in U.S., Egypt, Greece, Turkey, and Italy. Six studies were single-center RCTs; one was multi-center RCT; and the remaining two were RCTs that did not report number of centers.

Regarding specific surgical procedures, the most commonly compared procedures were TAPP vs. TEP (7 studies). The other two studies compared different variants types of surgical approaches for TEP or TEP vs. IPOM. The RCTs enrolled between 44 and 144 patients each. The dates of patient enrollment were reported by five of the eight studies. The average length of the enrollment period was 3.9 years (range 1.5 to 5.8 years).

Four studies were conducted at university hospitals; one at a surgical laparoscopic institute; one at a non-university hospital; one at a surgery clinic; and the remaining two did not report the type(s) of hospitals. Funding for the study was not reported by six studies; government funding was reported in one study; university funding was reported in one study; and one did not report the funding source but did state that they had no manufacturer ties.

Patient enrollment criteria appear in Table 61 (hernia-related criteria), Table 62 (demographic and medical criteria), and Table 63 (other criteria) of Appendix C. Enrollment criteria varied widely among the nine studies. The most commonly used hernia-related exclusions were recurrent hernia (7 studies), bilateral hernia (7 studies), and incarcerated hernia (5 studies). Others were femoral hernia (excluded by one study) and giant hernia (one study). Overall, the studies paint an extraordinarily diverse portrait of the types of hernias deemed relevant to the studies, even though, by virtue of inclusion, they all compared TAPP repair of inguinal hernia to either TEP or IPOM repair of inguinal hernia.

Regarding patient age criteria, six of the nine studies stated that they included any adults or required age >18. Five excluded patients that were unfit for general anesthesia or those with anesthesia risk scores of 3 or 4 or more, and two studies excluded those who had undergone a prior surgery in the lower abdomen. Two studies excluded all females, one excluded patients with ascites, and two excluded those with coagulation disorders. As with the hernia-related exclusions, there was large variability in how studies selected patients for inclusion.

Treatment details appear in Table 64 of Appendix C. None of the studies reported the actual number of prior hernia repairs the surgeons had performed. Instead, all eight studies simply said surgeon had general skills that were not specific to hernia repair. Two of the nine studies stated that all operations were performed by one consultant surgeon.

All reported baseline patient characteristics in the studies included for this Key Question appear in Table 65 of Appendix C.

### Risk of Bias

Our risk-of-bias assessments for the nine studies appear in Table 66 of Appendix C. Seven RCTs were categorized as Moderate risk-of-bias for all of their reported outcomes. Two RCTs

were categorized as low risk-of-bias for all of their reported outcomes Common reasons for assigning a Moderate category to the studies were the same as those discussed in Key Question 2a: possible differences in prior surgical expertise, lack of concealment of allocation, and lack of outcome assessor blinding.

## Findings

Described below are studies that compared either TAPP vs. TEP or TAPP vs. IPOM.

### TAPP vs. TEP (seven studies)

**Hernia recurrence**

We performed a meta-analysis of four of the seven studies reporting this outcome, and found that the evidence was inconclusive (summary relative risk 0.84, 95% CI: 0.28 to 2.55) (Figure 30).

**Length of hospital stay**

Three of the six studies reported this outcome, and were included in a meta-analysis (Figure 31). The meta-analysis was inconclusive (summary difference in means -0.21 days, 95% CI: -0.6 to 0.18).

**Return to daily activities**

Two of the six studies reported this outcome, and were included in a meta-analysis (Figure 32). This meta-analysis of number of days before returning to normal daily activities was inconclusive (summary difference in means -5.88 days, 95% CI: -17.84 to 6.09).

**Return to work**

Three of the six studies reported return-to-work data, and were combined in a meta-analysis (Figure 33). The meta-analysis indicated shorter time-to-return-to-work after TAPP repair (summary difference in means -1.59 days, 95% CI: -3.05 to -0.12). The 95% confidence of interval spans the value that we defined as the MCSD for the outcome (one day). Therefore, it is unclear whether the difference found is clinically significant.

**Short-term Pain (measured in VAS)**

Four studies reporting short-term pain (≤1 month after surgery) on the Pain (measured in VAS) scale were included in a meta-analysis (Figure 34). This analysis found approximately equivalent rates of short-term pain (summary difference in means: -0.03, 95% CI: -0.21 to 0.15 points on a 0-10 scale).

**Intermediate-term pain**

None of the studies of this comparison reported this outcome.

**Adverse events**

We conducted meta-analyses of three types of events (hematoma, urinary retention, and wound infection were each reported by three studies) (Figure 35, Figure 36, and Figure 37, respectively). The evidence was inconclusive for hematoma (OR=1.17, 95% CI: 0.32 to 4.34), urinary retention (OR=0.66, 95% CI: 0.25 to 1.75), and wound infection (OR=1.7, 95% CI: 0.29 to 9.95).

### TAPP vs. IPOM (one study)

**Hernia recurrence**

One study reported this outcome. There were no cases of recurrence in the TAPP group (among 76 repairs) and there were eight cases of recurrence in the IPOM group (11.1% or 8 of 72 hernia repairs) ($p<0.05$ in favor of TAPP).

**Length of hospital stay**

One study reported this outcome, and concluded a shorter length of stay after the TAPP procedure (difference -1.1 days, 95% CI: -1.52 to -0.68). This is larger than what we defined as the MCSD (one day; see the *Methods* section).

**Return to daily activities**

None of the studies of this comparison reported this outcome.

**Return to work**

None of the studies of this comparison reported this outcome.

**Short-term Pain (measured in VAS)**

None of the studies of this comparison reported this outcome.

**Intermediate-term pain**

None of the studies of this comparison reported this outcome.

**Adverse events**

One study reported adverse events. The TAPP procedure was associated with one case of urinary retention and six cases of hematoma. The IPOM was associated with three cases of hematoma but no urinary retention. The evidence was inconclusive for both events.

## Applicability

Nine studies are included for review for Key Question 4. We evaluated these studies to identify factors that may potentially affect the applicability of the evidence. As described in the *Methods* section, the goal of the evaluation is to raise stakeholders' awareness of potential applicability issues embedded in the evidence rather than generating a rating or score for the applicability.

Seven of the nine studies compared two laparoscopic procedures for hernia repair—TAPP and TEP. One study compared TEP and IPOM,[127] while another study compare four different types of TEP.[128] Table 60 provides a detailed description of the procedures being compared in the studies. For Key Question 4, we summarized the evidence by different comparison of surgical procedures, because the evidence for one set of comparisons does not apply to a different set of comparisons.

Five of the nine studies included for review reported the date range of the surgeries performed.[57,83,84,127-129] In four of the five studies, the surgeries were performed in 1990s to early 2000s.[57,83,84,127,129] In the other study, the surgeries were performed from 2004-2008.[128] The other four studies reviewed for Key Question 4 did not report a date range of surgeries being performed. The body of evidence for Key Question 4 may not necessarily reflect the comparative performance of the procedures that are performed at the current time.

Surgeons' prior experience with the procedures being compared varied across the studies (not all studies reported this data). Some studies reported that more senior surgeons had been used, while other studies reported using surgeons who might have needed supervision. No study reported the number of prior cases or years of practice of the surgeons. Given the data reported, we were unable to judge what implication surgeons' experience may have for the applicability of the evidence. Table 64 provides additional detail on the surgical procedures compared in the studies, including data on surgeons' prior experience with the procedures.

Most of the studies reviewed for Key Question 4 excluded patients with recurrent, bilateral, or incarcerated. Most studies also excluded patients unfit for general anesthesia. The evidence might be less applicable to these patient populations being excluded from the studies. Other patient enrollment criteria used varied significantly across the studies. For example, studies excluded patients with giant or strangulated hernia, while other studies excluded female patients or patients with an ASA score >3. Detailed patient enrollment criteria and baseline characteristics of these studies are provided in Table 69 and Table 70.

Except for a smaller study (with 66 patients),[47] all other studies were performed outside of the United States—two studies from Austria, two studies from China, and one study from Egypt, Greece, Italy, or Turkey, respectively. The differences in healthcare systems and practice patterns between the U.S. and other regions may potentially have an impact on the applicability of the evidence from the perspectives of the US stakeholders. The clinical settings in these studies range from general surgical clinics, specialized surgical institute, to academic medical centers. Based on the data reported, it is unclear how the clinical settings of the studies might have affected the applicability of the evidence. Detailed information on geographic and clinical settings of the six studies is provided in Table 60.

## Summary of Key Question 4

A summary of the comparisons and outcomes we examined for Key Question 4 is in Table 7 below. Of the 12 outcomes, the evidence was sufficient to permit a conclusion for four outcomes:

- One outcome favored TAPP compared to TEP (return to work)
- One outcome indicated equivalence for TAPP vs. TEP (short-term pain)
- One outcome favored TAPP compared to IPOM (recurrence)
- One outcome favored TAPP compared to IPOM (length of stay)

Our ratings of the strength of evidence for these outcomes also appear in Table 7. The majority of the studies were at Moderate risk of bias (see the pertinent section above); some inconsistencies were found for some outcomes based on effect sizes on opposite sides of a null effect; all of these outcomes are directly important to clinicians and patients; imprecision was found for some outcomes that precluded conclusions. One of the outcomes for the TAPP vs. TEP comparison was judged to potentially be associated with publication bias, specifically in the form of selective outcome reporting. Only two of the six studies reported return to daily activities, and the authors' choice to report that data may have been influenced by the nature of the findings.

**Table 7. Key Question 4: Strength of evidence ratings**

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| TAPP vs. TEP | Recurrence | 4 | MOD | C | D | I<br>*RR 0.84*<br>*(0.28 to 2.55)* | ? | INSUFF |
| TAPP vs. TEP | Length of stay (days) | 3 | MOD | I | D | I<br>*Diff in means -0.21*<br>*(-0.6 to 0.18)* | ? | INSUFF |
| TAPP vs. TEP | Return to daily activities (days) | 2 | MOD | I | D | I<br>*Diff in means -5.88*<br>*(-17.84 to 6.09)* | ? | INSUFF[@] |
| TAPP vs. TEP | Return to work (days) | 3 | MOD | C | D | P<br>*Diff in means -1.59*<br>*(-3.05 to -0.12)* | TAPP | MOD |
| TAPP vs. TEP | Short- term Pain (measured in VAS) | 4 | MOD | C | D | P<br>*Diff in means -0.03*<br>*(-0.21 to 0.15)* | EQ | MOD |
| TAPP vs. TEP | Hematoma | 3 | MOD | C | D | I<br>*OR 1.17*<br>*(0.32 to 4.34)* | ? | INSUFF |
| TAPP vs. TEP | Urinary retention | 4 | MOD | C | D | I<br>*OR 0.66*<br>*(0.25 to 1.75)* | ? | INSUFF |
| TAPP vs. TEP | Wound infection | 4 | MOD | C | D | I<br>*OR 1.7*<br>*(0.29 to 9.95)* | ? | INSUFF |
| TAPP vs. IPOM | Recurrence | 1 | MOD | U | D | P<br>(CI not reported, but $p<0.05$) | TAPP | LOW |
| TAPP vs. IPOM | Length of stay (days) | 1 | MOD | U | D | P<br>*Diff in means -1.1*<br>*(-1.52 to -0.68)* | TAPP | LOW |
| TAPP vs. IPOM | Hematoma | 1 | MOD | U | D | I<br>*OR 2.9*<br>*(0.12 to 72.62)* | ? | INSUFF |
| TAPP vs. IPOM | Urinary retention | 1 | MOD | U | D | I<br>*OR 2*<br>*(0.48 to 8.42)* | ? | INSUFF |

**Table Note:**
**For consistency,** C=consistent, I=inconsistent, U=unknown consistency because there was only one study.
**For directness,** D=direct and I=indirect. For precision, P=precise and I=imprecise.
**For the column labeled "Evidence favors,"** ? denotes inconclusive evidence, and EQ denotes approximate equivalence. SOE=strength of evidence, [@] indicates that the SOE was downgraded due to publication bias or selective outcome reporting.
**Other abbreviations:** OR=odds ratio, RR=relative risk, Diff=difference

One non-English study may potentially have met the inclusion criteria for this Key Question if we had not required that studies be published in English.[130] The study may have been randomized (the abstract was unclear on this point).The study compared TAPP vs. TEP and found reduced length of stay after TEP.

## Key Question 5. Do different mesh products differ in patient-oriented effectiveness outcomes and/or adverse events?

Surgical mesh products for hernia repair are typically made from polypropylene (PP) or polyester. However, other materials such as polytetraflourethylene (PTFE), polyglactin, polyglycolic acid, and polyamide are also used.[131] One reason a surgeon may debate the use of one mesh versus another is the mechanical support the mesh is reported to provide the deficient abdominal wall.[131] Mohamed et al.[131] listed seven important properties of the ideal mesh:

1. Strong enough to withstand physiologic stresses over a long period of time
2. Conform to the abdominal wall
3. Promote strong host tissue ingrowth, which mimics normal tissue healing
4. Resist the formation of bowel adhesions and erosions into visceral structures
5 Not induce allergic reaction or adverse foreign body reactions
6. Resist infection
7. Be non-carcinogenic.

PP mesh has been the standard material against which other materials are compared.[132] According to Robinson et al.,[132] an advantage of PP is that infections can be treated without mandatory removal of the mesh, while other materials such as PTFE may require removal. Biologic mesh materials such as porcine are decellularized living tissues composed of collagen matrix.[132] Two theoretical concerns for the use of biologic materials for hernia repair include potential transmission of diseases and the reduction in tensile strength of the mesh.[132]

### Study Characteristics

General information for the 29 studies addressing Key Question 5 can be found in Table 68 of Appendix C. Six were conducted in Germany; five in Sweden and/or Finland; three each in India and Italy; and two each in France and Poland. Hong Kong, the United States, Burkina Faso, Pakistan, Estonia, Belgium, and Bosnia each conducted one study. Eighteen studies were single-center RCTs; six RCTs reported multiple centers; and four RCTs did not report the type of center. One RCT was conducted in 15 centers in Poland.[133]

The identified studies assessed various mesh comparisons. Table 8 below lists the comparison types and the number of studies addressing each comparison. The RCTs enrolled between 25 and 600 patients. There were 23 studies that reported patient enrollment dates indicating that studies were conducted between 1996 and 2011.

**Table 8. Key Question 5: Mesh comparisons**

| Comparison | Number of Studies |
|---|---|
| PP vs. Low-weight PP | 4[134-137] |
| PP vs. Combination materials | 15[133,136,138-150] |
| PP vs. coated PP | 4[140,151-153] |
| PP vs. 3D PHS System | 2[154,155] |
| PP vs. Porcine | 2[148,156,157] |
| PP vs. PP[1] | 1[150] |
| Combination materials vs. porcine[1] | 1[148] |
| Low weight PP vs. combination materials[1] | 1[136] |
| PP vs. PTFE[1] | 1[137] |
| Low weight PP vs. PTFE[1] | 1[137] |
| PP vs. PVDF[1] | 1[158] |
| Combination materials vs. coated PP[1] | 1[140] |
| Coated PP light vs. Coated PP extra-light[1] | 1[159] |
| Nylon vs. combination materials[1] | 1[160] |
| ePTFE patch vs. ePTFE plus antimicrobial preservative agents patch[1] | 1[161] |

**Table Note:**
[1]No meta-analysis performed for this comparison.
ePTFE Expanded PTFE
PP Polypropylene
PTFE Polytetraflourethylene
PVDF Polyvinylidenfluoride

Nineteen studies were conducted at general and non-university hospitals; six were conducted at university hospitals; two included some university hospitals as well as some non-university hospitals; and the remaining three studies did not report the type(s) of hospitals. Eleven of the 29 studies for Key Question 5 reported their source of funding, six of which were supported by funding from Ethicon Endo-Surgery.

Patient enrollment criteria appear in Table 69 (hernia-related criteria), Table 70 (demographic and medical criteria), and Table 71 (other criteria) of Appendix C. Enrollment criteria varied among the 29 studies. The most commonly used hernia-related exclusions were recurrent hernia (14 studies), incarcerated hernia (12 studies), and bilateral and strangulated hernia (9 studies each). Patients were also excluded if they had an emergency repair or a femoral hernia (excluded by six studies each), scrotal hernia (three studies), asymptomatic hernia (two studies), and obstructed hernia (one study).

Twenty-eight studies enrolled patients of a minimum age of 18 years. Only one study set the minimum age for enrollment at 16 years. Ten studies excluded female patients; two studies each excluded patients with prior general anesthesia, an ASA score >4, pregnant women, and those with infection. Three studies each excluded patients with prior lower abdominal surgery and prior mesh surgery. Lastly, one study each excluded patients with prior treatment, coagulation disorders, advanced carcinoma, and an ASA score >2.

Treatment details appear in Table 72of Appendix C. Mesh sizes ranged from 4.5 x 10 cm to 15 x 15 cm. The mesh size most frequently reported was 10 x 15 cm. The following table (Table 9) lists various mesh materials, some of which were reported in our literature results for

Key Question 5.[132] Nine studies reported that surgeons had experience in hernia repair. Of these 9 studies, two mentioned the number of hernia repairs the surgeons had previously performed and one mentioned the number of years of surgeon experience in hernia repair. The surgical procedures performed included sixteen studies performing Lichtenstein, six performing TEP, four performing TAPP, and three studies did not specify the surgical procedure.

**Table 9. Key Question 5: Types of Mesh Materials**

| Material | Trade Name |
|---|---|
| Polypropylene (PP) | VISILEX™, PERFIX™, KUGEL™ Hernia Patch, 3DMAX™ (Davol Inc.)<br>PROLENE™ (Ethicon Endo-Surgery)<br>SURGIPRO™ (COVIDIEN)<br>Prolite™, Prolite™ Ultra (Atrium Medical Corp.) |
| Polyester | MERSILENE™ (Ethicon Endo-Surgery)<br>Parietex™ (COVIDIEN) |
| Polytetraflourethylene (PTFE) | GORE-TEX®, Gore® DUALMESH®, Gore® DUALMESH® Plus, Gore® MYCROMESH® (W.L. Gore & Associates Inc.)<br>DULEX™, Reconix® (Davol, Inc.) |
| PP/PTFE | Composix®, Composix ® EX, Ventralex® (Davol, Inc.) |
| PP/Cellulose | PROCEED™ (Ethicon Endo-Surgery) |
| PP/Seprafilm | SEPRAMESH™, SEPRAMESH™ IP (Davol, Inc.) |
| PP/Vicryl | VYPRO™, VYPRO™ II (Ethicon Endo-Surgery) |
| PP/Monocryl (poliglecaprone) | ULTRAPRO™ (Ethicon Endo-Surgery) |
| Polyester/Collagen Film | Parietex™ Composite (COVIDIEN) |
| Porcine | Surgisis® (Cook Biotech Inc.) |
| Human | AlloDerm® Regenerative Tissue Matrix (LifeCell Corp.) |

**Table Note:**

All reported baseline patient characteristics in the studies included for this Key Question appear in Table 73 of Appendix C. A summary of the most commonly reported baseline characteristics in studies included for Key Questions 2 through 7 appears in section Key Question 2a of this report along with Table 2 (please refer to Key Question 2a for further detail).

## Risk of Bias

The risk-of-bias assessments for the 29 studies appear in Table 74 of Appendix C. Twenty-six studies were categorized as Moderate risk-of-bias for all of their reported outcomes. One study was categorized as Low risk-of-bias for all outcomes,[150] and the category for two studies was mixed (Moderate and Low). One study with a mixed category had a Low risk-of-bias for most outcomes, and Moderate risk-of-bias for adverse events.[162] The second study was categorized as Moderate risk-of-bias for most outcomes, and Low risk-of-bias for adverse events and hospital stay.[163]

Many reasons underlie the Moderate rating for the 29 RCTs. Two of the most common reasons involved concealment of allocation (either not performed or not reported by 18 studies) and the blinding of outcome assessors (either not performed or not reported by 25 studies).

## Findings

The included data for Key Question five appears in Table 75 of Appendix C. We have organized this section by type of comparison and outcomes assessed through meta-analysis. We considered seven comparisons to be major:

- Standard polypropylene (PP) vs. low-weight PP
- Polypropylene (PP) vs. combination materials
- Polypropylene (PP) vs. coated PP
- Polypropylene (PP) vs. 3D PROLENE™ Hernia System (PHS)
- Polypropylene (PP) vs. porcine
- combination materials vs. porcine
- low-weight PP vs. combination materials

### Polypropylene (PP) vs. Low-weight PP

**Hernia recurrence**

We performed a meta-analysis of two studies comparing PP mesh to low-weight PP mesh, (Figure 38), and identified a summary RR of 1.63 (95% CI: 0.21 to 12.42). We defined the MCSD as a three-percentage-point difference between groups, so to aid interpretation; we calculated the overall rate of recurrence in the PP mesh group, which was 1.44%. Multiplying a 12.42 relative risk with this rate yielded a corresponding rate of 17.9% for low-weight PP mesh group. The difference between these rates is over 16 percentage points, which is greater than our predefined MCSD. Thus, the evidence is too imprecise to permit a conclusion.

**Quality of life**

Studies did not report this outcome.

**Patient satisfaction**

Studies did not report this outcome.

**Long-term pain**

Three studies reporting long-term pain (>6 months after surgery) as overall VAS scores were included in a meta-analysis (Figure 39) and we found a summary difference in means of 0.15 (95% CI: -0.28 to 0.59 points on a 0-10 scale). The results indicate approximate equivalence between the PP mesh and low-weight PP for the outcome of long-term pain.

**Adverse events**

We conducted meta-analyses of two types of events: feeling of foreign body (two studies), Figure 40) and infection (three studies) ( Figure 41). We identified a summary OR of 1.23 (95% CI: 0.48 to 3.17) for the outcome of feeling a foreign body and an OR of 1.59 (95% CI: 0.19 to 13.11) for the outcome of infection. These confidence intervals extend beyond our MCSD of 0.8 to 1.25. Thus, the evidence is too imprecise to permit a conclusion.

## Polypropylene (PP) vs. Combination Materials (e.g., PP and polyglactin)

### Hernia recurrence

We performed a meta-analysis of eight studies comparing PP mesh to combination material mesh (Figure 42), and identified a summary RR of 1.08 (95% CI: 0.54 to 2.17). We defined the MCSD as a three-percentage-point difference between groups, so to aid interpretation; we calculated the overall rate of recurrence in the PP mesh group, which was 1.78%. Multiplying a 2.17 RR with this rate yielded a corresponding rate of 3.87% for the combination material mesh group. The difference between these rates is only 2.09%, which is less than our predefined MCSD of three percentage points. This implies approximate equivalence between PP mesh and combination material mesh for this outcome.

### Quality of life

Four studies comparing PP mesh with combination material mesh reported quality of life data for various domains of the Short-form 36 (SF-36). Since these studies did not provide an overall quality of life score, we were unable to combine the data for meta-analysis, but provide some discussion of the studies' reported results.

One study assessing development of life quality reported that any differences identified between PP mesh and combination material mesh diminished beyond the 12th post-interventional week.[150] A second study, reporting scores for various domains found there was "no detectable difference in any dimension of quality of life on the SF-36 between the two treatment groups either before or six months after hernia repair."[147] Another study making the comparison of PP mesh with combination material mesh reported that "the SF-36 results showed few significant differences between groups."[133] The fourth study reported results of quality of life assessment at eight weeks and one year. At both timepoints, the authors found "no clinically relevant difference" between the treatment groups for various domains of the SF-36.[142,143]

### Patient satisfaction

Studies did not report this outcome.

### Long-term pain

Three studies reporting long-term pain (>6 months after surgery) as an overall score on the Visual Analog Scale (VAS) were included in a meta-analysis (Figure 43). We identified a summary difference in means of 0.09 (95% CI: -0.21 to 0.40). The results indicate approximate equivalence between these treatment groups for the outcome of long-term pain.

### Adverse events

We conducted meta-analyses of two types of events: feeling of foreign body (four studies), (Figure 44) and infection (five studies) (Figure 45). The summary OR for feeling of foreign body was 0.91 (95% CI: 0.35 to 2.40) and for infection was 1.29 (95% CI: 0.63 to 2.64). Neither of these outcomes permit a conclusion, due to low precision. The wide confidence intervals for both outcomes include our MCSD of 0.8 to 1.25. Thus, the evidence is too imprecise to permit a conclusion.

## Polypropylene (PP) vs. Coated PP (e.g., beta-D-glucan)

### Hernia recurrence

We performed a meta-analysis of two studies comparing PP mesh to coated PP mesh (Figure 46), and identified a summary RR of 1.47 (95% CI: 0.46 to 4.68). We defined the MCSD as a three-percentage-point difference between groups, so to aid interpretation; we calculated the overall rate of recurrence in the PP mesh group, which was 2.87%. Multiplying a 4.68 relative risk yielded a corresponding rate of 13.3% for the coated PP mesh group. The difference (13.3% vs. 2.87%) is greater than our predefined MCSD of three percentage points. Thus the evidence is too imprecise to permit a conclusion.

### Quality of life

One study comparing PP mesh with coated PP mesh reported quality of life.[153] At post-operative days seven and 30, the authors reported scores on the Short-Form 12 (SF-12). We calculated a difference in means of 0.40 (95% CI: -5.32 to 6.12); the wide CI indicates that the finding is inconclusive.

### Patient satisfaction

Studies did not report this outcome.

### Long-term pain

Two studies reporting long-term pain (>6 months after surgery) were included in a meta-analysis (Figure 47). This analysis found a summary OR of 2.84 (95% CI: 0.35 to 23.05). Although the summary OR appears to say patients with the coated PP mesh may experience more long-term pain, the wide confidence intervals for both outcomes include our MCSD of 0.8 to 1.25. Thus, the evidence is too imprecise to permit a conclusion.

### Adverse events

One study comparing PP mesh with coated PP mesh reported infection rates.[152] The authors reported a total of four infections identified in the PP mesh group and two in the coated-PP mesh group.[152] We calculated an OR of 1.63 (95% CI: 0.29 to 9.05) for this outcome, and the wide CI means that the evidence is inconclusive.

## Polypropylene (PP) vs. 3D PROLENE™ Hernia System (PHS) two studies

### Hernia recurrence

We performed a meta-analysis of two studies comparing PP mesh to 3D PHS System (Figure 48), and identified a summary RR of 1.05 (95% CI: 0.07 to 16.47). The studies included for this comparison reported zero events of hernia recurrence. The evidence is too imprecise to permit a conclusion.

### Quality of life

Studies did not report this outcome.

### Patient satisfaction

Studies did not report this outcome.

### Long-term pain

Studies did not report this outcome.

**Adverse events**

We conducted meta-analyses of two studies reporting infection (Figure 49). The analysis found a summary OR of 0.51 (95% CI: 0.09 to 2.88), which expands beyond our MCSD of 0.8 to 1.25. Thus, the evidence is too imprecise to permit a conclusion.

## Polypropylene (PP) vs. Porcine two studies

**Hernia recurrence**

We performed a meta-analysis of two studies comparing PP mesh with porcine mesh (Figure 50), and identified a summary RR of 1.93 (95% CI: 0.17 to 22.29). We defined the MCSD as a three-percentage-point difference between groups, so to aid interpretation; we calculated the overall rate of recurrence in the PP mesh group, which was 2%. Multiplying a 22.294 relative risk with this rate yielded a corresponding rate of 44.58% for the porcine mesh group. The difference between these rates is over 40 percentage points, which is greater than our predefined MCSD of three percentage points. Thus, the evidence is too imprecise to permit a conclusion.

**Quality of life**

Studies did not report this outcome.

**Patient satisfaction**

Studies did not report this outcome.

**Long-term pain**

One study comparing PP mesh with porcine mesh reported a VAS score for pain at rest and pain on movement at 3 years.[156,157] For the outcome of pain at rest we calculated a difference in means of 0.00 (95% CI: -0.94 to 0.94) and a difference in means of 0.39 (95% CI: -0.55 to 1.33) for the outcome of pain on movement. The results indicate approximate equivalence between the treatment groups for the outcome of long-term pain.

**Adverse events**

Studies did not report this outcome.

## Combination Materials vs. Porcine

**Hernia recurrence**

One study comparing combination material mesh with porcine mesh reporting hernia recurrence found zero events in each treatment group. We calculated a relative risk of 1.00 (95% CI: 0.02 to 47.38); the wide CI indicates that the finding is inconclusive.

**Quality of life**

The study did not report this outcome.

**Patient satisfaction**

The study did not report this outcome.

**Long-term pain (>6 months)**

The study did not report this outcome.

**Adverse Events**

One study comparing combination material mesh with porcine reported the feeling of stiffness and a foreign body in the groin.[148] We calculated an OR of 5.69 (95% CI: 0.94 to 34.46); the wide CI indicates that the finding is inconclusive.

### Low-weight PP vs. Combination Materials

**Hernia recurrence**

One study comparing low-weight PP mesh with combination material mesh reported hernia recurrence.[136] We calculated a RR of 0.51 (95% CI: 0.05 to 5.54); the wide CI indicates that the finding is inconclusive.

**Quality of life**

The study did not report this outcome.

**Patient satisfaction**

The study did not report this outcome.

**Long-term pain (>6 months)**

One study comparing low-weight PP mesh with combination material mesh reported overall VAS scores for the outcome of long-term pain.[136] We calculated a difference in means of 0.00 (95% CI: -0.65 to 0.65). This implies approximate equivalence between low-weight PP mesh and combination material mesh.

**Adverse Events**

One study comparing low-weight PP mesh with combination material mesh reported infection and the feeling of a foreign body.[136] We calculated an OR of 1.73 (95% CI: 0.54 to 5.55) for the outcome of feeling a foreign body. For the outcome of infection, the calculated odds ratio for this outcome is 0.35 (95% CI: 0.01 to 8.64). Both findings are inconclusive.

## Applicability

Twenty-nine studies are included for review for Key Question 5. We evaluated these studies to identify factors that may potentially affect the applicability of the evidence. As described in the *Methods* section, the goal of the evaluation is to draw stakeholders' attention to potential applicability issues embedded in the evidence rather than generating a rating or score for the applicability.

The twenty-nine studies compared different mesh products used in hernia repair. See Table 68 for a detailed description of the mesh products being compared in the studies. For Key Question 5, we summarized the evidence for each comparison of mesh products.

In 21 of the 29 studies reviewed for Key Question 5, the surgeries were performed 5 or more years ago (before 2006). The evidence may not necessarily reflect the comparative performance of the state-of-the-art mesh products that are currently used in clinical practice.

The majority of the 29 studies reviewed did not report data on surgeons' prior experiences with the hernia repair procedures or the mesh products being used. For the studies that did report such data, the meaning of "experience" was not explicitly defined (e.g., by the number of prior cases or years of practice). Given the data reported, we were unable to judge what implication surgeons' experience may have in the applicability of the evidence. Table 72 provides additional

detail on the surgical procedures compared in the studies, including data on surgeons' prior experience.

Patient enrollment criteria and reported baseline characteristics varied significantly across the 29 studies reviewed. The most commonly used exclusions were recurrent hernia (14 studies), incarcerated hernia (12 studies), bilateral hernia (9 studies), strangulated hernia (9 studies), hernia requiring emergency repair (6 studies), and femoral hernia (6 studies). From the reported data, we did not identify any general pattern in the patient population enrolled that may have a significant impact on the applicability of the overall evidence. Detailed patient enrollment criteria and baseline characteristics of these studies are provided in Table 69, Table 70, Table 73 of Appendix C.

Except for two studies, all other 27 studies were performed outside of the U.S., primarily in European countries. The differences in healthcare systems and practice patterns between the U.S. and other regions may potentially have an impact on the applicability of the evidence from the perspectives of the U.S. stakeholders. The clinical setting varied significantly across the studies, ranging from outpatient surgical clinics, community hospitals, and academic medical centers. Based on the data reported, it is unclear how the clinical settings of the studies might have affected the applicability of the evidence. Detailed information on geographic and clinical settings of the six studies is provided in Table 68.

## Summary of Key Question 5

A summary of the comparisons and outcomes we examined for this Key Question can be found in Table 10 below. Of the 11 outcomes, the evidence was sufficient to permit a conclusion for two outcomes assessed by the various comparisons of mesh types:

- Long-term pain (>6 months) for the comparisons of PP mesh vs. low-weight PP mesh; PP mesh vs. porcine; low-weight PP mesh vs. combination material mesh; and PP mesh vs. combination material mesh indicated approximate equivalence
- Recurrence for the comparison of PP mesh vs. combination material mesh indicated approximate equivalence.

Our ratings of the strength of evidence for these outcomes also appear in the table. Studies were typically a Moderate risk-of-bias (see risk of bias section above) and considered direct. The strength of evidence ratings for comparisons with meta-analytic results ranged from Low to Moderate. For the outcome of recurrence, the evidence indicated a non-substantial difference between treatment groups for the comparison of PP mesh vs. combination material mesh. The strength of evidence for this comparison was Moderate. Some imprecision was found for several comparisons and the analyzed outcomes of interest that precluded conclusions. For the outcome of feeling of foreign body, the finding was inconclusive for the following comparisons: PP mesh vs. low-weight PP mesh and PP mesh vs. combination material mesh. The outcome of infection was inconclusive for two comparisons: PP mesh vs. low-weight mesh; PP mesh vs. combination material mesh; PP mesh vs. coated PP mesh; and PP mesh vs. 3D PROLENE™ Hernia System. For the outcome of recurrence the finding was inconclusive for the comparisons of PP mesh vs. low-weight PP; PP mesh vs. coated PP mesh; PP vs. 3D PROLENE™ Hernia System; and PP vs. porcine. For the outcome of long-term pain the finding was inconclusive for the PP mesh vs. coated PP mesh comparison.

Questions about the relative importance of these outcomes need to be considered carefully. Some may believe the advantages of various "lighter weight," "partially absorbable" mesh types outweigh the disadvantages of the typical mesh material such as PP mesh.

The FDA has a web page devoted specifically to the topic of surgical mesh in the context of hernia repair.[164] It states: “Hundreds of thousands of hernia repair operations are performed each year both with and without surgical mesh, and patients generally recover quickly and do well after surgery. However, FDA has received reports of complications associated with the mesh. The complications include adverse reactions to the mesh, adhesions (when the loops of the intestines adhere to each other or the mesh), and injuries to nearby organs, nerves or blood vessels. Other complications of hernia repair can occur with or without the mesh, including infection, chronic pain and hernia recurrence. Most of the complications reported to us so far have been associated with mesh products that have been recalled and are no longer on the market.”[164] We searched the FDA website for any official product calls, and identified three:

- The first, involving Bard Composix Kugel Extra Large Oval Patches, was initiated in December 2005 and was expanded in March 2006 and also January 2007.[165] The Class I recall applies to this specific product and only to meshes manufactured before October 2005. The stated reason for the recall on the FDA website was “The "memory recoil ring" that opens the Bard® Composix® Kugel® Mesh Patch can break under the stress of placement of the large sized products in the intra-abdominal (inside the belly area) space.”.
- The second product recall was for 14 lot numbers of the XenMatrix Surgical Graft. This was a Class I recall initiated in January 2011 and applies only to the products distributed between July 1, 2010 through October 31, 2010. The stated reason for the recall on the FDA website was “Testing cannot confirm that all units of XenMatrix Surgical Graft are within FDA requirements for endotoxin levels. Several lots have been found to have elevated endotoxin levels.”[166]
- The third product recall was for 15 lot numbers of the Bard Flat Mesh; this Class I recall was initiated in March 2010 and applies to products distributed between October 21, 2008 and October 27, 2009. The stated reason for the recall on the FDA website was “The product was deemed a counterfeit. The product does not meet manufacturer's specifications.”[167]

**Table 10. Key Question 5: Strength of evidence ratings**

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| PP vs. Low-weight PP | Recurrence | 4 | MOD | C | D | I (RR 0.21 to 12.42) | ? | INSUFF |
| PP vs. Low-weight PP | Long term Pain (≥6 months) (0-10 scale) | 4 | MOD | I | D | P (Diff. -0.28 to 0.59) | EQ | LOW |
| PP vs. Low-weight PP | Feeling of Foreign Body | 4 | MOD | C | D | I (OR 0.48 to 3.17) | ? | INSUFF |
| PP vs. Low-weight PP | Infection | 4 | MOD | C | D | I (OR 0.19 to 13.11) | ? | INSUFF |
| PP vs. Combination materials | Recurrence | 15 | MOD | C | D | P (RR 0.54 to 2.17) | EQ | MOD |
| PP vs. Combination materials | Long term Pain (≥6 months) (0-10 scale) | 15 | MOD | I | D | P (Diff.-0.21 to 0.40) | EQ | LOW |
| PP vs. Combination materials | Feeling of Foreign Body | 15 | MOD | C | D | I (OR 0.35 to 2.40) | ? | INSUFF[@] |
| PP vs. Combination materials | Infection | 15 | MOD | C | D | I (OR 0.63 to 2.64) | ? | INSUFF |
| PP vs. Coated PP | Recurrence | 4 | MOD | C | D | I (RR 0.46 to 4.68) | ? | INSUFF |
| PP vs. Coated PP | Quality of Life | 4 | MOD | U | D | I (Diff. -5.3 to 6.1) | ? | INSUFF |
| PP vs. Coated PP | Long term Pain (≥6 months) | 4 | MOD | C | D | I (OR 0.35 to 23.05) | ? | INSUFF |
| PP vs. Coated PP | Infection | 4 | MOD | U | D | I (OR 0.29 to 9.05) | ? | INSUFF |
| PP vs. 3D PHS System | Recurrence | 2 | MOD | C | D | I (RR 0.07 to 16.47) | ? | INSUFF |
| PP vs. 3D PHS System | Infection | 2 | MOD | C | D | I (OR 0.09 to 2.88) | ? | INSUFF |
| PP vs. porcine | Recurrence | 2 | MOD | C | D | I (RR 0.17 to 22.29) | ? | INSUFF |

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| PP vs. porcine | Long term Pain (≥6 months) VAS at rest (0-10 scale) | 2 | MOD | U | D | P (Diff. -0.94 to 0.94) | EQ | LOW |
| PP vs. porcine | Long term Pain (≥6 months) VAS on movement (0-10 scale) | 2 | MOD | U | D | P (Diff. -0.55 to 1.33) | EQ | LOW |
| Combination materials vs. porcine | Recurrence | 1 | MOD | U | D | I (RR 0.02 to 47.38) | ? | INSUFF |
| Combination materials vs. porcine | Feeling of foreign body | 1 | MOD | U | D | I (OR 0.94 to 34.46) | ? | INSUFF |
| Low-weight PP vs. combination materials | Recurrence | 1 | MOD | U | D | I (RR 0.05 to 5.54) | ? | INSUFF |
| Low-weight PP vs. Combination materials | Long-term Pain (≥6 months) (0-10 scale) | 1 | MOD | U | D | P (Diff. -0.65 to 0.65) | EQ | LOW |
| Low-weight PP vs. Combination materials | Feeling of foreign body | 1 | MOD | U | D | I (OR 0.54 to 5.55) | ? | INSUFF |
| Low-weight PP vs. combination materials | Infection | 1 | MOD | U | D | I (OR 0.01 to 8.64) | ? | INSUFF |

**Table Note:**
**For consistency,** C=consistent, I=inconsistent, U=unknown consistency because there was only one study.
**For directness,** D=direct and I=indirect.
**For precision,** P=precise and I=imprecise.
**For the column labeled "Evidence favors,"** ? denotes inconclusive evidence, and EQ denotes approximate equivalence. SOE=strength of evidence. RR=relative risk.
[@]=Evidence downgraded for this outcome because of possible publication bias.

Three non-English studies may potentially have met the inclusion criteria for this Key Question if we had not required that studies be published in English.[168-170] Two of these were stated to be randomized trials and we are unsure if the fourth study was randomized, however it was a comparison study. We summarize the results as follows:

- One study[168] comparing Bard Corporation meshes with Auto Suture Company hernia link plug and netted patch found that after 12 months of followup, a total of 42 patients reported having a foreign body sensation, 47 patients experienced other complications, and four infections were recorded. The authors concluded that there was no statistically significant difference between the two treatment groups and that these particular meshes had similar effectiveness. These results are consistent with the conclusions of our review. Our results indicated an inconclusive finding for the outcome of feeling of foreign body and infection rates for all comparisons
- One RCT[169] comparing a rigid PP mesh with a softer PP mesh found that patients with the rigid PP mesh reported testicular sensitivity to touch, pain upon ejaculation, and pulling sensation during urination. These complications are stated to be reported less frequently in patients with the softer PP mesh group. These individual domains of pain were not discussed for this report; instead we assessed overall pain scores. Our results indicated approximate equivalence for the outcome of long-term pain (>6 months) for the following comparisons: PP vs. low-weight PP; PP vs. combination material; PP mesh vs. porcine; and low-weight PP vs. combination material mesh.
- Another RCT[170] comparing PP mesh with expanded polytetrafluroethylene mesh and a control group found there was no difference in VAS pain between the two meshes, as well as no significant difference of incidence of infections and other adverse events. The authors concluded that both of the included mesh types were safe and effective with a low recurrence rate. Our results indicated approximate equivalence for the outcome of long-term pain (>6 months) for the following comparisons: PP vs. low-weight PP; PP vs. combination material; PP mesh vs. porcine; and low-weight PP vs. combination material mesh. For the outcome of recurrence, our results indicated approximate equivalence for the comparison of PP mesh vs. comparison material mesh.

## Key Question 6. Do different mesh-fixation methods (e.g., no fixation, sutures, glue) differ in patient-oriented effectiveness outcomes and/or adverse events?

### Study Characteristics

General information about the 19 studies included for Key Question 6 can be found in Table 76 of Appendix C. Four were conducted in Italy, three in the United States, two each in Australia and Spain, and one each in Switzerland, China, Germany, United Kingdom, Poland, Finland, India, and Sweden. Fifteen studies were single-center RCTs; two RCTs were conducted in at least two centers; one RCT was conducted in three centers, and one RCT did not report the type of center.

The identified studies assessed various mesh fixation comparisons. Table 11 below lists the comparison types and the number of studies addressing each comparison. Eighteen RCTs enrolled between 27 and 600 patients and the Swedish registry included 142,578 hernias. Fifteen studies reported patient enrollment dates between the years 1996 and 2011.

**Table 11. Key Question 6: Mesh Fixation Methods Comparisons**

| Comparison | Number of Studies |
|---|---|
| Tacks or Staples vs. No fixation | 6[171-176] |
| Fibrin glue vs. Staples | 4[177-180] |
| Sutures vs. Tacks | 3[181-183] |
| Sutures vs. Glue | 4[184-187] |
| Comparing different types of staples (e.g., EndoANCHOR™ staples vs. EMS™ staples, Ethicon Endo-Surgery) | 2[180,183] |
| Absorbable Sutures (short or long term) vs. Nonabsorbable | 1[188] |
| Glue vs. No Fixation | 1[189] |

**Table Note:**

Thirteen studies were conducted at general and non-university hospitals; one study was conducted at a university hospital; and five studies did not report the type(s) of hospitals. Three studies reported their funding source. One study received funding from a public foundation in Spain,[178] one study received funding from a hospital group in China,[177] and the Swedish registry received funding from various sources (e.g., Sweden's National board of Health and Welfare, etc.).[119]

Patient enrollment criteria appear in Table 77 (hernia-related criteria), Table 78 (demographic and medical criteria), and Table 79 (other criteria) of Appendix C. Enrollment criteria varied among the 19 studies. The most commonly used hernia-related exclusions were recurrent hernia (7 studies), incarcerated hernia (5 studies), and bilateral and strangulated hernia (4 studies each). Others were emergency hernia (6 studies), femoral hernia (two studies), giant hernia (two studies), scrotal hernia (one study), and giant scrotal hernia (one study).

Seventeen studies enrolled patients of a minimum age of 18 years and two studies enrolled patients of a minimum age of 15 years. Five studies excluded female patients; four studies excluded those with prior general anesthesia; two studies excluded patients with ASA scores of >4. The following exclusions were reported in one study each: patients with prior abdominal surgery, prior mesh surgery, prior infection, and coagulation disorders.

Treatment details appear in Table 80 of Appendix C. There were various manufacturers of mesh fixation material represented in the included studies. Some of the fixation materials identified included Vivostat®, Autosuture™, ENDOPATH®, and Indermil® Tissue Adhesive. Seven studies reported that surgeons had experience in hernia repair. However, the literature did not specify the number of previous procedures or years of experience. The surgical procedures reported in the studies varied. Lichtenstein method was reported in six studies, TEP in five studies, TAPP in five studies, and three studies did not specify the surgical procedure.

All reported baseline patient characteristics in the studies included for this Key Question appear in Table 81 of Appendix C. A summary of the most commonly reported baseline characteristics in studies included for Key Questions 2 through 7 appears in section Key Question 2a of this report along with Table 2 (please refer to Key Question 2a for further detail).

## Risk of Bias

The risk-of-bias assessments for the 19 studies can be found in Table 82 of Appendix C. Sixteen studies were categorized as Moderate risk-of-bias for all of their reported outcomes. One study was categorized as Low risk-of-bias for all outcomes[183] except testicular swelling and evidence of atrophy; these outcomes were categorized as Moderate risk-of-bias. Another study was categorized as Low risk-of-bias for all outcomes except for return to work which was categorized as Moderate risk-of-bias.[175] Lastly, one study was categorized as Moderate risk-of-bias for most outcomes,[179] but the outcomes of recurrence, post-op hospital stay, recovery time to normal activity, and adverse events (e.g., hematoma, infection, etc.) were categorized as Low risk-of-bias.

Many reasons underlie the Moderate rating for the 19 RCTs. Two of the most common reasons involved concealment of allocation (either not performed or not reported by 11 studies) and the blinding of outcome assessors (either not performed or not reported by over 11 studies).

## Findings

All included data for this Key Question appear in Table 83of Appendix C. We have organized this section by type of comparison, followed by outcomes assessed through meta-analysis. We considered five comparisons to be major:

- Tacks or Staples vs. No Fixation
- Fibrin Glue vs. Staples
- Suture vs. Tacks
- Suture vs. Glue
- Absorbable sutures vs. non-absorbable sutures

### Tacks or Staples vs. No Fixation

#### Hernia recurrence

We performed a meta-analysis of three studies comparing tacks or staples with no fixation method (Figure 51), and identified a summary RR of 0.412 (95% CI: 0.055 to 3.075). We defined the MCSD as a three-percentage-point difference between groups, so to aid interpretation; we calculated the overall rate of recurrence in the tacks or staples group, which was 1.9%. Multiplying a 3.075 relative risk with this rate yielded a corresponding rate of 5.84% for the no fixation group. The difference between these rates is over 3 percentage points, which is greater than our predefined MCSD. Thus, the evidence is too imprecise to permit a conclusion.

**Quality of life**

Studies did not report this outcome.

**Patient satisfaction**

Studies did not report this outcome.

**Long-term pain**

Studies did not report this outcome.

**Adverse Events**

One study comparing tacks or staples with no fixation method reported two adverse events, bleeding and infection.[173] There were 11 patients in the tacks or staples group and 10 patients in the no fixation group who experienced bleeding. We calculated an OR of 1.12 (95% CI: 0.45 to 2.78) for the outcome of bleeding. We calculated an odds ratio of 3.036 (95% CI: 0.12 to 75.57) for the outcome of infection. The wide confidence intervals indicate the evidence is inconclusive.

## Fibrin Glue vs. Staples

**Hernia recurrence**

We performed a meta-analysis of three studies comparing fibrin glue with staples (Figure 52), and identified a summary RR of 0.832 (95% CI: 0.24 to 2.93). One study entailed three different comparisons (three different staple groups). We defined the MCSD as a three-percentage-point difference between groups, so to aid interpretation; we calculated the overall rate of recurrence in the fibrin glue group, which was 0.53%. Multiplying a 2.93 relative risk with this rate yielded a corresponding rate of 1.54% for the staples group. The difference between these rates is only 1.016%, which is less than our predefined MCSD of three percentage points. This implies approximate equivalence in recurrence rates between fibrin glue and staples.

**Quality of life**

One study comparing fibrin glue with staples reported quality of life.[179] We calculated a difference in means of 0.00 (95% CI: -0.09 to 0.09) for this outcome. This implies approximate equivalence between fibrin glue and staples for the outcome of quality of life.

**Patient satisfaction**

Studies did not report this outcome.

**Long-term pain**

Two studies reporting long-term pain (>6 months after surgery) as an overall score on the Visual Analog Scale (VAS) were included in a meta-analysis (Figure 53). This analysis found a difference in means of -0.33 (95% CI: -0.84 to 0.18) and indicates approximate equivalence between the treatment groups for long-term pain.

**Adverse Events**

Studies did not report this outcome.

## Sutures vs. Tacks

### Hernia recurrence

We performed a meta-analysis of two studies comparing sutures with tacks (Figure 54), and identified a summary relative risk of 1.98 (95% CI: 0.16 to 22.21). We defined the MCSD as a three-percentage-point difference between groups, so to aid interpretation; we calculated the overall rate of recurrence in the sutures group, which was 0.69%. Multiplying a 22.21 relative risk with this rate yielded a corresponding rate of 15.3% for the tacks group. The difference between these rates is over 14 percentage points, which is greater than our predefined MCSD. Thus, the evidence is too imprecise to permit a conclusion.

### Quality of life

Studies did not report this outcome.

### Patient satisfaction

Studies did not report this outcome.

### Long-term pain

Studies did not report this outcome.

### Adverse Events

Studies did not report this outcome.

## Sutures vs. Glue

### Hernia recurrence

One study comparing sutures with glue reported zero events of hernia recurrence for all treatment groups.[187] We calculated a RR for this outcome of 0.88 (95% CI: 0.02 to 43.75); the wide CI indicates that the evidence is insufficient for a conclusion.

### Quality of life

Studies did not report this outcome.

### Patient satisfaction

Studies did not report this outcome.

### Long-term pain

One study comparing fibrin glue with staples reported long-term pain at six months.[186] We calculated a difference in means of 0.88 (95% CI: -0.24 to 2.00); the wide CI indicates that the evidence is insufficient for a conclusion.

### Adverse Events

We conducted meta-analyses of infection for two studies comparing sutures with glue (Figure 56). Our analysis found a summary OR of 0.477 (95% CI: 0.039 to 5.885. The wide confidence interval includes our pre-determined MCSD of 0.8 to 1.25. Thus, the evidence is too imprecise to permit a conclusion.

### Absorbable sutures vs. Non-absorbable sutures

**Hernia Recurrence**

One study comparing absorbable sutures with non-absorbable sutures reported one event of hernia recurrence in each treatment group.[188] We calculated a RR of 1.00 (95% CI: 0.06 to 15.72); the wide confidence interval indicates that the evidence is insufficient for a conclusion.

**Long-term pain**

One study comparing absorbable sutures with non-absorbable sutures reported long-term pain.[188] At a mean followup of 2.1 years, 21 (26%) patients in the absorbable sutures group reported having pain within the last month, and 19 (23.4%) patients in the non-absorbable group reported the same. We calculated an OR of 1.14 (95% CI: 0.56 to 2.33). The wide confidence interval includes our MCSD of 0.8 to 1.25. Thus, the evidence is too imprecise to permit a conclusion.

**Quality of life**

The study did not report this outcome.

**Patient satisfaction**

One study comparing absorbable sutures with non-absorbable sutures reported satisfaction.[188] At mean follow-up of 2.1 years, 73(90%) patients in the absorbable suture group and 77 (95%) patients in the non-absorbable suture group reported being satisfied with the operation. We calculated an OR of 0.47 (95% CI: 0.14 to 1.64). The wide confidence interval includes our MCSD of 0.8 to 1.25. Thus, the evidence is too imprecise to permit a conclusion.

**Adverse Events**

One study comparing absorbable sutures with non-absorbable sutures reported infection.[188] We calculated an odds ratio of 3.04 (95% CI: 0.12 to 75.67); the wide CI indicates that the evidence is inconclusive.

## Applicability

Nineteen studies are included for review for Key Question 6. As described in the *Methods* section, the goal of the evaluation is to raise stakeholders' attention to potential applicability issues embedded in the evidence rather than generating a rating or score for the applicability.

The 19 studies reviewed for Key Question 5 compared different mesh fixation methods. Table 76 provides a detailed description of the fixation methods being compared in the studies. For Key Question 6, we summarized the evidence by different comparison of mesh fixation methods. In the vast majority of these studies, the surgeries were performed in the 1990s or early 2000s. The evidence may not necessarily reflect the comparative performance of the state-of-the-art mesh fixation methods that are currently used in clinical practice.

Seven studies reported that surgeons had experience in hernia repair. Six of the studies reported having used experienced surgeons, but did not define the meaning of "experienced" (e.g., by the number of prior cases or years of practice). One study reported having used first or second-year residents. The remaining 12 studies did not report surgeons' prior experiences with hernia repair. Given the data reported, we were unable to judge what implication surgeons' experience may have in the applicability of the evidence. Table 80 provides additional detail on the surgical procedures compared in the studies, including data on surgeons' experiences.

Patient enrollment criteria and reported baseline characteristics varied significantly across the 19 studies reviewed. From the reported data, we did not identify any general pattern in the patient population enrolled that may have a significant impact on the applicability of the overall evidence. Detailed patient enrollment criteria and baseline characteristics of these studies are provided in Table 77, Table 78, and Table 81.

Except for three studies,[171,176,181] all other studies were performed outside of the United States, primarily in European countries. The differences in healthcare systems and practice patterns between the U.S. and other regions may potentially have an impact on the applicability of the evidence from the perspectives of the United States stakeholders. The clinical setting varied significantly across the studies, ranging from outpatient surgical clinics, an infirmary, community hospitals, and academic medical centers. Based on the data reported, it is unclear how the clinical settings of the studies might have affected the applicability of the evidence. Detailed information on geographic and clinical settings of the six studies is provided in Table 76.

## Summary of Key Question 6

A summary of the comparisons and outcomes we examined for the Key Question six can be found in Table 12 below. Of the 11 outcomes, the evidence was sufficient to permit a conclusion for two outcomes assessed by the various comparisons of mesh fixation types:

- Long-term pain (>6 months) for the comparison of fibrin glue with staples indicated approximate equivalence
- Recurrence for the comparisons of fibrin glue vs. staples indicated approximate equivalence

Our ratings of the strength of evidence for these outcomes also appear in the table. Studies were typically a Moderate risk-of-bias (see risk of bias section above). Our strength of evidence ratings for comparisons with meta-analytic results ranged from Low to Moderate. For the outcome of long-term pain the comparison of fibrin glue vs. staples received a Low strength of evidence rating. The comparison of fibrin glue vs. staples received a Moderate strength of evidence rating for the outcome of recurrence. Imprecision was identified for several comparisons and the analyzed outcomes, precluding any conclusions.

Questions about the relative importance of these outcomes need to be considered carefully. Some may believe the advantages of various mesh fixation methods that prevent significant tension (e.g., glue) may outweigh the disadvantages of other types of fixation methods (e.g., staples).

**Table 12. Key Question 6: Strength of evidence ratings**

| Com-parison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| Tacks or Staples vs. No Fixation | Recurrence | 6 | MOD | C | D | I (RR 0.06 to 3.08) | ? | INSUFF |
| Tacks or Staples vs. No Fixation | Bleeding | 1 | MOD | U | D | I (OR 0.45 to 2.78) | ? | INSUFF |
| Tacks or Staples vs. No Fixation | Infection | 1 | MOD | U | D | I (OR 0.12 to 75.57) | ? | INSUFF |
| Fibrin Glue vs. Staples | Recurrence | 4 | MOD | C | D | P (RR 0.24 to 2.93) | EQ | MOD |
| Fibrin Glue vs. Staples | Quality of Life | 1 | MOD | U | D | I (Diff. -0.09 to 0.09) | ? | INSUFF |
| Fibrin Glue vs. Staples | Long term Pain (≥6 months) (0-10 scale) | 4 | MOD | I | D | P (Diff. -0.84 to 0.18) | EQ | LOW |
| Sutures vs. Tacks | Recurrence | 3 | MOD | C | D | I (RR 0.16 to 22.21) | ? | INSUFF |
| Sutures vs. Glue | Recurrence | 1 | MOD | U | D | I (Diff. -0.24 to 2.00) | ? | INSUFF |
| Sutures vs. Glue | Long term Pain (≥6 months) (0-10 scale) | 1 | MOD | U | D | I (OR 0.04 to 5.89) | ? | INSUFF |
| Sutures vs. Glue | Infection | 4 | MOD | C | D | I (RR 0.06 to 15.72) | ? | INSUFF |
| Absorbable sutures vs. Non resorbable sutures | Recurrence | 1 | MOD | U | D | I (OR 0.56 to 2.33) | ? | INSUFF |
| Absorbable sutures vs. Non resorbable sutures | Long term Pain (≥6 months) (0-10 scale) | 1 | MOD | U | D | I (OR 0.14 to 1.64) | ? | INSUFF |
| Absorbable sutures vs. Non resorbable sutures | Satisfaction | 1 | MOD | U | D | I (OR 0.12 to 75.67) | ? | INSUFF |
| Absorbable sutures vs. Non resorbable sutures | Infection | 1 | MOD | U | D | I (OR 0.12 to 75.67) | ? | INSUFF |

**Table Note:**
**For consistency,** C=consistent, I=inconsistent, U=unknown consistency because there was only one study.
**For directness,** D=direct and I=indirect. For precision, P=precise and I=imprecise.
**For the column labeled "Evidence favors,"** ? denotes inconclusive evidence, and EQ denotes approximate equivalence. SOE=strength of evidence, RR=relative risk.

One non-English study may potentially have met the inclusion criteria for this Key Question if we had not required that studies be published in English.[190] This study is an RCT that compared resorbable suture material with non-absorbable suture material. The authors report that differences in the recurrence rates following the use of these fixation methods were not statistically significant. Our results indicate approximate equivalence for the outcome of hernia recurrence for the comparison of fibrin glue with staples.

## Key Question 7. For each type of laparoscopic mesh repair, what is the association between surgical experience and hernia recurrence?

### Study Characteristics

Thirty two studies were included for this question (Table 13). Sixteen involved only TEP; 12 involved only TAPP; one reported separate data on TEP and TAPP; and three provided combined data on TAPP and TEP. Thus, the totals per procedure were 17 TEP, 13 TAPP, and 3 combined TEP/TAPP. Within each of these subgroups, most studies reported data by stages (e.g., the recurrence rate among the first A patients was x%, whereas the recurrence rate among the subsequent C patients was y%). Other studies reported data comparing surgeons or centers with different levels of prior experience.

**Table 13. Overview of Key Question 7 studies**

| Procedure | Total number of studies | Number that compared stages | Number that compared surgeons or centers |
|---|---|---|---|
| TEP | 17 | 15 | 4 |
| TAPP | 13 | 12 | 4 |
| Combined TAPP/TEP | 3 | 0 | 3 |

**Table Note:**
Two TEP studies and three TAPP studies reported data in two ways (compared stages and also compared surgeons/centers). Also, one study reported separate data on TEP and TAPP.

Hernia recurrence rate is a time-sensitive outcome, therefore studies should *factor out the length of followup* when measuring the association between surgical experience and hernia recurrence. The problem is that those undergoing earlier operations have had more time to experience recurrence, and so an observed higher rate of recurrence may be caused simply by a time confound. Unfortunately, a full 26 of the 32 included studies (81%) failed to report data that factored out the length of followup. Some of these 26 verbally acknowledged the time confound, however these still did not report their data in a more interpretable way (e.g., comparing *one-year recurrence rates* between the first half of the series and the last half of the series).

Another problem with interpreting surgical experience data involves the evolution of surgical techniques over time. If a surgeon changes the mesh over time, or the details of the procedure for inserting the mesh, then a reduction in recurrence rates may be due not to surgical expertise but rather procedural differences. Thirteen of the 32 included studies (41%) reported changing important procedural aspects over time, such as the size of the mesh (which typically involved the use of larger meshes in later time periods).

Another concern involves selective outcome reporting. Not all studies of laparoscopic hernioplasty have reported data on the association between surgical experience and hernia recurrence. Of the 47 studies included for other laparoscopy Key Questions (Key Question 2 and/or Key Question 4), only 4/47 were included for this Key Question 7. The other 43 studies were focused on treatment comparisons rather than surgical experience; most of the 32 included studies for Key Question 7 were case series of laparoscopy.

This question focuses on surgical experience specific to *laparoscopic hernia* repair. Wright et al., 1998[72] asserted that *general* laparoscopic experience (i.e., experience with non-hernia laparoscopic procedures) does not necessary apply to laparoscopic hernia repair:[72]
"In addition, the fact that a surgeon has ample experience in one particular area of laparoscopic

surgery does not mean that he or she will be able to operate in other areas without appropriate training. As pointed out by Grundfest, a surgeon who has performed 250 laparoscopic cholecystectomies will not be qualified to perform a laparoscopic colon resection. Additional training is required for any particular procedure before the surgeon incorporates it into his or her practice." (page 227).[72]

## Risk of Bias

We did not formally assess risk-of-bias for this Key Question, because the intent of the question is not to attribute cause. Above, we discussed our concerns about interpretation of the reported results on the association between surgical experience and hernia recurrence.

## Findings

Unfortunately, the included studies reported data in markedly different ways (Table 14). Among studies comparing an early set to later set(s) of repairs, the size of the early set varied from a low of 10 repairs to a high of 825 repairs. The compared portions of the series were typically of different sizes. Granted, this can be addressed by using recurrence *rates*, but nevertheless it is unclear how authors chose their cutpoints; one possibility is that they structured their data with an eye towards showing the largest possible reduction in recurrence rates over time. The reporting differences mean that one cannot use the data to estimate the length of the learning curve for TEP or TAPP in the context of hernia repair. Interpretation is further compounded by common problems (mentioned above) of ignoring the time confound, procedural evolutions over time, and selective outcome reporting.

**Table 14. Variation in Reporting of Key Question 7 data**

| Study | How the stages were reported |
|---|---|
| Bittner et al., 2002[191-195] | First 600 hernia repairs vs. last 7,450 hernia repairs<br>First 500 vs. next 1,700 vs. next 500<br>First 600 vs. next 4,405<br>First 132 vs. next 132 |
| Bobrzynski et al., 2001[196] | First 10 vs. last 326 |
| Cheah et al., 2004[197] | First 119 vs. last 63 |
| Davies et al., 1995[198,199] | First 10 vs. next 90 vs. next 100 vs. last 100 |
| Dulucq et al., 2009[200] | First 200 vs. next 1,254 vs. last 902 |
| Edwards et al., 2000[201] | First 30 vs. last 30<br>First 30 vs. last 27<br>First 30 vs. last 22 |
| Feliu-Pala et al., 2001[202] | First 100 vs. next 400 vs. last 491 |
| Ferzli et al., 1995[203] | First 100 vs. last 149 |
| Geis et al., 1993[204] | First 50 vs. last 314 |
| Kapiris et al., 2001[205] | First 325 vs. last 3,205 |
| Kieturakis et al., 1994[206] | First 20 vs. last 130 |
| Lal et al., 2004[207] | First 10 vs. next 10 vs. next 10 vs. last 26 |
| Lau et al., 2002[208] | First 20 vs. next 20 vs. next 20 vs. next 20 vs. next 20 vs. last 20 |
| Liem et al., 1997[72,209-214] | First 10 vs. next 10 vs. last 10 |
| MRC et al., 1999[27,66-73] | First 10 vs. next 10 vs. last 10 |
| Pikoulis et al., 2002[215] | First 50 vs. next 50 vs. last 209 |
| Ramshaw et al., 2001[216] | First 300 vs. last 624 |
| Schultz et al., 2000[217] | First 500 vs. next 500 vs. next 500 vs. next 500 vs. last 500 |
| Swadia et al., 2011[218] | First 412 vs. next 535 vs. last 592 |
| Tamme et al., 2003[219] | First 825 vs. last 4,378 |
| Voitk et al., 1998[220] | First 50 vs. last 50 |
| Zendejas et al., 2011[221] | First 40 vs. next 40 vs. next 40 vs. next 40 vs. next 40 vs. next 40 vs. last 24<br>First 110 vs. last 866 |

**Table Note:**

Given this large variation, no meta-analysis was conducted. Instead, we present a general summary of the results in Table 15 below. Most studies reported results in the expected direction: lower recurrence rates with increased experience. This was also true when examined more specifically for TEP (11/17 studies) and TAPP (11/13 studies).

**Table 15. Summary of Results of Key Question 7 studies**

| Procedure | Lower recurrence with increased experience | Mixed results, no effect, or no recurrences observed | Higher recurrence with increased experience |
|---|---|---|---|
| TEP | 11 | 6 | 0 |
| TAPP | 11 | 3 | 0 |
| Combined TAPP/TEP | 1 | 1 | 1 |

**Table Note:**
One study reported separate data on TEP and TAPP, so it is represented twice in the table (specifically in the column labeled "lower recurrence with increased experience").

## Applicability

Thirty-two studies are included for review for Key Question 7. We evaluated these studies to identify factors that may potentially affect the applicability of the evidence. As described in the *Methods* section, the goal of the evaluation is to raise stakeholders' attention to potential applicability issues embedded in the evidence rather than generating a rating or score for the applicability.

The 32 studies reviewed for Key Question 7 compared the recurrence rates of TAPP, TAP, or combined TAPP and TEP between surgeons or medical centers with varying experience or between surgeries operated earlier versus later in the series. Table 84 provides a detailed description of the laparoscopic procedures being studied. For Key Question 7, we summarized the findings separately by different procedures (Table 15), because the evidence for one type of laparoscopic procedure may not apply to a different type of procedure.

Except for three studies,[218,221,222] the surgeries were all performed in 1990s or early 2000s. The findings about the experience-recurrence association may not necessarily apply to the current state of the art of the procedures.

Patient enrollment criteria and reported baseline characteristics varied significantly across the 32 studies. It is unclear if any of the reported patient characteristics or enrollment criteria has a significant implication in the applicability of the overall evidence. Detailed patient enrollment criteria and baseline characteristics of these studies are provided in Table 85, Table 86, Table 87, and Table 89.

Except for eight studies[26,74-79,201,203,204,206,216,221,223] all other twenty-four studies were performed outside of the U.S., primarily in European countries. The differences in healthcare systems and practice patterns between the U.S. and other geographic regions may potentially have an impact on the applicability of the evidence from the perspectives of the U.S. stakeholders. The clinical setting varied significantly across the studies, ranging from community hospitals, teaching or university hospitals, to specialized hernia or laparoscopy centers. The reported data do not allow us to judge whether the geographic or clinical settings have any significant impact on the applicability of the overall evidence. Based on the data reported, it is unclear how the clinical settings of the studies might have affected the applicability of the evidence. Detailed information on geographic and clinical settings of the six studies is provided in Table 84.

## Summary of Key Question 7

This section found a large amount of evidence reporting that greater surgical experience with laparoscopic herniorrhaphy is associated with lower recurrence rates. The variations in reporting, however, made it impossible to estimate the length of the learning curve. There were also key problems in interpreting the data in three areas: the possibility of a time confound (that earlier patients had been followed for longer and had more time to have recurrences), procedural evolutions (that details of the procedure often changed over time making it difficult to pinpoint the effect of expertise), and selective outcome reporting (that the studies reporting this association may have chosen to do so because of the nature of the data).

We examined the abstracts of studies excluded for being non-English and found that 17 of them might possibly have met all of the other inclusion criteria for this Key Question.[224-240] Thirteen involved TAPP, two involved TEP, one combined TAPP/TEP data, and one did not report which laparoscopic procedure had been performed. These studies were substantially similar to the 32 already included, with similar reports of decreasing recurrence over time,

as well as the same problems in interpretation (e.g., no control for the time confound). Thus, their inclusion would not have altered our discussion of the evidence for this Key Question.

## Key Question 8. Pediatric patients: For a possible contralateral hernia, does same-operation repair/exploration differ from watchful waiting in patient-oriented effectiveness outcomes and/or adverse events?

No studies that met the inclusion criteria for this question. The Discussion section contains a detailed discussion of this topic.

## Key Question 9. Pediatric patients: Does open hernia repair without a mesh differ from laparoscopic hernia repair without a mesh in patient-oriented effectiveness outcomes and/or adverse events?

### Study Characteristics

General information about the two studies included for this Key Question appears in Table 92 of Appendix C. One study was conducted in Finland and the other one was in China. Both studies were single-center RCTs conducted at a university hospital with an enrollment of 89 patients and 83 patients, respectively. The length of the enrollment period was 5.3 years for one study and 1 year for the second study. The second study indicated that they had no financial relationship for disclosure.

Patient enrollment criteria appear in Table 93 (hernia-related criteria), Table 94 (demographic and medical criteria), and Table 95 (other criteria) of Appendix C. Enrollment criteria varied between the studies. Hernia-related study exclusion criteria included recurrent hernia (1 study), bilateral hernia (1 study), incarcerated hernia (both studies), femoral hernia (both studies), and "emergency" hernia (both studies). Regarding patient age criteria, one study enrolled patients aged 4 months to16 years, the other study enrolled patients aged >3 months to 9 years. As with the hernia-related exclusions, there was variability in how studies selected patients for inclusion.

Treatment details appear in Table 96 of Appendix C. Neither of the studies reported the actual number of prior laparoscopic hernia repairs the surgeons had performed. One study didn't mention surgeons' prior experience; the other one mentioned that surgeon had general laparoscopy skills. Both studies reported baseline patient characteristics included for this Key Question (Table 97 of Appendix C). The patient age in the two studies ranged from 4 months to 16 years; most were males.

### Risk of Bias

Our risk-of-bias assessments for both studies appear in Table 98 of Appendix C. Both RCTs were categorized as Moderate risk-of-bias for all of their reported outcomes. Common reasons for assigning a Moderate category to the studies were similar to those discussed in Key Question 2a: possible differences in prior surgical expertise, lack of concealment of allocation, and lack of outcome assessor blinding.

### Findings

All included data for this Key Question appear in Table 99 of Appendix C.

### Hernia recurrence

We performed a meta-analysis of both studies reporting this outcome (Figure 57), and found that the evidence was inconclusive (summary relative risk 1.54, 95% CI: 0.2 to 11.6).

### Length of hospital stay

Both studies reported an outcome in this category, and were included in a meta-analysis (Figure 58). The meta-analysis found that length of stay was shorter after laparoscopic surgery than after open surgery (summary difference -1.13 hours, 95% CI: –1.77 to -0.49). Given the confidence interval included values below 1 (what we defined as the MCSD) as well as values above 1, the finding's clinical significance remains unclear.

### Return to daily activities

Both studies reported an outcome in this category, and were included in a meta-analysis of number of hours before returning to normal daily activities (Figure 59). The result of the meta-analysis was equivalent (summary difference -2.77 hours, 95% CI: -11.24 to 5.69).

### Long-term patient satisfaction

One study reported this outcome. One study reported this outcome. Patient satisfaction was recorded (unsatisfactory=0, satisfactory=1, good=2, and excellent=3) by patients or parents, the attending nurse, and the surgeon (minimum points=0, maximum points=9). The parents were more satisfied (difference in satisfaction points 1, 95% CI: 0.47 to 1.53) in the laparoscopic group compared to the open group.

### Long-term cosmesis

One study reported this outcome. Cosmesis was recorded (unsatisfactory=0, satisfactory=1, good=2, and excellent=3) by patients or parents, the attending nurse, and the surgeon (minimum points=0, maximum points=9). The parents in the laparoscopic group were more content with cosmesis than those in the open group (difference in satisfaction points 0.25, 95% CI: 0.12 to 0.38).

## Applicability

Two studies are included for review for Key Question 9. We evaluated these studies to identify factors that may potentially affect the applicability of the evidence. As described in the *Methods* section, the goal of the evaluation is to draw stakeholders' attention to potential applicability issues embedded in the evidence rather than generating a rating or score for the applicability.

Both studies compared open with laparoscopic procedures. The procedures in the Chan study were performed seven years ago (2003-2004),[241] and those in the Koivusalo study were performed four to nine years ago (2002-2007).[242] The evidence may not reflect the comparative effectiveness and safety of the current state-of-the-art open vs. laparoscopic procedures. Surgeons' prior experiences for the procedures being compared were not reported in the studies. We were unable to judge if there is any applicability issues related to surgeons' prior experiences.

Neither study included very young patients. The Chan study excluded patients younger than 3 months, and the Koivusalo study excluded patients younger than 4 months. Meanwhile, both studies excluded patients with incarcerated or strangulated hernia. The findings of the studies may not apply to the patient populations being excluded. Both studies also used additional patient exclusion criteria. For example, the Chan study did not include patients with recurrent

hernia, and the Koivusalo study did not include patients with bilateral hernia. Other patient enrollment criteria used by the two studies are provided in Table 93, Table 94, and Table 95 of Appendix C. The findings of the studies may have a more restricted applicability in the populations being excluded from the studies.

Both studies were conducted outside of the U.S.; the Chan study was conducted in Hong Kong, and the Koivusalo study was conducted in Finland. The differences in healthcare systems and practice patterns between the U.S. and other regions may potentially have an impact on the applicability of the evidence from the perspectives of the U.S. stakeholders. Both studies were conducted in a university hospital. The evidence is potentially more applicable to academic settings.

## Summary of Key Question 9

A summary of the comparisons and outcomes we examined in this Key Question is in Table 16 below. Of the five outcomes reported, the evidence was sufficient to permit a conclusion for three outcomes:

- Three outcomes favored laparoscopy (length of stay, long-term patient satisfaction, and long-term cosmesis)
- One outcome indicated approximate equivalence comparing laparoscopy to open repair (return to daily activities)

Our ratings of the strength of evidence for these outcomes also appear in Table 16. Studies were all at Moderate risk of bias (see the pertinent section above); some inconsistencies were found for some outcomes based on effect sizes on opposite sides of a null effect; all of these outcomes are directly important to clinicians and patients; imprecision was found for some outcomes that precluded conclusions. Questions about the relative importance of these outcomes need to be considered carefully. We examined the studies that had been excluded for being non-English language publications, and none of them would have been included for this Key Question.

**Table 16. Key Question 9: Strength of evidence ratings**

| Comparison | Outcome | # studies | Overall risk of bias | Consistency | Directness | Precision | Evidence favors | SOE rating |
|---|---|---|---|---|---|---|---|---|
| Laparoscopic vs. open repair | Length of stay (hours) | 2 | MOD | C | D | P<br>*Diff in means -1.13 (-1.77 to -0.49)* | Laparoscopic | MOD |
| Laparoscopic vs. open repair | Return to daily activities (hours) | 2 | MOD | I | D | P<br>*Diff in means -2.77 (-11.24 to 5.69)* | EQ | LOW |
| Laparoscopic vs. open repair | Recurrence | 2 | MOD | I | D | I<br>*RR 1.54 (0.2 to 11.6)* | ? | INSUFF |
| Laparoscopic vs. open repair | Long-term patient satisfaction | 1 | MOD | U | D | P<br>*Diff in means 1 (0.47 to 1.53)* | Laparoscopic | LOW |
| Laparoscopic vs. open repair | Long-term cosmesis | 1 | MOD | U | D | P<br>*Diff in means 0.25 (0.12 to 0.38)* | Laparoscopic | LOW |

**Table Note:**
**For consistency,** C=consistent, I=inconsistent, U=unknown consistency because there was only one study.
**For directness,** D=direct and I=indirect.
**For precision,** P=precise and I=imprecise.
**For the column labeled "Evidence favors,"** ? denotes inconclusive evidence, and EQ denotes approximate equivalence. SOE=strength of evidence.
**Other abbreviations:** RR=relative risk, Diff=difference

# Discussion

## Summary of Key Findings

A comprehensive list of our conclusions appears in Table 17 below. Clinically significant differences are boldfaced (see further discussion below). Data on other comparisons or other post-surgical outcomes were either insufficient to permit conclusions, or were not considered major comparisons/outcomes.

For Key Question 1, the only conclusion permitted by the evidence was that quality of life which was reported as "overall change in health status in previous 12 months" at one year was greater after repair than after watchful waiting. The evidence on long-term pain interfering with activities was inconclusive due to low precision of the estimate of the difference between groups (odds ratio=0.42, 95% CI: 0.17 to 1.04, which meant that the effect could be as much as OR=0.17 in favor of the repair group or it could be 1.04 in favor of the watchful waiting group). The actual rates of long-term pain interfering with activities were 2.2% in the repair group and 5.1% in the watchful waiting group. The primary risk of watchful waiting is hernia strangulation, but the evidence was also inconclusive on this outcome. The primary benefit of watchful waiting is that one avoids (at least temporarily) the risks of surgery.

For Key Question 2, most outcomes favored laparoscopy, with the key exception of recurrence in the repair of primary hernia, which found lower rates after open surgery. Most outcomes favoring laparoscopy involved short-term recovery (hospital stay, return to daily activities, return to work) and certain types of adverse events (lower rates of wound infection and hematoma). Several of these outcomes showed clinically significant differences. These findings are consistent with the typical reasons why laparoscopy is performed. Interestingly, for recurrent hernia, the risk of a second recurrence was actually lower with open surgery than with laparoscopy. Another interesting finding was that long-term pain was less likely after laparoscopy (also a clinically significant difference), which we found for both primary hernia and recurrent hernia.For Key Question 3, comparing open mesh procedures, the Lichtenstein procedure is currently believed by many to be the best option, but we found that for most comparisons, its results are similar to other prominent open procedures such as mesh plug, Prolene Hernia System, open preperitoneal mesh, and Kugel procedure. The two exceptions to this were when Lichtenstein had better outcomes than mesh plug regarding return to work (a clinically significant difference) and rates of seroma..

For Key Question 4, comparing laparoscopic mesh procedures, the most commonly performed comparison was between TAPP and TEP, and the evidence permitted two conclusions: that return to work is shorter after TAPP, and that short-term pain rates are approximately equivalent. The other laparoscopic mesh procedure is IPOM, which we found to be worse than TAPP regarding hernia recurrence and length of stay.

For Key Question 5, comparing types of meshes, we found approximate equivalence for several outcomes of several comparisons. Standard polypropylene (PP) mesh had similar rates of recurrence as combination materials. Three types of meshes (standard PP, low-weight PP, and combination materials) had approximately equivalent rates of long-term pain. Long-term pain was also similar between standard PP and porcine.

For Key Question 6, comparing fixation approaches, we also found approximate equivalence in recurrence rates among glue vs. staples. Also, long-term pain was approximately equivalent between glue and staples.

For Key Question 7, many studies have reported that surgical experience lowers the risk of recurrence after laparoscopic repair, but the data were reported inconsistently, and do not permit any estimate of the length of the learning curve.

For Key Question 8, no studies have compared surgical exploration to watchful waiting, and in a section below we discuss the pertinent issues.

For Key Question 9, comparing laparoscopy to open repair, we found that return to daily activities was similar for both groups. However, the length of stay was shorter after laparoscopy (as one would expect). Also, long-term patient satisfaction and long-term cosmesis were greater after laparoscopy, and this likely involves the smaller scar.

**Table 17. Conclusions**

| Population | Comparison | Outcome | Conclusion | Strength of evidence |
|---|---|---|---|---|
| Adults with pain-free inguinal hernia | Repair vs. WW | Quality of life at one year | Favors repair<br>On a 0-100 scale, estimated difference 7 points (CI 0.4 to 14.3) | Low |
| Adults with painful inguinal hernia, primary | Lap. vs. open | Recurrence | Favors open<br>Relative risk 1.43 (CI 1.1 to 1.8) | Low |
| Adults with painful inguinal hernia, primary | Lap. vs. open | Hospital stay | Equivalence | Low |
| Adults with painful inguinal hernia, primary | Lap. vs. open | Time to return to daily activities | Favors Lap.<br>3.9 days earlier (CI 2.2 to 5.6) | High |
| Adults with painful inguinal hernia, primary | Lap. vs. open | Time to return to work | Favors Lap.<br>4.6 days earlier (CI 3.1 to 6.1) | High |
| Adults with painful inguinal hernia, primary | Lap. vs. open | Long-term pain | Favors Lap.<br>Odds ratio 0.61 (CI 0.48 to 0.78) | Mod. |
| Adults with painful inguinal hernia, primary | Lap. vs. open | Epigastric vessel injury | Favors Open<br>Odds ratio 2.0 (CI 1 to 3.9) | Low |
| Adults with painful inguinal hernia, primary | Lap. vs. open | Hematoma | Favors Lap.<br>Odds ratio 0.70 (CI 0.54 to 0.89) | Low |
| Adults with painful inguinal hernia, primary | Lap. vs. open | Wound infection | Favors Lap.<br>Odds ratio 0.61 (CI 0.48 to 0.78) | Mod. |
| Adults with painful inguinal hernia, bilateral | Lap. vs. open | Time to return to work | Favors Lap.<br>14 days earlier (CI not calculable) | Low |
| Adults with painful inguinal hernia, recurrent | Lap. vs. open | Recurrence | Favors Lap.<br>Relative risk 0.82 (CI 0.70 to 0.96) | Low |
| Adults with painful inguinal hernia, recurrent | Lap. vs. open | Time to return to daily activities | Favors Lap.<br>7.4 days earlier (CI 3.4 to 11.4) | High |

| Population | Comparison | Outcome | Conclusion | Strength of evidence |
|---|---|---|---|---|
| Adults with painful inguinal hernia, recurrent | Lap. vs. open | Long-term pain | Favors Lap.<br>Odds ratio 0.24 (CI 0.08 to 0.74) | Mod. |
| Adults with painful inguinal hernia | Lichtenstein vs. Mesh plug | Recurrence | Equivalence | Mod. |
| Adults with painful inguinal hernia | Lichtenstein vs. Mesh plug | Return to work | Favors Lich.<br>4 days earlier (CI 1 to 7) | Low |
| Adults with painful inguinal hernia | Lichtenstein vs. Mesh plug | Seroma | Favors Lich.<br>Odds ratio 0.39 (CI 0.16 to 0.94) | Mod. |
| Adults with painful inguinal hernia | Lichtenstein vs. PHS | Short-term pain | Equivalence | Mod. |
| Adults with painful inguinal hernia | Lichtenstein vs. OPM | Short-term pain | Equivalence | Low |
| Adults with painful inguinal hernia | Mesh plug vs. PHS | Short-term pain | Equivalence | Mod. |
| Adults with painful inguinal hernia | Lichtenstein vs. Kugel | Short-term pain | Equivalence | Low |
| Adults with painful inguinal hernia | Lichtenstein vs. Kugel | Intermediate-term pain | Equivalence | Low |
| Adults with painful inguinal hernia | TAPP vs. TEP | Return to work | Favors TAPP<br>1.6 days earlier (CI 0.1 to 3.1) | Mod. |
| Adults with painful inguinal hernia | TAPP vs. TEP | Short- term pain | Equivalence | Mod. |
| Adults with painful inguinal hernia | TAPP vs. IPOM | Recurrence | Favors TAPP<br>0% vs 11% (CI not calculated) | Low |
| Adults with painful inguinal hernia | TAPP vs. IPOM | Length of stay | Favors TAPP<br>1.1 days earlier (CI 0.7 to 1.5) | Low |
| Adults with painful inguinal hernia | PP vs. Low-weight PP | Long term Pain (≥6 months) | Equivalence | Low |
| Adults with painful inguinal hernia | PP vs. Combination mate rials | Recurrence | Equivalence | Mod. |
| Adults with painful inguinal hernia | PP vs. Combination mate rials | Long term Pain (≥6 months) | Equivalence | Low |
| Adults with painful inguinal hernia | PP vs. Porcine | Long term Pain (≥6 months) VAS at rest | Equivalence | Low |
| Adults with painful inguinal hernia | PP vs. Porcine | Long term Pain (≥6 months) VAS on movement | Equivalence | Low |
| Adults with painful inguinal hernia | Low-weight PP vs. Combination materials | Long-term Pain (≥6 months) | Equivalence | Low |
| Adults with painful inguinal hernia | Fibrin Glue vs. Staples | Recurrence | Equivalence | Mod. |

| Population | Comparison | Outcome | Conclusion | Strength of evidence |
|---|---|---|---|---|
| Adults with painful inguinal hernia | Fibrin Glue vs. Staples | Long term Pain (>6 months) | Equivalence | Low |
| Pediatric patients with inguinal hernia | Lap. vs. open | Return to daily activities | Equivalence | Low |
| Pediatric patients with inguinal hernia | Lap. vs. open | Length of stay | Favors Lap. 1.1 hours earlier (CI 0.5 to 1.8) | Mod. |
| Pediatric patients with inguinal hernia | Lap. vs. open | Long-term patient satisfaction | Favors Lap. Difference in satisfaction points 1.0 (CI: 0.5 to 1.5) | Low |
| Pediatric patients with inguinal hernia | Lap. vs. open | Long-term cosmesis | Favors Lap. Difference in satisfaction points 0.25 (CI: 0.12 to 0.38) | Low |

## Implications, clinical context and applicability

The typical adult in the included studies was a man in his mid-50s of average weight suffering from a primary unilateral hernia. About a quarter of the men worked in physically strenuous jobs; for these men, a durable repair is relatively important in order to prevent a recurrence. Our review can inform numerous treatment decisions faced by these men. These treatment decisions include:

- Whether to undergo surgery at an earlier time, or wait. Our data was mostly inconclusive on this point, however we did conclude that quality of life one year later is better among those who received surgery than those who waited.
- Whether to choose open surgery or laparoscopic surgery. For primary hernia, we found that some outcomes favor open surgery, and others favor laparoscopy (see summary above). Laparoscopic hernia repair was introduced around 1990.[243] In 1999, DeTurris et al., 2002)[244] found that the average surgical resident had performed only about seven laparoscopic hernia repairs during the previous five years of residency, whereas the average number of open repairs in the same timeframe was over 50. This suggests that laparoscopic repair did not receive widespread adoption in the first decade after introduction.
- Which type of open surgery. For some outcomes, open procedures yielded approximately similar outcomes, whereas for other outcomes, the evidence favored the Lichtenstein procedure over other open procedures.
- Which type of laparoscopic surgery. Evidence generally favored TAPP over other laparoscopic procedures.
- Choosing among meshes or fixation approaches. These surgical aspects are generally chosen by the surgeon based on prior experience and beliefs. Thus, the clinical audience for these questions is surgeons and manufacturers. We generally found equivalence among a variety of fixation approaches, including no fixation.
- Consideration of expertise with laparoscopic hernia repair. We found numerous reports that the risk of hernia recurrence decreases when a more experienced surgeon performs the procedure, or when the surgical center has greater procedure volume.

The evidence-based conclusions listed in the previous section are only applicable to the types of patients enrolled in the studies underlying those conclusions. For example, for Key Questions 2-7, the large majority of enrolled patients were middle-aged men, therefore the applicability to women or to older or younger men is unknown. Similarly, for Key Question 9 on pediatric hernia open vs. laparoscopic repair, both studies excluded cases <3 months old, and so the conclusions do not apply to patients younger than 3 months old.

## Limitations

One limitation of this review is that we only included studies published in English. Many studies have been published in other languages, and the inclusion of those studies may have resulted in additional conclusions, or may have contradicted some conclusions. In an attempt to address this possibility, we summarized the abstracts from non-English language publications that may have potentially been included for each Key Question. We also provided citations for these articles so that interested readers can obtain these articles and determine the possible impact had they been included.

Another limitation of this review is that for many outcomes, the evidence was inconclusive due to low precision. In general, the included studies were well-conducted, but small. We maximized the power of the data by conducting meta-analyses wherever appropriate and possible. Nevertheless, the data often precluded conclusions, because they suggested contradictory conclusions (i.e., that the evidence could favor option A or option B by a clinically significant amount).

A third limitation is that no studies met our inclusion criteria for Key Question 8 on pediatric contralateral hernia. No studies have compared surgical exploration with watchful waiting in this population. Therefore, in the next section, we describe informally some of the existing research in this area, such as the percentage of pediatric patients with a unilateral inguinal hernia who have a contralateral patent processus vaginalis (which is a risk factor for inguinal hernia).

## Pediatric contralateral hernias

As noted above, our searches included no studies for Key Question 8, which involved pediatric inguinal hernia and whether to surgically explore for a contralateral hernia, or use a wait-and-see approach. This section discusses the pertinent clinical issues.

Some pediatric patients with a unilateral hernia that requires surgical repair may develop hernia on the contralateral side later in life. Key Question 8 aimed to answer if same-operation exploration/repair differs from watchful waiting in health outcomes or adverse events among these patients. Some surgeons suggest performing routine contralateral groin exploration/repair during the operation for repairing unilateral hernia.[245-247] The potential benefits of the same-operation exploration/repair include the elimination of the need for a second operation (as well as a second anesthesia) for repair of a contralateral inguinal hernia and minimization of the risk of incarcerated contralateral hernia (as well as its associated morbidity).[246,248]

Contralateral hernia exploration/repair can be achieved via open surgery or laparoscopic approaches (e.g., transinguinal, via umbilical route or via hernia sac, etc.).[245,249]Laparoscopic approaches became increasingly popular in recent years due to their lesser invasiveness, which may help to reduce the risk of damage to the spermatic cord structures.[246,248] Some clinicians also believed that laparoscopic approaches allow a more accurate evaluation of the presence of contralateral patent processus vaginalis (CPPV).[249]

During the contralateral groin exploration, a large percentage (more than 30 to 40%) of the patients were found to have patent processus vaginalis,[248,250] which is a risk factor for the

development of inguinal hernia. This finding is one of the main reasons for some researchers to recommend routine same-operation contralateral hernia exploration/repair.[245,250] These researchers also argue that the procedure is generally simple, quick, and safe, rarely causing severe complications.[245,250]

However, not all CPPV identified during the contralateral exploration will develop into a clinical hernia. Despite the high percentage of the CPPV identified, the incidence of contralateral hernia is fairly low, ranging from 5.6 to 11.2 percent (followup of 2 to 29 years) according to several studies that we found.[251-255] In addition, there is a small risk of complications associated with the exploration/repair, including damage to vas deferens and spermatic vessels, recurrences of hernia, or iatrogenic cryptorchidism (undescended testes).[251,256,257] Due to the low incidence and potential risk of complications, more researchers believe that routine contralateral groin exploration is not justified and unnecessary.[245,246,251-255]

From the perspective of patients or families, the decision on whether watchful waiting or same-operation contralateral exploration should be opted for would always involve trade-offs among the aforementioned benefits and risks that are potentially associated with the two treatment options. The ideal study design for addressing Key Question 8 is an RCT in which the researchers assign patients with unilateral hernia randomly into a same-operation exploration/repair group and a watchful waiting group, follow up the patients for a long period of time after the intervention, and then compare health outcomes that reflect the trade-offs the patients have to make (e.g., quality of life and patient or parent satisfaction). For this evidence review, we also accepted non-randomized, prospective comparative studies which made appropriate adjustment on key baseline difference between the two treatment groups. However, our literature search did not identify any studies that met the inclusion criteria for Key Question 8. None of the clinical studies that we have scanned concurrently compared same-operation exploration with watchful waiting.

While RCTs are desirable for addressing Key Question 8, it could be technically challenging to conduct this type of study, due to the extremely long period of followup that would be required and anticipated difficulty in patient recruitment. Studies examining the risk of developing contralateral hernia for patients by age, sex and side of the symptomatic hernia would be helpful. Data on the incidence of various adverse events associated with either treatment option (e.g., incidence of strangulated or incarcerated hernia among patients on watchful waiting and the incidence of surgery-related complications among patients undergoing same-operation exploration) would also be required to assist patients and families in making decisions about their options.

## Future Research

A large portion of the existing literature on inguinal hernia has been conducted outside the United States. The differences in healthcare systems and practice patterns between the United States and other regions may potentially have an impact on the applicability of the evidence from the perspectives of the United States stakeholders. Future United States studies should define the unique needs of the United States population, describe how its needs may differ from those of Europeans (who comprise the majority of patients in studies conducted outside the United States), and target research to these unique areas. Surgical registry may help to define unique needs, but existing registries may be inadequate because they are voluntary. For example, an analysis of the voluntary SAGES database (Society of American Gastrointestinal and Endoscopic Surgeons) found that it contained only 1,607 inguinal hernia

repairs in a 5.4 year period (September 1999 to February 2005).[258] This is about 300 per year, which is less than one in every 2,000United States inguinal hernia repairs.

A large registry may also help address a widespread problem we encountered in our evidence review: low precision. Many randomized trials have investigated important questions, but their modest size limits the usefulness of the data. Rare events such as hernia recurrence require much larger sample sizes in order to permit clear inferences. Registry data require sophisticated analytic techniques, such as propensity scores or instrumental variables, in order to reduce selection bias. The registries that we assessed (e.g., Swedish Hernia Registry) were quite large (e.g., 143,000 hernias), but authors did not utilize these techniques, so it was difficult to determine the potential impact of selection bias.

Another key focus of future research should be on recurrence rates in the *very long-term*. The typical patient was middle-aged, so he likely has a few decades of life ahead. Studies have not generally reported recurrence rates past 5-10 years, but conceivably patients and clinicians would be interested in much longer timeframes (e.g., 30 years). One surgeon[259] proposed projection factors to predict 25-year recurrence risk from specific short-term rates: to estimate the 25-year recurrence rates, multiply the one-year rate by 5; multiply the two-year rate by 2.5, multiply the five-year rate by 1.5; and multiply the 10-year rate by 1.2. These projection factors reveal that a small difference in the short term can correspond to a large difference in the long term (e.g., 1% vs. 2% risk at one year corresponds to 5% vs. 10% risk at 25 years). These projections are a step in the right direction, but they have not been tested empirically. We also encourage greater focus on outcomes that matter most to patients, such as chronic pain, long-term quality of life, satisfaction, and the feeling of a foreign body. These outcomes may be associated with the type of mesh or mesh fixation methods, but our evidence review neither revealed nor ruled out key components, due to low precision.

Below, we summarize additional future research needs, separately for each Key Question. We identified only two studies that met the inclusion criteria for Key Question 1. Both studies compared mesh-based open surgery with watchful waiting. No study was identified comparing laparoscopic repair with watchful waiting. In regards to the two studies included for review, the strength of the evidence on the outcomes reported is rated as either “insufficient” or “low.” One of the studies only reported outcomes up to 12 months, which is barely sufficient for comparing the two interventions. There is a need for future studies of high quality that compare hernia repair—particularly laparoscopic repair—with watchful waiting. These studies should place more emphasis on the outcomes not reported in existing literature or were insufficient to permit conclusions, such as long-term pain limiting daily activities.

For comparing open and laparoscopic hernia repair, future studies would be easier to interpret if surgeons’ prior experience with the study procedures were similar. Long-term recurrence rates would be expected to be higher for procedures performed with less prior experience. For primary hernia comparing open repair vs. laparoscopy, the evidence was sufficient to permit conclusions for several outcomes, but for bilateral hernia and recurrent hernia there was far less evidence and therefore fewer conclusions. Recurrence data has often been reported at median followup (e.g., x% recurrence, and patients had been followed for a median of two years with a range from one month to seven years), but given the wide range of followup, this is more difficult to interpret than recurrence data at specific timepoints (i.e., x% recurrence at two years after surgery).

We identified 21 studies that met the inclusion criteria for Key Question 3. Only one of the studies was conducted in the United States (see discussion above). Meanwhile, given that the strength of the evidence on most of the outcomes reported is rated as “insufficient” or “low,” future studies should be conducted to address the uncertainty with the evidence on these outcomes, particularly recurrence, long-term pain, and severe adverse events.

Only one of the nine studies included for review for Key Question 4 was conducted in the United States. Again, the differences in healthcare systems and practice patterns between the U.S. and other regions may potentially have an impact on the applicability of the evidence from the perspectives of the US stakeholders. There is a need for more studies conducted in the U.S. in the future. Meanwhile, the strength of the evidence on most of the outcomes reported in the evidence base is rated as “insufficient” or “low”; future studies should be conducted to address the uncertainty with the evidence on these outcomes, particularly recurrence, long-term pain, return to daily activities, return to work, and severe adverse events.

The literature largest literature base for Key Question 5 was found for the comparisons of PP mesh with combination material mesh (15 studies). One of the issues with this literature base that prevented all studies from being combined in a meta-analysis for a specific outcome was how the data was reported. Not all studies reported data in a similar format (e.g., number of patients vs. number of hernias treated). Meta-analysis was based on the ability to combine the reported data. Theoretically, some meta-analyses may have remained the same or change if all data was reported in a similar format. Future research should work to report data in a consistent manner and continue to assess differences in mesh materials.

For Key Question 6, the challenge we faced when assessing the identified literature base was also the inconsistency of reported data (e.g., number of patients vs. number of hernias). For some outcomes, the authors reported data in a different format or not at all and this precluded the combination of data, and ultimately the identification of any conclusions. Overall consensus for identifying the most important patient oriented outcomes and standards for reporting these outcomes would facilitate analysis in future CERs. Future research may also want to continue to assess fixation methods such as fibrin glue, absorbable sutures, etc., to determine if the there is a difference between these methods when securing surgical mesh for inguinal hernia repairs.

Regarding Key Question 7, future studies of the relation between laparoscopic surgical experience and subsequent hernia recurrence should take care to control for a possible time confound (see discussion of this point above) by reporting recurrence data at a specific timepoint (e.g., the two-year recurrence rate was x% for hernias repaired in the first half of the series and was y% for hernias repaired in the second half of the series). Studies that investigate surgical experience by comparing different centers or comparing different surgeons need to ensure that hernia recurrence is measured in the same way across centers or surgeons and also that the case-mix is similar (to rule out the possibility that more experienced surgeons had lower recurrence rates because they operated on lower-risk patients).

We did not identify any studies that met the inclusion criteria for Key Question 8. The ideal study design for addressing Key Question 8 is an RCT in which the researchers assign patients with unilateral hernia randomly into a same-operation exploration/repair group and a watchful waiting group, follow up the patients for a long period of time after the intervention, and then compare health outcomes that reflect the trade-offs the patients have to make (e.g., quality of life and patient or parent satisfaction). While RCTs are desirable for addressing Key Question 8, it could be technically challenging to conduct this type of study, due to the required extremely long period of followup and anticipated difficulty in patient recruitment. In the near future, non-RCT

studies are welcome. These studies should focus on the identification of the sub-population (by age, sex, and left or right side of the unilateral hernia) at high risk for developing contralateral hernia. Future studies should also further investigate the incidences of severe adverse events associated with either same-operation exploration/repair (e.g., surgery-related complications) or watchful waiting (e.g., strangulated or incarcerated hernia). The findings of these studies would provide crucial information that patients need for making the choice between the two treatment options.

We identified only two studies that met the inclusion criteria for Key Question 9. Both studies enrolled fewer than 100 patients, and both were conducted outside of the United States. Only five health outcomes of interest were reported in the two studies, and the strength of evidence for most of these outcomes is rated as either “insufficient” or “low.” There is a need for future U.S. studies with larger enrollment that address the uncertainty in the evidence on these outcomes. Studies are also needed to address the outcomes that were not reported in the evidence base (e.g., quality of life and patient/parent satisfaction).

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# Glossary of Procedures

**Open mesh procedures:**

- Kugel patch repair: a hernia repair procedure wherein an oval-shaped mesh that is held open by a memory recoil ring is inserted behind the hernia defect and held in place with a single absorbable suture.
- Lichtenstein technique: a tension-free open hernia repair procedure wherein mesh is sutured in front of the hernia defect (anteriorly)
- Mesh plug technique: a hernia repair procedure wherein a pre-shaped mesh plug is introduced into the hernia weakness during open surgery and a piece of flat mesh is positioned on top of the hernia defect.
- Open preperitoneal mesh (OPM) technique: a tension-free open hernia repair procedure wherein mesh is sutured posteriorly.
- Prolene Hernia System (PHS): a one-piece mesh device constructed of an onlay patch connected to a circular underlay patch by a mesh cylinder.
- Read-Rives repair: a tension-free hernia repair procedure where in mesh is placed just over the peritoneum.
- Stoppa technique: a hernia repair wherein a large polyester mesh is interposed in the preperitoneal connective tissue between the peritoneum and transversalis fascia to prevent visceral sac extension through the myopectineal orifice.
- Trabucco technique: a hernia repair procedure that involves placing a single pre-shaped mesh without using sutures.

**Laparoscopic mesh procedures**

- Intraperitoneal onlay mesh (IPOM) technique: a hernia repair procedure wherein a mesh is placed over the hernia defect intra-abdominally to circumvent a groin dissection.
- Totally extraperitoneal (TEP) technique: a laparoscopic hernia repair procedure wherein peritoneal cavity is not entered and a mesh is used to seal the hernia from the outside of the peritoneum.
- Transabdominal preperitoneal (TAPP) technique: a laparoscopic hernia repair procedure that involves entering the peritoneal cavity to place a mesh through an incision over likely hernia sites.

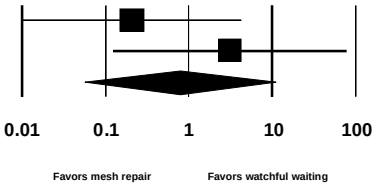
# List of Abbreviations

| | |
|---|---|
| AAS | Activity assessment scale |
| ADV | Adverse event |
| AHRQ | Agency for Healthcare Research and Quality |
| ANOVA | Analysis of variance |
| BMI | Body mass index |
| CI | Confidence interval |
| CMA | Comprehensive Meta-Analysis software |
| CPPV | Contralateral patent processus vaginalis |
| EHCP | Effective Health Care Program |
| EPC | Evidence-based Practice Center |
| ePTFE | Expanded PTFE |
| FDA | Food and Drug Administration |
| HOSP | Hospital-related outcomes |
| Hrs | Hours |
| INSUFF | Insufficient evidence SOE rating |
| IPOM | Intraperitoneal onlay mesh |
| IQR | Interquartile range |
| KQ | Key Question |
| Lich. | Lichtenstein procedure |
| LOS | Length of hospital stay |
| MCSD | Minimum clinically significant difference |
| Mdn | Median |
| Mg | Milligrams |
| N | Number of patients |
| n.s. | Not statistically significant |
| NR | Not reported |
| OPM | Open preperitoneal mesh |
| OR | Odds ratio |
| PCS | Physical Component Scale |
| PHS | Prolene Hernia System |
| PP | Polypropylene |
| PTFE | Polytetraflourethylene |
| PVDF | Polyvinylidenfluoride |
| QALYs | Quality adjusted life years |
| QOL | Quality of life |
| RC | Hernia recurrence |
| RCT | Randomized controlled trial |
| RR | Relative risk |
| RTDA | Return to daily activities |
| RTW | Return to work |
| SD | Standard deviation |
| SEM | Standard error of the mean |
| SF-36 | Short Form 36 quality of life instrument |
| SFN | Satisfaction |
| SOE | Strength of evidence |
| TAPP | Transabdominal preperitoneal repair (laparoscopic) |
| TEP | Totally extraoperitoneal repair (laparoscopic) |
| TOO | Task Order Officer |
| VAS | Visual analog scale |
| WW | Watchful waiting |

# Figures

**Figure 3. Key Question 1: Meta-analysis of acute hernia/strangulation**

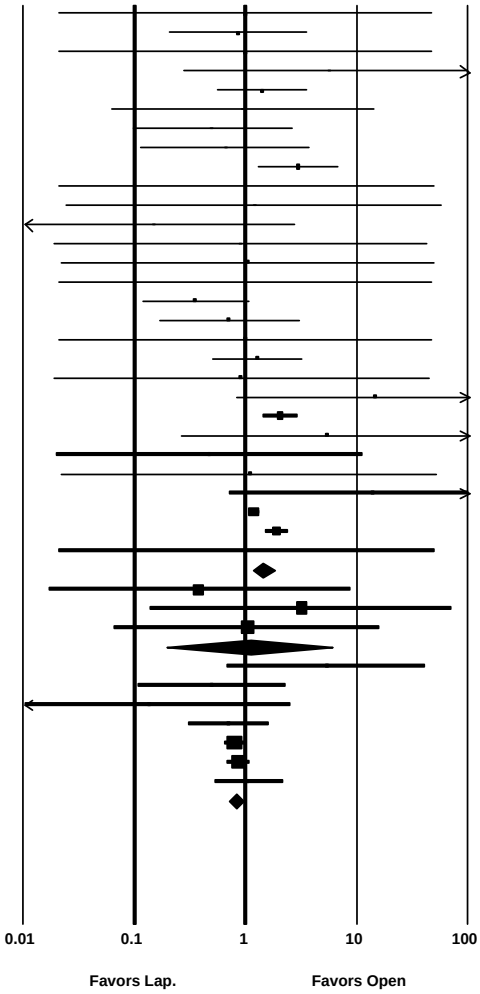
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Odds ratio | Lower limit | Upper limit | p-Value |
| Fitzgibbons et al., 2006 | 0.211 | 0.010 | 4.406 | 0.315 |
| O'Dwyer et al., 2006 | 3.118 | 0.125 | 77.715 | 0.488 |
| | 0.769 | 0.055 | 10.753 | 0.845 |




($I^2$=30%, tau=1.08)

## Figure 4. Key Question 2: Meta-analyses of recurrence

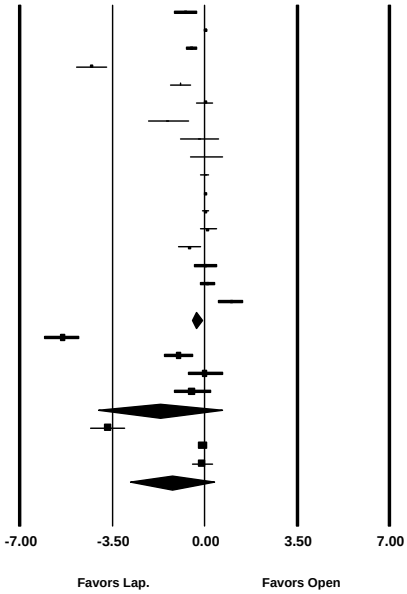
| Group by kq | Study name | Statistics for each study: Risk ratio | Lower limit | Upper limit |
|---|---|---|---|---|
| 2a | Anadol et al. (2004) | 1.000 | 0.021 | 48.524 |
| 2a | Andersson et al. (2003) | 0.848 | 0.197 | 3.656 |
| 2a | Bostanci et al. (1998) | 1.000 | 0.020 | 48.917 |
| 2a | Bringman et al. (2003) | 5.659 | 0.275 | 116.344 |
| 2a | Bueno et al. (2004) | 1.429 | 0.555 | 3.678 |
| 2a | Butters et al. (2007) | 0.938 | 0.060 | 14.737 |
| 2a | Colak et al. (2003) | 0.500 | 0.095 | 2.638 |
| 2a | Douek et al. (2003) | 0.656 | 0.112 | 3.855 |
| 2a | Eklund et al. (2006) | 2.915 | 1.249 | 6.805 |
| 2a | Gokalp et al. (2003) | 1.016 | 0.020 | 50.411 |
| 2a | Gong et al. (2011) | 1.189 | 0.024 | 58.892 |
| 2a | Gunal et al. (2007) | 0.150 | 0.008 | 2.812 |
| 2a | Heikkinen et al. (1997) | 0.905 | 0.019 | 43.398 |
| 2a | Heikkinen et al. (1998) a | 1.043 | 0.022 | 50.428 |
| 2a | Heikkinen et al. (1998) b | 1.000 | 0.021 | 48.086 |
| 2a | Johansson et al. (1999) | 0.351 | 0.114 | 1.083 |
| 2a | Khoury et al. (1998) | 0.710 | 0.162 | 3.117 |
| 2a | Lal et al. (2003) | 1.000 | 0.021 | 48.524 |
| 2a | Langeveld et al. (2010) | 1.250 | 0.484 | 3.231 |
| 2a | Lau et al. (2006) | 0.913 | 0.018 | 45.503 |
| 2a | MRC et al. (1999) | 14.463 | 0.829 | 252.276 |
| 2a | Neumayer et al. (2004) | 2.053 | 1.434 | 2.939 |
| 2a | Paganini et al. (1998) | 5.377 | 0.264 | 109.447 |
| 2a | Pavlidis et al. (2002) | 0.468 | 0.019 | 11.241 |
| 2a | Payne et al. (1994) | 1.082 | 0.022 | 53.469 |
| 2a | Pokorny et al. (2008) | 13.750 | 0.684 | 276.233 |
| 2a | Sevonius et al. (2009) | 1.177 | 1.025 | 1.352 |
| 2a | Wara et al (2005) | 1.873 | 1.449 | 2.420 |
| 2a | Zieren et al. (1998) | 1.000 | 0.020 | 49.750 |
| | | 1.430 | 1.135 | 1.803 |
| 2b | Sarli et al. (2001) | 0.381 | 0.016 | 8.859 |
| 2b | Suter et al. (2002) | 3.150 | 0.136 | 72.885 |
| 2b | Wara et al (2005 | 1.035 | 0.066 | 16.351 |
| | | 1.072 | 0.190 | 6.057 |
| 2c | Beets et al. (1999) | 5.286 | 0.667 | 41.904 |
| 2c | Dedemadi et al. (2006) | 0.492 | 0.104 | 2.334 |
| 2c | Kouhia et al. (2009) | 0.137 | 0.007 | 2.585 |
| 2c | Neumayer et al. (2004) | 0.700 | 0.298 | 1.648 |
| 2c | Sevonius et al. (2009) | 0.790 | 0.625 | 0.998 |
| 2c | Wara et al (2005) | 0.837 | 0.649 | 1.077 |
| 2c | Eklund et al. (2007) | 1.063 | 0.516 | 2.190 |
| | | 0.818 | 0.696 | 0.963 |




KQ2a: $I^2$=24%, tau=0.22
KQ2b: $I^2$=0%, tau=0
KQ2c: $I^2$=0%, tau=0

## Figure 5. Key Question 2: Meta-analyses of length of stay

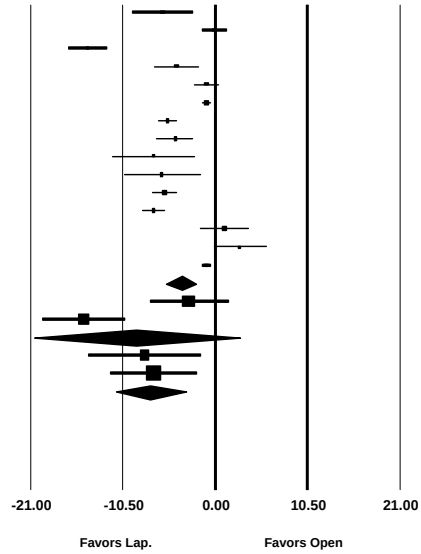
| Group by kq | Study name | Difference in means | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|---|---|
| 2a | Anadol et al. (2004) | -0.720 | 0.219 | 0.048 | -1.150 | -0.290 | -3.285 | 0.001 |
| 2a | Andersson et al. (2003) | 0.050 | 0.042 | 0.002 | -0.033 | 0.133 | 1.178 | 0.239 |
| 2a | Bueno et al. (2004) | -0.500 | 0.120 | 0.015 | -0.736 | -0.264 | -4.152 | 0.000 |
| 2a | Champault et al. (1997) | -4.300 | 0.306 | 0.094 | -4.899 | -3.701 | -14.060 | 0.000 |
| 2a | Colak et al. (2003) | -0.930 | 0.213 | 0.045 | -1.348 | -0.512 | -4.361 | 0.000 |
| 2a | Gokalp et al. (2003) | 0.000 | 0.180 | 0.033 | -0.353 | 0.353 | 0.000 | 1.000 |
| 2a | Gong et al. (2011) ov | -1.400 | 0.402 | 0.162 | -2.188 | -0.612 | -3.483 | 0.000 |
| 2a | Heikkinen et al. (1997) | -0.200 | 0.374 | 0.140 | -0.932 | 0.532 | -0.535 | 0.592 |
| 2a | Lal et al. (2003) | 0.080 | 0.325 | 0.106 | -0.558 | 0.718 | 0.246 | 0.806 |
| 2a | Langeveld et al. (2010) | 0.000 | 0.091 | 0.008 | -0.178 | 0.178 | 0.000 | 1.000 |
| 2a | Lau et al. (2006) | 0.000 | 0.006 | 0.000 | -0.012 | 0.012 | 0.000 | 1.000 |
| 2a | MRC et al. (1999) | 0.000 | 0.076 | 0.006 | -0.149 | 0.149 | 0.000 | 1.000 |
| 2a | Neumayer et al. (2004) | 0.100 | 0.174 | 0.030 | -0.241 | 0.441 | 0.575 | 0.565 |
| 2a | Pavlidis et al. (2002) | -0.600 | 0.222 | 0.049 | -1.034 | -0.166 | -2.708 | 0.007 |
| 2a | Payne et al. (1994) | 0.010 | 0.230 | 0.053 | -0.441 | 0.461 | 0.043 | 0.965 |
| 2a | Picchio et al. (1999) | 0.100 | 0.141 | 0.020 | -0.177 | 0.377 | 0.707 | 0.479 |
| 2a | Zieren et al. (1998) | 1.000 | 0.250 | 0.063 | 0.510 | 1.490 | 4.000 | 0.000 |
| 2a | | -0.333 | 0.097 | 0.009 | -0.523 | -0.144 | -3.452 | 0.001 |
| 2b | Champault et al. (1997) 2b | -5.400 | 0.344 | 0.118 | -6.073 | -4.727 | -15.715 | 0.000 |
| 2b | Ozmen et al. (2010) | -1.000 | 0.288 | 0.083 | -1.563 | -0.437 | -3.478 | 0.001 |
| 2b | Sarli et al. (2001) | 0.000 | 0.352 | 0.124 | -0.689 | 0.689 | 0.000 | 1.000 |
| 2b | Suter et al. (2002) | -0.500 | 0.368 | 0.136 | -1.222 | 0.222 | -1.357 | 0.175 |
| 2b | | -1.725 | 1.209 | 1.463 | -4.096 | 0.645 | -1.426 | 0.154 |
| 2c | Champault et al. (1997) 2c | -3.700 | 0.352 | 0.124 | -4.389 | -3.011 | -10.523 | 0.000 |
| 2c | Dedemadi et al. (2006) | -0.080 | 0.069 | 0.005 | -0.215 | 0.055 | -1.165 | 0.244 |
| 2c | Kouhia et al. (2009) | -0.100 | 0.218 | 0.048 | -0.528 | 0.328 | -0.458 | 0.647 |
| 2c | | -1.254 | 0.810 | 0.656 | -2.841 | 0.333 | -1.549 | 0.121 |




KQ2a: $I^2$=94%, tau=0.34
KQ2b: $I^2$=98%, tau=2.39
KQ2c: $I^2$=98%, tau=1.38

## Figure 6. Key Question 2: Meta-analyses of return to activities of daily living

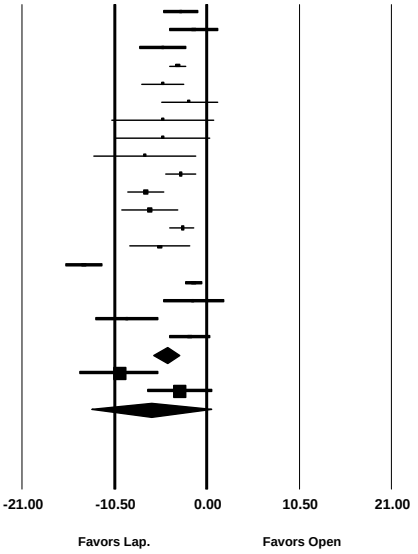
| Group by kq | Study name | Difference in means | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|---|---|
| 2a | Andersson et al. (2003) | -6.000 | 1.799 | 3.236 | -9.526 | -2.474 | -3.335 | 0.001 |
| 2a | Bender et al. (2009) | -0.100 | 0.772 | 0.597 | -1.614 | 1.414 | -0.129 | 0.897 |
| 2a | Bringman et al. (2003) overall | -14.500 | 1.166 | 1.359 | -16.785 | -12.215 | -12.437 | 0.000 |
| 2a | Colak et al. (2003) | -4.400 | 1.377 | 1.896 | -7.099 | -1.701 | -3.196 | 0.001 |
| 2a | Douek et al. (2003) 2a | -1.000 | 0.764 | 0.583 | -2.497 | 0.497 | -1.309 | 0.190 |
| 2a | Gokalp et al. (2003) | -1.000 | 0.286 | 0.082 | -1.560 | -0.440 | -3.498 | 0.000 |
| 2a | Gong et al. (2011) overall | -5.400 | 0.587 | 0.344 | -6.550 | -4.250 | -9.202 | 0.000 |
| 2a | Hamza et al. (2010) ov | -4.580 | 1.117 | 1.249 | -6.770 | -2.390 | -4.099 | 0.000 |
| 2a | Heikkinen et al. (1998) st1 | -7.000 | 2.469 | 6.097 | -11.840 | -2.160 | -2.835 | 0.005 |
| 2a | Heikkinen et al. (1998) st2 | -6.000 | 2.266 | 5.137 | -10.442 | -1.558 | -2.647 | 0.008 |
| 2a | Johansson et al. (1999) | -5.800 | 0.755 | 0.569 | -7.279 | -4.321 | -7.687 | 0.000 |
| 2a | MRC et al. (1999) | -7.000 | 0.656 | 0.431 | -8.286 | -5.714 | -10.665 | 0.000 |
| 2a | Paganini et al. (1998) | 1.000 | 1.464 | 2.142 | -1.869 | 3.869 | 0.683 | 0.494 |
| 2a | Picchio et al. (1999) | 2.800 | 1.566 | 2.452 | -0.269 | 5.869 | 1.788 | 0.074 |
| 2a | Zieren et al. (1998) | -1.000 | 0.316 | 0.100 | -1.620 | -0.380 | -3.162 | 0.002 |
| 2a | | -3.897 | 0.864 | 0.747 | -5.590 | -2.203 | -4.509 | 0.000 |
| 2b | Douek et al. (2003) 2b | -3.000 | 2.301 | 5.295 | -7.510 | 1.510 | -1.304 | 0.192 |
| 2b | Suter et al. (2002) | -15.000 | 2.435 | 5.928 | -19.772 | -10.228 | -6.161 | 0.000 |
| 2b | | -8.974 | 6.000 | 35.999 | -20.733 | 2.786 | -1.496 | 0.135 |
| 2c | Beets et al. (1999) | -8.000 | 3.282 | 10.771 | -14.432 | -1.568 | -2.438 | 0.015 |
| 2c | Dedemadi et al. (2006) | -7.000 | 2.581 | 6.661 | -12.059 | -1.941 | -2.712 | 0.007 |
| 2c | | -7.382 | 2.029 | 4.116 | -11.358 | -3.406 | -3.639 | 0.000 |




KQ2a: $I^2$=95%, tau=3.11
KQ2b: $I^2$=92%, tau=8.15
KQ2c: $I^2$=0%, tau=0

## Figure 7. Key Question 2: Meta-analyses of return to work

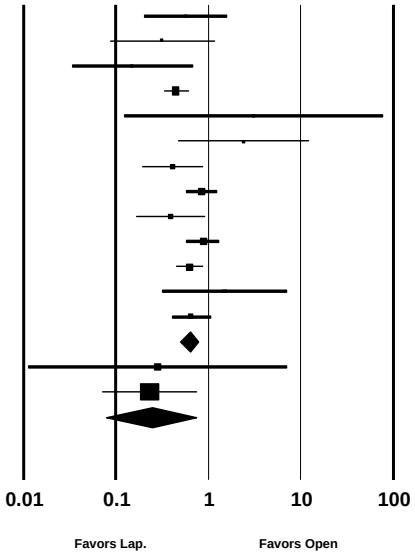
| Group by kq | Study name | Difference in means | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|---|---|
| 2a | Andersson et al. (2003) | -3.000 | 1.038 | 1.078 | -5.035 | -0.965 | -2.890 | 0.004 |
| 2a | Butler et al. (2007) ov | -1.500 | 1.417 | 2.008 | -4.277 | 1.277 | -1.058 | 0.290 |
| 2a | Douek et al. (2003) | -5.000 | 1.384 | 1.916 | -7.713 | -2.287 | -3.612 | 0.000 |
| 2a | Eklund et al. (2006) | -3.300 | 0.515 | 0.265 | -4.309 | -2.291 | -6.413 | 0.000 |
| 2a | Gokalp et al. (2003) | -5.000 | 1.277 | 1.630 | -7.502 | -2.498 | -3.916 | 0.000 |
| 2a | Hamza et al. (2010) ov | -2.030 | 1.674 | 2.803 | -5.312 | 1.252 | -1.212 | 0.225 |
| 2a | Heikkinen et al. (1997) | -5.000 | 3.022 | 9.130 | -10.922 | 0.922 | -1.655 | 0.098 |
| 2a | Heikkinen et al. (1998) st | -5.000 | 2.773 | 7.692 | -10.436 | 0.436 | -1.803 | 0.071 |
| 2a | Heikkinen et al. (1998) st | -7.000 | 3.022 | 9.130 | -12.922 | -1.078 | -2.317 | 0.021 |
| 2a | Johansson et al. (1999) | -3.000 | 0.923 | 0.852 | -4.810 | -1.190 | -3.249 | 0.001 |
| 2a | Khoury et al. (1998) | -7.000 | 1.089 | 1.186 | -9.134 | -4.866 | -6.429 | 0.000 |
| 2a | Lal et al. (2003) | -6.500 | 1.660 | 2.756 | -9.754 | -3.246 | -3.915 | 0.000 |
| 2a | Langeveld et al. (2010) | -2.800 | 0.739 | 0.547 | -4.249 | -1.351 | -3.787 | 0.000 |
| 2a | Lau et al. (2006) | -5.400 | 1.827 | 3.337 | -8.980 | -1.820 | -2.956 | 0.003 |
| 2a | MRC et al. (1999) | -14.000 | 1.048 | 1.099 | -16.055 | -11.945 | -13.353 | 0.000 |
| 2a | Neumayer et al. (2004) | -1.500 | 0.560 | 0.314 | -2.598 | -0.402 | -2.677 | 0.007 |
| 2a | Pavlidis et al. (2002) | -1.600 | 1.792 | 3.211 | -5.112 | 1.912 | -0.893 | 0.372 |
| 2a | Payne et al. (1994) | -9.100 | 1.861 | 3.465 | -12.748 | -5.452 | -4.889 | 0.000 |
| 2a | Zieren et al. (1998) | -2.000 | 1.188 | 1.413 | -4.329 | 0.329 | -1.683 | 0.092 |
| 2a | | -4.614 | 0.758 | 0.574 | -6.099 | -3.129 | -6.088 | 0.000 |
| 2c | Beets et al. (1999) | -10.000 | 2.340 | 5.475 | -14.586 | -5.414 | -4.274 | 0.000 |
| 2c | Kouhia et al. (2009) | -3.100 | 1.899 | 3.605 | -6.822 | 0.622 | -1.633 | 0.103 |
| 2c | | -6.415 | 3.447 | 11.884 | -13.171 | 0.342 | -1.861 | 0.063 |




KQ2a: $I^2$=88%, tau=2.93
KQ2c: $I^2$=81%, tau=4.39

## Figure 8. Key Question 2: Meta-analyses of long-term pain

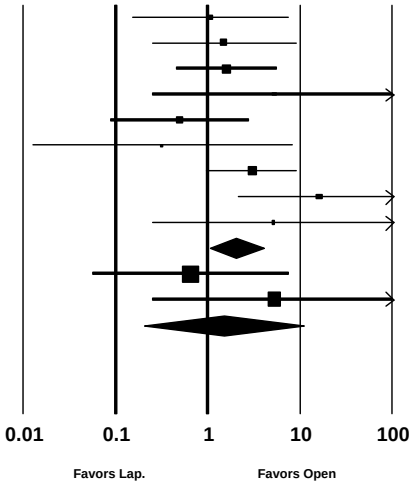
| Group by kq | Study name | Odds ratio | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|
| 2a | Andersson et al. (2003) | 0.570 | 0.199 | 1.628 | -1.050 | 0.294 |
| 2a | Bringman et al. (2003) | 0.317 | 0.084 | 1.191 | -1.701 | 0.089 |
| 2a | Douek et al. (2003) | 0.150 | 0.033 | 0.685 | -2.447 | 0.014 |
| 2a | Eklund et al. (2006) | 0.448 | 0.321 | 0.626 | -4.712 | 0.000 |
| 2a | Gokalp et al. (2003) | 3.099 | 0.124 | 77.572 | 0.688 | 0.491 |
| 2a | Johansson et al. (1999) | 2.448 | 0.469 | 12.774 | 1.062 | 0.288 |
| 2a | Koninger et al. (2004) | 0.414 | 0.193 | 0.891 | -2.257 | 0.024 |
| 2a | Langeveld et al. (2010) | 0.834 | 0.559 | 1.245 | -0.887 | 0.375 |
| 2a | Lau et al. (2006) | 0.396 | 0.167 | 0.940 | -2.100 | 0.036 |
| 2a | MRC et al. (1999) | 0.879 | 0.574 | 1.345 | -0.594 | 0.552 |
| 2a | Neumayer et al. (2004) | 0.629 | 0.440 | 0.899 | -2.543 | 0.011 |
| 2a | Pokorny et al. (2008) ov | 1.500 | 0.316 | 7.123 | 0.510 | 0.610 |
| 2a | Sevonius et al. (2009) | 0.653 | 0.393 | 1.085 | -1.646 | 0.100 |
| 2a | | 0.614 | 0.483 | 0.782 | -3.961 | 0.000 |
| 2c | Beets et al. (1999) | 0.285 | 0.011 | 7.221 | -0.761 | 0.447 |
| 2c | Kouhia et al. (2009) | 0.232 | 0.070 | 0.776 | -2.371 | 0.018 |
| 2c | | 0.238 | 0.077 | 0.738 | -2.488 | 0.013 |




KQ2a: $I^2$=39%, tau=0.25
KQ2c: $I^2$=0%, tau=0

**Figure 9. Key Question 2: Meta-analyses of epigastric vessel injury**

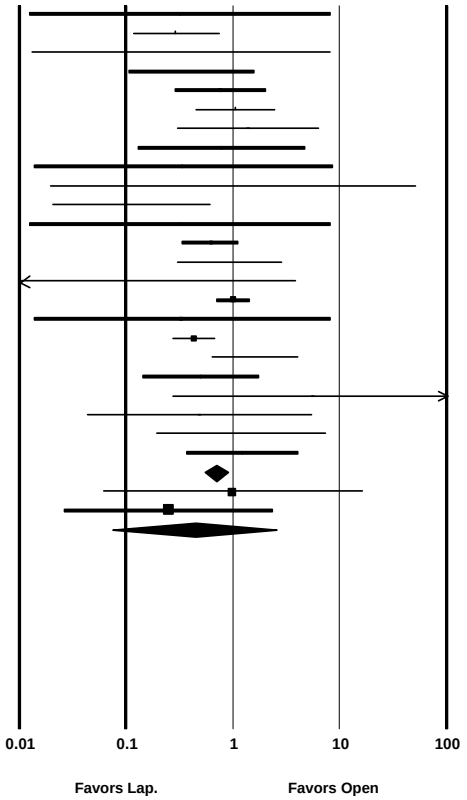
| Group by kq | Study name | Odds ratio | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|
| 2a | Andersson et al. (2003) | 1.078 | 0.148 | 7.841 | 0.074 | 0.941 |
| 2a | Bueno et al. (2004) | 1.508 | 0.249 | 9.121 | 0.447 | 0.655 |
| 2a | Eklund et al. (2006) | 1.598 | 0.449 | 5.688 | 0.724 | 0.469 |
| 2a | Gokalp et al. (2003) | 5.252 | 0.247 | 111.684 | 1.063 | 0.288 |
| 2a | Gunal et al. (2007) | 0.500 | 0.086 | 2.894 | -0.774 | 0.439 |
| 2a | Heikkinen et al. (1998) | 0.317 | 0.012 | 8.260 | -0.691 | 0.490 |
| 2a | Langeveld et al. (2010) | 3.019 | 0.963 | 9.463 | 1.896 | 0.058 |
| 2a | MRC et al. (1999) | 16.215 | 2.141 | 122.789 | 2.697 | 0.007 |
| 2a | Zieren et al. (1998) | 5.127 | 0.242 | 108.509 | 1.050 | 0.294 |
| 2a | | 2.001 | 1.018 | 3.934 | 2.011 | 0.044 |
| 2c | Dedemadi et al. (2006) | 0.652 | 0.056 | 7.642 | -0.340 | 0.734 |
| 2c | Eklund et al. (2007) | 5.210 | 0.246 | 110.409 | 1.059 | 0.289 |
| 2c | | 1.502 | 0.204 | 11.060 | 0.399 | 0.690 |




KQ2a: $I^2$=16%, tau=0.41
KQ2c: $I^2$=7%, tau=0.4

## Figure 10. Key Question 2: Meta-analyses of hematoma

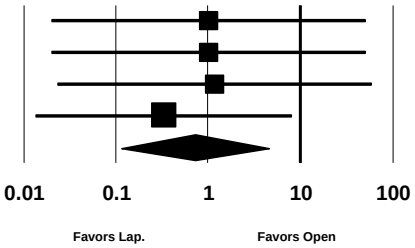
| Group by kq | Study name | Odds ratio | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|
| 2a | Anadol et al. (2004) | 0.320 | 0.012 | 8.245 | -0.687 | 0.492 |
| 2a | Andersson et al. (2010) | 0.290 | 0.113 | 0.748 | -2.561 | 0.010 |
| 2a | Bostanci et al. (1998) | 0.323 | 0.013 | 8.232 | -0.684 | 0.494 |
| 2a | Bringman et al. (2003) | 0.405 | 0.104 | 1.576 | -1.303 | 0.192 |
| 2a | Bueno et al. (2004) | 0.770 | 0.281 | 2.109 | -0.509 | 0.611 |
| 2a | Eklund et al. (2006) | 1.063 | 0.439 | 2.569 | 0.135 | 0.893 |
| 2a | Gokalp et al. (2003) | 1.380 | 0.296 | 6.441 | 0.410 | 0.682 |
| 2a | Gong et al. (2011) | 0.787 | 0.126 | 4.896 | -0.257 | 0.797 |
| 2a | Gunal et al. (2007) | 0.342 | 0.014 | 8.632 | -0.652 | 0.514 |
| 2a | Hamza et al. (2010) | 1.000 | 0.019 | 52.362 | 0.000 | 1.000 |
| 2a | Heikkinen et al. (1997) | 0.111 | 0.020 | 0.626 | -2.491 | 0.013 |
| 2a | Heikkinen et al. (1998) | 0.317 | 0.012 | 8.260 | -0.691 | 0.490 |
| 2a | Johansson et al. (1999) | 0.617 | 0.333 | 1.145 | -1.530 | 0.126 |
| 2a | Khoury et al. (1998) | 0.944 | 0.297 | 2.999 | -0.097 | 0.923 |
| 2a | Lal et al. (2003) | 0.184 | 0.008 | 4.041 | -1.073 | 0.283 |
| 2a | Langeveld et al. (2010) | 1.016 | 0.692 | 1.488 | 0.074 | 0.941 |
| 2a | Lau et al. (2006) | 0.330 | 0.013 | 8.199 | -0.676 | 0.499 |
| 2a | MRC et al. (1999) | 0.433 | 0.267 | 0.703 | -3.382 | 0.001 |
| 2a | Neumayer et al. (2004) | 1.584 | 0.612 | 4.104 | 0.948 | 0.343 |
| 2a | Paganini et al. (1998) | 0.500 | 0.141 | 1.772 | -1.074 | 0.283 |
| 2a | Payne et al. (1994) | 5.645 | 0.264 | 120.628 | 1.108 | 0.268 |
| 2a | Picchio et al. (1999) | 0.490 | 0.043 | 5.579 | -0.575 | 0.566 |
| 2a | Pokorny et al. (2008) | 1.212 | 0.193 | 7.624 | 0.205 | 0.838 |
| 2a | Zieren et al. (1998) | 1.216 | 0.356 | 4.159 | 0.312 | 0.755 |
| 2a | | 0.695 | 0.544 | 0.888 | -2.914 | 0.004 |
| 2b | Ozmen et al. (2010) | 1.000 | 0.060 | 16.713 | 0.000 | 1.000 |
| 2b | Sarli et al. (2001) | 0.250 | 0.026 | 2.448 | -1.191 | 0.234 |
| 2b | | 0.433 | 0.074 | 2.550 | -0.925 | 0.355 |




KQ2a: $I^2$=10%, tau=0.19
KQ2b: $I^2$=0%, tau=0

## Figure 11. Key Question 2: Meta-analysis of small bowel injury

| Group by kq | Study name | Odds ratio | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|
| 2a | Colak et al. (2003) | 1.000 | 0.020 | 51.132 | 0.000 | 1.000 |
| 2a | Douek et al. (2003) | 1.000 | 0.020 | 50.644 | 0.000 | 1.000 |
| 2a | Gong et al. (2011) | 1.190 | 0.023 | 61.033 | 0.087 | 0.931 |
| 2a | MRC et al. (1999) | 0.326 | 0.013 | 8.027 | -0.686 | 0.493 |
| 2a | | 0.715 | 0.112 | 4.555 | -0.356 | 0.722 |

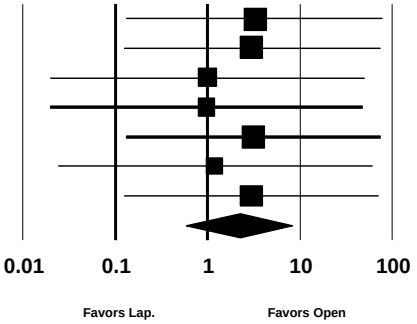



KQ2a: $I^2$=0%, tau=0

## Figure 12. Key Question 2: Meta-analysis of small bowel obstruction

| Group by kq | Study name | Odds ratio | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|
| 2a | Andersson et al. (2003) x x | 3.264 | 0.131 | 81.293 | 0.721 | 0.471 |
| 2a | Bueno et al. (2004) x x | 3.015 | 0.122 | 74.457 | 0.675 | 0.500 |
| 2a | Colak et al. (2003) x | 1.000 | 0.020 | 51.132 | 0.000 | 1.000 |
| 2a | Douek et al. (2003) x | 0.967 | 0.019 | 49.007 | -0.017 | 0.987 |
| 2a | Eklund et al. (2006) x x | 3.153 | 0.128 | 77.551 | 0.703 | 0.482 |
| 2a | Gong et al. (2011) x x x | 1.190 | 0.023 | 61.033 | 0.087 | 0.931 |
| 2a | MRC et al. (1999) x x x | 2.967 | 0.120 | 73.069 | 0.665 | 0.506 |
| 2a | | 2.159 | 0.583 | 8.001 | 1.152 | 0.249 |

Odds ratio and 95% CI

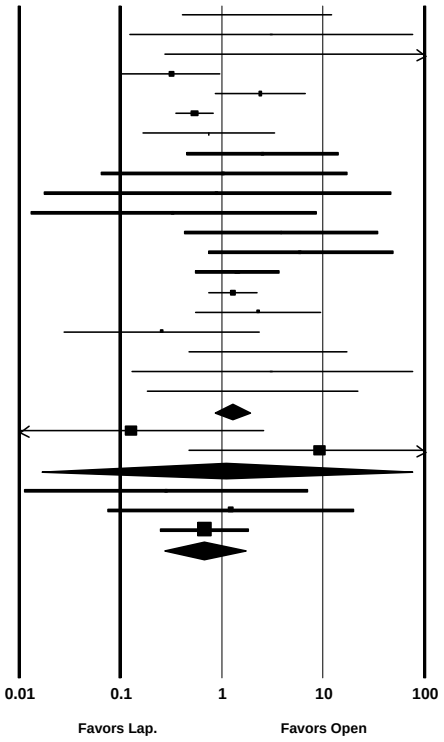



KQ2a: $I^2$=0%, tau=0

## Figure 13. Key Question 2: Meta-analyses of urinary retention

| Group by kq | Study name | Odds ratio | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|
| 2a | Andersson et al. (2003) x x | 2.247 | 0.400 | 12.627 | 0.919 | 0.358 |
| 2a | Bostanci et al. (1998) x | 3.095 | 0.121 | 78.868 | 0.684 | 0.494 |
| 2a | Bringman et al. (2003) x x | 5.791 | 0.274 | 122.236 | 1.129 | 0.259 |
| 2a | Bueno et al. (2004) x x | 0.320 | 0.101 | 1.009 | -1.945 | 0.052 |
| 2a | Douek et al. (2003) x x | 2.414 | 0.833 | 7.001 | 1.622 | 0.105 |
| 2a | Eklund et al. (2006) x x x | 0.542 | 0.338 | 0.867 | -2.553 | 0.011 |
| 2a | Gokalp et al. (2003) x x | 0.750 | 0.161 | 3.500 | -0.366 | 0.714 |
| 2a | Gong et al. (2011) x x x x | 2.500 | 0.439 | 14.233 | 1.033 | 0.302 |
| 2a | Gunal et al. (2007) x x x | 1.051 | 0.064 | 17.397 | 0.035 | 0.972 |
| 2a | Heikkinen et al. (1997) x | 0.902 | 0.017 | 47.815 | -0.051 | 0.960 |
| 2a | Heikkinen et al. (1998) x x | 0.333 | 0.013 | 8.627 | -0.662 | 0.508 |
| 2a | Johansson et al. (1999) x | 3.901 | 0.432 | 35.212 | 1.213 | 0.225 |
| 2a | Langeveld et al. (2016) x x | 6.981 | 0.716 | 49.965 | 1.651 | 0.099 |
| 2a | MRC et al. (1999) x x x x | 1.420 | 0.535 | 3.774 | 0.704 | 0.481 |
| 2a | Neumayer et al. (2004) x x | 1.287 | 0.731 | 2.266 | 0.875 | 0.381 |
| 2a | Paganini et al. (1998) x x | 2.304 | 0.545 | 9.736 | 1.135 | 0.256 |
| 2a | Payne et al. (1994) x x | 0.255 | 0.028 | 2.369 | -1.201 | 0.230 |
| 2a | Pokorny et al. (2008) x x | 2.859 | 0.454 | 17.997 | 1.119 | 0.263 |
| 2a | Simmermacher et al. (2010) x | 3.000 | 0.125 | 77.560 | 0.692 | 0.489 |
| 2a | Zieren et al. (1998) x x | 2.026 | 0.180 | 22.797 | 0.572 | 0.568 |
| 2a | | 1.247 | 0.836 | 1.861 | 1.081 | 0.280 |
| 2b | Ozmen et al. (2010) x x | 0.130 | 0.006 | 2.617 | -1.332 | 0.183 |
| 2b | Sarli et al. (2001) x | 9.400 | 0.455 | 193.994 | 1.451 | 0.147 |
| 2b | | 1.100 | 0.017 | 73.157 | 0.044 | 0.965 |
| 2c | Beets et al. (1999) x | 0.286 | 0.011 | 7.244 | -0.759 | 0.448 |
| 2c | Dedemadi et al. (2006) x x | 0.440 | 0.074 | 20.833 | 0.149 | 0.881 |
| 2c | Eklund et al. (2007) x x | 0.679 | 0.243 | 1.892 | -0.741 | 0.459 |
| 2c | | 0.675 | 0.268 | 1.699 | -0.835 | 0.404 |

Odds ratio and 95% CI

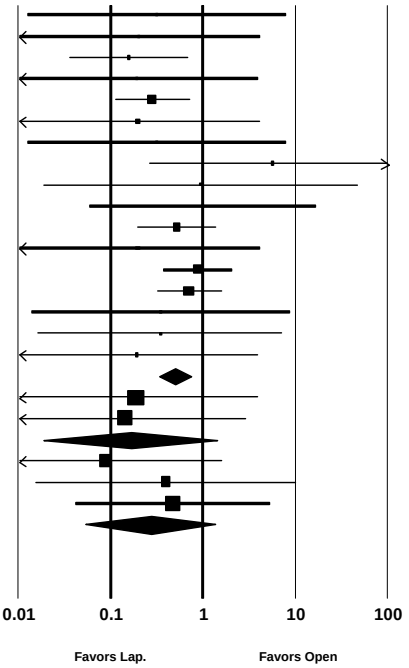



KQ2a: $I^2$=31%, tau=0.45
KQ2b: $I^2$=74%, tau=2.61
KQ2c: $I^2$=0%, tau=0

## Figure 14. Key Question 2: Meta-analyses of wound infection

| Group by kq | Study name | Odds ratio | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|
| 2a | Anadol et al. (2004) x | 0.320 | 0.012 | 8.245 | -0.687 | 0.492 |
| 2a | Andersson et al. (2003) x x x | 0.202 | 0.010 | 4.282 | -1.026 | 0.305 |
| 2a | Bueno et al. (2004) x x x x | 0.158 | 0.035 | 0.716 | -2.393 | 0.017 |
| 2a | Colak et al. (2003) x x | 0.194 | 0.009 | 4.120 | -1.052 | 0.293 |
| 2a | Douek et al. (2003) x x x | 0.282 | 0.110 | 0.723 | -2.634 | 0.008 |
| 2a | Gokalp et al. (2003) x x x | 0.197 | 0.009 | 4.184 | -1.042 | 0.297 |
| 2a | Hamza et al. (2010) x x x x | 0.320 | 0.012 | 8.245 | -0.687 | 0.492 |
| 2a | Heikkinen et al. (1998) x x x | 5.732 | 0.260 | 126.420 | 1.106 | 0.269 |
| 2a | Khoury et al. (1998) x | 0.947 | 0.019 | 48.038 | -0.027 | 0.978 |
| 2a | Lal et al. (2003) x | 1.000 | 0.059 | 16.928 | 0.000 | 1.000 |
| 2a | Langeveld et al. (2010) x x x | 0.527 | 0.192 | 1.441 | -1.248 | 0.212 |
| 2a | Lau et al. (2006) x | 0.196 | 0.009 | 4.135 | -1.047 | 0.295 |
| 2a | MRC et al. (1999) x x x x x | 0.894 | 0.375 | 2.131 | -0.254 | 0.800 |
| 2a | Neumayer et al. (2004) x x | 0.715 | 0.316 | 1.617 | -0.805 | 0.421 |
| 2a | Payne et al. (1994) x x | 0.354 | 0.014 | 8.899 | -0.631 | 0.528 |
| 2a | Pokorny et al. (2008) x x x x | 0.346 | 0.016 | 7.422 | -0.678 | 0.498 |
| 2a | Zieren et al. (1998) x x x | 0.195 | 0.009 | 4.127 | -1.050 | 0.294 |
| 2a | | 0.495 | 0.335 | 0.730 | -3.541 | 0.000 |
| 2b | Ozmen et al. (2010) x x | 0.188 | 0.009 | 4.069 | -1.066 | 0.286 |
| 2b | Sarli et al. (2001) x x | 0.143 | 0.007 | 2.944 | -1.260 | 0.207 |
| 2b | | 0.163 | 0.019 | 1.413 | -1.646 | 0.100 |
| 2c | Beets et al. (1999) x x | 0.088 | 0.005 | 1.684 | -1.614 | 0.106 |
| 2c | Dedemadi et al. (2006) x x x x | 0.396 | 0.015 | 10.138 | -0.560 | 0.576 |
| 2c | Kouhia et al. (2009) | 0.469 | 0.041 | 5.349 | -0.610 | 0.542 |
| 2c | | 0.271 | 0.053 | 1.375 | -1.576 | 0.115 |

Odds ratio and 95% CI

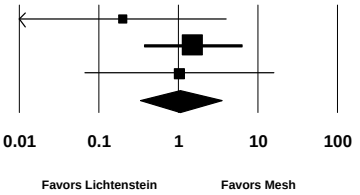



KQ2a: $I^2$=0%, tau=0
KQ2b: $I^2$=0%, tau=0
KQ2c: $I^2$=0%, tau=0

## Figure 15. Key Question 3: Lichtenstein vs. mesh plug, Meta-analysis of recurrence

| Study name | Risk ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Bringham et al., 2003 | 0.200 | 0.010 | 4.115 | 0.297 |
| Frey et al., 2007 | 1.553 | 0.375 | 6.442 | 0.544 |
| Dalenback et al., 2009 | 1.034 | 0.065 | 16.373 | 0.981 |
| | 1.065 | 0.332 | 3.419 | 0.916 |

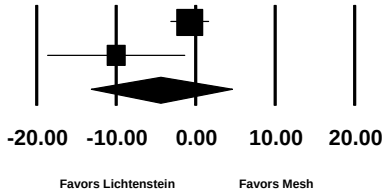
Risk ratio and 95% CI




($I^2$=0%, tau=0)

**Figure 16. Key Question 3: Lichtenstein vs. mesh plug, Meta-analysis of return to activities of daily living**

| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Kingsnorth et al., 2000 | -0.800 | -3.310 | 1.710 | 0.532 |
| Abu-Own et al., 2000 | -10.000 | -18.849 | -1.151 | 0.027 |
| | -4.381 | -13.173 | 4.411 | 0.329 |




($I^2$=74%, tau=31.3)

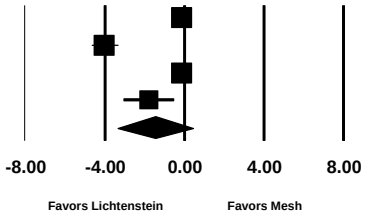
**Figure 17. Key Question 3: Lichtenstein vs. mesh plug, Meta-analysis of return to work**

| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Kingsnorth et al., 2000 | -3.800 | -6.872 | -0.728 | 0.015 |
| Abu-Own et al., 2000 | -7.000 | -19.070 | 5.070 | 0.256 |
| | -3.995 | -6.972 | -1.018 | 0.009 |

($I^2$=0%, tau=0)

**Figure 18. Key Question 3: Lichtenstein vs. mesh plug, Meta-analysis of short-term pain**

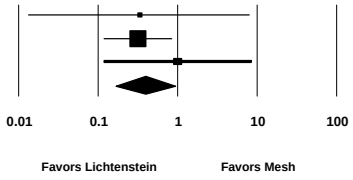
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Nienhuija et al., 2004 | -0.100 | -0.624 | 0.424 | 0.708 |
| Kingsnorth et al., 2000 | -4.000 | -4.661 | -3.339 | 0.000 |
| Dalenback et al., 2009 | -0.100 | -0.540 | 0.340 | 0.656 |
| Abu-Own et al., 2000 | -1.800 | -3.074 | -0.526 | 0.006 |
| | -1.484 | -3.357 | 0.390 | 0.121 |




($I^2$=97%, tau=3.5)

**Figure 19. Key Question 3: Lichtenstein vs. mesh plug, Meta-analysis of seroma**

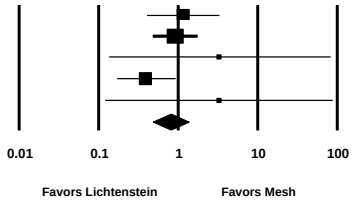
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Bringham et al., 2003 | 0.330 | 0.013 | 8.198 | 0.499 |
| Frey et al., 2007 | 0.314 | 0.113 | 0.874 | 0.027 |
| Abu-Own et al., 2000 | 1.000 | 0.119 | 8.421 | 1.000 |
| | 0.385 | 0.159 | 0.935 | 0.035 |




($I^2$=0%, tau=0)

**Figure 20. Key Question 3: Lichtenstein vs. mesh plug, Meta-analysis of hematoma**

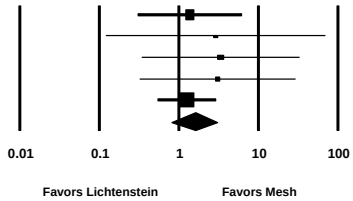
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Bringham et al., 2003 | 1.155 | 0.403 | 3.313 | 0.789 |
| Frey et al., 2007 | 0.914 | 0.463 | 1.804 | 0.795 |
| Kingsworth et al., 2000 | 3.267 | 0.131 | 81.564 | 0.471 |
| Darlenback et al., 2009 | 0.393 | 0.167 | 0.926 | 0.033 |
| Abu-Own et al., 2000 | 3.240 | 0.120 | 87.125 | 0.484 |
| | 0.797 | 0.465 | 1.367 | 0.410 |




($I^2$=14%, tau=0.06)

**Figure 21. Key Question 3: Lichtenstein vs. mesh plug, Meta-analysis of infection**

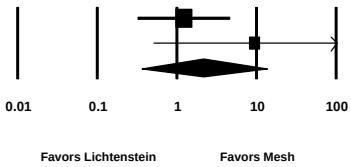
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Bringham et al., 2003 | 1.347 | 0.294 | 6.176 | 0.701 |
| Frey et al., 2007 | 2.924 | 0.119 | 72.019 | 0.512 |
| Kingsworth et al., 2000 | 3.323 | 0.337 | 32.746 | 0.304 |
| Darlenback et al., 2009 | 3.058 | 0.315 | 29.719 | 0.335 |
| Nienhuijs et al., 2004 | 1.248 | 0.516 | 3.020 | 0.622 |
| | 1.551 | 0.790 | 3.046 | 0.203 |




($I^2$=0%, tau=0)

**Figure 22. Key Question 3: Lichtenstein vs. mesh plug, Meta-analysis of urinary retention**

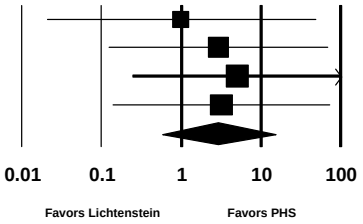
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Frey et al., 2007 | 1.218 | 0.324 | 4.574 | 0.770 |
| Darlenback et al., 2009 | 9.291 | 0.496 | 174.022 | 0.136 |
| | 2.171 | 0.360 | 13.095 | 0.398 |




($I^2$=35%, tau=0.72)

**Figure 23. Key Question 3: Lichtenstein vs. PHS, Meta-analysis of recurrence**

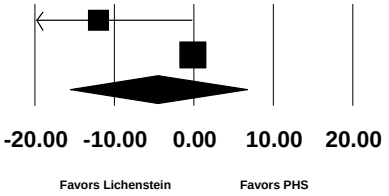
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Risk ratio | Lower limit | Upper limit | p-Value |
| Vironen et al., 2006 | 1.007 | 0.020 | 50.404 | 0.997 |
| Dalenback et al., 2009 | 2.960 | 0.122 | 72.077 | 0.505 |
| Kingsnorth et al., 2002 | 5.000 | 0.243 | 102.885 | 0.297 |
| Sanjay et al., 2006 | 3.187 | 0.135 | 75.432 | 0.473 |
| | 2.915 | 0.567 | 15.000 | 0.201 |




($I^2$=0%, tau=0)

**Figure 24. Key Question 3: Lichtenstein vs. PHS, Meta-analysis of return to work**

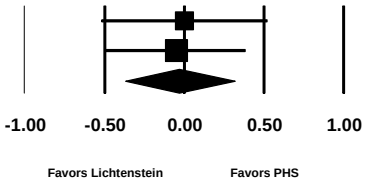
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Sanjay et al., 2006 | -12.000 | -23.853 | -0.147 | 0.047 |
| Vironen et al., 2006 | -0.200 | -1.583 | 1.183 | 0.777 |
| | -4.571 | -15.740 | 6.598 | 0.422 |




($I^2$=0%, tau=0)

**Figure 25. Key Question 3: Lichtenstein vs. PHS, Meta-analysis of short-term pain**

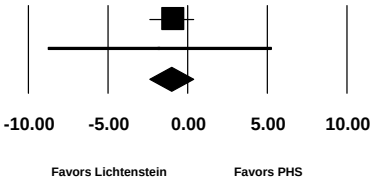
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Nienhuija et al., 2004 | 0.000 | -0.527 | 0.527 | 1.000 |
| Dalenback et al., 2009 | -0.050 | -0.493 | 0.393 | 0.825 |
| | -0.029 | -0.369 | 0.310 | 0.866 |




($I^2$=0%, tau=0)

**Figure 26. Key Question 3: Lichtenstein vs. PHS, Meta-analysis of intermediate-term pain**

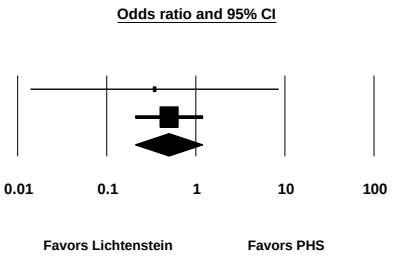
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Sanjay et al., 2006 | -1.000 | -2.386 | 0.386 | 0.157 |
| Kingsnorth et al., 2002 | -1.800 | -8.834 | 5.234 | 0.616 |
| | -1.030 | -2.390 | 0.330 | 0.138 |




($I^2$=0%, tau=0)

**Figure 27. Key Question 3: Lichtenstein vs. PHS, Meta-analysis of hematoma**

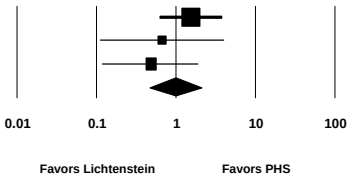
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Odds ratio | Lower limit | Upper limit | p-Value |
| Sanjay et al., 2006 | 0.344 | 0.013 | 8.763 | 0.518 |
| Dalenback et al., 2009 | 0.498 | 0.205 | 1.210 | 0.124 |
| | 0.485 | 0.206 | 1.143 | 0.098 |




($I^2$=0%, tau=0)

**Figure 28. Key Question 3: Lichtenstein vs. PHS, Meta-analysis of infection**

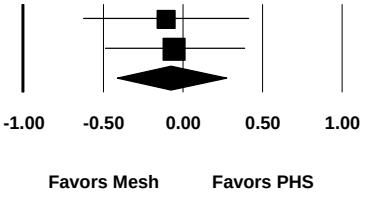
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Odds ratio | Lower limit | Upper limit | p-Value |
| Nienhuijs et al., 2004 | 1.545 | 0.606 | 3.942 | 0.362 |
| Vironen et al., 2006 | 0.667 | 0.110 | 4.048 | 0.660 |
| Dalenback et al., 2009 | 0.481 | 0.118 | 1.957 | 0.306 |
| | 0.990 | 0.475 | 2.062 | 0.978 |




($I^2$=3%, tau=0.02)

**Figure 29. Key Question 3: Mesh plug vs. PHS, Meta-analysis of short-term pain**

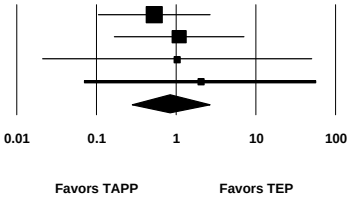
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Nienhuija et al., 2004 | -0.100 | -0.625 | 0.425 | 0.709 |
| Dalenback et al., 2009 | -0.050 | -0.492 | 0.392 | 0.825 |
| | -0.071 | -0.409 | 0.268 | 0.682 |




($I^2$=0%, tau=0)

**Figure 30. Key Question 4: TAPP vs. TEPP, Meta-analysis of recurrence**

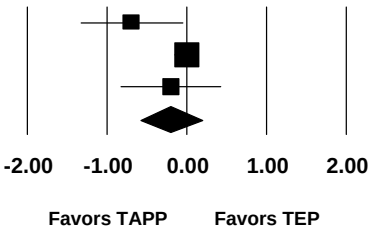
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Risk ratio | Lower limit | Upper limit | p-Value |
| Pokorny et al., 2008 | 0.541 | 0.106 | 2.772 | 0.461 |
| Dedemadi et al., 2006 | 1.083 | 0.165 | 7.098 | 0.933 |
| Gong et al., 2011 | 1.039 | 0.021 | 51.393 | 0.985 |
| Gunal et al., 2007 | 2.050 | 0.071 | 59.414 | 0.676 |
| | 0.840 | 0.277 | 2.549 | 0.758 |




($I^2$=0%, tau=0)

**Figure 31. Key Question 4: TAPP vs. TEPP, Meta-analysis of length of stay**

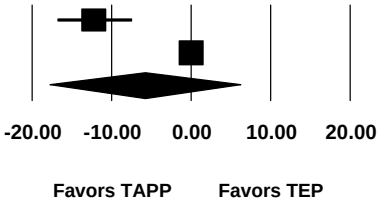
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Schrenk et al., 1996 | -0.700 | -1.352 | -0.048 | 0.035 |
| Dedemadi et al., 2006 | -0.010 | -0.162 | 0.142 | 0.898 |
| Gong et al., 2011 | -0.200 | -0.840 | 0.440 | 0.540 |
| | -0.209 | -0.601 | 0.183 | 0.297 |




($I^2$=53%, tau=0.07)

**Figure 32. Key Question 4: TAPP vs. TEPP, Meta-analysis of return to activities of daily living**

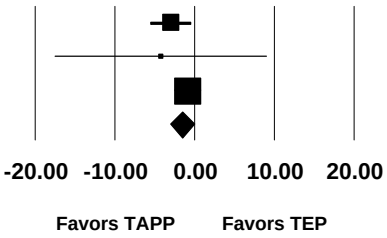
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Dedemadi et al., 2006 | -12.220 | -16.932 | -7.508 | 0.000 |
| Gong et al., 2011 | 0.000 | -0.622 | 0.622 | 1.000 |
| | -5.878 | -17.844 | 6.089 | 0.336 |




($I^2$=93%, tau=0.98)

**Figure 33. Key Question 4: TAPP vs. TEPP, Meta-analysis of return to work**

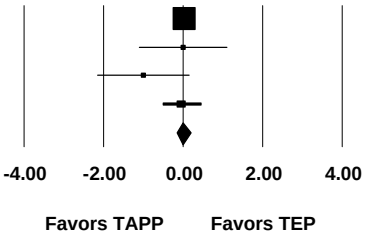
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Butler et al., 2007 | -3.000 | -5.634 | -0.366 | 0.026 |
| Schrenk et al., 1996 | -4.200 | -17.582 | 9.182 | 0.538 |
| Hamza et al., 2010 | -0.900 | -2.676 | 0.876 | 0.321 |
| | -1.588 | -3.052 | -0.124 | 0.033 |




($I^2$=0%, tau=0)

**Figure 34. Key Question 4: TAPP vs. TEPP, Meta-analysis of short-term pain**

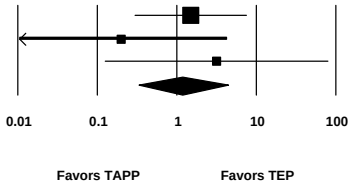
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Gong et al., 2011 | 0.000 | -0.194 | 0.194 | 1.000 |
| Schrenk et al., 1996 | 0.000 | -1.110 | 1.110 | 1.000 |
| Butler et al., 2003 | -1.000 | -2.182 | 0.182 | 0.097 |
| Gunal et al., 2007 | -0.050 | -0.538 | 0.438 | 0.841 |
| | -0.029 | -0.205 | 0.147 | 0.749 |




($I^2$=25%, tau=0.06)

**Figure 35. Key Question 4: TAPP vs. TEPP, Meta-analysis of hematoma**

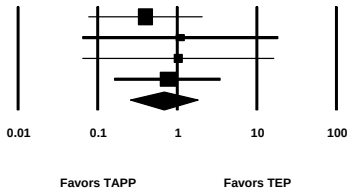
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Pokorny et al., 2008 | 1.500 | 0.296 | 7.606 | 0.624 |
| Gong et al., 2011 | 0.200 | 0.009 | 4.271 | 0.303 |
| Hamza et al., 2010 | 3.122 | 0.121 | 80.391 | 0.492 |
| | 1.168 | 0.314 | 4.336 | 0.817 |




($I^2$=0%, tau=0)

**Figure 36. Key Question 4: TAPP vs. TEPP, Meta-analysis of urinary retention**

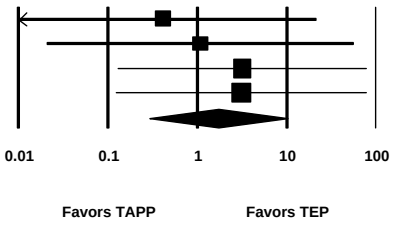
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Pokorny et al., 2008 | 0.395 | 0.076 | 2.061 | 0.270 |
| Dedemadi et al., 2006 | 1.087 | 0.064 | 18.402 | 0.954 |
| Gunal et al., 2007 | 1.026 | 0.062 | 17.006 | 0.986 |
| Gong et al., 2011 | 0.766 | 0.163 | 3.609 | 0.736 |
| | 0.655 | 0.245 | 1.751 | 0.399 |




($I^2$=0%, tau=0)

**Figure 37. Key Question 4: TAPP vs. TEPP, Meta-analysis of infection**

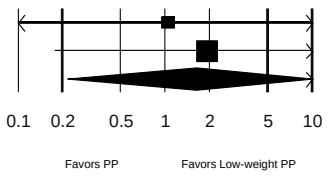
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Pokorny et al., 2008 | 0.420 | 0.008 | 21.591 | 0.666 |
| Dedemadi et al., 2006 | 1.082 | 0.021 | 56.639 | 0.969 |
| Gong et al., 2011 | 3.182 | 0.127 | 79.960 | 0.482 |
| Hamza et al., 2010 | 3.122 | 0.121 | 80.391 | 0.492 |
| | 1.695 | 0.289 | 9.948 | 0.559 |




($I^2$=0%, tau=0)

## Figure 38. Key Question 5: PP vs. Low-weight PP, Meta-analysis of recurrence

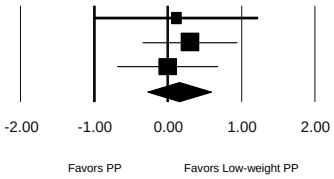
| Study name | Risk ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Nikkolo et al. (2010) | 1.046 | 0.021 | 51.950 | 0.982 |
| Paajanen et al. (2007) | 1.920 | 0.178 | 20.716 | 0.591 |
| | 1.629 | 0.214 | 12.422 | 0.638 |




($I^2$=0%, tau=0)

## Figure 39. Key Question 5: PP vs. Low-weight PP, Meta-analysis of long-term pain

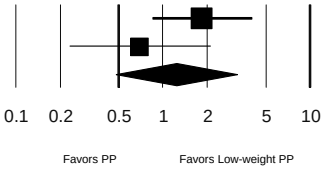
| Study name | Difference in means | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Agarwal et al. (2009) | 0.120 | -0.989 | 1.229 | 0.832 |
| Paajanen et al. (2007) | 0.300 | -0.347 | 0.947 | 0.363 |
| Nikkolo et al. (2010) | 0.000 | -0.685 | 0.685 | 1.000 |
| | 0.153 | -0.280 | 0.586 | 0.489 |




($I^2$=0%, tau=0)

## Figure 40. Key Question 5: PP vs. Low-weight PP, Meta-analysis of feeling of foreign body

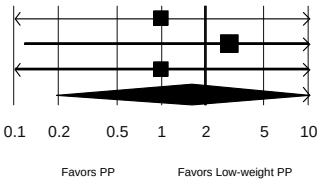
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Nikkolo et al. (2010) | 1.849 | 0.842 | 4.061 | 0.126 |
| Paajanen et al. (2007) | 0.696 | 0.229 | 2.115 | 0.522 |
| | 1.231 | 0.479 | 3.165 | 0.666 |




($I^2$=50%, tau=0.49)

## Figure 41. Key Question 5: PP vs. Low-weight PP, Meta-analysis of infection

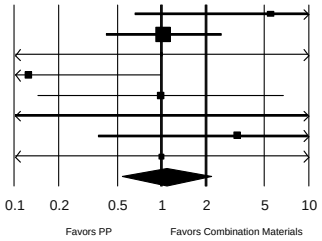
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Agarwal et al. (2009) | 1.000 | 0.019 | 52.362 | 1.000 |
| Paajanen et al. (2007) | 2.923 | 0.117 | 72.874 | 0.513 |
| Paradowski et al. (2009) | 1.000 | 0.019 | 52.362 | 1.000 |
| | 1.588 | 0.192 | 13.112 | 0.668 |




($I^2$=0%, tau=0)

## Figure 42. Key Question 5: PP vs. Combination material, Meta-analysis of recurrence

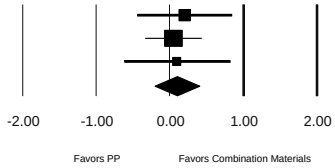
| Study name | Risk ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Chowbey et al. (2010) | 5.524 | 0.651 | 46.858 | 0.117 |
| Bringman et al. (2004) | 1.033 | 0.417 | 2.558 | 0.944 |
| Di Vita et al. (2010) | 1.000 | 0.021 | 47.380 | 1.000 |
| O'Dwyer et al. (2005) | 0.125 | 0.016 | 0.986 | 0.049 |
| Paajanen et al. (2007) | 0.987 | 0.143 | 6.821 | 0.989 |
| Puccio et al. (2005) | 1.000 | 0.021 | 47.380 | 1.000 |
| Collaborative group (2008) | 3.293 | 0.371 | 29.197 | 0.284 |
| Langenbach et al. (2008) | 1.000 | 0.064 | 15.608 | 1.000 |
| | 1.080 | 0.538 | 2.169 | 0.829 |




($I^2$=6%, tau=0.26)

## Figure 43. Key Question 5: PP vs. Combination material, Meta-analysis of long-term pain

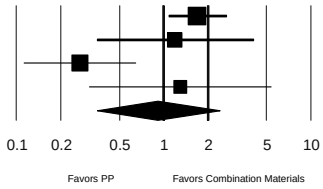
| Study name | Difference in means | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Paajanen et al. (2007) | 0.200 | -0.442 | 0.842 | 0.542 |
| Collaborative group (2008) | 0.050 | -0.348 | 0.448 | 0.805 |
| Langenbach et al. (2008) | 0.100 | -0.628 | 0.828 | 0.788 |
| | 0.093 | -0.214 | 0.400 | 0.552 |




($I^2$=0%, tau=0)

## Figure 44. Key Question 5: PP vs. Combination material, Meta-analysis of feeling of foreign body

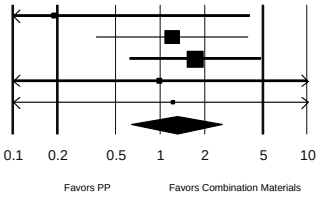
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Bringman et al. (2004) | 1.692 | 1.068 | 2.682 | 0.025 |
| Paajanen et al. (2007) | 1.200 | 0.350 | 4.117 | 0.772 |
| Post et al. (2004) | 0.268 | 0.110 | 0.651 | 0.004 |
| Puccio et al. (2005) | 1.306 | 0.311 | 5.483 | 0.715 |
| | 0.913 | 0.347 | 2.403 | 0.854 |




($I^2$=77%, tau=0.84)

## Figure 45. Key Question 5: PP vs. Combination material, Meta-analysis of infection

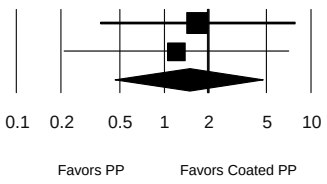
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Heikkinen et al. (2006) | 0.191 | 0.009 | 4.061 | 0.289 |
| Bringman et al. (2004) | 1.208 | 0.365 | 4.003 | 0.757 |
| O'Dwyer et al. (2005) | 1.745 | 0.619 | 4.921 | 0.293 |
| Paajanen et al. (2007) | 0.987 | 0.061 | 16.066 | 0.993 |
| Collaborative group (2008) | 1.214 | 0.024 | 61.495 | 0.923 |
| | 1.285 | 0.625 | 2.641 | 0.495 |




($I^2$=0%, tau=0)

## Figure 46. Key Question 5: PP vs. Coated PP, Meta-analysis of recurrence

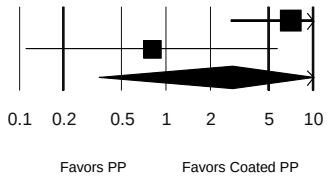
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Risk ratio | Lower limit | Upper limit | p-Value |
| Champault et al. (2007) | 1.698 | 0.367 | 7.860 | 0.498 |
| Khan et al. (2010) | 1.207 | 0.205 | 7.095 | 0.835 |
| | 1.467 | 0.460 | 4.675 | 0.517 |




($I^2$=0%, tau=0)

## Figure 47. Key Question 5: PP vs. Coated PP, Meta-analysis of long-term pain

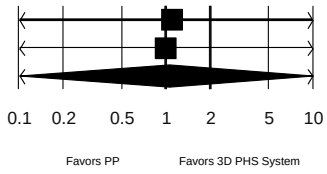
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Odds ratio | Lower limit | Upper limit | p-Value |
| Champault et al. (2007) | 7.001 | 2.728 | 17.968 | 0.000 |
| Khan et al. (2010) | 0.801 | 0.111 | 5.782 | 0.826 |
| | 2.839 | 0.350 | 23.049 | 0.329 |




($I^2$=73%, tau=1.3)

## Figure 48. Key Question 5: PP vs. 3D PHS System, Meta-analysis of recurrence

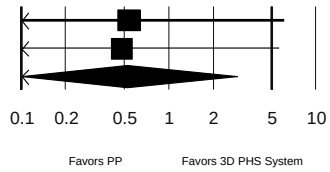
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Risk ratio | Lower limit | Upper limit | p-Value |
| Chauhan et al. (2007) | 1.098 | 0.022 | 54.061 | 0.963 |
| Sutalo et al. (2010) | 1.000 | 0.020 | 49.203 | 1.000 |
| | 1.048 | 0.067 | 16.474 | 0.974 |




($I^2$=0%, tau=0)

## Figure 49. Key Question 5: PP vs. 3D PHS System, Meta-analysis of infection

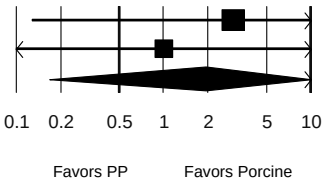
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Odds ratio | Lower limit | Upper limit | p-Value |
| Chauhan et al. (2007) | 0.538 | 0.047 | 6.176 | 0.619 |
| Sutalo et al. (2010) | 0.487 | 0.042 | 5.599 | 0.564 |
| | 0.512 | 0.091 | 2.877 | 0.447 |




($I^2$=0%, tau=0)

## Figure 50. Key Question 5: PP vs. Porcine, Meta-analysis of recurrence

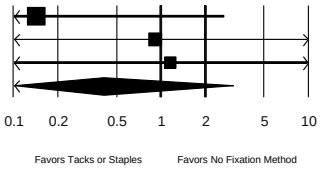
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Risk ratio | Lower limit | Upper limit | p-Value |
| Ansaloni et al. (2009) | 3.000 | 0.126 | 71.215 | 0.497 |
| Puccio et al. (2005) | 1.000 | 0.021 | 47.380 | 1.000 |
| | 1.928 | 0.167 | 22.294 | 0.599 |




($I^2$=0%, tau=0)

## Figure 51. Key Question 6: Tacks or Staples vs. No fixation, Meta-analysis of recurrence

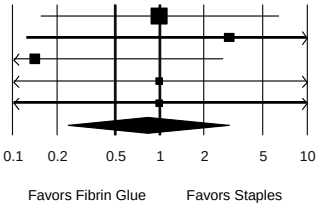
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Risk ratio | Lower limit | Upper limit | p-Value |
| Moreno-Egea et al. (2004) | 0.143 | 0.007 | 2.724 | 0.196 |
| Parshad et al. (2005) | 0.923 | 0.019 | 44.720 | 0.968 |
| Ferzli et al. (1999) | 1.159 | 0.023 | 57.212 | 0.941 |
| | 0.412 | 0.055 | 3.075 | 0.387 |




($I^2$=0%, tau=0)

## Figure 52. Key Question 6: Fibrin Glue vs. Staples, Meta-analysis of recurrence

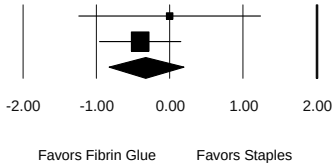
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Risk ratio | Lower limit | Upper limit | p-Value |
| Boldo et al. (2008) | 1.000 | 0.154 | 6.480 | 1.000 |
| Lovisetto et al. (2007) | 2.970 | 0.122 | 72.030 | 0.503 |
| Olmi et al. (2007) Tissucol vs. EMS | 0.143 | 0.007 | 2.742 | 0.197 |
| Olmi et al. (2007) Tissucol vs. EndoAnchor | 1.000 | 0.020 | 50.071 | 1.000 |
| Olmi et al. (2007) Tissucol vs. Protrack | 1.000 | 0.020 | 50.071 | 1.000 |
| | 0.832 | 0.236 | 2.933 | 0.775 |




($I^2$=0%, tau=0)

## Figure 53. Key Question 6: Fibrin Glue vs. Staples, Meta-analysis of long-term pain

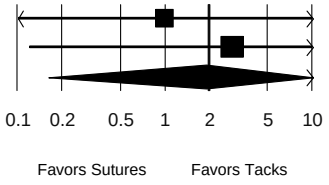
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Boldo et al. (2008) | 0.000 | -1.256 | 1.256 | 1.000 |
| Lovisetto et al. (2007) | -0.400 | -0.959 | 0.159 | 0.160 |
| | -0.334 | -0.844 | 0.176 | 0.200 |




($I^2$=0%, tau=0)

## Figure 54. Key Question 6: Sutures vs. Tacks, Meta-analysis of recurrence

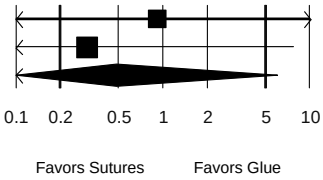
| Study name | Risk ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Mills et al. (1998) | 1.000 | 0.021 | 48.524 | 1.000 |
| Leibl et al. (2002) | 2.901 | 0.119 | 70.492 | 0.513 |
| | 1.888 | 0.161 | 22.209 | 0.613 |




($I^2$=0%, tau=0)

## Figure 56. Key Question 6: Sutures vs. Glue, Meta-analysis of infection

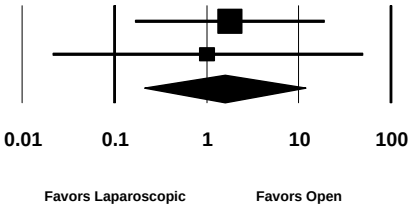
| Study name | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Helbling et al. (2003) | 0.918 | 0.017 | 48.247 | 0.966 |
| Kapischke et al. (2010) | 0.307 | 0.012 | 7.917 | 0.476 |
| | 0.477 | 0.039 | 5.885 | 0.564 |




($I^2$=0%, tau=0)

## Figure 57. Key Question 9: Meta-analysis of recurrence

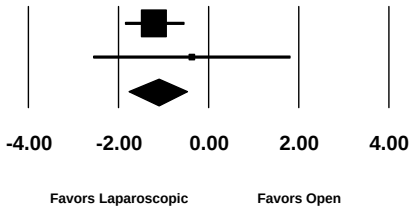
| Study name | Risk ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Koivusalo et al., 2009 | 1.787 | 0.168 | 19.006 | 0.630 |
| Chan et al., 2005 | 1.024 | 0.021 | 50.417 | 0.991 |
| | 1.538 | 0.204 | 11.612 | 0.676 |




($I^2$=0%, tau=0)

**Figure 58. Key Question 9: Meta-analysis of length of stay**

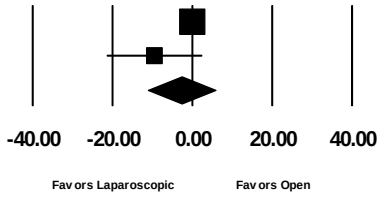
| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Koivusalo et al., 2009 | -1.200 | -1.864 | -0.536 | 0.000 |
| Chan et al., 2005 | -0.360 | -2.564 | 1.844 | 0.749 |
| | -1.130 | -1.766 | -0.494 | 0.000 |




($I^2$=0%, tau=0)

**Figure 59. Key Question 9: Meta-analysis of return to daily activities**

| Study name | Statistics for each study | | | |
|---|---|---|---|---|
| | Difference in means | Lower limit | Upper limit | p-Value |
| Koivusalo et al., 2009 | 0.000 | -0.785 | 0.785 | 1.000 |
| Chan et al., 2005 | -9.500 | -21.540 | 2.540 | 0.122 |
| | -2.772 | -11.237 | 5.692 | 0.521 |




($I^2$=58%, tau=26)