Reoperation for Inguinal Hernia Recurrence in Ontario: A Population-Based Study

By:

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Institute of Medical Science

University of Toronto

Thesis Abstract

Thesis Title: Reoperation for Inguinal Hernia Recurrence in Ontario: A Population- Based Study

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University: University of Toronto

Objective: To compare the rate of reoperation for recurrent inguinal hernia after primary repair.

Methodology: A population-based retrospective cohort study, using administrative data including adult patients in Ontario, Canada undergoing primary inguinal hernia repair (IHR) from April 1, 2003 - December 31, 2012, followed to August 31, 2014.

Exposure: Primary IHR techniques: open repair with mesh; open repair without mesh; laparoscopic repair

Results: We identified 109,106 adults undergoing primary IHR with 5.6 year median follow-up. The 5-year cumulative risk of recurrent IHR was 1.7% in the open with mesh group, 3.2% in the open without mesh group and 3.0% in the laparoscopic group. After adjusting for patient, surgeon and institution factors, as compared to patients undergoing open repair with mesh, those undergoing open

without mesh or laparoscopic repair had higher risk of recurrent IHR (hazard ratio 1.53, 95% CI, 1.33- 1.77 and 1.88, 95% CI, 1.61- 2.20 respectively, $p<0.001$).

Acknowledgements

This research project would not be possible without the assistance of multiple individuals.

I would like to first thank my supervisor, Dr. Nancy Baxter for her support, wisdom, guidance and exemplary leadership. Her mentorship over the last two years has been a constant source of inspiration and encouragement. She embodies all of the attributes of the surgeon I hope to become.

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Thank you to all the members of the Baxter Research Group – especially Corinne Daly and Anne Sorvari, who are always willing to help and have made the fluorescent lights and maze of cubicles a welcoming alternative to the operating room.

Lastly, I'd like to thank my family. I remain grateful to my parents for the many opportunities they have provided, love and constant support irrespective of circumstance. Thank you to my grandparents for being an ever-present source of motivation and to my brother Joel for occasionally answering my text messages. Finally, to my life teammate and wife (to be) – Lauren – thank you for taking this two-year journey to Toronto with me. There is no other person that I would like to share my adventures in surgery with.

Contributions

Drs. David Urbach, Nancy Baxter and Joshua Ramjist conceptualized the main thesis objective. Longdi Fu (Institute of Clinical Evaluative Sciences) completed the primary data coding and cohort generation. Joshua Ramjist led the analysis of results with significant statistical input from Drs. Therese Stukel, David Urbach and Nancy Baxter. Joshua Ramjist compiled this thesis with incorporation of revisions suggested by the entire program advisory committee.

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1. Literature Review

1.1 Inguinal Hernia Epidemiology

Inguinal hernia repair is one of the most commonly performed surgical procedures - an estimated 20 million inguinal hernia repairs are performed worldwide annually (Kingsnorth and LeBlanc 2003), with country specific operative rates varying from 100-300 per 100 000 per year. In Canada this represents ~70,000 repairs annually (Poulin and Marcaccio 1997). In the United States, 45 million adults have an inguinal hernia and at least 25% of American males will develop an inguinal hernia in their lifetime(Ruhl and Everhart 2007). Although some remain asymptomatic or minimally symptomatic, the cumulative probability of a patient presenting with symptoms is reported to be as high as 90% within 10 years of diagnosis (Hair, Paterson et al. 2001). Despite the frequency of surgery for this condition, there is no consensus regarding the optimal surgical approach to minimize hernia recurrence (Scott, McCormack et al. 2002, McCormack, Scott et al. 2003). There are a number of options for repair; the procedure can be performed in an open fashion using a prosthetic mesh or without mesh using a suture technique, or by a laparoscopic approach with placement of an extra-peritoneal mesh. Each technique has advantages and disadvantages (Bittner, Sauerland et al. 2005, Schmedt, Sauerland et al. 2005) with regards to cost, chronic pain, and wound infection. With no consensus in the literature, all approaches are performed in the United States and Canada.

1.2 Management and Repair of Inguinal Hernias

Inguinal hernias occur due to a combination of genetic and acquired factors. Patients who develop hernias have been shown to have a higher ratio of type III to type I collagen and a positive family history (Klinge, Zheng et al. 1999). Similarly, medical diseases associated with collagen disorders such as hiatal hernias and aneurysmal disease have been described in association in patients with inguinal hernias (Olsson, Eriksson et al. 2014). Acquired factors that contribute to a hernia development include heavy lifting as part of a patient's occupation, chronic cough (Ma, Yang et al. 2003) or straining due to constipation(Sarosi, Wei et al. 2011).

There are multiple classification schemes to describe an inguinal hernia. The most frequently used is the Nyhus system, which describes hernias as being direct, indirect, femoral or recurrent. Indirect hernias occur due to a patent processus vaginalis and represent the type of hernia most commonly seen in men. Direct hernias occur due to weakness in the transversalis fascia. Femoral hernias, commonly seen in females due to an enlarged femoral space secondary to a broader pelvis found in females relative to males (Figure 1.1).

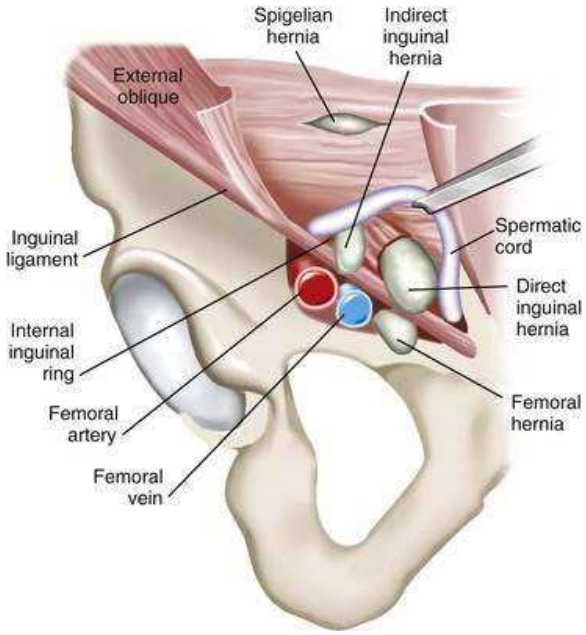


Figure 1.1: Pelvic Anatomy – An inguinal hernia is found superior to the inguinal ligament and deep to the spermatic cord (in males). Note the position of a direct or indirect inguinal hernia relative to the internal inguinal ring. A femoral hernia is found inferior to the inguinal ligament(Jacob and Ramshaw 2012)

Patients typically present after the onset of groin pain, which may be exacerbated by physical activity. The diagnosis of an inguinal hernia is primarily based on physical examination. On standing, male patients commonly demonstrate a bulge in the groin that may or may not reduce on digital palpation. A hernia that does not reduce is termed an incarcerated hernia and necessitates immediate operative intervention. In females, the presence of a hernia may not be as obvious; a palpable mass, bulge or defect may not be found on physical examination. Physical examinations that do not yield a definitive diagnosis can be supplemented with radiographic studies including ultrasound, computed tomographic (CT) imaging (Figure 1.2) and magnetic resonance imaging.

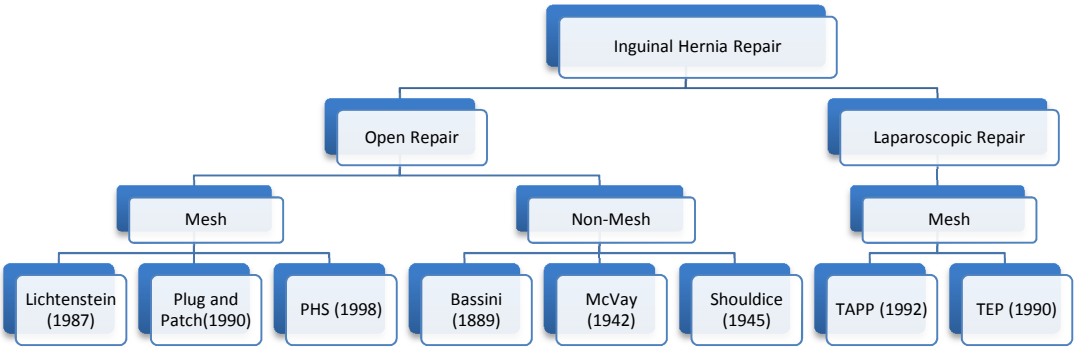
Figure 1.2: CT Image of Inguinal Hernia (circle). This is a cross-sectional CT scan without intravenous or oral contrast at the level of the mid pelvis. The pelvic bones and femur are in white; soft tissue appears in grey. The inguinal hernia is located on the patient's left side, off the midline, extending into the surrounding soft tissue(Heilman 2011).

There are limited options for non-operative management of an inguinal hernia. A hernia truss is a belt with a flexible and bendable metal spring sheet that is worn externally over the hernia. The truss provides external pressure over the defect and prevents the protrusion of the hernia sac and its contents. Cheek et al estimated that 40 000 trusses were issued annually in the UK and that the use may be higher in other countries with limited surgical access (Cheek, Williams et al. 1995).

Inguinal hernia repair is one of the earliest described and most common procedures in general surgery. While the techniques of repair have evolved

(Figure 1.3), the primary objectives of repair remain the same: closure of the pelvic floor defect, prevention of incarceration and reduction in patient pain/physical activity limitations.

FIGURE 1.3: Overview of Inguinal Hernia Repair



Acronyms: PHS- Prolene Hernia System; TAPP- Trans-Abdominal Pre-Peritoneal; TEP: Totally Extra-Peritoneal

To provide the greatest benefit for patients, while minimizing the risk of intra- and post-operative complications, it is essential that surgical repair is optimally timed. Previously, it was believed that all inguinal hernias should be repaired immediately due to the risk of incarceration or strangulation. Clinical trials have demonstrated that well-selected asymptomatic or minimally symptomatic patients can safely undergo a period of watchful waiting, with the risk of incarceration calculated to be only 0.18% annually (Fitzgibbons, Giobbie-Hurder et al. 2006, Sarosi, Wei et al. 2011). The risk of complication post-inguinal hernia repair has

been shown to be low; in a trial of males' ages 55 and older, there was an improvement in overall health without a significant increase in comorbidity (O'Dwyer, Norrie et al. 2006). Emergency surgery is indicated for patients with an incarcerated or strangulated hernia. Unlike inguinal hernias, elective repair of femoral hernias is indicated regardless of symptomology. This is due to the increased risk of emergency repair - one third of femoral hernias are repaired urgently compared to 6% of inguinal (Dahlstrand, Wollert et al. 2009, Lundstrom, Sandblom et al. 2012, Andresen, Bisgaard et al. 2014).

The two predominant modalities of repair are tissue repair (also termed a non-mesh repair) and mesh repair. While a mesh repair is the recommended type of repair in North America and Europe (Simons, Aufenacker et al. 2009, Sarosi, Wei et al. 2011), worldwide and in areas where mesh repair is recommended both repairs are performed. Choice of surgical repair technique will vary depending on an individual surgeon, however a tissue repair is commonly indicated for patients with (a) pre-existing chronic pain issues, or (b) those at a higher risk of a post-operative infection(Bay-Nielsen, Perkins et al. 2001, Fränneby, Sandblom et al. 2006, Inaba, Okinaga et al. 2012), for example, patients who present with an incarcerated or strangulated hernia. The goal of all tissue repairs, of which there are hundreds of techniques described, is closure of the defect and reinforcement of the pelvic floor. A relaxing incision may be used to decrease the tension on the repair.

The Bassini repair was first described in 1890 and involves opening pelvic floor transversely to reduce the pre-peritoneal contents and hernia sack back into

the abdominal cavity (Figure 1.4).

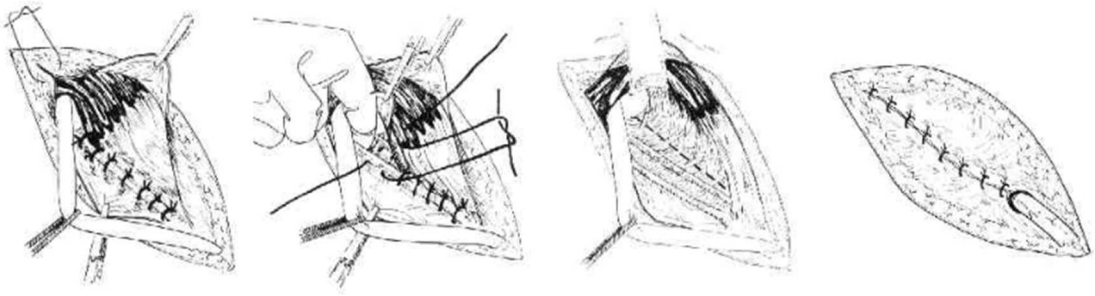


Figure 1.4: Bassini Inguinal Hernia Repair –(from left to right) re-approximation of the conjoint tendon to the inguinal ligament with non-absorbable suture and closure of the external oblique muscle superficially (Luzietti 2014).

The conjoint tendon is re-approximated to the inguinal ligament using an interrupted non-absorbable suture; this differs from the McVay repair, which sutures the conjoint tendon to Coopers ligament. Both repairs start medially at the anterior rectus fascia and ends laterally at the internal ring. The external oblique is closed over the repair. These repairs differ significantly from the Shouldice repair, which is a four-layered closure of the pelvic floor.

The mesh repair is considered the predominate repair by which all other techniques are judged in the Canada, the United States and Europe (Poulin and Marcaccio 1997, Grant, Go et al. 2000, Simons, Aufenacker et al. 2009). It involves the placement of a prosthetic mesh to bolster the pelvic floor and bridge the defect. An on-lay mesh approach places the mesh in the space above the external oblique/rectus muscles under the skin. The Lichtenstein technique

utilizes an on-lay mesh that is sutured in place after reduction of the hernia sac and pre-peritoneal fat (Figure 1.5).

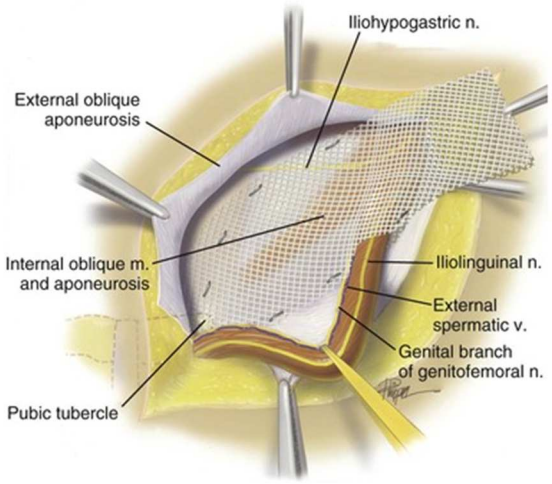


Figure 1.5: Lichtenstein Hernia Repair. Placement of onlay prosthetic mesh, fixed at pubic tubercle(Jacob and Ramshaw 2012)

The recurrence rate after primary inguinal hernia repair with the Lichtenstein technique has been reported between 2-6% (Lichtenstein 1987, Danielsson, Isacson et al. 1999, Amid 2003, Muldoon, Marchant et al. 2004, Bisgaard, Bay-Nielsen et al. 2007, Butters, Redecke et al. 2007). While the technique achieves a reasonable rate of recurrence, the mesh repair has also been associated with an increased level of postoperative and chronic pain compared to a tissue repair (Nienhuijs, Staal et al. 2007, Inaba, Okinaga et al. 2012). The increase in acute pain is thought to occur secondary to the amount of dissection required in order for the prosthetic mesh to lay flat or in the case of chronic pain, the use of non-absorbable sutures used to hold the mesh in place and ensure adequate coverage of the defect (Amid 2003).

To further reduce the rate of recurrence and decrease the dissection required, the Lichtenstein technique was modified to include a plug into the defect after reduction of the hernia sac (Nienhuijs, van Oort et al. 2005). Finally, the Prolene Hernia System connected a sub-lay mesh to the Lichtenstein on-lay mesh that was already being used – also known as the sandwich technique. A sub-lay mesh involves placement between the rectus muscles and the posterior sheath. Effectiveness of this repair requires appropriate dissection of the hernia sac and retro-muscular preperitoneal space in order for the mesh to lie flat and minimize the likelihood of a recurrence(Amid 2003, Bisgaard, Bay-Nielsen et al. 2007, Eher, Langeveld et al. 2012).

Until the early 1990s, inguinal hernia repair was performed solely through an anterior or open fashion. With the advent of laparoscopy and minimally invasive surgery, the totally extraperitoneal (TEP) and transabdominal with preperitoneal dissection (TAPP) techniques have become increasingly common. With TAPP, the peritoneal cavity is entered and the peritoneum is incised to gain access to the preperitoneal space. In the TEP procedure, a dissecting balloon is used to potentiate the preperitoneal space, providing access to the groin for mesh placement. In these laparoscopic repairs, the peritoneal sac and preperitoneal fat are dissected from the posterior abdominal wall and pelvic floor. The end result is the same for both approaches; a prosthetic mesh is placed in the preperitoneal space to cover the myopectineal orifice with fixation retromuscularly and extraperitoneally (Figure 1.6).

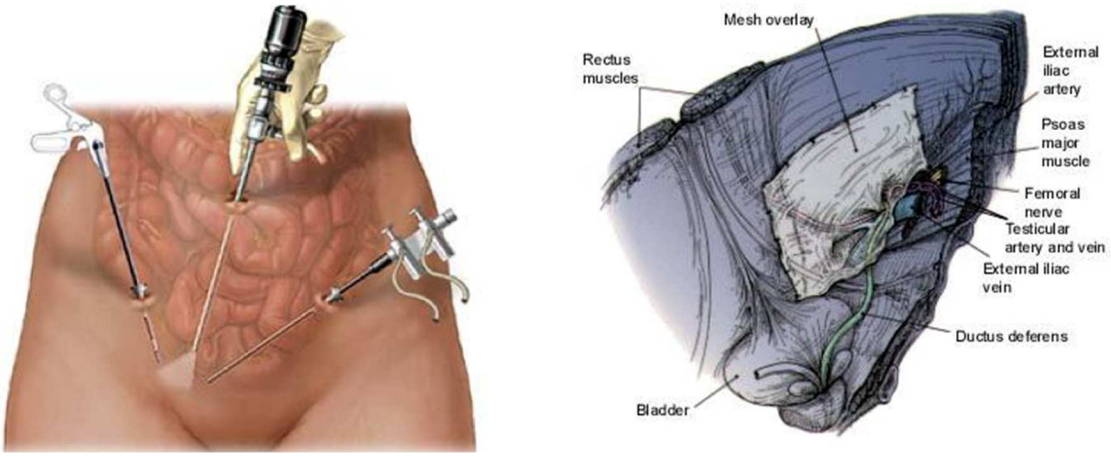


Figure 1.6: Laparoscopic Inguinal Hernia Repair. (Left) Port placement for TAPP repair, umbilical port for camera insertion, left and right groin port for dissecting instruments. (Right) End result of laparoscopic inguinal hernia repair, placement of sublay mesh over the myopectineal orifice after repair(Jacob and Ramshaw 2012).

1.3 Primary Outcome: Recurrence

Inguinal hernia recurrence is classified as the presence of a hernia after primary repair of the hernia site. The rate of recurrence ranges from 0.5 to 15% depending upon numerous patient factors including the hernia site, type of repair, surgeon specific characteristics and clinical circumstance, as well as the study type and length of follow-up.

Clinically, the presentation of a recurrent inguinal hernia (like a primary hernia) is a bulge in the groin typically at the pubic tubercle with extension into the scrotum. Symptomology of a recurrent inguinal hernia varies, though often there is a component of chronic groin pain that may be present with/without a

recurrent inguinal hernia(Nienhuijs, Staal et al. 2007). Given the variable presentation, diagnosing a recurrent inguinal hernia presents a challenging clinical scenario. An ultrasound of the groin can be performed when the patient is standing, supine and performing a Valsalva maneuver to evaluate for small defects in the fascia. However, the quality of the images is highly dependent on the experience of the ultrasonographer. A more consistent modality is a computed tomographic scan of the groin that can be used to identify a fascial defect or presence of bowel or fat in the inguinal canal (Figure 1.2). The most accurate and invasive means of diagnosing an inguinal hernia recurrence is with the use of laparoscopy (and if the abdominal wall defect is located, the hernia can be repaired simultaneously) (Shah, Mikami et al. 2011). In Sweden, Haapaniemi et al prospectively followed patients after inguinal hernia repair using a mailed questionnaire followed by a complete physical examination to evaluate the recurrence rate and chronic groin pain. Highlighting the challenge of making a definitive diagnosis of recurrence, they found that the rate of recurrence varied from 10-15% depending on the definition of recurrence and completeness of the physical exam (Haapaniemi and Nilsson 2002).

The clinical challenge of diagnosing a recurrent inguinal hernia creates difficulty at the provider level that can generate inaccurate data at the population research level. For that reason, disease specific registries offer a means to improve the quality of administrative data. The Swedish Hernia Register started in 1992 with the purpose of improving hernia care in Sweden within the founding 8 medical units; it has since expanded to over 90 clinical units

and includes data on virtually all groin hernias repaired in patients over the age of 15 in Sweden, and includes information on over 200,000 patients undergoing repairs (Nilsson, Kald et al. 1997). The register includes information on the repair technique, anesthesia, anatomical position, surgeon/patient demographic information, complications and surgical wait times. Patients who undergo an inguinal hernia repair are followed from repair until death using the healthcare registries. The use of reoperation for recurrence was validated as a measure of recurrence risk. Kald et al followed 1,565 hernia repairs for three years post-operatively and evaluated them for recurrence first by mailed questionnaire and then subsequent clinical examination. They found that total recurrence rate exceeded the reoperation rate for recurrence by 39% (Kald, Nilsson et al. 1998, Sevonius, Gunnarsson et al. 2011). Furthermore, they noted that all clinical recurrences that were underwent reoperation were confirmed recurrences at the time of intervention – indicating a high specificity. A similar registry exists in Denmark with more than 10,000 inguinal hernia and 400 femoral repairs recorded annually and over 130,000 repairs in the last 11 years (Rosenberg, Bisgaard et al. 2011). As with the Swedish Hernia Registry, the Danish Hernia Database uses reoperation as a measure of recurrence. It has been able to capture longer follow-up than most randomized trials, with >8 years of post-procedure data for some patients (Bisgaard, Bay-Nielsen et al. 2007, Bisgaard, Bay-Nielsen et al. 2008). Reoperation has been assessed as a surrogate measure of recurrence for ventral hernias as well. In 2012, Helgstrand et al compared reoperation versus clinical recurrence after umbilical and incisional

hernia. They found that reoperation rate underestimated the overall risk of recurrence by 4-5x the actual clinical recurrence. They do however note that the more serious recurrence – those that cause pain or physical impairment on follow-up, are more likely to present for reoperation (Helgstrand, Rosenberg et al. 2012). It has also been suggested that the more clinically important inguinal hernia recurrences present for reoperation (Hair, Paterson et al. 2001).

There are multiple associated factors that have been evaluated for their impact on inguinal hernia recurrence. These include the site of the hernia, use of prosthetic mesh, surgical approach, technical proficiency – demonstrated by a learning curve, physician and hospital volume, specialty centers, choice of anesthetic and patient characteristics. These factors as they relate to hernia recurrence is discussed in the remainder of section 1.3.

1.3a Hernia site

Administrative data from the Danish Hernia Database has shown a 2.7% vs 5.2% rate of reoperation for an indirect compared to a direct inguinal hernia(Burcharth, Andresen et al. 2014). Specifically, a direct hernia at primary operation had a Hazard ratio for recurrence of 1.90 as compared to an indirect inguinal hernia (Burcharth 2014). The Swedish Hernia Register has demonstrated an increased risk of reoperation for recurrence if the primary repair

is a femoral hernia as compared to an inguinal hernia (direct or indirect), OR: 1.30, 95% CI: 1.14-1.48 (Lundstrom, Sandblom et al. 2012).

1.3b Use of Prosthetic Mesh

There is a large body of evidence that demonstrates a reduced rate of recurrence when comparing repairs that utilize a prosthetic mesh to those that do not. The non-mesh repair was the only surgical approach for inguinal hernia repair for nearly a century until the inclusion of a prosthetic mesh by Lichtenstein in 1987(Lichtenstein 1987). The Bassini and Cooper techniques had a recurrence rate of ~ 8-18%(Tran, Putz et al. 1992, Hay, Boudet et al. 1995, Dirksen, Beets et al. 1998). The variability in recurrence rates have been thought to be secondary to surgeon experience(Tran, Putz et al. 1992), hernia type (Burcharth, Andresen et al. 2014), patient population(Burcharth 2014), type of study (Wara, Bay-Nielsen et al. 2005), length of follow-up (Magnusson, Nordin et al. 2010) and the use of absorbable versus non-absorbable sutures(Nilsson, Kald et al. 1997). The 4-layer Shouldice technique performed within the Shouldice hospital has been consistently reported with recurrence rates as low as 1-2% (Malik, Bell et al. 2015). The Shouldice hospital is an 89 bed hospital in Ontario that performs 7,000 abdominal wall hernia repairs annually (Hay, Boudet et al. 1995, 2015, Malik, Bell et al. 2015). This is a unique institution and questions about the generalizability of these results have been raised. To evaluate the effectiveness of the Shouldice repair in the general surgical practice, a study in

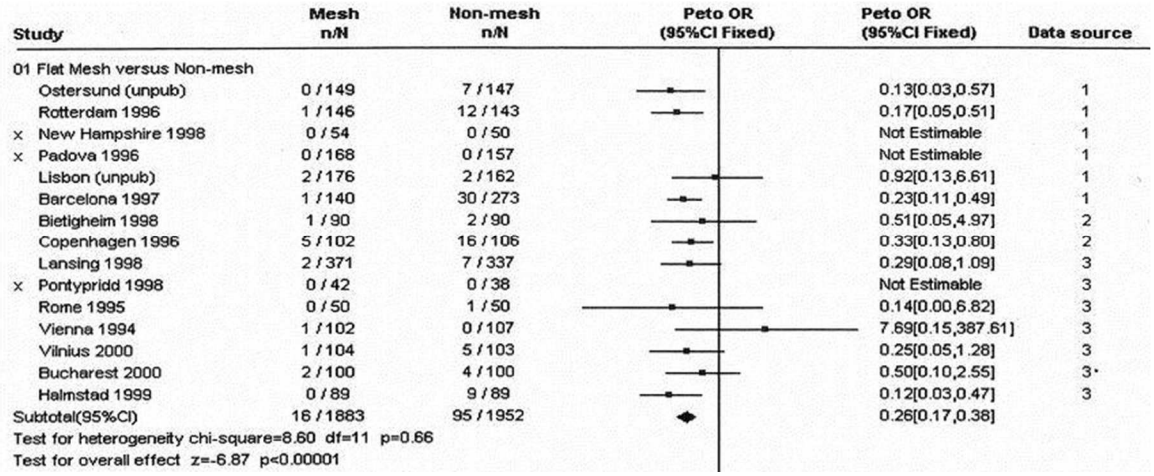
Sweden randomized 300 patients to undergo inguinal hernia repair via the Shouldice procedure or Lichtenstein hernia repair. After a follow-up of 36-77 months, they found 7 recurrences (95% CI 1.3 – 8.1) in the Shouldice group compared to 1 (95% CI 0.0 – 2.0) in the Lichtenstein repair group (Nordin, Bartelmess et al. 2002). In the mid 1990s, when non-mesh repairs were the mainstay of hernia repair, in a prospectively randomized trial with a 5-year median follow-up (Hay, Boudet et al. 1995) the Shouldice technique produced a recurrence rate of 6% compared to the Bassini (8.6%) and Cooper's ligament (11.2%) non-mesh techniques. More recently in 2012, a Cochrane Review identified 16 trials that included 2,566 hernias repaired with the Shouldice technique to 1,121 mesh and 1,608 non-mesh repairs. They found that the recurrence rate with the Shouldice techniques was higher than with mesh (OR 3.80, 95% CI 1.99 – 7.26) but lower than non-mesh techniques (OR 0.62, 95% CI 0.45 – 0.85)(Amato, Moja et al. 2012). While the Shouldice technique may produce the lowest recurrence rates amongst non-mesh repairs, in the general population of surgeons and patients it fails to produce a recurrence rate as low as the prosthetic mesh repairs.

There are many systematic reviews evaluating inguinal hernia repair, however there are three most recent and frequently cited. The review by Scott et al in 2002 compared outcomes between mesh and non-mesh repairs. Also in 2002, Grant et al compared the outcomes – including recurrence between open with mesh and laparoscopic primary repair. Finally, Memon et al evaluated the impact of technique on returning to work and daily activities after primary repair.

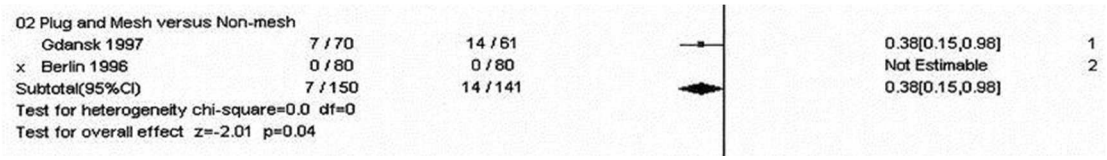
The first systematic review and meta-analysis of 20 individual trials evaluated the outcomes of patients who underwent open inguinal hernia repair with (17 used flat mesh, 2 plug and mesh and 1 preperitoneal mesh) and without mesh placement (Figure 1.7). Recurrence was 50-75% lower after primary mesh inguinal hernia repair compared to non-mesh repairs, OR: 0.37, 95% CI 0.26-0.51, p<0.001(Scott, McCormack et al. 2002) irrespective of repair technique. A more detailed systematic review and meta-analysis of 58 randomized control trials compared elective, mesh and non-mesh repairs, as well as laparoscopic and open with mesh techniques. Collectively, this included patient data from 11,174 inguinal hernia repairs performed. When comparing mesh to non-mesh, they corroborated the reduction in recurrence between the two repair modalities (OR: 0.43, 95% CI 0.34-0.55)(2002).

Figure 1.7: Mesh versus Non Mesh Hernia Repair

(a)



(b)



(c)

Mesh versus non-mesh: hernia recurrence. (a) flat mesh (open) versus non-mesh – OR: 0.26, 95%CI: 0.17-0.38 in favour of mesh. (b) Plug and Mesh versus non-mesh – OR:0.38, 95% CI: 0.15-0.98 in favour of mesh. (c) Preperitoneal mesh versus non-mesh – OR: 3.14, 95% CI: 1.19-6.29 in favour of non-mesh.

X denotes no recurrences in either mesh or non-mesh group. The solid squares denote individual odds ratio and the horizontal lines represent 95% confidence intervals. The diamonds denote pooled odds ratio. MRC, Medical Research Council; SCUR, Scandinavian Clinics United Research. Data source codes: 1 = individual patient data; 2 = additional aggregate data; 3 = published data only (2002).

Since these systematic reviews were published, Vrijland et al published a prospective, randomized trial that followed patients for 3 years and compared the difference in hernia recurrence between mesh and non-mesh primary inguinal hernia repair. They demonstrated a difference in recurrence rate of 1% and 7% between the two repairs respectively (Vrijland, van den Tol et al. 2002). These results have remained consistent in long-term follow-up; van Veen et al found a 10-year cumulative recurrence rate of 1% and 17% (P=0.005) after randomization into mesh and non-mesh groups respectively (van Veen, Wijsmuller et al. 2007).

1.3c Surgical Approach

Open surgical repair of an inguinal hernia has been practiced for over a century; however using a laparoscopic approach is a new technique with an unclear recurrence rate that offers some potential advantages to the traditional open technique. The challenges associated with the early laparoscopic studies are that many surgeons were still learning the procedure and on their learning curve for the first 80-100 procedures (Edwards and Bailey 2000). Early comparisons of laparoscopy to open inguinal hernia repair are not applicable to current practice because of the inclusion of a prosthetic mesh in the laparoscopic repair and the lack of mesh in the open non-mesh repair. In a randomized, multicenter trial of 994 patients, 6% of patients in the open without mesh group had a recurrence compared to 3% in the laparoscopic group (Liem, vanderGraaf et al. 1997). However Neumayer et al performed a similar randomized control trial of 2,164 patients and found that recurrence was more common after laparoscopic repair (10.0%) compared to open primary repair (4.0%) (Neumayer, Giobbie-Hurder et al. 2004). The reported recurrence rates after either laparoscopic or open procedure have varied in the literature. In 2010, Langeveld et al randomized 336 patients to a Lichtenstein or total extra peritoneal repair arm. After a mean follow-up of 49 months they found similar recurrence rates between the two procedures (3.8% and 3.0%, P=0.64)(Langeveld, van't Riet et al. 2010). A similar multicenter randomized trial with 5-year follow-up demonstrated an equivalent recurrence rate between a total extraperitoneal patch laparoscopic repair and Lichtenstein open repair (2.4% to 1.2%, P = 0.1090)(Eklund, Montgomery et al. 2009).

The EU Hernia Trialists Collaboration conducted a systematic review to compare laparoscopic and open methods of hernia repair (Grant, Go et al. 2000). They identified 34 trials that included 6,804 patients who underwent open and laparoscopically primary inguinal hernia repair and were followed from 6 week to 36 months. When comparing recurrence rate, they did not find a difference between the two techniques (OR: 1.26, 95% CI: 0.76-2.08), forest plot presented in figure 1.8. Two studies, one TAPP versus open with mesh (favouring TAPP) and one TEP versus open with mesh (favouring open) reported a difference in recurrence rate (Grant and Collaboration 2002). Both of these studies were limited by short follow-up of only 1 year and were conducted in a time period (1993-1996 and 1994-1997 respectively) when laparoscopy was not a common procedure performed by most general surgeons(Group 1999, Johansson, Hallerback et al. 1999, Zendejas, Ramirez et al. 2012).

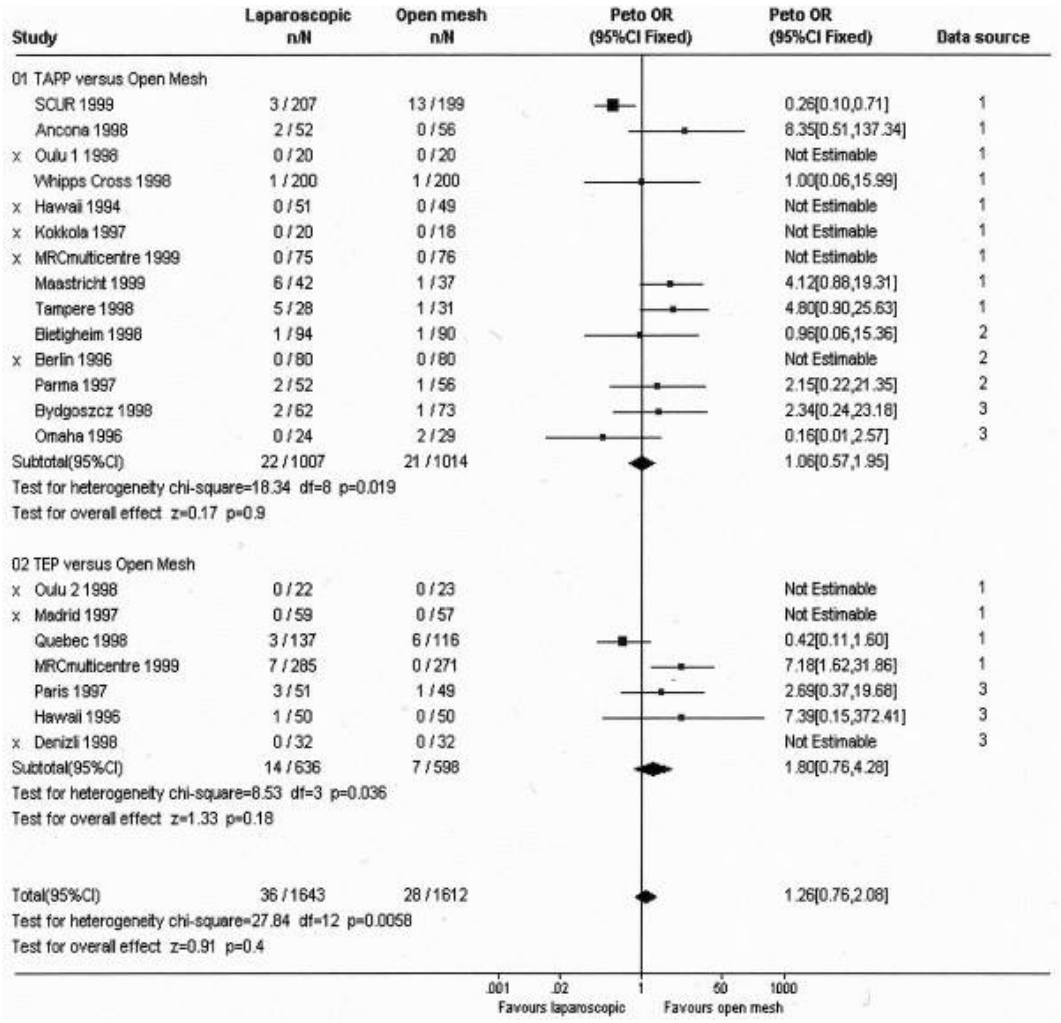


Figure 1.8: Laparoscopic versus Open Mesh – hernia recurrence

Laparoscopic versus open mesh: hernia recurrence. X denotes no recurrences in either laparoscopic or open mesh group. The solid squares denote individual odds ratio and the horizontal lines represent 95% confidence intervals. The diamonds denote pooled odds ratio. CI, confidence interval; df, degrees of freedom; OR, Odds Ratio; TAPP, transabdominal preperitoneal; TEP, totally extraperitoneal; MRC, Medical Research Council; SCUR, Scandinavian Clinics United Research. Data source codes: 1 = individual patient data; 2 = additional aggregate data; 3 = published data only(Grant and Collaboration 2002).

Though the systematic review by Grant et al found no difference between TEP or TAPP laparoscopic repairs and open with mesh repairs, additional non randomized trials not included in the review have compared TAPP and TEP

directly. Felix et al described the early experience with TEP and TAPP repairs in 1995 at the Annual Meeting of the Society of American Gastrointestinal Endoscopic Surgeons. They compared 733 TAPP and 382 TEP repairs, finding 2 recurrences and 9 intraperitoneal complications in the TAPP group compared to 1 recurrence and 0 intraperitoneal complications in the TEP group(Felix, Michas et al. 1995). A Cochrane Systematic Review in 2005 found insufficient evidence to compare the two techniques because of limited availability of prospective trials in the literature (McCormack, Wake et al. 2005).

There are a number of mechanisms proposed for hernia recurrence when mesh is used; recurrence may occur secondary to mesh folding, inadequate mesh size, porosity of material or failure of the mesh to remain flat after placement (Kukleta 2006). Recurrence after laparoscopic repair is thought to be secondary to inadequate lateral dissection, which ultimately results in poor mesh placement and the subsequent recurrence (Felix, Scott et al. 1998). For direct hernias, Felix et al reported that laparoscopic primary inguinal hernia repair was more likely to result in a recurrence compared to a Lichtenstein open with mesh primary repair (Felix, Michas et al. 1995).

1.3d Learning Curve

In 2005, Neumayer et al evaluated compared the risk of recurrence if surgical trainees at various years of training were involved in the case. There was an increased risk of recurrence for open inguinal hernia repairs found if the

participating resident was in the first two years of training (Neumayer, Gawande et al. 2005), however recurrence rates are unaffected after the third year of training.

The relationship between level of training and proficiency required for laparoscopy appears to be different from open hernia repairs. The surgical learning curve for inguinal hernia repair has been well studied; many of the early studies in laparoscopy were aimed at demonstrating equivalency to the open technique. With the introduction of laparoscopy in the early 1990s, early studies of laparoscopic inguinal hernia repair noted the increased operative time from 70 minutes versus 55 minutes p=0.003 and an increased risk of recurrence when inexperienced surgeons were compared to experienced laparoscopic surgeons (Liem, Van Steensel et al. 1996, Edwards and Bailey 2000). Further studies have identified that recurrence rates from laparoscopic repairs are highest in the first 2 years of learning the procedure (Tamme, Scheidbach et al. 2003). In fact, some studies have suggested that the recurrences associated with the learning curve may represent as many as 61% of recurrences over a surgeon's career (Feliu-Pala, Martin-Gomez et al. 2001). One strategy proposed by the European Hernia Society to overcome the learning curve was to establish a "school for hernia repair" that would provide mentorship for newly practicing surgeons(Simons, Aufenacker et al. 2009).

When evaluating the effect of the laparoscopic learning curve on recurrence, Neumayer et al classified a surgeon as "inexperienced" if they had performed <250 procedures during their career. Amongst these inexperienced

surgeons, surgeons >45 years old had an increased odds ratio of recurrence of 1.72 (P=0.045) compared to younger surgeons <45 years of age (Neumayer, Gawande et al. 2005).

1.3e Physician Volume

Physician volume has been used as a surrogate measure of technical proficiency. Using the Swedish Hernia Register, the relationship between rate of reoperation for recurrence and physician volume of hernia repairs in the previous year for 96,601 hernia repairs was explored. Nordin et al found a relative risk of reoperation for recurrence of 1.20, 95% CI 1.01-1.42 between low volume providers, those that performed 1-5 procedures annually and providers who performed >75 procedures annually. For surgeons performing more than 5 procedures, no relationship was found between volume and recurrence (Nordin and van der Linden 2008). In this study, they included all repair techniques and commented that the majority of low volume providers used Licthenstein or other open hernia repair methods more often than laparoscopy (3.7% vs 11.5% when comparing providers <5 procedure to those that performed > 5 in a year) (Nordin and van der Linden 2008). More recently, Aquina et al analyzed a cohort of patients undergoing open inguinal hernia repair in New York state and found that low-volume surgeons, i.e. those that performed <25 procedures annually had a higher rate of reoperation for recurrence compared to surgeons performing >25 procedures (HR: 1.23, 95% CI: 1.11-1.36)(Aquina, Probst et al. 2015). Finally, Al-

Jamal et al compared 3 groups of staff surgeons who performed 2,410 laparoscopic TEP inguinal hernia repairs at the Mayo Clinic (Rochester, Minnesota) between 1995- 2011. The high volume group performed >30 annual procedures (n=1), the middle volume group performed 15-30 (n=3) and the low volume group performed <15 (n=17). The high volume individual had a lower rate of intra- (1% compared to 2.6% and 5.6%, respectively) and post-operative complications (13% compared to 27% and 36%, respectively). The high volume surgeon also had a lower rate of recurrence (1% compared to 4% and 4.3% respectively) all $p<0.05$ (AlJamal, Zendejas et al. 2016). The study authors suggest that at least 15 annual TEP repairs are associated with improved quality metrics, however given the disproportionate number of surgeons in each group (there was only 1 high volume surgeon), the differences found may reflect differences in surgical skill and other confounders, rather than a pure volume-outcome relationship (Urbach 2015).

1.3f Hospital Volume

The volume of procedures performed annually in a single centre has been shown to affect the outcome of patients undergoing a variety of surgical procedures(Sosa, Bowman et al. 1998, Katz, Losina et al. 2001, Birkmeyer, Siewers et al. 2002, McAteer, LaRiviere et al. 2013, Aquina, Probst et al. 2015). Andersen et al evaluated 5,186 different surgeons who performed 14,532 laparoscopic primary inguinal hernia repairs between January 1, 1998 and

December 30, 2013. They demonstrated that patients who underwent primary inguinal hernia repair at centers that perform less than 50 annual laparoscopic inguinal hernia repair have an increased risk of reoperation, 3.5% when annual volume $\geq$ 50 procedures versus 4.5% when annual volume < 50 procedures (Andresen, Friis-Andersen et al. 2015). A key criticism of this study was the inability to control for surgeon volume, as the authors were unable to uniquely identify which surgeon performed a given repair. Since inguinal hernia repair is predominately an outpatient procedure, the intra-operative and surgeon specific factors likely have a substantial impact on hernia repair; adjusting for surgeon volume would be important to truly identify a relationship between institution volume and recurrence. Furthermore, there was an element of patient selection bias associated with the study – the study also found that repairs performed at a public institution had a higher risk of recurrence than those undergoing repair at a private institution (4.5% vs 2.8%) (Andresen, Friis-Andersen et al. 2015). For this study, the selection bias undermines the internal validity of the results as they were unable to adjust for patient and surgeon characteristics that may have impacted on the rate of recurrence.

In addition to volume, hospitals can also be classified based on the type of institution. In the Swedish hernia registry, the risk of re-operation was lower in medium sized and university hospitals compared to smaller institutions (those that only provided ambulatory day procedures) 0.88, $p < 0.01$ and 0.87, $p < 0.05$ respectively(Nordin and van der Linden 2008). In a systematic review comparing the influence of surgeon experience versus hospital volume on pediatric patient

outcomes after multiple procedures, including inguinal hernia repair, hospital level factors were associated with outcomes for high complexity procedures, while surgeon factors were associated with outcomes for common procedures such as primary inguinal hernia repair(McAteer, LaRiviere et al. 2013).

1.3g Specialty Centers

The Shouldice Hospital in Ontario performs over 7000 abdominal wall hernia repairs annually, representing a special scenario where surgeon and institutional volume are extremely high. Patients whose hernia are repaired at the Shouldice hospital, have a lower risk of subsequent surgery for recurrent hernia (1.15%, 95% CI 1.05%-1.25%) compared to patients who undergo inguinal hernia repair at a high volume general hospital (4.79%, 95% CI 4.54%-5.04%) (Malik, Bell et al. 2015).

1.3h Patient Factors

There are a number of patient factors that are clearly associated with an increased risk of recurrence. Analysis of the Swedish Hernia Register has shown that emergency procedures (OR: 1.53, 95%CI: 1.43-1.63) and recurrent inguinal hernia repair (OR: 1.39, 95% CI: 1.27-1.52) are risk factors for reoperation for recurrent inguinal hernia repair (Lundstrom, Sandblom et al. 2012).

Obesity, defined as a body mass index (BMI) of >30kg/m^2 is a known risk factor for recurrence (Matthews, Anthony et al. 2007, Zendejas, Hernandez-Irizarry et al. 2014). Evaluation of the Swedish Hernia Registry further demonstrated that being overweight (BMI of 25-30 kg/m^2) increases the risk for reoperation for recurrence (hazard ratio 1.20, 95% CI 1.00-1.40) (Rosemar, Angeras et al. 2010).

Smoking has been demonstrated in multiple studies to increase the risk of hernia recurrence after repair, the hypothesis being that there is connective tissue destruction secondary to free radical formation that causes inappropriate wound healing (Sorensen, Friis et al. 2002, Junge, Rosch et al. 2006). Chronic cough secondary to smoking causes an increase in intra-abdominal pressure and is a risk factor for inguinal hernia occurrence (Sorensen, Friis et al. 2002, Burcharth 2014).

Other patient factors that have been evaluated for their relationship with inguinal hernia recurrence include age, sex and size of the defect. With regards to age, a meta-analysis of 15 studies that examined age as a risk factor in 422,824 inguinal hernia repairs did not demonstrate a difference in risk of recurrence (relative risk 0.99 (95% CI: 0.84 – 1.17)(Burcharth, Pommergaard et al. 2015). The same meta-analysis evaluated 12 studies that evaluated the relationship between sex and hernia recurrence in 447,968 patients and found female sex to be a risk factor (relative risk 1.38 (95% CI: 1.28-1.48) (Burcharth, Pommergaard et al. 2015). The two studies that evaluate the relationship between size of the hernia defect and recurrence were both observational

studies and when pooled, did not demonstrate a difference in recurrence if the defect was <3cm or >3cm (relative risk 1.09, 95% CI: 0.92-1.30).

Single studies have evaluated the relationship between miscellaneous social factors and inguinal hernia recurrence. Unemployment did not lead to higher recurrence rates after repair compared to employed patients (Sorensen, Friis et al. 2002). In another study, the absence of a caregiver at home has been found to correlate with recurrence (Matthews, Anthony et al. 2007). Ingestion of 1-7 alcoholic drinks per week was found to be protective against the risk of recurrence with an odds ratio of 0.30, 95% CI: 0.10-0.93 compared to alcohol abstinence (Sorensen, Friis et al. 2002). Finally, the use of medication for chronic conditions (including steroids and ACE inhibitors) had no effect on the risk of recurrence (Junge, Rosch et al. 2006).

1.3i Repair of Recurrences

After the primary inguinal hernia repair, any subsequent repair for recurrence carries with it an increased risk of re-recurrence. The Swedish Hernia Registry demonstrated that a 4.6% risk of reoperation after a recurrent inguinal hernia repair compared to a 1.7% risk of reoperation after primary inguinal hernia repair (Haapaniemi, Gunnarsson et al. 2001). To study the impact of technique on re-recurrence in Denmark analysis of the Danish Hernia Database has demonstrated that using an open or laparoscopic technique for repair of a

recurrent inguinal hernia has no impact on subsequent reoperations for re-recurrence (Bisgaard, Bay-Nielsen et al. 2008).

1.3j Anesthesia Factors

From an anesthetic perspective, multiple studies have compared the effectiveness of local, spinal and general anesthesia for inguinal hernia repair. General anesthesia allows for more extensive surgery to be performed if the case is difficult but requires a certain level of patient fitness and may lead to post-operative coughing and straining. Spinal anesthesia is considered an acceptable alternative for unfit patients but has been shown to increase the risk of post-operative urinary retention and can cause profound hypotension (Petros, Rimm et al. 1991). Epidural anesthesia has similar risks/benefits as spinal anesthesia except for having a lower likelihood of causing urinary retention (Finley Jr, Miller et al. 1991). Finally, local anesthesia is advantageous because it allows for rapid patient mobilization relative to the other modalities and does not require extensive preoperative anesthesia evaluation. However, it is limited by the maximum dose of the local agent and cannot be used for a laparoscopic repair. The Swedish Hernia Registry reviewed 59,823 inguinal hernia repair and found that local anesthesia significantly increased the relative risk of reoperation for recurrence when compared to the other types of anesthesia(Nordin, Haapaniemi et al. 2004). This likely reflects an element of confounding; patients with multiple comorbidities are at a higher risk of recurrence (Malik, Bell et al. 2015) and would

are not good candidates for general anesthesia, and would therefore be more likely to undergo repair using local anesthesia (Rogers and Guzman 2011).

1.4 Secondary Outcomes

1.4a Pain

Chronic pain post inguinal hernia repair is not a rare occurrence but has a variable frequency reported in the literature between 0%-37%(Callesen and Kehlet 1997, Liem, vanderGraaf et al. 1997). Chronic pain may lead to functional impairment that limits physical activity in 8%-16.6% of patients (Bay-Nielsen, Perkins et al. 2001). Post-operative pain is believed to be secondary to a combination of factors, including wide dissection, mesh fixation, damage to the pubic periosteum, and entrapment of the ilioinguinal nerve (Callesen and Kehlet 1997, Nienhuijs, Staal et al. 2007, Bjurstrom, Nicol et al. 2014). Studies using validated questionnaires to asses chronic pain after inguinal hernia repair (Franneby, Gunnarsson et al. 2008), suggest that chronic post-hernia repair pain may last 3 years post-procedure. In a meta-analysis of prospective studies that evaluated post-operative pain as an outcome, there was an overall incidence of 11% (Nienhuijs, Staal et al. 2007) – 64% of the 11% experiencing pain described it as an aching pain, 9% with numbness and 9% with testicular pain. Overall, patients who underwent laparoscopic repairs had less pain than those undergoing an open repair with mesh 5 years after the index procedure, odds ratio 0.61, (95% CI: 0.49 – 0.77) (Nienhuijs, Staal et al. 2007). In a comparison of

8 trials that compared laparoscopic to open with mesh primary inguinal hernia repair, a total of 133/1,571 laparoscopic patients reported pain symptoms compared to 207/1,653 open with mesh patients after a median follow up of 21 months, resulting in an odds ratio of 0.61 (95% CI: 0.49-0.77) (Nienhuijs, Staal et al. 2007). They did note that chronic pain tended to decrease as the length of follow-up increased.

1.4b Complications

The primary intraoperative complications that can occur are during inguinal hernia repair include hemorrhage, injury to the vas deferens, injury to the vascular supply to the testis and the genitofemoral nerve, ilioinguinal nerve and sympathetic and visceral afferent fibers(Gaines 1978). The potential for serious intra-operative complications is higher with laparoscopic inguinal hernia repair compared to open(Gaines 1978, Gong, Zhang et al. 2011, Lundstrom, Sandblom et al. 2012). While the risk for vascular injury can occur with either open or laparoscopic approaches, the risk of damage to the epigastric vessel was higher in laparoscopic inguinal hernia repair (OR: 2.1 CI: 1.1-3.9)(Memon, Cooper et al. 2003, Science 2013). Additionally, the likelihood of bowel injury is elevated in laparoscopic repair either from trocar injury or dissection of non-reducible hernias(Felix, Harbertson et al. 1999).

Post-operatively, the issue of a surgical site infection can have a varied presentation and management. A superficial wound infection with mild erythema

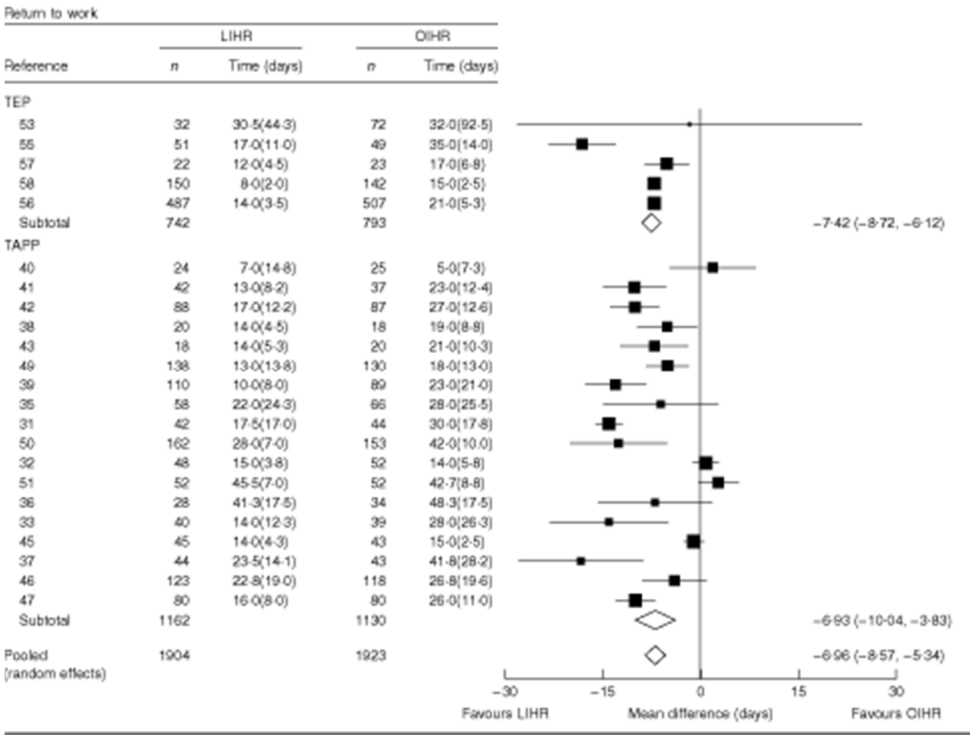
can be managed non-operatively with a course of antibiotics and a low likelihood of further infection. For deeper infected wounds, the presentation may be similar except for an obvious area of fluctuance on palpation of the surgical site – these require drainage and antibiotics. The most concerning scenario is that of an infected mesh with or without a draining sinus. A meta-analysis of RCTs found a lower incidence of wound infections with laparoscopic inguinal hernia repair compared to a Lichtenstein repair – odds ratio 0.39, 95% CI: 0.26-0.61 (Schmedt, Sauerland et al. 2005). From major hernia centers, wound infections are reported as being a rare complication (Amid 2003). However the opposite has been found in population studies, for example in Finland, 17% of patients developed a post-operative wound infection, all after an open repair and none after laparoscopic primary inguinal hernia repair (Paajanen, Scheinin et al. 2010). Taylor et al conducted a phone survey of 2,665 patients 30 days after they underwent an inguinal hernia repair and found 5.3% developed a surgical site infection and an additional 2.1% believed the wound was infected (Taylor, Duffy et al. 2004). The reduced rate of wound infection after laparoscopic repair is thought to be a result of trocar placement being located away from the actual myopectineal orifice where the mesh is placed (Gong, Zhang et al. 2011). To reduce the rate of post-operative wound infections in certain high risk individuals (operation for recurrent inguinal hernia, advanced age, immunosuppressive conditions), the use of antibiotic prophylaxis prior to skin incisions is recommended and decreases the rate of infection by upwards of 55% (Li, Lai et

al. 2012). However, in conventional patients undergoing a hernia repair, antibiotic prophylaxis is not recommended (Simons, Aufenacker et al. 2009).

1.4c Return to Daily Activities

Resumption of daily activities is a common measure of assessing the recovery period post inguinal hernia repair. A randomized, multicenter trial in the Netherlands found that laparoscopic inguinal hernia repair resulted in faster resumption of daily activity (6 vs 10 days), time to work (10 vs 21 days) and athletic activities (24 vs 36 days) [P<0.001 for all comparisons], when compared to open repairs (Liem, vanderGraaf et al. 1997). In a systematic review and meta-analysis, Memon et al (Figure 1.9) analyzed the outcomes of 5 trials that compared TEP to open inguinal hernia repair and 18 trials that compared TAPP to open inguinal hernia repair. They demonstrated a faster return to normal activities and work in the laparoscopic group, compared to the open group (4.7 days (95% CI 3.51-5.96); 7.0 days (95% CI 5.34-8.58); P<0.001 respectively) (Memon, Cooper et al. 2003). From this meta-analysis, laparoscopic repair does offer a speedier recovery than open inguinal hernia repair , however the difference appears small.

Figure 1.9: Pooled Analysis of Laparoscopic versus Open Inguinal Hernia for Return to Work



Values in left panel are mean(s.d.). Squares indicate point estimates of treatment effect (weighted mean difference), with the size of square representing the weight attributed to each study. Ninety-five per cent confidence intervals are indicated by horizontal bars. The summary weighted mean difference from the pooled studies with 95 per cent confidence intervals is represented by a diamond. Values to the left of the vertical line at zero favour laparoscopic inguinal hernia repair. Point estimates are significant at the P < *0.050 level if their confidence intervals exclude the vertical line at zero(Memon, Cooper et al. 2003).*

1.4d Economic Evaluation

The cost effectiveness of laparoscopic and open inguinal hernia repair has been compared in a number of trials and reviews. In a systematic review, McCormack

et al identified 14 studies that identified both the cost and outcomes associated with inguinal hernia repair. Procedure specific data included recurrences, time to return to usual activities and cost. Using a Markov model incorporating study data, they found laparoscopic inguinal hernia repair to be more expensive compared to open repair (McCormack, Wake et al. 2005) at the level of the provider. However, at a patient level, the increased initial costs of laparoscopic inguinal hernia repair were offset by quicker return to work, and a perceived increase in productivity by patients (McCormack, Wake et al. 2005). A second systematic review of similar studies, 3 from the UK, 3 from the Netherlands, 3 from other parts of Europe, 2 from France and the United States and 1 from Asia found that laparoscopic inguinal hernia repair increased the direct cost of the procedure from 41.1% - 84.2% compared with open with mesh(Vale, Grant et al. 2004). In the United Kingdom, the cost of a laparoscopic repair was $600 (Canadian dollars) more than open repair due to increased operating time and equipment costs(Group 1999).

1.4e Study Design

Prospective randomized trials are considered the benchmark for comparison of treatment modalities. A RCT as compared to other study designs offers the opportunity to control known and unknown factors, this controls for unmeasured confounders, which should be randomly assigned. The challenges of conducting a RCT may result in small studies underpowered for important outcomes. Thus

far, RCTs have been unable to demonstrate a difference in recurrence between laparoscopic and open with mesh inguinal hernia repair and it would be logistically and financially difficult to sufficiently power future studies. The generalizability of the patients within the trial to the larger population of patients who undergo repair is essential. Recruitment of patients who do not wish to leave their outcome up to chance can be difficult (McCulloch, Taylor et al. 2002) and may result in ideal patients that are not representative of the greater population who undergo procedure (Solomon and McLeod 1995). Just as the patients may be ideal, the surgeons conducting the trials may have a high degree of technical proficiency that is not found outside of specialized institutions. For that reason, RCTs may not be generalizable to the average practitioner in the health system.

In contrast, observational studies using administrative data enable the creation of a large cohort of patients, without the same logistical burden found in coordinating a clinical trial (Solomon and McLeod 1995), and can be performed quickly. The use of administrative data also enables inclusion of the entire population of patients undergoing a specific procedure and thus is generalizable to a wide range of patients, providers and institutions. .

There are unique limitations with the early randomized control trials before 2000 that compared laparoscopy to open procedures. First, there is a learning curve associated with new procedures and the wider adoption of them within the surgical population. For hernia, the learning curve is well established (Liem, Van Steensel et al. 1996) and many studies using laparoscopy pre-2000 would not

have reflected true outcomes attainable with this technique (Feliu-Pala, Martin-Gomez et al. 2001)- this is a limitation that would be encountered by other study methodologies as well. Secondly, there is variability in procedural technique and overall proficiency even after a surgeon has surpassed the learning curve (McCulloch, Taylor et al. 2002) and unless a range of technical proficiencies are sampled, it will not reflect the actual population of surgeons who perform the procedure. Third, trials take a long period of time to recruit patients and then follow prospectively for a recurrence (Magnusson, Nordin et al. 2010). Fourth, the results of trials are not necessarily generalizable if 'ideal' patients (young, low BMI, non-smokers) are recruited who do not represent the larger population who typically undergo repair (Rutkow and Robbins 1993, Sorensen, Friis et al. 2002, Burcharth 2014).

1.5 Limitations in the Literature:

Inguinal hernia repair is a common procedure that is performed routinely worldwide and has been extensively studied, yet there are limitations with the current literature. Though hernia repair has its historical origins in the late 1800s, at present the three common techniques for surgical repair include an open approach with or without prosthetic mesh placement or a laparoscopic approach. Prosthetic mesh repairs placed by either an open or laparoscopic approach are clearly superior to non-mesh repairs in the general population of patients and

providers. However, neither open with mesh nor laparoscopic repair have definitively been demonstrated to reduce the rate of recurrence in the population.

1.5a Skill and Expertise

Inguinal hernia repair is a challenging procedure with a well-described learning curve (Liem, Van Steensel et al. 1996, Edwards and Bailey 2000, Feliu-Pala, Martin-Gomez et al. 2001, Kukleta 2006, Cavazzola and Rosen 2013, Schouten, Elshof et al. 2013). Early studies compared surgeons with unequal levels of technical proficiency. In some cases, surgeons performing open mesh repairs were high volume experienced providers, while those performing laparoscopic procedures had not passed the learning curve for the procedure. (Liem, vanderGraaf et al. 1997, Dirksen, Beets et al. 1998, Heikkinen, Haukipuro et al. 1998, Grant, Go et al. 2000). These early studies are therefore not applicable to current practice where laparoscopic inguinal hernia repair is common (Liem, Van Steensel et al. 1996, Felix, Scott et al. 1998, Edwards and Bailey 2000, Kukleta 2006, Schouten, Elshof et al. 2013).

1.5b: Frequency of Procedure

Older studies have limited relevance today as they do not reflect the current practice patterns. Pre-2000, laparoscopic inguinal hernia repair was not widely practiced and only found in specialized centres. The frequency of each

inguinal hernia repair technique continues to fluctuate. The number of laparoscopic inguinal hernia repairs continues to increase over time, while the number of open without mesh repairs has decreased. In a study of Olmsted County, Minnesota from 1989 to 2008 Zendejas et al. found that non-mesh inguinal hernia repair represented 94% of repairs in 1989 but declined to 4% in 2008 (Zendejas, Ramirez et al. 2012). In the same study, laparoscopic repairs, which were 6% of repairs in 1992 increased to 41% of all inguinal hernia repairs, performed in 2008 (Zendejas, Ramirez et al. 2012). There is some variability in the adoption of laparoscopic hernia repair throughout the United States; in Florida from 2002-2003, laparoscopy represented 19.5% of all inguinal hernia repairs (Smink, Paquette et al. 2009). New population studies are required to accurately represent the changes in procedure frequency. (Primatesta and Goldacre 1996, DesCoteaux and Sutherland 1999, Rutkow 2003, Zendejas, Ramirez et al. 2012, Burcharth 2014, Trevisonno, Kaneva et al. 2015).

1.5b Generalizability

In general, randomized trials that are conducted by experts in expert centers cannot necessarily be generalized to all practitioners. Although randomized control trials have shown that laparoscopic and open with mesh inguinal hernia repair results in similar rates of recurrence (Grant, Go et al. 2000), we need population-based studies to evaluate the generalizability of the randomized control trial findings of equivalence. The use of administrative data

allows for a “real-world” analysis amongst practitioners within the Ontario health system. Where many population-based studies include few non-mesh and laparoscopic repairs (DesCoteaux and Sutherland 1999, Atkinson, Nicol et al. 2004, Nordin and van der Linden 2008, Burcharth 2014, Trevisonno, Kaneva et al. 2015), we find all techniques utilized in Ontario (Malik, Bell et al. 2015). A summary of population-based studies that evaluated for recurrence after procedure or other outcomes is provided in Table 1.1. While they have investigated different factors that impact on inguinal hernia recurrence, there is a need for new studies that account for the current practice patterns within Ontario and represent the current patient exposure to inguinal hernia repair.

We therefore planned our study using the linkage of Ontario healthcare administrative databases to assess if recurrence after laparoscopic and open with mesh inguinal hernia repair are equivalent in the general population of patients, surgeons, and institutions.

Table 1.1: Summary of Population-Based Studies for Inguinal Hernia Repair

Authors	Year	Country	Study Population	Exposure(s)	Findings
Trevisonno et al	2015	Canada (Quebec)	49,657 inguinal hernia repairs	Open repair (n=45,855) Laparoscopic (n=3,802)	-11 surgeons perform 61% of laparoscopic inguinal hernia repairs -56% of surgeons do not perform laparoscopic inguinal hernia repair
Bay-Nielsen et al	2001	Denmark	26,304 inguinal hernia repairs	Open with mesh (n=14,832) Open without mesh (n=4,373) Laparoscopic (n=547) Recurrent Repairs (n=3,943)	-Overall reoperation rate (all procedures) after primary repair of 1.6% (95% CI 1.5-1.8%); reoperation rate after recurrent hernia of 4.0% (95% CI 3.4-4.6%) -Similar reoperation rate <30 months for open with mesh and laparoscopic repair (2.2% and 2.6%); both lower than open without mesh (4.4%, P<0.0001) -Reoperation rate at 30 months, laparoscopic: 3.4%, open with mesh 6.1% (p=0.01); lower than open without mesh 10.6% (p<0.0001).
Mikkelsen et al	2002	Denmark	34,849 patients	Femoral hernia repair (n=1,297)	-Femoral hernias account for 7.9% of all reoperations for recurrent groin hernia (when the primary was believed to be inguinal) -Time to reoperation 10 months for inguinal hernia
Wara et al	2005	Denmark	43,143 patients	Lichtenstein (n=39,537) Laparoscopic (n=3606)	-Equal reoperation rate for unilateral primary inguinal hernia repair irrespective of technique -Higher rate of reoperation for bilateral inguinal hernia if laparoscopic compared to Lichtenstein (7.6%, 95% CI 4.1-12.6) vs (2.6%, 95% CI 1.4-4.4)
Bisgaard et al	2007	Denmark	47,975 primary inguinal hernia repairs	Open with Mesh (n=43,043) Open without	-Reoperation lower after Lichtenstein repair compared to sutured repair (hazard ratio 0.45, 95% CI 0.39-0.51) in first 30 months, 30-60 months (hazard ratio 0.38, 95% CI 0.29-0.49) and 60+ months (hazard ratio 0.25, 95% CI 0.16-0.40)

				mesh (n=4,932)	
Burcharth	2013	Denmark	85,314 males	Lichtenstein (n= 75,404) Laparoscopic (n=9,910)	-Overall reoperation rate of 3.8% -Indirect hernia reoperation: 2.7%, direct hernia reoperation rate: 5.2%. -Laparoscopic repair a risk factor for reoperation (hazard ratio: 1.07, 95% CI 1.01-1.13)
Burcharth	2013	Denmark	5,893 females	Indirect hernia (n=3,595) Direct hernia (n=2,298)	-Direct hernia a risk factor for reoperation (hazard ratio 3.1, 95% CI 2.4-3.9) -Laparoscopic inguinal hernia repair lower risk of recurrence to open when a direct hernia is present (hazard ratio: 0.57, 95% CI 0.43-0.75)
Paajenen et al	2010	Finland	55,000 inguinal hernia repairs	Open with Mesh (n=45298) Open without mesh (n=4422) Laparoscopic (n=4059) Femoral (n=891)	-Early recurrence 9% of open with mesh repair compared to 5% in laparoscopic repair (not significant) -Increased rate of wound infection with open with mesh compared to laparoscopic (17% vs 0%) -Increased rate of post-operative ileus with laparoscopy compared to open repair (26% vs 4%)
Kouhia et al	2015	Finland	93,000 inguinal and femoral hernia repairs	Open with mesh (n=74, 961) Open without mesh (n=4,706) Laparoscopic (n=87)	-Higher rate of recurrence between open without mesh and open mesh repair (15% vs 3.5%, $p<0.05$) -Greater rate of deep infection, visceral complications and deep bleeding between open with mesh and laparoscopic
Van der Linden et al	2011	Sweden	123,917 primary inguinal hernia repairs	Open with mesh (n=80,754) Open without	-Relative risk of reoperation for recurrence 26% higher if the operation >66 minutes versus <36 minutes (1.26, 95% CI: 1.11-1.43)

				mesh (n=2,505) Laparoscopic (n=1,044)	
Sevonius et al	2009	Sweden	16,648 recurrent hernia repairs	-	-Used Lichtenstein as a reference category; laparoscopic repair reduced risk of reoperation for first 2 recurrent repairs (0.79, 95% CI 0.62-0.99 and 0.48, 95% CI 0.32-0.74)
Koch et al	2005	Sweden	90,648 inguinal hernia repairs	Open with mesh (n=57,126) Open without mesh (n=24,593) Laparoscopic (n=8,929)	-Higher proportion of emergency procedures in women than men (16.9% vs 5%) - Women more commonly found to have a femoral hernia (41.5% vs 4.6%)
Nordin et al	2008	Sweden	86,409 patients 96,601 inguinal hernia repairs	-	-Low volume surgeons (<5 annual procedures) associated with higher relative risk 1.2, 95% CI 1.01-1.42
Lundstrom et al	2012	Sweden	150,514 hernia repairs	Open with mesh (n=123,556) Open without mesh (n=14,323) Laparoscopic (n=12,635)	-Risk factors for 30 day post-operative complications include laparoscopic repair (OR: 1.31), emergency procedure (OR: 1.53), recurrent hernia (OR: 1.39) and age >65 (OR:1.26)
Gass et al	2011	Switzerland	6,505 patients	Unilateral TEP (n=3,457) Bilateral TEP (n=3,048)	-Unilateral TEP vs bilateral TEP: shorter (67 min vs 86 min), lower rate of intraoperative complications (1.9% vs 3.1)/ post-operative complications (2.3% vs 3.2%)

Gass et al	2012	Switzerland	4,552 laparoscopic repairs	TAPP (n=1,095) TEP (n=3,457)	-Increased intraoperative complications with TEP vs TAPP (1.9% vs 0.9%, p=0.029) and post-operative complications (2.3% vs 0.8%, p=0.003)
Smink et al	2009	USA	58,712 outpatient hernias	Open (n=46,776) Laparoscopic (n=11,351)	-Laparoscopic patients tend to be younger than those undergoing open repair (ages 52 vs 57) and have less comorbidities
Hernandez-Irizarry et al	2012	USA	4,026 inguinal hernia repairs	-	-Overall incidence of emergent inguinal hernia repair is 3.8% -Non mesh repairs more likely to be performed in an emergent inguinal hernia repair (OR: 1.8, p=0.008)
Zendejas et al	2012	USA	4,433 inguinal hernia repairs	-	-Increased prevalence of laparoscopic repairs (6% in 1992 to 41%in 2008)
Keller et al	2015	Taiwan	5,806 patients	Open with mesh (n=5,550) Open without mesh (n=52)	-Overall recurrence rate of 9.73% -No laparoscopic repairs; median number of annual repairs per surgeon: 1.41

2. Research Aims and Hypotheses

2.1 Specific Aim: To evaluate the difference in reoperation for recurrent inguinal hernia after primary inguinal hernia repair.

2.1a Hypothesis: Open with mesh inguinal hernia repair will have a lower rate of reoperation compared to laparoscopic and open without mesh primary inguinal hernia repair

The existing literature for inguinal hernia repair very strongly advocates for the use of a prosthetic mesh when performing a primary inguinal hernia repair (Scott, McCormack et al. 2002). Despite the presence of the Shouldice hospital in Ontario and surgeons who are familiar with the technique, mesh repairs will still have a lower rate of re-operation when compared to non-mesh primary inguinal hernia repair.

Surgical intervention is accepted as the preferential treatment for a symptomatic inguinal hernia. While previous trials and meta-analyses have identified a clear reduction in recurrence after a prosthetic mesh repair compared to a non-mesh repair, they have failed to demonstrate a difference between a laparoscopic or open with mesh repair. The goal of this research project is to assess the rate of reoperation for recurrent inguinal hernia. Within Ontario, all three common approaches (open with/without mesh and laparoscopic) are utilized for inguinal hernia repair.

Between laparoscopic and open inguinal hernia repairs that both utilize prosthetic mesh, it is unclear which will have the lowest recurrence rate. When comparing mesh to non-mesh inguinal hernia repair, it is expected that mesh repairs will be superior to non-mesh inguinal hernia repair and will have a lower recurrence rate. While open inguinal hernia is less technically demanding than laparoscopy both utilize a prosthetic mesh and have similar recurrence rates reported in the literature.

3. Methodology

3.1 Study Design

This study is a retrospective cohort study that utilizes population-based administrative health data within the province of Ontario. The patient cohort, exposure and outcome were identified retrospectively. This allowed for an efficient strategy to analyze the outcome of interest while following patients for an extended period of time. Healthcare administrative data is supposed to reflect the population the population base, since Ontario is a single-payer health system and virtually all citizens are covered by the same provincial health insurance plan with little movement, it provides an accurate description of the healthcare resource utilization within the province (Branch 2012). The data sources are consolidated and can be gathered without the logistical and financial burden associated with a prospective randomized trial. While administrative data may be limited by the available data elements, it is immediately available and avoids the effort and limited generalizability of an institutional chart abstraction study. Given the large number of observations that are included, the use of population-based health care data allows for evaluation of common as well as rare outcomes. In Ontario there is minimal loss-to-follow-up because there is little migration out of the healthcare system (Roos, Black et al. 1996). Furthermore, through a retrospective analysis, it provides continued long-term follow-up of patients without the extended observation period found in prospective studies(Roos, Black et al. 1996). Conveniently, multiple healthcare databases can be linked using a patient's OHIP

number to evaluate the relationships between patient, provider and institutional factors (Roos, Roos et al. 1987, Virnig and McBean 2001).

3.2 Data Sources

The study utilized linked population-based health care administrative databases at the Institute for Clinical Evaluative Sciences (ICES). ICES is a non-profit research institute that encompasses a community of research, data and clinical experts to ensure accessibility to Ontario's health related data (Juurlink D 2006). The Ontario Health Insurance Plan (OHIP) database contains all physician claims (including procedural code and service date) and was used to identify patients undergoing primary inguinal hernia repair. OHIP datum is updated in ICES bi-monthly and contains patient information from July 1991 to as recently as 3 months ago (as of February 2016). Ontario residents are eligible for OHIP if they are (1) a Canadian citizen, permanent resident who is (2) present in Ontario for 153 days in any 23-month period and (3) physically present in Ontario for at least 153 days of the first 183 days after establishing residency in Ontario and (4) their primary place of residence is in Ontario. The datum found in OHIP is generated through claims/billing information supplied for services delivered by registered providers. While the data garnered from procedural codes is informative for the specific disease, purpose and provider, there is limited contextual information of what was done or the indications for procedure. The validity of the procedural codes is discussed in the next section, however the

same accuracy has not been demonstrated for diagnostic codes, with respect to timing of the diagnosis or validity of the code itself, thus it cannot be used to monitor for hernia recurrence.

To determine type of repair we used Canadian Classification of Health Interventions (CCI) codes (Table 3.1) recorded in the Canadian Institute for Health Information (CIHI) Discharge Abstracts Database (DAD) and the CIHI-Same Day Surgery (SDS) database and National Ambulatory Care Reporting System (NACRS) database. CIHI datum is collected directly from the participating health facilities, regional health authority or the ministry/department of health. The Discharge Abstract Database was first developed in 1963 and captures administrative, clinical and demographic patient information on hospital discharges. The datum is typically released annually in August and includes information from the previous fiscal year, from as far back as April 1988 to March 2015 (as of August 2015). Data prior from 1963- 1988 is not linkable and therefore not part of the database. From 2004 to present, all DAD records reflect ICD-10-CA and CCI codes, prior to that ICD-9, CCP and ICD-CM were used. By comparison, NACRS (also a CIHI holding) provides information with respect to ED visits, day surgery and outpatient clinics. Similar to DAD, it is updated each fiscal year annually and received at ICES in August, however it only includes data from July 2000 onward.

Surgeon data were extracted from the ICES Physician database (IPDB), which is a repository with information for all practicing physicians in Ontario. The

database combines information from the Ontario Physician Human Resource Data Centre, the OHIP Corporate Provider Database and the OHIP database of physician billing. The database includes demographic (ie. age and sex) and specialization information for the physicians who were/are licensed to provide care in Ontario from 1992- September 14, 2015. It also contains the year a physician graduated from a medical school, where each physician was trained and their practice location (Schultz, Simunovic et al. 2008). It is possible to assess a surgeon's case volume in a given time period by finding the frequency that a procedural codes is used for billing claims within a given time period.

The ICES facilities database provides information about Ontario health care institutions that are funded by the Ministry of Health and Long Term Care and was used to identify repairs performed at the Shouldice hospital. We were able to identify other institutions by their institution number at ICES. By analyzing the frequency that the OHIP S323 for primary inguinal hernia repair was billed at the institution, we calculated the annual hospital primary inguinal hernia repair volume. The database is updated annually, with the most recent update being October 10, 2015.

The Statistics Canada Census assigns income quintiles to each neighborhood community based on self-reported income or income reported in tax files. From this, an individual's income quintile is assigned based on the address listed in their Canadian Census Profile. The Canadian census data is updated every 5 years and contains population and demographic information from

1991, 1996, 2001 and 2006. The Registered Persons Database contains information, such as address, date of birth and sex of individuals registered with OHIP. It is updated bimonthly and contains data from April 1990 to March 2015.

3.3 Validation

The CIHI-DAD is considered the standard to evaluate health-care utilization within hospitals within Ontario and the accuracy of the database has been demonstrated in previous studies (Hawker, Coyte et al. 1997, Lee, Donovan et al. 2005). The validity of the CIHI-DAD 1SY80 code for inguinal hernia repair have been previously studied by ICES in 2006. Trained chart abstractors performed detailed chart abstraction to evaluate the accuracy of CIHI-DAD codes to the original charts between April 1, 2002 and March 31, 2004. A total of 215 inguinal hernia procedures, laparoscopic and open were re-abstracted from the original charts and evaluated for accuracy. The re-abstractor agreed that 93.3% of the procedures that were coded as “open inguinal hernia repairs” were accurately designated. In addition to the procedural category, the CCI code for a hernia repair can also include a location code to designate the laterality of the procedure. When the laterality designation was used, there was an 85% agreement between abstracted data and original chart, however for greater than 30% of procedures no location information was provided (Juurlink D 2006). For

this reason, the CCI code can be used to specify the type of repair, but not to indicate laterality of procedure.

3.4 Study Population

We identified patients between 18 and 90 years of age undergoing a primary, non-recurrent inguinal hernia repair from April 1, 2003 through December 31, 2012. The cohort of patients who underwent surgical procedure during our study period was identified using the S323 OHIP billing code for inguinal hernia repair. This code indicates a non-recurrent, non-emergent, elective primary inguinal hernia repair. A licensed physician in Ontario must perform the procedure for a patient with health coverage within the province. We selected 18 years old as our minimum age to ensure we were accurately capturing adult inguinal hernia repairs with the administrative data and that there was limited likelihood that the patient would be undergoing a pediatric repair of an inguinal hernia (Ma, Yang et al. 2003). While inguinal hernia repair in the elderly is well documented (Amato, Compagna et al. 2012), 90 years old was our maximum age to ensure there was adequate follow-up for reoperation for recurrence (Rogers and Guzman 2011). Our time period captures all three categories of repairs in Ontario, and practice patterns elsewhere in Canada (DesCoteaux and Sutherland 1999, Trevisonno, Kaneva et al. 2015).

Using procedure and billing codes (Table 3.1) we excluded patients at a higher risk of hernia recurrence and complications as identified by having a repair

performed in an emergent setting,(Kingsnorth and LeBlanc 2003, Burcharth 2014) in the presence of bowel strangulation (Hair, Paterson et al. 2001, Kulah, Kulacoglu et al. 2001), whose procedure was performed by an extremely low volume surgeon (one who performed 5 or fewer inguinal hernia repair of any type in the preceding year (Nordin and van der Linden 2008)), or whose hernia was classified as massive (Lowham, Filipi et al. 1997). We excluded patients who had evidence of a previous inguinal hernia repair from January 1991 (the earliest date we could identify inguinal hernia repair) to the start of the accrual period or if the type of inguinal hernia repair could not be determined based on administrative data. Additionally, we excluded patients who underwent inguinal hernia repair at the Shouldice hospital (2015). Results of repairs performed at this institution are superior but not generalizable to the patient and surgeon populations of Ontario(Malik, Bell et al. 2015).

Table 3.1: Codes used for cohort identification and group stratification

Identification Codes	Description
OHIP Codes	
S323	Primary, non-recurrent inguinal hernia repair
S345	Massive sliding inguinal hernia
S329	Strangulated hernia without resection
S330	Strangulated hernia with resection
E725	Recurrent inguinal hernia
E726	Repeat recurrent inguinal
CIHI Codes	

1SY80DA 1SY80DAXXN	Laparoscopic Inguinal Hernia Repair
1SY80LAXXN	Open with Mesh Inguinal Hernia Repair
1SY80LA 1SY80W	Open without Mesh Inguinal Hernia Repair

3.5 Exposures

After identification of the initial cohort and exclusion of those patients deemed to be at a higher risk of recurrence, the remaining group of patients was stratified by type of primary inguinal hernia repair. Using CCI codes (Table 3.1), each patient was placed into one of three categories: open repair with mesh (1SY80LAXXN), open repair without mesh (1SY80LA or 1SY80W), or laparoscopic repair (1SY80DA or 1SY80DAXXN).

3.6 Covariates

We adjusted for covariates in our analysis including age-sex groups (males and females in the categories of 18 – 34, 35 – 44, 45 – 64, 65 – 84 and 85+ years). We grouped age and sex to control for confounding and to adjust for extreme data distributions (Faresjö and Faresjö 2010). In addition, urban/rural residence and quintile of median neighborhood household income. To adjust for comorbidities we used the resource utilization bands (RUB) of the Adjusted

Clinical Group System (2008, Austin and Walraven 2011), stratifying patients into RUBs of 0, 1-5, 6-9 and 10+ - this will be discussed in further detail in the next section. Finally we adjusted for volume, at the hospital level and physician level. Hospital volume was calculated as the number of primary inguinal hernia repairs performed at a single institution in the previous 365 days prior to the index procedure and treated as a continuous variable. Physician volume, defined as the number of primary inguinal hernia repairs performed in the 365 days prior to the index procedure was separated into technique specific volume and non-technique specific volume.

3.6a Multi-Morbidity Scoring

Adjustment for comorbidities using multi-morbidity scoring is common in health services research as it provides a standardized means to capture multiple patient comorbidities and assess healthcare resource utilization. There are two modalities of multi-morbidity scoring – simple counts of a disease per patient and an index of morbidity that is weighted according to a range of conditions or diseases(Huntley, Johnson et al. 2012). Failure to account of severity of illness reduces the predictive value of multi-morbidity scores (Concato, Horwitz et al. 1992). The Johns Hopkins Aggregated Diagnosis Group (ADGs) uses categorical information to assess patient comorbidity from International Classification of Disease (ICD) diagnostic codes. For ACG, the data is an accumulation of

diagnoses over a period of time, including all encounters during a hospitalization and in an out-patient ambulatory setting. It was originally designed to predict future morbidity and health resource allocation (Starfield, Weiner et al. 1991). Other multi-morbidity scoring systems include the Chronic Disease Score (CDS), Charlson Index, Cumulative Index Illness Rating Scale (CIRS) and Duke Severity of Illness (DUSOI). The Chronic Disease Score uses medication from pharmacy dispensing data as a proxy for chronic disease; within Ontario there is limited information available about drug benefit claims; the score would not be available for many of the patients in our cohort and thus the Chronic Disease Score would not accurately capture the comorbidity of the patient cohort. Cumulative Illness Rating Scale scores the severity for 14 body systems on a scale from 1-5, where 1 would imply no impairment to the organ system and 5 denotes an impairment that is life threatening requiring urgent treatment (such as a myocardial infraction). It can be compiled from pre-existing medical records or directly from the patient (Hudon, Fortin et al. 2005). As it does not rely on specific diagnoses, it would be poorly applied to the administrative database. Duke Severity of Illness accounts for each diagnosis based on its symptoms, complications, prognosis without treatment and treatment potential (Parkerson, Broadhead et al. 1993). Similar to CIRS, this information is not routinely available within the ICES database holdings thus making it poorly applicable in this study. The Charlson Index was originally developed in hospital and specialist settings for use in longitudinal studies to predict mortality based on the comorbid disease (Charlson, Pompei et al. 1987). It

has been adapted for use with ICD-9 and has predictive validity with various outcomes like mortality, disability, readmission and length of stay(Poses, McClish et al. 1996). While the Charlson Index has been extensive studied in relation to mortality (Sharabiani, Aylin et al. 2012), its utility requires hospitalization and many of our cohort were not hospitalized in the years prior to their inguinal hernia repair. The Charlson Index was originally developed with 19 categories in 1987, in 1992 it was modified to 17 categories (Deyo, Cherkin et al. 1992), with the list of specific ICD codes modified in 1993 and 2005 to reflect changes from ICD-9 to 10 (Quan, Sundararajan et al. 2005). Finally the weights that were originally assigned in 1987 were modified in 2003 to better predict mortality amongst elderly Medicare populations (Schneeweiss, Wang et al. 2003). Comparatively, ACG has been demonstrated to be effective when accounting for resource utilization from administrative data (Huntley, Johnson et al. 2012). A comparison of the Charlson Index to other comorbidity scores amongst diabetic patients in the Veterans Affairs Hospital system found that the Charlson Index was a better predictor of mortality than ACG, however the ACG better predicted healthcare expenditures and comorbidity risk than the Charlson Index (Maciejewski, Liu et al. 2009). For our study, where inguinal hernia repair has a low perioperative mortality (Primatesta and Goldacre 1996, Hernandez-Rosa, Lo et al. 2011), we are more concerned with accurately adjusting for the common burden of comorbidity amongst the majority of patients who undergo primary repair.

3.6b Surgeon Volume

Because of the relationship between volume of hernia repair and recurrence (Nordin and van der Linden 2008), we controlled for the effect of volume. For each patient in our cohort we measured the total volume of all hernia repairs at their hospital in the year before the index procedure (continuous). For surgeons, we controlled for technique-specific volume (open with mesh, open without mesh, and laparoscopic). Using volume cut-points established in previous studies, we categorized technique-specific surgeon volume into quartiles (0-5, 6-25, 26-50, 51+ repairs) (Nordin and van der Linden 2008, Aquina, Probst et al. 2015) based on the total number of hernia repairs of the specific type in the year prior to the index procedure. Because surgeons who perform high volumes of inguinal hernia repair irrespective of technique should have more experience with the disease and hernia anatomy, we created a second continuous variable measuring surgeon volume of other repair methods in the year prior to the date of the index surgery to control for total volumes of inguinal hernia repair. In addition we performed an analysis restricting our patient population to those undergoing primary inguinal hernia repair by a surgeon performing more than 25 technique-specific hernia repairs in the previous year, as reduced rates of recurrence have been found for such surgeons relative those who perform <25 hernia repairs annually in previous studies (Aquina, Probst et al. 2015).

Table 3.2: Covariate Description and Source

Covariate	Definition	Source
Age	Patient age at time of index surgery (years)	RPDB
Sex	Patient sex	RPDB
ADG Comorbidity	Patient comorbidity	CIHI-DAD, NACRS and OHIP
Surgeon Volume (procedure specific)	Number of procedures performed 1 year prior of index surgery using specific technique	OHIP, IPDB and CIHI
Surgeon Volume (Non-procedure specific)	Number of procedure performed 1 year prior to index surgery using other 2 surgical techniques	OHIP, IPDB and CIHI
Hospital Volume	Number of inguinal hernia repair performed at an institution 1 year prior to the index surgery	NACRS and CIHI-DAD
Socioeconomic Status	Patient income based on neighborhood income from the 2001 (1999 – 2004) and 2006 (2005 –	RPDB and Census Data

	2010) census	
Rural Status	A census subdivision that had an acute care hospital in 2001/02 and <5 subspecialists in the geographical community.	RPDB and Census Data

3.7 Primary Outcome

Patients were followed to August 31, 2014. Our primary outcome was surgically treated recurrent inguinal hernia repair. During follow-up, individuals in our cohort undergoing an inguinal hernia repair with an accompanying billing code for recurrent disease were classified as having a recurrent inguinal hernia repair when this occurred more than 2 days after primary inguinal hernia repair to differentiate from a contralateral repair (it has been common in some practices to perform bilateral inguinal hernia repair in Ontario sequentially over a 2-day period (Malik, Bell et al. 2015)).

3.8 Statistical Analyses

We calculated the rate of patients undergoing a recurrent inguinal hernia repair after the three types of primary inguinal hernia repair procedures. Our unit analysis was the individual patient undergoing primary repair, stratified by

exposure (open with mesh, open without mesh, laparoscopic) and followed for our primary outcome – reoperation for recurrent inguinal hernia. We did not continue to follow patients after reoperation for a subsequent reoperation for re-recurrence. The rate of reoperation for recurrence was calculated by dividing the total number of reoperations for recurrence over the period of time that the patient was followed. Hospital volume and physician volume were summarized as a mean (SD) for the entire cohort. Reoperation for recurrence was stratified by type of primary inguinal hernia repair and compared using a t-test or ANOVA (continuous variables) and a χ^2 test (categorical variables). Cumulative incidence curves (a measure of disease frequency during a period of time) for recurrent inguinal hernia repair were generated by procedure type using the Kaplan-Meier method and compared using the log rank test. To evaluate the relationship between procedure type and recurrent inguinal hernia repair, we performed a time-to-event analysis using Cox proportional-hazards model with an endpoint of recurrent inguinal hernia repair. Patients were censored at death or at the end of the study period. We created models adjusting for age-sex groups, urban vs rural residence, income quintile, comorbidity (RUBs), hospital procedure volumes and surgeon procedure volumes. Models accounted for clustering of patients within surgeons using generalized estimating equations(Zeger, Liang et al. 1988), as patients of a given surgeon are to likely to interrelate. By clustering, we avoid yielding smaller standard errors than expected if we only assumed independent observations (Panageas, Schrag et al. 2003). Number needed to harm (i.e. the

number of hernia repairs that have to be performed to prevent one recurrence) was calculated using the hazard ratio from the Cox proportional hazards model(Altman and Andersen 1999). We analyzed the data using SAS software, version 9.1 (SAS Institute, Cary, North Carolina). All statistical tests were 2-sided and we considered a *P* value < 0.05 to be statistically significant.

3.8a Analytic Methods

Survival analysis is the analysis of the time to an event, death, device failure, or in the case of this study – hernia recurrence. There are a few unique features of survival data; first, there is a staggered entry and exit, whereby patients are able to enter and exit the study at different time points, i.e. variable follow up time after inguinal hernia repair. The patients can be censored, which in the context of inguinal hernia repair means that the study period can end without all patients experiencing a recurrence. This is an example of right censoring, and is the most common form encountered in survival analysis. Another form of right censorship is a patient that is lost to follow-up, however was “event free” when last observed – in this case, the hernia had not recurred. The two assumptions that must be met in survival analysis is that a patient’s probability of experiencing the outcome event is unchanged through the entirety of the study and that censored patients have the same prognosis as those remaining in the study (Altman and Bland 1998).

3.8b Univariate Analysis

For our univariate analysis, we used the Kaplan-Meier method. The Kaplan-Meier method is most popular form of survival analysis, using the log-rank test to evaluate for differences between groups. We planned to use a Kaplan-Meier model that would allow us to account for non-parametric data (Rich, Neely et al. 2010). An alternative approach to survival analysis would be using the actuarial or life-table method. This method will divide the overall time period into equivalent intervals and then calculate the proportion that has an event (in our case, reoperation for recurrent inguinal hernia) within each interval (Lee and Wang 2003). When calculating the Kaplan-Meier estimate, our population at risk only included those individuals at risk of hernia recurrence during that time period – participants who had already recurred or died were excluded. It is most applicable when the outcome and censored observations are already organized in time intervals, which is not the case within our study. Thus we elected to use the Kaplan-Meier method and compared the survival curves using the log-rank test.

3.8b Log-Rank Test

The log-rank test compares the survival of two (or more) groups of individuals. When comparing two survival curves, it is possible to arbitrarily select any specific point in time and compare the proportions, however this fails to capture the overall

survival of both groups and only serves for point comparisons. The log-rank test accounts for the follow-up period, without requiring the shape of the curve or distribution of survival times(Bland and Altman 2004). The null hypothesis with the log rank test is that there is no difference between the populations and the probability of the event. A χ^2 test of the null hypothesis is used, where the sum of the [(observed – expected)^2/expected] for each group is calculated, along with the degrees of freedom (number of groups -1) and a compared to a table of χ^2 distributions for significance. The log-rank test has numerous assumptions that are true in inguinal hernia repair. It assumes that the survival probability is uniform regardless of when patients are recruited – this is true for patients undergoing inguinal hernia repair (Trevisonno, Kaneva et al. 2015), even if we expect to see a difference in reoperation for recurrent inguinal hernia between the three techniques. The log-rank test assumes that censoring does not relate to prognosis (Lee, Donovan et al. 2005). The log-rank test has its limitations, specifically as a univariate test it cannot account for the effect of covariates or estimate the size of a difference groups. In order for use to evaluate this we utilized the Cox proportional hazards model.

3.c Multivariate Analysis

While the Kaplan-Meier curves can be used to plot the data, they do not account for covariates that may contribute to the outcome and so the multivariate Cox proportional hazards model is commonly utilized (discussed in further detail

below). We plotted the cumulative incidence of hernia recurrence which is a measure of rate per person-time (Fletcher, Fletcher et al. 2012). It is calculated by the number of new cases during a period divided by the number of subjects at risk in the population at the beginning of the study(Fletcher, Fletcher et al. 2012).

Two alternative analytic methods to survival analysis would be logistic or linear regression. Linear regression would be used to model time as a function of predictor covariates (Buckley and James 1979, Aalen 1989, Aalen 1993); however this is not ideal as it does not account for censoring and would require the outcome variable to be continuous. Again, one of the key advantages of survival analysis is the ability to include both censored and uncensored observation.

A third approach could be logistic regression, which is used for multivariable analysis of dichotomous outcomes – in this case, presence or absence of an inguinal hernia recurrence when censoring is not required. Logistic regression can be used when there is a non-linear relationship between the outcome and predictor variable. It is able to assess the effects of multiple predictor variables that are continuous and/or categorical. In the case of hernia repair, this would occur at pre-specified time points after procedure such as 1, 3 and 5 years post-operatively. They key disadvantage of logistic regression is an inability to analyze the time to an event and account for censoring which is present in survival analysis. While it can provide information about the likelihood, logistic regression is unable to make an inference about the event rate. It also

does not account for person-time at risk, which is found in survival analysis using the Cox proportional hazards model.

3.8c Cox Proportional Hazards Model

Introduced by Sir David Cox, the hazard is considered the instantaneous probability that the event of interest occurs at a specific time (David 1972). It allows for both the comparison of two or more groups and to adjust for covariates. The effect of the covariates multiplies the hazard function by a function of the explanatory covariates (Fisher and Lin 1999). The model allows for examination of the predictive value of an outcome in terms of its covariates. Cox models can include time-dependent covariates; the proportional hazards assumption means that the hazards are proportional between covariates across the time spectrum. It is possible to graphically check if the proportional hazard assumption is violated, however this is a subjective interpretation and relies on a distinct crossing of the survival plots to be visualized. A second option is to assess if the proportional hazards assumptions holds is by plotting the Schoenfeld residuals against time to assess the relationship (Schoenfeld 1982). If there is a significant interaction between the predictor and event time, then proportionality does not hold. The crossing of two survival curves is an extreme example of a violation of the proportional hazards assumption but has been previously described in the literature (Le, Balakrishnan et al. 2004, Delarue, Tilly et al. 2013). For the log-rank

test to be effective, the assumption of proportional hazard rates must remain intact (Li, Han et al. 2015). Crossing curves would violate this assumption and may indicate a treatment that offers short-term benefit but does not have a long-term advantage. We planned to compare the hazard ratio during the time period before and after the curves cross (Logan, Klein et al. 2008) if the assumption of proportional hazards was violated. While the semi-parametric Cox model provides an accurate estimate of the survival probability (Hjort 1992), it is necessary that both the assumption of non-informative censoring and proportional hazards is not violated. Non-informative censoring refers to the patients leaving the study for reasons unrelated to their health status or other factors related to potential outcomes (Ranganathan and Pramesh 2012).

In survival analysis, competing risks events are *intervening events that result in patient censoring due to some other event that may or may not be related to the disease* (Satagopan, Ben-Porat et al. 2004). The Kaplan-Meier approach generates a curve that portrays the estimated cumulative probability of an outcome event based on the rise in the curve over time. The competing risk approach would generate two curves, one that represents the event of interest (reoperation for inguinal hernia recurrence) and a second that for the competing risk event. The overall survival is reduced when either an event of interest or an event of competing risk occurs(Satagopan, Ben-Porat et al. 2004). In the case of our study, the outcome measure is reoperation for recurrent inguinal hernia with a competing risk event of death prior to reoperation. Primary inguinal hernia repair

is a relatively low morbidity procedure; in a group of octogenarians both laparoscopic and open repairs had zero perioperative mortality (Hernandez-Rosa, Lo et al. 2011). Over a 9-year period in Vermont performing primary inguinal hernia repairs in an elderly population with 5 years of follow-up, there was again zero mortality irrespective of procedure (Rogers and Guzman 2011). The issue of competing risks arises if those who die have a different risk of recurrence than those who live. Given that most inguinal hernias recurrences occur and are repaired within 3 years of the index procedure, it is a low mortality procedure and we had adequate follow-up (>5 years), it is not likely that patients who have the greatest risk of dying also have the greatest risk of recurrence (Heikkinen, Bringman et al. 2004, van Veen, Wijsmuller et al. 2007, Magnusson, Nordin et al. 2010).

3.8d Sensitivity Analysis

A sensitivity analysis can estimate the potential effect of missing data or accuracy of results by assuming various degrees of maldistribution of the variable. This is also known as a "what if" analysis to assess the best and worst possible distribution (Fletcher, Fletcher et al. 2012). In the case of our group of patients, we defined high volume providers as those who performed >25 annual procedures based on the findings of Nordin et al and Aquina et al who previously found the risk of recurrence to be lowest amongst these providers (Nordin and

van der Linden 2008, Aquina, Probst et al. 2015). By restricting our analyses to only these providers, we were able to control for an interaction between volume and outcome, in order to evaluate the effect of technique on recurrence. We performed a multivariable analysis for recurrence in the group of patients who had their primary inguinal hernia repair performed by a high volume surgeon.

3.8e Number Needed to Harm

The number needed to harm (NNH) is the number of patients who need to be treated to prevent one additional event and a common measure to quantify a treatment's impact in a simple term. The NNH was calculated from the hazard ratio using the equation by Altman et al: $NNH=1/([S_c(t)]^h - S_c(t))$ (Altman and Andersen 1999) . Where $[S_c(t)]^h$ is the survival probability (i.e. the risk of recurrent inguinal hernia repair) of the treatment group, h represents the hazard ratio and $S_c(t)$ is the survival probability of the control group.

3.9 Ethics Statement

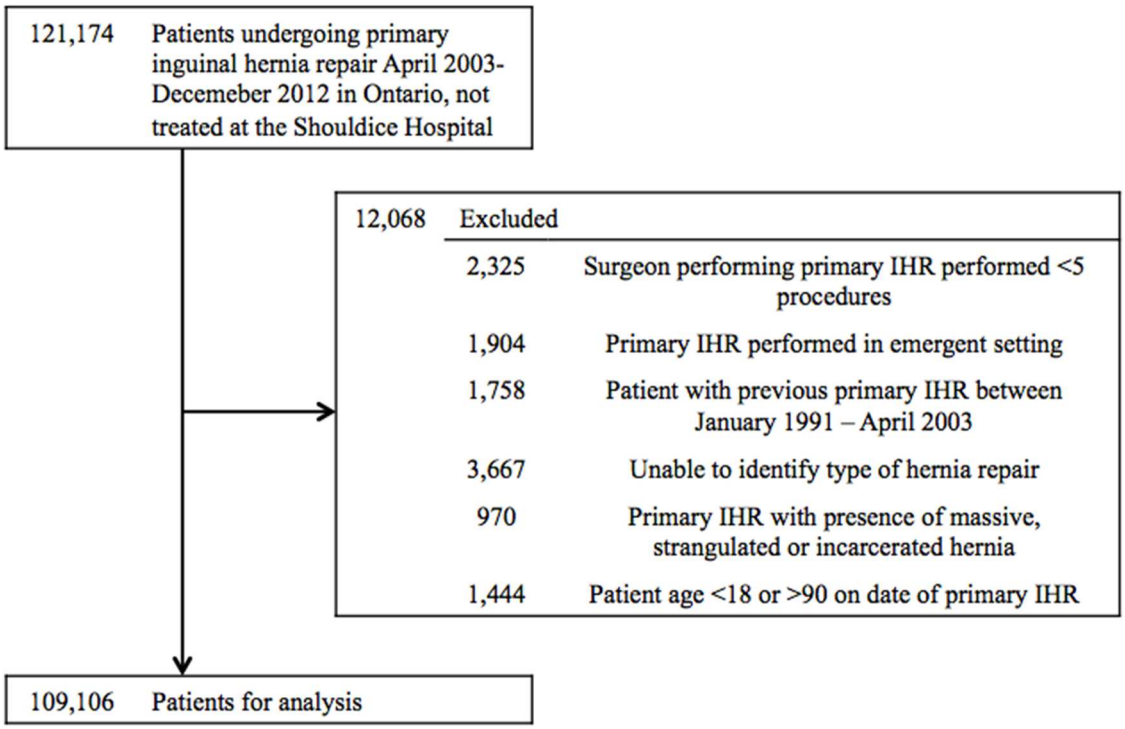
The study protocol was approved by the research ethics board of Sunnybrook Health Sciences Centre, Toronto, Canada. Healthcare databases were anonymously linked using a unique encrypted identifier to safeguard patient confidentiality.

4. Results

4.1 Patient Cohort – Inclusion / Exclusion

A total of 121,174 patients were identified using the S322 OHIP billing code from April 1, 2003 through December 31, 2012 in Ontario, at hospitals other than the Shouldice hospital (Figure 4.1). We excluded patients when the procedure was performed by a very low volume surgeon (<5 of any type of primary inguinal hernia repair in a year) (n=2,325), occurred in an emergent setting (n=1,904), the first identified inguinal hernia repair was for a recurrent hernia (n=1,758), the type of inguinal hernia repair indeterminate (n=3,667), the primary inguinal hernia repair occurred in the presence of a massive, strangulated or incarcerated hernia (n=970) or the patient at the time of primary inguinal hernia repair was <18 or >90 years old (n=1,444). Of the 109,106 patients remaining, a total of 79,888 (73.2%) underwent an open repair with prosthetic mesh placement, 15,605 (14.3%) underwent an open repair without prosthetic mesh placement and 13,613 (12.5%) underwent a laparoscopic repair. A total of 640 surgeons were included in our analysis; 619 performed open inguinal hernia repair with prosthetic mesh placement, 578 performed open inguinal hernia repair without mesh, and 453 performed laparoscopic inguinal hernia repair.

Figure 4.1: Inclusion and Exclusion Criteria



4.2 Cohort Description

Descriptive characteristics are found in Table 4.1. The majority of patients were male (89.7%) and over the age of 45 (75.8%). The majority of patients were non-rural (83.2% overall), with 18% of open with mesh inguinal hernia repair patients being in a rural community, compared to 11.1% of laparoscopic inguinal hernia repair (P<0.001). Comorbidity was fairly evenly distributed across patients undergoing the three techniques, however a lower percentage of patients in the highest comorbidity level (10+) underwent a laparoscopic repair compared to the other techniques (P<0.001). At the provider level, primary inguinal hernia repair was a common procedure (Table 4.1). Overall surgeons had a median annual

volume of 45 patients (IQR: 30-63) of all techniques combined. The median annual hospital volume of primary inguinal hernia repair was 194 patients (IQR: 124 – 265). The annual, technique-specific volume varied; surgeons who performed an open with mesh primary inguinal hernia repair had a median annual volume of 36 procedures (IQR: 23-51). This is compared to 13 procedures (IQR: 5-34) annually by surgeons performing an open without mesh primary inguinal hernia repair and 27 procedures (IQR: 13-48) annually by surgeons performing laparoscopic primary inguinal hernia repair ($P<0.001$).

Table 4.1: Patient Cohort Characteristics, According to Primary Inguinal Hernia Repair Type

		Primary Inguinal Hernia Repair Type			
Cohort Characteristics		**Open Repair with Mesh n=79,888**	**Open Repair without Mesh n=15,605**	**Laparoscopic Repair n=13,613**	**TOTAL n=109,106**
Patient Characteristics					
Age Group	18-34	8,401 (10.5%)	2,019 (12.9%)	1,623 (11.9%)	12,043 (11.0%)
	35-44	10,058 (12.6%)	2,091 (13.4%)	2,205 (16.2%)	14,354 (13.2%)
	45-64	32,473 (40.6%)	6,105 (39.1%)	6,306 (46.3%)	44,884 (41.1%)
	65-84	27,042 (33.8%)	4,965 (31.8%)	3,344 (24.6%)	35,351 (32.4%)
	85-90	1,914 (2.4%)	425 (2.7%)	135 (1.0%)	2,474 (2.3%)
Sex	F	7,549 (9.4%)	2,766 (17.7%)	957 (7.0%)	11,272 (10.3%)
	M	72,339 (90.6%)	12,839 (82.3%)	12,656 (93.0%)	97,834 (89.7%)
	Missing	254 (0.3%)	71 (0.5%)	35 (0.3%)	360 (0.3%)
Income Quintile	1 (lowest)	14,215 (17.8%)	2,936 (18.8%)	2,658 (19.5%)	19,809 (18.2%)
	2	16,016 (20.0%)	3,187 (20.4%)	2,733 (20.1%)	21,936 (20.1%)
	3	16,075 (20.1%)	3,213 (20.6%)	2,763 (20.3%)	22,051 (20.2%)
	4	16,695 (20.9%)	3,183 (20.4%)	2,802 (20.6%)	22,680 (20.8%)
	5 (highest)	16,633 (20.8%)	3,015 (19.3%)	2,622 (19.3%)	22,270 (20.4%)
	Missing	69 (0.1%)	19 (0.1%)	9 (0.1%)	97 (0.1%)
Rural Status	Not Rural	65,463 (81.9%)	13,170 (84.4%)	12,089 (88.8%)	90,722 (83.2%)
	Rural	14,356 (18.0%)	2,416 (15.5%)	1,515 (11.1%)	18,287 (16.8%)
	Missing	69 (0.1%)	19 (0.1%)	9 (0.1%)	97 (0.1%)
Aggregated Diagnosis	0-5	31,915 (39.9%)	5,928 (38.0%)	5,807 (42.6%)	43,650 (40.0%)
	6-9	30,898 (38.7%)	6,027 (38.6%)	5,383 (39.5%)	42,308 (38.8%)

Group	10+	17,075 (21.4%)	3,650 (23.4%)	2,423 (17.8%)	23,148 (21.2%)
Provider Characteristics					
Surgeon Overall Volume (1 year prior to the index case)	Mean ± SD	48.05 ± 26.34	47.57 ± 26.30	59.13 ± 31.57	49.37 ± 27.29
	Median (IQR)	43 (30-61)	44 (29-63)	55 (35-77)	45 (30-63)
Surgeon Technique-Specific Volume (1 year prior to the index case)	Mean ± SD	39.69 ± 23.75	21.55 ± 20.65	32.85 ± 25.76	36.24 ± 24.45
	Median (IQR)	36 (23-51)	13 (5-34)	27 (13-48)	32 (18-49)
Surgeon Technique-specific Volume (1 year prior to the index case)	51+	20,258 (25.4%)	1,921 (12.3%)	3,146 (23.1%)	25,325 (23.2%)
	26-50	35,801 (44.8%)	3,155 (20.2%)	3,942 (29.0%)	42,898 (39.3%)
	6-25	22,703 (28.4%)	6,381 (40.9%)	4,795 (35.2%)	33,879 (31.1%)
	0-5	1,126 (1.4%)	4,148 (26.6%)	1,730 (12.7%)	7,004 (6.4%)
Surgeon 'Other-Technique'✦ Volume (1 year prior to the index case)	Mean ± SD	7.06 ± 10.53	24.63 ± 24.45	24.84 ± 18.52	11.79 ± 16.45
	Median (IQR)	4 (2-8)	18 (5-37)	21 (11-34)	5 (2-15)
Yearly Hospital Volume (1 year prior to the index case)	Mean ± SD	207.30 ± 125.08	190.09 ± 104.89	263.11 ± 165.68	211.80 ± 129.85
	Median (IQR)	193 (121-264)	179 (122-240)	218 (151-320)	194 (124-265)

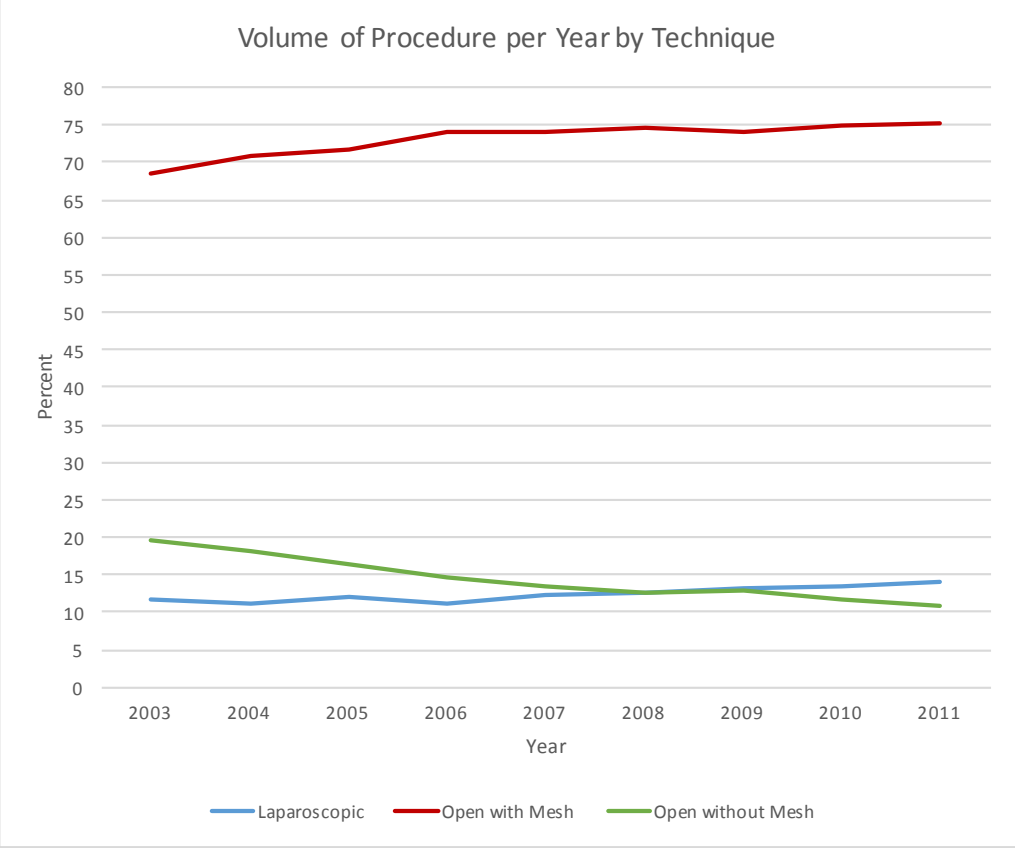
Abbreviations: M- male, F- female, IQR- interquartile range, SD- standard deviation

✦ 'Other technique' volume refers to the number inguinal hernia repairs performed by a single surgeon using either of the other two techniques in the preceding year prior to the index case, expressed as a continuous variable.

4.3 Procedure Volume

Procedure volume was fairly constant for the duration of our study period for laparoscopic and open with mesh repairs. There was a slight increase from 2003 – 2011 in laparoscopic repairs increasing from 11% all repairs annually to 14% by the end of the 9.75 year accrual window. Open with mesh repair also increased slightly from 68% of all repairs annually to 75% by the end of the study period. Open without mesh volume decreased from 19% of all repairs annually in 2003 to 11% of all repairs in 2011 (Figure 4.2).

Figure 4.2- Volume of Repair over Study Period



When comparing procedural volume between providers and institutions, the highest volume surgeons (those with 51+ procedures annually) are mostly located in the highest volume hospitals. However, the lower volume surgeons (<50 procedures) are found at all hospitals (Table 4.2).

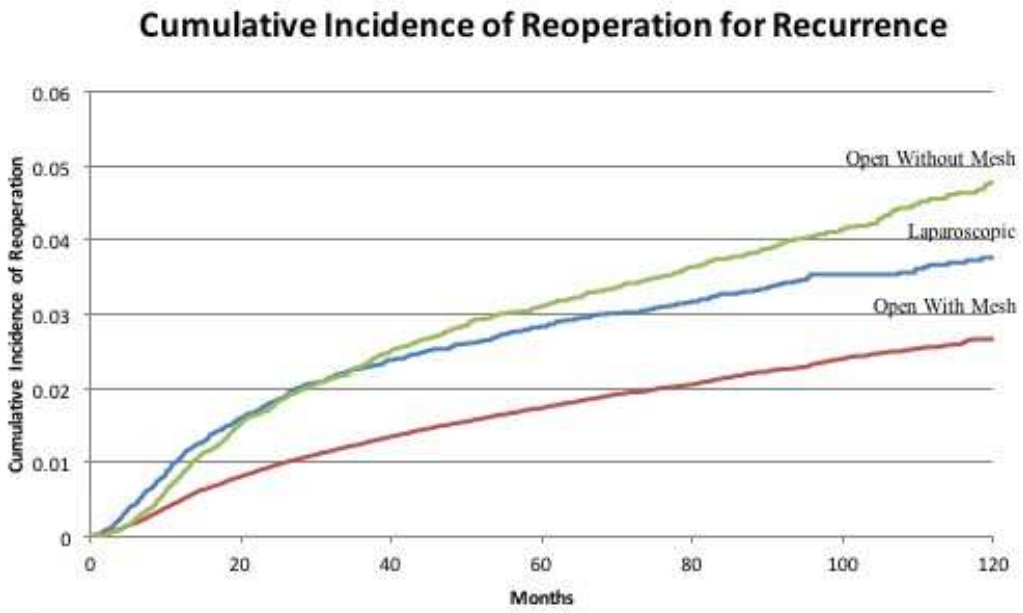
Table 4.2: Hospital – Physician Volume Relationship

	High Hospital Annual Volume (≥194 procedures)	Low Hospital Annual Volume (<194 procedures)
Highest surgeon volume (51+ procedures)	14,554 (16.9%)	6,113 (7.1%)
High surgeon volume (26-50 procedures)	16,394 (19.0%)	17,319 (20.1%)
Low surgeon volume (6-25 procedures)	10,098 (11.7%)	16,451 (19.1%)
Lowest surgeon volume (<5 procedures)	2,087 (2.4%)	3,326 (3.8%)

4.4 Inguinal Hernia Recurrence

Over a median follow-up time of 5.6 years, 2,690 (2.5%) of our patients underwent reoperation for a recurrent inguinal hernia repair, 1,621 (2.0%) of patients in the open repair with mesh group, 605 (3.9%) of patients in the open repair without mesh group, and 464 (3.4%) of patients in the laparoscopic group. The cumulative 5-year risk, the proportion of the population at risk of recurrent inguinal hernia repair in a 5 year period was 2.1% overall; 1.7% in the group undergoing an open repair with mesh, 3.2% in the group undergoing open repair without mesh and 3.0% in the group undergoing laparoscopic repair ($p<0.001$) (Figure 4.3).

Figure 4.3 –Cumulative Incidence of Reoperation for Recurrence



Subjects at risk (109,106)							
Time Period	0	20 months	40 months	60 months	80 months	100 months	120 months
Open with Mesh	79,888	74,314	59,352	45,183	31,363	18,557	7,001
Open without Mesh	15,605	14,489	11,996	9,516	7,060	4,505	1,910
Laparoscopic	13,613	12,609	9,982	7,551	5,246	3,241	1,321

4.5 Multivariable Analysis

4.5a Primary Exposure: Type of Surgical Repair

Rate of recurrent inguinal hernia repair was strongly associated with type of surgical repair. Compared with those undergoing open repair with mesh, patients undergoing an open repair without mesh had an adjusted hazard ratio for recurrent inguinal hernia repair of 1.53 (95% CI 1.33-1.77, p<0.001) and patients undergoing a laparoscopic inguinal hernia repair had an adjusted hazard ratio for recurrent inguinal hernia repair of 1.88 (95% CI 1.61 – 2.20, p<0.001) (Table 4.3). The cumulative incidence curves for the laparoscopic and open repair without

mesh groups crossed around year 3, indicating that the hazard functions of the 2 groups were not proportional to the baseline hazard function. We therefore tested the time to recurrence among the 3 procedures restricted to patients who had not recurred after 3 years. The findings did not change (Table 4.5).

4.5b Sensitivity Analysis

In analyses restricted to patients undergoing primary inguinal hernia repair by a surgeon performing > 25 procedure-specific repairs in the previous year, compared with those undergoing open repair with mesh, patients undergoing an open repair without mesh had an adjusted hazard ratio for recurrent inguinal hernia repair of 2.60 (95% CI 1.77- 3.82, p<0.001) and patients undergoing a laparoscopic inguinal hernia repair had an adjusted hazard ratio for recurrent inguinal hernia repair of 2.07 (95% CI 1.41- 3.06, p<0.001) (Table 4.4).

We calculated the number needed to harm for open inguinal hernia repair without mesh and laparoscopic repairs. For every 31 patients treated with a laparoscopic or open repair without mesh (vs. an open repair with mesh) 1 additional recurrent inguinal hernia repair would be expected within 5 years.

Table 4.3: Multivariable Analysis of Recurrent Inguinal Hernia Repair

Characteristic	Covariate	Hazard Ratio	Confidence Interval	P-Value
Type of Primary Inguinal hernia repair	Ref - open with mesh	1	.	.
	Laparoscopic	1.88	(1.61, 2.20)	<0.001
	Open without Mesh	1.53	(1.33, 1.77)	<0.001
ADG Comorbidity Category	Ref – 0-5	1	.	.
	6-9	1.22	(1.12, 1.34)	<0.001
	10+	1.25	(1.12, 1.39)	<0.001
Age-Sex Group	Ref - 18-34 F	1	.	.
	18-34 M	1.54	(0.87, 2.71)	0.14
	35-44 F	2.24	(1.20, 4.18)	0.01
	35-44 M	2.27	(1.30, 3.97)	0.004
	45-64 F	3.60	(2.04, 6.38)	<0.001
	45-64 M	2.58	(1.49, 4.48)	0.001
	65-84 F	2.78	(1.56, 4.94)	0.001
	65-84 M	2.88	(1.66, 5.00)	0.001
	85-90 F	1.57	(0.63, 3.96)	0.33
	85-90 M	2.03	(1.06, 3.92)	0.03
Income Quintile	Ref – 1 (highest)	1	.	.
	2	0.93	(0.82, 1.05)	0.26
	3	1.01	(0.90, 1.15)	0.82
	4	1.02	(0.90, 1.15)	0.76
	5 (lowest)	1.00	(0.88, 1.14)	0.95
	Missing	0.80	(0.33, 1.94)	0.62
Rural Status	Ref – No	1	.	.
	Yes	1.05	(0.92, 1.19)	0.47
	Missing	0.0001	(0.00, $133e^{68}$)	0.91
Hospital Volume (1y prior to the index)	Ref - low	1	.	.

	High	1.03	(0.90, 1.18)	0.65
Physician technique-specific Volume (1y prior to the index)	Ref- 51+	1	.	.
	26-50	1.01	(0.87, 1.19)	0.86
	6-25	1.19	(0.98, 1.45)	0.08
	1-5	1.13	(0.87, 1.47)	0.35
Physician non-procedure-specific Volume (1y prior to the index)	-	0.99	(0.99, 1.00)	0.56

Abbreviations: ADG- Aggregated Diagnosis Group; M- male; F- female; Ref- reference

Table 4.4: Multivariable Analysis of Recurrent Inguinal Hernia Repair (Limited to Surgeons with a 1 year technique specific volume >25 procedures)

Characteristic	Covariate	Hazard Ratio	Confidence Interval	P-Value
Type of Primary Inguinal hernia repair	Ref - open with mesh	1	.	.
	Laparoscopic	2.07	(1.41, 3.06)	<0.001
	Open without Mesh	2.60	(1.77, 3.82)	<0.001
ADG Comorbidity Category	Ref – 0-5	1	.	.
	6-9	1.18	(1.05, 1.34)	0.007
	10+	1.21	(1.04, 1.40)	0.016
Age-Sex Group	Ref - 18-34 F	1	.	.
	18-34 M	0.62	(0.32, 1.21)	0.16
	35-44 F	1.33	(0.63, 2.81)	0.46
	35-44 M	0.96	(0.51, 1.84)	0.92
	45-64 F	1.84	(0.94, 3.60)	0.08
	45-64 M	1.22	(0.65, 2.29)	0.53
	65-84 F	1.42	(0.72, 2.78)	0.31
	65-84 M	1.36	(0.72, 2.54)	0.34
	85-90 F	0.85	(0.26, 2.72)	0.78
	85-90 M	0.71	(0.31, 1.64)	0.43
Income Quintile	Ref – 1 (highest)	1	.	.
	2	0.98	(0.82, 1.16)	0.79
	3	0.99	(0.83, 1.18)	0.90
	4	1.08	(0.91, 1.28)	0.37
	5 (lowest)	1.06	(0.89, 1.26)	0.49
	Missing	0.44	(0.06, 3.18)	0.42
Rural Status	Ref – No	1	.	.
	Yes	0.99	(0.83, 1.18)	0.93
	Missing	0.0001	(0.00, $272e^{92}$)	0.94

Hospital Volume (1y prior to the index)	Ref - low	1	.	.
	High	1.01	(0.84, 1.21)	0.90
Physician non-procedure-specific Volume (1y prior to the index)	-	1.00	(0.99, 1.01)	0.41

Abbreviations: ADG- Aggregated Diagnosis Group; M- male; F- female; Ref- reference

Table 4.5: Sensitivity Analysis: Risk of Reoperation for Recurrent Inguinal Hernia after 3 years

Table 4.5a: Univariate Analysis of Recurrent Inguinal Hernia Repair

Characteristic	Covariate	Hazard Ratio	Confidence Interval	P-Value
Type of Primary Inguinal hernia repair	Ref - open with mesh	1	.	.
	Laparoscopic	1.24	(1.03, 1.50)	0.025
	Open without Mesh	1.78	(1.53, 2.07)	<0.001

Table 4.5b: Multivariable Analysis of Recurrent Inguinal Hernia Repair*

Characteristic	Covariate	Hazard Ratio	Confidence Interval	P-Value
Type of Primary Inguinal hernia repair	Ref - open with mesh	1	.	.
	Laparoscopic	1.53	(1.16, 2.02)	0.003
	Open without Mesh	1.44	(1.14, 1.82)	0.002

*Covariates controlled for include hospital volume, physician procedure-specific and non-specific volume, patient ADG category, patient age-sex group, income quintile and rural status.

5. Discussion

5.1 Thesis Summary

We analyzed a population-based cohort of patients undergoing primary inguinal hernia repair in Ontario over a 10-year period and found the rate of reoperation for recurrence varied depending on the type of initial procedure performed. As compared to patients undergoing an open repair with mesh, we found an increased risk of recurrent inguinal hernia repair over time for patients undergoing an open repair without mesh (hazard ratio 1.53) or a laparoscopic repair (hazard ratio 1.88), after controlling for covariates that might affect risk of recurrence. Even when restricted to high procedure-specific volume surgeons, the risk of recurrent inguinal hernia repair was higher after an open repair without mesh (hazard ratio 2.60) or a laparoscopic repair (hazard ratio 2.07).

5.2 Recurrence Rates

A number of investigators have evaluated the influence of surgical technique on the risk of recurrence after inguinal hernia repair. Our finding of a higher risk of reoperation for recurrence when inguinal hernia repair was performed in an open fashion without mesh adds further evidence to a very consistent literature (Scott, McCormack et al. 2002, McCormack, Scott et al. 2003, Bittner, Sauerland et al. 2005). Furthermore, the presence of increased

early recurrence rates for laparoscopic inguinal hernia repair has been found elsewhere in randomized trials (Andersson, Hallen et al. 2003, Neumayer, Giobbie-Hurder et al. 2004). In contrast, the majority of randomized trials and meta-analyses comparing laparoscopic and open with mesh inguinal hernia repair did not demonstrate a difference between the two groups (Wright, Paterson et al. 2002, Andersson, Hallen et al. 2003, Heikkinen, Bringman et al. 2004, Neumayer, Giobbie-Hurder et al. 2004, Butters, Redecke et al. 2007). However, it is unclear if the results of trials comparing laparoscopic to open inguinal hernia repair are generalizable to typical practice settings; some studies report recurrence rates as low as 1.0% (Grant, Go et al. 2000, van Veen, Wijsmuller et al. 2007) after primary inguinal hernia repair, rates not typically reproducible in other settings(Malik, Bell et al. 2015). Trials may enroll 'ideal' patients at low risk of recurrence. Additionally, trials conducted in specialized centres reflect the recurrence rates of highly skilled expert surgeons. Given that technical proficiency takes longer to attain for laparoscopic inguinal hernia repair vs. open with mesh repair (Neumayer, Gawande et al. 2005) and the majority of recurrences after laparoscopic inguinal hernia repair appear to be technical failures(Edwards and Bailey 2000, Neumayer, Gawande et al. 2005), outcomes of laparoscopic inguinal hernia repair may be worse in the general population of surgeons than in the hands of experts.

5.2a Relation to Other Population Studies

Other population-based studies have described the risk of hernia recurrence after inguinal hernia repair. These studies are typically national hernia registries and analyze the impact of various factors such as physician volume(Nordin and van der Linden 2008), type of hernia, or technique(Burcharth, Andresen et al. 2014). As in our study, they also found a higher risk of recurrence than described in randomized trials of inguinal hernia repair(Zhao, Gao et al. 2009). However, many of these studies are limited by a small number of surgeons performing laparoscopic inguinal hernia repair (Zendejas, Ramirez et al. 2012) and are reflective of the early experience with laparoscopy, which has an identifiable learning curve(Edwards and Bailey 2000). In contrast, our study, conducted during a time period when laparoscopic inguinal hernia repair was an established procedure, included over 13,000 patients undergoing a laparoscopic inguinal hernia repair by any surgeon, and 7,088 undergoing a laparoscopic repair by surgeons who performed more than 25 laparoscopic inguinal hernia repairs per year. Our study has a large sample of patients recently undergoing all types of repairs including laparoscopy and open without mesh.

5.2b Effect of Comorbidity

Our study found that increased Aggregated Diagnosis Groups comorbidity was associated with an increased hazards ratio for recurrent inguinal hernia repair, for

both categories 6-9 and 10+. This indicates that patients with greater comorbidity were more likely to undergo reoperation for recurrence than patients with fewer comorbid conditions. The ACG System has the ability to capture the inter-relationships between comorbidities through the use of the Aggregated Diagnosis Groups. Similar diagnoses (in terms of severity and likelihood of chronicity) are pooled together into 1 of 32 potential Aggregated Diagnosis Group clusters. Individuals with 6+ ACG categories will have multiple conditions of varying duration and severity(Starfield, Weiner et al. 1991). Rogers et al. performed a multivariate analysis to examine the factors predictive of hernia recurrence in elderly patients from 1995-2005. In this retrospective database study, they failed to demonstrate association between comorbid condition and recurrence (Odds ratio=1.1, P=093)(Rogers and Guzman 2011). This study is limited by including the experience of a single surgeon performing the procedure, with an overall recurrence rate of 0.05% that is not reflective of surgical practices elsewhere. More recent trials corroborate our findings and reflect the surgical experience described in the literature. In 2012, Amato et al compared a group of patients over the age of 70 with a higher American Society of Anesthesiologist to a group under 70, with fewer comorbidities and found a higher rate of recurrence (7.5%) in the older/chronically ill group compared to the younger group (3.6%) (Amato, Compagna et al. 2012).

5.2c Effect of Rural Status and Socio-Economic Status

Neither rural nor socioeconomic status was found to be associated with an increased hazards ratio for recurrent inguinal hernia repair. In a case series of 108 patients who underwent a laparoscopic inguinal hernia repair performed in the rural southern United States, only one had a recurrence at 1 year follow-up(Morrison and Jacobs 2008) with similar findings in another study that had a mean follow-up of 3.7 years(Napier, Olson et al. 2008). It is difficult to isolate a single factor to explain why socioeconomic status did not contribute to recurrent inguinal hernia repair; this may in part be due to equality of access within Ontario, as well as the presence of an inguinal hernia across all SES quintiles.

5.2d Effect of Physician Volume

The common theory to connect procedural volume to patient outcomes is that 'practice makes perfect' and that as a surgeon performs more procedures, their technical proficiency and therefore outcomes also improve. Physician volume and its impact on patient outcomes are extensively reported and discussed in the surgical literature. In a highly influential and widely cited study, Birkmeyer et al demonstrated an inverse relationship between surgeon volume and operative mortality for eight different cardiovascular or cancer procedures (Birkmeyer, Stukel et al. 2003). More recently, Aquina et al evaluated 151,322 patients who underwent inguinal hernia repair in New York State from 2001 to 2008 and found that patients having operations performed by surgeons who performed < 25 inguinal hernia repairs annually had a greater risk of recurrent

inguinal hernia repair than those having operations performed by higher volume surgeons (hazard ratio 1.23, 95% CI 1.11-1.36) (Aquina, Probst et al. 2015). Volume likely represents a surrogate measure of procedure-specific technical proficiency and once a minimal volume is attained, the volume-outcome relationship is less appreciated (Urbach 2015). In 2008, Nordin et al demonstrated a higher rate of recurrent inguinal hernia repair in surgeons who carried out 1-5 inguinal hernia repair annually (RR: 1.20, 95% CI 1.01-1.42, P=0.035) compared to surgeons who performed >75 inguinal hernia repair / year (Nordin and van der Linden 2008). No other volume categories >5 annual inguinal hernia repairs were found to confer similar risk or be significant when compared to the surgeons who performed >75 procedures. Based on this, we excluded patients whose surgeries were performed by surgeons who performed <5 inguinal hernia repairs in the year prior to the index procedure. After this exclusion, we did not find that surgeon volume at any volume category (1-5, 6-24, 25-49, 50+) was associated with an increased hazard ratio for recurrent inguinal hernia repair. In our analysis, we considered it important to control for volume by accounting for surgeon technique specific and non-technique specific volume, in addition to the hospital volume. It is possible that in doing so, we have masked a volume effect. As stated, high volume surgeons may have greater procedure specific technical ability, familiarity with anatomy and thus lower rate of reoperation for recurrence. Our primary exposure was repair technique, if surgeon volume had been our primary exposure there might have been a

relationship as there may be an element of collinearity between technique and surgeon/hospital volume.

5.2e Effect of Hospital Volume

We found that hospital volume did not contribute to reoperation for recurrent inguinal hernia, hazard ratio: 1.03 (95% CI 0.90-1.18) P=0.65 when comparing hospital volume as a continuous measure. Our results differ from a study from the Swedish Hernia Registry in 2008. Nordin et al demonstrated a reduced risk of recurrent inguinal hernia repair if the procedure was performed in a university hospital (relative risk: 0.87, 95% CI 0.751-0.998, P=0.047) or medium sized hospital (defined as those not associated with a teaching hospital and with a 24 hour emergency department) (relative risk: 0.88, 95% CI 0.795-0.964, P=0.007) when compared to small units (defined as only available for day surgery) (Nordin and van der Linden 2008). It is possible that this reflects a hospital characteristics rather than a volume issue. Andresen et al demonstrated a higher rate of recurrence at hospitals who performed less than 50 procedures annually, 9.97% recurrence vs 6.06% at hospitals > 50 procedures annually. Our median hospital volume was 194 overall, IQR: 124-265 suggesting that the majority of hospitals in our study treated at least 10 patients with an inguinal hernia and exceeded the minimum hospital volume to show a difference in recurrence.

5.3 Cox-Proportional Hazards Model

With the Cox-proportional hazards model, there are no assumptions made about the baseline hazard, however there are two key assumptions that must be assessed for its application. First, the cause of censoring for an individual must not be related to the probability of the event occurring. The second assumption is that if one curve dominates the other throughout the trial, they (the hazards) must be proportional (Sooriyarachchi and Whitehead 1998). However, since the curves are not parallel, dominance alone does not imply proportionality.

In our study, the laparoscopic and open without mesh curves cross at ~3 years post-index event (Figure 4.3) and is a violation of the proportional hazard assumption. It is necessary to note that in our primary comparison of laparoscopic to open with mesh inguinal hernia repair, the proportional hazards remain separate for the duration of the study period and therefore the assumption is not violated. For the crossing laparoscopic and open without mesh survival curves, there are three approaches that can be adopted (Logan, Klein et al. 2008).

The first approach would be to use a weighted log rank test with differential weighting on the early or later events (Fleming and Harrington 1981). The limitation of this approach is that the test is still designed to evaluate for differences over the entire survival curve and by weighting for late events, it is overly sensitive for differences between early events (Logan, Klein et al. 2008) and vice versa if weighted for early events. Clinically, weighting either the early or

late period of the survival curve would not be appropriate. Magnusson et al demonstrated that within a 5 year period after surgery, open without mesh and laparoscopic inguinal hernia repair tend to undergo recurrent inguinal hernia repair earlier post-operatively than open with mesh inguinal hernia repair (open without mesh odds ratio: 1.199 (95% CI 1.018-1.414 P=0.030) and laparoscopic odds ratio: 1.177 (95% CI 1.02-1.352, P=0.021) with open with mesh as the reference). The variability in recurrence eliminates the ability to weight for early or late events in the survival curve.

Secondly, we could have selected a single time point after the curves cross and compared the survival estimates (Klein, Logan et al. 2007). This would have limited our results to only the time point chosen and would ignore the events after the selected time point. This may have been an acceptable approach, since most recurrences occur and undergo re-operation within three years of the index procedure (Magnusson, Nordin et al. 2010). However, this would have failed to assess the long term outcomes after 3 years, which is a limitation noted of prospective studies (Neumayer, Giobbie-Hurder et al. 2004, Arvidsson, Berndsen et al. 2005).

The final approach (and method we utilized for our sensitivity analysis) was the identification of time regions before and after the survival curves cross (Parzen, Wei et al. 1997). Unlike the comparison of a single time point, this was able to account for all events within the two separate time intervals, maintaining the long-term follow-up. While it is limited by the larger number of time points to

adjust for (Logan, Klein et al. 2008), this method is able to evaluate for early and late recurrences with equivalent accuracy(Zhang and Klein 2001). In comparing the overall and >3 year period, the overall hazard ratio for recurrent inguinal hernia repair when the primary repair was performed laparoscopically is 1.88 (95% CI 1.61-2.20) compared to >3 year hazard ratio: 1.53 (95% CI 1.16-2.02)). Open without mesh inguinal hernia repair (overall hazard ratio: 1.53 (95% CI 1.33-1.77) versus >3 year hazard ratio: 1.44 (95% CI 1.14-1.82)).

5.4 Economic Implications

There are considerable economic implications of an inguinal hernia recurrence. There is an estimated 70,000 inguinal hernia repair performed annually in Canada (Poulin and Marcaccio 1997) and as many as 600,000 inguinal hernia repair in the United States (Ruhl and Everhart 2007). Inguinal hernias are estimated to limit the activity of 400,00 persons annually in the US resulting in a significant number of work days lost (Everhart 1994). Appropriate technique at the time of primary repair can significantly reduce the comorbidity associated with condition, specifically by prevent recurrences that cause further debilitation and are at greater risk to re-recur after repair (Haapaniemi, Gunnarsson et al. 2001). We calculated a NNH to be 31, meaning that for every 31 patients treated with a laparoscopic procedure an additional recurrence will occur that could have been prevented, if the practitioner had used an open with mesh approach. This is potentially 1,000 recurrences in North America annually that could be prevented

by performing all hernia repairs using an open with mesh technique. Given the current cost to treat a recurrent inguinal hernia in Canada, there is approximately $500,000 annually that could be saved with the appropriate change in technique (Vale, Grant et al. 2004, McCormack, Wake et al. 2005, Eklund, Carlsson et al. 2010).

5.5 Strengths

Our study has numerous additional strengths. We captured the population of patients undergoing elective primary inguinal hernia repair by excluding patients who underwent emergent or recurrent inguinal hernia repair. Our study included a large number of patients during a time period when all three techniques were established and performed frequently. With respect to volume, we excluded surgeons who performed <5 inguinal hernia repair per year, carefully controlled for provider and hospital volume, and conducted a sensitivity analysis restricting surgeons to those performing >25 procedure-specific repairs yearly. Though the literature reports that the majority of recurrent inguinal hernia repairs occur within 5 years of the primary repair, we found that repair for recurrence continues after 5 years as the cumulative incidence curves continue to increase for all repairs. Thus our median post-operative surveillance of 5.59 years is an adequate duration to assess this outcome(Wright, Paterson et al. 2002,

Arvidsson, Berndsen et al. 2005). Our study presents results that are generalizable for patients, surgeons and institutions.

5.6 Limitations

Our study does have limitations. We used administrative data and were not able to identify patient characteristics such as obesity (Rosemar, Angeras et al. 2010) and smoking (Sorensen, Friis et al. 2002) or hernia size and type (direct, indirect or femoral) that are known to influence recurrence rates. We had no additional information regarding specific type of technique performed or type of mesh used, however there is no evidence that recurrence rates differ between types of mesh (Sajid, Leaver et al. 2012) or techniques of open mesh insertion (Zhao, Gao et al. 2009). Our outcome was recurrent inguinal hernia repair and we therefore underestimate the overall rate of recurrence (Haapaniemi, Gunnarsson et al. 2001). Though recurrences after laparoscopic primary repair tend to occur earlier, there is no evidence to suggest that reoperation resulted in bias - the decision to repair a recurrent hernia is unlikely to be influenced by the technique used for the primary repair (Eklund, Carlsson et al. 2010, Burcharth, Andresen et al. 2014). The limitations of our study are unlikely to result in bias favoring any approach to primary inguinal hernia repair and therefore our findings remain generalizable to the population of patients considering surgery for their hernia and surgeons who perform inguinal hernia repair outside specialized, high volume centers.

Despite the strengths of administrative data, these data are not collected for research purposes; in the case of our study, we are using procedural codes as part of billing claims data. Elsewhere, such as Sweden and Denmark, there are dedicated disease registries for hernia repairs (Bay-Nielsen, Kehlet et al. 2001, Haapaniemi, Gunnarsson et al. 2001) that do not rely on administrative data, however amongst their populations, they do not have as many patients undergoing laparoscopic repair or open without mesh. The accuracy of secondary data sources in Ontario is routinely monitored to ensure that it is both current and accurate (Hawker, Coyte et al. 1997, Virnig and McBean 2001, Juurlink D 2006).

We have taken steps to ensure that our administrative data accurately represents the study population of interest. The risk of misrepresentation is especially true for certain diseases that are under diagnosed within the population, such as depression (Perez-Stable, Miranda et al. 1990) and may affect the quality of data generated; however inguinal hernia repair is a common, widely practiced procedure (Rutkow 2003). By using CIHI procedural codes for hernia repair that are specifically designed for health services research and routinely scrutinized for accuracy and validity, we are able to capture the specific procedure and date of service rendered with greater accuracy than with diagnostic or billing codes alone (Juurlink D 2006). Similarly, the use of multimorbidity scoring systems allow us to account for patient comorbidities as

they occur in a variety of practice settings, including in-patient, ambulatory and emergency department settings (Carlsson, Borjesson et al. 2002, 2008).

Finally, given that the data are collected for the purpose of billing clinically relevant information, such as patient factors (ex. vital signs, cardiac function, etc) are generally not included as part of administrative databases. In Canada however, administrative data within CIHI is collected specifically for health system analysis and is routinely scrutinized to ensure accuracy and validity. In the case of inguinal hernia repair, a useful patient attribute would be a patient's obesity status at the time of repair. While an obesity code is exists in ICD-9 and 10, it has not been widely used in Canadian administrative health data and underestimates the true prevalence of obesity (Kuhle, Kirk et al. 2011).

6. Conclusions

In summary, in typical practice settings, patients undergoing an open inguinal hernia repair with mesh have a lower risk of recurrence than patients undergoing an open inguinal hernia repair without mesh or a laparoscopic inguinal hernia repair. Based on our data, conversion of the 160,000 laparoscopic primary inguinal hernia repairs performed each year in North America to open repairs with mesh technique could avoid the need for repair of a recurrence in over 1,000 patients annually. There may be specific indications for a laparoscopic repair, for example patients undergoing bilateral repairs in expert centers. Those undergoing laparoscopic inguinal hernia repair in these centers may have reduced acute post-operative pain and quicker recovery. However, given the increased cost burden and risk of recurrence, the technique of choice for primary inguinal hernia repair for most patients and surgeons appears to be an open repair with mesh.

6.1 Specific Aim 1: To evaluate the difference in reoperation for recurrent inguinal after laparoscopic and open with mesh primary inguinal hernia repair.

We have demonstrated a difference in reoperation rates for recurrent inguinal hernia repair between the three common surgical approaches for primary inguinal hernia repair – laparoscopic, open without mesh and open with mesh. We found an overall rate of reoperation for recurrent inguinal hernia of 2.5%. When

stratified, the rate of reoperation for laparoscopic primary inguinal hernia repairs was 3.4%, 3.9% for open without mesh and 2.0% for open with mesh.

When analyzing the risk of reoperation for recurrent inguinal hernia using open with mesh as a reference, we found that laparoscopic and open without mesh confer an increased risk of reoperation – 1.88 and 1.53, respectively.

The practice patterns within Ontario changed over the accrual period. The frequency of laparoscopic primary inguinal hernia repair increased over the study period. Conversely, the frequency of open without mesh repair decreased from the start to end of the accrual period. There was no change in the rate of open with mesh primary inguinal hernia repair.

We excluded surgeons who performed less than 5 primary inguinal hernia repairs within a year. After exclusion of these low volume providers, provider volume at any level (6-25, 26-50, 51+) did not increase the risk of reoperation for inguinal hernia. Similarly, when analyzing the impact of non-specific procedure volume, that also did not affect the risk of reoperation for recurrent inguinal hernia.

We analyzed the effect of hospital volume on inguinal hernia recurrence. Comparing the high to low volume institutions (by dividing at the median), we found that hospital volume did not affect the risk of reoperation for recurrent inguinal hernia.

We evaluated the significance of patient level characteristics for their impact on risk of reoperation for recurrent inguinal hernia. We found that patients with increased comorbidity, that is those with higher ACG scores were at an increased risk of reoperation. Male patients from the age of 35-90 were at an increased risk of reoperation, compared to females whose risk was higher in 35-84 ranges.

Our findings are generalizable to the greater population of surgeons who perform inguinal hernia repair. Administrative data in Ontario allows us to account for providers at all skill levels in a variety of practice settings. Similarly, our patient population is representative of the larger population who undergo elective primary inguinal hernia repair. Laparoscopic primary inguinal hernia repair continues to have indications, specifically bilateral hernia repairs where it has been shown to decrease operative time. Though we did not find that volume of procedure affected the risk of reoperation, independent high-volume laparoscopic centers may achieve reoperation rates that are similar to the rates we found with the open with mesh repair. However, amongst the average practitioner performing primary inguinal hernia repair, then the procedure of choice is an open with mesh repair.

6.1 Future Directions

Our study found that the open with mesh primary inguinal hernia repair resulted in a lower rate of reoperation for recurrent inguinal hernia compared to laparoscopic inguinal hernia repair. Active dissemination of these results is important, through a combination of professional meetings, academic conferences, and publication in scientific journals and in the general media.

Ultimately, these results should impact on current surgical practice. Within Ontario, all three categories of inguinal hernia repair are practiced. For surgeon who perform laparoscopic primary inguinal hernia repair, there should be a mechanism in place to monitor the reoperation rate for recurrence amongst these surgeons. This could be performed via a personal audit, where individual surgeons must follow their patients for 3-5 years post-operatively to demonstrate recurrence rates as low as afforded by the open with mesh repair or at specialty institutions such as the Shouldice Hospital. If there were a hernia registry in Ontario, this would be another means to track individual surgeon performance.

With respect to open without mesh primary inguinal hernia repair, though it is decreasing in use, it is a technique that is still practiced in Ontario. Routine use of these procedures should be limited, except by those within the Shouldice hospital or in cases where use of prosthetic mesh is contraindicated (such as a contaminated surgical site). For patients deciding which procedure to undergo, patient education should focus on explaining the different technique options and reflect that low recurrence rate attained at the Shouldice hospital may not be attainable elsewhere and similar disparities may exist amongst laparoscopic

providers. For that reason, when consider the typical provider to electively repair a unilateral inguinal hernia, the procedure of choice is an open with mesh repair.

6.1a: Hernia Repair Mentorship

There are multiple future directions for inguinal hernia repair within Ontario; the first is on a practice level. There is a known learning curve with both open and laparoscopic techniques for inguinal hernia repair (Liem, Van Steensel et al. 1996, Edwards and Bailey 2000, Schouten, Elshof et al. 2013), which surgeons even after they have completed their residency training may still be overcoming. Previous studies have demonstrated that the majority of recurrences occur when a surgeon who has performed <5 repairs in the preceding 365 days performs the primary inguinal hernia repair. We, however, did not find a relationship between surgeon volume and recurrence after elimination of these low volume providers. Therefore, for surgeons who perform the procedure infrequently, the recommendation to have a second, “experienced” surgeon present would be advisable. An alternative approach might be hernia repair clinics, similar to what has been suggested in Europe (Simons, Aufenacker et al. 2009). This would foster active mentorship from senior surgeons to junior surgeons and provide a forum to update new advances in mesh technology and surgical technique.

6.1b Special Circumstances

We were able to demonstrate a difference in reoperation for recurrence that was previously unappreciated between laparoscopic and open with mesh inguinal hernia elective primary inguinal hernia repair. There are other circumstances that warrant study, specifically the technique of choice for recurrent inguinal hernias and in the case of emergency hernia repair.

There is no consensus within the literature as to which technique affords the lowest rate of re-recurrence (Bisgaard, Bay-Nielsen et al. 2008, Sevonius, Gunnarsson et al. 2011, Shah, Mikami et al. 2011). The study methodology to evaluate this would use the same parameters as in our study. However, rather than the index event being the S323 OHIP procedural code alone, it would have to be coded with an E725 or E726 code to designate a recurrent or repeat recurrent inguinal hernia, respectively. As in our study, the initial recurrent repair can be stratified using the CIHI procedural codes and then patients followed for a subsequent reoperation for recurrent or repeat recurrent inguinal hernia. In our study's time period we found 2,690 recurrent inguinal hernias, each of these patients could be followed to assess if they develop a re-recurrence. Our 2,690 reoperations is greater than the 2,117 reoperations previously reported from the Danish Hernia Database (Bisgaard, Bay-Nielsen et al. 2008) and could be increased if primary inguinal hernia repairs from the Shouldice center were included and the accrual period lengthened.

As part of our analysis, we eliminated emergency procedures or those performed 'after hours' so that we could focus specifically on elective inguinal hernia repairs. Instead, by stratifying the 1,904 patients that we identified who underwent an emergent inguinal hernia repair into one of the three technique categories, we could then follow them for the risk of reoperation for recurrent hernia. This is potentially a more difficult analysis, as there is a small number of patients who patients undergo an emergent procedure, with a higher risk of dying in the post-operative period, therefore leaving a small sample of patients with adequate time to recur. Regardless, this remains an area for future analysis.

6.1c Robotic Inguinal Hernia Repair

Minimally invasive surgery continues to advance with the adoption of robotic surgery. While urologists have reported repairing inguinal hernias concurrent with radical prostatectomies, general surgeons are now reporting the feasibility of robotic inguinal hernia repairs with respect to intraoperative complication and post-operative course (Escobar Dominguez, Ramos et al. 2015). If the wider surgical population adopts this as an acceptable technique for inguinal hernia repair, this would present a fourth treatment group to evaluate for differences in recurrence. Potentially, robotic surgery affords greater range of motion from the surgical instruments and improved visualization, which may improve lateral dissection and mesh placement in pre-peritoneal space.

6.1d Inguinal Hernia Registry

Given the presence of all inguinal hernia repair techniques in Ontario, it is an excellent location to establish a hernia registry to further improve the quality of hernia care delivered. The registry would provide an instrument to identify surgeons with higher than average rates of reoperation/recurrences and can be used to ensure the appropriate level of technical proficiency is uniformly delivered across Ontario. The volume of hernia repairs in Ontario would parallel or surpass other population registries that exist. Inclusion of repairs performed at the Shouldice Hospital in Ontario would add unique elements, such as patient selection criteria, repair at a specialized center, high volume practitioners and use of the Shouldice repair to the registry that are not found elsewhere.

Much of the required infrastructure for the hernia registry already exists within Ontario. The first element required is the ability to identify individuals though a unique identifier – this is present in Ontario using the Ontario Health Insurance Plan number. Coupled with the administrative databases housed at the Institute of Clinical Evaluative Sciences, specifically the Registered Persons Database, it is possible to accurately follow a patient until death.

The use of reoperation as a measure of recurrence is accepted in other hernia registries (Kald, Nilsson et al. 1998). To establish a new hernia registry, it will be necessary to demonstrate the internal validity of both the exposures and outcome measures. This would require primary chart review to ensure the accuracy of the codes used to identify laparoscopic and open inguinal hernia

repair. To evaluate the relationship between reoperation and recurrence, it would be necessary to prospectively follow patients after surgery to evaluate for recurrence and then to determine the number who undergo surgical repair. Prospective follow-up could take the form of a mailed questionnaire (Haapaniemi and Nilsson 2002) to determine presence or absence of symptoms consistent with a recurrence (groin pain or appreciable bulge in the area of the hernia). However, to make a definitive diagnosis, a physical examination by a physician would be required to term if a true recurrence were present.

There is additional hernia and patient level information that would be necessary for completeness of the registry. With regards to hernia, the laterality of the procedure would need to be documented at the time of procedure. For patients who undergo repairs of different sides over a two day period (as is common practice in the Shouldice Hospital) or over a longer period time, it would be possible to capture which hernia repair resulted in a recurrence and had to undergo repair. Where possible, incorporation of additional procedural codes to distinguish between the subtypes of repairs would provide a level of detail that does not exist within other population-based studies currently. Other hernia related data would include whether it is a direct, indirect, pantaloon or femoral hernia, with similar designations at the time of reoperation for recurrence. On the patient level, while there is a diagnostic code for BMI within the healthcare administrative databases, it is not often coded and given the importance of obesity in the development and recurrence of a hernia, is an element that requires

inclusion. Further information regarding social aspects of the patient would also be beneficial, including smoking and occupational status. Both smoking and occupation have been linked to the development of an inguinal hernia and contributing to recurrence (Sorensen, Friis et al. 2002, Rosemar, Angeras et al. 2010). The type of occupation can be useful when evaluating "time to return to work" after laparoscopic or open repair since as Gunwaldt et al speculated, a construction worker will take longer to return to work than an individual who works in an office (Grunwaldt, Schwaitzberg et al. 2005).

The major barrier to creating such a database would be securing the financial resources to establish and then maintain the registry. The second would be patient privacy to ensure confidentiality of all participants enrolled in the registry. A third major hurdle would be participation of all institutions that perform hernia repairs. This would have to be a gradual process, such as the development of the Swedish Hernia Registry that originally started with 8 institutions that performed inguinal hernia repairs and then subsequently expanded to nationwide coverage (Nilsson, Kald et al. 1997).

6.1e Economic Evaluation

There is a need to understand the financial impact of inguinal hernia recurrence from a Canadian perspective. Previous studies that have evaluated the cost of recurrence have been in the United States or Europe (McCormack, Wake et al.

2005) and fail to account for the practice patterns within Canada (Trevisonno, Kaneva et al. 2015). The economic evaluation would be at the provincial healthcare level and would assess the cost to OHIP for the primary procedure and (where applicable) cost of reoperation for recurrence. As demonstrated in our study, we found the number of procedures performed and the number of reoperations that occurred within the study period. The increased cost of a laparoscopic inguinal hernia repair compared to an open repair is usually justified on the basis of quicker return to daily activities and a reduced recurrence rate (McCormack, Wake et al. 2005). Given that we found an increased rate of reoperation for laparoscopic primary inguinal hernia repairs, a true economic evaluation that accounts for the high cost of primary procedure and reoperation may find that it is too costly of a procedure to be reimbursed outside of certain situations (such as a bilateral repair or when performed by a surgeon with a verifiable low reoperation rate).

6.1f Technical Skill and Hernia Repair

It has been discussed throughout this thesis that volume is often used as a surrogate measure of technical skill. There are pre-existing metrics to evaluate surgical skill, specifically the Objective Structured Assessment of Technical Skill (OSATS), which was originally designed to evaluate surgical trainees (Martin, Regehr et al. 1997). It has also been used to assess technical skill in bariatric, urological and gynecological practitioners (Birkmeyer, Finks et al. 2013, Alici,

Buerkle et al. 2014, Argun, Chrouser et al. 2015). OSATS consists of several domains – respect for tissue, time and motion, instrument handling, knowledge of instruments, flow of operation, use of assistants and knowledge of specific procedure. A future study would be to analyze the effect of a surgeon's technical skill, as measured by OSATS on the rate of reoperation for inguinal hernia. It would be expected that more technically skilled surgeons (those with higher OSATS scores) should have fewer recurrences; however this may identify the minimum threshold of technical proficiency that a surgeon must demonstrate to have an acceptably low rate of recurrence.

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