Abdominal Wall Reconstruction: Improving Research Quality and Identifying the Predictors of Ventral Hernia Recurrence

Samuel George Parker

University College London

Doctor of Philosophy, PhD

I, Sam Parker, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

To my wife, Henrietta.

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Table of Contents

Abstract

Abdominal wall reconstruction (AWR) is an emerging subspecialty within general surgery. To date, research has focused mostly on surgical reconstruction techniques without sufficient regard to research quality. As a result, much published work has produced spurious data with unstandardised variable definitions. Published data is therefore challenging to interpret, giving little robust evidence to guide AWR surgeons.

Consequently, the first part of this thesis focuses on improving research quality. Initially, I performed two systematic reviews analysing variable reporting amongst interventional trials, demonstrating the current heterogeneous reporting of perioperative variables, post-operative outcomes, and patient reported outcomes as well as poor trial methodology. Next, I targeted “loss of domain” (LOD) and published a systematic review and a clinician survey which revealed current inconsistent definitions, both in the literature and amongst practicing surgeons. Whilst performing these systematic reviews, I also identified that terms used to defined and name abdominal wall planes were used inconsistently.

To rectify this, I performed a series of consensus studies. First, I performed a Nominal Group Technique study and established minimum datasets for primary and incisional ventral hernia interventional trials. These datasets reached consensus on standardised peri-operative variable definitions and detection methods, outcomes reporting, follow-up duration, and criteria to improve trial methodology. Next, I performed two Delphi studies with 20 international hernia experts. The first established new written and volumetric definitions for LOD. The second study created ‘ICAP’, an International Classification of Abdominal wall Planes, which defines and names the tissue planes into which mesh can be placed for ventral hernia repair.

The second part of this thesis uses systematic review and meta-analysis across 20 years of AWR literature to identify peri-operative factors that significantly predispose to hernia recurrence after apparently curative repair. This systematic review forms the evidence-base from which to develop a prognostic model of ventral hernia recurrence.

Impact Statement

This work has already demonstrated significant impact within academic circles. At the time of completion, eight chapters of this thesis have been published in indexed journals with 74 citations. Over the last 4 years, I have made 12 podium presentations, and 5 poster presentations to learned international AWR conferences. This confirms my work is of interest to the academic AWR community and addresses topical issues faced by this surgical subspecialty.

The creation of ICAP has been my most significant contribution. After publication, Altmetrics reached 214 within the first week, which scores it within the top 5% of all research ever published. Multiple Tweets forecasted this publication as 'landmark' work within the subspecialty of AWR, and in March 2020 the European Hernia Society (EHS) endorsed ICAP; further promoting and propagating this work. Our standardised written and volumetric definitions for LOD have been acknowledged and well received, with invitations for me to present these on the international stage at both EHS and AHS (American Hernia Society). Using standardised definitions for LOD will allow for its consistent and comparable investigation as a post-operative outcomes predictor. Analogous to this, Chapter 7 presents much-needed AWR interventional trial minimum datasets. These datasets contain defined peri-operative variables and post-operative outcomes, and aim to standardise published trial data making it consistent, easier to interpret and more comparable between trials. This will materially improve AWR research quality.

Outside academia, my work has an evident impact on clinical work. Standardised unambiguous nomenclature describing the planes of the abdominal wall allows for accurate description of mesh placement during reconstructive surgery. Previous ambiguity may well have resulted in placement of mesh into incorrect abdominal wall planes, inaccurate descriptions of reconstruction surgery, and potentially unsafe practice. Our new standardised definitions for LOD will also improve clinical practice. Many AWR centres now use an MDT (multidisciplinary team) platform to review preoperative CT scans. LOD is a key hernia descriptor and is often discussed amongst clinicians at these meetings. Our standardised

definitions will result in a common understanding, accurate decision-making and safer practice.

AWR has strong ties to industry because new mesh implants are constantly being designed. New products aim to improve mesh tissue integration and lower hernia recurrence rates, and require interventional trials to evaluate their clinical effectiveness. Companies designing these trials will be able to use our minimum datasets to create meaningful and comparable data. Our paper also introduces methodology criteria for trials, which will produce robust, unbiased data, with meaningful results.

Chapter 10 comprises a prognostic systematic review that identifies predictors of ventral hernia recurrence. This is the first stage of developing a prognostic model for ventral hernia recurrence. Once developed this model will have significant clinical potential, informing a clinician when and when not to operate; thus avoiding fruitless high-risk major surgery if the chances of hernia recurrence are too high.

Chapter 1

Abdominal Wall Reconstruction: The Current Status Quo

1. The Scale of the Problem

Introduction

There has been a striking increase in prevalence and complexity of ventral hernia (VH) disease over the last decade (1). This is due to an ageing population (2), the rise in obesity (3), and a rise in the number of intra-abdominal operations (4). This increase has not been checked by the development of minimally invasive operating techniques, in part due to the requirement of an extraction site (5). To stall this surge in prevalence, rigorous research is required to reduce VH recurrence rates. In this thesis, I assess the present state of the literature and introduce new ways of how to improve research quality and output. The final section presents a systematic review, which analyses the current evidence-base and identifies predictors of VH recurrence informing us when not to operate, thus preventing pointless, high-risk major surgery.

In this chapter, the current status quo of hernia research is outlined. Initially, the impact of VH disease on patients is described, which explains why VHs need to be repaired. Then the increase in prevalence of VH is illustrated, from worldwide and UK perspectives. Next the aetiology of VH disease is explored with a brief discussion on the theory of 'herniosis'. The current research methods used by academic hernia surgeons are then discussed as they attempt to improve hernia repair outcomes by focusing on randomised trials, creating VH grading systems, new surgical repair techniques, national VH databases and VH sub-specialisation programmes. Next, the concept of VH complexity is addressed, and the only published classification system for complexity to date is presented. Lastly, the current difficulties with defining peri-operative variables and trial outcomes are discussed focusing on surgical site infection (SSI), surgical site occurrence

(SSO), and hernia recurrence. This will lead onto chapter 2, which gives an outline of how this thesis attempts to solve some of these challenges.

The Impact of Ventral Hernia Disease

Despite being commonly misunderstood and neglected, VH disease does require operative intervention. If patients do not have their VHs repaired electively, the frequency of emergency surgery increases, often requiring bowel resections due to strangulation or obstruction (6). If patients do not require an emergency repair, their hernias get larger, causing chronic morbidity. Mesenteric stretching (as the bowel prolapses into the hernia sac) can cause bowel ischaemia, chronic abdominal pain, and diarrhoea. Malalignment and degeneration of the abdominal wall muscles leads to an unsupported diaphragm and spine. This can precipitate paradoxical respiratory failure and degenerative osteoarthritis. Obese patients with large VHs are often wheelchair bound and, consequently, have a low quality of life. However, repairing large complex VHs is challenging, with a high chance of post-operative complications and a 30% risk of repair failure, even in specialist centres (7).

In 2014, after accepting the role as Director of Cleveland Clinic's Hernia Centre, Mike Rosen stated;

"hernia surgery is the most common surgery performed but the most neglected. When hernia surgery goes wrong, it results in some of the most despondent, challenged patients with the worst quality of life, who are desperate for improvements. There has been very little innovation for patients with hernias during the past 50 years and the field is ripe for improving outcomes." [1]

In the same year, Professor Ben Poulose, from Vanderbilt Medical Centre, USA, stated;

[1] https://consultqd.clevelandclinic.org/qa-with-dr-michael-rosen-new-hernia-center-director/

"if a patient has colon cancer he can expect virtually the same treatment anywhere in the world but if a patient has an abdominal wall hernia, his treatment can vary significantly between countries, states, hospitals and even within the same practice. That's because the quality of medical evidence just isn't there. We simply don't know what works best. Is a $15,000 mesh device better than a $500 one? We have to stop the madness." [2]

To provide clear evidence and guidelines of how best to reconstruct the abdominal wall, further work is required.

A Worldwide Perspective

Over one-third of Western individuals undergo intra-abdominal surgery during their life-time (4). Approximately 20% will develop a subsequent incisional hernia, the commonest long term complication after abdominal surgery (8). Despite invention of many new operative techniques and mesh implants, recurrence rates after hernia repair remain high. If operative repair fails, the chance of recurrence increases with each subsequent repair (9, 10). These phenomena, together with an increase in the three main risk factors (age, obesity, and number of intra-abdominal procedures), has led to a surge in VH disease prevalence.

In the US, a study published in 2012 found 154,278 inpatient VH repairs were performed in 2006, costing $15,899 per case, totalling $32 billion. This was an increase of nearly 30,000 repairs compared to the 126,548 performed in 2001 (11). The authors estimated that reducing hernia recurrence by just 1% would save $32 million, concluding that hernia research must be given higher priority. By 2015, the number of annual inpatient VH repairs in the US surpassed 200,000 (12), further escalating cost. In 2013, the estimated number of inpatient VH repairs performed in Europe was approximately 300,000, with Germany and France each performing over 60,000 (13).

[2]https://www.mc.vanderbilt.edu/documents/eckharma/files/innovations_1_2013.pdf

Looking at the worldwide literature, a systematic review performed by Bosanquet et al. from Cardiff University reported an overall primary incisional hernia (IH) rate after midline laparotomy of 12.8% at two years follow up (14). This review also reported an increase in prevalence of primary midline IH, averaging 8% in 1980 rising to 16% in 2012 (13); a doubling over 30 years. Again, this is likely due to increases in age (2) and obesity (3).

Ventral Hernia Disease in the UK

The situation is no different in the UK. The obesity epidemic is still on the rise. In 1993, 15% of UK adults were classified as obese, rising to 27% in 2015 (15). In addition, the population is ageing. In 2014, the median UK age passed 40 for the first time, up from 33.9 years in 1974, and the gradual increase in life expectancy and average age is projected to continue (16). To complete the triad of primary risk factors, the total number of all abdominal surgical interventions performed annually in the UK has also risen from 1,810,926 in 2013, to 2,158,201 in 2018 (figure. 1), a 16% rise over 6 years (1). The result, unsurprisingly, is a significant rise in the total number of VH repairs performed each year. In 2010, 19,453 umbilical hernia repairs were performed, increasing to 22,273 in 2018; and the total number of VH repairs has risen from 44,471 in 2010, to 46,395 in 2018 (figure 2) (1). As the number of VH repairs increases, general surgeons are also facing an increase in the number of complex VH repairs. National data concerning this is hard to come by, as there is no accepted definition for complex VH and there is no ICD-10 code. However, Kalms and Partners Medical Device Consultancy have estimated that 20% of all UK VH operations performed are for complex VHs, meaning over 8,000 are performed annually. These abdominal reconstructions are major operations, with an annual estimated cost surpassing £100m (13). Further data relating to the number of repairs on VH recurrences and the number of concomitant procedures performed at the time of VH repair, on a national scale, is currently unavailable. Many major VH repairs require stoma resiting, bowel resections, and complex panniculectomies. To obtain meaningful estimates about the growing impact of VH disease, a national database is warranted.

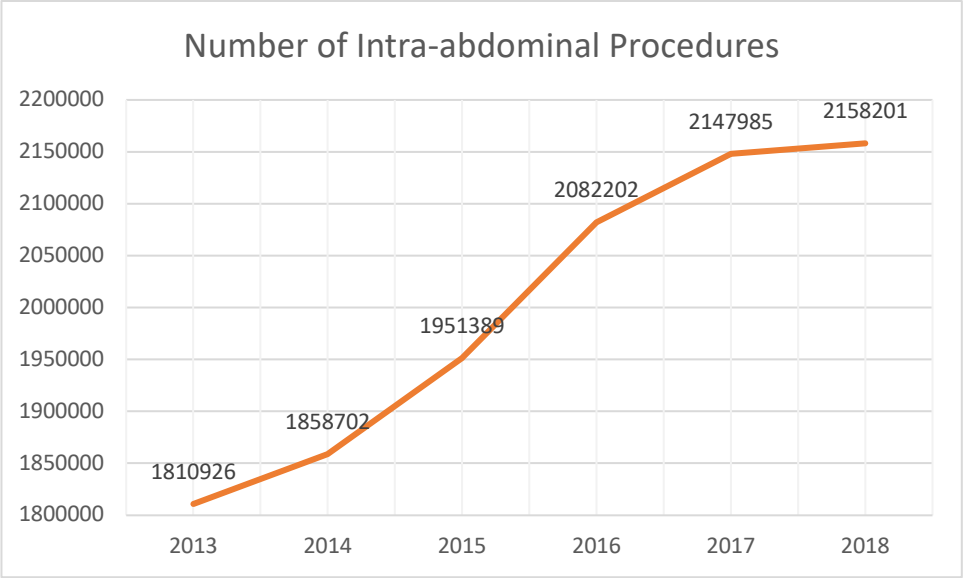


Figure 1. Annual number of intra-abdominal procedures performed in the UK (includes minimally invasive procedures).

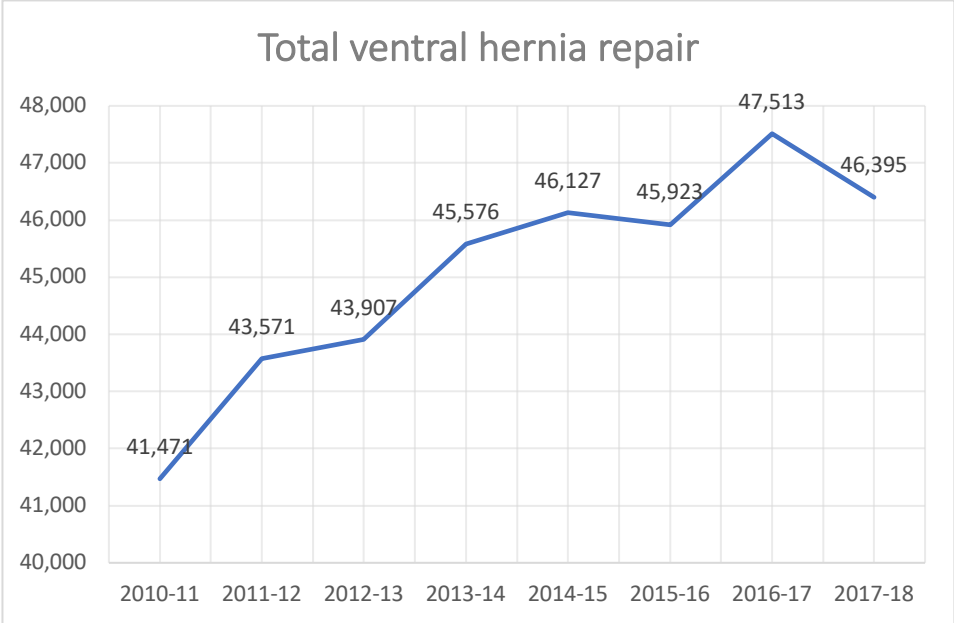


Figure 2. Annual number of VH (VH) repairs in the UK

Aetiology of Ventral Hernia

When considering the aetiology of VH disease, it is helpful to think of primary VH and IH components as two separate pathologies. Primary VHs are referred to as 'de novo' and are typically epigastric, umbilical, para-umbilical, or Spigelian in origin. Primary VHs are prone to develop with any risk factor that is likely to increase intra-abdominal pressure, such as obesity, chronic constipation, benign prostatic hypertrophy (BPH), chronic cough, prolonged manual labour, and pregnancy. In contrast, IHs arise from abdominal incisions (i.e. port sites, midline, Kocher's etc). They can manifest as a primary IH after a previous incision or as a recurrent VH. The aetiology of IH is similar to that of wound dehiscence (17). Often surgeons take tight suture bites spaced too far apart ("large bites" technique) during abdominal wall closure, which can cause ischaemia and tissue necrosis. Thereafter, sutures can slip through necrotic tissue causing the wound edges to pull apart, so that a gap results leading to protrusion of abdominal viscera and IH (17). Alternatively, necrotic tissue can act as a nidus for infection and a resulting wound infection predisposes to impaired wound healing and subsequent IH (18). Smoking, diabetes, obesity, malignancy, malnutrition, steroid usage, advanced age, jaundice, and previous hernia repair all predispose to an increased risk of wound infection, followed by delayed wound healing, and subsequent IH.

"Herniosis" as a concept dates back to the early 20th century and to Sir Arthur Keith, a Scottish surgeon and anatomist who believed that *'herniae'* were not the result of bad luck, but rather were a reflection of the aging process:

'*We are so apt to look on tendons, fascial structures and connective tissues as dead passive structures. They are certainly alive, and the fact that hernias are so often multiple in middle aged and old people leads one to suspect that a pathological change in the connective tissues of the belly wall may render certain individuals particularly liable to hernia*' (19).

In essence 'herniosis' is a term used to describe patients who have a predisposition to both primary VH and IH. Later, in 1948, Charles Saint published

Saint's triad (gallstone disease, diverticulosis and hiatus hernia), and ever since surgeons have been exploring the possibility of a familial or genetic link to the origins of hernia disease and 'herniosis' (20). Indeed, a range of interesting if circumstantial evidence has been published.

In the early 1970's, a study identified that the rectus sheath of inguinal hernia patients was thinner and weighed less than matched controls without hernia, with smaller and more irregular collagen fibrils (21). Lathyrism in rats inhibits collagen cross-linking and significantly increases the rate of hernia formation; if a similar state of affairs is deliberately induced in a rat model, by chemical inhibition of collagen cross-linking, the rate of hernia formation increases (22). Furthermore, patients who have their abdominal aortic aneurysms (AAA) repaired have a much higher incidence of both incisional and inguinal hernia (23, 24), suggesting there is a genetic effect influencing both AAA and hernia formation. Analogous to this, numerous connective tissue disorders such as Ehlers-Danlos, Marfans and Congenital Hip Dislocation have been shown to be associated with increased rates of herniation and abnormalities in biosynthesis of type III collagen (25, 26).

More recently, clinical studies have confirmed a possible association between gallstone disease, diverticulosis, and hernia formation. In 2009, the modified Saint's triad was proposed, which includes hernia formation and not just hiatus hernia formation (27). This phenomenon may be evident clinically, but the biological reasons for why this triad should occur have not been established. However, a genetic explanation for the observed association between hernia formation and diverticulosis (28) is beginning to emerge. Connective tissue analysis shows that in both diverticulosis and hernia patients there is decreased ratio of type I and type III collagen and reduced levels of mature collagen I (29, 30). Consequently, these patients have abnormally weak connective tissue, prone to developing diverticular and hernia defects. As research into the genetic causes of hernia disease continues, there has been particular focus on the role of matrix metalloproteinases (MMPs) in the pathogenesis of abdominal wall hernias, but tissue analysis results have been inconclusive thus far (31). Further research is required to fully define and isolate the multifactorial genetic disorder of "herniosis".

When considering the aetiology of VH disease, a grasp of the pathophysiological process that leads to worsening VH disease is required to understand why VHs are notoriously difficult to repair. If left untouched, VHs enlarge over time. After a defect has occurred in the linea alba, the abdominal strap muscles contract and retract laterally due to mechanical unloading. Due to disuse atrophy, irreversible muscular fibrosis follows and the muscles become stiffer, shorter, thicker and less elastic (32). These anatomical changes have physiological side effects. As intra-abdominal viscera herniate out of the abdominal cavity, intra-abdominal pressure reduces, causing diaphragmatic descent and respiratory dysfunction. Portal venous stasis often occurs, causing mesenteric and bowel wall oedema, and swelling of the hernia sac (33). Venous stasis leads to congested bowel, ischaemic bowel, diarrhoea, and abdominal pain. Lastly, malalignment of the rectus muscles, atrophy of the strap muscles, and reduced intra-abdominal pressure results in an unsupported spine, precipitating chronic back pain. The pathological consequences of large VH was first described by Rives in 1973 and was given the name “eventration disease” (34). Stiff strap muscles, oedematous herniated viscera, and diaphragm descent all make it challenging to return the abdominal contents back into the abdominal cavity. These large VHs with significant eventration are said to have “loss of abdominal domain” or “loss of domain”. Surgeons are using various methods in an attempt to reverse these physiological changes, such as pre-operative botulinum injections or pre-operative pneumoperitoneum. Further work is required to develop the specific indications for each pre-operative technique.

2. Trials and Innovations in Abdominal Wall Reconstruction

Randomised Interventional Trials of Ventral Hernia Repair

The ultimate aim of research is to improve and change clinical practice. Randomised controlled trials (RCTs) report level 1 evidence (Oxford Centre for Evidence Based Medicine (35)), the strongest evidence upon which to base published guidelines and to change practice. In Europe, a series of RCTs

concerning VH have been performed over the last two decades. Some of the most influential are described here.

In 2000, Luijendijk et al published an RCT comparing suture versus mesh repair of incisional VH. At 3 years follow-up, they reported a significant difference in recurrence; 43% of the suture repair patients recurred versus 23% of the mesh repair patients (36). These results were confirmed by a subsequent publication from Berger et al (37), in 2004, which reported a cumulative recurrence of 63% for suture repair and 32% for mesh repair at 10 years follow-up. These results supported the use of mesh in everyday clinical practice, which has been normal clinical practice throughout the 21st century. Recently, Kaufmann et al (38) confirmed that mesh repair was recommended even for small primary umbilical hernias with a maximal diameter between 1 and 4cm. Subsequent guidelines now recommend mesh for VH whose width is 1cm or greater (39).

Over the last 20 years, IH prophylaxis has become a 'hot topic'. Investigators first explored whether the 'small bites' wound closure technique was more effective than 'large bites' closure post midline laparotomy. Israelsson, from Sweden, pioneered this research, and published a single centre RCT in 2009, showing that his 'small bites' technique did significantly reduce IH occurrence at 12 months follow-up (18.0% IH rate 'large bites' vs 5.6% IH rate 'small bites'; p value = <0.001) (40). This triggered a Dutch multi-centre trial, the STITCH trial (41), published in 2015, which confirmed these results, with a 21% IH rate for 'large bites' versus a 13% IH rate for 'small bites', again at 12 months follow-up. Shortly afterwards, RCTs investigating the use of prophylactic mesh after midline laparotomy began to emerge. Muysoms et al (42) published a multi-centre RCT from Belgium in which the interventional group had a large-pore, light-weight, polypropylene mesh inserted into the retro-rectus plane after aortic aneurysm repair. At 2 years follow-up, the intervention group had an IH rate of 0% compared to 28% after conventional suture closure. In the following year, a multi-centre European trial, the PRIMA trial (43), was published. For this trial, prophylactic mesh was placed in either onlay or sublay planes and again compared to conventional suture closure. Only patients with an aortic aneurysm or a BMI greater than 27 were included, thereby selecting a group of patients who were at

higher risk of IH. The results showed IH rates of 13%, 18%, and 30% for onlay mesh, sublay mesh, and suture repair groups respectively at 2 years follow-up; yielding a significant p value of 0.016 for onlay mesh versus suture repair. These trials do suggest that prophylactic mesh does have a place in clinical practice. Consequently, guidelines for abdominal wall closure do suggest mesh usage in high risk patients (44).

Ventral Hernia Grading Scales

At an international meeting of herniologists in Suvretta, Austria, in 1998, Volker Schumpelick called for a classification of IHs, which would enable *'multi-centre trials'* and *'comparison of the literature'*. Consequently, IH classification systems began to be described. Schumpelick published his own grading scale (45) and at a similar time Chevrel and Rath published their own, perhaps better known, classification scale (46). Many other early classification systems were published but none were externally validated nor adopted widely for clinical use. At the European Hernia Society's (EHS) 29th Congress in May 2007, Andrew Kingsnorth, the Society's president, stressed that a classification of VH and IH was important as the literature was comparing 'apples and oranges' (47). This led to the development of the EHS classification systems for primary and incisional abdominal wall hernia (47). This classification system has been adopted widely in the literature, as it is relatively easy to use and attempts to describe and classify VH morphology accurately. Indeed, abdominal wall reconstruction (AWR) surgeons worldwide have adopted this taxonomy and it is currently being used in both European and American VH databases. Due to its popularity, it is useful to consider this classification system in more detail. Firstly, this classification system distinguishes between primary hernias and incisional hernias due to their differing aetiology. The classification system identifies four types of primary hernia: two midline (epigastric and umbilical) and two lateral (Spigelian and lumbar), and has three size categories (small <2cm, medium ≥2-4cm and large≥4cm) (table 1). The incisional hernia classification is more complex. Midline hernias, bordered either side by the rectus abdominis muscles, are classified by their vertical distance from the umbilicus, xiphisternum, and

pubis (Figure 5). Lateral hernias have a similar description but they are classified as lateral to the semilunar line (Figure 6).

E H S **Primary Abdominal Wall Hernia** **Classification**		**Diameter** **cm**	**Small** <2cm	**Medium** ≥2-4cm	**Large** ≥4cm
Midline	Epigastric				
	Umbilical				
Lateral	Spigelian				
	Lumbar				

Table 1. EHS classification system for primary ventral hernia

E H S **Incisional Hernia Classification**			
Midline	subxiphoidal	M1	
	epigastric	M2	
	umbilical	M3	
	infraumbilical	M4	
	suprapubic	M5	
Lateral	subcostal	L1	
	flank	L2	
	iliac	L3	
	lumbar	L4	
Recurrent incisional hernia?		Yes O No O	
length: cm		**width**: cm	
Width **cm**	**W1** <4cm O	**W2** ≥4-10cm O	**W3** ≥10cm O

Table 2. EHS classification system for incisional ventral hernia

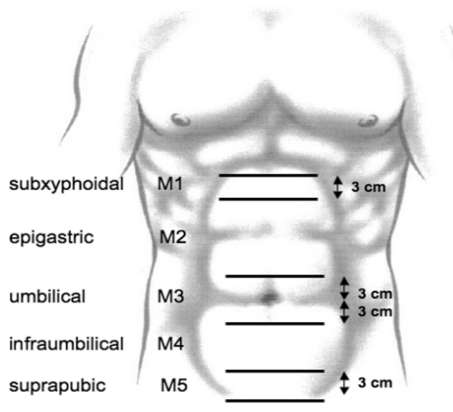


Figure 5. Midline hernias are assessed M1 to M5 and the medial to both semilunar ligaments. M1 (subxiphoidal) is 3cm below the xiphisternum. M3 is 3cm either side of the umbilicus. M5 is 3cm above the pubic bone. M2 and M4 fill in the gaps between M1 and M3, and M3 and M5 respectively.

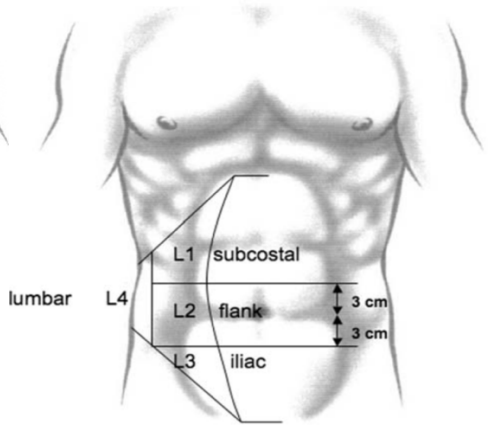


Figure 6. Lateral hernias are lateral to the semilunar ligaments. L1 has the borders of the subcostal margin, the semilunar ligament, a tranverse line 3cm above the umbilicus, and the anterior axillary line. L2 is bordered craniocaudally by two transverse lines 3cm above and below the umbilicus, the semilunar ligament medially and the anterior axillary line laterally. L3 is bordered by the inguinal ligament inferiorly, the semilunar ligament medially, and a transverse line 3cm below the umbilicus. L4 is the region lateral to the anterior axillary line.

Size is defined by greatest width and, if a patient has multiple hernias derived from the same incision, the widths and lengths are summed and taken as a single entity (Figure 7). Again, size is divided into three categories but with higher thresholds; <4cm, 4-10cm and >10cm. Recurrence is classified as “yes” or “no” (table 2). To date, two publications externally validate the EHS classification system. One publication shows a dependence of surgical site occurrences according to EHS classification (48) and the other a dependence of post-operative complications (graded according to the Clavien-Dindo scale) on EHS IH width subgroups (49).

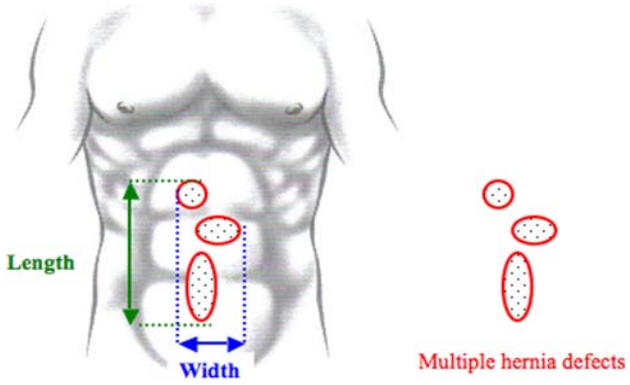


Figure 7. Schematic diagram which shows how to measure the width and length of multiple ventral hernia defects, which have been created by one incision. Essentially, the defects are grouped together and the combined maximal width and length of all defects is used.

In 2010, the VH Working Group (VHWG) grading scale was published by a group of American surgeons (50). This grades VHs according to patient co-morbidity and risk of wound contamination (Figure 4). Patients are categorised into four groups according to their individual risk of post-operative wound morbidity. Grade 1 patients are essentially fit and well, whereas Grade 2 patients have co-morbidities known to increase the risk of wound complication or surgical site occurrence (SSO). Grade 3 patients either have a surgical history of post-operative wound infection or have a repair that involves controlled enterotomy or opening of the abdominal viscera. Lastly, Grade 4 patients have a hernia repair in the presence of active infection. When considering grade 2, what was unknown at the time of creating this grading scale (and remains unknown), is the relative contributions of each co-morbidity; for instance, is it worse to be diabetic or obese? And, if so, how much worse? Clearly, in practice many of these co-morbidities co-exist and, likewise, the weighted cumulative risk is also unknown. The VHWG scale, as well as the EHS classification system, has been widely adopted by many AWR surgeons as it is quick and easy to use (50). Its use has shown promising results when subjected to external validation (51, 52). Several other VH classification systems have been published in recent years (53-57) in an attempt to predict post-operative outcomes, but few have been externally validated and, if so, with limited success (51, 58, 59).

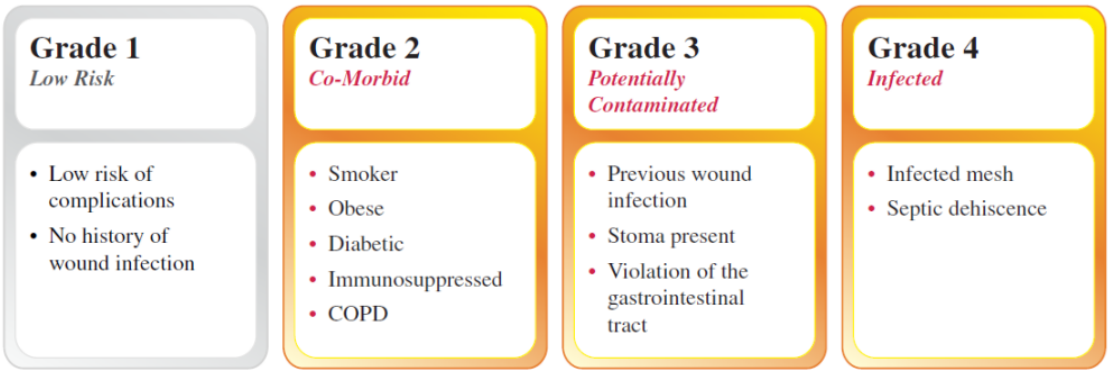


Figure 4. Ventral Hernia Working Group (VHWG) scale for grading ventral hernia (50).

National Ventral Hernia Databases

Throughout surgical practice, multicentre databases have emerged. Pooled data from large population samples can be used by academic surgeons and others to determine complication rates, discover preoperative risk factors to predict operative success, and improve our knowledge concerning the consequences of variations in surgical technique. Worldwide, several VH databases have been implemented; the American Hernia Society's Quality Collaborative (AHSQC) (60), the Danish Ventral Hernia Database (DVHD) (61), the German national ventral hernia database, called HerniaMed (62), and the European registry for abdominal wall hernias (EURAHS) (63) are perhaps the best known. The Danish VH database was the first to be founded, in 2007, and has become a major resource of informative publications. In 2012, a DVHD study of 902 primary and IH patients demonstrated that reoperation rate under-estimates the recurrence rate by a factor of four to five-fold, simply because most recurrences are not repaired (64). In 2013, a publication of 3258 incisional hernia repairs showed that hernia recurrence was significantly more likely after an open VH repair with mesh placed in either onlay or intraperitoneal positions, than when compared to sublay. The same paper showed that an open VH repair (compared to laparoscopic repair) and a hernia width of >7cm significantly subjects a patient to an increased risk of recurrence (65). In 2015, the DVHD published their results for small VH repairs of <2cm in width. This study of 1313 patients demonstrated that, at 43 months follow up, open mesh repair halved the recurrence rate from 21% to 10% compared to suture only repair, with no increase in the rate of post-operative

chronic pain (6% after mesh repair and 5% after suture repair), thereby justifying the use of mesh for the open repair of small ventral hernias (66). Lastly, the DVHD have recently published their long term (5 year) complication rates after elective incisional hernia repair. This showed long-term hernia recurrence rates of 10.6%, 12.3% and 17.1% following laparoscopic repair with mesh, open repair with mesh, and open repair without mesh, respectively (67). The most interesting results from this publication are the other repair-related complication rates of 3.7%, 5.6% and 0.8% respectively, and showed a significant increase in morbidity due to a mesh implant, whether inserted laparoscopically or via open surgery (67). Furthermore, the same publication reported that for both open and laparoscopic repair, an increase in mesh size was directly proportional to an increase in the rate of mesh-related complications (67).

These databases will contribute much to the future literature and to our understanding of VH disease. In particular, they should be used to externally validate VH grading scales, which aim to predict repair success and failure. A validated VH grading scale would be an extremely useful tool for clinical practice.

Surgical Innovation

In the mid 1800s, Billroth predicted the development of prosthetic mesh by writing;

"*if we could artificially produce tissues of the density and toughness of fascia and tendon, the secret of the 'radical cure' for hernia would be discovered*" (68).

Since then, throughout the 20th century, researchers have been seeking a perfect mesh implant. Prosthetic mesh was first made from silver filigree and used by Goepel in Germany (69). Subsequently, other metallic meshes were trialled but their use was unpopular due to a propensity to cause sinus tracts and chronic pain. Polypropylene mesh was first used in 1956, when Sir Francis Usher used a flat sheet of polypropylene mesh (Marlex) to bridge a hernia defect (70). Since then, polypropylene has become widely used. Polyester and expanded polytetrafluoroethylene (ePTFE) are two other plastics used to make synthetic

mesh. In the 1980s, Rives and Stoppa helped to popularise the mesh repair with their independent publications describing the placement of mesh in the retrorectus plane (71, 72).

As well as focusing on surgical mesh, VH research has tried to improve outcomes by using new repair techniques. In 1899, William Mayo announced that his *'radical cure'* for VH involved interrupted silver wire mattress sutures to overlap the edges of the VH defect (73). Nuttall, from the UK, described his technique of *'rectus translocation in the treatment of ventral herniae'* in 1926. In an attempt to close midline ventral defects, Nuttall resected the rectus muscles off the pubis bone and re-inserted them onto the contra-lateral side. Although this technique has not been widely adopted, this encouraged reconstructive surgeons to use more imaginative and complex techniques to try and improve outcomes. In the same publication, Nuttall acknowledges that;

'the difficulties of obtaining a 'radical cure' for large ventral herniae are well known' (74).

Over the last thirty years, many surgeons have designed new and innovative ways to repair VH. To give a detailed description of all these new techniques is beyond the scope of this thesis. However, a list of references of these novel reconstructive techniques can be found in Appendix 1. Despite the discovery of numerous new techniques and the synthesis of many complex new meshes, the complication rates and hernia recurrence rates after repair remain high and the, *'difficulties of obtaining a 'radical cure",* for large VH still remain.

Sub-Specialisation

VH repair is becoming increasingly complex. This is partly due to the rising prevalence of obesity, advancing age, and the high recurrence rate of VH (as each subsequent hernia repair becomes increasingly challenging). Therefore, the presentation of obese, elderly patients with multiple previous VH repairs and a significant history of abdominal surgery (either for cancer or not) is now not unusual. These patients with multiple comorbidities combined with a large,

complex recurrent VHs are extremely difficult to treat. As a result, many European countries have started to introduce national centres for hernia surgery with varying degrees of formality. Germany has the most well-established hernia centre certification system with two processes of certification; either a centre can be certified as a COEHS (Centre Of Excellence in Hernia Surgery) by an independent not-for-profit organisation called the Surgical Review Corporation (SRC), or a centre is certified as a Hernia Centre by the German Hernia Society (DHS) (75).

Established in 2003, the SRC is an internationally recognised organisation that promotes safety, efficacy and efficiency of surgical care worldwide. To achieve its aims, the SRC developed a validated methodology that involves two independent initiatives; a rigorous centre-of-excellence program and a central outcomes database. This integrated approach exemplifies the concept of the "Hawthorne effect" and overtime, program participants improve the quality of their care simply by entering their data and subjecting it to evaluation. The SRC subjects COEHSs to regular site inspections to maintain its high standards (75). The second system of accreditation has been designed and set up by the DHS and comprises three tiers of competence in hernia surgery. To achieve level 1 status, '*certification of quality assurance',* centres must operate on at least 30 hernia patients a year, centres must participate in the national HerniaMed database (62), and the surgeons must be members of the DHS and the EHS with an institutional subscription to the hernia journal. Level 2 status, *'certification of competence'*, involves achieving level 1 status for at least a year, operating on over 200 hernias a year with at least 30 being incisional hernias, offering specialist hernia outpatient clinics, offering day-case surgery for the small hernias, holding a hernia morbidity meeting at least once a month, and evidence of conforming to hernia guidelines. Level 3 status, *'certified hernia reference centre'*, consists of evidence of achieving level 2 status, operating on over 250 hernia a year with at least 50 being incisional hernias, performing both laparoscopic and open surgery, having a contracted plastic surgeon assisting in the complex cases, and publishing at least two papers or posters a year. In addition, all three levels have their own criteria of acceptable post-operative complication rates. By March 2014 the DHS had certified 286 institutions with

their seal of quality assurance, 18 hospitals as centres of competence, and 3 centres as hernia reference centres. Less formal tier systems exist in Denmark with five national hernia specialist centres (76), and Italy (77, 78). In the UK, complex VH patients have traditionally been referred to national intestinal failure units. However there are plans to create hernia centres (79) and to introduce a national triage system for VH (80).

Worldwide, many specialist hernia centres have introduced the multi-disciplinary team (MDT) to their practice (81). During MDT meetings, AWR surgeons can discuss their complex cases with medical nutritionists, radiologists, anaesthetists, bariatric surgeons, and plastic surgeons, with the aim of improving management of pre-operative risk factors and improving post-operative outcomes. MDT meetings allow for clinicians to collaborate and discuss optimal patient management, with a pooled knowledge of the literature, best practice, and expert opinion. High-risk patients with a poor quality of life and desperate for a cure can be discussed in a forum that allows clinicians to debate whether or not surgery should be attempted.

3. Complex Ventral Hernia (CVH)

Complex AWR is a highly skilled procedure often involving many other operations 'patched' together resulting in a bespoke repair. Often there may be an old mesh in situ which may or may not be infected. Commonly, patients have complicated surgical histories which have caused CVH. Has a component separation already been performed? Was the abdomen closed previously or was a skin graft placed over a planned damage control laparostomy? What was the cause of laparostomy? Trauma in a young fit man or an anastomotic leak in a comorbid elderly patient? The range of permutations is exhaustive, which is why the seemingly plentiful literature is insufficient in most cases to tell a surgeon how to proceed in an individual patient based on evidence. So, in the face of all this uncertainty, what defines complexity? Is it the hernia itself or the method chosen to repair it? What contribution does the patient make to complexity? Answering these questions is hindered further by the absence of a precise definition of "AWR", with or without the epithet "complex". Do all complex hernias need an

AWR and are all AWRs done for complex hernias? Is AWR synonymous with component separation or does a Rives-Stoppa repair count as AWR?

These challenges are well illustrated in an American paper detailing 26 AWRs from a single centre using a biologic mesh; 12/28 repairs were for defects smaller than 100cm^2, with seven actually being less than, or equal to, 30cm^2. Two were performed as day cases and another three cases spent only one night in hospital. The reported outcomes (11% recurrence at 16 months) seem reasonable, but it is worth questioning whether all patients actually underwent AWR reconstruction and whether using this paper as supportive evidence for reconstructive surgery would be flawed (82).

Most hernia surgeons will be able to reel off a list of what they think makes a hernia complex, and such a list would probably include size, infection, co-morbidities, and the number of previous attempts at repair. In an attempt to standardise definitions, a series of three industry-sponsored consensus meetings were held to answer the question, “What makes a hernia repair complex?” based on literature review and expert opinion. The output was published in the journal “Hernia” and usefully divided ‘complexity’ into four relevant areas: size and location, contamination and soft tissue condition, patient history and risk factors and, finally, clinical scenario (56). Thus a classification scheme was published that attempts to clarify what constitutes a ‘complex ventral hernia’ (56). It is not my intention to regurgitate the consensus meeting results, but these four sub-headings do provide a useful framework around which to consider complexity. At the time of writing, this is only published definition of CVH (56).

Size and Location

Evidence suggests that increasing hernia size / volume contributes to an increasing risk of complications (83) and recurrence (84, 85). The evidence for how wide a hernia must be in order to be classed as complex is not well supported but opinion leaders quote a width of >10cm (56). Furthermore, proximity of bony prominences (subcostal, lumbar, lateral hernias) increases difficulty of mesh anchorage, thereby increasing recurrence risk, and warrants ‘complexity’; as a

result midline hernia are, in general, less complex than lateral ones. Measurement of hernia volume (86) is a relatively new concept that allows estimation of the chances of tension-free closure; 20% loss of domain is a quoted threshold (87) (i.e. a hernia volume to peritoneal cavity volume ratio of 0.2) above which tension-free repair becomes unfeasible. Consequently, advanced AWR techniques are required, such as component separation, to increase the volume of the abdominal domain. Hernias with a loss of domain greater than 20% are therefore classed as complex. The implication of this are that a pre-operative CT scan, or alternative, should be mandatory to assess size, location, proximity of bony landmarks, and if large, hernia volume and content.

Contamination and Soft Tissue Condition

Evidence of wound contamination contributing to delayed wound healing and greater rates of surgical site infection, surgical site occurrences, and hernia recurrences is compelling (18, 88). Levels of contamination can be divided into four categories according to the American College of Surgeons and the US Centre for Disease Control (Table 3), and serves as a useful descriptor of bacterial load (89).

Class	Definition	Examples	Comments
Clean	An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered. Clean wounds are primarily closed.	Mastectomy, neck dissection, thyroid, vascular, hernia, splenectomy	Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.
Clean-Contaminated:	Operative wounds in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination.	Cholecystectomy, Whipples procedure, liver transplant, gastric surgery, colon surgery	Operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.
Contaminated:	Open, fresh, accidental wounds. Operations with	Inflamed appendix, bile spillage in	

	major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, non-purulent inflammation is encountered including necrotic tissue without evidence of purulent drainage (e.g., dry gangrene) are included in this category.	cholecystectomy, diverticulitis, rectal surgery, penetrating wounds.	
Dirty or Infected:	Includes old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera.	Incision and drainage of abscesses, perforated bowel, peritonitis, wound debridement, positive wound cultures pre-op.	This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

Table 3. The Centre for Disease Control classification system of wound contamination (89).

The consensus meetings agreed that contaminated and dirty wounds should be classified as complex due to their higher risk of local wound complications and recurrence; furthermore, situations that degrade the quality of residual tissues are regarded as complex. Often, this may involve an old laparostomy wound covered with granulation tissue or a skin graft; thus, incisional hernia repair after an open abdomen is again classified as complex. More seldom, this may involve a full thickness abdominal wall defect after either trauma, enterocutaneous fistula resection, tumour resection, or necrotising infection. AWR surgeons working in tertiary care units are often referred patients who have had multiple previous abdominal procedures which have led to the current presenting hernia. Abdominal wall scarring that has occurred as a result of these procedures reduces tissue strength and integrity, making AWR more challenging. This group of clinicians recognised the importance of healthy, clean, well-vascularised soft tissue for hernia repair, and any condition which degrades this implies a more complex surgical undertaking.

Of note, in recent years, there has been much research around prevention of post-operative wound infections (surgical site infections, SSIs). One technique that has been instrumental in lowering SSIs is the design of negative pressure wound dressings. Comparative studies (90, 91) post abdominal wall

reconstruction have shown negative pressure dressings to significantly reduce wound infections rates. These negative pressure dressings are now being used in clinical practice for SSI prophylaxis, particularly for contaminated procedures.

Patient History and Risk Factors

A patient may present with many factors that could mean a hernia repair is either not feasible or the risk vs. benefit balance lies strongly in favour of not operating. A history of hernia recurrence after prior repair is a de facto risk for further recurrence (9, 10). Multiple recurrences may suggest an underlying defect in collagen synthesis (herniosis). Likewise, a previous component separation reduces reconstruction options and increases complexity, as does a previous mesh repair. The literature extensively explores the patient risk factors that increase the chance of recurrence after abdominal wall reconstruction. The consensus meetings (56) determined that the evidence-based risk factors for recurrence were; obesity, diabetes, old age, steroid use and poor nutritional status (albumin <30g/dl), chronic obstructive pulmonary disease, history of previous mesh infection or wound dehiscence, and recurrence repair after previous mesh repair and/or previous component separation.

Clinical Scenario

The final domain felt to be essential for its incorporation into a classification system of complexity was clinical scenario. An acutely irreducible and painful hernia needs urgent attention. If hernias are reducible in the emergency department, they can be managed in the standard fashion with a scheduled repair. Emergency VH repairs with bowel resection was considered to be complex, as was removal of a previously placed mesh. Often this requires extensive adhesiolysis, longer operating times, and an increased risk of enterotomies. If the mesh is infected, then mesh explantation and hernia repair is again even more complex. The group also added a few other clinical scenarios to the classification system; they regarded an abdominal wall with multiple hernia defects, a non-healing abdominal wound, an inability to achieve primary fascial closure, and presence of an enterocutaneous fistula all as complex scenarios.

Complexity

The criteria from each of the four domains were then combined into a complex VH classification system consisting of three classes of severity: 'Minor', 'Moderate' and 'Major' (table 4). This classification system can be used by AWR surgeons for operative planning. With increased complexity, the peri-operative management is increasingly demanding. For example, patients with entero-cutaneous fistulas may require weeks of pre-operative parenteral nutrition so that the active intra-abdominal inflammation settles down, facilitating subsequent surgery. Likewise, patients with burst abdomen may require a temporary procedure before comprehensive AWR. The classification system presented in table 4 is the first published system that attempts to classify complex VH and is an important milestone in VH taxonomy and research (56).

Minor	Moderate	Major
Only one wound healing impairing risk factor[i]	Two or more wound healing impairing risk factors	Two or more wound healing impairing risk factors and one or more 'Moderate' class criteria
	Hernia ≥ 10cm in width, or no primary closure possible without component separation	Surgical wound class III ('Contaminated') or IV ('Dirty').
	Loss of domain ≥ 20%	Open (burst) abdomen
	Parastomal, lumbar, lateral and subcostal hernias	Disease related: necrotizing fasciitis
	Full-thickness defects, loss of substance, distorted anatomy (multiple previous procedures) or multiple hernia defects	Current mesh infection
	Skin grafts, wound ulcers, non-healing wound	Enterocutaneous fistula present
	Disease related: omphalocele.	
	Increased intra-abdominal pressure COPD, obesity	
	History of wound dehiscence or wound/mesh infection	
	Intraperitoneal mesh removal	
	Emergency operation with bowel resection	

Table 4. Ventral hernias defined as either 'Minor', 'Moderate', or 'Major' according their description and the patient's past history. [i] Obesity, diabetes, steroid use, smoking, old age, poor nutritional state (albumin <30 g/dl) (56).

4. Current Outcomes

Studies reporting VH repair predominantly use either surgical site infection (SSI), surgical site occurrence (SSO), or hernia recurrence as the primary outcome. As a rule, these outcomes are used to measure operative success. In addition, many trials use patient reported outcome measures (PROMs) to assess operative intervention (e.g. SF36 (92), EuraHS-QOL (63), EQ-5D (93), HerQLes (94), Carolinas Comfort Scale (95)). These will not be discussed here, but are currently an important component of VH research. Despite their importance, SSI, SSO and hernia recurrence remain poorly defined, and the methods used to detect SSIs, SSOs and recurrence are also highly heterogeneous. These range from patient questionnaires and telephone surveys, to clinical examination and imaging, i.e. USS and CT. If defined, trials may use the EHS's definition for hernia recurrence;

'A protrusion of the contents of the abdominal cavity or pre-peritoneal fat through a defect in the abdominal wall at the site of a previous repair of an abdominal wall hernia' (63).

The Centre for Disease Control's criteria for SSIs are often used, and these divide wound infections into superficial, deep and organ space subtypes (96). Other SSI classification systems exist, including the ASEPSIS score (97, 98). The VHWG defines an SSO as either a wound infection, wound dehiscence, seroma, or development of an entero-cutaneous fistula (50), but many trials define SSOs simply as '*any wound complication'* (99) or *'any event that resulted in delayed healing of the incision'* (18). To assess seroma rates after laparoscopic VH repair, the Morales-Conde classification has been adopted by academics (100). If trials do not use these definitions, then outcomes are often either left undefined, or adhoc definitions are used.

As with many areas of surgical science, post-operative outcomes are dependent upon multiple pre-operative, intra-operative, and post-operative variables. To

discuss each variable in turn would be a lengthy process. As my work is focusing on hernia recurrence, this commentary will focus on hernia recurrence rates. SSI and SSO outcomes will be discussed briefly. As a caveat, in addition to poorly defined outcomes, trials are often not specific enough in their inclusion and exclusion criteria, and interpreting outcomes for clinical use can therefore often be challenging.

Surgical Site Infections and Surgical Site Occurrences

Concerning VH repair, CDC contamination grade has been known to significantly affect wound complication rates, as shown by Choi et al's publication (101). This paper used National Surgery Quality Improvement Project (NSQIP) data to analyse outcomes from 33,832 patients. All modes of surgery and hernia types (primary and incisional) were included. Her results show SSI rates of 3.0%, 5.0% and 10% for clean, clean-contaminated and contaminated VH repairs respectively, with a significant individual difference between all groups. Reported case series have confirmed this phenomenon: Cobb et al reported an SSI rate of 15.6% in clean open VH repairs, significantly increasing to 25.7% in open repairs at risk of contamination (p value = 0.046) (18). Furthermore, in 2013, Mike Rosen reported a series of 128 open complex VH repairs, again all at risk of contamination[iii]. He reported an SSO of rate of 48%, and a rate of major SSIs requiring operative intervention of 22%.

In 1999, Bruce Ramshaw published a retrospective study comparing open and laparoscopic VH repair. This study included 253 patients; primary VHs with a diameter greater than 4cm, and all patients with recurrent VHs, were included. His results suggested a lower SSI rate (2.5% vs 3%) and a lower SSO rate (5% vs 10%) for laparoscopic surgery (102). Since then, other trials and systematic reviews have confirmed this. Rogmark et al (103) published a randomised controlled trial (RCT) in 2013, including 131 participants, all with VH defects of less than 10 centimetres in diameter. Post-operative SSI (1.5% vs 23%) and SSO (4.6% vs 37.7%) rates significantly favoured laparoscopic compared to open surgery. A Cochrane review, including 10 RCTs comparing laparoscopic and

open VH repair, stated, *'the most clear and consistent result was that laparoscopic surgery significantly reduced the risk of wound infection'* (104).

The anatomical plane of mesh insertion has also been shown to affect SSI rates. Timmermans et al meta-analysed 10 studies, showing sublay mesh placement significantly reduces SSI rates (OR: 2.42; 95% CI, 1.02 to 5.74; P = 0.05), compared to onlay placement (105). This is supported by a systematic review published in 2016 that compared sublay mesh insertion to onlay, inlay, and intra-peritoneal mesh locations. This review concludes that, *'sublay was associated with the lowest risk of SSI (OR 0.449 (95 % CI 0.12–1.16)) and was the best of all 4 treatment modalities assessed'*. Seroma rates were also shown to be lowest with sublay mesh insertion (106).

Surgical technique used for hernia repair is of particular interest to academic hernia surgeons. Briefly, primary fascial closure seems to reduce incidence of both SSIs and SSOs significantly when compared to a bridging mesh implant (107, 108). Krpata et al compared 111 open VH repairs treated with either anterior component separation (ACS) or posterior component separation (PCS) (109). They found ACS to be significantly more pre-disposed to SSOs compared to PCS. However, in a recent systematic review, no difference was found in SSO rates when comparing ACS and PCS (110). Endoscopic component separation (ECS) is a technique becoming more in vogue. In theory, it should reduce wound complication rates as the superficial perforator vessels supplying the skin are preserved. In a recent systemic review, which included 5 retrospective comparative studies and 163 patients, ECS was found to significantly reduce the incidence of SSOs compared to open ACS (111).

Hernia Recurrence

VH recurrence is an outcome of particular relevance to this thesis. In this section, the key variables that affect hernia recurrence are discussed. Thereafter, the changes in recurrence rates over the last twenty years are reviewed, as well as whether or not the true rates of VH recurrence and IH occurrence are actually known.

Regarding mode of surgery, the literature reports no difference in recurrence rates when comparing laparoscopic and open surgery (104). Large case series of open VH repairs report recurrence rates ranging from 8% (112) for simple VH repairs to 31% (7) for complex repairs, with recurrence rates increasing with levels of contamination (113) and size of hernia defect. The Danish Ventral Hernia Database has shown recurrence rates to increase significantly when the maximal hernia defect width exceeds 7cm. Other papers have found a significant increase in defect width to correlate positively with higher recurrence rates; however, the chosen cut-off point varies. Booth et al showed a maximal diameter greater than 15cm is associated with increased recurrence (114), whereas Kurmann et al, found a significant increase in recurrence above 10cm (115).

Perhaps the two most important patient factors predisposing to hernia recurrence are BMI and number of previous VH repairs, with a number of publications demonstrating this (9, 10, 116). Studies show recurrence estimates as high as 37%, 66% and 73%, after primary, secondary and tertiary repairs respectively, at 10 years follow up (10). Many other publications have investigated other patient factors, such as diabetes, smoking, chronic obstructive pulmonary disease, benign prostatic hypertrophy, to determine if they predispose to recurrence, and many have found an association. However, further research is required to definitively identify the clinical parameters associated with recurrence (see Chapter 2 and Chapter 10).

Other variables that appear to play a key role in determining whether or not VHs recur are the intra- and post-operative variables. These include mesh versus suture repair, the plane of mesh insertion, a bridging mesh versus primary fascial closure, anterior versus posterior component separation, endoscopic or perforator sparing repairs, and post-operative wound infections. Level I evidence exists for mesh repair rather than suture-only repair to significantly reduce VH recurrence (37). Regarding plane of mesh insertion, both database studies (65) and systematic reviews (105, 117) have shown the sublay plane (retro-rectus plane) to be optimal and result in lower recurrence rates but, as will be shown later, the plane of mesh insertion is often poorly defined in primary studies,

making conclusions drawn from the secondary literature (meta-analysis and systematic review) uncertain (Chapter 9). Much like SSI and SSO rates, recurrence rates have been shown to increase with a bridged mesh repair rather than when primary fascial closure has been achieved (107, 114). Comparative analyses of open VH repairs using either ACS or PCS have shown trends towards lower recurrence rates with the PCS technique, but without statistical significance (109, 110). Endoscopic and perforator sparing techniques have both shown promise in reducing recurrence rates with statistically significant results (107). Lastly, post-operative SSIs and SSOs are well known to delay wound healing and predispose to recurrence (118, 119), much like wound infection post laparotomy has been shown to predispose to incisional hernia (17, 18).

When assessing the 'state of the literature', it is important to take study type into account when analysing the operative outcomes, particularly hernia recurrence. Anecdotal hernia recurrence rates reported from single surgeon case series do seem to report lower recurrence rates, at around 5% (99, 120, 121). This could be due to a reduced length of follow-up, as authors are eager to publish their new repair techniques. It may be due to the hernia recurrence detection method used, whereby patient telephone calls and questionnaires are unlikely to be as sensitive for detecting recurrence as imaging techniques (ultrasound, CT or MRI). In addition, there may well be publication bias, as authors are keen to publish low complication rates. Comparative trials with improved trial methodology, and database studies with regional or national follow-up data, appear to report higher recurrence rates. Burger et al published cumulative recurrence rates of 32% and 63% after mesh and suture VH repair respectively, after 10-year follow-up (37). The DVHD published a cumulative risk of reoperation for recurrence of 18.3% with 48 months follow-up (65).

Whether VH recurrence rates have improved over the last twenty years, despite much surgical innovation, is debateable. Insertion of a prosthetic mesh undoubtedly lowers recurrence rates but, excepting this, there has been no obvious new intervention with such a significant impact. Flum et al. in 2003 published primary IH repair recurrence rates from a database of 10,822 patients. The results were reported pre- and post-1995, and both periods reported

recurrence at 12.3%. 1995 was used as a cut-point to assess whether the introduction of laparoscopic surgery improved recurrence rates which, in this population, it did not. Similarly, in 2016, the DVHD published its recurrence rates after open elective VH repair at 12.3%, after 59 months follow up (67). Consequently, it seems that recurrence rates have not changed significantly over the last 20 years, and so the search for a 'radical cure' for VH continues.

There is, however, some doubt as to whether true VH and IH recurrence rates are ever reported. Results from the DVHD have demonstrated that reoperation rates (frequently used to estimate VH recurrence rates) under-estimate hernia recurrence four- to five-fold (64). In addition, a publication from Spain reported the true umbilical trocar IH rate at 26% after laparoscopic cholecystectomy at 47 months of follow up. Previous estimates of umbilical trocar IH rates had been reported at between 1-2% from clinical examination (122). Consequently, it seems that VH recurrence rates and IH rates are likely to be grossly under-reported due to either use of re-operation rates or loss to follow-up.

Summary

The current status quo within VH surgical science has been outlined. Worldwide and UK evidence shows VH prevalence is increasing. Quotes from international hernia experts illustrate why urgent research into VH repair is warranted. Thereafter, how VH repair has evolved over the last 20 years as a sub-specialty has been illustrated; by highlighting key trials and studies that have changed practice, by mentioning innovative changes in surgical practice, new international and national databases, and by describing novel VH grading scales. In the last two sections, two of the most challenging issues for VH academics were highlighted; firstly, how is a 'complex VH' defined, and secondly, that clinical outcomes (SSIs, SSOs, hernia recurrence, PROMs), and other peri-operative variables (e.g. mesh location) are poorly defined and are unstandardised. Both challenges introduce bias into VH interventional trials and must be tackled by academics so that high quality robust and comparable research is produced.

Chapter 2

Improving Research Quality and Identifying Predictors of Ventral Hernia Recurrence: Hypotheses and Aims.

Chapter 2 outlines how our research evolved from the initial concept of creating a prognostic model for VH recurrence, to a project mainly based on improving research quality prior to development of our model. Our work on research quality stems from the issues raised in Chapter 1; namely, that many variables in VH academia are poorly defined and lack standardisation.

Prognostic Model Development

As the prevalence of VH increases (11) and as recurrence rates remain high (7), the burden of VH disease on healthcare systems escalates. Currently, recurrence rates after repair are reported at between 15-30% (7, 18), despite much surgical innovation (Appendix 1). To help avoid recurrence, and to prevent pointless, high-risk surgery, our research group hypothesised that a VH prognostic model, predicting hernia recurrence, could be built using predictors extracted from the literature and developed using data from our own series of VH repairs at University College London Hospital. A validated prognostic model for VH recurrence will help inform surgeons and patients when the risk of recurrence is too high to attempt surgical repair. It will also help them to pre-operatively optimise patients prior to surgery taking the risk of recurrence from high to low.

Stage 1 of Model Development

The development of our prognostic model has four stages. Stages 2 to 4 are explained in the final Chapter of this thesis. Stage 1 (Chapter 10) involves extensive systematic review of the indexed literature, extraction of prognostic data for hernia recurrence, and subsequent meta-analysis. Meta-analysis is used to identify the peri-operative predictors that predispose significantly to VH recurrence. These predictors (and others if deemed clinically important) will be then incorporated into the prognostic model.

At the start of my PhD tenure, I began work on stage 1. Our research group decided to review the literature from January 1st 1995 to 1st January 2018. Prognostic data for recurrence were extracted in the form of 2x2 tables, odds ratios, risk ratios, and hazards ratios. All pre-, intra-, and post-operative variables associated with hernia recurrence were extracted, together with the method of recurrence detection, study characteristics, and a risk of bias assessment was performed for each included study. Risk of bias was assessed using an adapted version of the PROBAST tool (Prediction model risk of bias assessment tool (123)), hernias were divided into primary and incisional hernia subgroups in keeping with published guidelines, that recommend primary and incisional hernia be investigated as separate entities (124).

However, after embarking on stage 1 of model development and after starting data extraction, it became apparent that there was a drastic lack of standardisation throughout the AWR literature, sufficient to prevent my work progressing without first addressing these problems. In particular, during review of the literature, I identified poorly defined and unstandardised pre- and intra-operative variables, inadequate trial methodology, unstandardised outcome definitions and detection methods, variable definitions used to describe ‘loss of domain’ and a lack of consistency for terms used to describe the abdominal wall planes. This lack of consistency and standardisation made interpretation of the literature challenging, and often meaningless. After discussing these findings amongst our research group, we concluded there was a large amount of work to be done to establish common definitions and detection methods for many

variables within this field of surgical science, and that this work was needed urgently. As a result, my initial research objectives changed and were aimed at establishing a common language amongst abdominal wall academics, with standardised peri-operative variables and defined outcomes. Once established, this common language would achieve the very important aim of subsequent robust high quality unambiguous research. Part 1 of this research therefore focuses on improving research quality, and part 2 reports the initial stages of prognostic model development.

Research plan

- Part 1: Improving research quality; demonstrating and correcting the current inconsistencies in the literature, specifically aiming at;
  1) outcome definitions and detection methods, peri-operative variable definitions, standardised minimum datasets and methodology for interventional trials of VH repair.
  2) the definitions used for 'loss of domain'
  3) the terms used to name abdominal wall planes,

- Part 2: Extensive systematic review, extraction of prognostic data and subsequent meta-analysis in order to identify predictors that may be incorporated into a prognostic model for VH recurrence.

Research Hypotheses and Aims

Part 1: Improving Research Quality

Systematic Review: **Outcome definitions and detection methods, peri-operative variable definitions, minimum datasets and methodology for interventional trials of VH repair.**

Hypothesis 1

I hypothesize that randomised controlled interventional trials of VH repair collect highly heterogenous data, with poorly defined peri-operative variables and post-operative outcomes. Focusing on trial outcomes, particularly hernia recurrence, I hypothesize that trials have no standardized outcome definitions and detection methods, and no standardised follow-up times. I also hypothesize that randomised controlled trials generally have poor research methodology that leads to a high risk of bias.

Aim 1

To demonstrate that the peri-operative variables and post-operative outcomes collected by VH randomised controlled trials are heterogeneous. I aim to show, via systematic review, there is an urgent need for clear variable and outcome definitions, and for standardised minimum datasets for VH randomised controlled trials.

Hypothesis 2

I hypothesize that non-randomised interventional trials of VH repair generally have poor methodology and do not adhere to published guidelines. Regarding peri-operative data collection, I hypothesize that trials generally collect varied and poorly defined variables. Focusing on trial outcomes, particularly hernia recurrence, I hypothesize that trials generally have no standardized outcome definitions and detection methods, and lack standardised follow-up times.

Aim 2

To demonstrate that current VH non-randomised interventional trial methodology is generally poor, and that data collection is highly heterogeneous with poorly defined peri-operative variables and post-operative outcomes. I aim to show, via systematic review, there is an urgent need for clear peri-operative variable and outcome definitions, and for standardised minimum datasets for VH interventional trials.

Systematic Review: Definitions for Loss of Domain

Hypothesis

I hypothesize that throughout the literature the term 'loss of domain' is poorly defined. I hypothesize that several written and volumetric definitions exist in the literature, with no standardisation.

Aim

To demonstrate, via systematic review of the indexed literature, the current heterogeneity of both the written and volumetric definitions for 'loss of domain'.

Clinician Survey: Definitions for Loss of Domain

Hypothesis

I hypothesize that general surgeons, who regularly perform VH repairs, have a poor understanding of the concept of loss of domain, with no generally accepted volumetric definition amongst clinicians and no therapeutic cut-point above which surgeons should not operate.

Aim

To demonstrate, via face-to-face survey, that loss of domain is poorly understood amongst practising surgeons with no standardised volumetric definition or diagnostic cut-point

Nominal Group Technique: **Outcome definitions and detection methods, peri-operative variable definitions, minimum datasets and methodology for interventional trials of VH repair.**

Hypothesis

I hypothesize that by using a group of expert panelists (i.e. key opinion leaders) and a solution generating technique, such as the Nominal Group Technique (125), I can reach group consensus on minimum datasets for VH interventional trials. As guidelines suggest that primary and incisional VHs should be investigated separately, I hypothesize that two minimum datasets should be generated.

Aim

To create standardised minimum datasets for interventional trials of both primary and incisional VH using a group of expert panelists and the Nominal Group Technique. In doing so, I aim to standardise peri- and post-operative data collection for VH trials. These datasets will include defined perioperative variables, clear outcome definitions and standardised detection methods, patient reported outcomes and guidance/criteria for high quality trial methodology.

Delphi Methodology: **Definitions for Loss of Domain**

Hypothesis

I hypothesize that by using a group of expert panelists (key opinion leaders) and an interactive forecasting technique, such as Delphi methodology, I can use group consensus to reach written and volumetric definitions to describe 'loss of domain'.

Aim

To establish, using Delphi methodology, precise written and volumetric definitions for 'loss of domain'.

Delphi Methodology: An International Classification of Abdominal Wall Planes

Hypothesis

I hypothesize that by using a group of expert panelists (key opinion leaders) and an interactive forecasting technique, such as Delphi methodology, we can reach consensus on the correct terms to use to describe the abdominal wall planes.

Aim

To establish, using Delphi methodology, a new classification system for the abdominal wall planes used for mesh insertion during the VH repair.

Part 2: Prelude to Prognostic Model Development

Systematic Review and Meta-analysis: Identifying the Predictors of VH recurrence.

Hypothesis

I hypothesize that by systematic review, prognostic data extraction, and subsequent meta-analysis I can identify potentially significant predictors of VH recurrence.

Aim

To carry out extensive systematic review of the indexed literature to identify and extract available prognostic data. Subsequent meta-analysis will identify which variables are statistically significant, and which thereby may predispose to VH recurrence. This will aid selection of which predictors are used to develop a prognostic model.

The following chapters will address the hypotheses and aims outlined above.

Chapter 3

A Systematic Methodological Review of Reported Perioperative Variables and Postoperative Outcomes from Randomised Controlled Trials of Elective Ventral Hernia Repair

Part 1: Improving Research Quality

Systematic Review: Outcome definitions and detection methods, peri-operative variable definitions, minimum datasets and methodology for interventional trials of VH repair.

Hypothesis 1

I hypothesize that randomised controlled trials of VH repair collect highly heterogenous data with poorly defined peri-operative variables and post-operative outcomes. Focusing on trial outcomes, particularly hernia recurrence, I hypothesize that trials have no standardised outcome definitions and detection methods, and no standardised follow-up times. I also hypothesise that trials have poor trial methodology with high risk of bias.

Aim 1

To demonstrate the heterogeneous peri-operative variables and post-operative outcomes collected by VH randomised controlled trials. Our aim was to show, via systematic review, there is an urgent need for clear variable and outcome definitions, and for standardised minimum datasets for VH interventional trials.

Introduction

During data extraction the VH prognostic model development, I found that VH trials and observational studies collected highly heterogenous data with poorly defined perioperative variables and post-operative outcomes. In particular, I noticed that studies used different definitions for recurrence as well as a variety of techniques to detect recurrence. As a result, I decided to investigate this

formally via systematic review.

In this systematic review, I analysed randomised controlled trials (RCTs) of adult patients undergoing elective VH repair. All VH repair RCTs were included irrespective of the intervention and comparator groups. I analysed all perioperative variables and post-operative outcomes reported, paying particular attention to the different methods used to detect and define hernia recurrence. My objective was to demonstrate the inconsistencies in variable and outcome reporting by RCTs and the necessity for standardised trial datasets as well as clear definitions of hernia recurrence and recurrence detection methods. Validated datasets for VH repair studies would make reported data consistent, allowing for greater accuracy of trial comparison and meta-analysis.

Methods

Reporting and Registration

This systematic review was reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (126). A protocol was developed and registered with PROSPERO, the international prospective register of systematic reviews (CRD42016043071).

Inclusion and exclusion criteria

Inclusion criteria for studies

We aimed to identify RCTs that described clinical outcomes in patients following VH repair between 1st January 1995 and 31st March 2016 inclusive. We excluded trials with less than 10 patients in an individual study arm since such data are likely to be weak. Only RCTs written in English were included.

Target condition

The target condition was surgical VH repair. All different VH morphologies were eligible as were all VH working group (VHWG) grades (50). Studies describing femoral and/or inguinal hernias (i.e. groin hernia) were excluded. Emergency VH repair was excluded as was primary closure after damage control laparotomy. However, patients having elective VH repair after primary closure from damage control laparotomy were eligible, as were RCTs of elective VH repair with bridging repair (i.e. failure to establish primary fascial closure). RCTs of parastomal hernia repairs were excluded. Trials with concomitant bowel resection were included (since this is often intended) and as long as the primary objective of surgical repair was VH repair. We excluded trials with either concomitant tumour removal or bariatric surgery.

Participants

Adult participants having a surgical VH repair. We excluded paediatric studies (defined as 18 years or less) since these are not representative of 'typical' VH patients.

Follow up

We stipulated no minimum length of follow-up.

Comparison

There was no restriction placed on any study arm comparator (e.g. operative technique, mesh type, position of mesh).

Search strategy and string

I searched the PubMed database from 1st January 1995 to 31st March 2016 inclusive limiting the search using the following terms: "adult 19+", "human studies" and to those written in English. My search string identified and combined the two following criteria to identify relevant articles:

- To identify studies of VH disease including complex disease we used the MESH terms “hernia”, “abdominal hernia”, “umbilical hernia” and “ventral hernia”. These were combined with keywords: “abdominal wall reconstruction”; “herniorrhaphy”; “ventral defect” and “entero-cutaneous fistula”.
- To identify studies of surgical techniques used for VH repair we used the MESH terms “general surgery”; “reconstructive surgical procedures” and “surgical mesh”. This was combined with keywords: “pneumoperitoneum”, “botox”, “botulinium”, “two-stage”, “two step”, “staged repair”, “component separation”, “transversus abdominis”, “retro-rectus”, “bridging”, “bridge repair”, “silo”, “open” and “laparoscopic”.

Our complete search string is shown in Appendix 2.

Citation management and screening

I stored identified citations in an Excel spreadsheet (Microsoft Excel for Mac 2011 Version 14.5.9, Microsoft Corporation, Washington, USA), up-loading these subsequently into a reference manager able to access online original articles directly (Mendeley Desktop Version 1.17 for Windows XP and Mac OS X, London, UK). After the search filters were applied and duplicates were excluded, the citations were divided into two equal groups. The titles of the first half of the citations were screened by myself and the second half by a second research fellow, Dr Chris Wood (CPJW). The researchers screened for comparative studies of VH disease. They discarded articles that were ‘clearly unsuitable’ for the review (e.g. subject not VH) and retained any regarded as ‘uncertain’ or ‘definitely possible’. These two latter groups were combined and researchers, CPJW, Richard Boulton (RWB) and I then independently screened the titles and abstracts of the ‘uncertain’ and ‘definitely possible’ results with the aim of identifying all comparative studies. Any discrepancies were settled by face-to-face discussion amongst the three researchers. A third hand search of the full text by CPJW, RWB, and I then divided the selected comparative studies into respective methodological designs; case-control studies, cohort studies and RCTs. Any article where uncertainty persisted was discussed with senior

members of the research group face-to-face. An exclusion log was kept at all stages. The PRISMA diagram (figure 1) shows the flow of article selection.

Data extraction

James Butterworth (JB) and I extracted data independently from all RCTs selected for the review, which were cross-checked subsequently face-to-face. Data were entered by the researchers into an Excel datasheet and categorised into broad groups as follows: study design; hernia morphology; pre-operative patient factors including comorbidities; intraoperative variables and clinical outcomes, including complication rates and hernia recurrence.

Study demographics and risk of bias

Information extracted for RCT study design included: the study setting (multi-centre vs. single centre), the country of publication, the date of publication and the number of patients in each study arm. JB and I used the Cochrane Collaboration's tool to assess the risk of bias (127). Any differences in opinion were discussed face-to-face and settled by discussion with senior authors if required.

Hernia morphology

For hernia morphology, we intended to record dimensions of the hernia defect, including area, loss of domain, the ventral hernia working group (VHWG) grade (50) and the CDC wound classification (89). We recorded whether the study included patients with either primary or incisional VHs, or both, and if so the proportion of these two hernia types. However, I anticipated that many trials would not report these details of hernia morphology and grade, and we recorded when these items were not reported. Similarly, we recorded the number of previous attempts at hernia repair where documented. We noted prior surgical site infection in patients undergoing repair since this is known to predispose to subsequent recurrence (128).

Pre-operative patient characteristics and co-morbidities

Baseline patient characteristics extracted were mean patient age and the proportion of male to females. Comorbidity data included the mean and standard deviation of body mass index (BMI), the proportion of patients with chronic obstructive pulmonary disease (COPD), liver cirrhosis, diabetes, steroid use, and the proportion of each American Society of Anaesthesiologists (ASA) grade (and mean ASA grade) in each study group. Proportion by smoking status, arteriopath status (previous diagnosis of ischaemic heart disease (IHD), peripheral vascular disease (PVD), cerebrovascular accidents (CVAs)) and a diagnosis of benign prostatic hypertrophy (BPH) were also noted.

Intra-operative variables

We recorded the mode of surgery used (e.g. laparoscopic or open), the type of mesh (where used), the anatomical layer within the abdominal wall into which the mesh was implanted (i.e. intraperitoneal, pre-peritoneal, retro-rectus, inlay or onlay), operative duration, intra-operative blood loss, and the experience of the principal surgeon where documented.

Reported Clinical Outcomes

Hernia recurrence

Our outcomes of primary interest were; hernia recurrence, the post-operative recurrence rates, the timing of recurrence, the definitions for VH recurrence used, and the test method(s) used to diagnose recurrence (for example clinical examination, CT scan, US scan); all were recorded. These data were analysed to investigate whether the method used to detect recurrence influenced recurrence rate. As I was aware of no generally accepted imaging definition of VH recurrence, I anticipated considerable inter-observer variability for reporting recurrence.

I did not pre-specify the definition of post-operative hernia recurrence. I did not restrict by timing of recurrence, the definitions for VH recurrence used, or the test method(s) used to diagnose recurrence.

Secondary outcomes

Post-operative complications

All post-operative complications described were recorded. Complications were grouped into intraoperative, early postoperative, late post-operative, and general or standardised outcomes. Early postoperative complications were sub-grouped into local wound complications (wound infection, seroma formation, wound dehiscence, skin necrosis) and systemic complications (hospital acquired pneumonia, myocardial infarction, pulmonary embolism). Early post-operative complications were defined as those occurring within 30 days of surgery and late post-operative complications as those occurring thereafter. Late complications were extracted for the timespan presented in the paper.

Standardised outcomes

Where reported, we recorded all standardised post-operative outcome measures used. I anticipated that RCTs would use a variety of outcome measures such as length of hospital stay, 30-day re-operation rate and 30-day re-admission rate. If trial complications were measured using a standardised post-operative complication scale, the value was recorded.

Patient reported outcome measures

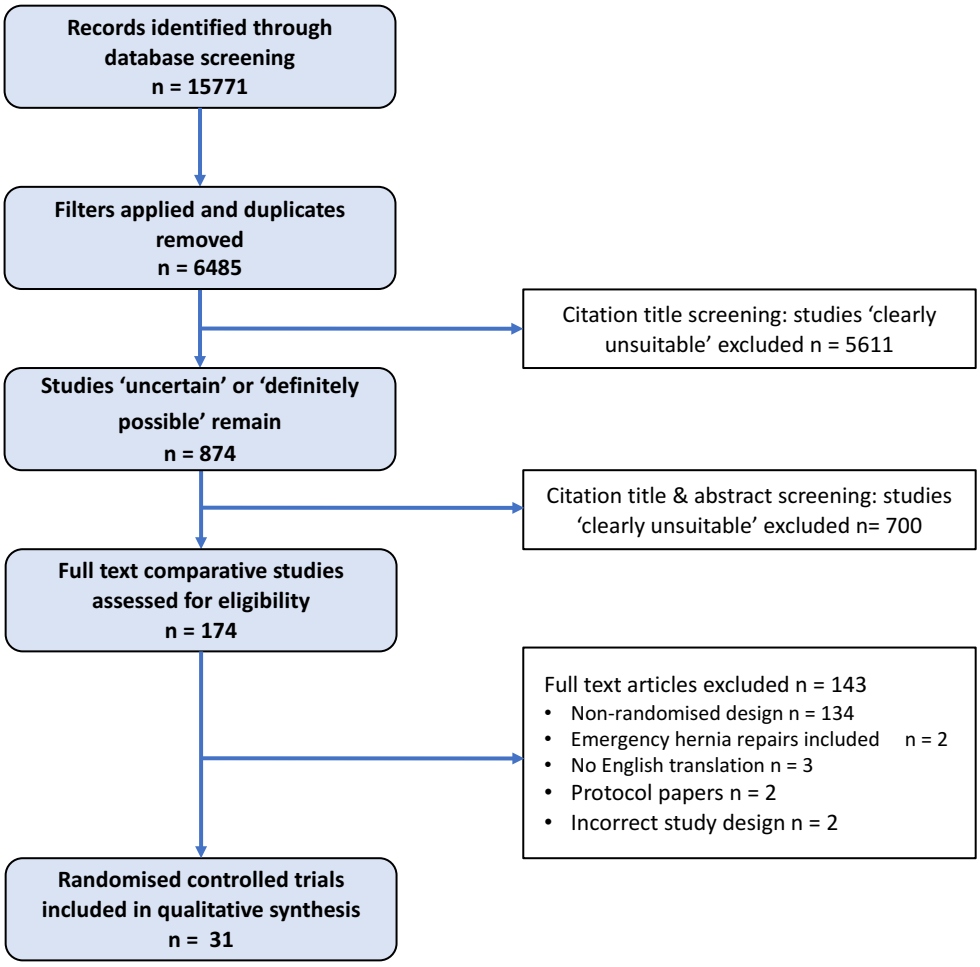
I foresaw that some trials may use standardised patient reported outcome measures (PROMs) to measure operative success. These may include visual analogue scales for pain or overall health status. They may also report the time to first bowel movement or the time taken to return to normal activities. All such outcomes were recorded, along with the timing of the assessment.

Results

Search results

Our initial search retrieved 15771 results (fig 1.). After applying search filters (studies published between 1st January 1995 to 31st March 2016, human trials only, participants aged ≥19, studies written in English), we excluded 9286 studies, resulting in 6485 papers for our initial review. After screening the citation titles, we ultimately categorised 874 studies as 'definitely possible' or 'uncertain'. This fell to 174 comparative studies after title and abstract screening. The full text of all 174 articles was assessed for details of study methodology. This identified 31 RCTs included in the present systematic review.

Figure 1. PRISMA diagram showing selection of RCTs for this review



Study demographics

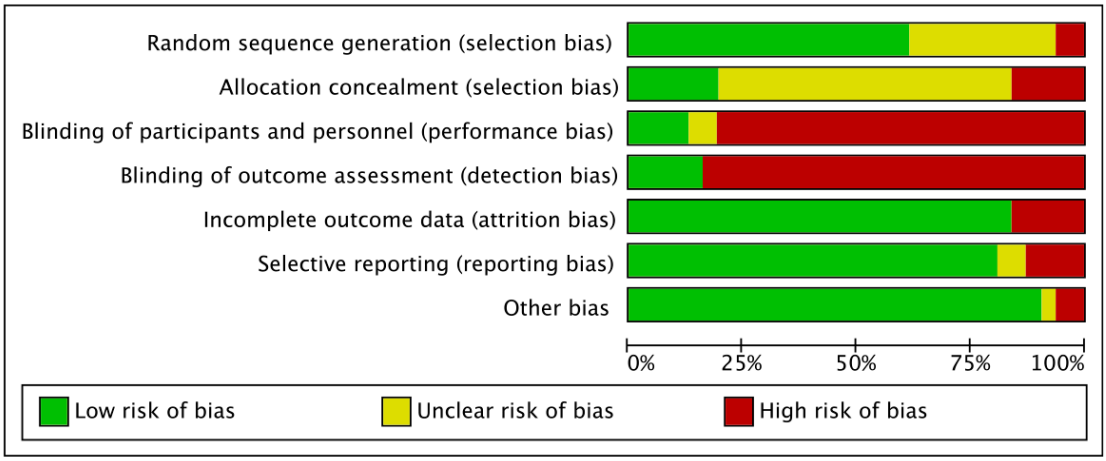
Study demographics and design characteristics are shown in Table 1. The 31 RCTs included 3,367 patients with a mean of 109 patients, range 24 to 337. One study (129) appears twice since it divided patients into simple and complex hernia groups, creating two individual trials (suture vs mesh repair and prosthetic mesh vs auto-dermal graft repair). Five RCTs were carried out in both the Netherlands (36, 130-133) and Spain (134-138). Thirteen RCTs were multi-centre and 18 were single centre. Over the past 20 years the number of RCTs performed increased, with 8 published between 1995 to 2005 versus 23 published from 2005 to 2016. There were 3 groups where RCTs compared the same interventions: Eleven studies compared laparoscopic versus open repair; 5 studies (36, 129, 136, 139, 140) compared suture versus mesh repair and 3 studies (137, 141, 142) compared tack versus suture mesh fixation in laparoscopic VH repair.

Table 1. Demographic and characteristics of the 31 RCTs included in the Systematic Review.

Included Studies - Demographics		
Characteristic	**Subgroup**	**No. of RCTs**
-Country of Publication	Netherlands (36, 130-133) Spain (134-138)	5
	India (141-143) Egypt (144-146)	3
	Pakistan (140, 147) Turkey (139, 148) Italy (149, 150) Germany (129, 151)	2
	Sweden (103) USA (152) Australia (153) Lithuania (154) France (155) Belgium (156) Denmark (157)	1
-Multi vs Single-centre	Multi centre (36, 103, 129, 130-1, 133-4, 140, 147, 150-2, 156-7)	13
	Single centre (132, 135-9, 141-6, 148-9, 153-5)	18
-Year of Publication	1995-2005 (36, 133, 135-6, 139, 146, 151)	7
	2006-2016 (103, 129-32, 134, 137-8, 140-4, 145, 147-150, 152-7)	24
Included Studies		
Characteristic	**Subgroup**	**No. of RCTs**
-Trial Groups	Laparoscopic vs. Open (103, 131, 134-5, 141, 149-150, 153, 147-8, 152)	11
	Open mesh vs. suture (36, 236, 240, 243-4)	5
	Laparoscopic mesh fixation; Tacks vs. Sutures (238, 241, 245, 246)	4
	• Open VH repair:	
	Onlay vs. Sublay (144, 154)	2
	Light weight vs. Heavy weight mesh (133)	1
	Medium weight vs. Medium weight mesh (129)	1
	*Autograft vs. Prosthetic mesh** (151*)	1
	Component separation vs. Prosthetic mesh (130)	1
	Onlay vs. Underlay (145)	1
	Intraperitoneal vs. Onlay (bridging) (146)	1
	Ventralex patch vs Biomesh composite mesh (155)	1
	• Laparoscopic VH repair:	
	Double crown tack vs. suture and tack mesh fixation (132), (156)	2

	Double crown tack vs. fibrin sealant mesh fixation (157)	1
	Light weight mesh vs. Medium weight mesh (138)	1
	Total	32*
	*Large hernias from Korenkov et al. (a suture vs. mesh RCT) were analysed as a separate category. This makes this total 32 rather than 31.	
-Hernia type	Primary hernias only (136, 139-140, 144-5, 147)	6
	Incisional hernias only (36, 103, 129-31, 133-4, 138, 146, 149, 150-2, 154)	14
	Primary and incisional hernias (132, 135, 137, 141-3, 148, 153, 155-7)	11
-Primary outcomes	Hernia recurrence (153, 151, 148, 155)	4
	Quality of life/ Health questionnaires (103, 134, 129, 133)	4
	Pain (measured using visual analogue scores) (131, 132, 156, 157)	4
	Pain and hernia recurrence (two primary outcomes) (138)	1
	Mesh shrinkage (137)	1
	Total complications rates (152)	1
	Unclear (36, 130, 135-6, 139-49, 154)	16
-Risk of Bias: Cochrane Collaboration's tool	High risk of bias (36, 103, 130-57)	30
	Low risk of bias (129)	1

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



Risk of bias and study design

Thirty RCTs were assessed as at high risk of bias with just one (151) considered at low risk. Figure 2 shows that this high level of bias is mostly due to the failed blinding of trial participants, personnel (surgeons) and outpatient assessors. Only two trials (151), (132) achieved blinding for both these criteria.

Hernia morphology

Twenty-three of 30 (76.6%) RCTs used hernia dimensions as an inclusion criteria and one RCT (129) divided hernias into simple and complex categories using a 10cm defect width cut-point. Seven trials had no selection criteria that used hernia dimension. The exact nature of dimension inclusion criteria varied across trials, ranging from hernias with a width of less than 4cm (139), to hernias with a width of greater than 10cm (6,24). Fourteen trials (45.2%) recorded the average defect surface area, which ranged from 3.4cm^2 to 141.2cm^2, with a mean of 43.1cm^2. Eleven trials (35.5%) recorded the average or median hernia width within each comparison group, which ranged from 3.6cm to 17cm with a mean of 7.5cm. None of the RCTs reported loss of domain or used loss of domain for patient selection (Table 2.).

As anticipated, no RCT recorded either VHWG grade or CDC wound classification of included hernias. Indeed, no RCT used a VH grading scale of

any description. Six trials (19.3%) included primary VHs only, 14 trials (45.2%) included incisional hernias only, and 11 trials (35.5%) included both primary and incisional hernias. Ten of these 11 trials, including both primary and incisional VHs, reported the proportion of primary to incisional hernias, with a mean of 32 primary to 41 incisional hernias. Seven of the 25 trials (28%) analysing incisional hernias included the ratio of primary incisional hernias to recurrent incisional hernias (mean of 84.1 primary to 28.3 incisional hernias, range 160:3 (149) to 24:30 (129)). Only two trials (36, 147) reported the number of patients with previous ventral wound infection.

Table 2. Summarising the hernia morphology data reported.

Hernia dimension	*No. of RCTs reporting variable*
Average hernia defect surface area	14 (103, 132-3, 135, 137-8, 141-2, 149, 152-6)
Average hernia defect width	11 (103, 130-1, 133-4, 138, 140, 144, 149-51)
Loss of Domain	0

Pre-operative patient characteristics and co-morbidities

Table 3 summarises the patient characteristics and comorbidities reported.

The pre-operative patient characteristics and comorbidities reported differed between trials. While many reported basic patient demographics of age, gender and BMI, few went beyond this to report patient comorbidities, including smoking status, diabetic status and steroid use.

Table 3. Preoperative patient characteristics and comorbidities reported.

Patient characteristic/comorbidities	*No. of RCTs reporting variable*
Age (mean)	30 (36, 103, 129-39, 141-57)
Gender (male/female ratio)	29 (36, 103, 130-39, 141-57)
Obesity (as a ratio >/< 35 or mean (SD))	25 (36, 103, 129-34, 137-8, 140-5, 148-52, 154-7)
No. patients ASA 3	10 (103, 129, 131-2, 136-7, 139, 145, 150, 152)
COPD	8 (103, 129, 134, 138, 141, 145, 151-2)
Smoking status	8 (36, 103, 129, 145, 151-2, 156-7)
No. patients with Diabetes	7 (103, 129, 134, 138, 144, 152, 155)
No. patients ASA 1	7 (103, 131, 135-6, 137-8, 150)
No. patients ASA 2	7 (103, 129, 131-2, 145, 150, 152)
SF-36 QoL questionnaire (59)	3 (129, 133, 149)
No. patients using steroids	3 (129, 151, 152)
No. of arteriopaths (IHD/PVD/CVA)	3 (103, 144, 151)
No. patients ASA 4	3 (129, 131, 150)
Average ASA score	2 (134, 154)
Liver cirrhosis / Childs-Pugh A	1 (144)
SF-12 QoL questionnaire (59)	1 (155)

Intra-operative variables

Table 4 shows that intraoperative variables were reported with increased frequency compared to pre-operative variables and patient comorbidities. Mode of surgery, type of mesh implanted (prosthetic, composite, biosynthetic or biologic) and anatomical layer were recorded in all 31 RCTs. Operation duration, intra-operative blood loss and the experience of the principal operating surgeon were all reported less frequently.

Table 4. Intra-operative variables reported.

Intra-operative variable	*No. of RCTs reporting variable*
Mode of Surgery (laparoscopic/open)	31 (36, 103, 129-57)
Category of mesh used	31 (36, 103, 129-57)
Anatomical layer of mesh placement	31 (36, 103, 129-57)
Duration of operation	27 (36, 103, 130-2, 134-45, 148-57)
Experience of the principal surgeon	14 (103, 130-2, 134, 136, 146-7, 150, 152-4, 156-7)
Intra-operative blood loss	3 (130-1, 141)

Clinical outcomes

Sixty-four different clinical outcomes were reported overall, with little consistency between trials, even when reporting similar intervention groups and primary outcomes. Indeed, 16 (51.6%) RCTs stated no primary outcome explicitly (Table 1). Of the 15 RCTs (48.4%) stating a primary outcome; 4 (129, 149, 153, 155) used hernia recurrence and 4 (103, 132, 134, 151) employed quality of life. Three trials (103, 132, 151) used the SF-36 questionnaire (158) and 1 trial (134) used the EQ-5D questionnaire (159). Four trials (130, 131, 156, 157) used pain as their primary outcome, assessed via visual analogue scales (VASs). One trial stated both pain and recurrence as two separate primary outcomes (138). The remaining two trials used mesh shrinkage (137) or standardised complication rates (152) as their primary outcomes respectively. Multiple different primary outcomes led to many different clinical and patient reported outcomes overall (as shown in Appendix 3).

Length of follow-up was reported in all studies and averaged 24.5 months (range 1 month to 64 months). Fifteen of 31 (48%) trials had follow-up of at least 24 months. One trial (103) did not report hernia recurrence rate. Of the 30 trials reporting hernia recurrence, 1 RCT (136) reported recurrence at 5 years post repair, 4 RCTs (36, 130, 141, 155) reported recurrence at 3 years, 15 RCTs at 2 years, 13 RCTs at 1 year, 5 RCTs (137, 141, 143, 150, 151) at 6 months and 1 RCT (134) at 3 months. Six (20%) of 30 RCTs defined recurrence: definitions are shown in table 5. Only three trials used the same definition. Eight (29%) of 30 trials did not specify the method used to detect recurrence. Twelve trials (43%)

used clinical examination alone to detect recurrence. Ten (33%) trials used imaging if recurrence was in doubt, or to confirm a recurrence suspected clinically. Five (50%) of these 10 trials (130, 131, 133, 143, 156) used either CT or USS to detect recurrence, 3 (30%) trials (36, 142, 157) used USS alone and 2 (20%) trials (138, 146) used CT alone. Recurrence rates increased when imaging was used. Trials using clinical examination had a 4% median recurrence rate whereas trials using USS or CT, USS alone, or CT alone had median recurrence rates of 7%, 9% and 7% respectively. Trials that did not specify test methods for recurrence had a mean re-herniation rate of 7%. The method used to detect hernia recurrence did not depend on the size or type of hernia included in the trial (as shown in Appendix 4). Patient reported outcomes used the SF-36 (158), SF-12 (158), EQ-5D (159), and GIQL (160) questionnaires as well as VASs, to assess pain and overall health status. These were also carried out at varying time intervals. The Clavien-Dindo (161) scale for post-operative complications was used in 9 of the trials to classify complication severity.

Table 5. Six definitions of hernia recurrence encountered in the systematic review.

Reference	*Definition*
Arroyo et al. (136) (2001)	'the presence of a defect on the central part of the midline aponeurosis around the umbilicus, where the operation had been performed previously.'
Bensaadi et al. (155) (2014)	'a defect of the midline aponeurosis around the umbilicus at the site where the operation was performed.'
Lal et al. (140) (2012)	'the presence of a defect on the central part of the midline aponeurosis where the operation had been performed previously.'
Luijendijk et al. (36) (2000)	'any fascial defect that was palpable or detected by ultrasound examination and was located within 7cm of the site of hernia repair.'
Pring et al. (153) (2008)	'a clinically detectable defect, associated with the protrusion of viscera on straining'.
Muysoms et al. (156) (2013)	'Patients were considered free from recurrence if at clinical examination, no hernia was felt in an upright position during Valsalva manoeuver.'

Discussion

This systematic review has analysed the reported perioperative variables and postoperative outcomes from randomised controlled trials of elective VH repair, performed over the last twenty years. Important findings include the general absence of: a standardised pre-operative patient variable dataset; a universally accepted definition of recurrence; standardised test methods to detect recurrence; standardised assessment times for the key primary and secondary outcomes, and standardised evaluation tools for post-operative pain and quality of life. This lack of standardisation limits the validity of trial comparisons made by meta-analyses and comparison of trials by practicing surgeons. Our review provides evidence-based justification for urgent investment in a core perioperative and clinical outcome dataset applicable to trials of VH surgery. This should be developed and validated with key stakeholders to improve the quality of outcome reporting in this rapidly developing field.

As VH research evolves, academics are searching increasingly for outcome predictors. Potentially reliable predictors can be identified from the primary literature only when they are reported. Our review has found that randomised

controlled trials are focusing on surgical technique and failing to report variables that would normally be regarded as important predictors. For example, many pre-operative patient comorbidities and, in particular, measures of hernia morphology (e.g. hernia width and area) were omitted from most reports. Loss of domain was not reported by any trial. Because current evidence is contradictory, with some studies suggesting that hernia width does correlate with recurrence (54) whereas others do not (162, 163), future trials need to report apparently important predictors to facilitate subsequent analysis. Investigators should also grade hernias using appropriate scales, for example the VHWG scale (50) and the CDC wound classification scale (128) as these scales themselves may prove to be outcome predictors. Our review demonstrates that a trial dataset with multiple pre-operative patient variables (diabetes, COPD, BMI, hernia grade etc), including pre-operative CT scan dimensions (hernia defect area, hernia width, loss of domain etc) and intra-operative variables (operation time, anatomical plane of mesh insertion, reconstructive technique etc) is required.

While 8 of the 30 trials (26.7%) reporting hernia recurrence did not even define how recurrence was detected, the remaining trials used differing recurrence detection methods ranging from undefined clinical examination to undefined imaging methods. This introduces bias depending on the differing examination and imaging methods used. There was much variation in the timing of assessment for hernia recurrence. This observed lack of consensus regarding assessment timing, test methods for recurrence, and definitions of recurrence limits data availability and consistency, and impairs meta-analysis. To achieve standardisation a clear definition of VH recurrence is required. Imaging is likely the most precise method with which to determine recurrence, but a radiological definition of recurrence is required that incorporates measurements of clinically important and unimportant reherniation. Currently, there is considerable variability in recurrence reporting for CT scans (164). Our review suggests that the use of imaging does increase reported recurrence rates, which would be anticipated, since subclinical recurrences will be identified.

RCT dataset designers should also consult the recommendations made by Muysoms et al. following a consensus meeting in Palmero, Italy in 2012 (165).

This work gives detailed advice on how to carry out statistically sound research (interventional studies, observational studies, systematic review, and meta-analysis) in abdominal wall repair. Of particular relevance, this article advises using the EuraHS definition for hernia recurrence (63); "*a protrusion of the contents of the abdominal cavity or preperitoneal fat through a defect in the abdominal wall at the site of a previous repair of an abdominal wall hernia*", which I support. Muysoms et al. recommend using the EHS hernia classifications scales and measuring post-operative complications using the Clavien-Dindo classification system, but do not define or list any other peri-operative or post-operative outcome variables that sound be measured. Importantly, they do allow for variability in the method used for recurrence detection and the time to outpatient assessment, which we feel should be standardised, especially in RCTs. To standardise trial outcomes, a dataset with clear definitions and follow up assessment times is warranted.

A standardised dataset should include tools to assess chronic pain and quality of life (QoL). When comparing different surgical techniques, chronic pain and QoL are important patient-centred endpoints, as patients frequently place more emphasis on these outcomes than the operative surgeon. In this review, simple visual analogue scales were used by the RCTs to assess pain. However, these analogue scales, and the timings of assessment, were not standardised. A future dataset must standardise pain assessment. QoL was measured using many different questionnaires (SF-36 (158), SF-12 (158), EuroQoL (159) and GIQL (160)). These questionnaires are commonly used and they allow for health economic analysis across different disease states. However, they are not disease specific, and may miss important patient reported outcomes specific to hernia surgery. Due to the unique set of complications arising from VH surgery, the importance of chronic pain and QoL, a hernia-specific patient reported outcome assessment tool, such as the Carolinas Comfort Scale (95) or the EuraHS-QoL questionnaire (63), should be used.

When constructing a VH perioperative variable and postoperative outcome dataset for randomised control trials, workers should also consult the VH databases currently being used in America (60), Europe (63), Denmark (61) and

Spain (166). These databases collect data prospectively from large cohorts of patients and will generate sizeable observational studies. These databases have been constructed by VH experts with multiple peri-operative and post-operative data-points, many of which could be included in an RCT dataset.

As well as focusing on standardised definitions and datasets, academic surgeons carrying out RCTs should make concerted efforts to reduce methodological bias. Thirty of the 31 included trials were assessed as at high risk of bias. Many of the included trials performed poorly in 3 out of the 7 domains of the Cochrane Collaboration's tool for risk of bias (127). Many trials failed to specify how participant group allocation was concealed, failed to blind participant and surgeon from the allocated treatment, and there was no blinding in the outpatient assessment clinic. Traditionally, surgical trials are usually at high risk of bias due to the impossibility of blinding the primary surgeon. However, if visible skin changes to the participant do not differ between the treatment groups (e.g. open VH repair with onlay vs. sublay mesh), it is possible to blind both the participant and an independent assessor. In addition, concealment of treatment allocation should follow the standards set by the Cochrane Collaboration. In surgery, the allocated treatment should only be revealed to an independent surgeon after the participant is under general anaesthetic and after the participant has been consented to take part in the trial and both possible treatments.

Further bias can arise in RCTs due to commercial funding and readers should be aware of this. I accept there are difficulties in achieving non-commercial funding for RCTs in hernia research and that without proper funding scrupulous methodology can be challenging due to the high workload. Eight out of 31 of the trials received commercial funding (131, 132, 137, 151, 153, 155-157), one trial received non-commercial funding (152) and one trial received both commercial and non-commercial funding (103). In the remaining 21 trials the funding method was not specified. The practical difficulty of obtaining non-commercial funding can only be addressed by researchers, who whilst applying for funding must clearly explain the technical difficulties faced by reconstructive surgeons and the high prevalence of morbidity suffered by patients after hernia repair; namely chronic pain and recurrence. If researchers face difficulties with funding or carry

out research with commercial funding, little can be done apart from carrying out research to highest possible standards. I note that any data is better than no data, as supported by Lilford et al (167).

Conclusion

To date, systematic reviews of elective VH RCTs have focused on comparing surgical outcomes, for example open versus laparoscopic VH repair (104, 168, 169). This review is the first to assess the methodology of VH RCTs. The results show that the perioperative variables and postoperative outcomes reported by RCTs of VH repair lack definition and consistency. To solve this, a defined minimum dataset of variables and outcomes is required. Recurrence is a prime outcome and requires standard clinical and radiological definitions, together with a minimum period of follow-up. I propose that key opinion leaders should form an international task force to create this dataset.

Chapter 4

A systematic methodological review of non-randomised interventional studies of elective ventral hernia repair

Part 1: Improving Research Quality

Systematic Review: Outcome definitions and detection methods, peri-operative variable definitions, minimum datasets and methodology for interventional trials of VH repair.

Hypothesis 2

I hypothesize that non-randomised interventional trials of VH repair have poor methodology. Regarding peri-operative data collection, I hypothesize that trials collect varied and poorly defined variables. Focusing on trial outcomes, particularly hernia recurrence, I hypothesize that trials have no standardized outcome definitions and detection methods, and no standardised follow-up times.

Aim 2

To demonstrate that current VH non-randomised interventional trial methodology is poor, and that data collection is highly heterogeneous with poorly defined peri-operative variables and post-operative outcomes. Our aim was to show, via systematic review, there is an urgent need for clear peri-operative variable and outcome definitions, and for standardised minimum datasets for VH interventional trials.

Introduction

Following the systematic review of RCTs described in Chapter 3 (170), I next decided to assess non-randomised studies hoping to gain further evidence that currently reported data is highly heterogenous and lacks precision, especially as

I anticipated that non-randomised studies would be far greater in number than RCTs.

The fact that some surgical studies lack methodological rigour has been identified previously, and a recent systematic review found that 62% of surgical journals do not require authors to adhere to recognised reporting guidelines (171). Reporting tools have been designed specifically to enhance reporting of surgical interventions (172). For this methodological review we designed our own methodological assessment tool for non-randomised VH studies using a combination of reporting guideline tools already published (Downs and Black (173), ROBINS-I (174), Newcastle-Ottawa (175), TIDieR (172) and STROBE (176)) and our own expert knowledge of the VH literature.

The aim of this systematic review was to evaluate the methodological quality of non-randomised interventional studies of VH repair. Furthermore, we aimed to establish evidence from non-randomised studies, that clear outcome definitions along with a standardised minimum dataset are required in this field of surgical science.

Methods

Registration and reporting

As previously, this systematic review is reported in line with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement (126). A protocol was developed and registered with PROSPERO, the international prospective register of systematic reviews (CRD42016043071).

Eligibility criteria

Study design

I included non-randomised interventional studies of VH repair. I anticipated finding fewer prospective than retrospective studies. In order to compare their methodological quality, I included all eligible prospective studies identified, matching each with a single retrospective study.

Participants

I included studies of adults. I excluded paediatric studies (defined as 18 years or less) since these are not representative of 'typical' VH patients. As this review was methodological, I included all hernia populations and included studies than restricted participants according to specific diseases, conditions, or metabolic disorders (e.g. a study of participants with BMI>30).

Target condition

I defined VH as any anterior abdominal wall defect associated with abnormal protrusion of intra-abdominal viscera (63). I therefore included a range from simple primary umbilical/epigastric hernias to large complex hernias. Studies combining multiple types of hernia were eligible, as I was interested in how hernias were graded.

Interventions

All interventions addressing VH repair were eligible. So, I included all types of comparative study, including those comparing mesh, plane of mesh insertion, surgical technique, with/without component separation, with/without panniculectomy, etc. Studies comparing the same intervention with minimal alteration were also eligible (e.g. "double-crown" versus "single row" tacks for laparoscopic repair).

Comparators

All interventional comparators were eligible. Studies that compared an intervention to conservative management (i.e. non-operative management of VH) were excluded.

Outcomes

Any study outcome was eligible.

Timing

I stipulated no minimum follow-up.

Setting

All settings were eligible.

Language

I restricted our search to the English language.

Information sources

I searched the PubMed database (US National Library of Medicine, National Institutes of Health, Bethesda MD, 20894, USA) from 1st January 2005 to 1st January 2018. My prior experience of systematic review of clinical interventions suggests that this is the most comprehensive database and little additional benefit is gained from searching other databases.

Search string

The search string was the same string I used for my first systematic review which combined two search criteria. The first criteria identified studies investigating VH disease, the second investigated innovative or novel surgical techniques being used for VH repair. The complete search string is shown in Appendix 2.

Study records:

Data management

Identified citations were entered into a spreadsheet (Microsoft Excel for Mac 2011 v. 14.5.9, Microsoft Corporation, Washington), and uploaded subsequently into a reference manager able to access online original articles directly (Mendeley Desktop v. 1.17, London, UK).

Citation management and screening

Citation management and screening was carried out with the same method as for the review in Chapter 3. Citations were divided up into two equal groups, then screened by CPJW and I. Articles that were "clearly unsuitable" were discarded (e.g. subject not VH), retaining any regarded as "uncertain" or "definitely possible". These two latter groups were then combined and all assessed independently; CPJW, RWB, and I identified eligible studies i.e. non-randomised prospective or retrospective interventional studies. Any article where uncertainty persisted was discussed face-to-face with senior authors. An exclusion log was kept at all stages.

The following data were extracted from remaining studies; journal, impact factor, publication year. Each prospective study was matched to a retrospective study. We attempted to match each prospective study to a retrospective study published in the same journal and year. If no studies met this criterion, we matched to retrospective studies published in the same journal but not in the same year. If no relevant articles were published in the same journal, we matched the prospective study to a retrospective study published in a journal with the closest impact factor. This procedure created a group of matched prospective and retrospective studies. A log of the matching process was kept. The flow of article selection is shown in the PRISMA diagram (Figure 1).

Data extraction

Marios Erotocritou (ME) and I extracted data independently from selected studies. To ensure consistency, data were cross-checked subsequently face-to-face and disagreement resolved by senior authors, if discrepancy persisted. Data were entered into an Excel datasheet and categorised into methodological groups as follows: introduction, study design, participants, reported outcomes, statistical analysis.

Data items

To assess methodological quality, I designed a methodological assessment tool relevant to this review by combining the most important data points from the following reporting and risk of bias guidelines tools: TIDieR (172), Downs and Black (173), ROBINS-I (174), STROBE (176), Newcastle Ottawa (175). The tool is described in Appendix 5. To analyse the introduction, we (Marios and I) attempted to identify a rationale, primary aim or objective, and a pre-specified hypothesis with references to existing literature. To analyse design, we identified whether data was collected prospectively and according to a protocol. We also analysed whether studies described the equipment used and the proposed intervention adequately, using pre-specified criteria (Appendix 5a and 5b; Appendix 5). We identified whether a primary outcome was described and whether a sample size calculation had been performed.

Regarding participants, we identified how patients were selected. We identified whether participants' selection criteria or process was described adequately, and whether participants in intervention and comparator groups were drawn from the same population. To assess selection bias and to differentiate between patients meeting inclusion criteria versus number of participants included, we identified whether the study reported eligibility. We collected data on hernia morphology, assessing whether number of previous repairs were reported, maximal hernia width, defect area, whether primary or incisional hernias were reported, and whether a hernia grading scale was used. To assess participant characteristics, we identified whether a table of basic demographics was reported according to pre-specified criteria (Appendix 5c; Appendix 5). To assess participant

recruitment, we recorded whether recruitment start date, finish date, and end of follow-up date were reported. We identified whether the number of participants deviating from the intended intervention was reported.

Regarding reported outcomes, we assessed whether the assessor and/or participant were blinded to the intervention. Remaining information collected under this heading related to primary and secondary outcomes (see sections below).

For statistical analysis, we identified whether median length of follow-up and the number of participants with missing data were reported. We identified whether an adjusted analysis was performed and whether any adjustment factors were reported. We identified whether prediction estimates were reported for standard clinical variables. We also assessed whether confidence intervals were stated for all reported estimates. We identified whether an intention-to-treat or complete case analysis had been performed since this is most realistic in the clinical setting.

Outcomes and prioritisation

Our primary outcome of interest was hernia recurrence, so we extracted post-operative recurrence rates. We also extracted the timing of recurrence, definitions for VH recurrence, and the test method(s) used for diagnosis (for example, clinical examination, CT scan, US scan). Our secondary outcomes were surgical site infection and surgical site occurrence, and we extracted definitions used to define them in the component studies. We also assessed whether a patient reported outcome measure was reported and, if so, its identity. Lastly, manuscripts were reviewed to see whether a visual analogue scale (VAS) was used to assess post-operative pain.

Risk of bias in individual studies

Existing reference tools were analysed (172-176) and my assessment tool designed to identify the following categories of potential bias:

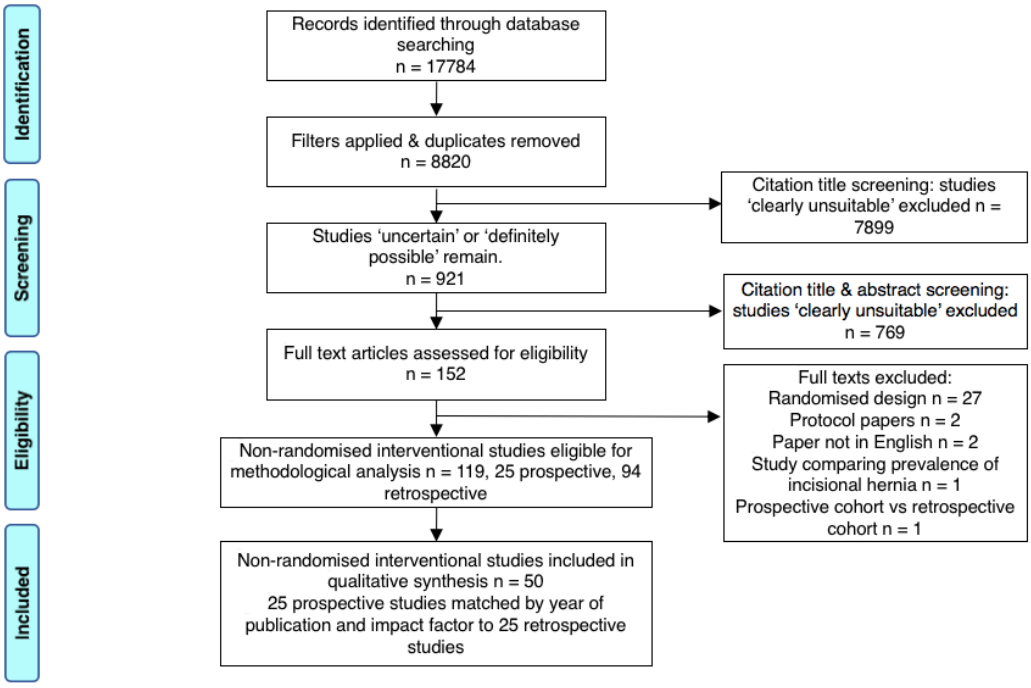
1) To assess selection bias we identified whether a study reported the number of eligible versus included participants.
2) To assess bias from intervention classification we included two questions from the TIDieR assessment tool (4): 1) Was a detailed description of equipment used reported (according to Appendix 5a, Appendix 5)? And, 2) Was a detailed description of the intervention reported (according to Appendix 5b, Appendix 5)?
3) To assess bias regarding outcome measurement, we identified whether participants and/or assessor were blinded to the intervention.
4) To assess missing data bias, we identified if analysis was restricted to patients with full data.

Studies were assumed to be at low risk of bias if they adhered to all these criteria. 'Unclear' criteria were classified as moderate risk. 'High' risk of bias was determined by clear non-adherence to any criteria.

Data synthesis

I used descriptive tables of frequencies for study items for prospective and retrospective studies. Box and whisker diagrams were used to present total methodological scores and to compare prospective and retrospective studies, enabling me to assess overall methodological quality. Scatter plots were used to show whether methodological quality was related to publication year and/or impact factor.

Figure 1. PRISMA diagram showing selection of non-randomised interventional studies for this review



Results

Search results

My initial search retrieved 17,784 results (Fig. 1). After applying filters (studies published 1st January 2005 to 1st January 2018; human; age >18; English language), I excluded 8,964 studies, leaving 8,820. After title screening, 921 studies were categorised 'definitely possible' or 'uncertain', falling to 152 after abstract screening. After full text assessment, there were 119 non-randomised interventional studies; 25 prospective, 94 retrospective. Thus, after matching the prospective studies as described previously, the final review comprised 50 studies in total.

Study demographics

Study demographics are shown in Table 1. The 50 studies reported 17,608 patients overall, 2800 (16%) prospective patients and 14,808 (84%) retrospective. Twenty-one studies (42% of total) were from the United States; 17 retrospective and 4 (177-180) prospective. Just five (10%) studies were multi-

centre (181-185). There were 5 categories of study with the same comparison groups: Nineteen laparoscopic versus open repair, 5 mesh versus suture repair (186-190), 2 primary fascial closure versus bridged repair (114, 191), 2 heavyweight versus lightweight mesh (192, 193), and 2 endoscopic component separation versus open component separation (194, 195). Twenty-one (42%) studies (8 prospective, 13 retrospective) reported compliance with national or regional ethical standards. Three (6%) prospective studies (188, 196, 197) reported approval from an ethics committee, 3 more (6%) (178-180) referenced approval from the institutional review board, 1 (2%) study (198) reported 'compliance with ethical standards', and 1 (2%) study (199) reported compliance with 'National Patient Rights Regulations'. Twelve (24%) of the retrospective studies reported approval from the institutional review board and 1 (2%) (189) reported approval from the hospital research ethics committee. Hernia type was specified by 32 (64%) studies; 18 prospective, 14 retrospective. Thirteen studies analysed both primary ventral and incisional hernia, eleven analysed incisional hernia only, 3 analysed primary incisional hernia only (180, 197, 200), 3 analysed primary VH (187, 201, 202) and 2 analysed primary umbilical hernia only (188, 203).

Characteristic	Prospective study	No. of Studies	Retrospective studies	No. of Studies
Country of Publication	USA (177-180), Spain (196, 204-206)	4	USA (109, 114, 182, 183, 185, 191, 194, 195, 207-215)	17
	Switzerland (216, 217), India (218, 219), Germany (192, 220), Belgium (193, 203)	2	Italy (200, 201, 221)	3
	Sweden (188), Italy (187), Poland (198), Norway (181), Singapore (222), Serbia (223), Austria (197), Turkey (199), Egypt (186)	1	France (184), UK (202), Germany (224), Pakistan (190), Saudi Arabia (189)	1
Multi vs single-centre	Multi centre (181)	1	Multi centre (182-5)	4
	Single centre (177-80, 186, 187-8, 192-3, 196-9, 203-6, 216-20, 222-3)	24	Single centre (109, 114, 189-91, 194, 195, 200-2, 207-15, 221, 224)	21
Study groups	Laparoscopic vs Open (177, 196, 199, 204, 205, 216-7, 219-20, 222)	10	Laparoscopic vs Open (185, 201, 202, 210, 212, 213, 214, 221, 224)	9
	Suture vs mesh (186-8)	3	Suture Vs Mesh (189, 190)	2
	Heavyweight vs lightweight mesh (192-3)	2	Primary fascial closure Vs Bridged (114, 191)	2
	Suture vs tack (178)	1	Endoscopic C/S Vs Open C/S (194, 195)	2
	Sublay vs Onlay (218)	1	Laparoscopic vs Open C/S (182)	1
	Primary fascial closure Vs Bridged (197)	1	Panniculectomy Vs No Pannicculectomy (215)	1
	Bridging Vs Primary fascial closure (IPOM Vs IPOMplus) (198)	1	Posterior component separation Vs Anterior component separation (109)	1
	Autograft Vs Polypropylene mesh (223)	1	Polyester mesh Vs PTFE (207)	1
	Single incision Vs Standard laparoscopic (181)	1	Concomitant Vs no concomitant procedure (183)	1
	Flex HD Vs Alloderm (179)	1	Mesh Vs Mesh+Pedicle flap (200)	1
	Barbed suture & mesh Vs Mesh (180)	1	Suture Vs Tack (208)	1
	Fibrin sealant Vs no fibrin sealant (206)	1	Permacol Vs Alloderm mesh (209)	1
	Open ventralex patch vs sublay mesh (203)	1	Ventralight ST Vs Control group (184)	1
			Laparoscopic Vs Robotic (211)	1
Hernia type	Primary ventral hernia (187)	1	Primary ventral hernia (201-2)	2
	Primary umbilical hernia (188, 203)	2	Primary incisional hernia (200)	1
	Primary incisional hernia (180, 197)	2	Incisional hernia (183, 189, 207, 212, 224)	5

	Incisional hernia (179, 193, 216, 217, 219, 223)	6	Primary and incisional hernia (184, 190, 208, 210, 214, 221)	6
	Primary and incisional hernia (198-9, 204-6, 220, 222)	7	Unclear (109, 114, 182, 185, 191, 194, 195, 209, 211, 213, 215)	11
	Unclear (177, 178, 181, 186, 192, 204, 218)	7		

Table 1. Demographics of the 50 non-randomised interventional studies included in the Systemic Review.

Figure 2. Graph of risk of bias item for prospective and retrospective studies. (blue – studies reporting the criteria, grey – unclear, red – studies omitting the criteria)

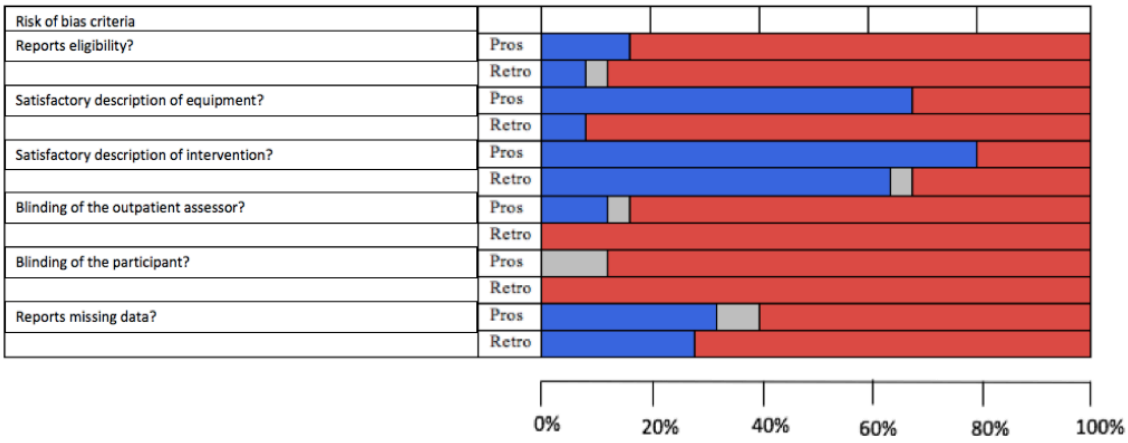


Figure 3. Box and whisker plots showing methodology scores for prospective and retrospective studies. A – Introduction, B - Study design score, C – Participants score, D – Outcomes score, E – Statistics score, F – Total methodology score

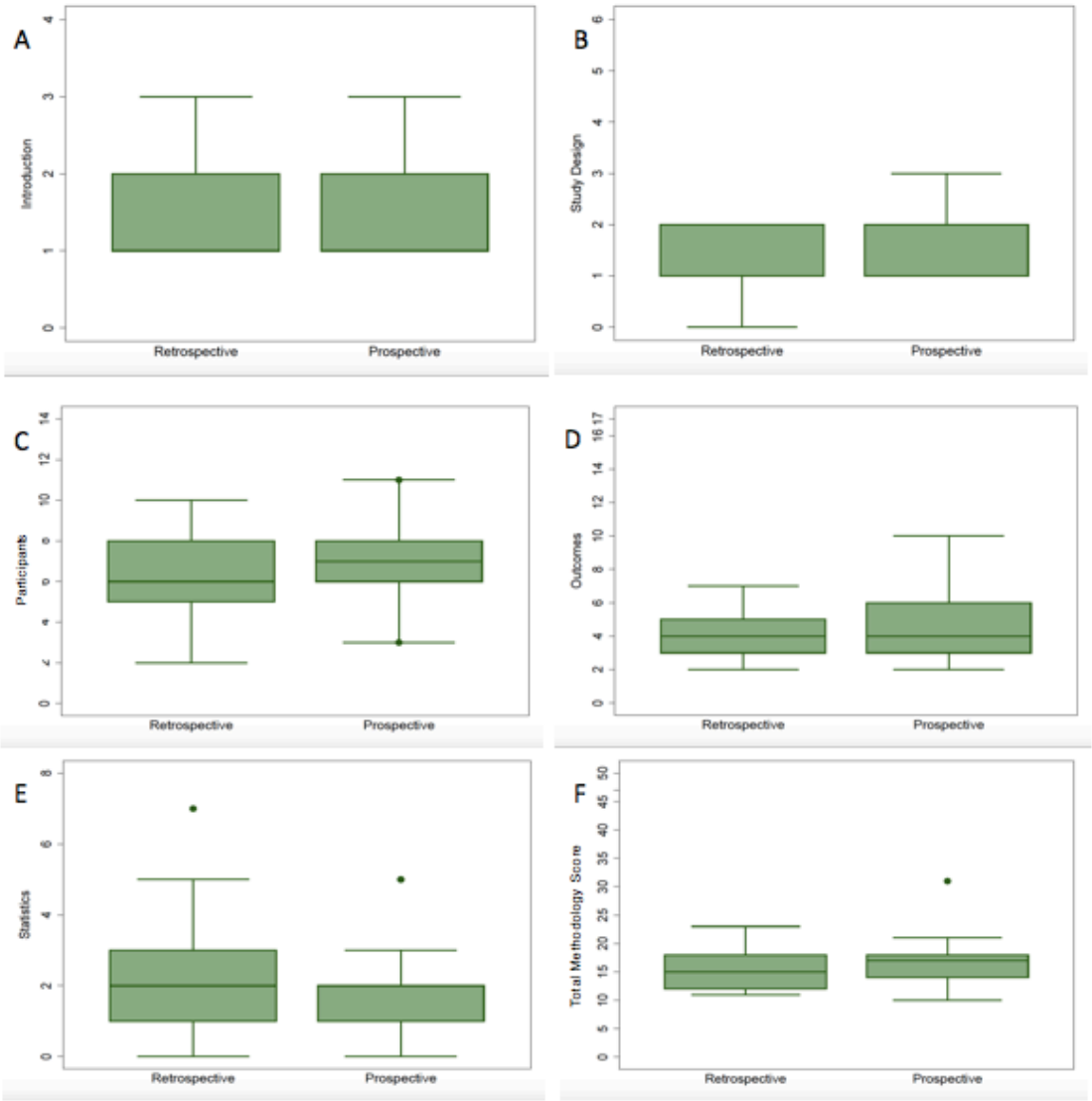


Figure 4. Scatter plots comparing methodological scores for prospective and retrospective studies. A – Impact factor versus total methodology score, B - Year of publication versus total methodology score.

Risk of bias assessment

All studies were rated as at high risk of bias. Figure 2 shows that this was mostly due to unblinding of both participants and assessors; only three (6%) studies (179, 206, 217), all prospective, achieved blinding of the outpatient assessor. Although we aimed to assess selection bias, only six studies reported participant eligibility; four prospective (197-199, 217), two retrospective (109, 189).

Methodology scores

Appendix 6 shows tabulated results from data extracted.

As our data extraction sheet had 46 items, the maximum possible methodology score for any single study was 46. Total and sub-category median methodology scores with their interquartile ranges (IQRs) are depicted using Box plots in Figure 3. The overall median score was 16 (IQR: 14 to 18), with a range of 11 to 31. Prospective and retrospective studies had median and IQRs of 17 (IQR: 14-18) and 15 (IQR: 12-18) respectively, with prospective studies having marginally better average methodological quality. For the sub-groups 'introduction', 'study design' and 'participants' prospective studies achieved higher median scores relative to the matched retrospective studies with median scores of 2 vs 1, 2 vs 1, 7 vs 6 respectively. For the subgroup 'reported outcomes' prospective and retrospective studies had equal median scores, 4 vs 4. In the 'statistics' subgroup the retrospective and prospective median scores were 2 vs 1 (Figure 3). Scatter plots of methodological quality against publication year and impact factor (Figure 4) showed no clear relationship for either prospective or retrospective studies. One study, Kurmann et al (217), scored 31 and was 8 points higher than the next best methodological score.

Introduction

All 50 studies (100%) provided a scientific rationale for their purpose. Twenty-nine studies (58%) described a primary aim or objective, with improved reporting for prospective (18 studies, 72%) versus retrospective (11 studies, 44%) studies. Only 3 studies (109, 114, 177) provided a hypothesis, and none of these referenced their hypothesis to the literature.

Study design

No study (0%) stated that a study protocol had been published or written. Studies were generally poor at accurately describing the equipment used for hernia repair but were informative about the interventions performed. Nineteen (38%) and 36 (72%) studies reported these criteria respectively. Only 18 (36%) studies defined a primary outcome, with similar proportions for prospective and retrospective

studies; 8 (32%) vs 10 (40%). Only 2 (4%) studies performed a power calculation (197, 206).

Participants

Thirty-five (70%) studies reported selection criteria beyond elective VH repair, time and place. Only 17 (34%) studies reported a basic list of baseline characteristics meeting our pre-specified criteria (17c). Amongst the 34 (68%) studies that did report baseline characteristics (including the 17 studies that met our criteria), 18 (36%) studies showed equivalence between the intervention and comparator groups, whereas 16 (32%) studies reported a difference in one or more baseline characteristics indicating a difference in the group populations.

Reported hernia characteristics also varied. Excluding studies that included only primary hernias (8 studies, 16%), the number of prior hernia repairs was only reported in 18 out of 42 (43%) studies. Twenty (40%) studies reported maximal hernia diameter, 12 (48%) prospective and 8 (32%) retrospective. Hernia defect area was reported by 21 studies, again with no detectable difference between the prospective and retrospective studies; 9 (36%) vs. 12 (48%). Thirty-two (64%) studies stated whether hernias were primary, incisional, or both, leaving 18 (36%) that did not state the hernia type included. Only 3 studies (184, 205, 217), graded hernias using either the EHS scale (184, 217) or their own pre-specified scale (205).

Participant recruitment start and finish dates were reasonably reported with 36 (72%) studies reporting both. In contrast, no study reported the end of follow-up date and only 18 (36%) reported the number of deviations from the intended intervention.

Prospective studies	Hernia recurrence definition	Referenced?
Kurmann et al. (217)	'Recurrence was defined as any abdominal wall gap with or without bulge that is not covered by mesh in the area of the postoperative scar'.	No
Anadol et al. (199)	'Recurrence was defined as the presence of a defect and/or lump in the original location'.	No
Moreno-Egea et al. (196)	'Hernia recurrence was defined on physical examination and confirmed on CT'.	No
Bochicchio et al. (179)	'We defined a true hernia recurrence as herniation of bowel or omentum through a defect in the biological mesh or through a defect at the mesh/fascial interface after the initial operation'.	No
Retrospective studies	**Hernia recurrence definition**	**Referenced?**
Al-Salamah et al. (189)	'Recurrence was defined as any fascial defect, palable or detected on CT scan and located within 7cm of the site of hernia repair'.	No
Jin et al. (191)	'Patients with recurrent hernias were defined as requiring another hernia reoperation or noting a significant bulge'.	No
Ballem et al. (214)	'recurrence was defined by the presence of a new or similar bulge which increased in size upon straining'.	No
Booth et al. (114)	'Recurrent hernia was a contour abnormality associated with a fascial defect'.	No
Iacco et al. (209)	'Recurrence was defined by the presence of a bulge on physical examination, imaging, or by patient self-reporting'.	No

Table 2. Nine definitions of hernia recurrence encountered in the systematic review

Reported outcomes

Hernia recurrence rate was reported in 47 (94%) studies. Three retrospective studies (183, 211, 212) did not report recurrence. However, only 9 (18%) studies defined recurrence; 4 (16%) prospective and 5 (20%) retrospective. None of these studies used the same definition and none referenced a definition of recurrence (Table 2). Two studies (186, 216) reported recurrence but the overall follow-up duration was unclear. Of the remaining 45 studies, recurrence rate, follow-up duration, and detection method varied. Follow-up duration ranged from 3 (206) to 81 months (188), with a median of 27 months. Ten (20%) studies reported a follow-up of between 6 and 12 months. Follow-up duration for the remaining 35 (70%) studies lacked any consistency (Appendix 6). In 21 (42%) studies the follow-up duration differed between treatment arms. Fifteen different methods to detect recurrence were reported across 37 (74%) studies (Appendix 6), ranging from re-operation rate (192) to telephone interview (221). Seven different detection methods were reported by prospective studies versus 12

different methods for retrospective studies. The most prevalent method used to detect recurrence was clinical assessment followed by a CT scanning if a recurrence was suspected.

Surgical site infection (SSI) was reported by 32 (64%) studies. However, only six (12%) studies, 3 prospective (179, 188, 217) and 3 retrospective (189, 210, 214), defined SSI with only 3 definitions referencing the literature (179, 214, 217). Two definitions used Centers for Disease Control and Prevention (CDC) wound infection criteria (179, 217), 1 study referenced NSQIP criteria (214), and the remaining 3 unreferenced definitions differed (188, 189, 195). Surgical site infection was reported using an anecdotal grading scale by one study (215). While one study provided the CDC SSI definition but the results then failed to use this for reporting wound infection rates (179).

Surgical site occurrence (SSO) was reported by 4 (8%) studies (194, 195, 199, 211). Only 1 study (195) defined SSO but without providing a reference. Ten (20%) studies, 7 prospective and 3 retrospective (184, 190, 208), stated patient reported outcomes. Two used the EQ-5D questionnaire (193, 203), 1 used the French Hernia Club questionnaire (184) and the remaining 7 asked ad hoc outcome questions (e.g. time to normal activity, time to return to work). Nine (18%) studies used visual analogue scores to assess pain.

Statistical analysis

Forty-five (90%) studies reported follow-up duration. Multivariable adjusted analysis for hernia recurrence was reported by 10 studies; 7 retrospective and 3 (177, 178, 217) prospective. All 3 prospective studies (177, 178, 217) reported the adjustment factors compared to 5 of 7 for retrospective studies (114, 183, 195, 209, 210). Eight (16%) studies reported confidence intervals for odds ratios and hazard ratios; 6 (24%) retrospective and 2 (8%) prospective (177, 178). Only one study (218) reported a complete-case analysis with 100% follow-up at 24 months. No study used imputation to handle missing data so analysis was limited to patients with complete data.

Discussion

In my first methodological systematic review described in Chapter 3 (170), I found that reported variables in randomised controlled trials (RCTs) of VH were heterogenous and lacked standardisation, concluding that clear outcome definitions and a standardised minimum dataset are needed if VH research is to be clinically useful and methodologically credible. Because RCTs are the highest level of evidence (35), we can hypothesise that perioperative variables reported in non-randomised interventional studies of VH repair would be at least as deficient. Therefore, for the present review my focus was upon assessment of study methodology. To achieve this, I designed a specific methodological assessment tool using published guidelines (172-176) (Appendix 5).

I found that there was no generally accepted definition of hernia recurrence, no standardised test methods to detect recurrence, no standardised length of follow-up, no universally accepted definition for both surgical site infection (SSI) or surgical site occurrence (SSO), and no standardised evaluation tools for post-operative quality of life and pain. General markers of poor methods included an absence of study protocols and power calculations. This lack of standardisation and methodological vigour limits the validity of published results and, furthermore, impacts upon meta-analytical synthesis.

Perhaps the most pressing issue is a lack of definitions for study outcomes. Historically, the most studied outcomes are surgical site infection (SSI), surgical site occurrence (SSO), and hernia recurrence (50), yet I found researchers defined these items poorly. Regarding hernia recurrence, as stated previously (Chapter 3) I advocate using the EHS definition for recurrence (63), as a broad definition for recurrence. However, it is imprecise and an additional definition of recurrence for VH trials that is far more precise and stipulates the exact findings on physical examination and includes the use of imaging to increase accuracy requires development (225). Indeed, the previous review found that studies employing cross-sectional imaging reported double the hernia recurrence rate

than other studies (170). Standardised accurate definitions and detection methods are warranted.

Similarly, I found that SSI and SSO were seldom defined and, even then, rarely reference standardised definitions from the literature. These findings will not surprise hernia academics since they echo a recent review by Haskins et al (226), who stated that of the 50 most cited papers describing VH repair, only 9 (18%) used standardised definitions for SSIs and SSOs. Haskins went onto propose definitions for SSI, SSO and SSOPI (surgical site occurrence requiring procedural intervention) that should be adopted by all studies of VH repair. The response from DeBord et al (227) stated difficulties with the proposal but accepted the need for a "common language". This editorial concluded by calling for an 'international task force' to establish common language for reporting wound complications in the field of abdominal wall reconstruction. I support this.

As well as identifying a paucity for defining outcomes, this methodology review identified additional major reporting deficiencies. No study mentioned writing a protocol, only 2 (4%) performed a power calculation, and only 18 described a primary outcome. These factors are pivotal to good-quality research. Protocols ensure that research is pre-planned and not haphazard, are important for research governance, and demonstrate that authors recognise that 'quality control needs to be built in from the start rather than the failures being discarded' at the end (228). Power calculations are essential; small samples risk type 2 errors whereas too large a sample results in unnecessarily large and costly research, wasting time and effort. Just 18 studies described a primary outcome, an item fundamental to reporting research. In essence, non-randomised interventional studies of VH repair need improved study design and reporting in order to produce meaningful results.

Surgeons performing such studies should make concerted efforts to reduce bias. All 50 studies included were deemed as at high risk of bias. For example, good research practice demands eligibility criteria and keeping a screening log. However, only six studies reported eligibility and when they did so it was implied rather than reported specifically (e.g. '57 patients were diagnosed with incisional

hernia, 44 underwent surgical repair' (216)), leaving exclusion criteria in doubt. Poor reporting of 'eligibility' exposes studies to concern about potential for selection bias. In general, prospective studies described both the equipment and the intended intervention well and, as a consequence, were at low risk of bias regarding classification of interventions. In contrast, retrospective studies described interventions poorly, suggesting high risk of bias in this category, as retrospective studies cannot control the exact equipment and intervention that was performed on each participant. As with the RCT systematic review, studies scored poorly for blinding the participant and assessor. While blinding of surgical studies can be difficult, visible skin changes give no clue as to where a mesh was placed or its nature or whether a component separation was performed. Accordingly, blinding should be possible for many hernia studies.

I found that recent publication or higher journal impact factor did not improve quality. This is disappointing because STROBE (176), Newcastle-Ottawa (175), and TIDieR (172) guidelines were published over the time-span of this review, suggesting that hernia researchers are unaware of these recommendations and not party to efforts to improve research quality over the last twenty years (229). The Ventral Hernia Working Group's classification of SSO was published in 2010 (50), which I would expect hernia researchers to endorse and use. Systematic reviews of other specialties have demonstrated improved methodology (230) and scoping reviews have shown quality improvement throughout the profession with both publication date and impact factor (231). As VHs become increasingly prevalent, combined with high recurrence rates, these results highlight an urgent need to improve methodology in non-randomised interventional studies of VH repair.

This systematic review has identified a need to construct a standardised minimum dataset for non-randomised VH trials (which greatly outnumber randomised trials). Definition of core variables and outcomes is vital to move the academic hernia community forwards. This endeavour will require international collaboration across academic hernia surgeons. Once achieved, such a minimum dataset will enable trials and registries to report the same peri-operative variables and outcomes, which will facilitate comparisons across them via meta-analysis

and multivariate logistic regression, improving our understanding of how each perioperative variable effects outcome. In research generally, there is a worldwide move towards establishing minimum datasets (232, 233). In this review, and my review of randomised trials (170), I have established evidence that the data collected is currently highly heterogeneous and undefined; clear outcome definitions and a standardised minimum dataset are warranted.

Chapter 5

What exactly is meant by 'loss of domain' for ventral hernia? Systematic review of definitions.

Part 1: Improving Research Quality

Systematic Review: Defining Loss of Domain

Hypothesis

I hypothesize that throughout the literature the term 'loss of domain' is poorly defined. I hypothesize that several written and volumetric definitions exist in the literature with no standardisation.

Aim

To demonstrate, via systematic review of the indexed literature, the current heterogeneity of both the written and volumetric definitions for 'loss of domain'.

Introduction

The second inconsistency I identified while performing data extraction for prognostic model development was the unstandardised use of the phrase 'loss of domain'. 'Loss of domain' (LOD) is a term used commonly in the literature to describe the distribution of abdominal contents between the hernia and residual abdomino-pelvic cavity. As the incidence of VH disease increases (11), so too has the proportion of large complex VH (CVH), partly due to increasing age (2), obesity (3), and operative intervention (1), but also because of improvements in intensive care medicine (234). For many patients, following intra-abdominal sepsis and laparostomy, the ventral defect is left open and covered only via skin grafting, culminating in large VHs. These CVH contain a significant proportion of the abdominal viscera outside the abdomino-pelvic compartment and large hernias present the sternest surgical challenge.

After repairing hernias with significant LOD (i.e. large hernias with much of the abdominal viscera outside the abdominal compartment), serious physiological changes arise. The rise in abdominal pressure increases tension along the laparotomy incision, which can be pulled apart, thereby causing wound complications (17) and hernia recurrence (17, 119, 235). LOD may have prognostic value and, accordingly, a standardised definition is warranted. A standardised definition will allow for comparable pre-operative assessment of hernia patients. Studies of hernia repair would then be able to use this definition and subsequent study comparison via meta-analysis will allow researchers to investigate LOD as an outcome predictor.

Previously, other articles have suggested that written definitions of LOD are inconsistent (236). Researchers have also noted that volumetric definitions of LOD differ (237, 238). To our knowledge, a systematic review of definitions has never been performed. To rectify this, I performed such a review, aiming to demonstrate that inconsistent definitions existed, and to document these (239).

Methods

Reporting and Registration

This systematic review was performed and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (126). Ethical permission is not required by UCL for systematic reviews of available primary literature.

Inclusion criteria for studies

I identified indexed studies that used the term ‘loss of domain’ in their methods when describing hernia morphology. There was no limit according to manuscript type, allowing for the inclusion of both the primary and secondary literature in our review. Only articles written in English were included.

Target condition

The target condition was hernia with LOD. My search strategy did not exclude any specific sub-types or aetiologies of hernia (e.g. large inguinal or diaphragmatic hernias), as my aim was to investigate all definitions of LOD, which can be applied to hernia irrespective of hernia aetiology. I wished to encompass definitions used not only by specialist abdominal wall surgeons but also those used by general, trauma, plastic, transplant, bariatric and paediatric surgeons.

Participants

Participants were defined as those with large hernia with LOD, either as part of a primary study or as part of a secondary review or editorial. I included paediatric patients, as the literature commonly describes the surgical repair of gastroschisis and omphalocele using the term loss of domain.

Search strategy and string

I searched the PubMed database with no date limitation. Filters were applied limiting the search to “human studies”. Our search string used the keywords; “loss of domain”, “loss of abdominal domain” and “hernia”. These terms were combined as two criteria to identify relevant articles:

1) “Loss of domain” OR “Loss of abdominal domain”
   AND
2) “hernia”

MESH terms were not used as ‘loss of domain’ is indexed under multiple terms. After entering the above keywords our search strategy was transformed to search for articles indexed under any mesh term containing the keyword ‘hernia’ combining this with the keywords ‘loss’ and ‘domain’ (our search string is shown in Appendix 7).

Citation management and screening

Identified citations were entered into a spreadsheet (Microsoft Excel for Mac 2011 v.14.5.9, Microsoft Corporation, Washington), and uploaded subsequently into a reference manager able to access the online original articles directly (Mendeley

Desktop v 1.17.13, London, UK). After the search filters were applied and duplicates excluded, the citation titles were screened by two researchers; Sarena Blackburn (SB) and I. Citations were excluded that were clearly unsuitable for full text assessment. Where there was uncertainty between the two researchers for citation inclusion, differences were discussed by face-to-face discussion. The full-text of the remaining articles was assessed for eligibility, and articles were excluded if they were not written in English, not describing abdominal loss of domain, and if they were unavailable (even after using our institution's interlibrary loan service).

Data extraction

Two researchers, SB and I, reviewed the full text of each article selected independently. Any data discrepancies were discussed face-to face, and if persistent they were discussed with a senior researcher. Data were extracted into an Excel spreadsheet. Data extracted related to study type, year and country of publication and surgical specialty (our classification for abdominal wall specialist surgeons is shown in Appendix 8). My primary aim was to extract definitions for LOD used in the literature. My anecdotal experience was that authors used the phrase 'loss of domain' as a concept to describe large hernias but without precise definition. However, any reported written and/or volumetric definitions were extracted. Free text space was also available to record any additional features regarding an individual study's definition of LOD. Where documented, we also collected authors' opinions of the 'cut-off' threshold or percentage proportion above which they believed LOD became clinically significant, i.e. the point at which closing the abdomen becomes very challenging and physiological complication increasingly likely.

We deemed that studies originating from the same research group were acceptable as groups may use a different definition of LOD as the literature evolves. This also applied to studies who reported overlapping patient groups since this review concentrates on definitions rather than treatment effects.

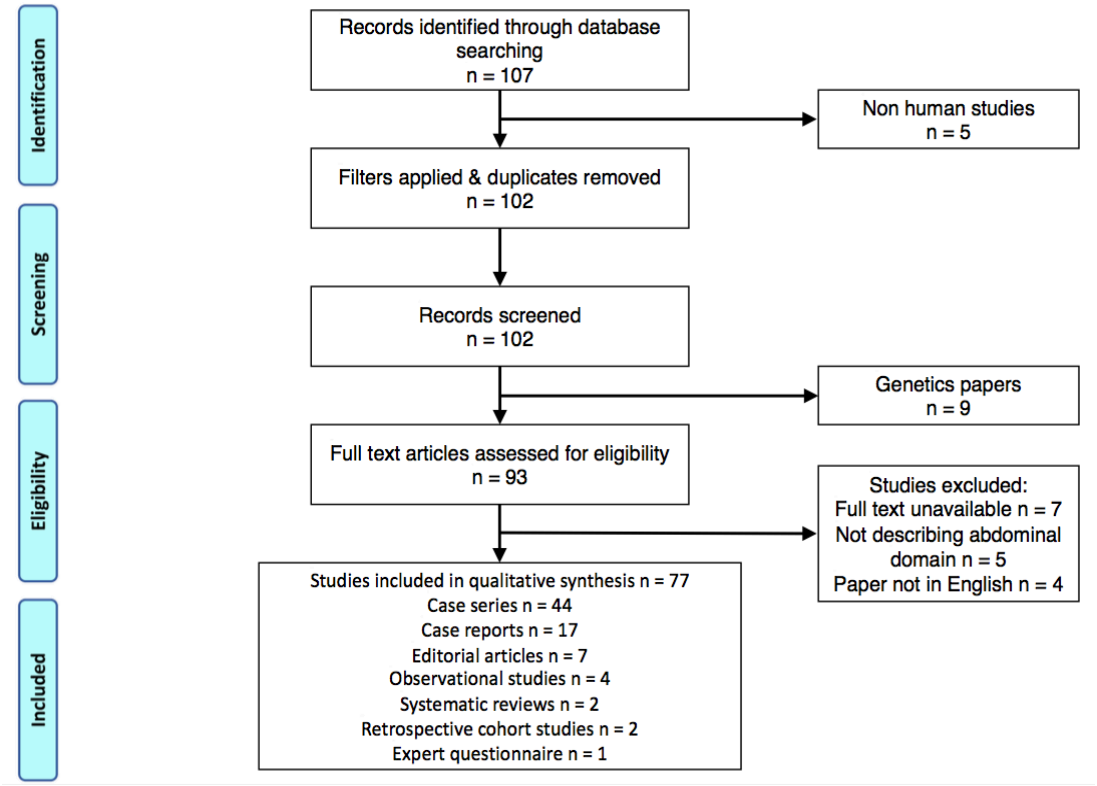
Risk of Bias

I did not assess risk of bias because I was interested in definitions of loss of domain rather than methodological quality.

Results

My initial search retrieved 107 results (Fig. 1). After applying search filters and removing duplicates, I excluded a further 5 non-human studies, leaving 102 records for title and abstract review. After title screening, I excluded a further 9 genetics studies, leaving 93 articles for full-text review. A further 16 studies were excluded during this final stage, 7 articles could not be found despite attempts to obtain them using the University's inter-library loan service, 5 articles did not describe LOD, and 4 articles were not written in English; leaving 77 articles for inclusion in the systematic review (Appendix 9).

Figure 1. PRISMA flow chart of study selection.



The majority of the articles, 39, originated from the United States; 5 were from France (87, 237, 240-242), 4 from the UK (170, 238, 243, 244), and 2 from Italy (245, 246), India (247, 248) and Brazil (33, 86). Six manuscripts were published prior to 2000 (249-254), 20 were published between 2000 and 2009, and 51 were published from 2010 onwards. Sixty-five articles described LOD in the context of VH patients, 9 articles described LOD caused by giant inguinal hernia, and 3 articles described giant diaphragmatic hernia. Sixty-seven articles were from the primary literature, comprising 44 case series, 17 case reports, 4 retrospective database analyses (243, 255-257) and 2 retrospective interventional studies (252, 258). Ten articles were from the secondary literature comprising 7 editorials, 2 systematic reviews (170, 259) and 1 consensus questionnaire (237). The primary literature reported a total of 1528 patients; 419 of these were retrospective database analyses.

Thirty-eight of the articles were written by abdominal wall specialists, 16 articles were written by general surgeons, 7 by paediatric surgeons, 6 by trauma surgeons, 6 by plastic surgeons, and 2, 1, and 1 by Transplant (260, 261), Vascular (262) and Bariatric (263) surgeons respectively. Twenty-eight (36%) of

articles presented a written definition for LOD (Appendix 10), meaning that the remaining 49 (64%) articles used the phrase “loss of domain” as a concept without definition. The written definitions reported were inconsistent. Definitions varied but could be categorised into 6 groups (Table 1). Four out of these six groups used definitions based around four theoretical concepts. Four articles defined LOD by describing a hernia as so large that “the herniated organs have lost their right of domain inside the abdominal cavity” (87, 241, 251, 257). Six articles use the principle of lateral contraction of the abdominal wall muscles leading to a reduced volume of the abdominal cavity and progressive visceral protrusion (261, 264-268). Five articles use the concept of the hernia sac being a “second abdomen”, and included the argument that restoring the hernia sac back into the abdominal cavity would create physiological disturbances and complications (86, 240, 244, 269, 270). Lastly, five articles describe LOD as a large irreducible hernia containing abdominal viscera residing outside the abdominal cavity and adherent to the hernial sac (33, 237, 271-273). Six of the definitions were miscellaneous (274-279) and two of the articles were editorials (236, 238), which highlighted inconsistencies when defining LOD. Twenty-three of the 28 (82%) articles reporting LOD definitions were written by Abdominal Wall Specialists. After categorising results by reporting specialty, the definitions remained inconsistent and were not dependent on the reporting surgical specialty (Table 1).

Table 1. The frequency of the concepts used to define 'loss of domain". Also broken down into the reporting specialties.

Specialty	Loss of the "right of domain"	Contraction of the lateral abdominal wall muscles leading to reduce volume of the abdominal cavity	The concept of a second abdomen	Chronic large irreducible hernia	Miscellaneous	Editorial/Literature review detailing multiple definitions	Total
AWR specialists	3 (87, 241, 257)	3 (264, 266, 268)	5 (86, 240, 244, 269, 270)	5 (33, 237, 271-273)	5 (274-276, 278, 279)	2 (236, 238)	23
General Surgeons	1 (251)	-	-		1 (277)	-	2
Plastics	-	1 (267)	-	-	-	-	1
Transplant	-	1 (261)	-	-	-	-	1
Trauma	-	1 (265)	-	-	-	-	1
Total	4 (87, 241, 251, 257)	6 (261, 264-268)	5 (86, 240, 244, 269, 270)	5 (33, 237, 271-273)	6 (274-279)	2 (236, 238)	28

Table 2. The frequency of the volumetric techniques used to define 'loss of domain"; Also broken down into the reporting specialties.

Specialty	Tanaka et al: Ratio of the Hernia Sac Volume/Abdominal Cavity Volume	Sabbagh et al: Percentage of the Hernia Sac Volume/total Peritoneal Volume	Unclear: Tanaka or Sabbagh	Both described	Other	Total
AWR specialists	7 (33, 86, 237, 266, 268, 273, 280)	5 (87, 240, 241, 271, 272)	4 (244, 270, 277, 281)	1 (238)	1 (257)	18
General Surgeons	1 (282)	-	-	-	-	1
Paediatric Surgeons	-	-	-	-	1 (283)	1
Total	8 (33, 86, 237, 266, 268, 273, 280, 282)	5 (87, 240, 241, 271, 272)	4 (244, 270, 277, 281)	1 (238)	2 (257, 283)	20

Volumetric definitions used for LOD were also inconsistent. In total, 20 studies used cross sectional imaging combined with volumetric analysis pre-operatively (Table 2). Eight studies (33, 86, 237, 266, 268, 273, 280, 282) reported the ratio of the Hernia Sac Volume (HSV) to the Abdominal Cavity Volume (ACV), commonly referred to as the Tanaka method (86). Five studies (87, 240, 241, 271, 272) reported the ratio or percentage of the HSV to the Total Peritoneal Volume (TPV = HSV + ACV), known as the Sabbagh method (87). Four of the papers describe volumetric analyses but were unclear how LOD was calculated (244, 270, 277, 281). Finally, 2 studies calculated HSV and ACV but simply stated these two volumes without using a ratio or a proportion (257, 283). One editorial review discussed both methods used to calculate LOD (238). Only 2 studies (282, 283) using volumetric analysis were not reported by Abdominal Wall Specialists. Therefore, a volumetric definition for LOD remained inconsistent even amongst hernia specialists (Table 2). Fifteen papers also reported a threshold at which they believed LOD became clinically significant, but this appeared anecdotal in all, based on clinical expertise rather than any independent research. Values ranged from 10% (281) to 50% (271), with the most frequently reported value being 20% (87, 273, 280, 282).

Discussion

This systematic review found that definitions for LOD are either not described or are disparate. Written definitions seemed to fall into six broad groupings. Two groups included 6 articles giving miscellaneous definitions (274-279) which could not be categorised and 2 editorials listing multiple definitions (236, 238). The remaining four groups were based on four theoretical concepts. Some articles defined LOD as the loss of the ‘right of domain’, a meaning that is unclear (87, 241, 251, 257). Interestingly, ‘right of domain’ is a phrase used in UK common law and refers to a citizen’s right to the ownership or possession of land. It is unclear how or when this phrase was used to refer to abdominal viscera; the earliest reference we could find was from 1972. In this paper, Willard Johnson from Chelsea, Massachusetts, writes, “*Infrequently a hernia is seen that has such a large sac that a significant portion of the abdominal viscera is residing outside the abdominal cavity. Over time no space is left in the abdomen to accommodate*

the replacement of such viscera. The contents of the sac have lost the right of domain in the abdomen" (284). Thus, this first definition suggests that the abdominal viscera lose the right to 'belong' inside the abdominal cavity.

The second definition we identified is based on pathological processes that occur due to large abdominal defects (261, 264-268). This was described in Chapter 1, but in essence the abdominal strap muscles contract, shorten and thicken, resulting in visceral protrusion. This definition uses the term 'domain' to refer to abdominal cavity volume and contraction of the lateral strap muscles, reduces the abdominal volume. Loss of domain, sometimes referred to as 'loss of abdominal domain', in this case means loss of abdominal cavity volume.

Five articles used the term 'loss of domain' without referring to abdominal cavity volume (86, 240, 244, 269, 270). Perhaps the authors assume that readers are aware that 'loss of domain' refers to 'loss of abdominal volume?' Instead these authors focus their definition on hernias being so large that a 'second abdomen cavity' is created inside the hernia sac. Three out of these five articles (86, 244, 270) add an additional aspect to their definition mentioning the significant physiological difficulties that may occur if this 'second abdomen' is reduced back into the patient's abdominal cavity. The origins of this description of the hernia sac as a "second abdomen" are unknown.

Lastly, five articles used definitions that appeared similar or equivalent to the definition of a large irreducible ventral hernia (33, 237, 271-273). Previous manuscripts have noticed that definitions for LOD and irreducible hernia are sometimes not dissimilar (33). These articles use terms like, "*the volume of the hernia can no longer be reduced into the abdominal cavity"* (33) and, "*hernia contents are set by adhesions and not reducible into the abdominal cavity"* (237). Clearly a standardised definition should distinguish hernias with LOD alone from those with irreducible and incarcerated components. Finally, it is important to mention that 49 articles, 64% of the total, use the phrase 'loss of domain' without any definition at all, or any reference to a standardised definition. Consequently, I must conclude that a knowledge or understanding of the concept of LOD is often assumed by authors despite there being no standardised definition.

Volumetric definitions exist already, although these are not consistent and are based around two equations. In the first case the hernia sac volume (HSV) is defined as a proportion of the residual abdominal cavity volume (ACV) (the Tanaka method, HSV/ACV (86)). This definition was used by 8 studies in our systematic review (33, 86, 237, 266, 268, 273, 280, 282). The alternative is to describe hernia volume as a proportion of the total peritoneal volume (TPV) (the Sabbagh method, ACV+HSV = TPV, HSV/TPV (87)). This definition was used by 5 studies in our systematic review (87, 240, 241, 271, 272). It is presently unclear which of these two definitions would be most appropriate or which operating surgeons feel would be the most meaningful and intelligible. Our group feel it is more logical and comprehensible to describe hernia volume as a proportion of total peritoneal volume, as this describes the percentage of abdominal viscera that has herniated, and outside the abdominal cavity.

Furthermore, a future volumetric definition of LOD may include subtypes of hernia by incorporating hernia neck width into the classification. Large hernias with narrow necks present a different surgical challenge compared to those with wide necks. In clinical practice, abdominal wall surgeons use hernia morphology to decide upon surgical approach and reconstructive techniques. In doing so they consider, other morphological parameters such hernia neck width, abdominal surface area to hernia defect area ratio, and proximity to bony prominences. The possible array of post-operative outcomes is likely to be dependent on hernia morphology and these parameters. As yet a descriptor that combines LOD with these other parameters does not exist and future work on this is warranted.

Via systematic review I have demonstrated that definitions of LOD are either disparate or omitted altogether. I found four concepts within the literature that described LOD and two volumetric definitions. Since LOD is a prime descriptor of hernia size and likely to be correlated with operative outcomes, an internationally accepted standardised definition is needed urgently, and this aim formed the basis of the work described in Chapter 7. In the following Chapter, Chapter 6, I explore exactly what is understood by the term ‘loss of domain’ on an individual surgeon level.

Chapter 6

What exactly is meant by 'loss of domain' for ventral hernia? A survey of 100 surgeons.

Part 1: Improving Research Quality

Clinician Survey: Defining Loss of Domain

Hypothesis

I hypothesize that general surgeons, who regularly perform VH repairs, have a poor understanding of the concept of loss of domain, with no generally accepted volumetric definition amongst clinicians and no therapeutic cut-point above which surgeons should not operate.

Aim

To demonstrate, via face-to-face survey, that loss of domain is poorly understood amongst practising surgeons with no standardised volumetric definition or therapeutic cut-point

Introduction

The systematic review described in the previous Chapter demonstrated considerable heterogeneity, finding multiple written and volumetric definitions, and without any consensus (239). Importantly we discovered that only 36% of included articles defined LOD, leaving 64% without a definition. These articles, therefore, used the phrase 'loss of domain' assuming that readers would instantly understand its meaning, without requiring further clarity. To investigate this, and to confirm that there was no known informal definition used widely by surgeons, I decided to perform a survey of surgeons regularly performing VH repair. My aim was to gain a deeper understanding of exactly what the term 'loss of domain' meant to them. Again, my hypothesis was based on inconsistency, predicting that

LOD was poorly understood, without a consistent definition. I aimed to determine if any single definition appeared to be dominant. I also asked clinicians whether there was a cut-point above which they chose not to operate as the risks outweighed benefit.

Methods

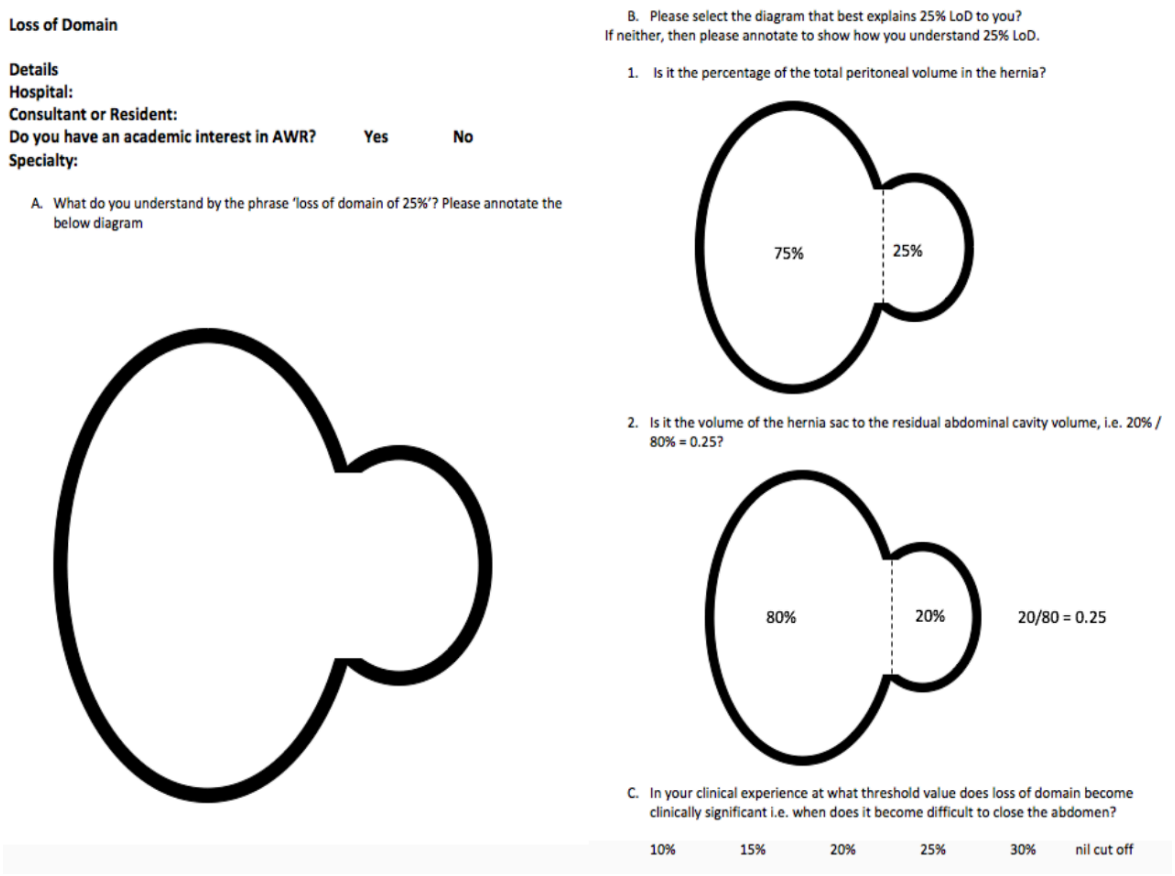
I designed a simple questionnaire to assess surgical understanding of the phrase 'loss of domain' (figure 1). A priori, I decided that a sample size of 100 would be sufficient to provide representative data concerning beliefs regarding LOD. The questionnaire was administered face-to-face by myself.

I first collected respondents' hospital location and professional grade, whether they had an academic interest in abdominal wall reconstruction, and their chosen sub-specialty. Only surgeons who performed VH repair as part of their routine practice were asked to complete the questionnaire. I decided that a proportion of our respondents should be surgical residents or trainees, as I wanted to assess which volumetric definition of LOD was most intuitive, not only to surgical consultants, but also to trainees.

I then asked the respondent to annotate a blank schematic diagram of a VH (figure 1), to illustrate their understanding of what 'loss of domain of 25%' meant to them. Once they had done this (or if they declared they were unable to), I then showed the surgeon a second diagram (figure 1) that illustrated two volumetric definitions of LOD: One; the Sabbagh definition, i.e. hernia sac volume (HSV) divided by total peritoneal volume (TPV) (87), and two; the Tanaka definition, i.e. HSV divided by abdominal cavity volume (ACV) (86). The surgeon was then asked to indicate which of the two options appeared most intuitive to them.

Lastly, I asked surgeons to give their own intrinsic threshold beyond which they believed VH repair was too risky, i.e, that threshold at which the hernia was likely too large to be repaired safely. Alternatively, surgeons could select "nil cut off".

Figure 1. Our questionnaire asking general surgeons about their understanding of LOD.



I conducted the survey over 12 months, from 1st February 2018 to 23rd January 2019 inclusive. The questionnaire was distributed by myself via the following methods: Face-to-face to delegates attending two hernia conferences (Abdominal Wall Reconstruction Europe, London, UK, February 2018 and Americas Hernia Society, Miami, USA, March 2018); to abdominal surgeons at three London hospitals; and ad hoc to abdominal wall surgeons known to our centre. Responses were collated by myself in a spreadsheet (Microsoft Excel for Mac 2011 Version 14.5.9, Microsoft Corporation, Washington, USA) and descriptive statistics derived.

Results

I achieved the planned sample size of 100 surgeons: 43 (43%) were from the conferences (18 London; 25 Miami) 52 (52%) from London Hospitals (28 UCL, 12 Princess Alexandra Hospital, 12 Chelsea and Westminster Hospital); Five (5%) from other hospitals (Table 1). Sixty (60%) worked in a university hospital, whilst the remaining 40 (40%) worked in district general hospitals (DGHs). Sixty-seven (67%) were consultants, leaving 33 (33%) as residents, i.e. surgeons still in training. Chosen surgical subspecialties varied, with colorectal surgery being the most prevalent (35%) and hepatobiliary surgery being the least (1%). Twenty-nine (29%) of respondents claimed to have an academic interest in Abdominal Wall Reconstruction (AWR) (Table 1).

Table 1: Characteristics of questionnaire respondents.

Characteristics		**No. of Respondents**
Location of questionnaire completion	AWR Europe 2018	18
	AHS 2018	25
	University College London Hospital	28
	Chelsea and Westminster	12
	Princess Alexandra Hospital	12
	Other	5
University / District General	University Hospital	60
	District General Hospital (DGH)	40
Level of training	Consultant	67
	Resident	33
Academic AWR interest	Yes	29
	No	71
Chosen sub-specialty	Colorectal	35
	Upper GI	17
	General Surgery	17
	Plastic Surgery	8
	AWR Surgeon	8
	Endocrine	7
	Bariatric Surgery	5
	Hepatobiliary	1
	Unclear/Did not fill in	2

Concerning their understanding of 25% LOD, 53 (53%) surgeons annotated the diagram in such a way that the hernia sac volume was 25% and the residual abdominopelvic cavity volume 75% (i.e. the Sabbagh method (87)). Eighteen (18%) respondents annotated the diagram in such a way that the hernia sac volume was 20% and the residual abdominopelvic cavity volume of 80% (i.e. the Tanaka method (86)). A further 21 (21%) were unable to annotate the diagram at all, while 8 (8%) made miscellaneous or incomprehensible annotations (Table 2). Therefore, of the 71 surgeons whose annotation designated either Sabbagh or Tanaka, 75% (53) indicated Sabbagh and 25% (18) Tanaka. Of these, consultant respondents drew the Sabbagh method predominantly, a trend also seen amongst university surgeons, DGH surgeons, non-academic surgeons, and residents (Table 2). Only academic abdominal wall surgeons drew the Tanaka method with greater frequency (Table 2). The miscellaneous annotations included two declaring 50% of the TPV within the hernia sac; four showing the hernial ostium as a 25% defect of the total abdominal circumference; one showing a 25% defect of the coronal surface area of the anterior abdominal wall; and one diagram annotated with an arrow pointing to the hernial ostium stating, “25% loss of the abdominal wall integrity”.

Table 2: Schematic diagram annotation (75/25 TPV/HSV ratio = Sabbagh method, 80/20 TPV/HSV ratio = Tanaka method). TPV: Total peritoneal volume, HSV: Hernia sac volume

Subgroups (n)	Sabbagh 75/25 (%)	Tanaka 80/20 (%)	Miscellaneous (%)	Unclear/Not able to fill in (%)
Total (100)	53 (53)	18 (18)	8 (8)	21 (21)
Consultant surgeons (67)	33 (49)	14 (21)	6 (9)	14 (21)
Resident surgeons (33)	20 (61)	4 (12)	2 (6)	7 (21)
University surgeons (60)	33 (55)	13 (22)	5 (8)	9 (15)
DGH surgeons (40)	20 (50)	5 (12)	3 (8)	12 (30)
Academic AWR interest (29)	12 (41)	16 (55)	0 (0)	1 (4)
No academic AWR interest (71)	41 (58)	2 (3)	8 (11)	20 (28)

When asked to exhibit a preference between the two diagrams showing the Sabbagh (87) and Tanaka (86) definitions, 60 (60%) surgeons chose Sabbagh method and 40 (40%) Tanaka. (Table 3). Again, the only subgroup exhibiting a

preference for the Tanaka definition overall were the surgeons with an academic interest in AWR (Table 3).

Table 3: Table showing the proportions of preferred volumetric method to describe loss of domain according to respondent subgroup.

Subgroups (n)	Sabbagh Method (%)	Tanaka Method (%)
Total (100)	60 (60)	40 (40)
Consultant surgeons (67)	41 (61)	26 (39)
Resident surgeons (33)	19 (58)	14 (42)
University surgeons (60)	36 (60)	24 (40)
DGH surgeons (40)	24 (60)	16 (40)
Academic AWR interest (29)	12 (41)	17 (59)
No academic AWR interest (71)	48 (68)	23 (32)

The most frequently chosen threshold value for significant LOD was 20%, which was selected by 35/100 surgeons. Thresholds of 25%, 30%, 15%, and 10% were selected by 26 (26%), 10 (10%), 5 (5%), and 3 (3%) surgeons respectively (Table 4). Six surgeons documented other values as follows: 50%, 35%, 33%, 20 to 25% (two surgeons), and 30 to 40%. Therefore, 63 surgeons (63%) selected a threshold value ranging between 20 to 25% inclusive for clinically significant LOD. Fifteen surgeons selected the “nil cut off” alternative.

For all subgroups, except residents, 20% was the most prevalent threshold. Twenty-five percent was the value selected most frequently by residents. ‘Nil cut off’ was selected by 22% of university surgeons, 20% of consultant surgeons, and 17% of academic AWR surgeons. ‘Nil cut off’ was selected least by 6% and 5% of resident and DGH surgeons respectively.

Table 4: Table showing the % LOD thresholds (cut off point) selected by respondents, according to surgical subgroup.

Sub-group (n)	10% (%)	15% (%)	20% (%)	25% (%)	30% (%)	Nil cut off (%)	Other (%)
Total (100)	3 (3)	5 (5)	35 (35)	26 (26)	10 (10)	15 (15)	6 (6)
Consultant surgeons (67)	1 (1)	2 (3)	25 (37)	13 (20)	8 (12)	13 (20)	5 (7)
Resident surgeons (33)	2 (6)	3 (9)	10 (30)	13 (40)	2 (6)	2 (6)	1 (3)
University surgeons (60)	1 (2)	1 (2)	21 (34)	13 (22)	6 (10)	13 (22)	5 (8)
DGH surgeons (40)	2 (5)	4 (10)	14 (35)	13 (33)	4 (10)	2 (5)	1 (2)
Academic AWR interest (29)	0 (0)	1 (3)	10 (35)	6 (21)	3 (10)	5 (17)	4 (14)
No academic interest (71)	3 (4)	4 (6)	25 (35)	20 (28)	7 (10)	10 (14)	2 (3)

Discussion

This survey aimed to gain a deeper understanding of the range of individual surgeons' beliefs regarding LOD, explore which of two proposed published volumetric definitions was most intuitive, and investigate the threshold beyond which surgery was believed to be particularly challenging. Our survey confirms that individual surgeons performing VH repair have a poor understanding of LOD overall. Given the physiological and biomechanical changes that occur during and following large VH repair, poor understanding and/or differing definitions work against improving postoperative outcomes. This survey suggests that generally accepted written and volumetric definitions of LOD are required.

Asking participants to annotate a blank diagram was intended to discover whether surgeons had any prior knowledge regarding LOD, and, if so, whether that was correct. I found a general lack of understanding of LOD as a concept, as 21% of respondents were unable to annotate the diagram at all. Beyond this, some participants offered "explanations" that were irrational and not compatible with any existing recognised definition. Of those offering recognised annotations, the majority overall favoured the Sabbagh description, i.e. that a LOD of 25% means simply that 25% of the total peritoneal volume resides within the hernia sac. Interestingly, all of the subgroups examined favoured Sabbagh over Tanaka with the sole exception of surgeons with an academic interest in AWR. The most plausible explanation is that the Tanaka definition has gained more traction within the academic community, possibly because the relevant publication preceded the Sabbagh method.

I then presented diagrams illustrating the Tanaka and Sabbagh methods and asked participants to offer a preference. This allowed those participants previously unfamiliar with one or both methods to offer an opinion, in addition to opinions from participants familiar with both. We were exploring which definition was the most logical and easiest to comprehend overall. Again, overall the group favoured the Sabbagh method, suggesting it is the more intuitive. However, again the sole subgroup preferring Tanaka was surgeons with an academic interest in AWR.

My final question explored the threshold at which surgeons believed the risk of VH repair becomes significant, e.g. from post-operative complications and/or recurrence. Overall, a LOD of 20% was the most popular cut-point. However, during face-to-face discussions when completing their responses, most clinicians stated that their answer was not based on evidence but a “hunch” based on their personal clinical experience. Many stated that LOD could not be considered in isolation, and that additional patient factors were equally or more important. Suggestions offered included abdominal wall laxity and patient co-morbidities such as respiratory and cardiovascular compromise. A frequently offered response was that, ‘if I can reduce the hernia manually in clinic, then loss of domain is reversible and I can attempt a repair’.

Threshold LOD values are reported in the literature but are mostly anecdotal. In 2004, Kingsnorth et al (244) suggested that if the hernial volume exceeds 15 to 20% of the abdominal compartment, then returning the contents of the sac will require, ‘significant patient physiological adaptation’. Tanaka (86) and Sabbagh (87) both published their own threshold values. Tanaka used 25% LOD as the cut point at which to introduce pre-operative pneumoperitoneum but did not explain how this threshold was conceived (86). Sabbagh demonstrated that, in a series of 17 large VHs, LOD less than 20% resulted in a tension free repair. When considering these thresholds, the method used for their calculation must be acknowledged. As my questionnaire made clear, 25% LOD calculated using the Tanaka method is exactly equal to 20% LOD calculated using the Sabbagh method. Accordingly, both are describing the same threshold value. It is clear that further work to establish an evidence-based cut-point for LOD is required.

Many ventral hernia grading scales have been published (47, 50, 53, 55, 57, 285). Most seem academic, with little clinical utility. None of these proposed scales account for LOD. Indeed, hernias with significantly different LOD can attract the same grade (e.g. EHS grade: M3, M4, W3, recurrent, can be used for hernias with very different LOD). It seems plausible that LOD would have useful prognostic value concerning the success or failure of subsequent surgical repair, in combination with other factors known to be important. In order to incorporate

LOD into an internationally accepted grading system, we first require an accepted standardised written and volumetric definition for LOD.

As stated in Chapter 1, previous work has attempted to classify and define large VHs or complex ventral hernias (CVHs), yet there is little consensus. Slater et al (56) published a rather involved classification system, dividing CVHs into “mild”, “moderate” and “major” subgroups. In a recent survey (237) 48 French surgeons defined ‘giant ventral hernia’ as those having LOD, and a hernia volume to abdominal volume ratio of greater than 30%. They defined LOD as when ‘hernia contents is set by adhesions and not reducible into the abdominal cavity’. This written definition has been recognised, but is as yet unstandardized (239). Both Slater et al (56) and Passot et al (237) used LOD criteria, >20% and >30% respectively, within their classification systems. However, their volumetric definitions differ, with Slater using Sabbagh’s definition (87), and Passot using Tanaka’s (86).

In summary, our survey found that LOD is poorly understood; Many surgeons were unable to express the concept. Overall, the Sabbagh method (87) appeared the most acceptable and intuitive but the Tanaka (86) method has specific traction amongst academic AWR surgeons. Since LOD is a prime descriptor of hernia size and likely correlated with operative outcomes, a standardised and generally accepted definition is required, which forms the basis of the work presented in Chapter 8.

Chapter 7

Proposed Minimum Dataset, Patient Reported Outcomes, and Methodology Criteria for Interventional Trials of Primary Ventral and Incisional Ventral Hernia Repair.

Part 1: Improving Research Quality

Nominal Group Technique: Outcome definitions and detection methods, peri-operative variable definitions, minimum datasets and standardised methodology for interventional trials of VH repair.

Hypothesis

I hypothesize that by using a group of expert panelists (key opinion leaders) and a solution generating technique, such as the Nominal Group Technique, we can reach group consensus on a minimum dataset for VH interventional trials. As guidelines suggest that primary and incisional VH should be investigated separately I hypothesise that two minimum datasets should be generated.

Aim

To create standardised minimum datasets for interventional trials of both primary and incisional VH using a group of expert panelists and the Nominal Group Technique. In doing so we aim to standardise peri- and post-operative data collection for VH trials. These datasets will include defined perioperative variables, clear outcome definitions and standardised detection methods, patient reported outcomes, and guidance/criteria for high quality trial methodology.

Introduction

Whilst assessing the 'state of the literature', the two systematic reviews described in Chapters 3 and 4 of this thesis (170, 286) revealed that VH interventional trials collect data that is poorly defined, has little consistency between trials, and

contain post-operative outcomes that are measured and detected in many different ways. This lack of consistency creates highly heterogenous data, which hinders trial comparison via both narrative review and meta-analysis.

To rectify this, I aimed to construct a minimum dataset for VH interventional trials. Our early discussions identified that primary ventral hernia (PVH) and incisional ventral hernia (IVH) are increasingly being investigated and treated as separate pathologies, since their aetiologies differ (47). Indeed, published guidelines recommend that, *"when studying ventral hernias, the analysis of primary ventral hernias should be done separately from the analysis of incisional and recurrent ventral hernias"* (124). Consequently, our panelists decided to develop two minimum datasets, for primary and incisional VHs respectively. In this study, I used an expert panel to identify and define variables, and to standardise their measurement and detection.

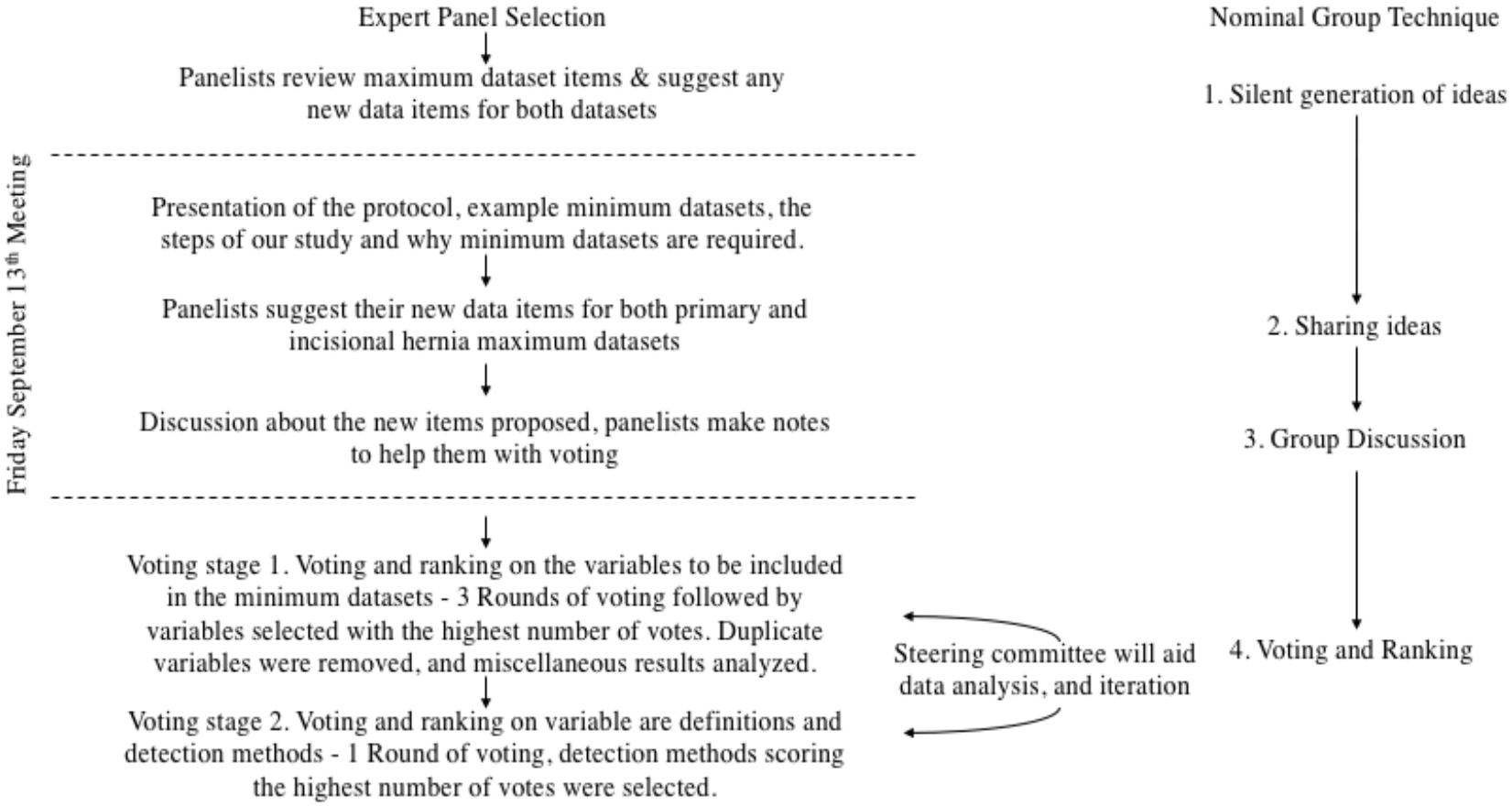
Methodology and Design

The methodology was based on the Nominal Group Technique (NGT). NGT is a procedure that facilitates effective group decision making by giving each individual an equal chance to provide input into a defined problem (125). NGT provides large amounts of data over a short period of time (287), reduces 'social loafing' (288), and can be used to establish priority lists (289).

Before the exercise began, panelists were asked to assume that the minimum datasets will be for interventional VH trials being conducted in a modern hospital with routine follow up and outpatient diagnostic tests. Panelists were asked to assume that these datasets will provide a template for interventional trials of elective VH repair where this is the primary indexed procedure. This is particularly important for retrospective studies where the primary procedure is sometimes unclear; i.e. the minimum dataset does not apply to operations where the primary indexed procedure is not VH repair or is unclear. Parastomal hernias were excluded, but it was anticipated the dataset could be adaptable for these. SH, SM, and I acted as the steering committee throughout and did not vote. As per NGT stipulations, during group discussions they remained impartial and

encouraged panelists to debate while not contributing themselves. Development consisted of four phases; expert panel selection (phrase 1), development of a maximum dataset (phase 2), a focused group meeting and maximum dataset completion (phrase 3), followed by rounds of voting and ranking (phase 4). The four phases of NGT; silent generation of ideas, ideas sharing, group discussion, and voting and ranking, were used to create the minimum trial datasets (125). The four phases of dataset development are displayed in the flowchart, Figure 1.

Figure 1: Flowchart showing the stages of minimum dataset development. The Nominal Group Technique to guide our methodology.



Phase 1: Expert Panel Selection

Being surgeons, ACJW and I selected a group of European panelists with well-established specialist academic and clinical interest in VH repair. Several panelists are leading members of the European, British, and Danish Hernia Societies. In total, 15 expert panelists were asked to take part. All panelists gave written consent to their participation and were asked to complete the study, to add variables to the maximum dataset, to attend a focused group meeting in Hamburg at the European Hernia Society's 2019 conference, to participate in rounds of voting, and to adhere to NGT format during group discussions. Panelists were also asked to adhere to COPE criteria (290), thereby authenticating their co-authorship. Lastly, panelists were asked to declare any conflicts of interest (COIs) on their consent form. Those with COIs were asked to withdraw if they believed these would affect their judgement, none withdrew.

Because patient and public involvement is deemed essential when formulating patient reported outcomes measures (PROMs), I included two patient advocates. Consequently, 17 panelists contributed to suggesting, disputing, prioritising and ranking PROMs. The 15 expert hernia surgeons also contributed to the analysis and prioritising of the clinical variables.

Phase 2: Development of a Maximum Dataset

To develop a maximum dataset, the two prior systematic reviews described in Chapters 3 and 4 of this thesis (170, 286) were interrogated to identify and extract variables collected during VH interventional trials. These variables were listed in Microsoft Excel (Microsoft Excel for Mac 2011 v. 14.5.9, Microsoft Corporation, Washington), (Appendix 11). This list contains an extensive catalogue of variables that could be potentially incorporated into the minimum datasets. The same list was used to develop both primary and incisional hernia minimum datasets. SM and I grouped these variables into four categories; 1) pre-operative variables (patient and hernia variables), 2) intra-operative variables, 3) post-operative variables, 4) patient reported outcomes measures. A fifth section of methodological criteria was also compiled from interventional trial tools used for

previous methodological analysis (172-176, 291). The provisional maximum dataset was emailed to panelists for analysis and review. Panelists were asked to add any additional variables that they felt warranted inclusion (satisfying NGT, Silent generation of ideas, (125)).

Phase 3: Focused Group Meeting and Maximum Dataset Completion

All panelists were then asked to attend a focused group meeting to debate and discuss the contents of the maximum datasets. Initially, I gave a presentation explaining the protocol and meeting purpose. Reasons for establishing a standardised minimum dataset for interventional trials was presented and example datasets from other disciplines given to all panelists. Thereafter, panelists fulfilled two tasks:

1) Via 'round robin' structured discussions, individual panelists were given the opportunity to detail any additional variables they had added and their rationale for this (satisfying NGT, sharing ideas, (125)).
2) The additional variables were then discussed and their inclusion debated (satisfying NGT, group discussion, (125)). If further new variables arose from these discussions, these were also added to the maximum dataset if deemed appropriate. During discussions panelists could make notes. The two patient advocates contributed to discussions concerning PROMs.

Phase 4: Voting and Ranking

Panelists were sent the finalised maximum dataset following the meeting. Voting occurred in three stages (NGT: Voting and Ranking, (125)). Initially panelists were sent a table asking for the number of individual variables they considered suitable for each category of both datasets (Appendix 12). Thereafter, they selected from the maximum dataset those variables they considered should be included in the minimum datasets. Finally, panelists voted on variable definitions and detection methods. Voting occurred via electronic mail. During voting the steering committee facilitated results tabulation, data interpretation and analysis,

and iteration. Voting for both primary and incisional hernia datasets occurred concurrently.

Stage 1: Number of dataset variables

I collected these votes, the results were analysed by the steering committee, and a final number of variables was proposed to panelists for approval.

Stage 2: Variables in the Datasets

As described above, a proposed number of variables, X, had been defined for each dataset category. From the maximum dataset, for each category, panelists were then asked to rank their chosen variables/items, from X (most preferred) to 1 (least preferred). Variables scoring greater than 50% of the maximum possible score for a category (maximum = 15 x X; 17 x X, for PROMs) were defined as achieving consensus, and were included in the final minimum dataset. Variables attracting no votes were deleted from the next round of voting. If Y variables reached consensus for a category in Round 1, then panelists voted on X-Y variables in that category for Round 2, from X-Y (most preferred) to 1 (least preferred). Again, 50% of the maximum possible score was deemed as reaching consensus. Results from each voting round were disclosed to panelists, and voting continued for three rounds. Thereafter, results of the three voting rounds were analysed by the steering committee. For incomplete categories, remaining variables were selected in order of popularity and duplicate variables removed. Miscellaneous results were discussed amongst the steering committee and removed if appropriate. Thereafter, the finalised minimum datasets were compiled and sent to all panelists for approval.

Stage 3: Variable Definitions and Detection Methods

Panelists then voted on variable definitions and detection methods. For most variables, definitions used commonly by hernia surgeons were selected and proposed by the steering committee. Free text space was available for panelists to propose alternative definitions. Where multiple choices were possible for a

detection method (e.g. imaging), panelists voted for their preference. Panelists also selected their preferred follow-up duration, selecting more than one duration where they deemed appropriate. To improve efficiency, if a variable existed in both minimum datasets, panelists were asked to vote only on how they would detect it for PVH. After voting, panelists were asked if they were happy for their responses to also apply to variables in the IVH dataset and if not, why? Comments and feedback were encouraged. Detection methods and follow-up times achieving the highest number of votes were selected.

At the end of the process, the finalised minimum datasets with their respective variable definitions and detection methods were sent to all panelists for approval.

Results

1. **Panelist Selection**

All expert hernia surgeons approached agreed to take part in the study. Three panelists MM, MS, and AM joined the study late and after voting on the number of variables in the datasets. They therefore did not take part in development of our maximum dataset or in our focused group meeting. Both expert patients approached, SB and ND, agreed to take part.

2. **Development and completion of the Maximum Dataset**

The maximum dataset initially contained 245 variables; 22 (9%) patient variables, 19 (8%) hernia characteristics, 20 (8%) intra-operative variables, 32 (13%) post-operative outcomes, 116 (47%) patient reported outcomes, and 36 (15%) methodology criteria, all derived from previous systematic review (170, 286). 109 new variables were suggested by panelists;19 (17%) patient variables, 15 (14%) hernia characteristics, 32 (29%) intra-operative variables, 9 (8%) post-operative outcomes, 30 (27%) patient reported outcomes, and 4 (4%) methodology criteria, expanding our maximum dataset to 354 variables. The focused group meeting occurred during the European Hernia Society's 41st conference in Hamburg, on Friday September 13th 2019. After structured 'round robin' and group discussions

30 variables were eliminated leaving 324 variables in the maximum dataset; 40 (12%) patient variables, 29 (9%) hernia characteristics, 35 (11%) intra-operative variables, 39 (12%) post-operative outcomes, 141 (44%) patient reported outcomes, and 40 (12%) methodology criteria (Appendix 13).

3. Voting and Ranking

Stage 1: Number of dataset variables

For the PVH minimum dataset panelists voted for a mean of 60 variables (range 29 to 97). For each category votes averaged 15 (25%) patient variables, 10 (17%) hernia characteristics, 19 (32%) intra-operative variables, and 16 (26%) post-operative outcomes. For the IVH minimum dataset panelists voted for a mean of 71 variables (range 36 to 104); 16 (22%) patient variables, 17 (24%) hernia characteristics, 21 (29%) intra-operative variables, and 17 (24%) post-operative outcomes. Panelists, including the patient representatives, voted for 25 patient reported outcomes. Finally, panelists voted for an average of 37 methodology criteria. At this early stage the steering committee felt an intervention was required as the number of chosen variables was considered as excessive for a minimum dataset. After reviewing the literature and analysing current registries (61, 63) and trial datasets (292), and the number of variables collected by previous hernia trials (36, 141, 143, 157, 293) the steering committee proposed 31 variables for the PVH dataset (8 (26%) patient variables, 6 (19%) hernia characteristics, 10 (32%) intra-operative variables, 7 (23%) post-operative outcomes), and 39 variables for the IVH dataset (8 (20%) patient variables, 10 (26%) hernia characteristics, 14 (36%) intra-operative variables, 7 (18%) post-operative outcomes), with 25 PROMs, and 38 methodology criteria. The steering committee informed the panelists of their proposal to reduce the number of variables to reasonable levels, and the rationale for this. All panelists then agreed with the final number of variables (Appendix 14).

Stage 2: Variables in the Datasets

Voting commenced on 1st October 2019 and was completed on 10th July 2020 (example voting sheet for Round 1, Appendix 15). For the PVH dataset 9 variables reached consensus in Round 1; 4 (44%) patient variables, 3 (33%) intra-operative variables, and 2 (23%) post-operative outcomes. After Round 2, 8 more variables reached consensus; 2 (25%) patient variables, 2 (25%) hernia characteristics, 3 (37.5%) intra-operative variables, and 1 (12.5%) post-operative outcomes. A further 7 variables reached consensus after Round 3; 1 patient variable, 2 hernia characteristics, 2 intra-operative variables, and 2 post-operative outcomes. Consequently, 24 of the 31 (77%) variables were selected after 3 rounds of voting (Appendix 16). For 6 of the 7 remaining, the variables scoring highest and selected most frequently by panelists were added to the dataset. The steering committee made two interventions: 'COPD' which had received a surprisingly low score after Round 3, was added as the last patient variable. 'COPD' had achieved high scores in Rounds 1 and 2, and was therefore selected over 'Frailty', 'Anti-coagulation', and 'No. of co-morbidities'. The committee also decided to add, 'Re-operation rate in 30 days' as an additional outcome, making a total of 8 post-operative outcomes and 32 variables in the final PVH dataset, Table 1 (Appendix 16).

For the IVH dataset 12 variables reached consensus in Round 1; 5 (42%) patient variables, 1 (8%) hernia characteristic, 4 (33%) intra-operative variables, 2 (17%) post-operative outcomes. After Round 2, 9 more variables reached consensus; 2 (22%) patient variables, 1 (11%) hernia characteristic, 4 (45%) intra-operative variables, and 2 (22%) post-operative outcomes. A further 9 variables reached consensus after Round 3; 4 (45%) hernia characteristics, 3 (33%) intra-operative variables, and 2 (22%) post-operative outcomes. Consequently, 30 of the 39 variables were selected after 3 rounds of voting (Appendix 17). For 8 of the 9 remaining, variables scoring highest and selected most frequently by the panelists were added to the dataset. Again, the steering committee intervened twice. 'Pre-operative pneumoperitoneum' was removed as a possible option as it was deemed too rare. 'Mesh overlap' was therefore added to the dataset as an intra-operative variable. To standardise post-operative outcomes, the committee

also added ‘chronic pain’, the next most popular outcome selected. This resulted in a total of 8 post-operative outcomes for both datasets and 40 variables in the final IVH dataset, Table 2 (Appendix 17). The rationale for all steering groups interventions were explained to and accepted by the expert panelist group.

For the PROMs 11 of the 25 outcomes reached consensus after the 3 rounds of voting; 4 (36%) during Round 1, 5 (46%) during Round 2, and a further 2 (18%) after Round 3 (Appendix 18). The 4 remaining PROMs from EURAHS QoL (63) and the 6 remaining PROMs from SF-12 (294) scored sufficiently for selection. The last 4 PROMs to achieve a higher enough score, without duplication of previously included PROMs, were proposed by the patient representatives on our panel. Two of these assessed mental health, sexual activity, and 2 focused on decisional regret. For one PROM the steering committee made a small adjustment. For the question; ‘Moderate activities, such as moving a table, vacuum cleaning, bowling, or playing golf’, ‘vacuum cleaning’ was changed to ‘getting dressed’ and ‘cooking’ (Appendix 18). The final list of 25 PROMs can be seen in Table 3.

For the methodology criteria, panelists could not reach consensus regarding which criteria should be removed from the original list of 40 recommendations. Consequently, during Round 3 we asked all panelists; ‘please state whether you agree or disagree with the following’: ‘I think all 40 of the original methodology criteria can be used in a checklist for ventral hernia interventional trials’ (Appendix 19). All 15 hernia specialists agreed with this statement. These recommended methodological criteria are displayed in Table 4.

Stage 3: Variable Definitions and Detection Methods

This stage involved a single round of voting (Appendix 20). After panelist review of the proposed variable definitions, two definitions were altered by the steering committee. Three panelists objected to the proposed definition for smoking status, with one panelist stating; ‘*Two months abstinence should be required for an ex-smoker, that is clinically relevant in terms of reduction of complications from surgery’*. Consequently, the existing EURAHS definition of smoking status was

adopted (63). Secondly, an existing definition for mesh infection could not be identified prior to voting. Therefore, panelists were asked to suggest a definition. Five panelists proposed a new definition, after review and a new definition devised; '*A chronic wound infection, wound sinus, or wound abscess in the location of a prosthetic mesh implant'*. Regarding loss of domain, the Sabbagh volumetric definition was chosen, after receiving 10 votes (67%), compared to 5 for the Tanaka definition. The finalised definitions can be found in column 2 of the completed datasets, Table 1 and Table 2.

Votes for variable detection methods are shown in Appendix 20. Where panelists were indecisive, they often chose more than one option or occasionally proposed an alternative. For 4 out of 6 pre-operative hernia variables (67%); number of ventral hernia defects, hernia width, diastasis, and loss of domain, panelists selected CT as their preferred option. To grade PVH using the EHS classification system, 'clinical examination' was the most popular detection method and for reducibility 'clinical examination +/- CT' was most popular. Overall, 12 panelists (80%) chose CT scanning as the method to assess and characterise PVH pre-operatively. For hernia defect area, the only IVH variable panelists were required to vote on, 14 panelists (93%) selected CT.

Panelists also voted for post-operative outcome detection methods (Appendix 20). For wound infection 8 (53%) panelists voted for clinical diagnosis via history and examination. This was adapted by the steering committee to meet the CDC criteria; see Table 1 & 2. For surgical site occurrence, 12 (75%) panelists voted for history and examination. Votes for mesh infection detection methods varied but were based predominantly on clinical diagnosis with positive culture. Consequently, we devised a statement based on CDC criteria for wound infection; *'Purulent discharge from a wound containing a prosthetic mesh implant OR a positive culture from a chronic wound containing a mesh implant using a wound swab, fluid aspirate, or an explanted piece of mesh OR a positive culture from intra-operative fluid surrounding a mesh'*. Eleven panelists (73%) voted for 'clinical examination +/- CT scan' to detect hernia recurrence. When asked whether all inpatient post-operative complications should be recorded, 14 panelists (93%) suggested they should if part of trial follow up and data analysis.

Overall, all panelists (100%) chose CT scanning to detect post-operative outcomes after PVH repair. Regarding follow-up duration, votes varied; 30 days, 1 year and 5 years received 14, 8, and 5 votes respectively, and were recommended by the steering committee as standardised follow-up durations.

After voting, panelists were asked whether their votes for detection methods for PVH variables could be applied to the same IVH variables. All panelists agreed to the same detection methods for IVH variables. As a caveat, the group added a cautionary note regarding pre-operative CT scanning for trials of PVHs: While there was consensus regarding CT as the optimal detection method, panelists considered that trials should adopt low-dose targeted scanning to minimise radiation exposure where there was no clinical requirement for pre-operative CT. The finalised detection methods can be found in column 3 of the completed datasets, Table 1 and Table 2.

For our PROMs dataset, during the final round panelists were asked to vote on the timing of assessment. Fourteen panelists (93%) agreed that pre-operative baseline PROMs should be recorded. Concerning post-operative follow-up, again votes varied; however, 30 days, 1 year, and 5 years received 6, 10, and 6 votes respectively and the steering committee proposed these as standardised intervals for participant assessment.

Table 1. Minimum Dataset for Primary Ventral Hernia

Pre-operative Variables	**Definition**	**Detection Method**
Age	Years since birth	Age on the day of VH repair
Sex	Male/Female	Sex on the day of VH repair
Obesity/BMI	Kilograms/Height in meters squared	Calculated on the day of VH repair
COPD	Previous diagnosis of COPD	Taking repeat medications for COPD on the day of VH repair.
Smoker	EURAHS definitions (63): Never smoked, Ex-smoker (>12 months), Occasional smoker, Daily smoker No. pack years: No cigarettes/day x years of smoking / 20	Status selected on the day of VH repair
Diabetes (type I/II)	Previous diagnosis of type I/II DM.	Taking repeat medications for Diabetes on the day of VH repair.
Immunosuppression/Steroid use	Previous diagnosis requiring immunosuppression therapy.	Immunosuppression/steroids taken over the perioperative period.
ASA	American Society of Anaesthetists score.	Score on the day of VH repair
Hernia variables	**Definition**	**Detection Method**
No of hernia defects	No of defects in the anterior abdominal wall	CT*
Hernia width	Maximal defect width; if more than one defect, measure the width according EHS classification (47).	CT*
Loss of Domain	Written: A ventral hernia large enough such that simple reduction in its contents and primary fascial closure either cannot be achieved without additional reconstructive techniques or cannot be achieved without significant risk of complications due to the raised intra-abdominal pressure. Volume: Sabbagh Method: Hernia sac vol / Peritoneal cavity vol (295).	CT*
EHS score	EHS classification for Primary Ventral Hernias. Graded according to: Position; epigastric, umbilical, Spigelian, Lumbar. Maximal defect width; small <2cm, medium 2-4cm, large >4cm (47).	Clinical exam

Divarification	A separation of >2 cm is considered to be a rectus diastasis (296).	1. CT*
Reducible	Reducible Irreducible without skin changes Irreducible with skin changes Irreducible with bowel contents causing obstruction	1. Clinical exam +/- CT

Best imaging modality for pre-op assessment of hernia: CT*

Peri-operative variables	**Definition**	**Detection Method**
Lap/Open/Robotic (as treated, not ITT)	Mode of surgery	Intra-operative details
Mesh/suture repair	Method of repair	Intra-operative details
Mesh repair		
-Exact mesh name; material/type/brand	Document trade name. Type: biologic, biosynthetic, synthetic.	Intra-operative details
-Mesh fixation technique	Suture: absorbable/non-absorbable. Tacks: absorbable/non-absorbable	Intra-operative details
-Position of mesh – plane of insertion	ICAP nomenclature: Onlay, Anterectus, Inlay, Interoblique, Retrooblique, Retrorectus, Retromuscular, Transversalis Fascial, Preperitoneal, Intraperitoneal (297).	Intra-operative details
-Mesh size	Intraoperative measurement	Intra-operative details (cm^2)
-Bridging Vs Primary fascial closure	EHS definitions (63): Bridging: the anterior fascia of the hernia defect is not **completely** closed. Primary fascial closure: the anterior fascia of the hernia defect is **completely** closed	Intra-operative details
Suture repair		
-Suture type: absorbable/non-absorbable	Absorbable/Non-absorbable material used	Intra-operative details
VHWG grade	Four VHWG grades: Grade 1: Low risk; no history of wound infection, no co-morbidities. Grade 2: Co-morbid; smoker, obese, diabetic, immunosuppressed, COPD.	Intra-operative details

	Grade 3: Potentially contaminated; Previous wound infection, stoma present, violation of GI tract. Grade 4: Infected; Infected mesh, septic dehiscence (50).	
CDC score	Four CDC grades: Grade 1: Clean; uninfected wounds with no inflammation, the alimentary tract is not entered. Grade 2: Clean-contaminated; operative wounds in which the alimentary tract is entered under controlled conditions, without spillage. Grade 3: Contaminated; operative wounds with a major breech in sterility or spillage from the alimentary tract, includes incisions where acute, non-purulent inflammation is encountered. Grade 4: Dirty; pre-existing infected operative wound prior to the start of the operation, includes mesh infection and enterocutaneous fistula (89).	Intra-operative details
Post-operative outcomes	**Definition**	**Detection Method**
Wound infection (SSI)	CDC definition: A surgical site infection (SSI) is an infection that occurs after surgery in the part of the body where the surgery took place. Surgical site infections can sometimes be superficial infections involving the skin only. Other surgical site infections are more serious and can involve tissues under the skin or organs (298).	**Superficial**: Involves the skin and subcutaneous tissue, occurs within 30 days of surgery, AND; Patient has at least ***one*** of the following: -Purulent drainage from the superficial incision. -An organism identified by a positive culture. -Wound is deliberately opened by a surgeon or physician AND patient has at least one of these signs and symptoms localized pain or tenderness, localized swelling, erythaema, or heat. -Diagnosis of a superficial incision SSI by a surgeon or physician. **Deep**: Involves deep soft tissues of the incision, eg fascia or muscle, occurs within 30 or 90 days of surgery, AND; Patient has at least ***one*** of the following: -Purulent drainage from the deep incision.

		-A deep incision that spontaneously dehisces, or is deliberately opened by a surgeon or physician AND an organism identified by positive culture AND patient has at least one of the following fever (>38°C), localized pain, or tenderness. - an abscess or other evidence of infection involving the deep incision that is detected on gross anatomical or histopathologic exam, or imaging test. **Organ-space**: Involves any part of the body deeper than the fascial/muscle layers that was opened or manipulated during the surgery, occurs within 30 or 90 days of surgery, AND; Patient has at least ***one*** of the following: -Purulent drainage from a drain that is placed into the organ/space. -An organism identified by a positive culture. -An abscess or other evidence of infection involving the organ/space that is detected on gross anatomical or histopathologic exam, or imaging test.
Surgical site occurrence (SSO)	Any SSI as well as wound cellulitis, non-healing incisional wound, fascial disruption, skin or soft tissue ischemia, skin or soft tis- sue necrosis, wound serous drainage, chronic sinus drainage, localized stab wound infection, seroma, haematoma, exposed biological/synthetic mesh, myocutaneous anastomotic disruption, and development of an enterocutaneous fistula (226).	History and Clinical examination, medical records
Surgical site occurrence requiring procedural intervention (SSOPI)	SSOs requiring a procedural intervention, defined as wound opening or debridement, suture excision, percutaneous drainage, or mesh removal (299).	History and Clinical examination, medical records
Mesh infection	New definition: A chronic wound infection, wound sinus, or wound abscess in the location of a prosthetic mesh implant.'	Purulent discharge from a wound containing a prosthetic mesh implant OR a positive culture from a chronic wound containing a mesh implant using a wound swab, fluid aspirate, or an explanted piece of mesh OR a

		positive culture from intra-operative fluid surrounding a mesh.
Chronic pain	Pain lasting longer than 3 months post-surgery .	History and Clinical examination
Hernia recurrence	EHS definition: A protrusion of the contents of the abdominal cavity or preperitoneal fat through a defect in the abdominal wall at the site of a previous repair of an abdominal wall hernia (63).	Clinical examination +/- CT
Clavien-Dindo complication score	Clavien-Dindo Classification: Grade 1: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Includes drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. Includes wound infections opened at the bedside. Grade 2: Requiring pharmacological treatment with drugs other than those allowed for grade I complications. Blood transfusions and total parenteral nutrition are included. Grade 3a: Requiring surgical, endoscopic or radiological intervention not under general anaesthetic. Grade 3b: Requiring surgical, endoscopic or radiological intervention under general anaesthetic. Grade 4: Life-threatening complication requiring IC/ICU management. Grade 5: Death of a patient (161).	Post-operative hospital medical records
30 day re-operation rate	An abdominal operation under GA or Regional anaesthesia within 30 days of primary VH repair.	Post-operative hospital medical records

Best imaging modality for post-op assessment of hernia: CT. Post op complications should be recorded at: 30 days, 1 year, 5 years

*This consensus group is not advocating a CT diagnosis for all patients that present to the general surgical clinic with a PVH. We are supporting and recommending the use of CT scanning for the measurement of pre-operative hernia characteristics/variables of participants entered into PVH interventional trials. If there is no clinical indication for a pre-operative CT scan then the trial participant should have a low-dose, targeted CT scan to obtain the pre-operative measurements (a radiation dose of approximately 4 CXRs). If the practicalities of a low dose, targeted CT are tricky then the patient should not be subjected to the radiation of a normal CT scan with intra-venous contrast.

Table 2. Minimum Dataset for Incisional Ventral Hernia

Pre-operative Variables	**Definition**	**Detection Method**
Age	Years since birth	Age on the day of VH repair
Sex	Male/Female	Sex on the day of VH repair
Obesity/BMI	Kilograms/Height in meters squared	Calculated on the day of VH repair
COPD	Previous diagnosis of COPD	Taking repeat medications for COPD on the day of VH repair.
Smoker	EURAHS definitions (63): Never smoked, Ex-smoker (>12 months), Occasional smoker, Daily smoker No. pack years: No cigarettes/day x years of smoking / 20	Status selected on the day of VH repair
Diabetes (type I/II)	Previous diagnosis of type I/II DM.	taking repeat medication for diabetes on the day of VH repair.
Immunosuppression/Steroid use	Previous diagnosis requiring immunosuppression therapy.	Immunosuppression/steroids taken on the day of VH repair
ASA	American Society of Anaesthetists score.	Score on the day of VH repair
Hernia variables	**Definition**	**Detection Method**
Previous abdominal surgery/operations	No. of previous midline laparotomies: ___ No. of previous right sided subcostal incisions: ___ No. of previous right sided RIF incisions: ___ No. of previous right flank incisions: ___ No. of previous left flank incisions: ___ Other:	Clinical records
No previous VH repairs & details of previous mesh	No. of previous ventral hernia repairs at same site: ___ No. of previous meshes at same site:___ Previous planes used (ICAP nomenclature: Onlay, Anterectus, Inlay, Interoblique, Retrooblique, Retrorectus, Retromuscular, Transversalis Fascial, Preperitoneal, Intraperitoneal (297)): ___	Clinical records
Previous surgical site infection	Previous surgical site infection either following previous incision at hernia site or after previous hernia repair: Yes/No	Clinical records

Hernia width	Maximal defect width: if more than one defect, measure the width according to EHS classification (47).	CT
Loss of domain	Written: A ventral hernia large enough such that simple reduction in its contents and primary fascial closure either cannot be achieved without additional reconstructive techniques or cannot be achieved without significant risk of complications due to the raised intra-abdominal pressure. Volume: Sabbagh Method: Hernia sac volume / Peritoneal cavity volume (295).	CT
Hernia defect area	New definition: 'The area of the hernia defect as the hernial sac passes through the abdominal wall muscles'	CT – Area calculated as an area of an ellipse (Area = a x b x π, a = major radius, b = minor radius)
EHS score	EHS classification for Incisional Ventral Hernias. Graded according to: Position; medial M1-5, Lateral L1-4, Recurrent incisional; yes/no, Maximum Defect Length, Maximal Defect Width, Width divided up into groups <4, 4-10cm, >4cm (47).	Clinical exam
Stoma present?	Abdominal wall ostomy present: Yes/No	Clinical records, intra-operative details
Previous component separation	Previous anterior component separation: Yes/No Previous transversus abdominis release: Yes/No	Clinical records, intra-operative details
Current mesh infection	New definition: 'A chronic wound infection, wound sinus, or wound abscess in the location of a prosthetic mesh implant'.	Purulent discharge from a wound containing a prosthetic mesh implant OR a positive culture from a chronic wound containing a mesh implant using a wound swab, fluid aspirate, or an explanted piece of mesh OR a positive culture from intra-operative fluid surrounding a mesh.

Best imaging modality for pre-op assessment of hernia: CT

Peri-operative variables	**Definition**	**Detection Method**
Pre-operative botox injection	Pre-operative intramuscular injection of Botulinum Toxin A into the abdominal strap muscles.	Pre-operative clinical details Total number of units given: Length of time pre-op: _____ (eg. 6 weeks)
Lap/Open/Robotic (as treated, not ITT)	Mode of surgery	Intra-operative details

Mesh/suture repair	Method of repair	Intra-operative details
Mesh repair		
-Exact mesh name; material/type/brand	Document trade name. Type: biologic, biosynthetic, synthetic.	Intra-operative details
-Mesh fixation technique	Suture: absorbable/non-absorbable. Tacks: absorbable/non-absorbable	Intra-operative details
-Position of mesh – plane of insertion	ICAP nomenclature: Onlay, Anterectus, Inlay, Interoblique, Retrooblique, Retrorectus, Retromuscular, Transversalis Fascial, Preperitoneal, Intraperitoneal (297).	Intra-operative details
-Mesh size	Intraoperative measurement	Intra-operative details (cm^2)
-Bridging vs Primary fascial closure	EHS definitions (63): Bridging: the anterior fascia of the hernia defect is not **completely** closed. Primary fascial closure: the anterior fascia of the hernia defect is **completely** closed.	Intra-operative details
-Mesh overlap	Mesh overlap area/defect area ratio: Circle: Overlap = (πR^2 - πr^2) , R = radius of mesh, r = radius of hernia defect Ellipse: Overlap = πAB - πab. AB = major & minor radii of mesh, ab = major & minor radii of hernia defect (300).	Intra-operative clinical details/measured and calculated during the operation. Parameters calculate: mesh area & defect area If defect closed: just calculate mesh area.
Suture repair		
-Suture type – absorbable/non-absorbable	Absorbable/Non-absorbable material used	Intra-operative details
Type of component separation	Anterior component separation Transversus abdominis release	Intra-operative details
Concomitant GI bowel procedure	-Small bowel resection -Ileo-caecal resection -Colonic resection -Stoma formation -Other	Intra-operative details
VHWG grade	Four VHWG grades:	Intra-operative details

	Grade 1: Low risk; no history of wound infection, no co-morbidities. Grade 2: Co-morbid; smoker, obese, diabetic, immunosuppressed, COPD. Grade 3: Potentially contaminated; Previous wound infection, stoma present, violation of GI tract. Grade 4: Infected; Infected mesh, septic dehiscence (50).	
CDC score	Four CDC grades: Grade 1: Clean; uninfected wounds with no inflammation, the alimentary tract is not entered. Grade 2: Clean-contaminated; operative wounds in which the alimentary tract is entered under controlled conditions, without spillage. Grade 3: Contaminated; operative wounds with a major breech in sterility or spillage from the alimentary tract, includes incisions where acute, non-purulent inflammation is encountered. Grade 4: Dirty; pre-existing infected operative wound prior to the start of the operation, includes mesh infection and enterocutaneous fistula (89).	Intra-operative details
Accurate reporting of intra-operative complications	-Enterotomy -Bleeding -Bladder injury -Systemic complications (eg. cardiac) -Equipment malfunction Other	Intra-operative details
Post-operative outcomes	**Definition**	**Detection Method**
Wound infection (SSI)	CDC definition: A surgical site infection (SSI) is an infection that occurs after surgery in the part of the body where the surgery took place. Surgical site infections can sometimes be superficial infections involving the skin only. Other surgical site infections are more serious and can involve tissues under the skin or organs (298).	**Superficial**: Involves the skin and subcutaneous tissue, occurs within 30 days of surgery, AND; Patient has at least ***one*** of the following: -Purulent drainage from the superficial incision. -An organism identified by a positive culture. -Wound is deliberately opened by a surgeon or physician AND patient has at least one of these signs

		and symptoms localized pain or tenderness, localized swelling, erythaema, or heat. -Diagnosis of a superficial incision SSI by a surgeon or physician. **Deep**: Involves deep soft tissues of the incision, eg fascia or muscle, occurs within 30 or 90 days of surgery, AND; Patient has at least ***one*** of the following: -Purulent drainage from the deep incision. -A deep incision that spontaneously dehisces, or is deliberately opened by a surgeon or physician AND an organism identified by positive culture AND patient has at least one of the following fever (>38°C), localized pain, or tenderness. - an abscess or other evidence of infection involving the deep incision that is detected on gross anatomical or histopathologic exam, or imaging test. **Organ-space**: Involves any part of the body deeper than the fascial/muscle layers that was opened or manipulated during the surgery, occurs within 30 or 90 days of surgery, AND; Patient has at least ***one*** of the following: -Purulent drainage from a drain that is placed into the organ/space. -An organism identified by a positive culture. -An abscess or other evidence of infection involving the organ/space that is detected on gross anatomical or histopathologic exam, or imaging test.
Surgical site occurrence (SSO)	Any SSI as well as wound cellulitis, non-healing incisional wound, fascial disruption, skin or soft tissue ischemia, skin or soft tis- sue necrosis, wound serous drainage, chronic sinus drainage, localized stab wound infection, seroma, haematoma, exposed biological/synthetic mesh, myocutaneous	History and Clinical examination, medical records.

	anastomotic disruption, and development of an enterocutaneous fistula (226).	
Surgical site occurrence requiring procedural intervention (SSOPI)	SSOs requiring a procedural intervention, defined as wound opening or debridement, suture excision, percutaneous drainage, or mesh removal (299).	History and Clinical examination, medical records
Mesh infection	New definition: 'A chronic wound infection, wound sinus, or wound abscess in the location of a prosthetic mesh implant.'	Purulent discharge from a wound containing a prosthetic mesh implant OR a positive culture from a chronic wound containing a mesh implant using a wound swab, fluid aspirate, or an explanted piece of mesh OR a positive culture from intra-operative fluid surrounding a mesh
Chronic pain	ICD 11 classification of chronic pain. 'Pain lasting longer than 3 months post-surgery'.	History and Clinical examination
Hernia recurrence	EHS definition: A protrusion of the contents of the abdominal cavity or preperitoneal fat through a defect in the abdominal wall at the site of a previous repair of an abdominal wall hernia (63).	Clinical examination +/- CT
Clavien-Dindo complication score	Clavien-Dindo Classification: Grade 1: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Includes drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. Includes wound infections opened at the bedside. Grade 2: Requiring pharmacological treatment with drugs other than those allowed for grade I complications. Blood transfusions and total parenteral nutrition are included. Grade 3a: Requiring surgical, endoscopic or radiological intervention not under general anaesthetic. Grade 3b: Requiring surgical, endoscopic or radiological intervention under general anaesthetic.	Post-operative hospital medical records

	Grade 4: Life-threatening complication requiring IC/ICU management. Grade 5: Death of a patient (161).	
30 day re-operation rate	An abdominal operation under GA or Regional anaesthesia within 30 days of primary VH repair.	Post-operative hospital medical records

Best imaging modality for post-op assessment of hernia: CT. Post op complications should be recorded at: 30 days, 1 year, 5 years

Table 3: Patient reported outcomes (PROMs) for Interventional Trials assessing Ventral Hernia repair

EURAHS QoL score (63):
Pain at hernia site:
1.Pain at rest (lying down) (0-10)
2.Pain during activities (walking, biking, sports) (0-10)
3.Pain felt during the last week (0-10)
Restrictions of activities because of pain or discomfort at the site of the hernia:
4.Restriction from daily activities (inside the house) (0-10)
5.Restriction outside the house (walking, biking, driving) (0-10)
6.Restriction during sports (0-10)
7.Restriction during heavy labour (0-10)
Cosmetic discomfort:
8.Shape of abdomen (0-10)
9.Site of hernia (0-10)
SF12 (294):
10.In general, would you say your health is: Excellent, Very good, Good, Fair, Poor
11.Moderate activities, such as moving a table, getting dressed, cooking, bowling, or playing golf: Yes, Limited a lot, Yes, limited a little, No, not limited at all.
12.Climbing several flights of stairs: Yes, Limited a lot, Yes, limited a little, No, not limited at all.
13.Due to physical health problems over the past 4 weeks: Have you accomplished less than you would like? Yes/No
14. Due to physical health problems over the past 4 weeks: Have you been limited in the kind of work/other activities? Yes/No
15.Due to emotional health problems over the past 4 weeks: Have you accomplished less than you would like? Yes/No
16.Due to emotional health problems over the past 4 weeks: Have you been limited in the kind of work/other activities? Yes/No
17.During the past 4 weeks, how much did pain interfere with your normal work? Not at all, A little bit, Moderately, Quite a bit, Extremely
18.Over the past 4 weeks: Have you felt calm and peaceful? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.
19. Over the past 4 weeks: Did you have lots of energy? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.
20.Over the past 4 weeks: Have you felt down hearted and blue? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.
21.Over the past 4 weeks: how much has your physical or emotional problems interfered with your social activities? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.
Expert patient questions:
22.My mental health currently is (answers: awful, poor, fair, good, very good, excellent)
23.My sexual activity currently is (answers: awful, poor, fair, good, very good, excellent)
24. Having the operation was the right decision (answers: strongly agree, agree, neither agree or disagree, disagree, strongly disagree)
25. I would go for the same choice if I had to do it over again (answers: strongly agree, agree, neither agree or disagree, disagree, strongly disagree)

PROMS should be recorded at: 30 days, 1 year, 5 years

Table 4. Forty methodology recommendations for PVH and IVH interventional trials. These criteria were devised using existing methodology tools; Downs & Black (173), ROBINS-I (174), CONSORT statement (291), STROBE (176), TIDieR checklist (172), and the Newcastle Ottawa Scale (175).

Methodology Criteria for Primary and Incisional VH Interventional Trials
General
Funding
Protocol
Registered Trial
Ethical Approval
Introduction
Background and rationale
Primary aim or objective
A pre-specified referenced hypothesis
Method
Randomised trials
Method of generating random allocation sequence
Method of implementing the random allocation
Blinding of the participant to the intervention received
Blinding of the care providers
Non-randomised trials/studies
Explain how the study groups/arms were selected, avoiding selection bias
All Interventional (Randomised and non-Randomised Interventional Trials)
Description of trial design
Trial setting (single/multicentre),names of centres where data will be collected
Describe the intended periods of recruitment and follow up
Description of the interventions, with sufficient detail to allow replication
Defined and referenced primary outcome, with well described methods for detection and measurement
Secondary outcome measures, defined and referenced, with described methods for detection and measurement
Power/Size calculation
Specific inclusion/exclusion criteria
Reports eligibility and number included
Blinding of the outpatient assessor/independent blinded outpatient assessor
Describe methods of follow-up
Results
Recruitment dates - Start date?, Finish date, End of follow-up date
Participant flow chart - for each group showing the no. of participants meeting inclusion criteria, then no. included, no. receiving the intended treatment, no. analysed for primary outcome (includes explanations for participant losses)
A table showing baseline characteristics/pre-operative variables between each group
Report all harmful events in each group
Deviations from the intended intervention reported?
Statistics
Length of follow-up reported
Details on Per Protocol analysis or Intention to Treat analysis
Number of participants with missing data

Statistic methods for comparing the groups; for primary and secondary outcomes
Additional methods for subgroup analyses and adjusted analyses
Reports adjusted analysis (with adjustment factors clearly listed)
Explains how missing data will be addressed
Reports estimated effect size with 95% confidence intervals
Discussion
Summarises key results with reference to study objectives
Trial limitations, addressing sources of potential bias, imprecision
Interpretation consistent with results, balancing benefits and harms
Generalisability of the study results

Discussion

Informed by systematic review and via expert consensus, I have constructed minimum datasets for interventional trials of primary and incisional VH. The two systematic reviews described in Chapters 3 and 4 of this thesis (170, 286) illustrated a requirement for minimum datasets, so too have calls from hernia surgeons, asking that a 'common language' be used for outcome reporting and research. Indeed, Debord et. al. called for, "an international task force to establish the definitions for wound events after hernia repair" (227). This work has used an international group to both standardise post-operative wound events, and define pre-operative patient variables, hernia characteristics, reported peri-operative variables, post-operative outcomes, and patient reported outcomes for VH trials. I have also included trial methodology criteria to try and create a 'handbook' or 'manual' to help and facilitate those researchers planning VH trials. A greater wealth of standardised data will facilitate pooling and comparisons, including meta-analysis, so that new knowledge regarding optimal treatment options and outcome predictors has a more substantial evidence base.

I am aware the results of this study will challenge investigators because it will demand they adhere to the stipulated variables and definitions. Adhering to the intricacies of variable definitions and detection methods may appear laborious. However, my argument is sound; hernia scientists must collect accurate data that is comparable across studies, centres, and countries. Much of the current difficulties in herniology stem from poorly defined variables and heterogenous data. If the hernia community is to discover which variables (patient, hernia, or

peri-operative) are most predictive of outcomes and which treatments are most beneficial, accurate and comparable data must be collected. I hope that by providing all variable definitions and detection methods in one manuscript, this will simplify understanding and adherence to these minimum datasets.

The group has recommended CT scanning as the optimal modality for pre-operative hernia assessment including trials of PVH. This recommendation maybe seem problematic as it relies on CT scanning being available for research, which competes with clinical demand, and scanning involves radiation exposure, an issue high-lighted by three panelists. However, it is well-established that CT scanning is superior and more reproducible than clinical examination when attempting to diagnose hernia and its location, morphology, and content, and these recommendations are made in the setting of prospective interventional trials. Because patient safety is paramount, our panelists advocate for low-dose targeted CT scanning in the absence of a defined clinical indication for pre-operative CT.

It is important readers understand this work is a consensus. Accordingly, not all panelists agreed with every variable, definition, or detection method. For example our chosen definition for loss of domain was rejected by one panelist stating, '*this would mean that every patient where you perform an anterior component separation or a transversus abdominis release there is loss of domain, I would tend to disagree with that; for me the cut-off is 20%* (Sabbagh)*'.* Our definition for loss of domain doesn't stipulate a volumetric cut-point because, as yet, a generally accepted threshold to discriminate between significant and insignificant loss of domain does not exist; only a written definition has been established (295). Another definition prompting ample group feedback was the definition of mesh overlap. We settled on a ratio, the mesh overlap:defect area ratio, which overlooks several important factors. Firstly, it assumes that both the implanted mesh and the hernial defect are either circular or elliptical, and does not account for either a rectangular mesh or multiple defects. In this situation, the data collectors (investigators) should still use basic mathematics to divide the mesh area by the defect(s) area, as the forces causing and preventing eventration are still proportional to both these areas (300). Secondly, it assumes a bridging repair.

If the defect is closed completely, the defect area and eventration force become zero (Force = Pressure x Area (300)), and mesh overlap area to defect area ratio becomes infinity. In such cases, the group advises that investigators simply document mesh area; if a closed wound breaks down then the value of mesh area represents the force of eventration resistance and may be inversely proportional to hernia recurrence. Lastly, mesh porosity was not a variable chosen for either dataset, but was discussed at our group meeting. Panelists were aware that porosity is an important variable, which has been shown to correlate with outcomes such as mesh infection (301), chronic pain (302), bacterial load (303) and surgical site occurrence (304). However, the group felt that a separate variable for porosity was unnecessary because it was imperative the exact name and type of mesh was recorded. Given this, porosity could be deduced.

Hernia academics reading this chapter will recognise that its contents bear resemblance to two previously published articles. The first is the published outcomes of a 2012 consensus meeting in Palermo, which made recommendations for reporting outcomes for abdominal wall repair and also advised hernia surgeons regarding study design (165). The second is an article from the European Hernia Society containing a dataset to launch the European registry for abdominal wall hernias (EuraHS) (63), also from 2012. In essence, our current work updates both of these articles. As new knowledge emerges and new definitions are established (295, 297), updates of standardised trial design and data accuracy are required to drive continuous improvement (305). In addition, although this article aims to improve interventional trial design and trial data quality, two international hernia societies (the British Hernia Society and the European Hernia Society) have already expressed interest in using these datasets to create and launch their new hernia registries. All the authors would encourage this.

In summary, using a panel of expert hernia surgeons and patient advocates, we have produced minimum datasets for PVH and IVH interventional trials, a set of standardised patient reported outcomes, and a checklist of methodology criteria, with the aim of improving trial design and resultant research quality. I hope this

“manual” will aid hernia researchers intending to perform such trials. If trials collect consistent, well defined data, comparison of their results across centres and countries will be facilitated, with the aim of improving investigation of the effect of peri-operative variables on patient and surgical post-operative outcomes.

Chapter 8

International Written and Volumetric Classifications of Loss of Domain

Part 1: Improving Research Quality

Delphi Methodology: Defining Loss of Domain

Hypothesis

I hypothesise that by using a group of expert panelists (key opinion leaders) and an interactive forecasting technique, such as Delphi methodology, I can reach group consensus on the correct written and volumetric definitions to use to describe 'loss of domain'.

Aim

To establish, using Delphi methodology, new written and volumetric definitions for 'loss of domain'.

Introduction

Our systematic review (239), Chapter 5, and clinician survey (306), Chapter 6, demonstrated that despite being used commonly, the phrase 'loss of domain' (LOD) lacks a single standardised written and volumetric definition. VHs with significant LOD have been reported to recur frequently after repair (162) but as no standardised volumetric description exists, the true prognostic value of LOD has not been properly investigated. In order to rectify this, I used the Delphi method and an international panel of recognised hernia surgeons (Appendix 21), to reach consensus regarding standardised written and volumetric definitions of LOD. Indeed, both ICAP, Chapter 9, (297) and this study (295) used the same group of international experts and Delphi Methodology, and were performed at

the same time; Professor Steve Halligan and I facilitated both studies simultaneously.

Method and Design

The Delphi method (307) is a consensus-based forecasting technique that provides a systematic framework to collect and aggregate informed opinion from a group of experts, via multiple iterations (308). The process consists of five phases; questionnaire development (phase 1), expert panel selection (phase 2), followed by three rounds of questionnaire distribution, data acquisition and analysis, and iteration (phases 3, 4 and 5). Controlled feedback from sequential rounds encourages panelists to reassess, deliberate and either confirm or alter their responses. Delphi methodology has been used extensively for research purposes (309-311), but has not previously been used to define loss of domain.

Questionnaire Development

I, in combination with SH (Professor Steve Halligan, UCL, UK), MKL (Professor Mike Liang, Texas, USA), FM (Professor Filip Muysoms, Ghent, Belgium) and ACJW (Mr Alastair Windsor, UCL, UK), constructed a PowerPoint presentation (Microsoft PowerPoint for Mac 2016, Version 16.0, Microsoft Corporation, Washington, USA) (Appendix 22) and distributed it to panelists. This presentation comprised 8 slides;

Slide 1: Explained the Delphi method and voting process.

Slide 2,3: The existing written definitions of LOD were listed in alphabetical order to eliminate bias. Panelists were asked to select their preferred definition.

Slide 4: A free text slide followed allowing panelists to insert additional definitions and/or to make comments.

Slide 5,6: To establish a volumetric definition. The lead researchers designed two different schematic diagrams depicting the abdominal and hernia sac cavities. Panelists were asked to select their preferred definition (Figure 1a).

Slide 7: A free text slide for additional comments regarding volumetric definitions.

Slide 8: The panelists were asked to vote on a threshold value for LOD, above which they believed the risk of post-operative complications becomes clinically significant, and therefore the value above which they might consider not operating at all.

The written and volumetric definitions of LOD were taken from those identified by my systematic review (239). The four written definitions and two volumetric definitions (Tanaka (86) and Sabbagh (87)) were presented.

Before distribution to the panelists, I piloted the questionnaire on volunteers at University College London Hospital. Recommendations were made regarding presentation and comprehension, and adjustments made by me accordingly.

Expert Panel Selection

The panelists were selected based on a combination of academic record and geographical location, so as to obtain a widely representative sample. For example, criteria included prominent membership of the American Hernia Society (AHS), British Hernia Society (BHS), European Hernia Society (EHS), German Hernia Society (DHS), and the Asian and Pacific Hernia Society (APHS). A priori it was determined that 20 panelists would be sufficient as a representative group. A list of our exert panelists can be found in Appendix 21.

Although patient and public involvement (PPI) can enhance Delphi studies (312), it was decided not to pursue their involvement given the nature and technicalities of this topic.

Questionnaire Distribution, Data acquisition and Analysis, and Iteration

Prior to questionnaire distribution, panelists were sent a consent form asking them to maintain anonymity until voting was concluded, this avoids undue pressures from dominant or dogmatic individuals. Anonymity also allows

individuals to reconsider options and maintain independence. Panelists were also asked to consent to COPE criteria (290), thereby authenticating co-authorship. The study protocol was also sent to and approved by each panelist. Panelists also received copies of our systematic review (239) and our clinician survey (306) that highlighted the inconsistencies, giving panelists further insight and focus. All panelists were asked to declare any conflicts of interest (COIs) on the consent form and to remove themselves from the study if these would affect their votes.

The rounds of voting were administered by SH and I who did not vote but acted as study facilitators. Data transfer occurred via electronic mail. Lead researchers, MK, FM and ACJW did vote and were blinded to co-panelist responses during voting to maintain anonymity. We planned to carry out three rounds of voting. If consensus did not occur, a teleconference between all panelists was planned (phase 6), in accordance with the “modified” Delphi technique (313). Consensus was pre-defined as ≥80% of panelists selecting the term. If <20% of the panelists selected a term, it was deleted from subsequent rounds. Anonymised responses were communicated to all panelists after each voting round via a table totaling the definitions selected and another detailing any extra definitions, comments and alterations suggested by panelists. The suggested definitions were added as possible options for subsequent rounds. Figures were presented as frequencies and percentages. We anticipated that establishing a written definition for LOD would be difficult as we believed previously published definitions were convoluted, counter-intuitive, and unlikely to reach consensus (239). We recognised that the facilitators may need to become more involved, possibly suggesting or synthesizing new definitions, in order to achieve consensus.

Table 1. Results of voting Rounds 1 to 3. The panelist's thresholds for operative cut off are also presented.

Round 1		**Round 2**		**Round 3**	
<u>Written definitions</u>		**<u>Written definitions</u>: Panelists suggested many alternatives***		**<u>Written definitions</u>: Facilitator intervention**	
1. Chronic large irreducible hernia	0 (0%)	1. Hernia sac forms a second abdomen	11 (55%)	A ventral hernia large enough such that simple reduction of its contents and primary fascial closure either cannot be achieved without additional reconstructive techniques or cannot be achieved without significant risk of complications due to raised intra-abdominal pressure.	**<u>20 (100%)</u>**
2. Hernia sac forms a second abdomen	7 (35%)	2. Lateral retraction of the rectus abdominis and the abdominal strap muscles	6 (30%)		
3. Loss of the “right of domain”	1 (5%)	**New suggested definitions**			
4. Lateral retraction of the rectus abdominis and the abdominal strap muscles	9 (45%)	3. A hernia where the fascia cannot be approximated even with component separation	1 (5%)		
5. Nil vote	3 (15%)	4. Irreducible hernia due lack of space or volume	6 (30%)		
		5. LOD is when the abdominal contents protrude through a hernia defect and is not able to be reduced and allow for abdominal closure	3 (15%)		
		6. Irreversible/Reversible loss of domain. Irreversible - the viscera cannot be replaced into the abdominal cavity by any technique. Reversible loss of domain means the ventral hernia can be reconstructed using any technique	5 (25%)		
		7. Loss of domain is when the abdomen cannot be closed primarily without the help of any augmentation technique	8 (40%)		

		8. A hernia where the fascia cannot be approximated without developing abdominal compartment syndrome	3 (15%)		
		9. Closure of the fascia is either impossible, or can lead to high intra-abdominal pressures, fascial dehiscence, or abdominal compartment syndrome	15 (75%)		
Volumetric definitions		**Volumetric definitions**		**Volumetric definitions**	
1. Tanaka Method	8 (40%)	1. Tanaka Method	7 (35%)	1. Tanaka Method	2 (10%)
2. Sabbagh Method	8 (40%)	2. Sabbagh Method	11 (55%)	2. Sabbagh Method	**17 (85%)**
3. Nil vote	4 (20%)	3. Nil vote	2 (10%)	3. Nil vote	1 (5%)
LOD cut-off point		**LOD cut-off point**		**LOD cut-off point**	
1. 15%	1 (5%)	1. 20%	5 (25%)	1. 20%	4 (20%)
2. 20%	5 (25%)	2. Nil value	15 (75%)	2. 30%	1 (5%)
3. 25%	1 (5%)			3. Nil value	15 (75%)
4. 30%	2 (10%)				**No consensus**
5. 33%	1 (5%)				
6. 35%	0 (0%)				
7. 40%	1 (5%)				
8. 45%	0 (0%)				
9. 50%	1 (5%)				
10. Nil value	8 (40%)				

*Panelists allowed to select ≥1 written definition.

Table 2. Combining the three concepts to design a new definition for loss of domain.

Concepts	**Round 2 (%)**
1. Irreducible due to lack of space	15 (75%)
2. Primary facial closure cannot be achieved without using an augmentation technique.	13 (65%)
3. Primary closure would lead to compartment syndrome.	18 (90%)
Definition designed by the facilitators	**Round 3**
A ventral hernia large enough such that simple reduction of its contents and primary fascial closure either cannot be achieved without additional reconstructive techniques or cannot be achieved without significant risk of complications due to raised intra-abdominal pressure.	20 (100%)

Figure 1a. Two schematic diagrams used in Round 1 to illustrate the Tanaka and Sabbagh methods for describing loss of domain.

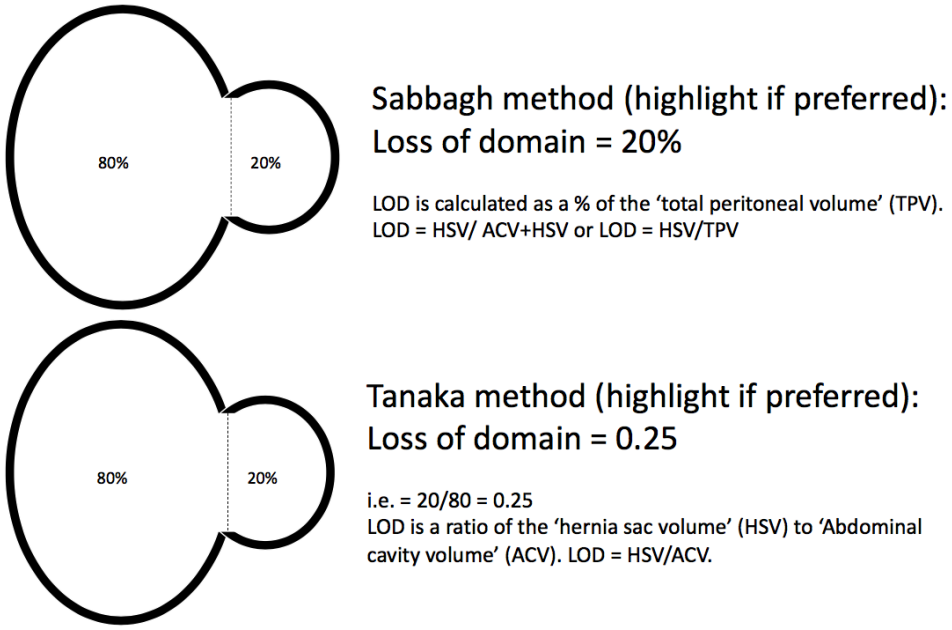
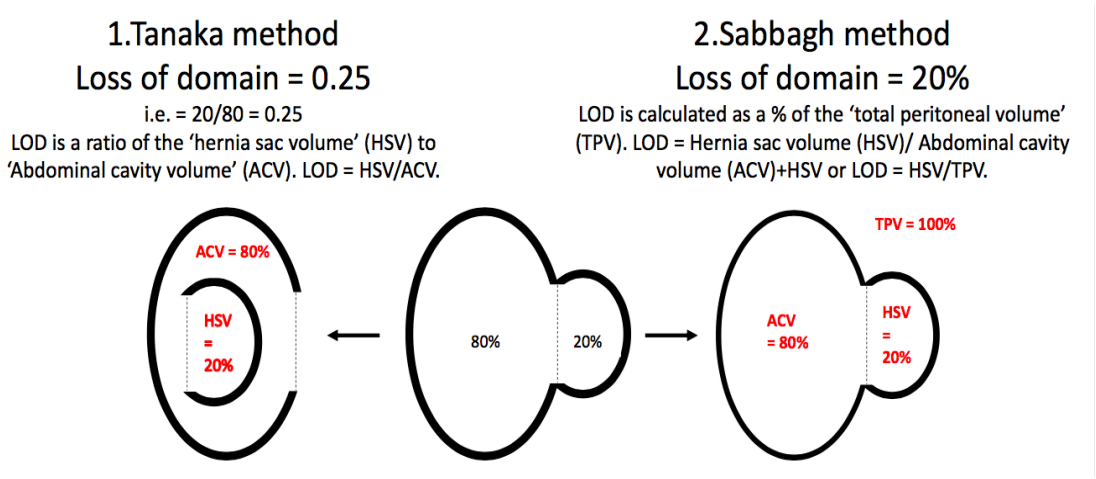


Figure 1b. Schematic diagram to facilitate understanding and accurately describe the Tanaka and Sabbagh volumetric definitions. Diagram used for Rounds 2 & 3.



Results

All the surgeons approached agreed to participate and consented; six panelists represented the USA (MKL, GLA, CMD, MTH, BTH and KMFI), 6 represented mainland Europe (FM, UAD, LNJ, AM, SMC, and YR), 5 represented the UK (ACdeB, DLS, NJS, JT, and ACJW), and 3 represented the rest of the worldwide surgical community; 1 South African (AB), 1 South Korean (JPH) and 1 Australian (NI), (Appendix 21). Voting started 24th August 2018 and completed 24th January 2019. All panelists completed the study.

Round 1

Table 1 shows results from each Delphi round. During Round 1, two of the written definitions, ('chronic large irreducible hernia' and 'loss of the right of domain'), were eliminated. In addition, panelists made 18 comments (Appendix 23), and suggested an additional seven definitions, which were then presented in Round 2. Panelists were inconclusive regarding their preferred volumetric definition for LOD, with both Tanaka and Sabbagh each scoring 8 (40%) votes. Four panelists abstained, citing a lack of evidence to support either (e.g. 'need evidence to choose' and 'not sure either method is superior'). For their preferred LOD threshold/cut-point panelists indicated a range of values from 15% to 50%. Five (25%) panelists voted for a threshold of 20%, two (10%) for 30%, and cut-points 15%, 25%, 33%, 40%, and 50% received one (5%) vote each. Eight panelists chose 'nil value', with accompanying feedback comments such as, 'an absolute value is not relevant', 'I adjust for clinical factors such as stiffness/thickness of lateral abdominal musculature, COPD etc', and 'LOD is clinically significant simply because it exists'. Only '20%' and 'nil value' scored ≥20% of the votes, so only these two options were presented in Round 2.

Round 2

Nine written definitions were presented in Round 2, including the additional 7 definitions suggested by panelists during round one. Thematic analysis of the proposed definitions by SH and I revealed three common themes/concepts: 1) large hernias with LOD are irreducible due to inadequate space inside the abdominal cavity; 2) primary fascial closure cannot be achieved without surgical

augmentation; and, 3) primary fascial closure could cause compartment syndrome (Table 2). To determine which of these themes/concepts were most relevant, panelists were asked to select any of the possible 9 definitions they agreed with during Round 2, i.e. multiple selection was possible. To demonstrate the difference between the two volumetric methods, Tanaka and Sabbagh, a new schematic diagram was drawn for Round 2, Figure 1b.

Panelists agreed with several suggested written definitions, Table 1. The two literature definitions: 'hernia sac forms a second abdomen' and the physiological definition 'lateral retraction of the recti muscles', received 11 (55%) and 6 (30%) votes respectively. The number of votes for the remaining 7 definitions ranged from 1 (5%) to 15 (75%). All three concepts presented in the definitions proposed by panelists were selected repeatedly (Appendix 24 and Table 2); 'irreducibility due to lack of space' was selected by 15 (75%); 'no primary closure without using an augmentation technique' was selected by 13 (65%), and 'primary closure leading to possible compartment syndrome' was selected by 18 (90%) (Table 2). Regarding their preferred volumetric definition, panelists chose Sabbagh over Tanaka; 11 (55%) versus 7 (35%) with two abstentions. Twenty percent was chosen as a clinical cut-point by 5 (25%) panelists. Fifteen (75%) panelists selected 'nil value'.

Round 3

Because all three themes/concepts proposed in Round 2 were popular, SH and I designed a definition incorporating all three themes/concepts, proposing the following definition for Round 3:

'A ventral hernia large enough such that simple reduction of its contents and primary fascial closure either cannot be achieved without additional reconstructive techniques or cannot be achieved without significant risk of complications due to raised intra-abdominal pressure'.

SH and I viewed the definitions, 'hernia sac forming a second abdomen' and 'lateral retraction of the recti muscles' as both lacking precision, since all VHs

involve these to some extent. These two definitions were therefore removed from Round 3 following approval from MKL, FM, and ACJW.

During Round 3, the proposed written definition achieved complete consensus, attracting 20 (100%) votes. Regarding the volumetric definition, the Sabbagh method received 17 (85%) votes, thereby also achieving consensus. However, panelists remained undecided regarding the clinical threshold value with 'nil value' receiving 15 (75%) votes, 20% 4 (20%) votes, and one (5%) panelist again suggested a cut-point of 30%. Consensus on this point was therefore not achieved.

Discussion

Using Delphi methodology, a panel of internationally recognized experts in abdominal wall reconstruction agreed on standardised written and volumetric definitions for LOD. The written definition of LOD was created after thematic analysis of panelist feedback. By analysing the proposed written definitions, I identified three common themes: Irreducibility due to lack of intra-abdominal space; use of reconstructive techniques to facilitate reduction and repair; and an increased risk of complications due to raised intra-abdominal pressure. These were combined into a single definition that then achieved 100% consensus. This definition attempts to characterize those hernias whose repair is likely to be challenging and which therefore require specific expertise in abdominal wall surgery. The definition is explicit that additional reconstructive techniques are likely because primary fascial closure alone would precipitate potentially serious complications due to abruptly increased intra-abdominal pressure.

Initially panelists were undecided as to their preferred volumetric method, with Tanaka (86) and Sabbagh (87) both receiving equal votes in Round 1. Eventually, consensus settled on the Sabbagh method and panelists confirmed this in their private correspondence with the facilitators. For example, '*Sabbagh seems much easier than Tanaka for clinical use*', and '*the Tanaka method is confusing and conceptually difficult. Much like relative risk is much easier to understand compared to odds ratios, Sabbagh is much easier to understand compared to*

Tanaka.' These comments support the feasibility of using the Sabbagh method in a clinical setting. Indeed, a straw poll of the audience at "Abdominal Wall Reconstruction Europe 2019" (London, UK) by Professor Halligan found that Sabbagh was preferred by the large majority of those present. Furthermore, LOD is often reported as a percentage. When using Tanaka, the value will surpass 100 when more than 50% of the abdomino-pelvic volume lies outside the abdominal cavity, which appears counterintuitive. In contrast, Sabbagh is always less than 100, making it conceptually easier. This likely contributed to achieving consensus in its favour.

We were unable to establish consensus regarding a LOD threshold above which panelists would consider not operating. Most panelists, 15, (75%), selected 'nil value' stating that their decision whether to or not to operate was multifaceted, incorporating comorbidities and not based solely on hernia size. However, 5 (25%) panelists, did select threshold values in Round 3. Indeed, one panelist who voted consistently for 20% proposed a written definition that separated VHs into two categories; those with reversible LOD and those with irreversible LOD, i.e. those with large VHs that can be repaired and those that cannot. The concept that LOD may be irreversible in some patients is interesting. Despite considerable morbidity (abdominal pain, back pain, respiratory dysfunction), patients with giant VHs are often denied surgery because the surgeon believes they cannot return the abdominal viscera to the abdomino-pelvic cavity safely. There is little existing evidence to support this opinion beyond surgical experience. So, during this study, I was in effect asking panelists to declare their own threshold for discriminating between reversible and irreversible LOD. As consensus was not established this value remains unknown; it likely varies from patient to patient contingent on multiple patient and hernia variables. Further work is required around which factors impact on the decision to operate and, in particular, whether a LOD threshold predicts post-operative failure.

This study arose following the systemic review described in Chapter 5 (239) and clinical survey described in Chapter 6 (306) that called for standardised written and volumetric definitions for LOD. As the subspecialty of abdominal wall reconstruction continues to expand, these standardised definitions for LOD will

hopefully reduce clinical inconsistency and facilitate research investigating LOD as an outcomes predictor. Indeed future VH grading scales may incorporate LOD along with other parameters, such as hernia neck width, associated with post-operative outcomes. I also recognise that definitions are not static and must adapt to new knowledge. All co-authors hope the definitions proposed here are endorsed by surgeons and international hernia societies.

Chapter 9

An International Classification of Abdominal Wall Planes (ICAP)

Part 1: Improving Research Quality

Delphi Methodology: Defining a new standardised classification system for the planes of the abdominal wall

Hypothesis

I hypothesize that by using a group of expert panelists (key opinion leaders) and an interactive forecasting technique, such as Delphi methodology, we can reach consensus on the correct terms to use to describe the abdominal wall planes.

Aim

To establish, using Delphi methodology, a new classification system for the abdominal wall planes used for mesh insertion during the VH repair.

1. Introduction

Whilst reviewing the literature and performing data extraction for the systematic reviews reported in Chapters 3, 4, 5, and 10, I also noticed that terms used to describe and define the abdominal wall planes were used inconsistently in the primary literature. To highlight this, I wrote an editorial article which was published in the World Journal of Surgery (314). This article focused mainly on the inconsistent use of terms ‘inlay’, ‘sublay’, and ‘underlay’. For example, the retrorectus tissue plane is often referred to as the ‘inlay’ (134, 315), ‘sublay’ (144, 150, 151, 316), or ‘underlay’ (317) plane. The pre-peritoneal plane is often also referred to by all three terms; ‘inlay’ (149), ‘sublay’ (145) and ‘underlay’ (318). And finally, the intra-abdominal plane is also referred to as either ‘inlay’ (319), ‘sublay’ (153), or ‘underlay’ (117, 133). To add to the confusion, this inconsistent use in the primary literature becomes increasingly concerning when these terms

are used to analyse mesh location in systematic reviews (104, 117) and meta-analysis (105, 320), which have a greater potential to influence wider clinical practice. In a much-cited Cochrane review (104), 5 RCTs (135, 143, 149, 150, 321) were meta-analysed to compare local wound complication rates of open 'sublay' repairs versus laparoscopic repairs. Critical analysis shows that in two (135, 149) of the RCTs the mesh was in fact inserted into the 'underlay' plane, i.e. pre-peritoneal and not retro-rectus. As a result, this review pools RCTs with open 'sublay' and 'underlay' repairs into a larger open 'sublay' group and compares their local wound complication rates to laparoscopic repair. The evidence must therefore be interpreted with caution as the premise is misguided and wrongly assumes that all five trials used an open technique with the mesh in the 'sublay' retrorectus plane. My article pointed out these inconsistencies and argues that to establish accurate and unambiguous clinical practice and to produce robust high quality research the terms used to name the abdominal wall planes used for mesh insertion must be well defined and standardised.

The editorial received comments from the International Hernia Collaboration (IHC) (322) and the Texas Health Science Center (323). Both groups agreed that there was an urgent requirement for well-defined terms to describe the planes of the abdominal wall. A research meeting was planned with attendees from all three centres (UCL, Texas Health Science Center, and the IHC). We decided to meet during the American Hernia Society's conference in Miami, March 12th-15th 2018. Thereafter, email correspondence continued and we agreed the best approach would be to use a group of key opinion leaders (KOLs) to devise a new international classification of abdominal wall planes, or "ICAP". ICAP, we hoped, would be a popular unforgettable acronym that would propagate through the sub-specialty and aid standardisation. To guide our KOLs and to facilitate the project, we again chose to use Delphi methodology (307). This project took 18 months but we did meet our objective, devising a new classification system. The project finally concluded with ICAP being published on Christmas Day 2019 in the British Journal of Surgery (297).

2. Methods

To recap Chapter 8; the Delphi method is a consensus-based technique that stipulates a systematic framework to collect and aggregate informed judgements from a group of participants over multiple iterations (308). Again, five phases were used; questionnaire development (phase 1), expert panel selection (phase 2), followed by three rounds of questionnaire distribution, data acquisition and analysis, and iteration (phases 3, 4 and 5). Controlled feedback from sequential rounds encouraged panelists to reassess, deliberate and either confirm or alter their responses.

Questionnaire Development

I, in combination with lead researchers SH, MKL, FM, and ACJW designed two anatomical diagrams depicting the muscle and fascia of the abdominal wall cranial and caudal to the arcuate line (figure 1). A series of diagrams were then developed to show all possible abdominal wall planes employed currently for VH repair (figure 2). The diagrams included planes both frequently and infrequently used for abdominal wall reconstruction, since surgical innovation may well utilise additional planes in the future. Using these diagrams, a PowerPoint presentation was created (Microsoft PowerPoint for Mac 2016, Version 16.0, Microsoft Corporation, Washington, USA) highlighting the individual abdominal wall planes on consecutive slides. Eleven abdominal planes were labelled alphabetically, A to K (figure 2). Each slide also indicated the possible range of terms used previously for each plane, from which panelists were asked to identify their preferred term. To avoid bias, options were listed alphabetically. For Round 1 only, a free text space on each slide allowed panelists to add additional terms and to comment. There were 13 slides in total; 1 introductory slide explaining the questionnaire format, followed by 11 slides of individual planes, and a final slide for additional comments. Participants were encouraged to suggest additional anatomical terms, questionnaire alterations and anatomical diagram adjustments on this final slide. The final questionnaire can be found in Appendix 25.

Identification of possible terms was multifaceted. A combination of literature review, expert consensus, and private correspondence was used. Extensive review of the abdominal wall literature was completed by me. After title and abstract screening of 6485 citations, and full-text review of 174 articles (170), manuscripts with published abdominal wall classifications systems (54, 63, 117, 324-326) were analysed and the terms used were identified. The web-based survey conducted by the International Hernia Collaboration (IHC) Facebook platform listed 31 possible terms for abdominal wall planes, making up a major component of our initial list of terms (322). Our final list totalled 41 different possible terms (Appendix 26), many of which could be used to describe more than one anatomical plane and therefore appeared multiple times in our questionnaire, ultimately giving a total of 59 options (Appendix 26).

Before distribution, the questionnaire was piloted on volunteers at the University College London Hospital. Recommendations regarding presentation and usability were adopted.

Expert Panel Selection

As previously, the panelists were selected by the expert surgeons MKL, FM, and ACJW, The same 20 experts were recruited (Appendix 21). Panelists were asked to consent to the present study, separately and independently from the LOD study described in Chapter 8. Consent involved maintenance of anonymity, commitment to completing the study, and taking part according to COPE criteria (290), thereby authenticating co-authorship. Panelists were asked to declare any conflicts of interest (COIs) on the consent form. Those with COIs were asked to withdraw if they felt this influenced their voting. For this study, panelists also received copies of relevant publications (314, 322, 323) that highlighted inconsistencies in nomenclature, giving panelists further insight and focus.

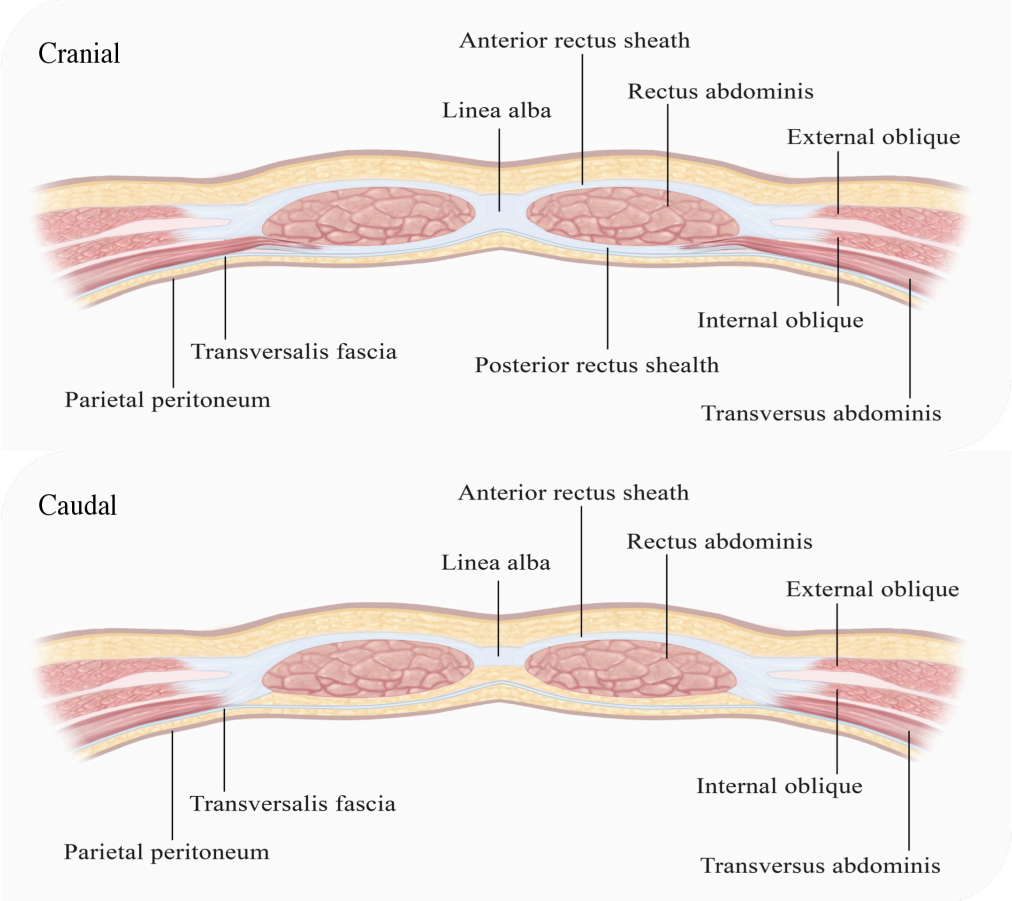
For a second time, we did consider whether patient and public involvement (PPI) should be incorporated into this Delphi study (312). Ultimately, we decided this was not warranted as the questions being asked required an understanding and

interpretation of complex surgical concepts and were targeted squarely at practicing abdominal surgeons.

Questionnaire distribution, Data acquisition and Analysis, and Iteration

SH and I did not vote but facilitated the study. We distributed the questionnaires, facilitated data acquisition, and performed data analysis. Between rounds, we re-distributed the results and questionnaires. Distribution and data acquisition occurred via electronic mail. It was anticipated that three voting rounds would be necessary to achieve consensus (327). If not, a teleconference was planned, i.e. a "modified" Delphi technique (313). Consensus was pre-defined as ≥80% of panelists selecting an individual term for an abdominal wall plane. If <20% of panelists choose a term, this term was eliminated from subsequent rounds. After each round, all the responses were counted and tabulated as frequencies and percentages. Round 1 responses were fed back to each panelist as a table totalling the responses given for each plane and as, for this round only, a word document with the additional suggested terms and feedback comments. After Rounds 2 and 3, responses were communicated as a table totalling the responses for each individual plane. An updated questionnaire for the subsequent round of voting was sent out to each panelist at the same time as the results.

Figure 1. Anatomical diagrams designed by the lead researchers showing the muscle and fascia of the anterior abdominal wall (cranial is above the arcuate line, caudal is below the arcuate line).



3. Results

Again, all surgeons approached agreed to participate and consented; 6 panelists were from the US, 6 were European, 5 from the UK, and 3 from countries elsewhere (panelist list; Appendix 21). All panelists completed all 3 rounds of voting. Voting started 24th August 2018 and was completed 24th January 2019. Appendix 27 details the voting results from each Delphi round.

Round 1

During Round 1, 43 of the original 59 (73%) terms proposed were selected by less than four panelists (<20%) and, as per protocol, were eliminated. In addition, panelists added 37 new terms to the questionnaire, which were carried forward to Round 2. One panelist designed a novel nomenclature system and voted for these new proposed terms. Eighteen (90%) panelists voted for the term 'onlay' for plane A, but consensus was not declared as a new term, 'Medial 1 and Lateral 1', was proposed, and carried forward to the next round. Panelists made a total of 50 free text comments. These were fed back to panelists along with Round 1 results (Appendix 28).

Round 2

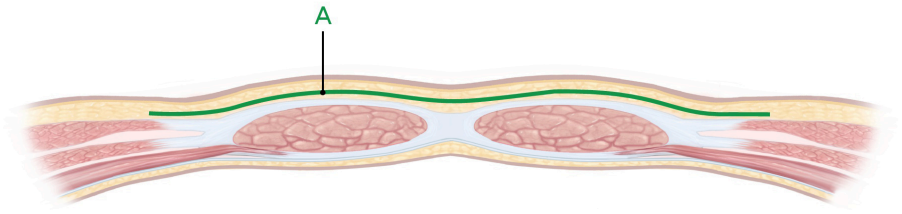
Fifty-three terms were offered to the panelists for Round 2s questionnaire. Consensus was achieved for planes A; 'onlay', C; 'inlay', J; 'preperitoneal' and K; 'intraperitoneal' (figure 2), each receiving 18 (90%), 16 (80%), 18 (90%), and 18 (90%) votes respectively. Thirty-five (66%) terms were selected by less than four panelists (<20%) and did not make it to Round 3.

Round 3

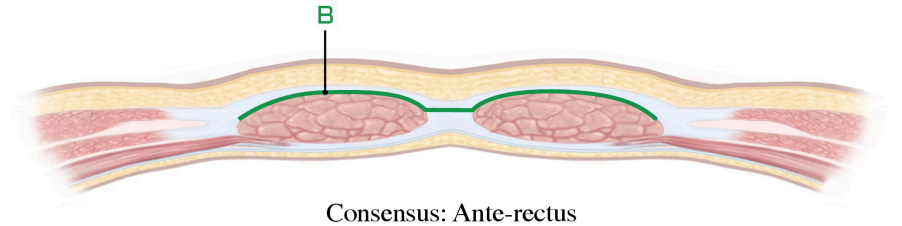
My analysis of Round 2 results suggested that panelists found it challenging to define and name planes G and I. As these planes are in continuum, with plane G being the lateral portion of plan I, the facilitators decided to remove plane G (figure 2) from Round 3's questionnaire, following approval by MKL, FM, and ACJW. Consequently, fifteen terms remained for 10 planes. Consensus was achieved for planes B; 'anterectus', D; 'interoblique', E; 'retrooblique, and H;

‘retromuscular’. For the 2 planes, F and I, only 1 possible term remained by default (i.e. all other terms were selected by 3 or less panelists (<20%) and were removed as per protocol). For these two planes, panelists were asked, ‘Do you have any strong objections to this term being the consensus term despite it being selected by default?’. For plane F, all 20 (100%) panelists did not object to the term ‘retrorectus’, which was consequently chosen. For plane I, 3 (15%) panelists objected, 1 (5%) preferred the term ‘retromuscular’ and 2 abstained. However, 17 (85%) panelists did not object, thus confirming the term ‘transversalis fascial’. Figure 2. shows the final results of the Delphi process and the chosen terms. Figure 3 is an anatomical image of the results showing all the planes with their respective terms chosen via consensus. Table 1 gives an anatomical description of each plane.

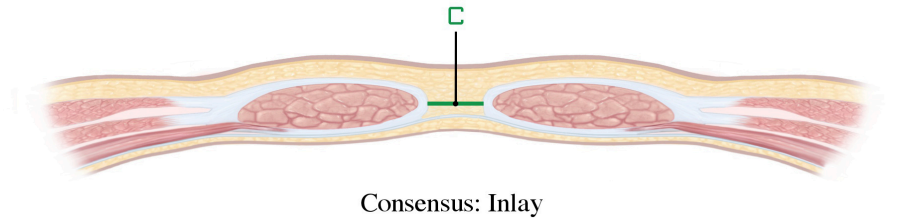
Figure 2. The results of the Delphi study showing all 11 planes. Terms for 10 out of 11 planes reached consensus. Planes H and I are divided into cranial and caudal sections as the posterior sheath is not present below the arcuate line. The anatomical difference between H and I is in the cranial images; medial to the semilunar line Plane I is posterior to the posterior sheath and Plane H is anterior to the posterior sheath. Plane H exists only if a transversus abdominis release is performed.



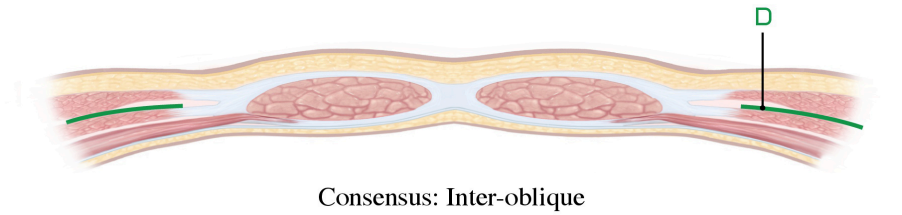
Consensus: Onlay



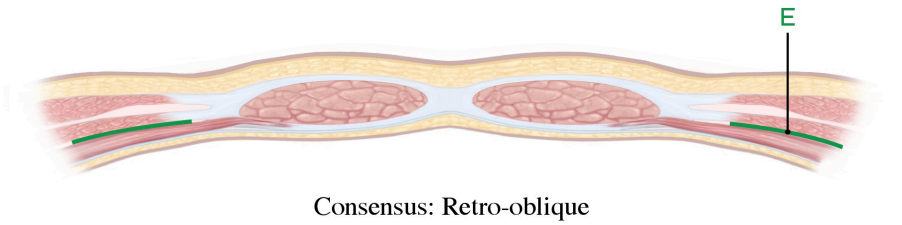
Consensus: Ante-rectus



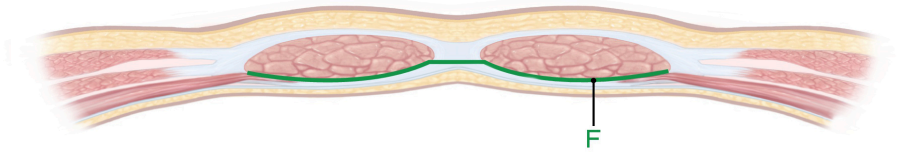
Consensus: Inlay



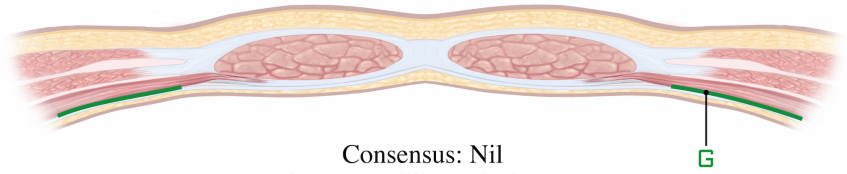
Consensus: Inter-oblique



Consensus: Retro-oblique

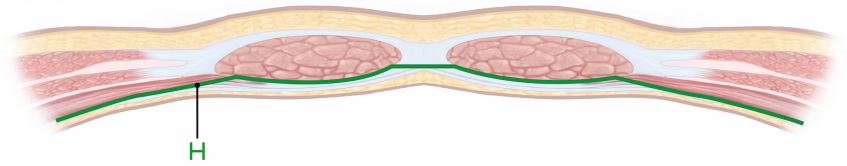


Consensus: Retro-rectus

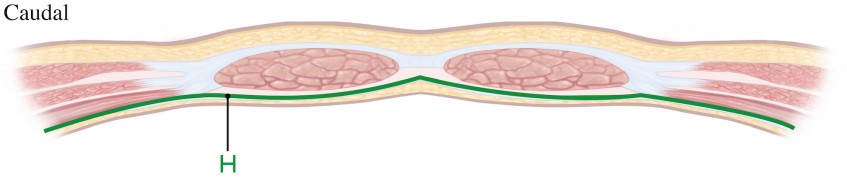


Consensus: Nil
(plane removed from Delphi study)

Cranial

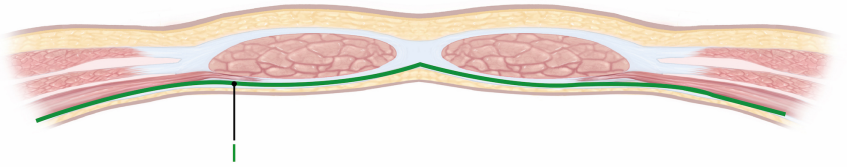


Caudal

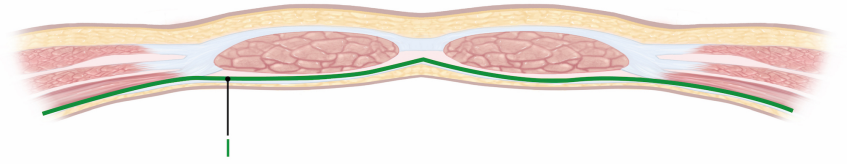


Consensus: Retro-muscular

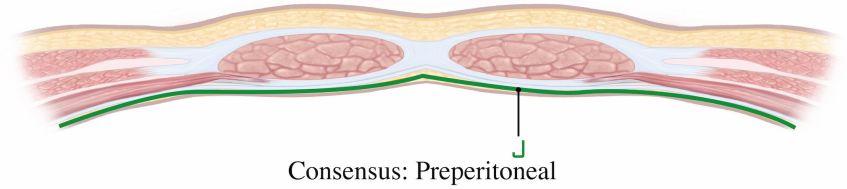
Cranial



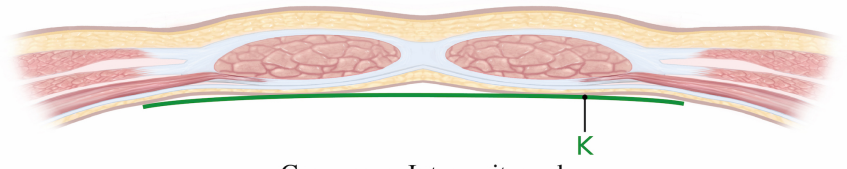
Caudal



Consensus: Transversalis fascial



Consensus: Preperitoneal



Consensus: Intraperitoneal

Figure 3. A summary diagram showing all the abdominal wall planes when their respect names chosen via Delphi consensus.

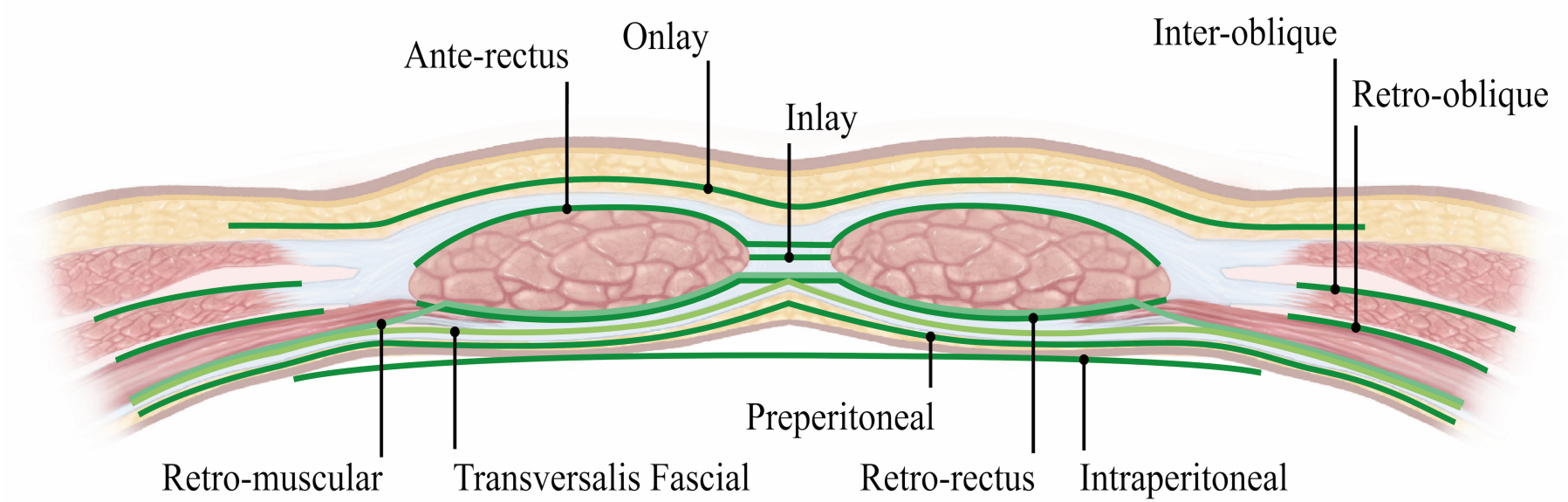


Table 1: Anatomical descriptions of each plane and their respective names chosen via Delphi consensus.

Delphi results: Name of plane	Anatomical description
A: Onlay	*Anterior:* Subcutaneous tissue *Posterior:* Anterior rectus sheath and external oblique
B: Ante-rectus	*Anterior:* Anterior rectus sheath *Posterior:* Rectus abdominis muscle
C: Inlay	Mesh attached to the edges of the hernia defect with no overlap.
D: Inter-oblique	*Anterior:* External oblique muscle *Posterior:* Internal oblique muscle
E: Retro-oblique	*Anterior:* Internal oblique muscle *Posterior:* Transversus abdominis muscle
F: Retro-rectus	*Anterior:* Rectus abdominis muscle *Posterior:* Posterior rectus sheath
H: Retro-muscular (TAR performed)*	*Anterior:* Medial: Rectus abdominis muscle Lateral: Transversus abdominis muscle *Posterior:* Medial: Posterior rectus sheath (not present caudally, therefore caudal posterior border is transversalis fascia). Lateral: Transversalis fascia
I: Transversalis Fascial*	*Anterior:* Medial: Posterior rectus sheath (not present caudally, therefore caudal anterior border is rectus abdominis muscle). Lateral: Transversus abdominis muscle *Posterior:* Medial: Transversalis fascia Lateral: Transversalis fascia
J: Preperitoneal	*Anterior:* Transversalis fascia *Posterior:* Peritoneum
K: Intraperitoneal	*Anterior:* Peritoneum *Posterior:* Abdominal cavity

*Below the arcuate line plane H & I have the same anatomical lie.

4. Discussion

Using Delphi methodology, a panel of internationally recognised experts in abdominal wall reconstruction agreed upon a standardised International Classification of Abdominal wall Planes (ICAP) to be used for mesh placement during VH repair. I would wish to see ICAP adopted by abdominal wall surgeons and the wider medical community. ICAP should facilitate comparison and eliminate ambiguous anatomical descriptions in both the clinical and research settings. Furthermore, adoption would also benefit others working with these anatomical planes, such as radiologists and anaesthetists. It is desirable that all clinicians “speak a common language” to describe abdominal wall anatomy. In the academic setting, variable nomenclature frustrates investigators studying surgical outcomes according to anatomical plane of mesh placement. The academic community would benefit from this new unambiguous and transparent classification system so that anatomical planes are defined precisely.

Academics have been calling for ‘a common language’ to describe hernia morphology since the turn of the century (328). Indeed, many grading scales have been published over the last 20 years (46, 54, 328). These grading scales, however, describe hernia location, length, and width and omit intra-operative variables. Since level 1 evidence suggests that using mesh for VH repair reduces recurrence (37), an accurate anatomical description of the plane into which mesh is implanted is required. Indeed, the exact ‘mechanism of recurrence’ may depend on mesh location (329). Once precise nomenclature is established, future grading systems incorporating exact location of mesh may have greater clinical utility.

Standardised nomenclature will also aid scrupulous monitoring and surveillance of outcomes related to mesh implanted into different planes. Mesh implanted in one plane may demonstrate a different risk/benefit profile than the same mesh implanted into a different plane. Awareness of the possible long-term complications should result in thoughtful and meticulous practice. The exact location for the mesh implant must be planned and described precisely. Our

unambiguous ICAP nomenclature system facilitates this. With the plane of insertion described clearly in the operation note, a reconstructive surgeon is able to scrutinise their previous actions should a hernia recurrence or other mesh complication occur. Moreover, planning future surgery, such as explantation and/or insertion of a new mesh, is simplified if the precise location of an existing mesh is known.

During this Delphi study, three panelists, raised concerns regarding the term 'bridging' for 'plane C', stating that, 'bridging is the opposite to primary fascial closure', and that, 'bridging is a term that should only be used in combination with the plane into which the mesh is inserted'. In response to these comments the facilitators compiled a definition for bridging as follows: *'Bridging is not a specific anatomical plane, it is a reconstruction method that can be used in many planes, e.g. bridging onlay, bridging retro-rectus, bridging intra-peritoneal etc".* Panelists were asked to vote for or against this definition at the end of the study and they agreed unanimously, implying that 'bridging' in-and-of itself should not be used to describe an individual plane. Furthermore, the authors agree with the European Hernia Society when it describes the *'mesh bridging technique'* as when *'the anterior fascia of the hernia defect is not completely closed'* and the *'mesh augmentation technique'* as when *'the anterior fascia of the hernia defect is closed'* (10). Abdominal wall surgeons must be explicit in their operation note as to whether the anterior fascia has or has not been completely closed as surgical outcomes are significantly worse after bridged repair (107).

Plane I, the transversalis fascial plane, caused some difficulties amongst panelists, stemming from the anatomy of the transversalis fascia, its landmarks, and its name. In both Mike Rosen's Abdominal Wall Reconstruction (AWR) Atlas (330) and in Gray's anatomical textbook (331), the transversalis fascia is labelled clearly. In Gray's, it is described as a, '*thin layer of connective tissue lying between the deep surface of the transversus abdominis and the extra-peritoneal fat*' (331). All panelists agreed that this fascial layer can be visualized posterior to the transversus abdominis. However, a few were uncertain whether this layer existed medial to the semilunar line and, if so, whether it could be dissected off the posterior rectus sheath to allow mesh placement. Gray's (331) describes this

fascia in detail. The description is complex and difficult to visualize. The fascia does cross the midline and is continuous with many other fascial structures such as the thoracolumbar fascial, iliac fascia and the diaphragmatic fascia. Indeed, all these fascial layers envelop the abdominal cavity in a continuous layer, which one panelist described as the 'endo-abdominal fascia', and is synonymous with the endo-pelvic fascia. Given that our expert panel had difficulty understanding the anatomy of this plane, and that AWR surgeons are designing new reconstructive techniques that place implants into planes not utilised previously, a thorough understanding of the anatomy of the transversalis fascia is required. Further work is needed to develop a concise and accurate anatomical description of this plane.

ICAP does name planes that to date have not been used commonly. To my knowledge, the anterectus plane has only been used in anecdotal instances known to ACJW[3]. The interoblique plane has reportedly been entered during variations of the peritoneal flap repair, a technique that has become popular in Europe after a case series was published in 2014 by the Royal Infirmary of Edinburgh (120). Surprisingly, the retrooblique plane, (more traditionally known as the neurovascular plane), has been used for mesh insertion. Carbonell et al (332) incised the posterior lamella of the internal oblique aponeurosis to access this plane. Their series of 20 repairs reported a recurrence rate of 5% at 12 months and no neurological complications, i.e. no long-term pain, abdominal wall paralysis, or abdominal wall dysfunction or asymmetry. Despite these results, this plane has not been investigated further, probably because of theoretical risks of neurovascular compromise. However, it cannot be predicted which planes will or will not be used in future. As surgery evolves and new bioprosthetic materials emerge, new planes may become appealing. This ICAP system attempts to pre-empt such developments by being exhaustive regardless of current preferences.

Lastly, it should be mentioned that it is not uncommon for AWR surgeons to use more than one plane. For example, if the posterior rectus sheath is exposed bilaterally and then a unilateral transversus abdominis release (TAR) is

[3] Zorraquino, A, Abdominal Wall Department, Hospital de Basurto, Bilbao, Spain

performed, as Renard et al (333) describe for lumbar hernia repair, the TAR side will use the retromuscular plane with the retrorectus plane used contralaterally. De Beaux combines the retrorectus and interoblique planes to tackle complex VHs arising from lateral oblique or transverse incisions (120). It follows that AWR surgeons must innovate, combining multiple planes where necessary in order to achieve the strongest repair.

Inevitably, such classification systems are not static and must be flexible and change as new knowledge is accumulated. Accordingly, future updates may be required. In the meantime, the ICAP classification is a precise description of the abdominal wall planes achieved by expert consensus via a Delphi process and abolishes ambiguous terms such as ‘sublay’, and ‘underlay’ (314). In January 2020, ICAP was formally endorsed by the European Hernia Society with an announcement in the society’s newsletter (334). All co-authors and I hope ICAP will also be endorsed by the remaining international hernia societies, AHS, BHS, DHS, and APHS, so that clinical and academic nomenclature becomes consistent worldwide.

Chapter 10

Identifying Predictors of Ventral Hernia Recurrence

Part 2: Prelude to Prognostic Model Development

Systematic Review and Meta-Analysis: Identifying the Predictors of VH recurrence

Hypothesis

I hypothesize that by systematic review, prognostic data extraction, and subsequent meta-analysis, we can identify predictors of VH recurrence.

Aim

To carry out extensive systematic review of the indexed literature and extract all available prognostic data. Subsequent meta-analysis will identify which variables are statistically significant with respect to the ability to predict recurrence. This will aid the selection of which variables would be selected to develop a prognostic model.

Introduction

Previous Chapters have described assessment of the literature and data extraction via systematic review, in order to identify methodological shortcomings with respect to available indexed studies of VH repair. In contrast, the review described in this Chapter is a "prognostic" systematic review (335). Prognostic reviews extract data that relate to the chance of a future event will occur or not, hernia recurrence after repair for example. This work aimed to identify the most significant predictive variables that might be incorporated into a prognostic model of hernia recurrence.

As mentioned in Chapter 2, hernia recurrence is an important post-operative outcome and assesses surgical efficacy. Indeed, recurrence reflects surgical

failure. The ability to predict recurrence accurately would have considerable clinical utility by informing surgeons when not to operate, for example by providing guidance as to when comorbidity or hernia complexity precludes repair. To date, there is an abundance of literature assessing VH repair that describes the pre-, intra-, and post-operative variables that may be associated with recurrence. However, publications are frequently small, vary in study design, are single-centre, and report divergent results (102, 221, 336). This frustrates interpretation of current evidence and findings are difficult to apply in clinical practice. Consequently, surgeons have limited guidance regarding when not to operate, and evidence for optimal repair is lacking. To rectify this, I performed a comprehensive prognostic systematic review of the published literature to identify potential predictors of VH recurrence. By using subsequent meta-analysis to synthesize these data, I aimed to identify those predictors significantly associated with post-operative recurrence, from across the whole range of published literature.

Methods and Design

Reporting and registration standards

This systematic review was reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement (126). Ethical permission is not required by our institution for systematic reviews of available primary literature. The protocol was registered with PROSPERO, the international prospective register of systematic reviews (CRD42016043071).

Inclusion and exclusion criteria

Inclusion criteria for studies:

As with my previous reviews, I aimed to identify studies reporting hernia recurrence in patients following elective VH repair with curative intent between 1st January 1995 and 1st January 2018. As before, I excluded studies with less

than 10 patients in any individual study group since such data are likely to be subject to small study bias. Only English language studies were included.

Participants:

I included studies of adult participants. Paediatric (defined as 18 years or less) studies were excluded since these are not representative of 'typical' VH patients.

Target condition:

The target condition was the same as for my two methodological reviews. Patients having elective VH repair were included. All different VH morphologies were eligible, as were all VH working group (VHWG (50)) grades. Femoral, inguinal hernias and parastomal hernia were excluded. Emergency VH repair was, in general, excluded; however a study was eligible if this proportion was <10%. Studies in which a proportion of patients had abdominal wall defects repaired with a bridging mesh after abdominal wall tumour excision were eligible. Studies with concomitant bowel resection were included (since this is often intended) as long as the primary surgical intention was VH repair. I excluded studies with concomitant GI tumour removal or bariatric surgery.

Follow-up:

No minimum length of follow up was stipulated.

Comparators:

I placed no restriction on any study comparator group (e.g. operative technique, mesh type, position or mesh).

Search strategy and string

PubMed database was searched from 1st January 1995 to 1st January 2018. As previously, the search was limited using the following terms: "adult 19+", "human

studies", and to publications written in English. I combined two different search strings to identify relevant articles for both VH repair and studies predicting VH recurrence. My first search string was the same search string I used for our two methodological systematic reviews, which identified studies of VH disease and of VH repair, Appendix 2. I combined this with a second search string aiming to identify prognostic studies predicting VH recurrence.

Our complete search string is shown in Appendix 29.

Citation management and screening

This process has previously been described in Chapter 8 & 9. I used Excel spreadsheet (Microsoft Excel for Mac 2011 version 14.5.9, Microsoft Corporation, Washington, USA) and Mendeley (Mendeley Desktop version 1.17 for Windows XP and Mac OS X, London, UK) for citation and reference management. Citation management and screening was undertaken by surgical trainees CPJW, RWB, and I in three stages. Stage 1; citation screening and article labelling; 'clearly unsuitable', 'uncertain' or 'definitely possible'. Stage 2; abstract screening, and stage 3 full text screening. Studies were labelled according to their methodological design as follows: randomised controlled trials (RCTs); prospective or retrospective interventional/cohort studies; observational/database studies. The PRISMA flow diagram (Figure 1) shows article selection.

Data extraction

I scrutinised included studies for prognostic data of VH recurrence. Data were extracted for all potential predictors from each article; for each predictor, risk-estimates (2x2 tables, odds ratios (ORs), Hazard Ratios (HRs), adjusted ORs, relative risk ratios (RRs)), and thresholds were recorded. Where overlapping articles included data for the same predictors from the same patients, data were only included from the study describing the larger cohort. Confidence intervals and p values were extracted for all estimates where available. Extracted predictors were grouped into pre-operative, intra-operative, and post-operative

subcategories. For each individual study I extracted the definition and method(s) used to identify hernia recurrence, and mean time-to-recurrence. Data from interventional trials tended to be 2x2 tables whereas data from larger database studies tended to be univariate and/or multivariable odds ratios.

Study characteristics and risk of bias

In addition to the pre-, intra-, and post-operative predictors, I also extracted data relating to study setting (multi-centre vs single centre), country of publication, publication date, recruitment dates, number of patients included, severity of VH disease, and whether the study included primary or incisional VHs, or both. Severe VH disease was classified as a hernia whose width exceeded 10cm and/or a contaminated hernia, graded as VHWG grade 4. Studies were scored as containing patients with either 'severe disease only', 'mild disease only', or as containing 'both' mild and severe disease. I recorded whether studies included participants with multiple grades or were restricted to severe disease.

I assessed 'risk of bias' for individual studies by using an adapted version of the PROBAST tool (123). PROBAST was developed to determine bias in published prediction models. Since few prognostic models have been published for VH disease, I adapted PROBAST for detection of bias from all study designs. This bias tool was categorized according to study participants, extracted predictors, definitions of hernia recurrence, and according to statistical analysis (Appendix 30).

All data were stored using Microsoft Excel (Microsoft Excel for Mac 2011 version 14.5.9, Microsoft Corporation, Washington, USA).

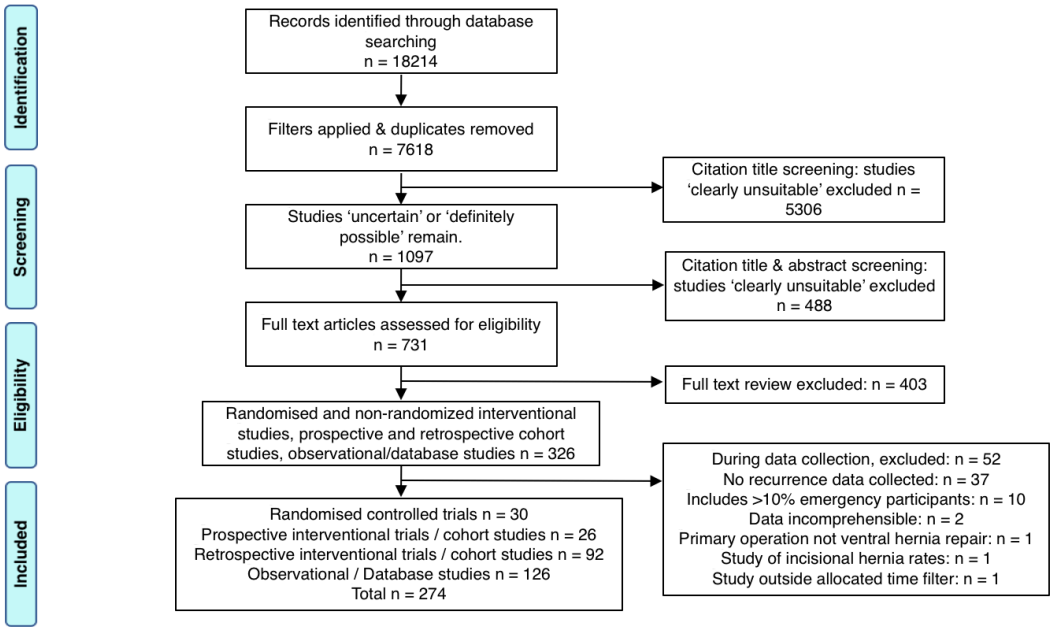
Statistical analysis

Because I anticipated heterogenous data, I looked for predictor association with recurrence rather than precise estimates of strength or inter-predictor comparison. I anticipated study designs would include different definitions of recurrence, follow-up, and patient populations that would cause variation in

predictor estimates. Accordingly, meta-analysis reflects general evidence across all studies rather than providing precise estimates regarding specific definitions, situations, measurements, and thresholds. Most results could be extracted as either 2x2 tables or univariable OR; 2x2 results were converted into OR for meta-analysis. Only OR results were sufficiently available to allow meta-analysis using the 'metan' command in STATA 14.2 (Timberlake Consultant Ltd, Richmond Upon Thames, London, UK).

Each study was included only once in each meta-analysis for a particular variable, to ensure patients were included only once. A study could be included in each subgroup within a predictor, e.g. where different thresholds of a predictor value were meta-analysed separately. To exclude predictors with data insufficient for meaningful meta-analysis, we excluded predictors available from fewer than five primary studies, except those predictors considered "clinically important" by surgical authors ACJW and I. Meta-analysis was considered for all predictors described in five or more individual studies if results were not considered heterogeneous based on visual inspection. A random effect meta-analysis used methods of DerSimonian and Laird with the estimate of heterogeneity taken from the inverse-variance fixed-effect model (335). Forest plots were used to present meta-analysis summaries across predictors and to present individual study results for each predictor. These plots indicate data characteristics including event, method of hernia recurrence detection, and whether incisional hernia, primary hernia, or both incisional and primary hernia populations were included.

Figure 1. PRISMA diagram showing selection of studies for this review.



Results

Study characteristics

The PRISMA flowchart is shown in Figure 1. In total, 18,214 abstracts were identified, and 731 full texts assessed for eligibility. Ultimately, prognostic data were extracted from 274 included studies; 30 (11%) randomised controlled trials, 26 (9%) prospective interventional or cohort studies, 92 (34%) retrospective interventional or cohort studies, and 126 (46%) database analyses. Most studies included originated from North America (137 of 274, 50%), with 116 (42%) European. Of the 274 studies, 212 (77%) were single centre, 63 (23%) were multi-centre, and one (0.5%) presented both multi- and single-centre data (337). Pre-operative, intra-operative, and post-operative prognostic factors were reported in 136 (35%), 204 (53%), and 46 (12%) articles respectively. Regarding hernia type; 129 (47%) studies assessed primary and incisional VH, 25 (9%) assessed primary VH only, 119 (43%) assessed incisional VH only, and one (0.5%) study provided no information. Individual study characteristics are shown in Table 1.

Characteristics	n (%)
Centre*	
Single	212 (77%)
Multi	63 (23%)
Study design	
Observational	126 (46%)
Prospective	26 (9%)
RCT	30 (11%)
Retrospective	92 (34%)
Continent	
Africa	3 (1%)
Asia	18 (7%)
Australia	1 (.5%)
Europe	116 (42%)
North America	137 (49%)
South America	1 (.5%)
Number of participants	
Median (IQR)	128 (77 to 251)
Range	21 to 13567
Prognostic factor type**	
Pre-operative	136 (35%)
Intra-operative	204 (53%)
Post-operative	46 (12%)
Population	
Primary and incisional	129 (47%)
Primary	25 (8%)
Incisional	119 (43%)
No information	1 (1%)
Method of detection	
Imaging with US or CT only	1 (1%)
Clinical assessment	54 (19%)
Clinical assessment with CT	43 (15%)
Clinical assessment with US	11 (4%)
Clinical assessment with imaging	22 (8%)
Clinical assessment with telephone	14 (5%)
Clinical assessment with questionnaire	2 (1%)
Medical records	19 (7%)
Re-operation rate	6 (2%)
Mixture of methods	79 (29%)
No information	24 (9%)
Severe disease included	
Yes	198 (72%)
No	51 (19%)
No information	25 (9%)
Follow up time***	
Months – median (IQR)	24 (15 to 39)
Range	2 to 116

Table 1. Study characteristics. Prognostic data was extracted from 274 VH studies from 1st January 1995 to 1st January 2018.

*One published manuscript contained two separate studies; one multi-centre and a second single-centre study.

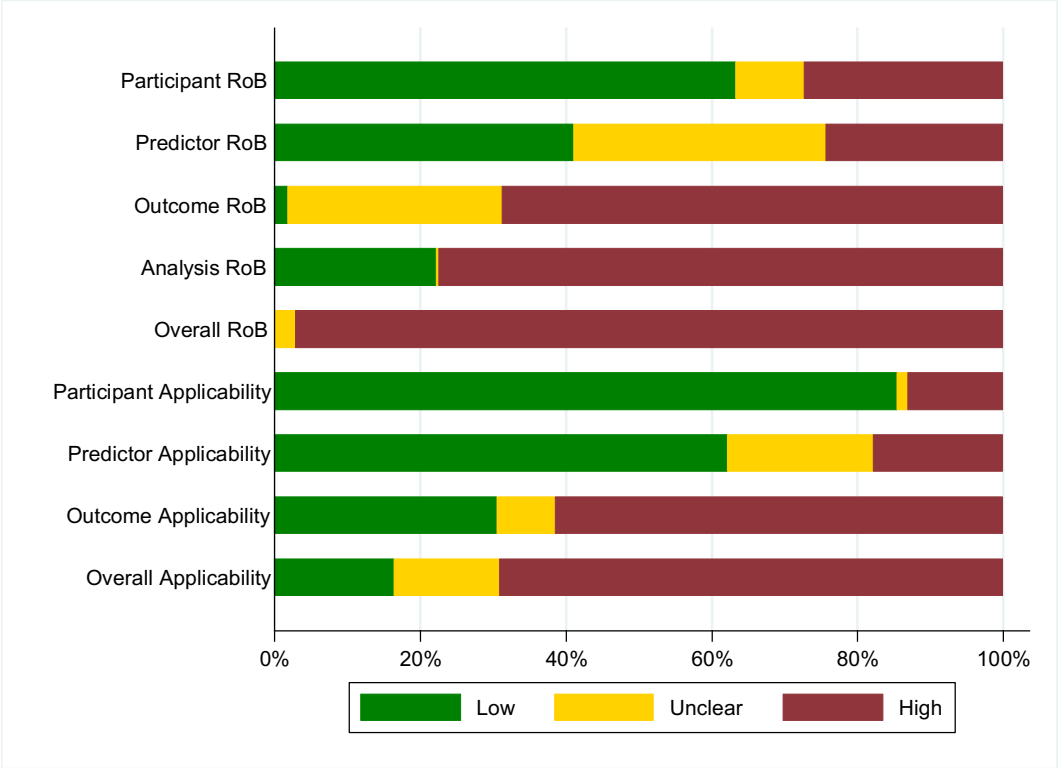
**Studies can have a mixture of pre/intra/post-operative prognostic factors

***Studies not reporting follow up time (5 studies). For studies split by subgroups; if difference was less than 4.5 months the average was taken (21 studies), if difference was more than 4.5 months, the minimum follow up was taken (22 studies).

Recruitment dates coincided with 109 studies describing overlapping patient cohorts (Appendix 31), and were excluded from meta-analysis as described above. 198 (72%) studies included both mild and severe disease, of which 16 (6%) assessed 'severe disease only', 51 (19%) included 'mild disease only', and 25 (9%) provided no severity information.

Concerning hernia recurrence, surprisingly only a minority of studies defined this: 66 (24%), using 41 different, unstandardized definitions (Appendix 32). Detection of hernia recurrence also varied widely, with 67 different detection methods used (Appendix 33). Duration of follow-up varied, with median 24 months (IQR 15 to 39 months), range 2 to 116 months.

Figure 2. Risk of bias graph using an adapted version of the PROBAST tool (123). Illustrates the authors' judgements about each risk of bias category presented as percentages across all included studies.



Risk of bias

Risk-of-bias (ROB) and applicability across all studies is presented in Figure 2. Most studies had high ROB in at least one domain, resulting in 266 (97%) studies rating "high" for ROB overall. Eight (3%) studies were rated "unclear". Not a single study reported acceptable data, at a "low" ROB. Notably, 272 (99%) studies rated

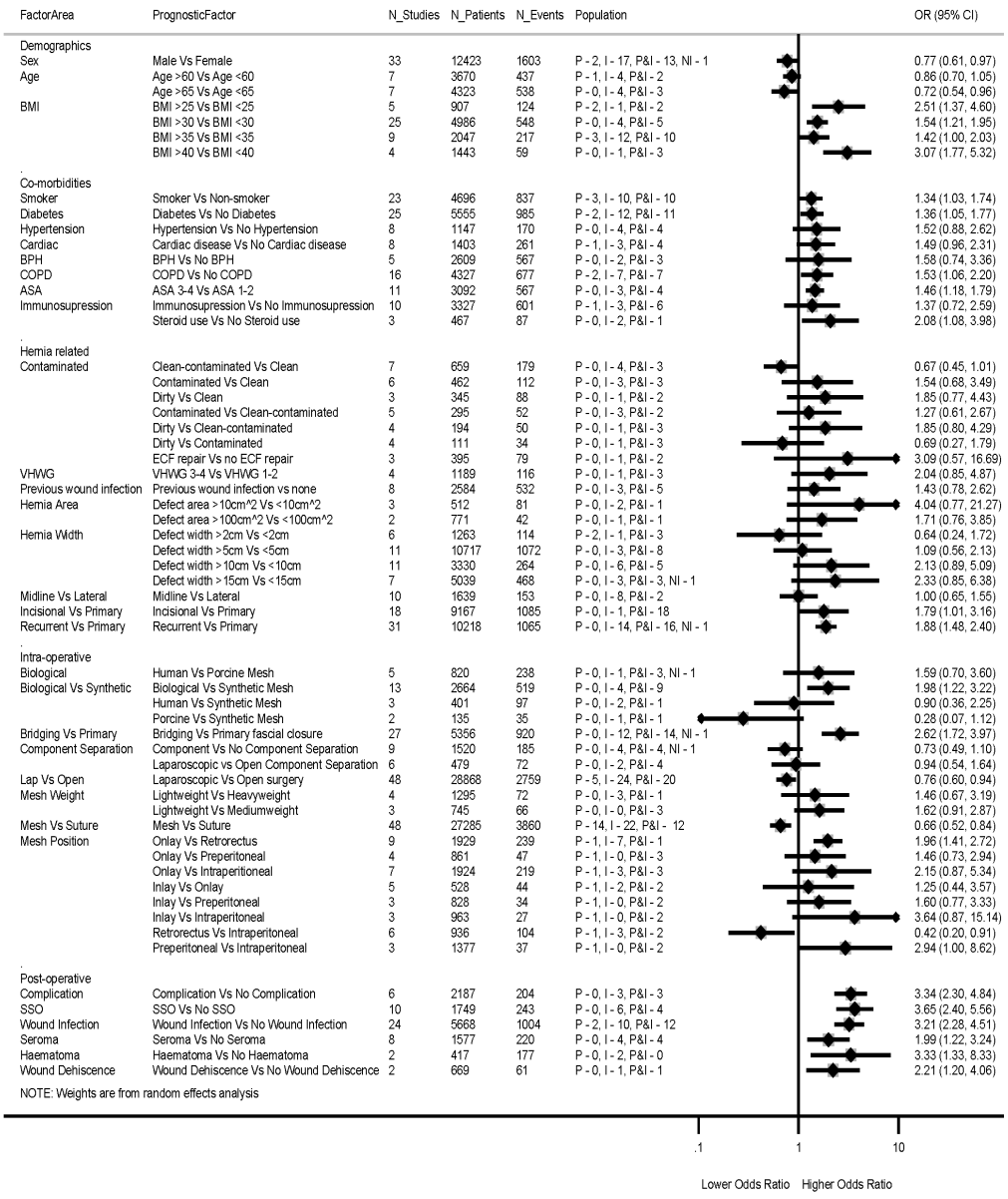
as either at “high” or “unclear” risk of bias when assessing the definition and detection of our outcome; recurrence. Concern regarding “Overall Applicability” was rated “low” in 45 (16%) studies, “unclear” in 40 (15%), and “high” in the remaining 189 (69%).

Predictors of hernia recurrence

Overall, 59 individual predictors of hernia recurrence were meta-analysed; 34 (54%) pre-operative (16 (25%) patient variables; 18 (29%) hernia variables), 19 (30%) intra-operative, and 6 (9%) post-operative predictors. Forty (63%) of these predictors had data provided by 5 or more individual studies and were therefore meta-analysed. An additional 19 (30%) predictors with data from less than five studies but labelled as “clinically important” and were also meta-analysed (Figure 3, Appendix 34). A remaining 4 (7%) predictors, with fewer than five studies providing data, were deemed clinically important enough for forest plots only (Appendix 35). Data were extracted for a further 172 predictors. These predictors were neither meta-analysed nor illustrated on forest plots as data were extracted from 4 or fewer studies, and data were either insufficient or uncomprehensive to permit meta-analysis or forest plot, or the predictors were considered clinically unimportant. A list of these predictors can be found in Appendix 36.

Figure 3 (and Appendix 34 & 37) presents overall meta-analysis results, number of studies, patients, hernia recurrence events and included study populations. Appendix 34 & 35 presents forest plots showing individual study results.

Figure 3. Overall meta-analysis results, showing the number of studies, patients, hernia recurrence events, and the included population/hernia type (P – primary, I – incisional, P&I – primary & incisional).



Pre-operative predictors

Patient predictors

Three patient factors, namely sex, age, and BMI were meta-analysed (Figure 3, Appendix 34): for age and BMI, data were provided for different thresholds including Age >/<60, Age >/<65, BMI >/< 25, BMI >/< 30, BMI >/< 35, BMI >/< 40. Male patients had significantly lower odds of recurrence (OR 0.77, 95%CI 0.61 to 0.97, 33 studies). Both age >60 compared to <60 and age >65 compared

to <65 decreased the odds of recurrence (OR 0.86, 95%CI 0.70 to 1.05, 7 studies, OR 0.72, 95%CI 0.54 to 0.96, 7 studies); this was not significant or marginally significant respectively. All BMI thresholds yielded significantly higher odds of recurrence for more obese patients (Figure 3, Appendix 34). The BMI cut-point 30 was reported in most studies; meta-analysis at this threshold gave OR of 1.54 (95% CI 1.21 to 1.95).

Meta-analyses of patient co-morbidities identified many factors potentially significantly associated with recurrence. Smoking, diabetes, COPD, ASA 3 to 4, and steroid use all had significantly higher odds of recurrence with ORs of 1.34, 1.36, 1.53, 1.46, and 2.08 respectively.

Meta-analysis of 'co-morbidity versus no co-morbidity' for hypertension, cardiac disease, benign prostatic hypertrophy, and any type of immunosuppression revealed the majority of individual study results in the direction of higher risk of recurrence; but these meta-analysis results were not statistically significant.

Hernia predictors

Two predictors relating to hernia morphology and contamination status were found to be significantly predictive of recurrence; namely incisional VH versus primary (OR 1.79, 95% CI 1.01 to 3.16, 18 studies), and recurrent VH versus primary (OR 1.88, 95% CI 1.48 to 2.40, 31 studies). Studies used a range of hernia widths to define thresholds for comparison: a wider defect appeared to predispose increasingly to recurrence, with cut-points >/< 2cm, 5cm, 10cm, and 15cm yielding progressively larger ORs of 0.64, 1.09, 2.13, and 2.33 respectively. However meta-analyses at these individual thresholds were not statistically significant. Hernia defect area was reported with thresholds of >/< 10cm^2 and 100cm^2 and gave ORs of 4.04 and 1.71 respectively; neither were significant. Hernia location (midline versus lateral) demonstrated no relationship with recurrence (OR 1.00, 95% CI 0.65 to 1.55, 10 studies).

For most of the remaining hernia related factors expected to be detrimental (Figure 3), the meta-analysis ORs exceeded 1, suggesting increased risk, but results were not statistically significant as the 95% confidence intervals spanned

1. Although 16 studies (5,279 patients, 1,018 recurrences) contributed to meta-analyses of Centre for Disease Control (CDC) wound criteria, these studies spanned six different comparisons (Figure 3) so no individual meta-analysis demonstrated a significant association with recurrence; even dirty wounds compared to clean were not significant (OR 1.85, 95% CI 0.77 to 4.43, 3 studies).

Data on VHWG grade (VHWG 4 to 3 vs. 2 to 1) was extracted from only 4 studies, and meta-analysis was not significant (OR 2.04, 95% CI 0.85 to 4.87). Previous wound infection versus no previous wound infection, another marker of contamination, was also not significant (OR 1.43, 95% CI 0.78 to 2.62, 8 studies).

Intra-operative predictors

Data were sufficient to meta-analyse 18 intra-operative predictors (Figure 3, Appendix 34). These were split into sub-groups according to operative technique, mesh versus suture, mesh type, mesh weight, and mesh location. For biological mesh, human acellular dermal matrix (ADM) compared to porcine ADM was not significant (OR 1.59, 95% CI 0.70 to 3.60, 5 studies). Several studies provided data comparing “any” biologic mesh to “any” synthetic mesh: meta-analysis suggested recurrence was significantly more frequent with biologic mesh (OR 1.98, 95% CI 1.22 to 3.22, 13 studies). However, data comparing biologic mesh subtypes to synthetic mesh were equivocal; human ADM versus synthetic mesh (OR 0.90, 95% CI 0.36 to 2.25, 3 studies), porcine ADM versus synthetic mesh (OR 0.28, 95% CI 0.07 to 1.12, 2 studies). Bridged repair was associated significantly with recurrence compared to primary fascial closure (OR 2.62, 95% CI 1.72 to 3.97, 27 studies). Component separation compared to no component separation did not reduce recurrence significantly (OR 0.73, 95% CI 0.49 to 1.10, 9 studies), with individual study results being divergent. Similarly, laparoscopic (endoscopic) component separation did not differ significantly from open (OR 0.94, 95% CI 0.54 to 1.64, 6 studies). Laparoscopic repair reduced the odds of recurrence significantly compared to open repair (OR 0.76, 95% CI 0.60 to 0.94, 48 studies).

Regarding mesh weight, lightweight mesh did not appear to provoke more recurrence than either heavyweight or mediumweight (OR 1.46, 95% CI 0.67 to 3.19, 4 studies; and OR 1.62, 95% CI 0.91 to 2.87, 3 studies, respectively). VH mesh repair versus suture only repair reduced recurrence odds significantly (OR 0.66, 95% CI 0.52 to 0.84, 48 studies). Mesh location was significant when comparing onlay to retrorectus positions (OR 1.96, 95% CI 1.41 to 2.72, 9 studies), retrorectus versus intraperitoneal (OR 0.42, 95% CI 0.20 to 0.91, 6 studies) and preperitoneal versus intraperitoneal (OR 2.94, 95% CI 1.00 to 8.62, 3 studies), ultimately favouring the retrorectus location significantly. Meta-analysis of other mesh locations (i.e. plane) were not significant (Figure 3, Appendix 34).

Post-operative predictors

Meta-analysis of post-operative predictors (Figure 3, Appendix 34) suggested that any post-operative complication (e.g. pneumonia, UTI, pulmonary embolus etc.) compared to none increased recurrence significantly (OR 3.34, 95% CI 2.30 to 4.84, 6 studies). Wound morbidity, defined as surgical site occurrence (SSO), also increased recurrence significantly (OR 3.65, 95% CI 2.40 to 5.56, 10 studies). In fact, all wound complication subtypes predisposed to recurrence significantly. This included post-operative wound infection versus no infection (OR 3.21, 95% CI 2.28 to 4.51, 24 studies), post-operative seroma versus no seroma (OR 1.99, 95% CI 1.22 to 3.24, 8 studies), post-operative haematoma versus no haematoma (OR 3.33, 95% CI 1.33 to 8.33, 2 studies), and post-operative wound dehiscence versus no dehiscence (OR 2.21, 95% CI 1.20 to 4.06, 2 studies).

Discussion

Over the last two decades hernia surgeons have published a considerable volume of research that describes the pre-, intra-, and post-operative variables that influence postoperative outcomes. Here, I investigate specifically how these variables influence recurrence, arguably the single most important outcome since it determines whether reconstruction was ultimately successful. To our

knowledge a prognostic systematic review and meta-analysis of these factors has not been performed previously. Identification of predictors of recurrence is pivotal because the decision whether to perform reconstruction or not pivots on the chance of success. However, clear signals of success are frustrated by individual primary studies that are usually relatively small, single-centre, and assess a limited handful of predictors. Moreover, small sample size bias causes divergent results that then frustrate identification of valid predictors. Synthesising all available evidence together by systematic review and meta-analysis, and then presenting results as forest plots allows individual clinicians to interpret data from multiple primary studies and facilitates discussion of evidence for clinical guidelines, clinical practice and future research. Furthermore, the strength of evidence is enhanced by excluding results for predictors with few reports (unless deemed “clinically important”).

I used an adapted version of the PROBAST tool to assess risk of bias (123) and found that most of the primary literature demonstrated high ROB. I confirmed that predictors were usually poorly defined and the methods and definitions used to detect recurrence also lacked standardisation. In addition, I also found that blinded reporting of both predictors and hernia recurrence was unusual. In other words, it was unclear whether predictor assessment was made blinded to recurrence, or vice versa (the former only being possible in retrospective studies). This is pivotal for unbiased prognostic data (338).

Because I aimed to evaluate the entirety of the prognostic literature, this review was very extensive; approximately 7,500 abstracts were screened. Surprisingly, I encountered very few true prognostic studies, i.e. those designed a priori specifically to identify predictors of VH recurrence (85, 119, 339, 340). Accordingly, I was obliged to extract a considerable amount of data from cohort studies (177, 198, 222), which analyse how one variable (e.g. open versus laparoscopic VH repair) affects outcome. Simple 2x2 tables could be constructed from these comparative studies and meta-analysed subsequently. Data were also extracted from large database studies (65, 67, 341), which record the effect of multiple peri-operative variables on multiple post-operative outcomes, often including hernia recurrence. I discovered a huge range in the amount of data

extractable for individual predictors. For some commonly quoted clinical risk factors for recurrence, such as previous abdominal aortic aneurysm (AAA) repair or connective tissue disorders (eg. Ehlers-Danlos), I found insufficient data for meta-analysis. Analogous with this, I could only categorize hernia location into medial and lateral subgroups as data was insufficient to identify subgroups such as supra-pubic versus umbilical, or sub-xiphisternal versus sub-costal. These subgroups are often discussed amongst hernia surgeons as 'difficult to repair', and with a high recurrence rate (342). In contrast, I could extract abundant data for other variables; for laparoscopic versus open and mesh versus suture repair we extracted data from 48 studies of 28,868 and 27,285 patients respectively. Accordingly, research appears focused on potential predictors related to surgical technique and less on others that may be equally or indeed more important. Further work is required on predictors that have had limited interrogation.

This work is presented methodically in Figure 3, where predictors are separated into groups; patient demographics, hernia characteristics, intra-operative, and post-operative variables. I found that BMI, smoking, diabetes, COPD, ASA class 3-4, and steroid use were patient variables associated significantly with recurrence. The analysis also suggests that male sex and age above 65 years is protective. Why males should be less vulnerable to recurrence is unclear and we can only speculate at this stage. For the age thresholds 60 and 65, Kokotovic et al (67), a publication from the Danish Ventral Hernia Database (DVHD) contributed the most patients, dominating the meta-analysis. The DVHD uses re-operation rate to surrogate for recurrence. Their large cohort suggests that elderly patients are significantly less likely than younger patients to undergo re-operation. This result is unsurprising as elderly patients would appear less fit for a second elective repair. The only hernia related variables associated significantly with increased recurrence were incisional versus primary VHs, and recurrent versus primary VHs, a finding that is well-established (9, 10). In other words, previous surgical intervention causes scarring, weakens the abdominal wall, and leads to impaired wound healing and hernia recurrence. Multiple studies described hernia width using different thresholds, each of which appeared unassociated with recurrence. However, I found that as defect width increased from cutpoints of 2cm, 5cm, 10cm, and 15cm, so did the odds of recurrence

(being 0.64, 1.09, 2.13, and 2.33 respectively). Even though their individual confidence intervals crossed one, this observation is consistent, suggesting that increasing hernia width is a genuine risk factor for recurrence. More data are required to confirm this. Furthermore, width may be measured clinically, intra-operatively, and by imaging, all of which will be subject to inter- and intra-observer variation, and to variation between methods. Larger defects require additional reconstructive techniques which may, in turn, confound the predictive power of defect width. Also, indexed publications usually arise from experienced centres, for whom larger width may be less challenging or, conversely, they attract the most difficult patients. Lastly, I was able to extract data for VHWG grade from only 4 studies (52, 108, 343, 344). This scale was proposed in 2010 (50), but few publications have validated it subsequently. I found no significant association with recurrence when comparing VHWG grade 3 or 4 to grade 1 or 2. Similarly, CDC status was not associated with recurrence but, again, few studies provided extractable data. Further prognostic research is required for these factors, and on creating a contamination scale that is potentially associated with postoperative outcomes/recurrence.

The analysis of intra-operative variables confirmed the well-known 'protective' effect of mesh over suture repair (37), and also that primary fascial closure (107) results in a more reliable repair than a bridged repair; both of these associations are well-established. Furthermore, the data was consistent with biological mesh being 'weaker' than synthetic mesh, with greater tendency towards recurrence, an association previously published (345, 346) but perhaps less well-known. In addition, laparoscopic VH repair appeared protective, again suggested by individual previous publications (65, 102), and similarly less well-known and clinically accepted. The variables of bridging versus primary fascial closure, mesh type, and mode of surgery are very much dependent on the individual surgeon and individual hernia morphology. For example, the reader must bear in mind that a bridged repair, a biologic mesh, and the open technique may be employed for more complex patients/hernias, which may then confound any association with recurrence. I described mesh location using the ICAP classification system recently published (297). The results concerning mesh location suggest that the retrorectus plane reduces recurrence compared to onlay and intraperitoneal

planes, and that intraperitoneal is superior to the preperitoneal plane. Observational studies, database studies, and systematic reviews support this finding (65, 105, 106, 347, 348). Lastly this review suggests that wound morbidity (defined as surgical site occurrence (SSO)) leads to delayed wound healing and subsequent recurrence. Indeed, I found that all local wound complications were associated with recurrence. Meta-analysis of six papers compared patients with 'any post-operative complication' (including systemic complications) with those that had 'no post-operative complication', suggesting increased recurrence in the former.

Although this was a prognostic systematic review, I found few prospective studies with an a priori intention to identify predictors of VH recurrence. Moving forwards, prospective VH prognostic studies should be performed to eliminate bias, with well-characterized participants, blinded assessment of potential predictors and outcomes, standardized definitions and detection methods for both predictors and outcomes. Expert statistical support from statisticians specifically interested in prognostic research is also required to assist both design and data collection to minimize ROB and so that the data generated are generalizable. If authors intend to use these prognostic data to develop prognostic models of post-operative outcomes, they should adhere to the TRIPOD statement, a 22-item checklist, which aims to improve the reporting of studies developing, validating, or updating prediction models (349, 350).

In summary, by systematic review and meta-analysis I have summarised the current evidence base for prediction of VH recurrence. The findings should be used to guide future prospective research aiming to identify predictors of VH recurrence. Figure 3 is a summary of the literature over the past 20 years.

Chapter 11

Limitations

Like all research this work does have its limitations that should to be taken into consideration. Readers will make their own critical appraisal of this work but in this chapter I outline some of the limitations that I identified during the course of my research.

After completing our first systematic methodological review that analysed VH randomised controlled trial (RCT) methodology and trial data collection (Chapter 3) we realised that our assessment of these trials could have been improved. Firstly, we hadn't assessed whether research quality had improved with date of publication or with journal impact factor. As RCTs are the highest level of evidence (level 1b, Oxford Centre of Evidence Based Medicine (35)) and are presumably carried out by the most laudable and up to date AWR researchers, we may have found an improvement in research quality as research has evolved over the last 20 years (particularly as the CONSORT (291) and TIDieR (172) checklists have been updated and published during this time). Consequently, we may have been able to publish a less pessimistic description of the literature, showing an improvement of research quality over time and with journal impact factor. However, the output from our systematic review still stands; i.e. that VH randomised controlled trials collect perioperative variables and post-operative outcomes that lack standardised definitions and detection methods. We did rectify this limitation in our next methodological review of non-randomised interventional trials, by collecting both publication date and impact factor, showing that there had been no improvement in research quality either with date of publication or increased impact factor. Secondly, we didn't assess whether these RCTs referenced a written protocol or whether they had performed a power calculation, both criteria being critical in performing robust high quality randomised trials and key indicators that allow us to evaluate the methodological quality of published trials. In our second review we did include these criteria, finding that none of the non-randomised trials referenced a written protocol and

only 2 trials performed a power calculation. Ultimately, our methodology checklist (soon to be published in the British Journal of Surgery along with our primary and incisional VH minimum datasets) does include these two criteria. Our hope is that publication of our defined minimum datasets and our methodological checklist will improved research quality within the VH domain.

When considering the LOD survey, Chapter 6, two limitations should be considered. Firstly, because I wished the data to be representative of a wide range of surgical expertise (within the general surgery specialty), I included surgeons from many different abdominal disciplines, but the number of individuals from each varied. I do not view this as a major limitation, as the most important contrast seen was between academic AWR surgeons and others. AWR surgeons being the only group who preferred the Tanaka definition to the Sabbagh. To get a better understanding of how each subspecialty perceived LOD and hernia morphology I could have interviewed an equal number of surgeons from each subspecialty. Secondly, during my analysis it also became apparent that the critical threshold for LOD (above which surgeons would not operate), depends on the precise definition used (i.e. Sabbagh or Tanaka) by the individual surgeon, and I did not record from which standpoint the surgeons were making their assessment. However, given that the only group to favour Tanaka were academic AWR surgeons, we can infer that most thresholds were made with the Sabbagh definition in mind. Also, the fact that there is a varied and unstandardized opinion on the preferred definition remains unchanged.

The NGT and Delphi consensus studies are presented in Chapters 7, 8, and 9. For the NGT study I used a group of European hernia experts and for both Delphi studies I used a worldwide group of hernia experts. The groups differed because for NGT studies a face-to-face focused group meeting is required; an impossible task to achieve with a worldwide group. A limitation that should be mentioned is how these two groups were selected as this was not clearly defined. For the NGT consensus study the group of European experts were selected by ACJW (Mr Alastair Windsor) and I. Surgeons well-known as hernia academics were selected. In addition, two expert patients known to have their own research activities within the field of AWR, were also chosen. For our LOD and ICAP Delphi

studies the worldwide group of experts was selected by lead researchers MK (Mike Liang), FM (Filip Muysoms), and AW. Again, panellists were selected adhoc, i.e. if they were known to the lead researchers and had a good reputation as hernia academics/surgeons. It could be argued that the experts included in both groups were self-selecting, being 'well-known' academics and hernia enthusiasts, who published research articles and attended academic conferences. However, we had no defined selection criteria for either group of experts. Predefined criteria could have included some or all of the following; performing in excess of a specific number of AWR operations each year, publishing more than a prespecified number of academic articles during a prespecified time period, working in a hospital with designated AWR operating lists and AWR outpatient clinics, or entering individual patient data into a national AWR database. Whatever the chosen selection criteria for panelist inclusion, specifying these prior to performing a consensus study, allows for selection of a homogenous group of experts with equal expertise and knowledge. Accordingly, each expert has an equally valid contribution to the consensus study. As we did not specify any selection criteria for panelist inclusion other than being 'well-known', the contributions of our panellists may not all have been equally valid. However, in our view this is unlikely to have material impact on the conclusions.

Furthermore, our worldwide chosen group of panelists mainly represents countries from the developed world, meaning that within our group there was no representation from Northern Africa, the Middle East, or the Indian subcontinent. Typical patient profiles in these regions differ, with lower rates of obesity (351) and sarcopenia (352), and higher rates of manual labour, trauma, late presentation, and emergency presentation of disease (353). This is likely to affect hernia aetiology with higher rates of primary and traumatic VH and lower rates of incisional hernia. Materials and techniques used to repair VHs may also differ due to a lack of healthcare resources and clinical knowledge that may have regional differences. Despite this, I believe the LOD definitions proposed and the abdominal wall planes described in ICAP, are straightforward, and easily applicable to all human populations and profiles. Indeed, even in developed countries there is a spectrum of patients that present to the outpatient clinic. I and

all co-authors believe that our new LOD definitions and abdominal wall nomenclature can be applied unreservedly.

Regarding the LOD Delphi study further limitations should be considered. As anticipated, as a facilitator, my role was relatively active, and required thematic analysis of proposed definitions to create a new written definition in order to achieve consensus. Two written definitions were removed, (despite not meeting the pre-defined criteria for removal) as they were deemed at variance with the definitions proposed by panelists. Facilitator intervention is sometimes necessary to achieve consensus and ultimately was judged acceptable in our study because the written definition proposed was approved by all panelists. Furthermore, it is possible that restricting panelists to expert abdominal wall surgeons may have introduced bias that could have resulted in an overly complex written definition for LOD. It also could have resulted in an overly high LOD threshold value, if consensus had been reached, since this group will likely be more willing to tackle complex cases. However, I would argue that expert surgeons will be the most appropriate “consumers” for these definitions once accepted, since I believe that complex abdominal wall reconstruction is not a problem that should be tackled by general surgeons with experience limited to a few individual cases.

The ICAP Delphi study resulted from an editorial article, which highlighted the inconsistent use of nomenclature for the abdominal wall planes (314). This article stimulated an academic debate amongst hernia experts and a research meeting in Miami, in March 2018. The meetings conclusion was to perform a Delphi study to standardise abdominal wall nomenclature. The terms we used for the abdominal wall planes at the start of this Delphi study were collected from our own knowledge of the literature, after performing systematic reviews, terms collected from an online survey performed by the IHC (322), and from our own private correspondence from surgeons worldwide who had emailed us in response to our editorial article. Consequently, a number of circumstantial events led to performing the ICAP study. Arguably, a systematic review should have been performed first. This would have allowed for a thorough and accurate assessment of the literature, a detailed summary of which terms are commonly and not commonly used, and identification of terms rarely used that may have

been missed out and therefore not used in our ICAP Delphi study. As all terms were presented to panelists in an unbiased manner, consensus may well have included a rarer term if proven to be a popular choice. Despite this limitation, our less conventional approach was nonetheless exhaustive; during this time we were performing extensive systematic review within the VH domain and developed a good knowledge of the literature and identified many studies describing the abdominal wall planes (54, 117, 354), in addition, 111 surgeons contributed to the IHC online survey (322), and 3 terms (ante-rectus, inter-oblique, and pre-transversalis facial) were identified to us via private email correspondence. ICAP is the only study in the literature that presents standardised nomenclature for the abdominal wall planes and should be adopted for robust research and accurate clinical practice.

Lastly the limitations of the prognostic systematic review presented in Chapter 10 should be discussed; the majority of which are contingent upon on the quality of primary component studies. As noted already, true prognostic research was surprisingly scarce. As anticipated, study methods were heterogeneous and we were obliged to meta-analyse across different study designs, definitions of recurrence, methods to detect recurrence, and different follow-up durations. Indeed, our risk of bias analysis, using PROBAST (123), found that 97% of included studies was high risk of bias and may cast doubt on the results of our meta-analysis. Such variability likely underlies disparity between the study effect estimates seen across results (Appendix 34). However, because data were heterogeneous, it is important to stress that interpretation of our findings should focus on which factors appeared predictive rather than on the precise strength of that prediction (i.e. whether or not the confidence interval was significant). The purpose of this review was not to confirm the existence of known predictors but to summarise the current evidence base and to identify new or unknown predictors that warrant future investigation. Our review also identifies predictors, like pre-operative wound contamination and mesh location, where to date, only a small number of studies have been performed such that findings from future larger and more rigorous studies will be important.

Furthermore, extracting overall study results from the published primary literature instead of individual patient data (IPD), means that I could not use multivariable analysis to account for confounding or ecological bias due to associations of multiple factors within individual patients. For example, biological mesh seems to predispose to recurrence compared to synthetic mesh, but multivariable analysis would be needed to understand if this is independent of mesh plane. Similarly, component separation did not appear to reduce recurrence, but multivariable analysis would be needed to understand if this result is confounded by more severe disease (in which this procedure is performed) and/or whether the repair was bridged or closed primarily.

In this chapter, I have mentioned some of the limitations of this work. I will not have identified all the shortcomings that exist. I look forward to future opportunities where I can present this work at national and international conferences and discuss its merits and limitations.

Chapter 12

Conclusion and Suggestions for Future work

Conclusion

The work described in this thesis has taken me four years. While the initial plan was to develop a prognostic model of ventral hernia recurrence after intended curative repair, I was immediately struck by the poor quality of available indexed literature, and this obliged me to change my research priorities. It was obvious to me and to my research collaborators that these deficiencies needed urgent attention, and it is this that has taken the large majority of my research effort. Accordingly, the majority of this thesis has aimed at establishing clear variable definitions and standardised trial datasets to improve VH research quality.

My initial work focused on interventional trials with the performance and subsequent publication of two systematic reviews that demonstrated the highly variable reporting of perioperative variables by trials investigating VH repair (170, 286). These reviews found that pre-, intra-, and post-operative data are often measured and reported differently frustrating data pooling and trial comparison. Focusing on hernia recurrence, I showed that trials use many different definitions and detection methods, and that recurrence rates differed according to these. Consequently, in Chapter 7, using the Nominal Group Technique and an international task force of hernia surgeons I established standardised reporting minimum datasets for trials investigating VH repair. During this project I also published a standardised methodology checklist for VH trials and a list of patient reported outcomes established via consensus. These datasets have been accepted for publication in the British Journal of Surgery.

Next, I focused on loss of domain (LOD), publishing a systematic review (239) and clinician survey (306) demonstrating that no standardised definition existed either within research or clinical practice. Using Delphi methodology and a second group of international hernia experts, I established new written and

volumetric definitions for LOD, and published these in 2019 (Chapter 8) (295). I have presented these on the international stage as well with presentations at EHS 2019, AWRE 2020, and AHS 2020. LOD could be a useful predictor for post-operative outcomes and needs to be reported with standardised definitions so that studies produce consistent comparable data.

My last project on research quality focused on nomenclature for the abdominal wall planes. I started by highlighting the current inconsistencies that existed in the literature by publishing a review article (314). This article triggered replies from the International Hernia Collaboration (322) and Texas Health Science Centre (323), both centres realising that standardisation was required. Again, using Delphi methodology and the same twenty international hernia experts I used for the LOD project, I created a new classification system, ICAP (International Classification of Abdominal Wall Planes), which was published in the British Journal of Surgery (297). Since then, ICAP has been endorsed by the European Hernia Society (EHS) and I am seeking endorsement from the American Hernia Society. To date, I have presented ICAP at four international hernia conferences, and will continue to submit the abstract to other international hernia meetings.

My final piece of work analysed twenty years of VH literature, searching for variables that might be significantly predictive of outcome following ventral hernia repair with curative intent. This systematic review involved extraction of prognostic data followed by meta-analysis to identify potential predictors of VH recurrence. Identification of potential predictors forms the basis for prognostic model development. As the extracted data was so poorly defined, with variable definitions for recurrence, detection methods for recurrence, and measuring of predictor variables, readers are asked to interpret our findings focusing on which factors appear potentially predictive rather than on the precise strength of that prediction (i.e. whether or not the confidence interval was significant, and the size of that interval). This is particularly the case for predictors where the number of included studies was small, meaning that findings from future larger and more rigorous studies will be especially important.

Further work: Prognostic model development

At University College London Hospital we have identified over 1100 individual patients who have had VH repair over the last 10 years. From this cohort, we will extract the predictors identified in Chapter 11 of this thesis. We anticipate that approximately 20% of our patients will have recurrence at 1-year; patients will be divided into those patients with and without VH recurrence. We have defined recurrence by clinical examination plus or minus CT or USS at 1-year, since not all patients undergo postoperative CT or US scanning.

We will develop two new models for recurrent VH at one-year post hernia repair. Model 1 using data collected in standard clinical practice, Model 2 using standard data enhanced with pre-operative CT scan data focusing on complex VH recurrence.

We will use logistic regression methods to develop predictions models for recurrent VH at 1 year. Multivariable logistic regression will retain continuous variables wherever possible (e.g. age, hernia size) to conserve statistical power. Our model will include five to 10 variables pre-specified and fixed in the model. We will use the full dataset for model development and for internal validation using 200 bootstrap datasets. We will use multiple imputation for missing covariates during development and validation. We will express results in terms of calibration, discrimination, net-benefit, and sensitivity at a fixed specificity identified by our expert clinicians as relevant (355).

We anticipate having approximately 220 recurrence events in 1100 VH individuals. Sample size calculation for prognostic studies is based on accepted “rule of thumb” rules that depend on whether the primary aim is to select variables suitable for inclusion in a new model (where the rule of thumb is to use a minimum of 10 events per variable used in selection procedures (356)), or to evaluate variables that are pre-specified and fixed (where simulation suggests at least 100 events are required for reliable validation (357)). We will conserve statistical power for both models by reducing the number of variables used in selection via pre-specification. We will include fixed variables in the model for patient

characteristics already known as important for CVH recurrence and for others required for acceptability by the clinical community, e.g. age, gender, BMI, hernia size, and others identified as plausible from our systematic review. In model 2 we will achieve this by using a simplified CT score. For example, principal component analysis (PCA) allows identification of best discrimination from combinations of CT parameters for patients with and without VH recurrence. PCA will allow multiple CT characteristics to be combined into relatively few individual predictor variables for inclusion in the model. We will then internally validate the model (358) using a minimum 200 bootstraps, or until estimates remain stable (359). Should the model prove reasonably predictive, we would then aim to perform an external validation to assess generalisability to other centres, updating the model as necessary via information gained from external validation.

Further work: Standardisation

Much research is needed throughout the domain of AWR to improve repair outcomes. Even within the subject of standardisation, there is still work to be done. Pre-clinical mesh testing is perhaps the most pressing area that requires standardisation. In the clinical setting, surgeons are eager their VH patients do not to suffer from morbid mesh-related complications (mesh infection, enteric fistulation), which have been reported in up to 5.6% of patients at 5 year follow-up (67). However, with over 200 mesh implants available on the market (344), choosing a surgical mesh implant is challenging. Aggressive marketing techniques quote anecdotal data from single arm animal studies and adhoc clinical comparative studies. At best, a marketed mesh product may have one or two published pre-clinical studies (360, 361) in addition to one or two published clinical comparative trials (207, 362); with the comparative trials comparing a new mesh to one of several possible products on the market. Furthermore, trial outcomes are poorly defined and unstandardized making trial comparison and interpretation challenging (170). The resulting chaos in the literature makes selecting a mesh implant almost impossible and surgeons have to rely on circumstantial data to make their choice.

This haphazard state of the literature is not accidental. Surgical mesh implants are categorised by the FDA as medical devices and are therefore not subjected

to the same levels of scrutiny as other new medical products (e.g. a new drug) (363). To license a new product for clinical use, mesh companies have to demonstrate 'substantial equivalence' to an already legally marketed product, and they apply to the FDA via the '510K mechanism'. 'Substantial equivalence' requires only that these materials have similarity to existing products without the need for rigorous clinical trials with long term follow up. Manufacturers therefore perform adhoc pre-clinical and clinical trials compiling the data enabling them to license their product. Importantly, there is no standardized test these mesh products have to surpass, and the demonstration of long term safety after implantation is not required.

This lack of standardization in the 21st century for marketed medical devices is absurd. Whilst other industries have governing bodies (many run by the International Organisation for Standardisation, https://www.iso.org) that control the quality and safety of their products, no such governance exists for the medical profession, a profession in which safety should be paramount. As the long-term safety of surgical meshes has become a major concern to both the public and to practicing surgeons, reference data of surgical mesh biocompatibility and performance is urgently required.

Further work: Prophylactic mesh

Over the past ten years VH hernia research has increasingly focused on the use of prophylactic mesh when closing a midline laparotomy. Currently, there is compelling evidence for mesh to be used in high-risk laparotomies (i.e. those with obesity and those having a laparotomy for AAA repair). Accordingly, in guidelines for abdominal wall closure this has been included as a 'weak' recommendation (44). Since publication of these guidelines further work has supported the use of prophylactic mesh but trial results do give contradictory evidence for the optimal plane of mesh insertion and the optimal mesh type (42, 43). A recent multicentre randomised controlled trial investigating ileostomy closure compared placement of an intraperitoneal biological mesh to suture only closure. The results were significant, with a 12% incisional hernia rate in the mesh group versus a 20% incisional hernia rate in the suture only group (364). Long term recurrence rates and cost analysis at 5 years follow-up are awaited but this trial supports use of

biological mesh for ileostomy closure and should change practice. However, to date, there has been limited use of mesh for hernia prophylaxis, possibly because of a fear of mesh long-term complications. As this would be a radical change to the practice of all general surgeons, further work is required to explore the long-term safety of this concept and to produce further robust evidence with clear guidance advising surgeons when and how to insert a prophylactic mesh.

Further work: Loss of Domain (LOD)

A large proportion of this thesis was dedicated to establishing standardised definitions for LOD. Both our Delphi study in Chapter 7 (295) and our clinician survey in Chapter 6 (306) supported using the Sabbagh method for volumetric LOD measurement and our Delphi study established a new written definition for LOD (295). As VH research progresses, using a standardised definition of LOD as a descriptor of large VH morphology is crucial to allow for further investigation into the clinical utility of LOD.

I hope to investigate LOD in future. In particular, it is clear that a single threshold for LOD that precludes repair, and that applies to all patients is vanishingly unlikely. Rather, it is likely that the threshold beyond which repair is likely to be fruitless will depend on multiple individual patient and hernia variables. It would be interesting to obtain examples of successful and unsuccessful VH repair from multiple centres to attempt to identify those morphological factors that best separate between these two groups. It would also be interesting to investigate how LOD volumes interact with various reconstructive techniques, thereby giving further guidance into the reconstructive techniques that should be utilised.

I hope that my work means that VH trials, studies, and databases will start reporting LOD consistently. Consistency within the primary literature will then allow for data pooling and analysis of LOD in the secondary literature as a post-operative outcomes predictor. I hope that future systematic reviews similar to the review performed in chapter 11 will be able to include LOD as a hernia descriptor and analyse whether this has prognostic utility regarding outcomes such as hernia recurrence, surgical site infection, or 30-day re-operation rate.

Summary

VH research is ever-increasing, from January 1st 1995 to January 1st 2005, 703 articles were published by PubMed within the domain of 'Abdominal Wall reconstruction'. In the following decade, January 1st 1995 to January 1st 2015, 1878 articles were published. This increase in research activity mirrors a surge in clinical prevalence of VH disease. Indeed, in the UK, we have seen a 13% increase in the number of VHs being repaired over the last 10 years (1). Consequently, it behoves surgeons to find both prevention and cure. Over the last four years I have manage to carry out a large amount of work aiming to improve VH research quality and identify the predictors for VH recurrence. I believe this work has made a significant contribution to surgical science specifically within the emerging subspecialty of Abdominal Wall Reconstruction. I have enjoyed my research tenure tremendously and I am looking forward to carrying out more research in the future.

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Publications and presentations

Publications

Published

Parker S.G, Wood C.P.J, Sanders D.L, Windsor A.C.J. Nomenclature in Abdominal Wall Hernias: Is it Time for Consensus? World Journal of Surgery 2017;41(10):2488-91. (Chapter 3)

Parker S.G, Wood C.P.J, Sanders D.L, Windsor A.C.J. Comment on: International Hernia Collaboration Consensus on Nomenclature of Abdominal Wall Hernia Repair: Reply. World Journal of Surgery 2018;42(1):305. (Chapter 3)

Parker S.G, Wood C.P.J, Sanders D.L, Windsor A.C.J. Comment on: Nomenclature in Ventral Hernia Repair. World Journal of Surgery 2018;42(6):1906. (Chapter 3)

Parker S.G, Halligan S, Liang M.K, et al. International classification of abdominal wall planes (ICAP) to describe mesh insertion for ventral hernia repair. British Journal of Surgery 2020;107(3):209-17. (Chapter 4)

Parker S.G, Halligan S, Blackburn S, et al. What exactly is meant by “Loss of Domain” for Ventral Hernia? Systematic Review of Definitions. World Journal of Surgery 2019;43(2):396-404. (Chapter 5)

Parker S.G, Halligan S, Erotocritou, et al. What exactly is meant by ‘loss of domain’ for ventral hernia? A survey of 100 surgeons. ANZ Journal of Surgery 2020;90(3):205-207. (Chapter 6)

Parker S.G, Halligan S, Liang M.K. Definitions for Loss of Domain: An International Delphi Consensus of Expert Surgeons. World Journal of Surgery 2019;44(4):1070-78. (Chapter 7)

Parker S.G, Wood C.P.J, Butterworth J.W, et al. A systematic methodological review of reported perioperative variables, postoperative outcomes and hernia recurrence from randomised controlled trials of elective ventral hernia repair: clear definitions and standardised datasets are needed. Hernia 2018;22(2):215-226. (Chapter 8)

Parker S.G, Halligan S, Erotocritou M, et al. A systematic methodological review of non-randomised interventional studies of elective ventral hernia repair: clear definitions and a standardised minimum dataset are needed. Hernia 2019;23:859-72. (Chapter 9)

Accepted

-British Journal of Surgery

Parker S.G, Halligan S, Berrevoet F, et al. Improving Research Quality: Proposed Minimum Datasets, Patient Reported Outcomes, and Methodology Criteria for Interventional Trials of Primary and Incisional Ventral Hernia Repair. (Chapter 10)

-BJS Open

Parker S.G, Mallett S, Quinn L, et al. Identifying Predictors of Ventral Hernia Recurrence: Systematic Review and Meta-Analysis. (Chapter 11)

Presentations

Podium

Parker S.G. Predicting Ventral Hernia Recurrence. AWR Europe February 2018, Royal College of Physicians, London, UK.

Parker S.G. A National Ventral Hernia Database. British Hernia Society November 2018, The Assembly Rooms, Edinburgh, UK

Parker S.G. Use of imaging for pre- and post-operative characterisation of ventral hernia: systematic review. British Hernia Society November 2018, The Assembly Rooms, Edinburgh, UK

Parker S.G. Incidence of Ventral Hernia Repair. AWR Europe February 2019, Royal College of Physicians, London, UK.

Parker S.G. An International Classification of Abdominal Wall Planes. European Hernia Society September 2019, Hamburg, Germany.

Parker S.G. A systematic methodological review of reported perioperative variables, postoperative outcomes and hernia recurrence from randomised controlled trials of elective ventral hernia repair: clear definitions and standardised datasets are needed. European Hernia Society September 2019, Hamburg, Germany.

Parker S.G. A systematic methodological review of non-randomised interventional studies of elective ventral hernia repair: clear definitions and a standardised minimum dataset are needed. European Hernia Society September 2019, Hamburg, Germany.

Parker S.G. What exactly is meant by “Loss of Domain” for Ventral Hernia? Systematic Review of Definitions. European Hernia Society September 2019, Hamburg, Germany.

Parker S.G. Definitions for Loss of Domain: An International Delphi Consensus of Expert Surgeons. European Hernia Society September 2019, Hamburg, Germany.

Parker S.G. An International Classification of Abdominal Wall Planes. Virtual European Hernia Society May 2020.

Parker S.G. An International Classification for Loss of Domain. Virtual American Hernia Society Conference September 2020.

Parker S.G. Ventral Hernia Repair; What to do before you operate? Virtual British Hernia Society November 2020.

Poster

Parker S.G, Wood C.P.J, Butterworth J.W, et al. A systematic methodological review of reported perioperative variables, postoperative outcomes and hernia recurrence from randomised controlled trials of elective ventral hernia repair: clear definitions and standardised datasets are needed. American and European Hernia Societies Joint International Hernia Congress March 2018, Fontainbleau Beach Hotel, Miami, Florida, USA.

Parker S.G, Halligan S, Plumb AAO, et al. Use of imaging for pre- and post-operative characterisation of ventral hernia: systematic review. British Hernia Society November 2018, The Assembly Rooms, Edinburgh, UK

Parker S.G, Wood C.P.J, Butterworth J.W, et al. A systematic methodological review of reported perioperative variables, postoperative outcomes and hernia recurrence from randomised controlled trials of elective ventral hernia repair: clear definitions and standardised datasets are needed. British Hernia Society November 2018, The Assembly Rooms, Edinburgh, UK.

Parker S.G, Halligan S, Blackburn S, et al. What exactly is meant by “Loss of Domain” for Ventral Hernia? Systematic Review of Definitions. British Hernia Society November 2018, The Assembly Rooms, Edinburgh, UK.

Parker S.G, Wood C.P.J, Sanders D.L, Windsor A.C.J. Nomenclature in Abdominal Wall Hernias: Is it Time for Consensus? British Hernia Society November 2018, The Assembly Rooms, Edinburgh, UK.

Appendix

Appendix 1

Surgical innovation and new techniques for ventral hernia repair developed over the last 100 years.

Midline hernias

Open

1. Mayo W.J. An operation for the radical cure of umbilical hernia. Ann Surg 1901;34:276-80.

2. Nuttal H.C. Rectus transplantation in the treatment of ventral herniae. Br Med J 1926;3395:138-39.

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11. Martin-Cartes J et al. Sandwich technique in the treatment of large and complex incisional hernias. ANZ Journal of Surgery 2016;86(5):343-347.

12. Mommers E H et al. A modified Chevrel technique for ventral hernia repair: long term results of a single centre cohort. Hernia 2017;21:591-600.

Laparoscopic

1. Le Blanc K et al. Laparoscopic repair of incisional abdominal hernias using expanded PTFE: preliminary findings. Surg Lap & Endoscopy 1993;3(1):39-41.

2. Chelala et al. Long term outcomes of 1326 laparoscopic incisional and ventral hernia repairs with the routine suturing concept: a single institution experience. Hernia 2016;20(1):101-10.

3. Belyansky I et al. Laparoscopic transversus abdominis release, novel minimal invasive approach to complex abdominal wall reconstruction. Surg Innov 2016;23(2):134-41.

4. Gomez-Menchero J et al. laparoscopic intra-corporeal rectus aponeuroplasty (LIRA): a step forward in minimally invasive abdominal wall reconstruction for ventral hernia repair. Surg Endosc 2018;32(8):3502-8.

Robotic

1. Warren J A et al. Standard laparoscopic versus robotic retromuscular ventral hernia repair. Surg Endosc 2017;31:324-332.

Hybrid

1. Lowe J B et al. Endoscopically assisted “Components separation” for Closure of Abdominal wall defects. Plastic and Reconstructive Surgery 2000;105(2):720-30.

2. Schwarz et al. Endoscopic mini/less open sublay technique (EMILOS) - a new technique for ventral hernia repair. Lang Arch Surg 2017;402(1):173-80.

3. Reinpold et al. Mini or less open Sublay Operation (MILOS): A new minimally invasive technique for the extra-peritoneal mesh repair of incisional hernias. Ann Surg 2018:16.

Lumbar/flank hernias

1. Lichenstein I L et al. Repair of large diffuse lumbar hernias by an extraperitoneal binder technique. Am J Surg 1986;151:501-504.

2. Renard Y et al. Open retromuscular large mesh reconstruction of lumbar incisional hernias including the atrophic muscular area. Hernia 2017:21:341-49.

Supra-pubic hernias

1. Blair L J et al.Bone anchor fixation in Abdominal Wall Reconstruction: A useful Adjunct in Suprapubic and Para-iliac hernia repair. Am Surg 2015;81:693-697.

2. Renard et al. Standard of Open Surgical Repair of Suprapubic Incisional Hernias. World J Surg 2017;41:1466-1474.

Subcostal hernias

1. Landau O et al. Laparoscopic repair of poststernotomy subxiphoid epigastric hernia. Surg Endosc 2001;15:1313-14.

Techniques for augmenting abdominal wall closure

1. Moreno I G. Giant chronic eventration prepared with pneumoperitoneum and operated. Preliminary report. Buenos Aires. 22nd Argentina Congress of Surgery 1940.

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4. Bueno-Lledo et al. Preoperative progressive pneumoperitoneum and botulinium toxin type A in patients with large hernia. Hernia 2017;21(2):233-243.

Appendix 2

Our complete PubMed search string:

(((((((("General Surgery"[MESH]) OR "Reconstructive Surgical Procedures"[MESH]))
OR ((("pneumoperitoneum"[Title/Abstract]) OR "botox"[Title/Abstract]) OR "botulinium"[Title/Abstract])) OR ((((("two stage"[Title/Abstract]) OR "stage repair"[Title/Abstract]) OR "staged repair"[Title/Abstract]) OR "two step"[Title/Abstract])) OR ((("component separation"[Title/Abstract]) OR "transversus
abdominis"[Title/Abstract]) OR "retrorectus"[Title/Abstract])) OR ((((("bridging"[Title/Abstract]) OR "bridge repair"[Title/Abstract]) OR "bridged repair"[Title/Abstract]) OR "silo"[Title/Abstract])) OR (("open"[Title/Abstract]) OR "laparoscopic"[Title/Abstract]))) AND (((((((hernia[Title/Abstract]) OR "abdominal wall defect"[Title/Abstract]) OR "abdominal wall reconstruction"[Title/Abstract]) OR "ventral defect"[Title/Abstract]) OR "enterocutaneous fistula"[Title/Abstract])) OR ("Hernia"[Mesh] OR "Hernia, Abdominal"[Mesh] OR "Hernia, Ventral"[Mesh] OR "Hernia, Umbilical"[Mesh]))

1) Systematic Review of RCTs - Filters: Publication date from 1995/01/01 to 2016/03/31; Humans; English; Adult: 19+ Years

2) Systematic Review of non-randomised interventional trials - Filters: Publication date from 1995/01/01 to 2017/12/31; Humans; English; Adult: 19+ Years

Appendix 3

Clinical outcomes reported in 31 RCTs included in the review.

Intra-operative complications/outcomes	No. of RCTs reporting outcome
Enterotomies	9[131],[36],[134],[142],[147, 148],[103, 152],[156]
Acute post-operative bleed	6[131],[36],[133],[150],[129],[152]
Wound dehiscence	3[131],[36],[147]
Early post-operative complications/outcomes	No. of RCTs reporting outcome
• **Local outcomes/complications**	
Superficial wound infection	30[36, 103, 129-155, 157]
Seromas	29[103, 129-36, 138-57]
Haematomas	21[103, 129-36, 139-40, 145-8, 151-2, 154-7]
Ileus	9[36],[131, 132],[147-8],[152],[154],[156-7]
Bowel Obstruction	5[151],[36],[135],[103],[155]
Flap necrosis	5[130],[135],[141],[152],[154]
Drain useage / days to drain removal	3[131],[144],[152]
Severe Constipation	2[150],[103]
• **Systemic outcomes/complications**	
HAP	8[151, 131, 36],[133],[132],[144],[103],[145],[147]
PE/DVT	6[151],[144],[146],[150],[153],[156]
UTI	4[131],[36],[103],[156]
Stroke	2[151],[154]
ACS/MI	2[151],[154]
Late post-operative complications/outcomes	No. of RCTs reporting outcome
Total recurrence (all papers reporting recurrence at any time during follow up)	30[36, 129-57]
Recurrence at 60 months	1[136]
Recurrence at 36 months	4[36, 131],[150],[155]
Recurrence at 24 months	15[151, 131, 36],[130, 133],[139],[138, 139],[142],[150, 147, 148],[152, 153],[156]
Recurrence at 12 months	13[151],[36],[132],[130, 134],[140, 142, 143, 146],[141, 144, 145],[154]
Recurrence at 6 months	5[137],[142],[141],[149, 129]
Recurrence at 3 months	1[134]

Chronic pain	11[131, 36, 132, 133],[137],[142, 143, 141],[146],[150],[155]
Mesh removal	7[130],[135],[141],[146],[148],[153],[155]
Mesh Infection	4[135],[141],[148],[153]
Serous leakage / sinus/ ascetic leak	4[140],[142],[146],[145]
Standardised outcomes	
Clavien-Dindo V[61]	1[103]
Clavien-Dindo IV	1[103]
Clavien-Dindo III [a/b]	9[132],[133],[135],[142],[141],[150, 148],[103],[146]
Clavien-Dindo II	1[103]
Clavien-Dindo I	2[132],[103]
Length of hospital stay	23[36], [131-5],[137-40], [142-3],[147-53], [103], [155-7].
30 day re-operation rate	12[36, 131-3],[135],[142],[141],[148],[149],[129],[103],[148]
30-day readmission	1[132]
Mortality	1[144]
Patient reported outcomes	**No. of RCTs reporting outcome**
Pain VAS score after surgery [24-48h]	15[131],[134],[138, 139],[144, 145, 141, 142, 143],[148],[103],[153, 154-6]
Pain VAS 0-10 days after surgery	2[134],[157]
Pain at day 15	1[134]
Pain VAS at 4 – 6 weeks	14[151],[131],[132],[141, 144],[137, 138],[142, 143],[129, 103],[155-7]
Pain VAS at 3 months	6[142],[144],[142],[143],[155, 156]
Pain VAS at 6 months	3[147, 148],[129]
Pain VAS at 12 months	3[151],[134],[148]
Return to work normal activity	11[151],[137, 138, 139, 140],[142],[144, 145],[153],[154],[157]
Health status using GIQL score at 12 months	1[151]
SF-12 questionnaire at 3 months	1[155]
SF-36 questionnaire at discharge	1[129]
SF-36 questionnaire at 1.5 weeks	1[103]

SF-36 questionnaire at 3 weeks	3[133],[129, 103]
SF-36 questionnaire at 1 month	1[103]
SF-36 questionnaire at 6 weeks	1[103]
SF-36 questionnaire at 2 months	1[103]
SF-36 questionnaire at 4 months	1[133]
SF-36 questionnaire at 6 months	1[129]
SF-36 questionnaire at 12 months	1[133]
SF-36 questionnaire at 24 months	1[133]
EQ-5D questionnaire at day 1	1[134]
EQ-5D questionnaire at day 2	1[134]
EQ-5D questionnaire at day 3	1[134]
EQ-5D questionnaire at day 7	1[134]
EQ-5D questionnaire at day 15	1[134]
EQ-5D questionnaire at 1 month	1[134]
EQ-5D questionnaire at 3 months	1[134]
EQ-5D questionnaire at 1 year	1[134]

Appendix 4

Methods used to detect hernia recurrence (only 30 RCTs included, as 1 trial didn't report hernia recurrence).

Method used to detect recurrence	No. of RCTs using this detection method	Median recurrence rates (%)	No. of RCTs including ventral hernia of width >10cm	Type of hernia
No detection method described	8(151),(134, 135),(147, 152),(149),(145)	7	6/8 (75%) (151),(134, 135), (148),(149),(152)	Incisional 5 (151),(134),(149),(152),(154) Primary 1 (147) Primary and Incisional 2 (135),(148)
Clinical examination	12 (133),(136, 137), (139, 140, 142) (144, 145), (150),(129),(153),(155)	4	4/12(33%) (133),(140),(129), (153)	Incisional 3 (133),(150),(129) Primary 5 (136),(139, 140),(144,145) Primary and Incisional 4 (137),(142),(153),(155)
Imaging – CT or USS	5 (131, 132,130,141, 156)	7	3/5 (60%) (131),(141),(156)	Incisional 2 (131), (130) Primary and Incisional 3 (132),(141),(156)
Imaging – USS	3 (36,143, 157)	9	0 (0%)	Incisional 1 (36) Primary and Incisional 2 (143), (157)
Imaging – CT	2 (138, 146)	7	1/2 (50%) (146)	Incisional 2 (138),(146)

Appendix 5

Data Extraction Sheet for Systematic Methodological Review of non-randomised Interventional Trials in Ventral Hernia repair.

Based on the ROBINS-I/ACROBAT assessment tool, Clinical reporting guidelines for cohort studies (STROBE), Template for intervention description (TIDieR), Downs and Black, Newcastle Ottawa, Expert opinion/knowledge of the literature.
Comparing 26 prospective interventional trials published since 2005, with 26 retrospective interventional trials (out of 94) published since 2005. Papers will be matched primarily according to Journal and the closest publication date, if no retrospective trial published in the same journal in the same year, then the prospective trial is matched with a trial performed in the similar impact journal, preferably published that year.

Reviewer details:

Reviewer:	
Date of data extraction:	

Study demographics

Multi or single centre	
Country of study	
Year of publication	
Number of Surgeons	
Consultant Surgeons or Trainees or both	
Paper number:	
Author of paper:	
Journal	
Impact factor	
Vol and page no	
Comparison groups	
Number of participants	
Ethical approval	

Inclusion Criteria:

Does the paper fulfil the following criteria:	Yes	No
▪ Published from 2005 onwards		
▪ Compares two different interventional techniques for ventral hernia repair		
▪ Aim of the study is to compare the outcomes of the two interventional techniques		
▪ Non-randomised participants		
▪ Published in English		

Introduction

Did the study report?	Yes	No
▪ A scientific rationale for the study?		
▪ A primary aim or objective?		
▪ A pre-specified hypothesis?		
▪ If a hypothesis was mentioned was there reference to the literature?		

Method

Study design

Did the study report?	Yes	No	Unclear	Page No.
▪ Was the data collected according to a protocol?				
▪ Description of equipment used? (Criteria see Appendix 5a)				
▪ Detailed description of the interventions? (Criteria see Appendix 5b)				
▪ Description of the primary outcome				
▪ Sample size/power calculation				

Participants

Did the study report?	Yes	No	Unclear	Page No.
▪ Is there any apparent selection other than ventral hernia, time, and place? (Yes if criteria are mentioned)				
▪ Reports a basic list of demographics? (Criteria see Appendix 5c)				
▪ Were the baseline characteristics measured the same in both groups? (the ones measured)				
▪ Number of patients meeting the inclusion criteria (eligibility)				
▪ Number of patients included				
▪ Number of previous hernia repairs reported				
▪ Hernia maximal width reported				
▪ Hernia defect area reported				
▪ Mentions whether participants had primary VHs, incisional VHs or both?				
o If so which one?				
▪ Was a hernia grading scale used?				
o If so which one?				
▪ Participant recruitment - start date?				
▪ Participant recruitment - finish date?				
▪ Participant recruitment - end of follow-up date?				

▪ Where deviations from intended intervention reported?				

Reported outcomes

Did the study report?	Yes	No	Unclear	Page No.
▪ Was there blinding of the outpatient assessor to the intervention received?				
▪ Was there blinding of the participant to the intervention received?				
▪ Is hernia recurrence reported by intervention?				
▪ Was hernia recurrence defined?				
▪ Was a standardised definition of hernia recurrence used and referenced?				
▪ Was the length of follow up the same between groups?				
▪ Was a hernia detection method reported?				
○ Questionnaire?				
○ Telephone?				
○ Clinical assessment only?				
○ Clinical assessment +/- USS?				
○ Clinical assessment +/- CT?				
○ Re-operation rate?				
○ Other?				
▪ What was the mean length of follow up?				
▪ Reoperation rate reported by intervention?				
▪ Surgical site infection reported by intervention?				
▪ Was surgical site infection defined?				
▪ Was a standardised definition of surgical site infection used and referenced?				
▪ Was a surgical site infection grading scale used?				
▪ Surgical site occurrence reported by intervention?				
▪ Was surgical site occurrence defined?				
▪ Was a standardised definition of surgical site occurrence used and referenced?				
▪ Were patient reported outcomes included?				
▪ If so which patient-reported-outcomes questionnaire was used?				
▪ Was a post-operative pain score used?				

Statistics

Does the paper fulfil the following criteria:	Yes	No	Unclear	Page No.
▪ Report the length of follow-up				

▪ Report the number of participants with missing data?				
▪ Report adjusted analysis				
▪ Report adjustment factors for adjusted analysis				
▪ Report estimate confidence intervals				
▪ Avoids restricting data analysis to patients with no missing data (complete case analysis)				
Studies conducting prognostic analysis				
▪ Report prediction estimates for standard clinical variables (Appendix 5c)				
▪ Avoids all reported predictors having a statistically significant effect				

Appendix 5a. – Description of the equipment used

Description of the equipment used contains details about:

1) The type of mesh used (material specified)
2) The type of suture used (if not the specific material - details whether absorbable or non-absorbable)
3) The type of tacks used (if not the specific material - details whether absorbable or non-absorbable)

-The authors define an adequate description of the intervention as containing at least 2 out of 3 of these items.

Appendix 5b. – Description of the intervention/s performed

Description of the intervention/s contains details about:

1) Whether the operation was open or closed?
2) Whether the operation was with or without mesh?
3) Whether the operation was with or without a component separation?
4) The plane used for mesh insertion?
5) Whether the defect was closed or bridged?
6) Mesh fixation technique?
7) Concomitant procedures described such bowel resection or panniculectomy?
8) Drains used or not?

-The authors define an adequate description of the intervention as containing at least 4 out of 8 of these items.

Appendix 5c. – Minimum list of participant demographics (any less than this list then the paper does not report enough informed)

Demographics table must contain the below three criteria:

Age
Sex
BMI

Demographics table must contain 2 out of the following 5 criteria:

Smoker
Diabetes
ASA
Primary hernia repair, or Incisional hernia repair, or both
Previous hernia repair

Appendix 6

Tables showing the number of studies reporting each item/criteria. A separate table for each methodological category; introduction, study design, participants, reported outcomes, and statistics.

Methodological criteria: Introduction	No. of Prospective studies reporting criteria	No. of Retrospective studies reporting criteria	Total
Scientific rationale	25 (100%)	25 (100%)	50 (100%)
Primary aim or objective	18 (72%)	11 (44%)	29 (58%)
Pre-specified hypothesis	1 (4%)	2 (8%)	3 (6%)
Hypothesis referenced in the literature?	0 (0%)	0 (0%)	0 (0%)

Methodological criteria: Study design	No. of Prospective studies reporting criteria	No. of Retrospective studies reporting criteria	Total
Was a protocol written?	0 (0%)	0 (0%)	0 (0%)
An accurate description of the equipment?	17 (68%)	2 (8%)	19 (38%)
A detailed description of interventions	20 (80%)	16 (64%)	36 (72%)
Study has a primary outcome?	8 (32%)	10 (40%)	18 (36%)
Was a power calculation performed?	2 (8%)	0 (0%)	2 (4%)

Methodological criteria: Participants	No. of Prospective studies reporting criteria	No. of Retrospective studies reporting criteria	Total
Other criteria apart from elective ventral hernia repair?	18 (72%)	17 (68%)	35 (70%)
Reports a basic list of baseline characteristics?	7 (28%)	10 (40%)	17 (34%)

Were the baseline characteristics the same in both groups?	12 (48%)	6 (24%)	18 (36%)
Reported eligibility?	4 (16%)	2 (8%)	6 (12%)
Reported no. included?	25 (100%)	25 (100%)	50 (100%)
Reported no. previous hernia repairs?	6/20 (30%)	12/22 (55%)	18/42 (43%)
Reported maximal hernia width?	12 (48%)	8 (32%)	20 (40%)
Reported hernia defect area?	9 (36%)	12 (48%)	21 (42%)
Mentions whether primary or incisional or both are included?	18 (72%)	14 (56%)	32 (64%)
If so which type?			
Primary VH	1 (4%)	2 (8%)	3 (6%)
Primary umbilical	2 (8%)		2 (4%)
Primary incisional	2 (8%)	1 (4%)	3 (6%)
Incisional	6 (24%)	5 (20%)	11 (22%)
Both primary and incisional	7 (28%)	6 (24%)	13 (26%)
Hernia grade used?	2 (8%)	1 (4%)	3 (6%)
If so which hernia grade?			
EHS	1 (4%)	1 (4%)	2 (4%)
Adhoc (hernia widths)	1 (4%)		
Reported recruitment start date?	19 (76%)	17 (68%)	36 (72%)
Reported recruitment finish date?	19 (76%)	17 (68%)	36 (72%)
End of follow-up reported?	0 (0%)	0 (0%)	0 (0%)
Reported deviations from the intended intervention?	10 (40%)	8 (32%)	18 (36%)

Methodological criteria: Reported Outcomes	No. of Prospective studies reporting criteria	No. of Retrospective studies reporting criteria	Total
Blinding of the outpatient assessor?	3 (12%)	0 (0%)	3 (6%)
Blinding of the participant?	0 (0%)	0 (0%)	0 (0%)
Length of follow-up the same in both groups?	14 (56%)	15 (60%)	29 (58%)
Re-operation rate?	17 (68%)	13 (52%)	30 (60%)
1)Hernia recurrence reported?	25 (100%)	22 (88%)	47 (94%)
Hernia recurrence defined?	4 (16%)	5 (20%)	9 (18%)
Definition referenced?	0 (0%)	0 (0%)	0 (0%)
Was the hernia recurrence detection method reported?	18 (72%)	19 (76%)	37 (74%)
2)Surgical site infection reported?	16 (64%)	16 (64%)	32 (64%)
Surgical site infection defined?	3 (12%)	3 (12%)	6 (12%)
Definition referenced?	2 (8%)	1 (4%)	3 (6%)
Surgical site infection grade used?	1 (4%)	1 (4%)	2 (4%)
3)Surgical site occurrence reported?	1 (4%)	3 (12%)	4 (8%)
Surgical site occurrence defined?	0 (0%)	1 (4%)	1 (2%)
Definition referenced?	0 (0%)	0 (0%)	0 (0%)
Were patient reported outcomes included?	7 (28%)	3 (12%)	10 (20%)
EQ-5D?	2 (8%)		2 (4%)
Adhoc functional questions?	5 (20%)	2 (8%)	7 (14%)

French Hernia Club questionnaire?		1 (4%)	1 (2%)
Was a VAS score used?	6 (24%)	3 (12%)	9 (18%)

Methodological criteria: Statistics	**No. of Prospective studies reporting criteria**	**No. of Retrospective studies reporting criteria**	**Total**
Reported the length of follow-up?	23 (92%)	22 (88%)	45 (90%)
Reported the no. of participants with missing data?	8 (32%)	7 (28%)	15 (30%)
Reported adjusted analysis?	3 (12%)	7 (28%)	10 (20%)
Reported adjustment factors for adjusted analysis?	3 (12%)	5 (20%)	8 (16%)
Report estimate confidence interval?	2 (8%)	6 (24%)	8 (16%)
Avoids restricting analysis to patients with no missing data?	1 (4%)	0 (0%)	1 (2%)

Total scores:

Methodological scores by criteria	**Prospective studies (median, IQR)**	**Retrospective studies (median, IQR)**	**Total score**
Introduction	2 (1-2)	1 (1-2)	2 (1-2)
Study design	1 (1-2)	1 (1-2)	2 (1-3)
Participants	7 (6-8)	6 (5-8)	7 (6-8)
Reported outcomes	4 (3-5)	4 (3-6.5)	4 (3-6)
Statistics	1 (1-2)	2 (1-3)	1 (1-2)
Total with statistics score	17 (14-18)	13 (11-15.5)	15 (12-17.25)
Total	17 (14-18)	15 (12-18)	16 (14-18)
Total (mean, SD)	16.96 (4.01)	15.4 (3.45)	16.16 (3.79)

Defining and referencing outcomes:

Hernia recurrence

Prospective studies	**Hernia recurrence definition**	**Definition referenced?**
Kurmann et al. (312)	'Recurrence was defined as any abdominal wall gap with or without bulge that is not covered by mesh in the area of the postoperative scar'.	No
Anadol et al (294)	'Recurrence was defined as the presence of a defect and/or lump in the original location'.	No
Moreno-Egea et al (291)	'Hernia recurrence was defined on physical examination and confirmed on CT'.	No
Boccicchio et al (274)	'We defined a true hernia recurrence as herniation of bowel or omentum through a defect in the biological mesh or through a defect at the mesh/fascial interface after the initial operation'.	No
Retrospective studies	**Hernia recurrence definition**	**Definition referenced?**
Al-Salamah et al (284)	'Recurrence was defined as any fascial defect, palable or detected on CT scan and located within 7cm of the site of hernia repair'.	No
Jin et al (286)	'Patients with recurrent hernias were defined as requiring another hernia reoperation or noting a significant bulge'.	No
Ballem et al (309)	'recurrence was defined by the presence of a new or similar bulge which increased in size upon straining'.	No
Booth et al (114)	'Recurrent hernia was a contour abnormality associated with a fascial defect'.	No
Iacco et al (304)	'Recurrence was defined by the presence of a bulge on physical examination, imaging, or by patient self-reporting'.	No

Surgical site infection

Prospective studies	Surgical site infection definition	Definition referenced?
Kurmann et al. (312)	'Surgical site infections were assessed according to the criteria developed by the Centers for Disease Control and Prevention (CDC)'.	Yes
Boccicchio et al (274)	'Surgical site infection as defined by Centers for Disease Control criteria'	Yes
Winsnes et al (283)	'defined as a wound infection treated with antibiotics'	No
Retrospective studies		
Al-Salamah et al (284)	'Wound infection was defined as systemic features associated with tender swelling, with or without apparent discharge, necessitating open drainage'.	No
Ballem et al (309)	'Our definition of a wound infection was quite liberal and based on National Surgical Quality Improvement Program (NSQIP) recommendations for surgical site infections'.	Yes
Froylich et al (305)	'Patients with wound infections were considered positive if there was at least wound cellulitis, at which point antibiotic treatment was initiated'.	No

Surgical site occurrence

Prospective Studies	Surgical site occurrence definition	Definition referenced?
Nil	Nil	Nil
Retrospective studies		
Azoury et al (290)	'Wound complications included any surgical site occurrence post-operatively which delayed or hindered primary wound healing, such as abscess, seroma requiring drainage, dehiscence, necrosis, cellulitis, and hematoma'.	No

Hernia recurrence detection method

	Prospective studies	**Retrospective studies**	**Total**
Clinical assessment +/- CT	6	1	7
Clinical assessment +/- USS	5	1	6
Clinical assessment	3	-	3
Clinical assessment +/- telephone	1	3	4
Clinical assessment +/- USS/CT	1	1	2
Clinical assessment +/- USS/CT +/- clinical records	1	-	1
Re-operation rate	1	-	1
Telephone	-	1	1
Telephone + clinical records	-	2	2
Clinical records	-	3	3
Clinical assessment +/- CT +/- telephone	-	3	3
Clinical assessment +/- CT/USS +/- reoperation	-	1	1
Prospective database +/- clinical records	-	1	1
Prospective database +/- clinical records +/- CT	-	1	1
Prospective database +/- re-operation rate	-	1	1

Mean length of follow-up	Prospective studies	Retrospectives studies	Total
Recurrence <= 6months	1		1
Recurrence >6months,≦12months	4	6	10
Recurrence >12months,≦18months	3	2	5
Recurrence >18months,≦24months	4	2	6
Recurrence >24months,≦36months	6	3	9
Recurrence >36months,≦48months	2	1	3
Recurrence >48months, ≦60months	1	4	5
Recurrence >60months	3	3	6
Unclear	2	3	5

Appendix 7

Search strategy and string

(((loss of domain) OR loss of abdominal domain)) AND hernia

Changed by the Pubmed search engine to

((loss[All Fields] AND ("domain"[All Fields])) AND ("hernia"[MeSH Terms] OR "hernia"[All Fields])

Appendix 8

For the purposes of this review we defined publications as written by Abdominal Wall Reconstruction surgeons if the following criteria were met:

Inclusion criteria

1. The authors affiliation was to an 'Abdominal Wall Unit' or 'Hernia Centre".
2. Manuscripts (not case reports) published using or describing complex abdominal wall reconstructive techniques (such as pre-operative pneumoperitoneum and pre-operative botox therapy).
3. The centre had a well-known international reputation for AWR, known to the authors of this review.
4. AWR case series published by both general surgeons and plastic surgeons.

Exclusion criteria

1. Manuscripts published by centres clearly belonging to other specialities (eg. Paediatrics, Trauma)
2. Case reports using complex reconstructive techniques that are written by authors not affiliated to a specialist 'Abdominal Wall Unit' or a 'Hernia Centre'

Appendix 9

Studies included in the Loss of Domain Systematic Review

Case reports - 17

1. Fernando EJ, Guerron AD, Rosen MJ. A case of splenic rupture within an umbilical hernia with loss of domain. Gastrointest Surg. 2015;19(4):789–91.
2. Hn D, Kumar CJ, N S. Giant inguinoscrotal hernia repaired by lichtensteins technique without loss of domain: a case report. J Clin Diagn Res. 2014;8(9):7–8.
3. Qaja E, Le C, Benedicto R. Repair of giant inguinoscrotal hernia with loss of domain. J Surg Case Rep. 2017;16(11):221.
4. Pakula A, Jones A, Syed J, Skinner R. A rare case of chronic traumatic diaphragmatic hernia requiring complex abdominal wall reconstruction. Int J Surg Case Reports. 2015;7C:157–60.
5. Obeid A, Sarhane K, Berjaoui T, Abiad F. Heterotopic intra-abdominal ossification in a complex ventral hernia defect. J Wound Care. 2014;23(2 Suppl):S5-9.
6. Suzuki T, Okamoto T, Hanyu K, Suwa K, Ashizuka S, Yanaga K. Repair of Bochdalek hernia in an adult complicated by abdominal compartment syndrome, gastropleural fistula and pleural empyema: Report of a case. Int J Surg Case Reports. 2014;5(2):82–5.
7. King J, Hayes JD, Richmond B. Repair of giant subcostal hernia using porcine acellular dermal matrix (Strattice™) with bone anchors and pedicled omental flap coverage: a case report. J Med Case Rep. 2013;11(7):258.
8. Hamad A, Marimuthu K, Mothe B, Hanafy M. Repair of massive inguinal hernia with loss of abdominal domain using laparoscopic component separation technique. J Surg Case Rep. 2013;22(3).
9. Todd H, Diaz D, Roth J. Rhabdomyolysis: An unusual complication following endoscopic component separation hernia repair. J Surg Case Rep. 2012;1(9):18.
10. Berrevoet F, Martens T, Van Landuyt K, de Hemptinne B. The anterolateral thigh flap for complicated abdominal wall reconstruction after giant incisional hernia repair. Acta Chir Belg. 2010;110(3):376–82.
11. Baird R, Gholoum S, Laberge JM, Puliganda P. Management of a giant omphalocele with an external skin closure system. J Paediatr Surg. 2010;45(7):E17-20.
12. Sonmez K, Onal E, Karabulut R, Turan O, Turkyilmaz Z, Hirfanoglu I, et al. A strategy for treatment of giant omphalocele. World J Paediatr. 2010;6(3):274–7.
13. Alaish SM, Strauch ED. The use of Alloderm in the closure of a giant omphalocele. J Pediatr Surg. 2006;41(3):e37-39.
14. Serpell JW, Polglase AL, Anstee EJ. Giant inguinal hernia. Aust N Z J Surg. 1988;58(10):831–4.
15. King JN, Didlake RH, Gray RE. Giant inguinal hernia. South Med J. 1986;79(2):252–3.

16. Wartman SM, Woo K, Brewer M, Weaver FA. Management of a Large Abdominal Aortic Aneurysm in Conjunction with a Massive Inguinal Hernia. Ann Vasc Surg. 2017;42:e302-7.
17. Harrison D, Taneja R, Kahn D, Rush BJ. Repair of a massive ventral hernia in a morbidly obese patient. N J Med. 1995;92(6):387–9.

Case series - 44

18. Kingsnorth AN, Sivarajasingham N, Wong S, Butler M. Open mesh repair of incisional hernias with significant loss of domain. Ann R Coll Surg Engl. 2004;86(5):363–6.
19. Gerlach UA, Pascher A. Technical advances for abdominal wall closure after intestinal and multivisceral transplantation. Curr Opin Organ Transpl. 2012;17(3):258–67.
20. Mayagoitia JC, Suarez D, Arenas JC, Daiz de Leon V. Preoperative progressive pneumoperitoneum in patients with abdominal-wall hernias. Hernia. 2006;10(3):213–7.
21. Elstner KE, Read JW, Rodriguez-Acevedo O, Ho-Shon K, Magnussen J, Ibrahim N. Preoperative progressive pneumoperitoneum complementing chemical component relaxation in complex ventral hernia repair. Surg Endosc Other Interv Tech. 2016;1–9.
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Appendix 10

Written definitions for Loss of Domain

Title	Study type	Written definition
Concept of "right of domain" – 4 papers		
Coopwood et al[251]	Case series	Loss of the "right of domain"
Sabbagh et al[87]	Case series	The hernia contents are held in place by adhesions and cannot be re-itegrated into the abdominal cavity [i.e. the herniated organs have lost their "right of domain" in the abdomen.
Sabbagh et al[241]	Case series	The hernias contents are held in place by adhesions and cannot be reintegrated into the abdominal cavity [i.e. the herniated organs have lost their "right of domain" in the abdomen].
Hadad et al [257]	Retrospective analysis of database	The abdominal 'right of domain'. This often used, but poorly defined term describes the patient with a massive hernia, in which primary repair has a high chance of leading to pulmonary and/or circulatory compromise.
Contraction of the lateral abdominal wall muscles leading to reduced volume of the abdominal cavity – 6 papers		

Agnew et al[264]	Case series	The term purports that the space inside the abdomen formerly occupied by the herniated viscera is forfeited over time. Irreversible decreases in abdominal muscle elasticity occurring as a result of mechanical disuse atrophy, as well as diaphragm descent are the cause of the loss of domain. The diagnosis of loss of abdominal domain does not require the hernia to be greater than a specific volume. iIt is a clinical diagnosis made by the surgeon who deems that abdominal wall compliance is insufficient for the hernia contents to be reduced and the defect to be repaired without an intolerable increase in intra-abdominal pressure.
Mangus et al[261]	Case series	Retraction of the abdominal wall with a loss of total volume in the peritoneal cavity
Dennis et al[265]	Case series	Domain loss describes this concept when applied to the lateral contractures of the abdominal wall
Bikhchandani et al[266]	Editorial Review	Lack of viscera in the abdominal cavity causes a decrease in the abdominal wall muscle elasticity, abdominal wall muscular atrophy, and reduced volume because of disuse.
Tobias et al[267]	Case series	Loss of domain: lateral migration of the rectus abdominis muscles in conjunction with flank muscle contraction leads to a progressive decrease in the volume of the abdominal cavity and worsening protrusion of the viscera.
Oprea et al[268]	Case series	In some instances, it is more important the volume of the exteriorized viscera and in those instances we are talking about “hernias with loss of domain”. Loss of domain by lateral musculo-aponeurotic retraction, relaxation of the diaphragm and frequent association of obesity and chronic cardio-respiratory diseases turns the patient into a biological and social invalid.
The concept of the second abdomen – 5 papers		

Kingsnorth et al[244]	Case series	This loss of domain [residence] implies that a proportion of the abdominal contents reside permanently [in a hernia sac = the second abdominal cavity] outside their natural compartment, and returning these contents will require significant physiological adaptation [mainly respiratory] if the volume exceeds > 15_20% of this compartment.
Tanaka et al[86]	Case series	This loss of domain means that the herniated viscera of the abdominal content inhabit, in a permanent way, the hernia sac, which behaves like a second abdominal cavity. Restoring the hernia sac contents to the abdominal cavity may lead to respiratory and circulatory disturbances.
Renard et al[240]	Case series	In patients with a giant incisional hernia with loss of domain, the herniated organs cannot be restored to the abdominal cavity and thereby create a "second abdomen".
Van Geffen et al[269]	Editorial Review	Loss of domain: in which some of the intraabdominal organs in a hernial sac form a "second abdominal cavity" and complete reduction of the hernial contents is impossible regardless of the size of the defect.
Berrevoet et al[270]	Case report	Loss of domain implies that a proportion of the abdominal content resides permanently outside its natural compartment, in the hernia sac, which acts as a second abdominal cavity. Returning these contents will require significant physiological adaptation [mainly res- piratory] if the volume exceeds > 15-20% of this compartment.
Chronic large irreducible hernia – 5 papers		

Valezi et al[33]	Case series	The volume of the hernia can no longer be reduced to the abdominal cavity, constituting the so called loss of domain hernias.
Mcadory et al[271]	Case series	Patients with 'loss of domain' have chronically herniated abdominal contents residing outside the abdominal cavity. The diagnosis of hernia with loss of domain was established if on physical examination there was a significant amount of herniated contents outside the abdominal cavity that could not be reduced with the patient in the supine position.
Passot et al[237]	Expert questionnaire	Hernia contents set by adhesions and not reducible to the abdominal cavity
Azar et al[272]	Case series	Loss of domain occurs when an abdominal wall defect progresses to a size at which it may no longer accommodate the viscera, leading to protrusion outside the abdominal wall and into the hernia sac
Bueno-Lledo et al[273]	Case series	Loss of domain occurs when an abdominal wall defect progresses to a size at which it may no longer accommodate the viscera, leading to protrusion outside the abdominal wall and into the hernia sac
Miscellaneous – 6 papers		
Zielinski et al[274]	Case series	Inability to primarily close the fascia after laparotomy
Baghai et al[275]	Case series	Loss of domain defines the inability of the abdominal cavity of fully accommodate the abdominal contents within its fascial boundaries. Laparoscopic LOD is the inability of the abdomen to keep the visceral contents within it whilst being insufflated with CO2.
King et al[276]	Case report	Majority of the patients abdominal contents were outside the abdominal cavity
Hamad et al[277]	Case report	The difficulty of returning herniated viscera to an abdominal cavity accustomed to being empty

Fernando et al[278]	Case report	"loss of domain" typically refers to a hernia in which greater than 15-20% of the intra-abdominal contents reside outside of the abdominal cavity proper.
Mayagoitia et al[279]	Case series	All patients had hernias with loss of domain, in which the volume of the sac and visceral contents was greater than the capacity of the abdominal cavity. These hernias are said to have ‘‘loss of domain’’ because the contents of the hernia exceed the capacity of the abdominal cavity.
Editorial/Reviews – 2 papers		
Kirkpatrick et al[32]	Editorial Review	Multiple referenced definitions for loss of domain
Halligan et al[238]	Editorial Review	The ratio of the hernia sac volume to the residual abdominopelvic cavity OR describes the extent to which the abdominal cavity has lost volume to the hernia

Appendix 11 – Preliminary Maximum Dataset for Systematic Review

Maximum Dataset for Interventional Trials of Ventral Hernia Repair

For this stage; Please can panellists read through the dataset and carry out 1 task

1. Pre-operative variables

Patient variables

Age
Sex
Obesity/BMI
COPD
Liver failure
Hypertension
Smoker
Alcohol abuse
Diabetes
Benign Prostatic Hypertrophy
Previous AAA repair
Coronary heart disease (IHD/stent/MI)
Peripheral vascular disease (PVD)
Cerebral vascular accident (CVA)
Arteriopath (all of the above - IHD/PVD/CVA)
Malignancy
Radiotherapy
Chemotherapy
Chronic kidney disease
Immunosupression/Steroid use
ASA score
No. of co-morbidities
22

Hernia variables

Previous abdominal surgery/operations
Previous abdominal incisions
No of Primary Ventral Hernias
No of Incisional Ventral Hernias

No of Primary Incisional Hernias

No of Recurrent Incisional Hernias

No previous VH repairs

Previous surgical site infection

Previous surgical site occurrence

No of hernia defects present

Hernia Width

Hernia Length

Hernia Defect Area

Loss of Domain

European Hernia Society score - For both Primary and Incisional hernias.

Hernia location: Midline Vs Lateral

Hernia location: Epigastric, Umbilical, Suprapubic, Subcostal (R/L), Flank (R/L), Iliac (R/L), Lumbar (R/L).

Stoma present

19

2. Intra-operative variables

General

Mode of Surgery - Laparoscopic/Open/Robotic

Surgeon experience - Consultant/trainee

Mesh variables

Mesh/suture repair

Exact mesh type/brand

Mesh weight

Position of mesh

Mesh fixation technique

Operative variables

Operative time

Anaesthetic type (Local, Spinal, General)

Bridged vs Primary fascial closure

Component separation (Y/N)

If suture repair - small bites/large bites

Preoperative Botox

Panniculectomy (Y/N)

Drains inserted and localation

Concomittment GI bowel procedure

Intra-operative blood loss

Enterotomies

VHWG score

CDC wound classification

20

3. Post-operative outcomes

Wound infection (SSI)
Surgical site occurrence (SSO)
Surgical site occurrence requiring procedural intervention (SSOPI)
Seromas
Haematomas
Wound dehisence
ECF formation
Mesh Infection
Mesh removal
Skin necrosis
Flap necrosis
Drain useage / days to drain removal
Severe Constipation
Ileus
Bowel Obstruction
Chronic pain
Bulging
Hernia recurrence
ACS/MI
Stroke
Post Op Intra-abdominal Bleed
Post Op GI Bleed
PE/DVT
HAP
UTI
Clavian-Dindo Complication Score (1-5)
Re-operation rate in 30 days
Re-opertion for hernia recurrence
Length of hospital stay
30-day hospital readmission
Mortality
32

4. Patient reported outcomes measures (PROMs)

(based on EURAHS QoL score, Carolinas Comfort Scale, HerQLes score, SF36, EQ-5D, GIQL)
Questions will be asked pre-operatively and post-operatively

GENERAL

Health VAS

Average inpatient pain VAS score (at rest)

Return to work

Retrun to normal activities

Outpatient Pain VAS score

EURAHS QoL score

Pain at hernia site:

Pain at rest (lying down) (0-10)

Pain during activities (walking, biking, sports) (0-10)

Pain felt during the last week (0-10)

Restrictions of activities because of pain or discomfort at the site of the hernia:

Restriction from daily activities (inside the house) (0-10)

Restriction outside the house (walking, biking, driving) (0-10)

Restriction during sports (0-10)

Restriction during heavy labour (0-10)

Cosmetic discomfort:

Shape of abdomen (0-10)

Site of hernia (0-10)

HERQLES (1-disagree to 6-strongly agree)

My abdominal wall has a huge impact on my health

My abdominal wall causes me physical pain

My abdominal wall interferes when I perform strenuous activitis eg heavy lifting

My abdominal wall interferes when I perfrom moderate activities, eg bowling, bending over

My abdominal wall interferes when I walk or climb stairs

My abdominal wall interferes when I dress myself, take showers and cook

My abdominal wall interferes with my sexual activity

I often stay at home because of my abdominal wall

I accomplish less at home because of my abdominal wall

I accomplish less at work because of my abdominal wall

My abdominal wall affects how I feel every day

I often feel blue becase of my abdominal wall

CAROLINAS COMFORT SCALE (each question has 3 parts, each marked 0-5 for severeity)

When lying down, do you have; Sensation of mesh? Pain?

When bending over, do you have; Sensation of mesh? Pain? Movement limitations?

While sitting up, do you have; Sensation of mesh? Pain? Movement limitations?

While performing activities of daily living (getting out of bed, bathing, getting dressed), do you have; Sensation of mesh? Pain? Movement limitations?

When coughing or deep breathing, do you have; Sensation of mesh? Pain? Movement limitations?

When walking or standing, do you have; Sensation of mesh? Pain? Movement limitations?

When walking up or down stairs, do you have; Sensation of mesh? Pain? Movement limitations?

When exercising (other than work-related), do you have? Sensation of mesh? Pain? Movement limitations?

SF36 Questionnaire

1.In general, would you say that your health is: Excellent, Very Good, Good, Fair, Poor

2.Compared to one year ago, how would you rate your health in general now: Much better, somewhat better, about the same, somewhat worse, much worse.

Limitations of activities: Does your health limit you in any of these activities: Answer; Yes a lot, Yes a little, Not at all

3.Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports

4.Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf

5.Lifting or carrying groceries

6.Climbing several flights of stairs

7.Climbing one flight of stairs

8.Bending, kneeling, or stooping

9.Walking more than a mile

10.Walking several blocks

11.Walking one block

12.Bathing or dressing yourself

Physical health problems: During the past 4 weeks have you had any of the following problems with work or other activities as a result of physical health? Answer; Yes/No

13.Cut down the amount of time you spent on work or other activities?

14.Accomplished less than you would like?

15.Were limited in the kind of work or other activities?

16.Had difficulty performing the work or other activities?

Emotional health problems: During the past 4 weeks have you had any of the following problems with work or other activities as a result of emotional health (such as feeling depressed or anxious)? Answer; Yes/No

17.Cut down the amount of time you spent on work or other activities?

18.Accomplished less than you would like?

19.Didn't do work or other activities as carefully as usual

20.Social activities: Emotional problems interferred with your normal social activities with family, friends, neighbors, or groups. (Not at all, slightly, moderately, severe, very severe)

21.Pain: How much bodily pain have you had during the past 4 weeks? (None, very mild, mild, moderate)

22.During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? (Not at all, A little, Moderately, Quite a bit, Extremely).

Energy and Emotions During the past 4 weeks: Answer: All of the time, Most of the time, A good bit of the time, some of the time, a little bit of the time, none of the time.

23.Did you feel full of pep?

24.Have you been a very nervous person?

25.Have you felt so down in the dumps that nothing could ever cheer you up?

26.Have you felt calm and peaceful?

27.Did you have a lot of energy?

28.Have you felt downhearted and blue

29.Did you feel worn out?

30.Have you been a happy person?

31.Did you feel tired?

32.Social Activities: During the past weeks, how much of the time has your physical or emotional problems interfered with your social activities? All of the time, Most of the time, Some of the time, A little bit of the time, None of the time

GENERAL HEALTH Answer: Definitely true, mostly true, don't know, mostly false, definitely false

33.I seem to get sick a little easier than other people

34.I am as healthy as anybody I know

35.I expect my health to get worse

36.My health is excellent

EQ-5D - select one of the four possiblities

1.Mobility: I have no problems in walking about?, I have some problems walking about? I am confined to bed?

2.Self-care: I have no problems with self-care?, I have some problems washing or dressing myself?, I am unable to wash or dress myself?

3.Usual activities: I have no problems with performing my usual activities?, I have some problems with performing my usual activities? I am unable to perform my usual activities?

4.Pain/Discomfort: I have no pain or discomfort? I have moderate pain or discomfort? I have extreme pain or discomfort?

5.Anxiety/Depression: I am not anxious or depressed?, I am moderately anxious or depressed?, I am extremely anxious or depressed?

6.Please state your level of overall health from 0-100.

GIQL

1.How often during the past 2 weeks have you had pain in the abdomen? All of the time, most of the time, some of the time, a little of the time, never.

2.How often during the past 2 weeks have you had a feeling of fullness in the upper abdomen? All of the time, most of the time, some of the time, a little of the time, never.

3.How often during the past 2 weeks have you had bloating? All of the time, most of the time, some of the time, a little of the time, never.

4.How often during the past 2 weeks have you been troubled by excessive passage of gas through the anus? All of the time, most of the time, some of the time, a little of the time, never.

5.How often during the past 2 weeks have you been troubled by strong burping or belching? All of the time, most of the time, some of the time, a little of the time, never.

6.How often during the past 2 weeks have you been troubled by gurgling noises from the abdomen?
all of the time, most of the time, some of the time, a little of the time, never

7.How often during the past 2 weeks have you been troubled by frequent bowel movements?
all of the time, most of the time, some of the time, a little of the time, never

8.How often during the past 2 weeks have you found eating to be a pleasure?
all of the time, most of the time, some of the time, a little of the time, never

9.Because of your illness, to what extent have you restricted the kinds of food you eat?
very much, much, somewhat, a little, not at all

10.During the past 2 weeks, how well have you been able to cope with everyday stresses?
Extremely poorly, poorly, moderately, well, extremely well

11.How often during the past 2 weeks have you been sad about being ill?
all of the time, most of the time, some of the time, a little of the time, never

12.How often during the past 2 weeks have you been nervous or anxious about your illness?
all of the time, most of the time, some of the time, a little of the time, never

13.How often during the past 2 weeks have you been happy with life in general?
never, a little of the time, some of the time, most of the time, all of the time

14.How often during the past 2 weeks have you been frustrated about your illness?
all of the time, most of the time, some of the time, a little of the time, never

15.How often during the past 2 weeks have you been tired or fatigued?
all of the time, most of the time, some of the time, a little of the time, never

16.How often during the past 2 weeks have you felt unwell?
all of the time, most of the time, some of the time, a little of the time, never

17.Over the past week, have you woken up in the night? every night, 5-6 nights, 3-4 nights, 1-2 nights, never

18.Since becoming ill, have you been troubled by changes in your appearance?
a great deal, a moderate amount, somewhat, a little bit, not at all

19.Because of your illness, how much physical strength have you lost?
a great deal, a moderate amount, some, a little bit, none

20.Because of your illness, to what extent have you lost your endurance?
a great deal, a moderate amount, somewhat, a little bit, not at all

21.Because of your illness, to what extent do you feel unfit? extremely unfit, moderately unfit, somewhat unfit, a little unfit,
fit

22.During the past 2 weeks, how often have you been able to complete your normal daily activities (school,work, household)?
all of the time, most of the time, some of the time, a little of the time, never

23.During the past 2 weeks, how often have you been able to take part in your usual patterns of leisure or recreational activities? all of the time, most of the time, some of the time, a little of the time, never

24.During the past 2 weeks, how much have you been troubled by the medical treatmentof your illness?
very much, much, somewhat, a little, not at all

25.To what extent have your personal relations with people close to you (family or friends) worsened because of your illness? very much, much, somewhat, a little, not at all

26.To what extent has your sexual life been impaired (harmed) because of your illness?
very much, much, somewhat, a little, not at all

27.How often during the past 2 week, have you been troubled by fluid or food coming up into your mouth (regurgitation)?
all of the time, most of the time, some of the time, a little of the time, never

28.How often during the past 2 weeks have you felt uncomfortable because of your slow speed of eating?
all of the time, most of the time, some of the time, a little of the time, never

29.How often during the past 2 weeks have you had trouble swallowing your food?
all of the time, most of the time, some of the time, a little of the time, never

30.How often during the past 2 weeks have you been troubled by urgent bowel movements?
all of the time, most of the time, some of the time, a little of the time, never

31.How often during the past 2 weeks have you been troubled by diarrhoea?
all of the time, most of the time, some of the time, a little of the time, never

32.How often during the past 2 weeks have you been troubled by constipation?
all of the time, most of the time, some of the time, a little of the time, never

33.How often during the past 2 weeks have you been troubled by nausea?
all of the time, most of the time, some of the time, a little of the time, never

34.How often during the past 2 weeks have you been troubled by blood in the stool?
all of the time, most of the time, some of the time, a little of the time, never

35.How often during the past 2 weeks have you be troubled by heartburn?
all of the time, most of the time, some of the time, a little of the time, never

36.How often during the past 2 weeks have you been troubled by uncontrolled stools?
all of the time, most of the time, some of the time, a little of the time, never

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5. Methodology

General

Funding

Protocol

Registered Trial

Ethical Approval

Introduction

Study rationale

Primary aim or objective

A pre-specified referenced hypothesis

Method

Randomised trials

Method of generating random allocation sequence

Method of implementing the random allocation

Blinding of the participant to the intervention received

Blinding of the care providers

All Interventional (Randomised and non-Randomised Interventional Trials)

Description of trial design

Trial setting (single/multicentre),names of centres where data will be collected

Description of the interventions, with sufficient detail to allow replication

Defined primary outcome, with well described methods for detection and measurement
Secondary outcome measures, defined, with described methods for detection and measurement

Power/Size calculation

Specific inclusion/exclusion criteria

Reports eligibility and number included

Same length of follow-up for each interventional/treament arm

Deviations from the intended intevention reported?

Blinding of the outpatient assessor/independent blinded out patient assessor

Results

Recruitment dates - Start date?, Finish date, End of follow-up date
Participant flow chart - for each group showing the no. of participants included, no. receiving the intended treatment, no. analysed for primary outome (includes explanations for patient losses)

A table showing baseline characteristics/pre-operative varibles between each group

Report all harmful events in each group

Statistics

Length of follow-up reported

Details on PP analysis or ITT analysis

Number of participants with missing data

Statistic methods for comparing the groups; for primary and secondary outcomes

Additional methods for subgroup analyses and adjusted analyses

Reports adjusted analysis (with adjustment factors listed)

Reports missing data

Reports estimated effect size with 95% confidence intervals

Discussion

Trial limitations, addressing sources of potential bias, imprecision

Interpretation consistent with results, balancing benefits and harms

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Appendix 12

Panellist voting on the number of variables in each category for the two minimum datasets

Category	Primary VH MD	Incisional VH MD
Pre-operative – Patient variables		
Pre-operative – Hernia variables		
Intra-operative variables		
Post-operative outcomes		
Patient reported outcomes		
Methodology		
Total		

Appendix 13: Finalised Maximum Dataset

1. Pre-operative variables
1a. Patient variables
Age
Sex
Weight
Height
Obesity/BMI
COPD
Hepatic disease
Ascites
Liver failure (Child Pugh or MELD score)
Hypertension
Smoker
Alcohol abuse (yes/no)
Alcohol intake
Diabetes (type I/type II)
Benign Prostatic Hypertrophy
Previous AAA repair
Coronary heart disease (IHD/stent/MI)
Peripheral vascular disease (PVD)
Cerebral vascular accident (CVA)
Arteriopath (all of the above – IHD/PVD/CVA)
Malignancy
Radiotherapy
Radiotherapy to the surgical field
Chemotherapy
Chronic kidney disease
Immunosupression/Steroid use
ASA score
No. of co-morbidities
Anaemia
Connective tissue disorders (eg Ehlers-Danlos, Marfans etc)
History of inflammatory bowel disease
Physical activity
Fitness level
Profession/Occupation
Anticoagulation
Current antibiotic therapy
Malnutrition
Pregnancy
Frailty
Sarcopaenia
1b. Hernia variables

Previous abdominal surgery/operations
Previous abdominal incisions
No of Primary Incisional Hernias
No of Recurrent Incisional Hernias
No previous VH repairs
Previous surgical site infection
Previous surgical site occurrence
No of hernia defects present
Hernia Width
Hernia Length
Hernia Defect Area
Loss of Domain
EHS score
Hernia location: Midline Vs Lateral
Hernia location: Epigastric, Umbilical, Suprapubic, Subcostal (R/L), Flank (R/L), Iliac (R/L), Lumbar (R/L).
Stoma present
Divarification of the recti
Reducible? Yes/No
Abdominal wall rigid/soft
Denervation incision present
Previous component separation
Signs of strangulation (pain/erythaema)
Type of previous hernia repair?
Previous mesh implant? If so where was mesh implanted
Enterocutaneous fistula
Current Mesh infection
AW muscle quality (rectus/obliques assessed: present (complete/partial) or absent)
Quality of Abdominal Wall Tissue (eg CT sarcopaenia index)
Abdominal wall function
Orientation of previous scars (difficult to think how to measure but possibly important to know)
2. Peri-operative variables
Operative work-up
Pre-operative botox injections
Pre-operative pneumoperitoneum
General
Mode of Surgery – Laparoscopic/Open/Robotic
Laparoscopic conversion to open with reason
Surgeon experience – Consultant/trainee (If trainee – then level of training reported)
Mesh variables
Mesh/suture repair
Exact mesh name; material/type/brand, (knowing this will tell us weight & porosity)
Position of mesh

Mesh fixation technique
Mesh size
Mesh overlap
Mesh 2 variable – with ALL the above details for this second mesh
Operative variables
For suture repair – suture type – absorbable/non-absorbable
Operative time
Anaesthetic type (Local, Spinal, General)
Bridged vs Primary fascial closure
Type of component separation
Small bites/large bites – suture repair
Whole scar repaired
Panniculectomy (Y/N)
Drains inserted and location
Concomitant GI bowel procedure
Concomitant non-GI procedure
Intra-operative blood loss
Enterotomies
VHWG score
CDC wound classification
Perioperative change in positive end expiratory pressure
Surgical antibiotic prophylaxis
Previous mesh removal
Post-operative analgesia (Epidural, Single dose TAPP block, PCA, wound catheters)
Negative pressure wound therapy
Epidural Yes/No
Miscellaneous: Accurate reporting of all intra-operative complications? (eg. Bladder injuries, enterotomies, allergies, cardiac arrests)
3. Post-operative outcomes
Wound infection (SSI)
Surgical site occurrence (SSO)
Surgical site occurrence requiring procedural intervention (SSOPI)
Seromas
Haematomas
Wound dehisence
ECF formation
Mesh Infection
Mesh removal
Skin necrosis
Flap necrosis
Drain useage / days to drain removal
Severe Constipation
Ileus
Bowel Obstruction

Chronic pain
Bulging
Hernia recurrence
ACS/MI
Stroke
Post Op Intra-abdominal Bleed
Post Op GI Bleed
PE/DVT
UTI
Clavian-Dindo Complication Score (1-5)
Re-operation rate in 30 days
Re-opertion for hernia recurrence
Length of hospital stay
30-day hospital readmission
Mortality
Post-operative antibiotics with indication
No. of days in ITU
Time to full mobilisation
Hospital acquired pneumonia
Atelectasis
Coughing
Renal failure
Delirium
Miscellaneous: Accurate reporting of all other medical complications during inpatient stay
4. Patient reported outcomes measures (PROMs)
(based on EURAHS QoL score, Carolinas Comfort Scale, HerQLes score, SF36, EQ-5D, GIQL, SF12, QLQ-C30, FACT – G, miscellaneous questions added by patient panellists)
Questions will be asked pre-operatively and post-operatively
GENERAL
Health VAS
Average inpatient pain VAS score (at rest)
Return to work
Return to normal activities
Outpatient Pain VAS score (plus baseline VAS)
EURAHS QoL score
Pain at hernia site:
Pain at rest (lying down) (0-10)
Pain during activities (walking, biking, sports) (0-10)
Pain felt during the last week (0-10)
Restrictions of activities because of pain or discomfort at the site of the hernia:
Restriction from daily activities (inside the house) (0-10)
Restriction outside the house (walking, biking, driving) (0-10)

Restriction during sports (0-10)
Restriction during heavy labour (0-10)
Cosmetic discomfort:
Shape of abdomen (0-10)
Site of hernia (0-10)
HERQLES (1-disagree to 6-strongly agree)
My abdominal wall has a huge impact on my health
My abdominal wall causes me physical pain
My abdominal wall interferes when I perform strenuous activitis eg heavy lifting
My abdominal wall interferes when I perfrom moderate activities, eg bowling, bending over
My abdominal wall interferes when I walk or climb stairs
My abdominal wall interferes when I dress myself, take showers and cook
My abdominal wall interferes with my sexual activity
I often stay at home because of my abdominal wall
I accomplish less at home because of my abdominal wall
I accomplish less at work because of my abdominal wall
My abdominal wall affects how I feel every day
I often feel blue becase of my abdominal wall
CAROLINAS COMFORT SCALE (each question has 3 parts, each marked 0-5 for severity)
When lying down, do you have; Sensation of mesh? Pain?
When bending over, do you have; Sensation of mesh? Pain? Movement limitations?
While sitting up, do you have; Sensation of mesh? Pain? Movement limitations?
While performing activities of daily living (getting out of bed, bathing, getting dressed), do you have; Sensation of mesh? Pain? Movement limitations?
When coughing or deep breathing, do you have; Sensation of mesh? Pain? Movement limitations?
When walking or standing, do you have; Sensation of mesh? Pain? Movement limitations?
When walking up or down stairs, do you have; Sensation of mesh? Pain? Movement limitations?
When exercising (other than work-related), do you have? Sensation of mesh? Pain? Movement limitations?
SF36 Questionnaire
1.In general, would you say that your health is: Excellent, Very Good, Good, Fair, Poor
2.Compared to one year ago, how would you rate your health in general now: Much better, somewhat better, about the same, somewhat worse, much worse.
Limitations of activities: Does your health limit you in any of these activities: Answer; Yes a lot, Yes a little, Not at all
3.Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports
4.Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf
5.Lifting or carrying groceries
6.Climbing several flights of stairs
7.Climbing one flight of stairs
8.Bending, kneeling, or stooping
9.Walking more than a mile
10.Walking several blocks
11.Walking one block

12.Bathing or dressing yourself
Physical health problems: During the past 4 weeks have you had any of the following problems with work or other activities as a result of physical health? Answer; Yes/No
13.Cut down the amount of time you spent on work or other activities?
14.Accomplished less than you would like?
15.Were limited in the kind of work or other activities?
16.Had difficulty performing the work or other activities?
Emotional health problems: During the past 4 weeks have you had any of the following problems with work or other activities as a result of emotional health (such as feeling depressed or anxious)? Answer; Yes/No
17.Cut down the amount of time you spent on work or other activities?
18.Accomplished less than you would like?
19.Didn't do work or other activities as carefully as usual
20.Social activities: Emotional problems interferred with your normal social activities with family, friends, neighbors, or groups. (Not at all, slightly, moderately, severe, very severe)
21.Pain: How much bodily pain have you had during the past 4 weeks? (None, very mild, mild, moderate)
22.During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? (Not at all, A little, Moderately, Quite a bit, Extremely).
Energy and Emotions During the past 4 weeks: Answer: All of the time, Most of the time, A good bit of the time, some of the time, a little bit of the time, none of the time.
23.Did you feel full of pep?
24.Have you been a very nervous person?
25.Have you felt so down in the dumps that nothing could ever cheer you up?
26.Have you felt calm and peaceful?
27.Did you have a lot of energy?
28.Have you felt downhearted and blue
29.Did you feel worn out?
30.Have you been a happy person?
31.Did you feel tired?
32.Social Activities: During the past weeks, how much of the time has your physical or emotional problems interfered with your social activities? All of the time, Most of the time, Some of the time, A little bit of the time, None of the time
GENERAL HEALTH Answer: Definitely true, mostly true, don't know, mostly false, definitely false
33.I seem to get sick a little easier than other people
34.I am as healthy as anybody I know
35.I expect my health to get worse
36.My health is excellent
EQ-5D - select one of the four possiblities
1.Mobility: I have no problems in walking about?, I have some problems walking about? I am confined to bed?
2.Self-care: I have no problems with self-care?, I have some problems washing or dressing myself?, I am unable to wash or dress myself?
3.Usual activities: I have no problems with performing my usual activities?, I have some problems with performing my usual activities? I am unable to perform my usual activities?
4.Pain/Discomfort: I have no pain or discomfort? I have moderate pain or discomfort? I have extreme pain or discomfort?

5.Anxiety/Depression: I am not anxious or depressed?, I am moderately anxious or depressed?, I am extremely anxious or depressed?
6.Please state your level of overall health from 0-100.
GIQL
1.How often during the past 2 weeks have you had pain in the abdomen? All of the time, most of the time, some of the time, a little of the time, never.
2.How often during the past 2 weeks have you had a feeling of fullness in the upper abdomen? All of the time, most of the time, some of the time, a little of the time, never.
3.How often during the past 2 weeks have you had bloating? All of the time, most of the time, some of the time, a little of the time, never.
4.How often during the past 2 weeks have you been troubled by excessive passage of gas through the anus? All of the time, most of the time, some of the time, a little of the time, never.
5.How often during the past 2 weeks have you been troubled by strong burping or belching? All of the time, most of the time, some of the time, a little of the time, never.
6.How often during the past 2 weeks have you been troubled by gurgling noises from the abdomen? all of the time, most of the time, some of the time, a little of the time, never
7.How often during the past 2 weeks have you been troubled by frequent bowel movements? all of the time, most of the time, some of the time, a little of the time, never
8.How often during the past 2 weeks have you found eating to be a pleasure? all of the time, most of the time, some of the time, a little of the time, never
9.Because of your illness, to what extent have you restricted the kinds of food you eat? very much, much, somewhat, a little, not at all
10.During the past 2 weeks, how well have you been able to cope with everyday stresses? Extremely poorly, poorly, moderately, well, extremely well
11.How often during the past 2 weeks have you been sad about being ill? all of the time, most of the time, some of the time, a little of the time, never
12.How often during the past 2 weeks have you been nervous or anxious about your illness? all of the time, most of the time, some of the time, a little of the time, never
13.How often during the past 2 weeks have you been happy with life in general? never, a little of the time, some of the time, most of the time, all of the time
14.How often during the past 2 weeks have you been frustrated about your illness? all of the time, most of the time, some of the time, a little of the time, never
15.How often during the past 2 weeks have you been tired or fatigued? all of the time, most of the time, some of the time, a little of the time, never
16.How often during the past 2 weeks have you felt unwell? all of the time, most of the time, some of the time, a little of the time, never
17.Over the past week, have you woken up in the night? every night, 5-6 nights, 3-4 nights, 1-2 nights, never
18.Since becoming ill, have you been troubled by changes in your appearance? a great deal, a moderate amount, somewhat, a little bit, not at all
19.Because of your illness, how much physical strength have you lost? a great deal, a moderate amount, some, a little bit, none
20.Because of your illness, to what extent have you lost your endurance? a great deal, a moderate amount, somewhat, a little bit, not at all
21.Because of your illness, to what extent do you feel unfit? extremely unfit, moderately unfit, somewhat unfit, a little unfit, fit

22.During the past 2 weeks, how often have you been able to complete your normal daily activities (school,work, household)? all of the time, most of the time, some of the time, a little of the time, never
23.During the past 2 weeks, how often have you been able to take part in your usual patterns of leisure or recreational activities? all of the time, most of the time, some of the time, a little of the time, never
24.During the past 2 weeks, how much have you been troubled by the medical treatmentof your illness? very much, much, somewhat, a little, not at all
25.To what extent have your personal relations with people close to you (family or friends) worsened because of your illness? very much, much, somewhat, a little, not at all
26.To what extent has your sexual life been impaired (harmed) because of your illness? very much, much, somewhat, a little, not at all
27.How often during the past 2 week, have you been troubled by fluid or food coming up into your mouth (regurgitation)? all of the time, most of the time, some of the time, a little of the time, never
28.How often during the past 2 weeks have you felt uncomfortable because of your slow speed of eating? all of the time, most of the time, some of the time, a little of the time, never
29.How often during the past 2 weeks have you had trouble swallowing your food? all of the time, most of the time, some of the time, a little of the time, never
30.How often during the past 2 weeks have you been troubled by urgent bowel movements? all of the time, most of the time, some of the time, a little of the time, never
31.How often during the past 2 weeks have you been troubled by diarrhoea? all of the time, most of the time, some of the time, a little of the time, never
32.How often during the past 2 weeks have you been troubled by constipation? all of the time, most of the time, some of the time, a little of the time, never
33.How often during the past 2 weeks have you been troubled by nausea? all of the time, most of the time, some of the time, a little of the time, never
34.How often during the past 2 weeks have you been troubled by blood in the stool? all of the time, most of the time, some of the time, a little of the time, never
35.How often during the past 2 weeks have you be troubled by heartburn? all of the time, most of the time, some of the time, a little of the time, never
36.How often during the past 2 weeks have you been troubled by uncontrolled stools? all of the time, most of the time, some of the time, a little of the time, never
SF12
1.In general, would you say your health is: Excellent, Very good, Good, Fair, Poor
2. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf: Yes, Limited a lot, Yes, limited a little, No, not limited at all.
3. Climbing several flights of stairs: Yes, Limited a lot, Yes, limited a little, No, not limited at all.
4. Due to physical health problems over the past 4 weeks: Have you accomplished less than you would like? Yes/No
5. Due to physical health problems over the past 4 weeks: Have you been limited in the kind of work/other activites? Yes/No
6. Due to emotional health problems over the past 4 weeks: Have you accomplished less than you would like? Yes/No
7. Due to emotional health problems over the past 4 weeks: Have you been limited in the kind of work/other activites? Yes/No
8. During the past 4 weeks, how much did pain interfere with your normal work? Not at all, A little bit, Moderately, Quite a bit, Extremely

9. Over the past 4 weeks: Have you felt calm and peaceful? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.
10. Over the past 4 weeks: Did you have lots of energy? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.
11. Over the past 4 weeks: Have you felt down hearted and blue? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.
12. Over the past 4 weeks: how much has your physical or emotional problems interfered with your social activities? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.
Expert Patient additions: Patient panellist 1:
General questions (awful, poor, fair, good, very good, excellent):
1.My abdominal body shape is:
2.My abdominal discomfort currently is:
3.My mental health currently is:
4.My sexual activity currently is:
5.My overall quality of life currently is:
Visual analogue scores (0-10):
Your abdominal pain:
Your pain at the hernia site:
Your back pain:
Your mobility:
Your relationship with your partner:
Patient panellist 2:
Decisional regret (answers: strongly agree, agree, neither agree or disagree, disagree, strongly disagree):
1.It was the right decision
2.I regret the choice that was made
3.I would go for the same choice if I had to do it over again
4.The choice did me a lot of harm
5.The decision was a wise one
QLQ-C30
1.Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase? Not at all, a little, quite a bit, very much
2.Do you have any trouble taking a long walk? Not at all, a little, quite a bit, very much
3.Do you have any trouble taking a short walk outside of the house? Not at all, a little, quite a bit, very much
4.During the past week Were you limited in doing either your work or other daily activities? Not at all, a little, quite a bit, very much
5.During the past week Were you limited in pursuing your hobbies or other leisure time activities? Not at all, a little, quite a bit, very much
6.During the past week Has your physical condition or medical treatment interfered with your family life? Not at all, a little, quite a bit, very much
7.During the past week has your physical condition or medical treatment interfered with your social activities? Not at all, a little, quite a bit, very much
8.During the past week has your physical condition or medical treatment caused you financial difficulties? Not at all, a little, quite a bit, very much
FACT – G
1.I feel close to my partner (or the person who is my main support). Not at all, not really, undecided, somewhat, very much
2.I am satisfied with my sex life. Not at all, not really, undecided, somewhat, very much
3.I am content with the quality of my life right now. Not at all, not really, undecided, somewhat, very much

4.I am enjoying the things I usually do for fun. Not at all, not really, undecided, somewhat, very much
5. Methodology
General
Funding
Protocol
Registered Trial
Ethical Approval
Introduction
Background and rationale
Primary aim or objective
A pre-specified referenced hypothesis
Method
Randomised trials
Method of generating random allocation sequence
Method of implementing the random allocation
Blinding of the participant to the intervention received
Blinding of the care providers
Non-randomised trials/studies
Explain how the study groups/arms were selected, avoiding selection bias
All Interventional (Randomised and non-Randomised Interventional Trials)
Description of trial design
Trial setting (single/multicentre),names of centres where data will be collected
Describe the intended periods of recruitment and follow up
Description of the interventions, with sufficient detail to allow replication
Defined primary outcome, with well described methods for detection and measurement
Secondary outcome measures, defined, with described methods for detection and measurement
Power/Size calculation
Specific inclusion/exclusion criteria
Reports eligibility and number included
Blinding of the outpatient assessor/independent blinded outpatient assessor
Describe methods of follow-up
Results
Recruitment dates - Start date?, Finish date, End of follow-up date
Participant flow chart - for each group showing the no. of participants meeting inclusion criteria, then no. included, no. receiving the intended treatment, no. analysed for primary outcome (includes explanations for participant losses)
A table showing baseline characteristics/pre-operative variables between each group
Report all harmful events in each group

Deviations from the intended intervention reported?
Statistics
Length of follow-up reported
Details on PP analysis or ITT analysis
Number of participants with missing data
Statistic methods for comparing the groups; for primary and secondary outcomes
Additional methods for subgroup analyses and adjusted analyses
Reports adjusted analysis (with adjustment factors clearly listed)
Explains how missing data will be addressed
Reports estimated effect size with 95% confidence intervals
Discussion
Summarises key results with reference to study objectives
Trial limitations, addressing sources of potential bias, imprecision
Interpretation consistent with results, balancing benefits and harms

Appendix 14: Round 1 – Panellists voting on the number of variables required in the minimum dataset:

Primary Ventral Hernia	**Panellist 1**	**Panellist 2**	**Panellist 3**	**Panellist 4**	**Panellist 5**	**Panellist 6**	**Panellist 7**	**Panellist 8**	**Panellist 9**	**Panellist 10**	**Panellist 11**	**Panellist 12**	**Total**	**Total Rounded**	**Steering Committee**
Criteria															
1a.Pre-operative – Patient variables	**11**	**7**	**28**	**11**	**23**	**8**	**10**	**16**	**15**	**21**	**16**	**16**	15.2	**15**	**8**
1b.Pre-operative – Hernia variables	**10**	**5**	**13**	**10**	**21**	**10**	**10**	**8**	**4**	**15**	**9**	**10**	10.4	**10**	**6**
2.Intra-operative variables	**20**	**10**	**28**	**18**	**27**	**24**	**14**	**13**	**22**	**27**	**19**	**10**	19.3	**19**	**10**
3.Post-operative outcomes	**12**	**7**	**28**	**15**	**23**	**14**	**6**	**21**	**19**	**16**	**23**	**14**	16.5	**16**	**7**
	53	29	97	54	94	56	40	58	60	79	67	50		**60**	**31**
Incisional Hernia															**Steering Committee**
Criteria															
1a.Pre-operative – Patient variables	**13**	**7**	**28**	**11**	**23**	**14**	**10**	**17**	**15**	**21**	**16**	**16**	15.9	**16**	**8**
1b.Pre-operative – Hernia variables	**12**	**10**	**19**	**11**	**24**	**26**	**10**	**20**	**14**	**22**	**17**	**19**	17.0	**17**	**10**
2.Intra-operative variables	**21**	**12**	**29**	**18**	**29**	**30**	**14**	**23**	**22**	**27**	**24**	**10**	21.6	**21**	**14**
3.Post-operative outcomes	**12**	**7**	**28**	**15**	**23**	**14**	**6**	**24**	**19**	**16**	**24**	**14**	16.8	**17**	**7**
	58	36	104	55	99	84	40	84	70	86	81	59		**71**	**39**
4.Patient reported outcomes	**18**	**21**	**20**	**13**	**34**	**78**	**5**	**21**	**16**	**37**	**38**	**21**	25.3	**25**	**25**
5.Methodology	**40**	**39**	**40**	**38**	**39**	**40**	**33**	**38**	**20**	**38**	**40**	**40**	37.1	**37**	**38**

Appendix 15: Voting Sheet for Stage 2: Round 1

Voting: Selecting Variables from the Maximum Dataset

The steering committee have met and decide to change to protocol slightly. We feel that a lot of panellists voted for far too many variables for inclusion into our minimum dataset for interventional trials in ventral hernia repair.

The changed protocol has been sent out to panellists. The desired number of variables for each minimum dataset is now:

Number of variables in Primary Ventral Hernia Minimum dataset – 31
Number of variables in Incisional Ventral Hernia Minimum dataset – 39
PROMS – 25
Methodology checklist – 38

Primary Ventral Hernia Minimum Dataset breakdown:
Patient demographics – 8
Hernia variables - 6
Peri-operative variables – 10
Post-operative outcomes – 7
(31)
Patient reported outcomes - 25
Methodology – 38

Incisional Ventral Hernia Minimum Dataset breakdown:
Patient demographics – 8
Hernia variables - 10
Peri-operative variables – 14
Post-operative outcomes – 7
(39)
Patient reported outcomes - 25
Methodology – 38

Voting instructions:
In each category please vote for the variables you would like to include in the 1) primary VH and the 2) incisional VH minimum datasets.

Please rank your most preferred variable with the highest number:

1. For example for Patient variables of the Primary VH dataset, your most preferred variable would score 8, your next would score 7 etc all the where down to 1.
2. Another example: For the hernia variables of the Incisional VH dataset, your most preferred variable would be 10, your next would be 9 etc all the where down to 1.

N.B. FOR THE PROMS: PLEASE REMEMBER IN THE MEETING WE LIKED THE EURAHS QUESTONS, AND THE SF12!!! OUR EXPERIENCE

PATIENTS SUE AND NICOLA HAVE ALSO ADDED SOME QUESTIONS! THERE WILL NOW ONLY BE ONE PROM QUESTIONNAIRE SHEET THAT APPLIES TO BOTH DATASETS.

N.B. FOR THE METHODOLOGY CATEGORY PLEASE SELECT THE *TWO* CRITERIA YOU WOULD LIKE TO EXCLUDE!!!!

Voting table:

1. Pre-operative variables	Primary VH	Incisional VH
No. of variables allowed:	8	8
1a. Patient variables		
Age		
Sex		
Weight		
Height		
Obesity/BMI		
COPD		
Hepatic disease		
Ascites		
Liver failure (Child Pugh or MELD score)		
Hypertension		
Smoker		
Alcohol abuse (yes/no)		
Alcohol intake		
Diabetes (type I/type II)		
Benign Prostatic Hypertrophy		
Previous AAA repair		
Coronary heart disease (IHD/stent/MI)		
Peripheral vascular disease (PVD)		
Cerebral vascular accident (CVA)		
Arteriopath (all of the above – IHD/PVD/CVA)		
Malignancy		
Radiotherapy		
Radiotherapy to the surgical field		
Chemotherapy		
Chronic kidney disease		
Immunosupression/Steroid use		
ASA score		
No. of co-morbidities		
Anaemia		
Connective tissue disorders (eg Ehlers-Danlos, Marfans etc)		
History of inflammatory bowel disease		
Physical activity		
Fitness level		
Profession/Occupation		
Anticoagulation		
Current antibiotic therapy		
Malnutrition		
Pregnancy		

Frailty		
Sarcopaenia		
No. of variables allowed:	**6**	**10**
1b. Hernia variables		
Previous abdominal surgery/operations		
Previous abdominal incisions		
No of Primary Incisional Hernias		
No of Recurrent Incisional Hernias		
No previous VH repairs		
Previous surgical site infection		
Previous surgical site occurrence		
No of hernia defects present		
Hernia Width		
Hernia Length		
Hernia Defect Area		
Loss of Domain		
EHS score		
Hernia location: Midline Vs Lateral		
Hernia location: Epigastric, Umbilical, Suprapubic, Subcostal (R/L), Flank (R/L), Iliac (R/L), Lumbar (R/L).		
Stoma present		
Divarification of the recti		
Reducible? Yes/No		
Abdominal wall rigid/soft		
Denervation incision present		
Previous component separation		
Signs of strangulation (pain/erythaema)		
Type of previous hernia repair?		
Previous mesh implant? If so where was mesh implanted		
Enterocutaneous fistula		
Current Mesh infection		
AW muscle quality (rectus/obliques assessed: present (complete/partial) or absent)		
Quality of Abdominal Wall Tissue (eg CT sarcopaenia index)		
Abdominal wall function		
Orientation of previous scars (difficult to think how to measure but possibly important to know)		
No. of variables allowed:	**10**	**14**
2. Peri-operative variables		
Operative work-up		
Pre-operative botox injections		
Pre-operative pneumoperitoneum		
General		
Mode of Surgery – Laparoscopic/Open/Robotic		
Laparoscopic conversion to open with reason		
Surgeon experience – Consultant/trainee (If trainee – then level of training reported)		

Mesh variables		
Mesh/suture repair		
Exact mesh name; material/type/brand, (knowing this will tell us weight & porosity)		
Position of mesh		
Mesh fixation technique		
Mesh size		
Mesh overlap		
Mesh 2 variable – with ALL the above details for this second mesh		
Operative variables		
For suture repair – suture type – absorbable/non-absorbable		
Operative time		
Anaesthetic type (Local, Spinal, General)		
Bridged vs Primary fascial closure		
Type of component separation		
Small bites/large bites – suture repair		
Whole scar repaired		
Panniculectomy (Y/N)		
Drains inserted and location		
Concomitant GI bowel procedure		
Concomitant non-GI procedure		
Intra-operative blood loss		
Enterotomies		
VHWG score		
CDC wound classification		
Perioperative change in positive end expiratory pressure		
Surgical antibiotic prophylaxis		
Previous mesh removal		
Post-operative analgesia (Epidural, Single dose TAPP block, PCA, wound catheters)		
Negative pressure wound therapy		
Epidural Yes/No		
Miscellaneous: Accurate reporting of all intra-operative complications? (eg. Bladder injuries, enterotomies, allergies, cardiac arrests)		
No. of variables allowed:	**7**	**7**
3. Post-operative outcomes		
Wound infection (SSI)		
Surgical site occurrence (SSO)		
Surgical site occurrence requiring procedural intervention (SSOPI)		
Seromas		
Haematomas		
Wound dehisence		
ECF formation		
Mesh Infection		

Mesh removal		
Skin necrosis		
Flap necrosis		
Drain useage / days to drain removal		
Severe Constipation		
Ileus		
Bowel Obstruction		
Chronic pain		
Bulging		
Hernia recurrence		
ACS/MI		
Stroke		
Post Op Intra-abdominal Bleed		
Post Op GI Bleed		
PE/DVT		
UTI		
Clavian-Dindo Complication Score (1-5)		
Re-operation rate in 30 days		
Re-opertion for hernia recurrence		
Length of hospital stay		
30-day hospital readmission		
Mortality		
Post-operative antibiotics with indication		
No. of days in ITU		
Time to full mobilisation		
Hospital acquired pneumonia		
Atelectasis		
Coughing		
Renal failure		
Delirium		
Miscellaneous: Accurate reporting of all other medical complications during inpatient stay		
	One column for both datasets	
No. of variables allowed:	**25**	N/A - Same checklist for both
N.B. FOR THE PROMS: PLEASE REMEMBER IN THE MEETING WE LIKED THE EURAHS QUESTONS, AND THE SF12!!! OUR EXPERIENCE PATIENTS SUE AND NICOLA HAVE ALSO ADDED SOME QUESTIONS!		
4. Patient reported outcomes measures (PROMs)		
(based on EURAHS QoL score, Carolinas Comfort Scale, HerQLes score, SF36, EQ-5D, GIQL, SF12, QLQ-C30, FACT – G, miscellaneous questions added by patient panellists)		
Questions will be asked pre-operatively and post-operatively		

GENERAL		
Health VAS		
Average inpatient pain VAS score (at rest)		
Return to work		
Return to normal activities		
Outpatient Pain VAS score (plus baseline VAS)		
EURAHS QoL score		
Pain at hernia site:		
Pain at rest (lying down) (0-10)		
Pain during activities (walking, biking, sports) (0-10)		
Pain felt during the last week (0-10)		
Restrictions of activities because of pain or discomfort at the site of the hernia:		
Restriction from daily activities (inside the house) (0-10)		
Restriction outside the house (walking, biking, driving) (0-10)		
Restriction during sports (0-10)		
Restriction during heavy labour (0-10)		
Cosmetic discomfort:		
Shape of abdomen (0-10)		
Site of hernia (0-10)		
HERQLES (1-disagree to 6-strongly agree)		
My abdominal wall has a huge impact on my health		
My abdominal wall causes me physical pain		
My abdominal wall interferes when I perform strenuous activitis eg heavy lifting		
My abdominal wall interferes when I perfrom moderate activities, eg bowling, bending over		
My abdominal wall interferes when I walk or climb stairs		
My abdominal wall interferes when I dress myself, take showers and cook		
My abdominal wall interferes with my sexual activity		
I often stay at home because of my abdominal wall		
I accomplish less at home because of my abdominal wall		
I accomplish less at work because of my abdominal wall		
My abdominal wall affects how I feel every day		
I often feel blue becase of my abdominal wall		
CAROLINAS COMFORT SCALE (each question has 3 parts, each marked 0-5 for severeity)		
When lying down, do you have; Sensation of mesh? Pain?		
When bending over, do you have; Sensation of mesh? Pain? Movement limitations?		
While sitting up, do you have; Sensation of mesh? Pain? Movement limitations?		
While performing activities of daily living (getting out of bed, bathing, getting dressed), do you have; Sensation of mesh? Pain? Movement limitations?		
When coughing or deep breathing, do you have; Sensation of mesh? Pain? Movement limitations?		
When walking or standing, do you have; Sensation of mesh? Pain? Movement limitations?		
When walking up or down stairs, do you have; Sensation of mesh? Pain? Movement limitations?		

When exercising (other than work-related), do you have? Sensation of mesh? Pain? Movement limitations?		
SF36 Questionnaire		
1.In general, would you say that your health is: Excellent, Very Good, Good, Fair, Poor		
2.Compared to one year ago, how would you rate your health in general now: Much better, somewhat better, about the same, somewhat worse, much worse.		
Limitations of activities: Does your health limit you in any of these activities: Answer; Yes a lot, Yes a little, Not at all		
3.Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports		
4.Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf		
5.Lifting or carrying groceries		
6.Climbing several flights of stairs		
7.Climbing one flight of stairs		
8.Bending, kneeling, or stooping		
9.Walking more than a mile		
10.Walking several blocks		
11.Walking one block		
12.Bathing or dressing yourself		
Physical health problems: During the past 4 weeks have you had any of the following problems with work or other activities as a result of physical health? Answer; Yes/No		
13.Cut down the amount of time you spent on work or other activities?		
14.Accomplished less than you would like?		
15.Were limited in the kind of work or other activities?		
16.Had difficulty performing the work or other activities?		
Emotional health problems: During the past 4 weeks have you had any of the following problems with work or other activities as a result of emotional health (such as feeling depressed or anxious)? Answer; Yes/No		
17.Cut down the amount of time you spent on work or other activities?		
18.Accomplished less than you would like?		
19.Didn't do work or other activities as carefully as usual		
20.Social activities: Emotional problems interferred with your normal social activities with family, friends, neighbors, or groups. (Not at all, slightly, moderately, severe, very severe)		
21.Pain: How much bodily pain have you had during the past 4 weeks? (None, very mild, mild, moderate)		
22.During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? (Not at all, A little, Moderately, Quite a bit, Extremely).		
Energy and Emotions During the past 4 weeks: Answer: All of the time, Most of the time, A good bit of the time, some of the time, a little bit of the time, none of the time.		
23.Did you feel full of pep?		

24.Have you been a very nervous person?		
25.Have you felt so down in the dumps that nothing could ever cheer you up?		
26.Have you felt calm and peaceful?		
27.Did you have a lot of energy?		
28.Have you felt downhearted and blue		
29.Did you feel worn out?		
30.Have you been a happy person?		
31.Did you feel tired?		
32.Social Activities: During the past weeks, how much of the time has your physical or emotional problems interfered with your social activities? All of the time, Most of the time, Some of the time, A little bit of the time, None of the time		
GENERAL HEALTH Answer: Definitely true, mostly true, don't know, mostly false, definitely false		
33.I seem to get sick a little easier than other people		
34.I am as healthy as anybody I know		
35.I expect my health to get worse		
36.My health is excellent		
EQ-5D - select one of the four possiblities		
1.Mobility: I have no problems in walking about?, I have some problems walking about? I am confined to bed?		
2.Self-care: I have no problems with self-care?, I have some problems washing or dressing myself?, I am unable to wash or dress myself?		
3.Usual activities: I have no problems with performing my usual activities?, I have some problems with performing my usual activities? I am unable to perform my usual activities?		
4.Pain/Discomfort: I have no pain or discomfort? I have moderate pain or discomfort? I have extreme pain or discomfort?		
5.Anxiety/Depression: I am not anxious or depressed?, I am moderately anxious or depressed?, I am extremely anxious or depressed?		
6.Please state your level of overall health from 0-100.		
GIQL		
1.How often during the past 2 weeks have you had pain in the abdomen? All of the time, most of the time, some of the time, a little of the time, never.		
2.How often during the past 2 weeks have you had a feeling of fullness in the upper abdomen? All of the time, most of the time, some of the time, a little of the time, never.		
3.How often during the past 2 weeks have you had bloating? All of the time, most of the time, some of the time, a little of the time, never.		
4.How often during the past 2 weeks have you been troubled by excessive passage of gas through the anus? All of the time, most of the time, some of the time, a little of the time, never.		
5.How often during the past 2 weeks have you been troubled by strong burping or belching? All of the time, most of the time, some of the time, a little of the time, never.		

6.How often during the past 2 weeks have you been troubled by gurgling noises from the abdomen? all of the time, most of the time, some of the time, a little of the time, never		
7.How often during the past 2 weeks have you been troubled by frequent bowel movements? all of the time, most of the time, some of the time, a little of the time, never		
8.How often during the past 2 weeks have you found eating to be a pleasure? all of the time, most of the time, some of the time, a little of the time, never		
9.Because of your illness, to what extent have you restricted the kinds of food you eat? very much, much, somewhat, a little, not at all		
10.During the past 2 weeks, how well have you been able to cope with everyday stresses? Extremely poorly, poorly, moderately, well, extremely well		
11.How often during the past 2 weeks have you been sad about being ill? all of the time, most of the time, some of the time, a little of the time, never		
12.How often during the past 2 weeks have you been nervous or anxious about your illness? all of the time, most of the time, some of the time, a little of the time, never		
13.How often during the past 2 weeks have you been happy with life in general? never, a little of the time, some of the time, most of the time, all of the time		
14.How often during the past 2 weeks have you been frustrated about your illness? all of the time, most of the time, some of the time, a little of the time, never		
15.How often during the past 2 weeks have you been tired or fatigued? all of the time, most of the time, some of the time, a little of the time, never		
16.How often during the past 2 weeks have you felt unwell? all of the time, most of the time, some of the time, a little of the time, never		
17.Over the past week, have you woken up in the night? every night, 5-6 nights, 3-4 nights, 1-2 nights, never		
18.Since becoming ill, have you been troubled by changes in your appearance? a great deal, a moderate amount, somewhat, a little bit, not at all		
19.Because of your illness, how much physical strength have you lost? a great deal, a moderate amount, some, a little bit, none		
20.Because of your illness, to what extent have you lost your endurance? a great deal, a moderate amount, somewhat, a little bit, not at all		
21.Because of your illness, to what extent do you feel unfit? extremely unfit, moderately unfit, somewhat unfit, a little unfit, fit		

22.During the past 2 weeks, how often have you been able to complete your normal daily activities (school,work, household)? all of the time, most of the time, some of the time, a little of the time, never		
23.During the past 2 weeks, how often have you been able to take part in your usual patterns of leisure or recreational activities? all of the time, most of the time, some of the time, a little of the time, never		
24.During the past 2 weeks, how much have you been troubled by the medical treatmentof your illness? very much, much, somewhat, a little, not at all		
25.To what extent have your personal relations with people close to you (family or friends) worsened because of your illness? very much, much, somewhat, a little, not at all		
26.To what extent has your sexual life been impaired (harmed) because of your illness? very much, much, somewhat, a little, not at all		
27.How often during the past 2 week, have you been troubled by fluid or food coming up into your mouth (regurgitation)? all of the time, most of the time, some of the time, a little of the time, never		
28.How often during the past 2 weeks have you felt uncomfortable because of your slow speed of eating? all of the time, most of the time, some of the time, a little of the time, never		
29.How often during the past 2 weeks have you had trouble swallowing your food? all of the time, most of the time, some of the time, a little of the time, never		
30.How often during the past 2 weeks have you been troubled by urgent bowel movements? all of the time, most of the time, some of the time, a little of the time, never		
31.How often during the past 2 weeks have you been troubled by diarrhoea? all of the time, most of the time, some of the time, a little of the time, never		
32.How often during the past 2 weeks have you been troubled by constipation? all of the time, most of the time, some of the time, a little of the time, never		
33.How often during the past 2 weeks have you been troubled by nausea? all of the time, most of the time, some of the time, a little of the time, never		
34.How often during the past 2 weeks have you been troubled by blood in the stool? all of the time, most of the time, some of the time, a little of the time, never		
35.How often during the past 2 weeks have you be troubled by heartburn? all of the time, most of the time, some of the time, a little of the time, never		
36.How often during the past 2 weeks have you been troubled by uncontrolled stools?		

all of the time, most of the time, some of the time, a little of the time, never		
SF12		
1.In general, would you say your health is: Excellent, Very good, Good, Fair, Poor		
2. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf: Yes, Limited a lot, Yes, limited a little, No, not limited at all.		
3. Climbing several flights of stairs: Yes, Limited a lot, Yes, limited a little, No, not limited at all.		
4. Due to physical health problems over the past 4 weeks: Have you accomplished less than you would like? Yes/No		
5. Due to physical health problems over the past 4 weeks: Have you been limited in the kind of work/other activites? Yes/No		
6. Due to emotional health problems over the past 4 weeks: Have you accomplished less than you would like? Yes/No		
7. Due to emotional health problems over the past 4 weeks: Have you been limited in the kind of work/other activites? Yes/No		
8. During the past 4 weeks, how much did pain interfere with your normal work? Not at all, A little bit, Moderately, Quite a bit, Extremely		
9. Over the past 4 weeks: Have you felt calm and peaceful? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.		
10. Over the past 4 weeks: Did you have lots of energy? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.		
11. Over the past 4 weeks: Have you felt down hearted and blue? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.		
12. Over the past 4 weeks: how much has your physical or emotional problems interfered with your social activities? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.		
Expert Patient additions: Patient panellist 1:		
General questions (awful, poor, fair, good, very good, excellent):		
1.My abdominal body shape is:		
2.My abdominal discomfort currently is:		
3.My mental health currently is:		
4.My sexual activity currently is:		
5.My overall quality of life currently is:		
Visual analogue scores (0-10):		
Your abdominal pain:		
Your pain at the hernia site:		
Your back pain:		
Your mobility:		
Your relationship with your partner:		
Patient panellist 2:		

Decisional regret (answers: strongly agree, agree, neither agree or disagree, disagree, strongly disagree):		
1.It was the right decision		
2.I regret the choice that was made		
3.I would go for the same choice if I had to do it over again		
4.The choice did me a lot of harm		
5.The decision was a wise one		
QLQ-C30		
1.Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase? Not at all, a little, quite a bit, very much		
2.Do you have any trouble taking a long walk? Not at all, a little, quite a bit, very much		
3.Do you have any trouble taking a short walk outside of the house? Not at all, a little, quite a bit, very much		
4.During the past week Were you limited in doing either your work or other daily activities? Not at all, a little, quite a bit, very much		
5.During the past week Were you limited in pursuing your hobbies or other leisure time activities? Not at all, a little, quite a bit, very much		
6.During the past week Has your physical condition or medical treatment interfered with your family life? Not at all, a little, quite a bit, very much		
7.During the past week has your physical condition or medical treatment interfered with your social activities? Not at all, a little, quite a bit, very much		
8.During the past week has your physical condition or medical treatment caused you financial difficulties? Not at all, a little, quite a bit, very much		
FACT – G		
1.I feel close to my partner (or the person who is my main support). Not at all, not really, undecided, somewhat, very much		
2.I am satisfied with my sex life. Not at all, not really, undecided, somewhat, very much		
3.I am content with the quality of my life right now. Not at all, not really, undecided, somewhat, very much		
4.I am enjoying the things I usually do for fun. Not at all, not really, undecided, somewhat, very much		
No. of variables allowed:	38	N/A - Same checklist for both
N.B. FOR THE METHODOLOGY CATEGORY PLEASE SELECT THE *TWO* CRITERIA YOU WOULD LIKE TO EXCLUDE!!!!		
5. Methodology		
General		
Funding		
Protocol		
Registered Trial		
Ethical Approval		

Introduction		
Background and rationale		
Primary aim or objective		
A pre-specified referenced hypothesis		
Method		
Randomised trials		
Method of generating random allocation sequence		
Method of implementing the random allocation		
Blinding of the participant to the intervention received		
Blinding of the care providers		
Non-randomised trials/studies		
Explain how the study groups/arms were selected, avoiding selection bias		
All Interventional (Randomised and non-Randomised Interventional Trials)		
Description of trial design		
Trial setting (single/multicentre),names of centres where data will be collected		
Describe the intended periods of recruitment and follow up		
Description of the interventions, with sufficient detail to allow replication		
Defined primary outcome, with well described methods for detection and measurement		
Secondary outcome measures, defined, with described methods for detection and measurement		
Power/Size calculation		
Specific inclusion/exclusion criteria		
Reports eligibility and number included		
Blinding of the outpatient assessor/independent blinded outpatient assessor		
Describe methods of follow-up		
Results		
Recruitment dates - Start date?, Finish date, End of follow-up date		
Participant flow chart - for each group showing the no. of participants meeting inclusion criteria, then no. included, no. receiving the intended treatment, no. analysed for primary outcome (includes explanations for participant losses)		
A table showing baseline characteristics/pre-operative variables between each group		
Report all harmful events in each group		
Deviations from the intended intervention reported?		
Statistics		
Length of follow-up reported		

Details on PP analysis or ITT analysis		
Number of participants with missing data		
Statistic methods for comparing the groups; for primary and secondary outcomes		
Additional methods for subgroup analyses and adjusted analyses		
Reports adjusted analysis (with adjustment factors clearly listed)		
Explains how missing data will be addressed		
Reports estimated effect size with 95% confidence intervals		
Discussion		
Summarises key results with reference to study objectives		
Trial limitations, addressing sources of potential bias, imprecision		
Interpretation consistent with results, balancing benefits and harms		
Generalisability of the study results		

Appendix 16: Results of Primary Ventral Hernia Minimum Dataset

Highlighted in yellow – round 1 consensus; Green – round 2 consensus, Pink – round 3 consensus, Grey – steering committee decision.

	Fraction of Max Score		Steering Committee	Reason
1a. Pre-operative variables				
No. of variables allowed:				
1a. Patient variables				
Age		**CONSENSUS**		
Sex		**CONSENSUS**		
Obesity/BMI		**CONSENSUS**		
COPD	0.07		**Include**	**Miscellaneous results - COPD scored much higher than Anticoag and frailty on previous rounds, fits with IVH dataset/results**
Smoker		**CONSENSUS**		
Diabetes (type I/type II)		**CONSENSUS**		
Previous AAA repair	0.00			
Immunosupression/Steroid use	0.87	**CONSENSUS**		
ASA score		**CONSENSUS**		
No. of co-morbidities	0.13			
Connective tissue disorders (eg Ehlers-Danlos, Marfans etc)	0.03			
Anticoagulation	0.23		OUT	
Malnutrition	0.03			

Frailty	0.13		OUT
1b. Hernia variables			
No. of variables allowed:			
Previous abdominal surgery/operations	0		
No of Primary Incisional Hernias	0		
No of Recurrent Incisional Hernias	0		
Previous surgical site infection	0		
No of hernia defects present	0.42		**Include**
Hernia Width		**CONSENSUS**	
Hernia Length	0.25		
Hernia Defect Area	0.02		
Loss of Domain	0.5	**CONSENSUS**	
EHS score		**CONSENSUS**	
Hernia location: Epigastric, Umbilical, Suprapubic, Subcostal (R/L), Flank (R/L), Iliac (R/L), Lumbar (R/L).	0.1		
Stoma present	0.02		
Divarification of the recti	0.62	**CONSENSUS**	
Reducible? Yes/No	0.25		**Include**
Denervation incision present	0		
Signs of strangulation (pain/erythaema)	0.017		
Previous mesh implant? If so where was mesh implanted	0.1		
Enterocutaneous fistula	0.05		
Current Mesh infection	0.15		

2. Peri-operative variables			
No. of variables allowed:			
Operative work-up			
Pre-operative botox injections	0.00		
Pre-operative pneumoperitoneum	0.05		
General	0.00		
Mode of Surgery – Laparoscopic/Open/Robotic		**CONSENSUS**	
Surgeon experience – Consultant/trainee (If trainee – then level of training reported)	0.12		
Mesh variables	0.00		
Mesh/suture repair		**CONSENSUS**	
Exact mesh name; material/type/brand, (knowing this will tell us weight & porosity)		**CONSENSUS**	
Position of mesh		**CONSENSUS**	
Mesh fixation technique	0.65	**CONSENSUS**	
Mesh size		**CONSENSUS**	
Mesh overlap	0.00		
Operative variables	0.00		
For suture repair – suture type – absorbable/non-absorbable	0.28		**Include**
Operative time	0.00		
Bridged vs Primary fascial closure		**CONSENSUS**	
Type of component separation	0.05		
Whole scar repaired	0.05		
Panniculectomy (Y/N)	0.00		
Concomitant GI bowel procedure	0.18		
Enterotomies	0.00		

VHWG score	0.38		Include	
CDC wound classification	0.72	CONSENSUS		
Miscellaneous: Accurate reporting of all intra-operative complications? (eg. Bladder injuries, enterotomies, allergies, cardiac arrests)	0.02			
3. Post-operative outcomes				
No. of variables allowed:				
Wound infection (SSI)		CONSENSUS		
Surgical site occurrence (SSO)	0.23		Include	
Surgical site occurrence requiring procedural intervention (SSOPI)	0.72	CONSENSUS		
ECF formation	0.00			
Mesh Infection		CONSENSUS		
Mesh removal	0.02			
Chronic pain	0.45		Include	
Bulging	0.05			
Hernia recurrence		CONSENSUS		
Clavian-Dindo Complication Score (1-5)	0.53	CONSENSUS		
Re-operation rate in 30 days	0.20		Include	**Decided on 8 post-operative outcomes to maintain consistency with the IVH outcomes**
Re-opertion for hernia recurrence	0.08			
Length of hospital stay	0.00			
30-day hospital readmission	0.22			
Mortality	0.00			
Time to full mobilisation	0.00			

Appendix 17: Results of Incisional Ventral Hernia Minimum Dataset

Highlighted in yellow – round 1 consensus; Green – round 2 consensus, Pink – round 3 consensus, Grey – steering committee decision.

	Fraction of Max Score		Steering Committee	Reason
1a. Pre-operative variables				
No. of variables allowed:				
1a. Patient variables				
Age		CONSENSUS		
Sex		CONSENSUS		
Obesity/BMI		CONSENSUS		
COPD	0.27		Include	
Smoker		CONSENSUS		
Alcohol intake	0			
Diabetes (type I/type II)		CONSENSUS		
Previous AAA repair	0			
Immunosupression/Steroid use	0.8	CONSENSUS		
ASA score		CONSENSUS		
No. of co-morbidities	0.10			
Anaemia	0.00			
Connective tissue disorders (eg Ehlers-Danlos, Marfans etc)	0.03			
Physical activity	0.00			
Anticoagulation	0.13			
Malnutrition	0.03			

Frailty	0.13		
1b. Hernia variables			
No. of variables allowed:			
Previous abdominal surgery/operations	0.51	**CONSENSUS**	
Previous abdominal incisions	0.01		
No of Recurrent Incisional Hernias	0.58	**CONSENSUS**	
No previous VH repairs	0.11		
Previous surgical site infection	0.44		**Include**
No of hernia defects present	0.06		
Hernia Width		**CONSENSUS**	
Hernia Length	0.05		
Hernia Defect Area	0.15		
Loss of Domain		**CONSENSUS**	
EHS score	0.61	**CONSENSUS**	
Hernia location: Midline Vs Lateral	0.00		
Hernia location: Epigastric, Umbilical, Suprapubic, Subcostal (R/L), Flank (R/L), Iliac (R/L), Lumbar (R/L).	0.19		
Stoma present	0.33		**Include**
Divarification of the recti	0.01		
Reducible? Yes/No	0.06		
Denervation incision present	0.00		
Previous component separation	0.20		**Include**
Signs of strangulation (pain/erythaema)	0.00		
Type of previous hernia repair?	0.11		

Previous mesh implant? If so where was mesh implanted	0.17			
Enterocutaneous fistula	0.47		Include	
Current Mesh infection	0.51	CONSENSUS		
2. Peri-operative variables				
No. of variables allowed:				
Operative work-up				
Pre-operative botox injections	0.56	CONSENSUS		
Pre-operative pneumoperitoneum	0.34		OUT	Currently too rare
	0.00			
General	0.00			
Mode of Surgery – Laparoscopic/Open/Robotic		CONSENSUS		
Laparoscopic conversion to open with reason	0.01			
Surgeon experience – Consultant/trainee (If trainee – then level of training reported)	0.17			
	0.00			
Mesh variables	0.00			
Mesh/suture repair		CONSENSUS		
Exact mesh name; material/type/brand, (knowing this will tell us weight & porosity)		CONSENSUS		
Position of mesh		CONSENSUS		
Mesh fixation technique		CONSENSUS		
Mesh size		CONSENSUS		
Mesh overlap	0.23		Include	
	0.00			
Operative variables	0.00			

For suture repair – suture type – absorbable/non-absorbable	0.09		
Operative time	0.00		
Bridged vs Primary fascial closure		CONSENSUS	
Type of component separation		CONSENSUS	
Whole scar repaired	0.17		
Concomitant GI bowel procedure	0.57	CONSENSUS	
Intra-operative blood loss	0.00		
Enterotomies	0.11		
VHWG score	0.40		Include
CDC wound classification	0.62	CONSENSUS	
Surgical antibiotic prophylaxis	0.00		
Previous mesh removal	0.00		
Negative pressure wound therapy	0.00		
Miscellaneous: Accurate reporting of all intra-operative complications? (eg. Bladder injuries, enterotomies, allergies, cardiac arrests)	0.23		Include
3. Post-operative outcomes			
No. of variables allowed:			
Wound infection (SSI)		CONSENSUS	
Surgical site occurrence (SSO)	0.40		Include
Surgical site occurrence requiring procedural intervention (SSOPI)	0.60	CONSENSUS	
Seromas	0.00		
ECF formation	0.02		
Mesh Infection		CONSENSUS	
Skin necrosis	0.07		

Chronic pain	0.31		Include
Hernia recurrence		CONSENSUS	
Clavian-Dindo Complication Score (1-5)		CONSENSUS	
Re-operation rate in 30 days	0.51	CONSENSUS	
Re-opertion for hernia recurrence	0.00		
30-day hospital readmission	0.18		
Mortality	0.00		
Time to full mobilisation	0.00		

Appendix 18: Results of Patient Reported Outcomes: Minimum Dataset

Highlighted in yellow – round 1 consensus; Green – round 2 consensus, Pink – round 3 consensus, Grey – steering committee decision.

4. Patient reported outcomes measures (PROMs)	Fraction of Max score		Steering Committee	Reason
No. of variables allowed:				
N.B. FOR THE PROMS: PLEASE REMEMBER IN THE MEETING WE LIKED THE EURAHS QUESTONS, AND THE SF12!!! OUR EXPERIENCE PATIENTS SUE AND NICOLA HAVE ALSO ADDED SOME QUESTIONS!				
(based on EURAHS QoL score, Carolinas Comfort Scale, HerQLes score, SF36, EQ-5D, GIQL, SF12, QLQ-C30, FACT – G, miscellaneous questions added by patient panellists)				
Questions will be asked pre-operatively and post-operatively				
GENERAL				
Health VAS	0.00			
Average inpatient pain VAS score (at rest)	0.03			
Return to work	0.13			In SF12
Return to normal activities	0.22			In SF12
Outpatient Pain VAS score (plus baseline VAS)	0.03			
EURAHS QoL score				
Pain at hernia site:				
Pain at rest (lying down) (0-10)		**CONSENSUS**		
Pain during activities (walking, biking, sports) (0-10)		**CONSENSUS**		
Pain felt during the last week (0-10)	0.56	**CONSENSUS**		
Restrictions of activities because of pain or discomfort at the site of the hernia:				
Restriction from daily activities (inside the house) (0-10)		**CONSENSUS**		

Restriction outside the house (walking, biking, driving) (0-10)		**CONSENSUS**	
Restriction during sports (0-10)	0.47		**Include**
Restriction during heavy labour (0-10)	0.41		**Include**
Cosmetic discomfort:			
Shape of abdomen (0-10)	0.47		**Include**
Site of hernia (0-10)	0.49		**Include**
CAROLINAS COMFORT SCALE (each question has 3 parts, each marked 0-5 for severeity)			
When bending over, do you have; Sensation of mesh? Pain? Movement limitations?	0.00		
While sitting up, do you have; Sensation of mesh? Pain? Movement limitations?	0.00		
While performing activities of daily living (getting out of bed, bathing, getting dressed), do you have; Sensation of mesh? Pain? Movement limitations?	0.00		
When coughing or deep breathing, do you have; Sensation of mesh? Pain? Movement limitations?	0.00		
SF36 Questionnaire	0.00		
2.Compared to one year ago, how would you rate your health in general now: Much better, somewhat better, about the same, somewhat worse, much worse.	0.09		
Limitations of activities: Does your health limit you in any of these activities: Answer; Yes a lot, Yes a little, Not at all	0.00		
8.Bending, kneeling, or stooping	0.00		
20.Social activities: Emotional problems interferred with your normal social activities with family, friends, neighbors, or groups. (Not at all, slightly, moderately, severe, very severe)	0.05		
GENERAL HEALTH Answer: Definitely true, mostly true, don't know, mostly false, definitely false	0.00		
1.Mobility: I have no problems in walking about?, I have some problems walking about? I am confined to bed?	0.00		
2.Self-care: I have no problems with self-care?, I have some problems washing or dressing myself?, I am unable to wash or dress myself?	0.00		

3.Usual activities: I have no problems with performing my usual activities?, I have some problems with performing my usual activities? I am unable to perform my usual activities?	0.00		
4.Pain/Discomfort: I have no pain or discomfort? I have moderate pain or discomfort? I have extreme pain or discomfort?	0.03		
5.Anxiety/Depression: I am not anxious or depressed?, I am moderately anxious or depressed?, I am extremely anxious or depressed?	0.03		
6.Please state your level of overall health from 0-100.	0.01		
GIQL	0.00		
18.Since becoming ill, have you been troubled by changes in your appearance?	0.05		
21.Because of your illness, to what extent do you feel unfit?	0.00		
SF12	0.00		
1.In general, would you say your health is: Excellent, Very good, Good, Fair, Poor		**CONSENSUS**	
2. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf: Yes, Limited a lot, Yes, limited a little, No, not limited at all.		**CONSENSUS**	
3. Climbing several flights of stairs: Yes, Limited a lot, Yes, limited a little, No, not limited at all.		**CONSENSUS**	
4. Due to physical health problems over the past 4 weeks: Have you accomplished less than you would like? Yes/No		**CONSENSUS**	
5. Due to physical health problems over the past 4 weeks: Have you been limited in the kind of work/other activites? Yes/No		**CONSENSUS**	
6. Due to emotional health problems over the past 4 weeks: Have you accomplished less than you would like? Yes/No	0.48		**Include**
7. Due to emotional health problems over the past 4 weeks: Have you been limited in the kind of work/other activites? Yes/No	0.36		**Include**
8. During the past 4 weeks, how much did pain interfere with your normal work? Not at all, A little bit, Moderately, Quite a bit, Extremely	0.54	**CONSENSUS**	

9. Over the past 4 weeks: Have you felt calm and peaceful? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.	0.35	**Include**	
10. Over the past 4 weeks: Did you have lots of energy? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.	0.37	**Include**	
11. Over the past 4 weeks: Have you felt down hearted and blue? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.	0.36	**Include**	
12. Over the past 4 weeks: how much has your physical or emotional problems interfered with your social activities? All of the time, Most of the time, A good bit of the time, Some of the time, A little of the time, None of the time.	0.41	**Include**	
Expert Patient additions: Patient panellist 1:			
General questions (awful, poor, fair, good, very good, excellent):			
1.My abdominal body shape is:	0.10		Similar to EURAHS QoL
2.My abdominal discomfort currently is:	0.11		Similar to EURAHS QoL
3.My mental health currently is:	0.08	**Include**	
4.My sexual activity currently is:	0.19	**Include**	
5.My overall quality of life currently is:	0.34		In SF12
Visual analogue scores (0-10):	0.00		
Your mobility:	0.03		
Patient panellist 2:			
Decisional regret (answers: strongly agree, agree, neither agree or disagree, disagree, strongly disagree):	0.10		
1.It was the right decision	0.26	**Include**	
2.I regret the choice that was made	0.24		Very similar to above

3.I would go for the same choice if I had to do it over again	0.28	**Include**	
4.The choice did me a lot of harm	0.09		Very similar to above
QLQ-C30			
5.During the past week Were you limited in pursuing your hobbies or other leisure time activities? Not at all, a little, quite a bit, very much	0.03		
6.During the past week Has your physical condition or medical treatment interfered with your family life? Not at all, a little, quite a bit, very much	0.03		
7.During the past week has your physical condition or medical treatment interfered with your social activities? Not at all, a little, quite a bit, very much	0.08		
8.During the past week has your physical condition or medical treatment caused you financial difficulties? Not at all, a little, quite a bit, very much	0.07		

Appendix 19: Results of voting on Methodology Criteria

5. Methodology		
So far, form rounds 1 & 2 there has been no consensus agreed to exclude any of the methodology criteria!		
Round 3 vote: 1 x Question: PLEASE STATE WHETHER YOU AGREE WITH THE FOLLOWING: I THINK ALL 40 OF THE ORIGINAL METHODOLOGY CRITERIA CAN BE USED IN A CHECKLIST FOR VENTRAL HERNIA INTERVENTIONAL TRIALS!	**100% 15 x Yes**	**CONSENSUS**

Appendix 20: Results from last round of voting: Detection Methods

Panellists voted for detection of these variables as primary ventral hernias and then all approved of the same detection methods for incisional ventral hernias.

Final Round Results						
	RESULTS					
Pre-operative variables						
	Yes	**No**	**Sort of**			
Smoking - Satisfied with suggested definition of smoking status	**11**	**3**	**1**			
Smoking - suggestions	**RESULTS**					
Primary hernia variables						
No of hernia defects	**CT**	**Clinical exam**	**MRI**	**US**	**Clinical exam (intra-op)**	**CT (during straining)**
	10	**5**	**2**	**2**	**1**	**1**
Hernia width	**CT**	**Clinical exam**	**US**	**Clinical exam (intra-op)**	**MRI**	
	11	**5**	**3**	**1**	**1**	
Loss of Domain - detection method	**CT**					
	15					
Loss of Domain - definition	**Sabbagh**	**Tanaka**				
	10	**5**				

EHS score	**Clinical exam** **8**	**CT** **7**	**Clinical exam (intra-op)** **1**	**MRI** **1**	**US** **1**
Rectus diastasis	**CT** **8**	**Clinical exam** **7**	**US** **4**	**Clinical exam (intra-op)** **1**	**MRI** **1**
Reducible/Irreducible	**Clinical exam +/- CT** **8**	**Clinical exam +/- US** **1**	**Clinical exam** **7**		
Overall modality	**CT** **12**	**Clinical exam** **2**	**Clinical exam (intra-op)** **1**		

Comments

RESULTS

Post-operative outcomes

Time point at which they should be measured:	**7 days** **2**	**30 days** **14**	**6 months** **0**	**1 year** **8**	**2 years** **3**	**5 years** **5**	**Short term follow-up (7 days, 30 days)** **16**	**Mid-term follow-up (6 months, 1 year)** **8**	**Long term follow-up (2 years, 5 years)** **8**
Wound infection	**Clinical diagnosis - history & examination**	**Wound swab**	**Clinical diagnosis & treatment**	**Draining abscess/wound**	**Clinical diagnosis +/- positive culture**				

			with oral/iv antibiotics								
	8	**5**	**2**	**1**	**1**						
Surgical site occurrence	**Clinical diagnosis - history & examination**	**CT**	**US**	**MRI**	**Fluid aspirate +/- IR drainage**						
	12	**5**	**2**	**1**	**1**						
Mesh infection - definition	**5 x suggested definitions**										
Mesh infection - detection method	**Wound swab**	**CT**	**Clinical diagnosis - history & examination only**	**Culture an explanted piece of mesh**	**US**	**MRI**	**CT PET**	**leukocyte scintigraphy**	**Intra-operative finding of pus in relation to mesh material**	**Positive percutaneous culture of aspirated fluid**	**Clinical diagnosis - wound infection with exposed mesh + positive culture from mesh**
	7	**6**	**3**	**4**	**3**	**2**	**1**	**1**	**1**	**1**	**1**
Hernia recurrence	**Clinical examination +/- CT**	**CT**	**Clinical examination +/- CT +/- USS**	**Clinical exam +/- CT during straining**	**Telephone/Questionnaire - followed by Clinical exam +/- CT**	**Clinical exam**					
	11	**6**	**2**	**1**	**1**	**1**					
Overall modality	**CT**										
	15										

Comments		
	Yes	**No**
Statement: All post-operative complications should be recorded	**14**	**1**

	RESULTS	
Incisional hernia dataset		
Hernia defect area	**CT**	**Other**
	14	**1**

PROMs	**Yes**	**No**
Baseline PROMs should be recorded?	**14**	**0**

	7 days	**30 days**	**6 months**	**1 year**	**2 years**	**5 years**	**Short term follow-up (7 days, 30 days)**	**Mid-term follow-up (6 months, 1 year)**	**Long term follow-up (2 years, 5 years)**
When should follow-up PROMs be measured?	**1**	**6**	**3**	**10**	**3**	**6**	**7**	**13**	**9**

Appendix 21

Experts panelists taking part in our Delphi studies (ICAP and Definitions of Loss of Domain):

USA panelists:

- Mike Liang - Texas Health Science Centre
- Gina Adrales - John Hopkins Hospital, Baltimore
- Todd Heniford - Carolinas Healthcare Systems
- Mary Hawn - Stanford University Medical Center
- Kamal Itani - Veterans Affairs Boston Healthcare System
- Celia Divino - Mount Sinai School of Medicine, New York

European panelists:

- Filip Muysoms - Maria Middelares Hospital, Ghent, Belgium
- Agneta Montgomery - Skåne University Hospital Malmö, Malmö, Sweden
- Lars Jorgensen - Bispebjerg University Hospital, Copenhagen, Denmark
- Yohann Renard - Robert-Debré University Hospital, Reims, France
- Ulrich - Kantonal Hospital of Olten, Olten, Switzerland
- Salvador Morales-Conde - University Hospital 'Virgen del Rocio', Seville, Spain

UK panelists:

- Alastair Windsor – Univeristy College London Hospital
- David Sanders – North Devon District General Hospital
- Andrew de Beaux – Royal Infirmary of Edinburgh
- Jared Torkington – University College of Wales
- Neil Smart – Royal Devon and Exeter Hospital

Worldwide panelists:

- Joon P Hong - Asan Medical Centre, Seoul, South Korea
- Nabeel Ibrahim - Macquarie University Hospital, Sydney, Australia
- Adam Bottal - Groote Schuur Hospital, Cape Town, South Africa

Appendix 22

Questionnaire for a Delphi consensus for an International Classification of Loss of Domain (LOD) - instructions 1

- Please make sure you have signed the co-authors consent form and email it back to samgparker@nhs.net.
- Please read the study protocol.
- Essentially, the literature contains many different written and volumetric definitions for LOD and these are presented in the following slides.
- Importantly, we are looking for a definition of LOD for **ventral hernia**, not for inguinal or diaphragmatic hernia.
- Empty slides are available for panelists to add comments or alterations to the definitions.
- When discussing LOD often authors give an anecdotal opinion about when LOD becomes clinically significant. The final slide of this questionnaire asks panelists to choose a threshold value above which LOD becomes clinically significant.
- Please highlight your preferred definitions in RED. Then email the presentation back to samgparker@nhs.net.

Preferred written definition for LOD 1

- Chronic large irreducible hernia (highlight if preferred):
  - Large ventral defect with hernia contents set by adhesions and not reducible to the abdominal cavity

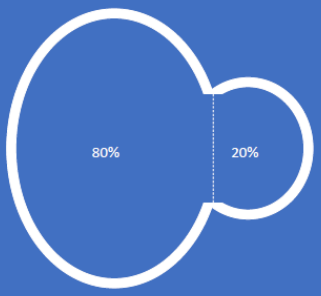
- Hernia sac forms a second abdomen (highlight if preferred):
  - Loss of domain implies that a proportion of the abdominal content resides permanently outside its natural compartment, in the hernia sac, which acts as a second abdominal cavity.

Preferred written definition for LOD 2

- Loss of the “right of domain” (highlight if preferred):
  - The hernia contents are held in place by adhesions and cannot be re-integrated into the abdominal cavity (i.e. the herniated organs have lost their "right of domain" in the abdomen).
- Pathophysiological definition (highlight if preferred):
  - Lateral migration of the rectus abdominis muscles in conjunction with flank muscle contraction leads to a progressive decrease in the volume of the abdominal cavity and worsening protrusion of the viscera.

Additional comments/feedback on what extra concepts a formal definition of “loss of domain” should contain?

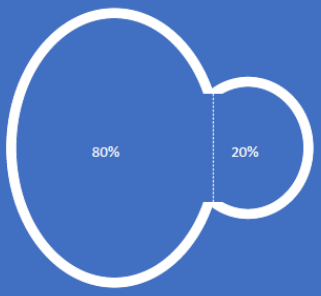
Preferred volumetric definition for LOD 1



Tanaka method (highlight if preferred):
Loss of domain = 0.25

i.e. = 20/80 = 0.25
LOD is a ratio of the 'hernia sac volume' (HSV) to 'Abdominal cavity volume' (ACV). LOD = HSV/ACV.

Preferred volumetric definition for LOD 1



Tanaka method (highlight if preferred):
Loss of domain = 0.25

i.e. = 20/80 = 0.25
LOD is a ratio of the 'hernia sac volume' (HSV) to 'Abdominal cavity volume' (ACV). LOD = HSV/ACV.

Any additional comments on how to define “loss of domain” via volumetric analysis? Do you know of any other commonly used volumetric definition?

Clinical threshold value?

- Authors use different threshold values for when LOD becomes clinically significant.
- Bearing in mind the volumetric definition you have just selected, when do you think LOD becomes clinically significant? i.e. the value above which post-operative complications (such as respiratory failure/pneumonia, wound dehiscence) become significantly more likely to occur, and at which point you might consider not operating at all:
- Write your preferred LOD threshold value below in RED:

Appendix 23

Panellist comments: Loss of Domain Delphi

Regarding the written definitions:

Panellist 1

- None are quite right. I don't think adhesions have anything to do with loss of domain. LOD is basically defined as not reducible – due to space, not adhesions.
- Also, does not necessary have to be a midline hernia. I've seen LOD with flank and ostomy site hernias.

Panellist 3

- Need to consider tissue loss (e.g. muscle resection due to tumour) , not just retraction.
- Ratio of defect width to total abdominal cavity circumference as measured at the musculoaponeurotic layer.

Panellist 4

- For me the problem is **not** adhesions ++++
- The problem comes from the volume outside the abdominal cavity and the problem of reintegration. My choice is proposition 2
- But the proposition 3 is also good but the existence of the word "adhesion" is a problem for me….
- I would rather have proposed: 'The hernia contents cannot be re-integrated into the abdominal cavity (i.e. the herniated organs have lost their "right of domain" in the abdomen)'. The choice would have be very difficult for me, between 2 and 3, if proposition 3 was written like this…

Panellist 6

- A hernia where the fascia cannot be approximated (1) even with a component separation and (2) without developing abdominal compartment syndrome
- Unlike mesh location, LOD will need evidence to be defined.

Panellist 7

- There is loss of domain that can be dealt with in contrast to irreversible loss of domain. Comorbidities, integrity of the layers of the abdominal wall, low BMI or nicotine consumption may be part of these.
- A means of staging LOD would be helpful:
    - Irreversible
    - Reversible
        - Size of tha gap and Tanakas' estimation
        - Quality of connective tissue
        - Commorbidities
        - Suitable for morphologic reconstruction (TAR / Ramirez / Botox)
        - Reversible only by enlargement of the abdominal wall

Panellist 10

- Sorry. -I have strong views on LOD. LOD for me is a volume phenomenon. It is defined as either a ratio or an absolute value as per subsequent slides. It has nothing to do with adhesions. Small hernia with adhesions is not LOD – while large hernia with no adhesions certainly is! Size of defect does not

matter. Its amazing how much colon and SB can get through a relatively small hole – but once reduced – the small defect gets bigger. As LOD increases – the girth or diameter of the original abd cavity actually gets smaller – as lateral muscles contract. You see this – large LOD and hernia down to knees – pt has flat abd when standing. Restore that to the abd cavity – and looks like a beer belly – and surgery/component separation/botox is all about increasing the diameter/girth of the abdomen. Pathophysiology statement true for midline – not for all the latertal hernias – no midline separation with nephrectomy scars etc. So I like none of the proposed definitions. See discussions later!

Panellist 12

- LOD is when the abdominal contents protrude through a hernia defect and would not be able to be reduced and allow abdominal closure

Panellist 14

- Adhesions are not always present in a large ventral hernia with LOD as observed by our group in 28 patients undergone PPP.

Panellist 15

- The pathophysiological definition is a correct statement, but it is not suitable as a definition of the condition

Panellist 16

- The amount of abdominal content in % outside the abdominal cavity that is warranted to be defined as loss of domain

Panellist 17

- The abdominal cavity is unable to fully accommodate the abdominal contents within its fascial boundaries. Closure of the fascia is either impossible, or can lead to high intra-abdominal pressures, fascial dehiscence, or abdominal compartment syndrome.

Regarding the volumetric definitions:

Panellist 2

- Both methods will require a CT scan and an experienced radiologist

Panellist 3

- Not sure either method is superior. Neither strikes me as easy to use of calculate with the everyday software we have on NHS computers. The whole debate is reminiscent of the argument about carotid stenosis measurements – "academic" in the sense of the 3rd definition in the OED – "of little practical use".
- Volumetric analysis completely misses the point of abdo wall compliance as a factor. The volumetric LODs may be equivalent, but patients will respond markedly differently due to the inherent elasticity of their abdo walls, which are governed by a myriad of factors.
- Not sure VOLUME is the correct measure. Maybe that pressure is better physiological parameter – airways pressure and intra-abdominal. This is extremely pertinent in the context of botox injections.

Panellist 6

- Need evidence. Any choice would be arbitrary right now.

Panellist 7

- The volumetric analysis needs to be supplemented by and correlated with further characteristics in order to become clinically relevant:
    - "preserved elasticity of the abdominal wall" in case of morphological reconstruction; in other words, absence or presence of scars lateral to the rectus.
    - Estimative of the expected increase of the diameter of the abdominal wall (volumetry) in case of relocation of all the extraabdominal organs. This would allow to compare the needed volume to the width-increase that can be obtained at each side by TAR or Ramirez.
    - Proportion rectus-width : defect-width as proposed by Carbonell?

Panellist 12

- Yes, if the abdomen can also not be closed primarily - this would not include the use of components separation

Panellist 14

- We have used " The Sabbagh " method since 2013 totally unaware of its existence 2016 when we were publishing our work on PPP , believing that we invented this method!

Panellist 15

- Sabbagh´s method seems easier than Tanaka´s for clinical use

Regarding the LOD threshold value:

Panellist 1

- I don't have a metric cutoff. Depends on whether primary, recurrent, what is in the hernia – amount of bowel versus omentum, etc.

Panellist 3

- Not appropriate in light of the answers above

Panellist 5

- Start to be concerned >10% - think ITU post op respiratory complications
- Be very concerned >20%

Panellist 6

- A hernia where the fascia cannot be approximated (1) even with a component separation and (2) without developing abdominal compartment syndrome. The volumetric size needs to be assessed and defined in multicenter trial.

Panellist 8

- 30% for which higher numbers would be associated with higher complication risk (but this does not mean that I would not consider operating. I would prepare the patient, possibly use pre-repair abdominal wall expansion methods such as botulinum A). I would adjust for other clinical factors such as stiffness/thickness of lateral abdominal musculature, COPD- may shoose a lower threshold as patient may not tolerate as well the restoration of the abdominal contents.

Panellist 10

- From my point of view, absolute value not that relevant. You could have a 40 % LOD in a morbidly obese midline incisional hernia – weight loss and botox could reduce this to 20 % - but also gained intra-abdominal vol from the weight loss – so easy to repair abdominal wall without much change in IAP. Could have 15 % in thin person, transverse wound – and no room for weight

loss and not so sure about Botox, so looking at resection/or elongation of other muscles such as component separation. I have rough rule of thumb – every 3 kg of total body weight lost, gain approx. 1 litre of intra-abd vol. Varies a bit if fat all over or more central obesity.

- So when reporting – are you reporting initial LOD, or prior to surgery – and how do you measure that – preop CT. 2 CT for benign disease?? So a bit more thought required here. It's a volume thing for sure – but also how modifiable is the LOD prior to surgery.

Panellist 11

- I also take into consideration other factors such as age, body habitus of the patient, height comorbidities that can influence ability of patient to compensate over time and affect their quality of life after surgery.

Panellist 12

- LOD is clinically significant simply because it exists – no symptoms are necessary

Panellist 14

- In our practice, 20% LOD is considered to be clinically significant, and about the level a range of pre-operative preparation is utilized including BTA Comp Relaxation as well as PPP.
- We have successfully operated on many patents with LOD between 50 -60 % , achieving mid line or near mid-line closure , either laparoscopic and laparoscopic assisted with endoscopic CS .
- We have declined surgery to only 3 patents out of approx. 120 patents with LOD of 30-40% , due to co-morbidities .
- Patients selection relevant to LOD should be carried out on a case by case basis and on clinical grounds , at the surgeons discretion , rather than defining ridged guidelines.

Panellist 15

- Clinically significant: Sabbagh´s ratio > 25%. This does not necessarily mean that I would not operate the patient. It rather reflects that I would tend to use preop. BTA and perhaps add component separation in these cases. There is no clear definition for me in terms of a specific cut-of level of Sabbagh's ratio, where I would avoid surgery. It depends on many other clinical parameters of the patient.

Panellist 17

- I discuss the case with the anesthesiologist and the patient. I tailor my decision.

Appendix 24

Amalgamation of suggested definitions to create a new written definition for loss of domain.

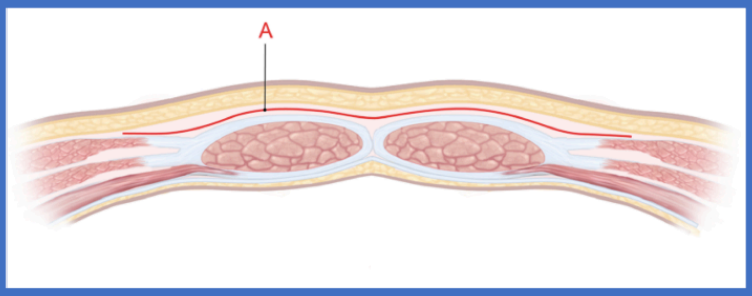
Many alternatives suggested - Panelists asked to select all the definitions they agreed with.	**Round 2 (%)**		Concept 1: Irreducible due to lack of space	Concept 2: Primary facial closure cannot be achieved without an augmentation technique	Concept 3: Primary closure would lead to compartment syndrome
1. Hernia sac forms a second abdomen	11 (55%)	Outdated			
2. Lateral retraction of the rectus abdominis and the abdominal strap muscles.	6 (30%)	Physiological definition			
New suggested definitions					
3. A hernia where the fascia cannot be approximated even with component separation.	1 (5%)		Yes		
4. Irreducible hernia due lack of space or volume.	6 (30%)		Yes		
5. LOD is when the abdominal contents protrude through a hernia defect and is not able to be reduced and allow for abdominal closure.	3 (15%)		Yes		
6. Irreversible/Reversible loss of domain. Irreversible - the viscera cannot be replaced into the abdominal cavity by any technique. Reversible loss of domain means the ventral hernia can be reconstructed using any technique.	5 (25%)		Yes	Yes	
7. Loss of domain is when the abdomen cannot be closed primarily without the help of any augmentation technique.	8 (40%)			Yes	
8. A hernia where the fascia cannot be approximated without developing abdominal compartment syndrome.	3 (15%)				Yes
9. Closure of the fascia is either impossible, or can lead to high intra-abdominal pressures, fascial dehiscence, or abdominal compartment syndrome.	15 (75%)				Yes

Appendix 25

Questionnaire for a Delphi consensus study for the International Classification of Abdominal wall Planes (ICAP)

- Please make sure you have signed the co-authors consent form and have emailed it back to samgparker@nhs.net.
- Please read the study protocol.
- Each slide depicts an abdominal wall plane. Please select your preferred term by highlighting the term in RED.
- Please use the free text box to add any alternative terms AND (if necessary) to suggest a changes to the format of the questionnaire.
- Please email your questionnaire to samgparker@nhs.net once it has been filled in.
- N.B. We have included all possible abdominal wall planes, both ones that are and ones that aren't commonly used for Abdominal Wall Reconstruction.

Plane A

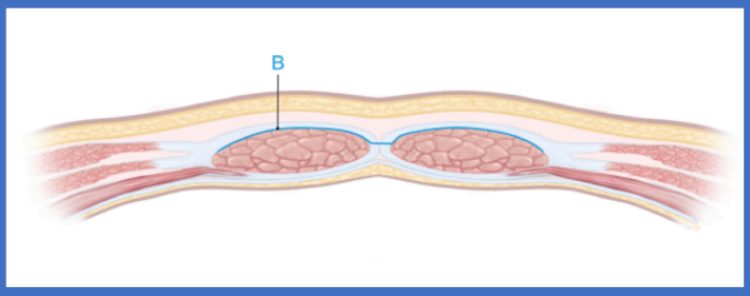


Onlay
Preaponeurosis
Prefascial
Premuscular
Prelay
Prerectus
Subcutaneous
Supraaponeurotic

Alternative term:

Comments:

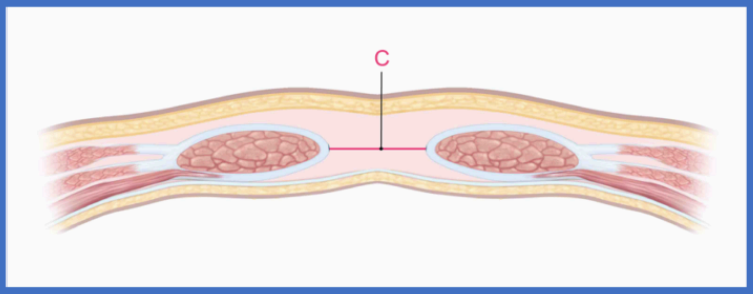
Plane B



Anterectus
Prerectus
Retroaponeurotic

Alternative term:
Comments:

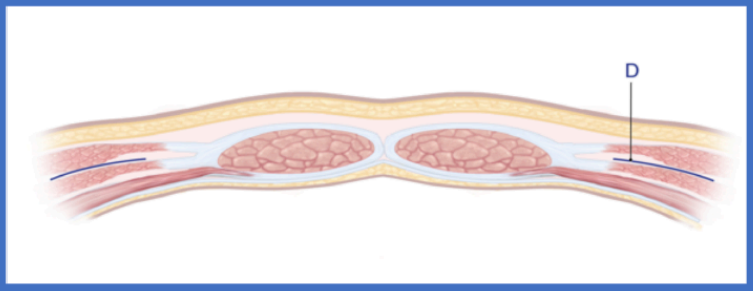
Plane C



Bridging
Inlay
Interaponeurotic
Interfascial
Interlay
Interposition
Intralay
Intramuscular
Transrectus

Alternative term:
Comments:

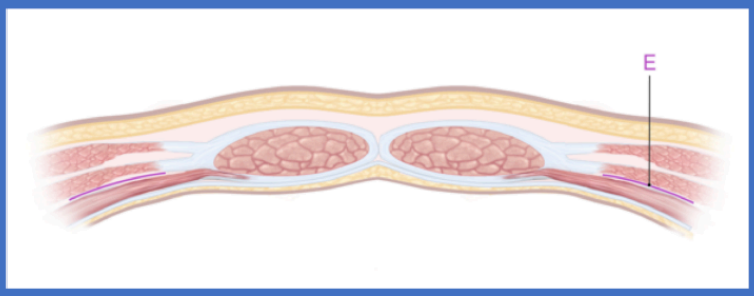
Plane D



Interoblique
Intraoblique

Alternative term:
Comments:

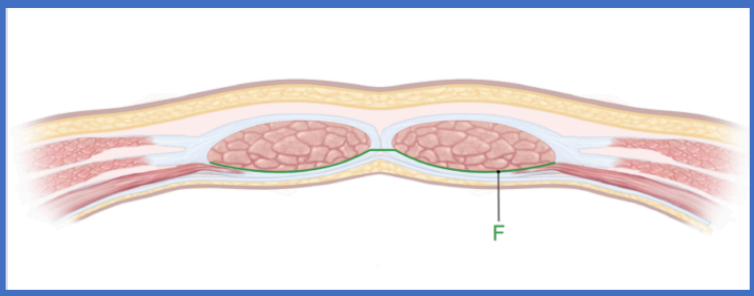
Plane E



Neurovascular
Retro-oblique

Alternative term:
Comments:

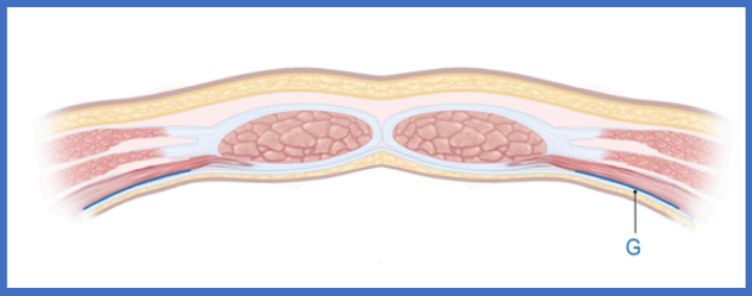
Plane F



Inlay
Postrectus
Rives-Stoppa
Retromuscular
Retrorectal
Retrorectus
Sublay
Underlay

Alternative term:
Comments:

Plane G

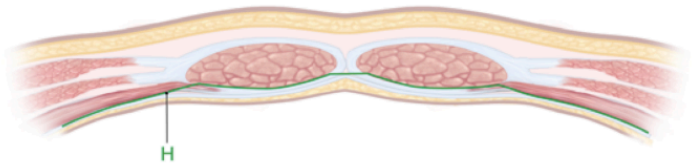


Retromuscular
Transversalis
Transversalis fascial
TAR
Underlay

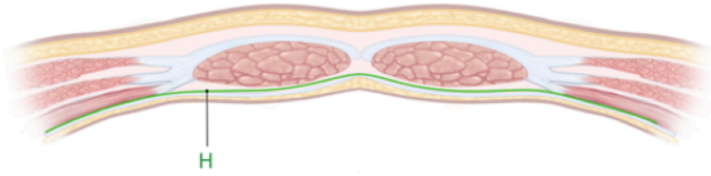
Alternative term:
Comments:

Plane H

Cranial



Caudal (inferior to the arcuate line)



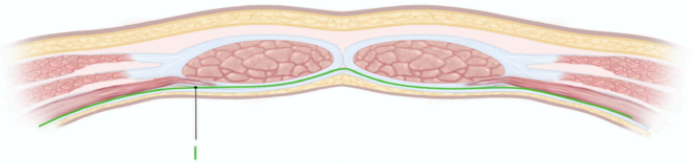
Inlay
Retromuscular
Sublay
TAR
Underlay

Alternative term:

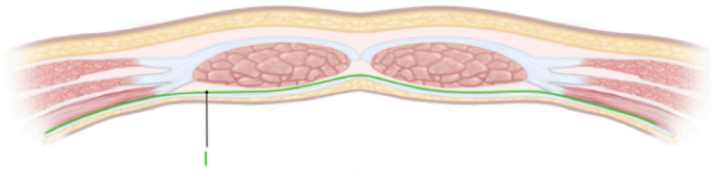
Comments:

Plane I

Cranial



Caudal (inferior to the arcuate line)

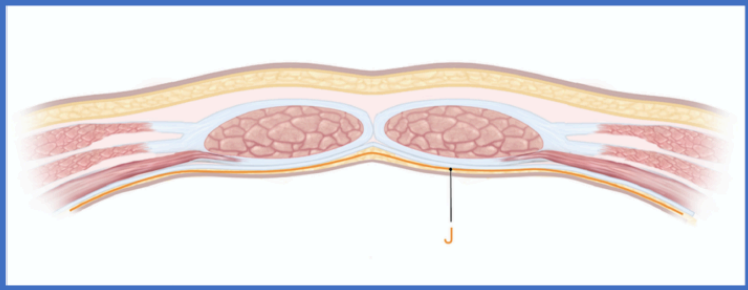


Prefascial
Retroaponeurotic
Sublay
TA
Transversalis
Transversalis fascial
Underlay

Alternative term:

Comments:

Plane J

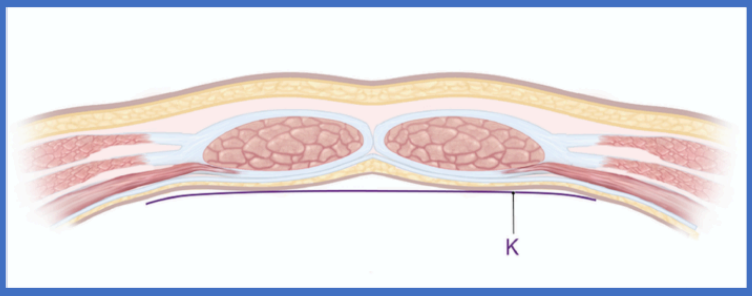


Extraperitoneal
Preperitoneal
Retromuscular
Subfascial
Sublay
Underlay

Alternative term:

Comments:

Plane K



Intraabdominal
Intraperitoneal
IPOM
Underlay

Alternative term:

Comments:

Any additional comments?

Appendix 26

Final list of terms (no duplicates)

1. Onlay
2. Preaponeurosis
3. Prefascial
4. Premuscular
5. Prelay
6. Prerectus
7. Subcutaneous
8. Supraaponeurotic
9. Anterectus
10. Prerectus
11. Retroaponeurotic
12. Bridging
13. Inlay
14. Interaponeurotic
15. Interfascial
16. Interlay
17. Interposition
18. Intralay
19. Intramuscular
20. Transrectus
21. Interoblique
22. Intraoblique
23. Neurovascular
24. Retrooblique
25. Postrectus
26. Rives-Stoppa
27. Retromuscular
28. Retrorectal
29. Retrorectus
30. Sublay
31. Underlay
32. Transversalis
33. Transversalis fascial
34. TAR
35. Transversus abdominis
36. Extraperitoneal
37. Preperitoneal
38. Subfascial
39. Intraabdominal
40. Intraperitoneal
41. IPOM

Final list of terms for each plane, including duplicates (i.e. one term can be used to refer to different planes).

Plane A

1. Onlay
2. Preaponeurosis
3. Prefascial
4. Premuscular
5. Prelay
6. Prerectus
7. Subcutaneous
8. Supra-aponeurotic

Plane B

9. Anterectus
10. Prerectus
11. Retro-aponeurotic

Plane C

12. Bridging
13. Inlay
14. Interaponeurotic
15. Interfascial
16. Interlay
17. Interposition
18. Intralay
19. Intramuscular
20. Transrectus

Plane D

21. Interoblique
22. Intraoblique

Plane E

23. Neurovascular
24. Retro-oblique

Plane F

25. Inlay
26. Postrectus
27. Rives-Stoppa
28. Retromuscular
29. Retrorectal
30. Retrorectus
31. Sublay
32. Underlay

Plane G

33. Retromuscular
34. Transversalis
35. Transversalis fascial
36. TAR
37. Underlay

Plane H

38. Inlay
39. Retro-muscular
40. Sublay
41. TAR
42. Underlay

Plane I

43. Prefascial
44. Retro-aponeurotic
45. Sublay
46. TA
47. Transversalis
48. Transversalis fascial
49. Underlay

Plane J

50. Extra-peritoneal
51. Preperitoneal
52. Retro-muscular
53. Subfascial
54. Sublay
55. Underlay

Plane K

56. Intraabdominal
57. Intraperitoneal
58. IPOM
59. Underlay

Appendix 27

Results of voting for Rounds 1 to 3 of the Delphi process for abdominal wall planes. *Extra terms added to the Delphi process by panellists. **Term added in by panellist in round 3 against protocol. IO: internal oblique, EO: external oblique, TA: transversus abdominis, TAR: transversus abdominis release.

Abdominal wall plane: anatomical description	Descriptive term	Round 1 (%)	Round 2 (%)	Round 3 (%)
Plane A: Anterior: subcutaneous tissue. Posterior: anterior sheath. and external oblique	Onlay	18 (90)	**18 (90)**	**20 (100)**
	Preaponeurosis	-		
	Prefascial	1 (5)		
	Premuscular	-		
	Prelay	-		
	Prerectus	-		
	Subcutaneous	-		
	Supraaponeurotic	-		
Extra terms*	Medial 1 and Lateral 1	1 (5)	2 (10)	
Plane B: Anterior: anterior sheath. Posterior: rectus muscle.	Anterectus	8 (40)	8 (40)	**20 (100)**
	Prerectus	9 (45)	10 (50)	0 (0)
	Retroaponeurotic	2 (10)		
Extra terms*	Medial 2	1 (5)	2 (10)	
Plane C: Mesh attached to edges of hernia defect, no mesh overlap.	Bridging	6 (30)	2 (10)	
	Inlay	12 (60)	**16 (80)**	**20 (100)**
	Interaponeurotic	-		
	Interfascial	-		
	Interlay	-		
	Interposition	-		
	Intralay	-		
	Intramuscular	-		
	Transrectus	1 (5)		
Extra terms*	Medial 0	1 (5)	2 (10)	
Plane D: Anterior: EO. Posterior: IO.	Interoblique	14 (70)	9 (45)	**20 (100)**
	Intraoblique	3 (15)		
Extra terms*	Between EO & IO	1 (5)	3 (15)	
	Lateral 2A	1 (5)	2 (10)	
	Preinternal oblique		-	
	Retroexternal oblique	1 (5)	1 (5)	
	Intramuscular: EO & IO		-	
	Intermuscular: EO & IO		5 (25)	0 (0)
Plane E: Anterior: IO. Posterior: TA	Neurovascular	1 (5)		
	Retrooblique	14 (70)	9 (45)	**20 (100)**
Extra terms*	Retrointernal oblique	1 (5)	1 (5)	
	Pre/Ante-transversus abdominis	1 (5)	-	
	Lateral 2B	1 (5)	2 (10)	
	Intramuscular: IO & TA	1 (5)	1 (5)	
	Intermuscular: IO & TA		4 (20)	0 (0)
	Between IO & TA	1 (5)	3 (15)	
Plane F: Anterior: rectus muscle. Posterior: posterior sheath	Inlay	-		
	Postrectus	-		
	Rives-Stoppa	-		
	Retromuscular	5 (25)	3 (15)	
	Retrorectal	-		

	Retrorectus Sublay	11 (55) 2 (10)	15 (75)	**<u>20 (100)</u>**
Extra terms*	Underlay Medial 3	1 (5) 1 (5)	2 (10)	
Plane G: Anterior: TA. Posterior: transversalis fascia.	Retromuscular Transversalis Transversalis fascial TAR Underlay	6 (30) 1 (5) 2 (10) 6 (30) -	3 (15) 5 (25)	 N/A
Extra terms*	Lateral 3 Retrotransversus Pretransversalis Lateral retromuscular TAR	1 (5) 1 (5) 1 (5) 2 (10)	2 (10) 4 (20) - 6 (30) -	 N/A N/A
Plane H: Anterior: rectus muscle and TA. Posterior: posterior sheath and transversalis fascia.	Inlay Retromuscular Sublay TAR Underlay	- 8 (40) - 6 (30) -	 8 (40) 1 (5)	 **<u>16 (80)</u>**
Extra terms*	Medial 3 and Lateral 3 Retromuscular sublay Retromuscular with TAR Retro-transversus Pre-transversalis No vote	1 (5) 1 (5) 3 (15) 1 (5) -	2 (10) 1 (5) 7 (35) 1 (5) -	 3 (15) 1 (5)
Plane I: Anterior: posterior sheath and TA. Posterior: transversalis fascia.	Prefascial Retroaponeurotic Sublay Transversus abdominis Transversalis Transversalis fascial Underlay	- 1 (5) 2 (10) 1 (5) 1 (5) 4 (20) 2 (10)	 6 (30) 	 **<u>17 (85)</u>**
Extra terms*	Medial 4a and Lateral 4a TAR Retromuscular without TAR Interfascial Retromuscular & pretransversalis extension Pretransversalis fascial Retromuscular Preperitoneal Preperitoneal & pretransversalis extension No vote	1 (5) 1 (5) 1 (5) 1 (5) 2 (10) 2 (10)	2 (10) - 2 (10) 1 (5) 3 (15) 1 (5) - 3 (15) 1 (5) 1 (5)	 1 (5)** 2 (10)
Plane J: Anterior: transversalis fascia. Posterior: peritoneum.	Extraperitoneal Preperitoneal Retromuscular Subfascial Sublay Underlay	1 (5) 14 (70) 1 (5) - 1 (5) 2 (10)	 **<u>18 (90)</u>** 	 **<u>20 (100)</u>**

Extra terms*	Medial 4b and Lateral 4b	1 (5)	2 (10)	
Plane K: Anterior: peritoneum. Posterior: abdominal cavity. Extra terms*	Intraabdominal Intraperitoneal IPOM Underlay Medial 5 and Lateral 5	- 15 (75) 3 (15) 1 (5) 1 (5)	**18 (90)** 2 (10)	**20 (100)**

Appendix 28

Round 1 – Comments

Plane A

Panellist 6
- Second choice – Onlay

Panellist 7
- Onlay (pragmatic)
- Prefascial (anatomical)
- the striked words are wrong from the perspective of the Terminologia Anatomica and should not be perpetuated in the literature.
  ~~Premuscular~~
  ~~Prelay~~
  ~~Prerectus~~
  ~~Supra-aponeurotic~~

Panellist 8
- This looks to be within the anterior fascia but I assume on top which I would designate as onlay. Otherwise if intended as the fascial layer I would designate as anterior fascia.

Panellist 17
- I would suggest to join onlay with the position in this plane and in the next one

Plane B

Panellist 6
- Second choice – Antrectus

Panellist 7
- In latin, ante- and pre- are synonymous, but pre- is preferentially used for describing something that is anterior to. Ex: Pretracheal, prevertebral, preauricular, precordial, prepatellaris, etc. I favour prerectus.

Panellist 10
- Rare event – but have occassionally gone here. Not really happy with any of the terms, but anterectus snappy, and ?? cannot think of a better one.

Plane C

Panellist 6
- Second choice – Inlay

Panellist 7
- The terminology should follow the anatomical principles across all definitions. Inter = between
  ~~Interlay~~
  ~~Intralay~~
  ~~Intramuscular~~
  ~~Transrectus~~

Panellist 8

- Inlay first choice, bridging mesh second choice

Panellist 10

- Modern man so going with European terminology to upset USA. Avoid term bridging here – it is – but bridging mesh can go in a variety of planes so bridging does not describe mesh position, with zero overlap.

Panellist 12

- Bridging – I choose this so it can be used in combination with other terms well, i.e. – a bridging or bridged retrorectus repair

Panellist 17

- We could suggest to use inlay but using the concept of bridging, as it is explain in the table after, use bridging adding what is being bridged, the edge of the sac, the anterior aponeurosis or the posterior aponeurosis

Plane D

Panellist 3

- Needs a "Ronseal" term – does what it says on the tin i.e. between the external and internal oblique

Panellist 4

- I would have added these 2 terms: intramuscular and intermuscular

Panellist 6

- Second choice - Sublay (external oblique)

Panellist 7

- Intra is absolutely wrong according to its latin meaning.

Panellist 8

- The ext, int and transversus abdo are considered by some to be the obliques which would warrant more specification here. To be anterior to the internal oblique- I think that would be less confusing and more exact.

Panellist 10

- Inter better – as between – not in the muscle.

Panellist 12

- Neither of the terms are not specific enough to describe which layer of the obliques is being used

Plane E

Panellist 3

- Needs a "Ronseal" term – does what it says on the tin i.e. between the internal oblique and the transversus abdominis

Panellist 4

- I would have add these 2 terms: intramuscular and intermuscular

Panellist 5

- This plane is not commonly used

Panellist 6

- Second choice – Sublay (internal oblique)

Panellist 8

- Pre or ante-transversus. This is the neurovascular plane but not all (such as trainees) may recognize this so a description based on the muscle may be more clear to many.

Panellist 12

- Neither of the terms are not specific enough to describe which layer of the obliques is being utilized

Plane F

Panellist 6
- Second choice: Sublay (rectus)

Plane G

Panellist 3
- Needs a “Ronseal” term – does what it says on the tin i.e. Lateral retromuscular or retrotransversus

Panellist 4
- Lateral pre-peritoneal should be proposed

Panellist 6
- Second choice: Sublay (transversus abdominus)

Panellist 12
- TAR is a technique. The terms are not specific enough to describe which layer of the obliques

Plane H

Panellist 6
- Second choice: Sublay (rectus and transversus abdominus)

Panellist 10
- I prefer accurate description. Mesh place behind the rectus muscles, anterior to the posterior rectus sheath, and continued out laterally behind the TA muscle.

Panellist 12
- There being a bit of the Transversalis muscle cut is technical, not mesh placement

Panellist 19
- Tricky!

Plane I

Panellist 3
- This is what some surgeons call “pre-peritoneal”. The difference between this and a TAR is negligible as far as I have ever been able to ascertain. The debate is about how medial the incision is made to release TA. The reality is that people are arguing over 5mm and the plane where the mesh sits is essentially the same.

Panellist 4
- The proposition TA is TAR ? If yes, it is my choice. If not I don’t know what TA means

Panellist 6
- Second choice: Sublay (pre-transversalis fascia)

Panellist 7

- The Plane ”l” is a virtual plane between H and J. As an anatomist, I don’t know this plane from cadaveric dissection or at least don’t know how to differentiate it in the fibers’ intersection at linea alba. As surgeon, I would not be sure. Not one from the offered alternatives is anatomically correct to define the plane between the aponeurosis of the transversus abdominis and the aponeurosis of the internal oblique. I’m unable to select any alternative. Interfascial would be theoretically adequate.

Panellist 10

- Probably possible – but never seen or heard of anyone doing this!

Panellist 12

- It is hard for me to tell where this mesh is supposed to be in this picture. Is it retro-rectus and then preperitoneal? This is what we called the preperitoneal extension of the retro-rectus repair?

Panellist 14

- A distinction between pure anatomical and surgical perspective terminology is needed.

Panellist 15

- This one was difficult….

Panellist 19

- Tricky!

Plane J

Panellist 6

- Second choice: Sublay (preperitoneal)

Panellist 7

- It is the plane of TEP/TAPP and ventral-TAPP
- Preperitoneal (1st), Subfascial (2nd), Underlay (pragmatic)

Panellist 8

- This is an underlay mesh but the designation as intraperitoneal further specifies this.

Plane K

Panellist 6

- Second choice: Underlay

Panellist 7

- In anatomy the peritoneum is defined to be inside de abdominal cavity (it is intraabdominal) Consequently, plane k is intraperitoneal.

Panellist 10

- IPOM means you have to be in the gang to know the jargon!

General Comments – Abdominal Planes:

Panellist 1

- A taxonomy is definitely needed! I think the more specific, the better.

Panellist 2

- It is obvious where the confusion comes from. I hope we can agree on the terms

Panellist 3

- You have missed out the plane proposed by Alfie Carbonell that extends from the Retrorectus space into the plane between IO & TA (see what I did there ☺ ?). This “posterior components separation” creates a different plane to either of those from Heniford or Novitsky.
- Carbonell AM, Cobb WS, Chen SM. Posterior components separation during retromuscular hernia repair. Hernia. 2008 Aug;12(4):359-62. doi: 10.1007/s10029-008-0356-2. Epub 2008 Feb 22.

Panellist 5

- I think there is a danger of having too many terms and the terms should be limited to the more common planes.

Panellist 6

- Does this classification apply to inguinal hernias? It should.

Panellist 7

- Medical and surgical terminology may have three main origins:
- it may parallel and correlate to vocabulary we use in every days communication (pragmatic definitions: ex. onlay or inlay, augmentation, IPOM, etc.); these terms are usually launched by surgeons who create and describe new techniques, but these terms will often not endure a critical terminology challenge.
- terminology may follow accepted international rules, as it is the case for the latin principles of Terminologia Anatomica (late Nomina Anatomica). Surgery is applied anatomy. We should invest every effort to follow the anatomical terminology.
- eponyms and acronyms are helpful in summarizing complex procedures, for example, Lichtenstein, Shouldice, McVay, etc. Maybe TAR-plane can become such a term.
- Last reminder: in times of electronic data-mining (registries, etc) it would be very important, that each term in hernia surgery is related to only one unique meaning.

Panellist 10

- Problem is legacy of old terminology. Pre-peritoneal been around so long that it wont change. In general – describing what layer is immediately in front or behind mesh helps/sensible. Hence trying to go with ante or retro in the terminology. Then in unusual cases may need to be more descriptive but using the terms defined – mesh laterally, behind recti and then lateral again. So could be retromuscular with inter oblique on the right and retro-TA on the left.

Panellist 14

- Efforts must be made to make terminology of surgical planes as simple as possible and less confusing fitting in with real life surgical mindset and perspective , rather than pure anatomical planes which may be variable or doesn’t exist, particularity in a complex ventral hernia setting .
- Surgical plane below the arcuate ligament and deep to the rectus , to avoid hair splitting should be referred to as pre- preperitoneal.

Panellist 17

- This could be an alternative interesting systematic to describe the position, recommending to introduce the “name” and the “last name”.

• *ONLAY*	• *Supraaponeurotic*
•	• *Retroaponeurotic*
• *INLAY*	• *Bridging Hernia sac*
•	• *Bridging Anterior fascia*
•	• *Bridging Posterior fascia*
• *SUBLAY*	• *Retromuscular*
•	• *Retromuscular with TAR*
•	• *Preperitoneal*
• *INTRAPERITONEAL*	•

Appendix 29

General Search

(((((((("General Surgery"[MESH]) OR "Reconstructive Surgical Procedures"[MESH]))
OR ((("pneumoperitoneum"[Title/Abstract]) OR "botox"[Title/Abstract]) OR "botulinium"[Title/Abstract])) OR ((((("two stage"[Title/Abstract]) OR "stage repair"[Title/Abstract]) OR "staged repair"[Title/Abstract]) OR "two step"[Title/Abstract])) OR ((("component separation"[Title/Abstract]) OR "transversus
abdominis"[Title/Abstract]) OR "retrorectus"[Title/Abstract])) OR ((((("bridging"[Title/Abstract]) OR "bridge repair"[Title/Abstract]) OR "bridged repair"[Title/Abstract]) OR "silo"[Title/Abstract])) OR (("open"[Title/Abstract]) OR "laparoscopic"[Title/Abstract]))) AND (((((((hernia[Title/Abstract]) OR "abdominal wall defect"[Title/Abstract]) OR "abdominal wall reconstruction"[Title/Abstract]) OR "ventral defect"[Title/Abstract]) OR "enterocutaneous fistula"[Title/Abstract])) OR ("Hernia"[Mesh] OR "Hernia, Abdominal"[Mesh] OR "Hernia, Ventral"[Mesh] OR "Hernia, Umbilical"[Mesh]))

Filters: Publication date from 1995/01/01 to 2017/12/31; Humans; English; Adult: 19+
Years

Prognostic/Predictive studies search

((((ventral hernia[MeSH Terms]) OR abdominal hernia[MeSH Terms])) AND (((predictive[Title/Abstract]) OR predictor[Title/Abstract]) OR factor[Title/Abstract])) AND ((recurrence[Title/Abstract]) OR recurrent hernia[Title/Abstract])

Filters: Publication date from 1995/01/01 to 2017/12/31; Humans; English; Adult: 19+ Years

Appendix 30

Risk of Bias (ROB) criteria based on PROBAST.

Possible answers: Yes (Y), probably yes (PY), probably no (PN), No (N), or No information (NI).

Participants	
Risk of Bias	
1.1: Were appropriate data sources used, e.g. cohort, RCT or nested case-control study data?	HIGH risk: Case-control studies Low risk: RCTs, cohort studies, database studies
1.2: Were all inclusions and exclusions of participants appropriate?	High risk: Studies including some emergency repairs some paediatric hernia repairs (only if participants were 10% emergency repairs, 10% paediatric repairs were the studies included), studies with primary hernias only. Low risk: Studies of elective ventral hernia repair (incisional only, and incisional & primary VH)
1.3: Were patients with severe disease included in analysis?	High risk: Severe disease defined as ventral hernias with a diameter of >10cm, or with active contamination (VHWG grade 4). If studies only included ventral hernias with severe disease then defined as high risk. Low risk: Studies including ALL ventral hernias (as our prognostic model wants to applied to ALL VHs)
Risk of bias introduced by selection of participants (low, high, unclear)	**High: Any of the domains answer is N or PN** **Unclear: All domains answer Y or PY or NI** **Low: All domains answered Y or PY**
Applicability	
Concern that the included participants and setting do not match the review question	High: Demographics or comorbidity limitations for study participants (e.g. diabetics, sex etc). If study is primary ventral hernia only, or contains 10% either emergency or paediatrics hernia repairs. If study contains hernias <5cm in diameter only. Unclear: If inclusion criteria are 'unclear' Low: If >5cm diameter incisional ventral hernia with or without primary ventral hernia
Predictors	
Risk of Bias	
2.1: Were predictors defined and assessed in a similar way for all participants?	High risk: Patient questionnaire, telephone consultation, non-clinician collecting predictor data (including filling database information), if multiple methods used. Low risk: Medical records, clinical notes, medical database, clinical review, imaging
2.2: Were predictor assessments made without knowledge of outcome data?	High risk: Retrospective data collection outcome data is likely to be present. Some predictors open to bias if outcome data known eg Predictors such as hernia characteristics (contamination status, width, LoD, wound infection/events). Low risk: Prospective data collection, Prospective maintained database – retrospectively reviewed – benefit of the doubt
Risk of bias introduced by predictors or their assessment	**High: Any of the domains answer is N or PN** **Unclear: All domains answer Y or PY or NI** **Low: All domains answered Y or PY**

Applicability	
Concern that the definition, assessment or timing of predictors in the model do not match the review question	High: Concern may be raised if a predictor was measured/detected outside standard clinical practice for example: smoking status using urine cotinine, COPD diagnosis using spirometry etc… Unclear: If there was little information about how predictors were assessed and defined and predictors were not discrete. Low: Our review question is relatively generalised with few specifics on predictor requirements eg. detection methods or definitions or timing of predictor evaluation.
Outcomes	
Risk of Bias	
3.1: Was the outcome determined appropriately?	High risk: Patient questionnaire, telephone questionnaire, medical records, and re-operation rate Low risk: Clinical detection of hernia recurrence e.g. clinical examination, US scan and CT
3.2: Was a pre-specified or standard outcome definition used?	High risk: If there is reason to suspect that a definition has been chosen so the study gets a positive results Low risk: If a pre-specified or standardised definition is used No information: No definition
3.3: Were predictors excluded from the outcome definition?	High risk: If recurrence definition includes a predictor variable Low risk: Likely to be low for all studies; currently no definition that includes a predictor variable
3.4: Was the outcome defined and determined in a similar way for all participants?	High risk: If multiple different methods used to detect the outcome (e.g. telephone and questionnaire). If multiple different reporters (non-consultants) detect recurrence (outcome) LOW risk: Same detection method for recurrence for all participants
3.5: Was the outcome determined without knowledge of predictor information?	High risk: In prospective trials where the outpatient assessor was unblinded, retrospective data collection where knowledge of the outcome is likely to be present. Low risk: Prospective trials with blinded outpatient assessment; includes independent blinded radiological assessment. Trials with no difference in abdominal scarring.
3.6: Was the time interval between predictor assessment and outcome determination appropriate?	High risk: Follow-up of less than 6 months, difference in follow-up in treatment arms of >4.5 months. Low risk: Follow-up of ≥6 months.
Risk of bias introduced by the outcome or its determination	**High: Any of the domains answer is N or PN** **Unclear: All domains answer Y or PY or NI** **Low: All domains answered Y or PY**
Applicability	
Concern that the outcome, its definition, timing or determination do not match the review question	High: Some studies may include bulging in their definition for recurrence. Bulging has no abdominal wall defect and therefore is outside the definition for recurrence. Unclear: No information about how recurrence was defined or detected. Low: Our review question includes all different definitions for recurrence that imply there is an abdominal wall defect.

Analysis	
Risk of Bias	
4.1: Were there a reasonable number of participants with the outcome? >10 events	High risk: <10 events per variable (if multivariate analysis performed). This will be the case from most studies. Low risk: ≥10 events per variable (if multivariate analysis performed), if univariate analysis performed only 10 events required.
4.2: Were all enrolled participants included in the analysis?	High risk: >10% of participants not included due to loss to follow up or another systematic reason (like missing data). Low risk: If this is <10% and there appears to be no selection or inclusion criteria for the final analysis
4.3: Were participants with missing data handled appropriately?	Not rated as not reported in any articles
4.4: Did they report estimates from at least 3 standard clinical variables, or justify why not?	High risk: Less than 3 of the standard clinical variables below reported* Low risk: At least 3 of the standard clinical variables below reported*
4.5: Were at least 3 predictor estimates reported with non-statistically significant results?	High risk: ≤2 predictor estimates with no statistical Low risk: ≥3 predictor estimates with no statistical significance
Risk of bias introduced by the analysis	**High: Any of the domains answer is N or PN** **Unclear: All domains answer Y or PY or NI** **Low: All domains answered Y or PY**
Overall judgement	
Overall judgement of risk of bias	**HIGH if risk of bias for any domain is HIGH** **LOW if risk of bias for all domains is LOW** **UNCLEAR if risk of bias for one or more domains is UNCLEAR and the other domains are all rated as LOW**
Overall judgement of applicability	**HIGH if concern for applicability for any domain is HIGH** **LOW if concern for applicability for all domains is LOW** **UNCLEAR if concern for applicability one or more domains is UNCLEAR and the other domains are all rated as low**

*Standard pre-operative clinical variables that should be reported:

Age

BMI

COPD

Smoker

Diabetes

Primary hernia or Incisional hernia

Previous hernia repair

Hernia defect size area/width

Appendix 31 – Recruitment

Study characteristics			
Study		**Recruitment**	
Name/year	**Country**	**Dates**	**Notes**
Sadava 2016	Argentina		
Pring 2008	Australia		
Werkgartner 2014	Austria	Nil	
Kohler 2015a	Austria	Jan 2009 to Oct 2013	Primary - no overlap
Kohler 2015b	Austria	2009 to 2013	Incisional - no overlap
Muysoms 2013	Belgium		
Berrevoet 2011	Belgium	Feb 2004 to Apr 2007	Primary - no overlap
Berrevoet 2010	Belgium	March 2000 to Apr 2006	Incisional - no overlap
Bontinck 2014	Belgium	Apr 2009 to Dec 2011	
Lahon 2009	Belgium	Jan 2003 to Feb 2007	
Hauters 2017	Belgium	2001 to 2014	
Chelala 2016	Belgium	Oct 2000 to Mar 2014	
Tollens 2011	Belgum	May 2004 to Feb 2009	
Park 1998	Canada		
Dinh Le 2013	Canada	Apr 2008 to Dec 2011	
Birch 2007	Canada	Aug 1999 to Jun 2004	
Chan 2005	Canada	Jan 1999 to Dec 2000	
Han 2007	China		
Vidovic 2006	Croatia		
Christoffersen 2015a	Denmark	Jan 2008 to Jan 2012	LIKELY OVERLAP WITH **HELGSTRAND 2013**
Christoffersen 2015b	Denmark	Jan 2008 to Dec 2010	LIKELY OVERLAP WITH **CHRISTOPHERSEN 2013**
Westen 2014	Denmark	Jan 2000 to Dec 2004	
Christoffersen 2013	Denmark	Jan 2007 to Dec 2010	LIKELY OVERLAP WITH **CHRISTOPHERSEN 2015b**
Helgstrand 2013	Denmark	Jan 2007 to Dec 2010	LIKELY OVERLAP WITH **CHRISTOPHERSEN 2015a**
Oma 2017	Denmark	Jan 2007 to Apr 2013	LIKELY OVERLAP WITH **CHRISTOPHERSEN 2015a, 2015b, 2013,** and **HELGSTRAND 2013** but ONLY FEMALES included
Kokotovic 2016	Denmark	Jan 2007 to Dec 2010	OVERLAP WITH **HELGSTRAND 2013** BUT **LONGER FOLLOW UP**
Bessa 2015	Egypt		
Afifi 2005	Egypt		

Youssef 2007	Egypt		
Bensaadi 2014	France	Jan 2007 to Aug 2011	
Luc 2014	France	Jan 2004 to Dec 2012	
Romain 2016	France	Jan 2010 to May 2013	Two different hospitals same university - no overlap
Mercoli 2017	France	2005 to 2014	Two different hospitals same university - no overlap
Bageacu 2002	France	Jan 1993 to Dec 1998	
Aura 2002	France	Jul 1994 to Oct 2001	
Renard 2017	France	Sep 2007 to Apr 2013	
Demetrashvili 2017	Georgia		
Korenkov 2002	Germany	1997 to 1999	SAME DATASET AS **SAUERLAND 2004**
Conze 2005	Germany	Jun 1999 to Dec 2000	
Schmidbauer 2005	Germany	Jan 1996 to Dec 2001	
Meyer 2015	Germany	Jan 2006 to Jan 2011	
Scheuerlein 2011	Germany	Jan 2008 to July 2010	
Wolter 2009	Germany	Jun 2004 to June 2006	
Langer 2005a	Germany	1976 to 2001	SAME DATASET AS **LANGER 2005b**
Sauerland 2005	Germany	1990 to 1999	
Dietz 2014	Germany	Jan 1999 to Dec 2006	
Sauerland 2004	Germany	1997 to 1999	SAME DATASET AS **KORENKOV 2002**
Lauscher 2013	Germany	Dec 2006 to Apr 2009	
Langer 2005b	Germany	1976 to 2001	SAME DATASET AS **LANGER 2005b**
Zografos 2007	Greece	Jan 1997 to Dec 2004	
Tsimoyiannis 2008	Greece	May 1996 to Dec 2005	
Pavlakis 2006	Greece	1990 to Mar 2004	
Misra 2006	India	Apr 2003 to Apr 2005	
Bansal 2012	India	May 2007 to Dec 2011	OVERLAP WITH **BANSAL 2011**
Bansal 2011	India	Apr 2008 to Mar 2010	OVERLAP WITH **BANSAL 2012**
Qadri 2010	India	Dec 2005 to Dec 2009	
Shukla 2005	India	Jan 1991 to August 2003	
Prasad 2011	India	Jan 2005 to Dec 2009	
Sharma 2011	India	Jan 1992 to Jun 2005	
Notash 2007	Iran		
Froylich 2016	Israel		

Olmi 2005	Italy	Sep 2001 to May 2003	OVERLAP WITH **OLMI 2007**
Olmi 2007	Italy	Sep 2001 to Dec 2004	OVERLAP WITH **OLMI 2005**
Navarra 2007	Italy	Sep 2003 to Jan 2010	
Ammaturo 2005	Italy	Jun 2002 to ?	
Stabilini 2009	Italy	Mar 1995 to Dec 2005	
Cavallaro 2013	Italy	no dates	Different Hosp from Brescia
Bencini 2003	Italy	Jan 2000 to Jun 2002	SOME OVERLAP WITH **BENCINI 2009** (BUT **BENCINI 2003** INCLUDES 49 OPEN REPAIRS WITH 42 LAP, **BENCINI 2009** IS JUST 146 LAP REPAIRS)
Brescia 2016	Italy	Jan 2013 to Dec 2015	Different Hosp from Cavallaro
Caruso 2017	Italy	Jan 2001 to Dec 2014	
Asti 2016	Italy	Sep 2001 to Dec 2014	
Soliani 2017	Italy	May 2004 to Jul 2014	
Ferrarese 2016	Italy	Mar 2008 to Mar 2014	
Bencini 2009	Italy	Jan 2000 to Dec 2006	SOME OVERLAP WITH **BENCINI 2003** (BUT **BENCINI 2003** INCLUDES 49 OPEN REPAIRS WITH 42 LAP, **BENCINI 2009** IS JUST 146 LAP REPAIRS)
Baccari 2013	Italy	Feb 2003 to Dec 2010	
Ferrai 2013	Italy	Jan 2002 to Nov 2011	
Tsuruta 2014	Japan		
Venclauskas 2010	Lithuania	2005 to 2008	Different years no overlap
Venclauskas 2007	Lithuania	1997 to 2000	Different years no overlap
Eker 2013	Netherlands	May 1999 to Dec 2006	Possible overlap with Van't Riet 2002 but only for 7 months recruitment out of 7 years - therefore … no overlap
Luijendijk 2000	Netherlands	Mar 1992 to Feb 1998	
Wassenaar 2010	Netherlands	Aug 2005 to Jul 2008	POSSIBLY A SMALL OVERLAP WITH **STIRLER 2014** - SAME AUTHORS AND LIKELY SAME LOCATION, BUT ONLY A FRACTION OF THE PATIENTS, ALSO OVERLAP WITH **WASSENAAR 2009** FOR 17 MONTHS
Stirler 2014	Netherlands	Jan 2000 to Sep 2012	POSSIBLY A SMALL OVERLAP WITH **WASSENAAR 2010**, BUT ONLY A FRACTION OF THE PATIENTS, OVERLAP WITH **WASSENAAR 2009**
Halm 2005	Netherlands	Jan 1998 to Dec 2002	
Van't Riet 2002	Netherlands	Jan 1996 to Jan 2000	Possible overlap with Eker 2013 but only for 7 months recruitment out of 4 years - therefore … no overlap
Wassenaar 2009	Netherlands	Jan 2001 to Dec 2007	100% OVERLAP WITH **STIRLER 2014,** 17 MONTHS OVERLAP WITH **WASSENAAR 2010**
Slater 2015a	Netherlands	2000 to 2010	OVERLAP WITH **SLATER 2015c**
Slater 2015b	Netherlands	2000 to 2009	
Slater 2015c	Netherlands	Sep 2000 to Mar 2013	OVERLAP WITH **SLATER 2015a**
Vrijland 2000	Netherlands	Sep 1982 to Aug 1998	Possible overlap with Van't Riet 2002 but only for 28 months for 16 years recruiment (192 months).
Atema 2017	Netherlands	Jan 2011 to Feb 2015	
Mommers 2017	Netherlands	2000 to 2012	
Lambrecht 2014	Norway	2007 to 2010	Same IH cohort as Lambrecht 2015, but tecting for different variables on datasheet so no overlap
Gronvold 2012	Norway	Mar 2008 to Jun 2010	

Lambrecht 2015a	Norway	2007 to 2010	Same IH cohort as Lambrecht 2014, but tecting for different variables on datasheet so no overlap
Lambrecht 2015b	Norway	Oct 2002 to Jun 2006	No overlap
Malik 2015	Pakistan	Jun 2011 to Jun 2013	No overlap
Lal 2012	Pakistan	Jan 2008 to Dec 2010	No overlap
Malik 2008	Pakistan	Jan 2000 to Dec 2004	No overlap
Memon 2013	Pakistan	Jan 2001 to Jun 2009	No overlap
Pawlak 2016	Poland	Nov 2012 ro Aug 2013	
Mitura 2017	Poland	May 2011 to Jun 2014	
Al-Salamah 2006	Saudi Arabia		
Stojiljkovic 2013	Serbia		
Lomanto 2005	Singapore		
Asencio 2009	Spain	no dates	
Carbajo 1999	Spain	Jan 1994 to Jan 1997	
Arroyo 2001	Spain	Jun 1992 to Jan 1998	OVERLAP WITH **ARROYO 2002**
Moreno-Egea 2016	Spain	Jan 2012 to Dec 2014	
Moreno-Egea 2007	Spain	Jan 1996 to Dec 2006	OVERLAP WITH **MORENO-EGEA 2012** - ONLY 18 LUMBAR HERNIAS - - PROBABLY CAN IGNORE, OVERLAP WITH **MORENO-EGEA 2012a** – ALL HERNIAS IN THAT STUDY
Arteaga-Gonzalez 2010	Spain	Jan 2005 to Oct 2008	
Moreno-Egea 2012	Spain	Jan 1995 to Dec 2008	OVERLAP WITH **MORENO-EGEA 2007** - ONLY 18/55 LUMBAR HERNIAS - PROBABLY CAN IGNORE
Moreno-Egea 2012a	Spain	Jan 1994 to Jan 2008	OVERLAP WITH **MORENO-EGEA 2012** - 33/73 NON MIDLINE HERNIAS ARE LUMBAR AND TREATED WITH LAP SURGERY, OVERLAP WITH MORENO-EGEA 2007 - 43/73 HERNIAS IN MORENO-EGEA 2007
Martinez 2017	Spain	Jan 2009 to Dec 2014	
Lorente-Herce 2015	Spain	Jan 2000 to Dec 2011	
Porrero 2015	Spain	Jun 2004 to Dec 2010	
Moreno-Egea 2012b	Spain	Jan 1994 to Jun 2009	OVERLAP WITH **MORENO-EGEA 2007, 2012, 2012a**
Arroyo 2002	Spain	Jun 1992 to Jan 1998	OVERLAP WITH **ARROYO 2001**
Rogmark 2016	Sweden	no dates	
Dalenback 2013	Sweden		
Israelsson 2006	Sweden		
Beldi 2011	Switzerland	Apr 2005 to Jan 2008	36 PATIENTS FROM HERE MAY WELL BE IN **KURMANN 2011**
Kurmann 2011	Switzerland	Feb 2003 to Jun 2009	MAY WELL CONTAIN THE 36 PATIENTS FROM **BELDI 2011**. Possible overlap with Kurmann 2010, but I think this is a separate cohort
Kurmann 2010	Switzerland	1994 to 2008	Liver transplant pateints only
Huang 2013	Taiwan		
Barbaros 2007	Turkey	Jan 2001 to Oct 2005	

Polat 2005	Turkey	Jan 2000 to Oct 2003	
Gecim 1996	Turkey		
Basoglu 2004	Turkey	Jan 1986 to Nov 2000	
Khan 2012	UK	Jan 2004 to Jul 2008	
Solomon 2010	UK	May 1998 to Dec 2008	No overlap with Sturt 2011 as this is primary only
Ching 2008	UK	Dec 2002 to Aug 2007	
Sanjay 2005	UK	no dates	
Shaikh 2013	UK	Jan 2007 to June 2009	
Tandon 2016	UK	Jan 2008 to Dec 2010	
Mann 2015	UK	Apr 2007 to Sep 2012	
Hornby 2015	UK	Jan 2004 to Dec 2010	
Giordano 2015.1&2	UK	no dates	
Jamal 2015	UK	2005 to 2012	
Shipworth 2014	UK	Feb 2009 to Sep 2012	
Sturt 2011	UK	1994 to 2008	No overlap with Solomon 2010 as this is incisional only
Light 2016	UK	2012 to 2015	
Warwick 2016	UK	Feb 2007 to Nov 2013	Possible small overlap with Giordano 2015.1&2 but no dates for giordano and Exeter only one of 7 centres so probably negligible
Itani 2010	USA	Feb 2004 to Jan 2007	
Wormer 2016	USA	Oct 2012 to Feb 2015	
Novitsky 2006	USA	Jul 1998 to Dec 2003	OVERLAP WITH **COBB 2006**
Cobb 2006	USA	Jul 1998 to Dec 2003	OVERLAP WITH **NOVITSKY 2006**
Heniford 2003	USA	Nov 1993 to Feb 2003	Multicentre probably cotains patients for Cobb 2006 and Novitsky 2006, difficult to know
Cox 2016	USA	2007-2011	OVERLAP - KLIMA 2014, HUNTINGTON 2016 BUT DIFFERENT PREDICTORS SO NIL CONCERNS
Klima 2014	USA	Sep 2005 to Jul 2010	OVERLAP - COX 2016, HUNTINGTON 2016 BUT DIFFERENT PREDICTORS SO NIL CONCERNS
Huntington 2016	USA	2005–2014	OVERLAP - COX 2016, KLIMA 2014 BUT DIFFERENT PREDICTORS SO NIL CONCERNS
Greenstein 2008	USA	Sep 2004 to Dec 2005	
Bingener 2007	USA	Oct 1995 to Dec 2005	
Bochicchio 2013	USA	Feb 2008 to Jan 2010	
De Maria 2000	USA	Jan 1996 to Jun 1997	
Nguyen 2016	USA	Mar 2012 to Jun 2014	
Le Blanc 2003	USA	Jul 1992 to May 2000	
Ng 2015	USA	Jan 2009 to Jul 2013	
Carbonell 2013	USA	Aug 2007 to Feb 2013	OVERLAP WITH **COBB 2015, WARREN 2017**, Some overlap with Warren 2015 but looking at different predictors so not a problem
Cobb 2015	USA	Aug 2006 to Aug 2013	OVERLAP WITH **CARBONELL 2013, WARREN 2017**. Some overlap with Warren 2015 but looking at different predictors so not a problem

Warren 2015	USA	Jul 2006 to Jul 2014	Some overlap with Warren 2017, Cobb 2015, and Carbonell 2013 - but looking at different predictors so not a problem
Warren 2017	USA	Mar 2006 to Jan 2013	OVERLAP WITH **COBB 2015, CARBONELL 2013**, Some overlap with Warren 2015 but looking at different predictors so not a problem
Iacco 2014	USA	Jan 2007 to Jun 2011	
Azoury 2014a	USA	Oct 2010 to Jul 2013	OVERLAP THE 42 **AZOURY 2014a** PATIENTS ARE IN **AZOURY 2014b**. DIFFERENT PREDICTORS FROM AZAR 2017
Azoury 2014b	USA	Oct 2010 to Jul 2013	OVERLAP THE 42 **AZOURY 2014a** PATIENTS ARE IN **AZOURY 2014b**. DIFFERENT PREDICTORS FROM AZAR 2017
Azar 2017	USA	2008 to 2015.	SOME OVERLAP WITH **AZOURY 2014a, AZOURY 2014b** BUT DIFFERENT PREDICTORS SO NO WORRIES.
Berger 2014	USA	Jan 2000 to Dec 2010	
Richmond 2014	USA	Jan 2006 to Dec 2012	
Fischer 2014	USA	2007 to 2012	OVERLAP WITH **WINK 2014**. No overlap with Basta 2015 as primary fascial closure only
Basta 2015	USA	Jan 2007 to Jan 2013	OVERLAP WITH **WINK 2014**. No overlap with Fischer 2014 as bridging mesh only
Wink 2014	USA	2007–2012	SOME OVERLAP WITH **BASTA 2015, FISCHER 2014**
Keating 2016	USA	Dec 2009 and Jan 2013	DIFFERENT PATIENT SET DIFFERENT SENIOR AUTHOR SERIES
Cheng 2014	USA	2007 to 2013	
Harth 2010	USA	Jan 2005 to Feb 2009	OVERLAP WITH **HARTH 2011, KRPATA 2012, ROSEN 2013, KANTERS 2012**
Harth 2011	USA	2007 to 2010	OVERLAP WITH **HARTH 2010, KRPATA 2012, ROSEN 2013, KANTERS 2012**
Petro 2015	USA	Patients from 2011	OVERLAP WITH **KRPATA 2012 (SMALL), ROSEN 2013, KANTERS 2012**
Krpata 2012	USA	Mar 2006 to Mar 2011	OVERLAP WITH **HARTH 2010, HARTH 2011, ROSEN 2013, KANTERS 2012, PETRO 2015**
Rosen 2013	USA	Sep 2005 to Feb 2012	OVERLAP WITH **HARTH 2010, HARTH 2011, KRPATA 2012, KANTERS 2012, PETRO 2015**
Kanters 2012	USA	Mar 2006 to Jan 2012	OVERLAP WITH **HARTH 2010, HARTH 2011, KRPATA 2012, ROSEN 2013, PETRO 2015**
Rosen 2009	USA	Dec 2005 to Apr 2008	One predictor - not in others
Petro 2016	USA	Jan 2006 to Jun 2013	OVERLAP WITH **FAYEZIZADEH 2016**. SOME OVERLAP WITH **ROSEN2013, KANTERS 2012** (Larger cohort - some ROSEN patients but also other
Fayezizadeh 2016	USA	2007 and 2014	OVERLAP WITH **PETRO 2016**. Not Rosen - Novitsky
Majumder 2016	USA	Jun 2009 to Mar 2015	Small overlap on dates with Harth 2010 and krpata 2012 but this is multicenter and contaminated probably very few if any overlap
Rosen 2012	USA	no dates	OVERLAP WITH **ITANI 2012,** (THIS STUDY IS AN INTERIM ANALSIS OF ITANI 2012 WITH LESS PATIENTS AND LESS FOLLOW UP TIME)
Jin 2007	USA	Jan 2004 to Dec 2005	I don't think this is an 11 month overlap with Harth 2010, Rosen not main author and not single surgeon
Brahmbhatt 2014	USA	Jan 2000 to Dec 2010	OVERLAP WITH **SUBRAMANIAN 2013, CARTER 2014** (BOTH CONTAIN LAP ONLY REPAIRS)
Carter 2014	USA	Jan 2000 to Dec 2010	OVERLAP WITH **SUBRAMANIAN 2013, BRAHMBHATT 2014** (BOTH CONTAIN LAP ONLY REPAIRS)
Subramanian 2013	USA	2000 to 2010	OVERLAP WITH **BRAHMBHATT 2014, CARTER 2014** (BOTH CONTAIN LAP ONLY REPAIRS)
Liang 2013	USA	2000 to 2010	GIVING BENEFIT OF THE DOUBT VERY DIFFICULT TO KNOW IF THESE SINGLE CENTRE PATIENTS ARE ALSO IN THE MULTI CENTRE PAPERS. Overlap with Farrow 2008, different predictors no concerns
Brown 2013	USA	Jan 2000 to Aug 2007	GIVING BENEFIT OF THE DOUBT VERY DIFFICULT TO KNOW IF THESE SINGLE CENTRE PATIENTS ARE ALSO IN THE MULTI CENTRE PAPERS
Clapp 2013	USA	Jan 2007 to Dec 2010	SOME OVERLAP WITH **BRAHMBHATT 2014**, **CARTER 2014** & **SUBRMANIAN 2013**, BUT DOESN'T MATTER AS DIFFERENT VARIABLE IN DATASHEET
Salameh 2002	USA	Jan 2000 to Jun 2001	VERY SMALL OVERLAP WITH **LIANG 2013**, **SUBRAMANIAN 2013**, **CARTER 2014, BRAHMBHATT 2014** AND **BROWN 2013**
Farrow 2008	USA	Oct 2003 to Sep 2007	Open overlap with Liang 2013 but different predictors so nil concerns

El-Gazzaz 2013	USA	Dec 1991 to Aug 2007	Unlikely overlap with Rosen 2003 or Ballem 2008
Rosen 2003	USA	Jan 1996 to Mar 2001	OVERLAP WITH **BALLEM 2008** FOR LAP CASES
Ballem 2008	USA	Jan 1996 to Dec 2001	OVERLAP WITH **ROSEN 2003** FOR LAP CASES
Zeichen 2013	USA	Jul 2000 to Sep 2011	
Fox 2013	USA	Oct 2009 to Nov 2011	Very different years, different authors unlikely overlap with Kanaan 2011
Kanaan 2011	USA	1995 and 2010	Very different years, different authors unlikely overlap with Fox 2013
Snyder 2011	USA	1997 and 2002	Overlap with Altom 2012 but different predictors so nil concern
Gleysteen 2009	USA	Feb 1988 to Sep 2001	I don't think overlap with Altom - different centres involved
Altom 2012	USA	1998 to 2002	Overlap with Synder 2011, but different predictors so nil concernI don't think overlap with Gleysteen - different centres involved
Singhal 2012	USA	Jan 2001 to Feb 2010	
Yannam 2011	USA	Apr 2005 to Mar 2009	
Kurian 2010	USA	Apr 2001 to Apr 2009	
Tsereteli 2008	USA	1993 to 2006	
Lee 2008	USA	2000 to 2006	
Saber 2008	USA	Jul to Jul 2006	
Raftopoulos 2003	USA	1994 and 2000	
Gonzalez 2003	USA	Nov 1995 to Oct 2000	
Wright 2002a	USA	Jan 1998 to Apr 2000	OVERLAP WITH **WRIGHT 2002b**
Wright 2002b	USA	Jan 1998 to Apr 2000	OVERLAP WITH **WRIGHT 2002a**
Booth 2013	USA	Feb 2000 to Oct 2011	OVERLAP WITH **GARVEY 2012, GARVEY 2014, GARVEY 2016, GHALI 2012, CLEMENS 2013**, **GIORDANO 2016, GIORDANO 2017a**, **GIORDANO 2017b, GIORDANO 2017c**
Garvey 2012	USA	June 2002 to Nov 2010	OVERLAP WITH **GARVEY 2014**, **GARVEY 2016, BOOTH 2013, GHALI 2012, CLEMENS 2013, GIORDANO 2016, GIORDANO 2017a, GIORDANO 2017b, GIORDANO 2017c**
Giordano 2017a	USA	Mar 2005 to Oct 2015	OVERLAP WITH **GARVEY 2012, GARVEY 2014, GARVEY 2016, BOOTH 2013, GHALI 2012, CLEMENS 2013, GIORDANO 2016, GIORDANO 2017b**, **GIORDANO 2017c**
Giordano 2017b	USA	Mar 2005 to Oct 2015	OVERLAP WITH **GARVEY 2012, GARVEY 2014, GARVEY 2016, BOOTH 2013, CLEMENS 2013, GHALI 2012**, **GIORDANO 2016, GIORDANO 2017a, GIORDANO 2017c**
Giordano 2017c	USA	Mar 2005 to Oct 2015	OVERLAP WITH **GARVEY 2012**, **GARVEY 2014**, **GARVEY 2016, BOOTH 2013**, **CLEMENS 2013**, **GHALI 2012**, **GIORDANO 2016**, **GIORDANO 2017a**, **GIORDANO 2017b**
Ghali 2012	USA	Mar 2005 to Oct 2010	OVERLAP WITH **GARVEY 2012, GARVEY 2014, GARVEY 2016, BOOTH 2013, CLEMENS 2013, GIORDANO 2016, GIORDANO 2017a, GIORDANO 2017b**, **GIORDANO 2017c**
Clemens 2013	USA	Jan 2008 to Mar 2011	OVERLAP WITH **GARVEY 2012, GARVEY 2014, GARVEY 2016, BOOTH 2013, GHALI 2012**, **GIORDANO 2016, GIORDANO 2017a, GIORDANO 2017b**, **GIORDANO 2017c**
Garvey 2014	USA	Mar 2005 to Mar 2013	OVERLAP WITH **GARVEY 2012, GARVEY 2016, CLEMENS 2013, BOOTH 2013, GHALI 2012**, **GIORDANO 2016, GIORDANO 2017a, GIORDANO 2017b**, **GIORDANO 2017c**
Garvey 2016	USA	Mar 2005 and Oct 2015	OVERLAP WITH **GARVEY 2012, GARVEY 2014, CLEMENS 2013, BOOTH 2013, GHALI 2012**, **GIORDANO 2016, GIORDANO 2017a, GIORDANO 2017b**, **GIORDANO 2017c**
Giordano 2016	USA	Mar 2005 and Oct 2015	OVERLAP WITH **GARVEY 2012, GARVEY 2014, GARVEY 2016, CLEMENS 2013, BOOTH 2013, GHALI 2012**, **GIORDANO 2017a, GIORDANO 2017b**, **GIORDANO 2017c**
Ko 2009a	USA	Sep 2004 to Sep 2007	Some possible overlap with Ko 2009b but different predictors tested not an issue
Ko 2009b	USA	Aug 1996 to Jul 2007	OVERLAP WITH **REID 2004**, Some possible overlap with Ko 2009a but different predictors tested not an issue
Ujiki 2004	USA	Apr 2000 to Feb 2003	No overlap with Ko 2009a+b due to this being laparascopic only (Ko not laparoscopic)
Reid 2004	USA	1997 to 2003	OVERLAP WITH **KO 2009b** - Small group of patients - Likely included in Ko 2009 b

Colon 2011	USA	2005 to 2009	OVERLAP WITH **DANZIG 2016** (NOT KITAMURA 2013 AS INCISIONAL ONLY)
Kitamura 2013	USA	2003 and 2009	OVERLAP WITH **DANZIG 2016** (NOT COLON 2011 AS INCISIONAL ONLY)
Groene 2016b	USA	no dates	THERE IS OVERLAP HERE BUT THIS IS ONLY A SUBSET OF 44 PATIENTS OF THE IHMR ? OVERLAP WITH **WORMER 2013, GROENE 2016a**
Colavita 2012	USA	Sep 2007 to Jul 2011	OVERLAP WITH **WORMER 2013**, **GROENE 2016a**
Wormer 2013	USA	Oct 2007 to Jun 2012	OVERLAP WITH **COLAVITA 2012**, **GROENE 2016a**
Groene 2016a	USA	no dates	OVERLAP WITH **WORMER 2013, COLAVITA 2012**
Johnson 2016	USA	2009 to 2013	
Karipineni 2016	USA	Aug 2010 to Jul 2013	
Parent 2016	USA	Jan 2010 to Jan 2016	Possible small overlap with Sandvall 2016 but minimal
Sandvall 2016	USA	Nov 2006 to Nov 2010	Possible small overlap with Parent 2016 but minimal
Wennergren 2016	USA	2010 to 2012	Possible overlap with some of the involved centres but only small proportion of patients
Desai 2016	USA	2002 to 2014	OVERLAP WITH **GHAZI 2011**, JUST LONGER PERIOD OF PATIENTS
Ghazi 2011	USA	2002 and 2009	OVERLAP WITH **DESAI 2016**, JUST SHORTER PERIOD OF PATIENTS
Ecker 2016	USA	2007 and 2011	
Danzig 2016	USA	Jan 2002 to Dec 2010	OVERLAP WITH **KITAMURA 2013, COLON 2011**
Henry 2013	USA	Jul 2008 to Oct 2011	POSSIBLE OVERLAP WITH **WON 2015 AND RINALDI 2016,** BUT NOT AN ISSUE DIFFERENT PREDICTORS
Rinaldi 2016	USA	Jul 2011 to Mar 2013	POSSIBLE OVERLAP WITH **WON 2015 AND HENRY 2013,** BUT NOT AN ISSUE DIFFERENT PREDICTORS
Won 2015	USA	May 2011 to Nov 2013	POSSIBLE OVERLAP WITH **RINALDI 2016 AND HENRY 2013**, BUT NOT AN ISSUE DIFFERENT PREDICTORS
Hultman 2014	USA	2000 to 2010	
Satterwhite 2012	USA	Sep 2002 to Feb 2010	
Iqbal 2007	USA	Oct 1991 to Oct 2003	
Krpata 2013	USA	Sep 2005 and Jan 2012	I don't thin overlap these are ECF repairs other case papers are not
Itani 2012	USA	no dates	OVERLAP WITH **ROSEN 2012** (ROSEN WAS AN INTERIM ANALSIS WITH LESS PATIENTS AND LESS FOLLOW UP TIME)
Anthony 2000	USA	Oct 1991 to Sep 1995	
Abdelfatah 2015	USA	Oct 2004 to Jun 2008	
Roth 2015	USA	2007 and 2010	Multicentre unlikely ovelap with Johnson 2016
Rosen 2017	USA	Feb 2011 to Dec 2014	
Chand 2014	USA	Aug 2010 to Oct 2011	
Sailes 2010	USA	Oct 1996 to Oct 2006	
DiCocco 2009	USA	Oct 1993 to Dec 2008	
Clarke 2010	USA	no dates	
Lin 2009	USA	May 2005 to Feb 2008	
Candage 2008	USA	May 2004 to Oct 2007	
Heartsill 2005	USA	1996 and 2000	No overlap with Franklin 2004 as Heartsill has open surgey

Perrone 2005	USA	May 2000 to Dec 2003	
Franklin 2004	USA	Feb 1991 to Nov 2002	No overlap with Heart 2005 as Franklin has Lap patients
Clark 2001	USA	Oct 2003 to Dec 1996	
Davidson 2009	USA	1999 and 2005	
Gassman 2015	USA	May 2008 to Jul 2011	
Holihan 2015	USA	2000 to 2012	OVERLAP WITH **HOLIHAN 2016** (MODEL DEV AND INTERNAL VALIDATION), SOME OVERLAP WITH **BONDRE 2016 BUT** SOME DIFFERENT CENTRES AND DIFFERENT DATES OF RECRUITMENT SO DISCOUNT
Bondre 2016	USA	Jan 2010 to Dec 2011	OVERLAP WITH **HOLIHAN 2016** (EXTERNAL VALIDATION), SOME OVERLAP WITH **HOLIHAN 2015 BUT** SOME DIFFERENT CENTRES AND DIFFERENT DATES OF RECRUITMENT SO DISCOUNT
Holihan 2016	USA	2009-2010	**OVERLAP TRICKY!!!** MODEL DEVELOPMENT AND INTERNAL VALIDATION OVERLAP WITH **HOLIHAN 2015,** EXTERNAL VALIDATION OVERLAP WITH **BONDRE 2016**
Diamond 2015	USA	2006 to 2011	
Flum 2003	USA	1987 to 1999	
Baucom 2016	USA	no dates	
Bender 2016	USA	Jan 1995 to Jun 2014	
Heimann 2017	USA	Jan 1976 to Dec 2014	
Shankar 2017	USA	Jan 1998 to Dec 2008	
Yao 2016	USA	Aug 2005 to Jul 2014	
Hadeed 2011	Germany	Jan 2005 to Sep 2009	

Appendix 32 – Definitions of Recurrence

Definitions

Yes - palpable lump at the site of previous repair

Yes - Abdo wall defect detectable on examination or imaging

Yes - Hernias at the same location

Yes - defined by clinical examination

Yes - protruding bulge whilst doing a valsalva at previous repair site
Yes - ‘‘Recurrence during follow-up’’ of an incisional hernia was defined as a repeat incisional hernia operation, abdominal wall weakness in the area of the incision, or localized bulging upon coughing.
Yes - defect of the midline aponeurosis around the umbilicus at the site where the operation had been performed

Yes - protrusion of contents of the abdominal cavity through a defect in the abdominal wall at the site of repair

Yes - bulge at hernia repair site

Yes - palpable lump at the site of previous repair

Yes - bulge at hernia repair site

Yes - new hernia within 7cm of the repair

Yes - central tissue eventration when hernia sac extends beyond the boundaries of the anterior abdom wall

Yes - abnormal contour associated with a fascial defect

Yes - recurrence involved more than one side of the hernia or large than 2.5cm

Yes - bulge at hernia repair site

Yes - hernia at repair site

Yes - defect in the midline, parastomal area, at the flap harvest site.

Yes - bulge/reoperation

Yes - recurrent fascial defect on examination or scan

Yes - palpable defect

Yes - patient complained of simliar symptom to what they had before the repair

Yes - isolated palpable defect at the site of the previous repair

Yes - recurrent bulge in the supine and standing positions

Yes - any gap in the abdominal wall identified on imaging

Yes - Reoperation

Yes - reoperation at the site of previous hernia repair

Yes - protrusion of fat through a defect in the abdominal wall at the site of previous repair of an abdominal wall hernia.

Yes - contour abnormality with a fascial defect

Yes - hernia at incision site OR ileostomy closure site

Yes - but defined as whether found during f/u

Yes - reoperation at the site of previous hernia repair

Yes - re-operation rate

Yes - fascial defect with contour abnormality

Yes - Radiological evidence of recurrence

Yes - palpable bulge

Yes - fascial defect with contour abnormality

Yes - bulge or defect at the site of VH repair

Yes - fascial defect with contour abnormality

Yes - re-operation rate

Yes - fascial defect with protrusion of bowel

Yes - fascial edges of defect palpable

Yes - re-operation, examination, CT, telephone

Yes - abdo wall defect

Yes - reoperation or clinical/radiological evidence of recurrence

Yes - fascial defect

Yes - palpable lump at the site of previous repair

Yes - palpable lump within 7cm of hernia repair site

Yes - requiring another op OR a significant bulge

Yes - defect in abdo wall at site of previous hernia

Yes - bulge at site of op getting bigger with coughing

Yes - defect in abdo wall at site of previous hernia

Yes - defect in abdo wall at site of previous hernia

Yes - abdo wall defect

Yes - central or port site

Yes - tissue protruding beyond the anterior plane of the anterior rectus fascia on CT scan
Yes - a palpable defect on exam as noted by the attending surgeon, further confirmed by CT imaging in all cases.
Yes - the presence of a bulge on physical examination, imaging, or by patient self-reporting
Yes - any abdominal wall gap with or without bulge that is not covered by mesh in the area of a postoperative scar
Yes - a symptomatic herniation or a herniation was detected via abdominal ultrasonography

Yes - a true hernia recurrence as herniation of bowel or omentum through a defect in the biologic mesh or through a defect at the mesh/fascial interface after the initial operation.

Yes - a clinically detectable defect, associated with the protrusion of viscera on straining.

Yes - any fascial defect that was palpable or detected by ultrasound examination and was located within 7 cm of the site of hernia repair

Yes - as the presence of a defect on the central part of the midline aponeurosis around the umbilicus, where the operation had been performed previously.

Yes - the presence of a defect on the central part of the midline aponeurosis where the operation had been performed previously
Yes - a defect of the midline aponeurosis around the umbilicus at the site where the operation had been performed

66 studies gave a definition for recurrence

Definition 1

Yes - palpable lump at the site of previous repair

Yes - palpable lump at the site of previous repair

Definition 2

Yes - Abdo wall defect detectable on examination or imaging

Definition 3

Yes - Hernias at the same location

Yes - hernia at repair site

Definition 4

Yes - defined by clinical examination

Definition 5

Yes - protruding bulge whilst doing a valsalva at previous repair site

Definition 6

Yes - defect of the midline aponeurosis around the umbilicus at the site where the operation had been performed

Yes - as the presence of a defect on the central part of the midline aponeurosis around the umbilicus, where the operation had been performed previously.

Yes - the presence of a defect on the central part of the midline aponeurosis where the operation had been performed previously

Yes - a defect of the midline aponeurosis around the umbilicus at the site where the operation had been performed

Definition 7

Yes - protrusion of contents of the abdominal cavity through a defect in the abdominal wall at the site of repair

Yes - protrusion of fat through a defect in the abdominal wall at the site of previous repair of an abdominal wall hernia.

Definition 8

Yes - bulge at hernia repair site

Yes - bulge at hernia repair site

Definition 9

Yes - new hernia within 7cm of the repair

Yes - palpable lump within 7cm of hernia repair site

Definition 10

Yes - central tissue eventration when hernia sac extends beyond the boundaries of the anterior abdom wall

Definition 11

Yes - abnormal contour associated with a fascial defect

Yes - contour abnormality with a fascial defect

Yes - fascial defect with contour abnormality

Yes - fascial defect with contour abnormality

Yes - fascial defect with contour abnormality

Definition 12

Yes - recurrence involved more than one side of the hernia or large than 2.5cm

Definition 13

Yes - defect in the midline, parastomal area, at the flap harvest site.

Definition 14

Yes - bulge/reoperation

Yes - requiring another op OR a significant bulge

Definition 15

Yes - palpable defect

Yes - fascial edges of defect palpable

Definition 16

Yes - patient complained of simliar symptom to what they had before the repair

Definition 17

Yes - isolated palpable defect at the site of the previous repair

Definition 18

Yes - recurrent bulge in the supine and standing positions

Definition 19

Yes - any gap in the abdominal wall identified on imaging

Yes - Radiological evidence of recurrence

Definition 20

Yes - Reoperation

Yes - re-operation rate

Yes - re-operation rate

Definition 21

Yes - reoperation at the site of previous hernia repair

Yes - reoperation at the site of previous hernia repair

Definition 22

Yes - hernia at incision site OR ileostomy closure site

Definition 23

Yes - ‘‘Recurrence during follow-up’’ of an incisional hernia was defined as a repeat incisional hernia operation, abdominal wall weakness in the area of the incision, or localized bulging upon coughing.

Definition 24

Yes - but defined as whether found during f/u

Definition 25

Yes - palpable bulge

Definition 26

Yes - bulge or defect at the site of VH repair

Definition 27

Yes - fascial defect with protrusion of bowel

Definition 28

Yes - re-operation, examination, CT, telephone

Definition 29

Yes - abdo wall defect

Yes - fascial defect

Yes - abdo wall defect

Definition 30

Yes - reoperation or clinical/radiological evidence of recurrence

Definition 31

Yes - defect in abdo wall at site of previous hernia

Yes - defect in abdo wall at site of previous hernia

Yes - defect in abdo wall at site of previous hernia

Definition 32

Yes - bulge at site of op getting bigger with coughing

Definition 33

Yes - central or port site

Definition 34

Yes - tissue protruding beyond the anterior plane of the anterior rectus fascia on CT scan

Definition 35

Yes - a palpable defect on exam as noted by the attending surgeon, further confirmed by CT imaging in all cases.

Definition 36
Yes - the presence of a bulge on physical examination, imaging, or by patient self-reporting

Definition 37

Yes - any abdominal wall gap with or without bulge that is not covered by mesh in the area of a postoperative scar

Definition 38
Yes - a symptomatic herniation or a herniation was detected via abdominal ultrasonography

Definition 39

Yes - a true hernia recurrence as herniation of bowel or omentum through a defect in the biologic mesh or through a defect at the mesh/fascial interface after the initial operation.

Definition 40

Yes - a clinically detectable defect, associated with the protrusion of viscera on straining.

Definition 41

Yes - any fascial defect that was palpable or detected by ultrasound examination and was located within 7 cm of the site of hernia repair

Appendix 33 – Methods of Detecting Recurrence

Method of detecting recurrence	Grouping
adhoc Clinical assessment	MI
Clinical assesment +/- CT +/- Telephone call	MI
Clinical Assessment	CA
Clinical assessment + CT	CC
Clinical assessment + medical records	MI
Clinical assessment + telephone call	CT
Clinical assessment + USS	CU
Clinical assessment +/- CT	CC
Clinical assessment +/- CT +/- medical records	MI
Clinical Assessment +/- CT +/- re-operation	MI
Clinical assessment +/- CT +/- telephone call	MI
Clinical assessment +/- CT/USS	CI
Clinical assessment +/- CT/USS +/- re-operation	MI
Clinical Assessment +/- CT/USS +/- telephone call	MI
Clinical Assessment +/- medical records	MI
Clinical assessment +/- medical records +/- telephone call +/- CT	MI
Clinical Assessment +/- Questionnaire	CQ
Clinical Assessment +/- Questionnaire +/- Telephone call	MI
Clinical assessment +/- re-operation	MI
Clinical Assessment +/- telephone call	CT
Clinical assessment +/- telephone call +/- questionnaire	MI
Clinical Assessment +/- telephone call +/- questionnaire +/- clinical notes	MI
Clinical assessment +/- US	CU
Clinical assessment +/- US/CT +/- re-operation	MI
Clinical Assessment +/- USS/CT	CI
Clinical Assessment +/- USS/CT +/- re-operation	MI
Clinical assessment/medical records/imaging	MI
Clinical assessment/telephone	CT
Clinical assessment/telephone&Questionnaire	MI
Clinical assessment+/-CT/re-operation	MI
Clinical notes & records + telephone call +/- clinical assessment +/- CT	MI
Clinical records +/- telephone call	CT
Medical records	MR
Medical records +/- Clinical assessment	MI
Medical records +/- clinical Assessment +/- CT	MI
Medical records +/- questionnaire +/- GP records +/- clinical assessment	MI
Medical records +/- Telephone +/- Clinical Assessment	MI
Medical records +/- telephone call	MI
Medical records +/- telephone call +/- CT +/- reoperation	MI
No information	NI
Prospectively maintained database	MI

Prospectively maintained database +/- Medical records	**MI**
Questionnaire	**MI**
Questionnaire +/- Clinical Assessment + US	MI
Questionnaire +/- Clinical Assessment +/- CT/USS	MI
Questionnaire +/- telephone call +/- clinical Assessment	MI
Questionnaire +/- telephone call +/- clinical assessment +/- CT	MI
Questionnaire +/- telephone call +/- clinical examination +/- CT/USS	MI
Questionnaire/GP records	**MI**
Re-operation	RO
Re-operation rate	RO
Re-operation rate +/- Clinical assessment +/- CT/USS	MI
Telephone +/- Clinical assessment	CT
Telephone +/- clinical assessment +/- CT	MI
Telephone call	**MI**
Telephone call + Questionnaire	MI
Telephone call +/- Clinical assessment	CT
Telephone call +/- Clinical assessment +/- CT	MI
Telephone call +/- Clinical assessment +/- CT/USS	MI
Telephone call +/- clinical assessment +/- medical records	MI
USS +/- CT	**IU/C**

Group codes

Imaging only with CT - IC (not many studies)
Imaging only with US - IU (not many studies)
Imaging only with USS or CT - IU/C
Clinical Assessment - CA
Clinical assessment combined with CT - CC
Clinical assessment combined with USS - CU
Clinical assessment combined with CT or USS - CI
Clinical assessment combined with telephone - CT
Clinical assessment combined with Questionnaire - CQ
Medical records synonymous with clinical records & clinical notes - MR
Re-operation - RO
Mixture - MI

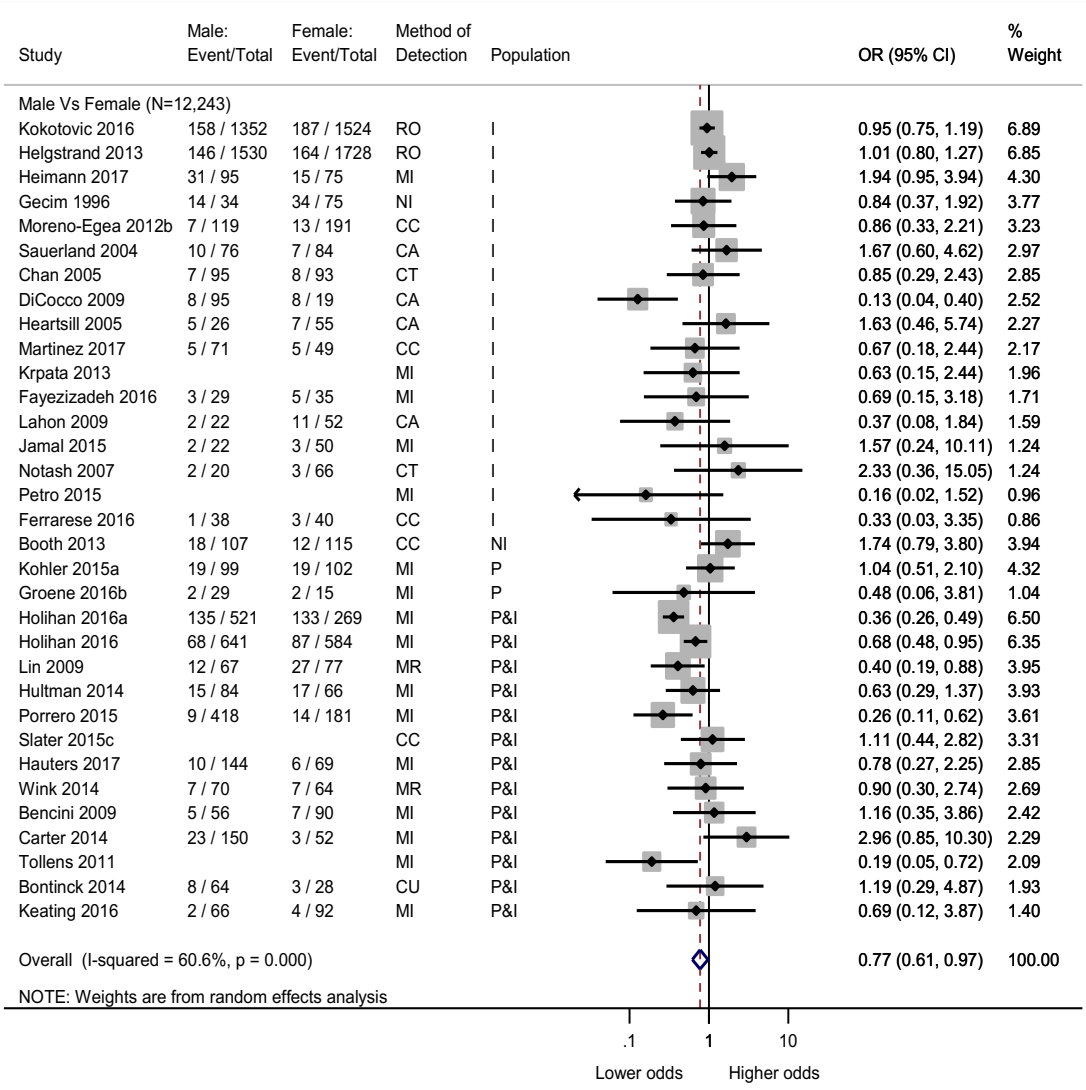
The Mixture group with include a lot - eg. Clinical assessment + clinical notes + telephone, OR Telephone + Questionnaire

NI - No Information

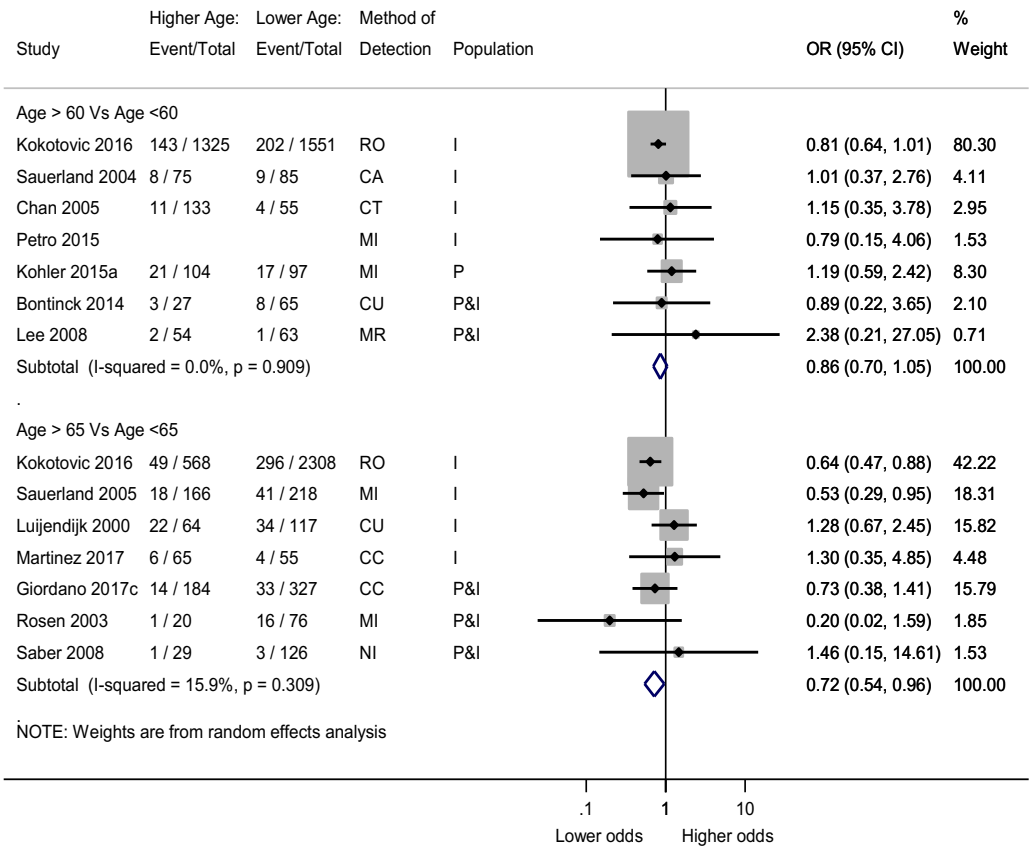
Appendix 34

Patient demographics

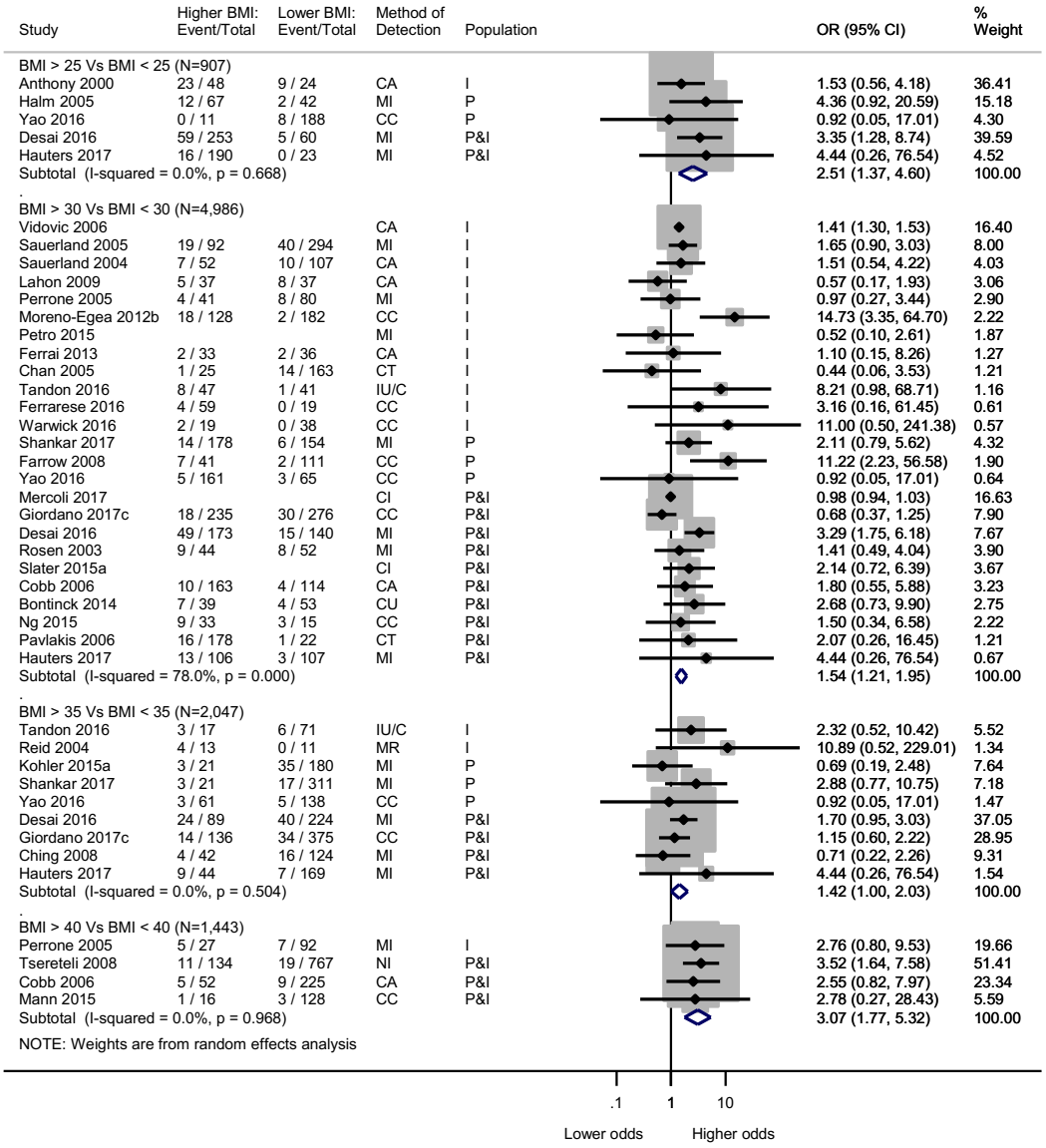
1.1 Sex



1.2 Age

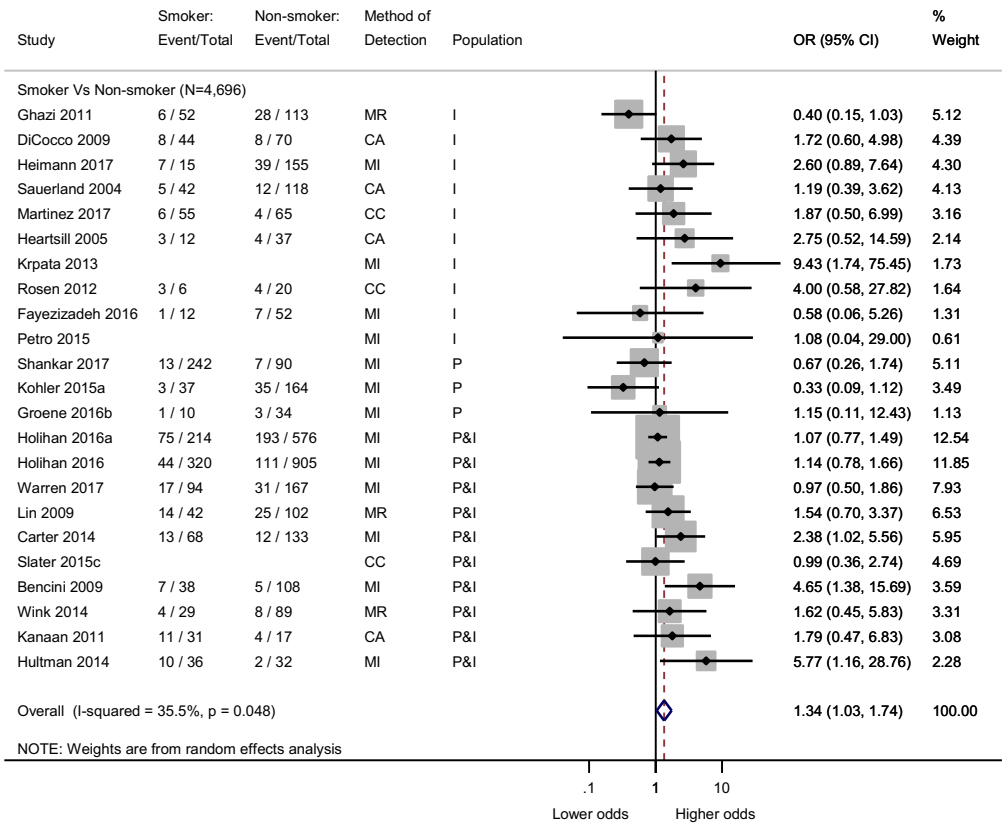

Study
Higher Age: Event/Total
Lower Age: Event/Total
Method of Detection
Population
OR (95% CI)
% Weight
Age > 60 Vs Age <60
Kokotovic 2016 143 / 1325 202 / 1551 RO I 0.81 (0.64, 1.01) 80.30
Sauerland 2004 8 / 75 9 / 85 CA I 1.01 (0.37, 2.76) 4.11
Chan 2005 11 / 133 4 / 55 CT I 1.15 (0.35, 3.78) 2.95
Petro 2015 MI I 0.79 (0.15, 4.06) 1.53
Kohler 2015a 21 / 104 17 / 97 MI P 1.19 (0.59, 2.42) 8.30
Bontinck 2014 3 / 27 8 / 65 CU P&I 0.89 (0.22, 3.65) 2.10
Lee 2008 2 / 54 1 / 63 MR P&I 2.38 (0.21, 27.05) 0.71
Subtotal (I-squared = 0.0%, p = 0.909) 0.86 (0.70, 1.05) 100.00
Age > 65 Vs Age <65
Kokotovic 2016 49 / 568 296 / 2308 RO I 0.64 (0.47, 0.88) 42.22
Sauerland 2005 18 / 166 41 / 218 MI I 0.53 (0.29, 0.95) 18.31
Luijendijk 2000 22 / 64 34 / 117 CU I 1.28 (0.67, 2.45) 15.82
Martinez 2017 6 / 65 4 / 55 CC I 1.30 (0.35, 4.85) 4.48
Giordano 2017c 14 / 184 33 / 327 CC P&I 0.73 (0.38, 1.41) 15.79
Rosen 2003 1 / 20 16 / 76 MI P&I 0.20 (0.02, 1.59) 1.85
Saber 2008 1 / 29 3 / 126 NI P&I 1.46 (0.15, 14.61) 1.53
Subtotal (I-squared = 15.9%, p = 0.309) 0.72 (0.54, 0.96) 100.00
NOTE: Weights are from random effects analysis
.1
1
10
Lower odds
Higher odds

1.3 BMI

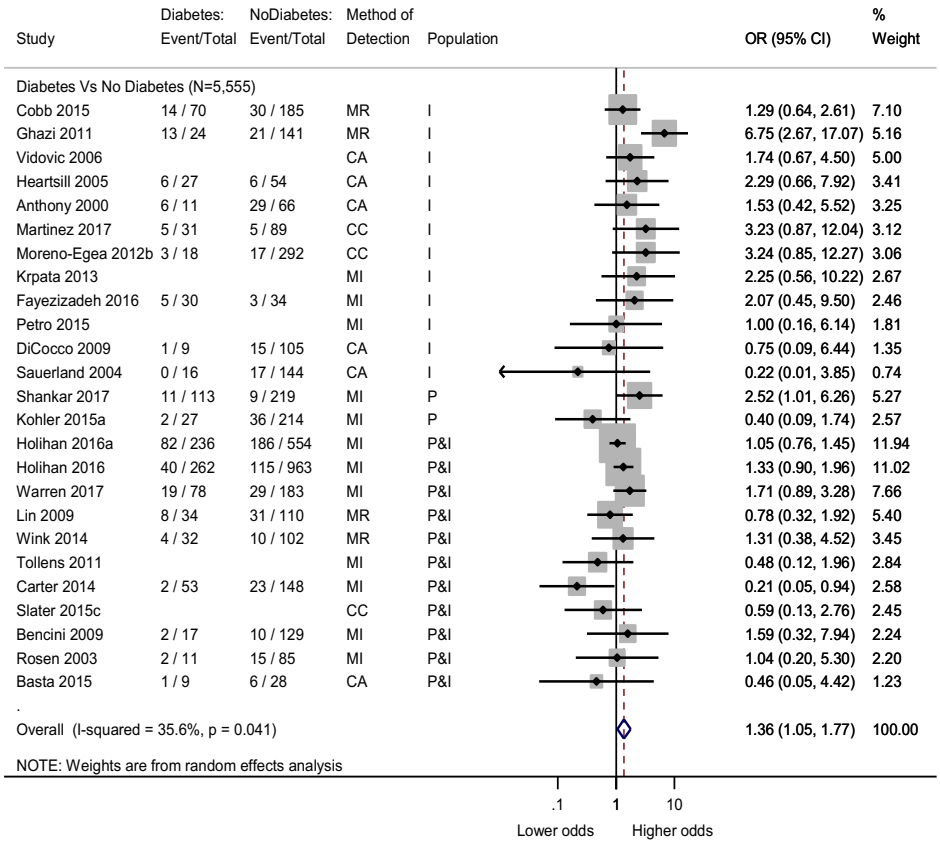

Study
Higher BMI: Event/Total
Lower BMI: Event/Total
Method of Detection
Population
OR (95% CI)
% Weight
BMI > 25 Vs BMI < 25 (N=907)
Anthony 2000 23 / 48 9 / 24 CA I 1.53 (0.56, 4.18) 36.41
Halm 2005 12 / 67 2 / 42 MI P 4.36 (0.92, 20.59) 15.18
Yao 2016 0 / 11 8 / 188 CC P 0.92 (0.05, 17.01) 4.30
Desai 2016 59 / 253 5 / 60 MI P&I 3.35 (1.28, 8.74) 39.59
Hauters 2017 16 / 190 0 / 23 MI P&I 4.44 (0.26, 76.54) 4.52
Subtotal (I-squared = 0.0%, p = 0.668) 2.51 (1.37, 4.60) 100.00
BMI > 30 Vs BMI < 30 (N=4,986)
Vidovic 2006 CA I 1.41 (1.30, 1.53) 16.40
Sauerland 2005 19 / 92 40 / 294 MI I 1.65 (0.90, 3.03) 8.00
Sauerland 2004 7 / 52 10 / 107 CA I 1.51 (0.54, 4.22) 4.03
Lahon 2009 5 / 37 8 / 37 CA I 0.57 (0.17, 1.93) 3.06
Perrone 2005 4 / 41 8 / 80 MI I 0.97 (0.27, 3.44) 2.90
Moreno-Egea 2012b 18 / 128 2 / 182 CC I 14.73 (3.35, 64.70) 2.22
Petro 2015 MI I 0.52 (0.10, 2.61) 1.87
Ferrai 2013 2 / 33 2 / 36 CA I 1.10 (0.15, 8.26) 1.27
Chan 2005 1 / 25 14 / 163 CT I 0.44 (0.06, 3.53) 1.21
Tandon 2016 8 / 47 1 / 41 IU/C I 8.21 (0.98, 68.71) 1.16
Ferrarese 2016 4 / 59 0 / 19 CC I 3.16 (0.16, 61.45) 0.61
Warwick 2016 2 / 19 0 / 38 CC I 11.00 (0.50, 241.38) 0.57
Shankar 2017 14 / 178 6 / 154 MI P 2.11 (0.79, 5.62) 4.32
Farrow 2008 7 / 41 2 / 111 CC P 11.22 (2.23, 56.58) 1.90
Yao 2016 5 / 161 3 / 65 CC P 0.92 (0.05, 17.01) 0.64
Mercoli 2017 CI P&I 0.98 (0.94, 1.03) 16.63
Giordano 2017c 18 / 235 30 / 276 CC P&I 0.68 (0.37, 1.25) 7.90
Desai 2016 49 / 173 15 / 140 MI P&I 3.29 (1.75, 6.18) 7.67
Rosen 2003 9 / 44 8 / 52 MI P&I 1.41 (0.49, 4.04) 3.90
Slater 2015a CI P&I 2.14 (0.72, 6.39) 3.67
Cobb 2006 10 / 163 4 / 114 CA P&I 1.80 (0.55, 5.88) 3.23
Bontinck 2014 7 / 39 4 / 53 CU P&I 2.68 (0.73, 9.90) 2.75
Ng 2015 9 / 33 3 / 15 CC P&I 1.50 (0.34, 6.58) 2.22
Pavlakis 2006 16 / 178 1 / 22 CT P&I 2.07 (0.26, 16.45) 1.21
Hauters 2017 13 / 106 3 / 107 MI P&I 4.44 (0.26, 76.54) 0.67
Subtotal (I-squared = 78.0%, p = 0.000) 1.54 (1.21, 1.95) 100.00
BMI > 35 Vs BMI < 35 (N=2,047)
Tandon 2016 3 / 17 6 / 71 IU/C I 2.32 (0.52, 10.42) 5.52
Reid 2004 4 / 13 0 / 11 MR I 10.89 (0.52, 229.01) 1.34
Kohler 2015a 3 / 21 35 / 180 MI P 0.69 (0.19, 2.48) 7.64
Shankar 2017 3 / 21 17 / 311 MI P 2.88 (0.77, 10.75) 7.18
Yao 2016 3 / 61 5 / 138 CC P 0.92 (0.05, 17.01) 1.47
Desai 2016 24 / 89 40 / 224 MI P&I 1.70 (0.95, 3.03) 37.05
Giordano 2017c 14 / 136 34 / 375 CC P&I 1.15 (0.60, 2.22) 28.95
Ching 2008 4 / 42 16 / 124 MI P&I 0.71 (0.22, 2.26) 9.31
Hauters 2017 9 / 44 7 / 169 MI P&I 4.44 (0.26, 76.54) 1.54
Subtotal (I-squared = 0.0%, p = 0.504) 1.42 (1.00, 2.03) 100.00
BMI > 40 Vs BMI < 40 (N=1,443)
Perrone 2005 5 / 27 7 / 92 MI I 2.76 (0.80, 9.53) 19.66
Tsereteli 2008 11 / 134 19 / 767 NI P&I 3.52 (1.64, 7.58) 51.41
Cobb 2006 5 / 52 9 / 225 CA P&I 2.55 (0.82, 7.97) 23.34
Mann 2015 1 / 16 3 / 128 CC P&I 2.78 (0.27, 28.43) 5.59
Subtotal (I-squared = 0.0%, p = 0.968) 3.07 (1.77, 5.32) 100.00
NOTE: Weights are from random effects analysis
.1
1
10
Lower odds
Higher odds

2.0 Co-morbidities

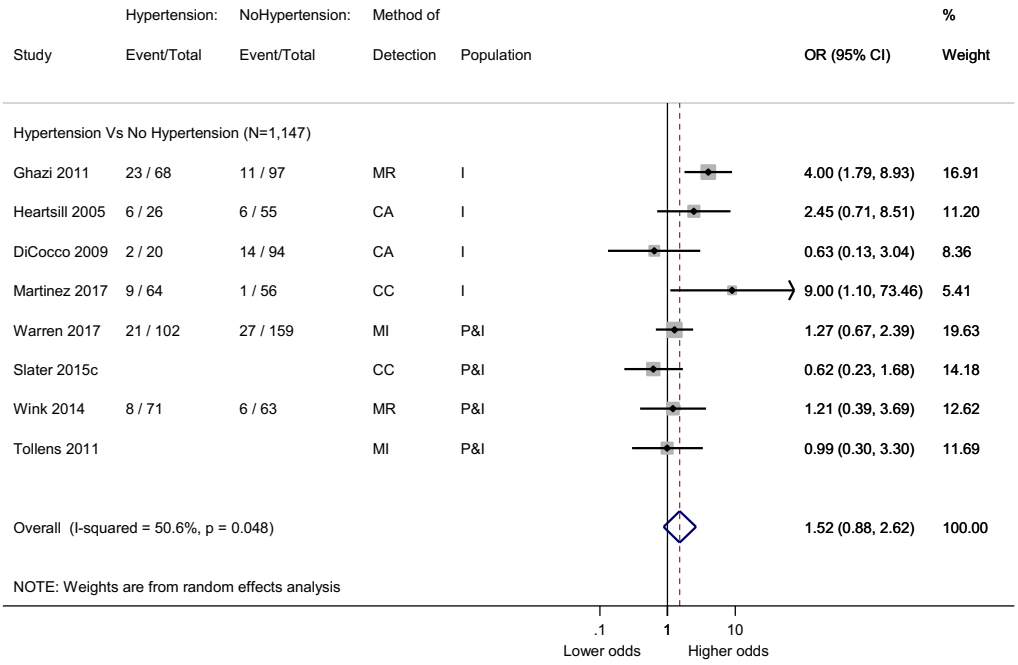
2.1 Smoker



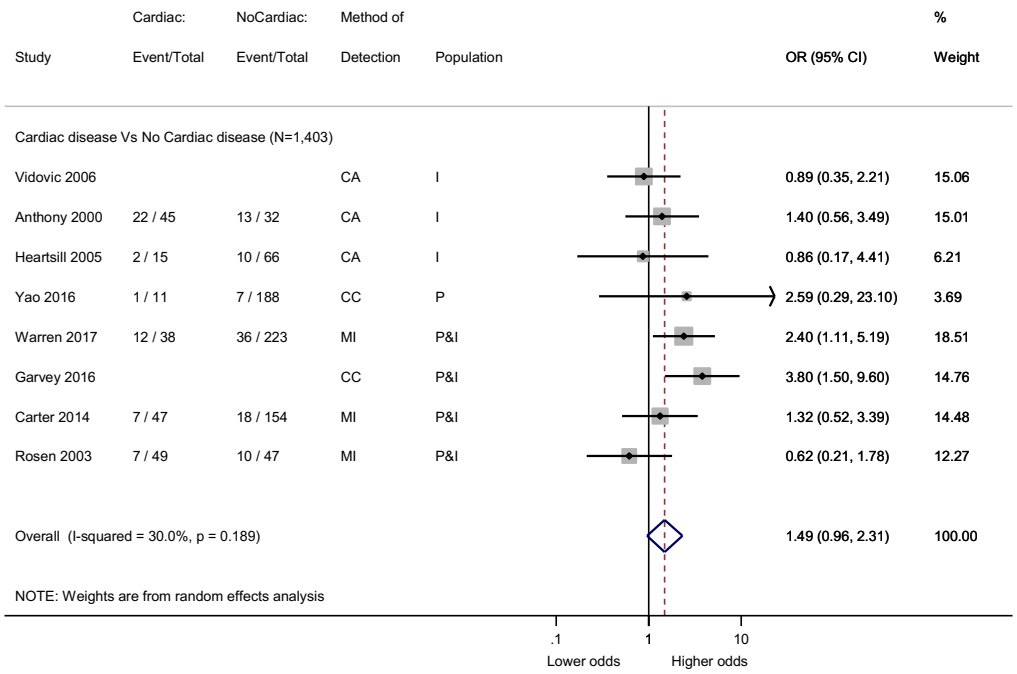
2.2 Diabetes


Study
Diabetes: Event/Total
NoDiabetes: Event/Total
Method of Detection
Population
OR (95% CI)
% Weight
Diabetes Vs No Diabetes (N=5,555)
Cobb 2015 14 / 70 30 / 185 MR I 1.29 (0.64, 2.61) 7.10
Ghazi 2011 13 / 24 21 / 141 MR I 6.75 (2.67, 17.07) 5.16
Vidovic 2006 CA I 1.74 (0.67, 4.50) 5.00
Heartsill 2005 6 / 27 6 / 54 CA I 2.29 (0.66, 7.92) 3.41
Anthony 2000 6 / 11 29 / 66 CA I 1.53 (0.42, 5.52) 3.25
Martinez 2017 5 / 31 5 / 89 CC I 3.23 (0.87, 12.04) 3.12
Moreno-Egea 2012b 3 / 18 17 / 292 CC I 3.24 (0.85, 12.27) 3.06
Krpata 2013 MI I 2.25 (0.56, 10.22) 2.67
Fayezizadeh 2016 5 / 30 3 / 34 MI I 2.07 (0.45, 9.50) 2.46
Petro 2015 MI I 1.00 (0.16, 6.14) 1.81
DiCocco 2009 1 / 9 15 / 105 CA I 0.75 (0.09, 6.44) 1.35
Sauerland 2004 0 / 16 17 / 144 CA I 0.22 (0.01, 3.85) 0.74
Shankar 2017 11 / 113 9 / 219 MI P 2.52 (1.01, 6.26) 5.27
Kohler 2015a 2 / 27 36 / 214 MI P 0.40 (0.09, 1.74) 2.57
Holihan 2016a 82 / 236 186 / 554 MI P&I 1.05 (0.76, 1.45) 11.94
Holihan 2016 40 / 262 115 / 963 MI P&I 1.33 (0.90, 1.96) 11.02
Warren 2017 19 / 78 29 / 183 MI P&I 1.71 (0.89, 3.28) 7.66
Lin 2009 8 / 34 31 / 110 MR P&I 0.78 (0.32, 1.92) 5.40
Wink 2014 4 / 32 10 / 102 MR P&I 1.31 (0.38, 4.52) 3.45
Tollens 2011 MI P&I 0.48 (0.12, 1.96) 2.84
Carter 2014 2 / 53 23 / 148 MI P&I 0.21 (0.05, 0.94) 2.58
Slater 2015c CC P&I 0.59 (0.13, 2.76) 2.45
Bencini 2009 2 / 17 10 / 129 MI P&I 1.59 (0.32, 7.94) 2.24
Rosen 2003 2 / 11 15 / 85 MI P&I 1.04 (0.20, 5.30) 2.20
Basta 2015 1 / 9 6 / 28 CA P&I 0.46 (0.05, 4.42) 1.23
Overall (I-squared = 35.6%, p = 0.041) 1.36 (1.05, 1.77) 100.00
NOTE: Weights are from random effects analysis
.1
1
10
Lower odds
Higher odds

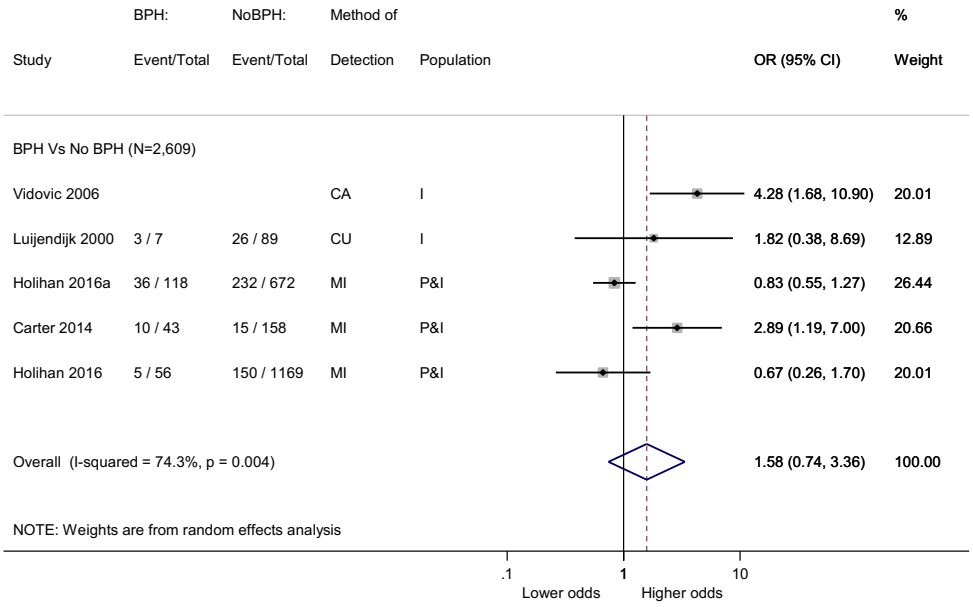
2.3 Hypertension



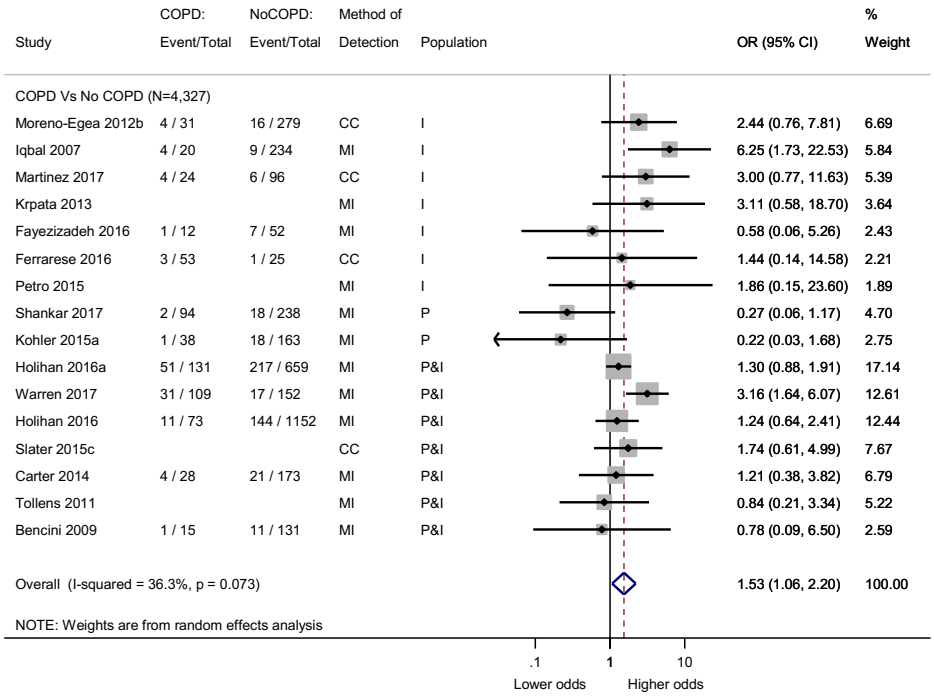
2.4 Cardiac



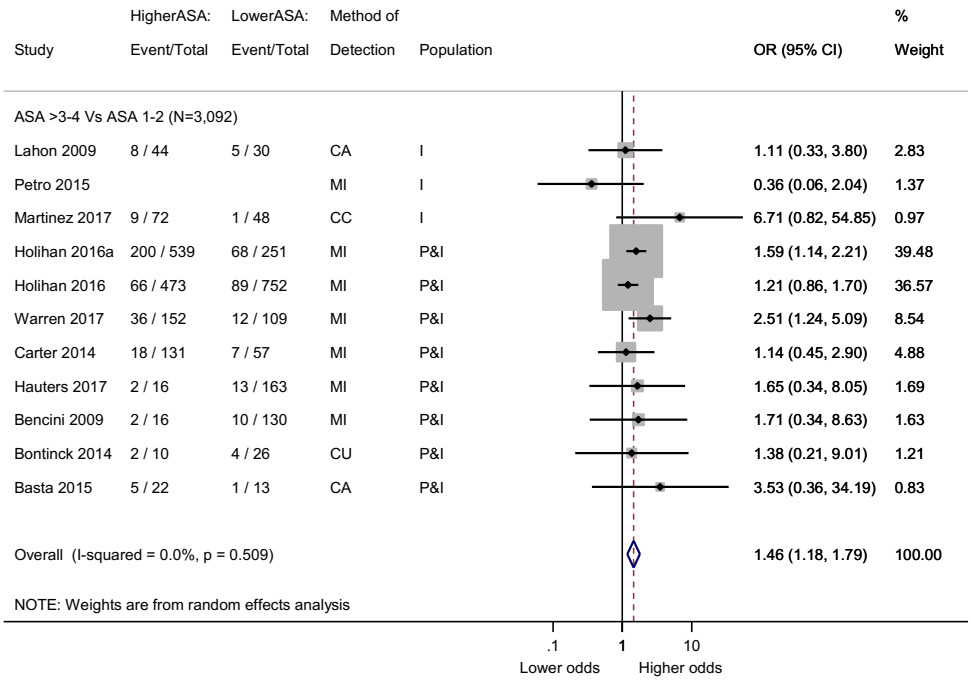
2.5 BPH



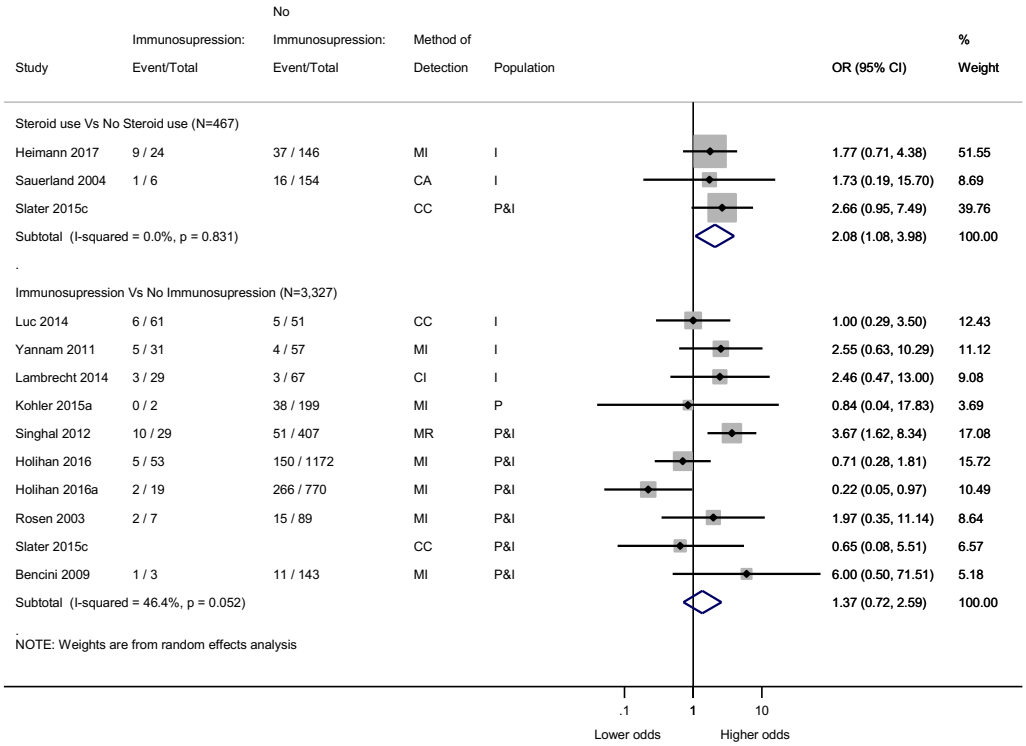
2.6 COPD



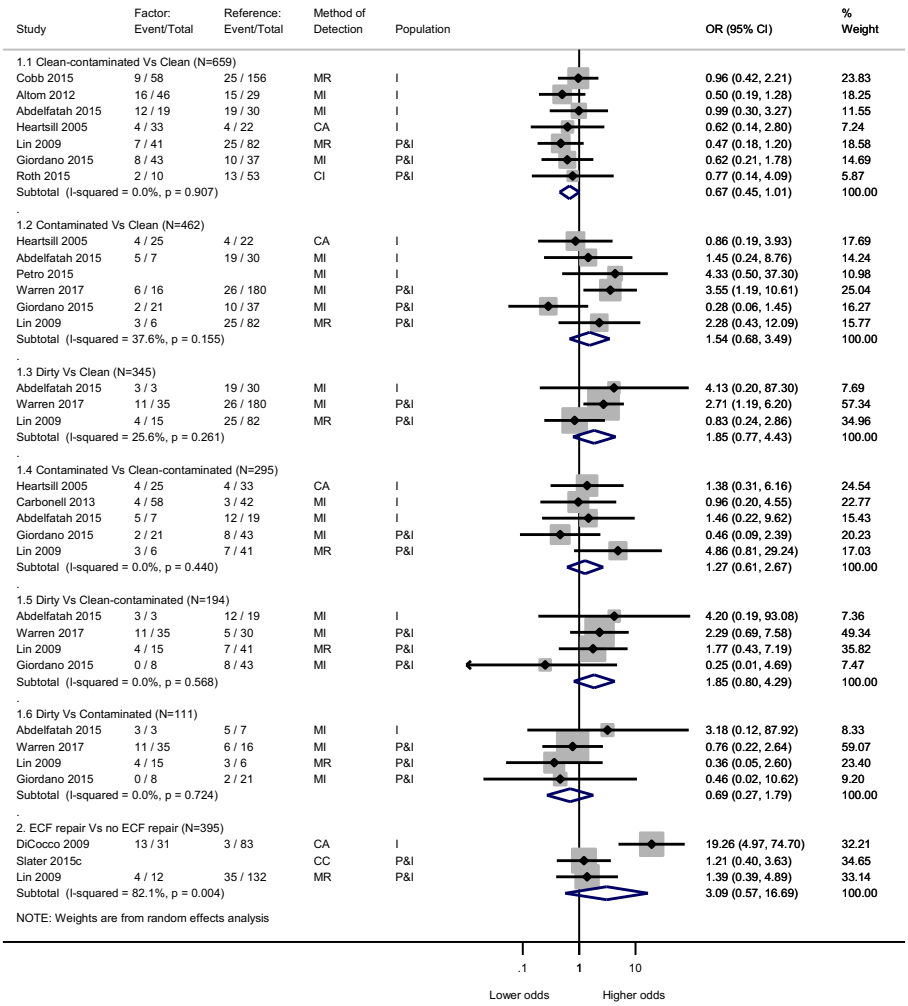
2.7 ASA 3-4 Vs ASA 1-2



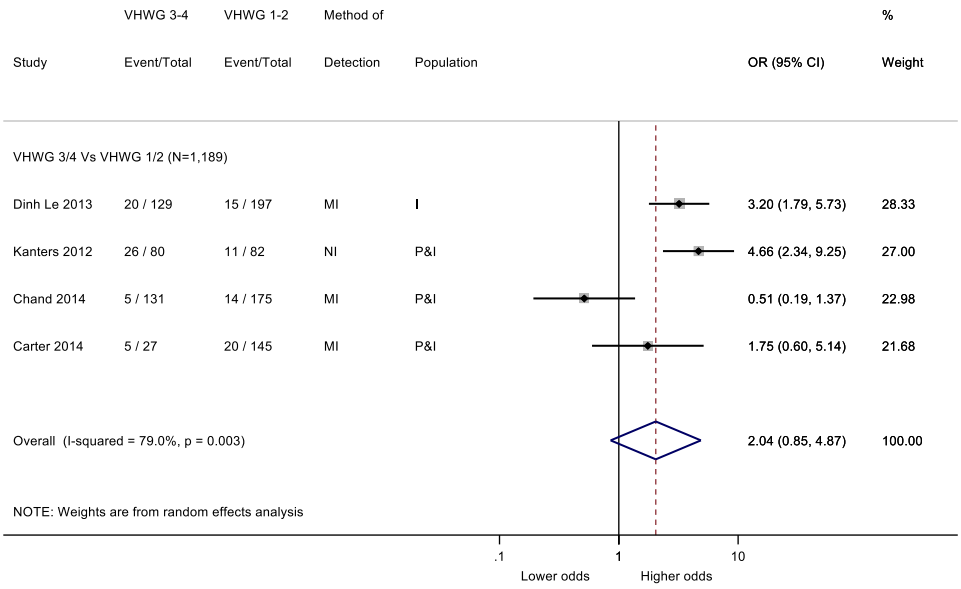
2.8 Immunosuppression



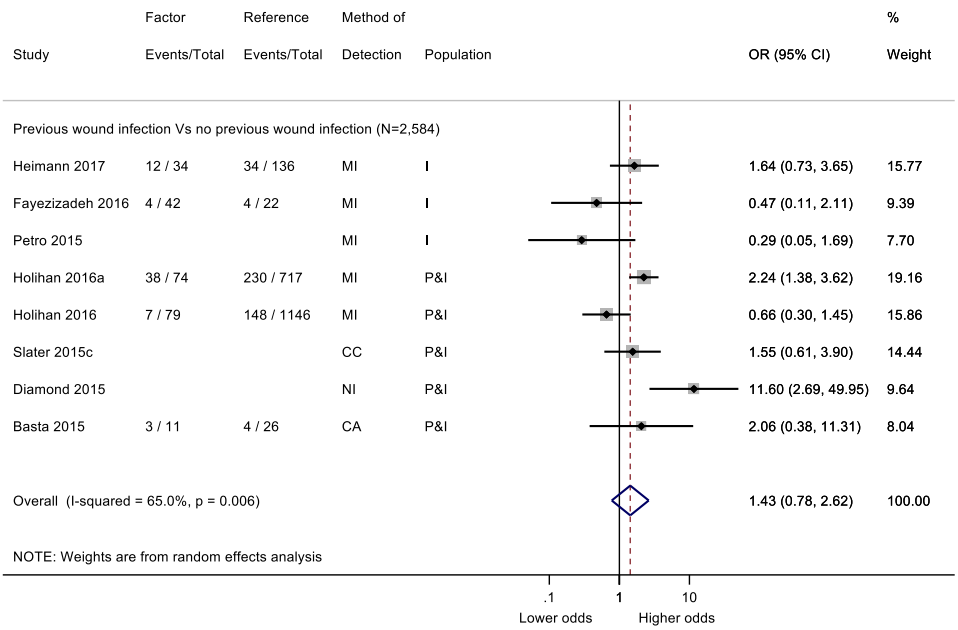
3.0 Hernia related
3.1 Contaminated



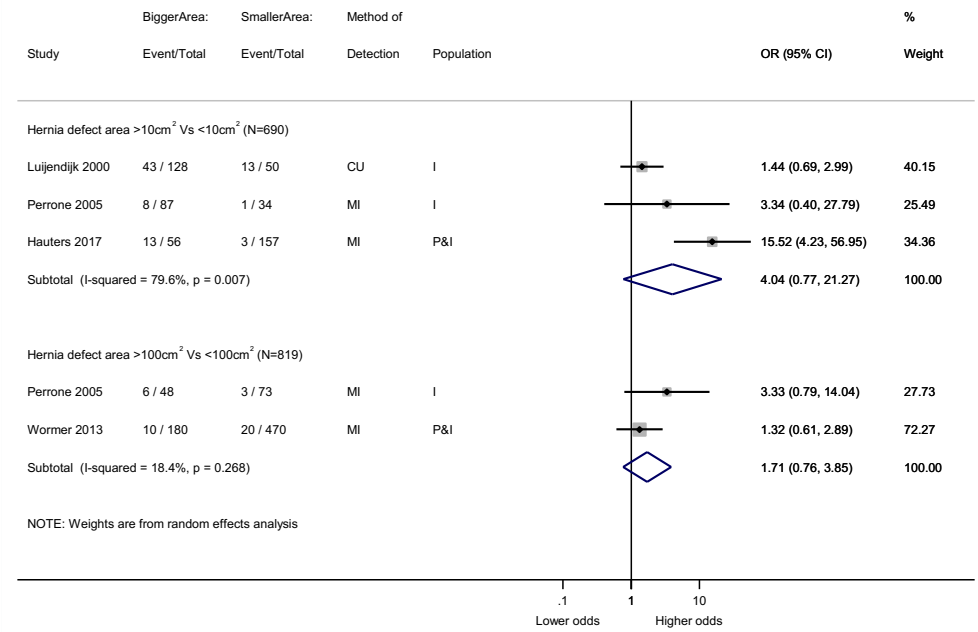
3.2 VHWG


VHWG 3-4
VHWG 1-2
Method of
%
Study
Event/Total
Event/Total
Detection
Population
OR (95% CI)
Weight
VHWG 3/4 Vs VHWG 1/2 (N=1,189)
Dinh Le 2013 20 / 129 15 / 197 MI I 3.20 (1.79, 5.73) 28.33
Kanters 2012 26 / 80 11 / 82 NI P&I 4.66 (2.34, 9.25) 27.00
Chand 2014 5 / 131 14 / 175 MI P&I 0.51 (0.19, 1.37) 22.98
Carter 2014 5 / 27 20 / 145 MI P&I 1.75 (0.60, 5.14) 21.68
Overall (I-squared = 79.0%, p = 0.003) 2.04 (0.85, 4.87) 100.00
NOTE: Weights are from random effects analysis
.1
1
10
Lower odds
Higher odds

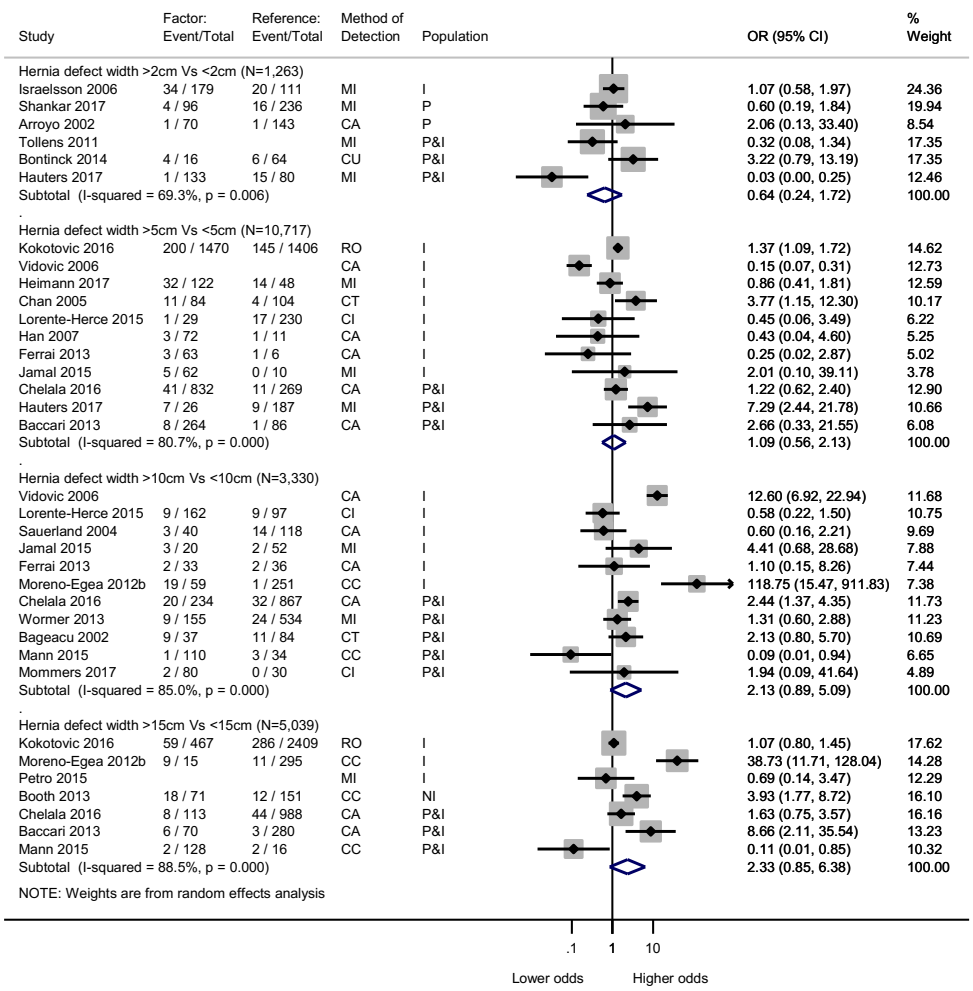
3.3 Previous wound infection



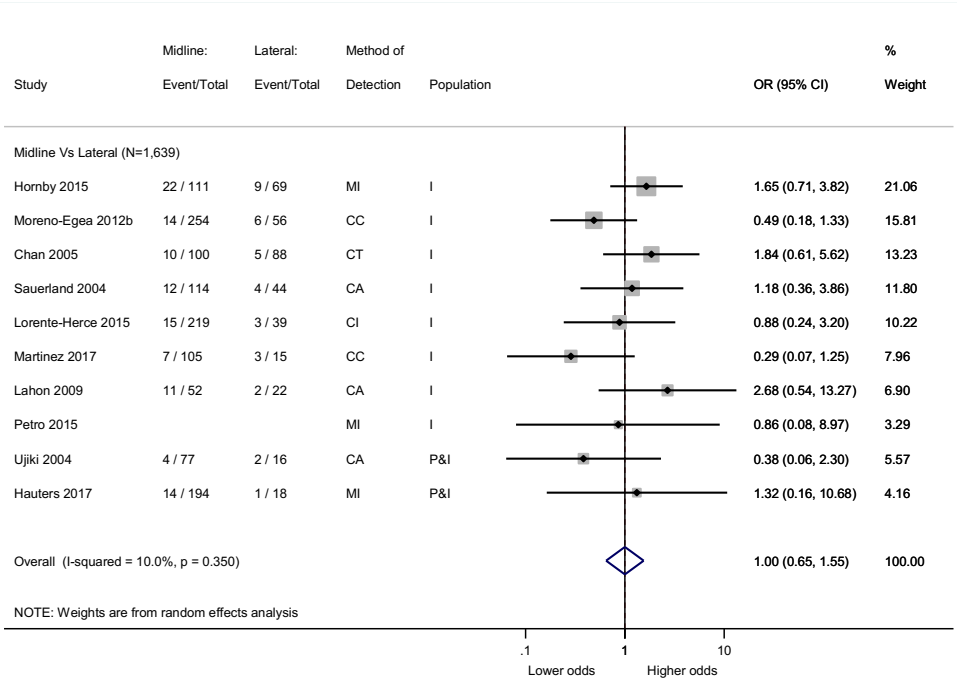
3.4 Hernia Area



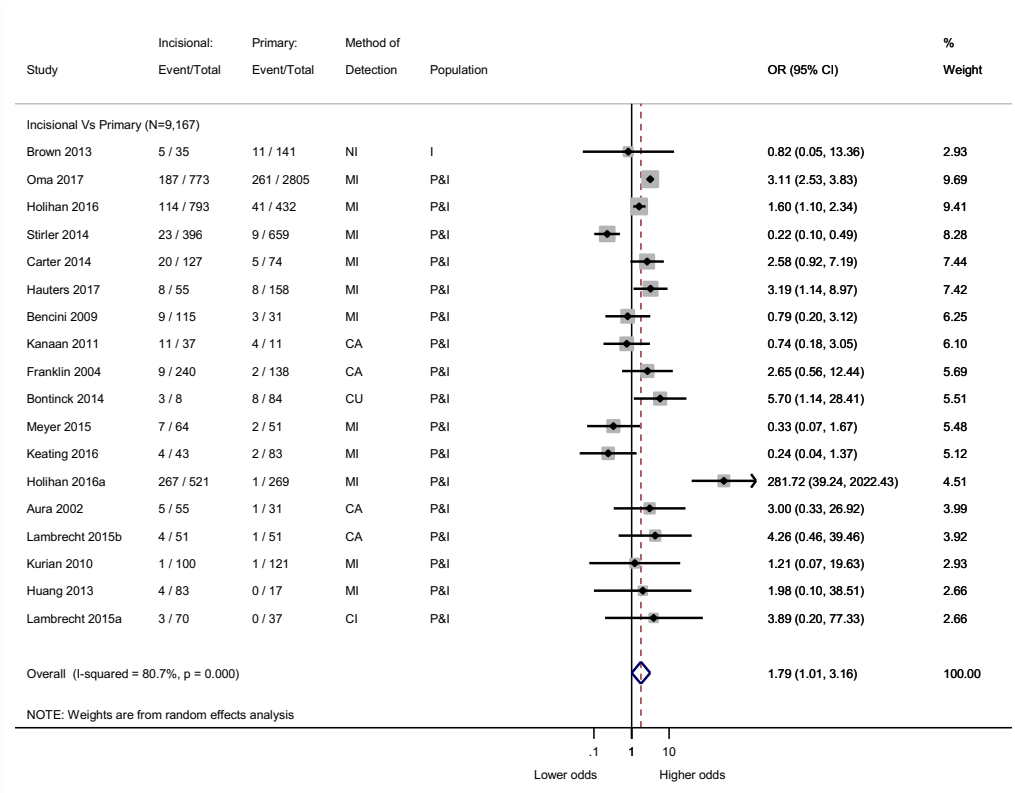
3.5 Hernia width



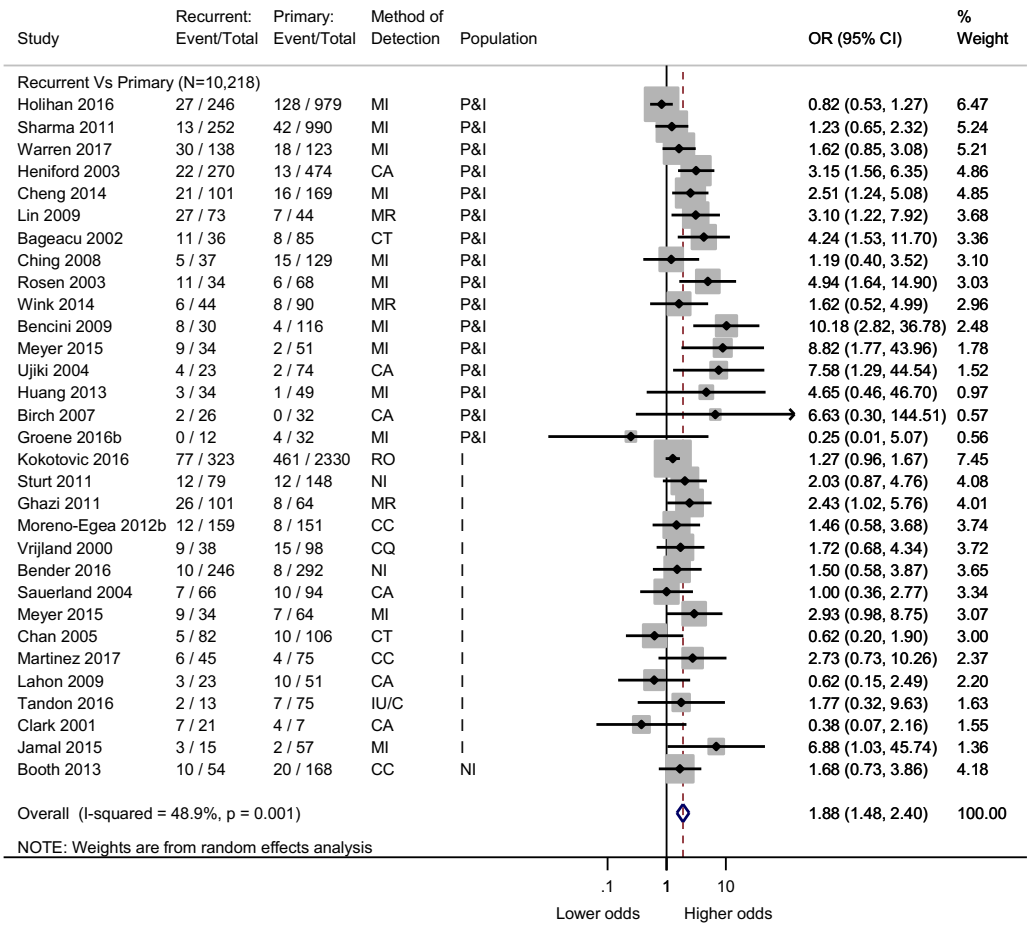
3.6 Midline Vs Lateral



3.7 Incisional Vs Primary

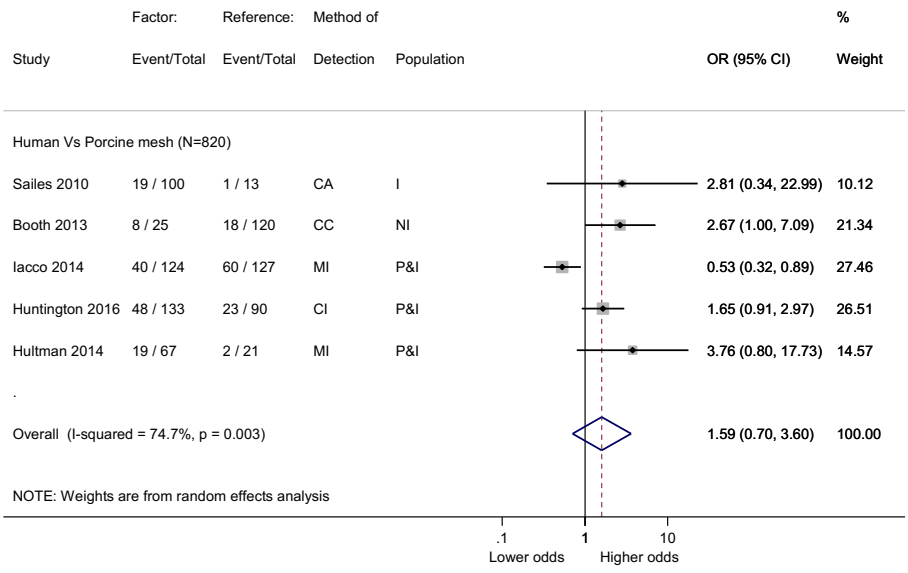


3.8 Recurrent Vs Primary

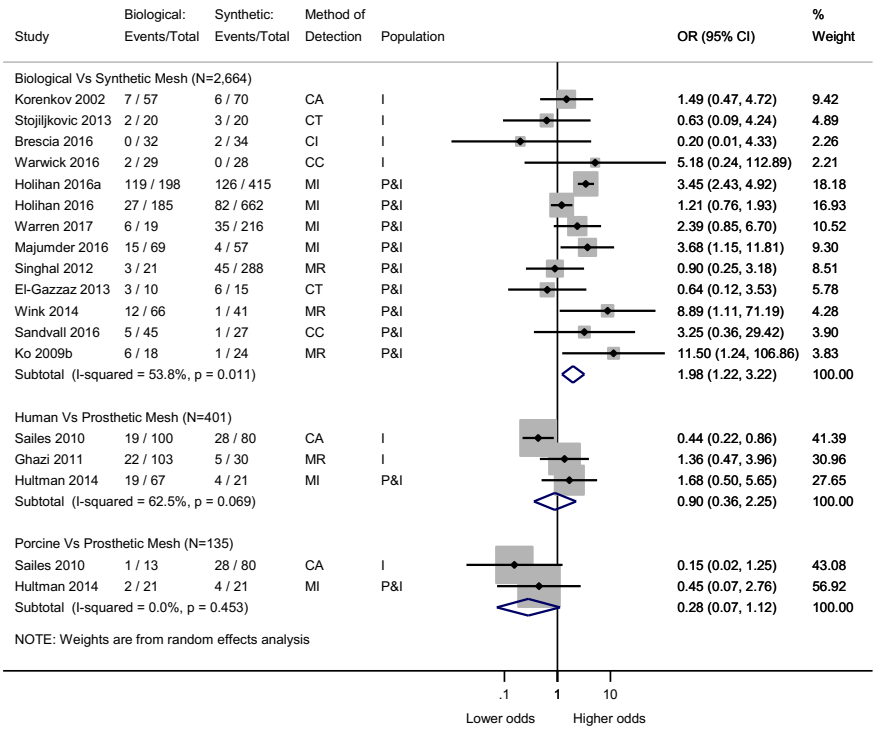


4.0 Intra-operative

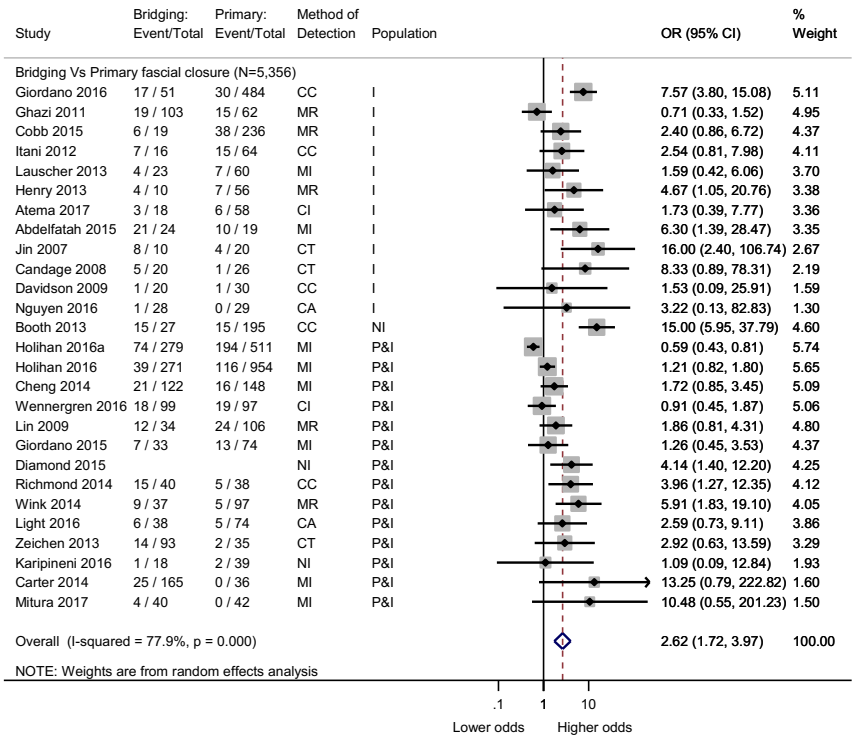
4.1 Human biologic Vs Porcine biologic



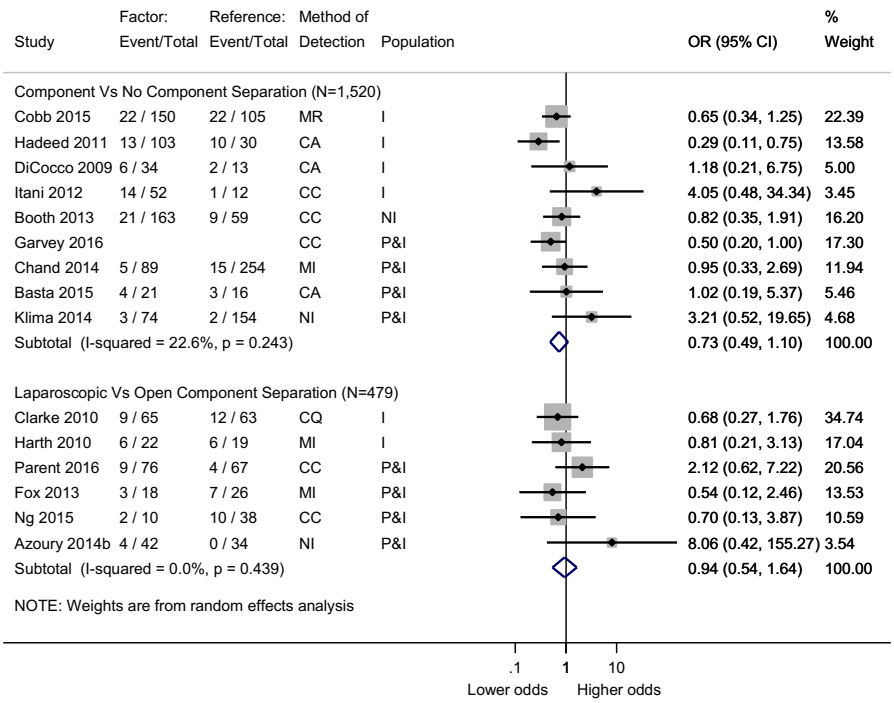
4.2 Biologic Vs Synthetic



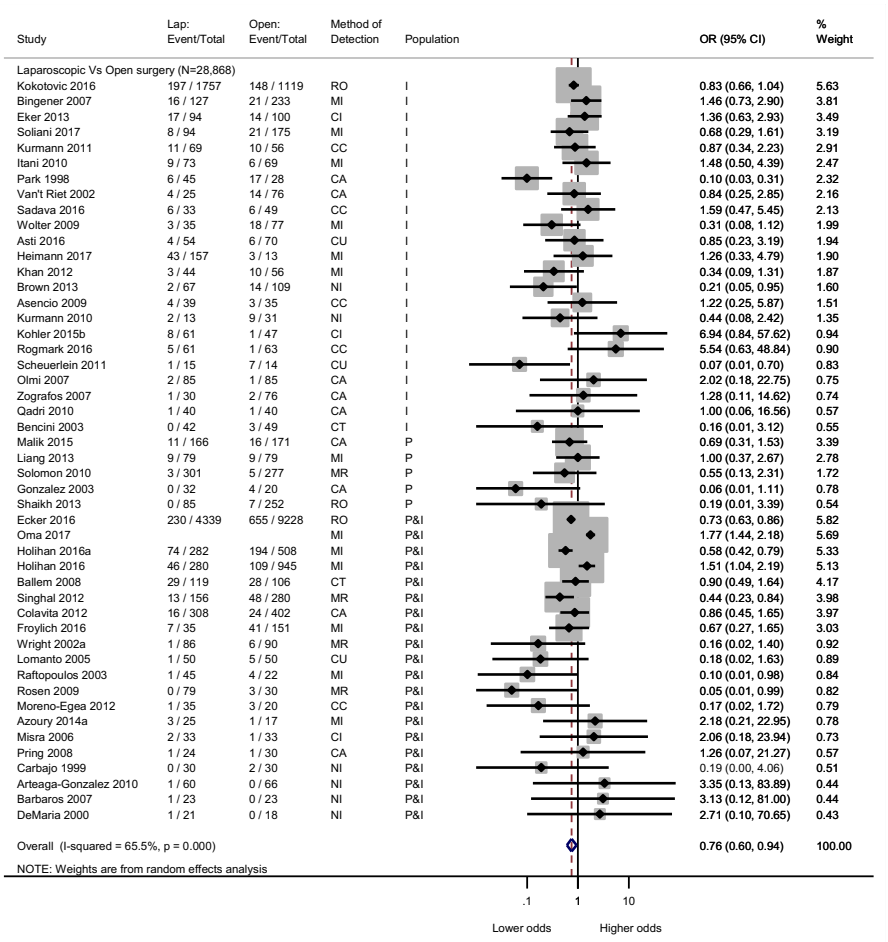
4.3 Bridging Vs Primary closure



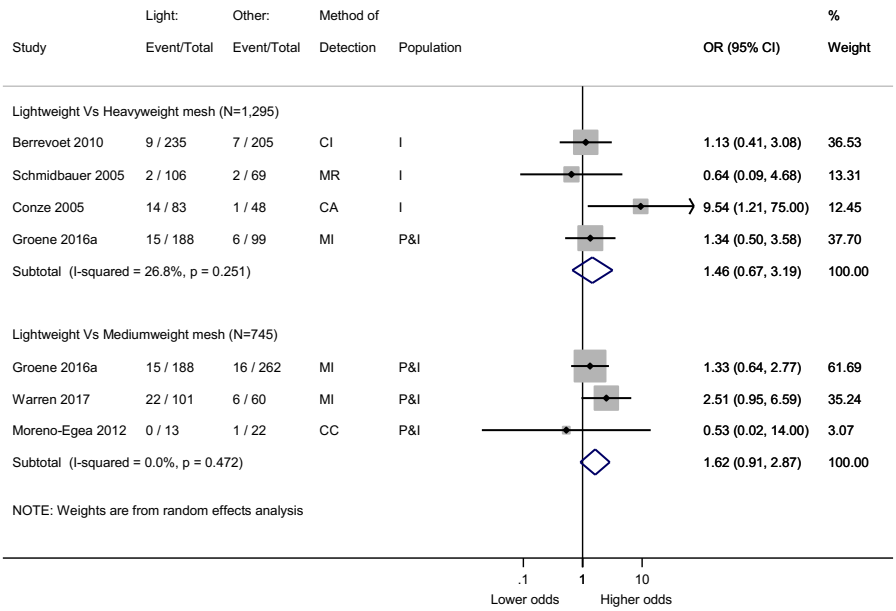
4.4 Component separation Vs no Component Separtion



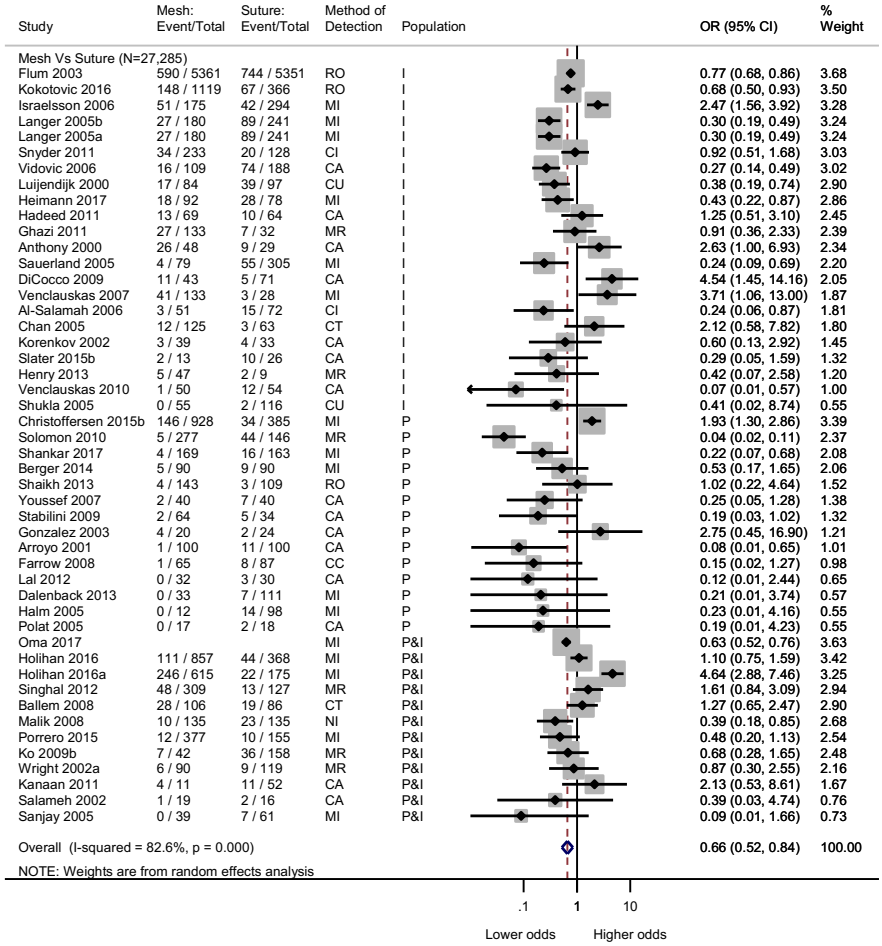
4.5 Laparoscopic Vs Open Surgery



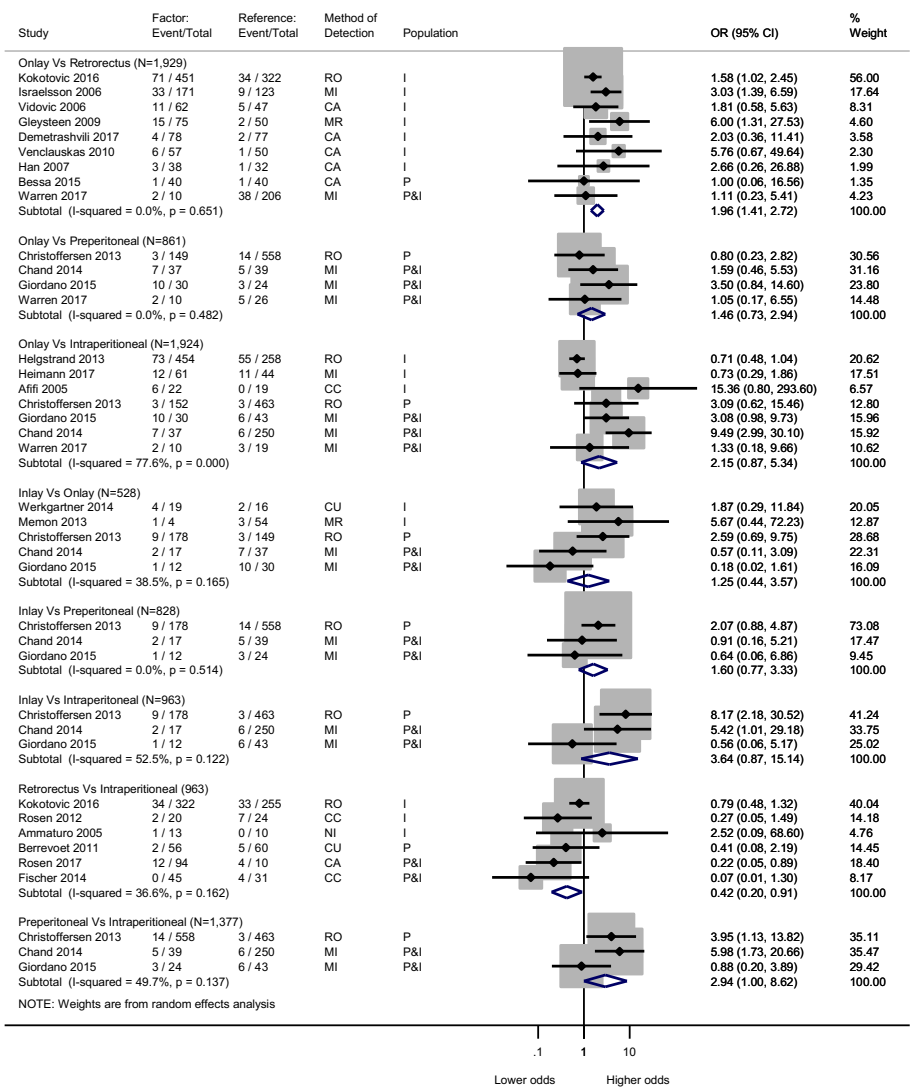
4.6 Lightweight mesh Vs other mesh



4.7 Mesh Vs Suture repair

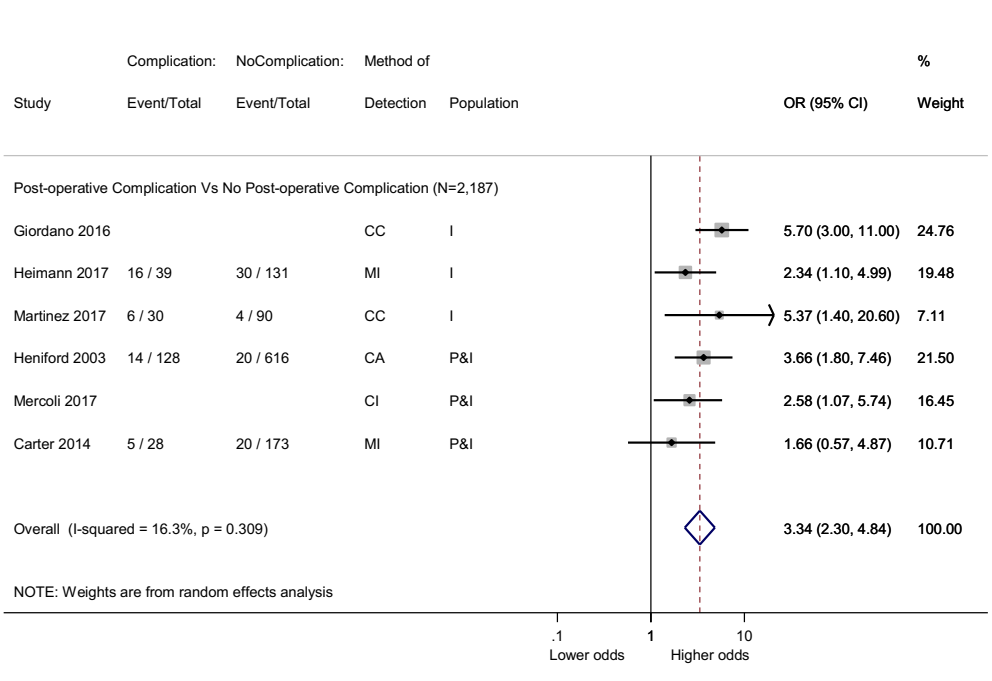


4.8 Position of mesh

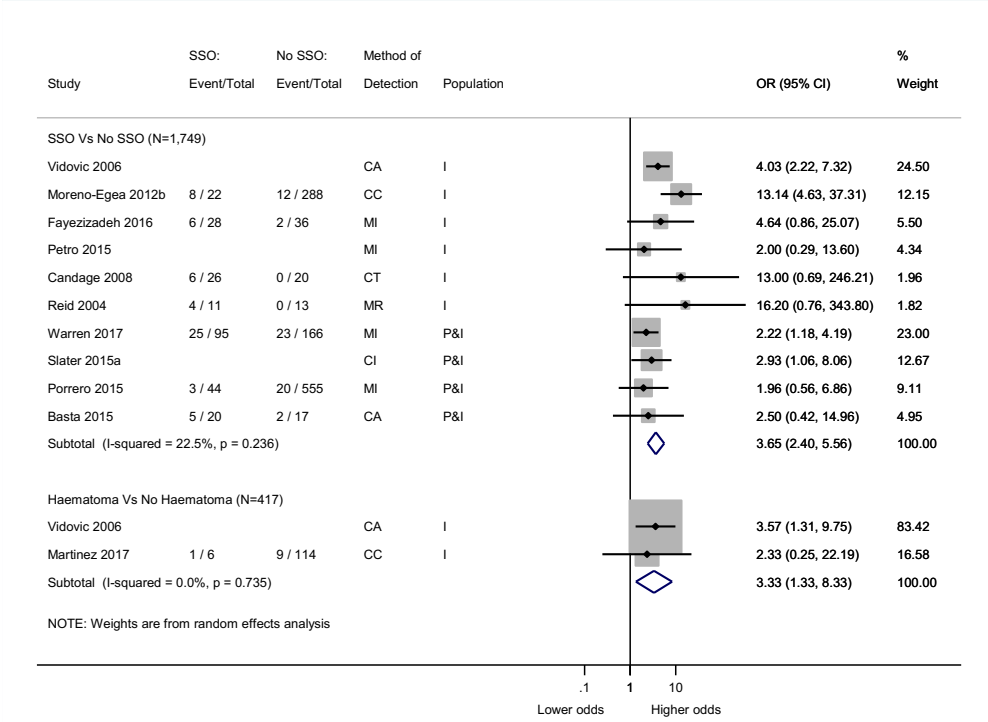


5.0 Post-operative

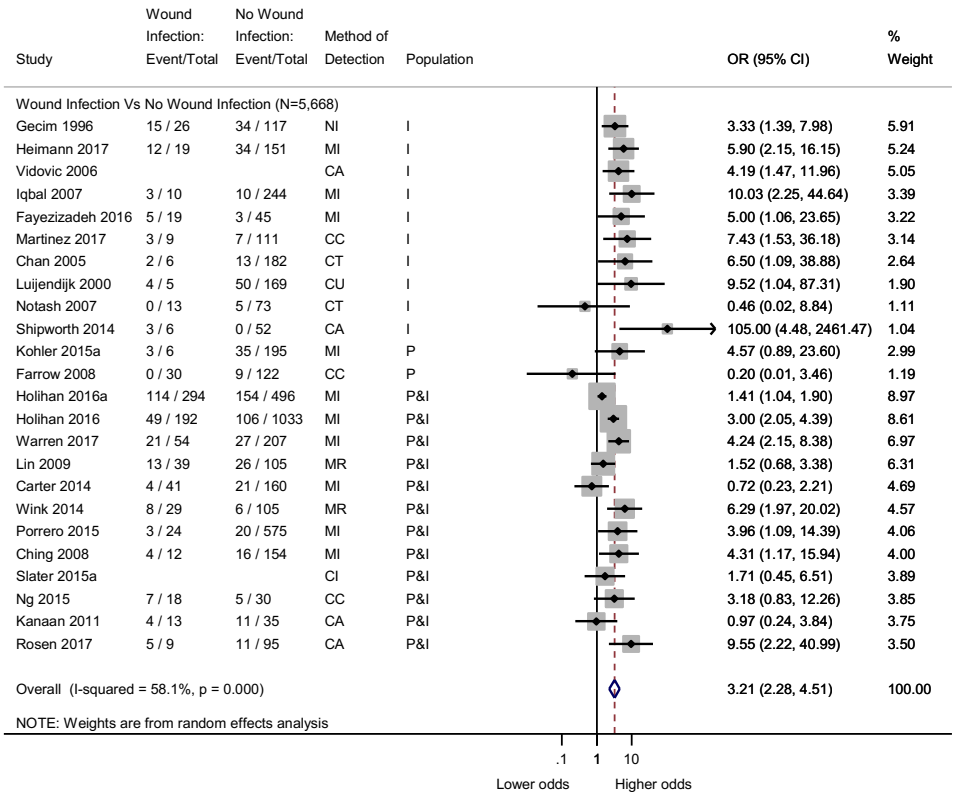
5.1 Post-operative complication



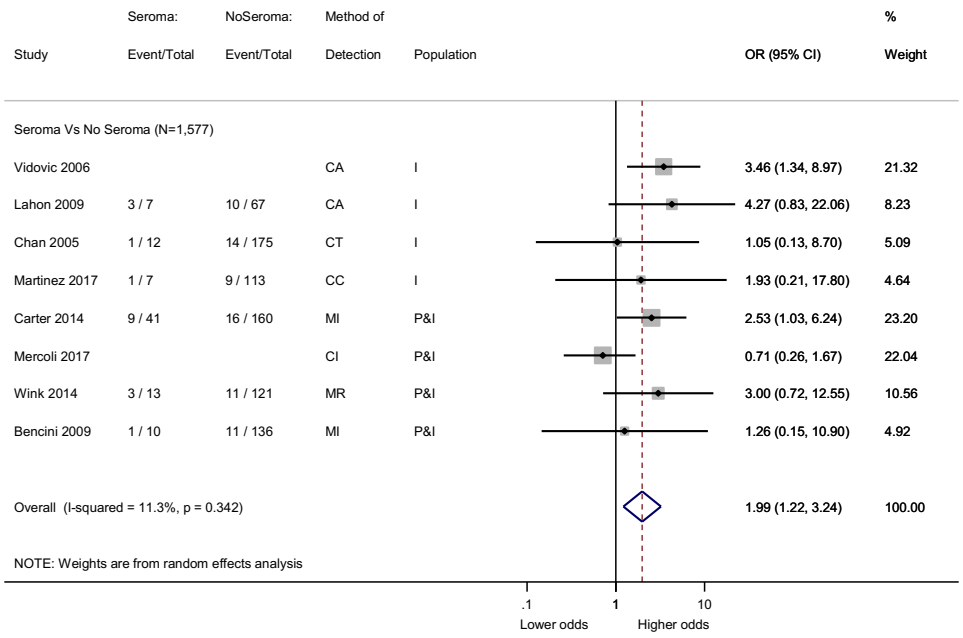
5.2 Surgical site Occurrence



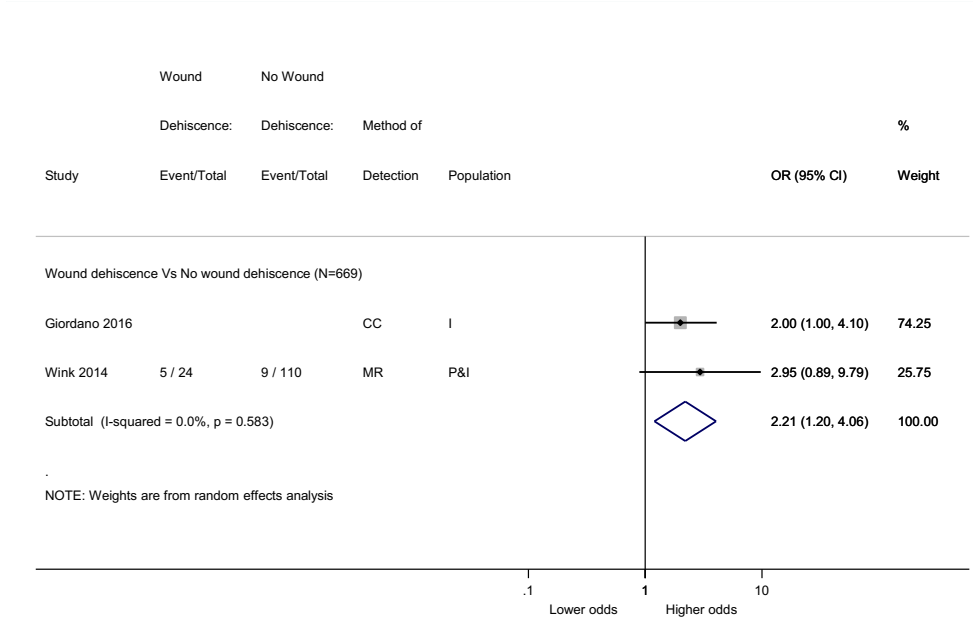
5.3 Wound infection



5.4 Seroma

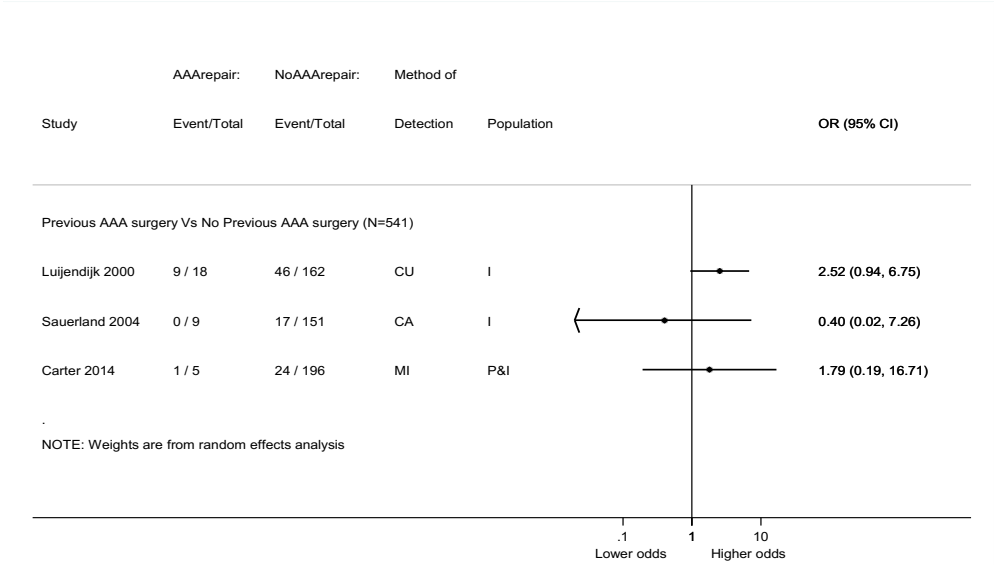

Seroma: Event/Total
NoSeroma: Event/Total
Method of Detection
Population
% Weight
Study
OR (95% CI)
Seroma Vs No Seroma (N=1,577)
Vidovic 2006 CA I 3.46 (1.34, 8.97) 21.32
Lahon 2009 3 / 7 10 / 67 CA I 4.27 (0.83, 22.06) 8.23
Chan 2005 1 / 12 14 / 175 CT I 1.05 (0.13, 8.70) 5.09
Martinez 2017 1 / 7 9 / 113 CC I 1.93 (0.21, 17.80) 4.64
Carter 2014 9 / 41 16 / 160 MI P&I 2.53 (1.03, 6.24) 23.20
Mercoli 2017 CI P&I 0.71 (0.26, 1.67) 22.04
Wink 2014 3 / 13 11 / 121 MR P&I 3.00 (0.72, 12.55) 10.56
Bencini 2009 1 / 10 11 / 136 MI P&I 1.26 (0.15, 10.90) 4.92
Overall (I-squared = 11.3%, p = 0.342) 1.99 (1.22, 3.24) 100.00
NOTE: Weights are from random effects analysis
.1
1
10
Lower odds
Higher odds

5.5 Wound dehiscence

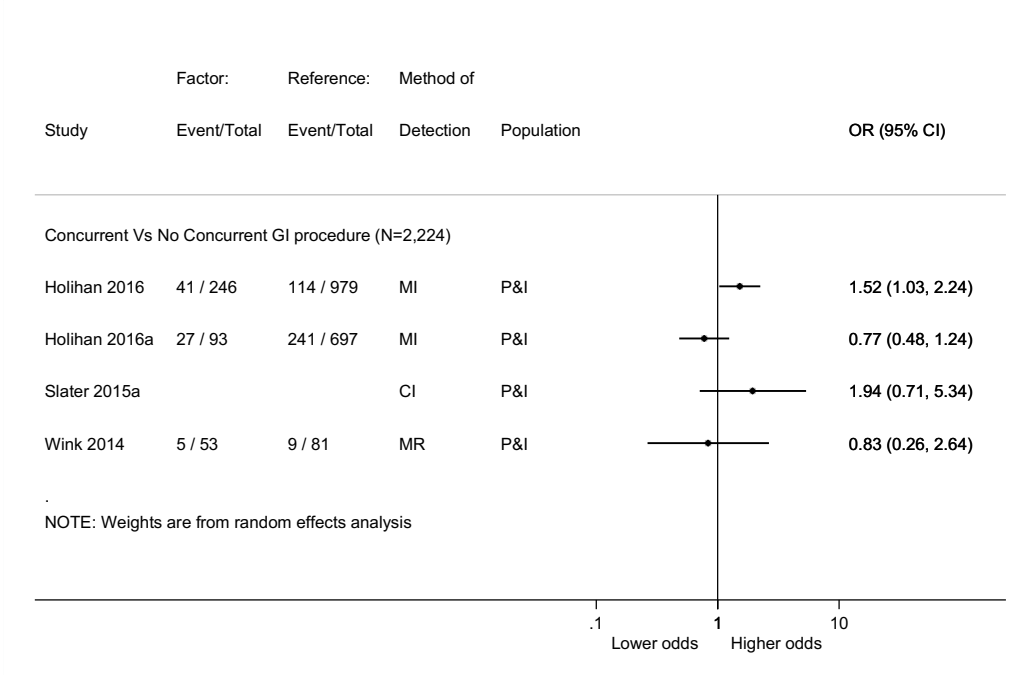


Appendix 35

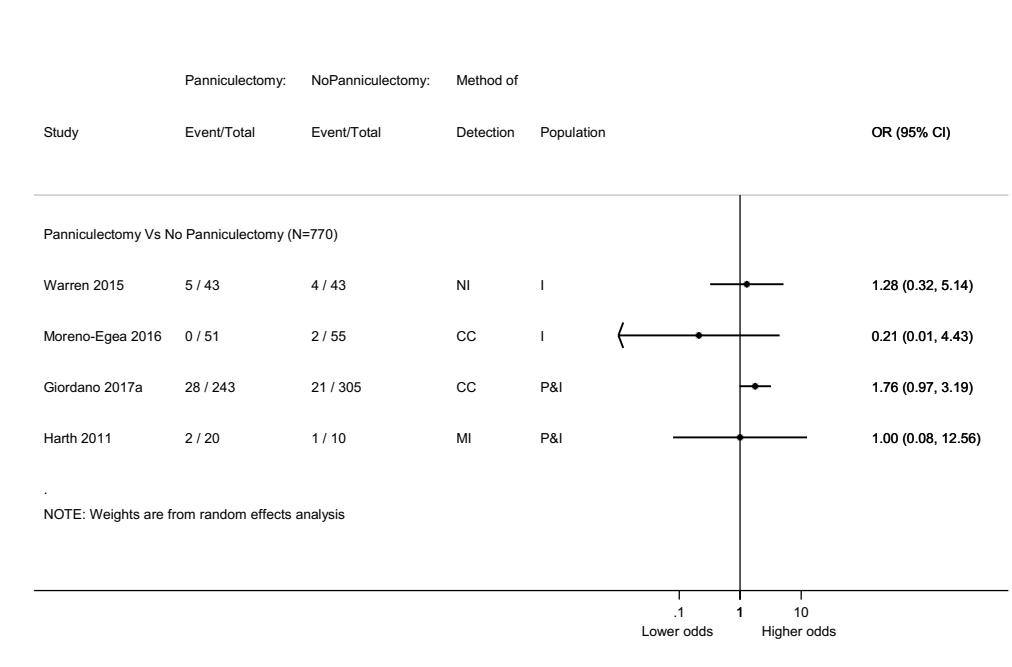
AAA repair – only 3 studies (hernia related variable)



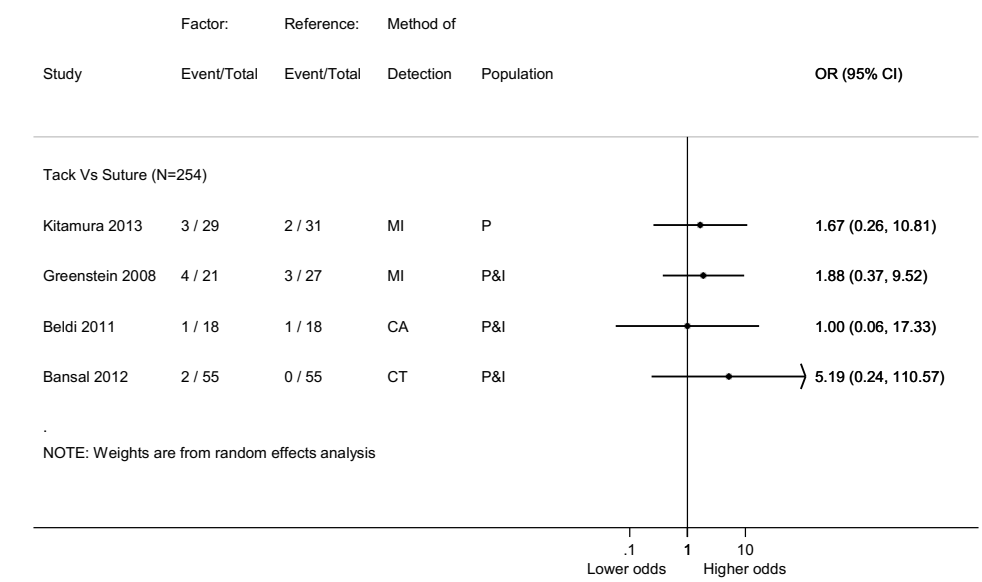
Concurrent GI – not enough studies (Intra-operative variable)



Panniculectomy - not enough studies (Intra-operative variable)



Tack Vs Suture - not enough studies (Intra-operative variable)



Appendix 36 – Deleted Predictors

PaperID	Area	Column1	PrognosticFactor
Christoffersen 2013	Absorable Vs Non-Abs Suture	OUT	Slow-absorbable Vs Fast absorbable suture]
Fayezizadeh 2016	Admission	OUT	ICU admission Vs no ICU admission
Hauters 2017	Hernia Area	Correct - BUT OUT - only data from the paper	Surface area of defect
Notash 2007	Hernia Area	Correct - OUT	Defect area+1cm^2 Vs defect area
Oma 2017	Hernia Area	Correct - Area+10cm^2/Area - OUT	Hernia defect area+10cm^2 Vs hernia defect area
Bontinck 2014	Hernia width	Correct - width+1/width - OUT	Hernia defect width+1cm Vs Hernia defect width
Helgstrand 2013	Hernia width	Correct - ? Subgroup (Probably OUT)	Hernia defect width 7-15cm Vs 0-2cm
Helgstrand 2013	Hernia width	Correct - ? Subgroup (Probably OUT)	Hernia defect width >20cm Vs 0-2cm
Helgstrand 2013	Hernia width	Correct - ? Subgroup (Probably OUT)	Hernia defect width 15-20cm Vs 0-2cm
Kokotovic 2016	Hernia width	Correct - ? Subgroup (Probably OUT)	Hernia defect width 7-15cm Vs 0-2cm
Petro 2016	Hernia width	Correct - width+10/width - OUT	Hernia defect width +10cm Vs hernia defect width
Ferrarese 2016	Location	Correct - OUT nil other	Suprapubic Vs Epigastric
Ferrarese 2016	Location	Correct - OUT nil other	Subcostal Vs Suprapubic
Ferrarese 2016	Location	Correct - OUT nil other	Epigastric Vs Lumbar
Ferrarese 2016	Location	Correct - OUT nil other	Epigastric Vs Non Epigastric
Ferrarese 2016	Location	Correct - OUT nil other	Suprapubic Vs Non suprapubic
Ferrarese 2016	Location	Correct - OUT nil other	Suprapubic Vs Lumbar
Ferrarese 2016	Location	Correct - OUT nil other	Subcostal Vs Epigastric
Ferrarese 2016	Location	Correct - OUT nil other	Lumbar Vs Non lumbar
Ferrarese 2016	Location	Correct - OUT nil other	Subcostal Vs Non subcostal
Ferrarese 2016	Location	Correct - Subcostal Vs Lumbar - OUT	Subcostal Vs Lumbar
Keating 2016	Location	Correct - Epigastric Vs Umbilical - OUT	Umbilical Vs Epigastric
Moreno-Egea 2012a	Location	Correct - OUT nil other	Iliac IH Vs Lumbar IH
Oma 2017	Location	Correct - OUT only one other	Incisional Vs Epigastric
Basoglu 2004	Material	Correct - PP Vs PE - OUT only 2	Polypropylene Vs Polyester
Brown 2013	Material	Correct - ePTFE vs non-ePTFE - OUT - only one	ePTFE Vs non-ePTFE
Carter 2014	Material	Correct - PTFE Vs PEL - OUT only 2	Polytetraflouroethylene Vs Polyethylene
Carter 2014	Material	Correct - PP Vs PEL - OUT only 2	Polypropylene Vs polyethylene
Carter 2014	Material	Correct - PP Vs PTFE - OUT only 2	Polytetraflouroethylene Vs Polypropylene
Hauters 2017	MD Ratio	Correct - OUT no other papers have this variable	MD-Ratio 13-16 Vs MD-Ratio 9-12
Hauters 2017	MD Ratio	Correct - OUT no other papers have this variable	MD-Ratio 9-12 Vs MD-Ratio ≦8
Hauters 2017	MD Ratio	Correct - OUT no other papers have this variable	MD-Ratio ≥17 Vs MD-Ratio ≦8
Hauters 2017	MD Ratio	Correct - OUT no other papers have this variable	MD-Ratio ≥17 Vs MD-Ratio 9-12
Hauters 2017	MD Ratio	Correct - OUT no other papers have this variable	MD-Ratio 13-16 Vs MD-Ratio ≦8
Hauters 2017	MD Ratio	Correct - OUT no other papers have this variable	MD-Ratio ≥17 Vs MD-Ratio 13-16
Hauters 2017	MD Ratio	Correct - OUT no other papers have this variable	M/D ratio
Groene 2016a	Medium Vs Heavy	Correct - OUT no other papers have this variable	Mediumweight Vs Heavyweight

Hauters 2017	Mesh overlap	Correct - OUT >/<5cm overlap - only 1 paper	Mesh overlap 5cm Vs 4cm
Hauters 2017	Mesh overlap	Correct - OUT ?only 1 so OUT	Mesh overlap
Hauters 2017	Mesh overlap	Correct - OUT >/<5cm overlap - only 1 paper	Mesh overlap 5cm Vs 3cm
Hauters 2017	Mesh overlap	Correct - OUT >/<5cm overlap - only 1 paper	Mesh overlap ≥6cm Vs 4cm
Hauters 2017	Mesh overlap	Correct - OUT >/<3cm - only 2 - OUT	Mesh overlap 4cm Vs 3cm
Hauters 2017	Mesh overlap	Correct - OUT >/<5cm overlap - only 1 paper	Mesh overlap ≥6cm Vs 3cm
Hauters 2017	Mesh overlap	Correct - OUT >/<5cm overlap - only 1 paper	Mesh overlap ≥6cm Vs 5cm
Lambrecht 2014	Mesh overlap	Correct - ?only 1 so OUT	Overlap coefficient
Tsimoyiannis 2008	Mesh overlap	Correct - >/<3cm - only 2 - OUT	Mesh overlap 2.5cm Vs 4.5cm
Bensaadi 2014	Mesh related	Correct - BUT OUT AS ONLY 1	Ventralex vs Biomesh Cabs'Air
Keating 2016	Mesh related	Correct - BUT OUT AS ONLY 1	Medium V-Patch Vs Small V-Patch
Keating 2016	Mesh related	Correct - BUT OUT AS ONLY 1	Large V-Patch Vs Small V-Patch
Keating 2016	Mesh related	Correct - BUT OUT AS ONLY 1	Large V-Patch Vs Medium V-Patch
Martinez 2017	Mesh related	Correct - BUT OUT AS ONLY 1	Kugel patch Vs Ventrio patch
Martinez 2017	Mesh related	Correct - BUT OUT AS ONLY 1	Kugel patch Vs Ventrio patch
Martinez 2017	Mesh related	Correct - BUT OUT AS ONLY 1	Kugel patch Vs Ventrio patch
Pawlak 2016	Mesh related	Correct - BUT OUT AS ONLY 1	Physiomesh (rigid) vs Ventralight(elastic)
Tandon 2016	Mesh related	Correct - BUT OUT AS ONLY 1	Parietex Vs Dynamesh
Cox 2016	No. Comorbidities	Correct - BUT OUT AS ONLY 1	≥2 Co-morbidity Vs <2 co-morbidities
Bencini 2009	Operation time	Correct - BUT OUT AS ONLY 1	Operating time (Continuous variable, Multivariable HR analysis)
Fischer 2014	Operation time	Corrct - BUT OUT AS ONLY 1	Prolonged Operating time Vs not prolonged
Greenstein 2008	Operation time	Correct - >/<120min - OUT as only 2	Operative time (>/< 120 mins)
Hornby 2015	Operation time	Correct - >/<90min - OUT as only 1	Duration of operation >90mins Vs <90mins
Rosen 2013	Operation time	Correct - >/<90min - OUT as only 1	Operating time+60mins Vs Operating time
Slater 2015c	Operation time	Correct - >/<120min - OUT as only 2	Operating time+120mins Vs Operating time
Heimann 2017	Other disease	Correct - BUT OUT AS ONLY 1	Crohn Vs Ulcerative colitis
Heimann 2017	Other disease	Correct - BUT OUT AS ONLY 1	Hypoalbuminaemia Vs no hypoalbuminaemia
Heimann 2017	Other disease	Correct - BUT OUT AS ONLY 1	Anaemia Vs no Anaemia
Shankar 2017	Other disease	Correct - Liver dis/no Liver dis - OUT ONLY 2	Liver disease Vs no Liver disease
Vidovic 2006	Other disease	Correct - BUT OUT AS ONLY 1	No Chronic disease Vs Any Chronic disease
Caruso 2017	Other Fixation	Correct - Non-absorbable Vs absorbable - OUT only 3	Titanium staples Vs absorbatacks
Caruso 2017	Other Fixation	Correct - BUT OUT AS ONLY 1	Titanium staples Vs titanium coils
Dalenback 2013	Other Fixation	Correct - BUT OUT AS ONLY 1	Mayo Vs Single row
Dalenback 2013	Other Fixation	Correct - BUT OUT AS ONLY 1	Double row suture Vs Single row
Dalenback 2013	Other Fixation	Correct - BUT OUT AS ONLY 1	Mayo Vs double row suture
Hauters 2017	Other Fixation	Correct - BUT OUT AS ONLY 1	Transfascial sutures
Hauters 2017	Other Fixation	Correct - BUT OUT AS ONLY 1	No Transfascial sutures Vs Transfascial sutures
Hornby 2015	Other Fixation	Correct - BUT OUT AS ONLY 1	Protack Vs no protack

Lambrecht 2014	Other Fixation	Incorrect - BUT OUT AS ONLY 1	Ingrowth area
Muysoms 2013	Other Fixation	Correct - BUT OUT AS ONLY 1	Double-crown tacks vs Sutures and Tacks
Baucom 2016	Pain	Correct - OUT ONLY 3	Post-op Symptomatic pain Vs non symptomatic pain
Carter 2014	Pain	Correct - OUT ONLY 3	Post chronic pain Vs no chronic pain
Groene 2016b	Pain	Correct - OUT ONLY 2	Pre-symptomatic pain Vs non symptomatic pain
Lauscher 2013	Pain	Correct - OUT only 1 paper	Pre-chronic pain Vs no chronic pain
Helgstrand 2013	Position of mesh	Correct - ? OUT as planes are combined	Onlay mesh Vs Sublay mesh (retrorectus or pre-peritoneal)
Helgstrand 2013	Position of mesh	Correct - - ? OUT as planes are combined	Onlay mesh Vs Sublay mesh (retrorectus or pre-peritoneal)
Helgstrand 2013	Position of mesh	Correct - - ? OUT as planes are combined	Sublay mesh (retrorectus or pre-peritoneal) Vs Intraperitoneal mesh
Petro 2015	Position of mesh	OUT	Prior intra-abdominal mesh Vs no prior intra-abdominal mesh
Prasad 2011	Position of mesh	OUT	TAPP Lap repair VS IPOM Lap repair
Rosen 2013	Position of mesh	Out - Only 2	Sandwich repair Vs Intra-peritoneal mesh
Slater 2015c	Position of mesh	OUT - difficult to tell what the sublay is reffered too	Sublay mesh Vs non-sublay mesh
Slater 2015c	Position of mesh	OUT- difficult to tell ? intraperitoneal mesh is referrenced too	Intra-peritoneal mesh Vs non-intra-peritoneal mesh
Slater 2015c	Position of mesh	OUT - difficult to tell what the onlay is reffered too	Onlay mesh Vs non-onlay mesh
Oma 2017	Pregnancy	Correct - PROB OUT AS ONLY 3	Pregnancy Vs No pregnancy
Booth 2013	Previous abdomial surgeries	Correct - Prior abdo surg y/n OUT ONLY 3	Previous abdominal surgery Vs no previous surgery
Diamond 2015	Previous abdomial surgeries	Correct - ≥4/<4PriorSurg (PORB OUT ONLY 2)	≥4prior abdominal operations Vs <4prior abdominal operations
Rosen 2013	Previous abdomial surgeries	Correct - PriorSurg+1VsPriorSurg (OUT ONLY 1)	No previous abdominal surgeries+1 Vs no previous abdominal surgeries
Flum 2003	Primary Vs Recurrent	Correct - ThirdIHrepairVsSecondIHrepair (4 - OUT)	2nd IH recurrence Vs 1st IH recurrence repair
Flum 2003	Primary Vs Recurrent	Correct - SecondIHrepairVsFirstIHrepair (6 - OUT)	1st IH recurrence Vs primary IH repair
Flum 2003	Primary Vs Recurrent	Correct - ThirdIHrepairVsFirstIHrepair - OUT ONLY 2	2nd IH recurrence VS primary IH repair
Gecim 1996	Primary Vs Recurrent	Correct - >2priorrepairs Vs <=2 (OUT ONLY 2)	Previous hernia repair >2 Vs Previous repir <=2
Gecim 1996	Primary Vs Recurrent	Correct - >=2priorrepairs Vs <2 (OUT ONLY 2)	Previous hernia repair >1 Vs Previous repir <=1
Holihan 2015	Primary Vs Recurrent	Correct - FourthVHrepairVsThirdVHrepair (OUT ONLY 2)	3rd IH repair Vs 2nd IH repair
Holihan 2015	Primary Vs Recurrent	Correct - FourthVHrepairVsSecondVHrepair (OUT ONLY 2)	3rd IH repair VS primary VH repair
Holihan 2015	Primary Vs Recurrent	Correct - FourthVHrepairVsFirstVHrepair (OUT ONLY 1)	3rd IH repair VS primary VH repair
Krpata 2013	Primary Vs Recurrent	Correct - Repair+1 Vs Repair (PROB OUT ONLY 3)	No previous hernia repair +1 Vs No previous hernia repairs
Wink 2014	Smoker	Correct - Only 2 prob OUT	Ex-smoker Vs non-smoker
Bencini 2009	Surgeon experience	Correct - ONLY 1 Prob OUT	Surgeon experience <10 procedures Vs >10 procedures
Gecim 1996	Surgeon experience	Correct - ONLY 2 Prob OUT	Registrar Vs Consultant
Kokotovic 2016	Tack Vs NoTack	Correct - OUT only 1 paper	Tack fixation Vs non-tack fixation

Sharma 2011	Tack Vs Suture	Incorrect - OUT only 1	Tacks Vs Suture
Wassenaar 2010	Tack Vs Suture	Incorrect - OUT only 1	Tacks vs Suture fixation
Basta 2015	VHWG	Incorrect - separate - prob OUT only 1	Modified VH grade 3 Vs modified VH grade 2
Slater 2015a	VHWG	Correct - VHWG+1/VHWG (Prob OUT, Only 4)	VHWG modified grade+1 Vs VHWG modified grade
Slater 2015a	VHWG	Correct - VHWG+1/VHWG (Prob OUT, Only 4)	VHWG grade+1 Vs VHWG grade
Slater 2015c	VHWG	Correct - VHWG+1/VHWG (Prob OUT, Only 4)	VHWG modified grade+1 Vs VHWG modified grade
Slater 2015c	VHWG	Correct - VHWG+1/VHWG (Prob OUT, Only 4)	VHWG grade+1 Vs VHWG grade
Booth 2013	Violated rectus	Correct- OUT only 4	Violated rectus Vs Non-violated rectus
Krpata 2012	Zno Group	OUT	Anterior Comp Sep Vs Posterior Comp Sep
Wink 2014	Zno Group	OUT	Bilateral C/S Vs Unilateral C/S
Danzig 2016	Zno Group	Prob OUT only 2 - Danzig and Martinez	Post operative ECF Vs no ECF
Carter 2014	Zno group	Prob OUT only 2 - Carter and Garvey	Mesh removal Vs no mesh removal
Hornby 2015	Zno group	OUT - unclear whether absorbable/non-absorbable	Suture Vs no suture
Lorente-Herce 2015	Zno group	OUT	Lower midline Vs Upper midline
Memon 2013	Zno group	OUT	Midline Vs Pfannenstiel
Altom 2012	ZNo group	OUT	Concomitant: same side Vs other side
Altom 2012	ZNo group	OUT	Concomitant Vs Non-Concomitant
Azar 2017	ZNo group	OUT	LOD >30% Vs LOD <30%
Basta 2015	ZNo group	OUT	Estimated blood loss + ml Vs estimated blood loss
Bencini 2009	ZNo group	OUT - only 1	Hospital stay (Continuous variable, Multivariable HR analysis)
Bondre 2016	ZNo group	OUT - only 2	Skin flap Vs no Skin flap
Carter 2014	ZNo group	OUT - only 1	Institution 1 Vs Institution 2
Carter 2014	ZNo group	OUT - only 1	Urine retention Vs no urine retention
Carter 2014	ZNo group	OUT - only 1	Ethnicity Afro-caribean Vs White caucassian
Carter 2014	ZNo group	OUT - only 2	Re-operation Vs no re-operation
Davidson 2009	ZNo group	OUT - Probably not the same as pannicculectomy	Body contouring procedures Vs no body contouring procedures
Diamond 2015	ZNo group	OUT - only 2	Active mesh infection Vs no active infection (CDC4/VHWG4)
Dietz 2014	ZNo group	OUT - only 1	>=3 risk factors ref to 0-2 risk factors
Gecim 1996	ZNo group	OUT - Constipation Vs no Constipation (ONLY 3)	Severe constipation Vs no severe constipation
Ghazi 2011	ZNo group	OUT - only 1	Risk factors >=2 Vs <2
Giordano 2016	ZNo group	OUT - only 1	Mesh exposure Vs no mesh exposure
Giordano 2017c	ZNo group	OUT - only 1	NSQUIP grade 3+4 Vs NSQUIP grade 1+2
Greenstein 2008	ZNo group	OUT - only 2	Number of defects (</>=2)
Groene 2016b	ZNo group	OUT - only 1	Symptomatic limited activity Vs non-symptomatic limited activity
Gronvold 2012	ZNo group	OUT - only 1	SingleSiteLap Vs StandardLap
Heimann 2017	ZNo group	OUT - only 1	No. of previous bowel resections+1 Vs no. of previous bowel resections
Helgstrand 2013	ZNo group	OUT - only 1	Longitudinal Vs Transverse incision
Hornby 2015	ZNo group	OUT - only 1	LOS >0 days Vs LOS 0 days
Hornby 2015	ZNo group	OUT - only 1	Use >3 ports Vs <=3 ports
Hultman 2014	ZNo group	OUT - only 1	Posterior release Vs no posterior release

Johnson 2016	ZNo group	OUT - only 1	Transabdominal Vs Total extraperitoneal approach
Kohler 2015a	ZNo group	OUT - only 1	Coagulopathy Vs No coagulopathy
Kohler 2015a	ZNo group	OUT - only 1	Rectus diastasis Vs no rectus diastasis
Korenkov 2002	ZNo group	OUT - only 1	Simple Hernia Vs Complex
Lahon 2009	ZNo group	OUT - only 1	Mesh size > 15x20 Vs Mesh size < 15x20
Le Blanc 2003	ZNo group	OUT - only 2	Early Vs Late
Mercoli 2017	ZNo group	OUT - only 1	Clavien Dindo >2 Vs Clavien Dindo <=2
Mercoli 2017	ZNo group	OUT - only 1	Clavien Dindo >2 Vs Clavien Dindo <=2
Notash 2007	ZNo group	OUT - only 1	Mesh size+1cm^2 Vs mesh size
Renard 2017	ZNo group	OUT - only 1	Absorbable mesh Vs non absorbable mesh
Rinaldi 2016	ZNo group	OUT - only 1	Sarcopaenic Vs non-sarcopaenic patients
Slater 2015c	ZNo group	OUT - only 2	No previous laparotomies+1 Vs No previous laparotomies
Slater 2015c	ZNo group	OUT - only 1	Blood loss+500mls Vs blood loss
Slater 2015c	ZNo group	OUT - only 2	Previous open abdomen Vs no previous open abdomen
Tollens 2011	ZNo group	OUT - only 1	Heavy manual work Vs no heavy manual work
Tollens 2011	ZNo group	OUT - only 1	Not another abdo wall hernia Vs presence of other abdo wall hernia
Tollens 2011	ZNo group	OUT - only 1	Not another abdo wall hernia Vs presence of other abdo wall hernia
Westen 2014	ZNo group	OUT - only 1	Chronic complaints Vs no chronic complaints
Wink 2014	ZNo group	OUT - only 2	Previous skin graft Vs previous primary closure
Wink 2014	ZNo group	OUT - only 1	Simultaneous stoma reversal Vs no simultaneous stoma reversal
Wink 2014	ZNo group	OUT - only 1	Previous mesh closure Vs previous primary closure
Wink 2014	ZNo group	OUT - only 1	Flap necrosis Vs no flap necrosis
Wink 2014	ZNo group	OUT - only 2	Traumatic hernia Vs non-traumatic hernia
Won 2015	ZNo group	OUT - only 1	Post operative hyperglycaemia Vs no post operative hyperglycaemia
Wormer 2016	ZNo group	OUT - only 1	indocyanine green vs no indocyanine green

Total 172 – deleted predictors

Appendix 37

Review question: Overview of prognostic factors for recurrent ventral hernias

Population: Primary, Incisional or Primary and Incisional

Prognostic factors: Demographics, co-morbidities, hernia related, intra-operative and post-operative

Studies: RCTs, prospective cohorts, retrospective cohort, observational

Meta-analysis estimates: Univariate odds ratios were used

Prognostic factor	No. studies	No. patients	No. events	Estimates reported	Meta-analysis estimate (95%CI) [no. studies]	Notes
Demographics						
Age	25	34,484	3,995	22 Uni OR 8 Multi OR 2 Uni HR 7 Multi HR 1 Multi RR	Age>60 Vs Age<60 0.86 (0.70 to 1.05) [7] Age>65 Vs Age<65 0.72 (0.54 to 0.96) [7]	• Age thresholds in meta-analysis: results were presented from the most frequently used thresholds. Related thresholds were grouped - namely 55 and 60, 70 with 65. Other presentations with fewer results are not presented in meta-analysis i.e. continuous age and threshold of 50 years. • Some patients will be counted more than once in the total number of patients, as they are included in both the meta-analyses at the two age thresholds. • One article was excluded as patients overlapped with another article.
BMI	49	14,454	1,703	49 Uni OR 9 Multi OR 3 Uni HR 6 Multi HR 1 Multi RR	BMI>25 Vs BMI<25 2.51 (1.37 to 4.60) [5] BMI>30 Vs BMI<30 1.54 (1.21 to 1.95) [25] BMI>35 Vs BMI<35	• BMI thresholds in meta-analysis: results were presented from the most frequently used thresholds. Related thresholds were grouped - namely 28 and 25, 32 with 30. Other presentations with fewer results are not presented in meta-analysis i.e. continuous BMI.

					1.42 (1.00 to 2.03) [9] BMI>40 Vs BMI<40 3.07 (1.77 to 5.32) [4]	• Some patients will be counted more than once in the total number of patients, as they are included in multiple meta-analyses at the different BMI thresholds. • Three articles were excluded as patients overlapped with other articles.
Sex	43	14,948	1,987	37 Uni OR 2 Multi OR 4 Uni HR 5 Multi HR	Male Vs Female 0.77 (0.61 to 0.97) [33]	• Three articles were excluded as patients overlapped with other articles.
Co-morbidities						
ASA	16	5,828	1,002	24 Uni OR 1 Multi OR 2 Uni HR 1 Multi HR	ASA 3-4 Vs ASA 1-2 1.46 (1.18 to 1.79) [11]	• ASA thresholds in meta-analysis: results were presented from the most frequently used threshold ASA 3-4 Vs ASA 2-1. Other presentations with fewer results are not presented in meta-analysis i.e. continuous ASA, ASA 2 Vs ASA 1 and ASA 4 Vs 3. For some articles different thresholds were combined in the comparison of ASA 3-4 Vs ASA 2-1.
BPH	5	2,705	596	5 Uni OR 1 Multi RR	BPH Vs No BPH 1.58 (0.74 to 3.36) [5]	
Cardiac disease	9	2,815	391	8 Uni OR 2 Multi OR 1 Uni HR 1 Multi HR	Cardiac disease Vs No cardiac disease 1.49 (0.96 to 2.31) [8]	

COPD	22	5,910	932	19 Uni OR 2 Multi OR 3 Uni HR 1 Multi HR	COPD Vs No COPD 1.53 (1.06 to 2.20) [16]	• Three articles were excluded as patients overlapped with other articles.
Diabetes	28	6,064	1,095	26 Uni OR 1 Multi OR 1 Uni HR	Diabetes Vs No Diabetes 1.36 (1.05 to 1.77) [25]	• One article was excluded as patients overlapped with another article.
Hypertension	10	1,379	216	10 Uni OR 1 Uni HR	Hypertension Vs No Hypertension 1.52 (0.88 to 2.62) [8]	• Two articles were excluded as patients overlapped with other articles.
Immunosuppression	13	4,018	734	13 Uni OR 1 Multi OR 1 Uni HR	Immunosuppression Vs No Immunosuppression 1.37 (0.72 to 2.59) [10] Steroid use Vs No Steroid use 2.08 (1.08 to 3.98) [3]	• Some patients will be counted more than once in the total number of patients, as they are included in both the meta-analyses at the two thresholds.
Smoker	32	14,454	1,307	29 Uni OR 2 Multi OR 5 Uni HR 3 Multi HR	Smoker Vs Non-smoker 1.34 (1.03 to 1.74) [23]	• Smoker thresholds in meta-analysis: results were presented from the most frequently used threshold smoker vs non-smoker. Three studies using different thresholds were not included in the meta-analysis i.e. past smoker vs no smoker, active smoker vs non-active smoker and ex-smoker vs non-smoker. • Three articles were excluded as patients overlapped with other articles.
Hernia related						

AAA repair*	3	721	152	3 Uni OR 1 Multi RR	Previous AAA surgery Vs No Previous AAA surgery [3]	• No meta-analysis completed due to only three studies having AAA repair information • None of the studies indicated statistically significance difference between surgery methods. Two studies show increased odds of recurrence with AAA surgery compared to no AAA surgery; one study shows lower odds of recurrence. See Online resource 7 for individual study results.
Contaminated	16	5,279	1,018	39 Uni OR 1 Multi OR 4 Uni HR	Clean-contaminated Vs Clean0.67 (0.45 to 1.01) [7] Contaminated Vs Clean 1.54 (0.68 to 3.49) [6] Dirty Vs Clean 1.85 (0.77 to 4.43) [3] Contaminated Vs Clean-contaminated 1.27 (0.61 to 2.67) [5] Dirty Vs Clean-contaminated 1.85 (0.8 to 4.29) [4] Dirty Vs Contaminated 0.69 (0.27 to 1.79) [4] ECF repair Vs no ECF repair 3.09 (0.57 to 16.69) [3]	• Contamination thresholds in meta-analysis: results were presented from the most frequently used thresholds. Thresholds with fewer results are not presented in meta-analysis i.e. continuous estimates and all contaminated vs clean. • Some patients will be counted more than once in the total number of patients, as they are included in multiple meta-analyses at the different contamination thresholds.
Previous wound infection	9	2,770	563	8 Uni OR 1 Multi OR	Previous wound infection Vs no previous wound infection	

					1.43 (0.78 to 2.62) [8]	
Hernia Area	11	9,554	1,224	10 Uni OR 2 Multi OR 2 Uni HR 1 Multi HR 1 Multi RR	Area>10cm^2 Vs <10cm^2 4.04 (0.77 to 21.27) [3] Area >100cm^2 Vs <100cm^2 1.71 (0.76 to 3.85) [2]	• Hernia area thresholds in meta-analysis: results were presented from the most frequently used thresholds. Related thresholds were grouped – namely 25cm^2 with 10cm^2. Other presentations with fewer results are not presented in meta-analysis i.e. continuous area. For one article 20cm^2 wasn't used as the 10cm^2 threshold was available. • Some patients will be counted more than once in the total number of patients, as they are included in both meta-analyses at the different thresholds. • One article was excluded as patients overlapped with another article.
Hernia Width	36	49,471	5,001	46 Uni OR 14 MultiOR 3 Uni HR 8 Multi HR	Width >2cm Vs <2cm 0.64 (0.24 to 1.72) [6] Width >5cm Vs <5cm 1.09 (0.56 to 2.13) [11] Width >10cm Vs <10cm 2.13 (0.89 to 5.09) [11] Width >15cm Vs <15cm 2.33 (0.85 to 6.38) [7]	• Hernia width thresholds in meta-analysis: results were presented from the most frequently used thresholds. Related thresholds were grouped – namely hernia width 3cm was grouped with 2cm, defect width 4cm, 6cm, 7cm was grouped was with 5cm. Other presentations with fewer results are not presented in meta-analysis i.e. continuous hernia width and 20cm hernia width. • Some patients will be counted more than once in the total number of patients, as they are included in multiple meta-analyses

						at the different thresholds. • Three articles were excluded as patients overlapped with other articles.
Midline Vs Lateral	14	3,391	427	11 Uni OR 2 Multi OR 1 Uni HR 2 Multi HR	Midline Vs Lateral 1.00 (0.65 to 1.55) [10]	• One article was excluded as patients overlapped with another article.
Incisional Vs Primary	23	12,299	1,543	22 Uni OR 5 Multi OR 1 Multi HR	Incisional Vs Primary 1.79 (1.01 to 3.16) [18]	• Two articles were excluded as patients overlapped with other articles.
Recurrent Vs Primary	52	56,548	11,223	55 Uni OR 11 MultiOR 6 Uni HR 3 Multi HR 1 Multi RR	Recurrent Vs Primary 1.88 (1.48 to 2.40) [31]	• For the meta-analysis, results were presented from the most frequently used threshold recurrent vs primary. Other presentations with fewer results are not presented in meta-analysis i.e. continuous estimates and more than two hernia repairs vs less than two hernia repairs. • Six articles were excluded as patients overlapped with other articles. • One article had separate estimates for incisional only patients and primary and incisional patients which were kept separate for meta-analysis. • One article had different thresholds combined in the comparison of recurrent vs primary.
VHWG*	7	5,020	739	28 Uni OR	VHWG 3-4 Vs VHWG 1-2	• No meta-analysis completed due to only

				2 Multi OR	2.04 (0.85 to 4.87) [4]	four studies having VHWG information. • Two studies estimates showed statistically significance results, with increased odds of recurrence if have had VHWG 3-4 vs VHWG 1-2. One study shows higher odds of recurrence and another study shows lower odds of recurrence. See Online resource 7 for individual study results • One article was excluded as patients overlapped with another article.
Intra-operative						
Biological	14	5,613	808	16 Uni OR 2 Multi OR 5 Uni HR 2 Multi HR	Human Vs Porcine Mesh 1.59 (0.70 to 3.60) [5]	• For meta-analysis: Human vs xenograft, human vs bovine, porcine vs bovine subgroups were not included in meta-analysis due to overlapping data with other studies. • One article was excluded as patients overlapped with another article.
Biological Vs Synthetic	19	3,786	742	20 Uni OR 1 Multi OR 1 Multi HR	Biological Vs Synthetic Mesh 1.98 (1.22 to 3.22) [13] Human Vs Synthetic Mesh0.9 (0.36 to 2.25) [3] Porcine Vs Synthetic Mesh0.28 (0.07 to 1.12) [2]	• Some patients will be counted more than once in the total number of patients, as they are included in multiple meta-analyses at the different thresholds. • One article was excluded as patients overlapped with another article.
Bridging Vs Primary	33	9,189	1,376	30 Uni OR 3 Multi OR 2 Uni HR	Bridging Vs Primary fascial closure 2.62 (1.72 to 3.97) [27]	• Two articles were excluded as patients overlapped with other articles.

				4 Multi HR		
Component Separation	18	3,944	461	16 Uni OR 1 Multi OR 3 Uni HR 2 Multi HR	Component Vs No Component Separation 0.73 (0.49 to 1.10) [9] Laparoscopic vs Open Component Separation 0.94 (0.54 to 1.64) [6]	• One article was excluded as patients overlapped with another article.
Concurrent GI*	6	3,849	725	5 Uni OR 2 Multi OR	Concurrent GI Vs No Concurrent GI [4]	• No meta-analysis completed due to only four studies having concurrent GI information. • One study estimate showed statistically significance results, with increased odds of recurrence if have had concurrent GI compared to no concurrent GI. • For the other studies, one showed increased odds and two showed lower odds of recurrence. See Online Resource 7 individual study results. • One article was excluded as patients overlapped with another article.
Lap Vs Open	55	40,020	3,891	55 Uni OR 2 Multi OR 1 Multi HR	Laparoscopic Vs Open surgery 0.76 (0.60 to 0.94) [48]	• Six articles were excluded as patients overlapped with other articles. • One article was excluded as there were no recurrences.
Mesh Weight	7	2,084	142	8 Uni OR	Lightweight Vs Heavyweight 1.46 (0.67 to 3.19) [4] Lightweight Vs Mediumweight	• Some patients will be counted more than once in the total number of patients, as they are included in both meta-analyses at the two thresholds.

					1.62 (0.91 to 2.87) [3]	• One article was excluded as patients overlapped with another article.
Mesh Vs Suture	55	43,587	5,515	54 Uni OR 12 MultiOR 4 Multi HR 1 Multi RR	Mesh Vs Suture 0.66 (0.52 to 0.84) [48]	• For meta-analysis: biological and synthetic mesh was combined in the comparison of mesh vs suture. • Three articles were excluded as patients overlapped with other articles.
Mesh Position	23	12,525	1,236	42 Uni OR 3 Uni HR 1 Multi HR	Onlay Vs Retrorectus 1.96 (1.41 to 2.72) [9] Onlay Vs Preperitoneal 1.46 (0.73 to 2.94) [4] Onlay Vs Intraperitioneal 2.15 (0.87 to 5.34) [7] Inlay Vs Onlay 1.25 (0.44 to 3.57) [5] Inlay Vs Preperitoneal 1.6 (0.77 to 3.33) [3] Inlay Vs Intraperitoneal 3.64 (0.87 to 15.14) [3] Retrorectus Vs Intraperitoneal 0.42 (0.20 to 0.91) [6] Preperitoneal Vs Intraperitoneal 2.94 (1 to 8.62) [3]	• Some patients will be counted more than once in the total number of patients, as they are included in multiple meta-analyses at the different thresholds.
Panniculectomy*	6	1,409	151	4 Uni OR	Panniculectomy Vs No	• No meta-analysis completed due to only

				2 Uni HR	Panniculectomy [4]	four studies having panniculectomy information. • None of the studies indicated statistically significance difference between panniculectomy and no panniculectomy. Two studies show increased odds of recurrence with panniculectomy compared to no panniculectomy; one study shows no difference and one study showed lower odds of recurrence. See Online Resource 7 for individual study results
Tack Vs Suture*	5	369	23	5 Uni OR 1 Multi HR	Tack Vs Suture fixation [4]	• No meta-analysis completed due to only four studies having fixation information. • None of the studies indicated statistically significance difference between tack and suture fixation. Three studies show increased odds of recurrence with tack compared to suture and one study shows no difference in odds of recurrence. See Online Resource 7 for individual study results • One article was excluded as patients overlapped with another article.
Post-operative						
Complication	8	4,433	445	9 Uni OR 3 Multi OR 1 Uni HR 2 Multi HR	Complication Vs No Complication 3.34 (2.30 to 4.84) [6]	• For meta-analysis: small bowel obstruction, chest infection and urinary tract infection thresholds were not included due to few articles at these thresholds.

Seroma	8	1,697	230	8 Uni OR 1 Uni HR	Seroma Vs No Seroma 1.99 (1.22 to 3.24) [8]	
SSO	15	4,165	621	12 Uni OR 1 Multi OR 5 Uni HR 1 Multi HR	SSO Vs No SSO 3.65 (2.40 to 5.56) [10] Haematoma Vs No Haematoma 3.33 (1.33 to 8.33) [2]	• Some patients will be counted more than once in the total number of patients, as they are included in both meta-analyses at the two thresholds.
Wound Dehiscence	5	2110	216	4 Uni OR 1 Multi OR 1 Uni HR 1 Multi HR	Wound Dehiscence Vs No Wound Dehiscence 2.21 (1.2 to 4.06) [2]	• Two articles were excluded as patients overlapped with other articles.
Wound Infection	31	8,563	1,500	27 Uni OR 4 Multi OR 3 Uni HR 2 Multi HR 1 Multi RR	Wound Infection Vs No Wound Infection 3.21 (2.28 to 4.51) [24]	• For meta-analysis: wound infection with mesh infection and ECG threshold was not included due to few articles at this threshold. • Two articles were excluded as patients overlapped with other articles.

* Prognostic factors were not included in meta-analysis, forest plots available in appendix