Roboterassistierte Chirurgie bei Indikationen im Bereich des Thorax und des Bauchraumes

EUnetHTA-Report

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EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

Ludwig Boltzmann Institut
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LBI-HTA Projektbericht Nr.: 108
ISSN: 1992-0488
ISSN-online: 1992-0496

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Vienna, May 2019

Zusammenfassung

Beschreibung der Technologie und der Komparatoren

Die Roboterassistierte Chirurgie ist eine Form der minimal-invasiven Chirurgie, bei der die Instrumente nicht unmittelbar durch die ChirurgInnen, sondern durch einen Telemanipulator gesteuert werden. Durch den Telemanipulator werden die Hand- und Fingerbewegungen an einen ferngesteuerten Roboter übermittelt; damit können die Objekte manipuliert werden. Der Roboter besitzt ein höheres Maß an Geschicklichkeit in der Manipulation im Vergleich zur Laparoskopie, wodurch eine Operation auf sehr engem Raum im Körper ermöglicht wird (dies wäre sonst nur durch offene Chirurgie möglich), mit dem Ziel, die klinischen Ergebnisse und den Ressourcenverbrauch zu verbessern.

minimal-invasive Chirurgie

durch einen Telemanipulator gesteuert,
Operation auf sehr engem Raum im Körper möglich

Bislang wurden 22 Robotersysteme entwickelt, von denen sich 13 allerdings noch in der Entwicklungsphase befinden, sieben sind derzeit kommerziell erhältlich (da Vinci SI®, da Vinci SP®, da Vinci XI®, da Vinci X®, Freehand v1.2, Surgenius Beta und SenhanceTM Surgical System), eins ist nur für Forschungszwecke verfügbar und eins ist nur für den transoralen und transanalen Einsatz. Ziel der derzeit verfügbaren Robotersysteme ist es, Technologien zur Unterstützung der ChirurgInnen bereitzustellen und somit eine weitere minimal-invasive Operationstechnik zu bieten, und nicht die ChirurgInnen zu ersetzen. Die Roboterassistierte Chirurgie ist aber (zurzeit) deutlich kostenintensiver als herkömmliche Operationstechniken (offene oder laparoskopische Chirurgie).

22 Robotersysteme:

13 in Entwicklungsphase,
7 kommerziell erhältlich

Unterstützung, nicht Ersatz von ChirurgInnen

deutlich teurer

Gesundheitsproblem

In diesem Bericht stehen Indikationen für Operationen im Bereich des Thorax- und des Bauchraumes im Zentrum.

Bericht zu Thorax- und Viszeralchirurgie (Bauchraum)

- Zu den Indikationen im Bereich des **Thorax** gehören Erkrankungen der Lunge, der Brustwand und des Zwerchfells (häufig bösartige Krebserkrankungen). In dem Bericht wurden die folgenden Verfahren im Bereich des Thorax untersucht: Lobektomie, Lungensegmentierung und Mediastinalchirurgie.

Thorax:
Lobektomie,
Lungensegmentierung,
Mediastinalchirurgie

- Zu den Indikationen im Bereich des **Bauchraumes** gehören die gutartigen und bösartigen Erkrankungen der Bauchorgane, des gesamten Magen-Darm-Traktes, der endokrinen Organe, der Bauchwand und des Peritoneums. Die Verfahren der Viszeralchirurgie, die in den Bericht einbezogen wurden, sind: Antireflux-Chirurgie/ Fundoplikatio, Ösophagektomie/ Ösophagus-Chirurgie, Heller Myotomie, Gastrektomie, Bariatrische Chirurgie, Dünndarmresektion, Kolektomie, Rektumresektion, Cholezystektomie, Leberresektion/ Hepatektomie und Hernienchirurgie.

Bauchraum:
Antireflux-Chirurgie,
Ösophagektomie, Heller Myotomie, Gastrektomie,
Bariatrische Chirurgie,
Dünndarmresektion,
Kolektomie,
Rektumresektion,
Cholezystektomie,
Leberresektion und Hernienchirurgie

Methoden

Für die Bewertung der Wirksamkeit und Sicherheit wurde eine systematische Literatursuche in mehreren Datenbanken (Cochrane CENTRAL Register of Controlled Trials, Embase über Elsevier und Ovid Medline), ergänzt um eine Hand- und Scopus-Suche, durchgeführt.

Suche in mehreren Datenbanken

Klinische Leitlinien wurden in der UptoDate Datenbank, durch eine Handsuche und durch Rücksprache mit klinischen Experten identifiziert.

Leitliniensuche

Darüber hinaus wurde eine Suche nach laufenden Studien in den folgenden Datenbanken durchgeführt:

Suche nach laufenden Studien

- ClincalTrials.gov
- EU Register für klinische Studien (EU-CTR)
- WHO International Clinical Trials Registry Platform (ICTRP).

Das Cochrane Risk of Bias Tool wurde für die Qualitätsbewertung von randomisierten kontrollierten Studien (RCTs) und das Tool ROBINS-I für die Bewertung von nicht-randomisierten Studien verwendet.

Cochrane RoB Tool, ROBINS-I

Zur Bewertung der Wirksamkeit und Sicherheit wurden RCTs mit zumindest zehn PatientInnen herangezogen. Wenn keine relevanten RCTs identifiziert werden konnten, wurden prospektive, nicht-randomisierte kontrollierte Studien mit mindestens zehn PatientInnen eingeschlossen. Potenziell relevante Studien wurden nach Studiendesign dann eingeschlossen, wenn sie auch Ergebnisse zu Wirksamkeit, Sicherheit oder perioperativen Ergebnissen und Ressourcenverbrauch berichteten. Es gab keine Einschränkung hinsichtlich der PatientInnenpopulationen; alle Studien mit PatientInnen mit Indikationen im Bereich des Thorax- oder des Bauchraumes wurden eingeschlossen.

Einschlusskriterien: RCTs mit ≥ 10 PatientInnen, nRCTs mit ≥ 10 PatientInnen

relevante Endpunkte

Ergebnisse

Verfügbare Evidenz

Die systematische Literatursuche identifizierte keine RCTs zu Indikationen im Bereich des Thorax. Es wurden drei nicht-randomisierte kontrollierte Studien zu Lobektomie/Lungensegmentierung und eine zu Mediastinalchirurgie eingeschlossen.

Thoraxchirurgie:

keine RCTs
4 nRCTs

<u>Thorax</u> (**insgesamt 114 PatientInnen mit Roboterassistierter Intervention**):

114 Pts mit Roboter

- 3 nRCTs (215 PatientInnen, davon 100 in der Interventionsgruppe) verglichen Roboterassistierte Lobektomie mit VATS (Videoassisierte thorakoskopischer) Lobektomie,
- 1 nRCT (36 PatientInnen, davon 14 in der Interventionsgruppe) verglich Roboterassistierte mediastinale Massereduktion mit offener Sternotomie.

Zu Indikationen im Bereich des Bauchraumes, insbesondere im Bereich der Speiseröhre, wurden fünf RCTs (sechs Publikationen) zu Antireflux-Chirurgie/ Fundoplikatio und Ösophagektomie identifiziert. Keine RCTs konnten zu Heller Myotomie gefunden werden, daher wurden zwei nicht-randomisierte kontrollierte Studien eingeschlossen.

Viszeralchirurgie: im Bereich…

Speiseröhre:

5 RCTs
2 nRCTs

170 Pts mit Roboter

Ösophagus (**insgesamt 170 PatientInnen mit Roboterassistierter Intervention**):

- 4 RCTs (160 PatientInnen, davon 79 in der Interventionsgruppe) verglichen Roboterassistierte (laparoskopische) Fundoplikatio mit laparoskopischer Fundoplikatio,
- 1 RCT (109 PatientInnen, davon 54 in der Interventionsgruppe) verglich Roboterassistierte (laparoskopische) Ösophagektomie mit offener Ösophagektomie,
- 2 prospektive nRCT (92 PatientInnen, davon 37 in der Interventionsgruppe) verglichen Roboterassistierte Myotomie mit partieller Fundoplikatio (1 Studie mit laparoskopischer Fundoplikatio).

Magen:

3 RCTs
80 Pts mit Roboter

Drei RCTs wurden zu Magenoperationen (zwei zu Gastrektomie und eine zu Bariatrie) und sieben RCTs zu Darmoperationen (eins zu Kolektomie, eins zu Rektopexie und fünf zu Rektumresektion) identifiziert. Im Bereich der Gallenblase/ Leber/ Milz konnten vier RCTs zu Cholezystektomie, und keine RCTs zur Leberresektion und Hernienreparatur identifiziert werden. Somit wurden zu Leberresektion zwei und zu Hernienreparatur eine nicht-randomisierte kontrollierte Studie eingeschlossen.

Magen (insgesamt 80 PatientInnen mit Roboterassistierter Intervention):

- 2 RCTs (474 PatientInnen, davon 255 in der Interventionsgruppe) verglichen Roboterassistierte Gastrektomie mit laparoskopischer oder offener Gastrektomie,
- 1 RCT (50 PatientInnen, davon 25 in der Interventionsgruppe) verglich Roboterassistierten laparoskopischen Roux-en-Y-Magenbypass (RYGB) mit laparoskopischen RYGB.

Darm:

7 RCTs
486 Pts mit Roboter

Darm (**insgesamt 486 PatientInnen mit Roboterassistierter Intervention**):

- 1 RCT (71 PatientInnen, davon 35 in der Interventionsgruppe) verglich Roboterassistierte Kolektomie mit laparoskopischer Kolektomie,
- 5 RCTs (866 PatientInnen, davon 435 in der Interventionsgruppe) verglichen Roboterassistierte Rektumresektion mit laparoskopischer Rektumresektion,
- 1 RCT (30 PatientInnen, davon 16 in der Interventionsgruppe) verglich Roboterassistierte Rektopexie mit laparoskopischer Rektopexie.

Gallenblase & Leber/ Hernie:

4 RCTs
3 nRCTs

173 Pts mit Roboter (Galle)
104 Pts (Leber)
16 Pts (Hernie)

Gallenblase (**insgesamt 173 PatientInnen mit Roboterassistierter Intervention**), **Leber** (**insgesamt 104 PatientInnen mit Roboterassistierter Intervention**) und **Hernie** (**16 PatientInnen mit Roboterassistierter Intervention)**:

- 4 RCTs (317 PatientInnen, davon 173 in der Interventionsgruppe) verglichen Roboterassistierte Cholezystektomie mit laparoskopischer Cholezystektomie,
- 2 nRCT (162 PatientInnen, davon 104 in der Interventionsgruppe) verglichen Roboterassistierte (partielle) Hepatektomie mit laparoskopischer Hepatektomie,
- 1 nRCT (32 PatientInnen, davon 16 in der Interventionsgruppe) verglich Roboterassistierte Hernienreparatur mit laparoskopischer Hernienreparatur.

Alle RCTs berichteten über Wirksamkeitsendpunkte, mit einer Ausnahme. Für die Bewertung der Sicherheit wurden dieselben Studien verwendet, zusätzlich eine weitere Studie. Alle prospektiven, nicht randomisierten kontrollierten Studien (nRCTs), die als Nachweis für die Wirksamkeit identifiziert wurden, berichteten auch Sicherheitsendpunkte.

Studien für Wirksamkeits- und Sicherheitsendpunkte

Klinische Wirksamkeit & Sicherheit

Die Vielfalt der unterschiedlichen Operationen, kombiniert mit dem Mangel an zuverlässiger Evidenz zu fast allen Indikationen, bereiten Schwierigkeiten bei der Analyse und Berichterstattung der Ergebnisse. Folgende Endpunkte wurden – auch basierend auf Erwartungen an die Roboterassistierte Chirurgie – analysiert:

Mangel an zuverlässiger Evidenz

gemessene und analysierte Wirksamkeits-/ Sicherheitsendpunkte

Mortalität: 3-, 5-Jahresüberleben

Morbidität:

- 3-, 5-Jahres DFS/ krankheitsfreies Überleben
- Intraoperative Komplikationsrate
- Postoperative Komplikationsrate

Lebensqualität:

- Funktionalität
- Postoperative Schmerzen

Ressourcenverbrauch:

- Spitalsaufenthaltsdauer
- Wiederaufnahmen
- Bedarf an Transfusionen

Mortalität
Morbidität
Lebensqualität
Ressourcenverbrauch

Aussagen zur Wirksamkeit waren nicht für alle, sondern nur für einen Teil der Endpunkte bei vier Verfahren (Ösophagektomie, Gastrektomie, Rektumresektion, Cholezystektomie) möglich, wobei die Evidenzqualität als niedrig oder höchstens moderat eingestuft wurde. Die relevanten Endpunkte wurden in den meisten Studien entweder nicht berichtet, nicht gemessen oder zeigten keine statistisch signifikanten Unterschiede. Es werden daher hier nur jene Endpunkte berichtet, die – wenngleich mit Unsicherheit behaftet – Unterschiede zeigten

die meisten Endpunkte: nicht berichtet oder bekannt

Aussagen nur für einen Teil der Endpunkte bei 4 Verfahren möglich:

- **Ösophagektomie**: die Roboterassistierte Chirurgie verbessert wahrscheinlich die postoperative Morbidität/Lebensqualität und reduziert postoperative Komplikationen im Vergleich zur offenen Chirurgie *(Evidenzqualität: moderat).* Intraoperative Komplikationen dürften durch Roboterassistierte Chirurgie im Vergleich zur offenen Chirurgie reduziert werden (*Evidenzqualität: niedrig).*

…verbessert wahrscheinlich postoperative Morbidität, reduziert intraoperative Komplikationen

- **Gastrektomie**: die Roboterassistierte Chirurgie dürfte postoperative Komplikationen im Vergleich zur konventionellen Laparoskopie reduzieren *(Evidenzqualität: niedrig).*

…dürfte postoperative Komplikationen reduzieren

- **Rektumresektion**: die Roboterassistierte Chirurgie dürfte die Sexualfunktion verbessern, aber Schlafstörungen im Vergleich zur konventionellen Laparoskopie verschlimmern *(Evidenzqualität: niedrig);* Roboterassistierte Chirurgie dürfte postoperative Komplikationen zwischen 30 Tagen und sechs Monaten verringern, aber intraoperative Komplikationen erhöhen *(Evidenzqualität: niedrig).*

…dürfte Sexualfunktion verbessern, postop. Komplikationen reduzieren, aber auch Schlafstörungen verschlimmern, intraop. Komplikationen erhöhen

- **Cholezystektomie**: die Roboterassistierte Chirurgie dürfte intraoperative Komplikationen und postoperative Komplikationen nach 30 Tagen im Vergleich zur Laparoskopie reduzieren *(Evidenzqualität: niedrig).*

…dürfte intraop. Komplikationen reduzieren

Bei allen anderen Endpunkten sowie Verfahren ist die Wirksamkeit der Roboterassistierten Chirurgie im Vergleich zur offenen Operation oder Laparoskopie

bei allen anderen Endpunkte und Verfahren:

- entweder *unsicher* (die Qualität der Evidenz wurde als sehr niedrig bewertet und daher sind die Ergebnisse unsicher),
- *unbekannt* (der Endpunkt wurde in der Studie einbezogen, aber die Studie berichtete keine relative Häufigkeit des Ereignisses aufgrund fehlender Daten in der Kontrollgruppe, daher konnte kein relativer Effekt berechnet werden)

unsichere oder unbekannte Wirksamkeit und Sicherheit

- oder die vorhandene Evidenz *berichtete nicht über die Endpunkte*.

Tabelle 1 gibt einen Überblick über die Ergebnisse zu den wichtigsten Wirksamkeits- und Sicherheitsendpunkten der einzelnen Verfahren.

Laufende Studien

Die Suche in Datenbanken für klinische Studien ergab viele laufende oder geplante Studien zum Einsatz der Roboterchirurgie im Bereich des Thorax- und Viszeralchirurgie.

viele laufende Studien:

überwiegend RCTs mit Abschlussdaten zwischen 2019 und 2024

Die Verfahren mit den meisten laufenden Studien sind Rektumresektion (17 Studien), Gastrektomie (14 Studien), Hernienreparatur (acht Studien) und Ösophagektomie (sechs Studien). Weiters wurden vier Studien zu Lobektomie/ Lungensegmentierung, eine Studie zu Antireflux-Chirurgie/ Fundoplikation, drei Studien zu Kolektomie, zwei Studien zu Cholezystektomie und zwei zu Leberresektion/ Hepatektomie gefunden. Die meisten Studien sind RCTs, die die Roboterassistierte Chirurgie mit Laparoskopie oder offener Operation vergleichen. Die laufenden oder geplanten Studien rekrutieren zwischen 20 und 5.000 PatientInnen und werden voraussichtlich zwischen 2019 und 2024 abgeschlossen sein.

Es ist hervorzuheben, dass es einige besonders große Studien gibt, von denen erwartet werden kann, dass sie weitere und relevantere Evidenz liefern. Insbesondere, da in fünf Studien voraussichtlich mehr als 1.000 PatientInnen aufgenommen werden. Die ersten Ergebnisse dieser laufenden Studien könnten ab 2021 vorliegen.

besonders große Studien könnten weitere relevante Evidenz liefern

Allerdings wurden nicht für alle in diesem Bericht berücksichtigten Indikationen/ Verfahren laufende Studien identifiziert, z.B. konnten keine Studien zur Mediastinalchirurgie, der Heller Myotomie/ Ösophagus-Chirurgie, der Bariatrischen Chirurgie oder der Dünndarmresektion identifiziert werden.

allerdings auch keine laufenden Studien in einigen Indikationen

Schlussfolgerung

zu 9 aus 13 Verfahren gibt es keine ausreichende Evidenz

Nutzen nur in wenigen Indikationen bei einzelnen Endpunkten

bei mehreren Verfahren nur ein einziger RCT oder gar keine vergleichende Evidenz

Zu neun der 13 Verfahren im Bereich des Thorax- und des Bauchraumes gibt es keine ausreichende Evidenz, um den Nutzen der Roboterassistierten Chirurgie gegenüber Laparoskopie und offener Chirurgie feststellen zu können. In der Ösophagektomie hat die Roboterassistierte Chirurgie im Vergleich zur offenen Chirurgie wahrscheinlich (Evidenzqualität: moderat) Zusatznutzen in Bezug auf Lebensqualität und postoperative Komplikationen. Jedoch konnte in der Gastrektomie kein Zusatznutzen im Vergleich zur offenen Chirurgie gezeigt werden; im Vergleich zur laparoskopischen Gastrektomie kann es Zusatznutzen in Bezug auf postoperative Komplikationen durch den Einsatz der Roboterassistierten Chirurgie geben. Die (qualitativ moderate) Evidenz legt nahe, dass die Roboterassistierte Cholezystektomie Komplikationen reduzieren kann. Die Evidenz zur Roboterassistierten Rektumresektion zeigt jedoch kein einheitliches Bild; einige Endpunkte weisen auf eine Verbesserung und andere auf eine Verschlechterung in Bezug auf Lebensqualität, postoperative- und intraoperative Komplikationen hin. Zu mehreren Verfahren stand nur ein einziger (oder kein) RCT zur Verfügung; demzufolge sind weitere Studien erforderlich.

Roboterassistierte Chirurgie mit höheren Kosten verbunden

ev. weniger Blutverlust

Einige der Studien berücksichtigten Kostenaspekte und die meisten berichteten über deutlich höhere Kosten im Zusammenhang mit Roboterassistierten Operationen. Dies ist oft auch auf die längere Operationsdauer, die in vielen Studien berichtet wurde, zurückzuführen. Die Evidenz zum Blutverlust war uneinheitlich, aber es gab etwas mehr Studien, in denen mit Roboterassistierter Operation signifikant weniger Blutverlust berichtet wurde.

Limitationen:

keine Stratifikation nach chirurgischer Erfahrung

Mindestfallzahlanalyse und Einschränkungen auf das Studiendesign

Zu den Limitationen des vorliegenden Berichts gehört das Fehlen von Stratifikation nach chirurgischer Erfahrung. Eine Analyse der Mindestfallzahl und zur Erfahrung in der Ausübung der Methode wäre nützlich, da dies erhebliche Auswirkungen auf die Wirksamkeit und Sicherheit im Zusammenhang mit der Anwendung der Technologie haben dürfte. Um die Leistungsfähigkeit der ChirurgInnen und der Operationsteams aufrechtzuerhalten, sind umfangreiche, hochspezialisierte Schulungen und ein ausreichendes Fallvolumen erforderlich. Die Entscheidung, nur RCTs mit wenigstens zehn PatientInnen einzuschließen und andere Art von Evidenz auszuschließen, kann als eine weitere Einschränkung insbesondere bei Aussagen zu Sicherheitsendpunkten angesehen werden.

Jedoch stehen die Schlussfolgerungen des Berichts im Einklang mit systematischen Übersichtsarbeiten und Metaanalysen von Beobachtungsstudien. Die Roboterassistierte Chirurgie ist ein sich rasch entwickelndes Aufgabengebiet: es gilt die Evidenz ebenso wie die Anbieter (und Kosten) zu beobachten.

Tabelle 1 gibt einen Überblick über die Ergebnisse zu den wichtigsten Endpunkten der einzelnen Verfahren

	Mortalität	Morbidität/Lebensqualität	Komplikationen
Thoraxchirurgie			
Lobektomie	Wirksamkeit unbekannt	keine Studien wurden gefunden, die über diesen Endpunkt berichteten	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)
Mediastinalchirurgie	Wirksamkeit unbekannt	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)
Viszeralchirurgie: Ösophagus			
Antireflux-Chirurgie/ Fundoplikatio	keine Studien wurden gefunden, die über diesen Endpunkt berichteten	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)
Heller Myotomie	keine Studien wurden gefunden, die über diesen Endpunkt berichteten	Wirksamkeit unbekannt	Wirksamkeit unbekannt
Ösophagektomie	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)	Roboterassistierte Chirurgie verbessert wahrscheinlich die post-operative Morbidität/ Lebensqualität im Vergleich zur offenen Chirurgie (Evidenzqualität: moderat)	Roboterassistierte Chirurgie reduziert wahrscheinlich die post-operative Komplikationen im Vergleich zur offenen Chirurgie (Evidenzqualität: moderat) Roboterassistierte Chirurgie dürfte die intra-operative Komplikationen reduzieren im Vergleich zur offenen Chirurgie (Evidenzqualität: niedrig)
Viszeralchirurgie: Magen			
Gastrektomie	Wirksamkeit unbekannt	Wirksamkeit ist unsicher im Vergleich zur Laparoskopie (Evidenzqualität: sehr niedrig); nicht berichtet in offener Chirurgie	Roboterassistierte Chirurgie verbessert wahrscheinlich die postoperative Komplikationen im Vergleich zur Laparoskopie (Evidenzqualität: niedrig); Wirksamkeit ist unsicher im Vergleich zur offenen Chirurgie (Evidenzqualität: sehr niedrig)
Bariatrie	keine Studien wurden gefunden, die über diesen Endpunkt berichteten	keine Studien wurden gefunden, die über diesen Endpunkt berichteten	Wirksamkeit unbekannt
Viszeralchirurgie: Darm			
Kolektomie	Wirksamkeit unbekannt (keine Informationen über die relative Häufigkeit des Ereignisses)	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)
Rektumresektion	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)	Roboterassistierte Chirurgie dürfte die Sexualfunktion verbessern, aber Schlafstörungen verschlimmern im Vergleich zur konventionellen Laparoskopie (Evidenzqualität: niedrig)	Postoperative Komplikationen vor Entlassung und postoperative Komplikationen innerhalb von 30 Tagen: Wirksamkeit unsicher (Evidenzqualität: sehr niedrig) Roboterassistierte Chirurgie dürfte intraoperative Komplikationen erhöhen und postoperative Komplikationen zwischen 30 Tagen und sechs Monaten verringern (Evidenzqualität: niedrig)
Rektopexie	keine Studien wurden gefunden, die über diesen Endpunkt berichteten	Wirksamkeit unbekannt	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)
Viszeralchirurgie: Gallenblase/ Leber/ Milz			
Cholezystektomie	keine Studien wurden gefunden, die über diesen Endpunkt berichteten	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)	Roboterassistierte Chirurgie dürfte intraoperative Komplikationen verringern (Evidenzqualität: niedrig) Roboterassistierte Chirurgie dürfte postoperative Komplikationen nach 30 Tagen im Vergleich zur Laparoskopie reduzieren (Evidenzqualität: niedrig)
Leberresektion	Wirksamkeit unbekannt	keine Studien wurden gefunden, die über diesen Endpunkt berichteten	Wirksamkeit unsicher (Evidenzqualität: sehr niedrig)
Hernienreparatur	keine Studien wurden gefunden, die über diesen Endpunkt berichteten	keine Studien wurden gefunden, die über diesen Endpunkt berichteten	Wirksamkeit unbekannt

EUnetHTA Joint Action 3 WP4

**Rapid assessment of other technologies using the HTA Core Model®
for Rapid Relative Effectiveness Assessment**

ROBOT-ASSISTED SURGERY IN THORACIC AND VISCERAL INDICATIONS

Project ID: OTCA14

Version 1.4, 06.05.2019

This report is part of the project/joint action '724130/EUnetHTA JA3' which has received funding from the European Union's Health Programme (2014-2020)

DOCUMENT HISTORY AND CONTRIBUTORS

Version	Date	Description
V1.0	**31.01.19**	First draft.
V1.1	**27.02.19**	Input from co-author has been processed.
V1.2	**29.03.19**	Input from dedicated reviewers has been processed.
V1.3	**30.04.19**	Input from external experts and manufacturer(s) has been processed.
V1.4	**06.05.19**	Input from medical editing has been processed.

Disclaimer

The assessment represents a consolidated view of the EUnetHTA assessment team members and is in no case the official opinion of the participating institutions or individuals.

EUnetHTA Joint Action 3 is supported by a grant from the European Commission. The sole responsibility for the content of this document lies with the authors and neither the European Commission nor EUnetHTA are responsible for any use that may be made of the information contained therein.

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Manufacturer(s) [v1.2] (factual accuracy check)	Intuitive Surgical

Conflict of interest

All authors, co-authors, dedicated reviewers, external experts and patients or patient representatives involved in the production of this assessment have declared they have no conflicts of interest in relation to the technology and comparator assessed according to the EUnetHTA Declaration of interest and confidentiality undertaking of interest (DOICU) statement form.

How to cite this assessment

Please, cite this assessment as follows:

Robot-assisted surgery in thoracic and visceral indications. Collaborative assessment. Diemen (The Netherlands): EUnetHTA; 2019. Report No.: OTCA14. Available from https://www.eunethta.eu.

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LIST OF ABBREVIATIONS

ASA	American Society of Anesthesiologist
BIQ	Body image Questionnaire
BMI	Body-Mass-Index
CE	Comunità Europea
CG	Control Group
CI	Confidence Interval
cm	Centimeter
DFS	Disease free survival
dl	deciliter
e.g.	For example
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer Quality of Life Group
EU	European Union
FSFI	Female Sexual Function Index
FU	Follow up
g	Gramm
GERD	Gastroesophageal reflux disease
GORD	Gastro-oesophageal reflux disease
GRACI	GERD Activity Index
GRADE	Grading of Recommendations Assessment Development and Evaluation
GSRS	Gastrointestinal Symptom Rating Scale
HCC	Hepatocellular carcinoma
ICU	Intensive Care Unit
IG	Intervention Group
IIEF	International Index of Erectile Function
Inc	Incorporated
IPSS	International Prostate Symptom Score
IQR	Interquartile range
Kg	Kilogramm
L	Liter
LOS	Length of the stay
max	Maximum
MD	Mean difference
Ø	Mean
M	Median
MeSH	Medical Subject Headings
mg	milligram

ml	milliliter
n	Number
n/a	Not applicable
NCCN	National Comprehensive Cancer Network
NIH	National Institute for Health
NR	Not reported
NRS	Numeric Rating Scale
ns	Not significant
NSCLC	Non-small cell lung Cancer
p	Power
PFDI	Pelvic Floor Distress Inventory
PFIQ	Pelvic Floor Impact Questionnaire
PISQ	Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire
PSQ	Photograph series questionnaire
QLQ-LC-13	Lung-cancer-specific questionnaire Module
QOL	Quality of Life
QOLRAD	Quality of Life in Reflux and Dyspepsia
R	Range
RATS	Robot-assisted thoracospic Surgery
RCT	randomised controlled trial
RR	Relative risk
SCLC	Small cell lung cancer
SD	standard deviation
SF-12	Short Form 12
SIRC	Single-incision robotic cholecystectomy
TM	Trade Mark
VAS	Visual Analogue Scale
VATS	Video-assisted thoracospic Surgery
Vs.	versus
WHO	World Health Organization

SUMMARY OF RELATIVE EFFECTIVENESS OF ROBOT-ASSISTED SURGERY IN THORACIC AND VISCERAL INDICATIONS

Scope

The aim of this HTA report was to assess the effectiveness and safety of robot-assisted surgery in the area of thoracic and visceral indications. The project plan (scope) conceived at the start of the project can be found here: Scope.

Introduction

Description of technology and comparators

Robotic surgery is a form of minimally-invasive surgery whereby the instruments of the robotic system are controlled by a telemanipulator, which is a device for transmitting hand and finger movements to a remote robotic device, allowing the consequent manipulation of objects. The robot has a higher degree of dexterity compared to the laparoscopic approach, which allows surgeons to operate in very tight spaces in the body (which would otherwise only be accessible through open surgery) with the rational of improving clinical outcomes and resource use.

22 systems have been developed, of which 13 are still in development, 7 are currently commercially available (da Vinci SI®, da Vinci SP®, da Vinci XI®, da Vinci X®, Freehand v1.2, Surgenius Beta and Senhance™ Surgical System), 1 is available for research purposes only and 1 is only for the transoral and transanal approach. The evidence suggests that robot-assisted surgery is more expensive than conventional surgical methods.

The aim of the currently available robotic systems is to provide technology to assist surgeons; they do not replace surgeons. These devices are a tool that surgeons can choose to use to provide their patients with a further minimally invasive surgical option. Comparators used in the clinical studies were conventional laparoscopic techniques or open surgery.

Health problem

This assessment looks at the use of robot-assisted surgery in the area of thoracic and visceral surgery. Thoracic surgery is concerned with conditions of the lungs, chest wall and diaphragm and is generally dominated by treatment of malignant disease. Thoracic procedures that were examined in the review included, in accordance with the project plan, pulmonary lobectomy, lung segmentectomy and mediastinal surgery. Visceral surgery deals with all aspects of the surgical treatment of benign and malignant diseases of abdominal organs, the entire gastrointestinal tract, endocrine organs, the abdominal wall and the peritoneum. Visceral procedures that were included in the review, in accordance with the project plan, were anti-reflux surgery/fundoplication, oesophagectomy or oesophageal repair, heller myotomy, gastrectomy, bariatric surgery, small bowel resection, colectomy, rectal resection, cholecystectomy, liver resection/hepatectomy and hernia repair.

Methods

To identify primary studies fulfilling the inclusion criteria outlined in the Scope of the present assessment, a systematic literature search in the following databases was performed:

- The Cochrane CENTRAL Register of Controlled
- Embase (via Elsevier)
- Ovid Medline

Detailed tables on the search strategy are included in Appendix 1. In addition, a hand search, supplemented by a Scopus-search, was performed.

Moreover, the following clinical trial databases were searched to identify ongoing studies:

- ClincalTrials.gov
- EU Clinical Trials Register (EU-CTR)
- The WHO International Clinical Trials Registry Platform (ICTRP).

Clinical Practice Guidelines (CPGs) were searched in the UptoDate database, through manual searching and through consultation with clinical experts, in addition to the systematic search.

The Cochrane Risk of Bias tool was used for the quality assessment of RCTs and the ROBINS-I was used for the assessment of non-randomised studies.

Randomised controlled studies (RCTs) with ≥ 10 patients were used for assessing the evidence in the effectiveness and safety domains. If no relevant RCTs could be identified, prospective non-randomised controlled studies with ≥ 10 patients were included. Perioperative outcomes and resource use were also considered. Potentially relevant studies according to study design were therefore included if they provided results on effectiveness, safety or perioperative events/resource use outcomes. Comparators were laparoscopic surgery or open surgery.There were no restrictions on patient populations; all studies on patients with indications for thoracic or visceral surgery were included.

Results

Available evidence

The systematic literature search did not identify any RCTs relating to thoracic surgery non-randomised controlled studies (3 for lobectomy/segmentectomy and 1 for mediastinal surgery) were included as the next best evidence level.

Regarding visceral surgery, and specifically surgery in the area of the oesophagus, 5 RCTs (6 publications) were identified relating to the procedure antireflux/fundoplication and oesphagectomy. For Heller myotomy no RCTs were found, hence non-randomised, controlled studies were included (two in total).

Three RCTS were included relating to stomach surgery (2 for gastrectomy and 1 for bariatric surgery) and 7 RCTs were identified relating to bowel procedures (specifically 1 RCT for colectomy, 1 RCT for rectopexy and 5 RCTs for rectal resection). Lastly in the area of gallbladder/liver/spleen, 4 RCTS were included for the cholecystectomy procedure whilst for liver resection and hernia repair, no RCTS could be identified thus again non-randomised, controlled studies were included (2 for liver resection and 1 for hernia repair).

All the RCTS identified in the systematic literature search reported on effectiveness, with one exception [1].The same RCT study pool was used for the safety domain with the addition of one study [1]. All the prospective non-randomised controlled studies that were identified as providing evidence for the effectiveness domain also reported on safety.

Clinical effectiveness & safety

The diverse range of surgeries included in this review, combined with the lack of reliable evidence for almost all indications, poses difficulties for the analysis and reporting of results. However, the following Table 1 provides an overview of the findings on key effectiveness and safety outcomes for the individual procedures. Where statements relating to effect can be made, these are also summarized below:

- *Oesophagectomy:* robot-assisted surgery probably improves post-operative morbidity/QoL and reduces post-operative complications compared to open surgery (evidence quality: moderate). Intra-operative complications may be reduced with robot-assisted surgery vs. open surgery but here the evidence quality is low.
- *Gastrectomy:* robot-assisted surgery may reduce postoperative complications vs conventional laparoscopy (evidence quality: low)
- *Rectal resection:* robot-assisted surgery may improve sexual functioning but worsen sleep disturbances compared with conventional laparoscopy (evidence quality: low); robot-assisted surgery may decrease postoperative complications between 30 days and 6 months, but increase intraoperative complications (evidence quality: low)
- *Cholecystectomy:* robot-assisted surgery may reduce intraoperative complications and postoperative complications at 30 days compared to laparoscopy (evidence quality: low)

For all other outcomes and procedures, the effect of robot-assisted surgery compared to open or laparoscopic surgery on the basis of the included study pool was either uncertain (we are uncertain whether robot-assisted surgery improves or reduces the outcome as the quality/certainty of the evidence has been assessed as very low), unknown (although included as an outcome in the study, relative effect could not be calculated as the study provided no information about the relative probability of the event, mainly due to missing events in one arm) or the available evidence did not measure the outcome.

Table 1: Summary of conclusions

	Mortality	Morbidity/QoL	Complications
Thoracic surgery			
Lobectomy	Effect unknown	No studies were found that considered this outcome	Effect uncertain *(evidence quality: very low)*
Mediastinal surgery	Effect unknown	Effect uncertain *(evidence quality: very low)*	Effect uncertain *(evidence quality: very low)*
Visceral surgery: Oesophagus			
Antireflux/ fundoplication	No studies were found that considered this outcome	Effect uncertain *(evidence quality: very low)*	Effect uncertain *(evidence quality: very low)*
Heller myotomy	No studies were found that considered this outcome	Effect unknown	Effect unknown
Oesophagectomy	Effect uncertain *(evidence quality: very low)*	Robot-assisted surgery probably improves post-operative morbidity/QoL compared to open surgery *(evidence quality: moderate)*	Post-op complications: Probably reduced with robot-assisted surgery vs open surgery *(evidence quality: moderate)* Intra-op complications: May be reduced with robot-assisted surgery vs open surgery *(evidence quality: low)*
Visceral surgery: stomach			
Gastrectomy	Effect unknown	Effect uncertain in laparoscopy comparison (*evidence quality: very low*); not reported in open surgery comparison	Robot-assisted surgery may reduce postoperative complications vs conventional laparoscopy (*evidence quality: low*); effect uncertain in open surgery comparison (*evidence quality: very low*)
Bariatric surgery	No studies were found that considered this outcome	No studies were found that considered this outcome	Effect unknown
Visceral surgery: bowel			
Colectomy	Effect unknown (no information about relative probability of event)	Effect uncertain (*evidence quality: very low*)	Effect uncertain (*evidence quality: very low*)
Rectal resection	Effect uncertain (*evidence quality: very low)*	Robot-assisted surgery may improve sexual functioning but worsen sleep disturbances compared with conventional laparoscopy *(evidence quality: low)*	Effect uncertain on postoperative complications to discharge and postoperative complications within 30 days (*evidence quality: very low*) Robot-assisted surgery may increase intraoperative complications and decrease postoperative complications >30 days and ≤ 6 months (*evidence quality: low*)

	Mortality	Morbidity/QoL	Complications
Rectopexy	No studies were found that considered this outcome	Effect unknown	Effect uncertain (*evidence quality: very low*)
Visceral surgery: gallbladder/liver/spleen			
Cholecystectomy	No studies were found that considered this outcome	Effect uncertain (*evidence quality: very low*)	Robot-assisted surgery may reduce intraoperative complications (*evidence quality: low*). Robot-assisted surgery may reduce postoperative complications at 30 days when compared to single-incision laparoscopic cholecystectomy (*evidence quality: low*)
Liver resection	Effect unknown	No studies were found that considered this outcome	Effect uncertain (*evidence quality: very low*)
Hernia repair	No studies were found that considered this outcome	No studies were found that considered this outcome	Effect unknown

Note: “Effect unknown”: although included as an outcome in the study, relative effect could not be calculated as the study provided no information about the relative probability of the event, mainly due to missing events in one arm. “Effect uncertain”: in the case of very low quality evidence we are undertain whether robot-assisted surgery improves or reduces the outcome as the quality/certainty of the evidence has been assessed as very low

Research in progress

The search within clinical trials databases identified many ongoing or planned trials on the use of robotic surgery in the field of thoracic and visceral surgery.

The procedures for which the largest numbers of ongoing studies were found were rectal resection (17 studies), gastrectomy (14 studies), hernia repair (8 studies), oesophagectomy (6 studies). 4 studies were found for lobectomy/segmentectomy, 1 study for antireflux/fundoplication, 3 studies for colectomy, 2 studies for cholecystectomy and 2 for liver resection/hepatectomy. Most of the studies are RCTs comparing the robotic approach with laparoscopic or open surgery. The ongoing or planned studies are recruiting from between 20 to 5,000 patients and they are expected to be completed between 2019 and 2024.

It is of note that there are some particularly large studies which can be expected to add further and more relevant evidence. In particular, 5 studies are expected to enroll more than a thousand patients. The first results from these ongoing studies could be available from 2021.

However, not all the indications/procedures considered in this assessment were found to have ongoing trials, for instance none could be identified for mediastinal surgery, Heller myotomy/oesophageal repair, bariatric surgery or small bowel resection.

Conclusion

For 9 of the 13 procedures within the area of thoracic and visceral surgery that we considered in this HTA, we conclude that there is insufficient evidence on which a judgement can be made about the relative merits of robot-assisted surgery compared to the alternatives (mostly conventional laparoscopic procedures). For 4 of the procedures there was evidence on some of the outcomes, but not all. Of the outcomes for which there is evidence we can report that when compared with open surgery in oesophagectomy, robot-assisted surgery probably (*evidence quality: moderate*) has advantages in terms of QoL and postoperative complications (although this was not shown for the comparison with open gastrectomy); when compared with laparoscopic gastrectomy, there may be advantages in terms of postoperative complications with the use of robot-assisted surgery. There is some low quality evidence that robot-assisted cholecystectomy may confer advantages in terms of reduced complications. The evidence for robot-assisted rectal resection was mixed with some areas of improvement and some areas of decline regarding quality of life outcomes and some reduced post-operative complications but some increased intraoperative complications. For several of the procedures only a single (or no) RCT was available; here further studies are necessary.

Several of the studies considered cost aspects and most reported higher costs associated with robot-assisted surgery. This is often due to the longer operation time necessary, which was reported by many studies; the evidence on blood loss was mixed.

Limitations of the present report include the lack of stratification according to surgical experience. In addition an analysis of the number of cases required to maintain training and knowledge related to the method would be useful, as this is likely to have a considerable impact on the effectiveness and safety associated with using the technique. Extensive, highly specialized training and an adequate volume of cases are required for surgeons and their surgical teams to maintain proficiency. A further limitation related to the decision to include only RCTs ≥ 10 patients where these are available, to the exclusion of other types of evidence. However it should be noted, that the conclusions drawn here are generally in accordance with systematic reviews and meta-analyses results of observational studies.

1 SCOPE

The aim of this HTA report was to assess the effectiveness and safety of robot-assisted surgery in the area of thoracic and visceral indications. The project plan concievd at the start of the project can be found in the table below.

Description	Project scope
Population	Patients with indication for thoracic surgery: • Pulmonary (sleeve) lobectomy [non-small cell lung cancer] o International classification of diseases **(ICD)-10-CM code**: e.g. Z90.2 Acquired absence of lung [part of], C34.1/C34.2/C34.3 Malignant neoplasm of upper/middle/lower lobe, bronchus or lung **MeSH Terms**: e.g. Lung Neoplasms [C04.588.894.797.520, C08.381.540, C08.785.520], Pulmonary Surgical Procedures [E04.928.600] • Lung segmentectomy/wedge resection [non-small cell lung cancer] o **ICD-10-CM code**: e.g. Z90.2 Acquired absence of lung [part of], C34.1/C34.2/ C34.3 Malignant neoplasm of upper/middle/lower lobe, bronchus or lung o **MeSH Terms**: e.g. Lung Neoplasms [C04.588.894.797.520, C08.381.540, C08.785.520], Pulmonary Surgical Procedures [E04.928.600] • Mediastinal surgery: e.g. Thymectomy [*Myasthenia gravis* (pseudoparalytica); thymoma]; (posterior) mediastinal lesion resection [(posterior) mediastinal mass/tumour, neurogenic tumour]; other mediastinal pathology [e.g.mediastinal bronchogenic cyst, lipoma, teratoma or fibrous tumour of the mediastinum] o **ICD-10-CM code**: e.g. G70.0 *Myasthenia gravis*, D15.0 Benign neoplasms of thymus, C37 Malignant neoplasms of the thymus, D15.2 Benign neoplasm of mediastinum, D21.3 Benign neoplasm of connective and other soft tissue of thorax, C38.1 Malignant neoplasm of anterior mediastinum, C38.2 Malignant neoplasm of posterior mediastinum, C38.3 Malignant neoplasm of mediastinum, part unspecified, J85.3 Abscess of mediastinum, J98.5 Diseases of mediastinum, not elsewhere classified, Q33.0 Congenital cystic lung, Q33.2 Sequestration of lung, Q33.5 Ectopic tissue in lung o **MeSH Terms**: e.g. *Myasthenia Gravis* [C10.114.656, C10.668.758.725, C20.111.258.500], Thymoma *[*C04.557.435.850, C04.588.894.949.500, C15.604.861.800], Mediastinum [A01.923.761.800.500], Thymectomy [E04.928.770] Patients with indication for visceral (abdominal) surgery: • Oesophagus: o Anti-reflux surgery/fundoplication [gastroesophageal reflux disease (GERD), hiatal hernia] ▪ **ICD-10-CM code**: e.g. K21 Gastro-esophageal reflux disease, K44 Diaphragmatic hernia ▪ **MeSH Terms**: e.g. Gastroesophageal Reflux [C06.405.117.119.500.484], Hernia, Hiatal [C23.300.707.500.467] o Oesophagectomy (total or partial)/transhiatal oesophagectomy [benign or malignant oesophageal tumours, oesophageal leimyoma, oesophageal diverticula] ▪ **ICD-10-CM code**: e.g. C15 Malignant neoplasm of esophagus, D13.0 Benign neoplasm of esophagus, K22.1 Ulcer of esophagus, K22.8 Other specified diseases of esophagus. K22.9 Disease of esophagus, unspecified, K22.5 Diverticulum of esophagus, acquired ▪ **MeSH Terms**: e.g. Esophageal Diseases [C06.405.117], Esophageal Neoplasms [C04.588.274.476.205, C04.588.443.353, C06.301.371.205, C06.405.117.430, C06.405.249.205], Diverticulosis, Esophageal [C06.405.117.136, C06.405.205.282.500.438], Esophagus [A03.556.875.500], Esophagectomy [E04.210.346]

Description	Project scope
	○ Oesophageal repair[1] [oesophageal perforation] ▪ **ICD-10-CM code**: e.g. K22.3 Perforation of esophagus ▪ **MeSH Terms**: e.g Esophageal Perforation [C06.405.117.468, C26.348], Esophagus [A03.556.875.500] ○ (Heller) Myotomy [swallowing disorder/achalasia] ▪ **ICD-10-CM code**: e.g. K22.0 Achalasia of cardia ▪ **MeSH Terms**: e.g. Esophageal Achalasia [C06.405.117.119.500.432], Myotomy [E04.515] • Stomach: ○ Gastrectomy [subtotal for gastric cancer <stage IB, radical for IB-III] ▪ **ICD-10-CM code**: e.g. C16 Malignant neoplasm of stomach ▪ **MeSH Terms**: e.g. Stomach Neoplasms [C04.588.274.476.767, C06.301.371.767, C06.405.249.767, C06.405.748.789], Gastrectomy [E04.210.419] ○ Bariatric surgery[2]: e.g. (ROUX-en-Y) gastric bypass, sleeve gastrectomy, gastric banding, implantable gastric stimulator, band revision; [obesity] ▪ **ICD-10-CM code**: e.g. E66 Overweight and obesity ▪ **MeSH Terms**: e.g. Obesity [C18.654.726.500, C23.888.144.699.500, E01.370.600.115.100.160.120.699.500, G07.100.100.160.120.699.500], Bariatric Surgery [E02.570.500.062, E04.062] • Bowel: ○ Small bowel resection[1] [bleeding, infection, ulcers, blockage, benign tumours, precancerous polyps, cancer, injuries, Meckel's diverticulum] ▪ **ICD-10-CM code**: e.g. K26 Duodenal ulcer, C17 Malignant neoplasm of small intestine, D13.2 Benign neoplasm of duodenum, C17.3 Meckel's diverticulum, malignant ▪ **MeSH Terms**: e.g. Intestine, Small [A03.556.124.684], Meckel Diverticulum [A03.556.124.684.249.612, A03.556.249.124.612, C01.539.463.199.750.750, C06.198.859, C06.405.205.282.750.750, C16.131.314.556, C23.300.415.750], Duodenal Diseases [C06.405.469.275], Duodenal Neoplasms [C04.588.274.476.411.445, C06.301.371.411.445, C06.405.249.411.445, C06.405.469.275.270, C06.405.469.491.445], Jejunal Neoplasms [C04.588.274.476.411.523, C06.301.371.411.523, C06.405.249.411.523, C06.405.469.491.523, C06.405.469.600.523], Ileal Neoplasms [C04.588.274.476.411.501, C06.301.371.411.501, C06.405.249.411.501, C06.405.469.420.501, C06.405.469.491.501] ○ Colectomy (total, partial)/hemicolectomy (left, right)/abdominal colectomy/ proctocolectomy/sigmoid colectomy/transverse colectomy [bleeding, bowel obstruction, cancer, Crohn's disease, ulcerative colitis, diverticulitis, cancer prevention] ▪ **ICD-10-CM code**: e.g. C18 Malignant neoplasm of colon, D12 Benign neoplasm of colon, rectum, anus and anal canal, K51 Ulcerative colitis, K50 Crohn's disease [regional enteritis], K56 Paralytic ileus and intestinal obstruction without hernia, K57 Diverticular disease of intestine ▪ **MeSH Terms**: e.g. Diverticulitis [C01.539.463.199.375, C06.405.205.282.500], Colorectal Neoplasms [C04.588.274.476.411.307, C06.301.371.411.307, C06.405.249.411.307, C06.405.469.158.356, C06.405.469.491.307, C06.405.469.860.180], Crohn Disease [C06.405.205.731.500, C06.405.469.432.500], Colitis [C06.405.205.265, C06.405.469.158.188], **Colectomy [E04.210.219]** ○ Rectal resection (anterior, low anterior, inter sphincteric, total)/colorectal resection/polyectomy/proctectomy/rectopexy/total mesorectal excision [e.g. rectal cancer, rectal prolapse]

[1] Intervention was recommended to be excluded from PICO by one external expert, but not by the manufacturers. Thus, the intervention was kept.

[2] Intervention was recommended to be excluded from PICO by one manufacturer (studies are currently underway). However, TransEnterix claims that the Senhance™ Surgical System is intended for use in bariatric surgery.

Description	Project scope
	▪ **ICD-10-CM code**: e.g. C20 Malignant neoplasm of rectal ampulla, D12.8 benign neoplasm of rectum, K62.3 Rectal prolapse ▪ **MeSH Terms**: e.g. Rectal Neoplasms [C04.588.274.476.411.307.790, C06.301.371.411.307.790, C06.405.249.411.307.790, C06.405.469.491.307.790, C06.405.469.860.180.500], Rectal Prolapse [C06.405.469.860.800, C23.300.842.624.500] • Gallbladder/Liver/Spleen: o Cholecystectomy[3] [biliary colic, acute cholecystitis, cholangitits (e.g. caused by symptomatic gallstones), gallbladder cancer] ▪ **ICD-10-CM code**: e.g. R10.83 Colic, K81 Cholecystitis, K83.0 Cholangitis, C23 Malignant neoplasm of gallbladder ▪ **MeSH Terms**: e.g. Colic [C16.614.166], Cholecystitis [C06.130.564.263], Cholangitis [C06.130.120.200], Gallbladder Neoplasms [C04.588.274.120.401, C06.130.320.401, C06.130.564.401, C06.301.120.401], Cholecystectomy [E04.210.120.172] o Liver resection (partial, total)/hepatectomy [liver cell carcinoma, hepatocellular carcinoma/adenoma, hepatic hemangioma, focal nodular hyperplasia] ▪ **ICD-10-CM code**: e.g. C22 Malignant neoplasm of liver and intrahepatic bile ducts, C22.0 Liver cell carcinoma, D13.4 Benign neoplasm of liver, D18.09 Hemangioma of other sites ▪ **MeSH Terms**: e.g. Liver Neoplasms [C04.557.470.200.025.255, C04.588.274.623.160, C06.301.623.160, C06.552.697.160], Carcinoma, Hepatocellular [C04.557.470.200.025.255, C04.588.274.623.160, C06.301.623.160, C06.552.697.160], Adenoma, Liver Cell [C04.557.470.035.120, C04.588.274.623.040, C06.301.623.040 C06.552.697.040], Hepatectomy [E04.210.556] o Hernia repair[3] ▪ **ICD-10-CM code**: e.g. K40-K46 Hernia, K40 inguinal hernia ▪ **MeSH Terms**: e.g. Hernia [C23.300.707], Hernia, Abdominal [C23.300.707.374], Hernia, Inguinal [C23.300.707.374.875], Herniorrhaphy [E04.680.325] **Rationale:** The population has been defined based on the suggested interventions for robot-assisted surgery in recent systematic reviews or studies [2] [3] [4], and informed by external experts and manufacturers. Moreover, since the interventions are in the focus of the assessment, the individual indications are examples, which the assessment is not limited to.
Intervention	• Robot-assisted surgery
Comparison	• Laparoscopic surgery (or thoracoscopic approach for thoracic surgery) • Open surgery **Rationale**: Appropriate comparators have been informed by selected guidelines [5] [6] and systematic reviews [7].
Outcomes[4]	Effectiveness (*critical* outcomes are highlighted in **bold**): • Survival (overall and disease-specific or disease-free) • Positive (surgical) margins • Recurrence (local, regional or distant) • Quality of life (e.g. measured by EQ-5D or SF-36) • Other disease-specific effectiveness-related outcomes • Conversion to laparoscopic/thoracoscopic/open surgery • Length of hospital stay • Time to resume work/daily activities • Patient satisfaction

[3] Intervention was recommended to be excluded from PICO by external experts and one manufacturer. However, Trans-Enterix claims that the Senhance™ Surgical System is intended for this intervention (cholecystectomy and inguinal hernia repair). Thus, the intervention was kept.

[4] Not all outcomes apply for every single population/indication

Description	Project scope
	Safety (*critical* outcomes are highlighted in **bold**): • **Intraoperative complications (e.g. bleeding, procedure-related mortality)** • Postoperative complications (e.g. 30-day overall complications, pain, infections) • Re-operations/additional surgeries Perioperative outcomes: • Blood loss • Operation time • Transfusions These are a type of outcome but we have not classified these under effectiveness as they are not necessarily patient-relevant outcomes but rather proxy outcomes. In accordance with the advice of the clinical expert, outcomes were considered at the individual procedure level and not across all procedures. **Rationale**: Appropriate clinical outcomes have been informed by systematic reviews [8] and the EUnetHTA guidelines [8] [9].
Study design	Effectiveness: • Randomised controlled studies (RCTs) with ≥ 10 patients (for effectiveness and safety) • Prospective non-randomised controlled studies with ≥ 10 patients in the absence of RCTs Safety: • Randomised controlled studies (RCTs) with ≥ 10 patients (for effectiveness and safety), • Prospective non-randomised controlled studies with ≥ 10 patients in the absence of RCTs Prospective studies with ≥100 patients and without a control group are eligible for inclusion in the absence of comparative evidence Data from good quality non-RCT studies may still be relevant even if RCTs exist however given the breadth of this topic the study design to be included was more restrictive than might be the case for other HTA topics.

2 METHODS AND EVIDENCE INCLUDED

2.1 Assessment Team

The distribution of the responsibilities and the workload between the author and co-authors was as follows:

LBI-HTA (author):

- Designed first draft of EUnetHTA project plan, amended the draft according to co-author's, dedicated reviewers', external experts, and manufacturers.
- Performed the literature search (systematic and by hand, supplemented by a Scopus-search)
- Performed literature selection for lobectomy, mediastinal and oesophagus (fundoplication and anti-reflux, oesophagectomy and heller myotomy)
- completed the checklist regarding potential ethical (ETH), organisational (ORG), social (SOC) and legal (LEG) aspects of the HTA Core Model® for Rapid Relative Effectiveness (REA)

JOANNEUM RESEARCH (author):

- Performed literature selection (for stomach, bowel, gallbladder, liver, spleen), data extraction for all studies, risk of bias assessment of the selected references, quality assessment of the body of evidence (GRADE)
- Carried out the assessment: answered assessment elements, checked the discrepancies with the co-author and reached consensus
- Compiled draft report, sent "draft versions" to dedicated reviewers and co-authors, compiled feedback from reviewers and co-authors and performed changes according to reviewer's comments.
- Sent "final draft" to external experts, compiled feedback from external experts and performed changes according to comments
- Prepared the final assessment and wrote a final summary of the assessment.

Azienda Zero Regione del Veneto (co-author):

- Reviewed and commented on EUnetHTA project plan.
- Checked and approved all steps (e.g. literature selection of included RCTs, data extraction, assessment of risk of bias assessment, quality of the body of evidence assessment).
- Wrote sections on technology (chapter 3) and ongoing research
- Reviewed draft assessment, proposed amendments where necessary and provided (written) feedback.

2.2 Source of assessment elements

The selection of assessment elements is based on the HTA Core Model Application for Rapid Relative Effectivenes Assessments. The selected issues (generic questions) were translated into actual research questions (answerable questions) for the selected domains of the assessment.

Please note that some research questions were answered together; that is, these questions can be listed below each other and the answer can then be provided subsequently.

2.3 Search

To identify recent primary studies fulfilling the inclusion criteria outlined in the Scope of the present assessment, a systematic literature search in the following databases was performed:

- The Cochrane CENTRAL Register of Controlled
- Embase (via Elsevier)
- Ovid Medline

Detailed tables on search strategy are included in Appendix 1. In addition, a hand search of the clinical trials database, supplemented by a Scopus-search, was performed.

Moreover, the following clinical trial databases were searched to identify ongoing studies:

- ClincalTrials.gov
- EU Clinical Trials Register (EU-CTR)
- The WHO International Clinical Trials Registry Platform (ICTRP).

Clinical Practice Guidelines (CPGs) were searched in the UptoDate database, through manual searching and through consultation with clinical experts in addition to the systematic search.

2.4 Study selection

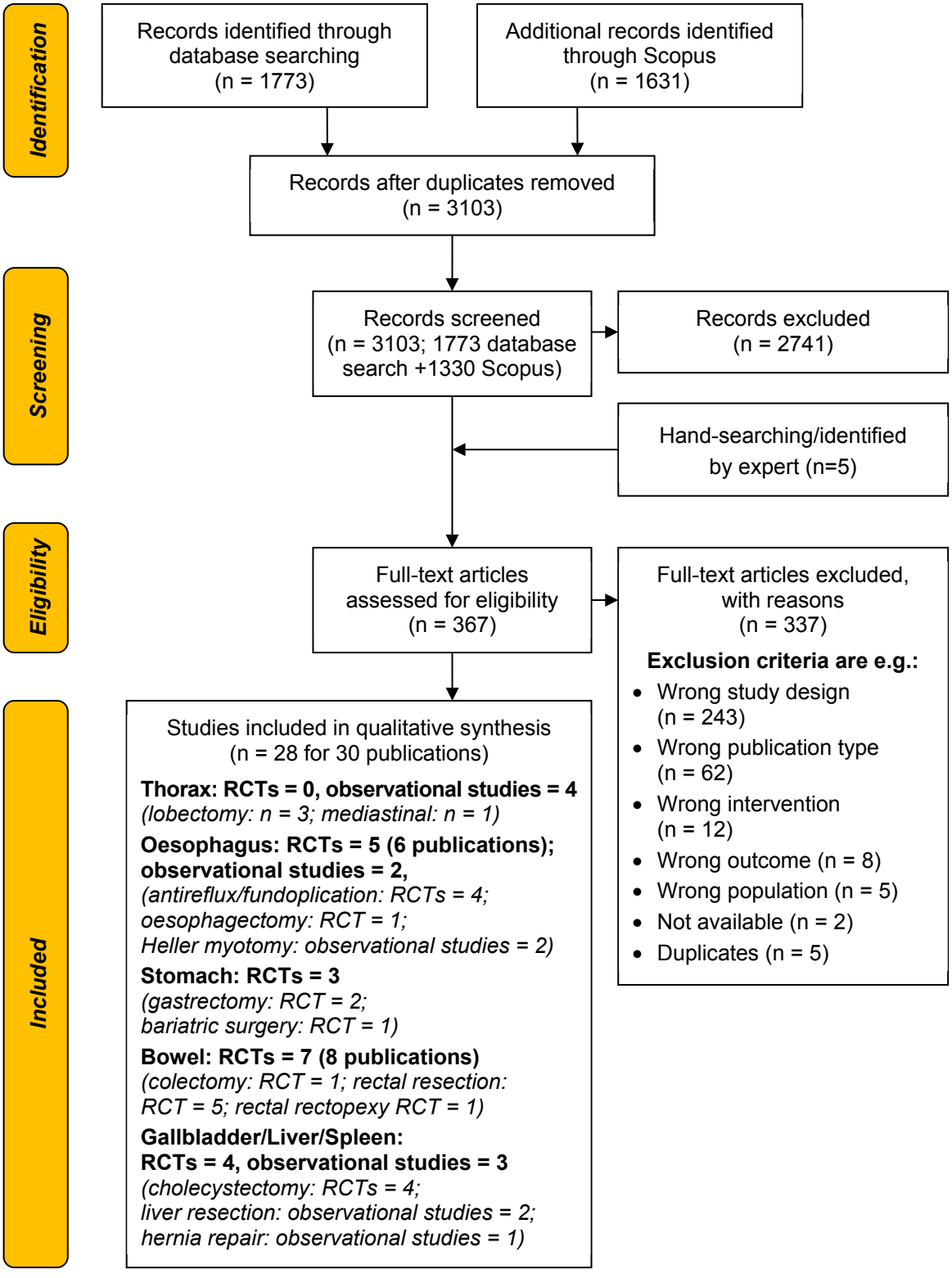

Figure 1: Flow chart

The systematic searches yielded 3103 records after accounting for duplicates. The author and co-author independently screened the titles and abstracts and selected studies according to the pre-defined inclusion as outlined in the Scope for further full-text examination. 2741 records were excluded at this screening stage, leaving 362 full-text articles which were assessed for eligibility. Of these 362 full-text articles, 337 were excluded on the grounds of wrong study design, wrong publication type, wrong intervention, wrong outcome or wrong population. 7 were either not available or turned out to be duplicates. An additional five relevant studies were identified via hand searching or contact with experts. For eight procedures (antireflux/fundoplication, oesphagectomy, gastrectomy, bariatric surgery, colectomy, rectal resection, rectal rectopexy, cholecystectomy), RCTs of ≥10 patients could be identified. For five procedures (lobectomy, mediastinal surgery, Heller myotomy, liver resection/hepatectomy, hernia repair), no RCTs ≥10 patients could be identified, hence (in accordance with the project protocol) nine non-randomised controlled studies were included (lobectomy:3; mediastinal surgery:1; Heller myotomy:2; liver resection/hepatectomy:2; hernia repair:1).

2.5 Data extraction and analyses

Data were extracted by the author and checked by the co-author. Evidence tables were created based on the predefined outcomes and information about the study. Continuous variables were reported using median, interquartile range or overall range, and/or mean with standard deviation, according to availability. Categorical variables were reported using frequencies and percentages. For the summary of findings table, data from RCTs were pooled, where homogenous outcome measures were available, to generate estimates of absolute and relative effect. This took the form of relative and absolute risk for categorical variables or mean differences for continuous variables. No meta-analysis was performed.

2.6 Quality rating

For Description and Technical Characteristics of Technology (TEC) and Health Problem and Current Use of the Technology (CUR) domains, no quality assessment tool were used; here multiple sources were used to generate a narrative description of the results of these domains, chiefly information from the manufacturer, clinical guidelines and published HTA reports.

For the Effectiveness (EFF) and the Safety (SAF) domains and following EUnetHTA guidelines, risk of bias at the study level was assessed using the Cochrane Risk of Bias tool[5] for RCTs and the ROBINS-I for non-randomised studies[6]. The author and co-authors performed the risk of bias assessment independently.

The quality of the body of evidence was assessed using Grading of Recommendations, Assessment, Development and Evaluation (GRADE), using the online programme https://gradepro.org/. The author performed the GRADE assessment and the co-author checked it. Disagreements were resolved by consensus.

[5] https://handbook-5-1.cochrane.org/

[6] https://www.riskofbias.info/welcome/home

2.7 Description of the evidence used

Table 2: Main characteristics of studies (RCTs) included

Author and year	Study type	Number of patients	Intervention (s)	Comparator (s)	Main endpoints	Included in clinical effective-ness and/ or safety domain
Oesophagus						
Antireflux/Fundoplication						
Draaisma et al, 2006 [10]	Single-centre RCT of patients with GORD	50 (IG: 25, CG: 25)	Robot-assisted laparoscopic Nissen fundoplication | da Vinci Robotic System	Laparoscopic Nissen fundoplication	Primary endpoints: clinical measures and symptoms Secondary endpoints: general health state (10-point VAS 0-100); QoL (Visick scale); self-rated reflux symptoms (instrument NR); satisfaction with outcome (instrument NR);	Effective-ness and safety
Morino et al, 2006 [11]	Single-centre RCT of patients with GORD	50 (IG:25, CG:25)	Robot-assisted fundoplication | da Vinci system	Laproscopic fundoplication	Primary endpoint: In-hospital cost of the procedure Secondary endpoints were skin-to-skin and total operating time	Effective-ness and safety
Mueller-Stich et al. 2007 & Mueller-Stich et al. 2009 [12] [13]	Single-centre RCT of patients with symptomatic GERD	40 (IG: 20, CG:20)	Robot-assisted laparoscopic fundoplication | da Vinci Surgical System	Laproscopic fundoplication	Primary: Quality of Life in Refux and Dsypepsia (QOLRAD); Gastrointestinal Symptom Rating Scale (GSRS); patient satisfaction; 4-step Likert scale for specific symptoms (2009) Secondary: Perioperative outcomes regarding operative time, perioperative complications, length of stay and costs (2007)	Effective-ness and safety
Nakadi et al, 2006 [14]	Single-centre RCT of patients with GERD	20 (IG: 9, CG: 11)	Robot-assisted Nissen fundoplication | da Vinci system	Laparoscopic Nissen fundoplication	Aims stated as: Feasibility, benefits and costs (postoperative complaints, satisfaction score, duration of surgical procedure, LOS, operative costs)	Effective-ness

Author and year	Study type	Number of patients	Intervention (s)	Comparator (s)	Main endpoints	Included in clinical effective-ness and/ or safety domain
Oesophagectomy						
Van der Sluis et al, 2018 [15]	Single centre RCT of patients with oesopgaeal cancer	109 (IG: 54, CG: 55)	Robot-assisted minimally invasive thoracolaparoscopic oesophagectomy | da Vinci Robotic System	Open transthoracic oesophaegctomy	Primary: Surgery-related postoperative complications. Secondary: mortality (in-hospital and within 30 days), pulmonary complications, cardiac complications, perioperative outcomes, quality of life, functioning, pain	Effective-ness and safety
Stomach						
Gastrectomy						
Pan et al, 2017 [16]	Single centre RCT of patients with gastric cancer	163 (IG: 102, CG: 61)	Robotic gastrectomy | NR	Laparoscopic gastrectomy	Assessed perioperative outcomes and postoperative complications	Effective-ness and safety
Wang et al, 2016 [17]	Single-centre RCT of patients with gastric cancer	311 (IG: 153, CG: 158)	Robotic gastrectomy | NR	Open gastrectomy	Primary: duration of hospitalization, clinical measures, surgery duration, proximal and distal resection margins, estimated blood loss, morbidity and mortality during the first 30 days after the procedure	Effective-ness and safety
Bariatric Surgery						
Sanchez et al, 2005 [18]	Single-centre RCT	50 (IG: 25, CG: 25)	Totally robotic laparo-scopic Roux-en-Y gastric bypass | da Vinci Surgical System	Laparoscopic Roux-en-Y gastric bypass	Not stated as such but included learning curve analysis, safety, operative times and length of stay	Safety
Bowel						
Colectomy						
Park et al. 2012 [19]	Single-centre RCT of patients with newly diagnosed right-sided colonic carcinoma	71 (IG: 35, CG: 36)	Robot-assisted colectomy | da Vinci Surgical System	Laparoscopic colectomy	Length of hospital stay Secondary endpoints: duration of operation, complications, pathological completeness of tumour excision and postoperative pain	Effective-ness and safety

Author and year	Study type	Number of patients	Intervention (s)	Comparator (s)	Main endpoints	Included in clinical effective-ness and/ or safety domain
Rectal resection						
Jayne et al. 2017 [20]	International multicentre RCT of patients with rectal adenocarcinoma (ROLARR clinical trial)	IG: 237 randomised; (1 withdrew before surgery) CG: 234 randomised; (4 had no surgery after randomisation)	Robot-assisted laparoscopic rectal cancer resection | da Vinci Surgical System	Laparoscopic rectal resection	Primary endpoint: Rate of conversion to open surgery Secondary endpoints: 30-day operative mortality, duration of operation, compli-cations, pathological completeness of tumour excision, patient-reported bladder symptoms (International Prostate Symp-tom Score, I-PSS) and sexual function-ing (International Index of Erectile Func-tion, and Female Sexual Function Index	Effective-ness and safety
Kim et al. 2018 [21]	Single-centre RCT of patients with mid to low-lying rectal cancer	IG: 81 randomised, 66 available for analysis CG: 81, 73 available for analysis	Robot-assisted laparoscopic rectal cancer resection | da Vinci Surgical System	Laparoscopic rectal resection	Primary endpoint: Completeness of total mesorectal excision Secondary outcomes: circumferential and distal resection margin; Global Operative Assessment of Laparoscopic Skills; bowel function; morbidity; post-operative pain (Present Pain Intensity Index and VAS); QoL (via Korean version of EORTC QLQ-C30 and the colorectal cancer module QLQ-CR38).	Effective-ness and safety
Tolstrup et al. 2018 [22]	Single-centre RCT of patients with rectal adenocarcinoma (ROLARR clinical trial): Denmark centre	51 (IG : 25, CG : 26)	Robot-assisted laparoscopic rectal cancer resection | da Vinci Surgical System	Laparoscopic rectal resection	The aim was to assess perioperative pain via numeric rating scale (NRS). Length of surgery and complications were also assessed.	Effective-ness and safety
Wang et al. 2017 [23]	Single-centre RCT of male patients with rectal cancer	137 (IG: 71; CG 66)	Robot-assisted total mesorectal excision (device unspecified)	Laparoscopic total mesorectal excision	Urinary function and sexual function at 12 months	Effectiveness and safety
Debakey et al. 2018 [24]	Single centre RCT of patients with rectal cancer	45 (IG: 21, CG 24)	Robot-assisted rectal cancer resection | da Vinci robotic system Intuitive	Laparoscopic rectal resection	Short-term operative outcomes (blood loss) and complications Oncologic outcomes	Effective-ness and safety

Author and year	Study type	Number of patients	Intervention (s)	Comparator (s)	Main endpoints	Included in clinical effective-ness and/ or safety domain
Ventral mesh rectopexy						
Mäkelä-Kaikonen et al. 2016 [25], [11]	Single-centre RCT of patients with rectal prolapse and intussusception	IG: 16 (total relapse 4, intras-susception 12) CG: 14 (total relapse 2, intras-susception 11, 1 excluded)	Robot-assisted ventral mesh rectopexy | da Vinci Surgical System	Laparoscopic ventral mesh rectopexy	Perioperative parameters, complications and restoration of anatomy, postoperative pain via VAS	Effective-ness and safety
Gallbladder/Liver Spleen						
Cholecystectomy						
Kudsi et al. 2017 [26]	International multi-centre RCT of patients with gallbladder disease	136 (IG: 83, CG: 53)	Robotic single-site cholecystectomy | da Vinci Single Site Instruments	Multiport laparoscopic cholecystectomy	Patient-perceived cosmesis, patient-reported satisfaction (BIQ, PSQ) and and QoL (SF 12) Secondary endpoint: perioperative outcomes	Effective-ness and safety
Pietrabissa et al. 2016 [27]	Single-centre RCT of patients with gall-bladder lithiasis or polyps with no evidence of choledocholithiasis	81 (IG: 40, CG: 41)	Single incision laparoscopic robotic cholecystectomy | NR	Four-port laparoscopic cholecystectomy	Primary: Pain at 24 h Secondary endpoints: VAS score and cosmetic outcome (subjective min 0-max 10). Further objectives: operative times, intra and postoperative morbidity, rate of incisional hernia.	Effective-ness and safety
Grochola et al. 2018 [28]	Single centre RCT of patients with benign gallbladder disease	60 (IG 30, CG 30)	Robot-assisted single-site cholecystectomy | Da Vinci single-site TM cholecystectomy robotic system	Single-port laparoscopic cholecstectomy	Surgeon's physical and mental stress load. Secondary: intraoperative outcomes, complications, health-related quality of life, cosmesis	Effective-ness and safety
Ruurda et al. 2003 [1]	Single centre RCT of patients with cholecystolithiasis	40 (IG: 20, CG: 20)	Robot-assisted single-site cholecystectomy | da Vinci telemanipu-lation system	Standard laparoscopic cholecystectomy	Procedure time	Safety

Table 3: Main characteristics of studies (non-randomised comparative) included

Author and year or study name	Study type	Number of patients	Intervention (s)	Comparator	Main endpoints	Included in clinical effective-ness and/ or safety domain
Thoracic						
Lobectomy/segmentectomy						
Augustin et al. 2013 [29]	Non-randomised comparison of all robot-assisted and consecutive conventional minimally invasive VATS lobectomies	52 (IG: 26, CG: 26)	Robot-assisted lobectomy (5 posterior and 21 anterior approach) | da Vinci Surgical System (3-arm)	VATS lung lobectomy (anterior approach)	Perioperative events	Effective-ness and safety
Gonde et al. 2017 [30]	Single-center 1 year prospective observational cost study	112 (IG: 57, CG: 55)	RATS | da Vinci Surgical System (3-arm)	VATS (modified anterior approach)	Perioperative events & resource use	Effective-ness and safety
Rinieri et al. 2016 [31]	Prospective observational study	51 (IG: 17, CG: 34)	RATS |da Vinci Surgical System (3-arm)	VATS (anterior approach)	Perioperative events and complications	Effective-ness and safety
Mediastinal surgery						
Balduyck et al. 2011 [32]	prospectivenon-randomised study	36 (IG: 14, CG: 22)	Robot-assisted anterior mediastinal mass resection | da Vinci robotic system	Open mediastinal mass resection by sternotomy	Quality of life using EORTC QLQ-C30 (cancer core questionnaire) and EORTC QLQ-LC-13 (lung-cancer-specific questionnaire module)	Effective-ness and safety
Oesophagus						
Heller myotomy						
Huffmanm et al. 2007 [33]	Single centre prospective observational study (conse-cutive patients over 6 years)	61 (IG: 24, CG: 37)	da Vinci Surgical System robot-assisted laparoscopic myotomy with partial fundoplication	Laparoscopic myotomy with partial fundoplication	Generic and disease-specific quality of life	Effective-ness and safety
Sanchez et al.2012 [34]	Single centre, prospective-comparative study of consecutive patients	31 (IG: 13, CG: 18)	da Vinci Surgical System robotic assisted laparoscopic Heller myotomy	Laparoscopic Heller myotomy	Efficacy and safety	Effective-ness and safety

Author and year or study name	Study type	Number of patients	Intervention (s)	Comparator	Main endpoints	Included in clinical effective-ness and/ or safety domain
Gallbladder/Liver Spleen						
Liver resection/hepatectomy						
Berber et al. 2010 [35]	Single centre prospective non-randomised study	32 (IG: 9, CG: 23)	Robotic resection of liver tumour	Laparoscopic liver resection	Survival, recurrence, perioperative outcomes	Effective-ness and safety
Lai and Tang 2016 [36]	Single centre prospective non randomised trial of consecutive patients	130 (IG: 95, CG:35)	da Vinci Surgical System robot-assisted laparascopic partial hepatectomy	Laparoscopic partial hepatectomy	Survival, perioperative outcomes	Effective-ness and safety
Hernia repair						
Tran et al. 2011 [37]	Single centre prospectivenon-randomized Study	32 (IG: 16, CG: 16)	Robotic Freehand® Robotic single-port total extraperi-toneal inguinal hernia repair	Laparoscopic single-port total extraperitoneal inguinal hernia repair	Perioperative outcomes and satisfaction	Effective-ness and safety

Abbreviations: ASA=score American Society of Anesthesiologists; BIQ=body image questionnaire; BMI=body mass index; EORTC QLQ-C30=European Organisation for Research and Treatment of Cancer Quality of Life Group; CG=control group; FU=follow-up; GERD=gastroesophageal reflux disease; GORD=gastro-oesophageal reflux disease; GORD HRQOL=Gastro-oesophageal Reflux Health-Related Quality of Life scale; GSRS=Gastrointestinal Symptom Rating Scale; ICU=intensive care unit; IG=intervention group; IQR=interquartile range; M=Median; MD=mean difference; NR=not reported; ns=not significant; PSQ=photograph series questionnaire; QoL=quality of life; QOLRAD=Quality of Life in Reflux and Dyspepsia; SF-12 (QoL-12)=short form 12; Ø=mean; R=Range; RATS=Robot-assisted thoracic surgery; SIRC=single-incision robotic cholecystectomy; TNM=Tumor, nodes, metastasis; VAS=visual analogue scale; VATS=Video-assisted thoracic surgery.

2.8 Deviations from project plan

No deviation has occurred.

3 DESCRIPTION AND TECHNICAL CHARACTERISTICS OF TECHNOLOGY (TEC)

3.1 Research questions

Element ID	Research question
B0001	What is robot-assisted surgery? What is open surgery? What is laparoscopic/video-assisted thoracoscopic surgery?
B0002	What is the claimed benefit of robot-assisted surgery in relation to open surgery and laparoscopy/VATS?
B0003	What is the phase of development and implementation of robot-assisted surgery?
B0004	Who administers robot-assisted surgery? In what context and level of care is robot-assisted surgery provided?
B0008	What kind of special premises are needed to use robot-assisted surgery?
B0009	What equipment and supplies are needed to use robot-assisted surgery?
A0020	For which indications/interventions has robot-assisted surgery received marketing authorisation or CE marking?

3.2 Results

Features of the technology and comparators

[B0001] – What is the technology and the comparator(s)?

In general, robot-assisted surgery is a form of minimally-invasive surgery. The aim of developing robotic surgery was to overcome the limitations (e.g. accessibility of difficult reachable areas) associated with pre-existing minimally-invasive surgery. The instruments of the robotic system are controlled by a direct telemanipulator [38].

A telemanipulator is a remote manipulator that allows the surgeon to perform the normal movements associated with the surgery, using the robotic arms [39].

Robot-assisted surgical systems in development include single-arm units designed to perform single-port surgery – also called single-incision surgery – and multi-arm systems typically used for multi-port, or multi-incision, procedures. Some manufacturers developing single-port systems designed to access the body via natural orifice describe their systems as allowing “scarless” surgery. A comparative potential benefit of multiarm systems over single-arm systems is the ability to perform a broader range of surgical procedures due to their allowing for a larger surgical field with corresponding greater visualization of the surgical field and their versatility in positioning instruments, thus increasing surgeons’ ability to access more anatomy with those instruments. Generally, single-port systems may be preferred for less complex surgery, whereas multi-port systems may be preferred for more technically challenging procedures[7].

[7] Emerging Robotic-assisted Surgery Systems, Health Thecnology Forecast, ECRI, 2017 (from: https://www.ecri.org/library/general-topics/robotics)

Currently there are 17 known manufacturers of robotic systems to aid in surgical procedures (although one of these is not yet planned for use in thoracic and visceral surgery), of which four are currently marketing their products as commercially available in the area of thoracic and visceral surgery. These companies are Intuitive Surgical, Inc., Surgica Robotica S.p.A., TransEnterix and Freehand 2010 Ltd.

Intuitive Surgical: da Vinci®:

Intuitive Surgical, an American corporation and market leader in surgical robots was founded in 1995 and has launched four generations of robotic surgical systems. The current generation includes: da Vinci® Xi, SP, and X.

- The da Vinci® Xi system has four robotic arms. The system includes the most advanced instrumentation, vision, and features such as integrated table motion. The Xi is used for a variety of complex procedures.
- The da Vinci® X has the same arm architecture as the Xi, but takes advantage of a number of cost-conscious options that reduce the overall price of the system.
- The da Vinci® SP is designed spefically for single-port accesss. Three multi-jointed instruments and a 3DHD camera are all delivered through a single arm.

All systems have CE mark and FDA approval. Each system composed of a surgeon console and a patient side-cart with boom-mounted robotic arm(s). The surgeon operates at a console (typically in the same room as the patient) while viewing a high definition 3D image from inside the patient's body to see anatomical structures in natural colours. The patient side cart(s) is a surgical robotic assistant, with multiple arms and detachable instruments, mounted on a cart that can be positioned at the surgical site. The system translates the surgeon's hand, wrist and finger movements into real-time movements of the wristed surgical instruments. The replaceable wristed instruments (EndoWrist®) are attached to the arms of the robot. The attached instruments have seven degrees of motion and every single instrument available is designed for a specific task (e.g. clamping, cutting, coagulating, dissecting, suturing). Another part of the surgical system is the Vision Cart: positioned tableside, the system's central processing unit component includes accessory equipment, a surgical video system, and a viewing monitor for the operating team. It is equipped with a high-definition, 3D endoscope (flexible tube with a camera and light) and image processing equipment that provides images of the patient's anatomy. This 3D HD endoscope is inserted through one of the small incisions and is held in place by one of the robotic arms[7, 8, 9].

Surgica Robotica: Surgenius:

Surgica Robotica, an Italian company, offers one system: Surgenius Beta. The former Alpha System was the first development and it would appear from the manufacturer's website that this product is not commercially available anymore. The Beta version is a further development of the Alpha version. The Surgenius Beta is able to cover the entire torso (four abdominal quadrants). The robotic tools reach nine degrees of freedom for the surgeon. Beta proved its capabilities with operations on the pancreas of mini-pigs and obtained approval in the European Economic Area through its CE (Conformité Europeene – European Conformity) Marking Certificate. Presently the company is developing the Surgenius Gamma[10].

[8] https://www.davincisurgerycommunity.com/Systems_I_A/da_Vinci_Si_Si_e

[9] https://www.intuitive.com/about-us/company/legal/safety-information

[10] http://www.surgicarobotica.com/

TransEnterix: Senhance™ Surgical System:

TransEnterix®, an American company, provides the Senhance™ Surgical System. Initially, the company marketed another surgical robot (SurgiBot™ System). The FDA rejected the submission for SurgiBot system in 2016. In 2015 TransEnterix® also acquired the surgical robot division of SOFAR S.p.A with its Telelap ALF-X®. The ALF-X system was renamed the Senhance™ Surgical System[11].

The new Senhance™ is a console type robotic platform consisting of a remote control station unit, manipulator arms, and a connection node. The robot system comprises three arms, each individually mounted on its own cart. It was designed to require only a minimal learning curve with familiar laparoscopic motion, trocars and approach. The surgeon sits at a console and telemanipulates the surgical robot. Furthermore, the surgeon has the ability to simultaneously control multiple robotic arms, instruments and a camera. Due to its open platform strategy, the Senhance™ System is compatible with other laparoscopic devices. Moreover, the surgical system provides eye-tracking that is intended to allow vision control during surgical operations without repositioning the camera: this is an evolution of current visualization technologies, such as the da Vinci Surgical System's binocular display controlled by foot-operated switches. Another feature is the haptic feedback that provides force feedback: this tactile force feedback translates sensation from an instrument's distal end to the surgeon's hand, contrasting da Vinci's feedback, which is displayed visually rather than felt by the controller [12] [40].

Freehand 2010 Ltd Freehand v1.2

Freehand 2010 Ltd is a company located in the United Kingdom. The company offers a robotic camera arm for minimally invasive surgery: this system is composed of a lockable articulating arm, an electronic control box, and a robotic motion assembly unit. Mounted on railings around the operating table, the camera can be moved in three dimensions, controlled via operator head movements and laser-pointed guidance. To select the direction of movement, the operator moves his/her head in the desired direction; an LED arrow with the selected direction is then displayed. In order to initiate movement, a foot switch is pressed until the camera is in the desired location; releasing the switch terminates movement [40][13].

22 systems have been developed, of which 13 are still in development, 7 are currently commercially available (da Vinci® Si/Si-e, da Vinci® SP, da Vinci® XI, da Vinci® X, Freehand v1.2, Surgenius Beta and Senhance TM Surgical System) and 1 is available for research purposes only. A further product Flex® Robotic System is commercially available but is only for transoral and transanal surgery. All systems are listed in Table 4.

[11] https://www.massdevice.com/transenterix-reboots-alf-x-robot-assisted-surgery-platform-senhance/

[12] https://www.senhance.com/us/laparoscopic-surgery-challenges

[13] http://freehandsurgeon.com/Products/Detail/2

Table 4: Features of the intervention and development status [40] [41][10,]

Manufacturer	Product name	Development status	Principal characteristics/Intended Use
Applied Dexterity	RAVEN™ (I, II and III)	Commercialized as an open research platform and distributed to university clinics and research labs	It was developed with a military's vision (aim: compactness, remote control). Multi-arms Generic intended use/
AVRA Medical Robotics	AVRA Surgical Robotic System (ASRS)	In development	Semi/autonomous systems incorporate artificial intelligence for enhanced diagnostic and therapeutic capabilities Generic intended use
Cambridge Medical Robotics	Versius	In development	Multiarms Generic intended use
CAST	MIVR (Miniature in vivo robot)	In development	Two Arms miniaturization of robotic arms and the motors that drive them
DLR Robotics	MiroSurge	In development	Multiarm Multipurpose (laparoscopic) Haptic fedback
Freehand®	FREEHAND V1.2	FDA approval (2009) CE Mark (2009	There is one robotic video arm, which one can be controlled by footswitch and a Headset.
Intuitive Surgical	First generation of products: da Vinci®	FDA approval (2003) CE Mark (2003)	da Vinci (IS1200) is no longer on the Notified Product List and Declaration of Conformity, so it is no longer supported as a CE-marked product
	Second generation of products: da Vinci® S	FDA approval (2009) CE Mark (2007)	da Vinci S (IS2000) is no longer on the Notified Product List and Declaration of Conformity, so it is no longer supported as a CE-marked product.
	Third generation of products: da Vinci® Si or Si-e Surgical System	FDA approval (2009/10) CE mark (2009/10)	Four robotics arms (Vinci® Si) Three robotic arms (da Vinci® Si-e) Multi intended use (for details see FDA and CE)
	Fourth generation of products: da Vinci® Xi; da Vinci® X; da Vinci® SP	Xi: FDA approval (2014); CE mark (2014) X : FDA approval (2017); CE mark (2017) SP : FDA approval (2018); no CE mark	Advancement of da Vinci® Si in particular arms are thinner and instruments longer. The Xi's arms also include a new "patient clearance joint" that is designed to facilitate intraoperative arm adjustments and to provide a wider range of motion than is possible with the Si and Si-e. X is similar to the da Vinci Xi architecture but at a lower cost Multi intended use (for details see FDA and CE)
Medical Robotic Technolgies	SOFIE (Surgeon's Operating Force-feedback Interface Eindhoven)	In development	Compact, Haptic feedback, Multi-arms Generic intended use

Medrobotics	Flex® Robotic System[14]	FDA clearances (2018) CE mark (2014)	highly articulated, serpentine scope but only for use in transanal or transoral surgery
Medtronic	Hugo	In development	multiarm, multipurpose
Meere Company	REVO-I	In development CE mark (planned for 2019)[15]	multiarm general endoscopic surgery, including cholecystectomy and prostatectomy
Nanyang Technological University and National University Health System	MASTER	In development	transluminal endoscopic robot two arms
Surgica Robotica S.p.A.[16]	Surgenius Beta	CE mark (2012)	Multiarms Generic intended use
	Surgenius Gamma	In development	Confidential
Titan Medical[17]	Single Sport Orifice Robotic Technology (SPORT™) Surgical System	In development (launch and approval planned for 2019)	Single-port access Multiarms Generic intended use (including general abdominal, gynecologic, and urologic indications)
TransEnterix	Senhance™ Surgical System (Former Telelap ALF-X ®)	FDA approval (2017) CE mark (2017)	Eye-tracking system , haptic feedback Multi-arms indicated for adult use and for laparoscopic surgery (although different indications for use between FDAand CE certification[18])
	SurgiBot	In development	Mobile, Single-port access
Verb Surgical	-	In development (launch planned for 2020)	Cooperation of Google parent Alphabet Inc.'s Verily Life Sciences and Johnson & Johnson
Virtual Incision	-	In development	Single-port Intended use abdominal surgery

[14] Robotic system marketed for transoral and transanal surgery.
Manufacturer is not commercially active in thoracic and visceral surgery.

[15] REVO-I has Korean FDA-approval so far (2017)

[16] Manufacturer was contacted via e-mail on the 16th May and 12th June 2018. However, no answer was received.

[17] Manufacturer was first contacted on the 16th May via the contact formula on the manufacturers website. After several e-mails and phone calls with representatives of the manufacturer the contact was discontinued without any additional information from the manufacturer.

[18] FDA: The Senhance Surgical System is intended for use in laparoscopic gynecological surgery, colorectal surgery, cholecystectomy, and inguinal hernia repair. CE: is intended to be used for laparoscopic surgery in the abdomen, pelvis and limited uses in the thoracic cavity excluding the heart and greater vessels.
(from: https://www.senhance.com/us/senhance-indication)

What is open surgery?

Open surgery is a type of surgery in which an incision is made using a scalpel to fully expose the area of the body on which the operation will be performed. The surgeon inserts the instruments through the incision and conducts the surgery. Selected surgeries are still performed using the traditional open incision (especially for the resection of larges masses), but many more are conducted using minimally invasive techniques [42].

What is laparoscopic/video-assisted thoracoscopic surgery?

Laparoscopic and video-assisted thoracoscopic surgeries (VATS) are minimally invasive approaches, meaning that the incision is smaller than the usual open incision. It is also known as keyhole surgery. Whereas one incision is required to place the laparoscope (a viewing telescope attached to a camera and light source) that allows the surgeon to see the operative area on the video monitor, two or three other small incisions are made to place the surgical instruments [38].

In laparoscopic surgery, the surgeon performs the procedure holding rigid instruments and views the surgical area through an endoscopic camera that is projected onto a monitor. The laparoscopic tools move in the opposite direction of the surgeon's hands due to the pivot point design. Furthermore, the instruments used in traditional laparoscopy normally have four degrees of movement. In some cases, a surgery may start out as a minimally invasive procedure, but then convert to the larger open incision procedure if the surgeon needs more flexibility of movement or due to an occurring adverse event [38].

VATS is a type of minimally invasive surgery, comparable to laparoscopy, which does not require the formal thoracotomy incisions, especially the cuts through the ribs or breastbone (sternum). VATS is principally performed in the management of pulmonary, mediastinal, and pleural pathology. The instrumentation for VATS includes the use of a camera-linked optic scope and either conventional thoracic instruments or laparoscopic instruments. In general, VATS and laparoscopic surgery are similar surgical approaches. However, unlike with laparoscopy, carbon dioxide insufflation is not generally required with VATS [43].

[B0002] – What is the claimed benefit of the technology in relation to the comparator(s)?

Minimally invasive surgery is generally considered superior to open surgery since, assuming surgeons are equally skilled in both procedures, the minimally invasive technique is associated with a lower risk of infection, shorter recovery times and equally successful outcomes[19]. These claimed benefits of laparoscopic surgery over open surgery also apply for robotic surgery vs. open surgery.

Nevertheless, robotic surgery is an advanced form of minimally invasive or laparoscopic surgery requiring the surgeon to operate a robot. The robot has a higher degree of dexterity compared to the laparoscopic approach, allowing surgeons the ability to operate in very tight spaces in the body that would otherwise only be accessible through open surgery.

Robot-assisted surgery is supposed to achieve the safety established with open surgery and the reduced patient burden associated with minimally-invasive surgery. However, the robotic approach may also confer additional clinical and economic benefits beyond open and laparoscopic surgery. The benefits are claimed to relate to improved quality of life, reduction in healthcare resource utiliza-

[19] https://www.sages.org/publications/patient-information/patient-information-for-laparoscopic-appendectomy-from-sages/

tion, improved perioperative and oncological clinical outcomes. It is also thought to allow surgeons to work more ergonomically, resulting in less strain. The degree of improvement varies across modalities but tends to be most apparent when comparing robot-assisted surgery with open surgery. The claimed benefits of robot-assisted surgery compared to open surgery and/or laparoscopic surgery are as follows [39][20]

Healthcare Utilization:

- Reduced length of stay
- Fewer Readmissions
- Reduced ICU Time
- Fewer post-surgery diagnostic tests
- Reduction in need for catheters and other accessories
- Hospital bed utilization
- Shift to outpatient surgery

Clinical Outcomes:

- Reduced blood loss volume
- Fewer transfusions
- Lower overall complication rate
- Fewer conversions to open or laparoscopic surgery
- Lower Positive Surgical Margins
- Reduced surgical trauma to tissue

Improved Quality Of Life:

- Improvement in patient reported outcomes
- Faster return to work for patients
- Reduced burden on caregivers
- Reduced operative pain and discomfort
- Less carring and improved cosmesis

[B0003] – What is the phase of development and implementation of the technology and the comparator(s)?

Robotic surgery has been increasingly implemented during the last 10 to 15 years. Minimally-invasive interventions, performed by laparoscopy, are very common in certain areas (e.g. cholecystectomy). However, in more complex surgeries (e.g. prostatectomy) laparoscopy is associated with a longer learning curve and surgeons often face technical challenges. It is these challenges that surgical robots are intended to assist surgeons in overcoming. Robot-assisted surgery is very common in certain interventions (e.g. prostatectomy) whilst the list of eligible surgeries for robotic support is growing. The da Vinci Surgical System for example is at present employed most extensively in the areas of urological, visceral, head and neck, and thoracic surgery [39].

[20] https://www.intuitive.com/about-us/company/legal/safety-information

[B0004] – Who administers the technology and the comparator(s) and in what context and level of care are they provided?

In robot-assisted surgery, performed with the commercially available systems in the European Union, a trained surgeon is always in control of the device.

The aim of the currently available robotic systems is to provide technology to assist surgeons; they do not replace surgeons. These devices are a tool that surgeons can choose to use to provide their patients with a further minimally invasive surgical option. There are no additional personnel requirements according to the manufacturers; the personnel required is the same as for an open or laparoscopic intervention. However, additional training and learning is required to operate all systems[21, 22]

Other issues associated with robot-assisted surgery are the need for additional pre- and postoperative procedures related to preparing, cleaning, and maintaining the system and proprietary instrumentation. TransEnterix has stated that switching the reusable surgical instruments for its Senhance system is a quick and simple process and that the Senhance system offers per-procedure costs comparable to those of conventional laparoscopic surgery [10, 14].

[B0008] – What kind of special premises are needed to use the technology and the comparator(s)?

The robotic systems typically consist of a surgeon's console and a patient-side cart with three to four interactive robotic arms controlled from the console. The arms are for tools that hold objects and can also act as scalpels, scissors, or graspers. The surgeon uses the console's master controls to manoeuvre the patient-side cart's robotic arms. The robotic surgical system is large and although it may fit in most operating room suites, renovation or new construction of operating rooms may be needed in some cases. In order to justify the cost of robotic systems, hospitals may need to apportion its use among several clinical departments[10, 14].

[B0009] – What equipment and supplies are needed to use the technology and the comparator(s)?

The capital costs include upgrades and accessories typically purchased with each system (e.g. for the da Vinci system these may include da Vinci Skills Simulator, endoscope and Integrated Table Motion). There are also specialized surgical instruments designed to offer surgeons better dexterity and a full range of motion through small incisions. Each interchangeable instrument has a specific function including grasping, cutting, blunt and sharp dissection, approximation, ligation, suturing, and electrocautery.

In the literature there are several studies detailing costs, but the heterogeneity and publication bias of the studies make analysis difficult. For example studies report costs incurred at different time periods of the learning curve (which may impact staff and material costs), use different techniques in laparoscopic and robotic groups (such as the type of device, hybrid versus totally robotic techniques etc.) and have different volumes of patients which may affect the distribution of organisation and related costs. Added to which there is the general variability in costs between hospitals and countries.

[21] https://www.intuitive.com/about-us/company/legal/safety-information

[22] https://www.senhance.com/us/laparoscopic-surgery-challenges

In a systematic review and meta-analysis of the literature, Fuertes-Guiró et al. [44] reported the differences in the total cost of surgery and operative time in traditional laparoscopic surgery and da Vinci robotic surgery as follows: da Vinci robot-assisted surgery is associated with signfiicantly higher costs compared with traditional laparoscopic surgery (p<0.00001). Robotic surgery takes longer (8.0–65.5 min) than traditional surgery (p<0.00001), and this difference represents an average opportunity cost for robot use of € 489.98, with a unit cost factor/time which varies according to the pathology dealt with, from € 8.2 to 18.7/min.

10 of the studies included in this HTA considered cost aspects, all of which reported higher costs with robot-assisted surgery than with the comparator. 2 studies related to the area of thoracic surgery [29], [30]. One of these studies found procedural costs to be 44% higher for the robotic approach, equating to a difference of € 770.55 per operation [29]. The other study reported a median cost per procedure of € 10,972 for robot-assisted surgery and € 9,637 for VATS (p<0.01). All 3 of the antireflux/fundoplication studies that measured costs [14] [11] [12] reported higher costs with the robot-assisted technique. In one study, robot-assisted surgery was more than four times more expensive than the comparator; individual cost elements that were significantly higher included disposable materials, re-usable materials, staffing (nurse) costs, investment and maintenance [14]. In another study, mean total costs per procedure were €3244 ± 512 in the robot-assisted fundoplication group vs. € 2743 ± 483 in the laparoscopic fundoplication group (p<0.01) [12]. Similarly Morino et al [11] reported significantly higher mean total costs per procedure of € 3157 in the robot-assisted group versus €1527 in the laparoscopic fundoplication group (p<0.001). Two studies in the area of bowel surgery reported cost results: in the rectal resection study [20], mean costs per procedure in the robot-assisted group were £11,853 vs. £ 10,874 in the conventional laparoscopy group (mean difference of £980, p<0.05). Main drivers of higher costs in this study were longer use of the operating theatre and the cost of instruments. Park et al [19] similarly attributed the higher costs associated with robot-assisted surgery (US $12,235 vs. $10,320, p<0.05) to the costs of surgery, primarily consumables. Lastly, robot-assisted cholecystectomy was also found to be more expensive than laparoscopic single-incision cholecystectomy (median 9734 CHF vs. 6900 CHF respectively, p=0.001) [28].

Extensive, highly specialized training and an adequate volume of cases are required for surgeons and their surgical teams to maintain proficiency. The surgical team requires training to learn how to set-up the system and how to make any necessary adjustments during a procedure. The learning curve may result in longer surgical times that can reduce the number of procedures that can be scheduled in a day until clinical staff gain experience.

Robot-specific consumables for the da Vinci system also represent a high cost and are significantly more expensive than those required to perform open surgery or conventional minimal invasive surgery. For example, the da Vinci system's EndoWrist instruments – which can be used 10 times, after which the system refuses to accept them – are expensive compared to their traditional-surgery counterparts and make up the bulk of the additional consumable cost[23].

Surgeons require training on how to learn to use the system. Some experts advise that new surgeons should already have extensive experience in minimally invasive surgery before attempting robot-assisted surgery. If there is a malfunction or emergency during the surgery, the surgeon will need the skills to finish the surgery manually. The manufacturer provides onsite and offsite training for surgeons and clinical support staff. Offsite training consists of lectures and hands-on sessions that address system skills for various applications. Typically, surgeons or hospitals request that a surgeon experienced in robot-assisted procedures be present to supervise new surgeons for initial cases[10, 14].

[23] DA VINCI DECISIONS HEALTH DEVICES JANUARY 2013 www.ecri.org

Intuitive Surgical recommends different learning programs, which are intended for surgeons who seek to develop the knowledge and skills necessary to use da Vinci surgical systems and da Vinci technology.[24] However, these programs are said to only cover the initial phase of the learning process. It is claimed that self-directed study and practice are additionally required to master the technology. Intuitive Surgical refers to the learning process as the "da Vinci Technology Training Pathway" (TTP) which consists of the following phases and elements:

- Phase 1 – Introduction to da Vinci Technology
- Phase 2 – da Vinci Technology Training
- Phase 3 – Initial Case Series Plan
- Phase 4 – Continuing Development

Whilst acknowledging that the responsibility of developing and updating the training program for any surgical area must be led and managed by its respective professional surgical societies, Intuitive proffers to provide support and services including simulation, core technology, and skill advancement. In addition, the company states that there are procedure analytics to help optimize the effectiveness of each hospital's surgical program[25].

TransEnterix established surgical training and innovation centers in Orlando, FL, USA, in August 2017, and Milan, Italy, in December 2016.

However, no consensus or recognized standards exist regarding optimal training programs for robot-assisted surgery. To address this need, some professional organizations have begun developing guidance to help healthcare facilities address the need for adequate training in robot-assisted surgery as it pertains generally to their respective clinical disciplines or to specific surgical procedures. For example, the American Association of Gynecologic Laparoscopists has published guidelines for recognising clinicians as proficient in robot-assisted gynecologic laparoscopy [41]. Similarly, the American Urological Association has formulated standard operating practices to guide hospitals in granting urologists credentials and privileges to perform robotic surgery at their institutions [41]. The Society of American Gastrointestinal and Endoscopic Surgeons and the Minimally Invasive Robotic Association published a consensus statement on robotic surgery, including guidelines for training and credentialing, in 2008, which recommends the following [41]:

- Training in robot-assisted surgery should involve both the acquisition of technical skills and practical use of the robot in specific operations.
- Training programs should involve an expert instructor who provides didactic lessons on the "technology, device function, altered functional status, basic troubleshooting, other technical issues, and device parameters and limitations."
- Instructors should also discuss team interaction and procedure-specific information, including "indications, workup, patient selection, instrumentation, preoperative preparation, patient and system positioning, port placement, procedural steps, complications, and management."
- Didactic training should also include a "discussion of issues related to the learning curve, reported outcomes, and expected perioperative course."
- Didactic training should be followed by live case observation, including "procedure preparation, system setup, patient positioning, review of case selection, and intraoperative technical aspects."

[24] The learning programs outlined in this section are based on information gathered from Intuitive Surgical. Since the other manufacturers did not answer our requests, no further information can be provided.

[25] https://www.intuitive.com/about-us/company/legal/safety-information

- After observing at least one complete procedure, trainees should receive hands-on experience, including “nonclinical simulation encompassing system setup, connections, operation, and troubleshooting,” initial skill training to develop procedure-specific skills, and clinical simulation.

However, TransEnterix, Titan Medical, and other manufacturers in earlier development have stated generally that their robotic systems are designed to take advantage of laparoscopic surgeons’ existing skills and experience and will be technically familiar to laparoscopic surgeons[10, 14].

[A0020] – For which indications has the technology received marketing authorisation or CE marking?

Please see Table 4 for a summary of the regulatory status.

4 HEALTH PROBLEM AND CURRENT USE OF THE TECHNOLOGY (CUR)

4.1 Research questions

Element ID	Research question
A0002	What is the thoracic or visceral surgery and for which diseases or health conditions is it used?
A0003	What are the known risk factors for the diseases or health conditions treated by thoracic or visceral surgery?
A0004	What is the natural course of the diseases or health conditions treated by thoracic or visceral surgery?
A0005	What are the symptoms and the burden of diseases or health conditions for the patient?
A0006	What are the consequences of the diseases or health conditions for the society?
A0007	What are the target populations in this assessment?
A0023	How many people belong to the target populations?
A0024	How are the diseases or health conditions currently diagnosed according to published guidelines and in practice?
A0025	How are the diseases or health conditions currently managed according to published guidelines and in practice?
A0011	How much is robot-assisted surgery utilised?

Questions A0003-A0006 are answered together since it is beyond the scope of this HTA to detail each possible disease – as well as its causes and effects – for which thoracic and visceral surgery can be employed as a treatment option.

4.2 Results

Overview of the disease or health condition

[A0002] – What is thoracic or visceral surgery and for which diseases or health condition is it used?

This assessment looks at the use of robot-assisted surgery in the area of thoracic and visceral surgery. Thoracic surgery is concerned with conditions of the lungs, chest wall and diaphragm and is generally dominated by treatment of malignant disease. Visceral surgery deals with all aspects of the surgical treatment of benign and malignant diseases of abdominal organs, the entire gastro-intestinal tract, endocrine organs, the abdominal wall and the peritoneum.

Within this HTA-assessment of surgical procedures performed with the assistance of robots, the following specific disease areas and procedures were included:

Surgical procedures for ***thoracic surgery*** relates to diseases of the lung, ribs and pulmonary pleura, mediastinum and chest. Often these diseases are specifically related to cancer. Here included operative procedures, in accordance with the project plan, were pulmonary lobectomy, lung segmentectomy and mediastinal surgery[26].

[26] Pleurectomy and pleurla/pulmonary decortication were recommended to be excluded from PICO by manufacturer and by external clinical expert

Surgical procedures for ***visceral (abdominal) surgery*** are related to surgery of the intestinal system (gastroenterological surgery), the oesophagus, stomach, small and large intestine, spleen, liver and gall bladder system. Here included operative procedures, in accordance with the project plan, were anti-reflux surgery/fundoplication, oesophagectomy or oesophageal repair, heller myotomy, gastrectomy, bariatric surgery, small bowel resection, colectomy, rectal resection, cholecystectomy, liver resection/hepatectomy and hernia repair[27].

As defined in the project proposal, diseases and diagnoses for which thoracic surgery was considered appropriate included lung neoplasms and neoplasms of the thymus, thorax and mediastinum. For visceral (abdominal) surgery underlying diseases or conditions for which surgical procedures could be deemed relevant included reflux disease, diseases and neoplasm of the oesophagus, swallowing disorders/achalasia, stomach neoplasms, obesity, neoplasms of the colon, rectum and anus, Crohn's disease, ulcerative colitis, rectal prolapse, cholecystitis, neoplasm of the gallbladder, liver and bile, and hernia.

Effects of the disease or health condition

[A0003] – What are the known risk factors for the diseases or health conditions treated by thoracic or visceral surgery?

[A0004] – What is the natural course of the diseases or health conditions treated by thoracic or visceral surgery?

[A0005] – What are the symptoms and the burden of disease or health condition for the patient?

[A0006] – What are the consequences of the disease or health condition for the society?

As stated above, visceral and thoracic surgery covers a variety of individual surgical procedures and is employed to treat a wide variety of conditions, both malignant disease and non-cancerous disease.

Lung & chest

Thoracic surgery (pulmonary lobectomy, lung segmentectomy and mediastinal surgery) is primarily used to treat non-small-cell-***lung cancer*** and small-cell lung cancer[28]. Primary lung cancer remains the most common malignancy after non-melanocytic skin cancer, and deaths from lung cancer exceed those from any other malignancy worldwide. The number of lung cancer-related deaths in Europe for 2017 was estimated to represent the leading cause of cancer deaths in both genders (24% in males and 15% in females) [45]. Non-small cell lung cancer (NSCLC) accounts for 80%–90% of lung cancers, while small cell lung cancer (SCLC) has been decreasing in frequency in many countries over the past two decades whilst around 70% of lung cancer is attributed to tobacco smoking [45]. Aside from lung cancer, conditions requiring thoracic surgery include tuberculosis (TB), lung abscess, emphysema, non-cancerous tumors, and fungal infections[29].

[27] Appendectomy was recommended to be excluded by the external expert whilst splenectomy/pancreatectomy was recommended to be excluded by both the external clinical expert and by the manufacturer

[28] https://www.nice.org.uk/guidance/cg121/chapter/1-Guidance#treatment

[29] https://www.uabmedicine.org/patient-care/treatments/lobectomy-lung-

Mediastinal tumors are benign or cancerous growths that form in the area of the chest that separates the lungs and are in general rare. Mediastinal tumors are usually diagnosed in patients aged 30 to 50 years and almost 40% of people who have mediastinal tumors experience no symptoms[30]. Most of the growths are often discovered on a chest x-ray that is performed for another reason[31]. Thymic epithelial tumours are the most frequent cause of anterior mediastinal mass, accounting for 35% of cases [46].

Oesphagus

Turning to visceral surgery, ***gastroesophageal reflux disease (GERD)*** is one of the most frequent benign disorders of the upper gastrointestinal tract. Gastroesophageal reflux disease can be defined as troublesome symptoms that are sufficient to impair an individual's quality of life that result from the retrograde flow of gastric contents into the esophagus, oropharynx, and/or respiratory tract [47]. The two most frequently reported symptoms of GERD, heartburn or acid regurgitation, are reported by one out of five people on a weekly basis and two out of five people experience heartburn or acid regurgitation at least once a month[32]. Barrett's esophagus (BE) refers to the endoscopic presence, confirmed histologically, of columnar-lined esophagus. This is currently the only identifiable complication of GERD that is known to have malignant potential.

Oesophageal cancer has two main subtypes – oesophageal squamous cell carcinoma – which accounts for the vast majority of cases, and oesophageal adenocarcinoma. Oesophageal carcinoma is rare in young people and increases in incidence with age; main risk factors for oesophageal squamous cell carcinoma in Western countries are smoking and alcohol consumption, whereas the rarer subtype predominantly occurs in patients with chronic gastro-oesophageal reflux disease and their risk is correlated with the patient's body mass index with a higher risk among obese persons [48].

Perforation of the oesophagus results in significant morbidity and potential mortality, depending on the cause and location of the injury, as well as time to diagnosis and treatment. It can have instrumental causes such as endoscopy and non-instrumental causes such as operative trauma [49].

Achalasia is a relatively rare oesophageal motor disorder with an estimated incidence of 0.7 to 1.6 per 100,000 inhabitants/year [50] whilst oesophageal cancer is the 19th most common cancer in the European Union (EU), with around 45 900 new cases diagnosed in 2012 [48].

Stomach

Almost one million new cases of ***gastric cancer*** were diagnosed globally in 2012; gastric cancer displays significant global variation in incidence with lower rates in North America and Western Europe [51]. Risk factors for gastric cancer include male gender, Helicobacter pylori infection, tobacco use, atrophic gastritis, partial gastrectomy and Ménétrier's disease [51]. Tumours of the proximal stomach (cardia) are associated with obesity, and tumours of the gastroesophageal junction are associated with reflux and Barrett's oesophagus and are more common in non-Asian countries [51].

[30] https://my.clevelandclinic.org/health/diseases/13792-mediastinal-tumor

[31] https://my.clevelandclinic.org/health/diseases/13792-mediastinal-tumor

[32] https://www.aboutgerd.org/prevalence.html

One-third of U.S. adults were considered obese in 2009–2010 (BMI ≥30 kg/m^2), with ***obesity*** being associated with an increased hazard ratio for allcause mortality, as well as significant medical and psychological comorbidity [52]. The prevalence of obesity has tripled since the 1980s in many countries of the WHO European Region with overweight and obesity thought to affect 50% of the population in many European countries [53].

Bowel/small and large intestine

The incidence of ***rectal cancer*** in the European Union is estimated at 125,000 per year, which corresponds to 35% of the total colorectal cancer incidence [54]. Risk factors for rectal cancer are high BMI, body or abdominal fatness, diabetes type II with longstanding ulcerative colitis and Crohn's disease. Excessive consumption of red or processed meat and tobacco as well as moderate/heavy alcohol act to increase the risk [54].

Colorectal cancer is the third most common tumour in men and the second in women, accounting for 10% of all tumour types worldwide, and is rare before 40 years of age (nearly 70% of patients with colon cancer are over 65 years of age) [54]. Mortality has declined progressively in many Western countries due to cancer screening programmes, removal of adenomas, early detection of cancerous lesions and the availability of more effective therapies for early stage disease [55]. Risk factors are lifestyle or behavioural factors (such as smoking, high red meat consumption, obesity, physical inactivity) and genetically determinant factors [55].

According to the American College of Gastroenterology, benign anorectal disorders include disorders of function such as defecation disorders, fecal incontinence, and proctalgia syndromes, whereas disorders of structure include rectal prolapse, anal fissure and hemorrhoids [56]. ***Rectal prolapse*** is a condition in which the rectum (the last part of the large intestine) loses the normal attachments that keep it fixed inside the body, allowing it to slide out through the anal opening[33]. Rectal prolapse affects mostly adults and women ages 50 and older have six times the risk as men. It is a condition that can be very embarrassing and impacts negatively quality of life[34].

Spleen, liver and gallbladder

Small stones can form in the gallbladder as a result of an imbalance in the substances that make up bile which occasionally block the flow of bile and irritate the gallbladder (acute cholecystitis) or pancreas (acute pancreatitis). This can cause symptoms such as sudden and intense abdominal pain, nausea and jaundice[35], however most people with ***gallstone disease*** have asymptomatic gallbladder stones and the disease – if diagnosed– is often identified as a result of investigations for other conditions [57]. In Europe about 10% of all adults have gallstones, with women having 3 times the prevalence of men during the fertile period; the prevalence rises with age in both sexes [58].

Liver cancer (or hepatocellular carcinoma) was the fifth most common cancer in men and the ninth in women, and the second most common cause of cancer-related death worldwide in 2012 [59]. In Europe, the estimated incidence rate in 2012 was 10 in men and 3.3 in women per 100,000 [59]. The incidence of HCC shows a strong male preponderance and increases progressively with advancing age in all populations; risk factors include obesity, type 2 diabetes and alcohol consumption [59].

[33] https://www.fascrs.org/patients/disease-condition/rectal-prolapse-0

[34] https://www.fascrs.org/patients/disease-condition/rectal-prolapse-0

[35] https://www.nhs.uk/conditions/gallbladder-removal/

The lifetime occurrence of ***hernia*** (viscera or adipose tissue protrusions through the inguinal or femoral canal) is reported to be 27–43% in men and 3–6% in women; inguinal hernias are almost always symptomatic and the only cure is surgery [60]. Risk factors include inheritance, abnormal collagen metabolism, male gender, age, previous prostatectomy and low BMI [60].

Target population

[A0007] – What is the target population of this assessment?

The target population in question is patients requiring surgery for a number of different thoracic and visceral conditions.

[A0023] – How many people belong to the target population?

This question is not answered as several different surgical procedures are included in the HTA covering many different target populations, as described earlier in this chapter. However some information on epidemiology is provided in the preceding section.

Current clinical diagnosis and management of the disease or health condition

[A0024] – How is the disease or health condition currently diagnosed according to published guidelines and in practice?

[A0025] – How is the disease or health condition currently managed according to published guidelines and in practice?

Lung & chest

Starting with the main indication for thoracic surgery, which is ***lung cancer***, symptoms for this disease occur late in the stage of the disease, so the majority of patients with lung cancer present with advanced disease. The cornerstone of treatment of potentially resectable lung cancer is surgical removal of the tumour. Whether surgery should be done through standard open thoracotomy, or a video-assisted thoracoscopic surgery (VATS) procedure, is probably less important from an oncological perspective, according to the European Society for Medical Oncology [55], since comparative margin clearance and nodal dissection can be achieved with both methods. This organisation recommends surgery is offered to all patients with stage I and II NSCLC, and specifically that VATS should be the approach of choice in stage 1 tumours. However this recommendation only has a grading of V (evidence from studies without control group, case reports, expert opinions) and C (Insufficient evidence for efficacy). The guideline makes no mention of whether robotic approaches to VATS should be considered [55]. The NCCN guideline recommends that VATS or minimally invasive surgery (including robot-assisted approaches) should be strongly considered in patients suitable for surgery, however this guideline notes that robotic VATS seems to be more expensive and associated with longer operating times than conventional VATS [61].

The treatment used for ***mediastinal tumors*** depends on the type of tumor and its location with thymic cancers and neurogentic tumors treated surgically[36]. There is no recognised clinical staging system and the treatment strategy depends on whether it is possible to resect the tumour upfront or not [46]. Minimally invasive surgery, including robotic approaches, is considered to be an option for presumed stage I and possibly stage II tumours, assuming appropriately trained thoracic surgeons are available; evidence level IV (retrospective cohort studies or case-control studies); grade of recommendation C (insufficient evidence for efficacy) [46]. The European Society of Medical Oncology considers robotic surgery might allow a better visualisation of the tumour when compared to VATS although no recommendation level is provided [46].

Oesphagus

Turning to visceral surgery, one of the main indications for non-cancer surgery relates to antireflux surgery for an oesophageal ***GERD syndrome***. This is recommended where a patient is intolerant of acid suppressive therapy (grade A recommendation) as well as those with persistent, troublesome symptoms despite PPI therapy (grade B recommendation). For those with an *extra*oesophageal GERD syndrome and persistent, troublesome symptoms despite PPI therapy, the balance of benefits and harms is however too close to justify a general recommendation. Generally, patients who are well maintained on medical therapy should not be recommended for surgery [62]. At the European level, the European Association of Endoscopic Surgery considers laparoscopic fundoplication as one of the most successful surgical operations for GERD [63] although the World Gastrological Organisation considers surgical intervention (usually fundoplication) to be rarely indicated in GERD patients [47]. None of these guidelines mention the use of robot-assisted approaches to laparoscopy.

According to the Society of American Gastrointestinal and Endoscopic Surgeons Guidelines for the Surgical Treatment of Esophageal ***Achalasia*** [64], laparoscopic Heller myotomy with partial fundoplication provides superior and longer-lasting symptom relief with low morbidity for patients with achalasia compared with other treatment modalities and should be considered the procedure of choice to treat achalasia (high quality of evidence ++++; strong recommendation). This US guideline specifically mentions robotic assistance which it considers has been demonstrated to decrease the rate of intraoperative esophageal mucosal perforations (low quality of evidence ++; weak recommendation), although it states that there are no clear described differences in postoperative morbidity, symptom relief, or long-term outcomes between robotic and conventional laparoscopic techniques [64].

Surgery is the treatment of choice in limited ***oesophageal cancer*** (where local or locoregional disease only is present). This can take the form of endoscopic resection or oesophagectomy, depending on the stage of disease and risk criteria [48]. Oesophageal repair is necessary in cases of ***oesophageal perforation*** [49].

Stomach

Surgical resection of ***gastric cancer***, specifically at early stages, is potentially curative with the extent of resection necessary determined by the preoperative stage [51]. For stage IB–III gastric cancer, radical gastrectomy is indicated. Laparoscopic surgery is becoming one of the recommended options for patients with early gastric cancer; however, it remains to be shown whether laparoscopic surgery can achieve the same results as open surgery in gastric cancers requiring D2 lymphadenectomy [51].

[36] https://my.clevelandclinic.org/health/diseases/13792-mediastinal-tumor/management-and-treatment

Bariatric surgery has proven to be the most effective mode of treatment for morbidly ***obese*** patients. It is reported that recent long-term studies provide evidence of a substantial reduction in mortality among bariatric surgery patients, as well as a decreased risk of developing new health-related co-morbidities, together with decreased health care utilization and a drop in direct health care costs [53]. Patients are indicatd for bariatric surgery if they are 18 to 60 years old with BMI ≥ 40 kg/m 2 or with BMI 35–40 kg/m 2 with co-morbidities and should have failed to lose weight or to maintain long-term weight loss, despite appropriate surgical and/or non-surgical comprehensive medical care [53]. Standard bariatric and metabolic procedures include adjustable gastric banding, sleeve gastrectomy, Roux-en-Y gastric bypass, biliopancreatic diversion and duodenal switch [53]. The European guideline recommends that a laparoscopic technique should be considered as the preferable approach to the operation in bariatric surgery, providing no contraindications for the laparoscopic approach are present. However robot-assisted approaches are not mentioned by this guideline [53]. The U.S. guideline concurs that in general, laparoscopic bariatric procedures are preferred over open bariatric procedures due to lower early postoperative morbidity and mortality but again makes no specific mention of robot-assisted techniques [52].

Bowel/small and large intestine

A variety of surgical approaches, depending on the location and extent of disease, are used to treat primary ***rectal cancer*** lesions, both local procedures, such as transanal endoscopic microsurgery, and more invasive procedures involving a transabdominal resection e.g. low anterior resection or radical total mesorectal excision [65]. According to the NCCN guideline, conflicting results have been documented regarding open surgery versus laparoscopic techniques but the guidelines note that studies comparing conventional laparoscopic resection with robot-assisted resection have generally seen comparable results [65]. The NCCN Guidelines Panel defined principles by which minimally invasive resection of rectal cancer can be considered: the procedure can be considered by an experienced surgeon, should include thorough abdominal exploration, and should be limited to lower-risk tumors [65]. The European guideline notes that robot-assisted rectal cancer surgery provides some technical advantages for surgeons compared with conventional laparoscopy, but is still under evaluation [54].

Non-metastatic ***colon cancer*** is generally treated with curative intent by colectomy [65] where the goal of surgery is a wide resection of the involved segment of bowel together with the removal of its lymphatic drainage. The laparoscopic approach has now received wide acceptance for several types of surgical procedures in major abdominal surgery and laparoscopic colectomy can be safely carried out for colon cancer, particularly for left-sided cancer laparoscopic approach [55]. However the European guideline states that the laparoscopic approach should only be carried out if, amongst other criteria, technically experienced surgeons are available [55].

Surgery should be considered for clinically significant structural abnormalities for example, ***rectal prolapse*** or large rectocele [56].

Spleen, liver and gallbladder

It is difficult to agree which symptoms are specifically biliary and therefore will be cured by cholecystectomy; where there are no symptoms at all, cholecystectomy confirms no benefit in patients with asymptomatic ***gallstones*** [57]and even in patients with one attack of uncomplicated gallstone pain [58]. NICE advises offering early laparoscopic cholecystectomy (to be carried out within 1 week of diagnosis) to people with acute cholecystitis and to reconsider laparoscopic cholecystectomy for people who have had percutaneous cholecystostomy once they are well enough for surgery [57]. Robot-assisted techniques are not mentioned.

Liver resection (also referred to as hepatectomy) is the surgical removal of all or a portion of the liver and is one of the potentially curative modalities for patients with ***HCC***, particularly in patients with single tumours and well-preserved liver function [59]. Compared with open liver resection, laparoscopic liver resection shows advantages regarding blood loss and faster postoperative recovery and is recommended for liver resection in cirrhosis; robot-assisted techniques are not mentioned [59].

Worldwide, inguinal ***hernia*** repair is one of the most common surgeries, performed on more than 20 million people annually [60]. Surgical treatment is successful in the majority of cases, but recurrences necessitate reoperations in 10–15% and long-term disability due to chronic pain occurs in 10–12% of patients [60]. Many different repair methods are available, including non-mesh techniques, open mesh techniques and endoscopic techniques (the latter includes robotic repair techniques), which makes the choice of technique challenging [60]. Provided that resources and expertise are available, laparo-endoscopic techniques have faster recovery times, lower chronic pain risk and are cost-effective but their use requires the availability of an experienced surgeon [60].

[A0011] – How much are the technologies utilized?[37]

A Belgian HTA into the clinical effectiveness and potential benefit of the currently marketed robotic surgical systems reported that at least 20 robotic surgical systems were in use in Belgium and that compared to the rest of the world, Belgium had the second highest number of robotic surgical systems per capita, after the US [66].

According to a U.S. HTA, as of the first quarter of 2012, 37 da Vinci Surgical Systems had been installed in the State of Washington [67].

The manufacturer of the da Vinci® surgical system reports that since the year 2007, more than 5 million minimally invasive procedures have been performed in the U.S. (where it is used in all 50 states) and 66 countries worldwide. The system is used in over 4,400 hospitals worldwide and there are more than 43,000 da Vinci trained surgeons[38].

As of October 2017, TransEnterix reported to have installed seven Senhance systems in five countries (presumably in Europe) where surgeons continue to gather clinical data, with a goal of expanding FDA-cleared indications in the United States in coming years. In August 2017, the company established its first Senhance training and surgical innovation center in the United States at Florida Hospital (Orlando, FL, USA) to train U.S. surgical teams on its robotic technology [41].

[37] No information could be found regarding the Surgica Robotica (Surgenius) system

[38] https://www.intuitive.com/

5 CLINICAL EFFECTIVENESS (EFF)

5.1 Research questions

Element ID	Research question
D0001	What is the expected beneficial effect of robot-assisted surgery on mortality/survival?
D0005	How does robot-assisted surgery affect symptoms and findings (severity, frequency) of the disease or health condition?
D0006	How does robot-assisted surgery affect progression (or recurrence) of the disease or health condition?
D0011	What is the effect of robot-assisted surgery on patients' bodily functions?
D0012	What is the effect of robot-assisted surgery on generic health-related quality of life?
D0013	What is the effect of robot-assisted surgery on disease-specific health-related quality of life?
D0016	How does the use of robot-assisted surgery affect activities of daily living?
D0017	Were patients satisfied with robot-assisted surgery?

5.2 Results

The inclusion criteria for assessing the clinical effectiveness of robot-assisted surgery were initially restricted to RCTs with more than or equal than 10 patients or – in the absence of these – non-randomised prospective studies with control groups of more than or equal to 10 patients. The characteristics of all included studies can be found in Appendix 1. The systematic literature search did not identify any RCTs relating to thoracic surgery hence non-randomised controlled studies (3 for lobectomy/segmentectomy and 1 for mediastinal surgery) were included as the next best evidence level.

Regarding visceral surgery, and specifically surgery in the area of the oesophagus, 5 RCTs (6 publications) were identified relating to the procedure antireflux/fundoplication and oesphagectomy. For Heller myotomy no RCTs were found, hence non-randomised, controlled studies were included (two in total).

Three RCTS were included relating to stomach surgery (2 for gastrectomy and 1 for bariatric surgery) and 7 RCTs were identified relating to bowel procedures (specifically 1 RCT for colectomy, 1 RCT for rectopexy and 5 RCTs for rectal resection). Lastly in the area of gallbladder/liver/spleen, 4 RCTS were included for the cholecystectomy procedure whilst for liver resection and hernia repair, no RCTS could be identified thus non-randomised, controlled studies were included (2 for liver resection and 1 for hernia repair).

All the RCTS identified in the systematic literature search reported on effectiveness, with the exception of one [1]. The robotic procedure in most of the cases involved the da Vinci Surgical System. In all but three studies, the comparison was laparoscopic surgery. In the oesphagectomy study [15], one gastrectomy study [17] and the mediastinal surgery study [32], the comparison was with open surgery.

Seven procedures (lobectomy, mediastinal mass resection, gastrectomy, colectomy, rectal resection, liver resection/hepatectomy and oesophagectomy) related to patients undergoing surgical treatment for cancer.

Lobectomy/segmentectomy for lung cancer: here 100 patients underwent robot-assisted surgery in the intervention group and 115 patients underwent videothoracoscopy procedures in the control group across the 3 non-randomised, controlled studies [29], [30], [31]. Median age across the 3 studies was 62 in the IG and 64 in the CG whilst 46% and 42% were female in the IG and CG respectively. For mediastinal mass resection for lung cancer, 1 non-randomised, controlled study was found [32]. The intervention and control groups in this study differed in median age and sex distribution, although this was not statistically significant. The gastrectomy procedure for patients with gastric cancer was assessed in 2 RCTs [16], [17] with a total of 255 patients in the IG and 219 in the CG. These 2 studies differed in the control procedure: Pan et al [16] used a laparoscopic procedure as control, whereas Wang et al [17] used an open gastrectomy procedure, therefore the patient data was not pooled. One RCT was identified for oesophagectomy for patients with oesophageal cancer [15] with a total of 109 patients (IG 54; CG 55) and with a mean age of 64 in the IG and 65 in the CG. A lower proportion of patients in the IG was female compared to the CG (15% vs. 24%); the difference was not subjected to statistical testing. Colectomy for colonic carcinoma was assessed in one study [19] with 35 in the robot-assisted group and 36 in the laparoscopically assisted colectomy group. Two non-randomised controlled trials were identified for liver resection/hepatectomy [35], [36] with a combined patient pool of 104 in the robot-assisted group and 58 in the control group. Both studies included patients with malignant lesions although in one study a large proportion of patients had colorectal metastases [35]. Across both studies median age in the IG was 64 vs. 62 in the CG and the proportion of women was similar in each arm (40% IG, 39% CG). Lastly robot – assisted rectal resection for rectal adenocarcinoma was assessed in 5 studies for a total of 435 patients in the intervention group and 431 patients in the control group (undergoing laparoscopic rectal resection). Here the median age (across all studies) was 60.4 in the IG and 59.7 in the CG, with 32% female in both treatment allocation groups.

The other non-cancer related procedures (six) were antireflux/fundoplication, Heller myotomy, cholecystectomy, bariatric surgery, ventral mesh rectopexy and hernia repair.

Across the 4 antireflux/fundoplication RCTs there were a total of 79 patients in the robot-assisted intervention group and 81 in the control group (laparosopic fundoplication). The median age across these studies was 46 in the IG and 49 in the CG with 31.5% females in the IG and 32.5% in the CG. Two controlled (non-randomised) studies were identified for Heller myotomy with a total of 37 patients with achalasia in the IG and 55 patients with achalasia in the CG. In Huffmanm et al (2007) [33] 58% and 38% of patients in the IG and CG respectively were female (the other study did not report on sex characteristics); both intervention and control procedures in this study also included a partial fundoplication, in addition to the Heller myotomy (these procedures were nevertheless combined in the summary of findings). Median age in Sanchez et al (2012) [34] was 38 in the IG and 40.7 in the CG (Huffmanm only reports a very wide age range).

Four studies were available for cholecystectomy for gallbladder disease for a total of 163 patients in the robot-assisted cholecystectomy (intervention) group and 134 in the laparoscopic cholecystectomy (control) group, although one study used single-port laparoscopic cholecystectomy as control and was therefore analysed separately from the others in the Summary of Findings table [28]. The median age across available studies (Pietrabissa et al, 2016, did not report age and sex characteristics and so was excluded from the pooling) was 46.8 in the IG and 51.5 in the CG. Overall in the cholecystectomy studies, 78% of patients were female in the IG; the corresponding figure for the CG was 80. In 3 studies patients had gallbladder disease and in 1 study patients had

cholecystolithiasis. For bariatric surgery, 1 RCT was available with 25 participants in the robot-assisted gastric bypass (intervention) group and 25 participants in the laparoscopic gastric bypass (control) group. One non-randomised controlled study looked at robot-assisted hernia repair with 16 participants in both intervention and control (conventional single-port inguinal hernia repair) groups. The patients (aged 46 in IG; aged 48 in CG; sex unknown) were followed up for 6 months and assessed on satisfaction, complications and perioperative outcomes/resource use. Lastly 1 RCT was included that assessed robot-assisted ventral mesh rectopexy for rectal prolapse and intussusception with 16 women in the IG group and 14 women in the laparoscopic ventral mesh rectopexy (control) group.

The critical outcomes to evaluate were effectiveness, safety and perioperative outcomes however since the included studies related to different disease areas with often different endpoints, the effectiveness of robot-assisted surgery was considered for each operative procedure separately. The summary of findings (GRADE) relating to effectiveness (mortality, morbidity/quality of life and recurrence) for the individual surgical procedures can be found at the end of this chapter (Table 5).

Included studies

Thoracic surgery

Lobectomy

In the absence of any suitable RCTs, three non-randomised controlled comparisons of robot-assisted and conventional minimally invasive VATS (video-assisted thoracic surgery) were identified, which together included a total of 100 subjects in the intervention group and 115 subjects in the comparison group. All three studies focused on perioperative events as the main outcome, whereby Gonde et al, 2017 [30], focused specifically on the costs associated with both procedures (it should be noted that one of the co-authors of this paper undertook activities for Intuitive Surgical, Inc). The study by Augustin et al, 2013 [29], incorporated two types of robot-assisted lobectomy (both the posterior and anterior approach) and also in this study the intervention and control procedures were not conducted during the same time period (the latter point could also be observed by Rinieri et al [31]. In all three studies it is unclear how patients were assigned to the two groups; in one study [30], IG and CG were significantly different at baseline regarding sex and the presence of pulmonary comorbidities. The degree of surgeon's experience was not consistently reported across the studies. All 3 studies were assessed as having a moderate to critical risk of bias, depending on the outcome.

Mediastinal

No RCTs and only one non-randomised, controlled study [32] could be identified for mediastinal surgery which compared robot-assisted anterior mediastinal mass resection with open mediastinal mass resection by sternotomy. This is one of the relatively few studies that focused on quality of life using a standardised, valid instrument (although even here the authors note that the EORTC questionnaire has only been tested for validity and reliability among stage III and stage IV lung-cancer patients). The sample size was however small (total 36 participants) and the study was assessed as having a moderate to critical risk of bias, depending on the outcome considered

Visceral surgery

Oesophagus

Antireflux/fundoplication

Five publications on four RCTS for antireflux/fundoplication operations were included [10], [11], [12], [13], [14]. All studies were on patients with gastro-oesophageal reflux disease and all compared robot-assisted laparoscopic fundoplication with conventional laparoscopic fundoplication. In total there were 79 in the IG and 81 in the CG. Patients were followed up for a maximum of 6 to 22 months. Patient characteristics across studies were similar in terms of age; the Mueller-Stich et al study [13], [12] had a higher proportionally of female participants than the other studies. Two of the studies measured quality of life as an endpoint [10] [12], although quality of life was measured in different ways. Two studies focused on costs and perioperative events [11], [14].One study was assessed as having a low risk of bias at the study level [11]; the other 3 studies were assessed as having a potentially high risk of bias at the study level, principally due to missing information regarding study design.

Heller myotomy

Two non-randomised controlled studies were included [33], [34]. Both studies were on patients with achalasia but were different in that the intervention and control in one study included a partial fundoplication [33]. Both studies were small (61 and 31 participants) and followed patients up for at least 6 months. Both studies measured QoL/morbidity: Huffman et al with the SF-36 whilst Sanchez et al 2012 looked at relief of symptoms. Intraoperative complications were assessed in both studies, as were perioperative events/resource use. Huffman was assessed as having a critical risk of bias on both the health-related QoL outcomes and the safety & perioperative events whilst Sanchez 2012 was also rated as critical for QoL outcome but slightly better (serious risk of bias) on the safety & perioperative outcome.

Oesophagectomy

One relevant RCT was identified [15] which was conducted in the Netherlands with a total sample size of 109 and compared robotic thoracolaparoscopic oesophagectomy with open transthoracic oesophagectomy. Median follow up was for 40 months and the main endpoints related to complications (primary endpoint) as well as mortality and quality of life. Patient characteristics were reasonably similar although there was a higher proportion of women in the control group (25% vs. 15%), significance testing not reported. The risk of bias at the study level was assessed as low.

Stomach

Gastrectomy

The two RCTS assessing robotic gastrectomy used different comparisons: one used laparoscopic gastrectomy as the comparison [16] whilst the other used open gastrectomy [17]; for this reason the outcomes were not combined in the summary of findings table. Both studies included over 200 patients and included patients with gastric cancer. Perioperative outcomes and postoperative complications were the focus of both studies. Both studies failed to report on study design and for this reason are considered to have a high risk of bias.

Bariatric surgery

1 RCT was identified [18] which compared robotic laparoscopic Roux-en-Y with laparoscopic Roux-en-Y gastric bypass in a total of 50 patients (25 in each group) with a focus on safety and resource use. This study poses a high risk of bias at the study level as there is unclear information on allocation and blinding, and no sample size calculations were performed.

Bowel

Colectomy

Park et al [19] was the only RCT to consider a robot-assisted colectomy procedure versus laparoscopic colectomy in a study sample of 71 patients with newly diagnosed right-sided colonic carcinoma. Perioperative events and resource use were the main endpoints, alongside completeness of tumour excision. This study has a high risk of bias since there is insufficient information on many key aspects of the study and the possibility of selective reporting exists (pain score at 72 hours was not reported).

Rectal resection

Five RCTs [20], [21], [22], [24], [23] compared robot-assisted laparoscopic rectal resection with laparoscopic rectal resection for patients with rectal carcinoma. Jayne et al [20] reported on the ROLARR clinical trial, which was a multicentre RCT conducted in 10 countries with a total sample size of 471 randomised particiapnts. Jayne et al [20] and Kim et al [21] (latter with a sample size available for analysis of 139 patients) had clinical endpoints as primary endpoints (rate of conversion to open surgery and completeness of total mesorectal excision respectively) but also considered QoL and complications whilst Tolstrup et al [22], with a total sample of 51, assessed postoperative pain and complications. The Tolstrup RCT appeared to be the Danish results of the ROLARR trial. Wang et al [23] also considered quality of life, focusing on a 12 month assessment of urinary and sexual functioning. Debakey et al [24] reported on the results of a single-centre study in Egypt (45 patients) focussing on short-term operative and oncologic outcomes and complications. Three of the RCTs, Tolstrup et al [22] Debakey et al [24] and Wang et al [23] were assessed as having a high risk of bias at the study level.

Rectopexy

The RCT published by Mäkelä-Kaikonen et al [25] compared robot-assisted ventral mesh rectopexy with laparoscopic ventral mesh rectopexy in 28 female patients with rectal prolapse or intussception and looked at perioperative events, complications and pain. This study was judged to have a low risk of bias.

Gallbladder/liver/spleen

Cholecystectomy

Three RCTS compared robotic cholecystectomy with multiport or four-port laparoscopic robotic cholecystectomy [26] [27] [1], with a total sample size across the studies of 237 patients with a diagnosis of gallbladder disease. All RCTs measured perioperative events and quality of life and/or satisfaction. Kudsi et al [26] was classed as having a high risk of bias principally due to missing quality of life data, inconsistent reporting of blinding and a high proportion of inexperienced surgeons. Pietrabissa al [27] was judged to have a low level of bias at the study level. We inferred that another RCT, Ruurda et al [1], compared robotic cholecystectomy with multi-port laparoscopy (although not

clearly stated in the publication); here the focus was on procedure time and the study was assessed as having a high risk of bias. Grochola et al [28] compared robotic cholecystectomy with single-port laparoscopic cholecystectomy in a small trial in Switzerland focusing on surgeon's physical and mental stress load, but with secondary outcomes relevant to this HTA. This study as a whole was assessed as having a low risk of bias but the risk of bias associated with the QoL outcome was high.

Liver resection

Two non-randomised controlled studies (one conducted in the USA and one in China) were available for analysis [36] [35]. The exact robotic system used is not stated in Berber et al [35]. In both studies the control group was operated on usin reported to be laparoscopy (this was the control in both studies). Both studies report on survival and recurrence, as well as safety and perioperative outcomes. Follow-up was relatively long (mean 14 months in 1 study and 26 or 62 months, depending on allocation group, in the other). Lai and Tang [36] performed a partial hepatectomy whilst Berber et al [35] performed a liver tumour resection. As assessed with the ROBINS-I both studies have critical risk of bias.

Hernia repair

Tran [37] was a small, single-centre, non-randomised, controlled, Australian study comparing the Robotic Freehand with laparoscopic hernia repair, focussing on patient satisfaction, safety-related outcomes and resource use (length of operation). As assessed with the ROBINS-I it has a critical risk of bias.

The detailed extraction tables and risk of bias tables per study can be found in the Appendix 1.

Mortality

[D0001] – What is the expected beneficial effect of the technology on mortality/survival?

Thoracic surgery

Lobectomy

Three observational studies considered mortality [29], [30], [31]. Results were either non-significant or – where the control group had a marginally lower survival rate – there was no statistical testing performed [30], [31].

Mediastinal

100% intraoperative survival was reported in both groups [32]. At the outcome level this study was assessed to have a critical risk of bias.

Visceral surgery

Oesophagus

Antireflux/fundoplication: None of the RCTs assessed mortality.

Heller myotomy: Not reported by the studies.

Oesophagectomy

Van der Sluis et al [15] did not find any statistically significant differences between the intervention and control groups regarding in-hospital mortality, 30-day, 60-day or 90-day mortality. Disease-free survival was a median of 26 months in the IG and 28 months in the CG (not statistically significant).

Stomach

Gastrectomy

Both gastrectomy RCTs (both with the open gastrectomy and the laparoscopic gastrectomy comparisons) reported 100% survival. Both RCTS were assessed as having a high risk of bias at the outcome level due to insufficient information and a high risk of bias at the study level.

Bariatric surgery: Mortality was not assessed.

Bowel

Colectomy

Parks et al [19] reported on a 30-day survival rate of 100% in both groups: this study has a high risk of bias.

Rectal resection

Three RCTs reported on survival [20], [24], [23]. In Jayne et al [20] 30-day mortality was similar in both groups (0.8% IG vs. 0.9% CG). This study was assessed as having a low risk of bias at the outcome level. The sample size in Debakey et al [24] was very small and the study was assessed as having a high risk of bias; in this study one patient died in the control group and none in the intervention group within the 1 month follow-up period. Wang et al [23] reported no deaths in either group at 30 days.

Rectopexy: Not reported.

Gallbladder/liver/spleen

Cholecystectomy: None of the studies reported on mortality.

Liver resection

In one study survival data was only presented in graphs [35] but it is reported that disease-free survival at 14 months was equivalent in both groups (p=ns). Numerical data is reported by Lai and Tang [36] which shows 0% mortality in both groups at 90 days but differences between groups in 5-year survival (overall: IG 65% vs CG 48% and disease-free: IG 42% vs. CG 38%), but these were not reported to be statistically significant. Both studies were classed as having a critical risk of bias.

Hernia repair: Not reported.

Morbidity

[D0005] – How does the technology affect symptoms and findings (severity, frequency) of the disease or health condition?

Thoracic surgery

Lobectomy: Symptoms were not assessed in these observational studies.

Mediastinal

As reported by Balduyck et al [32] both procedures (robot-assisted and sternotomy) resulted in increased thoracic pain at 1 month; this persisted only in the sternotomy group at the 3 month point. Sternotomy but not robot-assisted surgery was associated with increased fatigue at 1 month after surgery ($p<0.01$). The robot-assisted group showed an increase in shoulder pain/dysfunction at 3 months, which was not observed in the sternotomy group ($p<0.05$). The open surgery group showed deterioration on 5 out of 10 QoL/symptom subscales at 1 month; in the robot-assisted surgery group there is deterioration in only 1 out of 10 subscales. At the outcome level this study was assessed as having a medium risk of bias.

Visceral surgery

Oesophagus

Antireflux/fundoplication

All four RCTs considered symptoms, albeit using different measurement instruments. Draaisma et al [10] found no significant difference between the groups in self-rated change in reflux state compared with the preoperative state; Morino et al [11] failed to detect a difference in symptoms or oesophagitis between the groups using the Gastro-oesphageal Reflux Health-Related Quality of Life scale; Mueller-Stich et al [13] [12] found no significant difference in reflux syndrome measured by the GSRS instrument at 12 months after surgery (this was the only RCT judged to have a low risk of bias at the outcome level); in Nakadi et al [14] symptoms occurred in a similar proportion in both groups after 1 month (in approximately one-third of patients), persisted at 3 months in the IG group and were relatively similar in both groups at 12 months after surgery (IG 1/19 vs CG 2/11), however no statistical testing was performed.

Heller myotomy

Symptoms were measured in Sanchez et al [34]. At 18 months 100% of patients reported relief of symptoms in the IG whilst 94.5% reported relief of symptoms at 18 months in the CG (not statistically significant). No information was given on how symptom relief was assessed. In Huffman et al [33], both groups reported statistically significant improvements in the GERD activity index (GRACI) at 6 days postoperatively (although no exact results were reported).

Oesophagectomy

Postoperative pain at 14 days was significantly lower in the intervention group, as measured by the VAS [15].

Stomach

Gastrectomy

Pan et al [16] reported significantly lower VAS pain scores in the intervention group for up to 3 days postoperatively (high risk of bias at the outcome level); this outcome was not considered in the study by Wang et al [17].

Bariatric surgery: No results.

Bowel

Colectomy

Park et al [19] reported non-significant results on the VAS assessment for pain (high risk of bias).

Rectal resection

Non-significant differences were reported on the prostate symptom score [20]; this study has a low risk of bias at the outcome level. Significant differences between treatment groups on the same prostate symptom score were reported in another study (with the robotic surgery group scoring better than the laparoscopically treated group) however this study has a high risk of bias [23]. Non-significant differences on pain were reported by Kim et al, [21] although this study has a high risk of bias at the outcome level. Tolstrup et al [22] similarly reported non-significant differences on pain (using the numerical rating scale).

Rectopexy

Mäkelä-Kaikonen [25] [68] (high level of bias at the outcome level) reported non-significant differences in mean pain scores via the VAS at 2 weeks and no differences in symptom scores (exact results are not provided).

Gallbladder/liver/spleen

Cholecystectomy

Pietrabissa et al [27] reported non-significant findings on the VAS pain measurement (low risk of bias).

Liver resection: Not reported.

Hernia repair: Not reported.

[D0006] – How does the technology affect progression (or recurrence) of the disease or health condition?

Information on recurrence was only available for mediastinal surgery, antireflux/fundoplication and liver resection/hepatectomy.

In the RCT by Draaisma et al [10] on antireflux/fundoplication there was a 12% recurrence of hiatal hernia in the CG and 4% recurrence in the IG; statistical significance testing was not reported and there is a high risk of bias at the outcome level. In the observational study by Balduyck et al

[32], recurrence occurred in 1/22 patients in the control group and none in the intervention group, which was reported as non-statistically significant (low to medium risk of bias).

The positive surgical margin clinical outcome is relevant for all of the cancer-related procedures, however the three non-randomised, controlled studies for lobectomy did not report data on this outcome (although Rinieri et al [31] stated that all patients undergoing cancer surgery had tumour-free margins); neither was information on this outcome available on the mediastinal surgery study [32] or the liver resection/hepatectomy studies [35], [36]. This outcome was however reported for the colectomy procedure [19] where there was a non-significant difference using the proximal margin and distal margin outcomes. In the rectal resection studies, Jayne et al [20] reported a non-significant difference on circumferential resection margin positivity between groups and Kim et al [21] also reported non-significant differences on this measure as well as on comparisons of proximal and distal resection margins between groups. Tolstrup et al [22] and Wang et al [23] did not report results on this outcome. Lastly this is a relevant outcome for the gastrectomy procedures for gastric cancers and Wang et al [17] provided results on this outcome: non-statistically significant results for proximal resection margins and distal resection margins were reported between the intervention and control groups.

Recurrence occurred in slightly fewer patients in the IG compared to the CG (22% vs. 26% at a mean of 14 months) but the difference was not statistically significant [35]. Elsewhere the difference was more considerable (IG 34% vs. CG 63% after a mean follow-up of 26 months in the IG and 62 months in the CG) but this study did not report statistical testing and the difference is likely to be attributed to the much later mean follow-up in the control group [36]. Recurrence occurred in one patient in the CG but it was not statistically significant (23).

[D0011] – What is the effect of the technology on patients' body functions?

[D0016] – How does the use of technology affect activities of daily living?

These two questions are answered in the next chapter together with quality of life outcomes.

Health-related quality of life

[D0012] – What is the effect of the technology on generic health-related quality of life and

[D0013] – What is the effect of the technology on disease-specific quality of life?

Thoracic surgery

Lobectomy: Not reported.

Mediastinal

Functioning deteriorated (statistically significant) in the CG at 1 month (but not thereafter); no deterioration was observed in the IG (medium risk of bias in this non-randomised, controlled study), [32].

Visceral surgery

Oesophagus

Antireflux/fundoplication

One study reported no significant differences in general quality of life at 6 months between the groups [10], neither were there any significant differences between groups at 12 months after surgery as measured by the QOLRAD, a disease-specific QOL instrument [12] [13]. No pooling was possible as different measuring systems and time periods were used.

Heller myotomy

All categories of the SF-36 showed statistically significant improvements in the pre-op vs. post-op comparison but there were no data on between group comparisons [33].

Oesophagectomy

As measured by the QLQ-C30, the robot-assisted surgery group reported statistically significantly better overall health-related quality of life and physical functioning both at discharge and at 6 weeks [15]. A statistically significant higher proportion of patients in the intervention group reported functional recovery at 2 weeks: 70% vs. 51% [15].

Stomach

Gastrectomy

With the exception of pain (reported in morbidity, see question D0005 above), there was no reported data on patient-related outcomes.

Bariatric surgery: Not reported.

Bowel

Colectomy

With the exception of pain (reported in morbidity, see question D0005 above), there was no reported data on patient-related outcomes.

Rectal resection

Here 3 RCTs reported quality of life results however no pooling was possible as different measuring systems and time periods were used. Jayne et al [20] reported no statistically significant differences between the groups regarding erectile function or female sexual function at 6 months following surgery however Wang et al [23] reported a lower incidence of partial or complete erectile dysfunction post-operatively, compared to the laparoscopically treated group. Kim et al [21] reported no differences between groups after 3 weeks, 3 months or 12 months except for insomnia scores at 12 months (IG significantly more sleep disturbances) and sexual functioning at 12 months (IG showed significantly better functioning), using the Korean version of the QLQ-C30. Both Jayne et al [20] and Kim et al [21] show a low risk of bias at the outcome level.

Rectopexy

Mäkela-Kaikonen et al [25] (59) reported no significant differences for pain at 2 weeks in comparison with pre-surgery for all patients combined and QoL improvements 3 months post-surgery especially for symptoms and sexual function but there was no comparison between study arms. This study has a high risk of bias at the outcome level since data on between group comparisons were not presented for any of the measures (data on Pelvic Floor Impact Questionnaire and Prolapse/ Incontinence Sexual Questionnaire were missing).

Gallbladder/liver/spleen

Cholecystectomy

Kudsi et al [26] reported no statistically significant results using the SF-12 between the groups at 2 weeks, 6 weeks or 3 months. Grochola et al [28] similarly reported no statistically significant differences at 1 month and 12 months post-operatively on the Gastrointestinal Quality of Life Index. Both studies have a high risk of bias at the outcome level.

Liver resection: Not reported.

Hernia repair: Not reported.

Satisfaction

[D0017] – Were patients satisfied with the technology?

Thoracic surgery

None of the identified thoracic surgery non-randomised, controlled studies reported on patient satisfaction.

Visceral surgery

Oesophagus

Antireflux/fundoplication

Draaisma et al [10] reported higher satisfaction in the IG (92% vs. 88%), although this was not statistically significant and this study has a high risk of bias, both at study and outcome level. Mueller-Stich et al [12] reported no statistically significant differences between the groups regarding self-reported satisfaction with change in condition or satisfaction with operative result (low risk of bias at the outcome level, although high risk of bias overall at the study level).

Heller myotomy: Not reported.

Oesophagectomy: Not reported.

Stomach

Gastrectomy: Not reported.

Bariatric surgery: Not reported.

Bowel

Colectomy: Not reported.

Rectal resection: Not reported.

Rectopexy: Not reported.

Gallbladder/liver/spleen

Cholecystectomy

Kudsi et al [26] reported results for the BIQ (which measures satisfaction with body image) and the PSQ (relating to satisfaction with surgical scar) which showed statistically significant differences between the two groups in favour of robot-assisted surgery at 2 weeks and 3 months (but not at 6 weeks) whilst all PSQ results, at all 3 follow-up points, were statistically significantly better for the robot-assisted surgery group. Similarly, Pietrabissa et al [27] found that robot-assisted surgery conferred a statistically significant cosmetic advantage. However Grochola et al [28] reported no statistically significant differences at 1 month and 12 months post-operatively on the Body Image Questionnaire. Only Pietrabissa et al (18) was assessed as having a low risk of bias at the outcome level.

Liver resection: Not reported.

Hernia repair

The same proportion of patients were highly satisfied and satisfied in both intervention and control groups (88% highly satisfied; the rest were satisfied). As assessed with the ROBINS-I, this result is associated with a critical risk of bias [37].

Table 5: Summary of findings table regarding effectiveness for robot-assisted surgery in thoracic and visceral indications[39]

Thoracic Surgery

Robot-assisted lobectomy vs. VATS					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative mortality; in-hospital mortality	0 deaths in both arms of all studies except for Gonde et al in 1 arm (2 deaths in CG) and Rinieri et al in 1 arm (1 death in CG) Relative effect cannot be calculated as the study provides no information about the relative probability of the event (see Cochrane handbook 5-1, section 9.2.2.2)		164 (2 RCTs)	⊕◯◯◯ Very low	Differences in surgery performed and in group characteristics; no power calculations
Morbidity	Outcome not reported				

Robot-assisted mediastinal surgery vs. open mediastinal mass resection					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
In-hospital mortality	0 deaths in both arms Relative effect cannot be calculated as the study provides no information about the relative probability of the event (see Cochrane handbook 5-1, section 9.2.2.2)		36 (1 RCT)	⊕◯◯◯ Very low	unclear how group allocation operated, no information on tumour size, no sample size calculations
Morbidity	Less short-term deterioration in QoL and symptoms following surgery reported in robot-assisted group vs open surgery group		36 (1 RCT)	⊕◯◯◯ Very low	unclear which surgeons conducted surgery and with what type of experience, unclear how patients were assigned to treatment groups

[39] Relative risk calculations performed via https://www.medcalc.org/calc/relative_risk.php; absolute effect estimates obtained via from GradePro https://gdt.gradepro.org/app/#

Visceral surgery

Oesophagus

Robot-assisted laparoscopic fundoplication vs. laparoscopic fundoplication					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality	Outcome not reported				
Morbidity, quality of life	None of the studies reported significant differences on symptoms between the 2 approaches		160 (4 RCTs)	⊕◯◯◯ Very low	Different measurement instruments prevents pooling; 3/4 RCTS with high risk of bias at the outcome level

Robot-assisted Heller myotomy vs. laparoscopic Heller myotomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality	Outcome not reported				
Morbidity, quality of life	Statistically significant improvements in symptoms post-op vs. pre-op in both IG and CG groups on the SF-36 (no between group comparisons) and symptom relief at 6 days as measured on the GERD (GRACI) index in IG and CG. High level of symptom relief in both IG and CG groups at 18 months (non- statistically significant differences).		92 (2 non-randomised studies)	⊕◯◯◯ Very low	Lack of data on between group differences. Critical/serious risk of bias on ROBINS-I

Robot-assisted thoracolaparoscopic oesophagectomy compared to open transthoracic oesophagectomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality	In-hospital mortality: 19 more per 1,000 (from 15 fewer to 378 more) 30-day mortality: not estimable (0 events in CG) 60-day mortality: 37 more per 1,000 (from 12 fewer to 499 more) 90-day mortality: 74 more per 1,000 (from 7 fewer to 749 more)	RR 2.04 (0.19 to 21.81) - RR 3.06 (0.33 to 28.47) RR 5.09 (0.62 to 42.17)	109 (1 RCT)	⊕◯◯◯ Very low	Serious risk of bias; 95% confidence intervals around the absolute and relative effects includes the possibility of both increased postoperative complications and reduced postoperative complications

Robot-assisted thoracolaparoscopic oesophagectomy compared to open transthoracic oesophagectomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Morbidity, quality of life	On QLQ-C30 statistically significant better overall health-related QoL and physical functioning at discharge and at 6 weeks. Functional recovery @ 2 weeks: 70% in IG and 51% in CG (p<0.05)		109 (1 RCT)	⊕⊕⊕◯ Moderate	High risk of bias at the outcome level as study not powered to detect QoL differences

Stomach

Robot-assisted gastrectomy vs. laparoscopic gastrectomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality	Intraoperative: 0 deaths in both arms Relative effect cannot be calculated as the study provides no information about the relative probability of the event (see Cochrane handbook 5-1, section 9.2.2.2)		163 (1 RCT)	⊕◯◯◯ Very low	Relative and absolute rates cannot be calculated (no events); sample size likely to be too small for a reliable mortality estimate
Morbidity, quality of life	Significantly lower VAS scores for pain in IG vs. CG, post-operative days 1 to 3		163 (1 RCT)	⊕◯◯◯ Very low	Very serious risk of bias, and serious imprecision whilst inconsistency was not estimable

Robot-assisted gastrectomy vs. open gastrectomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality	Intraoperative: 0 deaths in both arms Relative effect cannot be calculated as the study provides no information about the relative probability of the event (see Cochrane handbook 5-1, section 9.2.2.2)		296 (1 RCT)	⊕◯◯◯ Very low	Relative and absolute rates cannot be calculated (no events); sample size likely to be too small for a reliable mortality estimate
Morbidity, quality of life	Outcome not reported				

Robot-assisted laparoscopic gastric bypass vs. laparoscopic gastric bypass					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality	Outcome not reported				
Morbidity, quality of life	Outcome not reported				

Bowel

Robot-assisted right colectomy vs. laparoscopic right colectomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality at 30 days	0 deaths in both groups Relative effect cannot be calculated as the study provides no information about the relative probability of the event (see Cochrane handbook 5-1, section 9.2.2.2)		70 (1 RCT)	⨁◯◯◯ Very low	
Morbidity, quality of life	non-significant results on the VAS assessment for pain		70 (1 RCT)	⨁◯◯◯ Very low	Insufficient information and selective reporting possible (missing data on pain score at 72 hours)

Robot-assisted laparoscopic rectal resection compared to laparoscopic rectal resection					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality within 30 days	3 fewer per 1,000 (from 8 fewer to 27 more)	RR 0.65 (0.11 to 3.87)	648 (3 RCTs)	⨁◯◯◯ Very low	95% confidence intervals around the absolute and relative effects includes the possibility of both increased postoperative complications and reduced postoperative complications; 2 studies had high risk of bias

Robot-assisted laparoscopic rectal resection compared to laparoscopic rectal resection					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Morbidity, quality of life	No statistically significant differences were reported in erectile function or female sexual function in the 2 studies with a low risk of bias, but significant differences in favour of robotic surgery in one study measuring erectile function with a high risk of bias. Some evidence that sexual functioning is significantly better in the IG although sleep disturbances at 12 months were significantly more prevalent in the IG. One study reporting better prostate symptom scores in the robotic surgery group (high risk of bias), which was not observed in the other study. No reported differences in pain.		742 (3 RCTs)	⨁⨁◯◯ Low	2 studies are assessed as having a low risk of bias; 1 study as having high risk of bias

Robot-assisted ventral mesh rectopexy vs. laparoscopic ventral mesh rectopexy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality	Outcome not reported				
Morbidity, quality of life	Mäkelä-Kaikonen reported non-significant differences in mean pain scores via the VAS at 2 weeks and no differences in symptom scores (data not given).		(1 RCT)	⨁◯◯◯ Very low	high level of bias at the outcome level; only 1 study so inconsistency cannot be assessed

Gallbladder/liver/spleen

Single-site laparoscopic robotic cholecystectomy vs. multiport laparoscopic cholecystecomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality	Outcome not reported				
Morbidity, quality of life	Non-statistically significant differences in quality of life (SF-12) at 2 weeks, 6 weeks and 3 months and in VAS (pain) at 24 h, 7 days and 30 days		196 (2 RCTs)	⨁◯◯◯ Very low	High risk of bias with the Kudi (2017) RCT that provided QoL assessment via SF-12

Single-site laparoscopic robotic cholecystectomy vs. single-incision laparoscopic cholecystecomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality	Outcome not reported				
Morbidity, quality of life	Non-statistically significant differences on Gastrointestinal Quality of Life Index and Body Image Questionnaire at 1 month and 12 months post-op		60 (1 RCT)	⊕◯◯◯ Very low	No power calculations performed; it is possible study is too small to detect QoL differences between the arms.

Robot-assisted liver resection/hepatectomy compared to laparoscopic liver resection/hepatectomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Recurrence	154 fewer per 1,000 (from 261 fewer to 5 fewer)	RR 0.68 (0.46 to 0.99)	162 (2 non-randomised, controlled studies)	⊕◯◯◯ Very low	Critical risk of bias for this outcome at the ROBINS-I: much longer follow up in CG (Lai and Tang 2016); little information on amount of surgical experience and type and approach of resection (Berber et al, 2010); no power calculations for this outcome

Robot-assisted hernia repair vs. laparoscopic single-port inguinal hernia repair					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Mortality	Outcome not reported				
Morbidity, quality of life	Outcome not reported				

6 SAFETY (SAF)

6.1 Research questions

Element ID	Research question
C0008	How safe is robot-assisted surgery in relation to open or laparoscopic/thoracoscopic surgery?
C0002	Are the harms related to dosage or frequency of applying robot-assisted surgery?
C0004	How does the frequency or severity of harms change over time or in different settings?
C0005	What are the susceptible patient groups that are more likely to be harmed through the use of robot-assisted surgery?
C0007	Is robot-assisted surgery associated with user-dependent harms?
B0010	What kind of data/records and/or registry is needed to monitor the use of the robot-assisted surgery?

6.2 Results

In accordance with the pre-defined HTA project protocol, the study inclusion criteria for assessing safety, as with the assessment of clinical effectiveness, defined RCTs with ≥10 patients as relevant for inclusion. In the absence of RCTs, the project plan permitted the inclusion of prospective, non-randomised controlled studies with ≥10 patients.

The critical outcomes used to evaluate the evidence were intraoperative complications, postoperative complications, re-operations/additional surgeries and conversion to laparoscopic/thoracoscopic or open surgery. Several of the studies reported complications using the Clavien-Dindo classification which allows comparison across studies. The results of studies reporting Clavien-Dindo complications are given in Table 6. The summary of findings (GRADE) tables relating to safety can be found at the end of this chapter. In the summary of findings table (Table 7), complications relate to the total number of all complications i.e. the analysis is not restricted to complications classified by Clavien-Dindo.

No specific questions regarding perioperative events and resource use were set in the project plan but the following indicators were defined: blood loss; operation time; transfusions. Subsequently, drain duration (days) and length of hospital stay (days) were also added as potentially relevant indicators. No specific study design was stipulated in the project plan hence the same pool of studies was used as in the EFF and SAF domains.

Included studies

The same study pool was used as in the effectiveness domain, in addition Ruurda et al was included [1]. In Table 6 the studies that presented complications according to the Clavien-Dindo classification[40] are summarised.

[40] https://www.baus.org.uk/patients/surgical_outcomes/grading_of_surgical_complications.aspx

Patient safety

[C0008] – How safe is robot-assisted surgery in relation to open or laparoscopic surgery?

Thoracic surgery

Lobectomy

The three non-randomised controlled studies for lobectomy all reported non-statistically significant differences in total postoperative complications however Gonde et al [30] reported a statistically significant difference in conversion to laparoscopic or open surgery, with conversion occurring more often in the control group (IG 2% vs. CG 16%, p<0.01) although this finding was not statistically significant in the other two studies [29], [31]. None of the studies reported on intraoperative complications and there was no relevant information on reoperations.

Augustin et al [29] reported significantly more blood loss in the robot-assisted surgery group and a significantly longer median operation time. There were non-significant differences in drain duration and length of stay but no relevant data on transfusions. Gonde et al [30] did not report on blood loss and found non-statistically significant differences in operation time, drain duration and length of stay between the groups. Rinieri et al [31] however found a statistically significant difference in blood loss between the groups, with the robot-assisted surgery group associated with significantly less blood loss (median 50ml compared with median 100ml in the CG); there were no statistically significant differences in operation time, drain duration or length of hospital stay. No information on transfusions was reported. None of these studies had a low risk of bias at the outcome level.

Mediastinal

This single non-randomised, controlled study for mediastinal surgery – using open surgery as the comparator – reported non-statistically significant differences between the groups regarding postoperative complications (IG 3/14 or 22% vs. CG 2/22 or 9%) [32]. Intraoperative complications did not occur in either group. Reoperations occurred more often in the CG (IG 0% vs. CG 2/22 or 9%) but conversion to laparoscopic/open surgery occurred in the IG but not CG (IG 1/14 or 7% vs CG 0). At the outcome level this study was assessed to have a medium risk of bias.

There were no statistically significant differences between groups in operation time or length of hospital stay according to Balduyck et al [32]. No other outcomes were reported. At the outcome level this study was assessed to have a medium risk of bias.

Visceral surgery

Oesophagus

Antireflux/fundoplication

There were no intraoperative complications reported in Morino et al [11] and this outcome was not reported in Nakadi et al [14]. Draaisma et al [10] reported minor intraoperative complications in 16% of the IG (4/25) und 28% of the CG (7/25); corresponding figures for the Mueller-Stich study [13] [12] were 5% (1/20) and 10% (2/20).

Postoperative complications were slightly less common in the IG than CG (0% vs. 8%) in the Draaisma [10] study (p=NR), but were not observed in either group in the Morino [11] study. In the

Mueller-Stich study (with a low risk of bias at the outcome level and the only study to subject postoperative complications to inferential statistical testing), there were no significant differences between the groups regarding minor postoperative complications and no major postoperative complications were observed in either groups [13], [12]. Nakadi et al [14] did not report on postoperative complications.

As to conversions to laparoscopic or open surgery, Draaisma et al [10] reported more conversions in the control group (0% vs 8%), while Morino et al [11] and Nakadi et al [14] reported more conversions in the intervention groups (4% vs. 0% and 11% vs. 0% respectively). In Mueller-Stich et al (2007) [12] no conversions were reported in either group. No statistical testing was performed on this outcome in these studies.

No significant differences in blood loss were observed by Draaisma [10]. This outcome was not reported in the other 3 RCTs. No significant difference in operation time was reported by Draaisma [10] however all the other studies did report statistically significant differences on this outcome; in 2 instances the operation time with robot-assisted surgery was significantly longer [14], [11] and in 1 RCT robot-assisted surgery was found to be associated with a shorter operation time [13] [12]. One of the studies reported on blood loss, but the difference between groups was not statistically significant (2). No statistically significant differences were found regarding overall length of stay. No information on transfusions or drain duration was reported. The strongest evidence is considered to come from Morino et al [11] which showed a low risk of bias at the study and outcome level.

Heller myotomy

Intraoperative complications were similar across groups in the Heller myotomy non-randomised controlled studies with 0 intraoperative complications in both intervention groups and 3/37 (8%) and 1/18 (5.5%) in the two control groups [33, 34]. One of the studies [34] reported that statistical testing showed non-significant differences; the other study did not report a p value (25). There were no conversions in the Sanchez et al study (25); this outcome was not reported in Huffman et al [33]. Neither study reported on postoperative complications.

Blood loss was reported in one study [33], where less blood loss was observed in the control group (no statistical testing performed). Operation time was longer in the robot-assisted group (355 vs. 287 minutes) but no statistical testing was reported [33]. In Sanchez et al 2012, there was no significant difference in operation length between the groups [34]. Overall length of stay was reported in one study and the result showed similar length of stays between arms [33].

Oesophagectomy

Intraoperative complications were 13% in the IG group and 16% in the CG (difference was not statistically significant) [15]. There were statistically significantly fewer overall surgery-related postoperative complications (Clavien-Dindo ≥2) RR RR 0.74 $CI_{95\%}$ [0.57; 0.96], $p<0.05$ and overall postoperative complications (MCDC grade≥2) RR 0.79 $CI_{95\%}$ [0.62; 1.00], $p=0.05$ in the robotic surgery thoracolaparoscopic group compared with open transthoracic oesophagectomy [15].

There were more re-operations in the control group (33%) as opposed to the intervention group (24%) but this difference was not statistically significant (van der Sluis, [15]). There was significantly less blood loss in the robotic surgery group compared to the open surgery group (IG M 400ml vs. CG M 568, $p<0.001$) however operation time was significantly longer in the robotic surgery group (IG Ø 349 minutes vs. CG Ø 296, $p<0.001$) [15].There was no statistically significant difference regarding overall length of hospital stay. Conversion to laparoscopic/open surgery was reported only for the IG [15].

Stomach

Gastrectomy

There were no intraoperative complications observed in Wang et al [17] and Pan et al [16] did not report on this outcome. Both studies reported no statistically significant differences between the two groups regarding postoperative complications (Pan et al at 11 months and Wang et al at 30 days). In the Wang study, a high proportion of patients in both groups required reoperations due to anastomotic leakages (IG 4/14 or 29% vs CG 3/15 or 20%); the comparator in this study was open surgery. Conversion was not reported in Wang and was an exclusion criterion in Pan. Both studies had a high risk of bias at the outcome level.

Both RCTs found statistically significantly lower blood loss levels in the robot-assisted surgery group [16], [17]. Pan et al found no difference in operation time whilst Wang et al found the operation time for the IG group was significantly longer than the control group. Both found statistically significantly shorter hospital length of stay days with the robot-assisted surgery group. Wang reported that 1 transfusion had occurred in each group. No information on drain duration was reported.

Bariatric surgery

There were no major intraoperative complications in either groups and 1/25 minor intraoperative complications in the IG versus none in the CG (for a high risk of bias at the outcome level) [18]. There were no postoperative complications observed. 1 patient of 25 required conversion in the IG (none in the CG). Reoperations were not included as an outcome measure [18].

Sanchez et al (2005) [18] reported that operation time was significantly shorter in the IG ($p<0.05$) but found no overall difference in hospital length of stay. Information on blood loss, transfusions and drain duration were not reported.

Bowel

Colectomy

In the only RCT (Park et al, [19] with a low risk of bias at the study level), there were no intraoperative complications observed. There was a statistically non-significant difference between the groups in observed post-operative complications (IG 6/35 vs. CG 7/35) and no conversions were performed. Information on reoperations was not included.

Park et al [19], with a low risk of bias also at the outcome level, reported significantly lower operating time with robot-assisted surgery but no difference in blood loss or in the length of overall hospital stay. There were no transfusions performed and drain duration was not reported.

Rectal resection

Jayne et al [20], with a low risk of study bias, found no statistically significant differences between the groups regarding intraoperative complications or post-operative complications (at 30 days, and between 30 days and 6 months). Conversion occurred in 19/236 (8%) of the IG and 28/230 (12%) of the CG, with an unadjusted risk difference of 4.1% (95% CI -1.4% to 9.6%)[41]. Reoperations were not mentioned in the publication. Kim et al, [21] also with a low risk of bias at the outcome level, reported non-statistically significant differences in intraoperative and perioperative com-

[41] In a separate analysis on the ROLARR trial data, multi-level logistic regression (Corrigan et al, 2018)

plications (there was no information on postoperative complications). Tolstrup (high risk of bias at outcome level) did not report on intraoperative complications or reoperations but reported 10/25 postoperative complications in the IG and 10/26 in the CG (not statistically significant) [22]. There was however a statistically significant difference in the rate of conversions between the groups which occurred among 1/25 patients in the IG and 10/26 patients in the CG ($p<0.01$) [22]. Debakey et al (high risk of bias) reported a high rate of postoperative complications within 30 days, although this was the same in both groups (29%) and most were grade 1 complications [24]. Conversions and re-operations occurred slightly more frequently in the control group (8% in the CG vs. 5% in the IG and 4% in the CG vs. 0% in the IG respectively), no statistical testing reported [24]. Wang et al [23] reported postoperative complications, but not which time period they related to, so could not be included in the GRADE quantitative summary in Table 7. In this study slightly more postoperative complications were observed in the control group (15%) than in the intervention group (1%); conversions and reoperations were not reported [23].

Jayne reported longer operating times with robot-assisted surgery (no statistical testing performed) but no difference in length of stay [20]. Blood loss was not reported. Kim also reported longer operating time ($p<0.0001$) and significantly more blood loss with the robot-assisted surgery group ($p<0.00001$) [21]. Both these studies had a low risk of bias rating at the study and outcome level. Debakey et al [24] (high risk of bias at the outcome level) also reported significantly longer operating time with robot-assisted surgery ($p<0.001$) but more blood loss in the control group ($p=0.05$) whilst overall length of hospital stay did not differ between the groups. Wang et al [23] similarly reported statistically significantly longer operation times with robotic surgery; blood loss and length of stay were not reported. Tolstrup [22] reported non-significant differences in operating time and did not report on the other outcomes (high risk of bias).

Rectopexy

The ventral mesh rectopexy study by Mäkelä-Kaikonen et al [68] reported non-statistically significant differences on intraoperative complications and on postoperative complications (low risk of bias at outcome level). There were no conversions and information on reoperations was not reported.

Non-significant differences between the groups were observed regarding operation time and length of stay [25]. No other outcomes were reported (low risk of bias at the outcome level).

Gallbladder/liver/spleen

Cholecystectomy

All three RCTs on robot-assisted cholecystectomy that reported on complications [26], [27], [28] reported no statistically significant differences between the groups regarding intraoperative or postoperative complications. Grochola et al [28] reported 10% conversion to conventional laparoscopy in the control group and 7% in the intervention group (not statistically significant); in all RCTs [26], [27], [1], there were no conversions. No information on reoperations was given. Pietrabissa et al. and Grochola et al were classed as having a low risk of bias.

Kudsi et al [26] and Grochola et al [28] reported on blood loss and found no significant differences between IG and CG. Operation time was significantly longer in the robot-assisted surgery group in 1 RCT [26] but not significantly different between groups in the other RCTs [27] [1] [28] Length of hospital stay was reported in three studies [26] [27] [28] and was found not to be (significantly) different between groups in 2 RCTs but statistically significantly shorter in the robot-assisted surgery group in Grochola et al [28]. Pietrabissa et al [27] and Grochola et al [28] have a low risk of bias whereas the Kudsi et al [26] and Ruurda et al [1] studies are associated with a high risk of bias.

Liver resection

Total complications (intraoperative and postoperative) in the non-randomised, controlled studies occurred in 11% and 20% of the robot-assisted group compared with 17% and 20% in the control group ([35], [36] respectively). The differences were not statistically significant [36] or not reported [35]. 1 conversion (11%) was needed in the IG group as opposed to none in the CG [35]; 4 conversions (4%) were needed in the IG as opposed to 2 in the CG (6%), p=ns [36]. Reoperations were observed in Lai and Tang [36]: 5% in IG and 3% in CG and were not reported in Berber et al [35]. Both studies were classed as having a critical risk of bias.

There was no statistically significant difference between the groups regarding blood loss in either study. Lai and Tang [36] reported that operation time was statistically significantly longer in the robot-assisted group (207 minutes vs. 134 minutes) although Berber et al [35] found no statistically significant difference. Length of hospital stay and transfusions were reported by Lai and Tang [36]; there were no statistically significant differences on these outcomes and they were not reported in the Berber study [35]. Neither study reported on drain duration. Both studies were classed as having a critical risk of bias.

Hernia repair

There were no wound infections reported in either group [37]. No other complications were considered. As assessed with the ROBINS-I it has a critical risk of bias

The operation time was shorter in the robot-assisted group (48 vs. 52 minutes) but there is no statistical reporting. As assessed with the ROBINS-I, this study is associated with a critical risk of bias [37].

Table 6: Frequency and severity of adverse events in studies that used the Clavien-Dindo classification

Clavien-Dindo classification								
Clavien-Dindo grade class/adverse events	**Cholecystectomy**				**Rectal resection**			
	Grochola et al. 2018 [28]		**Kim et al. 2018** [21]		**Tolstrup et al. 2018** [22]		**Debakey et al. 2018** [24]	
	IG	**CG**	**IG**	**CG**	**IG**	**CG**	**IG**	**CG**
Grade I	2/30 (7%)	4/30 (13%)	6/66 (9.1%)	3/73 (4.1%)	1/25 (4%)	4/26 (25%)	4/21 (19%)	5/24 (21%)
Grade II	2/30 (7%).	1/30 (3%)	11/66 (16.7)	10/73 (13.7%)	6/25 (24%)	1/26 (4%)	1/21 (5%)	1/24 (4%)
Grade III (Total)	NR	NR	NR	NR	2/25 (8%)	4/26 (25%)	1/21 (5%)	0/24 (0%)
Grade IIIa	0	1/30 (3%)	4/66 (6.4%)	2/73 (2.7%)	NR	NR	NR	NR
Grade IIIb	0	0	2/66 (3.0%)	2/73 (2.7%)	NR	NR	NR	NR
Grade IV (Total)	NR	NR	NR	NR	0/25 (0%)	1/26 (4%)	NR	NR
Grade IVa	0	0	NR	NR	NR	NR	0/21 (0%)	0/24 (0%)
Grade IVb	0	1/30 (3%)	NR	NR	NR	NR	NR	NR
Grade V	0	0	NR	NR	1/25 (4%)	0/26 (0%)	0/21 (0%)	1/24 (4%)

Clavien-Dindo classification								
	Lobectomy/Segmentectomy		**Colectomy**		**Oesophagectomy**		**Gastrectomy**	
	Rinieri et al. 2016 [31]		**Park et al. 2012** [19]		**Van der Sluis et al. 2018** [15]		**Wang et al. 2016** [17]	
Grade I	2/17 (12%)	2/34 (6%)	5/35 (14%) (Grade I and II)	6/35 (17%) (Grade I and II)	22/54 (41%)	11/55 (20%)	7/14 (50.0%)	6/15 (40.0%)
Grade II	0/17 (0%)	1/34 (3%)			32/54 (59%) (Grade II to V)	44/55 (80%) (Grade II to V)	3/14 (21.4%)	4/15 (26.7%)
Grade III (Total)	1/17 (6%)	4/34 (12%)	1/35 (3%) (Grade III and IV)	1/35 (3%) (Grade III and IV)			4/14 (28.6%)	4/15 (26.7%)
Grade IIIa	NR	NR					NR	NR
Grade IIIb	NR	NR					NR	NR
Grade IV (Total)	1/17 (6%)	2/34 (6%)					0/14 (0%)	1/15 (6.7%),
Grade IVa	NR	NR					NR	NR
Grade IVb	NR	NR					NR	NR
Grade V	0/17 (0%)	1/34 (3%)	NR	NR			NR	NR

Abbreviations: CG= control group; IG=intervention group; NR= not reported

Table 7: Summary of findings regarding safety for thoracic and visceral indications

Thoracic Surgery

Robot-assisted lobectomy vs. VATS					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Postoperative complications	68 fewer per 1,000 (from 170 fewer to 77 more)	RR 0.84 (0.60 to 1.18)	215 (3 RCTs)	⊕◯◯◯ Very low	unclear which surgeons conducted surgery and with what type of experience, unclear how patients were assigned to treatment groups, small sample size; wide CIs around results;

Robot-assisted mediastinal surgery vs. open mediastinal mass resection					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Postoperative complications	124 more per 1,000 (from 50 fewer to 1,000 more)	RR 2.36 (0.45 to 12.38)	36 (1 RCT)	⊕◯◯◯ Very low	unclear which surgeons conducted surgery and with what type of experience, unclear how patients were assigned to treatment groups, small sample size; wide CIs around results.

Visceral surgery

Oesophagus

Robot-assisted laparoscopic fundoplication vs. laparoscopic fundoplication					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative complications	57 fewer per 1,000 (from 103 fewer to 73 more)	RR 0.56 (0.20 to 1.57)	140 (3 RCTs)	⨁◯◯◯ Very low	2 studies with high risk of bias at the study level; all 3 studies are small with wide CIs around results
Postoperative complications at discharge	57 fewer per 1,000 (from 157 fewer to 117 more)	RR 0.80 (0.45 to 1.41)	140 (3 RCTs)	⨁◯◯◯ Very low	All 3 studies are small with wide CIs around results; 2 studies have a high risk of bias
Postoperative complications at 30 days	18 more per 1,000 (from 139 fewer to 379 more)	RR 1.07 (0.46 to 2.47)	60 (2 RCTs)	⨁◯◯◯ Very low	High risk of bias at the study level (but low for this outcome); both studies are small with wide CIs around results
Postoperative complications at 12 months	119 fewer per 1,000 (from 224 fewer to 163 more)	RR 0.59 (0.23 to 1.56)	60 (2 RCTs)	⨁◯◯◯ Very low	High risk of bias at the study level (but low for this outcome); both studies are small with wide CIs around results

Robot-assisted Heller myotomy vs. laparoscopic Heller myotomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative complications	IG: 0/37 (0%) vs. CG: 4/55 (7.3%) Relative effect cannot be calculated as the study provides no information about the relative probability of the event (see Cochrane handbook 5-1, section 9.2.2.2)		92 (2 non-randomised studies)	⨁◯◯◯ Very low	Critical/serious risk of bias on ROBINS-I

Robot-assisted thoracolaparoscopic oesophagectomy compared to open transthoracic oesophagectomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative complications	34 fewer per 1,000 (from 111 fewer to 160 more)	RR 0.79 (0.32 to 1.98)	109 (1 RCT)	⊕⊕◯◯ Low	95% confidence intervals around the absolute and relative effects includes the possibility of both increased postoperative complications and reduced postoperative complications
Postoperative complications (overall surgery-related, Clavien-Dindo ≥ grade 2)	208 fewer per 1,000 (from 344 fewer to 32 fewer)	RR 0.74 (0.57 to 0.96)	109 (1 RCT)	⊕⊕⊕◯ Moderate	Inconsistency uncertain as only 1 study
Postoperative complications (overall, MCDC ≥ grade 2)	168 fewer per 1,000 (from 304 fewer to 0 fewer)	RR 0.79 (0.62 to 1.00)	109 (1 RCT)	⊕⊕◯◯ Low	95% confidence intervals around the absolute and relative effects includes the possibility of both increased postoperative complications and reduced postoperative complications

Stomach

Robot-assisted gastrectomy vs. laparoscopic gastrectomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative complications	Outcome not reported				
Postoperative complications	148 fewer per 1,000 (from 179 fewer to 65 fewer)	RR 0.25 (0.09 to 0.67)	163 (1 RCT)	⊕⊕◯◯ Low	High risk of bias

Robot-assisted gastrectomy vs. open gastrectomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative complications	0 events in both groups Relative effect cannot be calculated as the study provides no information about the relative probability of the event (see Cochrane handbook 5-1, section 9.2.2.2)		296 (1 RCT)	⨁◯◯◯ Very low	High risk of bias at the outcome and study level
Postoperative complications	10 fewer per 1, 000 (from 57 fewer to 82 more)	RR 0.90 (0.45 to 1.79)	296 (1 RCT)	⨁◯◯◯ Very low	95% confidence intervals around the absolute and relative effects includes the possibility of both increased postoperative complications and reduced postoperative complications

Robot-assisted laparoscopic gastric bypass vs. laparoscopic gastric bypass					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative complications	Not estimable Relative effect cannot be calculated as the study provides no information about the relative probability of the event (see Cochrane handbook 5-1, section 9.2.2.2)		50 (1 RCT)	⨁◯◯◯ Very low	0 complications in the control group and only 1 complication in the intervention group
Postoperative complications	Not estimable Relative effect cannot be calculated as the study provides no information about the relative probability of the event (see Cochrane handbook 5-1, section 9.2.2.2)		50 (1 RCT)	⨁◯◯◯ Very low	0 complications in both groups

Bowel

Robot-assisted right colectomy vs. laparoscopic right colectomy					
Intraoperative complications	Outcome not reported				
Postoperative complications	28 fewer per 1000 (from 136 fewer to 258 more)	RR 0.86 (0.32 to 2.29)	70 (1 RCT)	⨁◯◯◯ Very low	High risk of bias, small sample size, wide CI

Robot-assisted laparoscopic rectal resection compared to laparoscopic rectal resection					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative complications	13 more per 1,000 (from 33 fewer to 8 more)	RR 1.11 (0.73 to 1.68)	605 (2 RCTs)	⨁⨁◯◯ Low	95% confidence intervals around the absolute and relative effects includes the possibility of both increased postoperative complications and reduced postoperative complications
Postoperative complications (timeframe unclear)	39 fewer per 1,000 (from 105 fewer to 117 more)	RR 0.74 (0.31 to 1.77)	137 (1 RCT)	⨁◯◯◯ Very low	95% confidence intervals around the absolute and relative effects includes the possibility of both increased postoperative complications and reduced postoperative complications
Postoperative complications to discharge	90 more per 1,000 (from 35 fewer to 281 more)	RR 1.33 (0.87 to 2.03)	190 (2 RCTs)	⨁◯◯◯ Very low	95% confidence intervals around the absolute and relative effects includes the possibility of both increased postoperative complications and reduced postoperative complications; 1 RCT had a high risk of bias
Postoperative complications within 30 days	13 more per 1,000 (from 33 fewer to 8 more)	RR 1.04 (0.81 to 1.34)	511 (2 RCTs)	⨁◯◯◯ Very low	95% confidence intervals around the absolute and relative effects includes the possibility of both increased postoperative complications and reduced postoperative complications
Postoperative complications > 30 days and ≤ 6 months	21 fewer per 1,000 (from 71 fewer to 55 more)	RR 0.87 (0.57 to 1.33)	466 (1 RCT)	⨁⨁◯◯ Low	95% confidence intervals around the absolute and relative effects includes the possibility of both increased postoperative complications and reduced postoperative complications

Robot-assisted ventral mesh rectopexy vs. laparoscopic ventral mesh rectopexy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative complications	116 more per 1000 (from 49 fewer to 1000 more)	RR 2.62 (0.31 to 22.46)	30 (1 RCT)	⨁◯◯◯ Very low	Single study with small sample size and few events. CI around estimates are wide, including both beneficial and harmful effects.
Postoperative complications	54 more per 1000 (from 59 fewer to 1000 more)	RR 1.75 (0.18 to 17.30)	30 (1 RCT)	⨁◯◯◯ Very low	Single study with small sample size and few events. CI around estimates are wide, including both beneficial and harmful effects.

Gallbladder/liver/spleen

Single-site laparoscopic robotic cholecystectomy vs. multiport laparoscopic cholecystecomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative complications	91 fewer per 1000 (from 124 fewer to 9 more)	RR 0.37 (0.14 to 0.94)	196 (2 RCTs)	⨁⨁◯◯ Low	One of the studies constituted a low risk of bias (Pietrabissa et al, 2017); the 95% confidence interval around the absolute effect includes the possibility of both increased postoperative complications and reduced postoperative complications
Postoperative complications	29 more per 1000 (from 13 fewer to 233 more)	RR 2.20 (0.46 to 10.65)	196 (2 RCTs)	⨁◯◯◯ Very low	The 95% confidence interval around the absolute effect includes the possibility of both increased postoperative complications and reduced postoperative complications

Single-site laparoscopic robotic cholecystectomy vs. single-incision laparoscopic cholecystecomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Intraoperative complications	65 fewer per 1,000 (from 243 fewer to 247 more)	RR 0.86 (0.48 to 1.53)	60 (1 RCT)	⊕⊕◯◯ Low	Small sample size; absolute and relative risk effects include the possibility of both more and fewer events
Postoperative complications at 30 days	100 fewer per 1,000 (from 189 fewer to 175 more)	RR 0.57 (0.19 to 1.75)	60 (1 RCT)	⊕⊕◯◯ Low	Absolute and relative risk effects include the possibility of both more and fewer events

Robot-assisted liver resection/hepatectomy compared to laparoscopic liver resection/hepatectomy					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Total complications (intra- and postoperative)	61 fewer per 1,000 (from 102 fewer to 2 fewer)	RR 0.68 (0.46 to 0.99)	162 (2 non-randomised, controlled studies)	⊕◯◯◯ Very low	Critical risk of bias for this outcome at the ROBINS-I: little information on amount of surgical experience and type and approach of resection (Berber et al, 2010); potentially missing complications data (Berber et al, 2010)

Robot-assisted hernia repair vs. laparoscopic single-port inguinal hernia repair					
Outcome	**Anticipated absolute effects (95% CI)**	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality**	**Comments**
Wound infections	O events in both groups Relative effect cannot be calculated as the study provides no information about the relative probability of the event (see Cochrane handbook 5-1, section 9.2.2.2)		32 (1 non-randomised controlled study)	⊕◯◯◯ Very low	Critical risk of bias

[C0002] – Are the harms related to dosage or frequency of applying robot-assisted surgery?

This question does not apply to the da Vinci Surgical System or any of the other robotic systems, as there is no varying dosage or frequency associated with the device.

[C0004] – How does the frequency or severity of harms change over time or in different settings?

This question is not relevant to the da Vinci Surgical System, as the device is used typically once for a given intervention.

[C0005] – What are the susceptible patient groups that are more likely to be harmed through the use of robot-assisted surgery?

No evidence was found to answer this research question.

[C0007] – Is robot-assisted surgery associated with user-dependent harms?

No evidence was found to answer this research question from the included study pool. Robot-assisted surgery is claimed to be a more ergonomically-friendly method of operating for the surgeon[42] and there is some evidence to support this [69].

[B0010] – What kind of data/records and/or registry is needed to monitor the use of the technology and the comparator?

No evidence was found to answer this research question.

[42] https://www.intuitive.com/about-us/company/legal/safety-information

7 DISCUSSION

Robotic surgery is a form of minimally-invasive surgery whereby the instruments of the robotic system are controlled by a direct telemanipulator, which is a remote manipulator that allows the surgeon to perform the normal movements associated with surgery. The robot has a higher degree of dexterity compared to the laparoscopic approach, which it is claimed allows surgeons to operate in very tight spaces in the body that would otherwise only be accessible through open surgery, with the rational of improving clinical outcomes and resource use. There are currently 16 manufacturers of robotic systems for use in thoracic and visceral surgery; four of these are currently actively marketing a total of seven products (da Vinci SI®, da Vinci SP®, da Vinci XI®, da Vinci X®, Freehand v1.2, Surgenius Beta, Flex Robotic System and Senhance TM Surgical System). The robotic procedure used in most of the studies included in this HTA involved the da Vinci® Surgical System. Evidence suggests that robot-assisted surgical methods result in a higher mean cost per procedure than conventional surgical methods.

This HTA had the aim of assessing the effectiveness and safety of robotic surgery applied to the areas of thoracic and visceral surgery. Thoracic surgery is concerned with conditions of the lungs, chest wall and diaphragm and is generally dominated by treatment of malignant disease. Visceral surgery deals with all aspects of the surgical treatment of benign and malignant diseases of abdominal organs, the entire gastrointestinal tract, endocrine organs, the abdominal wall and the peritoneum.

In accordance with the advice of a clinical expert, the evidence on effectiveness and safety was assessed for each procedure at the operation level. Different procedures are often associated with different outcome categories hence the reporting of results differs according to the procedure under consideration. In total 2 thoracic procedures were assessed, namely lobectomy and mediastinal surgery. Visceral surgery covers a much wider number of organs. Here procedures relating to the oesophagus (antireflux/fundoplication, oesophagectomy and Heller myotomy), stomach (gastrectomy, bariatric surgery), bowel (colectomy, rectal resection, rectal rectopexy) and gallbladder/ liver/spleen (cholecystectomy, liver resection and hernia repair) were assessed.

There is a serious lack of evidence available from RCTs on the performance of robot-assisted surgery compared to open or laparoscopic surgery. Statements of effect were only possible for some of the outcomes (but not all) for 4 procedures (oesophagectomy, gastrectomy, rectal resection, cholecystectomy) and even here the quality of evidence was generally low and at most, moderate. Of these statements of effect, most were in favour of robot-asisted surgery. For all other outcomes and procedures there are evidence gaps. In terms of ongoing studies, we can report that there are many ongoing trials on the use of robotic surgery in the field of thoracic and visceral surgery. It is expected that the studies will add further evidence, at least for some of the procedures considered.

7.1 Interpretation of findings/level of evidence

For eight procedures (antireflux/fundoplication, oesphagectomy, gastrectomy, bariatric surgery, colectomy, rectal resection, rectal rectopexy, cholecystectomy), RCTs of ≥10 patients could be identified. For five procedures (lobectomy, mediastinal surgery, Heller myotomy, liver resection/hepatectomy, hernia repair), no RCTs ≥10 patients could be identified, hence (in accordance with the project protocol) nine prospective studies non-randomised controlled studies were included (lobectomy: 3; mediastinal surgery: 1; Heller myotomy: 2; liver resection/hepatectomy: 2; hernia repair: 1). All studies included in this HTA were comparative, prospective studies.

A total of 28 studies were therefore included; of these 19 were RCTs and 9 were prospective, controlled, non-randomised studies. All the RCTS identified in the systematic literature search reported on effectiveness, with the exception of one [1]. In the majority of studies laparoscopy (not open surgery) was used as the comparator.

Seven procedures (lobectomy, mediastinal mass resection, gastrectomy, colectomy, rectal resection, liver resection/hepatectomy and oesophagectomy) of the total 13 procedures related to patients undergoing surgical treatment for cancer.

Thoracic surgery: lobectomy

Intraoperative and in-hospital mortality shows non-significant differences between the arms; relative risk estimates are not possible since no events are observed in at least one arm. Regarding postoperative complications, the point estimate suggests a relative risk reduction but wide confidence intervals include the possibility of both more and fewer complications occurring with robot-assisted surgery.

Evidence on blood loss is conflicting (one study found significantly more and one study significantly less blood loss with robot-assisted surgery). 1 out of the 3 studies found statistically significantly longer operation times with robot-assisted surgery whilst the other two did not. None of these studies had a low risk of bias.

Thoracic surgery: mediastinal

In the non-randomised, controlled study by Balduyck et al (2011) [32], recurrence occurred in 1/22 patients in the control group and in no cases in the intervention group, which was not statistically significant (low to medium risk of bias). The relative effect on intraoperative mortality could not be assessed as there were no events in either arm; there was a conversion in the IG (7%) and one re-operation in the CG (9%) but no statistical testing was reported. Quality of life and symptoms deteriorated significantly in the short-term in several subscales in the open surgery group but much less so in the robotic surgery group. There was no statistically significant difference in operation time and length of hospital stay. The evidence has been assessed as very low.

Visceral surgery: Oesophagus

Antireflux/fundoplication

Up to four RCTs were available for analysis (depending on endpoint), for a total of up to 160 patients. Mortality associated with the procedure could not be assessed, since it was not reported in any of the studies. There were no reported differences in symptoms. In terms of intraoperative and postoperative complications, we are uncertain whether robotic fundoplication surgery improves or reduces intraoperative and postoperative complications compared to laparoscopic fundoplication surgery as the certainty of the evidence has been assessed as very low. Therefore no consistent advantage for robot-assisted antireflux surgery has been demonstrated. In one RCT there was a 12% recurrence of hiatal hernia in the CG and 4% recurrence in the IG but statistical significance testing was not reported and there is a high risk of bias at the outcome level**.** Neither study reporting on satisfaction found statistically significant differences.

1 study reported on blood loss; no statistically significant differences were reported. The evidence on operation time is conflicting: 3 studies reported significant differences but these went in different directions (two found robot-assisted surgery took longer and the other reported that it took a shorter time than the control procedure) and 1 found a non-significant difference. The strongest evidence came from one of the studies reporting a significantly longer operation time.

Heller myotomy

2 controlled, non-randomised studies for a total of 92 patients were available for analysis. Mortality was not assessed as an outcome. Both the robot-assisted Heller myotomy group and the laparoscopic Heller myotomy groups showed post-operative improvements in quality of life and symptoms, but no between-group assessments were made in the studies. For this reason we are uncertain whether robotic surgery improves morbidity or quality of life compared with laparoscopy for this procedure. We cannot infer from the study data whether robotic surgery is associated with more or fewer intraoperative complications compared to laparoscopic Heller myotomy. Neither study reported significant differences on resource use outcomes.

Oesophagectomy

1 RCT was available (109 patients) comparing thoracolaparoscopic oesophagectomy with open transthoracic oesophagectomy. Confidence intervals around the absolute and relative effect estimates around the point estimate for mortality include the possibility of both increased postoperative complications and reduced postoperative complications hence we are uncertain whether robotic surgery is associated with more or fewer fatal events. Robotic surgery probably improves quality of life and functional recovery and reduces postoperative complications when compared to open surgery for this procedure (quality of evidence: moderate). In terms of intraoperative complications, robotic surgery may reduce intraoperative complications, but the 95% confidence interval includes the possibility of both reduced complications and increased complications. This study found significantly less blood loss in the robot-assisted surgery arm compared to open surgery but statistically significantly longer operation time and no statistically significant difference on reoperations.

Visceral surgery: stomach

Gastrectomy

2 RCTS were available, each with different comparators (open gastrectomy for a total of 296 patients and laparoscopic gastrectomy for a total of 163 patients). In both studies, no mortality events were reported in either arm. Morbidity and quality of life was not reported in the open gastrectomy comparison; in the laparoscopy comparison significant (statistically) lower VAS scores were reported in early post-operative days in the robot-assisted group but the certainty of this evidence is assessed as very low. Robot-assisted surgery may reduce postoperative complications compared to conventional laparoscopic surgery (low quality/certainty of evidence). The comparison with open gastrectomy did not show any clear results in terms of reduction or increase in postoperative complications. There were no statistically significant differences in proximal resection margins (in comparison with conventional laparoscopy). Both RCTs found statistically significantly lower blood loss levels and significantly shorter hospital length of stay days with the robot-assisted surgery group. Operation time was statistically significantly longer for the robot-assisted group compared to the conventional laparoscopy arm (there was no difference in the comparison with open surgery).

Bariatric surgery/gastric bypass

Here 1 RCT was available (50 patients), which did not report on mortality or morbidity/quality of life. Due to the very few events (only 1 intraoperative complication and 0 postoperative complications) observed in this study in both arms relative effect estimates were not possible.1 patient required conversion to traditional laparoscopy in the intervention group (p=NR). We therefore have no basis on which to make any statements about effects or safety for this procedure. In terms of resource use, the included RCT reported a significantly shorter operation time with robot-assisted surgery, although the sample size is small and there was insufficient information on patient characteristics i.e. serious risk of bias.

Visceral surgery: bowel

Colectomy

In a single RCT (70 patients) comparing robot-assisted surgery with conventional laparoscopic surgery, mortality could not be assessed as there were no events in either arm. Pain assessment scores showed no statistically significant results between the groups. Intraoperative complications were not reported and postoperative complications showed a relative effect in favour of robot-assisted colectomy surgery (RR 0. 86), but given the very low quality of this study and the wide CI around this effect estimate, we must conclude that we are uncertain whether robot-assisted surgery reduces postoperative complications compared with traditional laparoscopic colectomy. Proximal margin and distal margin outcomes were not influenced by the type of surgery in this study. In terms of resource use, significantly shorter operating time was reported with robot-assisted surgery and in terms of perioperative outcomes, there was no stastically significant difference regarding blood loss or length of hospital stay.

Rectal resection

5 RCTS were included in this HTA on rectal resection. For the outcome mortality within 30 days (2 RCTS; 511 patients) we are uncertain whether robot-assisted surgery reduces mortality compared to conventional laparoscopic surgery. Quality of life results were mixed, with some aspects (sexual functioning) better in the IG and others (sleep disturbances) worse (both studies reporting on this outcome had a low risk of bias). Intraoperative and postoperative complications were genereally more prevalent in the robot-assisted group (particularly in the studies with a slightly lower risk of bias) but the CI crossed the line of no effect so we are uncertain whether robot-assisted surgery increases complications compared with conventional laparoscopic surgery. Proximal margin and distal margin outcomes were not influenced by the type of surgery in these studies.

In terms of resource use, 5 RCTs reported on operative time; in 4 studies, robot-assist surgery took longer (in 3, significantly so). In terms of perioperative outcomes, 2 studies reported on blood loss with conflicting results.

Rectopexy

1 RCT was identified that compared robot-assisted ventral mesh rectopexy with laparoscopic ventral mesh rectopexy for rectal prolapse and intussusception. We are uncertain whether robot-assisted rectopexy results in more or fewer intraoperative and postoperative complications as the evidence has been assessed as very low. No comparisons between arms were made regarding morbidity/quality of life. Regarding resource use, no statistically significant differences were reported on operation time and length of hospital stay.

Visceral surgery: Gallbladder/liver/spleen

Cholecystectomy

In total 4 RCTs were available with either single-port or muilt-port laparoscopy as the comparator. No data was available on mortality. Quality of life and satisfaction results showed no statistically significant differences between the arms (3 RCTs, total 256 patients), although the quality of evidence is very low. Robot-assisted surgery may reduce intraoperative complications, but the quality of evidence is low. Robot-assisted surgery may reduce postoperative complications at 30 days when compared to single-incision laparoscopic cholecystectomy (low certainty evidence) however the 95% CI includes the possibility of both reduced complications and increased complications. Two studies reporting on satisfaction found it was statistically significantly higher with robot-assisted surgery (one of the studies had a low risk of bias) but a third study (also with a low risk of bias) reported no statistically significant differences (the overall evidence has been assessed as very low).

Blood loss was reported in 2 studies: both found no significant differences. Operation time was significantly longer in 1 of 4 studies but not found to be different in 3 of 4 studies (the evidence has been assessed as low).

Liver resection

No RCTS were identified for this procedure so non-randomised, controlled studies were identified and included (2 in total, 162 patients). There were fewer recurrences with robot-assisted surgery compared to conventional liver resection but we are uncertain whether robot-assisted surgery reduces recurrences as the quality of the evidence has been assessed as very low. Similarly fewer overall complications were reported with robot-assisted surgery compared to conventional liver resection but we are uncertain whether robot-assisted surgery reduces complications as the quality of the evidence has been assessed as very low. Rates of recurrence were either not statistically significant in one study or sizable but without statistical testing in another study.

Neither study found a difference regarding blood loss. Regarding operation time, 1 study found it was significantly longer in the robot-assisted surgery group; the other found no difference.

Hernia repair

No RCTS were identified for this procedure so non-randomised, controlled studies were identified and included (1 in total with 32 patients). Mortality results were not reported, neither were quality of life/morbidity results. The study only provides information on wound infections, for which no cases were reported in either arm (very low certainty of evidence). Satisfaction rates did not differ between the two arms.

Operation time was shorter in the robot-assisted group but there was no statistical testing reported.

7.2 Limitations of the present report

Limitations of the present report include the lack of stratification according to surgical experience; this information was often not available in a way that would enable a structured classification. Also an analysis of the number of cases required to maintain training and knowledge related to the method would be useful (this was beyond the scope of this HTA).

Another limitation is the focus on RCTs where these were available, to the exclusion of potentially good quality prospective non-randomised studies. This was a decision taken at the project protocol stage to enable a manageable evidence pool given the magnitude of the topic (namely the inclusion of all procedures existing within the field of thoracic and visceral surgery). Given the range of outcomes reported on, which often differed between the procedures, we did not assess whether an RCT was available at the outcome level but only at the procedure level.

8 CONCLUSION

There is insufficient evidence to determine whether robot-assisted **lobectomy** is more effective and/or has a better safety profile compared with VATS.

There is insufficient evidence to determine whether robot-assisted **mediastinal surgery** is more effective and/or has a better safety profile compared with open mediastinal mass resection.

There is insufficient evidence to determine whether robot-assisted **antireflux/fundoplication** mediastinal surgery is more effective and/or has a better safety profile compared with conventional laparoscopic fundoplication.

There is insufficient evidence to determine whether robot-assisted **Heller myotomy** is more effective and/or has a better safety profile compared with conventional laparoscopic Heller myotomy.

There is insufficient evidence to determine the effect of robot-assisted **oesophagectomy** upon mortality compared with open surgery. Robot-assisted **oesophagectomy** surgery probably improves post-operative morbidity/QoL compared to open surgery (evidence quality: moderate) and robot-assisted oesophagectomy surgery probably reduces postoperative complications compared to open surgery (evidence quality: moderate). Intra-operative complications may be reduced with robot-assisted surgery compared to open surgery, although the 95% confidence interval includes both the possibility of reduced complications and increased complications.

There is insufficient evidence to determine whether robot-assisted **gastrectomy** is more effective than conventional laparoscopy or open surgery. Robot-assisted gastrectomy may reduce postoperative complications compared to conventional laparoscopy (evidence quality: low).

There is insufficient evidence to determine whether robot-assisted **bariatric surgery** is more effective and/or has a better safety profile compared with conventional laparoscopic surgery.

There is insufficient evidence to determine whether robot-assisted **colectomy** is more effective and/or has a better safety profile compared with conventional laparoscopy.

There is insufficient evidence to determine the effect of robot-assisted **rectal resection** upon mortality compared with conventional laparoscopic rectal resection. There is evidence that robot-assisted rectal resection improves some aspects of QoL but worsens others (evidence quality low). It may increase intraoperative complications and decrease postoperative complications >30 days and ≤6 months (evidence quality: low).

There is insufficient evidence to determine whether robot-assisted **rectal rectopexy** is more effective and/or has a better safety profile compared with conventional laparoscopic rectal rectopexy.

There is insufficient evidence to determine whether robot-assisted **cholecystectomy** is more effective compared with conventional laparoscopy. There is some evidence that robot-assisted surgery may reduce intraoperative complications (evidence quality: low) and reduce postoperative complications at 30 days when compared to single-incision laparoscopic cholecystectomy (evidence quality: low).

There is insufficient evidence to determine whether robot-assisted **liver resection** is more effective and/or has a better safety profile compared with conventional laparoscopic liver resection.

There is insufficient evidence to determine whether robot-assisted **hernia repair** is more effective and/or has a better safety profile compared with conventional laparoscopic hernia repair.

Several of the studies considered cost aspects and most reported higher costs associated with robot-assisted surgery. This is often due to the longer operation time necessary, which was reported by many studies. The evidence on blood loss was mixed but there were more studies reporting significantly less blood less with robot-assisted surgery than significantly more blood loss.

Multicenter studies are needed in order to evaluate the outcomes in a higher number of subjects. Pending results from some large studies could contribute to solving at least some of uncertainties. For instance, 2 of the ongoing studies with more than a thousand patients will evaluate the long term impact on mortality following robot-assisted gastrectomy.

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APPENDIX 1: METHODS AND DESCRIPTION OF THE EVIDENCE USED

DESCRIPTION OF THE EVIDENCE USED

Guidelines for diagnosis and management

Table A1: Overview of guidelines with specific recommendations regarding robot-assisted surgery

Name of society/organisation issuing guidance	Date of issue	Country/ies to which applicable	Summary of recommendation	Level of evidence (A,B,C)/class of recommendation (I, IIa, IIb, III)
European Society for Medical Oncology [54]	2017	Europe	Robot-assisted rectal cancer surgery provides some technical advantages for surgeons compared with conventional laparoscopy but it is still under evaluation	No recommendation level given
National Comprehensive Cancer Network [65]	July 2018	USA	Several rectal cancer studies have looked at outcomes of robot-assisted surgery versus conventional laparoscopic resection with comparable results in terms of conversion to open resection, quality of total mesorectal excision, postoperative complications and quality of life	2a
National Comprehensive Cancer Network [61]	21st Feb. 2018	USA	VATS or minimally invasive surgery (including robotic-assisted approaches) should be strongly considered for patients with no anatomic or surgical contraindications, as long as there is no compromise of the standard oncologic and dissection principles of thoracic surgery	No recommendation level given
European Society for Medical Oncology [46]	September 2015	Europe	Minimally invasive surgery conducted by trained thoracic surgeons (including robotic approaches) is an option for presumed stage I and possibly stage II tumors	IV, C
American Gastrointestinal and Endoscopic Surgeons [64]	May 2011	America	Compared with laparoscopy, robot- assisted surgery has been demonstrated to decrease the rate of intraoperative oesophageal mucosal perforations but no clear differences in postoperative morbidity, symptom relief or long-term outcomes have been described. Further evaluation is necessary to better establish the role of robot-assisted myotomy.	++, weak

Evidence tables of individual studies included for clinical effectiveness and safety

Table A2: Characteristics & risk of bias of randomised controlled studies

Oesophagus		
	Antireflux/Fundoplication	**Antireflux/Fundoplication**
Author, year [reference number]	**Draaisma et al. 2006** [10]	**Morino et al. 2006** [11]
Study design	Single-centre RCT of patients with GORD	Single-centre RCT of patients with GORD
Country	The Netherlands	Italy
Funding/Sponsor	NR	NR
Intervention (IG) | Product	robot-assisted laparoscopic Nissen fundoplication | da Vinci Robotic System	Robot-assisted fundoplication | da Vinci system
Comparator (CG)	Laparoscopic-assisted laparoscopic Nissen fundoplication	Traditional laparoscopic fundoplication
Experience of surgeon(s), time period	Surgeons had performed more than 30 laparoscopic Nissen fundoplications and more than 20 robot-assisted laparoscopic procedures. Operations were performed January 2003-October 2005	3 surgeons all proficient in laparoscopic procedures Operations were performed February 2002-February 2004
Number of patients	IG: 25 CG: 25	IG:25 CG:25
Inclusion/exclusion criteria	Inclusion: • Age >18 • Diagnosed with GORD via upper endoscopy, barium oesophagram series, oesophaegeal manometry, 24-hr pH monitoring Exclusion: • General contraindications for laparoscopy, psychiatric illness, previous abdominal surgery • 12 patients excluded prior to randomisation	Inclusion: • Clinical GORD that necessitated surgery according to the criteria of Hinder et al. • ASA score I-II Exclusion: • Giant hiatal hernia (larger than 6 cm on preoperative barium meal) • ASA score III–IV • Previous upper abdominal surgery • Contraindications to pneumoperitoneum
Primary/secondary endpoints	• Primary endpoints: (nadir) end-expiratory LOS pressure, total oesophageal acid exposure time, symptom index, symptom association probability • Secondary endpoints: general health state (10-point VAS 0-100); QoL (Visick scale); self-rated reflux symptoms (instrument NR); satisfaction with outcome (instrument NR);	• Primary endpoint: In-hospital cost of the procedure • Secondary endpoints were skin-to-skin and total operating time
Follow-up (months)	3-6	Ø 22.3 (R 6-32)
Drop-outs (n (%)	IG: 2/25 (8%) CG: 0	none
Patient characteristics		
Age of patients (yrs.)	IG: M 48 (R 20-74) CG: M 52 (R 27-71), p=ns	IG: Ø 43.0 ±12.8 CG: Ø 46.3 ±11.3, p=ns
Sex (% female)	IG: 36% CG: 32%, p=NR	IG: 24% CG: 28%, p=ns
BMI (kg/m²)	IG: M 25.6 (R 19.1-37.2) CG: M 28.7 (R 19.5-46.6), p=ns	IG: Ø 25.5 ±2.9 CG: Ø 26.1 ±2.3, p=ns
Clinical classification	Los Angeles classification of	NR

Oesophagus		
	Antireflux/Fundoplication	**Antireflux/Fundoplication**
Author, year [reference number]	**Draaisma et al. 2006** [10]	**Morino et al. 2006** [11]
	oesophagitis (IG vs.CG) Grade A: 24% vs. 20% Grade B: 28% vs. 24% Grade C: 12% vs. 0 Grade D: 8% vs. 4% No oesophagitits: 24% vs. 32% Unknown: 4% vs. 20%	
Patient-relevant outcomes		
Survival (overall and disease-specific or disease-free)	NR	NR
Recurrence (local, regional or distant)	IG: 1/25 (4%) hiatal hernia CG: 3/25 (12%) hiatal hernia, p=NR	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	General quality of life IG vs CG @ 6 months after surgery, NR $CI_{95\%}$ [-18.1;9.2], p=ns[43] : IG: M 22.5 (R 12-99) vs. M 72.0 (R21-98) CG: M 32.5 (R 0-96) vs. M 76.0 (R 26-100) Self-rated change in reflux symptoms compared with preoperative state (IG vs CG): Resolved: 14/25 (56%) vs. 15 (60%), p=ns Improved: 9/25 (36%) vs. 9/26 (36%), p=ns Unchanged: 1/25 (4%) vs. 0, p=ns Worsened: 1/25 (4%) vs 1/25 (4%), p=ns Self-rated change in general quality of life compared with preoperative state (IG vs. CG): Improved: 22/25 (88%) vs. 20/25 (80%), p=ns Unchanged: 0 vs. 3/25 (12%), p=ns Worsened: 3/25 (12%) vs. 2/25 (8%), p=ns	Symptoms @ 1 month (IG vs. CG), p=NR Mild transient dysphagia: 3/25 (12%) vs. 3/25 (12%), @ 6 months, p=NR Oesophagitis: 0 vs. 0 Authors report that no clinical differences between the two groups were found using the GORD-HRQOL at 3, 6 and 12 months.
Time to resume work/daily activities	NR	NR
Patient satisfaction	IG: 23/25 (92%) CG: 22/25 (88%) p=ns, $CI_{95\%}$ [-0.13.0.21][1]	NR
Safety-related outcomes		
Intraoperative complications (e.g. air-leakage)	Minor complications (IG vs. CG) p=NR: • Liver capsule tear: 2/25 (8%) vs. 4/25 (16%) • Spleen capsule tear: 0 vs. 2/25 (8%) • Pneumothorax: 0 vs. 1/25 (4%) • Minor bleeding: 2/25 (8%) vs. 0	IG: 0 CG: 0
Postoperative complications (e.g. infections)	IG vs. CG, p=NR: Pneumonia: 0 vs. 1/25 (4%)	IG: 0 CG: 0

[43] No summary statistic reported, only that the CI relates to CG vs. IG 6 months after surgery

Oesophagus		
	Antireflux/Fundoplication	**Antireflux/Fundoplication**
Author, year [reference number]	**Draaisma et al. 2006** [10]	**Morino et al. 2006** [11]
	Urinary tract infection: 0 vs. 1/25 (4%)	
Re-operations/additional surgeries	@ 6 months FU, p=NR: IG: 2/25 (8%), because of dysphagia and an incisional hernia CG: 2/25 (8%), because of dysphagia	NR
Conversion	IG: 0 CG: 2/25 (8%), p=NR	IG: 1/25 (4%) because of difficulty in pursuing the dissection by robotic techniques with a prolonged operating time. CG: 0, p=NR
Perioperative events & resource use		
Blood loss (in ml)	IG: M 20 (R 0-200) CG: M 45 (R 0-200) Mean Difference 25; $CI_{95\%}$[-58.2;8.9], pü=ns	NR
Operation time in min.	IG: M 120 (R 80-180) CG: M 95 (R 60-210) Mean Difference 25, $CI_{95\%}$[-6.0;32.0]	IG: Ø 131.3 ±18.3 CG: Ø 91.1 ± 10.6, p<0.001
Transfusions	NR	NR
Drain duration (days)	NR	NR
Length of hospital stay (days)	IG: M 3 (R 2-6) CG: M 3 (R 1-13), p=NR	IG: Ø 2.9 (R 2-6) CG: Ø 3.0 (R 2-7), p=ns

Oesophagus	
	Antireflux/Fundoplication
Author, year [reference number]	**Mueller-Stich et al. 2007** [12] **& Mueller-Stich et al. 2009** [13]
Study design	Single-centre RCT of patients with symptomatic GERD
Country	Germany
Funding/Sponsor	German Research Foundation.
Intervention (IG) | Product	Robot-assisted laparoscopic fundoplication | da Vinci Surgical System
Comparator (CG)	Conventional laparoscopic fundoplication
Experience of sur-geon(s), time period	All surgeons were reported to be highly experienced in laparoscopy, with at least 30 conventional laparoscopic fundoplications Operations were performed August 2004-December 2005 by 1 surgeon (IG) and 3 surgeons (CG)
Number of patients	IG: 20 CG:20
Inclusion/exclusion criteria	Inclusion: • Age >18 • History of more than 6 months of symptomatic GERD requiring acid suppressive therapy of a minimal standard dosage of the applied proton pump inhibitor (PPI) for at least 3 months in the preceding year • GERD had to be proven endoscopically or by severe clinical symptoms which resolved with PPI therapy (positive PPI test) Exclusion: • Previous major upper abdominal surgery, hiatal hernias with paraesophageal involvement • Obesity with a body mass index of over 40 kg/m2 • Evidence of primary oesophageal disorders such as achalasia, sclerodermia or malignant

Oesophagus	
	Antireflux/Fundoplication
Author, year [reference number]	**Mueller-Stich et al. 2007** [12] **& Mueller-Stich et al. 2009** [13]
	diseases 12 patients excluded prior to randomisation
Primary/secondary endpoints	• Primary: Quality of Life in Refux and Dsypepsia (QOLRAD); Gastrointestinal Symptom Rating Scale (GSRS); patient satisfaction; 4-step Likert scale for specific symptoms • Secondary: Perioperative outcomes regarding operative time, perioperative complications, length of stay and costs
Follow-up (months)	12 (also 1, 3, 6 months)
Drop-outs (n (%))	none
Patient characteristics	
Age of patients (yrs.)	IG: Ø 49.6 ±12.0 (R 23-71) CG: Ø 50.5 ±12.4 (R 25-75), p=ns
Sex (% female)	IG: 50% CG: 60%, p=NR
BMI (kg/m²)	IG: Ø 29.2 ±5.8 (R 21-40) CG: Ø 26.2 ±3.4 (R 19-31), p=ns
Clinical classification	Los Angeles classification of oesophagitis (IG vs.CG), p=ns: Grade A: 45% vs. 55% Grade B: 50% vs. 35% Grade C: 5% vs. 10% Grade D: 0 vs. 0
Patient-relevant outcomes	
Survival (overall and disease-specific or disease-free)	NR
Recurrence (local, regional or distant)	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	QOLRAD (min. 1-max. 7) before vs. 12 months after surgery: IG: Ø 3.7 ±1.3 vs. Ø 1.3 (R 1.0-4.6), p=ns CG: Ø 3.7 ±1.2 vs Ø 1.1 (R1.0-2.2), p=ns GSRS (reflux syndrome, min. 1-max. 7) before vs. 12 months after surgery: IG: Ø 4.0 ±1.7 vs. Ø 1.3 (R 1.0-3.5) CG: Ø 4.4 ±1.5, vs. Ø 1.3 (R 1.0-4.0), p=ns
Time to resume work/daily activities	NR
Patient satisfaction	Change of condition (IG vs. CG): Normalised: 11/20 (55%) vs. 5/20 (25%), p=ns Improved: 7/20 (35%) vs. 14/20 (70%), p=ns Unchanged: 2/20 (10%) vs. 1/20 (5%), p=ns Worsened: 0 vs. 0, p=ns Operative result (IG vs. CG): Excellent: 6/20 (5%) vs. 2/20 (10%), p=ns Very good: 7/20 (35%) vs. 9/20 (45%), p=ns Good: 6/20 (30%) vs. 8/20 (40%), p=ns Sufficient: 0 vs. 1/20 (5%), p=ns **Would you decide in favour of an operation again**? (ratio Yes:No) IG: 19:1 CG: 20:0
Safety-related outcomes	
Intraoperative compli-cations (e.g. air-	IG: 1/20 (5%), 1 pneumothorax CG: 2/20 (10%), 2 bleedings

Oesophagus	
	Antireflux/Fundoplication
Author, year [reference number]	**Mueller-Stich et al. 2007** [12] **& Mueller-Stich et al. 2009** [13]
leakage)	p=NR
Postoperative complications (e.g. infections)	Minor complications (IG vs. CG): • Mild dysphagia at discharge: 16/20 (80%) vs. 18/20 (90%), p=ns • Dysphagia 30 days postoperatively: 5/20 (25%) vs. 4/20 (20%), p=ns • Mild reflux symptoms 30 days postoperatively: 2/20 (10%) vs. 3/20 (15%), p=ns • Reflux score: Ø 1.3 ±0.7 vs. Ø1.6 ±1.3, p=ns Major complications (IG vs. CG): 0 vs. 0 Complications @ 12 months FU (IG vs. CG): • Mild reflux symptoms: 0 vs. 2/20 (10%), p=NR • Gastritis: 0 vs. 1/20 (5%), p=NR • Dysphagia: 0 vs. 0 • Gas bloat: 3/20 (15%) vs. 2/20 (10%), p=ns • Diarrhoea 1/20 (5%) vs. 0, p=ns • Impeded vomiting: 0 vs. 1/20 (5%), p=ns • Regurgitation: 0 vs. 1/20 (5%), p=ns
Re-operations/ additional surgeries	@ 12 months FU, p=NR IG: 1/20 (5%), because of dysphagia CG: 0
Conversion	IG: 0 CG:0
Perioperative events & resource use	
Blood loss (in ml)	NR
Operation time in min.	IG: Ø 88 ±18 CG: Ø 102 ±19, p<0.05
Transfusions	NR
Drain duration (days)	NR
Length of hospital stay (days)	IG: Ø 2.9 ±0.8 CG: Ø 3.3 ±0.8, p=ns

Oesophagus	
	Antireflux/Fundoplication
Author, year [reference number]	**Nakadi et al. 2006** [14]
Study design	Single-centre RCT of patients with GERD
Country	Belgium
Funding/Sponsor	NR
Intervention (IG) | Product	Robot-assisted Nissen fundoplication | da Vinci system
Comparator (CG)	Laparoscopic Nissen fundoplication
Experience of surgeon(s), time period	All the procedures were performed by 2 surgeons: 1 digestive surgeon experienced in Nissen fundoplication and 1 general surgeon used to laparoscopic techniques. Operations were performed between: NR
Number of patients	IG: 9 CG: 11
Inclusion/exclusion criteria	Inclusion: • Symptoms of pathologic GERD

Oesophagus	
	Antireflux/Fundoplication
Author, year [reference number]	**Nakadi et al. 2006** [14]
	• Age >16 • proven complications of GERD like esophagitis, strictures, Barrett without dysplasia and extra digestive symptoms • Recurrence of symptoms or failure following 3 months of proton pump inhibitor (PPI) treatment Exclusion: • Achalasia and diffuse esophageal spasms • Brachyesophagus • Recurrence following previous surgery • History of previous gastric surgery
Primary/secondary endpoints	• Aims stated as: Feasibility, benefits and costs (specifically postoperative complaints, satisfaction score, duration of surgical procedure, LOS, operative costs)
Follow-up (months)	1-12
Drop-outs (n (%))	None
Patient characteristics	
Age of patients (yrs.)	IG: Ø 44 ±4 CG: 48 ±4, p=ns
Sex (% female)	IG: 27% CG: 33%, p=NR
BMI (kg/m²)	IG: Ø 24.8 ±0.7 CG: Ø 25.3 ±1.2, p=NR
Clinical classification	NR
Patient-relevant outcomes	
Survival (overall and disease-specific or disease-free)	NR
Recurrence (local, regional or distant)	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	IG vs. CG, p=NR *1 month after surgery:* • Dysphagia for solids: 1/9 (11%) vs. 2/11 (18%) • Epigastric pain: 1/9 (11%) vs. 0 • Flatulence: 1/9 (11%) vs. 2/11 (18%) *3 months after surgery* • Dysphagia for solids: 1/9 (11%) vs. 0 • Epigastric pain: 2/9 (22%) vs. 0 • Flatulence: 1/9 (11%) vs. 0 *12 months after surgery* • Dysphagia for solids: 0 vs. 0 • Epigastric pain: 0 vs. 0 • Flatulence: 0 vs. 2/11 (18%) Soft stools: 1/9 (11%) vs. 0
Time to resume work/daily activities	NR
Patient satisfaction	NR
Safety-related outcomes	
Intraoperative complications (e.g. air-leakage)	NR
Postoperative compli-	NR

Oesophagus	
	Antireflux/Fundoplication
Author, year [reference number]	**Nakadi et al. 2006** [14]
cations (e.g. infections)	
Re-operations/additional surgeries	IG: 1/9 (11%), because of gastric torsion CG: 0, p=NR
Conversion	IG: 1/9 (11%) CG: 0, p=NR
Perioperative events & resource use	
Blood loss (in ml)	NR
Operation time in min.	IG: Ø 137 ±12 CG: Ø 94 ±5, p<0.01
Transfusions	NR
Drain duration (days)	NR
Length of hospital stay (days)	IG: Ø 4.4 ±0.2 CG: Ø 4.1 ±0.3, p=ns

Oesophagectomy	
Author, year [reference number]	**Van der Sluis et al. 2018** [15]
Study design	Single centre RCT
Country	Netherlands
Funding/Sponsor	None (but affiliations to Intuitive Surgical Inc.)
Intervention (IG) | Product	Robot-assisted minimally invasive thoracolaparoscopic oesophagectomy | da Vinci Robotic System
Comparator (CG)	Open transthoracic oesophagectomy
Experience of surgeon(s), time period	All surgical procedures were performed by 2 surgeons, who performed at least 50 of both procedures each. January 2012 to August 2016
Number of patients	IG: 54 CG: 55
Inclusion/exclusion criteria	Inclusion Criteria[44]: • Histologically proven squamous cell carcinoma, adenocarcinoma or undifferentiated carcinoma of the intrathoracic esophagus (including Siewert I and II). • Surgical resectable (T1-4a, N0-3, M0) • Age ≥18 and ≤80 years. • European Clinical Oncology Group (ECOG) performance status 0,1 or 2 • Written informed consent Exclusion Criteria: • Carcinoma of the cervical esophagus • Carcinoma of the gastro-esophageal junction (GEJ) with major tumor in the gastric cardia (Siewert III) • Prior thoracic surgery at the right hemithorax or thorax trauma (rationale: these patients will undergo open resection)
Primary endpoint	Primary: Surgery-related postoperative complications. Secondary: mortality (in-hospital and within 30 days), pulmonary complications, cardiac complications,

[44] Inclusion and exclusion information extracted from the clinical trials website

Oesophagectomy	
Author, year [reference number]	**Van der Sluis et al. 2018** [15]
	perioperative outcomes, quality of life, functioning, pain
Follow-up (months)	M: 40 Months
Drop-outs (n, %)	41% for quality of life data
Patient characteristics	
Age of patients (yrs.)	Ø 64 (±8.9) CG: Ø 65 (±8.2) p=NR
Sex (% female)	IG: 15% CG: 24% p=NR
BMI (kg/m²)	IG: Ø 26.1 (±4.4) CG: Ø 25.5 (±4.7) p=NR
Disease	Oesophageal Cancer
Clinical classification	Clinical stage, p=NR IA: IG 7%; CG 7% IIA: IG 9%; CG 6% IIB: IG 20%; CG 33% IIIA: IG 24% CG 38%; IIIB: IG 24%; CG 11% IIIC: IG 15%; CG 6% Clinical stadium, p=NR cT1N0: IG 7%; CG 7% cT1N1: IG 2%; CG 4% cT2N0: IG 9%; CG 6% cT2N1: IG 7%; CG 7% cT2N2: IG 2%; CG 0 cT2N3: IG 2%; CG 0 cT3N0: IG 11%; CG 22% cT3N1: IG 22%; CG 38% cT3N2: IG 24%; CG 11% cT3N3: IG 11%; CG 4% cT4aN2: IG 2%; CG 0 cT4aN3: IG 0; CG 2%
Clinically-relevant outcomes[45]	
Positive surgical margins	NR
Patient-relevant outcomes	
Survival (overall and disease-specific or disease-free)	In-hospital mortality: IG: 2/54 (4%); CG: 1/55 (2%), p=ns 30-day mortality: IG: 1/54 (1%); CG 0, p=ns 60-day mortality: IG: 3/54 (6%); CG: 1/55 (2%), p=ns 90-day mortality IG: 5/54 (9%); CG: 1/55 (2%), p=ns Disease-free survival: IG: M 26 months; CG M 28 months, p=ns[46]
Recurrence (local, regional or distant)	NR
Quality of life (e.g. measured by EQ-5D	QLQ-C30:

[45] Entered as potential endpoint category only in cancer-relevant procedures

[46] Overall survival (Kaplan-Meier) plots are shown but data is unclear

Oesophagectomy	
Author, year [reference number]	**Van der Sluis et al. 2018** [15]
or SF-36)	Health-related quality of life @ discharge: IG: Ø 57.9 $CI_{95\%}$ [49.9;66.1] vs. Ø CG: 44.6 $CI_{95\%}$ [36.7;52.5], p=<0.05 Health-related quality of life @ 6 wk: IG: Ø 68.7 $CI_{95\%}$ [61.5;75.9] vs.CG: Ø 57.6 $CI_{95\%}$ [50.6;64.6], p<0.05 Physical functioning @ discharge: IG: Ø 54.5 $CI_{95\%}$ [45.8;63.3] vs.CG: Ø 41.0 $CI_{95\%}$ [32.4;49.6], p< 0.05 Physical functioning @ 6 wk: IG: Ø 69.3 $CI_{95\%}$ [61.6;76.9] vs.CG: Ø 58.6 $CI_{95\%}$ [51.1;66.0], p=0.05 Postoperative pain @ 14 days (VAS): IG: Ø 1.86 vs. CG: 2.62, p<0.001
Time to resume work/daily activities	Functional recovery within 2 weeks[47]: IG: 38/54 (70%); CG 28/55 (51%), p<0.05
Patient satisfaction	NR
Safety-related outcomes	
Intraoperative complications (e.g. air-leakage)	IG: 7/54 (13%) vs. CG: 9/55 (16%) p=ns
Postoperative complications (e.g. infections)	Overall surgery-related postoperative complications (Clavien-Dindo ≥2): IG: 32/54 (59%) vs. CG: 44/55 (80%), RR 0.74 $CI_{95\%}$ [0.57;0.96], p<0.05 Overall postoperative complications (MCDC grade≥2) IG: 34/54 (63%) vs CG: 44/55 (80%), RR 0.79 $CI_{95\%}$ [0.62;1.00], p=0.05 Pulmonary complications: IG 17/54 (32%) vs. CG 32/55 (58%), RR 0.54 $CI_{95\%}$, [0.34;0.85], p = 0.005 ➢ Pneumonia: IG 15 vs. CG 30, p<0.01 ➢ Pneumothorax: IG 0 vs. CG 3, p=ns ➢ Pulmonary embolism: IG 3 vs. CG 1, p=ns ➢ ARDS: IG 0 vs. CG 1, p=ns Cardiac complications: IG 17/45 (22%) vs. CG 26/55/47%) 0.47 $CI_{95\%}$, [0.27;0.83], p <0.01 ➢ Atrial fibrillation: IG 12; CG 25, p=0,01 ➢ Cardia asthma:IG 1; CG 1, p=ns Wound infections: IG 2/54 (4%) vs. CG 8/55 (15%), p=ns ➢ Cervical : IG 2 vs. CG 1, p=ns ➢ Thoracic: IG 0 vs. CG 5, p=ns ➢ Abdominal: IG 0 vs. CG 2, p=ns Anastomic leakage ➢ Type I (conservative): IG 0 vs. CG 0 ➢ Type II (non-surgical intervention) : IG 1 vs. CG 0 ➢ Type III (surgical intervention) : IG 12 vs. CG 11 Mediastinitis : IG 12 vs. CG 11, p=ns Thoracic epymea: IG 2 vs. CG 3, p=ns Gastric conduit necrosis Type III (conduit necrosis extensive, treated with resection and diversion): IG 1 vs. CG 2, p=NR Chylothorax, p=NR ➢ Type I (dietary, low-fat elemental formula gavage): IG 9 vs. CG 6 ➢ Type II (total parenteral nutrition): IG 6 vs. CG 5 ➢ Type III (operative): IG 2 vs. CG 1 Recurrent laryngeal nerve injury ➢ Type I (no therapy): IG 5 vs. CG 6, p=NR Postoperative bleeding: IG 2 vs. CG 2, p=ns Dehiscence of abdominal fascia: IG 0 vs. CG 1, p=ns

[47] Defined as: removal of thoracic tubes; no requirement of intravenous fluid resuscitation; tolerance for solid oral intake; ability to mobilize independently; adequate pain control with analgesics

Oesophagectomy	
Author, year [reference number]	**Van der Sluis et al. 2018** [15]
Re-operations/additional surgeries	IG: 13/54 (24%) vs. CG:18/55 (33%), p=ns
Conversion to laparoscopic/open surgery	IG: 3/54 (5%) vs. CG: NA
Perioperative events & resource use	
Blood loss (in ml)	IG M 400 (IQR 258–581) vs. CG: M 568 (IQR 428–800), p<0.001
Operation time in min.	IG: Ø 349 (±56.9) vs. CG: Ø 296 (±33.9) p<0.001
Transfusions	NR
Drain duration (days)	NR
Length of hospital stay (days)	IG:M 14 (IQR 11–25) CG: M 16 (IQR 11–27), p=ns

Stomach		
	Gastrectomy	**Gastrectomy**
Author, year [reference number]	**Pan et al. 2017** [16]	**Wang et al. 2016** [17]
Study design	Single centre RCT of patients with gastric cancer	Single-centre RCT of patients with gastric cancer
Country	China	China
Funding/Sponsor	Supported by the Social Development Fund of Jiangsu Province	National Natural Science Foundation of China
Intervention (IG) | Product	Robotic gastrectomy | NR	Robotic gastrectomy | NR
Comparator (CG)	Laparoscopic gastrectomy	Open gastrectomy
Experience of surgeon(s), time period	The surgical team had experience with >550 cases of robotic gastrectomy. Operations were performed January 2015-August 2016	NR Patients were recruited May 2012-December 2014
Number of patients	IG: 102 CG: 61	IG: 153 CG: 158
Inclusion/exclusion criteria	Inclusion: • Endoscopy-considered and biopsy-proven gastric cancer; clinical stage of I, II, or III based on the 7th version of the pathologic classification of the International Union Against Cancer • ASA score of ≤2 Exclusion • Serious cardiovascular or respiratory disorders; hepatic or renal failure; other tumors or metastases; surgical failure (conversion to open surgery); D1/D3/D4 lymphadenectomy	Inclusion: • Patients with gastric cancer, pathologically confirmed via gastroscopy Exclusion: • Patients who had remote metastasis • Preoperative chemotherapy • A history of abdominal surgery • ASA scores above Grade III • Patients with detected abdominal cavity metastases during surgery or who were transferred to open gastrectomy • Patients with factors known to influence fast-track recovery, such as pregnancy, cardiopulmonary dysfunction, chronic kidney or liver disease, complicated diabetes, or anti-cholinergic drug administration,
Primary/secondary endpoints	• Assessed perioperative outcomes and postoperative complications	• Primary: duration of hospitalization, number of nodes retrieved in lymph node dissection, resection type, reconstruction type, surgery duration, proximal and distal resection margins, estimated blood loss, and morbidity and mortality during the first 30 days after the procedure
Follow-up (months)	11	NR

Stomach		
	Gastrectomy	**Gastrectomy**
Author, year [reference number]	**Pan et al. 2017** [16]	**Wang et al. 2016** [17]
Drop-outs (n (%))	None	IG: 7/158 (4.43%) CG: 8/153 (5.23%)
Patient characteristics		
Age of patients (yrs.)	IG: Ø 65.1 ±11.8 CG: Ø 65.7 ±13.6, p=ns	IG: Ø 57.5 ±12.7 CG: Ø 55.9 ±13.1, p=ns
Sex (% female)	IG: 36% CG: 26%, p=ns	IG: 27.82% CG: 38.62%, p=ns
BMI (kg/m²)	IG: Ø 24.1 ±1.7 CG: Ø 23.9 ±1.6, p=ns	IG: Ø 22.1 ±2.9 CG: Ø 21.3 ±2.5, p=ns
Clinical classification	ASA (IG vs. CG), p=ns I: 77% vs 77% II: 23 vs. 23% TNM (IG vs. CG), p=ns I: 22% vs. 11% II: 46% vs. 64% III: 32% vs. 25%	ASA (IG vs. CG), p=ns I: 39% vs. 35% II: 54% vs. 53% III: 7% vs. 7% TNM (IG vs. CG), p=ns Ia: 11% vs. 9% Ib: 5% vs. 6% IIa: 11% vs. 15% IIb: 22% vs. 26% IIIa: 17% vs. 16% IIIb: 27% vs. 25% IIIc: 7% vs. 5%
Clinically-relevant outcomes		
Positive surgical margins	NR	Proximal resection margin (cm) IG: Ø 5.3 ±1.5 CG: Ø 5.1 ±1.9, p=ns Distal resection margin (cm) IG: Ø 5.5 ±1.7 CG: Ø 5.3 ±1.5, p=ns
Patient-relevant outcomes		
Survival (overall and disease-specific or disease-free)	IG: 102/102 (100%) CG: 61/61 (100%)	Intraoperative IG: 151/151 (100%) CG: 145/145 (100%)
Recurrence (local, regional or distant)	NR	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	VAS for pain (IG vs. CG) 1st postoperative day: Ø 2.6 ±0.7 vs Ø 7.5 ±1.2, p<0.00 2nd postoperative day: Ø 0.8 ±0,8 vs Ø 3.5 ±1.3, p<0.00 3rd postoperative day: Ø 0.1 ±0.3 vs. Ø 1.0 ±1.0, p<0.00	NR
Time to resume work/daily activities	NR	NR
Patient satisfaction	NR	NR
Safety-related outcomes		
Intraoperative complications (e.g. air-leakage)	NR	IG: 0 CG: 0
Postoperative complications (e.g. infections)	IG vs. CG during 11-months FU, p=ns:	At 30 days (p=ns):

Stomach		
	Gastrectomy	**Gastrectomy**
Author, year [reference number]	**Pan et al. 2017** [16]	**Wang et al. 2016** [17]
	• Ileus: 0 vs. 1/61 (1.6%) • Wound infection: 2/102 (2.0%) vs. 4/61 (6.6%) • Pneumonia: 2/102 (1.96%) vs. 4/61 (6.6%) • Oesphago-jejunal anastomosis leak: 0 vs. 2/61 (3.3%) • Duodenal stump leak: 1/102 (1.0%) vs. 1/61 (1.6%) • None: 97/102 (95.1%) vs. 49/61 (80.3%)	IG: 14/151 (9.3%) CG: 15/145 (10.3%) Clavien Dindo classification (IG vs. CG), p=ns I: 7/14 (50.0%) vs. 6/15 (40.0%), of these: • Surgical site infection: 3/14 (21.4%) vs. 4/15 (26.7%) • Fever: 3/14 (21.4%) vs. 2/15 (13.3%) • Fluid collection/abscess: 1/14 (7.1%) vs. 0 II: 3/14 (21.4%) vs. 4/15 (26.7%) of these: • Pneumonia: 2/14 (14.3%) vs. 3/15 (20.0%) • Intra-abdominal bleeding: 1/14 (7.1%) vs. 1/15 (6.7%) III: 4/14 (28.6%) vs. 4/15 (26.7%), of these: • Fluid collection: 0 vs. 1/15 (6.7%) • Anastomotic leakage: 4/14 (28.6%) vs. 3/15 (20.0%) IV: 0 vs 1/15 (6.7%), of these: • Acute renal failure: 0 vs. 1/15 (6.7%)
Re-operations/additional surgeries	1 patient in the CG group required Braun anastomosis on postoperative day 10 because of jejunal afferent loop obstruction.	IG: 4/14 (28.6%) CG: 3/15 (20.0%), p=NR (all due to anastomotic leakages).
Conversion	Conversion as exclusion criterion	NR
Perioperative events & resource use		
Blood loss (in ml)	IG: Ø 41.3 ±20.2 CG: Ø 83.7 ±32.8, p<0.01	IG: Ø 94.2 ±51.5 CG: Ø 152.8 ±76.9, p<0.001
Operation time in min.	IG: Ø 153.1 ±16.4 CG: Ø 152.0 ±23.6, p=ns	IG: Ø 242.7 ±43.8 CG: Ø 192.4 ±31.5, p<0.01
Transfusions	NR	IG: 1/14 (7.1%) CG: 1/15 (6.7%), p=NR
Drain duration (days)	NR	NR
Length of hospital stay (days)	IG: Ø 3.8 ±0.7 CG: Ø 5.4 ± 1.2, p<0.001	IG: Ø 5.7 ±2.3 CG: Ø 6.4 ±2.5, p<0.05

Stomach	
	Bariatric Surgery
Author, year [reference number]	**Sanchez et al. 2005** [18]
Study design	Single-centre RCT
Country	USA
Funding/Sponsor	NR
Intervention (IG) | Product	Totally robotic laparoscopic Roux-en-Y gastric bypass | da Vinci Surgical System
Comparator (CG)	Laparoscopic Roux-en-Y gastric bypass
Experience of surgeon(s), time period	Standard Food and Drug Administration mandated training on the da Vinci system Operations were performed July 2004-April 2005
Number of patients	IG: 25 CG: 25

Stomach	
	Bariatric Surgery
Author, year [reference number]	**Sanchez et al. 2005** [18]
Inclusion/exclusion criteria	Inclusion: NR Exclusion: NR All patients met the minimal criteria for bariatric surgery proposed by the National Institute of Health Consensus Development Panel report of 1991
Primary/secondary endpoints	Not stated as such but included, learning curve analysis, safety, operative times and length of stay
Follow-up (months)	NR
Drop-outs (n (%))	None
Patient characteristics	
Age of patients (yrs.)	IG: M 43.3 (R 27-58) CG: M 44.4 (R 20-59), p=ns
Sex (% female)	IG: 92% CG: 88%, p=ns
BMI (kg/m²)	IG: M 45.5 (R 35-62) CG: M 43.4 (R 37-55), p=ns
Clinical classification	NR
Patient-relevant outcomes	
Survival (overall and disease-specific or disease-free)	NR
Recurrence (local, regional or distant)	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	NR
Time to resume work/daily activities	NR
Patient satisfaction	NR
Safety-related outcomes	
Intraoperative complications (e.g. air-leakage)	Complication rate IG vs CG, p=ns Minor complications (IG vs. CG): Oversewed gastrojejunostomy leak after positive bubble test: 1/25 (4%) vs. 0. Major complications (IG vs. CG): 0 vs. 0
Postoperative complications (e.g. infections)	IG: 0 CG: 0
Re-operations/additional surgeries	NR
Conversion	IG: 1/25 (4%) required conversion to traditional LRYGB because of exterior anatomy, p=NR CG: 0
Perioperative events & resource use	
Blood loss (in ml)	NR
Operation time in min.	IG: Ø 130.8 CG: Ø 149.4, p<0.02
Transfusions	NR

Stomach	
	Bariatric Surgery
Author, year [reference number]	**Sanchez et al. 2005** [18]
Drain duration (days)	NR
Length of hospital stay (days)	IG: Ø 2.7 (R 2-4) CG: Ø 2.7 (R 2-3), p=ns

Bowel	
	Colectomy
Author, year [reference number]	**Park et al. 2012** [19]
Study design	Single-centre RCT of patients with newly diagnosed right-sided colonic carcinoma
Country	Korea
Funding/Sponsor	Supported by the Basic Science Research Programme through the National Research Foundation of Korea funded by the Ministry of Education, Science and Technology
Intervention (IG) | Product	Robot-assisted colectomy | da Vinci Surgical System
Comparator (CG)	Laparoscopically assisted colectomy
Experience of surgeon(s), time period	Single surgeon The operating team had undertaken 30 robotic surgery procedures (including five robotic right colectomies) before starting this clinical trial. Operations were performed September 2009-July 2011
Number of patients	IG: 35 CG: 36
Inclusion/exclusion criteria	Inclusion: • Age (≥18 years) with newly diagnosed right-sided colonic carcinoma were potential candidates Exclusion: • Patients who were unfit for operative treatment • Patients who presented with an acute surgical emergency, including intestinal obstruction or perforation; • Patients with distant metastasis on preoperative evaluation • Patients with an advanced tumour with adjacent organ invasion requiring en bloc multiple organ resection.
Primary/secondary endpoints	• Length of hospital stay • Secondary endpoints: duration of operation, complications, pathological completeness of tumour excision and postoperative pain
Follow-up (months)	24-120 hours
Drop-outs (n (%))	IG: 0 CG: 1/36 (2.78%) did not receive intervention due to intraperitoneal chemotherapy
Patient characteristics	
Age of patients (yrs.)	IG: Ø 62.8 ±10.5 CG: Ø 66.5 ±11.4, p=ns
Sex (% female)	IG: 60% CG: 54%, p=ns
BMI (kg/m²)	IG: Ø 24.4 ±2.5

Bowel	
	Colectomy
Author, year [reference number]	**Park et al. 2012** [19]
	CG: Ø 23.8 ±2.7, p=ns
Clinical classification	TNM (IG vs. CG) p=ns: I: 26% vs. 29% II: 46% vs. 46% III: 29% vs. 26% ASA (IG vs. CG) p=ns: I: 43% vs. 60% II: 46% vs. 34% III: 11% vs. 6%
Clinically-relevant outcomes	
Positive surgical margins	Proximal margin (cm) IG vs CG: Ø18.6 ±7.3 vs. Ø18.3 ±9.9, p=ns Distal margin (cm) IG vs CG: Ø18.0 ±9.0 vs. Ø14.5 ±8.0, p=ns
Patient-relevant outcomes	
Survival (overall and disease-specific or disease-free)	At 30-day: IG: 35/35 (100%) CG: 35/35 (100%), p=ns
Recurrence (local, regional or distant)	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	VAS (IG vs. CG) 24 hours: Ø 6.1 ±2.2 vs. Ø 6.1 ±2.2, p=ns 120 hours: Ø 2.0 ±1.8 vs. Ø 2.2 ±1.9, p=ns
Patient satisfaction	NR
Safety-related outcomes	
Intraoperative complications (e.g. air-leakage)	IG: 0 CG: 0
Postoperative complications (e.g. infections)	IG vs. CG Total morbidity 6/35 vs 7/35 p=ns: • Wound infection: 2/35 (5.71%) vs. 2/35 (5.71%) • Anastomosis leakage: 1/35 (2.86%) vs. 0 • Intra-abdominal abscess: 0 vs. 1/35 (2.86%) • Bleeding: 1/35 (2.86%) vs. 3/35 (8.57%) • Ileus: 1/35 (2.86%) vs. 1/35 (2.86%) Grade of morbidity (Clavien-Dindo (IG vs. CG)) p=ns: • I-II: 5/35 (14.29%) vs. 6/35 (17.14%) • III-IV: 1/35 (2.86%) vs. 1/35 (2.86%)
Re-operations/additional surgeries	NR

Bowel	
	Colectomy
Author, year [reference number]	**Park et al. 2012** [19]
Conversion	IG: 0 CG:0, p=ns
Perioperative events & resource use	
Blood loss (in ml)	IG: Ø 35.8 ±26.3 CG: Ø 56.8 ±31.3, p=ns
Operation time in min.	IG: Ø 195 ±41 CG: Ø 130 ±43, p<0.001
Transfusions	IG: 0 CG: 0, p=ns
Drain duration (days)	NR
Length of hospital stay (days)	IG: Ø 7.9 ±4.1 CG: Ø 8.3 ±4.2, p=ns

Bowel		
	Rectal resection	**Rectal resection**
Author, year [reference number]	**Jayne et al. 2017** [20]	**Kim et al. 2018** [21]
Study design	International multicentre RCT of patients with rectal adenocarcinoma (ROLARR clinical trial)	Single-centre RCT of patients with mid to low-lying rectal cancer.
Country	29 sites across 10 countries (UK, Italy, Denmark, US, Finland, South Korea, Germany, France, Australia, Singapore)	South Korea
Funding/Sponsor	Medical Research Council and NIH	National Cancer Center
Intervention (IG) | Product	Robot-assisted laparoscopic rectal cancer resection | da Vinci Surgical System	Robot-assisted laparoscopic rectal cancer resection | da Vinci Surgical System
Comparator (CG)	Laparoscopic rectal cancer resection	Laparoscopic surgery
Experience of surgeon(s), time period	40 surgeons with minimum 30 previous minimally invasive rectal cancer resections, of which 10 conventional and 10 robot-assisted. Patients assessed for eligibility January 2011-September 2014.	2 surgeons; each had performed laparoscopic rectal cancer in over 500 patients and robot-assisted surgeries in over 30 patients. Randomisation occurred February 2012-March 2015
Number of patients	IG: 237 randomised; 1 withdrew before surgery CG: 234 randomised; 4 had no surgery after randomisation	IG: 81 randomised, 66 available for analysis (rest excluded after randomisation) CG: 81, 73 available for analysis (rest excluded after randomisation)
Inclusion/exclusion criteria	Inclusion: • Diagnosis of adenocarcinoma of the rectum Exclusion: • Patients with benign lesions of the rectum, cancers of the anal canal, local advanced cancers not amenable to curative surgery or synchronous colorectal tumors requiring multisegment surgical resection	Inclusion: • Patients with mid or low-lying rectal cancer without distant metastases • All patients had rectal adenocarcinoma located within 9 cm of the anal verge Exclusion: • Cancer invading adjacent organs, distant metastases, severe concomitant disease • any other malignancy,

Bowel		
	Rectal resection	**Rectal resection**
Author, year [reference number]	**Jayne et al. 2017** [20]	**Kim et al. 2018** [21]
		• pregnant or breastfeeding females, • hereditary colorectal cancer, • emergency operation. • Patients with c3NO-2 tumors received preoperative chemoradiotherapy
Primary/secondary endpoints	• Primary endpoint: Rate of conversion to open surgery • Secondary endpoints: 30-day operative mortality, duration of operation, complications, pathological completeness of tumour excision, patient-reported bladder (International Prostate Symptom Score, I-PSS) and sexual function (International Index of Erectile Function, IIEF, and Female Sexual Function Index, FSFI)	• Primary endpoint: Completeness of total mesorectal excision • Secondary outcomes: circumferential and distal resection margin; Global Operative Assessment of Laparoscopic Skills; bowel function; morbidity (postoperative complications using Clavien-Dindo); postoperative pain (Present Pain Intensity Index and VAS); QoL (via Korean version of EORTC QLQ-C30 and the colorectal cancer module QLQ-CR38).
Follow-up (months)	30 days and 6 months (latter for QoL)	QOL: postoperative; 3 weeks; 3 months; 12 months
Drop-outs (n (%))	IG: 1/236 (0.4%) CG: 4/230 (1.7%) PROP bladder data available on 351/466 (75%) PROP sexual function data available on 181/230 men (57%) and 54/15 (36%) women	NR
Patient characteristics		
Age of patients (yrs.)	IG: Ø 64.4 ±10.98 CG: Ø 65.5 ±11.93, p=NR	IG: Ø 60.4±9.7 CG: Ø 59.7±11.7, p=ns
Sex (% female)	IG: 32% CG: 32%, p=NR	IG: 23% CG: 29%, p=ns
BMI (kg/m²)	IG vs. CG, p=NR Underweight/normal (BMI 0-24.9): 39% vs 37% Overweight (BMI 25.0-29.9): 38% vs. 39% Obese (BMI ≥ 30.0): 23% vs 24%	IG: Ø 24.1 ± 3.3 CG: Ø 23.6 ± 3.0, p=ns
Clinical classification	T stage (IG vs. CG), p=NR: 0: 9% vs. 10% 1: 10% vs. 9% 2: 27% vs. 27% 3: 50% vs. 50% 4: 4% vs. 2% Tx or missing: 2% vs. 1% N stage: 0: 62% vs. 65% 1:27% vs. 25% 2:11% vs. 9%	ASA (IG vs. CG), p=ns: I: 30% vs. 41% II: 70% vs. 59% p/ypT classification, p=ns T0: 8% vs. 8% Tis: 3% vs. 6% T1: 12% vs 10% T2: 26% vs. 25% T3: 46% vs. 49% T4a: 3% vs. 1% T4b: 3% vs. 1%

Bowel		
	Rectal resection	**Rectal resection**
Author, year [reference number]	**Jayne et al. 2017** [20]	**Kim et al. 2018** [21]
	ASA (IG vs. CG) I: 17% vs. 22% II: 63% vs. 53% III: 19% vs. 22% IV: 0% vs. 0.4% Missing: 1% vs 2%	p/ypN classification, p=ns N0: 70% vs. 77% N1a: 14% vs. 7% N1b: 11% vs. 8% N1c: 3% vs. 3% N2a: 3% vs. 4% N2b: 0% vs. 1%
Clinically-relevant outcomes		
Positive surgical margins	Circumferential resection margin positivity[48]: IG: 12/235 (5.1%) CG: 14/224 (6.3%) OR 0.78 $CI_{95\%}$ [0.35 ;1.76], p=ns	Circumferential resection margin positivity[1]: IG:4/66 (6.1%) CG: 4/73 (5.5%), p=ns Proximal resection margin cm IG: M12.3 (R 4.7-35.8) CG: M 13.2 (R6.8-29.0), p=ns Distal resection margin cm IG: M 1.5 (R 0.04-6.7) CG: M 0.7 (R 0-2.5), p=ns
Patient-relevant outcomes		
Survival (overall and disease-specific or disease-free)	Mortality within 30 days: IG: 2/236 (0.8%) CG: 2/230 (0.9%), p=ns	NR
Recurrence (local, regional or distant)	NR	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	IPSS score difference of 0.74 $CI_{95\%}$[-0.59;2.07], p=ns IIEF score difference of 0.80 $CI_{95\%}$[-4.10;5.70], p=ns FSFI score difference of 1.23 $CI_{95\%}$[-3.54;6.00], p=ns	PPI pain score postoperative day: IG M 1 (R 0-4) vs. CG M 1 (R 0-4), p=ns VAS score postoperative day: IG M 3(R 1-9) vs. CG M 2 (R 0-8), p=ns Authors report no difference in scores on QLQ-C30 after 3 weeks, 3 months and 12 months except for insomnia scores, where IG showed more sleep disturbances: IG Ø 28.3 $CI_{95\%}$[19.6;37] vs. CG Ø 15.7 $CI_{95\%}$[8.1;23.3], p<0.05 Reported that there were no significant differences on QLQ-CR38 scores except for sexual function after 12 months, where IG showed better functioning: Ø 35.2 $CI_{95\%}$[26.9;43.5] vs. Ø 23.0 $CI_{95\%}$[15.7;30.2], p<0.05
Time to resume work/daily activities	NR	NR
Patient satisfaction	NR	NR
Safety-related outcomes		

[48] Defined as tumor cells within 1mm of the circumferential resection margin on histological analysis

Bowel		
	Rectal resection	**Rectal resection**
Author, year [reference number]	**Jayne et al. 2017** [20]	**Kim et al. 2018** [21]
Intraoperative complications (e.g. air-leakage)	IG: 36/236 (15.3%) CG: 34/230 (14.8%), p=ns	Intraoperative (p=ns) IG: 5/66 (7.6%) CG: 3/73 (4.1%) Perioperative complications (p=ns) IG: 23/66 (34.8) CG: 17/73 (23.3%) Clavien-Dindo classification (IG vs. CG), p=ns: I: 6/66 (9.1%) vs. 3/73 (4.1%) II: 11/66 (16.7) vs. 10/73 (13.7%) IIIa: 4/66 (6.4%) vs. 2/73 (2.7%) IIIb: 2/66 (3.0%) vs. 2/73 (2.7%)
Postoperative complications (e.g. infections)	Within 30 days: IG: 78/236 (33.1%) CG: 73/230 (31.7%), p=ns >30days and ≤6months: IG: 34/236 (14.4%) CG: 38/230 (16.5%), p=ns	NR
Re-operations/additional surgeries	NR	NR
Conversion	IG: 19/236 (8.1%) CG:28/230 (12.2%) Unadjusted risk difference 4.1% $CI_{95\%}$[-1.4%;9.6%]	IG: 1/66 (1.5%) CG: 0, p=ns
Perioperative events & resource use		
Blood loss (in ml)		IG: M 100 (R 0-1000) CG: M 50 (R 0-300), p<0.0001
Operation time in min.	IG: Ø 298.5 ±88.71 CG: Ø 261.0 ±83.24, p=NR Difference in use of operating theatre (IG minus CG): Ø 50.88 minutes $CI_{95\%}$[-20.26;81.56], p=0.001	IG: Ø 339.2 ±80.1 CG: Ø 227.8 ±65.6, p<0.0001
Transfusions	NR	NR
Drain duration (days)	NR	NR
Length of hospital stay (days)	IG: Ø 8.0 ±5.85 CG: Ø 8.2 ±6.03, p=NR	IG: Ø 10.3 ±3.4 CG: Ø 10.8 ±7.4, p=ns

Rectal Resection		
Author, year [reference number]	**Debakey et al. 2018** [24]	**Wang et al. 2017** [23]
Study design	Single centre RCT	Single centre RCT
Country	Egypt	China
Funding/Sponsor	Funded by the National Cancer Institute,	National Natural Science Foundation of China

Rectal Resection		
Author, year [reference number]	**Debakey et al. 2018** [24]	**Wang et al. 2017** [23]
	Cairo University,Egypt.	(Grant no. 81500417)
Intervention (IG) | Product	Robot-assisted rectal cancer resection | Da Vinci robotic system Intuitive Surgical Inc, (Sunnyvale, CA)	Robot-assisted total mesorectal excision | device unspecified
Comparator (CG)	Conventional laparoscopic rectal resection	Conventional laparoscopic total mesorectal excision
Experience of surgeon(s), time period	Procedures were performed by the same surgeon team but no information on experience. Randomisation performed April 2015 to February 2017	No information on experience of surgeons Randomisation performed November 2010 to September 2013
Number of patients	IG: 21 CG: 24	IG: 71 CG: 66
Inclusion/exclusion criteria	Inclusion criteria: • Histological diagnosis of adenocarcinoma of rectum located within 15 cm from the anal verge. • No anesthesiological contraindications to minimally invasive surgery • age ≤ 75 years • ASA ≤ 2 Exclusion Criteria: • Metastatic disease • Malignant bowel obstruction (MBO) • Unresectable tumor	Inclusion criteria • Male patients with medium (7-12 cm from the anal verge) to low (≤ 7 cm from the anal verge) rectal cancer Exclusion criteria: • Pre-operative sexual dysfunction (n=61) • History of: prior rectum or urinary tract surgery, abdominal perineal resection, partial mesorectal resection, local or distant recurrence (n=102) • Death within 12 months (n=25) • Incomplete follow-up data (n=11)
Primary endpoint	Short-term operative outcomes and complications, oncological outcomes	Urinary function (via International Prostate Symptom Score where higher scores indicate more severe symptoms) and sexual function (via International Index of Erectile Function where higher score indicates better functioning) Complete erectile dysfuntion defined as domain score < 10; partial erectile dysfunction defined as domain score <17 but ≥19)
Follow-up (months)	1 Month	12 months
Drop-outs (n, %)	NR	Only patients with follow-up data included in analysis
Patient characteristics		
Age of patients (yrs.)	IG: M 53.4 (R 32-67) vs.CG: M 50.3 (R 36-64) p=ns	IG: Ø 60.3 (R 36-68) vs. CG Ø 58.7 (R 36-71), p=ns
Sex (% female)	IG: 48% vs. CG:46%, p=NR	IG: 0% vs CG 0%
BMI (kg/m²)	MBI (kg/m2), p=ns MBI< 30 IG: 48% vs. CG: 33% MBI >/= 30 IG: 11 (52%) vs. CG16 (67%)	IG: Ø 22.9 (R 19.1-30.1) vs. CG: Ø 22.4 (R 18.3-30.6), p=ns
Disease	Rectal cancer	Rectal cancer
Clinical classification	Clinical stage, p=ns I: IG: 1/21 (5%) vs. CG: 4/24 (17%) II: IG:15/21(71%) vs 17/24 (71%) III: IG: 5/21(24%) vs. 3/24 (13%)	TNM (tumour, node, metastasis system) 0/1: IG: 9/71 (13%); CG: 8/66 (12%) II: IG: 22/71 (31%); CG 24/66 (36%) III: IG 40/71 (56%); CG: 34/66 (52%)

Rectal Resection		
Author, year [reference number]	**Debakey et al. 2018** [24]	**Wang et al. 2017** [23]
Clinically-relevant outcomes		
Positive surgical margins	Proximal margin (cm) • IG: M 13 (R 10-20) vs. CG: M 15 (R 11-239; p=ns Distal margin (cm) • IG: M 2.8 (R 1.4-4) vs. CG: M 1.8 (R 1-2.8), p<0.001 Completeness of resection (% complete) • IG: 86% vs. CG: 63%,p=ns	NR
Patient-relevant outcomes		
Survival (overall and disease-specific or disease-free)	30-day mortality: IG: 0/21 (0%) vs. CG: 1/24 (4%) p=NR	30-day mortality: IG: 0/71 (0%); CG: 0/66 (0%)
Recurrence (local, regional or distant)	NR	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	NR	Urinary function IG post-op vs pre-op IPSS: 6.79 vs. 4.04, p=ns CG post-op vs. pre-op IPSS: 9.66 vs. 4.12, p<0.05 Total IPSS scores postoperatively: IG 6.79 vs CG 9.66, p<0.05 Sexual function IG post-op vs. pre-op IIEF: 46.2 vs 56.4, p<0.05 CG post-op vs. pre-op IIEF: 40.1 vs. 57.9, p<0.05 Total IIEF scores postoperatively: IG 46.2 vs CG 40.1, p<0.05 Incidence of partial and complete erectile dysfunction: IG 19/71 (27%); CG 32/66 (48%), p<0.05
Time to resume work/daily activities	NR	Return of gastrointestinal function: IG: 37 h vs CG: 51 h, p<0.05
Patient satisfaction	NR	NR
Safety-related outcomes		
Intraoperative complications (e.g. air-leakage)	NR	NR
Postoperative complications (e.g. infections)	Total number, p=ns: IG: 6/21 (29%) vs.CG: 7/24 (29%) • Anastomotic leakage: IG 1; CG 1 • Ileus (median days): IG: 2; CG 3 • Wound problems: IG 2; CG 2 • Others: IG 1 (DVT); CG 1 (erectile dysfunction) Severity: • No complications: IG 15/21 (71%) vs. 18/24 (75%), p=ns • Grade I: IG 4/21 (19%) vs. CG 5/24 (21%) • Grade II: IG 1/21 (5%) vs. CG 1/24 (4%) • Grade III: IG 1/21 (5%) vs. 0 • Grade IV: IG 0 vs.CG 0 • Grade v: IG 0 vs. CG 1/24	IG: 8/71 (11%): 2 anastomic leakages, 2 lung infections, 1 urinary tract infection, 1 intraabdominal abcess, 1 abdominal cavity bleeding, 1 incisional wound infection CG: 10/66 (15%): 3 anastomic leakages, 3 lung infections, 1 urinary tract infection, 3 incisional wound infections.

Rectal Resection		
Author, year [reference number]	**Debakey et al. 2018** [24]	**Wang et al. 2017** [23]
	(4%)	
Re-operations/additional surgeries	IG: 0 vs. CG: 1/24 (4%), p=NR	NR
Perioperative events & resource use		
Conversion to laparoscopic/open surgery	IG 1/21 (5%) vs. CG: 2/24 (8%), p=NR	NR
Blood loss (in ml)	IG: M 200 (R 50-650) vs. CG: M 325 (R 100-800), p=0.05	NR per treatment group
Operation time in min.	IG: M 201 (R 140-280) vs. CG: M 134.5 (R 110-190), p<0.001	IG: Ø 246.9 (R 210-330) vs CG: 207.3 (R 170-230), p<0.01
Transfusions	NR	NR
Drain duration (days)	NR	NR
Length of hospital stay (days)	IG: M 3 (R 2-14) vs. CG: M 2 (R 2-11), p=ns	NR

Bowel		
	Ventral mesh rectopexy	**Rectal resection**
Author, year [reference number]	**Mäkelä-Kaikonen et al. 2016 (2 references)** [25] [68]	**Tolstrup et al. 2018[49]** [22]
Study design	Single-centre RCT of patients with rectal prolapse and intussusception	Single-centre RCT of patients with rectal adenocarcinoma (ROLARR clinical trial): Denmark centre
Country	Finland	Denmark
Funding/Sponsor	State funding of the Medical Research Center Oulu University and Finnish Menopause Society	NR
Intervention (IG) | Product	Robot-assisted ventral mesh rectopexy | da Vinci Surgical System	Robot-assisted laparoscopic rectal cancer resection | da Vinci Surgical System
Comparator (CG)	Laparoscopic ventral mesh rectopexy	Laparoscopic rectal cancer resection
Experience of surgeon(s), time period	3 experienced surgeons performed IG; 4 (these +1 additional surgeon) performed CG. NR: No of prior operations. Operations performed February to May 2012	30 previous minimally invasive rectal cancer resections, 10 conventional and 10 robot-assisted. Study conducted November 2012 to April 2014.
Number of patients	IG: 16 (total relapse 4, intrassusception 12) CG: 14 (total relapse 2, intrassusception 11, 1 excluded)	IG : 25 CG : 26
Inclusion/exclusion criteria	Inclusion: • females; • age 18-85; • ASA 1-3; • symptomatic, uncomplicated, isolated, rectal prolapse; symptomatic intusseception and enterocele Exclusion: • male; • ASA 4-5;	NR

[49] This study reports on a subset of patients from the ROLARR trial pertaining to the Denmark centre. To avoid double-counting, only those results which are not reported in the main trial publication by Jayne et al are reported here.

Bowel		
	Ventral mesh rectopexy	**Rectal resection**
Author, year [reference number]	**Mäkelä-Kaikonen et al. 2016 (2 references)** [25] [68]	**Tolstrup et al. 2018[49]** [22]
	• previous surgery; pregnancy now or future; suspicion of frozen pelvis	
Primary/secondary endpoints	Perioperative parameters, complications and restoration of anatomy, postoperative pain via VAS	The aim was to assess perioperative pain via numeric rating scale (NRS). Length of surgery and complications were also assessed.
Follow-up (months)	Pain assessment 2 weeks after surgery Quality of life (Pelvic Floor Distress Inventory, Pelvic Floor Impact Questionnaire, Prolapse/Incontinence Sexual Questionnaire) also condition-specific symptom and quality of life questionnaires (unspecified) at 3 months	Discharge from recovery ward
Drop-outs (n (%)	QoL data on total of between 19 and 26 patients; drop-out 35% to 52%	NR
Patient characteristics		
Age of patients (yrs.)	IG: Ø 60.8 ±11.5 CG: Ø 66.0 ±10.1, p=NR	IG: Ø 63 ±10.9 CG: Ø 68 ±9.9, p=ns
Sex (% female)	IG and CG: 100%, p=NR	IG: 72% CG 77%; p=ns
BMI (kg/m²)	IG: Ø 25.6 ±4.5 CG: Ø 24.3 ±3.0, p=NR	IG: Ø 27 ±4.5 CG: Ø 28 ±4.3, p=ns
Clinical classification	ASA (% IG vs. % CG), p=NR 1: 19% vs. 21% 2: 63% vs. 36% 3: 19% vs. 36%	ASA (% IG vs % CG), p=ns: 1: 44% vs. 38% 2: 28% vs. 31% 3: 0 vs. 4% 4: 0 (y)pT-stage (% IG vs. % CG), p=ns: 0: 12% vs. 12% 1: 12% vs. 4% 2: 16% vs. 12% 3: 52% vs. 58% 4: 0 vs. 15%
Clinically-relevant outcomes		
Positive surgical margins	n/a	NR
Patient-related outcomes		
Survival (overall and disease-specific or disease-free)	NR	NR
Recurrence (local, regional or distant)	NR	NR
Quality of life or symptoms (e.g. measured by EQ-5D or SF-36)	VAS @ 2 weeks: IG: Ø 2.9 ±1.8 CG: Ø 2.6 ±1.4, p=ns QoL @ 3 months, mean difference (95% CI): PFDI-20: -61.9 $CI_{95\%}$ [40.9 ;82.8%], p<0.01 PFIQ-7: -57.0 $CI_{95\%}$ [29.3;84.5%], p<0.01 PISQ-12: 3.4 $CI_{95\%}$ [-6.2;-7.6%], p<0.05	NRS mean (recovery[50]): IG: 1.800 (0-5) CG: 2.000 (0-5), p=ns NRS max (recovery): IG: 4 (0-10) CG: 5 (0-9), p=ns

[50] Unclear whether these values relate to actual number, mean or median

Bowel		
	Ventral mesh rectopexy	**Rectal resection**
Author, year [reference number]	**Mäkelä-Kaikonen et al. 2016 (2 references)** [25] [68]	**Tolstrup et al. 2018[49]** [22]
	No significant differences were found in symptom and condition-specific QoL scores in the between-group comparison as reported for the PFDI and 2 subscales (CRADI and POPDI). No between group results reported for PFIQ or PISQ.	
Time to resume work/daily activities	NR	NR
Patient satisfaction	NR	NR
Safety-related outcomes		
Intraoperative complications (e.g. air-leakage)	Perioperative bleeding: IG 2/16; CG 0/14, p=ns	NR
Postoperative complications (e.g. infections)	Vascular complication: IG 1; CG 0, p=ns Minor complications, p=ns: Haemotoma: IG 1/16; CG 0 Perineal pain: IG 1/16; CG 0 Fever: IG 0; CG 1/14	Not clearly stated but likely to be period until discharge: Total IG 10/25, CG 10/26 p=ns. Clavien-Dindo classification: 1: IG 1; CG 4 2: IG 6; CG 1 3: IG 2; CG 4 4: IG 0; CG 1 5: IG 1; CG 0
Re-operations/ additional surgeries	NR	NR
Conversion	IG 0 CG 0	IG: 1/25 CG: 10/26, p<0.01
Perioperative events & resource use		
Blood loss (in ml)	NR	NR
Operation time in min.	IG: Ø 125 ±27 CG: Ø 130 ±25, p=ns	IG: 152±43 CG: 170±57, p=ns
Transfusions	NR	NR
Drain duration (days)	NR	NR
Length of hospital stay (days)	IG: Ø 2.2 ±1.5 CG: Ø 2.5 ±0.9, p=ns	NR

Gallbladder/Liver Spleen		
	Cholecystectomy	**Cholecystectomy**
Author, year [reference number]	**Kudsi et al. 2017** [26]	**Pietrabissa et al. 2016** [27]
Study design	International multicentre RCT of patients with gallbladder disease	Single-centre RCT of patients with gallbladder lithiasis or polyps with no evidence of choledocholithiasis
Country	7 institutions in the USA and 1 institution in Greece	Italy
Funding/Sponsor	Intuitive Surgical, Inc., Sunnyvale, CA, USA in association with the identified study investigators under a cooperative clinical trial agreement	None
Intervention (IG) | Product	Robotic single-site cholecystectomy | da Vinci Single Site Instruments	Single incision laparoscopic robotic cholecystectomy | NR

Gallbladder/Liver Spleen		
	Cholecystectomy	**Cholecystectomy**
Author, year [reference number]	**Kudsi et al. 2017** [26]	**Pietrabissa et al. 2016** [27]
Comparator (CG)	Multiport laparoscopic cholecystectomy	Four-port laparoscopic cholecystectomy
Experience of surgeon(s), time period	At the onset of the study, 8 of the 10 surgeons were new to the single-site technique; however, all 10 surgeons were experienced in laparoscopic and robot-assisted multiport techniques. The RSSC cases include procedures in which the surgeons were learning the technique Enrollment of patients occurred from September 2013-August 2015	Surgeons with prior experience with both operation techniques Operations were performed September 2011-May 2013
Number of patients	IG: 83 CG: 53	IG: 40 CG: 41
Inclusion/exclusion criteria	Inclusion: • Age 18–80 • Diagnosis of symptomatic gallbladder disease Exclusion: • Requirement of emergency procedure, acute cholecystitis, pregnancy, presence of upper midline visible abdominal scar(s) or keloid • Presence of umbilical hernia or prior umbilical hernia repair • Inability of patient to tolerate Trendelenburg position • Pneumoperitoneum • Cirrhosis • Mental impairment	Inclusion: • Diagnosis of gallbladder lithiasis or polyps with no evidence of choledocholithiasis • Age 18- 80 • BMI < 30 kg/m2, • Ability to adhere to the protocol Exclusion • Evidence of acute cholecystitis or stones in the common duct as assessed by liver function tests and abdominal ultrasound • Gallbladder stone > than 3 cm • Previous abdominal surgery through a midline or a right subcostal laparotomic incision • Ongoing pregnancy • Liver cirrhosis • ASA>II • Known allergy to the analgesic drugs adopted in the study protocol
Primary/secondary endpoints	• Patient-perceived cosmesis, patient-reported satisfaction (BIQ, PSQ) and quality of life (QoL-SF 12) • Secondary endpoint: perioperative outcomes	• To evaluate the reduction by 50% of SIRC patients with moderate to severe pain at 24 h after surgery compared to the laparoscopy group • Secondary endpoints: VAS score and cosmetic outcome (subjective min 0-max 10) of the surgical scars. Further objectives: operative times, intra and postoperative morbidity, rate of incisional hernia.
Follow-up (months)	Max. 3 months	IG: M 32.0 IQR [22.4-30.1] CG: M 36.8 IQR [26.9-39.5], p=ns
Drop-outs (n (%))	@ 2 weeks IG: 6/83 (7.2%) CG: 1/53 (1.9%) @ 6 weeks IG: 16/83 (19.3%) CG: 3/48 (6.3%) @ 12 weeks IG: 17/83 (20.5%) CG: 5/53 (9.4%)	IG: 10/40 (25.0%) CG. 10/41 (24.4%)

Gallbladder/Liver Spleen		
	Cholecystectomy	**Cholecystectomy**
Author, year [reference number]	**Kudsi et al. 2017** [26]	**Pietrabissa et al. 2016** [27]
Patient characteristics		
Age of patients (yrs.)	IG: Ø 46.8 ±15.5 CG: Ø 46.5 ±17.3, p=ns	NR, but it was reported "the groups were comparable in terms of age, sex and BMI"
Sex (% female)	IG: 78% CG: 92%, p<0.05	
BMI (kg/m²)	IG: Ø 30.4 ±6.5 CG: Ø 31.7 ±6.7, p=ns	
Clinical classification	ASA (IG vs. CG), p=ns I: 20% vs. 21% II: 63% vs. 64% III: 16 vs. 15% IV: 1 vs. 0	NR
Patient-relevant outcomes		
Survival (overall and disease-specific or disease-free)	NR	NR
Recurrence (local, regional or distant)	NR	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	SF-12: @ 2 weeks, IG vs. CG (Ø±SD): 39±4.19 vs. 39.5±3.95,p=ns @ 6 weeks, IG vs. CG: 39.23 ±3.79 vs. 40±3.41, p=ns @ 3 months, IG vs CG: 40.45±3.05 vs. 41.18±5.53, p=ns	VAS (IG vs. CG), p=ns @ 24h: M 3 IQR [1-8] vs. CG: M 4 IQR [1-9], Δ-1 $CI_{95\%}$ 1 [-5;3] @ 7 days: M 0 IQR [0-2] vs. M 0 IQR [0-2], Δ 0 $CI_{95\%}$ [-2;2], ns @ 30 days: M 0 IQR [0-0] vs. M 0 IQR [0-0], Δ 0 (NA)
Time to resume work/daily activities	NR	NR
Patient satisfaction	BIQ (IG vs. CG) @ 2 weeks Questions 1-5: Ø 5.5 ±1.0 $CI_{95\%}$[5.3;5.8] vs. Ø 6.4 ±1.80 $CI_{95\%}$[5.9;6.9], p<0.01 Questions 6-8: Ø 20.5 ±3.3 $CI_{95\%}$[19.8;21.3] vs. Ø18.5 ±4.5 $CI_{95\%}$[17.3;19.7], p<0.01 @ 6 weeks Questions 1-5: Ø 5.5 ±1.2 $CI_{95\%}$[5.2;5.8] vs. Ø 6.2 ±2.2 $CI_{95\%}$[5.5;6.9], p=ns Questions 6-8: Ø 21.2 ±3.2 $CI_{95\%}$[20.4;22.0] vs. Ø 19.8 ±3.8 $CI_{95\%}$[18.7;21.0], p=ns @ 12 weeks Questions 1-5: Ø 5.4 ±1.4 $CI_{95\%}$[5.1;5.8] vs. Ø 6.1 ±1.5 $CI_{95\%}$[5.6;6.5], p<0.05 Questions 6-8: Ø 22.3 ±2.3 $CI_{95\%}$[21.7;22.8] vs. Ø 20.2 ±3.5 $CI_{95\%}$[19.2;21.2], p<0.01 PSQ (IG vs. CG) @ 2 weeks Questions 1: Ø 8.3 ±2.0 $CI_{95\%}$[5.3;5.7] vs. Ø 7.2 ±2.1 $CI_{95\%}$[5.9;6.9], p<0.01 Questions 5: Ø 7.8 ±2.7	Cosmetic outcome (IG vs. CG) M 9 IQR [8-10] vs. M 8 IQR [7-8], Δ 1 $CI_{95\%}$[0 to 2], p=<0.01

Gallbladder/Liver Spleen		
	Cholecystectomy	**Cholecystectomy**
Author, year [reference number]	**Kudsi et al. 2017** [26]	**Pietrabissa et al. 2016** [27]
	$CI_{95\%}$[7.1;8.4] vs. Ø 6.6 ±2.4 $CI_{95\%}$[5.9;7.3], p<0.05 @ 6 weeks Questions 1: Ø 8.8 ±1.6 $CI_{95\%}$[8.4;9.2] vs. Ø 8.1 ±1.9 $CI_{95\%}$[7.6;8.7], p<0.05 Questions 5: Ø 8.9 ±1.6 $CI_{95\%}$[8.6;9.3] vs. Ø 8.2 ±1.8 $CI_{95\%}$[7.7;8.8], p<0.05 @ 12 weeks Questions 1: Ø 9.2 ±1.1 $CI_{95\%}$[9.0;9.5] vs. Ø 8.1 ±1.9 $CI_{95\%}$[7.5;8.6], p<0.01 Questions 5: Ø 9.4 ±1.1 $CI_{95\%}$[9.2;9.7] vs. Ø 8.2 ±1.8 $CI_{95\%}$[7.6;8.7], p<0.01	
Safety-related outcomes		
Intraoperative complications (e.g. air-leakage)	IG: 0 CG: 0, p=ns	IG vs. CG, p=ns Major adverse events: 0 vs. 0 Bile spillage: 2/30 (6.7%) vs. 5/30 (16,7%), ns Minor bleeding: 3/30 (10.0%) vs. 4/30 (13.3%), ns Liver damage at gallbladder fossa: 1/30 (3.3%) vs. 3/30 (10.0%)
Postoperative complications (e.g. infections)	Total IG 4/83 (5%) vs. CG 2/53 (4%) @ 3 months, p=ns • Bile leakage: 0 vs. 1/53 (1.9%) • Wound infection: 2/83 (2.4%) vs. 1/53 (1.9%) • Inflammatory bowel disease: 1/83 (1.2%) vs. 0 • Deep vein thrombosis/pulmonary embolism: 1/83 (1.2%) vs. 0	IG vs. CG @ 6 months • Wound infection: 2/30 (6.7%) (of these 1 required incisional hernia) vs. 0, p=ns
Re-operations/additional surgeries	NR	NR
Conversion to laparoscopic/open surgery	IG: 0 CG: 0	IG: 0 CG: 0, p=ns
Perioperative events & resource use		
Blood loss (in ml)	IG: 13.1 CG: 15.8, p=ns	NR
Operation time in min.	IG: Ø 61.0 ±27.5 CG: Ø 44.0 ±19.9, p<0.01	IG: Ø 98 ±34 CG: Ø 87 ±30, p=ns
Transfusions	IG: 0 CG: 0	NR
Drain duration (days)	NR	NR
Length of hospital stay (days)	IG: 16.7 hours CG: 13.9 hours, p=ns	IG: M 1.2 (R 1-3) CG: M 1.2 (R 1-3), p=NR

Cholecystectomy	
Author, year [reference number]	**Grochola et al. 2018** [28]
Study design	Single centre RCT
Country	Switzerland
Funding/Sponsor	None
Intervention (IG) | Product	Robot-assisted single-site cholecystectomy | da Vinci single-site ™ cholecystectomy robotic system (Intuitive Surgical Inc, Sunnyvale, CA)
Comparator (CG)	Single-port laparoscopic cholecystectomy
Experience of surgeon(s), time period	Operations performed by three senior surgeons with training and experience in both surgical techniques.
Number of patients	IG 30; CG 30
Inclusion/exclusion criteria	Inclusion: adults with benign gallbladder disease admitted for elective cholecystectomy Exclusion: pregnant or breastfeeding, systemic disease, mental or organic disorders affecting consent/participation, malignant disease, previous abdominal surgery, obesity (BMI > 35.0 kg/m^2).
Primary/secondary endpoints	Surgeon's physical and mental stress load. Secondary: intraoperative outcomes, complications, health-related quality of life, cosmesis
Follow-up (months)	1 year
Drop-outs (n, %)	IG: 0 vs. CG 3/30 (10%) (three patients did not return the HRQoL and BIC questionnaires in the CG group at 1-year follow-up and were therefore excluded from the analyses)
Patient characteristics	
Age of patients (yrs.)	IG Ø 52.4 (R 26-82) vs CG Ø 51.5 (R 30-78), p=ns
Sex (% female)	IG 67% vs. CG 53%, p=ns
BMI (kg/m^2)	IG Ø 27.3 ± 3.9 vs. CG Ø 27.3 ± 4.2, p=ns
Disease	Cholecystolithiasis: IG 29/30 vs. CG 29/30 Galbladder polyps: IG 1 vs. CG 1
Clinical classification	NR
Patient-relevant outcomes	
Survival (overall and disease-specific or disease-free)	NR
Recurrence (local, regional or distant)	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	Gastrointestinal Quality of Life Index: 1 month post-op: IG M 123 (R 83-140) vs. CG M 120 (R55-142), p=ns. 12 months post-op: IG ; 123 (R 105-141) vs. CG ; 128 (94-143), p=ns
Time to resume work/daily activities	
Patient satisfaction	Body Image Questionnaire: 1 month post-op: IG M 37 (R 24-40) vs. CG 38 (19-40), p=ns 12 months post-op: IG M 35.5 (R 20-40) vs. CG M 39 (22-40)NR
Safety-related outcomes	
Intraoperative complications (e.g. air-leakage)	EAES grade: • No complications: IG 18/30 (60%) vs. CG 16/30 (53%), p=ns • Grade I: IG 8/30 (27%) vs. CG 11/30 (37%), p=ns • Grade II: IG 4/30 (13%) vs. CG 3/30 (10%), p=ns • Grade III-IV: IG 0 vs, CG 0. Type of complication, p=ns: • Peritoneal tear (EAES I^o): IG 8/30 (27%) vs. CG 11/30 (37%) • Minor bleeding (EAES II^o): IG 4/30 (13%) vs.CG 3/30 (10%) • Major bleeding (EAES > 11^o): IG 0 vs. CG 0

Cholecystectomy	
Author, year [reference number]	**Grochola et al. 2018** [28]
	• Bile duct injury: IG 0 vs. CG 0
Postoperative complications (e.g. infections)	Complications within 30 days: IG 4/30 (13%) vs. CG 7/30 (23%), p=ns Dindo-Clavien IG vs. CG, p=NR: • No complications: 25/30 (83%) vs. 23/30 (77%) • Grade I: 2/30 (7%) vs. 4/30 (13%) • Grade II: 2/30 (7%) vs. 1/30 (3%) • Grade IIIa: 0 vs. 1/30 (3%) • Grade IIIb: 0 vs. 0 • Grade IVa: 0 vs. 0 • Grade IVb: 0 vs 1/30 (3%) • Grade V: 0 vs. 0 Type of complication (IG vs. CG), p=ns: ➢ Superficial wound infection: 2/30 (3%) vs. 1/30 (3%) ➢ Periumbilical hematoma: 1/30 (3%) vs. 0 ➢ Self-limiting fever episode: 0 vs 1/30 (3%) ➢ Bowel paralysis: 0 vs 1/30 (3%) ➢ Renal function impairment: 0 vs. 1/30 (3%) ➢ Urinary retention: 1/30 (3%) vs. 0 ➢ Nausea: 0 vs. 1/30 (3%) ➢ Common bile duct stones: 0 vs. 1/30 (3%) ➢ Multi-organ failure: 0 vs. 1/30 (3%) Incisional hernia (within 1 post-op year): IG 2/30 (7%) vs. CG 2/30 (7%), p=ns
Re-operations/ additional surgeries	Rate of postoperative complications requiring re-intervention (Dindo-Clavien grade ≥IIIa): IG: 0 vs CG 2/30, p=ns
Conversion to laparoscopic/open surgery	Conversion to conventional laparoscopy: IG 2 (7%) vs. CG 3 (10%), p=ns Conversion to open surgery: IG 0 vs. CG 0
Perioperative events & resource use	
Blood loss (in ml)	IG: M 5.0 (R 0-150) vs. CG: M 3.5 (R 0-300), p=ns
Operation time in min.	IG: M 85.5 (R 48-148) vs. CG: M 74 (R 31-135), p=ns
Transfusions	NR
Drain duration (days)	NR
Length of hospital stay (days)	IG: Ø 1.9 (R 1-4) vs. CG Ø 3.06 (R 1-26) Median: IG 2 (R 1–4) vs CG: 2 (R 1–26) p<0.05

Cholecystectomy	
Author, year [reference number]	**Ruurda et al, 2003** [1]
Study design	Single centre RCT
Country	Netherlands
Funding/Sponsor	NR
Intervention (IG) | Product	Robot-assisted single-site cholecystectomy | da Vinci telemanipulation system (Intuitive Surgical Inc, Mountain View, CA)
Comparator (CG)	Standard laparoscopy cholecystectomies[51]
Experience of surgeon(s), time period	3 experienced surgeons and assisting team with experience of >15 robotic procedures performed IG procedures; 5 surgical residents under supervision of qualified surgeon, performed laparoscopic cholecystectomies
Number of patients	IG 10 CG 10
Inclusion/exclusion	Elective symptomatic cholelithiasis patients with cholecystolithiasis confirmed by ultrasound.

[51] Not clearly stated but probably multi-port laparoscopy

Cholecystectomy	
Author, year [reference number]	**Ruurda et al, 2003** [1]
criteria	
Primary/secondary endpoints	Procedure time
Follow-up (months)	None
Drop-outs (n, %)	None
Patient characteristics	
Age of patients (yrs.)	IG: M 46 (R 29-72) CG: M 54 (R 24-87), p=NR
Sex (% female)	IG: 80% CG: 80%, p=NR
BMI (kg/m²)	IG: 26[52] (R 18-47) CG: 25 (22-30), p=NR
Disease	Cholecystolithiasis (chronic in IG 4/10 and CG 1/20)
Clinical classification	NR
Patient-relevant outcomes	
Survival (overall and disease-specific or disease-free)	NR
Recurrence (local, regional or distant)	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	NR
Time to resume work/daily activities	NR
Patient satisfaction	NR
Safety-related outcomes	
Intraoperative complications (e.g. air-leakage)	NR
Postoperative complications (e.g. infections)	NR
Re-operations/ additional surgeries	NR
Conversion to laparoscopic/open surgery	IG 0, CG: 0
Perioperative events & resource use	
Blood loss (in ml)	NR
Operation time in min.	[53] IG: M 144 (R 111-234) vs. CG M 119 (R 71-189), p=ns
Transfusions	NR
Drain duration (days)	NR
Length of hospital stay (days)	NR

Abbreviations: ASA=score American Society of Anesthesiologists; BIQ=body image questionnaire; BMI=body mass index; EORTC QLQ-C30=European Organisation for Research and Treatment of Cancer Quality of Life Group; CG=control group; FU=follow-up; GERD=gastroesophageal reflux disease; GORD=gastro-oesophageal reflux disease;

[52] Not stated if mean or median

[53] Defined as time between entry of the patient into the OR and departure from OR

GORD HRQOL=Gastro-oesophageal Reflux Health-Related Quality of Life scale; GSRS=Gastrointestinal Symptom Rating Scale; ICU=intensive care unit; IG=intervention group; IQR=interquartile range; M=Median; MD=mean difference; NR=not reported; ns=not significant; PSQ=photograph series questionnaire; QoL=quality of life; QOLRAD=Quality of Life in Reflux and Dyspepsia; SF-12 (QoL-12)=short form 12; Ø=mean; R=Range; RATS=Robot-assisted thoracic surgery; SIRC=single-incision robotic cholecystectomy; TNM=Tumor, nodes, metastasis; VAS=visual analogue scale; VATS=Video-assisted thoracic surgery.

Risk of bias – study level (RCTs)

Trial	Adequate generation of randomization sequence	Adequate allocation concealment	Blinding		Selective outcome reporting unlikely	No other aspects increasing risk of bias	Risk of bias – study level
			Patient	Treating person[54]			
Gallbladder/Liver Spleen							
Kudsi et al. 2017 [26]	Y	Y	U Inconsistently reported	U Inconsistently reported	N Outcomes regarding quality of life just reported "for female patients with non-missing data: controlled for age, BMI, and prior abdominal surgery"	N Single-site (IG) vs multi-port (CG) Experience of surgeons (8/10 new to single-site technique) Probably inadequate sample size	H
Pietrabissa et al. 2016 [27]	Y	Y	Y	Y	Y	N Comparison was not made with a standard single-incision technique No detailed information about patient characteristics was provided	L
Grochola et al, 2018 [28]	Y	Y	Y	Y	Y	N Several surgeons involved, experience not detailed; study not powered for our endpoints of interest	L
Ruurda et al, 2003 [1]	N	U Insufficient information for a judgement	U Insufficient information for a judgement	U Insufficient information for a judgement	Y	N No power calculations, residents in training performed control procedure	H

[54] Since it impractical for the surgeon to be blinded, we refer here to other healthcare professionals involved in patient care

Bowel							
Jayne et al. 2017 [20]	Y	Y	N Patients were not blinded	N Healthcare professionals were not blinded	Y	Y	L
Wang et al, 2017 [23]	U Only reported that rndomisation was performed using opaque sealed envelopes	U No information	U No information	U No information	N Patients that died or did not provide follow-up data were excluded	N No details on experience of surgeons	H
Kim et al, 2018 [21]	Y	Y	N Patients were not blinded	N Health care professionals were not blinded	Y	Y	L
Mäkelä-Kaikkonen et al, 2016 x2 [25] [68]	Y	Y	Y	N Health care professionals were not blinded	N Not all outcomes were reported	N No details on experience of surgeons Power of the study is unclear	L
Park et al. 2012 [19]	U Insufficient information for a judgement	Y	U No information	U No information	Y	Y	H
Tolstrup et al, 2018 [22]	U	U	N Patients were not blinded in the Rolarr trial	N Other healthcare professionals were not blinded in the Rolarr trial	N Results data unclear	Y	H
Debakey et al, 2018 [24]	U Insufficient information for a judgement	U Insufficient information for a judgement	U Insufficient information for a judgement	U Insufficient information for a judgement	N Intraoperative complications analysed but not reported	N No power calculations, no information regarding surgical experience	H

Trial	Adequate generation of randomization sequence	Adequate allocation concealment	Blinding		Selective outcome reporting unlikely	No other aspects increasing risk of bias	Risk of bias – study level
			Patient	Treating person[55]			
Oesophagus							
Draaisma et al. 2009 [10]	U Insuffi-cient infor-mation for a judge-ment	U Insuffi-cient infor-mation for a judge-ment	U Insuffi-cient infor-mation for a judge-ment	U Insuffi-cient infor-mation for a judge-ment	Y	U Unclear how many patients results refer to	H
Mueller-Stich et al. 2007, 2009 [13] [12]	U No infor-mation	U No infor-mation	Y	U Insufficient infor-mation for a judge-ment	Y	N Lack of sample size calculation	H
Morino et al. 2006 [11]	Y	Y	U Insuffi-cient infor-mation for a judge-ment	U Insuffi-cient infor-mation for a judge-ment	Y	Y	L
Nakadi et al. 2006 [14]	U “Ran-domised by enve-lopes”	U “Random-ised by enve-lopes”	N Patients were not blinded	U Insuffi-cient infor-mation for a judge-ment	N No out-comes regarding satisfaction score, although predefined	N Lack of sample size calculation	H
van der Sluis, 2018 [15]	Y	Y	U Insuffi-cient infor-mation for a judge-ment	U Insuffi-cient infor-mation for a judge-ment	Y	N No power calculations, no information regarding surgical experience	L
Stomach							
Pan et al. 2017 [16]	U Insuffi-cient infor-mation for a judge-ment	U Insuffi-cient infor-mation for a judge-ment	U No infor-mation	U No infor-mation	Y	N Lack of sam-ple size calculation	H
Sanchez et al. 2005 [18]	U No infor-mation	U No infor-mation	U No infor-mation	U No infor-mation	Y	N Lack of sam-ple size calculation	H
Wang et al. 2016 [17]	U Insuffi-cient infor-mation for a judge-ment	Y	U No infor-mation	U No infor-mation	Y	N Lack of sample size calculation	H

[55] Since it impractical for the surgeon to be blinded, we refer here to other healthcare professionals involved in patient care

Risk of bias – outcome level (RCTs)

Endpoint Trial	Risk of bias – study level	Blinding – outcome assessors	ITT principle adequately realized	Selective outcome reporting unlikely	No other aspects increasing risk of bias	Risk of bias – out-come level
OVERALL MORTALITY						
Galllbladder/Liver Spleen						
Kudsi et al. 2017 [26]	Not defined as outcome					
Pietrabissa et al. 2016 [27]	Not defined as outcome					
Grochola et al, 2018 [28]	Not defined as outcome					
Ruurda et al, 2003 [1]	Not defined as outcome					
Bowel						
Park et al. 2012 [19]	Not defined as outcome					
Jayne et al. 2017 [20]	L	Y	Y	N	Y	L
Kim et al. 2018 [21]	Not defined as outcome					
Mäkelä-Kaikkonen et al, 2016 x2 [25] [68]	Not defined as outcome					
Tolstrup et al, 2018 [22]	Not defined as outcome					
Wang et al, 2017 [23]	H	U No infor-mation	N Those not providing follow-updata were excluded before ran-domisation	N No infor-mation on mortality during fol-low-up	N Not powered to detect mortality differences	H
Debakey et al, 2018 [24]	H	U Insufficient information for a judgement	Y	Y	N Not powered to detect survival difference	H
PATIENT-ASSESSED OUTCOMES (QoL, symptoms, satisfaction)						
Gallbladder/Liver Spleen						
Kudsi et al. 2017	H	U No infor-mation	U No infor-mation	N Outcomes regarding quality of life just “for female patients with non-missing data: con-trolled for age, BMI, and prior abdominal surgery”	Y	H
Pietrabissa et al. 2016 [27]	L	U No infor-mation	Y	Y	Y	L
Grochola et al, 2018 [28]	L	U Insufficient information for a judge-ment	Y	Y	N Study not powered to detect quali-ty of life difference	H

Ruurda et al, 2003 [1]	Not defined as outcome					
Bowel						
Jayne et al. 2017 [20]	L	U Stated that blinding of assessments was conducted "where possible"	Y	Y	Y	L
Kim et al. 2018 [21]	L	U Insufficient information	Y	U No outcome tables	Y	L
Mäkelä-Kaikkonen et al. 2016 x2 [25] [68]	L	U Insufficient information	Y	Y	U No detailed reporting of condition-specific symptom measures	H
Park et al. 2012 [19]	H	U No information	Y	N Pain score at 72 h not reported	Y	H
Tolstrup et al. 2018 [22]	H	U Insufficient information	Y	N (results data unclear)	Y	H
Wang et al, 2017 [23]	H	U No information	N Patients not providing follow-up data were excluded before randomisation	N No information on patents not providing follow-up	N Power of study unclear	H
Debakey et al, 2018 [24]	Not defined as outcome					
SAFETY & PERIOPERATIVE OUTCOMES						
Gallbladder/Liver spleen						
Kudsi et al. 2017 [26]	H	U Insufficient information for a judgement	U No information	Y	Y	H
Pietrabissa et al. 2016 [27]	L	U No information	Y	Y	Y	L
Grochola et al, 2018 [28]	L	U	Y	Y	U Not powered for this outcome	L
Ruurda et al, 2003 [1]	H	U Insufficient information for a judgement	Y	Y	N Limited experience of surgeons in the control group could affect operating time; unclear if sample size adequate	H
Bowel						

Jayne et al. 2017 [20]	L	U Stated that blinding of assessments was conducted "where possible"	Y	Y	Y	L
Kim et al. 2018 [21]	L	U Insufficient information for a judgement	Y	Y	Y	L
Mäkelä-Kaikkonen et al. 2016 [25] [68]	L	U Insufficient information for a judgement	Y	Y	Y	L
Park et a. 2012 [19]	H	U No information	Y	Y	Y	L
Tolstrup et al. 2018 [22]	H	U Insufficient information for a judgement	Y	N Results data unclear	Y	H
Wang et al, 2017 [23]	H	U No information	U Unclear	Y	N	H
Debakey et al, 2018 [24]	H	U Insufficient information for a judgement	Y	Y	U Unclear if sample size adequate	H

Endpoint Trial	**Risk of bias – study level**	**Blinding – outcome assessors**	**ITT principle adequately realized**	**Selective outcome reporting unlikely**	**No other aspects increasing risk of bias**	**Risk of bias – outcome level**
OVERALL MORTALITY						
Oesophagus						
Draaisma et al. 2009 [10]			Not defined as outcome			
Mueller-Stich et al. 2007, 2009 [13] [12]			Not defined as outcome			
Morino et al. 2006 [11]			Not defined as outcome			
Nakadi et al. 2006 [14]			Not defined as outcome			
van der Sluis et al, 2018 [15]	L	U No information	Y	Y	N Survival data unclear; not powered to detect survival difference	H
Stomach						
Pan et al. 2017 [16]	H	U No information	U No information	U Insufficient information	Y	H

				for a judgement		
Sanchez et al. 2005 [18]	Not defined as outcome					
Wang et al. 2016 [17]	H	U No information	U No information	U Insufficient information for a judgement	Y	H
Endpoint Trial	**Risk of bias – study level**	**Blinding – outcome assessors**	**ITT principle adequately realized**	**Selective outcome reporting unlikely**	**No other aspects increasing risk of bias**	**Risk of bias – outcome level**
PATIENT-ASSESSED OUTCOMES (QoL, symptoms, satisfaction)						
Oesphagus						
Draaisma et al. 2009 [10]	H	U Insufficient information for a judgement	U Insufficient information on drop-outs	Y	U Insufficient information for a judgement	H
Mueller-Stich et al. 2009 [13]	H	Y	U No information	Y	Y	L
Morino et al. 2006 [11]	L	U	U	Y	N Study not powered to detect QoL differences	H
Nakadi et al. 2006 [14]	Not defined as outcome					
van der Sluis et al, 2018 [15]	L	U Insufficient information for a judgement	U Insufficient information on drop-outs	U Data on quality of life missing (“will be reported extra”)	N Study not powered to detect quality of life difference	H
Stomach						
Pan et al. 2017 [16]	H	U No information	U No information	Y	Y	H
Wang et al. 2016 [17]	Not defined as outcome					
Sanchez et al. 2005 [18]	Not defined as outcome					
Endpoint Trial	**Risk of bias – study level**	**Blinding – outcome assessors**	**ITT principle adequately realized**	**Selective outcome reporting unlikely**	**No other aspects increasing risk of bias**	**Risk of bias – outcome level**
SAFETY & PERIOPERATIVE OUTCOMES						
Oesophagus						
Draaisma et al. 2009 [10]	H	U Insufficient information for a judgement	U Insufficient information for a judgement	Y	U Insufficient information for a judgement	H
Mueller-Stich et al.	H	Y	U	Y	Y	L

2007 [12]			Insufficient information for a judgement			
Morino et al. 2006 [11]	L	U Insufficient information for a judgement	U Insufficient information for a judgement	Y	Y	L
Nakadi et al. 2006 [14]	H	Y	U Insufficient information for a judgement	Y	Y	L
van der Sluis, 2018 [15]	L	U Insufficient information for a judgement	Y	Y	Y	L
Stomach						
Pan et al. 2017 [16]	H	U Insufficient information for a judgement	U Insufficient information for a judgement	Y	Y	H
Wang et al. 2016 [17]	H	U Insufficient information for a judgement	U Insufficient information for a judgement	Y	Y	H
Sanchez et al. 2005 [18]	H	U No information	U Insufficient information for a judgement	Y	Y	H

Table A3: Characteristics & risk of bias of non-randomised studies

Thoracic surgery		
Lobectomy/Segmentectomy		
Author, year [reference number]	**Augustin et al. 2013** [29]	**Gonde et al. 2017** [30]
Study design	Non-randomised comparison of all robot-assisted and consecutive conventional minimally invasive VATS lobectomies	Single-centre 1 year prospective observational cost study
Country	Austria	France
Funding/Sponsor	None	NR but conflict of interest present
Intervention (IG) | Product	Robot-assisted lobectomy (5 posterior and 21 anterior approach) | da Vinci Surgical System (3-arm)	RATS | da Vinci Surgical System (3-arm)
Comparator (CG)	VATS lung lobectomy (anterior approach)	VATS (modified anterior approach)
Experience of surgeon(s), time period	RATS was performed by 1 surgeon, who had completed formal training in robotic surgery. VATS was performed by 3 surgeons with reported extensive experience in minimally invasive surger.y RATS procedures undertaken 2001-2008; VATS procedures undertaken in 2009	Minimal invasive surgery for major pulmonary resection was established in 2008; in 2012 RATS was added; over 100 robotic procedures were performed in 2014 before the present study Study conducted: 09/2014-09/2015
Number of patients	IG: 26	IG: 57

Thoracic surgery		
Lobectomy/Segmentectomy		
Author, year [reference number]	**Augustin et al. 2013** [29]	**Gonde et al. 2017** [30]
	CG: 26	CG: 55
Inclusion/exclusion criteria	Inclusion: • histologically proven lung cancer, centrally located solitary lung metastasis, and aspergilloma • early stage NSCLC cT1-2N0M0	Inclusion: • Patients who underwent minimally invasive lobectomy or segmentectomy Exclusion: • Wedge resection, sleeve resection, pneumonectomy, resection of a tumour >8cm.
Primary/secondary endpoints	Perioperative events and complications	Perioperative events, resource use and complications
Follow-up (months)	NR	90 days
Drop-outs (n, %)	none	none
Patient characteristics		
Age of patients (yrs.)	IG: M 65 (R 47-82) CG: M 65 (R 37-79), p=ns	IG: M 61 (IQR 57-64) CG: M 63 (IQR 60-65), p=ns
Sex (% female)	IG: 46% CG: 42%, p=ns	IG: 46% CG: 25%, p<0.05
BMI (kg/m²)	NR	IG: M 25 (IQR 23-26) CG: M 26 (IQR 24-27), p=ns
Disease	Primary lung cancer, p=ns: IG: 24/26 (92%) CG: 25/26 (96%) Of these, clinical stage >1B: IG: 0/24 CG: 6/25 (24%), p<0.05 Aspergilloma (benign disease): IG: 0/26 CG: 1/26 (3.85%)	Indication, p=ns Lung cancer: IG: 44/57 (77%) CG: 44/55 (80%) Pulmonary metastasis: IG: 5/57 (9%) CG: 4/55 (7%) Benign lesion: IG: 8/57 (14%) CG 7/55 (13%)
Clinical classification	Pathological stage (UICC 7th edition) IG vs. CG, p=ns: Ia: 18/24 (75%) vs. 12/25 (48%) Ib: 5/24 (21%) vs. 6/25 (24%) II: 1/24 (4%) vs. 2/25 (8%) III, IV[56]: 0 vs. 5/25 (20%)	TNM (IG vs. CG), p=ns Ia: 17/39 (44%) vs. 20/44 (45%) Ib: 6/39 (15%) vs. 9/44 (20%) IIa: 6/39 (15%) vs. 6/44 (14%) IIb: 5/39 (13%) vs. 6/44 (14%) IIIa: 4/39 (10%) vs. 2/44 (5%) IIIb: 1/39 (3%) vs. 0 IV: 0/39 vs. 1/44 (2%) ASA score, p=ns 1: 8/57 (14%) vs. 7/55 (13%) 2: 21/57 (37%) vs. 20/55 (36%) 3: 23/57 (40%) vs. 22/55 (40%) 4: 4/57 (7%) vs. 6/55 (11%) 5 and 6: 0 vs. 0 Unknown: 1/57 (2%) vs. 0
Clinically-relevant outcomes		
Positive surgical margins	NR	NR
Patient-relevant outcomes		

[56] Histologically proven bilateral bronchioloalveolar carcinoma confined to the upper lobes

Thoracic surgery		
Lobectomy/Segmentectomy		
Author, year [reference number]	**Augustin et al. 2013** [29]	**Gonde et al. 2017** [30]
Survival (overall and disease-specific or disease-free)	Intraoperative: IG: 26/26 (100%) CG: 26/26 (100%), p=ns In-hospital: IG: 26/26 (100%) CG: 26/26 (100%), p=ns	Intraoperative: IG: 57/57 (100%) CG: 55/55 (100%), p=ns In-hospital: IG: 57/57 (100%) CG: 53/55[57] (96%), p=NR Survival to 90 days: IG: 57/57 (100%) CG: 53/55 (96%), p=NR
Recurrence (local, regional or distant)	NR	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	NR	NR
Time to resume work/daily activities	NR	NR
Patient satisfaction	NR	NR
Safety-related outcomes		
Intraoperative complications (e.g. air-leakage)	NR	NR
Postoperative complications (e.g. infections)	Total complications, p=ns: IG: 11/26 (42%) (5 air leaks, 2 atrial fibrillations, 1 wound infection, 1 urinary tract infection, 1 empyema, 1 colonic perforation) CG: 10/26 (38%) (4 air leaks, 2 atrial fibrillations, 2 pleural fluid collections, 2 atelectasis) Minor complications, p=ns: IG: 8/26 (31%) CG: 9/26 (35%) Major complications, p=ns: IG: 3/26 (12%) CG: 1/26 (4%)	IG: 21/57 (37%) CG: 29/55 (53%), p=ns Minor complications: IG: 19/57 (33%) CG: 21/55 (38%), p=ns Major complications: IG: 2/57 (4%) CG: 8/55 (15%), p=ns Complications requiring readmission: IG: 3/57 (5%) CG:5/55 (9%), p=ns
Re-operations/additional surgeries	NR	NR
Conversion to laparoscopic/open surgery	IG: M 5/26 (19%) CG: M 2/26 (8%), p=ns	IG: 1/57 (2%) CG: 9/55 (16%), p<0.01
Perioperative events & resource use		
Blood loss (in ml)	Blood loss by comparing hemoglobin levels preoperative vs. postoperative: IG: Median change 2.40 g/dl vs. CG 1,85 g/dl, p<0.05 CG: NR	NR
Operation time in min.	IG: M 215 (R 162-375) CG: M 183 (R 113-379), p<0.05	IG: M 255 (IQR 225-300) CG: M 255 (IQR 217-305), p=ns
Transfusions	1 patient required transfusion, group was	NR

[57] During hospital stay: a heart transplant patient because of acute respiratory distress of infectious origin; a second patient died of multiple organ failure.

Thoracic surgery		
Lobectomy/Segmentectomy		
Author, year [reference number]	**Augustin et al. 2013** [29]	**Gonde et al. 2017** [30]
	not reported	
Drain duration (days)	IG: M 7 (R 3-15) CG: M 6 (R 3-18), p=ns	IG: M 4 (IQR 3-5) CG: M 4 (IQR 3-7), p=ns
Length of hospital stay (days)	IG: M 11 (R 7-53) CG: M 9 (R 4-23), p=ns	IG: M 5 (IQR 5-7) CG: M 6 (IQR 5-11), p=ns

Lobectomy/Segmentectomy	
Author, year [reference number]	**Rinieri et al. 2016** [31]
Study design	Prospective observational study
Country	France
Funding/Sponsor	None
Intervention | Product	RATS |da Vinci Surgical System (3-arm)
Comparator	VATS (anterior approach)
Experience of surgeon(s), time period	Surgeons performing VATS (n=?) had performed >100; 1 surgeon performed RATS (no information on experience) Videothoracoscopy procedures: 2010-06/2014 Robotic procedures: 2013-06/2014
Number of patients	IG:17 CG: 34
Inclusion/exclusion criteria	Inclusion: patients undergoing RATS or VATS segmentectomy
Primary/secondary endpoints	Perioperative events and complications
Follow-up (months)	NR
Drop-outs (n, %)	None reported
Patient characteristics	
Age of patients (yrs.)	IG:M 62 (IQR 57-67) CG: M 64 (IQR 55-69), p=ns
Sex (% female)	IG: 29% CG: 50%, p=ns
BMI (kg/m²)	NR
Disease	Benign or infectious lesion: IG: 3/17 (17.65%) CG: 4/34 (20.59%), p=ns Preinvasive lesion or minimally invasive adenocarcinoma: IG: 2/17 (12%) CG: 10/34 (29%), p=NR Invasive adenocarcinoma: IG: 4/17 (24%) CG: 12/34 (35%) p=NR Other lung cancer: IG: 2/17 (12%) CG: 4/34 (12%) p=NR Pulmonary metastasis: IG: 6/17 (35%) CG: 4/34 (12%) p=NR

Lobectomy/Segmentectomy	
Author, year [reference number]	**Rinieri et al. 2016** [31]
Clinical classification	TNM (IG vs. CG), p=ns Ia: 4/6 (67%) vs. 12/15 (80%) Ib: 1/6 (17%) vs. 2/15 (13%) IIa: 1/6 (17%) vs. 1/15 (7%)
Clinically-relevant outcomes	
Positive surgical margins	No data but reported that all patients had tumor-free margins
Patient-relevant outcomes	
Survival (overall and disease-specific or disease-free)	In-hospital: IG: 17/17 (100%) CG: 33/34 (97%)[58], p=NR
Recurrence (local, regional or distant)	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	NR
Time to resume work/daily activities	NR
Patient satisfaction	NR
Safety-related outcomes	
Intraoperative complications (e.g. air-leakage)	NR
Postoperative complications (e.g. infections)	Clavien-Dindo classification (IG vs CG), p=ns 0: 13/17 (76%) vs. 24/34 (71%) I: 2/17 (12%) vs. 2/34 (6%) II: 0/17 vs. 1/34 (3%) III: 1/17 (6%) vs. 4/34 (12%) IV: 1/17 (6%) vs. 2/34 (6%) V: 0/17 vs. 1/34 (3%)
Re-operations/additional surgeries	1 reoperation for air leak, NR which group
Conversion to laparoscopic/open surgery	Lobectomy: IG: 1/17 (5.88%) CG: 2/34 (5.88%), p=ns Thoracotomy: IG: 1/17 (5.88%) CG: 3/34 (8.82%), p=ns
Perioperative events & resource use	
Blood loss (in ml)	IG:M 50 (IQR 10-100) CG: M 100 (IQR 50-200), p<0.05
Operation time in min.	IG: M 140 (IQR 120-170) CG: M 150 (IQR 120-180), p=ns
Transfusions	NR
Drain duration (days)	IG: M 3 (IQR 3-4) CG: M 3 (IQR 3-4), p=ns
Length of hospital stay (days)	IG: M 4 (IQR 4-5)

[58] this patient died on postoperative day 1 due to cardiac arrest (ventricular fibrillation due to hyperkalemia)

Lobectomy/Segmentectomy	
Author, year [reference number]	**Rinieri et al. 2016** [31]
	CG: M 5 (IQR 4-7[59]), p=ns

Mediastinal Surgery	
Author, year [reference number]	**Balduyck et al. 2011** [32]
Study design	prospective, non-randomised study
Country	Belgium
Funding/Sponsor	NR
Intervention | Product	Robot-assisted anterior mediastinal mass resection | da Vinci robotic system (Intuitive Surgical, Inc., Mountain View, CA, USA)
Comparator	Open mediastinal mass resection by sternotomy
Experience of surgeon(s), time period	NR Recruitment: 01/2004-12/2008
Number of patients	IG: 14 CG: 22
Inclusion/exclusion criteria	Inclusion: patients with a surgical resectable, anterior mediastinal mass Exclusion criteria for robot-assisted surgery: anterior mediastinal mass with maximal diameter >4cm, inability to sustain single-lung ventilation, local invasiveness in surrounding great vessels
Primary, secondary endpoints	Quality of life using EORTC QLQ-C30 (cancer core questionnaire) and EORTC QLQ-LC-13 (lung-cancer-specific questionnaire module
Follow-up (months)	IG: Ø 34.2 ±11.6 CG: Ø 50.1 ±16.1, p<0.05
Drop-outs (n, %)	22/36 (61%) returned questionnaires at all 5 time periods. Non-response (IG vs. CG) 6 months questionnaire: 5/14 (36%) vs. 4/22 (18%) 12 months questionnaire: 3/14 (21%) vs. 2/22 (9%)
Patient characteristics	
Age of patients (yrs.)	IG: M 49 (R 18-63) CG: M 56 R(23-84), p=ns
Sex (% female)	IG: 71% CG: 45% p=ns
BMI (kg/m²)	NR
Disease	Pathological diagnosis after resection, IG vs. CG, p=ns: Thymic hyperplasia: 4/14 (29%) vs. 5/22 (23%) Thymic cyst: 4/14 (29%) vs. 2/22 (9%) Thymoma WHO type A: 1/14 (7%) vs. 1/22 (5%) Thymoma WHO type B1: 2/14 (14%) vs. 2/22 (9%) Thymoma WHO type B2: 1/14 (7%) vs. 5/22 (23%)

[59] Postoperative stay

Mediastinal Surgery	
Author, year [reference number]	**Balduyck et al. 2011** [32]
	Thymoma WHO type B3: 0 vs. 1/22 (5%) Thymoma WHO type AB: 1/14 (7%) vs. 3/22 (14%) Thymic carcinoma: 0 vs. 1/22 (5%) Metastasis of second primary: 1/14 (7%) vs. 0 Extragonadal germ cell tumour: 0 vs. 2/22 (9%)
Clinical classification	NR
Clinically-relevant outcomes	
Positive surgical margins	NR
Patient-relevant outcomes	
Survival (overall and disease-specific or disease-free)	Intraoperative IG: 22/22 (100%) CG: 14/14 (100%), p=NR
Recurrence (local, regional or distant)	IG: 0 CG: 1/22 (4.55%), p=ns
Quality of life (e.g. measured by EQ-5D or SF-36)	Measured by EORTC-QLQ-C30 (IG vs CG) **QoL functioning scores** *Physical functioning* @1 month after surgery: Ø 76.9 (p=ns) vs. Ø 66.3 (p=0.001) No significant differences at 3, 6 or 12 months after surgery *Role functioning* @ 1 month after surgery: Ø 62.1 (p=ns) vs. Ø 40.8 (p=0.001) No significant differences at 3, 6 or 12 months after surgery *Cognitive functioning*: no significant differences at any time period *Social functioning* @ 1 month after surgery: Ø 72.7 (p=ns) vs. Ø 66.7 (p<0.05) No significant differences at 3, 6 or 12 months after surgery *Global QoL*: no significant differences at any time period **QoL symptom scores** *Dyspnoea*: no significant differences at any time period *Coughing*: no significant differences at any time period *Fatigue* @ 1 month after surgery: Ø 35.4 (p=ns) vs. Ø 50.5 (p<0.01) No significant differences at 3, 6 or 12 months after surgery *Thoracic pain* @ 1 month after surgery: Ø 24.3 (p<0.05) vs. Ø 31.7 (p<0.05) 3 months after surgery: Ø 23.8 (p=ns) vs. Ø 26.7 (p<0.05) No significant differences at 6 or 12 months after surgery *Shoulder dysfunction* @ 3 months after surgery 3 months after surgery: Ø 30.9 (p<0.05) vs. Ø 11.7 (p=ns) No significant differences at 1,6 or 12 months after surgery
Time to resume work/daily activities	NR
Patient satisfaction	NR
Safety-related outcomes	
Intraoperative complications (e.g. air-leakage)	IG: 0 CG: 0
Postoperative complications (e.g. infections)	IG vs CG: Cardiac tamponade: 0 vs. 1/22 (5%), p=ns

Mediastinal Surgery	
Author, year [reference number]	**Balduyck et al. 2011** [32]
	Phrenic paralysis: 2/14 (14%) vs. 0, p=ns Deep vein thrombosis: 1/14 (7%) vs. 0,p=ns Sternal keloid scarring: 0 vs. 1/22 (5%), p=NR
Re-operations/additional surgeries	IG: 0 CG: 2/22 (9.09%) : 1 re-operation for pleural recurrence and 1 re-operation for sternal instability, p=NR
Conversion to laparo-scopic/open surgery	IG: 1/14 (7%) CG: 0, p=NR
Perioperative events & resource use	
Blood loss (in ml)	NR
Operation time in min60.	IG: Ø 224.2 ±66.5 CG: Ø 243.8 ± 55.5, p=ns
Transfusions	NR
Drain duration (days)	NR
Length of hospital stay (days)	IG: Ø 9.6 ±3.9 CG: Ø 11.8 ± 5.7, p=ns

Oesophagus		
Heller myotomy		
Author, year [reference number]	**Huffmanm et al.2007** [33]	**Sanchez et al. 2012** [34]
Study design	Single centre prospective observational Study (consecutive patients over 6 years)	Single centre, prospective, comparative study of consecutive patients
Country	USA, Ohio	Venezuela
Funding/Sponsor	NR	NR
Intervention (IG) | Product	da Vinci Surgical System Robot-assisted laparoscopic myotomy with partial fundoplication	da Vinci Surgical System Robotic assisted laparoscopic Heller myotomy
Comparator (CG)	Laparoscopic myotomy with partial fundoplication	Laparoscopic Heller myotomy
Experience of surgeon(s), time period	Single surgeon for all procedures Operations performed between 2004 and 2006 (intervention); operations performed between 2000 and 2004 (comparator)	The same surgical team for every case Study conducted: January 2008 to November 2010
Number of patients	IG: 24 CG: 37	IG: 13 CG: 18
Inclusion/exclusion criteria	Patients suitable for a Heller myotomy were included	Inclusion: patients with achalasia confirmed by oesophagogram and manometry
Primary, secondary endpoints	Generic and disease-specific quality of life, perioperative outcomes and complications	Postoperative complications and recurrence of symptoms
Follow-up (months)	1-6 months but: CG: M 43 months IG: M 15 months	1 week, 1 month and 4 months after surgery then every 6 months (latter by telephone)

[60] Total operation room occupation

Oesophagus		
Heller myotomy		
Author, year [reference number]	**Huffmanm et al.2007** [33]	**Sanchez et al. 2012** [34]
Drop-outs (n, %)	0	IG: 0% at 18 Months CG: 5.5% at 18 Months
Patient characteristics		
Age of patients (yrs.)	IG: R 22-92 CG: R 25-85	IG: M 38.0 CG: M 40.7, p=ns
Sex (% female)	IG: 58% CG:38%, p=NR	NR
BMI (kg/m²)	NR	NR
Disease	Achalasia	Achalasia
Clinical classification	NR	NR
Clinically-relevant outcomes		
Positive surgical margins	NR	NR
Patient-relevant outcomes		
Survival (overall and disease-specific or disease-free)	NR	NR
Recurrence (local, regional or distant)	NR	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	SF-36 general health perceptions post-op vs. pre-op: IG: 53 vs. 34, p<0.05 CG: 68 vs. 56, p<0.05 All categories showed improvement (post-op vs pre-op) for both groups, p<0.05 (data in diagram) No data on between group comparisons GERD Activity Index (GRACI) showed an improvement in severity of symptoms in both groups at 6 days postoperatively (P <0.05) (no exact results reported).	At 18 months (method of measurement not stated): IG: 100% relief of symptoms CG: 94.5% relief of symptoms p=NS
Time to resume work/daily activities	NR	NR
Patient satisfaction	NR	NR
Safety-related outcomes		
Intraoperative complications (e.g. air-leakage)	IG:0 CG:3/37 (8%) operative oesophageal perforations, p=NR	IG: 0 CG: 1/18 (5.5%) (oesophageal perforations), p=ns
Postoperative complications (e.g. infections)	NR	NR
Re-operations/ additional surgeries	NR	NR
Conversion to laparoscopic/open surgery	NR	IG=0 CG=0
Perioperative events & resource use		
Blood loss (in ml)	IG: 67 ml CG: 57 ml p=NR	NR

Oesophagus		
Heller myotomy		
Author, year [reference number]	**Huffmanm et al.2007** [33]	**Sanchez et al. 2012** [34]
Operation time in min.	IG: M 355± 23 CG: M 287 ± 9, p=NR[61]	IG: M 79 ± 20 CG: M 76 ± 13 p=ns[2]
Transfusions	NR	NR
Drain duration (days)	NR	NR
Length of hospital stay (days)	IG: 2.8 days CG: 2.6days, p=NR	NR

Gallbladder/liver/spleen		
Liver resection/hepatectomy		
Author, year [reference number]	**Berber et al. 2010** [35]	**Lai and Tang 2016** [36]
Study design	Single centre prospective non-randomised study	Single centre prospective non randomised trial of consecutive patients
Country	USA	China
Funding/Sponsor	NR	NR
Intervention | Product	Robotic resection of liver tumour	da Vinci Surgical System robot-assisted laparascopic partial hepatectomy
Comparator	Laparoscopic resection of liver tumour	Conventional laparoscopic partial hepatectomy
Experience of surgeon(s), time period	NR Robotic procedures conducted October 2008 to September 2009	Consultant surgeons with expertise in hepatobiliary and laparoscopic surgery Procedures undertaken October 1998 to February 2015
Number of patients	IG: 9 CG: 23	IG: 95 CG:35
Inclusion/exclusion criteria	Inclusion: Patients with a peripherally located malignant lesion measuring <5 cm Exclusion: NR	Inclusion: Patients with hepatocellular carcinoma Exclusion: NR
Primary endpoint	Survival, recurrence, perioperative outcomes	Survival, perioperative outcomes
Follow-up (months)	Mean (both groups) of 14 months	IG: M 26.4±11.8 CG: M 61.6±44.5
Drop-outs (n, %)	NR	0
Patient characteristics		
Age of patients (yrs.)	IG: M 66.6 ±6.4 CG: M 66.7±9.6, p=ns	IG: M 62.1±10.8 CG: M 57.9±10.3, p=0.05
Sex (% female)	IG: 22% CG:48%, p=ns	IG: 31% CG: 26%, p=ns
BMI (kg/m²)	NR	NR
Disease	Tumour type, p=ns Colorectal metastasis: IG 4/9 (44%) vs CG 14/23 (61%) Hepatocellular cancer IG 3/9 (33%) vs. CG 7/23 (30%)	Hepatocellular Carcinoma

[61] Definition: from induction of anesthesia to extubation

[2] Definition: from incision to closure of the wounds

Gallbladder/liver/spleen		
Liver resection/hepatectomy		
Author, year [reference number]	**Berber et al. 2010** [35]	**Lai and Tang 2016** [36]
Clinical classification	NR	NR
Clinically-relevant ouctomes		
Positive surgical margins	NR	NR
Patient-relevant outcomes		
Survival (overall and disease-specific or disease-free)	Data NR (diagram unclear) Reported that disease-free survival at 14 months was equivalent in both groups (p=ns)	Operative mortality (within 90 days): IG: 0% vs. CG: 0% 5-year overall survival: IG: 65% vs. CG: 48%, p=ns 5-year disease-free survival: IG 42% vs. CG: 38%, p=ns
Recurrence (local, regional or distant)	IG: 2/9 (22%) CG: 6/23 (26%), p=ns	IG: 32/95 (34%) CG: 22/35 (63%), p=NR
Quality of life (e.g. measured by EQ-5D or SF-36)	NR	NR
Time to resume work/daily activities	NR	NR
Patient satisfaction	NR	NR
Safety-related outcomes		
Intraoperative complications (e.g. air-leakage)	Intra-operative bleeding requiring conversion: IG: 1/9 (11%) vs. CG: 0, p=NR	Not specified if occurred intraoperatively
Postoperative complications (e.g. infections)	Total (intra-operative and post-operative), p=NR: IG: 1/9 (11%) vs. CG:4/23 (17%)	All complications/all procedures: IG: 20/100 (20%) vs. CG 7/35 (20%), p=NR N patients with complications: IG: 14/100 procedures (14%) vs CG: 7/35 (20%), p=ns
Re-operations/additional surgeries	NR	IG: 5/95 (5.26%) CG: 1/35 (2.9%), p=NR
Conversion to laparoscopic/open surgery	IG: 1/9 (11%) vs. CG: 0, p=ns	IG 4/100 procedures (4%) vs. CG 2/35 (6%), p=ns
Perioperative events & resource use		
Blood loss (in ml)	IG:M 136 ± 61 cc CG: M 155 ± 54 cc, p=ns	IG: M 334.6 (R 5-3500) CG: M 336.0 (R 5-2000), p=ns
Operation time in min.	IG: M 258.5 ± 27.9 CG: M 233.6 ± 16.4, p=ns	IG:M 207.4±77.1 CG: M 134.2±41.7[62], p=0.001
Transfusions	NR	IG: 9/100 procedures (9%) CG: 4/35 (11.4%), p=ns
Drain duration (days)	NR	NR
Length of hospital stay (days)	NR	IG:M 7.3 ± 5.3 CG: M 7.1 ± 2.6, p=ns

[62] Defined as time between skin incision and last port skin closure

Hernia repair	
Author, year [reference number]	**Tran, 2011** [37]
Study design	Single centre prospective, non- randomized, controlled study
Country	Australia
Funding/Sponsor	NR
Intervention | Product	Robotic Freehand® Robotic single-port total extraperitoneal inguinal hernia repair
Comparator	Conventional single-port inguinal hernia Repair (laparoscopy)
Experience of surgeon(s), time period	NR Study period October 2010 to December 2010
Number of patients	IG: 16 CG: 16
Inclusion/exclusion criteria	Inclusion: Patients listed for LESS TEP inguinal hernia repair Exclusion: NR
Primary endpoint	Perioperative outcomes and satisfaction
Follow-up (months)	6
Drop-outs (n, %)	0 at 6 months
Patient characteristics	
Age of patients (yrs.)	IG: 46 vs. CG: 48, p=NR
Sex (% female)	NR
BMI (kg/m²)	IG: 28.4 vs. CG 29.2, p=NR
Disease	Inguinal hernia, p=NR % Direct: IG 6/10 (60%) vs. CG 6/10 (60%)
Clinical classification	ASA: IG 1 vs. CG 1
Clinically-relevant outcome	
Positive surgical margins	NR
Patient-relevant outcomes	
Survival (overall and disease-specific or disease-free)	NR
Recurrence (local, regional or distant)	NR
Quality of life (e.g. measured by EQ-5D or SF-36)	NR
Time to resume work/daily activities	NR
Patient satisfaction	Highly satisfied: IG: 14/16 (88%) vs. CG 14/16 (88%), p=NR Satisfied: IG: 2/16 (13%) vs. CG 2/16 (13%), p=NR
Safety-related outcomes	
Intraoperative complications (e.g. air-leakage)	NR
Postoperative complications (e.g. infections)	Wound infections: IG 0 vs. CG 0.
Re-operations/	NR

Hernia repair	
Author, year [reference number]	**Tran, 2011** [37]
additional surgeries	
Conversion to laparoscopic/open surgery	NR
Perioperative events & resource use	
Blood loss (in ml)	NR
Operation time in min	IG: 48 (R 35-95) CG: 52 (R 40-125), p=NR
Transfusions	NR
Drain duration (days)	NR
Length of hospital stay (days)	NR

Risk of bias – outcome-level of non-randomised studies comparing robot-assisted surgery versus open or laparoscopic surgery

Trial	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall bias
Thorax								
OVERALL MORTALITY								
Augustin et al. 2013 [29]	M Different surgeons performed surgery;d IG surgery performed in different ways	C Unclear how IG group was defined	L	L	L	C Study sample very small for survival outcome	L	C
Gonde et al. 2017 [30]	S Significant differences in groups on pulmonary comorbidities and sex	C Unclear how groups were constructed	L	L	L	C Study sample likely to be too small for assessment of survival	C No statistical testing on mortality result	C
Rinieri et al. 2016 [31]	C Long study period, no information how many surgeons conducted VATS or experience level of RATS surgeon, some patients chosen specifically for VATS	C Unclear how groups were constructed	L	L	L	C Sample size too small for outcome	L	C
Balduyck et al. 2011 [32]	C Unclear how participants were assigned to group and NI about	C No information and no comparable characteristics for tumour	L	L	L	C Sample size too small for outcome and only short follow-up for	L	C

Trial	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall bias
	surgeon experience	size				recurrences		
PATIENT-ASSESSED OUTCOMES (QoL, symptoms, satisfaction)								
Augustin et al. 2013 [29]	Not defined as outcome							
Gonde et al. 2017 [30]	Not defined as outcome							
Rinieri et al. 2016 [31]	Not defined as outcome							
Balduyck et al. 2011 [32]	M See above	NI	L	L	L	NI	L	M
SAFETY & PERIOPERATIVE OUTCOMES								
Augustin et al. 2013 [29]	M See above	C See above	L	L	L	M Small sample size	M Missing results on blood loss in CG	M
Gonde et al. 2017 [30]	S See above	C See above	L	L	L	L	L	S
Rinieri et al. 2016 [31]	C See above	C See above	L	L	L	L	L	C
Balduyck et al. 2011 [32]	M See above	M No information and no comparable charateristics for tumour size	L	L	L	L	L	M

Trial	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall bias
Heller myotomy								
OVERALL MORTALITY								
Huffmanm et al. 2007 [33]	Not defined as outcome							
Sanchez et al. 2012 [34]	Not defined as outcome							
PATIENT-ASSESSED OUTCOMES (QoL, symptoms, satisfaction)								
Huffmanm et al. 2007 [33]	C Unclear for how long follow- up was per-formed	C 2 groups were treated at different times	L	L	C Missing numerical data on GERD activity index GRACI	C No informatio n on data collection and small sample size	C Missing data for GERD and GRAC	C
Sanchez et al. 2012 [34]	H No infor-mation on sex or BMI	L	L	L	L	C No informatio n on measure ment of symptom s and small sample size	L	C
SAFETY & PERIOPERATIVE OUTCOMES								
Huffmanm et al. 2007 [33]	C See above	C See above	L	L	L	NI Unclear if sample size adequate	L	C
Sanchez et al. 2012 [34]	S Insufficie nt informatio n on patient characteri	L	L	L	L	NI Unclear if sample size adequate	L	S

Trial	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall bias
	stics							
Liver resection/ hepatectomy								
OVERALL MORTALITY								
Berber et al, 2010 [35]	C Experience of surgeons not reported, insufficient information on inclusion/ exclusion criteria, on clinical and pathologic variables	M NI on type and approach of resection	L	L	S Data not clearly reported	C Small sample size for survival, no power calculation	L	C
Lai & Tang, 2016 [36]	C Experience of surgeons with robotic procedure unclear, insufficient information on inclusion/ exclusion criteria	NI	L	S Cross-over of procedures and multiple procedures performed	L	C No sample size calculations, sample too small for outcome, NI on loss to follow-up	L	C
PATIENT-ASSESSED OUTCOMES (QoL, symptoms, satisfaction)								
Berber et al, 2010 [35]	Not defined as outcome							
Lai & Tang, 2016 [36]	Not defined as outcome							
SAFETY & PERIOPERATIVE OUTCOMES								
Berber et al, 2010 [35]	S See above	NI	L	L	C Not all complications data reported	L	C Complications data missing	C
Lai & Tang, 2016 [36]	S See above	NI	L	S See above	L	C Reported on complications per	L	C

Trial	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall bias
						procedures not patients		
Hernia repair								
OVERALL MORTALITY								
Tran, 2011 [37]	Not defined as outcome							
PATIENT-ASSESSED OUTCOMES (QoL, symptoms, satisfaction)								
Tran, 2011 [37]	C NI on experience of surgeons, insufficient information on inclusion/ exclusion criteria and on clinical and pathological variables	C Unclear how selection performed	L	L	L	C No information on how satisfaction was measured	L	C
SAFETY & PERIOPERATIVE OUTCOMES								
Tran, 2011 [37]	C See above	C See above	L	L	C Only information on wound infection given	S Only information on wound infection given	S Only information on wound infection given	C

Applicability tables

Table A4: Summary table characterising the applicability of a body of studies

Thoracic surgery: lobectomy and mediastinal surgery

Domain	Description of applicability of evidence
Population	All thoracic surgery procedures included in this HTA were performed due to lung cancer. The enrolled populations in the studies do not differ substantially from the target population; therefore the findings are generalizable to the target population.
Intervention	**Lobectomy/segmentectomy** studies used robot-assisted lobectomy (RATS) with the da Vinci system whilst the **mediastinal surgery study** used robot-assisted anterior mediastinal mass resection, again with the da Vinci system.
Comparators	Videothoracoscopy (VATS) was the control procedure for the lobectomy studies and open mediastinal mass resection by sternotomy was the control procedure for the mediastinal surgery study.
Outcomes	The main outcomes considered were perioperative events, complications and resource use. All four observational studies (3 for lobectomy/segmentectomy and 1 for mediastinal surgery) were included in the effectiveness and safety domains. The 3 lobectomy/ segmentectomy studies considered perioperative events, perioperative events and resource use, and perioperative events and complications. One study had a follow-up for 1 year but this was primarily a cost study; information on endpoints relevant for this HTA was only available for up to 90 days. None of the lobectomy studies considered quality of life. The mediastinal surgery study considered quality of life using a standardized and valid instrument although the sample size was small.
Setting	All the lobectomy/segmentectomy studies were conducted in Europe. In 2 studies the intervention and control procedures were undertaken in different time periods. In one of the studies there was no information on the level of experience or training of the surgeon. The mediastinal surgery study was also conducted in Europe. No information was provided on the training or experience of the surgeon.

Visceral surgery: Oesophagus

Domain	Description of applicability of evidence
Population	**(i) Antireflux/fundoplication**: patients had gastro-oesophageal reflux disease. **(ii) Heller myotomy**: patients had achalasia. **(iii) Oesophagectomy**: patients had carcinoma. The enrolled populations in the studies do not differ substantially from the target population; therefore the findings are generalizable to the target population.
Intervention	(i) One of the Heller myotomy studies used a partial fundoplication in addition to the robot-assisted laparoscopic Heller myotomy, the other only used robot-assisted laparoscopic Heller myotomy (ii) robotic fundoplication was used in the antireflux/fundoplication studies (iii) robotic thoracolaparoscopic oesophagectomy was used in the oesophagectomy RCT. All of the studies, regardless of specific procedure, used the da Vinci robotic system as the intervention.
Comparators	(i) conventional laparoscopic fundoplication (ii) laparoscopic Heller myotomy (in one study partial fundoplication was added to this) (iii) open transthoracic oesophagectomy

Domain	Description of applicability of evidence
Outcomes	**Antireflux/fundoplication**. 3 studies contributed to the effectiveness and safety domains whilst one study provided evidence on effectiveness only. Mortality associated with the procedure could not be assessed, since it was not reported in any of the studies. Morbidity/quality of life was reported by all 4 studies although different instruments were used which makes comparison difficult. **Oesophagectomy**. The single RCT reported on both safety and effectiveness parameters including mortality, quality of life and functional recovery as well as providing data on perioperative events/resource use. **Heller myotomy**. Neither observational study considered mortality or recurrence but both measured quality of life (with a follow-up of up to 6 months) whereby one of the studies used a standardized, valid instrument (although no results on between group comparisons were reported). Most information relates to perioperative events/resource use. Two of the studies in this area considered outcomes relating to patient satisfaction whilst one considered time to work/daily activities.
Setting	Both the antireflux/fundoplication and the oesophagectomy studies were conducted in Europe whilst the Heller myotomy studies were conducted outside of Europe (USA and Venezuela). Neither the oesophagectomy study nor the Heller myotomy studies provided information on surgical training or experience. In one antireflux study, surgeons had undertaken 20 robotic surgery procedures whilst in 3 studies no information was given on the experience with robotic surgery.

Visceral surgery: Stomach

Domain	Description of applicability of evidence
Population	Gastric cancer patients were included in the gastrectomy studies; the samples relate to Chinese patients. No patient details were given for the bariatric surgery study.
Intervention	The specific device used for robotic gastrectomy was not reported whilst for the bariatric surgery, robotic laparoscopic Roux-en-Y gastric bypass with the daVinci Surgical System was implemented.
Comparators	For the gastrectomy studies, one used laparoscopic gastrectomy whilst the other used open gastrectomy as the comparator. In the bariatric surgery study laparoscopic Roux-en-Y gastric bypass was the comparator.
Outcomes	**Bariatric**. Only information relating to the safety domain was provided but here there were very few events so relative effect estimates were not possible. Resource implications– notably operation time– was reported although the sample size was small and there was insufficient information on patient characteristics i.e. serious risk of bias. **Gastrectomy**. In the comparison with open gastrectomy, morbidity and quality of life was not reported; in the laparoscopy comparison the certainty of the evidence was assessed as very low. Both studies reported complications and perioperative events/resource use, namely blood loss, length of stay and operation time.
Setting	In one study, surgeons were very experienced with robotic gastrectomy; in the other study no information was given. Both gastrectomy studies took place in China. The bariatric surgery study took place in the USA; surgeons were reported to have had mandatory FDA training in the da Vinci system.

Visceral surgery: Bowel

Domain	Description of applicability of evidence
Population	**(i) Colectomy**: colonic carcinoma patients for colectomy **(ii) Rectal resection**: rectal cancer patients **(iii) Rectal rectopexy**: rectal prolapse/intrasusception patients. The enrolled populations in the studies do not differ substantially from the target population; therefore the findings are generalizable to the target population.

Domain	Description of applicability of evidence
Intervention	(i) Robot-assisted colectomy with the da Vinci system (ii) robot-assisted laparoscopic rectal cancer resection with the da Vinci system (iii) robot-assisted ventral mesh rectopexy with the da Vinci system
Comparators	(i) Laparoscopically-assisted colectomy (ii) laparoscopic rectal resection (iii) laparoscopic ventral mesh rectopexy
Outcomes	**Colectomy**: follow-up was for a maximum of 30 days (not clearly stated); outcomes were positive surgical margins, pain scores (VAS), complications and perioperative events/resource use. 30-day mortality was reported but the sample size was too small for this outcome. **Rectal resection**: outcomes related to survival, clinically-relevant outcomes, quality of life (measured with different instruments), pain and complications. One was an international mutlicentre RCT. The longest follow-up was 12 months. 2 studies were of a low risk of bias. **Rectal rectopexy**: This RCT only considered pain, complications and perioperative outcomes with a maximum follow-up of until discharge.
Setting	(i) RCT took place in Korea; the operating team had previously undertaken 30 robotic procedures (5 specifically of this type) (ii) the RCTs covered a number of European and international countries; 3 of 4 studies reported on the existence of surgeon experience with robot-assisted surgery (iii) study took place in Finland with “experienced” surgeons (no details reported).

Visceral surgery: Gallbladder/Liver/Spleen

Domain	Description of applicability of evidence
Population	**(i) Cholestectomy**: patients had benign gallbladder disease and in one study, gallstones. **(ii) Liver resection**: patients with liver tumours (no details on exclusion criteria). **(iii) Hernia repair**: patients recommended for hernia repair (no details on exclusion criteria). As far as could be assessed, the enrolled populations in the studies do not differ substantially from the target population, therefore the findings are generalizable to the target population.
Intervention	(i) Single-site cholecystectomy with da Vinci (in 1 trial the product type was not specified) (ii) robot-assisted laparoscopic hepatectomy/liver resection (in 1 study da Vinci system was used; in 1 study product was not reported) (iii) robotic single-port total extraperitoneal inguinal hernia repair with the Freehand system was used
Comparators	(i) Single-port, four-port or multiport laparoscopic cholecystectomy (ii) laparoscopic resection/partial hepatectomy (iii) laparoscopic single-port inguinal hernia repair
Outcomes	**Cholecystectomy**: follow-up varied between none (only operation itself considered) to around a maximum of 3 years. 3 RCTs considered QoL (using SF-12 or gastrointestinal quality of life index) and 2 studies measured satisfaction (using Body Image Questionnaire). Pain, complications, and perioperative events/resource use were also reported. **Liver resection**: follow-up was long (> 1 year) but variable. Survival, recurrence, complications and perioperative events/resource use were assessed. **Hernia repair**: 6 month follow-up looking at satisfaction and complications.
Setting	(i) RCTs were conducted in 4 different European countries; surgeons often had prior experience but also included surgeons who were learning the robotic technique (ii) studies took place in USA and China; no information on experience with robot-assisted surgery (iii) study took place in Australia; no information on the experience of surgeons

DOCUMENTATION OF THE SEARCH STRATEGIES

Strategies for identifying literature on robotic thoracic and visceral surgery (systematic search)

1. Robotic (Pulmonary) Lobectomy:

Search strategy for Medline (Ovid MEDLINE(R) <1946 to June Week 3 2018>, Ovid MEDLINE(R) Epub Ahead of Print <June 25, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <June 25, 2018>, Ovid MEDLINE(R) Daily Update <June 25, 2018>). Date of search: 26.06.2018

1 ((pulmonar* or lung*) adj5 (segmentectom* or lobectom*)).mp. (3776)
2 ((excis* or resect*) adj5 (lobe* or lung*)).mp. (20369)
3 1 or 2 (22911)
4 exp Robotic Surgical Procedures/ (3932)
5 robot*-assisted*.mp. (9971)
6 (robot* adj5 (surger* or surgical*)).mp. (12260)
7 4 or 5 or 6 (16830)
8 3 and 7 (193)
9 limit 8 to (clinical trial, all or randomized controlled trial) (10)
10 ((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3665363)
11 8 and 10 (41)
12 9 or 11 (47)
13 remove duplicates from 12 (47)

Search strategy for Embase (via Elsevier). Date of search: 26.06.2018

No.	Query	Results
#14.	#10 OR #12 OR #13	57
#13.	#9 AND ('clinical trial'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de)	26
#12.	#9 AND #11	47
#11.	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,247,422
#10.	#4 AND #8 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	15
#9.	#4 AND #8	545
#8.	#5 OR #6 OR #7	66,212
#7.	((excis* OR resect*) NEAR/5 (lobe* OR lung*)):ti,ab,de	57,124
#6.	((pulmonar* OR lung*) NEAR/5 (segmentectom* OR lobectom*)):ti,ab,de	18,430
#5.	'lung lobectomy'/exp	9,251
#4.	#1 OR #2 OR #3	26,594
#3.	robot* NEAR/5 surg*	26,594
#2.	'robotic surgical procedure'/exp	2,001
#1.	'robot assisted surgery'/exp	6,055

Search strategy for Cochrane (CENTRAL). Date of search: 26.06.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	robot*-assisted* (Word variations have been searched)
#3	robot* near surg* (Word variations have been searched)
#4	#1 or #2 or #3
#5	(pulmonar* or lung*) near (segmentectom* or lobectom*) (Word variations have been searched)
#6	(excis* or resect*) near (lobe* or lung*) (Word variations have been searched)
#7	#5 or #6
#8	#4 and #7 in Trials (Word variations have been searched)

21 Hits

2. Robotic Mediastinal Surgery (incl. Thymectomy):

Search strategy for Medline (Ovid MEDLINE(R) <1946 to June Week 4 2018>, Ovid MEDLINE(R) Epub Ahead of Print <July 02, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <July 02, 2018>, Ovid MEDLINE(R) Daily Update <July 02, 2018>). Date of search: 04.07.2018

1 exp Mediastinum/su [Surgery] (850)
2 (mediastin* adj5 (surg* or resect*)).mp. (4209)
3 exp Thymectomy/ (7687)
4 thymectom*.mp. (10046)
5 exp Thymus Gland/su [Surgery] (470)
6 (thymus adj5 (surg* or resect* or excis* or remov*)).mp. (770)
7 1 or 2 or 3 or 4 or 5 or 6 (15261)
8 exp Robotic Surgical Procedures/ (3961)
9 robot*-assisted*.mp. (9982)
10 (robot* adj5 (surger* or surgical*)).mp. (12294)
11 8 or 9 or 10 (16863)
12 7 and 11 (187)
13 limit 12 to clinical trial, all (6)
14 ((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3667967)
15 12 and 14 (31)
16 13 or 15 (35)
17 remove duplicates from 16 (35)

Search strategy for Embase (via Elsevier). Date of search: 04.07.2018

No.	Query	Results
#19.	#14 OR #16 OR #18	34
#18.	#17 AND ('clinical trial'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de)	15
#17.	#13	345
#16.	#13 AND #15	29
#15.	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,251,819
#14.	#4 AND #12 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	10
#13.	#4 AND #12	345
#12.	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	22,143
#11.	(thymus NEAR/5 (surg* OR resect* OR excis* OR remov*)):ti,ab,de	1,804
#10.	'thymus'/exp/dm_su	178
#9.	thymectom*:de,ti,ab	12,113
#8.	'thymectomy'/exp	10,168
#7.	(mediastin* NEAR/5 (surg* OR resect*)):ti,ab,de	9,026
#6.	'mediastinum'/exp/dm_su	263
#5.	'mediastinum surgery'/exp	25
#4.	#1 OR #2 OR #3	26,691
#3.	robot* NEAR/5 surg*	26,691
#2.	'robotic surgical procedure'/exp	2,027
#1.	'robot assisted surgery'/exp	6,096

Search strategy for Cochrane (CENTRAL). Date of search: 04.07.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	robot*-assisted* (Word variations have been searched)
#3	robot* near surg* (Word variations have been searched)
#4	#1 or #2 or #3
#5	MeSH descriptor: [Mediastinum] explode all trees and with qualifier(s): [Surgery – SU]
#6	mediastin* near (surg* or resect*) (Word variations have been searched)
#7	MeSH descriptor: [Thymectomy] explode all trees
#8	thymectom* (Word variations have been searched)
#9	MeSH descriptor: [Thymus Gland] explode all trees and with qualifier(s): [Surgery – SU]
#10	thymus near (surg* or resect* or excis* or remov*) (Word variations have been searched)
#11	#5 or #6 or #7 or #8 or #9 or #10
#12	#4 and #11 in Trials (Word variations have been searched)

11 Hits

3. Oesophageal Surgery

3.1. Robotic Fundoplication (Anti-reflux surgery)

Search strategy for Medline (Ovid MEDLINE(R) <1946 to July Week 3 2018>, Ovid MEDLINE(R) Epub Ahead of Print <July 31, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <July 31, 2018>, Ovid MEDLINE(R) Daily Update <July 31, 2018>). Date of search: 01.08.2018

1 exp Robotic Surgical Procedures/ (4119)
2 robot*-assisted*.mp. (10146)
3 (robot* adj5 (surger* or surgical*)).mp. (12496)

4 1 or 2 or 3 (17130)
5 exp Gastroesophageal Reflux/ (25014)
6 gastro?esophageal reflux.mp. (30221)
7 gastro-?esophageal reflux.mp. (1488)
8 GER.mp. (3281)
9 GERD.mp. (7602)
10 GORD.mp. (791)
11 5 or 6 or 7 or 8 or 9 or 10 (33322)
12 surgery.fs. (1840672)
13 (plication* or fundic wrap*).mp. (3415)
14 12 or 13 (1841448)
15 11 and 14 (8318)
16 ((anti?reflux or reflux) adj3 (surg* or management)).mp. (3983)
17 exp Gastroesophageal Reflux/su [Surgery] (5022)
18 15 or 16 or 17 (10463)
19 exp FUNDOPLICATION/ (4170)
20 fundoplication*.mp. (6573)
21 18 or 19 or 20 (12997)
22 4 and 21 (187)
23 limit 22 to clinical trial, all (18)
24 ((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3687346)
25 22 and 24 (46)
26 23 or 25 (55)
27 remove duplicates from 26 (55)

Search strategy for Embase (via Elsevier). Date of search: 02.08.2018

No.	Query	Results
#29.	#24 OR #26 OR #28	67
#28.	#23 AND #27	53
#27.	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,266,299
#26.	#25 AND ('clinical trial'/de OR 'controlled clinical trial'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de)	42
#25.	#23	370
#24.	#4 AND #22 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	14
#23.	#4 AND #22	370
#22.	#5 OR #6 OR #19 OR #20 OR #21	22,366
#21.	fundoplication:ti,ab,de	10,812
#20.	'stomach fundoplication'/exp	9,762
#19.	#15 AND #18	13,359
#18.	#16 OR #17	18,421
#17.	plication* OR 'fundic wrap*'	5,390
#16.	#15 AND 'surgery'/lnk	13,214
#15.	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	64,050
#14.	gord:ab,ti	1,308
#13.	gerd:ab,ti	14,624
#12.	ger:ab,ti	3,630
#11.	'gastro-oesophageal reflux':ab,ti,de	5,035
#10.	'gastro-esophageal reflux':ab,ti,de	2,793
#9.	'gastrooesophageal reflux':ab,ti,de	545
#8.	'gastroesophageal reflux':ab,ti,de	52,805
#7.	'gastroesophageal reflux'/exp	57,419
#6.	((antireflux OR 'anti reflux' OR reflux) NEAR/2 (surg* OR management)):ti,ab,de	5,183
#5.	'antireflux operation'/exp	11,662
#4.	#1 OR #2 OR #3	26,978
#3.	robot* NEAR/5 surg*	26,978
#2.	'robotic surgical procedure'/exp	2,091
#1.	'robot assisted surgery'/exp	6,220

Search strategy for Cochrane (CENTRAL). Date of search: 02.08.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	robot*-assisted* (Word variations have been searched)
#3	robot* near surg* (Word variations have been searched)
#4	#1 or #2 or #3
#5	MeSH descriptor: [Gastroesophageal Reflux] explode all trees and with qualifier(s): [Surgery – SU]
#6	gastro*esophageal reflux (Word variations have been searched)
#7	GER:ti,ab,kw (Word variations have been searched)
#8	GERD:ti,ab,kw (Word variations have been searched)
#9	GORD:ti,ab,kw (Word variations have been searched)
#10	#6 or #7 or #8 or #9
#11	MeSH descriptor: [General Surgery] explode all trees
#12	surg* or operat* (Word variations have been searched)
#13	#11 or #12
#14	#10 and #13
#15	(anti*reflux or reflux) near (surg* or operat* or management) (Word variations have been searched)
#16	MeSH descriptor: [Fundoplication] explode all trees
#17	fundoplication* (Word variations have been searched)
#18	plication* or fundic wrap* (Word variations have been searched)
#19	#5 or #14 or #15 or #16 or #17 or #18
#20	#4 and #19 in Trials (Word variations have been searched)

24 Hits

3.2. Robotic Oesophagectomy

Search strategy for <u>Medline</u> (Ovid MEDLINE(R) <1946 to July Week 4 2018>, Ovid MEDLINE(R) Epub Ahead of Print <August 07, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <August 07, 2018>, Ovid MEDLINE(R) Daily Update <August 07, 2018>). Date of search: 08.08.2018

1	exp Robotic Surgical Procedures/ (4178)
2	robot*-assisted*.mp. (10167)
3	(robot* adj5 (surger* or surgical*)).mp. (12570)
4	1 or 2 or 3 (17192)
5	exp Esophagectomy/ (8641)
6	Oesophagectom*.mp. (1464)
7	Esophagectom*.mp. (11939)
8	(Trans?hiat* adj3 (Oesophagectom* or Esophagectom*)).mp. (725)
9	((oesophag* or esophag*) adj3 (remov* or excis* or resect*)).mp. (5787)
10	5 or 6 or 7 or 8 or 9 (15424)
11	4 and 10 (188)
12	limit 11 to clinical trial, all (10)
13	((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3690476)
14	11 and 13 (39)
15	12 or 14 (45)
16	remove duplicates from 15 (45)

Search strategy for <u>Embase</u> (via Elsevier). Date of search: 08.08.2018

No.	Query	Results
#16.	#12 OR #13 OR #15	45
#15.	#11 AND #14	33
#14.	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,268,330
#13.	#11 AND ('clinical trial'/de OR 'clinical trial (topic)'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de)	31
#12.	#4 AND #10 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	9
#11.	#4 AND #10	297
#10.	#5 OR #6 OR #7 OR #8 OR #9	24,210
#9.	((oesophag* OR esophag*) NEAR/2 (remov* OR excis* OR resect*)):ti,ab,de	22,584
#8.	((transhiat* OR 'trans hiat*') NEAR/2 (oesophagectom* OR esophagectom*)):ti,ab,de	989
#7.	esophagectom*:ab,ti,de	12,057
#6.	oesophagectom*:ab,ti,de	2,077

#5. 'esophagus resection'/exp 18,631
#4. #1 OR #2 OR #3 27,005
#3. robot* NEAR/5 surg* 27,005
#2. 'robotic surgical procedure'/exp 2,091
#1. 'robot assisted surgery'/exp 6,236

Search strategy for Cochrane (CENTRAL). Date of search: 08.08.2018

ID Search
#1 MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2 robot* NEAR assisted*
#3 robot* NEAR surg*
#4 #1 OR #2 OR #3
#5 MeSH descriptor: [Esophagectomy] explode all trees
#6 Oesophagectom*
#7 Esophagectom*
#8 (Transhiat* OR Trans-hiat*) NEAR (Oesophagectom* OR Esophagectom*)
#9 (oesophag* OR esophag*) NEAR (remov* OR excis* OR resect*)
#10 #5 OR #6 OR #7 OR #8 OR #9
#11 #4 AND #10 in Trials

13 Hits

3.3. Heller Myotomy (Robotic oesophageal repair)

Search strategy for Medline (Ovid MEDLINE(R) <1946 to August Week 2 2018>, Ovid MEDLINE(R) Epub Ahead of Print <August 21, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <August 21, 2018>, Ovid MEDLINE(R) Daily Update <August 21, 2018>). Date of search: 22.08.2018

1 exp Robotic Surgical Procedures/ (4274)
2 robot*-assisted*.mp. (10223)
3 (robot* adj5 (surger* or surgical*)).mp. (12657)
4 1 or 2 or 3 (17300)
5 exp Esophageal Perforation/ (4092)
6 ((oesophag* or esophag* or Heller*) adj3 (repair* or perforat* or myotom*)).mp. (7221)
7 exp Heller Myotomy/ (37)
8 LHM.ti,ab. (268)
9 exp Esophageal Achalasia/ (6437)
10 achalasia*.mp. (7954)
11 ((oesophag* or esophag*) adj3 (swallow* adj3 (disorder* or difficult* or problem* or impair*))).mp. (64)
12 ((oesophag* or esophag*) adj3 dysphagia*).mp. (1267)
13 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 (15841)
14 4 and 13 (83)
15 limit 14 to clinical trial, all (9)
16 ((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3702283)
17 14 and 16 (21)
18 15 or 17 (28)
19 remove duplicates from 18 (28)

Search strategy for Embase (via Elsevier). Date of search: 22.08.2018

#21. #17 OR #18 OR #20 21
#20. #16 AND #19 16
#19. 'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti 2,273,818
#18. #16 AND ('clinical trial'/de OR 'randomized controlled trial (topic)'/de) 12
#17. #4 AND #15 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim) 4
#16. #4 AND #15 193
#15. #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #13 OR #14 30,237
#14. ((oesophag* OR esophag*) NEAR/2 dysphagia*):de,ab,ti 11,166
#13. #11 AND #12 1,448
#12. oesophag*:de,ab,ti OR esophag*:de,ab,ti 284,072

#11.	(swallow* NEAR/2 (disorder* OR difficult* OR problem* OR impair)):ti,ab,de	7,781
#10.	achalasia*:ti,ab,de	11,603
#9.	'esophagus achalasia'/exp	10,777
#8.	lhm:ti,ab	397
#7.	'cardioesophagomyotomy'/exp	1,628
#6.	'esophagus perforation'/exp	6,612
#5.	((oesophag* OR esophag* OR heller*) NEAR/2 (repair* OR perforat* OR myotom*)):ti,ab,de	11,545
#4.	#1 OR #2 OR #3	27,092
#3.	robot* NEAR/5 surg*	27,092
#2.	'robotic surgical procedure'/exp	2,115
#1.	'robot assisted surgery'/exp	6,281

Search strategy for Cochrane (CENTRAL). Date of search: 22.08.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	robot* NEAR assisted*
#3	robot* NEAR surg*
#4	#1 OR #2 OR #3
#5	MeSH descriptor: [Esophageal Perforation] explode all trees
#6	(oesophag* OR esophag* OR Heller*) NEAR (repair* OR perforat* OR myotom*) (Word variations have been searched)
#7	MeSH descriptor: [Heller Myotomy] explode all trees
#8	(LHM):ti,ab,kw (Word variations have been searched)
#9	MeSH descriptor: [Esophageal Achalasia] explode all trees
#10	(achalasia*)
#11	((oesophag* OR esophag*) NEAR (swallow* NEAR (disorder* OR difficult* OR problem* OR impair*)))
#12	((oesophag* OR esophag*) NEAR dysphagia*)
#13	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14	#4 AND #13 in Trials

2 Hits

4. Stomach Surgery

4.1. Robotic Gastrectomy

Search strategy for Medline (Ovid MEDLINE(R) <1946 to August Week 3 2018>, Ovid MEDLINE(R) Epub Ahead of Print <August 23, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <August 23, 2018>, Ovid MEDLINE(R) Daily Update <August 23, 2018>. Date of search: 24.08.2018

1	exp Robotic Surgical Procedures/ (4282)
2	robot*-assisted*.mp. (10237)
3	(robot* adj5 (surger* or surgical*)).mp. (12668)
4	1 or 2 or 3 (17316)
5	exp Gastrectomy/ (32564)
6	Gastrectom*.mp. (41938)
7	Pylorectom*.mp. (71)
8	((stomach or pylor*) adj3 (remov* or excis* or resect*)).mp. (3395)
9	5 or 6 or 7 or 8 (43701)
10	4 and 9 (314)
11	limit 10 to clinical trial, all (19)
12	((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3702513)
13	10 and 12 (113)
14	11 or 13 (122)
15	remove duplicates from 14 (120)

Search strategy for Embase (via Elsevier). Date of search: 24.08.2018

No.	Query	Results
#15.	#11 OR #13 OR #14	198
#14.	#10 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	30
#13.	#10 AND #12	156
#12.	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl*	2,274,392

	NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	
#11.	#10 AND ('clinical trial'/de OR 'clinical trial (topic)'/de OR 'controlled clinical trial'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de)	122
#10.	#4 AND #9	1,092
#9.	#5 OR #6 OR #7 OR #8	97,081
#8.	((stomach* OR pylor*) NEAR/5 (surg* OR resect* OR excis* OR remov*)):ti,ab,de	52,698
#7.	pylorectom*:ab,ti,de	62
#6.	gastrectom*:ab,ti,de	59,831
#5.	'gastrectomy'/exp	55,460
#4.	#1 OR #2 OR #3	27,104
#3.	robot* NEAR/5 surg*	27,104
#2.	'robotic surgical procedure'/exp	2,117
#1.	'robot assisted surgery'/exp	6,287

Search strategy for Cochrane (CENTRAL). Date of search: 28.08.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	robot* NEAR assisted*
#3	robot* NEAR surg*
#4	#1 OR #2 OR #3
#5	MeSH descriptor: [Gastrectomy] explode all trees
#6	(Gastrectom*)
#7	(Pylorectom*)
#8	(stomach OR pylor*) NEAR (remov* OR excis* OR resect*)
#9	#5 OR #6 OR #7 OR #8
#10	#4 AND #9 in Trials

36 Hits

4.2. Robotic Bariatric Surgery

Search strategy for Medline (Ovid MEDLINE(R) <1946 to August Week 4 2018>, Ovid MEDLINE(R) Epub Ahead of Print <August 29, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <August 29, 2018>, Ovid MEDLINE(R) Daily Update <August 29, 2018>. Date of search: 30.08.2018

1	exp Robotic Surgical Procedures/ (4316)
2	robot*-assisted*.mp. (10256)
3	(robot* adj5 (surger* or surgical*)).mp. (12704)
4	1 or 2 or 3 (17343)
5	exp Bariatric Surgery/ (21860)
6	bariatric*.mp. (17322)
7	(Gastric adj3 (bypass* or band* or stimul*)).mp. (18304)
8	Roux*.mp. (12538)
9	RYGB.ti,ab. (2197)
10	(sleeve* adj3 gastrectom*).mp. (4077)
11	5 or 6 or 7 or 8 or 9 or 10 (40294)
12	4 and 11 (258)
13	limit 12 to clinical trial, all (9)
14	((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3704848)
15	12 and 14 (62)
16	13 or 15 (67)
17	remove duplicates from 16 (67)

Search strategy for Embase (via Elsevier). Date of search: 30.08.2018

No.	Query	Results
#19.	#15 OR #16 OR #18	72
#18.	#14 AND #17	54
#17.	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,276,938

#16. #14 AND ('clinical trial'/de OR 'clinical trial (topic)'/de OR 'controlled clinical trial'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de)	47
#15. #4 AND #13 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	16
#14. #4 AND #13	616
#13. #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	61,691
#12. (sleeve* NEAR/2 gastrectom*):ti,ab,de	11,248
#11. 'sleeve gastrectomy'/exp	10,141
#10. rygb:ti,ab	4,976
#9. roux*:ti,ab,de	22,907
#8. 'gastric bypass surgery'/exp	19,963
#7. (gastric NEAR/2 (bypass* OR band* OR stimul*)):ti,ab,de	31,140
#6. bariatric*:ti,ab,de	33,770
#5. 'bariatric surgery'/exp	35,121
#4. #1 OR #2 OR #3	27,132
#3. robot* NEAR/5 surg*	27,132
#2. 'robotic surgical procedure'/exp	2,121
#1. 'robot assisted surgery'/exp	6,308

Search strategy for Cochrane (CENTRAL). Date of search: 30.08.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	robot* NEAR assisted*
#3	robot* NEAR surg*
#4	#1 OR #2 OR #3
#5	MeSH descriptor: [Bariatric Surgery] explode all trees
#6	(bariatric*) (Word variations have been searched)
#7	(Gastric*) NEAR (bypass* OR band* OR stimul*) (Word variations have been searched)
#8	(Roux*) (Word variations have been searched)
#9	(RYGB):ti,ab,kw
#10	(sleeve* NEAR gastrect*) (Word variations have been searched)
#11	#5 OR #6 OR #7 OR #8 OR #9 OR #10
#12	#4 AND #11 in Trials

21 Hits

5. Stomach Surgery

5.1. Robotic Small Bowel Resection

Search strategy for Medline (Ovid MEDLINE(R) <1946 to August Week 4 2018>, Ovid MEDLINE(R) Epub Ahead of Print <August 30, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <August 30, 2018>, Ovid MEDLINE(R) Daily Update <August 30, 2018>). Date of search: 31.08.2018

1	exp Robotic Surgical Procedures/ (4320)
2	robot*-assisted*.mp. (10262)
3	(robot* adj5 (surger* or surgical*)).mp. (12711)
4	1 or 2 or 3 (17354)
5	exp Intestine, Small/ (156220)
6	((small bowel* or small intestine*) adj3 (remov* or excis* or resect*)).mp. (3762)
7	5 or 6 (157794)
8	4 and 7 (135)
9	limit 8 to clinical trial, all (3)
10	((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3705798)
11	8 and 10 (11)
12	9 or 11 (13)

Search strategy for Embase (via Elsevier). Date of search: 03.09.2018

No.	Query	Results
#13.	#9 OR #10 OR #12	53
#12.	#8 AND #11	48
#11.	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1	2,278,078

	blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	
#10.	#8 AND ('clinical trial (topic)'/de OR 'randomized controlled trial (topic)'/de)	16
#9.	#8 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	5
#8.	#4 AND #7	307
#7.	#5 OR #6	28,403
#6.	(('small bowel*' OR 'small intestine*') NEAR/5 (remov* OR excis* OR resect*)):ti,ab,de	9,044
#5.	'small intestine resection'/exp	22,983
#4.	#1 OR #2 OR #3	27,157
#3.	robot* NEAR/5 surg*	27,157
#2.	'robotic surgical procedure'/exp	2,126
#1.	'robot assisted surgery'/exp	6,326

Search strategy for Cochrane (CENTRAL). Date of search: 03.09.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	(robot* NEAR assist*) (Word variations have been searched)
#3	(robot* NEAR surg*) (Word variations have been searched)
#4	#1 OR #2 OR #3
#5	MeSH descriptor: [Intestine, Small] explode all trees
#6	(small bowel* OR small intestine*) NEAR (remov* OR excis* OR resect*) (Word variations have been searched)
#7	#5 OR #6
#8	#4 AND #7 in Trials

7 Hits

5.2. Robotic Colectomy

Search strategy for Medline (Ovid MEDLINE(R) <1946 to August Week 4 2018>, Ovid MEDLINE(R) Epub Ahead of Print <August 31, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <August 31, 2018>, Ovid MEDLINE(R) Daily Update <August 31, 2018>). Date of search: 04.09.2018

1	exp Robotic Surgical Procedures/ (4324)
2	robot*-assisted*.mp. (10264)
3	(robot* adj5 (surger* or surgical*)).mp. (12718)
4	1 or 2 or 3 (17362)
5	exp Colectomy/ (18986)
6	colectom*.mp. (21602)
7	procto?colectom*.mp. (4501)
8	hemi?colectom*.mp. (3636)
9	sigmoidectom*.mp. (923)
10	transversectom*.mp. (25)
11	((colon* or hemi*colon* or sigmoid*) adj3 (remov* or excis* or resect*)).mp. (8878)
12	5 or 6 or 7 or 8 or 9 or 10 or 11 (33558)
13	4 and 12 (341)
14	limit 13 to clinical trial, all (20)
15	((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3706833)
16	13 and 15 (101)
17	14 or 16 (113)
18	remove duplicates from 17 (113)

Search strategy for Embase (via Elsevier). Date of search: 04.09.2018

No.	Query	Results
#19.	#15 OR #16 OR #18	112
#18.	#14 AND #17	91
#17.	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,278,584
#16.	#14 AND ('clinical trial'/de OR 'randomized controlled trial (topic)'/de)	57
#15.	#4 AND #13 AND ([controlled clinical trial]/lim	19

OR [randomized controlled trial]/lim)
#14. #4 AND #13 755
#13. #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 60,627
#12. ((colon* OR hemi*colon* OR sigmoid*) NEAR/5 45,392
(remov* OR excis* OR resect*)):ti,ab,de
#11. transversectom*:ti,ab,de 40
#10. sigmoidectom*:ti,ab,de 3,519
#9. hemi*colectom*:ti,ab,de 9,415
#8. procto*colectom*:ti,ab,de 6,440
#7. 'proctocolectomy'/exp 5,454
#6. colectom*:ti,ab,de 17,766
#5. 'colon resection'/exp 38,801
#4. #1 OR #2 OR #3 27,173
#3. robot* NEAR/5 surg* 27,173
#2. 'robotic surgical procedure'/exp 2,134
#1. 'robot assisted surgery'/exp 6,335

Search strategy for Cochrane (CENTRAL). Date of search: 04.09.2018

ID Search
#1 MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2 (robot* NEAR assist*) (Word variations have been searched)
#3 (robot* NEAR surg*) (Word variations have been searched)
#4 #1 OR #2 OR #3
#5 MeSH descriptor: [Colectomy] explode all trees
#6 colectom* (Word variations have been searched)
#7 procto*colectom* (Word variations have been searched)
#8 hemi*colectom* (Word variations have been searched)
#9 sigmoidectom* (Word variations have been searched)
#10 transversectom* (Word variations have been searched)
#11 (colon* OR hemi*colon* OR sigmoid*) NEAR (remov* OR excis* OR resect*) (Word variations have been searched)
#12 #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
#13 #4 AND #12 in Trials

31 Hits

5.3. Robotic Rectal Resection

Search strategy for Medline (Ovid MEDLINE(R) <1946 to August Week 5 2018>, Ovid MEDLINE(R) Epub Ahead of Print <September 06, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <September 06, 2018>, Ovid MEDLINE(R) Daily Update <September 06, 2018>). Date of search: 07.09.2018

1 exp Robotic Surgical Procedures/ (4345)
2 robot*-assisted*.mp. (10297)
3 (robot* adj5 (surger* or surgical*)).mp. (12761)
4 1 or 2 or 3 (17417)
5 polypectom*.mp. (4528)
6 proctectom*.mp. (1131)
7 rectopex*.mp. (805)
8 ((rect* or colo?rect* or meso?rect* or polyp* or sphincter*) adj3 (remov* or excis* or resect*)).mp. (21331)
9 colo?rectom*.mp. (20)
10 rectom*.mp. (43)
11 5 or 6 or 7 or 8 or 9 or 10 (26117)
12 4 and 11 (498)
13 limit 12 to clinical trial, all (37)
14 ((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3709558)
15 12 and 14 (169)
16 13 or 15 (187)
17 remove duplicates from 16 (186)

Search strategy for Embase (via Elsevier). Date of search: 07.09.2018

No. Query Results
#21. #17 OR #18 OR #20 214
#20. #16 AND #19 178
#19. 'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* 2,280,161

NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	
#18. #16 AND ('clinical trial'/de OR 'controlled clinical trial'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de)	127
#17. #4 AND #15 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	54
#16. #4 AND #15	1,309
#15. #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	65,349
#14. ((rect* OR colo*rect* OR meso*rect* OR polyp* OR sphincter*) NEAR/5 (remov* OR excis* OR resect*)):ti,ab,de	55,886
#13. 'mesorectal excision'/exp	46
#12. rectopex*:ti,ab,de	1,367
#11. 'proctopexy'/exp	1,348
#10. proctectom*:ti,ab,de	1,796
#9. 'rectum resection'/exp	14,722
#8. polypectom*:ti,ab,de	12,108
#7. 'polypectomy'/exp	7,815
#6. rectom*:ti,ab,de	74
#5. colo*rectom*:ti,ab,de	46
#4. #1 OR #2 OR #3	27,214
#3. robot* NEAR/5 surg*	27,214
#2. 'robotic surgical procedure'/exp	2,141
#1. 'robot assisted surgery'/exp	6,354

Search strategy for Cochrane (CENTRAL). Date of search: 07.09.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	(robot* NEAR assist*) (Word variations have been searched)
#3	(robot* NEAR surg*) (Word variations have been searched)
#4	#1 OR #2 OR #3
#5	colo*rectom* (Word variations have been searched)
#6	rectom* (Word variations have been searched)
#7	polypectom* (Word variations have been searched)
#8	proctectom* (Word variations have been searched)
#9	rectopex* (Word variations have been searched)
#10	(rect* OR colo*rect* OR meso*rect* OR polyp* OR sphincter*) NEAR (remov* OR excis* OR resect*)
#11	#5 OR #6 OR #7 OR #8 OR #9 OR #10
#12	#4 AND #11 in Trials

73 Hits

6. Gallbladder, Liver and Spleen Surgery

6.1. Robotic Cholecystectomy

Search strategy for Medline (Ovid MEDLINE(R) <1946 to August Week 5 2018>, Ovid MEDLINE(R) Epub Ahead of Print <September 10, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <September 10, 2018>, Ovid MEDLINE(R) Daily Update <September 10, 2018>). Date of search: 11.09.2018

1	exp Robotic Surgical Procedures/ (4354)
2	robot*-assisted*.mp. (10309)
3	(robot* adj5 (surger* or surgical*)).mp. (12776)
4	1 or 2 or 3 (17436)
5	((gallbladder* or gall bladder*) adj3 (remov* or excis* or resect*)).mp. (1641)
6	exp Cholecystectomy/ (27234)
7	cholecystectom*.mp. (36376)
8	5 or 6 or 7 (36960)
9	4 and 8 (329)
10	limit 9 to clinical trial, all (25)
11	((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3711921)
12	9 and 11 (71)
13	10 or 12 (81)
14	remove duplicates from 13 (81)

Search strategy for Embase (via Elsevier). Date of search: 11.09.2018

No.	Query	Results
#14.	#10 OR #11 OR #13	90
#13.	#9 AND #12	75
#12.	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2,280,988
#11.	#9 AND ('clinical trial'/de OR 'controlled clinical trial'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de)	58
#10.	#4 AND #8 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	29
#9.	#4 AND #8	716
#8.	#5 OR #6 OR #7	54,211
#7.	((gallbladder* OR 'gall bladder*') NEAR/5 (remov* OR excis* OR resect*)):ti,ab,de	3,007
#6.	cholecystectom*:ti,ab,de	53,072
#5.	'cholecystectomy'/exp	47,382
#4.	#1 OR #2 OR #3	27,238
#3.	robot* NEAR/5 surg*	27,238
#2.	'robotic surgical procedure'/exp	2,146
#1.	'robot assisted surgery'/exp	6,366

Search strategy for Cochrane (CENTRAL). Date of search: 11.09.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	(robot* NEAR assist*) (Word variations have been searched)
#3	(robot* NEAR surg*) (Word variations have been searched)
#4	#1 OR #2 OR #3
#5	MeSH descriptor: [Cholecystectomy] explode all trees
#6	Cholecystectom* (Word variations have been searched)
#7	(gallbladder* OR gall bladder*) NEAR (remov* OR excis* OR resect*) (Word variations have been searched)
#8	#5 OR #6 OR #7
#9	#4 AND #8 in Trials

51 Hits

6.2. Robotic Herniorrhaphy

Search strategy for Medline (Ovid MEDLINE(R) <1946 to September Week 1 2018>, Ovid MEDLINE(R) Epub Ahead of Print <September 13, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <September 13, 2018>, Ovid MEDLINE(R) Daily Update <September 13, 2018>). Date of search: 14.09.2018

1	exp Robotic Surgical Procedures/ (4350)
2	robot*-assisted*.mp. (10290)
3	(robot* adj5 (surger* or surgical*)).mp. (12747)
4	1 or 2 or 3 (17399)
5	exp Herniorrhaphy/ (7050)
6	herniorrhaph*.mp. (8906)
7	hernioplast*.mp. (1561)
8	(hernia* adj3 repair*).mp. (12237)
9	5 or 6 or 7 or 8 (18213)
10	4 and 9 (184)
11	limit 10 to clinical trial, all (4)
12	((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3709223)
13	10 and 12 (45)
14	11 or 13 (47)
15	remove duplicates from 14 (47)

Search strategy for Embase (via Elsevier). Date of search: 14.09.2018

No.	Query	Results
#16.	#12 OR #13 OR #15	34
#15.	#11 AND #14	23
#14.	'crossover procedure':de OR 'double-blind	2,283,132

procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	
#13. #11 AND ('clinical trial'/de OR 'controlled clinical trial'/de OR 'randomized controlled trial'/de)	18
#12. #11 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	14
#11. #4 AND #10	423
#10. #5 OR #6 OR #7 OR #8 OR #9	27,239
#9. (hernia* NEAR/5 repair*):ti,ab,de	19,833
#8. herniorrhaph*:ti,ab,de	5,516
#7. 'herniorrhaphy'/exp	4,521
#6. hernioplast*:ti,ab,de	15,087
#5. 'hernioplasty'/exp	14,351
#4. #1 OR #2 OR #3	27,289
#3. robot* NEAR/5 surg*	27,289
#2. 'robotic surgical procedure'/exp	2,154
#1. 'robot assisted surgery'/exp	6,393

Search strategy for Cochrane (CENTRAL). Date of search: 14.09.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	(robot* NEAR assist*) (Word variations have been searched)
#3	(robot* NEAR surg*) (Word variations have been searched)
#4	#1 OR #2 OR #3
#5	MeSH descriptor: [Herniorrhaphy] explode all trees
#6	Herniorrhaph* (Word variations have been searched)
#7	Hernioplast* (Word variations have been searched)
#8	hernia* NEAR repair* (Word variations have been searched)
#9	#5 OR #6 OR #7 OR #8
#10	#4 AND #9 in Trials

22 Hits

6.3. Robotic Hepatectomy

Search strategy for Medline (Ovid MEDLINE(R) <1946 to September Week 1 2018>, Ovid MEDLINE(R) Epub Ahead of Print <September 12, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <September 12, 2018>, Ovid MEDLINE(R) Daily Update <September 12, 2018>). Date of search: 13.09.2018

1	exp Robotic Surgical Procedures/ (4343)
2	robot*-assisted*.mp. (10281)
3	(robot* adj5 (surger* or surgical*)).mp. (12734)
4	1 or 2 or 3 (17381)
5	((liver* or hepat*) adj3 (remov* or excis* or resect*)).mp. (24484)
6	exp Hepatectomy/ (27346)
7	Hepatectom*.mp. (34628)
8	5 or 6 or 7 (46729)
9	4 and 8 (230)
10	limit 9 to clinical trial, all (9)
11	((randomized controlled trial or controlled clinical trial).pt. or randomi#ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3708257)
12	9 and 11 (43)
13	10 or 12 (48)
14	remove duplicates from 13 (48)

Search strategy for Embase (via Elsevier). Date of search: 13.09.2018

No.	Query	Results
#14.	#10 OR #11 OR #13	46
#13.	#9 AND #12	33
#12.	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1	2,282,498

over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti		
#11. #9 AND ('clinical trial'/de OR 'clinical trial (topic)'/de OR 'randomized controlled trial (topic)'/de)	23	
#10. #9 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)	6	
#9. #4 AND #8	424	
#8. #5 OR #6 OR #7	74,835	
#7. hepatectom*:ti,ab,de	28,837	
#6. 'liver resection'/exp	51,090	
#5. ((liver* OR hepat*) NEAR/5 (remov* OR excis* OR resect*)):ti,ab,de	65,195	
#4. #1 OR #2 OR #3	27,285	
#3. robot* NEAR/5 surg*	27,285	
#2. 'robotic surgical procedure'/exp	2,154	
#1. 'robot assisted surgery'/exp	6,388	

Search strategy for Cochrane (CENTRAL). Date of search: 13.09.2018

ID	Search
#1	MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#2	(robot* NEAR assist*) (Word variations have been searched)
#3	(robot* NEAR surg*) (Word variations have been searched)
#4	#1 OR #2 OR #3
#5	(liver* OR hepat*) NEAR (remov* OR excis* OR resect*) (Word variations have been searched)
#6	MeSH descriptor: [Hepatectomy] explode all trees
#7	Hepatectom* (Word variations have been searched)
#8	#5 OR #6 OR #7
#9	#4 AND #8 in Trials

11 Hits

Search strategies for the identification of ongoing clinical trials (trial register search)

1. Robotic (Pulmonary) Lobectomy
   Date of search**:** 28.06.2018

ClinicalTrials.gov (Advanced Search Mode)
(robotic OR robot) AND (pulmonary segmentectomy OR pulmonary lobectomy OR lung segmentectomy OR lung lobectomy OR lung excision OR lung resection OR pulmonary resection OR pulmonary excision) [DISEASE]
10 Hits

WHO ICTRP (Advanced Search Mode)
robot* **in the Title**
segmentectomy OR lobectomy OR pulmonary segmentectomy OR pulmonary lobectomy OR lung segmentectomy OR lung lobectomy OR lung excision OR lung resection OR pulmonary resection OR pulmonary excision **in the Intervention**
5 (3 additional) Hits

EU-CTR
robot* AND (segmentectomy OR lobectomy OR pulmonary OR lung)
No studies identified

2. Robotic Mediastinal Surgery (incl. Thymectomy):
   Date of search**:** 04.07.2018

ClinicalTrials.gov
No studies identified

WHO ICTRP (Advanced Search Mode)
robot* **in the Title**
thymus OR thymectomy OR mediastinal OR mediastinum **in the Intervention**
12 Hits

EudraCT (Basic Search Mode)
robot* AND (segmentectomy OR lobectomy OR pulmonary OR lung)
No studies identified

3. Oesophageal Surgery

3.1. Robotic Fundoplication (Anti-reflux surgery):
Date of search**:** 03.08.2018

ClinicalTrials.gov (Expert Search Mode)
(robotic OR robot*) AND (Antireflux OR Anti-reflux OR reflux OR Fundoplication)
3 Studies identified

WHO ICTRP (Advanced Search Mode)
robot* **in the Title**
(Antireflux OR Anti-reflux OR Fundoplication) **in the Intervention**
2 further studies identified

EudraCT (Basic Search Mode)
robot* AND (Antireflux OR Anti-reflux OR reflux OR Fundoplication)
No studies identified

3.2. Robotic Oesophagectomy
Date of search**:** 10.08.2018

ClinicalTrials.gov (Expert Search Mode)
(robotic OR robot*) AND (Esophagectomy OR Oesophagectomy OR (remov* OR excis* OR resect*) AND (Esophagectomy OR Oesophagectomy)) [TREATMENT]
5 Studies identified

WHO ICTRP (Basic Search Mode)
robot* AND Esophagectomy
18 (15 further) studies identified

EudraCT (Basic Search Mode)
robot* AND (Esophagectom* OR Oesophagectom*)
No studies identified

3.3. Heller Myotomy (Robotic oesophageal repair)
Date of search**:** 28.08.2018

ClinicalTrials.gov (Expert Search Mode)
(robotic OR robot*) AND (Myotom* OR Heller* OR Achalasia* OR oesophageal repair* OR esophageal repair*)) [TREATMENT]
No Studies identified

WHO ICTRP (Basic Search Mode)
robot* AND Myotom* No results
robot* AND Heller* No results
robot* AND (o)esophageal repair* No results
robot* AND Achalasia* 1 Study identified

EudraCT (Basic Search Mode)
(robotic OR robot*) AND (Myotom* OR Heller* OR Achalasia* OR oesophageal repair* OR esophageal repair*)
No studies identified

4. Stomach Surgery

4.1. Robotic Gastrectomy:

ClinicalTrials.gov (Expert Search Mode, Date of search**:** 28.08.2018)
(robotic OR robot) AND gastrectomy [DISEASE]
24 Studies identified

WHO ICTRP (Basic Search Mode, Date of search**:** 30.08.2018)
robot* AND gastrectom*
47 (29 additional) studies identified

EudraCT (Basic Search Mode, Date of search**:** 30.08.2018)
robot* AND gastrectom* No studies identified
robot AND gastrectom* No studies identified
robot* AND gastrectomy No studies identified
robot AND gastrectomy No studies identified
robotic AND gastrectom* No studies identified
robotic AND gastrectomy No studies identified
robotic gastrectom* No studies identified
robotic gastrectomy No studies identified

4.2. Robotic Bariatric Surgery
Date of search**:** 31.08.2018

ClinicalTrials.gov. (Expert Search):
(robotic OR robot) AND (bariatric OR roux OR gastric bypass OR gastric stimul* OR gastric band* OR sleeve gastrectom*) [TREATMENT]
8 Studies identified

WHO-ICTRP (Basic Search Mode):
robot* AND bariatric 3 studies identified
robot* AND roux* No studies identified
robot* AND gastric bypass 3 studies identified

robot* AND sleeve* 1 study identified

3 (1 additional) studies identified

EU Clinical Trials (Basic Search Mode):
robot* AND bariatric No relevant studies identified
robot* AND roux* No relevant studies identified
robot* AND gastric bypass No relevant studies identified
robot* AND stomach bypass No relevant studies identified
robot* AND sleeve* No relevant studies identified
robot* AND gastric No relevant studies identified

5. Bowel Surgery

5.1. Robotic Small Bowel Resection
Date of search**:** 03.09.2018

ClinicalTrials.gov (Expert Search Mode)
(robotic OR robot) AND (small bowel OR small intestine) [TREATMENT]
2 Studies identified
WHO ICTRP (Basic Search Mode)
robot* AND small bowel
2 further (potentially relevant) studies identified
EudraCT (Basic Search Mode)
robot* AND ("small intestine" OR "small bowel")
No studies identified
5.2. Robotic Colectomy
Date of search**:** 06.09.2018

ClinicalTrials.gov (Expert Search Mode)
(robotic OR robot) AND (colectomy) [TREATMENT]
21 Studies identified
WHO ICTRP (Basic Search Mode)
robot* AND colectom*
16 (9 further) studies identified
EudraCT (Basic Search Mode)
robot* AND colectom*
1 additional study identified
5.3. Robotic Rectal Resection
Date of search**:** 10./11.09.2018
ClinicalTrials.gov (Expert Search Mode)
(robotic OR robot) AND (colorectal OR rectal OR mesorectal OR polypectomy OR proctectomy OR rectopexy OR rectomy OR colorectomy OR mesorectomy OR sphincter OR polyp) [TREATMENT]
45 Studies identified
WHO ICTRP (Basic Search Mode)
robot* AND colorect* 28 Studies identified
robot* AND colo-rectal 2 Studies identified
robot* AND rectal 37 Studies identified

⇨ 67 (38 further) studies identified

EudraCT (Basic Search Mode)
robot* AND (colorectal OR color-ectal OR rectal OR mesorectal OR meso-rectal OR polypectom* OR proctectom* OR rectopex* OR rectom* OR colorectom* OR mesorectom* OR sphincter OR polyp*)
5 (1 further) studies identified
6. Gallbladder, Liver and Spleen Surgery

6.1. Robotic Cholecystectomy
Date of search**:** 12.09.2018

ClinicalTrials.gov (Expert Search Mode)
(robotic OR robot) AND (Cholecystectomy OR gallbladder OR gall bladder) [TREATMENT]

12 Studies identified

WHO ICTRP (Basic Search Mode)
robot* AND cholecystectomy
13 (5 further) Studies identified

EudraCT (Basic Search Mode)
robot* AND (cholecystectom* OR gall bladder OR gallbladder)
No studies identified
6.2. Robotic Herniorrhaphy
Date of search**:** 14.09.2018

ClinicalTrials.gov (Expert Search Mode)
(robotic OR robot) AND (herniorrhaphy OR hernioplasty OR hernia repair) [TREATMENT]
13 Studies identified

WHO ICTRP (Basic Search Mode)
robot* AND hernia repair 13 Studies identified
robot* AND herniorrhaphy NOT hysterectomy 13 Studies identified
robot* AND hernioplasty 13 Studies identified

⇨ 13 (0 further) studies identified

EudraCT (Basic Search Mode)
robot* AND (hernia* OR herniorrhaph* OR hernioplast*)
No studies identified
6.3. Robotic Hepatectomy
Date of search**:** 13.09.2018
ClinicalTrials.gov (Expert Search Mode)
(robotic OR robot) AND (hepatectomy OR liver OR hepatic) [TREATMENT]
10 Studies identified
WHO ICTRP (Basic Search Mode)
robot* AND hepatectomy * 3 Studies identified
robot* AND hepatic 8 Studies identified
robot* AND liver 7 Studies identified

⇨ 18 (6 further) studies identified

EudraCT (Basic Search Mode)
Robot* AND (hepatectom* OR liver OR hepatic)
3 (0 further) studies identified
Search strategies for <u>Guidelines</u>
Search date: 23.10.2018
<u>G-I-N Guideline Search</u>
Search term(s) entered: Robot*, Robotic
1 Hit
<u>Trip-database (advanced search mode)</u>
Searchstring: (robot* OR robotic)
42 Hits (in category “Guidelines”)
N.B.: The National Guidelines Clearinghouse (NGC) has ceased compiling/making accessible Guidelines on 16th July 2018. Archived contents have been incorporated into the TRIP-Database

APPENDIX 2 : LIST OF ONGOING AND PLANNED STUDIES

List of ongoing and planned studies

Lobectomy/Segmentectomy

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
NCT02804893	Not date given (status unknown)	Prospective randomized study, Parallel assignment	300	VATS	RATS	• Age older than 18 years old • Known or suspected lung cancers • Patients in clinical stage T1-T2, N0-N1 candidate to surgery lobectomy or anatomical segmentectomy • ASA-1-2	Primary endpoints • Intraoperative complications: conversion rate, defined as procedures that start with minimally invasive access and are converted to open surgery due to different reasons (bleeding, anatomical reasons, oncological reasons, technical reasons, other) [Time Frame: date of Surgery] • Postoperative complications: surgical complications, higher or equal grade II assessed by Clavien-Dindo scale, within 90 days [Time Frame: within 90 days]
NCT03134534	January 2020	randomized study, Parallel assignment	300	RATS lobectomy	VATS lobectomy	• surgical indication for lobectomy; • minimal invasive surgery; • ASA (American Society of Anesthesiologists) stage: I-III; • signed informed consent	Primary endpoints • 3-year overall survival (OS) [Time Frame: 3 year after surgery] OS at 3 year after surgery
NCT02617186	March 2018 (recruiting)	RCT	186	Robotic thoracic surgery	Video-assisted thoracoscopic surgery	• Age > 18 years • clinical stage I, II or IIIa non-small cell lung cancer (NSCLC) • Candidates for minimally invasive pulmonary lobectomy, as determined by the operating surgeon.	• Difference in HRQOL scores between the treatment groups, as measured by the EQ-5D-5L questionnaire at week 12 weeks. [Time Frame: Assessed at 12 weeks, presented average 1 year from end of study]
NCT01933828	June 2015 (status unkown, no	Randomized prospe	176	VATS lobectomy Robot-	open lobectomy	• Non-small cell lung carcinoma, pathologically confirmed or strong suspicion based on	Primary endpoints • Quality of life (EQ5D) [Time Frame: up to12 month] Primary endpoints include Quality of life assessed by EQ5D for VATS

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
	publication identified)	ctive trial, Parallel Assignment		assisted lobectomy		imaging. • T1 or T2a (≤ 5 cm) on computer tomography (CT). • Primary aim is lobectomy. • Tumor not in close relation to the hilar structures (bronchus,vessels) based on CT. • Clinically staged N0 (no regional lymph node metastasis) or N1 (metastasis to ipsilateral, hilar, interlobar- and/or intrapulmonary lymph nodes), M0 (no distant metastasis) after clinical staging according to the current Dutch guideline (may 2011).	versus open lobectomy in patients with early stage non small cell lung carcinoma. • Hospital length of stay [Time Frame: day of discharge from hospital after surgery (expected within 2 weeks).] .

Mediastinal Surgery

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
No relevant ongoing trials were identified							

Antireflux/Fundoplication

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
DRKS00014690	Not date given (ROLAF Trial)	RCT	40	Robotic fundoplication	Conventional laparoscopic fundoplication	• Age > 18 years • Male and female	Primary endpoints • Quality Of Life in Reflux and Dyspepsia (QOLRAD) questionnaire [Time Frame: 10 years after initial surgery]

Heller Myotomy/Oesophageal Repair

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
No relevant ongoing trials were identified							

Oesophagectomy

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
NCT02292914	November 2017 (Status unknown)	Randomized prospective trial, Parallel Assignment	1120	Robot-assisted: esophagectomy; gastrectomy; pancreatectomy;rectal resection; radical cistectomy; prostatectomy ; Partial Nephrectomy; hysterectomy; Resection of malignant tumors of the mouth and orofaringolaringe; lung lobectomy	Procedure: Conventional Surgery Thoracoscopic oesophagectomy; Open rectal resection and rectal laparoscopy resection; Open radical cistectomy; Open prostatectomy ; Open Partial Nephrectomy; Laparoscopic hysterectomy; Laparoscopic lung lobectomy	• Patients eligible for robot-assisted surgery	Primary endpoints • Postoperative Complications [Time Frame: 30 days .] The postoperative complications will be measured by clavien-dindo scale
NCT03094351	December 2024	RCT	300	Robot-assisted Thoraco-laparoscopic Esophagecto	Conventional Thoraco-laparoscopic oesophagectomy	• Histologically proven squamous cell carcinoma of the intrathoracic esophagus. • Surgical resectable (T1b-3, N0-2, M0)	Primary endpoints • Overall Survival Rate [Time Frame: 5 years]

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
				my		• Age ≥ 18 and ≤ 75 years • European Clinical Oncology Group performance status 0, 1 or 2 • Written informed consent	
ChiCTR-IIR-17012851	June 2020	RCT	272	Robot-assisted minimally invasive esophagectomy (RAMIE)	conventional open surgery (OE)	• squamous cell carcinoma was diagnosed by gastroscopy or cytologic examination; • primary tumor in thoracic oesophageal cancer, • according to the inspection, confirmed the preoperative clinical stage cT3-4aN0-1M0 (AJCC/UICC eighth) of the patients with oesophageal cancer • Aged 18 to 75 years, physical condition, ECOG score of 0 to 1, expected survival time more than 12 months; • subjects without major organ dysfunction, blood, lung, liver, kidney function and heart function • informed consent	Primary endpoints • 3-year overall survival
ChiCTR-INR-16009408	December 2019	RCT	300	Robot-assisted oesophagectomy	Conventional minimally invasive thoraco-laparoscopic oesophagectomy	• Aged 20 to 80 years; • Karnofsky score above 80; • Histologically proven squamous cell carcinoma of the intrathoracic oesophagus; • Primary tumor located in the thoracic oesophagus. • Surgically resectable (T1-3, N0-	Primary endpoints • 3-year overall survival

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
						3, M0, excluding T4) based on the 7th UICC-TNM classification. • No prior treatment of chemotherapy or radiation therapy against any other malignancies. • No prior lateral thoracotomy (or thoracoscopic surgery) on the right side or no prior lobectomy or more extended surgery on the left side has been performed; • Sufficient organ functions • R0 oesophagectomy is expected; • Written informed consent.	
ChiCTR-TRC-13003318	2015-07-16	RCT	200	three-field robot-assisted esophagectomy	three-field thoracic-laparoscopic esophagectomy	• Patients with esophageal cancer (Age from 18 to 75); • No chemotherapy or radiotherapy was performed before operation; • Understood the experiment, informed consent.	• Pulmonary infection • Anastomotic leak • Anastomotic stricture • Chylothora
ChiCTR-TRC-13003312	2015-07-16	RCT	200	three-field robot-assisted esophagectomy	three-field thoracic-laparoscopic esophagectomy	• Patients with oesophageal cancer (Age from 18 to 75); • No chemotherapy or radiotherapy was performed before operation; • Understood the experiment, informed consent.	• Pulmonary infection • Anastomotic leak • Anastomotic stricture • Chylothora

Gastrectomy

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
NCT03313700	August 2022	RCT	300	Robot-assisted Distal Gastrectomy	Laparoscopic Assisted Distal Gastrectomy	• Age from over 18 to under 75 years • Primary gastric adenocarcinoma • cT1-4a(clinical stage tumor), N-/+, M0 • expected to perform distal gastrectomy • Performance status of 0 or 1 on Eastern Cooperative Oncology Group scale • American Society of Anesthesiology class I to III • Written informed consent	Primary endpints • 3-year disease free survival rate [Time Frame: 36 months] the rate of 3-year disease free survival
NCT03524300	November 2022	RCT	220	Robotic Assisted Total Gastrectomy	Laparoscopic Assisted Total Gastrectomy	• Age from over 18 to under 75 years • Primary gastric adenocarcinoma • The tumor is on the upper or middle third stomach and expected to perform total gastrectomy • Performance status of 0 or 1 on Eastern Cooperative Oncology Group scale • American Society of Anesthesiology class I to III • Written informed consent	Primary endpoints • 3-year disease free survival rate [Time Frame: 36 months] the rate of 3-year disease free survival
NCT02413476	May 2018 (Status	Non-rando	120	Robot-assisted	Laparoscopic-assisted	• Pathologically proven gastric cancer (early or advanced)	Primary endpoints • Five-year disease free survival rate [Time Frame: Up to 5

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
	unknown)	mized, prospective study, Parallel Assignment		gastrectomy	Gastrectomy	• Age: >18 and <80 • cT1-4a(surgically resectable tumor), N0-3,M0 • No obvious surgical contraindications • American Society of Anesthesiology score class I, II, or III • Written informed consent.	years post-operative]
NCT03273920	September 2022	RCT	1110	Robotic gastrectomy	Laparoscopic gastrectomy	• Pathologically proven gastric adenocarcinoma. • Tumor located in the lower third of the stomach, and is possible to be curatively resected by subtotal gastrectomy. • Preoperative stage of cT2-4aN0-3M0 • Eastern Cooperative Oncology Group performance status of 0 or 1 • American Society of Anesthesiology score of class I to III • informed consent	Primary endpoints • 3-year relapse-free survival [Time Frame: 3 years] Relapse-free survival is defined as days from surgery to recurrence or death from any cause, and it is censored at the latest day when the patient is alive without any evidence of recurrence
NCT03500471	December 2019	Non-randomised, prospective study	150	Robot-assisted Total Gastrectomy	Laparoscopic-assisted Total Gastrectomy	• Pathologically proven gastric adenocarcinoma; • Age: >18 and <80 • Tumor located in the upper third of the stomach or esophagogastric junction or other location, and is possible to be curatively resected by	Primary endpoints • Overall postoperative morbidity rates [Time Frame: 30 days]. Refers to the incidence of early postoperative complications. The early postoperative complication are defined as the event observed within 30 days after surgery.

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
						total gastrectomy; • Preoperative stage of cT2-4aN0-3M0; • American Society of Anesthesiology score of class I to III; • Eastern Cooperative Oncology Group performance status of 0 or 1; • informed consent	
NCT02751086	December 2024	Non-randomised, prospective cohort study	5000	Robot-assisted surgery Laparoscopic surgery Open surgery	-	• Histologically proven gastric cancer • Preoperative staging work-up performed by upper endoscopy and/or endoscopic ultrasound, and CT scan and in accordance to international guidelines • Early Gastric Cancer • Advanced Gastric Cancer • Patients treated with curative intent in accordance to international guidelines	Primary endpoints • Rate of patients with intraoperative adverse events [Time Frame: During surgery] events other than the normal course of the surgery • Mean of retrieved lymph nodes [Time Frame: Within 30 days after surgery] Count of retrieved lymph nodes at the histopathological examination of the surgical specimen • Rate of patients alive [Time Frame: 1 year after surgery] subjects alive at the planned endpoint • Rate of patients alive [Time Frame: 2 year after surgery] subjects alive at the planned endpoint • Rate of patients alive [Time Frame: 3 year after surgery] subjects alive at the planned endpoint • Rate of patients alive [Time Frame: 4 year after surgery] subjects alive at the planned endpoint • Rate of patients alive [Time Frame: 5 year after surgery] subjects alive at the planned endpoint
R000013738	No date given (no longer recruiting)	Non-randomised, prospective	650	Robotic gastrectomy	Conventional laparoscopic gastrectomy	• Age > 18 years • Male and female • Primary gastric cancer for	Primary endpoints • Morbidity

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
		study, Parallel Assignment				which surgical treatment was applicable (cStageI-III)	
R000011407	No date given (no longer recruiting)	Non-randomised, uncontrolled phase II study	100	robot assisted gastrectomy	-	• Age 20-80 years • Male and female • adenocarcinoma • Diagnosed as Stage IA or IB gastric cancer • Curative resection is expected by distal gastrectomy or total gastrectomy • Eastern clinical oncology group performance status is 0 or 1 • BMI < 30 • no prior upper abdominal surgery or intestinal resection other than appendectomy • No previous chemotherapy or radiation including those for other cancers	Primary endpoints • The incidence of post-operative intra-abdominal infectious complications (anastomotic leakage, pancreas related infection, and intra-abdominal abscess)
R000019689	No date given (open public recruiting)	Non-randomised, uncontrolled study	120	Robot-assisted laparoscopic gastrectomy	-	• Age > 20 years • Male and female • Histologically confirmed gastric cancer; clinically diagnosed T1 or T2N0 • Enough main organ functions to perform operation • informed consent obtained from the patient	Primary endpoints • The incidence of postoperative complication during 30 days after surgery

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
R000017904	No date given (open public recruiting)	historically controlled prospective cohort study	330	Robotic gastrectomy	-	• Operable patients under general anesthesia • Histologically diagnosed gastric adenocarcionoma • cStage I or II disease curably treated with total, distal, or proximal gastrectomy • Not indicated for endoscopic resection • Age over 18 • Informed consent is obtained	Primary endpoints • Postoperative complications greater than Grade III according to Clavien-Dindo classification
R000036007	No date given (preinitiation)	Randomised phase III study, Parallel Assignment	240	Robotic gastrectomy	Conventional laparoscopic gastrectomy	• Age 20-80 years • Histologically proven gastric carcinoma, resectable gastric cancer, excluding esophageal invasion • Eastern clinical oncology group performance status is 0 or 1 • BMI < 35 • No history of gastrointestinal surgery • No history of chemotherapy or radiotherapy • Normal function of the major organs • Proven written informed consent	Primary endpoints • Incidence of intra-abdominal infectious complications (pancreatic fistula, intra-abdominal abscess, and anastomotic leakage) with more than Clavien-Dindo grade 2
R000024081	No date given (open public recruiting)	historically controlled non-	110	Robotic gastrectomy	-	• Age > 20 years • Male and female • Pathologically confirmed gastric	Primary endpoints • Intraoperative complication • Postoperative complication (within 30 days)

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
		randomised study				cancer • Amenable to curative resection • ECOG Performance Status 0/1 • Written informed consent	• Operative mortality
ChiCTR-TRC-13003301	2015-07-01	RCT	200	robot surgery	laparoscopic surgery	• Patients with esophagogastric junctional adenocarcinoma	• Anastomotic leak • Pulmonary infection • Anastomotic stricture • Wound infection
ChiCTR-INR-17010404	2017-12-31	RCT	100	da Vinci robotic surgery group	Laparoscopic surgery group	• Patients with gastric cancer	• Recent clinical outcome measures • Markers of inflammat • immunologic function

Bariatric Surgery

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
No relevant ongoing trials were identified							

Colectomy

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
NCT02642978	September 2019	RCT	100	robot-assisted, simultaneous	Traditional open simultaneous	• Age ≥ 18 and ≤ 75 years; • Primary tumor has undergone	Primary endpoints • Disease-free survival(DFS) [Time Frame: 3 years disease-

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
				radical resection of both colorectal cancer and liver metastasis (RSRCLM)	radical resection of both colorectal cancer and liver metastasis	histologically confirmed colon adenocarcinoma • Together with clinical or radiological evidence of Stage II (T3-4, N0, M0) or Stage III (T1-4, N1-2, M0) disease • Performance status 0~1 • Adequate haematological, hepatic, renal function: • informed consent • liver resectability	free survival] DFS was defined as from the date of randomization to the date of tumor recurrence or death from any cause
ChiCTR1800017146	June 2026	RCT	746	Robot-assisted surgery	Laparoscopic surgery	• Aged 18 to 80 years; • Pathologic biopsy confirmed the right-sided colon adenocarcinoma; • Preoperative clinical stage: locally advanced right-sided colon adenocarcinoma（cT2-4,N0-2,M0AJCC-8); • R0 results are expected from right hemicolectomy and regional lymph node dissection; • Preoperative ECOG physical state score: 0/1; • Preoperative ASA score: I-III; • informed consent.	Primary endpoints • 3-year disease-free survival
NCT03650517	December 2021	Prospective, parallel cohort study	1200	Robot-assisted Right Colectomy with ICA and with ECA	-		Primary endpoints • Surgical wound infection [Time Frame: 30 days] (CDC definition) • Clavien Dindo Complication [Time Frame: 30 days] Complications according to Clavien Dindo Classification.

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
				Laparoscopic Right Colectomy with ICA and with ECA			

Small Bowel Resection

No relevant ongoing trials were identified	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
No relevant ongoing trials were identified							

Rectal Resection

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
NCT01130233	December 2014 (status unknown)	RCT	98	robotic assisted rectal resection	laparoscopic rectal resection	• Histologically proven new case of rectal cancer with the lower border within 15 cm from anal verge • Age >18 years • Informed consent obtained • American Society of Anesthesiologist class 1-3 • No contraindication to laparoscopic surgery • Acceptable operating risk	Primary endpoints • Bladder function [Time Frame: one year] Urodynamic Questionnaire •

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
NCT02673177	May 2019	Randomised, prospective study	225	Robot-assisted total mesorectal excision	Laparoscopic total mesorectal excision	• Patients who agree to both procedures • Match the diagnostic criteria; • Aged 18-70 years old; • Preoperative TNM staging (CT, laparoscopic exploration): cT1-3N0-3M0 (excluding M1, T4); • Preoperative ASA 3 scores; • no history of malignancy • no prior radiotherapy, chemotherapy or immunotherapy; • normal sexual function	Primary endpoint • Incidence of sexual and urinary dysfunction [Time Frame: One years after surgery]
NCT01736072	June 2018 (status unknown)	RCT	520	Robotic-assisted Resection of Rectal Cancer	Laparoscopic Resection of Rectal Cancer	• Aged ≥ 18 years • written informed consent • Diagnosis of rectal cancer amenable to curative surgery • Rectal cancer suitable for resection by either standard or robot-assisted laparoscopic procedure • Fit for robot-assisted or standard laparoscopic rectal resection • American Society of Anesthesiologists (ASA) physical status ≤ 3 • Capable of completing required questionnaires at time of consent	Primary endpoints • End of Conversion to Open Surgery [Time Frame: 1 day] The primary end point is the rate of conversion to open surgery as an indicator of surgical technical difficulty. Conversion is defined as the use of a laparotomy wound for any part of the mesorectal dissection. The use of a limited laparotomy wound to facilitate a low stapled anastomosis and/or specimen extraction is permissible and not defined as an open conversion.
NCT01591798	December	rando	146	Robot-	Laparoscopic	• mid or low rectal cancer (within	Primary endpoints

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
	2017 (status unknown)	mised phase II trial		assisted rectal resection	assisted rectal resection	9cm from anal verge) • pathologically proven as adenocarcinoma • written informed consent • no severe functional disability in lung and heart	• Quality of mesorectal excision [Time Frame: 7days after surgery (Pathologic report)] Evaluating the quality of mesorectal excision in rectal specimen
NCT01346436	May 2020	RCT	50	Roboti-assisted approach	Laparoscopic approach	• Aged ≥ 18 years • women • proven pelvic floor dysfunction • informed consent	Primary endpoints • Perioperative outcomes [Time Frame: up to 30 days] Including: blood loss, operative time, conversion rate, quality of dissection, pain, complications, hospital stay.
NCT03597126	September 2020	RCT	100	Robot-assisted Intersphincteri c Resection	Laparoscopic-assisted Intersphincteri c Resection	• 18 years to 80 years • Match diagnostic criteria; • tumor located 3 cm from anal verge • Clinically diagnosed cT1-3N0-2 M0 lesions • Tumor size of 4 cm or less • ASA 1-3 scores; • ECOG score is 0-1; • Adequate preoperative sphincter function	Primary endpoints • Change in urinary function [Time Frame: 6 months] The days of indwelling catheter after operation The overall efficiency of urination function • Change in International Index of Erectile Function [IIEF] score [Time Frame: 18 months] • Change in FIQL scores [Time Frame: 18 months] Alterations in Fecal Incontinence Quality of Life Instrument (FIQL) scores from baseline up to 18 months postoperatively • Change in Female Sexual Function Index [FSFI] [Time Frame: 18 months]
NCT02642978	September 2019	RCT	100	robot-assisted, simultaneous radical resection of both colorectal cancer and liver metastasis	Traditional open simultaneous radical resection of both colorectal cancer and liver	• Age ≥ 18 and ≤ 75 years; • Primary tumor has undergone histologically confirmed colon adenocarcinoma; • Together with clinical or radiological evidence of Stage II (T3-4, N0, M0) or Stage III (T1-4, N1-2, M0) disease	Primary endpoints • Disease-free survival(DFS) [Time Frame: 3 years disease-free survival] DFS was defined as from the date of randomization to the date of tumor recurrence or death from any cause

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
				(RSRCLM)	metastasis	• Performance status 0~1 • Adequate haematological, hepatic and renal function: • Written informed consent • liver resectability	
NCT01985698	October 2019	RCT	402	Robot-assisted resection	Laparoscopic resection Open Surgery	• Age 18-75 years • Histologically proven rectal adenocarcinoma • Inferior edge of the tumor located within 5 cm from the anal verge • No evidence of distant metastases • Tumor assessed as cT1-T3 or ycT1-T3 • No other malignancies • Suitable for both robot-assisted, laparoscopic and open surgery • American Society of Anesthesiologists (ASA) class I - III • No other preoperative treatment except neoadjuvant chemoradiotherapy • Informed consent	Primary endpoints • operative complications [Time Frame: 30 days post operatively] intra, and postoperative complications related to operation • assessed using a self-rating scale "International Index of Erectile Function" (IIEF-5). • self reported sexual function for female patients [Time Frame: at postoperative 3, 6 and 1 2 months] This section is assessed using a self-rating scale "Female Sexual Function Index" (FSFI).
NCT03209076	December 2020	Prospective, randomised study	120	Robot-assisted low anterior resection	Laparoscopic low anterior resection	• Age 18-70 years • Mid or low Rectal Adenocarcinoma • Performance Status (ECOG) 0	Primary endpoints • Urinary dysfunction [Time Frame: Change from Before surgery to 3 months after surgery] Urodynamic test

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
						- 2	
NCT03574493	June 2022	Prospective cohort study	1300	Open laparotomy Laparoscopic surgery Robot-assisted surgery Transanal surgery through the anus	-	• Age ≥ 18 years old • Rectal adenocarcinoma • High risk operative patients • Patients with adequate performance status • informed consent	Primary endpoints • Efficacy of surgical method (success determined by composite of Oncologic, morbidity and functional outcomes) [Time Frame: up to 4 years] completeness of resection, TME grade III, The absence of clavien dindo grade III-IV complications within 30 days post op
NCT02817126	October 2023	RCT	680	Robot-assisted resection	Laparoscopic resection	• Age 18-80 years • histologically proven rectal adenocarcinoma • inferior edge of the tumor located within 12 cm from the dentate line as determined by rigid rectoscopy • no evidence of distant metastases • tumor assessed as cT1-T3 • no other malignancies • suitable for both robot-assisted and laparoscopic surgery • informed consent	Primary endpoints • Disease-free survival [Time Frame: 3 years]
NCT01423214	December 2018	Prospective,	540	robot-assisted surgery	Laparoscopic surgery	• Eligibility rule of enrollment • Rectal adenocarcinoma that	Primary endpoints • Surgical quality based on pathological examination [Time

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
		randomised study, Parallel assignment				were 10 cm or less from the anal verge • 18 -80 years old • Clinically diagnosed cT3N0-2 disease • adequate hepatic, renal, and bone marrow function	Frame: up to 4 weeks after operation] A comparison of completeness of total mesorectal excision
ISRCTN14574075	February 2019	RCT	70	Robot-assisted rectal surgery	laparoscopic rectal surgery	• Patients with a diagnosis of rectal cancer • Male aged 18 years and over • informed consent • Fit enough to undergo minimally invasive surgery (ASA≤3) • Deemed suitable for minimally invasive surgery by local MDT • Elective case • Sexually active	Primary endpoints • Urological function is measured using the International Prostatic Symptoms Score (IPSS) pre-operatively and 3, 6 and 12 months after surgery • Sexual function is measured using the International Index of Erectile Function (IIEF) pre-operatively and 3, 6 and 12 months after surgery • Urodynamics (urine flow rate and post micturition residual urine volume) are assessed by a uroflow meter and a bladder scanner pre-operatively and 3, 6 and 12 months after surgery
ChiCTR-ICR-15007040	September 2020	RCT	215	Robot-assisted radical resection for rectal cancer	Laparoscopic-assisted radical resection for rectal cancer	• Patients who agree to both surgical procedures • Match diagnostic criteria; • Aged 18-70 years old; • Preoperative TNM staging (CT, laparoscopic exploration): cT1-3N0-3M0 (excluding M1, T4); • Preoperative ASA 3 scores; • no history of malignancy • no definitive treatment, such as radiotherapy, chemotherapy	Primary endpoints • The overall efficiency of urination function • The overall efficiency of sexual function • Sphincter-preserving rate of low rectal cancer

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
						• normal sexual function	
DRKS00011328	No date given (recruiting)	Non-randomised controlled study, Parallel Assignment	100	Robot-assisted rectal resection	Laparoscopic-assisted rectal resection Open rectal resection	• Age 18-80 years • Patients with rectal cancer • informed consent • BMI<=30 kg/m2 • No medical contraindication that exclude laparoscopy • Preoperatively normal bowel, bladder and sexual function	Primary endpoints • Functional outcome 6 and 12 months after surgery. Stool, urinary and sexual function as assessed by Wexner-score, EORTC QLQ-CR29 and EORTC QLQ-C30
NCT01196000	July 2013	RCT	0 (Study withdrawn)	Standard conventional laparoscopic resection	Robot-assisted laparoscopic resection	• •Able to provide written informed consent • •Diagnosis of rectal cancer amenable to curative surgery • ASA =< 3 • •Capable of completing required questionnaires at time of consent	• Rate of conversion to open surgery as an indicator of surgical technical difficulty

Cholecystectomy

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
NCT02485392	July 2017 (status unknown)	RCT	60	Single-Site robot-assisted cholecystectomy	Single-incision laparoscopic cholecystectomy	• Patient compliance and geographic proximity • Written informed consent • Women who are not breastfeeding and are not pregnant • Age ≥18 years	Primary endpoints • Surgeon's comfort as measured by LED and SMEQ questionnaires [Time Frame: 1 Day]

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
						• Symptomatic cholecystolithiasis • Chronic cholecystitis • Benign gallbladder polyps	
NCT03160157	December 2020	Prospective, randomised cohort study	200	Robotic Cholecystectomy	Laparoscopic Cholecystectomy	• 18 years or older • Any of the pre-operative diagnoses including chronic cholecystitis, acute cholecystitis, benign neoplastic disease of the gallbladder or pre-cancerous conditions of the gallbladder (polyps, adenomyomatosis), symptomatic cholelithiasis, porcelain gallbladder and biliary dyskinesia.	Primary endpoints • Determine which minimally invasive (small incisions) surgical approach is associated with the best outcomes when performing the removal of the gallbladder (cholecystectomy): laparoscopic or robotic? [Time Frame: 2 years] Outcome: open conversion • Determine which minimally invasive (small incisions) surgical approach is associated with the best outcomes when performing the removal of the gallbladder (cholecystectomy): laparoscopic or robotic? [Time Frame: 2 years] Outcome: biliary injuries • Determine which minimally invasive (small incisions) surgical approach is associated with the best outcomes when performing the removal of the gallbladder (cholecystectomy): laparoscopic or robotic? [Time Frame: 2 years] Outcome: biliary anomalies • Determine which minimally invasive (small incisions) surgical approach is associated with the best outcomes when performing the removal of the gallbladder (cholecystectomy): laparoscopic or robotic? [Time Frame: 2 years] Outcome: blood loss

Liver resection/Hepatectomy

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
NCT03297099	June 2020	Non-randomised, prospective	60	Robot-assisted Laparoscopic operation	Open surgery	• Age 18-70 years • Patients with intrahepatic bile duct stones or hepatolithiasis.	Primary endpoints • initial stone clearance rate [Time Frame: during the operation] rate of the removal of the stones from intrahepatic bile duct identified by ultrasonic or computed tomography or magnetic

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
		cohort study				• Liver function > Child-pugh level B, no severe biliary cirrhosis • Age: Between 18 to 70 years • Combined with severe liver atrophy hypertrophy syndrome, hepatic portal transposition or hilar biliary fibrosis/stenosis • Patients with good general condition, • Other organ lesions and previous biliary tract operation is not the absolute exclusion criteria • Written informed consent	resonance
ChiCTR-IOR-17011298	December 2020	RCT	20	Robot-assisted living donor hepatectomy	laparoscopic living donor hepatectomy	• healthy people without infectious disease,tumor and cardiopulmonary disorders; • Age over 18 years and under 55 years; • No history of upper abdominal surgery. • Normal liver function, normal coagulation function,no mental disease; • Voluntary donation of liver and in accordance with medical and ethics criteria; • Three generations lineal consanguinity	Primary endpoints • Intraoperative blood loss • Operation time

Hernia Repair

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
NCT03283982	September 2020	Registry-Based, prospective, RCT	74	Robotic Ventral Hernia Repair with IPOM	Laparoscopic Ventral Hernia Repair with IPOM	• Adult patients (>18 years old) • Primary or Incisional Ventral Hernia • informed consent • Considered eligible for minimally invasive ventral hernia repair • Willing to undergo mesh-based repair • Fascial closure is presumed to be achieved	Primary endpoints • Postoperative Pain Scores [Time Frame: Pain scores will be assessed on baseline, on postoperative days 1,7 and 30 and 365.] Pain scores will be assessed using the Numeric Pain Rating Scale (NRS-11)
NCT03007758	December 2019	RCT	100	Robot-assisted ventral hernia repair	open ventral hernia repair	• Age >18 years • Ventral or incisional hernia measuring ≥ 7 cm and ≤ 15 cm. • At least one of the following risk factors: Body Mass Index > 30, Chronic Obstructive Pulmonary Disease, Diabetes Mellitus, current smoker (within 1 month)	Primary endpoints • Composite outcome of diagnosis of surgical site occurrence or infection, hospital readmission, or hernia recurrence [Time Frame: Through study completion, an average of 2 years] A composite outcome of events which are clinically significant including but not limited to seroma requiring procedural intervention, skin dehiscence, cellulitis, hematoma, skin necrosis, and surgical site infections which may require interventions such as wound care or antibiotic therapy.
NCT02816658	May 2019	RCT	100	laparoscopic inguinal hernia surgery repair	Robot-assisted inguinal hernia repair	• 21 years or older • No prior open abdominal surgery at or below the umbilicus • Primary or recurrent unilateral inguinal hernia repair • No previous preperitoneal mesh placement • BMI less than or equal to	Primary endpoints • Pain Score [Time Frame: 2 Years] Differences in postoperative pain between those patients who undergo robotic inguinal hernia repair versus laparoscopic inguinal hernia repair.

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
						40kg/m2	
NCT03490266	April 2023	RCT	120	Robot-assisted Repair	Laparoscopic Repair	• 18 years and older • All patients undergoing elective ventral hernia repair deemed appropriate for minimally invasive repair.	Primary endpoints • Total number of days in the hospital [Time Frame: 90 days post-operative] Total number of days spent in the hospital.
NCT02715622	May 2021	Prospective cohort study	900	Open hernia repair Laparoscopic Hernia Repair Robotic Hernia Repair	-	• Age 18 years and older • All patients undergoing either an open, laparoscopic or robot-assisted • Incisional or Inguinal Hernia repair procedure • Non-Emergent Incisional or Inguinal Hernia Repair cases	Primary endpoints • Number of complications observed intraoperatively through 30 days [Time Frame: 30 days] Number of intraoperative and short-term complications related to hernia repair. • Number of patient reported complications post 30-days through 3 years post procedure [Time Frame: 30 days post-procedure to 3 years post-procedure] Number of long-term complications related to hernia repair directly reported by patients
NCT03133533 Note: Principal Investigator on an extended leave of absence	June 2023	RCT	0 (Study withdrawn)	Surgical inguinal hernia repair using laparoscopic approach Surgical inguinal hernia repair using robot-assisted approach	laparoscopic laparoscopic inguinal hernia repair robot-assisted robot-assisted inguinal hernia repair	• Surgeon determined need for inguinal hernia repair • Age 18 Years to 99 Years	Primary endpoints • Operative time
NCT03133715 Note: Study not approved by Institutional Review Board	June 2023	RCT	0	robot-assisted ventral hernia	laparoscopic ventral hernia repair	• Surgeon determined need for ventral hernia repair • Age 18 Years to 99 Years	Primary endpoints • Operative time
NCT00908193 Note: No	June 2012	RCT	70	robot-assisted coelioscopy	conventional coelioscopy	• over 18 years	• Evaluate the reduction in morphine consumption

Study Identifier	Estimated completion date	Study type	Number of patients	Intervention	Comparator	Patient population	Endpoints
Publication identified although study completed						• with indication of hernia repair • a collar with a diameter of less than 10cm • no antecedent of hernia treatment with poses plate • agreeing coelioscopy • agreeing to participate the clinical study, having sign an informed consent • agreeing a regular monitor	• Pain patient • Quality of life (questionary SF-36) • Length of stay in hospital, percentage return home to 24 hours of surgery • Morbidity • Resumption of work

Abbreviations: VATS =Video-assisted thoracoscopic surgery;RATS=Robot-assisted thoracoscopic surgery;ASA =American Society of Anaesthesiologists; EORTC QOL-30 =European Organisation for Research and Treatment of Cancer Quality of Life Group;OS= overall survival; LOS =length of stay;QOL= quality of life;DFS =disease free survival;NSCLC =non-small cell lung cancer;HRQOL= health-related quality of life;QOLRAD =Quality Of Life in Reflux and Dyspepsia;GSRS =Gastrointestinal Symptom Rating Scale;QLQ-C30 =Quality-of-Life-Questionnaire;CTCAE v4.0= Common Terminology Criteria for Adverse Events;FISI =Fecal Incontinence Severity Index;I-PSS =International Prostatic Symptom Score;IIEF =International Index of Erectile Function;FSFI= Female Sexual Function Index;MSKCC =Memorial Sloan Kettering Cancer Centre Bowel Function Instrument;ECOG =Eastern Cooperative Oncology Group;NCCN =National Comprehensive Cancer Network;ICA =intracorporeal anastomosis;ECA =extracorporeal anastomosis;VAS= Visual analogue scale;SSI =surgical site infection;SSO =surgical site occurrence;HerQLes =Hernia-Related Quality-of-Life Survey to Assess Abdominal Wall Function

Sources: ClinicalTrials.gov; WHO ICTRP; EU Clinical Trail (EudraCT) Register

APPENDIX 3: CHECKLIST FOR POTENTIAL ETHICAL, ORGANISATIONAL, PATIENT AND SOCIAL AND LEGAL ASPECTS

1	**Ethical**	
1.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new ethical issues?	Potentially, yes
	This has been discussed in the literature. Surgical robotics present challenges in the realm of law and ethics [70]	
1.2	Does comparing the new technology to the defined, existing comparators point to any differences that may be ethically relevant?	No
	If answered with 'yes', please provide a short statement explaining why.	
2	**Organisational**	
2.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) require organisational changes?	Yes
	If answered with 'yes', please provide a short statement explaining why. Introduction of robot-assisted surgery requires the device and adequate training of staff. If a hospital plans to purchase a robot, an adequate infrastructure is also required (e.g. room/space for robots).	
2.2	Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be organisationally relevant?	Yes
	If answered with 'yes', please provide a short statement explaining why. Some infrastructural changes may be needed to accommodate the equipment in the operating room.	
3	**Social**	
3.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new social issues?	No
	If answered with 'yes', please provide a short statement explaining why.	
3.2	Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be socially relevant?	No
	If answered with 'yes', please provide a short statement explaining why.	
4	**Legal**	
4.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any legal issues?	Yes
	If answered with 'yes', please provide a short statement explaining why. In case of any malfunction of the robotic system the question of liability could arise.	
4.2	Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be legally relevant?	No
	If answered with 'yes', please provide a short statement explaining why. Note: The assessment should not address patent-related issues.	