NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technologies evaluation programme

[GID-HTE10040] Robot-assisted Surgery for Soft-Tissue Procedures: Early Value Assessment

External Assessment Group Final Protocol

Produced by: York Health Economics Consortium

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None

Responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

1 Objective(s) and Research Question(s)

1.1 Purpose

Robot assisted surgery (RAS) for soft-tissue procedures has been identified by NICE for early value assessment (EVA). The objective of this EVA is to evaluate the use of RAS for soft-tissue procedures, outlining key considerations, clinical evidence, economic outcomes and where to prioritise future evidence generation.

1.2 Decision problem

1.2.1 Population

The population of interest is adults and children who require soft-tissue surgical procedures. A range of surgical specialties will be considered which are outlined in Table 2 of the NICE Scope.

Subpopulations have been identified and these will be considered in line with the availability of evidence. The subgroups of interest are detailed in Table 2 of the NICE Scope.

1.2.2 Intervention

Eligible interventions will be RAS interventions intended to be used in adults or children expected to undergo minimally invasive surgery (MIS), or people who would undergo open surgery (but may be eligible for RAS), across a broad range of clinical areas as highlighted in Table 2 of the NICE Scope.

Robotic platforms are defined as a technology that enables MIS to be performed across multiple interventional surgical procedures, using one or more mechanical arms to which an endoscope and surgical instruments are attached. The operator controls the apparatus from a remote console. For this EVA, we will consider robotic platforms that are used for soft-tissue procedures that meet the following criteria:

1. Are intended for use for:

    - adult or paediatric populations
    - procedures for cancer or benign disease in at least one of the following specialties:
        - urology (excluding prostatectomy)
        - gynaecology
        - colorectal
        - head and neck
        - thoracic
        - upper gastrointestinal (including bariatric and oesophago-gastric surgery)
        - general (including hernia repair)
        - hepato-pancreato-biliary
        - transplant
        - breast
        - reconstructive and plastic surgery

2. have a CE or UKCA mark and, if applicable, meet the standards within the digital technology assessment criteria (DTAC)

3. are available for use in the NHS.

1.2.3 Comparators

RAS will be compared with surgical standard of care. For most surgeries this will be laparoscopic or thoracoscopic surgery. For some procedures, like the Whipple procedure or bladder removal, the only current option is open surgery. For head and neck surgery, the main comparator is radical radiotherapy.

1.2.4 Outcomes

Key outcomes are reported in full in the NICE Scope published alongside this protocol.

1.2.5 Pathway

The care pathway varies between different specialties and indications for the procedures in scope for this assessment. The intended place of RAS in the pathway is to:

- Replace the surgical standard of care surgical technique (open or standard MIS) for the soft-tissue surgical procedure.
- Give an alternative option for the soft-tissue surgical procedure.

The NICE Scope provides further information on the expected pathway for different specialties of surgeries.

1.3 Research questions

The primary objectives of this EVA are:

- To identify, review and summarise evidence of the clinical effects and safety of RAS for soft-tissue procedures, when compared with the standard of care.
- To identify, review and summarise the economic evidence of RAS interventions, when compared with standard of care.

- To summarise information on the capacity, capabilities and practicalities of RAS for a range of soft-tissue procedures.
- To identify important evidence gaps and outline what data could be collected to address them.
- To develop an early economic model to provide an initial assessment of the potential cost-effectiveness of RAS.

2 Clinical Evidence

A review will be conducted to identify evidence that is available on the selected technologies and explore if the technologies have the potential to address the unmet need, using methods that conform to the NICE early value assessment interim statement [1].

The review will be undertaken according to the principles of systematic reviewing published by the Centre for Reviews and Dissemination (CRD) [2]. While a fully systematic review is beyond the scope of an EVA, the review methods, search approach and synthesis will be conducted in a transparent manner.

Initial scoping searches suggest there is a reasonably large evidence base for the included technologies which will be identified through our planned search. However, if the number of studies identified is large then the EAG will prioritise studies for inclusion based on the most relevant evidence, and the highest quality evidence. We will prioritise studies in this order:

- studies conducted in the UK
- studies reporting data for the prioritised outcomes
- prospective comparative studies followed by retrospective comparative and non-comparative studies analysing the highest numbers of patients

- the most recent evidence.

Equally, if few or no eligible studies are identified in line with the scope for any of the included technologies, the EAG will consider adding broadly relevant evidence identified by the searches but excluded at full text for not meeting all of the population, intervention, comparator and outcome (PICO) criteria, for example, in terms of population or comparator.

2.1 Inclusion and exclusion criteria

The eligibility criteria for included studies are summarised in Table 2.1 and reflect the decision problem as set out in the NICE scope.

Table 2.1: Summary of the review eligibility criteria

	Inclusion criteria	Exclusion criteria
Population	Adults or children having a surgical procedure on soft-tissues in the following specialties: • urology (excluding prostatectomy) • gynaecology • colorectal • head and neck • thoracic • upper gastrointestinal (including bariatric and oesophago-gastric surgery) • general (including hernia repair) • hepato-pancreato-biliary • transplant • breast • reconstructive and plastic surgery The following subgroups will be included: • Children under the age of 18 • Procedures for cancer • Procedures for benign disease	Patients having prostatectomy Studies conducted in cadavers
Intervention	RAS conducted with the following technologies: • Versius (CMR surgical) • da Vinci X and Xi (Intuitive) • da Vinci SP (Intuitive) • Hugo (Medtronic)	RAS conducted with technologies other than those listed as eligible Studies where the device name is not reported

Comparators	RAS will be compared with surgical standard of care. For most surgeries this will be laparoscopic or thoracoscopic surgery. For some procedures, like the Whipple procedure or bladder removal, the only current option is open surgery. For head and neck surgery, the main comparator is radical radiotherapy.	Any comparators not listed. except for where RAS is compared with another RAS
Outcomes	**Studies reporting at least one of the following outcomes:** Patient level: • Conversion to open surgery (for RAS compared with other minimally invasive surgical techniques only) • Rate of MIS (other minimally invasive surgical techniques and RAS) compared with open surgery after RAS was introduced • Intraoperative and post-operative complications (e.g. Clavien-Dindo score) • Health-related quality of life Surgeon level: • Procedure-related discomfort and ergonomics (e.g. SURG-TLX) Organisation level: • Volume of procedures • Length of hospital stay • Capacity and wait list reduction **Secondary outcomes** Patient level: • Days alive and out of hospital at 30 days • Length of hospital stay (for RAS compared with open surgery only) • Post-operative pain • Satisfaction • Intraoperative blood loss (for RAS compared with open surgery only) • Revision surgery for the same indication • Condition/specialty specific outcomes: • Survival rate (cancer)	

	• Need for adjuvant treatment (cancer) • Feeding tube dependency (head and neck) Surgeon level: • Career longevity and musculoskeletal injury • Human factors • Learning curve Organisation level: • Readmission at 30 days • Operating time • Staffing requirements	
Study design	• RCTs • Cross-over RCTs if data presented at time of cross-over • Non-randomised comparative studies • Single-arm evidence, such as registry data including a minimum of 10 patients • HTA reports investigating the cost-effectiveness of treatments **Economic evaluations, including:** • Cost- effectiveness analyses (included cost-utility analyses) • Cost-benefit analysis • Cost-consequence analyses • Cost-minimisation analyses • Budget impact analyses • Cost models	• Case reports • Qualitative studies • Reviews (systematic or non-systematic)* • Meta-analyses
Limits	• English language studies • Studies published in the last ten years will be eligible • Preprints**	• Non-English language studies • Editorials and news articles • Conference abstracts

Key: HTA – Health Technology Assessment, MIS – Minimally invasive surgery, RAS – Robot assisted surgery, RCT – Randomised controlled trial, SOC – Standard of care.

*We will check the included studies lists of any retrieved relevant systematic reviews or meta-analyses published in the last five years for any eligible studies that may have been missed by the database searches. This timeframe will be shortened if the volume of literature from systematic reviews and meta-analyses is high.

** We will include preprint evidence; however, we will not search for it explicitly.

2.2 Search strategy

A MEDLINE (OvidSP) search strategy designed to identify studies of the four eligible RAS technologies for eligible soft-tissue surgical procedures is presented in Appendix 1.

The strategy comprises search terms for the brand names of the four eligible RAS technologies (search lines 1 to 4), combined with OR in search line 5.

The strategy excludes animal studies from MEDLINE using a standard algorithm (search line 7). The strategy also excludes some ineligible publication types which are unlikely to yield relevant study reports (editorials, news items and case reports) and records with the phrase 'case report' in the title (search line 8).

Reflecting the eligibility criteria, the strategy is restricted to studies published in English (search line 9). The strategy is also limited to studies published in the last ten years (search line 9).

The final Ovid MEDLINE strategy will be peer-reviewed before execution by a second Information Specialist. Peer review will consider the appropriateness of the strategy for the review scope and eligibility criteria, inclusion of key search terms, errors in spelling, syntax and line combinations, and application of exclusions.

Search limitations

The search is designed only to retrieve studies where the named RAS technologies are mentioned in the title, abstract, keyword or original title fields of the database record. Database records that do not clearly state the named technologies could be missed by the searches. The approach taken in the search strategy is designed to strike an appropriate balance of sensitivity and precision.

2.2.1 Resources to be searched

We will conduct the literature search in the databases and information sources shown in Table 2.2.

Table 2.2: Databases and information sources to be searched

Resource	Interface / URL
Databases	
MEDLINE(R) ALL	OvidSP
Embase	OvidSP
Cochrane Database of Systematic Reviews (CDSR)	Cochrane Library/Wiley
Cochrane Central Register of Controlled Trials (CENTRAL)	Cochrane Library/Wiley
HTA database	https://database.inahta.org/
NHS Economic Evaluation Database (NHS EED)	https://www.crd.york.ac.uk/CRDWeb/HomePage.asp
EconLit	OvidSP
Trials Registers	
ClinicalTrials.gov	https://clinicaltrials.gov/
WHO International Clinical Trials Registry Platform (ICTRP)	https://trialsearch.who.int/
Reference list checking	n/a

The resources include sources of both clinical and economic studies. The trials register sources listed above (ClinicalTrials.gov and ICTRP) will be searched to identify information on studies in progress.

Reflecting the eligibility criteria, records in Embase that are indexed as conference abstracts will be excluded from the Embase search results, but preprints will be included in the search.

We will also check included studies lists of any industry submissions to NICE as well as retrieved relevant systematic reviews or meta-analyses published in the last five years, for additional eligible studies. If the volume of literature from systematic reviews and meta-analyses is high, we may shorten this timeframe.

2.2.2 Running the search strategies and downloading results

We will conduct searches using each database or resource listed in the protocol, translating the agreed Ovid MEDLINE strategy appropriately. Translation includes consideration of differences in database interfaces and functionality, in addition to variation in indexing languages and thesauri. The final translated database strategies will be peer-reviewed by a second Information Specialist. Peer review will consider the appropriateness of the translation for the database being searched, errors in syntax and line combinations, and application of exclusions.

We will document all search strategies and search results and we will provide this in the final report to meet standard requirements for clear formal reporting of the search process. The report of search methods will be informed by the PRISMA-S (Preferred Reporting Items for Systematic reviews and Meta-Analyses literature search extension) checklist [3] and the PRISMA 2020 statement [4, 5].

Where possible, we will download the results of searches in a tagged format and load them into bibliographic management software (EndNote) [6]. The results will be deduplicated using several algorithms and the deduplicated references held in a duplicates EndNote database for checking if required. Results from resources which do not allow export in a format compatible with EndNote will be saved in Word or Excel documents as appropriate and manually deduplicated.

2.3 Study selection

Record assessment will be undertaken as follows:

- A single researcher will remove obviously irrelevant records such as those ineligible conditions.
- The titles and abstracts of remaining records will be assessed in detail for relevance against the protocol eligibility criteria by a single

experienced reviewer, with a 10% sample checked by a second reviewer and any queries regarding eligibility addressed in discussion with the second reviewer.

- The full text of potentially relevant studies will be obtained and assessed for relevance against the protocol criteria by a single experienced reviewer, with a 10% sample checked by a second reviewer and any queries regarding eligibility addressed in discussion with the second reviewer.

We will list studies excluded after assessment of the full document in an excluded studies table, with the reasons for exclusion.

2.4 Data extraction strategy

A bespoke data extraction template will be developed in Word and piloted on 10% of the included studies. One researcher will extract data and a second researcher will check all data points. Any discrepancies will be resolved by discussion, and by involvement of a third researcher when required. Data extraction will be targeted, involving the limited extraction of key details describing the study reference (bibliographic details), study design, key patient characteristics, key intervention / comparator characteristics and outcomes.

Subject to available evidence and time, the EAG will consider extracting outcome data for subgroups with health inequalities (as identified in the NICE Scope) and co-morbidities.

2.5 Quality assessment strategy

Formal risk of bias assessment is not required in the EVA process and so will not be conducted. However, the EVA report will include discussion of any concerns regarding the reliability of the key included studies, due to study designs used and consequently how the risk of bias might have affected key

outcomes. The report will comment on the generalisability of the results to clinical practice in the NHS.

2.6 Methods of analysis/synthesis

The data will be summarised in tables and synthesised in a narrative review.

3 Economic Evidence

3.1 Identifying and reviewing published economic evaluations

3.1.1 Eligibility criteria

For the rapid review of economic evaluations, studies will be eligible if they report total costs, effectiveness, incremental analyses or other economic evaluation outcomes, or measure any relevant cost or resource use associated with the use of RAS in the relevant clinical areas and population. Recent studies and those conducted in a UK NHS setting will be prioritised. If a large volume of potentially relevant evidence is identified, further prioritisation will focus on economic evaluations and cost analyses covering broad pathways only (i.e. excluding studies of specific pathways).

3.1.2 Search strategy

The searches for clinical evidence will not be restricted by study design and will be screened for relevant economic evidence. The resources being searched includes sources of economic evidence (Table 2.2).

3.2 Evaluation of costs, quality of life and cost-effectiveness

In parallel to the rapid review of economic evaluations, the EAG will develop an early economic model of RAS for soft-tissue surgery compared to the use of open or soft-tissue MIS. It is important to explore the differences in both of these comparators, given the impact of RAS will be different depending on the surgery they will be acting as a replacement for.

The model will address the decision problem set out in Section 1.2. The aim of an early economic model is to identify key drivers of costs and effectiveness for the use of RAS, when compared to standard of care.

We expect given the focus will be on short- and medium-term outcomes, the model will take the structure of a decision tree, with a time horizon of 1 year. This will allow us to make best use of available evidence without introducing a high level of uncertainty within the results associated with mapping out long-term outcomes. The economic model will be aligned with the NICE reference case [7]. Clinical experts will be consulted to determine the exact design of the model and make sure key outcomes are captured. The focus of this model is likely to be the change in resource use and change in complication rates / surgery-related adverse events, rather than long-term recovery from the underlying disease. As part of our evaluation of the economic evidence, we will recommend a model structure that may be more appropriate for very specific decision problems that can be modelled over a longer time-horizon.

The model will incorporate the difference in costs and resource use of employing RAS compared to the standard of care, focusing on the short- and medium-term outcomes. This is because due to the wide range of surgical specialties, there will be a wide range of long-term outcomes, which cannot be reflected in the short evaluation period. The model will include any key clinically reported measures, which may include length of stay, complications, rate of hospital readmissions, and any additional primary or secondary care resource use, subject to the availability of evidence. Costs associated with the use of RAS may include the cost of the technology to a department / NHS site, staff time to carry out the procedure, and any training or ongoing equipment maintenance costs. The model will explore different intervention cost structures such as leasing, annualised capital investment, and free loan with consumable contracts. Model inputs will be sourced from published literature, company data, or expert clinical opinion.

To identify cost and resource use evidence, the EAG will also search the same sources identified for the economic evidence, together with NHS cost collection data, the Unit Costs of Health and Social Care (Personal Social Services Research Unit [PSSRU] and the British National Formulary (BNF). All costs will be updated to the price year 2022/23. Given the short-time horizon associated with this analysis, it is likely the model will be a cost-comparison model. If there is evidence to suggest that there is a material difference in HRQoL within in the first year, based on the procedure type and change in the distribution of complications, then these will be incorporated into the economic model but any impact of patient outcomes will be discussed in the qualitative report.

Scenario and sensitivity analysis will be conducted on key parameters that are associated with the highest amount of uncertainty and variability. This will particularly focus on the cost of purchasing, implementing, and maintaining a surgical robot, as this varies by manufacturer and robot functionality. The upper and lower limit of incorporating a robotic surgical device will be calculated and used in scenario analysis to capture the potential impact of this variability on the model results.

The EAG will also identify evidence gaps as described in section 4. This gap analysis will be used to recommend a model structure that could be developed for future analysis, once more mature data has been collected on the use of RAS. This will be important to develop a more robust evaluation of the cost-effectiveness of RAS.

4 Gap Analysis

Evidence gaps identified pertaining to the intermediate and final outcomes from the scope and those pertaining to the economic modelling will be summarised in tabular and narrative form. If appropriate, a ‘traffic light’ scheme will be used to highlight relative importance of the gap. Key areas for

evidence generation will be summarised in tabular form. Narrative text will also address missing clinical evidence for other parts of the scope, such as population, setting and comparators.

5 Handling Information

The EAG will consider any data or evidence supplied by the companies or stakeholders involved. If the data meet the inclusion criteria for the review they will be considered. It will not be possible to include data received later than 05/07/2024.

Any ‘commercial in confidence’ data provided and specified as such will be highlighted in blue and underlined in the assessment report. Any ‘academic in confidence’ data provided will be highlighted in yellow and underlined in the assessment report. Any ‘’depersonalised data’ (DPD) in the assessment report document should be underlined and highlighted in pink.

If confidential information is included in any economic models produced, then a version using dummy data or publicly available data in place of confidential data will be provided.

6 References

1. National Institute for Health and Care Excellence. Early value assessment interim statement. NICE,; 2022. Available from: https://www.nice.org.uk/process/pmg39/chapter/introduction.

2. Centre for Reviews and Dissemination. Systematic reviews: CRD's guidance for undertaking reviews in health care. 2008. Available from: https://www.york.ac.uk/media/crd/Systematic_Reviews.pdf.

3. Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Matthew JP, et al. PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst Rev. 2021.39doi: https://doi.org/10.1186/s13643-020-01542-z

4. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Systematic Reviews. 2021.10(1):89. doi: 10.1186/s13643-021-01626-4

5. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021.372:n160. doi: 10.1136/bmj.n160

6. Clarivate. EndNote 20. Clarivate; 2021. Available from: http://endnote.com/.

7. National Institute for Health and Care Excellence. NICE health technology evaluations: the manual. NICE; 2022. Available from: https://www.nice.org.uk/process/pmg36/resources/nice-health-technology-evaluations-the-manual-pdf-72286779244741.

7 Appendix 1

Search strategy for Ovid MEDLINE® ALL

1 versius*.ti,ab,kf,ot. (71)
2 ((da vinci* or davinci*) adj6 (x* or sp*)).ti,ab,kf,ot. (977)
3 (davincix* or davincisp* or IS4200 or IS4000 or SP1098).ti,ab,kf,ot. (12)
4 (hugo* and robot*).ti,ab,kf,ot. (99)
5 or/1-4 (1133)
6 exp animals/ not humans/ (5232910)
7 (news or editorial or case reports).pt. or case report.ti. (3378249)
8 5 not (6 or 7) (948)
9 limit 8 to (english language and yr="2014 -Current") (865)

Key to Ovid symbols and commands:

*	Unlimited right-hand truncation symbol
ti,ab,kf,ot	Searches are restricted to the Title (ti), Abstract (ab), Keyword Heading Word (kf), and Original Title (ot) fields
adjN	Retrieves records that contain terms (in any order) within a specified number (N) of words of each other
/	Searches are restricted to the Subject Heading field
pt.	Search is restricted to the publication type field
yr	Limits the search to the year of publication field

Saved in Ovid as: temp - MTAC309 - scoping search - tech names only