Early Value Assessment (EVA)

HTE10043 Robot-assisted surgery for orthopaedic procedures:

EVA Final Protocol

Produced by: Newcastle External Assessment Group (EAG)

Authors: Kim Keltie, Lead Evaluation Healthcare Scientist, The Newcastle upon

Tyne Hospitals NHS Foundation Trust (NuTH);

Rachel O'Leary, Clinical Scientist, NuTH;

Paula Leslie, Pre-registrant Clinical Scientist, NuTH;

David Muir, Clinical Scientist, NuTH;

Elliot Blacklock, EAG Administrator, NuTH;

Andrew Goldsborough, Trainee Healthcare Scientist, NuTH;

Emma Belilios, Project Co-ordinator, NuTH;

Alex Inskip, Research Assistant, Information Specialist, Newcastle University;

Hannah O'Keefe, Research Associate, Information Specialist, Newcastle University;

Luke Vale, Professor of Health Economics, London School of Hygiene and Tropical Medicine; NuTH;

Andrew Sims, EAG Director, NuTH

Correspondence to: Dr Andrew Sims

Northern Medical Physics and Clinical Engineering,

NMPCE (Medical Physics, NCCC Level 2)

Freeman Hospital High Heaton,

Newcastle upon Tyne

NE7 7DN

nuth.nmpce.hta@nhs.net

Date completed: 04/07/2024

Contains confidential information: No

Number of attached appendices: 1

Contents

	Abbreviations	2
	1. Background	3
	2. Decision Problem	3
	2.1 Population	3
	2.2 Intervention	3
	2.3 Comparators	5
	2.4 Healthcare setting	5
	2.5 Outcomes	6
	2.6 Care Pathways	6
3.	Objective	7
4.	Methods	8
	4.1 Evidence Review	8
	4.4 Use in the NHS	11
	4.5 Economic modelling	12
	4.6 Gap Analysis	12
	4.7 Handling of company submissions	12
	4.8 Competing interests of authors	12
Re	eferences	13
Αŗ	opendix A – Example Search Strategy	14

Abbreviations

Term	Definition
CT	computed tomography
DTAC	Digital Technology Assessment Criteria
EAG	External Assessment Group
EVA	Early Value Assessment
PROMs	Patient Reported Outcome Measures
RAS	robotic-assisted surgery
RCS	Royal College of Surgeons

1. Background

The topic has been identified by NICE for Early Value Assessment (EVA). The objective of an EVA is to identify promising technologies in health and social care where there is significant need and potentially enable early conditional access to these while informing further evidence generation. A rapid appraisal of the evidence is conducted to determine if these offer plausible value to the NHS. The evidence developed will demonstrate if the expected benefits of the technologies are realised and will be used to inform a subsequent final NICE evaluation when a decision will be made on the routine use of the technologies in the NHS.

2. Decision Problem

The decision problem is described in the Final Scope and summarised here.

2.1 Population

As per the final scope, the eligible population for this Early Value Assessment includes people undergoing the following orthopaedic procedures:

- Total and partial knee replacement, including revision.
- Total hip replacement, including revision and repair.
- Shoulder replacement.

Due to differences in patient demographics and outcomes, the Newcastle External Assessment Group (EAG) will treat the following cohorts separately across the procedure (where appropriate):

- Patients undergoing total and partial replacement will be considered separately.
- Patients undergoing primary and revision surgery will be considered separately.

2.2 Intervention

Six robotic platforms have been included in the scope.

ApolloKnee (Corin)

The ApolloKnee robot-assisted surgical platform has recently been launched and

is indicated for total knee arthroplasty. The system features the BalanceBot for pre-resection knee balancing and a gesture-controlled workflow.

CORI Surgical System (Smith+Nephew)

The CORI Surgical System is used for total knee arthroplasty, partial knee arthroplasty and total hip arthroplasty. CORI does not require preoperative imaging; it uses real-time data and intraoperative imaging to create a virtual 3D model of the patient's anatomy. The CORI system is designed to be portable with a small operating room footprint. The system controls the surgical cut based on its proximity to the planned bone surface, offering real-time feedback and visual indicators throughout the procedure. The NAVIO Surgical System is the predecessor technology to the CORI Surgical system; Smith and Nephew acquired NAVIO from Blue Belt Technologies in 2016.

MAKO SmartRobotics System (Stryker)

The Mako SmartRobotics System is indicated for partial knee arthroplasty including patellofemoral knee replacement, total knee arthroplasty and total hip arthroplasty. The Mako system provides computed tomography (CT)-based anatomical models and software-defined spatial boundaries for precise implant placement. It is used in surgical knee and hip procedures where stereotactic surgery is appropriate. The Acrobot and RIO systems are predecessor technologies; Stryker acquired Mako Surgical Corp and the RIO system in 2013 and Stanmore Implants and the Acrobot system in 2016.

ROSA Knee System (Zimmer Biomet)

ROSA is a robotic system designed to assist surgeons and is indicated as a stereotaxic instrumentation system for total knee arthroplasty and hip arthroplasty. It allows the surgeon to control and execute cutting with support from the robotic arm, which uses intra-operatively captured patient-specific metrics such as range of motion, alignment, and soft tissue laxity. The system facilitates intra-operative planning, including gap balancing and implant positioning, without the need for pre-operative images.

SkyWalker (MicroPort MedBot)

The SkyWalker system is indicated for assisting in total knee arthroplasty surgeries. Its preoperative planning system generates personalised prosthetic implantation plans based on patient-specific anatomical characteristics using preoperative CT scan data. The company is in the process of obtaining CE marking for partial knee arthroplasty and for total hip arthroplasty and is planning to introduce the technology to the NHS.

VELYS Robotic-Assisted Solution (Johnson & Johnson)

The VELYS Robotic-Assisted Solution is indicated for total knee arthroplasty using the ATTUNE total knee system. This semi-active robotic system is imageless as it relies on an infrared camera to track reflective arrays on the patient's femur and tibia during surgery. The system maintains the saw blade within planned resection planes and allows bone resections without cutting blocks.

Intrinsic to the EVA process (<u>PMG39, 2022</u>), each robotic system will have appropriate regulatory requirements (for example valid CE or UKCA certification, and Digital Technology Assessment Criteria (DTAC) status, where applicable) as determined by NICE, and this will not be checked by the EAG. The EAG will consider evidence for the included robotic systems, and their predecessors as identified by completed Request for Information forms submitted by the Companies. Evidence will only be included where conducted in populations and procedures that are not explicitly contraindicated according to the device Instructions for Use.

2.3 Comparators

The comparator considered is conventional manual surgery. At the Scoping meeting, Clinical Experts advised that computer-assisted navigation is not currently representative of standard care within joint replacement procedures in the NHS.

2.4 Healthcare setting

The healthcare setting is admitted patient services including emergency and elective surgery.

2.5 Outcomes

Outcomes listed in the final scope were ranked by those attending the Scoping meeting. Due to the breadth of the published evidence in robotic-assisted surgery, the EAG will focus on prioritised outcomes, and will consider additional outcomes if time permits.

High priority

- Patient level: frequency and grade of complication, Patient Reported
 Outcome Measures (PROMs), including function, pain, activity, Health related
 quality of life, revision surgery.
- Surgeon level: learning curve.
- Organisation level: revision surgery, cost of additional equipment (including device and single use instrumentation, maintenance and servicing costs, training costs), procedure volume, operating times, case mix (for example, proportion of partial knee replacements rather than total knee replacements).

Other (where feasible)

- Patient level: Need for further imaging with associated radiation exposure (CT scans), mortality, health related quality of life.
- Surgeon level: procedure-related discomfort and ergonomics, career longevity and musculoskeletal injury, loss of experience with manual techniques, precision/accuracy measures such as alignment on imaging.
- Organisation level: Staff requirements including time to undergo training, length of hospital stay, readmission to hospital within 30 days, people in whom the procedure without use of RAS may not be feasible, adverse events related to equipment, requirement for transfer of images to industry to allow planning which can introduce delays, environmental costs of additional disposable equipment and associated packaging, manufacture and distribution.

2.6 Care Pathways

The NICE guideline on primary joint replacement (hip, knee and shoulder) does not explicitly mention RAS. Interventional procedure guidance for minimally-invasive total hip replacement does not mention RAS either, but this is because RAS is considered a minor modification of an existing procedure. For orthopaedic

procedures there are not many differences in care before and after the surgery.

There may be a requirement for some additional imaging or planning time before surgery depending on the procedure and robotic system employed.

The National Joint Registry (NJR) for England, Wales, Northern Ireland, the Isle of Man and states of Guernsey, is a mandatory audit of joint replacement procedures with over 95% capture of primary procedures. The primary outcome measures are revision surgery and 90-day mortality. In shoulder surgery the NJR also collects various PROMs to assess the quality of care and outcomes for joint replacement surgeries delivered to people having NHS funded treatment. People undergoing elective inpatient surgery for hip and knee replacement, are asked to complete questionnaires before and after their operations. PROMs collected by NHS Digital through the national PROMS programme can be linked to the National Joint Registry (NHS Digital, 2023).

The EAG note that in 2019, the National Joint Registry added a data field for "<u>robotic surgery used</u>" for hip and knee primary forms, including the name of the robot used. The EAG will explore whether uptake of robotic surgery in knee, hip and shoulder can be determined from NJR data. Alternatively, the EAG will explore whether aggregated uptake (since manufacturer and model cannot be identified) can be determined from routine administrative data from Hospital Episode Statistics using appropriate procedure codes.

3. Objective

The purpose of this evidence assessment is to summarise and critically appraise existing evidence for the robotic platforms included in the Final Scope. The aim is to evaluate clinical-effectiveness and cost-effectiveness, identify evidence gaps, and highlight any risks associated with the potential use of these technologies in the NHS whilst further evidence is generated. It should be noted that the purpose of the review is not to compare the technologies with each other. Based on the scope developed by NICE, the following specific primary objectives are proposed:

• To identify, review and summarise evidence of the clinical effects and safety of RAS for orthopaedic procedures, when compared with the standard of care.

- To identify, review and summarise the economic evidence of RAS interventions in orthopaedics, when compared with standard of care.
- To summarise information on the capacity, capabilities and practicalities of RAS for a range of orthopaedic 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 for orthopaedic procedures.

4. Methods

4.1 Evidence Review

A rapid review will be undertaken to identify evidence for the plausible clinical and cost effectiveness of included technologies. A systematic literature review to comprehensively search for all relevant evidence for the appraisal is beyond the scope of an EVA. However, the review methods, including the literature search strategy and evidence synthesis, will be rigorous and conducted in a transparent manner, with the aim to produce a comprehensive overview of the key literature as relevant to the decision-making context.

Based on initial scoping searches, the EAG expects there to be a large body of evidence for robotic-assisted surgery in orthopaedics. The EAG plans to conduct focused searches which will incorporate the technology names (including predecessor version). If the evidence base identified is large, the EAG will prioritise the inclusion of evidence that is of the best quality and most pertinent to the objectives of the EVA.

At study commencement, NICE will request that the manufacturers supply published evidence relating to their robotic platform, which will be considered and reviewed by the EAG.

4.3.1 Search strategy

Searches for clinical and cost-effectiveness evidence will be conducted in a combined search.

Search strategies will be developed by one of the EAG's information specialists for MEDLINE and then translated, adapted and run independently for each individual database (MEDLINE including In-Process and In-Data-Review & Other Non-Indexed, Embase, Cochrane Library CENTRAL, National Institute for Health and Care Research). Additional pragmatic searches will include grey literature sources (NIHR Journal Library) including unpublished or pre-print papers (EngRxiv, MedRxiv). Additional databases will also be explored for economic evidence (RePEC IDEAS, CEA Registry, INAHTA). The EAG has already identified 2 overviews of systematic reviews, which will be used to inform the literature search strategy (Appendix A):

- The umbrella review by <u>Hasan et al. (2020)</u> which included 42 systematic reviews on total knee or total hip arthroplasty.
- The systematic overview of meta-analyses by <u>Kort et al. (2022)</u> which included 10 meta-analyses, 4 on unicompartmental knee arthroplasty and 7 on total knee arthroplasty.

Language limits will be applied (English only). For articles naming the device within the title and abstract, a time limit of 5 years will be applied; depending on volume of evidence obtained, additional time restrictions may be considered. Pragmatically, for articles not naming the device in the title and abstract, a shorter time limit (for example within 2 years) will be applied to ensure achievable within timescales.

Ongoing trials will be searched for (ScanMedicine, Clinicaltrials.gov) applying a limit to UK studies.

MHRA field safety notices will be searched for adverse events.

4.3.2 Study Selection

This assessment will look across a range of evidence types including experimental and observational. Systematic reviews meeting the inclusion criteria will also be identified and checked for additional eligible studies. Studies may report either quantitative or qualitative evidence for the scoped outcomes. The following evidence types will be excluded:

- Studies not explicitly reporting the robotic system used, unless one of the companies submitted the study and confirmed that their technology was used.
- Animal or cadaver studies
- Narrative reviews, editorials, opinions, letters.
- Meeting abstracts, for studies where full-text papers are available. If studies
 are only available as meeting abstracts, inclusion will depend on sufficient
 information being available to offer meaningful critique.
- Studies not available in the English language.

Full economic evaluations, costing studies and studies reporting health related quality of life measures that inform either the design of the EAG's own analysis or provide a source of input data will be included where they meet the inclusion criteria set out for the review of clinical effectiveness. Prioritisation of clinical and economic evidence will be based on the following criteria, in descending 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 highest number of patients
- The most recent evidence.

Three levels of study selection will be conducted:

- Step 1: Titles and abstracts of records identified in literature searches will be screened against a subset of the inclusion criteria (population, intervention, comparator).
- Step 2: Full publications will be retrieved for records included at Step 1 and will be screened according to the inclusion criteria.
- Step 3: If the evidence base identified is large and infeasible to appraise in full
 within the timeline of the EVA, publications included at Step 2 will be screened
 and a subset of publications will be prioritised for inclusion. At least one
 publication will be included for each intervention, and publications will be
 prioritised where these are higher evidence quality and of greater relevance to
 the decision problem.

Independent, second review of study selection may be conducted subject to time and resource availability. Studies excluded after full paper review will have the reason for exclusion documented and tabulated within the report.

4.3.3 Quality assessment strategy

Formal risk of bias assessment will not be conducted. Discussion will be included in the EAG report on potential biases in key studies and how the risk of bias could affect key outcomes. The report will explicitly detail the potential sources of bias such as the main confounding factors and will comment on the generalisability of the results to clinical practice in the NHS.

4.3.4 Data extraction strategy

Data will be extracted from included studies into a bespoke spreadsheet to enable descriptive statistics. Independent, second review of data extraction may be conducted subject to time and resource availability. Data points to be extracted include information about the study reference, setting, design, population characteristics, intervention characteristics and relevant outcomes.

4.3.5 Methods of analysis / synthesis

Clinical evidence will be tabulated and narratively synthesised. Additional synthesis (for example meta-analysis) may be conducted subject to time and resource availability and will be considered by outcome depending on data availability.

Methods and findings from included published economic evaluations will be summarised in a tabular format and synthesised in a narrative review. Economic evaluations carried out from the perspective of the UK NHS and Personal Social Services perspective will be presented in greater detail.

Key sources of risk of bias will be discussed. The generalisability of findings to clinical practice in the NHS will be considered.

4.4 Use in the NHS

To give committee context of the relative uptake of RAS, compared with manual, orthopaedic procedures the EAG will consider national data collections (for example the National Joint Registry or Hospital Episode Statistics). These datasets may be explored to determine both national uptake of robotic assisted procedures within the NHS, and hospital procedure volume.

4.5 Economic modelling

Following review of published economic evaluations, the EAG will construct an economic model built in R Programming language using *rdecision* package. The EAG will describe the appropriate characteristics of the model (for example structure, setting, input parameters, sources of data, assumptions). The structure of the model will be determined on the basis of the clinical evidence and economic evaluations identified and advice sought from Clinical Experts regarding assumptions and parameter values where evidence is lacking. Time horizon will be considered by procedure of interest but is expected to be up to the patient lifetime. Costs will be considered from an NHS and Personal Social Services perspective. Where appropriate, and if data allow, sensitivity analysis will be undertaken to explore uncertainty. These may include deterministic and probabilistic sensitivity analysis.

4.6 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.

4.7 Handling of company submissions

Data received from the company will be appraised and, where consistent with the decision problem, will be extracted and appraised in accordance with the procedures outlined in this protocol. Data provided (for example cost and resource use data) will be assessed against NICE's manual (2022), for the reasonableness of assumptions made and appropriateness of the data used. Any academic or commercial in confidence data taken from a company submission will be marked appropriately in the report. It will not be possible to include data received later than 05 July 2024.

4.8 Competing interests of authors

None.

References

Hasan MM, Zhang M, Beal M, Ghomrawi HMK. (2020) An umbrella review comparing computer-assisted and conventional total joint arthroplasty: quality assessment and summary of evidence. BMJ Surg Interv Health Technol. 2(1):e000016

Kort N, Stirling P, Pilot P, Müller JH. (2022) Robot-assisted knee arthroplasty improves component positioning and alignment, but results are inconclusive on whether it improves clinical scores or reduces complications and revisions: a systematic overview of meta-analyses. Knee Surg Sports Traumatol Arthrosc. 30(8):2639-2653

Appendix A – Example Search Strategy

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions <1946 to July 03, 2024>

#	Searches	Results
1	Robotic Surgical Procedures/	18732
2	Robotics/	29379
3	Surgery, Computer-Assisted/ and robot*.mp.	3068
4	robot*.ti,kf.	53329
5	robot*.ab. /freq=3	27499
6	(robot* adj2 assist*).ab.	21745
7	(or/1-6) and robot*.ti,ab.	60923
8	arthroplasty/ or arthroplasty, replacement/ or arthroplasty, replacement, hip/ or arthroplasty, replacement, knee/ or arthroplasty, replacement, shoulder/ or hemiarthroplasty/	82191
9	(knee or hip or shoulder).ti. and ((surger* or surgical).ti,kf,hw. or su.fs.) and (ortho* or arthro*).af.	66922
10	(exp Hip Injuries/su or exp Knee Injuries/su or exp Shoulder Injuries/su or hip/su or knee/su or shoulder/su or exp hip joint/su or exp knee joint/su or shoulder joint/su) and (ortho* or arthro*).af.	70351
11	(exp Hip Injuries/ or exp Knee Injuries/ or exp Shoulder Injuries/ or hip/ or knee/ or shoulder/ or exp hip joint/ or exp knee joint/ or shoulder joint/) and (surger* or surgical).hw. and (ortho* or arthro*).af.	10411
12	(arthroplas* or knee replacement* or hip replacement* or shoulder replacement* or joint replacement*).ti,kf,hw.	108834
13	((tka or uka or pka).ti,kf,hw. and knee arthroplas*.mp.) or (tha.ti,kf,hw. and hip arthroplas*.mp.)	3843
14	arthroplas*.ab. /freq=3 or tka.ab. /freq=3 or uka.ab. /freq=3 or pka.ab. /freq=3 or tha.ab. /freq=3	44653
15	or/8-14	176926
16	7 and 15	1542
17	limit 16 to english language	1445
18	(apolloknee* or apollo knee or balancebot* or balance-bot or balance-bottm or cori or coritm or navio* or mako* or acrobot* or rio or rosa or rosar or rosatm or rosaknee or (skywalker* not MIT-skywalker*) or velys* or attune total knee*).mp. and robot*.af. and (knee* or hip or hips or shoulder* or musculoskelet* or patell* or arthroplas*).mp.	251
19	(corin or corinr or corintm or (smith adj2 nephew*) or stryker* or zimmer* or biomet* or microport* or medbot* or "think surgical*" or "Johnson and Johnson*" or "johnson & johnson*" or depuy*).in,mp.	113715
20	19 and 17	165
21	18 or 20	340
22	limit 21 to (comment or editorial or news or newspaper article)	0
23	21 not 22	340
24	limit 23 to (english language and yr="2019 - Current") [results with relevant named	285
25	technologies from 2019 onwards] (systematic review or meta-analysis).pt.	352740

#	Searches	Results
26	meta-analysis/ or systematic review/ or systematic reviews as topic/ or meta-	394659
	analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp	
27	technology assessment, biomedical/ or network meta-analysis/ ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or	369332
	overview*))).ti,ab,kf.	
28	((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf.	17680
29	((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf.	42968
30	(data synthes* or data extraction* or data abstraction*).ti,ab,kf.	45778
31	(handsearch* or hand search*).ti,ab,kf.	11650
32	(mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf.	38759
33	(met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf.	13169
34	(meta regression* or metaregression*).ti,ab,kf.	16589
35	(meta-analy* or metaanaly* or systematic review* or biomedical technology	525404
26	assessment* or bio-medical technology assessment*).mp,hw.	200050
36	(medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.	386650
37	(cochrane or (health adj2 technology assessment) or evidence report).jw.	21951
38	(comparative adj3 (efficacy or effectiveness)).ti,ab,kf.	19235
39	(outcomes research or relative effectiveness).ti,ab,kf.	11809
40	((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).ti,ab,kf.	4670
41	(multi* adj3 treatment adj3 comparison*).ti,ab,kf.	310
42	(mixed adj3 treatment adj3 (meta-analy* or metaanaly*)).ti,ab,kf.	179
43	umbrella review*.ti,ab,kf.	2090
44	(multi* adj2 paramet* adj2 evidence adj2 synthesis).ti,ab,kf.	14
45	(multiparamet* adj2 evidence adj2 synthesis).ti,ab,kf.	19
46	(multi-paramet* adj2 evidence adj2 synthesis).ti,ab,kf.	12
47	or/25-46 [CADTH SR filter from https://searchfilters.cadth.ca/link/33]	762250
48	(17 and 47) not 24	103
49	limit 48 to yr="2022 -Current" [results without relevant technologies named, systematic reviews from 2022 onwards]	55
50	limit 17 to (address or autobiography or bibliography or biography or comment or dictionary or directory or editorial or news or newspaper article or observational study, veterinary or personal narrative or portrait)	35
51	limit 17 to ("review articles" or meta analysis or "systematic review")	222
52	51 and ((review or overview or literature).ti. or "this* review".ab. or "this* systematic review".ab.)	111
53	17 not (50 or 52)	1300
54	limit 53 to yr="2022 -Current"	680
55	exp United Kingdom/	396306
56	(national health service* or nhs*).ti,ab,in.	293613
57	(english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab.	129647
58	(gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in.	2564895

#	Searches	Results
59	(bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("london not (ontario* or ont or toronto*)) or ("london not (ontario* or ont or toronto*)) or ("newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or or "pipmouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or stalbans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("not or not or toronto*))))).ti,ab,in.	1849871
60	(bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in.	74895
61	(aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in.	272137
62	(armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in.	36175
63	or/55-62	3287587
64	(exp africa/ or exp americas/ or exp antarctic regions/ or exp arctic regions/ or exp asia/ or exp australia/ or exp oceania/) not (exp united kingdom/ or europe/)	3438621
65	63 not 64 [UK filter from https://doi.org/10.1111/hir.12252]	3082764
66	(54 and 65) not 24 [results without relevant technologies named, (potential) primary research, from 2022 onwards, limited to UK]	85
67	24 or 49 or 66	420
68	Economics/	27535
69	exp "costs and cost analysis"/	271543
70	Economics, Dental/	1922
71	exp economics, hospital/	25881
72	Economics, Medical/	9288
73	Economics, Nursing/	4013
74	Economics, Pharmaceutical/	3141
75	(economic\$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic\$).ti,ab.	1129040
76	(expenditure\$ not energy).ti,ab.	39134
77	value for money.ti,ab.	2243
78	budget\$.ti,ab.	37695
79	or/68-78	1297333
80	79 not (((energy or oxygen) adj cost) or (metabolic adj cost) or ((energy or oxygen) adj expenditure)).ti,ab.	1288993

#	Searches	Results
81	80 not (letter or editorial or historical article).pt.	1247911
82	81 not (exp animals/ not humans/)	1167937
83	17 and 82	205
84	limit 83 to yr="2019 -Current"	166
85	84 not 67 [econ papers, since 2019, not in other results]	106
86	24 or 49 or 66 or 85	526