# [GID-HTE10066] Ex-situ machine perfusion for deceased donor liver transplants: routine use assessment

## Final Protocol

Produced by: York Health Economics Consortium

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# 1 Decision problem

Ex-situ liver perfusion technologies have been identified by NICE for assessment. As described in the NICE scope, the aim of this assessment is to evaluate whether ex-situ machine perfusion technologies for deceased donor liver transplants are a clinical and cost-effective use of NHS resources and to identify gaps in the evidence base. This document was prepared in response to the NICE Scope and presents the methods that the external assessment group (EAG) commissioned by NICE will undertake to produce the assessment.

This assessment will consider the use of ex-situ machine perfusion technologies for the preservation and functional assessment of livers from deceased donors, initiated on arrival at the hospital of the person having the transplant, after the liver has been transported using conventional static cold storage. Where possible, the assessment will also consider potential changes to the national liver transplantation pathway, in line with proposals by NHS Blood and Transplant, including the use of ex-situ machine perfusion technologies during transportation of donor organs, as applicable.

Table 1.1 summarises the decision problem to be addressed in this assessment. Further detail on each element can be found in the published scope for the assessment.

### Table 1.1. Summary table of the decision problem

| Item | Description |
|---|---|
| **Population(s)** | People active on the UK waiting list for liver transplantation from deceased donors. |
| **Subgroups** | Subgroup data for adult and paediatric populations will be eligible where reported. Within these population subgroups the following subgroups will be considered (where data permits, with adult and paediatric subpopulations treated separately within each subgroup):<br>• Higher risk donors, including higher risk donors for children and young person (CYP) recipients. These might include extended criteria donors (particularly with steatotic livers) and donors following circulatory death. If possible, use of normothermic regional perfusion (NRP) of livers donated after circulatory death will also be considered. If possible, ex-situ machine perfusion during liver splitting will also be considered.<br>• Complex recipients, including CYP recipients. These might include people who have previously had a transplant or abdominal surgery, or those with advanced comorbidities and haemodynamic instability. If possible, ex-situ machine perfusion during liver splitting will also be considered.<br>• Logistical considerations, including for CYP recipients. These might include complex multi-organ transplants, challenging hepatectomies, liver splitting and prolonged preservation to allow time for allocation, transport and/or in-hospital logistics such as enabling day-time surgery. If possible, use of ex-situ machine perfusion during liver splitting will also be considered. |
| **Intervention(s)** | Ex-situ machine perfusion devices initiated on arrival at the hospital of the person having the transplant after the liver has been transported using conventional static cold storage (SCS).<br>The following ex-situ machine perfusion devices will be considered:<br>• Liver Assist (XVIVO B.V.).<br>• Organ Care System (OCS) Liver (TransMedics).<br>• metra (OrganOx Ltd).<br>• PerLife Pro (Aferetica S.R.L.).<br>• VitaSmart Hypothermic Oxygenated Machine Perfusion System (Bridge to Life Ltd).<br>Where possible, the assessment will also consider potential changes to the national liver transplantation pathway, in line with proposals by NHS Blood and Transplant, including the use of ex-situ machine perfusion technologies during transportation of donor organs, as applicable. |
| **Comparators** | SCS of donated livers. |
| **Setting** | Secondary and tertiary care, including retrieval and transportation of organs from donors to recipient hospitals. |
| **Outcomes eligible for inclusion (organised by outcome type)** | **Waiting list and utilisation outcomes:**<br>• Transplant utilisation (proportion of donor organs that proceeded to transplant rather than being discarded).<br>• Size and duration of liver transplant waiting list.<br>• Mortality on liver transplant waiting list.<br>**Clinical outcomes**<br>• Overall participant survival at 1 year and maximum follow-up. |

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| | • Graft survival at 1 year and maximum follow-up.<br>• Re-transplantation at 1 year and maximum follow-up.<br>• Biliary complications at 6 months, 12 months and maximum follow-up (total and if data permits separately for biliary leakage, anastomotic biliary strictures and non-anastomotic biliary strictures, and separately for DCD and DBD liver subgroups).<br>• Primary non-function of the graft (defined as irreversible graft dysfunction leading to recipient death or emergency retransplant within 7 days, excluding due to hepatic artery thrombosis).<br>• Hepatic artery thrombosis within 28 days (total and if data permits separately for hepatic artery thrombosis leading to recipient death and emergency retransplant).<br>• Inhospital incidence of post-reperfusion syndrome.<br>• Acute kidney injury post transplantation measured using a validated classification system (e.g. stage 2 or 3 on the Acute Kidney Injury Network classification system).<br>• Post-operative requirement for renal replacement therapy (total and if data permits separately for dialysis [including duration of dialysis] and kidney transplantation).<br>• Early allograft function, measured with a validated model (7 days) (e.g., Early Allograft Dysfunction or Model for Early Allograft Function criteria).<br>• Transaminase release during the first week post-transplant (participant serum) (until 7 days).<br>• Mechanical failure of machine perfusion technology (if data permits, separately for mechanical failure leading to organ discard and change in method of preservation).<br>• Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher) including bowel perforation, post-transplant lymphoproliferative disorder, bleeding and infections (both donor-related and surgical infections).<br>• Device related adverse events.<br>**Patient-reported outcomes:**<br>• HRQoL, assessed using any validated scale (also from carer and/or family perspective).<br>Other:<br>• Healthcare professional satisfaction and/or wellbeing.<br>**Costs and resource use:**<br>• Cost of technology, including purchase costs/lease fee, consumable costs and cost of training, including cost of transplants that do not proceed to surgery.<br>• Cost of organ retrieval and transplant surgery (encompassing cases that do not proceed to transplantation), including:<br>  • Hospital length of stay (including ICU separately)<br>  • management of complications and adverse events (including dialysis, rehospitalisation and re-transplantation)<br>  • Transportation of organs (including method of transport and whether ex-situ machine perfusion was used).<br>  • Cost of returning perfusion devices.<br>  • Cost of managing condition on the transplant waiting list, including hospitalisation episodes.<br>  • Staff time and cost according to specialism and level of pay, including theatre staff. |

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|---|---|
| | • Proportion of daytime transplant procedures (different costs associated with daytime and night-time procedures will also be taken into account). |
| **Economic analysis** | • The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality adjusted life year.<br>• Costs will be considered from an NHS and PSS perspective. The availability of any commercial arrangements for the interventions or comparator will be taken into account. |
| **Time horizon** | • The time horizon for estimating clinical and cost effectiveness will be sufficiently long to reflect potential for differences in costs or outcomes between the technologies being compared. |

**Key:** DBD – donation after brain death, DCD – donation after circulatory death, HRQoL - health related quality of life, NRP – normothermic regional perfusion, ICU - intensive care unit, PSS - personal social services, SCS - static cold storage.

## 1.1 Objectives

The purpose of this assessment is to address the following key decision questions:

- What is the clinical effectiveness of using ex-situ machine perfusion technologies for deceased donor liver transplants?
- What is the cost effectiveness of using ex-situ machine perfusion technologies for deceased donor liver transplants?
- What evidence is available to support the value proposition of ex-situ machine perfusion devices outlined in the scope, i.e.:
    - increasing the number of livers suitable for transplant?
    - improving the clinical outcomes of transplant recipients?
    - extending preservation time to allow more flexibility in the timing of the transplant operation?
- What are the key gaps in the evidence base?

# 2 Evidence review methods

We will conduct a systematic review to identify the clinical and economic evidence that is available on the selected technologies and explore if the technologies address the unmet need, using methods that conform to the NICE health technology evaluations manual and with reference to guidance from the NICE Decision Support Unit (NICE Decision Support Unit 2025). The review will follow the principles of systematic reviewing published by the Centre for Reviews and Dissemination (CRD) (Centre for Reviews and Dissemination 2008). The review methods, search approach, and synthesis will be conducted in a transparent manner. We will conduct a systematic search for relevant published evidence and incorporate any relevant evidence submitted by manufacturers through the NICE request for company evidence. Data sourced from NHS Blood and Transplant will also be considered for the meta-analysis, if applicable. Retrieved evidence will be screened according to the eligibility criteria described in Section 2.1. We will extract and synthesise relevant data from the eligible documents. Relevant clinical and health-related quality of life (HRQoL) data will inform the parameters of an Excel-based economic model.

## 2.1 Inclusion criteria

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

**Table 2.1: Summary of the review eligibility criteria**

| | Inclusion criteria | Exclusion criteria |
|---|---|---|
| **Population** | Subgroup data for adult and paediatric populations will be eligible where reported. Within these population subgroups the following subgroups will be considered (where data permits):<br>• Higher risk donors. These might include extended criteria donors (particularly with steatotic livers) and donors following circulatory death. If possible, use of NRP of livers donated after circulatory death will also be considered.<br>• Complex recipients. These might include people who have previously had a transplant or abdominal surgery, or those with advanced comorbidities and haemodynamic instability.<br>• Transplants subject to logistical considerations. These might include complex multi-organ transplants, challenging explant surgery, split livers (e.g., transport of right lobe for adult recipient) or other cases where it may be predicted that transport, allocation or in-hospital logistics would lead to cold ischaemia times too long to proceed with transplantation without the use of ex-situ machine perfusion. | • Non-liver transplant recipients, except where the recipient is receiving a multi-organ transplant which includes a donor liver. |
| **Intervention** | Ex-situ machine perfusion devices initiated on arrival at the hospital of the recipient after the liver has been transported using conventional static cold storage (back-to-base perfusion).<br><br>This includes cases where ex-situ perfusion is performed post-NRP after the circulatory death of the donor.<br><br>The following ex-situ machine perfusion devices will be considered:<br>• Liver Assist (XVIVO B.V.).<br>• Organ Care System (OCS) Liver (TransMedics).<br>• metra (OrganOx Ltd).<br>• PerLife Pro (Aferetica S.R.L).<br>• VitaSmart Hypothermic Oxygenated Machine Perfusion System (Bridge to Life Ltd). | Ex-situ machine perfusion devices other than those listed as eligible. |

| | | |
|---|---|---|
| | Where possible, the assessment will also consider potential changes to the national liver transplantation pathway, in line with proposals by NHS Blood and Transplant, including the use of ex-situ machine perfusion technologies during transportation of donor organs, as applicable. | |
| **Comparators** | • SCS of donated livers.<br>• No comparator. | Any comparator not listed. |
| **Outcomes** | All outcomes listed in the NICE final scope. | Studies not reporting outcomes relevant to the NICE final scope. |
| **Study design** | **For the clinical review:**<br>• RCTs.<br>• Non-randomised comparative studies, including:<br>  • Non-randomised comparative trials.<br>  • Cohort studies.<br>  • Case-control studies.<br>• Single arm studies.<br>Real-world evidence will be considered for the meta-analysis if applicable.<br>**For the economic review:**<br>• Cost-effectiveness analyses (including cost-utility analyses).<br>• Cost-benefit analyses.<br>• Cost-consequence analyses.<br>• Cost-comparison analyses.<br>• HTA reports investigating the cost-effectiveness of treatments. | • Case reports.<br>• Bench studies.<br>• Reviews, both systematic and non-systematic. |
| **Limits** | • Studies in English language only.<br>• Studies published from 2010 onwards.<br>• Conference abstracts published from 2022 onwards. | • Studies not in the English language.<br>• Studies published in 2009 or earlier.<br>• News items, opinion pieces and editorials. |

**Key:** HTA – health technology assessment, NRP – normothermic regional perfusion, RCT – randomised controlled trial, SCS - static cold storage.

Initial scoping searches indicate that first-in-human studies for hypothermic machine perfusion for liver transplants were published in 2010 (Guarrera et al. 2010). This is reflected in the eligibility criteria.

Scoping suggests a reasonable evidence base for the included technologies. Therefore, we do not anticipate the need to prioritise evidence. However, if we identify a large number of studies we will prioritise those that provide the most relevant and rigorous evidence.

For the review of clinical evidence, we will prioritise:

- randomised controlled trials
- prospective studies reporting comparative evidence.

Prioritisation will be done per technology taking the use case into account; for example, single arm studies may be included if there is limited comparative evidence for a particular technology, or for a particular use case.

For the economic review, we will prioritise:

- studies reporting full economic evaluations over partial economic evaluations, on an intervention-by-intervention basis, taking the use case into account.
- studies conducted in the UK, or if not in the UK, Europe, or Canada.

## 2.2 Search strategy

A MEDLINE (OvidSP) search strategy designed to identify clinical and economic evidence on the eligible technologies is presented in Appendix 1.

The strategy comprises search terms for liver transplants (search lines 1 to 4), liver perfusion devices (search lines 5 to 13), and terms associated with the eligible technologies (search line 15). The search is structured: (liver transplants AND perfusion devices) OR eligible technologies.

The strategy excludes animal studies from MEDLINE using a standard algorithm (search line 17). 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 18).

Reflecting the eligibility criteria, the strategy is restricted to studies published in the English language (search line 20) since 2010 (search line 21).

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.

### 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/ |
| Conference Proceedings Citation Index – Science (CPCI-S) | Web of Science |
| 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.

The CPCI-S search results and records indexed in Embase as conference abstracts will be restricted to studies published from 2022 to date.

We will also check included studies lists of any industry submissions to NICE, and evidence received from NHS Blood and Transplant, as well as retrieved relevant systematic reviews or meta-analyses published in the last 5 years, for additional eligible studies.

### 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 (Rethlefsen et al. 2021) and the PRISMA 2020 statement (Page et al. 2021a, Page et al. 2021b).

Where possible, we will download the results of searches in a tagged format and load them into bibliographic management software (EndNote) (Clarivate 2021). 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 assess the search results according to their relevance in providing information on clinical and cost-effectiveness, and will remove the obviously irrelevant records such as those about ineligible diseases.

- Two reviewers will independently assess the titles and abstracts of remaining records for relevance against the eligibility criteria, with disagreements adjudicated by a third reviewer.

- We will obtain the full text of potentially relevant studies. Two reviewers will independently assess the full texts for relevance against the eligibility criteria. A third reviewer will adjudicate any disagreements.

- We will record the number of records included and removed at each selection stage in the PRISMA flow diagram. We will list studies excluded after assessment of the full document in an excluded studies table, with the reasons for exclusion.

- Where results for one study are reported in more than one paper, all related papers will be identified and grouped together to ensure that participants in individual trials are only included once.

## 2.4 Data extraction strategy

A data extraction template will be developed in Word and piloted on 3 included studies. One researcher will extract data and a second researcher will check all data points. Any discrepancies will be resolved by discussion, or the involvement of a third researcher when required. Data extraction will be targeted, involving the extraction of key details describing the study reference (bibliographic details), study design, key patient characteristics, key intervention / comparator characteristics, and outcomes.

## 2.5 Quality assessment strategy

One reviewer will assess the risk of bias of each included study using the relevant, validated tool for each study design. A second reviewer will check the risk of bias assessment.

We will summarise the results of the risk of bias assessment in a table and we will provide a detailed assessment in an Appendix to the main report. The report will comment on the generalisability of results to clinical practice in the NHS.

## 2.6 Methods of analysis/synthesis

The studies will be summarised in tables providing data on their methods and results. We will provide a narrative summary exploring the quality of the studies, the relationship between studies and patterns that we have discerned

in the data. We will provide an overall assessment of the strength of the research evidence in relation to the research question. The similarity of included studies and availability of data will be assessed, and a meta-analysis will be conducted if it is feasible.

We expect to group the technology according to key differences. These include:

- Perfusion type (hypothermic, normothermic, subnormothermic, controlled oxygenated rewarming following hypothermic perfusion).
- Mode of use (initiated at recipient transplant centre or initiated at donor hospital and continued during transport, with initiation at recipient centre being the use case for the primary analysis).

If the evidence allows, we will also group by the key population subgroups detailed in the inclusion criteria.

## 3 Economic analysis methods

We propose the development of an economic model to estimate the clinical and economic outcomes associated with the use of ex-situ MP devices in people (i.e., both adults and children) undergoing whole or split liver transplantation from deceased donors.

The model will address the decision problem outlined in the final scope (see Section 1 for the draft decision problem).

The primary aim of this economic analysis is to estimate the costs and clinical outcomes for ex-situ MP devices initiated at recipient liver centre when compared with SCS, either with or without the use of normothermic regional perfusion (NRP). The model will also identify key drivers of costs and clinical outcomes.

As a secondary aim, and contingent on data being available to inform we will perform scenario analyses to investigate the impact of MP devices during

transport. These scenarios could include the use of transport in different places in the pathway, most likely in its use from ARC to recipient hospital. These scenarios will be informed by NHSBT plans for system use using ARCs. Scenario analyses will not include the use of ex-situ machine perfusion technologies for transporting donor organs in any manner not considered under the NHSBT ARC pilot programme.

We will also consider the costs and clinical outcomes in specific risk groups, such as DCD livers, where data allows.

The economic evaluation will adopt an NHS and Personal Social Services (PSS) perspective, in line with NICE guidelines (National Institute for Health and Care Excellence 2022b).

## 3.1 Model development

This evaluation will include distinct analysis for adult and paediatric populations where possible, and conditional on evidence, disaggregated analyses will also be conducted to examine costs and clinical outcomes for relevant subgroups and scenarios as highlighted in Section 2. These may include specific risk groups, such as high-risk donors (e.g., DCD livers). We anticipate there will be differences in the level and quality of evidence available across subgroups and for the paediatric population. Where this is identified, we will reference and interpret this in the final report. Where appropriate, this will be used to inform recommendations for future data collection.

Expert clinical input will be used to guide the model design, use of subgroups, and to ensure that key clinical events and outcomes are appropriately captured. We will aim to include all outcomes listed in the NICE scope that either have suitable evidence to inform them, or where informed assumptions can be used. Taking into account expert clinical input, outcomes with the highest level of evidence will be prioritised, and those with greater uncertainty may be included in additional scenario analyses. For example, where

outcomes such as biliary complications or acute kidney injury are supported by some evidence, but with notable uncertainty, these may be included in the base model with the option to toggle their inclusion on or off in scenario analysis.

Costs associated with the use of ex-situ MP may include the cost of the technology to a department / NHS site, staff time for organ transport, procedure time, and any training or ongoing equipment maintenance costs. Where company-supplied evidence is available, the model will aim to explore different intervention cost structures such as leasing, annualised capital investment, and free loan with consumable contracts.

Clinical outcomes which influence costs may include unnecessary call-ins (i.e., where individuals on the liver transplant waitlist are called into hospital and subsequently sent home as the donor liver is unsuitable), hospital length of stay, complication and adverse event rates, the need for dialysis or re-transplantation, and other relevant interventions.

Model inputs will be informed by published literature, company submissions, NHS data sources, and expert opinion. To identify appropriate evidence for costs and resource use, we will conduct targeted searches of the economic literature, supplemented by data from the NHS Cost Collection data, the Unit Costs of Health and Social Care published by the Personal Social Services Research Unit (PSSRU), and the British National Formulary (BNF). All costs will be inflated to the 2023/24 price year.

While the model will include health-related quality of life outcomes (HRQoL) where available, particularly in the long-term, it may not be possible to fully reflect the impact of different patient pathways or additional time spent on the transplant waiting list. Where we are unable to quantify this, these issues will be discussed qualitatively in the final report. Equally, we acknowledge that broader societal outcomes, including personal and family costs and potential impacts on quality of life for family and caregivers, may not be captured in the model. These outcomes will also be discussed qualitatively in the final report.

Deterministic sensitivity analysis (DSA) will be used to test the impact of uncertainty in key model parameters. A tornado diagram will be included to display the parameters which have the highest impact on model outcomes. Additional scenario analysis will be conducted around key factors such as the ability of certain ex-situ MP devices to assess liver viability. These analyses will also consider potential future implementation strategies, where possible, in line with NHSBT Assessment and Recovery Centre (ARC) proposals. These scenarios will be high-level given the early nature of this pathway. Probabilistic sensitivity analysis (PSA) will also be conducted, though it is worth noting that, if there is a significant lack of data for some parameters, the results of the PSA may not be fully accurate as the underlying probability distributions may be less robust.

## 3.2 Conceptual modelling

A conceptual model will be developed to address the decision problem. While it is not possible at this point to provide a definitive outline of the model structure, we propose the development of a decision tree with a one-year time horizon leading into a high-level lifetime Markov model. The final model structure will be finalised following further exploration of the clinical pathways and the evidence assessment.

The base case model is expected to focus primarily on the short-term change in liver utilisation, alongside other important clinical and resource use outcomes such as re-transplantation rates, length of stay in hospital, and immediate patient survival. The lifetime model will aim to assess the long-term consequences of either receiving a liver transplant or remaining on the waiting list beyond one-year. This analysis will consider long-term impact on patient outcomes including survival where available. Costs and health outcomes in this longer-term model will be discounted at 3.5% per annum, in line with NICE guidance (National Institute for Health and Care Excellence 2022b). As robust data for this extended period may be limited, it may not be possible to

accurately model these outcomes. In this case, exploratory assumptions may be necessary to investigate the range of potential impacts.

Due to the wide range of sub-populations, as well as specific workflows and preferences of various speciality departments, there will be a wide range of additional long-term outcomes, which will not be possible to capture. YHEC will take expert advice into account to consider long-term outcomes such as the need for re-transplantation due to biliary complications or episodes of acute kidney injury leading to renal failure, where feasible. Model results will be reported disaggregated by short- and long-term outcomes; commentary will be provided on the relative robustness of each of these outcomes in the final report.

This outlined approach enables us to balance the use of existing evidence, capture both short-term events and select long-term cost and health outcomes, while limiting the structural uncertainty that may arise from the use of more complex modelling structures.

Once the model structure and key assumptions have been refined based on the final scope, evidence review, we will validate the approach with clinical experts. This will be done through dedicated meetings or email correspondence. Expert feedback will be used to test the face validity of the conceptual model, inform subgroup analysis, and ensure that key events and outcomes are appropriately captured.

In line with the draft scope, we plan to include people receiving repeat liver transplants within the broader population of interest. However, we acknowledge that this group may represent a higher-risk subgroup with distinct clinical trajectories and outcomes. Therefore, where evidence allows, we will consider conducting separate subgroup analyses for individuals receiving repeat transplants.

# 4 Gap analysis

Evidence gaps relating to all NICE scope outcomes 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 from the companies and other stakeholders

The EAG will consider all data submitted by the companies in evidence and information requests by NICE, or by other stakeholders, if received by 26th September 2025. Information arriving after this date will not be considered. If the data included in the information provided meets the inclusion criteria for the review, it will be extracted and quality assessed following the procedures outlined in this protocol. The EAG may seek clarification or additional information from companies and other stakeholders where necessary.

Any 'commercial in confidence' data provided by a company and specified as such will be highlighted in blue and underlined in the assessment report. Any 'academic in confidence' data provided by company(s), and specified as such, will be highlighted in yellow and underlined in the assessment report. If confidential information is included in the economic model, the EAG will provide a copy of the model with 'dummy variable values' for the confidential values (using non-confidential values).

# 6 Competing interests of authors

The EAG can confirm that there are no conflicts of interests to declare for the project team.

# 7 References


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# 8 Appendix A: Draft search strategy

1 liver transplantation/ (68408)

2 ((liver* or hepat*) adj5 (transplant* or allograft* or graft* or replac*)).ti,ab,kf. (98604)

3 ((liver* or hepat*) adj5 (donat* or donor*)).ti,ab,kf. (20976)

4 or/1-3 (112410)

5 organ preservation/ (10630)

6 perfusion/ (54461)

7 (machine* or oxygen* or hypotherm* or normotherm* or subnormotherm* or "ex vivo" or "ex situ").ti,ab,kf. (1279526)

8 (5 or 6) and 7 (12028)

9 ((machine* or oxygen*) adj5 perfus*).ti,ab,kf. (9046)

10 ((hypotherm* or normotherm* or subnormotherm*) adj5 perfus*).ti,ab,kf. (5025)

11 (("ex vivo" or "ex situ") adj5 perfus*).ti,ab,kf. (4150)

12 ((back to base or end ischemic or end ischaemic or device to donor* or transport*) adj5 perfus*).ti,ab,kf. (1180)

13 or/8-12 (22128)

14 4 and 13 (2097)

15 (bridge to life or vitasmart* or vita smart* or organox or organ ox or metra or metratm or metrar or xvivo or liver assist or liver assisttm or liver assistr or organ assist or organ assisttm or organ assistr or aferetica or

perlife* or perlife pro* or transmedics or trans medics or organ care system or organ care systemtm or organ care systemr or OCS liver*).ti,ab,kf,ot. (550)

16 14 or 15 (2608)

17 exp animals/ not humans/ (5375079)

18 (news or editorial or case reports).pt. or case report.ti. (3520555)

19 16 not (17 or 18) (1747)

20 limit 19 to english language (1669)

21 limit 20 to yr="2010 -Current" (1399)

Key to Ovid symbols and commands:

| | |
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| * | 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 |

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