IPG10405 (IP1890) - In-situ normothermic regional perfusion of the abdomen for livers donated after controlled circulatory death

Final Protocol

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1. Decision problem

The key objective for this evaluation is to assess the efficacy and safety of in-situ normothermic regional perfusion (NRP) of the abdomen for the recovery of donor livers following circulatory death, to determine whether it works well enough and is safe enough for use in the NHS.

Table 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. Summary table of the decision problem

Population	People receiving a liver transplant from donors who have died from controlled circulatory death
Intervention	In-situ NRP of the abdomen to retrieve the liver after the donor has died from controlled circulatory death
Key efficacy outcomes (may include but are not limited to)	• Transplant utilisation (use of livers or proportion not discarded) • Post-transplant liver function (serum aspartate aminotransferase AST, alanine aminotransferase, serum creatinine, total bilirubin, prothrombin time) • Long term (6-12 months post-transplant) liver function (e.g. ALP measurement to assess biliary damage) • Acute rejection of the donor liver by the recipient • Graft survival • Primary non-function of the graft • Early allograft dysfunction • Recipient mortality 7 days and 1 year after transplantation • Recipient mortality without relisting or retransplantation, recipient mortality after relisting and re-transplantation • Recipient re-listing • Recipient re-transplantation

	• Recipient time to recovery to normal functional status post-transplantation • Circuit failure during in-situ NRP (loss of blood volume, air or clots in the circuit) • NRP procedure-related failure that impacts the donor liver (failed cannulation of the donor, mechanical failure of the device)
Key safety outcomes (may include but are not limited to)	• NRP procedure-related adverse events that impact the recipient (e.g. infections, bleeding, cardiovascular complications, and thromboembolic complications related to the graft) • Biliary complications (e.g. ischaemic cholangiopathy, non-anastomotic strictures) • Recipient hospitalisation (total hospital admissions) after 1st year of transplantation • Renal complications

NRP: Normothermic Regional Perfusion; ALP: Alkaline Phosphatase.

1.1 Objectives

The purpose of this Interventional Procedures assessment is to assess the efficacy and safety of in-situ NRP of the abdomen for the recovery of donor livers following controlled circulatory death, to determine whether it works well enough and is safe enough for use in the NHS.

The research questions this assessment will aim to answer are:

- What is the clinical efficacy of in-situ NRP of the abdomen for the recovery of donor livers after controlled circulatory death?
- What are the risks and safety considerations associated with using this procedure?

The following objectives are proposed to address the research questions:

- Identify and assess evidence relating to the efficacy and safety of the interventional procedure as it pertains to the scope

- Report on any potential safety issues of the procedure

2. Evidence review methods

An independent search for and assessment of relevant evidence will be conducted by the EAG. Evidence relevant to the scope will be identified using databases of published evidence. If available, relevant evidence provided by technology manufacturers through NICE will be used. The EAG will adopt rapid review methods, guided by the Cochrane Rapid Review Methods Guidance (Garritty et al., 2024) and consistent with the Interventional Procedures Programme Manual (NICE, 2025).

Inclusion criteria

Table 2 outlines the inclusion and exclusion criteria considered for the evidence identified. If a large volume of evidence is identified, certain evidence may be prioritised for inclusion (see Section 2.2).

Table 2. Inclusion and exclusion criteria

	Inclusion Criteria	Exclusion Criteria
Population	People receiving a liver transplant from donors who have died from controlled circulatory death	• People receiving a liver transplant from donors who have died from non-circulatory death • People receiving a liver transplant from donors who have died from uncontrolled circulatory death • Studies reporting on organ transplantation for other organs (e.g heart, liver, lungs), where no specific data for the liver is reported
Intervention	In-situ NRP of the abdomen to retrieve the liver after the donor has died from controlled circulatory death	• Thoraco-abdominal NRP • Ex-situ Machine Perfusion (NMP/HOPE) in the absence of an in-situ NRP group
Comparators	• Static cold storage (SCS) only • Ex-situ Machine Perfusion (NMP/HOPE) only • Ex-situ Machine Perfusion (NMP/HOPE) with SCS	

Key outcomes	**Key efficacy outcomes** (may include but are not limited to): • Transplant utilisation (use of livers or proportion not discarded) • Post-transplant liver function (serum aspartate aminotransferase AST, alanine aminotransferase, serum creatinine, total bilirubin, prothrombin time) • Long term (6-12 months post-transplant) liver function (e.g. ALP measurement to assess biliary damage) • Acute rejection of the donor liver by the recipient • Graft survival • Primary non-function of the graft • Early allograft dysfunction • Recipient mortality 7 days and 1 year after transplantation • Recipient mortality without relisting or retransplantation, recipient mortality after relisting and re-transplantation • Recipient re-listing • Recipient re-transplantation • Recipient time to recovery to normal functional status post-transplantation • Circuit failure during in-situ NRP (loss of blood volume, air or clots in the circuit) • NRP procedure-related failure that impacts the donor liver (failed cannulation of the donor, mechanical failure of the device) **Key safety outcomes** (may include but are not limited to): • NRP procedure-related adverse events that impact the recipient (e.g. infections, bleeding, cardiovascular complications, and	

	thromboembolic complications related to the graft) • Biliary complications (e.g. ischaemic cholangiopathy, non-anastomotic strictures) • Recipient hospitalisation (total hospital admissions) after 1st year of transplantation • Renal complications	
Study design	• Randomised controlled trials (RCTs) • Non-randomised comparative studies • Systematic reviews and meta-analyses • Observational studies (retrospective and prospective) • Diagnostic accuracy studies • Surveys • Cross-sectional studies • Case series • Case reports	• Narrative review articles • Animal studies • Studies reporting only on physiological outcomes • Editorials • Commentaries • Cost-effectiveness or economic studies
Publication type	• Full text publications • Conference abstracts and proceedings (provided they contain sufficient detail on methods and outcomes) • Letters/correspondence that report novel research findings	• Studies reporting efficacy outcomes only reported in conference abstracts / proceedings or letters may be excluded if there is a large volume of relevant full-text publications available

ALP: Alkaline Phosphatase; HOPE: Hypothermic Oxygenated Perfusion; NMP: Normothermic Machine Perfusion; NRP: Normothermic Regional Perfusion.

2.1 Search strategy

As per section 5 of the Interventional Procedures Programme Manual (NICE, 2025), evidence relevant to the scope will be identified using a comprehensive and exhaustive search across a limited number of sources. Searches will be developed in MEDLINE (Ovid) by an experienced Information Specialist. Search terms will include free-text terms and controlled vocabulary where applicable (e.g. MeSH). The search strategy will be peer-reviewed by a second Information Specialist. A draft search strategy is available in Appendix A. The search strategy will be translated to each database. If needed, e.g. if other important search terms are identified during

the screening process, searches will be performed iteratively. To maximise retrieval of relevant evidence, the search strategy includes terms related to devices that are currently used, or were previously used, to perform in-situ NRP in the UK, guided by the information provided in the published scope and British Transplantation Society's guidelines on transplantations from donors who have died from circulatory death.

The following bibliographic databases will be searched:

- MEDLINE (ALL) via Ovid
- Embase via Ovid
- Cochrane Central Register of Controlled Trials (CENTRAL) via Cochrane Library
- Cochrane Database of Systematic Reviews (CDSR) via Cochrane Library
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCO
- Health Technology Assessment Database (INAHTA)

The following clinical trial registries will be searched:

- ClinicalTrials.gov
- International Clinical Trials Registry Platform (ICTRP)
- International Standard Randomised Controlled Trial Number (ISRCTN) registry

The following pre-print server will be searched for yet unpublished evidence:

- medRxiv

The following resources will be checked for adverse events:

- Medicines and Healthcare products Regulatory Agency (MHRA)
- US Food and Drug Administration's (FDA) Manufacturer and User Facility Device Experience (MAUDE) database

Where possible, the EAG will identify additional published and unpublished studies from the information companies provide to NICE. To identify studies that have not been retrieved by the database searches, company websites will also be searched for relevant publications. After the studies identified through the database searches

have been screened for inclusion, back citation searching will be performed on the eligible studies to identify other studies that may not have been identified through the database searches and those will be assessed for eligibility.

2.2 Study selection

The EAG will use the methodology outlined in section 5.2 of the interventional procedures programme manual for study selection (NICE, 2025).

Retrieved references will be imported into EndNote and deduplicated, after which they will be imported into the online screening tool Rayyan, where deduplication will be completed and records screened. The titles and abstracts of the identified studies will be screened by one reviewer and a minimum of 20% of excluded records will be checked by a second reviewer against the pre-specified inclusion and exclusion criteria (see Table 2). The AI screening tool available within Rayyan will not be used and all decisions will be made by the review team. Where a record appears to meet the eligibility criteria, or where a decision cannot be made based on the information provided in the titles and abstracts alone, it will be progressed to the full-text screening stage. The full texts of the articles progressed to this stage will be obtained and screened by one reviewer, with a random 20% of exclusions checked by a second reviewer. A list of studies excluded at the full-text stage, with reasons for their exclusion, will be presented in an appendix in the report.

Where a large volume of evidence is identified, a pragmatic approach to study selection may be taken, in line with the Technical Support Document 27: Prioritising studies and outcomes for NICE HealthTech literature reviews (Carroll et al., 2025). Prioritisation of studies to be included may be based on factors such as study design, sample size, availability of relevant patient-focused outcomes including safety outcomes, length of follow-up, and extent of generalisability to a UK population. Clinical experts may be consulted to inform these decisions. Any decisions made and approaches taken by the EAG will be flagged with the NICE team for discussion and presented transparently in the final report.

2.3 Data extraction strategy

Where available, the following data will be extracted from studies: study information (i.e., author, year), study design, study dates, intervention characteristics (i.e.,

intervention name), comparator, participant characteristics (i.e., demographics, comorbidities) and participant outcomes which are relevant to the scope. Data extraction will be conducted by one reviewer into a table in Microsoft Word and checked by a second reviewer.

2.4 Quality assessment strategy

In line with interventional procedures programme manual (NICE, 2025) a formal risk of bias assessment using validated critical appraisal checklists will not be performed. Instead, a narrative summary of the key strengths and limitations of the evidence will be presented. Consistent with section 5.3 of the interventional procedures programme manual, this analysis will address key features such as patient selection, operator training/experience, validity of outcome measurement, and completeness of follow-up. This summary will highlight potential biases in individual studies, discuss how these impact on the certainty of the results and outline how this might impact generalisability to NHS clinical practice.

3. Handling information from the companies and other stakeholders

All data submitted by the companies in evidence and information requests by NICE, or data submitted by other stakeholders will be considered by the EAG if received by 12/02/2026. Information arriving after this date will not be considered. If the data included in the information provided meets the inclusion criteria for the review, they 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. All correspondence between the EAG and companies will happen through NICE.

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.

4. Competing interests of authors

None.

5. References

British Transplantation Society (2023). UK guidelines on transplantation from deceased donors after circulatory death.

Carroll C, Cooper K, Harnan S, Wailoo A (2025) Technical Support Document 27: Prioritising studies and outcomes for NICE HealthTech literature reviews. Sheffield Decision Support Unit

Garritty C, Hamel C, Trivella M et al. (2024) Updated recommendations for the Cochrane rapid review methods guidance for rapid reviews of effectiveness. BMJ 384: e076335

Interventional procedures programme manual: NICE process and methods (2025) NICE process and methods guide PMG28

Appendix A: Draft search strategy

Ovid MEDLINE(R) ALL <1946 to January 16, 2026>

#	Query	Hits
1	Extracorporeal Membrane Oxygenation/	18166
2	((regional* or local* or abdom*) adj2 (perfus* or reperfus*)).tw.	6579
3	NRP.tw.	2288
4	abdominal-RP.tw.	5
5	((extracorpor* or extra-corpor*) adj1 (membran* oxygenat* or membran* reoxygenat* or membran* re-oxygenat*)).tw.	21872
6	((normotherm* or normo-therm*) adj2 (circulation or recirculation)).tw.	93
7	CardioHelp.tw.	33
8	GETINGE.tw.	66
9	Donor Assist.tw.	1
10	XVIVO.tw.	35
11	or/1-10	35761
12	Liver Transplantation/	69037
13	((liver* or hepat*) adj10 (donor* or donat* or recover* or retriev* or transplant* or procur* or graft* or allotransplant* or allograft*)).tw.	122564
14	or/12-13	131156
15	exp Heart Arrest/	60673
16	((circulatory or cardi* or heart) adj2 (arrest or death)).tw.	119953

17	(withdr* adj2 life support).tw.	728
18	non-heart beating donor*.tw.	982
19	DCD.tw.	4489
20	cDCD.tw.	229
21	NHBD.tw.	340
22	or/15-21	145418
23	11 and 14 and 22	237
24	exp animals/ not humans.sh.	5415384
25	23 not 24	219