NICE National Institute for Health and Care Excellence

Overview

HealthTech Programme

Medical Technologies Advisory Committee (MTAC) Advisory Committee

HTE10066 Ex-situ machine perfusion devices to preserve deceased donor livers for transplantation – 1st meeting

23 April 2026

Technical analyst:	Robbie Pitcher and Sam Baskerville
Technical adviser:	Rebecca Owens
Committee lead:	Katherine Boylan
Expert Lead:	Colin Wilson
EAG leads:	Anne Littlewood Luc Curtis-Gretton
Link to Experts register for topic:	expert-advisers.pdf

The following documents are made available to the Committee:

1. Cover sheet
2. Final Scope
3. External assessment report overview (ARO)
4. Patient group, professional group and NHS organisation submissions:
   4a. NHS England
5. Expert questionnaires
6. Updated External assessment report (EAR) 15 April 2026 – prepared by York Health Economics Consortium. Note, this report is an updated version to the one issued for company fact check on 17/03/2026. The updates are listed on pages 4-6 of the report
7. Company fact check comments and External Assessment Group (EAG) responses on the EAR

Any information supplied to NICE which has been marked as confidential, has been redacted. All personal information has also been redacted

Routine use assessment

HTE10066 Ex-situ machine perfusion devices for deceased donor liver transplants

Assessment report overview

This overview summarises key information from the assessment and sets out points for discussion in the committee meeting. It should be read together with the final scope and the external assessment report. As part of this assessment, NICE did a survey of people (and carers) who have undergone or are awaiting liver transplant surgery. The summary of the survey responses is included in appendix A and the survey questionnaire in appendix B. NICE would like to thank all the people who responded, for their time and for sharing their experiences and views. A list of abbreviations used in this overview is in appendix C.

1. The technology

This assessment included 4 ex-situ machine perfusion devices that can be used to preserve livers from deceased donors (Table 1). Although the Organ Care System (OCS) Liver was originally in scope, TransMedics later advised NICE that it would not be making the system available to the NHS for the relevant use case, and it has therefore been removed from the assessment.

Ex-situ machine perfusion systems typically comprise a reservoir, a pump, an oxygenator and a warming or cooling unit. The donor liver is placed in the device, which pumps a specially formulated solution (perfusate) through the organ's blood vessels. Machine perfusion is typically performed at hypothermic (4 to 12 °C) or normothermic (around 37 °C) temperatures. Normothermic machine perfusion requires an oxygen carrier; hypothermic machine perfusion does not. In hypothermic oxygenated machine perfusion (termed 'HOPE'), oxygenated perfusate can be delivered via both the hepatic

artery and portal vein, or via the portal vein only. With some devices, the viability of the donor liver can be assessed during normothermic perfusion. Some devices can also slowly rewarm livers from hypothermia to normothermia (termed ‘controlled oxygenated rewarming’) and/or provide a platform for liver splitting during machine perfusion.

The aims of machine perfusion technologies include:

- increasing utilisation of donated organs
- improving the quality of liver transplants and therefore clinical outcomes for transplant recipients
- extending how long the liver can be preserved. This could enable more day-time operations and help address organ allocation, transport and in-hospital logistical considerations. It may also support improved staff well-being and workforce sustainability.

2. The condition

Liver transplantation is a treatment option for people with end-stage liver disease (for example, because of alcohol-related liver disease, metabolic, autoimmune or infectious conditions) and some people with liver cancer or acute liver failure. In children, the most common reason for liver transplantation is congenital biliary atresia. People with end-stage liver disease are at increased risk of dying from complications of the condition and symptoms can severely affect quality of life.

Table 1 Summary of ex-situ machine perfusion technologies

Technology (company)	Intended population	Perfusion strategy	Liver function and viability assessment*	Regulatory status (machine unit) Use in NHS
Liver Assist (XVIVO BV)	• Adults • Children	• Hypothermic oxygenated machine perfusion (HOPE) • Normothermic machine perfusion (NMP) • Controlled oxygenated rewarming (COR)	Yes (during normothermic perfusion)	• CE marked class IIb • Currently used in NHS
metra (OrganOx Ltd)	Adults	NMP	Yes	• UKCA marked class IIa (CE class IIb) • Currently used in NHS
PerLife Pro (Aferetica Srl)	• Adults • Children	• HOPE • NMP • COR	No	CE marked class IIa. Currently working towards registering with MHRA, so that it can be available to NHS.
VitaSmart Hypothermic Oxygenated Machine Perfusion System (Bridge to Life Ltd)	• Adults • Children	HOPE	No	• CE marked class IIb • Currently used in NHS

***According to clinical experts, emerging evidence suggests that flavin mononucleotide (FMN) can be used as a surrogate marker of mitochondrial damage and organ quality during hypothermic machine perfusion.**

3. Current practice

Most liver transplants are planned as routine, elective procedures, but some people require an emergency 'super-urgent' transplant (NHSBT, 2025b). People identified as needing a liver transplant are placed on a waiting list. The national UK median waiting time for an elective liver only transplant from a deceased donor is about 5 months in adults and 6 months in children, but this varies across transplant centres (NHSBT, 2025b).

Within the NHS, transplants are done by specialist liver transplant surgeons in 7 centres for adults and 3 centres for children across the UK.

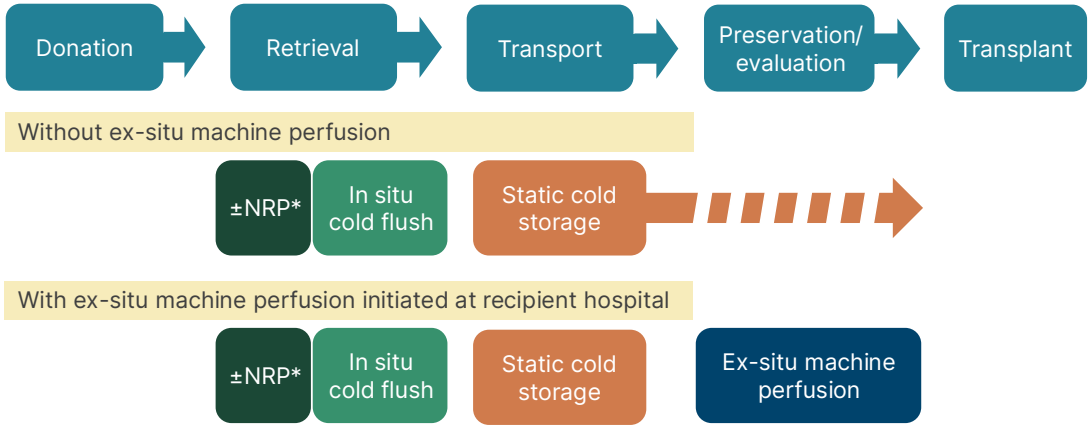
In the UK, the majority of livers suitable for transplantation come from deceased donors after either brainstem death (DBD) or circulatory death (DCD). The use of DCD livers is more common in adults than in children. In adults, the majority of donated livers are transplanted as a whole organ. In children and small adults, split liver transplants are more common. Split livers are usually obtained from carefully selected low-risk donors. The smaller left lobe is transplanted into a child or small adult. If usable, the larger right lobe may be transported to an adult liver transplant centre and used for an adult.

A donor liver for transplant is usually preserved using static cold storage (SCS). This involves flushing the donor liver with cold organ preservation solution and then placing it in a sterile bag in a cold storage icebox for transport to the selected hospital for transplant as soon as possible, to minimise ischaemic damage to the organ. Increasingly, organ retrieval teams do in-situ normothermic regional perfusion (NRP) before abdominal organs are removed from donors after circulatory death (NHSBT 2025c). During NRP, the function of the liver can be assessed. NRP and ex-situ machine perfusion can be used sequentially in the same pathway (Figure 1). NICE guidance on NRP is currently in development.

According to NICE HealthTech guidance 496, ex-situ machine perfusion should only be used with special arrangements for clinical governance, consent, and audit or research. Most UK liver transplant centres use ex-situ

machine perfusion devices to some degree, more commonly for organs for adults than for children. But practices vary between centres, leading to variation in access. In the UK, ex-situ machine perfusion devices are initiated on arrival at the hospital of the person having the transplant, after the liver has been transported using SCS. Although 1 of the devices included in the scope (i.e., *metra*) can also be initiated at the donor hospital and be used to transport the liver transplant instead of SCS, this is not current UK practice and therefore this functionality is outside the scope of this assessment.

Figure 1 Donation and transplantation pathway



*In situ normothermic regional perfusion (NRP) is done only for abdominal organs donated after circulatory death

4. Unmet need

There is a shortage of high-quality donor livers available for transplant in the UK and demand is rising due to the increasing prevalence of chronic liver diseases in the general population. This shortfall results in significant mortality and morbidity for people on the waiting list for liver transplants.

In the UK, many donated livers do not proceed to transplant, particularly organs from people who are older, who have conditions that affect liver function or who donated their liver after circulatory death. These organs are at higher risk of worse outcomes if they are preserved using static cold storage only. Because it is not possible to assess how well donor livers are functioning during cold storage, decisions about whether an organ is suitable for transplantation are based on characteristics of the donor and the appearance

of the liver. This uncertainty may lead some clinicians to decline to transplant organs that could potentially be used.

Further details, including descriptions of the interventions, comparator, care pathway and outcomes, are in the final scope.

5. Clinical effectiveness

The external assessment group (EAG) did literature searches to identify relevant published clinical evidence (on 15 September 2025). 168 studies were identified as relevant. Due to the large number of studies identified, studies were prioritised based on the quality of evidence and applicability to UK practice, for each device and perfusion method. The search and selection methods are in sections 4.1 and 4.2 of the external assessment report (EAR).

5.1 Overview of key studies

The EAG prioritised a total of 15 studies on 3 technologies (Liver Assist, *metra* and VitaSmart) for review. No relevant studies were identified for PerLife Pro. 14 studies were done in Europe (4 recruited participants from the UK) and 1 in the USA. None of the prioritised studies included children or young people. Table 2 summarises the characteristics of the prioritised studies.

Of the 15 prioritised studies, 7 randomised controlled trials (RCTs) reported on Liver Assist, 2 RCTs reported on VitaSmart and 6 non-randomised comparative studies reported on *metra*. All studies assessed ex-situ machine perfusion initiated at the hospital of the person having the transplant, after the liver has been transported using SCS, compared to SCS only. 1 study on *metra* included a third arm, NRP then SCS. Additional RCT evidence was identified on *metra* initiated at the donor hospital, but this was not prioritised as this use case was not included in the scope.

In 8 RCTs, hypothermic oxygenated machine perfusion was used (6 Liver Assist, 2 VitaSmart). In 7 studies normothermic machine perfusion was used; 1 RCT on Liver Assist and 6 non-randomised comparative studies on *metra*.

2 studies included DCD livers only, 9 DBD donors only, and 4 a mix of the two (<30% DCD). Where reported, studies including DBD livers typically restricted them to extended criteria donors.

Studies on LiverAssist

- 7 RCTs (798 participants in total)
- Normothermic machine perfusion was used in 1 study (20 participants). Hypothermic oxygenated machine perfusion was used in 6; in 1, hypothermic oxygenated perfusion was followed by controlled oxygenated re-warming. Of studies assessing hypothermic oxygenated machine perfusion, 3 perfused both the hepatic artery and portal vein, 3 perfused the portal vein only.
- 1 study included DCD livers only. The other studies used DBD livers only, typically from extended criteria donors.
- All studies were done in Europe (2 included UK participants)

Studies on *metra*

- 3 matched-case studies and 3 cohort studies (861 participants in total)
- All studies assessed normothermic machine perfusion
- 1 study included DCD livers only, 2 DBD livers only, and 3 a mix. Where reported, studies using DBD livers typically restricted them to extended criteria donors
- 2 studies were done in the UK; 4 were done in other European countries

Studies on VitaSmart

- 2 RCTs (329 participants in total)
- Both studies assessed hypothermic oxygenated machine perfusion; in both, only the portal vein was perfused.
- 1 study included a mix of DBD and DCD livers; 1 study included DBD livers only. Both studies only included DBD livers from extended criteria donors.
- 1 study was done in Europe and 1 in the USA

Information on the prioritised studies is detailed in section 4.2 of the EAR.

Outcomes

- Clinical experts identified transplant utilisation as the most important outcome, followed by waiting list outcomes (size, duration and mortality), then overall participant survival, graft survival, device-related adverse events and biliary complications. Biliary complications include anastomotic strictures, non-anastomotic strictures and bile leakage. Non-anastomotic biliary strictures are the most severe form of biliary complication and a major contributor to graft loss, morbidity and mortality post-transplant. DCD livers are more prone to non-anastomotic biliary strictures.
- Some experts also considered mechanical failure of device, re-transplantation, primary non-function of the graft, healthcare professional satisfaction/wellbeing, patient/carer quality of life and early allograft dysfunction (EAD) to be the most important outcomes. EAD is used to describe how well the donor liver is working in the first 7 days post-transplant, based on surrogate markers of liver injury and function. Some clinical experts questioned the clinical relevance of the EAD measures used in the prioritised clinical studies, as they are based on transaminase levels. Transaminases are washed out of donor livers during machine perfusion and therefore do not correlate well with actual liver injury.
- Additional outcomes not considered the most important by experts are also captured in the EAR, as per the scope of the assessment.

Study quality

Of the 9 RCTs, 8 were judged to be at a low risk of bias. 1 RCT (on LiverAssist) was judged to be at a moderate risk due to unclear handling of missing data. All RCTs were open-label or single-blind, as clinicians could not be blinded to the organ preservation method. But this was not considered a meaningful source of bias because all outcomes were objectively measured.

4 of the 6 non-randomised studies were judged to be at a moderate risk of bias, all due to potential imbalance in confounding factors between treatment groups. The other 2 were considered low risk.

Generalisability

Advice from clinical experts suggested that the prioritised studies were broadly applicable to the UK setting, with caveats around possible differences in donor case-mix, logistics, cold ischaemia times, allocations and peri-operative pathways.

It is uncertain whether clinical results obtained from a specific device can be applied to other devices using the same perfusion method, or whether findings from one perfusion method can be generalised to different perfusion methods. It is also uncertain whether outcomes observed in adult recipients of livers preserved using machine perfusion devices can be generalised to paediatric recipients.

Table 2 Summary of prioritised studies

All studies compare ex-situ machine perfusion devices to static cold storage (1:1), unless otherwise stated in study design column.

Study	Study design	Perfusion method	Study location	Donor type
Liver Assist				
van Rijn et al 2021	RCT (N=156)	HOPE; dual perfusion	Belgium, UK, Netherlands	DCD
Czigany et al 2021	RCT (N=46)	HOPE; single perfusion	Czech Republic, Germany	DBD; ECD
Minor et al 2021	RCT (N=40)	HOPE followed by controlled oxygenated re-warming; dual perfusion	France	DBD; ECD
Lesurtel et al 2025	RCT (N=262)	HOPE; single perfusion	France	DBD; ECD
Ghinolfi et al 2019	RCT (N=20)	Normothermic; dual perfusion	Italy	DBD; ECD
Grat et al 2023	RCT (N=104) ESMP vs SCS (1:3)	HOPE; dual perfusion	Poland	DBD; ~50% ECD
Schlegel et al 2023	RCT (N=170)	HOPE; single perfusion	UK, Belgium, Netherlands, France, Austria, Switzerland	DBD; ECD not reported
metra				
Vogt et al 2024	Prospective cohort study (N=37) ESMP vs SCS (5:1)	Normothermic; dual perfusion	Germany	DBD; ECD not reported
Krendl et al 2025	Retrospective cohort study (N=332)	Normothermic; dual perfusion	Austria	Mixed DBD/DCD (<20% DCD); >60% ECD

Study	Study design	Perfusion method	Study location	Donor type
	ESMP vs SCS (~1:1)			
Fodor et al 2021	Matched case study (N=118)	Normothermic; dual perfusion	Austria	Mixed DBD/DCD (<20% DCD); >70% ECD
Mathis et al 2024	Matched case study (N=54) ESMP vs SCS (1:2)	Normothermic; dual perfusion	Austria	Mixed DBD/DCD (<20% DCD); ECD included but number unclear
Hann et al 2022	Matched case study (N=82) ESMP vs historical SCS and contemporaneous SCS (~1:1:1)	Normothermic; dual perfusion	UK	DBD; ECD in the *metra* arm only
Puttappa et al 2025	Retrospective cohort (N=238) ESMP (n=78) vs SCS (n=59) vs NRP then SCS (n=101)	Normothermic; dual perfusion	UK	DCD
VitaSmart				
Reich et al 2024	RCT (N=219)	HOPE; single perfusion	USA	Mixed DBD/DCD (<30% DCD); ECD
Ravaioli et al 2022	RCT (N=110)	HOPE; single perfusion	Italy	DBD; ECD

DBD: donation after brain death, DCD: donation after circulatory death, ECD: extended criteria donor, ESMP: ex-situ machine perfusion, HOPE: hypothermic oxygenated machine perfusion, NRP: normothermic regional perfusion, RCT: randomised controlled trial, SCS: static cold storage

5.2 Results

None of the prioritised studies reported comparative evidence on transplant utilisation, waiting list outcomes or device related adverse events. There was also no evidence from the prioritised studies on healthcare professional satisfaction/ wellbeing or patient/ carer health-related quality of life.

For the prioritised outcomes, all RCTs did intent-to-treat (ITT) or modified ITT analyses (including all participants who underwent a transplant according to their allocated preservation method), except for 1 RCT on VitaSmart, which did per protocol analyses (participants were analysed according to the preservation method used during the transplant process).

The EAG did not do a meta-analysis due to heterogeneity across studies.

Full details of results from the prioritised studies are in section 5.2 of the EAR, including outcomes not considered by experts to be the most important, such as serious adverse events.

Hypothermic oxygenated machine perfusion

Table 3 summarises the results from the prioritised studies on the outcomes that experts considered to be the most important.

Overall survival

7 RCTs (5 on Liver Assist; 2 on VitaSmart) reported on overall survival at follow-up periods ranging from 6 months to 5 years. None reported a statistically significant difference between treatment groups, and the direction of effect was inconsistent across studies.

Graft survival

8 RCTs (6 on Liver Assist; 2 on VitaSmart) reported on graft survival, at follow-up periods ranging from 3 months to 5 years. Liver Assist and VitaSmart were consistently associated with improved graft survival compared to SCS. In 2 RCTs (1 on Liver Assist; 1 on VitaSmart) on DBD livers this benefit reached statistical significance.

Biliary complications

- 4 RCTs (all on LiverAssist) reported on total biliary complications at follow-up periods ranging from 90 days to 1 year. Liver Assist was consistently associated with fewer biliary complications compared to SCS, although this did not reach statistical significance in any study. 1 RCT on VitaSmart reported on biliary or vascular complications. At 6 months, there were fewer complications in the VitaSmart group, but this difference was not statistically significant.

- 2 RCTs (both on Liver Assist) reported on non-anastomotic biliary strictures. In the RCT on DCD livers, there were significantly fewer complications in the Liver Assist group at 6 months and 5 years. In the RCT on DBD livers, there were also fewer complications in the Liver Assist group at 1 year, but no statistical comparison between groups was reported.

- 3 RCTs (all on LiverAssist) reported on anastomotic biliary strictures at follow-up periods ranging from 90 days to 5 years. There was no statistical difference between comparators in any. In 2 RCTs there were fewer complications in the Liver Assist group. In 1 RCT, the number of complications was similar in both groups.

- 1 RCT on VitaSmart did not specify whether strictures were non-anastomotic or anastomotic. The number of strictures was similar in both groups at 6 months.

- 2 RCTs (1 on Liver Assist; 1 on VitaSmart) reported on biliary leakage at 6 months. Compared to SCS, biliary leakage was less common in the Liver Assist group, and more common in the VitaSmart group. There was no statistical difference between groups in either study.

Table 3 Hypothermic oxygenated machine perfusion: summary of results on key outcomes from prioritised studies

Outcome	Study	Study design	Technology	Effect (95% CI) ESMP versus SCS
Graft utilisation	Not reported			
Wait list outcomes	Not reported			
Overall survival	van Rijn 2021	RCT (N=156); DCD	Liver Assist	1-year HR: 2.45 (0.77 to 7.85) 5-year HR: 1.30 (0.75 to 2.26)
	Czigany 2021	RCT (N=46); DBD	Liver Assist	1-year Liver Assist vs SCS: 91% vs 83%; p=0.442 5-year Liver Assist vs SCS: 86.9% vs 64.9%; p=0.107
	Lesurtel, 2025	RCT (N=262); DBD	Liver Assist	1-year HR: 1.07 (0.49 to 2.34)
	Grat 2023	RCT (N=104); DBD	Liver Assist	2-year Liver Assist vs SCS: 92.3% vs 83.9%; p=0.23
	Schlegel 2023	RCT (N=170); DBD	Liver Assist	1-year OR: 1 (0.229 to 4.359)
	Reich 2024	RCT (N=219); mix	Vita Smart	6-month VitaSmart vs SCS: 95% vs 97%; p=NS
	Ravaioli 2022	RCT (N=110); DBD	Vita Smart	1-year VitaSmart vs SCS; p=0.52
Graft survival	van Rijn 2021	RCT (N=156); DCD	Liver Assist	1-year HR: 0.65 (0.18 to 2.29) 5-year HR: 0.91 (0.45 to 1.87)
	Czigany 2021	RCT (N=46); DBD	Liver Assist	1-year Liver Assist vs SCS: 91% vs 78%; p=0.253 5-year Liver Assist vs SCS: 86.9% vs 51.9%; p=0.029
	Lesurtel 2025	RCT (N=262); DBD	Liver Assist	1-year HR: 0.92 (0.46 to 1.81)
	Minor 2021	RCT (N=40); DBD	Liver Assist	3-month Liver Assist vs SCS: 100% vs 95%; p>0.999
	Grat 2023	RCT (N=104); DBD	Liver Assist	2-year Liver Assist vs SCS: 92.3% vs 81.4%; p=0.23
	Schlegel 2023	RCT (N=170); DBD	Liver Assist	1 year OR: 0.55 (0.14 to 1.896)
	Reich 2024	RCT (N=219); mix	VitaSmart	6-month VitaSmart vs SCS: 96% vs 94%

Outcome	Study	Study design	Technology	Effect (95% CI) ESMP versus SCS
	Ravaioli 2022	RCT (N=110); DBD	VitaSmart	1-year graft failure: VitaSmart vs SCS: 2% vs 13%, p=0.03; RD: 0.109 (0.014 to 0.204)
Biliary complications	van Rijn 2021	RCT (N=156); DCD	Liver Assist	Non-anastomotic biliary strictures 6-month adjusted HR: 0.32 (0.11 to 0.89) 5-year adjusted HR: 0.4 (0.23 to 0.99) Anastomotic biliary strictures 6-month adjusted HR: 1.07 (0.52 to 2.20) 5-year Liver Assist vs SCS: 45% vs 47%; p=0.748 Biliary anastomotic leakage 6-month RR: 0.69 (0.22 to 2.13)
	Czigany 2021	RCT (N=46); DBD	Liver Assist	1-year Liver Assist vs SCS: 17% vs 26%; p=0.722
	Lesurtel, 2025	RCT (N=262); DBD	Liver Assist	90-days Liver Assist vs SCS: 9.9% vs 16.8%; p=0.1
	Grat 2023	RCT (N=104); DBD	Liver Assist	Biliary complications 90-day Liver Assist vs SCS: 23.7% vs 43.4%; p=0.11 Anastomotic strictures 90-day Liver Assist vs SCS: 19.9% vs 33.7%; p=0.2
	Schlegel 2023	RCT (N=170); DBD	Liver Assist	Biliary complications: 1-year OR: 0.744 (0.35 to 1.58) Anastomotic biliary strictures 1-year Liver Assist vs SCS: 16.5% vs 21.2% Non-anastomotic biliary strictures 1-year Liver Assist vs SCS: 1.2% vs 3.5%
	Ravaioli 2022	RCT (N=110); DBD	VitaSmart	Hepatic biliary or vascular complications

Outcome	Study	Study design	Technology	Effect (95% CI) ESMP versus SCS
				6-month VitaSmart vs SCS: 16% vs 22%; p=0.47 Biliary strictures (no further details) 6-month VitaSmart vs SCS: 4% vs 4%; p=NS Biliary leak 6-month VitaSmart vs SCS: 4% vs 2%; p=NS
Device related AEs	Not reported			

AE: Adverse event, DBD: donation after brain death, DCD: donation after circulatory death, ESMP: ex-situ machine perfusion, HR: hazard ratio, mix: mixed DBD/DCD, NS: non-significant, OR: odds ratio, RCT: randomised controlled trial, RD: risk difference, RR: risk ratio, SCS: static cold storage.

Normothermic machine perfusion

Table 4 summarises comparative evidence from the prioritised studies on the outcomes that experts considered to be the most important.

Transplant utilisation

None of the prioritised studies reported comparative evidence on transplant utilisation. However, 1 study (Krendl et al 2025) noted that of the 174 grafts in the *metra* arm, 67 were considered to be viable only if preserved with machine perfusion. These livers included significantly more DCD livers (37% vs 8%, $p<0.001$) compared with livers that would have been accepted regardless of machine perfusion availability and had a significantly higher donor risk index (DRI) (median 2.13 vs 1.70, $p<0.001$). DRI measures the risk of graft failure after transplant, based on characteristics of the donor and the organ.

There is evidence from RCTs on the impact of machine perfusion devices (i.e., *metra*) on transplant utilisation, but these studies evaluated machine perfusion initiated at the donor hospital and were therefore excluded from the clinical review as this use case was not included in the scope of the assessment.

Overall survival

4 studies (1 on LiverAssist; 3 on *metra*) reported on overall survival at follow-up periods ranging from 18 days to 1 year, on mostly DBD livers. None reported a statistically significant difference between treatment groups, and survival rates were similar across groups in the 2 larger studies.

Graft survival

5 studies (1 on LiverAssist; 4 on *metra*) reported on graft survival at follow-up periods ranging from 6 months to 5 years. There was no statistical difference between comparators in any studies. In most studies, graft survival rates were similar across treatment groups.

Biliary complications

- 2 studies (1 on LiverAssist; 1 on *metra*) reported on total biliary complications at 6 months and 1 year. There was no statistical difference between

comparators in either study. 1 study (on *metra*) reported on bile duct complications at >30 days. The number of complications was lower in the *metra* group, but this difference did not reach statistical significance.

- 3 studies (all on *metra*) reported separately on non-anastomotic strictures and anastomotic strictures, on mostly DBD livers. In 2 studies, the follow-up period was unclear; in 1 study, the follow-up was 1 year. None reported a statistically significant difference between treatment groups for either outcome, and the direction of effect was inconsistent across studies for both outcomes.
- 3 studies (all on *metra*) reported on biliary leakage. In 2 studies, the follow-up period was unclear; in 1 study, the follow-up was 1 year. There was no statistical difference between comparators in any. Rates of biliary leakage were similar across *metra* and contemporaneous SCS treatment groups.

Table 4 Normothermic machine perfusion: summary of results on key outcomes from prioritised studies

Outcome	Study	Study design	Technology	Effect (95% CI)
Graft utilisation	Not reported			
Wait list outcomes	Not reported			
Overall survival	Ghinolfi 2019	RCT (N=20); DBD	Liver Assist	6-month Liver Assist vs SCS: 100% vs 90% p=1
	Fodor 2021	Matched case study (N=118); mix	*metra*	1-year *metra* vs SCS: 81% vs 82%; p=0.347
	Mathis 2024	Matched case study (N=54); mix	*metra*	Median of 18 days *metra* vs SCS: 0% vs 3%
	Hann 2022	Matched case study (N=82); DBD	*metra*	6-month *metra* vs SCS historical vs SCS contemporaneous: 88% vs 87% vs 92%; p=0.837
Graft survival	Ghinolfi 2019	RCT (N=20); DBD	Liver Assist	6-month Liver Assist vs SCS: 90% vs 100% p=1
	Krendl 2025	Retrospective cohort study (N=332); mix	*metra*	1-year *metra* vs SCS: 83.8% vs 81.3% 36-month *metra* vs SCS: 73.1% vs 73.9%
	Fodor 2021	Matched case study (N=118); mix	*metra*	1-year *metra* vs SCS: 81% vs 79%; p=0.784
	Hann 2022	Matched case study (N=82); DBD	*metra*	6-month *metra* vs SCS historical vs SCS contemporaneous: 84% vs 87% vs 88%; p=0.934
	Puttappa 2025	Retrospective cohort (N=238); DCD	*metra*	1-year *metra* vs SCS vs NRP then SCS: 94% vs 90% vs 94% 5-year HR SCS vs *metra*: 2.0 (0.9 to 4.4); p=0.089
Biliary complications	Ghinolfi 2019	RCT (N=20); DBD	Liver Assist	6-month Liver Assist vs SCS: 1% vs 0% p=1
	Krendl 2025	Retrospective cohort study (N=332); mix	*metra*	<u>Biliary complications</u> 1-year *metra* vs SCS: 42% vs 36.7%; p=0.329 <u>Anastomotic strictures</u>

Outcome	Study	Study design	Technology	Effect (95% CI)
				1-year *metra* vs SCS: 23.6% vs 18.4%; p=0.245 Non-anastomotic strictures 1-year *metra* vs SCS: 10.9% vs 8.9%; p=0.531 Bile duct leak 1-year *metra* vs SCS: 11.5% vs 12%; p=0.881
	Fodor 2021	Matched case study (N=118); mix	*metra*	Bile duct complications >30-days *metra* vs SCS: 27% vs 36%; p=0.321 Anastomotic strictures *metra* vs SCS (timepoint unclear): 36% vs 39%; p=0.70 Non-anastomotic strictures *metra* vs SCS (timepoint unclear): 8% vs 17%; p=0.167 Bile duct leak *metra* vs SCS (timepoint unclear): 17% vs 19%; p=0.81
	Hann 2022	Matched case study (N=82); DBD	*metra*	Anastomotic strictures *metra* vs SCS historical vs SCS contemporaneous (timepoint unclear): 3.8% vs 9.6% vs 8%; p=0.693 Non-anastomotic strictures *metra* vs SCS historical vs SCS contemporaneous (timepoint unclear): 3.8% vs 12% vs 8%; p=0.473 Bile leak *metra* vs SCS historical vs SCS contemporaneous (timepoint unclear): 0% vs 6.4% vs 0%; p=0.185
Device related AEs	Not reported			

AE: Adverse event, DBD: donation after brain death, DCD: donation after circulatory death, HR: hazard ratio, mix: mixed DBD/DCD, RCT: randomised controlled trial, SCS: static cold storage.

Data on subgroups

The decision problem detailed in the scope included the following subgroups of interest: children and young people, sequential use of NRP and ex-situ machine perfusion and people undergoing transplants with logistical considerations that require cold ischaemia times in excess of acceptable limits in the absence of machine perfusion.

No evidence on these groups was identified in the prioritised studies or the results were not reported separately, so the deprioritised studies were checked. Only limited relevant evidence was found:

- 2 studies reported on ex-situ machine perfusion in children and young people. In 1 cohort study (on Liver Assist) paediatric participants received livers split during SCS (n=12) or hypothermic oxygenated machine perfusion (n=8) (Rossignol et al. 2022). The study reported no significant differences between groups across a range of outcomes. The other study was a case report on 1 person, reported in a conference abstract (Todd et al. 2023).
- 2 small studies (both Liver Assist) reported on the use of sequential NRP and ex-situ machine perfusion. 1 RCT randomised DCD livers to NRP followed by hypothermic oxygenated (n=6) or normothermic (n=5) machine perfusion (Torri et al 2024). Graft survival was not significantly different at 3 months. The other study was a retrospective case series (Ghinolfi et al. 2021). 34 DCD livers underwent NRP then ex-situ machine perfusion; 18 were transplanted. There was 1 death at the median follow-up of 15 months.
- 3 studies with comparative data were identified that evaluated ex-situ machine perfusion initiated at the recipient centre in extended preservation scenarios (De Carlis et al. 2025, Bruggenwirth et al. 2024, Rossignol et al. 2022). All 3 assessed hypothermic oxygenated perfusion using Liver Assist. Across the studies, extended preservation did not result in significant differences between groups, except for 1 study that reported a lower rate of acute kidney injury with longer preservation.

Full details of data on subgroups are in section 5.4 of the EAR.

5.3 Ongoing studies

4 ongoing studies that align with the scope of this assessment were identified. 2 single arm studies on LiverAssist, 1 prospective case-matched study on *metra* and 1 RCT comparing SCS to hypothermic oxygenated perfusion using Liver Assist, VitaSmart and PerLife Pro in people with hepatocellular cancer (due to complete in 2028). A fifth UK-based study was also identified that partially addresses the decision problem. It will compare hypothermic oxygenated machine perfusion (VitaSmart), NRP and SCS in 36 DCD livers. In all 3 groups, normothermic machine perfusion will be used to allow viability assessment.

Additional ongoing studies were noted, but there was not enough information to determine whether they fall within the scope of this assessment.

Details of ongoing studies can be found in section 6.5 of the EAR.

6. Health economic evidence

The external assessment group (EAG) did literature searches to identify relevant health economic evidence (on 15 September 2025). 15 studies were identified and 4 were prioritised for detailed review based on relevance to the decision problem, applicability to UK practice and evaluation type. The prioritised studies assessed Liver Assist, *metra* and VitaSmart. No health economic studies evaluating PerLife Pro were identified. 3 studies used a Markov model structure, 1 was a trial-based cost-effectiveness analysis.

The direction of results differed across the studies. Economic evaluations done in the Netherlands and Canada suggested that ex-situ machine perfusion may be cost saving or dominant (more effective and less costly) compared with static cold storage (SCS), whereas a UK-based analysis concluded that machine perfusion was more costly and less effective than SCS. This contrast likely reflects differences in structural assumptions, and input parameters used across the studies. An overview of these 4 economic models is in section 6.1.1 of the external assessment report (EAR).

1 company (OrganOx) submitted a de novo economic model for consideration. This model suggested *metra* to be cost-effective compared to SCS over a lifetime time horizon, but the model structure was associated with moderate limitations. A critique of this model is in section 6.1.2 of the EAR.

Overall, none of the existing models were deemed suitable for direct use in addressing the decision problem outlined in the scope for this assessment. In particular:

- Key details about the modelling approach were unclear or not reported
- Important outcomes (such as re-transplantations and complications) were not described in sufficient detail.
- The impact of machine perfusion on transplant waitlists was not captured.

As a result, the EAG developed a de novo economic model to assess the impact of machine perfusion in the context of the decision problem.

6.1 Health economic model

The economic model developed by the EAG was designed to explicitly capture the impact of machine perfusion on waiting list outcomes, short-term post-transplant complications and long-term re-transplantations and mortality.

The model structure is detailed in Figure 2. It takes a cohort-based approach and is composed of a decision tree to capture short-term outcomes followed by a Markov model to estimate lifetime costs and benefits:

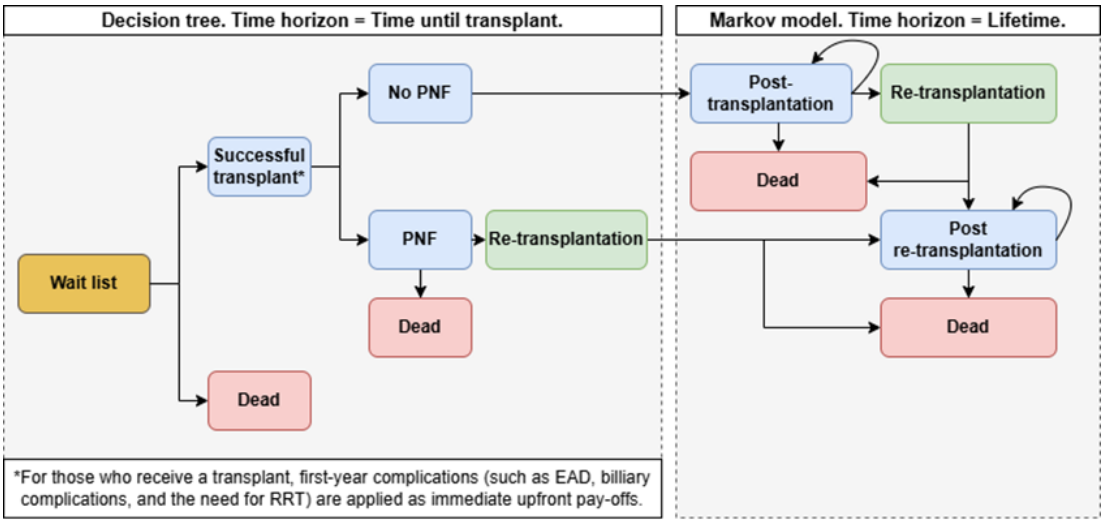
- The cohort of people eligible for a liver transplant enter the decision tree on the waiting list. Waitlist outcomes include time-to-transplantation, waitlist mortality, and the cost of being on the waitlist. Once a transplant is received, the model applies the cost of the transplant procedure, which in the intervention arm includes the cost of machine perfusion. At this stage, the model also incorporates the incidence of short-term post-transplant complications and associated costs as one-off events.
- 1 year after receiving a transplant, people enter the long-term component of the model, which is structured as a Markov model with 3 health states (i.e., post-transplantation, post-re-transplantation, and death) and yearly

cycles. An additional tunnel state is included to capture re-transplants, and all outcomes within the first year of having a re-transplant (including death). The long-term model applies survival and re-transplantation risks over a lifetime time horizon, with outcomes accrued until the entire cohort has transitioned to death.

For all outcomes, the number of events which occur and the associated costs are explicitly reported. In the long-term model, costs and QALYs are accrued according to the 3 health states.

Further details of the economic modelling are in section 6.2 of the EAR. A comparison of the economic model developed by the EAG to existing UK-based economic analyses is on pages 97-9 of the EAR and section 6.4.2.

Figure 2 Structure of EAG health economic model



EAD: early allograft dysfunction, PNF: primary non-function, RRT: renal replacement therapy

Key model assumptions (in base case)

- NHS Blood and Transplant (NHSBT) registry data was used to inform a number of model inputs assumed to reflect outcomes associated with SCS (e.g., organ utilisation and short-term complications).
- Where clinical evidence on a specific machine perfusion device is lacking it is assumed that it has the same clinical effectiveness as another device

that uses the same perfusion method. The modelling approach for each device is set out in Table 6.3 of the EAR.

- It is assumed that the utilisation rate of donated livers determines the proportion of patients who receive a transplant but does not affect the average waiting time. As a result, higher utilisation simply leads to a greater number of successful transplants being performed.
- The same organ utilisation rate (1.1; favouring machine perfusion) applies to all machine perfusion devices, based on studies on normothermic ex-situ machine perfusion initiated at the donor hospital.
- 70% of newly utilised organs were assumed to originate from donors after circulatory death.
- Complications are only explicitly captured in the first-year after the initial transplant. The model assumes that any complication costs beyond the first year are captured by the ongoing annual cost of living with a transplant. Complications following re-transplantation were assumed to be captured in the overarching cost of re-transplantation, mortality, and QALY outcomes.
- The same re-transplantation rate applies to all machine perfusion devices based on results from a single study on Liver Assist (hypothermic oxygenated perfusion) using DCD livers
- The impact of machine perfusion on re-transplantations is assumed to apply only for the first 5-years post-transplant, reflecting the available evidence base.
- Due to limited evidence, the cost and QALYs accrued in the post-transplant and post-re-transplantation health states are assumed to be the same.
- The same long-term mortality rate applies to all machine perfusion devices based on results from a single study on Liver Assist (hypothermic oxygenated perfusion) in DBD livers
- The impact of machine perfusion on mortality is assumed to apply only for the first 5-years post-transplant, reflecting the available evidence base.
- In the model, short-term complications (with the exception of primary non-function [PNF]) and re-transplantation do not affect mortality risk directly. Instead, long-term mortality is represented using survival estimates that

differ depending on whether a transplant was performed using machine perfusion or SCS.
- It was assumed that people who do not receive a transplant after 42 months on the wait list die before the end of the fourth year

Key structural and parameter uncertainties were explored through extensive sensitivity and scenario analyses.

Key modelling assumptions are detailed in Table 6.4 of the EAR.

Population

The demographic characteristics of the cohort included in the model were sourced from NHSBT registry data. Due to limited data on recipients of livers from extended criteria donors (ECD), the cohort age and sex distributions were assumed to be the same as those for the adult population.

Intervention

Each of the 4 ex-situ machine perfusion devices included in the scope is included as a separate intervention within the model.

There was insufficient clinical evidence to include the following perfusion strategies in the evaluation:

- Sequential hypothermic oxygenated machine perfusion then controlled oxygenated rewarming, followed by normothermic machine perfusion
- Sequential use of normothermic regional perfusion (NRP) followed by ex-situ machine perfusion.

Comparator

In the EAG model, ex-situ machine devices initiated on arrival at the hospital of the person having the transplant are compared to SCS.

Model inputs

Organ utilisation and waiting list parameters

The time spent on the waiting list in the model is based on the average duration people wait for a transplant according to NHSBT registry data.

The rate of organ utilisation associated with SCS was informed by NHSBT registry data. The impact of machine perfusion on organ utilisation was modelled using a utilisation risk ratio of 1.1 (favouring machine perfusion) for all machine perfusion devices. This value was obtained from a meta-analysis comparing normothermic ex-situ machine perfusion with SCS in liver transplantation. This pooled analysis included studies using devices initiated at the donor hospital that were excluded from the clinical review because they fall outside the scope of the assessment and do not reflect UK clinical practice.

Organ utilisation and waitlist parameters are set out in Table 6.6 of the EAR.

Complications

The model accounts for post-transplant complications including PNF, early allograft dysfunction, post-reperfusion syndrome, biliary complications, hepatic artery thrombosis and renal replacement therapy. PNF is assumed to lead to immediate re-transplantation or death.

Complications are only explicitly captured in the first-year after the initial transplant.

The rates of short-term complications associated with SCS were informed by NHSBT registry data. Complication rates for machine perfusion devices relative to SCS were obtained from published evidence. Most short-term complication rates associated with machine perfusion were not statistically significant. Therefore, the impact of machine perfusion devices on short-term complications is highly uncertain. This was tested in scenario analysis.

Complication parameters are set out in Table 6.7 of the EAR.

Re-transplantation

The rate of re-transplantation due to PNF was informed by NHSBT registry data. Long-term re-transplantation rates for SCS and all machine perfusion devices are based on a single study on Liver Assist (hypothermic oxygenated perfusion) using DCD livers.

There was no data identified on the proportion of people who receive a third transplant, or how this may impact long-term outcomes. The long-term outcomes of additional re-transplantations are therefore assumed to be captured indirectly through the long-term outcome data.

Re-transplantation parameters are detailed in Table 6.8 of the EAR.

Cost inputs

The key cost parameters used to inform the model were:

- Waiting list costs. The monthly cost of being on the waiting list was sourced from a published UK-based health economic study.
- Procedure and post-transplant costs. These were sourced from the National Cost Collection (NCC), published evidence, [redacted] According to experts, a dedicated perfusion team may be required for the machine perfusion procedure, though this will likely vary across transplant centres and evolve over time. Due to complexities in attributing a specific cost to this resource, it was excluded from the base case and instead addressed in scenario analyses.
- Technology costs. The cost of SCS was sourced from published evidence. The costs of machine perfusion devices were provided by the companies. But the reporting across devices was inconsistent due to variations in each company's pricing approach. As a result, different costing approaches were applied to each device depending on the cost data available. Whilst these prices are considered indicative, the impact of these inputs on the evaluation is associated with considerable uncertainty. This was tested in threshold analyses.

- Complication costs. The costs for short-term complications were applied as one-off costs at the point of transplant. Costs were sourced from NCC, BNF, NHSBT and published evidence. In most cases, the costs of complications were assumed to be the same across adults, children and young people, and ECD recipients.

Cost parameters are detailed in Tables 6.9 to 6.13 in the EAR.

Health state utilities

Annual utilities for people on the waitlist and living with a transplant were obtained from a UK study. The impact of these values on model results was explored in sensitivity analysis. Utilities were applied to UK population EQ-5D-3L background utilities, sourced from the NICE Decision Support Unit (2022), using a multiplicative approach rather than fixed penalties.

Mortality

Baseline survival data for liver transplant recipients were taken from NHSBT registry data. Survival data from the general population were applied in the model whenever post-transplant survival exceeded background mortality rates.

In the base case analysis, the impact of machine perfusion (all devices) on survival was obtained from a single study on Liver Assist (hypothermic oxygenated perfusion) in DBD livers and assumed to apply to all other devices.

6.2 Model results

Base case

Deterministic results

In the base case deterministic analysis, all machine perfusion technologies were more costly and more effective compared to SCS alone. In adults, ICERs ranged from around £5,600 (Liver Assist; hypothermic oxygenated perfusion) to £19,400 (PerLife Pro; normothermic perfusion) per QALY gained. Results are displayed in Table 6.14 in the EAR. Due to limitations in

the evidence used to inform the model, this evaluation should not be used to compare cost-effectiveness across devices. Clinical data for Liver Assist (normothermic perfusion) and PerLife Pro were very limited. Findings for these devices/perfusion methods should therefore be interpreted with caution.

Total costs are higher with machine perfusion due to the additional costs associated with machine perfusion and an increase in the number of people who receive a transplant. These increased costs are partially offset by cost savings associated with fewer re-transplants and reduced time spent on the waitlist.

Machine perfusion led to incremental QALY gains, driven primarily by increased numbers of transplants performed, reductions in PNF (and associated mortality) and improvements in long-term survival. On average, life expectancy is extended by approximately 2 years with machine perfusion compared with SCS alone.

Two subpopulations were also explored: children and young people, and recipients of livers from extended criteria donors. Due to limited subgroup-specific evidence, most model parameters remained consistent with the adult population. Results were broadly consistent with the base case:

- Machine perfusion is estimated to result in lower ICERs for children and young people than for adults, primarily because their longer life expectancy leads to greater QALY gains from each additional transplant. However, the long-term costs of treating children and young people and the impact of machine perfusion on re-transplants and mortality is not well understood. Results for the paediatric population are detailed in Table 6.15 in the EAR.
- The analysis in the ECD population is not detailed in the EAR as the results are associated with considerable uncertainty and show only marginal differences in ICERs compared with the adult population

Probabilistic results

PSA results are consistent with the deterministic findings.

The ICERs range from £6,300 to £20,900, and no higher than £12,200 when PerLife Pro is excluded. At a cost-effectiveness threshold of £20,000 per QALY gained, the probability that machine perfusion is cost-effective ranges from 61% to 100% (93% to 100% when PerLife Pro is excluded). At a threshold of £30,000 per QALY this probability increases to 87% to 100% (99% to 100% when PerLife Pro is excluded). As with the deterministic analysis, the lack of device-specific data for PerLife Pro, introduces considerable uncertainty into results for this device.

An additional PSA was conducted in which the mortality benefit associated with machine perfusion was removed. This analysis was undertaken to explore a key structural assumption, identified in the scenario analyses as an important driver of results. Under this assumption, at a willingness-to-pay threshold of £20,000 per QALY, Liver Assist (both hypothermic and normothermic perfusion), and VitaSmart, remained cost-effective; PerLife Pro (normothermic), PerLife Pro (hypothermic), and *metra* had ICERs of £46,000, £41,500, and £26,200, respectively. This evaluation should not be used to compare cost-effectiveness across devices due to data limitations. According to clinical experts, a reduction in mortality associated with machine perfusion is highly plausible, due to reductions in complication-related mortality, improved graft viability and longer-term transplant outcomes.

The deterministic and probabilistic results are in sections 6.3.1 and 6.3.2 of the EAR, respectively.

Scenario and sensitivity analyses

Due to data limitations, it was not possible at this time to undertake a well-informed scenario analysis on the use of ex-situ machine perfusion devices in liver transplantation pathways that include assessment and recovery centres (ARC).

Scenario and sensitivity analyses included in the EAR are detailed in Table 5. PerLife Pro was not included in these analyses due to the limited availability of clinical evidence.

According to threshold analyses the per procedure costs of Liver Assist, *metra* and VitaSmart [redacted]

In most sensitivity analyses, machine perfusion devices remained cost-effective. One-way and two-way sensitivity analyses demonstrate that the model results are most sensitive to assumptions regarding long-term mortality and organ utilisation rates.

Results from scenario analyses were broadly aligned with the base case findings. In most scenarios, variation in ICERs was modest, suggesting that the model results are relatively robust to plausible changes in structural and parameter assumptions. There were 2 notable exceptions, but clinical experts suggested that the assumptions underpinning these scenarios are unlikely to be plausible:

- If it is assumed that machine perfusion has no impact on long-term mortality, ICERs increased to between £9,800 and £23,600 per QALY gained. *metra* was the only device to exceed the £20,000 threshold.
- If it is assumed that (1) machine perfusion has no impact on long-term mortality and that (2) improvements in organ utilisation reduces time to transplant but does not increase the number of organs utilised, ICERs reached £115,000 to £6,000,000 per QALY gained. In this scenario, incremental QALY gain is negligible and therefore even a marginal difference in costs can lead to large ICERs. These results demonstrate the model's sensitivity to the removal of both primary drivers of clinical benefits.

The results of sensitivity and scenario analyses are in sections 6.3.3 and 6.3.4 of the EAR, respectively.

Table 5 Sensitivity and scenario analyses done

One-way sensitivity analysis	Scenario analyses (excluding PerLife Pro)
• Cost of machine perfusion was varied from £0 to £50,000 per procedure	• Applied the median wait time to transplant (as opposed to mean),

• Proportion of newly utilised livers which are DCD was varied from 0% to 100% • Impact of machine perfusion on mortality varied from a hazard ratio of 0 to 1 (base case: 0.32) • Impact of machine perfusion on organ utilisation was varied from 1 to 1.88 (1.88 is the theoretical maximum increase).	to account for the skewed nature of waitlist data. • Assumed improvements in organ utilisation reduces time to transplant but does not increase the number of transplants. • Assumed improvements in organ utilisation increases number of transplants and reduces time-to-transplant. • Assumed that machine perfusion has no impact on long-term mortality and that improvements in organ utilisation reduces time to transplant but does not increase the number of transplants. • Assumed that 50% of those who do not receive a transplant by 42 months receive a transplant by the end of the fourth year. • Mortality rate associated with machine perfusion compared to SCS extrapolated to 10 years. • Assumed machine perfusion has no impact on mortality. • Assumed that after 5 years the rate of re-transplantation is 1% (base case: 0%) and that the relative benefit of machine perfusion is maintained. • Assumed post-transplant complication rates for SCS and machine perfusion are the same. • Included additional costs relating to perfusionist staffing and time.
Two-way sensitivity analyses	
• Long-term impact of mortality associated with DBD and DCD organs was varied. • Long-term re-transplantation rate associated with DBD and DCD organs was varied.	

Additional benefits not captured in health economic model

Several additional potential benefits of ex-situ machine perfusion may not be captured in the economic model due to data limitations. By extending the safe preservation time of donor livers beyond what is possible with SCS, ex-situ machine perfusion devices allow transplants to be done as planned daytime surgeries rather than emergency overnight procedures, reducing logistical pressures and supporting staff well-being and workforce sustainability. In addition, viability testing of higher-risk organs may reduce anxiety among

people on the transplant waitlist by lowering the likelihood of cancelled procedures.

7. Equality considerations

The final scope and the scoping equality impact assessment describe equality considerations for this assessment. The EAG did not identify additional equality issues.

8. Key points, limitations and considerations

8.1 Clinical effectiveness

Key points

- 15 studies were prioritised for review, 7 randomised controlled trials (RCTs) on Liver Assist, 2 RCTs on VitaSmart and 6 non-randomised comparative studies on *metra*. All studies assessed ex-situ machine perfusion initiated at the hospital of the person having the transplant, after the liver has been transported using static cold storage (SCS), compared to SCS only.
- None of the devices were shown to reduce death
- Overall, hypothermic oxygenated machine perfusion appeared to be associated with improved graft survival and fewer non-anastomotic biliary strictures. Normothermic machine perfusion was not associated with these benefits.

Limitations

- None of the prioritised studies reported comparative evidence on transplant utilisation, waiting list outcomes (size, duration and mortality) or device related adverse events, which were considered the most important outcomes by clinical experts. There was also no evidence from the prioritised studies on healthcare professional satisfaction/ wellbeing or patient/ carer health-related quality of life.
- Limited evidence from non-randomised studies was found on *metra* initiated at the recipient hospital.
- No studies on PerLife Pro were identified.

- Very limited evidence was identified on ex-situ machine perfusion in children and young people.
- Very limited evidence was identified on the use of sequential normothermic regional perfusion (NRP) and ex-situ machine perfusion.

Considerations for committee:

- Is there sufficient clinical evidence to make recommendations on ex-situ machine perfusion?
  - For each of the devices and perfusion methods?
  - Across adults and children? (can outcomes observed in adult recipients of livers preserved using machine perfusion devices be generalised to paediatric recipients?)

8.2 Health economic evidence

Key points:

- None of the existing health economic models identified were deemed suitable for direct use in addressing the decision problem outlined in the scope for this assessment. Consequently, the external assessment group (EAG) developed a de novo economic model.
- In the base case deterministic analysis, all machine perfusion technologies were more costly and more effective compared to SCS alone. In adults, incremental cost-effectiveness ratios (ICER) ranged from around £5,600 to £19,400 per quality-adjusted life year (QALY) gained, but this evaluation should not be used to compare cost-effectiveness across devices due to data limitations. Results from probabilistic sensitivity analyses are consistent with the deterministic findings.
- Scenario analysis testing key structural assumptions and parameters indicated results were broadly robust to uncertainty within the model. Some scenarios led to high ICERs but clinical experts suggested that the assumptions underpinning these scenarios were unlikely to be plausible.

Limitations:

- Due to data limitations, it was not possible to consider potential changes to the national liver transplantation pathway in scenario analyses.
- NHS Blood and transplant (NHSBT) registry data was used to inform a number of model inputs. Because NHSBT registry data does not report outcomes by preservation method, and normothermic regional perfusion (NRP) and ex-situ machine perfusion are already used in UK practice, the model may underestimate the true incremental benefit of machine perfusion. Conversely, there is also a risk that incremental benefits have been applied in the model to a baseline that already includes these gains.
- Due to data limitations where clinical evidence on a specific machine perfusion device was lacking it was assumed that it has the same clinical effectiveness as another device.
- There was no clinical evidence on PerLife Pro to inform the economic model and very limited information on the use of ex-situ machine perfusion in children and young people.

Considerations for committee:

- Is the de novo economic model developed by the EAG suitable for addressing the decision problem outlined in the scope for this assessment?
- Are all potential benefits of ex-situ machine perfusion captured in the economic model?
- Is there sufficient health economic evidence to make recommendations on ex-situ machine perfusion?
  - For each of the devices and perfusion methods?
  - Across adults and children?
- Can outcomes obtained from a specific device be applied to other devices using the same perfusion method (e.g., post-transplant complications)?
- Can outcomes from one perfusion method be generalised to different perfusion methods (e.g., re-transplantation, mortality)?
- Is it reasonable to apply organ utilisation rates obtained from machine perfusion devices initiated at donor hospitals to the decision problem?

Appendix A – Survey on liver transplant experience

Survey participants

As part of this assessment, NICE did a survey to gather lived experiences and views on liver transplantation and machine perfusion. It received 121 responses from people who have undergone or are awaiting liver transplant surgery or are supporting someone who is. Table 6 shows the characteristics of the survey participants.

The survey questionnaire can be found in Appendix C.

Table 6 Characteristics of survey participants

Characteristic	Proportion
Transplant experience	
Have had a liver transplant	65%
On the waiting list for a liver transplant	21%
Supporting someone who is waiting for or has received a liver transplant (e.g. parent or carer)	14%
Time on waiting list	
Less than 3 months	36%
3 to 6 months	19%
6 to 12 months	16%
Over 12 months	17%
Over 24 months	12%

The main topic areas, and a summary of responses to each, are presented below.

Experience of living with a health condition that resulted in needing a liver transplant

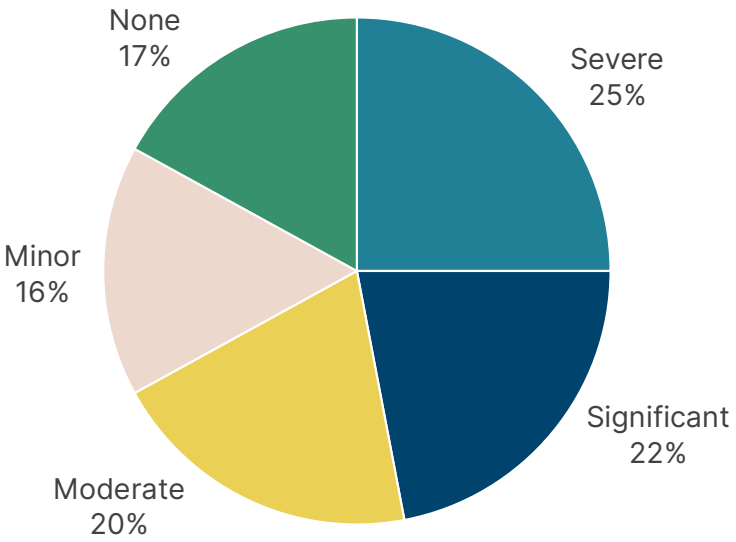
Most respondents described substantial and wide-ranging impacts across all aspects of daily life due to severe symptoms from health conditions that resulted in needing a liver transplant. Many reported reduced or complete loss of ability to work. Respondents frequently reported that their condition

disrupted family life, strained relationships, reduced participation in social activities, and led to significant emotional distress. Feelings of anxiety, depression and loss of confidence were consistently noted. Overall, the responses conveyed a sense of life becoming progressively smaller and more restricted.

Experience of waiting for a transplant

Figure 3 describes the impact of being on the waiting list on daily life. Most respondents felt that it disrupts daily life. Some respondents, often those with super-urgent listings or very short waits, reported minimal or no disruption. Respondents noted that waiting created a constant sense of uncertainty and need to be prepared. People frequently described the emotional burden of waiting, including anxiety and low mood. Several also noted that restrictions to travel affected social contact and personal relationships. Practical difficulties were also widely reported, including long journeys to specialist centres, frequent hospital appointments, and financial strain from unpaid leave, transport and accommodation. Respondents also referenced the pressure placed on carers and family members, who also needed to stay ready for sudden changes, and inability to plan ahead.

Figure 3 People's thoughts on the impact of being on the waiting list on daily life



Experience of attending transplant surgery, including cancellations.

Among respondents called to hospital for potential transplant surgery, many described the experience as emotionally intense. People often felt anxious, nervous or scared. 36% of respondents had been called to hospital for a transplant that did not go ahead. Cancellations were described as particularly emotionally challenging. Despite this, many emphasised that they understood the reasons for cancellations and trusted the judgement of transplant teams. Practical challenges varied depending on circumstances such as distance from transplant centres and availability of support. Many also highlighted positive interactions with healthcare professionals and feeling well supported in decision making.

Acceptance of machine perfusion

Figure 4 describes whether respondents would be happy to accept a donor liver preserved using machine perfusion technology. Most respondents were, supportive of machine perfusion technologies, particularly if clinicians recommended it.

Figure 4 People's thoughts on whether they would be happy to accept a donor liver preserved using machine perfusion technology

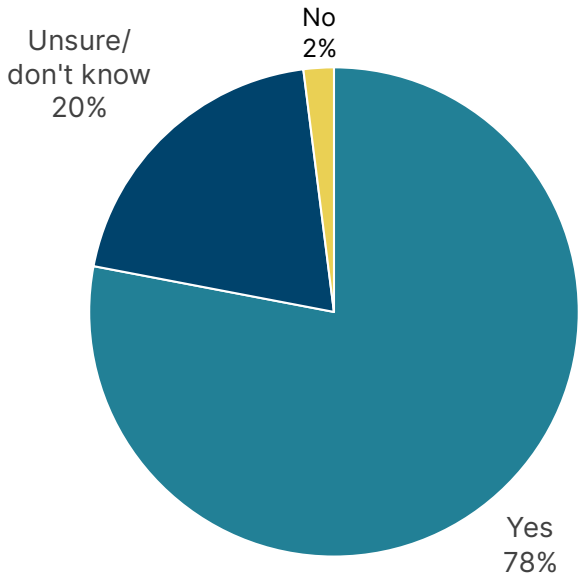
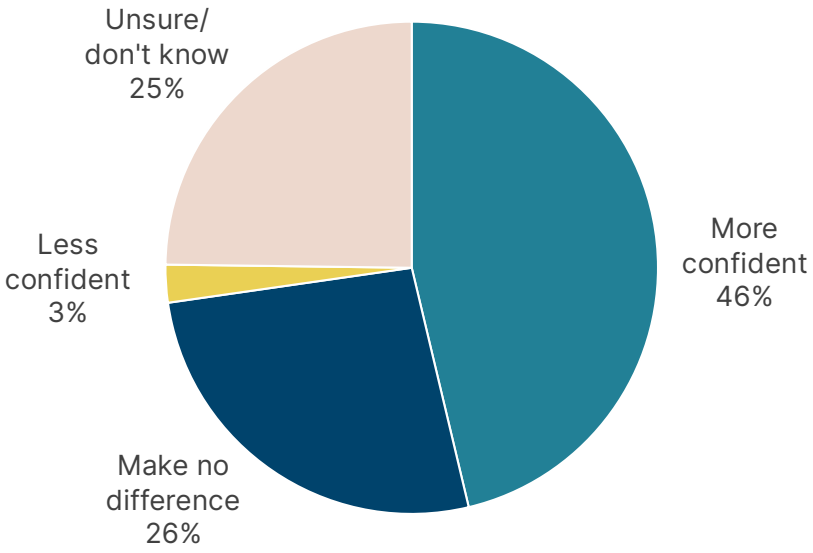


Figure 5 describes whether use of machine perfusion technology would affect confidence in the liver transplant. Some respondents said the use of machine perfusion would make them more confident in a liver transplant. Others indicated that it would make no difference to them, or that they were unsure, usually because they felt they did not have enough information about the technology, its risks, or its effectiveness.

Figure 5 People's thoughts on whether use of machine perfusion technology would affect confidence in the liver transplant



Barriers affecting access to liver transplantation services

Experiences of barriers varied considerably. Some respondents said they experienced no barriers. Among those reporting barriers, geographical distance from transplant centres was reported most. Other reported barriers included lack of tailored mental health support for younger people, sub-optimal communication between local services and transplant centres, challenges to accessing support, moving to adult care and delays in assessments. 1 respondent was concerned that people with variant conditions may be relatively disadvantaged by recent changes to the allocation system. This is because people with variant conditions often require DBD livers but are less likely to be prioritised as they typically have a lower mortality risk, even though quality of life may be severely affected. As a result, people with variant conditions are more reliant on a diminishing supply of DBD livers.

Appendix B Survey questionnaire

Background

NICE is evaluating a technology that could help people who need a liver transplant. The technology – known as '*ex-situ machine perfusion'* – works by keeping donated livers healthy outside the body, before they are transplanted. Some machines also allow assessment of liver function during this time, to help the surgeon decide if the liver is appropriate to transplant.

The aims of these technologies include:

- Enabling the use of more donated livers for transplantation, including those previously deemed too high-risk.
- Extending preservation times, allowing for more flexible and better-planned transplant procedures.
- Improving clinical outcomes for people undergoing liver transplantation.

NICE is assessing how well these devices work and whether they offer good value for the NHS. To better understand the impact of this technology we are asking if you could share your experience of waiting (or caring for someone waiting) for a liver transplant.

Find out more about NICE's assessment of ex-situ machine perfusion devices for liver transplants.

How NICE will use this information

The survey responses will be collected and then presented to our independent committee who will consider the evidence for ex-situ machine perfusion for liver transplant. Responses to this survey will be kept anonymous and will help NICE to understand what it's like to live with a condition that needs a liver transplant, and how waiting for a transplant affects people's lives. This information will support decision-making by NICE around the use of ex-situ machine perfusion devices.

This survey is designed to be completed by people aged 18 and over. We also welcome parents or carers of children younger than 18, to complete this survey on their behalf.

We ask that you answer the questions to the best of your knowledge based on your personal experience. There are no right or wrong answers.

The survey will take about 20 minutes to complete.

Thank you very much for sharing your views. If you have a question about the survey, please email Helen Crosbie at pip@nice.org.uk.

Data Protection

For more information about how your data will be processed please see our privacy notice (opens in new window).

Please note we use a third party, SNAP, to administer this survey. For more information about how SNAP process personal data please see their privacy notice (opens in new window).

Section 1: About you

1. Please check the relevant box to indicate your experience:

☐ Supporting someone who is waiting for or has received a liver transplant (e.g. parent or carer)

☐ On the waiting list for a liver transplant

☐ Have had a liver transplant. If so, how long ago? ……...

Comments:……...

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2. Please indicate where you live (city, town, village, borough)

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Section 2: Living with the condition

3. Please describe your experience of living with the health condition that resulted in you requiring a liver transplant.

   In your response, please include how it affects your daily life, for example: what it stops you from doing, how it affects your ability to work or study, your mental health, your social life, and your relationships with your family and friends.

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Section 3: Waiting for a transplant

4. How long have you (or your child, relative or someone close to you) been on the liver transplant waiting list?

☐ Less than 3 months

☐ 3–6 months

☐ 6–12 months

☐ Over 12 months

☐ Over 24 months

Comments:……...

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5. To what extent has being on the waiting list disrupted your daily life?

☐ 1: No disruption at all

☐ 2: Minor disruption

☐ 3: Moderate disruption

☐ 4: Significant disruption

☐ 5: Severe disruption

6. Please describe your experience of being listed and waiting on the waiting list for a liver transplant. *In your response, please consider how this affects your ability to work or study, your mental health, your social life, and your relationships with family and friends. You may also wish to reflect on the logistical challenges related to attending medical appointments while on the waiting list (e.g., travel, accommodation, childcare).*

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7. Have you ever been called to hospital for a potential transplant that did not go ahead?

☐ Yes. If yes, how many times has this happened..……..

☐ No

If known, please state the reason(s) the transplant(s) did not go ahead.

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8. Please describe your experience of attending transplant surgery, including cancellations.

In your response, you may wish to reflect on:

- *The practical challenges involved – such as arranging time off work, organising care for dependents, securing transport to the transplant centre.*
- *How you felt about coming to the hospital at short notice for a transplant surgery that might not go ahead.*
- *Your experience of deciding whether to accept or decline a liver transplant offer – how prepared did you feel to make the decision, based on your understanding of the benefits and risks?*

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Section 4: Machine perfusion

9. If offered a donor liver preserved using machine perfusion technology, would you be happy to accept it?

☐ Yes.

☐ No.

☐ Unsure / I don't know

Comments:……
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10. Would knowing that your donor liver had been assessed and/or preserved using a machine perfusion device make you more confident in the transplant?

☐ More confident.

☐ Less confident.

☐ Make no difference.

☐ Unsure / I don't know

Comments:……
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Section 5: Equality and inclusion considerations

11. Are there any barriers you have experienced that affected your access to liver transplantation services?

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12. NICE aims to promote equality, prevent discrimination and reduce avoidable differences in health between different groups of people. Are there any considerations you feel NICE should be aware of when assessing the impact of ex-situ machine perfusion devices for liver transplants in relation to equality and inclusion?

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Section 6: Any further comments

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Many thanks for your time completing this survey.

Appendix C Abbreviations

BNF	British National Formulary
DBD	Donated after brainstem death
DCD	Donated after circulatory death
DRI	Donor risk index.
EAD	Early allograft dysfunction
EAG	External assessment group
EAR	External assessment report
ECD	Extended criteria donor
ESMP	Ex-situ machine perfusion
HOPE	Hypothermic oxygenated machine perfusion
HR	Hazard ratio
ICER	Incremental cost-effectiveness ratio
ICU	Intensive care unit
ITT	Intent-to-treat.
MELD	Model for end-stage liver disease.
NCC	National Cost Collection
NHSBT	NHS Blood and Transplant
NMB	Net monetary benefit
NMP	Normothermic machine perfusion
NRP	Normothermic regional perfusion
OR	Odds ratio
QALY	Quality-adjusted life year
RCT	Randomised controlled trial
PNF	Primary non-function
PSA	Probabilistic sensitivity analysis
SCS	Static cold storage

HealthTech Programme

HTE10066: Ex-situ machine perfusion devices for liver transplants (provisional title)

NHS organisation submission

Thank you for agreeing to give us your organisation's views on this technology and its possible use in the NHS.

You can provide a unique perspective on the technology in the context of current clinical practice that is not typically available from the published literature.

To help you give your views, please use this questionnaire. You do not have to answer every question – they are prompts to guide you. The text boxes will expand as you type.

Information on completing this submission

- Please do not embed documents (such as a PDF) in a submission because this may lead to the information being mislaid or make the submission unreadable
- We are committed to meeting the requirements of copyright legislation. If you intend to include **journal articles** in your submission you must have copyright clearance for these articles. We can accept journal articles in NICE Docs. If you do not have copyright clearance, please provide us with the reference to the journal article only.
- Your response should not be longer than 10 pages.

About you

Your name	Sarah Watson
Name of organisation	NHS England
Job title or position	Highly Specialised Services Senior Commissioning Manager
Job role (please select Yes or No to all that apply):	Responsible for commissioning services for the NHS in general? No Responsible for commissioning services for the NHS for the condition for which NICE is considering this technology? Yes Expert in treating the condition for which NICE is considering this technology? No Expert in the clinical evidence base supporting the technology (for example, an investigator in clinical trials evaluating the technology)? No Other (please specify):

Current and proposed management

1. How and at which point in the pathway would the device be used in NHS clinical practice? What impact could it have on the care pathway? Please state any relevant clinical guidelines.	Ex-situ machine perfusion devices would be used between organ retrieval and transplantation, replacing or supplementing static cold storage. These devices maintain the liver, enabling assessment of function and viability prior to transplantation. Impact on the pathway: • Increased utilisation of marginal or extended criteria donor (ECD) livers. • Extended preservation time, improving logistical planning and potentially reducing night-time/emergency surgery. • Improved graft outcomes and reduced early allograft dysfunction. • May help address organ shortages and waiting list mortality. Relevant guidance includes: • NHS England Service Specification for Adult Liver Transplantation. • NHS Blood and Transplant operational standards.
2. Are there variations or specific issues in the current care pathway that should be considered in this assessment?	High variation in organ acceptance rates across centres No current method to objectively assess liver function during cold storage, leading to conservative discard decisions Inequities in access to marginal organs, with some patients less likely to receive transplants due to centre-level variation in organ risk tolerance Operational pressures (e.g., night-time transplants) could be mitigated with longer preservation time These devices could help standardise decision-making and reduce organ wastage.
3. Do the technologies have the potential to address a significant unmet need in the NHS? Please give details, including potential benefits	Yes, these technologies have the potential to address unmet need as follows: • High liver discard rates in the UK. • Waiting list mortality: Some patients die or deteriorate before a transplant becomes available.

to patients and the healthcare system.	• Poor graft outcomes in cases of marginal donor use without viability assessment. Potential benefits include**:** • Improve patient outcomes and survival. • Optimise use of donor organs. • Lead to fewer re-transplants and complications.
4. Is there a proportion of the target population who cannot access or do not receive the recommended treatment in the NHS currently? If so, do you have an estimate of the size of this proportion?	A proportion of patients: • Do not receive transplants in time due to organ unavailability. • Some patients are removed from the waiting list due to deteriorating health before a suitable liver is found • 5–10% of patients on the adult liver transplant list die while waiting • Liver utilisation in the UK is estimated at around 80%, meaning approximately 20% of retrieved livers are not transplanted, often due to concerns over quality These technologies could reclaim a proportion of currently discarded organs, improving equity and access.
5. Please list any technologies that you think should be included in this assessment.	• OrganOx • TransMedics OCS Liver
6. What investment and resources are needed to introduce the technologies in the NHS (e.g., facilities, equipment, training, staff time and grade, etc.)?	These technologies are widely use in liver transplant services in the UK largely funded from within baseline allocations for liver transplantation services. It is not clear what additional resources would be needed to support optimum use, equity of access and any additional workforce requirements.

7. Are there any pilots or evaluations of using the technologies in the NHS? If so, please provide details including how these align with this assessment.	NHS liver transplant centres have already implemented NMP used OrganOx. OrganOx metra has been evaluated in UK settings and published in peer-reviewed literature.

Equality

8. Are there any equality issues that should be considered for this assessment?	Geographic access: Non uniform access to these technologies could lead to unequal access to higher-quality organs or to transplants involving marginal livers. Variation in liver offer acceptance**:** Some groups—particularly older patients, those with comorbidities, or from ethnic minorities—may be disproportionately affected if centres are more likely to decline marginal organs in the absence of perfusion and assessment technologies. Socioeconomic barriers**:** Patients from more deprived areas may be more likely to present with advanced liver disease and should benefit from increased donor organ availability.
9. Could the technologies reduce or increase health inequalities? How?	Increased organ utilisation could benefit all patients on the waiting list, including those currently disadvantaged by low donor liver acceptance rates.

Other comments

10. Are there any other issues you would like the committee to consider when evaluating these technologies?	

NICE National Institute for Health and Care Excellence

HealthTech Programme

Medical Technologies Advisory Committee (MTAC) Advisory Committee

HTE10066 Ex-situ machine perfusion devices for deceased donor liver transplant – 1st meeting

23 April 2026

Expert questionnaires for committee:	
5a	Alba Bueno, Consultant Paediatric Liver, Kidney and Small Bowel Transplant Surgeon
5b	Charlotte Vockins, People and Communities Partner
5c	Colin Wilson, Consultant HPB and Transplant Surgeon, and Honorary Professor
5d	Dhiraj Tripathi, Consultant Hepatologist and Liver Transplant Physician, and Honorary Professor
5e	James Richards, Consultant in Machine Perfusion and Transplantation Surgery
5f	Keziah Crick, Lead Clinical Scientist in Organ Procurement
5g	Miriam Cortes-Cerisuelo, Consultant in Adult and Paediatric Liver Transplantation
5h	Monica Walsh, People and Communities Partner

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology name & indication: **Ex-situ machine perfusion devices for deceased donor liver transplants** GID-HTE10066

Name:	Alba Bueno
Job title:	Locum Consultant Paediatric HPB and Transplant Surgery
Organisation:	Birmingham Children's Hospital
Completed:	20/10/2025

Please answer the following questions as fully as possible to provide further information about the technologies and/or your experience

1	Please describe your level of experience with ex-situ machine perfusion technologies, for example: • Are you familiar with the technologies? • Have you used or are you currently using any? If so, please indicate your experience with each.	I am highly familiar with ex-situ liver perfusion systems and have been routinely using **hypothermic oxygenated perfusion (HOPE)** for paediatric deceased donor liver transplantation since MAY 2024. Our centre currently uses the **VitaSmart (Bridge to Life)** system for back-to-base perfusion. I have experience with HOPE applied both to whole paediatric grafts and reduced/split grafts (left lateral segments) from DBD and DCD donors. I am familiar with the principles of **normothermic machine perfusion (NMP)** but we do not currently use it in routine paediatric.
2	Please indicate your research experience relating to this technology (please choose one or more if relevant): Please highlight your choice(s)	I have participated in clinical service evaluation and observational data collection on outcomes following HOPE in paediatric liver transplantation. I have not yet published on this technology, though our data are being prepared for presentation. ☑ I have done clinical research on this technology involving patients or healthy volunteers. ☑ I have done bibliographic research on this technology.

Current and future management

3	At your liver transplant centre, approximately how many donated livers currently receive ex-situ machine perfusion each year? And approximately how many would be eligible in the future if NICE guidance supported use of this technology? Please provide estimates either as a number, or a proportion of the total.	Currently, approximately 15–20 paediatric liver grafts per year receive HOPE perfusion in our centre, representing around >90% of all deceased donor liver transplants. If NICE guidance supports wider implementation, we anticipate near-universal use (>90%), as the system is suitable for almost all deceased donor grafts used in children.

Potential patient benefits and impact on the health system

4	What do you consider to be the potential benefits to patients from using: • HOPE ex-situ machine perfusion • Normothermic ex-situ machine perfusion	HOPE has provided consistent improvements in early graft function, haemodynamic stability post-reperfusion, and reduction in biliary complications, particularly in DCD and marginal donors. In the paediatric setting, the main advantages are the ability to rescue grafts considered “marginal” according to split criteria, and to enable planned surgery and long hepatectomies for complex or very complex recipients, improving both surgical and anaesthetic outcomes. NMP may offer advantages in viability testing, but its clinical benefit in children remains unproven.
5	Are there any groups of patients who would particularly benefit from this technology? Are there any groups in which the technology would be less effective or would be less likely to benefit?	More effective: • Children receiving grafts from DCD or extended-criteria donors, where oxygenated perfusion mitigates ischaemia–reperfusion injury. • Split liver grafts (especially left lateral segments), where improved microcirculatory flow reduces risk of small-for-size injury and biliary strictures. • Re-transplants or recipients with haemodynamic instability. • Complex recipients in which long hepatectomy time is expected. Less effective: • Minimal difference expected in standard DBD grafts with short cold ischaemia times (<6h).

6	What do you consider to be the potential benefits to the system from using • HOPE ex-situ machine perfusion? • Normothermic ex-situ machine perfusion?	• Increased organ utilisation by recovering grafts previously declined for marginal features. • Reduction in early post-operative complications and ICU stay, thereby optimising bed usage. • Improved scheduling flexibility, enabling elective daytime transplantation. • Potential cost savings through avoidance of early graft dysfunction and re-transplantation.
7	What clinical facilities (or changes to existing facilities) are needed to implement this technology safely?	A small dedicated perfusion space adjacent to the transplant theatre or organ reception area is required, equipped with oxygen supply and temperature-controlled environment. The VitaSmart system footprint is modest and can be managed within existing facilities.
8	Is any specific training needed in order to use the technology with respect to efficacy or safety? Please advise if this varies across devices.	Training is straightforward and device-specific. Perfusion is usually managed by transplant perfusionists or junior surgical colleagues under the supervision of the transplant surgeon. Competency is achieved after two to three supervised procedures, and manufacturer training covers both efficacy and safety aspects.
9	What potential impact could roll-out of in-situ normothermic regional perfusion (NRP) to all livers donated after circulatory death (DCD) have on the utility of ex-situ machine devices in the future?	If normothermic regional perfusion (NRP) becomes standard for all DCD donors, the relative need for ex-situ oxygenated perfusion might reduce slightly for optimal DCD grafts. However, HOPE remains complementary, particularly for split grafts or paediatric recipients, as it provides additional mitochondrial recovery and microvascular stabilisation following NRP.

Safety and efficacy of the procedure/technologies

10	What are the potential harms of the technology, including theoretical adverse events?	No specific device-related adverse events have been observed. Theoretical risks include mechanical failure leading to graft discard, contamination, or oxygen toxicity, but these have not occurred in our practice. Overall, risk profile is low compared with potential benefits.
11	Please list any uncertainties or concerns about the efficacy and safety of this technology?	• Long-term outcomes beyond 5 years, especially for split grafts. • Limited paediatric-specific data (most evidence extrapolated from adult studies). • Optimal perfusion duration for small grafts remains to be standardised.
12	Please prioritise the 5 most important efficacy and safety outcomes for this	☒ Transplant utilisation (proportion of donor organs that proceeded to transplant)

	technology. Are there are any challenges in collecting key outcomes? Please explain your answer.	☒ Size and duration of liver transplant waiting list ☒ Mortality on liver transplant waiting list ☐ Overall participant survival at 1 year and maximum follow-up ☐ Graft survival at 1 year and maximum follow-up ☐ Re-transplantation at 1 year and maximum follow-up ☒ 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) ☐ Primary non-function of the graft (irreversible graft dysfunction leading to recipient death or emergency retransplant within 7 days, excluding due to hepatic artery thrombosis [HAT]) ☐ HAT within 28 days (total and if data permits separately for HAT leading to recipient death and emergency retransplant) ☐ Inhospital incidence of post-reperfusion syndrome ☐ Acute kidney injury post transplantation, measured using a validated classification system ☐ Post-operative requirement for renal replacement therapy (total and if data permits separately for dialysis and kidney transplantation) ☒ Early allograft function, measured with a validated model ☐ Transaminase release during the first week post-transplant ☐ Mechanical failure of machine perfusion technology ☐ Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher) ☐ Device related adverse events ☐ Health related quality of life, assessed using any validated scale (also from carer and/or family perspective) ☐ Healthcare professional satisfaction and/or wellbeing

		Challenges: paediatric sample sizes are small, requiring multi-centre data pooling for robust analysis.
13	Are you aware of any additional issues which would prevent (or have prevented) this technology being adopted in your organisation or across the wider NHS? This could include costs, resource, staffing for example.	• Initial device cost and consumable pricing. • Staffing and training resource, particularly for out-of-hours retrievals. • Limited paediatric-specific trial data, which may delay national adoption until evidence matures.
14	Is there any research that you feel would be needed to address uncertainties in the evidence base?	• Prospective, multicentre paediatric studies comparing HOPE vs SCS. • Cost-effectiveness modelling specific to paediatric graft sizes and outcomes. • Studies evaluating sequential NRP + HOPE protocols. • Long-term follow-up for biliary outcomes and re-transplantation rates.

Further comments

15	Please add any further comments on your particular experiences or knowledge of the technology that you would like to share	Our experience with HOPE at Birmingham Children's Hospital has been very positive. The technology integrates well into paediatric workflows, improves graft quality perception among surgeons, and enhances confidence in utilising extended-criteria donors. It represents a safe, feasible, and clinically meaningful advancement for paediatric liver transplantation.

NICE National Institute for Health and Care Excellence

Patient Expert Questionnaire

Technology name & indication: **Ex-situ machine perfusion devices for deceased donor liver transplants** **GID-HTE10066**

Name:	Charlotte Vockins
Completed:	19/10/2025

Please answer the following questions as fully as possible to provide further information to support this assessment of ex situ machine perfusion devices for deceased donors

1	**Your role and experience**	**Please indicate your role** (please delete those that aren't relevant to you): • Have had a liver transplant
2	**Living with the condition** Please describe your experience of living with your health condition that resulted in requiring a liver transplant. Consider how it affected your daily living, for example: what it stops you from doing, how it affects your ability to work or study, your mental health, your social life, and your relationships with your family and friends.	Living with Primary Sclerosing Cholangitis (PSC) had a major impact on every part of my daily life. The condition caused a range of difficult and debilitating symptoms that made it increasingly hard to function normally. One of the most challenging aspects was the extreme fatigue and no matter how much rest I got, I would still feel completely exhausted. This constant tiredness affected my ability to concentrate, work and even carry out basic day-to-day tasks. Another major symptom was severe itching, which was always worse at night. It often prevented me from sleeping properly, leaving me even more drained. I also experienced hepatic encephalopathy, which caused confusion and reversed sleep patterns. Because of this, there were periods when I wasn't allowed to drive, which made me more dependent on others and affected my independence. I had frequent hospitalisations due to episodes of bacterial cholangitis, which were both physically and emotionally exhausting. The jaundiced tinge to my skin was also very visible, which sometimes made me self-conscious in social situations. Overall, PSC affected every aspect of my life including my physical health, mental wellbeing, and social relationships. The constant fatigue and hospital visits made it difficult to maintain work, friendships and a normal routine. It was a very isolating experience at times, but I tried to stay positive and focus on managing my symptoms as best I could while waiting for the liver transplant.

3	**Waiting for a transplant** Please describe your experience of being listed and waiting on the waiting list for a liver transplant.	I waited nearly two and a half years for my perfect donor. Being on the transplant waiting list meant putting my entire life on hold. I had to stay close to the hospital at all times and live with the constant awareness that the call could come at any moment. The waiting was an enormous mental burden and I carried my phone on loud everywhere and thought about that call every single minute of the day and night. To remain active on the list, I had to attend my transplant centre every six weeks so my results could be monitored. My centre was 85 miles away from home, which made these regular visits tiring and stressful, especially as my health declined. During this time, I had several hospital admissions due to infections and my overall quality of life was poor. I was also told that I might have to wait longer than others because of my age, which was difficult to hear when I was already feeling so unwell. The uncertainty, combined with the physical symptoms of my condition, made the waiting period one of the hardest parts of my transplant journey.
4	**Transplant surgery** Please describe your experience of being called up for transplant surgery; including cancellations, declining or accepting an offer or successful surgeries where appropriate.	I was extremely lucky to be accepted for my first call, although I was told immediately upon admission that there was only a slim chance the surgery would actually go ahead. Many patients in the transplant community aren't as fortunate as me and usually those waiting are called up and admitted into hospital, only to be sent home again when their donor is not suitable. This can happen on multiple occasions when you are on the list - typically two to three times. When you receive that call, you go to the hospital filled with huge anticipation and anxiety. The emotional pressure is immense and it takes a real toll on your mental health, especially knowing that it rarely happens on the first call. So many factors have to align perfectly: there must be an available ICU bed, the donor liver must be functioning properly and all your test results (such as the COVID swab) must be clear. In my case, it was a split liver transplant, which adds another layer of complexity. The anatomy of the donor liver must be suitable for splitting and the timing of the retrieval has to be exact. Any delay can cause the liver cells to deteriorate. Ultimately, even when everything seems to line up, the final decision rests with the surgeon once the donor liver is on the operating table. The entire experience is a huge mental rollercoaster. You're hopeful but terrified, grateful yet anxious and it's a moment that tests your emotional resilience in every possible way. I feel incredibly fortunate that my surgery went ahead on that first call, but this is not the 'norm' within the community.
5	**Views on the technology**	In my view, there are huge advantages to using ex-situ machine perfusion devices for liver transplants from deceased donors. For patients like me who received a split liver transplant, these technologies are especially valuable because the retrieval and splitting process takes longer than for full lobe transplants.

	In your view, what are the benefits of using ex-situ machine perfusion devices for liver transplants from deceased donors? Please share your thoughts on: How you feel patient groups would benefit from the use of ex-situ machine perfusion technologies? What do you think the disadvantages / risks may be from the use of ex-situ machine perfusion technologies?	Machine perfusion helps keep the organ viable for longer periods, which can make the difference between a successful transplant and a missed opportunity. One of the most significant benefits is that more livers can be considered suitable for transplantation. Organs that might previously have been discarded can now be preserved and assessed in real time, meaning more transplants can go ahead. This could lead to shorter waiting times and, ultimately, fewer people dying on the waiting list because they didn't get their match in time. For patient groups, the use of these technologies brings real hope. It could increase the number of viable organs available, improve outcomes by allowing early identification of potential problems with liver function, and give transplant teams greater confidence in the organs they use. As with any technology, there may be disadvantages or risks, for example, the cost of equipment and training and the possibility of overreliance on machine data rather than clinical judgement. However, in my view, the benefits far outweigh these risks. Ex-situ machine perfusion represents a huge step forward in transplant medicine, giving more people the chance of life-saving surgery, less people dying on the waiting list and reducing the emotional and physical toll of waiting for a donor.
6	**Equality and Inclusion** NICE aims to promote equality, prevent discrimination and reduce avoidable differences in health between different groups of people. Are there any considerations you feel the committee should be aware of when assessing the impact of this technology in relation to equality and inclusion?	It is important that all patients have equitable access to this technology, regardless of where they receive care. At present, perfusion machines are only available in certain centres due to funding limitations, which creates geographical inequality. Patients in centres without access to these machines may be disadvantaged in both transplant opportunities and outcomes. Children and smaller adults are often offered split liver transplants, but the ability to safely split and use the right lobe is dependent on perfusion technology. Without routine access to perfusion machines, these patients are less likely to benefit from one liver saving two lives, resulting in an inherent disadvantage for this group. As a smaller-framed, younger female, I was informed that I might wait longer for a suitable liver, not only due to allocation algorithms but also because of my size. This technology could help address such inequities by making more organs viable for people of different sizes and demographics. In addition, perfusion technology enhances patient knowledge and autonomy. It allows for better assessment of organ function, enabling patients to make more informed decisions about whether to

		accept an organ. This supports inclusion by promoting informed choice and shared decision-making across all patient groups.
7	**Further comments** Please add any further comments on your particular experience or knowledge of the technology in this clinical pathway that you would like to share with us.	This technology is already being adopted across several liver transplant centres; however, it is not yet in routine use due to funding constraints. This variation in access is disadvantaging patients and may lead to the unnecessary discarding of otherwise viable organs when liver function cannot be adequately assessed. As a result, some patients may face longer waiting times or, in some cases, die while awaiting a suitable organ. Routine implementation of this technology is therefore vital to ensure equitable access to transplantation and to maximise the use of available donor organs.

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology name & indication: **Ex-situ machine perfusion devices for deceased donor liver transplants** GID-HTE10066

Name:	Colin Wilson
Job title:	Cons Transplant Surgeon/ Professor of Transplant Surgery
Organisation:	Freeman Hospital, Newcastle-upon-Tyne
Professional organisation or society membership/ affiliation (if applicable):	British Transplantation Society (BTS)/ European Society of Organ Transplant (ESOT)/ International Liver Transplant Society (ILTS)
Date completed:	02/10/2025

Please answer the following questions as fully as possible to provide further information about the technologies and/or your experience

1	Please describe your level of experience with ex-situ machine perfusion technologies, for example: • Are you familiar with the technologies? • Have you used or are you currently using any? If so, please indicate your experience with each.	Very familiar- was part of the initial normothermic liver perfusion trial in the UK 2012/3 based in Oxford and King's College. Then created and developed a hypothermic liver perfusion device which was used successfully in the research and clinical transplant arena for recipients of DCD grafts (2015-2020). In my routine clinical practice, I have used the OrganOx, VitaSmart and am currently using the Xvivo LiverAssist devices.
2	Please indicate your research experience relating to this technology (please choose one or more if relevant): Please highlight your choice(s)	I have done bibliographic research on this technology. Senior author on primary research papers and Cochrane systematic reviews I have done research on this technology in laboratory settings (e.g. device-related research). I have done clinical research on this technology involving patients or healthy volunteers. I have published this research. Other (please comment)

Current and future management

3	At your liver transplant centre, approximately how many donated livers currently receive ex-situ machine perfusion each year? And approximately how many would be eligible in the future if NICE guidance supported use of this technology? Please provide estimates either as a number, or a proportion of the total.	**Currently** Adults: 50-60% Children:N/A **Future** Adults: depending on criteria maybe 70% Children: N/A

Potential patient benefits and impact on the health system

4	What do you consider to be the potential benefits to patients from using: • HOPE ex-situ machine perfusion • Normothermic ex-situ machine perfusion	**HOPE ex-situ machine perfusion** Improved early outcomes (decreased ITU stay, need for kidney support) and reduced ischaemic cholangiopathy in the medium to long term, reduced need for retransplant, improved patient survival (Level 1A evidence), increased DCD utilisation, reduced waiting times **Normothermic ex-situ machine perfusion** Organ viability assessment, increased marginal organ utilisation, reduced waiting times Longer preservation times leading to better matching of patient and recipient
5	Are there any groups of patients who would particularly benefit from this technology? Are there any groups in which the technology would be less effective or would be less likely to benefit?	**HOPE ex-situ machine perfusion** More effective: DCD grafts Less effective: Steatotic DBD grafts (lack of clear viability testing)- better with NMP but HMP certainly better than ice box **Normothermic ex-situ machine perfusion** More effective: Steatotic DBD grafts Less effective: DCD livers

6	What do you consider to be the potential benefits to the system from using • HOPE ex-situ machine perfusion? • Normothermic ex-situ machine perfusion?	HOPE ex-situ machine perfusion: Increased utilisation of DCD grafts Reduced waiting times Normothermic ex-situ machine perfusion: Improved team resilience day time operating leading to better patient outcomes Increased use of suboptimal DBD grafts and assessment of marginal livers after normothermic regional perfusion (NRP)
7	What clinical facilities (or changes to existing facilities) are needed to implement this technology safely?	All these technologies are resource intensive and require skilled team members to both connect the organs to the machine and then monitor them on perfusion. Liver transplant centres are currently not remunerated for this extra activity and some centres have been more successful than others in establishing skilled rota's to deliver the technology. This has directly led to inequity of access and widely differing patient wait times for transplant.
8	Is any specific training needed in order to use the technology with respect to efficacy or safety? Please advise if this varies across devices.	Yes, normothermic machine perfusion devices (OrganOx, TransMedics) are particularly challenging to ensure that the organ is constantly supplied with oxygenated blood. Specific concerns are air bubbles in the perfusion tubing and blood loss from the organ leading to circuit failure and graft infarction. HMP devices where the organ is maintained at a cold temperature by ice in the bowl (VitaSmart) are the lowest risk, as inadvertent pump failure does not immediately compromise the graft. Intermediate risk are circuits where organ cooling is reliant on adequate flow of cold preservation fluid into the liver (LiverAssist).
9	What potential impact could roll-out of in-situ normothermic regional perfusion (NRP) to all livers donated after circulatory death (DCD) have on the utility of ex-situ machine devices in the future?	HOPE ex-situ machine perfusion devices: In theory universal NRP availability could potentially make the need for HMP redundant- however many centres still use HMP to improve outcomes and increase the cold preservation window. The extra gain in this situation is currently unclear from the literature, however a small Italian trial (Ghinolfi) does show improved patient outcomes for NRP then HMP rather than SCS or NMP. Normothermic ex-situ machine perfusion devices: Viability testing on NRP is still an imprecise science- many centres in the USA and UK as well as Europe (Italy) are routinely using NMP after NRP to enhance the safe utilisation of marginal DCD livers (Level 2b evidence)

Safety and efficacy of the procedure/technologies

10	What are the potential harms of the technology, including theoretical adverse events?	Children: NMP- damage to hepatic artery and portal vein from cannulas leading to hepatic artery or portal vein thrombosis in the immediate postoperative period. Inadequate perfusion (air bubble occlusion) or "toxic" perfusion (incorrect or contaminated perfusate) leading to primary non-function or septicaemia in the recipient. HMP- inadvertent or unrecognised graft warming leading to PNF, cannula damage as above. Adults: As above
11	Please list any uncertainties or concerns about the efficacy and safety of this technology?	Children: Less of an evidence base in children Adults: Very few concerns over safety but have been reports of bacterial contamination. Overall there is no doubt that patient outcomes are generally better when all factors are considered.
12	Please prioritise the 5 most important efficacy and safety outcomes for this technology. Are there are any challenges in collecting key outcomes? Please explain your answer.	☒ Transplant utilisation (proportion of donor organs that proceeded to transplant) **3** ☐ Size and duration of liver transplant waiting list ☐ Mortality on liver transplant waiting list ☒ Overall participant survival at 1 year and maximum follow-up **1** ☒ Graft survival at 1 year and maximum follow-up **2** ☐ Re-transplantation at 1 year and maximum follow-up ☐ 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) ☐ Primary non-function of the graft (irreversible graft dysfunction leading to recipient death or emergency retransplant within 7 days, excluding due to hepatic artery thrombosis [HAT]) ☐ HAT within 28 days (total and if data permits separately for HAT leading to recipient death and emergency retransplant) ☐ Inhospital incidence of post-reperfusion syndrome

		☐ Acute kidney injury post transplantation, measured using a validated classification system ☐ Post-operative requirement for renal replacement therapy (total and if data permits separately for dialysis and kidney transplantation) ☐ Early allograft function, measured with a validated model ☐ Transaminase release during the first week post-transplant ☐ Mechanical failure of machine perfusion technology ☐ Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher) ☒ Device related adverse events **4** ☐ Health related quality of life, assessed using any validated scale (also from carer and/or family perspective) ☒ Healthcare professional satisfaction and/or wellbeing **5** All the other outcomes stem from these Top 5
13	Are you aware of any additional issues which would prevent (or have prevented) this technology being adopted in your organisation or across the wider NHS? This could include costs, resource, staffing for example.	Adults: No doubt the biggest barrier to implementation is the lack of specific funding for these technologies within the UK system. Currently most hospitals are still using charity funding or have accepted a “cost pressure” to offer to the most challenging organs and cases. Most transplant centres cannot fill rotas to offer the technology, as the posts demand 24/7 availability and are under paid when compared with other less onerous but similarly banded roles. Children: As above.
14	Is there any research that you feel would be needed to address uncertainties in the evidence base?	The evidence base worldwide is constantly evolving to meet the changing landscape with donation after circulatory death (DCD) now the predominant donation type. The “real world experience” shows us that the only way we can meet this challenge is using machine perfusion technology.

Further comments

15	Please add any further comments on your particular experiences or knowledge of the technology that you would like to share	As with other areas of healthcare the United Kingdom led the development of this technology, but has lagged in its implementation. The challenge now is to create a sustainable resilient national framework to ensure liver transplant centres can offer this service in an equitable manner to improve local patient outcomes, increase organ utilisation and hence stop the increasing waiting time for current and future patients. Currently there is an exodus of highly trained surgeons and allied professionals to countries that have established liver perfusion services.

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology name & indication: Ex-situ machine perfusion devices for deceased donor liver transplants GID-HTE10066

Your information: Please complete your details as per instructions below. Please ensure you enter your details within the brackets provided below. The brackets expand to fit the length of the text. Thank you.

Name:	Professor Dhiraj Tripathi
Job title:	Consultant Hepatologist and Liver Transplant Physician
Organisation:	University Hospitals Birmingham
Professional organisation or society membership/ affiliation (if applicable):	British Society of Gastroenterology, British Association for the Study of the Liver, British Liver Transplant Group
Date completed:	October 2025

Please answer the following questions as fully as possible to provide further information about the technologies and/or your experience

1	Please describe your level of experience with ex-situ machine perfusion technologies, for example: • Are you familiar with the technologies? • Have you used or are you currently using any? If so, please indicate your experience with each.	I am familiar with the technology which is used extensively in my institution for both routine clinical care and research. I was the clinical lead for the previous NICE IPAC guidance (IPG636), which recommends that ex-situ machine perfusion for liver transplantation can be used with special arrangements. I am the senior author of the UK Guidelines on Liver Transplantation. The technologies have a particular role in marginal grafts, and we have revised our surgical protocol to reflect recent evidence with particular attention to DCD donor livers: All DCD liver grafts will be subjected to either Normothermic Regional Perfusion (NRP) at the time of retrieval or Hypothermic Machine Perfusion (HOPE). The use of cold storage only for DCD grafts is no longer acceptable.

		Ex-situ machine perfusion may be used to extend storage time for liver grafts (technical or logistical reasons) to minimise cold ischaemic time. Functional assessment can be considered for marginal grafts using ex-situ Normothermic Machine Perfusion (NMP).
2	Please indicate your research experience relating to this technology (please choose one or more if relevant): Please highlight your choice(s)	I have done bibliographic research on this technology. I have done research on this technology in laboratory settings (e.g. device-related research). I have done clinical research on this technology involving patients or healthy volunteers. I have published this research. I have had no involvement in research on this technology. Other (please comment) Although I have not had direct involvement with research, my institution has an extensive record of research in machine perfusion.

Current and future management

3	At your liver transplant centre, approximately how many donated livers currently receive ex-situ machine perfusion each year? And approximately how many would be eligible in the future if NICE guidance supported use of this technology? Please provide estimates either as a number, or a proportion of the total.	**Currently** Adults: 81 out of 171 transplants in 2024 (65% DCD donor liver) received ex-situ machine perfusion. A considerably greater proportion of DCD donor livers received ex-situ machine perfusion than DBD donor livers. Children: Adult only centre **Future** Adults: As mentioned above, cold storage alone is not advised in DCD donors. This can be combined with HOPE, and NMP can also be used for viability assessments. I would expect an increasing number of donor livers utilising this technology, particularly DCD donors, where the proportion could rise to as much as 90%. NMP could also see an increased use in assessing the viability of marginal donor livers, to expand the donor pool at this time of large waiting lists. Children: Adult only centre.

Potential patient benefits and impact on the health system

4	What do you consider to be the potential benefits to patients from using: • HOPE ex-situ machine perfusion • Normothermic ex-situ machine perfusion	**HOPE ex-situ machine perfusion** This technology has been shown to improve mitochondrial function, graft microcirculation and energy charge, resulting in reduced oxidative stress and inflammation upon normothermic reperfusion at the time of transplantation. In total, six randomised controlled trials (RCTs) comparing HOPE with static cold storage have shown reduced early allograft dysfunction, post-transplant complications and graft loss, with the benefit particularly in higher-risk recipients of DBD grafts. HOPE and DHOPE also reduce ischemic type biliary strictures in controlled DCD recipients. **Normothermic ex-situ machine perfusion** NMP provides close to physiological conditions for the donor liver and enables viability assessment using parameters such as lactate clearance, coagulation factor production, bile production, urea production, and other metabolic measures. Five RCTs have compared NMP with cold storage. Key efficacy outcomes include reduced ischaemic reperfusion injury, improved early allograft dysfunction, and reduced post-perfusion syndrome in all donor types.

		These benefits have so far not conclusively translated into improvement in hard clinical outcomes such as biliary complications and patient/graft survival.
5	Are there any groups of patients who would particularly benefit from this technology? Are there any groups in which the technology would be less effective or would be less likely to benefit?	**HOPE ex-situ machine perfusion** More effective: DCD grafts alone or in combination with NRP/NMP assessment. Less effective: Low-risk DBD grafts or low-risk recipients of DBD grafts. **Normothermic ex-situ machine perfusion** More effective: Assessing the viability assessment of marginal DBD grafts, which may otherwise be discarded. Less effective: DCD grafts, although NMP may have a role where DCD donors are not subject to NRP (logistic or regulatory reasons in some countries), to assess viability after HOPE and controlled oxygenated rewarming.
6	What do you consider to be the potential benefits to the system from using • HOPE ex-situ machine perfusion? • Normothermic ex-situ machine perfusion?	HOPE ex-situ machine perfusion: Can permit extended preservation for up to 20 hours, although the data is limited to an observational cohort (HOPE) and DEAL stage 2 prospective clinical trial (DHOPE). This can greatly facilitate logistics such that transplantation can take place during the day. Normothermic ex-situ machine perfusion: Unlike HOPE, there is good evidence that NMP can assist in assessing the quality/viability of donor livers and minimising the use of donor livers at risk of early graft failure with improved organ utilisation. Perfusion lactate levels in the first 2-6 hours of NMP are generally advised as a marker of outcomes following transplantation. However, the thresholds for the variables used in viability assessment are not well established or standardised due to heterogeneity in clinical protocols and studies.
7	What clinical facilities (or changes to existing facilities) are needed to implement this technology safely?	Although the technology has been extensively used in research and in clinical care by enthusiastic transplant teams without funding for additional human resources in some centres, further expansion requires a dedicated, appropriately resourced team. This is particularly the case for NMP ex-situ machine perfusion.

8	Is any specific training needed in order to use the technology with respect to efficacy or safety? Please advise if this varies across devices.	A clinical/lab-based training program is available for the use of all major technologies. As they are increasingly used in the UK, clinicians are significantly more ahead of the learning curve than they were, say, 5 years ago. Fully automated systems like OrganOx, which is used in my institution, do not require as much training and expert supervision. There is also a need to invest in capital and infrastructure with regular training programmes.
9	What potential impact could roll-out of in-situ normothermic regional perfusion (NRP) to all livers donated after circulatory death (DCD) have on the utility of ex-situ machine devices in the future?	HOPE ex-situ machine perfusion devices: See comments. NRP is already being used in all DCD livers with the option of HOPE before transplantation. Normothermic ex-situ machine perfusion devices: See above. May have a role in viability assessment. See diagram below for an overview of the options(reference: https://doi.org/10.1016/j.jhep.2025.01.042)

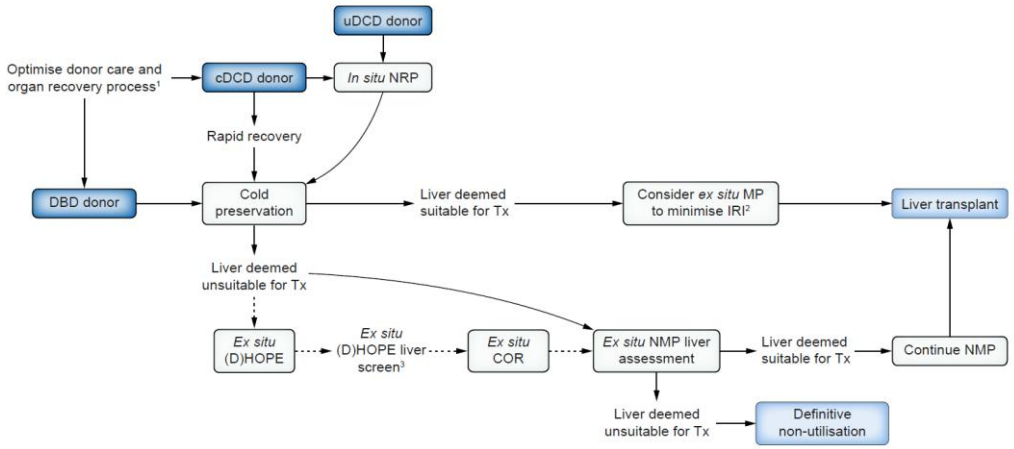

Fig. 1. Stepwise approach to management and assessment of livers arising from deceased donors. [1]Maneuvers in DBD and ventilator-dependent cDCD donors may include correction of hypovolemia, support of tissue perfusion, treatment of diabetes insipidus, neurohormonal support, and lung protective ventilation. See European Directorate for the Quality of Medicines and Healthcare, Ed. Management of the potential donor after brain death. In: Guide to the quality and safety of organs for transplantation. Council of Europe 2018;95-107. [2]*Ex situ* MP, including HMP (HOPE, DHOPE, $HMPO_2$) and NMP, may be used to minimise ischaemia-reperfusion injury, in particular in cases with donor, graft, and/or recipient risk factors. Risk factors include all livers with macrosteatosis >30%; uDCD livers; and cDCD livers with donor total warm ischaemia time >30 minutes, donor hepatectomy time >40 minutes, or cold ischaemia time >6 hours or transplanted into recipients on mechanical ventilation. For cDCD livers, while donor or recipient age >60 years, donor BMI >25, or recipient MELD >25 alone would not necessarily be considered high-risk, the combination of these with other risk factors may prompt application of *ex situ* perfusion preservation to minimise ischaemia-reperfusion injury in these grafts and their recipients. [3]Liver screen performed during an initial post-ischaemic period of (D)HOPE for research purposes but not necessarily used to guide clinical decision-making. cDCD, controlled donation after circulatory determination of death; COR, controlled, oxygenated rewarming; DBD, donation after brain death; DCD, donation after circulatory determination of death; (D)HOPE, hypothermic or dual hypothermic oxygenation perfusion; IRI, ischaemia-reperfusion injury; NMP, normothermic machine perfusion; NRP, normothermic regional perfusion; uDCD, uncontrolled donation after circulatory determination of death.

Safety and efficacy of the procedure/technologies

10	What are the potential harms of the technology, including theoretical adverse events?	Children: Can't comment Adults: The risk of long-term biliary complications remains uncertain with NMP, although data on HOPE are favourable.
11	Please list any uncertainties or concerns about the efficacy and safety of this technology?	Children: Adult only centre Adults: As mentioned above, long-term data are lacking, although favourable 5-year data have been published for HOPE.
12	Please prioritise the 5 most important efficacy and safety outcomes for this technology. Are there are any challenges in collecting key outcomes? Please explain your answer.	☒ Transplant utilisation (proportion of donor organs that proceeded to transplant) ☐ Size and duration of liver transplant waiting list ☒ Mortality on liver transplant waiting list ☒ Overall participant survival at 1 year and maximum follow-up ☒ Graft survival at 1 year and maximum follow-up ☐ Re-transplantation at 1 year and maximum follow-up ☒ 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) ☐ Primary non-function of the graft (irreversible graft dysfunction leading to recipient death or emergency retransplant within 7 days, excluding due to hepatic artery thrombosis [HAT]) ☐ HAT within 28 days (total and if data permits separately for HAT leading to recipient death and emergency retransplant) ☐ Inhospital incidence of post-reperfusion syndrome ☐ Acute kidney injury post transplantation, measured using a validated classification system ☐ Post-operative requirement for renal replacement therapy (total and if data permits separately for dialysis and kidney transplantation) ☐ Early allograft function, measured with a validated model ☐ Transaminase release during the first week post-transplant

		☐ Mechanical failure of machine perfusion technology ☐ Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher) ☐ Device related adverse events ☐ Health related quality of life, assessed using any validated scale (also from carer and/or family perspective) ☐ Healthcare professional satisfaction and/or wellbeing
13	Are you aware of any additional issues which would prevent (or have prevented) this technology being adopted in your organisation or across the wider NHS? This could include costs, resource, staffing for example.	Adults: Resource is a major issue. This is particularly the case for NMP. In our institution, the funding model has been local after making a case to the hospital executives on the need to move away from cold storage only for DCD donors. Children: Adult only centre.
14	Is there any research that you feel would be needed to address uncertainties in the evidence base?	With reference to the IDEAL framework, evidence for HOPE aligns with IDEAL states 3 and 4, for NMP it is IDEAL stages 2b and 3. NRP, prolonged HOPE, and a combination of the technologies need to progress to stage 3. Long-term hard clinical outcomes are an area of interest, particularly for NMP and combined technologies.

Further comments

15	Please add any further comments on your particular experiences or knowledge of the technology that you would like to share	Cost-effectiveness in the UK Healthcare system must be assessed. These technologies can be a significant cost pressure on the NHS. An independent assessment is urgently needed.

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology name & indication: **Ex-situ machine perfusion devices for deceased donor liver transplants** **GID-HTE10066**

Your information: Please complete your details as per instructions below. Please ensure you enter your details within the brackets provided below. The brackets expand to fit the length of the text. Thank you.

Name:	James Richards
Job title:	Consultant in General Surgery, Machine Perfusion and Transplantation Surgery
Organisation:	Cambridge University Hospitals NHS Foundation Trust
Professional organisation or society membership/ affiliation (if applicable):	Royal College of Surgeons of Edinburgh. British Association for the Study of the Liver, British Transplant Society
Date completed	October 2025

Please answer the following questions as fully as possible to provide further information about the technologies and/or your experience

1	Please describe your level of experience with ex-situ machine perfusion technologies, for example: • Are you familiar with the technologies? • Have you used or are you currently using any? If so, please indicate your experience with each.	I am one of a few surgeons nationally that have used more than one platform / device (Liver Assist, Organox) to deliver ex situ perfusion as well as a volume experience of normothermic regional perfusions and hypothermic oxygenated perfusion. I have been a consultant surgeon at 2 of the largest UK ex situ machine perfusion centres (Royal Free, Cambridge) and have experience using several different platforms, but importantly have not got any commercial/ academic / honoraria ties with any of the companies. Current use is predominantly on the Organox platform. I have published on clinical outcomes of patients transplanted with or without the adjunct of machine perfusion and have recruited patients to national ex situ perfusion studies.

2	Please indicate your research experience relating to this technology (please choose one or more if relevant): Please highlight your choice(s)	I have done clinical research on this technology involving patients or healthy volunteers. I have published this research.

Current and future management

3	At your liver transplant centre, approximately how many donated livers currently receive ex-situ machine perfusion each year? And approximately how many would be eligible in the future if NICE guidance supported use of this technology? Please provide estimates either as a number, or a proportion of the total.	**Currently** Adults: 60-80 per annum Children: 0 **Future** Adults: 60-80 per annum Children: 0

Potential patient benefits and impact on the health system

4	What do you consider to be the potential benefits to patients from using: • HOPE ex-situ machine perfusion • Normothermic ex-situ machine perfusion	**HOPE ex-situ machine perfusion** This is to be fully established and, in my opinion, requires appropriately powered and meaningful randomised trials to fully evaluate / justify. The biggest reported impact currently seems to be the reduction in ischemic cholangiopathy seen in DCD liver transplants perfused with HOPE (Zurich data), though more recently this has been brought in to question as other centres have failed to recreate the size of effect originally reported. There have been no appropriately powered large trials of HOPE versus Normothermic Regional Perfusion (NRP). There may be a role in prolonging the time from explant to reperfusion in the recipient (previously thought of as cold ischemia time) for logistics. There may or may not be benefit in HOPE during transportation, this needs appropriate trials. **Normothermic ex-situ machine perfusion**

		The main current roles for NMP are viability testing and logistics (prolonging the time from explant to reperfusion in the recipient). There is massive potential scope for improvements in viability testing and downstream therapeutic interventions that could lead to a step change in graft utilisation and outcomes. Work is also being done in acute liver failure, using ex situ perfusion as a form of "liver dialysis" to allow recovery.
5	Are there any groups of patients who would particularly benefit from this technology? Are there any groups in which the technology would be less effective or would be less likely to benefit?	**HOPE ex-situ machine perfusion** Patients with a long wait as a result of the current allocation system or who have a high waiting list mortality (as will likely improve organ utilisation). More effective: Retransplants / complex explants Less effective: None **Normothermic ex-situ machine perfusion** Patients with a long wait as a result of the current allocation system or who have a high waiting list mortality (as will likely improve organ utilisation). May benefit those with liver cancers and / or rare genetic conditions that could be managed by gene therapy / editing etc. More effective: Retransplants / complex explants Less effective: None
6	What do you consider to be the potential benefits to the system from using • HOPE ex-situ machine perfusion? • Normothermic ex-situ machine perfusion?	**HOPE ex-situ machine perfusion:** Increased utilisation of more marginal organs Reduction in ischemic cholangiopathy Logistics Potential for reconditioning **Normothermic ex-situ machine perfusion:** Increased utilisation of more marginal organs- especially in the context of more formal approaches to viability testing

		Reduction in ischemic cholangiopathy Logistics Potential for reconditioning including gene therapy / editing, cell therapy etc Use in non-transplant setting e.g. cancer surgery / treatment
7	What clinical facilities (or changes to existing facilities) are needed to implement this technology safely?	It is likely that as well as in centre perfusion, a dedicated Hub and Spoke Model will be the most efficient way to manage this technology with centralised perfusion of the most marginal organs which once deemed transplantable can then be transported to the recipient centres; this is often termed ARC (Assessment & Reconditioning Centre). Centres will likely have to develop in centre perfusion suites for the delivery of this technology.
8	Is any specific training needed in order to use the technology with respect to efficacy or safety? Please advise if this varies across devices.	Utilisation of this technology requires training of staff. This will need to be both at the surgeon level but also at the perfusionist level. Lots of centres are struggling with identifying, training, funding and retaining perfusion staff. One of the other key areas that requires development / education is in the interpretation of the data, so we do not see transplantable organs declined on the basis of poor interpretation / understanding of the data. We already see this to a greater or lesser extent with more experienced centres in this technology taking on transplantation of organs perfused (and rejected) by other centres where possible. Both of these factors would likely benefit from centralisation of perfusion services (ARC). This probably is similar across devices, though NMP is generally more technically challenging.
9	What potential impact could roll-out of in-situ normothermic regional perfusion (NRP) to all livers donated after circulatory death (DCD) have on the utility of ex-situ machine devices in the future?	**HOPE ex-situ machine perfusion devices:** NRP plus upcoming SCORE (rearrangement of retrieval to being overnight) may reduce the need for perfusion technology in DCD setting. Though the perfusion for logistics could increase if multiple organs are arriving at once. **Normothermic ex-situ machine perfusion devices:** NRP plus upcoming SCORE (rearrangement of retrieval to being overnight) may reduce the need for perfusion technology in DCD setting. Though the perfusion for logistics could increase if multiple organs are arriving at once.

Safety and efficacy of the procedure/technologies

10	What are the potential harms of the technology, including theoretical adverse events?	**Children:** Transplantable organs being declined based on poorly understood / poor understanding of perfusion parameters. Grafts lost due to device issues (rare) **Adults:** Transplantable organs being declined based on poorly understood / poor understanding of perfusion parameters. Grafts lost due to device issues (rare)
11	Please list any uncertainties or concerns about the efficacy and safety of this technology?	Children: Adults:
12	Please prioritise the 5 most important efficacy and safety outcomes for this technology. Are there are any challenges in collecting key outcomes? Please explain your answer.	☒ Transplant utilisation (proportion of donor organs that proceeded to transplant) ☐ Size and duration of liver transplant waiting list ☒ Mortality on liver transplant waiting list ☒ Overall participant survival at 1 year and maximum follow-up ☒ Graft survival at 1 year and maximum follow-up ☐ Re-transplantation at 1 year and maximum follow-up ☐ 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) ☐ Primary non-function of the graft (irreversible graft dysfunction leading to recipient death or emergency retransplant within 7 days, excluding due to hepatic artery thrombosis [HAT]) ☐ HAT within 28 days (total and if data permits separately for HAT leading to recipient death and emergency retransplant)

		☐ Inhospital incidence of post-reperfusion syndrome ☐ Acute kidney injury post transplantation, measured using a validated classification system ☐ Post-operative requirement for renal replacement therapy (total and if data permits separately for dialysis and kidney transplantation) ☐ Early allograft function, measured with a validated model ☐ Transaminase release during the first week post-transplant ☐ Mechanical failure of machine perfusion technology ☐ Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher) ☐ Device related adverse events ☒ Health related quality of life, assessed using any validated scale (also from carer and/or family perspective) ☐ Healthcare professional satisfaction and/or wellbeing Short term graft outcomes (like peak ALT, Early Allograft dysfunction (Olthoff, MEAF,L-GrAFT), reperfusion syndrome, AKI) have almost no bearing on longer term graft. Biliary complications are always difficult to define, have a lot of heterogeneity in the literature and open to bias as an outcome. If I was a patient, my post-listing/assessment survival is the most important outcome not overall survival. Post-transplant measures don't capture waiting list mortality etc.
13	Are you aware of any additional issues which would prevent (or have prevented) this technology being adopted in your organisation or across the wider NHS? This could include costs, resource, staffing for example.	Adults: Cost (devices are very expensive and likely to get more expensive especially as large corporations start cornering the market with a view to expansion into US market). Staffing: difficulty in training, recruiting, funding and retaining perfusion staff Children:

14	Is there any research that you feel would be needed to address uncertainties in the evidence base?	Lack of randomised control data comparing technologies Lack of cost-effectiveness data comparing the technologies

Further comments

15	Please add any further comments on your particular experiences or knowledge of the technology that you would like to share	

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology name & indication: Ex-situ machine perfusion devices for deceased donor liver transplants GID-HTE10066

Your information: Please complete your details as per instructions below. Please ensure you enter your details within the brackets provided below. The brackets expand to fit the length of the text. Thank you.

Name:	Keziah Crick
Job title:	Lead Clinical Scientist – Organ Procurement
Organisation:	Royal Free Hospital
Professional organisation or society membership/ affiliation (if applicable):	HCPC
Date completed:	October 2025

Please answer the following questions as fully as possible to provide further information about the technologies and/or your experience

1	Please describe your level of experience with ex-situ machine perfusion technologies, for example: • Are you familiar with the technologies? • Have you used or are you currently using any? If so, please indicate your experience with each.	
2	Please indicate your research experience relating to this technology (please choose one or more if relevant): Please highlight your choice(s)	I have done bibliographic research on this technology. YES I have done research on this technology in laboratory settings (e.g. device-related research).YES I have done clinical research on this technology involving patients or healthy volunteers. YES I have published this research. YES

		I have had no involvement in research on this technology. Other (please comment)

Current and future management

3	At your liver transplant centre, approximately how many donated livers currently receive ex-situ machine perfusion each year? And approximately how many would be eligible in the future if NICE guidance supported use of this technology? Please provide estimates either as a number, or a proportion of the total.	**Currently** Adults: 88 Children: 0 **Future** Adults: 100 Children:

Potential patient benefits and impact on the health system

4	What do you consider to be the potential benefits to patients from using: • HOPE ex-situ machine perfusion • Normothermic ex-situ machine perfusion	**HOPE ex-situ machine perfusion** - Reduced IRI - Reduce BC - Reduce CIT - Can be used for long reconstructions - Used for logistics **Normothermic ex-situ machine perfusion** - Liver viability assessment - Logistical use - Reduce CIT - Transportability - Extend liver donor pool - Assess ECD livers - Platform for therapeutic interventions

5	Are there any groups of patients who would particularly benefit from this technology? Are there any groups in which the technology would be less effective or would be less likely to benefit?	**HOPE ex-situ machine perfusion** More effective: DCDs from young donors with short downtime and short WIT/agonal phase, to stop CIT, to be used for logistics, post NRP for logistics or to mitigate any concerns on biliary damage Less effective: severely fatty livers, prolonged WIT, severe underlying pathology **Normothermic ex-situ machine perfusion** More effective: ECDs, DCD marginal grafts, DBD marginal grafts, Donors with increasing transaminases prior to retrieval, further functional assessment post NRP, logistics Less effective: standard DBDs
6	What do you consider to be the potential benefits to the system from using • HOPE ex-situ machine perfusion? • Normothermic ex-situ machine perfusion?	HOPE ex-situ machine perfusion: Normothermic ex-situ machine perfusion:
7	What clinical facilities (or changes to existing facilities) are needed to implement this technology safely?	- Secured and appropriate storage area for consumables and devices - maintenance and service contracts in place - Accessible POCT available - Appropriately trained staff - Governance and monitoring systems in place - Effective audit trails - Sterile facilities available for benching with adequate airflow
8	Is any specific training needed in order to use the technology with respect to efficacy or safety? Please advise if this varies across devices.	Yes, specific, multi-disciplinary training is mandatory for the safe and effective use of NMP & HOPE, and training protocols vary across devices. Due to the complexity and high stakes involved, transplant programs require extensive preparation and skilled personnel to establish a successful NMP program. - device operation & set up (perfusion practitioners) - Troubleshooting protocols (perfusion practitioners) - Local Waste management, Maintenance and cleaning, storage protocols and lifting and handling training (perfusion practitioners) - Monitoring & interpretation (perfusion practitioners & surgical staff)

		- Benching the liver- safety following a highly controlled and sterile process involving careful dissection, meticulous cannulation, and the use of a specialized perfusion device.
9	What potential impact could roll-out of in-situ normothermic regional perfusion (NRP) to all livers donated after circulatory death (DCD) have on the utility of ex-situ machine devices in the future?	HOPE ex-situ machine perfusion devices: **- Sequential Therapy**: offers mitochondrial protection and further reduction of ischemia-reperfusion injury just before transplantation - **Logistical Challenges:** n cases with prolonged cold ischemia time due to long transport distances, HOPE could be used to recondition the liver at the recipient's center, effectively mitigating the effects of extended preservation time. - Some centres may not have the necessary infrastructure, trained personnel, or ethical approval for NRP, especially for uncontrolled DCD. In these cases, HOPE could be the only available machine perfusion technology. -**Cost & logistics:** The financial implications and operational complexity of running both systems versus a single, streamlined process will influence adoption patterns and the Vitasmart disposable kit used in NMP costs: £4085.76 (VAT incl) and the OrganOx kit most commonly used for NMP costs £7200 (VAT incl). Normothermic ex-situ machine perfusion devices: **- Further functional assessment:** In cases where a liver does not meet viability criteria after NRP, it can be subsequently evaluated with an NMP. This second assessment allows for a more definitive decision on whether to proceed with transplantation, potentially salvaging livers that would have otherwise been discarded. **- Logistical Flexibility**: NMP can bridge the logistical gap for organs that need to be transported long distances or to coordinate with complex recipient surgeries. For example, if an NRP-treated organ has a long travel time to the transplant centre, it can be placed on a perfusion device to extend its preservation time and allow for daytime surgery. -**Minimal ischaemia model**: NRP + NMP at donor hospital, in transit until reperfusion in the recipient

Safety and efficacy of the procedure/technologies

10	What are the potential harms of the technology, including theoretical adverse events?	Children: NA to my centre - unable to comment Adults: 1) Technical or machine failure: Malfunction or sudden cessation of the perfusion device can lead to warm ischemia and potentially jeopardize the organ. 2) Vascular complications: Errors in cannulation of the blood vessels for perfusion carries the risk of damaging them, which can impact blood flow after transplantation.
11	Please list any uncertainties or concerns about the efficacy and safety of this technology?	Children: NA to my centre- unable to comment. The majority of research focuses on adults, and there is a lack of evidence regarding the efficiency of machine perfusion in paediatric liver transplantation Adults: 1) Predicting long -term outcomes 2) optimal protocol 3) viability assessment criteria lack consistency nationally (for eg., in RFH: the results are discussed amongst the same consultants to decide on liver viability) 4) Benefits vary slightly by perfusion type
12	Please prioritise the 5 most important efficacy and safety outcomes for this technology. Are there are any challenges in collecting key outcomes? Please explain your answer.	☒ Transplant utilisation (proportion of donor organs that proceeded to transplant) ☒ Size and duration of liver transplant waiting list ☒ Mortality on liver transplant waiting list ☐ Overall participant survival at 1 year and maximum follow-up ☐ Graft survival at 1 year and maximum follow-up ☐ Re-transplantation at 1 year and maximum follow-up ☐ 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)

		☐ Primary non-function of the graft (irreversible graft dysfunction leading to recipient death or emergency retransplant within 7 days, excluding due to hepatic artery thrombosis [HAT]) ☐ HAT within 28 days (total and if data permits separately for HAT leading to recipient death and emergency retransplant) ☐ Inhospital incidence of post-reperfusion syndrome ☐ Acute kidney injury post transplantation, measured using a validated classification system ☐ Post-operative requirement for renal replacement therapy (total and if data permits separately for dialysis and kidney transplantation) ☐ Early allograft function, measured with a validated model ☐ Transaminase release during the first week post-transplant ☒ Mechanical failure of machine perfusion technology ☐ Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher) ☒ Device related adverse events ☐ Health related quality of life, assessed using any validated scale (also from carer and/or family perspective) ☐ Healthcare professional satisfaction and/or wellbeing
13	Are you aware of any additional issues which would prevent (or have prevented) this technology being adopted in your organisation or across the wider NHS? This could include costs, resource, staffing for example.	Adults: NA Children: No. RFH has a fully functional 24/7 MP service covering HOPE & NMP (alongside NRP at 75% NORS availability)
14	Is there any research that you feel would be needed to address uncertainties in the evidence base?	1. Management of ischaemic cholangiopathy 2. Preventative strategies 3. Thrombolytic therapy 4. Biomarker validation 5. Advanced imaging during MP 6. Refining POCT for viability markers

		7. Prediction of HAT post-transplant 8. Treatment of steatotic livers 9. Long-term perfusion 10. Split liver transplant 11. Harmonized endpoints in clinical trial design 12. Collaborative networks

Further comments

15	Please add any further comments on your particular experiences or knowledge of the technology that you would like to share	I am a cardiac trained perfusionist with a BSc Biochemistry, Biology and Biotechnology and On the Job Training and education MSc in Cardiac Perfusion Science. I then transitioned to liver perfusion in 2015 at Cambridge University Hospital. There I trained in NRP and NMP technologies. As the profession developed, I wrote the competency package, organized department-wide training workshops, wrote SOP's, initiated the audit trails and also risk assessment documents associated with MP of the liver. There I completed my MSc in Blood Sciences with my dissertation on synthetic function of livers during NMP using the XVIVO machine. I was trained to use the OrganOx metra when it was made commercially available in 2017. In 2019, I moved to Royal Free Hospital; there I optimised the NMP programme, and introduced the NRP, HOPE and VVB programmes. I have been directly involved in the clinical implementation, optimisation, and governance of these programmes at RFH, where I led the introduction of these systems into routine transplant and retrieval practices. During which, I completed the NHS Elizabeth Garrett Anderson Programme MSc in Senior Healthcare Leadership, my dissertation being in the Implementation of Innovative Change in an Acute Hospital Trust-Machine Perfusion Technology in Liver Transplant. I am now currently a pre-Clinical Research Excellence Fellow (pCREF) at The Francis Crick Institute in collaboration with KCL and King's College Hospital, with the aim to pursue a PhD. My research topic is looking into the metabolomics of bile produced on NMP.

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology name & indication: **Ex-situ machine perfusion devices for deceased donor liver transplants** **GID-HTE10066**

Your information: Please complete your details as per instructions below. Please ensure you enter your details within the brackets provided below. The brackets expand to fit the length of the text. Thank you.

Name:	Miriam Cortes-Cerisuelo
Job title:	Consultant in Adult and paediatric Liver Transpalnt surgery
Organisation:	King's College Hospital
Professional organisation or society membership/ affiliation (if applicable):	GMC
Date completed:	Nov 2025

Please answer the following questions as fully as possible to provide further information about the technologies and/or your experience

1	Please describe your level of experience with ex-situ machine perfusion technologies, for example: • Are you familiar with the technologies? • Have you used or are you currently using any? If so, please indicate your experience with each.	I am very familiar with ex-situ perfusion in normothermia (NMP) and hypothermic oxygenated perfusion (HOPE) . I have both put livers on these devices and transplanted them. At King's College Hospital, we participated in the first in man trials with Organox more than 10 years ago. Regarding HOPE, we contributed to the first RCT in 2017 and 2018. Since then, we have done over 300 perfusions overall.
2	Please indicate your research experience relating to this technology (please choose one or more if relevant): Please highlight your choice(s)	**I have done bibliographic research on this technology.** I have done research on this technology in laboratory settings (e.g. device-related research).

		I have done clinical research on this technology involving patients or healthy volunteers. **I have published this research.** I have had no involvement in research on this technology. Other (please comment)

Current and future management

3	At your liver transplant centre, approximately how many donated livers currently receive ex-situ machine perfusion each year? And approximately how many would be eligible in the future if NICE guidance supported use of this technology? Please provide estimates either as a number, or a proportion of the total.	**Currently** Adults:80 Children:10 **Future** Adults:120 Children:25

Potential patient benefits and impact on the health system

4	What do you consider to be the potential benefits to patients from using: • HOPE ex-situ machine perfusion • Normothermic ex-situ machine perfusion	**HOPE ex-situ machine perfusion** HOPE has a clear effect in decreasing ischaemia reperfusion injury, restoring the ATP storage that got depleted during static cold storage, resulting in better graft function early after transplant, reducing the risk of primary non function and the risk of ischaemic type biliar lesions. All these translates into improving the quality of extended criteria donors and being able to use these livers safely in any patient, from less unwell to more deteriorated. These means, expanding the donor pool for all patients HOPE also allows extending safely the preservation time when required. Other benefits described have been the potential to reduce the risk of early acute cellular rejection in the patient, as well as splitting livers in HOPE for two recipients. In the later, the right lobe is generally used for an adult and has longer cold ischaemia time.

		In the last years, a few publications have shown the benefit of measuring FMN as a biomarker during HOPE to predict complications. Though further studies are required, it seems to discriminate well. **Normothermic ex-situ machine perfusion** The main benefit is that it allows real time assessment of the functionality of the liver before implantation, hence reducing the risk of primary non-function. It also reduces the risk of ischaemia/reperfusion injury immediately after implantation of the liver in the recipient, which translate in better early function. This effect also allows using extended criteria donor livers in very deteriorated patients. NMP also allows prolong preservation of the donor livers which can be very helpful when there is a complex transplant, when there are logistic problems in the hospital such as 2 livers arriving at the same time to the transplant centres,… NMP has also the potential to be used to treat donor livers with different therapies: from defatting strategies, to reducing immunogenicity…
5	Are there any groups of patients who would particularly benefit from this technology? Are there any groups in which the technology would be less effective or would be less likely to benefit?	**HOPE ex-situ machine perfusion** I believe ever liver can benefit from HOPE but the effects may be More effective: Donors after circulatory death (DCD) , extended criteria donors after brain death (DBD), or any liver with prolong cold ischaemia time. Less effective: the beneficial effect of HOPE may be less obvious in good DBD livers, transplanted into a straightforward recipient with short cold ischaemia time. **Normothermic ex-situ machine perfusion** More effective: in extended criteria donors, either DBD or DCD Less effective: very good quality DBD with normal cold ischaemia time.
6	What do you consider to be the potential benefits to the system from using • HOPE ex-situ machine perfusion? • Normothermic ex-situ machine perfusion?	HOPE ex-situ machine perfusion: expanding the donor pool, reducing the waiting list, and reducing the risk of complications in the recipient, resulting in shorter hospital and ICU stay and lower need for interventions or re-admissions after discharge from transplant.

		Normothermic ex-situ machine perfusion: expanding the donor pool further for extended criteria donor livers that need function assessment before implantation, increasing organ utilisation, reducing waiting list. Other benefit is helping with logistics such as transplanting very complex patients, moving transplant activity to daily hours, when two or more livers arrive at the same time at the transplant centres, or any challenge that requiring preserving the liver for longer before implantation.
7	What clinical facilities (or changes to existing facilities) are needed to implement this technology safely?	While most of the transplant units are perfusing livers safely, it would be required for a broader implementation to have dedicated space as close to the theatre as possible to perfuse donor livers as well as dedicated perfusionist.
8	Is any specific training needed in order to use the technology with respect to efficacy or safety? Please advise if this varies across devices.	There is specific training for all the devices that is provided by the different companies. In terms of efficacy, there is a vast amount of publications about the benefits of these technologies. Also, the transplant community as quite small, so generally more expert centres provide guidance to other units starting perfusion.
9	What potential impact could roll-out of in-situ normothermic regional perfusion (NRP) to all livers donated after circulatory death (DCD) have on the utility of ex-situ machine devices in the future?	HOPE ex-situ machine perfusion devices: It would still be required for those DCD livers that will have a long cold ischaemia time after NRP because of travel time or being used in difficult recipients. Normothermic ex-situ machine perfusion devices: It would still be required for those DCD livers than do not fulfil transplantability criteria in NRP but could potentially be assessed on NMP. Also, could be used for logistics after NRP.

Safety and efficacy of the procedure/technologies

10	What are the potential harms of the technology, including theoretical adverse events?	For any technology and for both children and adults, the danger is if it fails, however, as it is mainly used in the transplant centres, the liver can be quickly put on the ice box in the case of HOPE and in case of NMP, it would need to be perfused with preservation solution and then placed on ice.

11	Please list any uncertainties or concerns about the efficacy and safety of this technology?	Children: it is still unknown what is the smallest size of a liver to be perfused on normothermia. In HOPE, small livers of 300gms have been perfused safely. Adults: the current viability criteria are not fully validated. While it has shown to expand the donor pool, there is the possibility that we could discard transplantable livers.
12	Please prioritise the 5 most important efficacy and safety outcomes for this technology. Are there are any challenges in collecting key outcomes? Please explain your answer.	☒ Transplant utilisation (proportion of donor organs that proceeded to transplant) ☒ Size and duration of liver transplant waiting list ☐ Mortality on liver transplant waiting list ☐ Overall participant survival at 1 year and maximum follow-up ☐ Graft survival at 1 year and maximum follow-up ☒ Re-transplantation at 1 year and maximum follow-up ☒ 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) ☒ Primary non-function of the graft (irreversible graft dysfunction leading to recipient death or emergency retransplant within 7 days, excluding due to hepatic artery thrombosis [HAT]) ☐ HAT within 28 days (total and if data permits separately for HAT leading to recipient death and emergency retransplant) ☐ Inhospital incidence of post-reperfusion syndrome ☐ Acute kidney injury post transplantation, measured using a validated classification system ☐ Post-operative requirement for renal replacement therapy (total and if data permits separately for dialysis and kidney transplantation) ☐ Early allograft function, measured with a validated model ☐ Transaminase release during the first week post-transplant ☐ Mechanical failure of machine perfusion technology

		☐ Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher) ☐ Device related adverse events ☐ Health related quality of life, assessed using any validated scale (also from carer and/or family perspective) ☐ Healthcare professional satisfaction and/or wellbeing
13	Are you aware of any additional issues which would prevent (or have prevented) this technology being adopted in your organisation or across the wider NHS? This could include costs, resource, staffing for example.	Adults: initial cost, dedicated space, tight on call rota with expert staff Children: initial cost, dedicated space, some colleagues from the adult side questioning the benefit.
14	Is there any research that you feel would be needed to address uncertainties in the evidence base?	There are still many research questions such as: -Benefit of combining HOPE followed by NMP to further improve utilisation. -Benefit of ischaemia free donor livers

Further comments

15	Please add any further comments on your particular experiences or knowledge of the technology that you would like to share	In the UK, since NLOS was implemented, livers seem to travel longer distances, which include whole livers and split right lobe. This means that the cold ischaemia time is longer, which can decrease organ utilisation; hence the further need to use these technologies.

NICE National Institute for Health and Care Excellence

Patient Expert Questionnaire

Technology name & indication: Ex-situ machine perfusion devices for deceased donor liver transplants GID-HTE10066

Your information: Please complete your details as per instructions below. Please ensure you enter your details within the brackets provided below. The brackets expand to fit the length of the text. Thank you.

Name:	MONICA WALSH
Email address:	

Please answer the following questions as fully as possible to provide further information to support this assessment of ex situ machine perfusion devices for deceased donors

1	**Your role and experience**	**Please indicate your role** (please delete those that aren't relevant to you): • An individual • • Have had a liver transplant
2	**Living with the condition** Please describe your experience of living with your health condition that resulted in requiring a liver transplant. Consider how it affected your daily living, for example: what it stops you from doing, how it affects your ability to work or study, your mental health, your social life, and your relationships with your family and friends.	I WAS BORN WITH HEP B UNKNOWINGLY PASSED ONTO TO ME AT BIRTH.THIS WAS NOT DISCOVERED UNTIL MY MOTHER PASSED AWAY UNEXPECTLY FROM LIVER FAILURE AGED JUST 62. MONITORING/SURVEILLANCE WAS NEVER SUGGESTED FOR ME. ON MY ACTUAL 61ST BIRTHDAY I WAS SUBSQUENTLY DIAGNOSED WITH LIVER CANCER. MY TREATMENT OPTIONS WERE LIMITED, 6 MONTHS LATER I RECEIVED MY TRANSPLANT. THE SUBJECT WAS VERY DIFFICULT TO SHARE MAINLY DUE TO PERCEIVE STIGMA OF LIVER DISEASE AND THE LOSS OF MY MOTHER.
3	**Waiting for a transplant** Please describe your experience of being listed and waiting on the waiting list for a liver transplant.	I WAS ONLY ON THE WAITING LIST 9 DAYS SO MY WHOLE EXPERIENCE WAS ONE OF COMPLETE SHOCK AND NOT BELIEVING THIS WAS HAPPENING TO ME.

4	**Transplant surgery** Please describe your experience of being called up for transplant surgery; including cancellations, declining or accepting an offer or successful surgeries where appropriate.	MY TRANSPLANT COULDN'T HAVE GONE BETTER, TO QUOTE ONE OF THE SURGEONS 'MY TRANSPLANTED LIVER WAS NOT ONLY A PERFECT MATCH BUT PERFECT FIT AS WELL'. MY CALL CAME AT 11AM AND THAT EVENING AT 8PM MY OPERATION BEGAN.
5	**Views on the technology** In your view, what are the benefits of using ex-situ machine perfusion devices for liver transplants from deceased donors? Please share your thoughts on: How you feel patient groups would benefit from the use of ex-situ machine perfusion technologies? What do you think the disadvantages / risks may be from the use of ex-situ machine perfusion technologies?	MY VIEW ON THE TECHNOLOGY IS THAT IT CAN ONLY BE BENEFICAL FOR PATIENTS AWAITING LIVER TRANSPLANTS AS IT CAN HOPEFULLY GIVE THEM MORE TIME TO FIND A MORE SUITABLE LIVER. AS ABOVE I SEE A POTENTIAL DISADVANTAGE AS MAYBE COMING FROM THE DONOR'S FAMILIES NOT WANTING THEIR LOVED ONES ORGAN USED IN THIS MANNER. I GUESS AS WITH ANY PERFUSION METHODS THERE COULD BE A RISK OF INFECTION ETC….

6	**Equality and Inclusion** NICE aims to promote equality, prevent discrimination and reduce avoidable differences in health between different groups of people. Are there any considerations you feel the committee should be aware of when assessing the impact of this technology in relation to equality and inclusion?	THE WISHES OF DONORS AND THEIR FAMILIES. THE POTENTIAL CULTURAL DIFFERENCES OF USING THIS TYPE OF TECHNOGOLY.
7	**Further comments** Please add any further comments on your particular experience or knowledge of the technology in this clinical pathway that you would like to share with us.	MY ONLY OTHER COMMENT I FEEL I CAN ADD IS THAT HAVING BEEN A TRAINED PEER SUPPORT MENTOR (POST TRANSPLANT) I KNOW ONLY TO WELL THE TERRIBLE EFFECT PATIENTS & THEIR FAMILIES GO THROUGH WHILE BEING ON THE WAITING LIST, HAVING A NUMBER OF CANCELLATIONS, ARRIVING AT THE HOSPITAL ONLY TO BE INFORMED THE DONATED LIVER IS NOT SUITABLE ETC... SO, IF THIS TECHNOLOGY CAN CUT DOWN WAITING TIMES OR EVEN PROVIDE TEMPORARY MEDICAL CARE UNTIL PATIENT IS WELL ENOUGH TO GO BACK ONTO WAITING LIST, I WOULD BE AN ADVOCATE OF USING THIS TECHNOLOGY.

Document cover sheet - Please delete before publication

Routine use external assessment report: Ex-situ machine perfusion devices for liver transplant

EAG team: Anne Littlewood, Angel Varghese, Chris Bartlett, Ellen Telfer-Thomas, Emma Bishop, Emma Carr, Hayden Holmes, Luc Curtis-Gretton, Rebecca Watts, Rachael McCool

Project lead(s): Angel Varghese, Rachael McCool

Information specialist: Anne Littlewood

Clinical evidence reviewer: Emma Bishop, Emma Carr, Ellen Telfer-Thomas

Economic evidence reviewer: Chris Bartlett, Ellen Telfer-Thomas, Luc Curtis-Gretton

EAG sign-off: Hayden Holmes

Version number	Brief description of changes	Author/reviewer (e.g. J Smith)	Date (DD/MM/YY)	Date sent to NICE (if applicable)
1.0	Draft report submitted to NICE	Anne Littlewood Angel Varghese Chris Bartlett Ellen Telfer-Thomas Emma Bishop Emma Carr Hayden Holmes Luc Curtis-Gretton Rebecca Watts Rachael McCool	19/02/26	19/02/26
2.0	Draft report submitted to NICE	Anne Littlewood Angel Varghese Chris Bartlett Ellen Telfer-Thomas Emma Bishop Emma Carr Hayden Holmes Luc Curtis-Gretton Rebecca Watts Rachael McCool	06/03/26	06/03/26

3.0	Final report submitted to NICE	Anne Littlewood Angel Varghese Chris Bartlett Ellen Telfer-Thomas Emma Bishop Emma Carr Hayden Holmes Luc Curtis-Gretton Rebecca Watts Rachael McCool	12/03/26	12/03/26
4.0	Final report submitted to NICE with updated redactions	Anne Littlewood Angel Varghese Chris Bartlett Ellen Telfer-Thomas Emma Bishop Emma Carr Hayden Holmes Luc Curtis-Gretton Rebecca Watts Rachael McCool	17/03/26	17/03/26

HTE10066 Ex-situ machine perfusion devices for liver transplant

External assessment report

Produced by: York Health Economics Consortium

Authors:

Anne Littlewood, Information Specialist

Angel Varghese, Project Director, Digital Health and Technologies

Chris Bartlett, Senior Research Consultant, Reviews and Evidence Synthesis

Ellen Telfer-Thomas, Research Assistant, Digital Health and Technologies

Emma Bishop, Research Consultant, Reviews and Evidence Synthesis

Emma Carr, Research Consultant, Reviews and Evidence Synthesis

Hayden Holmes, Director of Digital Health and Technologies

Luc Curtis-Gretton, Research Consultant, Digital Health and Technologies

Rebecca Watts, Project Administrator

Rachael McCool, Director of Reviews and Evidence Synthesis

Correspondence to: Angel Varghese ([redacted])

Date completed: 19/02/2026

Contains confidential information: Yes

Number of attached appendices: 8

Purpose of the assessment report

The purpose of this external assessment report (EAR) by an external assessment group (EAG) for routine use assessment is to review the evidence and conduct an economic evaluation for technologies within the decision problem. NICE has commissioned this work and provided the template for the report. The report forms part of the papers considered by the Committee when it is making decisions about the assessment.

Declared interests of the authors

No interests to declare.

Acknowledgements

Clinical experts and company representatives for the scoped technologies provided input into this report. These are noted within the correspondence log submitted to NICE.

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.

EAR Amendments

The original EAG report was submitted to NICE on 14th April 2026. Since that submission, changes have been made to respond to correct errors or provide further clarifications. The changes are summarised in the table below.

Location in report	Edit made
Throughout	Minor grammatical changes.
Throughout	EAD abbreviation corrected from early allograft disorder to dysfunction throughout.
Executive summary	Amended to reflect that no studies were prioritised/included in the review for sequential use of NRP and ex-situ machine perfusion.
Executive summary	Amended to reflect that analysis for extended donor criteria was not included in the report.
Section 3	Primary non-function of the graft added to the prioritised outcomes.
Section 3	Reference added to the statement that one of the aims of normothermic perfusion is to reduce ischaemic reperfusion injury.
Section 4	Transplant history added to included and excluded studies.
Table 4.1, Table 5.1	Data for donor type in Krendl 2025 corrected.
Table 5.1	Data for overall survival in Mathis et al 2024 corrected.

Section 5	Clarified wording around transaminase release to recognise that this happens in hypothermic as well as normothermic perfusion.
Section 5	Correction of the reporting of biliary complications in Krendl 2025.
Section 5	Detail added for studies relating to non-anastomotic biliary strictures.
Section 6	Clarification around explanation for not explicitly modelling complications following re-transplantation.
Section 6	Clarification around QALY/HRQoL terminology used in regard to long-term outcomes.
Table 6.4	Amended explanation regarding the assumption that long-term mortality rates for all machine perfusion were informed by 5-year data from a single device in a DBD population.
Table 6.4	Clarification added for assumption regarding length of time on the waitlist.
Section 6	Data for utilisation rates of Nasralla et al corrected.
Table 6.7	Clarification added for relative risk of Lesurtel et al 2025.
Table 6.7	Amendment to source for VitaSmart HAT parameter.
Section 6	Mortality source amended to Czigany et al 2024.

Section 6	Amendment to deterministic results for PerLifePRO.
Table 6.22, Table 6.23, Table 6.24, Table 6.25	Length for waitlist scenarios amended.
Section 6	ICERs updated for base case.
Section 7	Amended to reflect that no studies were prioritised/included in the review for sequential use of NRP and ex-situ machine perfusion.
Section 9.2 (Appendix B), Table B.2	Reference amended to include Bruggenwirth et al 2022.
Section 9.7 (Appendix G)	Clarification added for Liver Assist (XVIVO Perfusion AB).

Contents

Abbreviations

Term	Definition
CI	Confidence interval
DBD	Donation after brain death
DCD	Donation after circulatory death
DHOPE	Dual hypothermic oxygenated machine perfusion
DSA	Deterministic sensitivity analysis
EAD	Early allograft dysfunction
EAG	External assessment group
ECD	Extended criteria donor
HAT	Hepatic artery thrombosis
HOPE	Hypothermic oxygenated machine perfusion
HR	Hazard ratio
HRQoL	Health-related quality of life
ICER	Incremental cost-effectiveness ratio
IQR	Interquartile range
ITT	Intention-to-treat
NA	Not applicable
NMB	Net monetary benefit
NMP	Normothermic machine perfusion
NR	Not recorded
NRP	Normothermic regional perfusion
MP	Machine perfusion
PNF	Primary non-function
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRS	Post-reperfusion syndrome
PSSRU	Personal Social Services Research Unit
QALY	Quality-adjusted life year
RCT	Randomised controlled trial
RFI	Request for information
RRT	Renal replacement therapy
SAE	Severe adverse event
SCS	Static cold storage

SD	Standard deviation

Executive summary

Clinical context

Liver transplantation in the UK is the standard treatment for end-stage liver disease, with patients currently facing median wait times of 144 days for adults and 183 days for children across specialised transplant centres. To address the critical shortage of high-quality organs and the high discard rates associated with circulatory death (DCD) donors, the clinical pathway has evolved from traditional static cold storage (SCS) towards machine perfusion technologies.

Ex-situ machine perfusion is used in transplant centres in the UK, most commonly as end-ischaemic perfusion initiated after the donor liver arrives at the transplant centre. In this process, the liver is placed in a perfusion device, typically comprising a reservoir, pump, oxygenator and temperature control unit, through which fluid is circulated before the organ is removed, prepared for surgery and transplanted.

Although some devices allow ex-situ perfusion during transportation of the liver, this is not standard practice in the UK.

Both hypothermic and normothermic ex-situ perfusion approaches are used. Hypothermic oxygenated perfusion (HOPE), including dual HOPE (DHOPE), circulates oxygenated fluid through the liver at low temperatures (4 to 10°C) with the aim of reducing ischaemia-reperfusion injury. Normothermic machine perfusion (NMP), conducted at approximately 37°C, maintains the liver in a metabolically active state by supplying oxygen and nutrients and can also facilitate pre-transplant viability assessment. In addition, in-situ normothermic regional perfusion (NRP) may be undertaken prior to organ retrieval, allowing viability assessment while the liver remains in the donor body. Although not yet routine across all UK transplant centres, NRP forms part of the NHS Blood and Transplant framework and is currently under review within NICE interventional procedures guidance.

Clinical evidence

Searches were conducted to identify clinical and economic evidence for 4 ex-situ machine perfusion technologies, used in liver transplantation in the UK. The included devices were Liver Assist, *metra*, PerLifePRO, and VitaSmart. Although originally included, the TransMedics OCS system was withdrawn from the assessment at the manufacturer's request. Eligible studies compared ex-situ machine perfusion to SCS, where perfusion was initiated at the transplant centre.

168 relevant studies were identified, and 15 were prioritised for detailed data extraction based on evidence quality and their alignment with the UK clinical pathway. Of these prioritised studies, 7 randomised controlled trials (RCTs) evaluated Liver Assist, 2 RCTs evaluated VitaSmart and 3 matched-case studies and 3 cohort studies evaluated *metra*. No eligible studies were identified for the PerLifePRO device. The quality of the RCTs was assessed using the Cochrane Risk of Bias tool. 6 out of 7 RCTs were considered to be low risk of bias, with 1 RCT at moderate risk of bias. 4 of the 6 non-randomised studies were judged to be at a moderate risk of bias using the ROBINS-I tool, with the remaining 2 at low risk of bias.

Clinical evidence review

While evidence exists for overall survival, graft survival, and biliary complications, significant gaps remain. The prioritised research offers no or limited data regarding organ utilisation, waitlist mortality, healthcare practitioner satisfaction, and patient or caregiver health-related quality of life.

8 studies, including RCTs for LiverAssist and VitaSmart, investigated hypothermic perfusion. This evidence base consistently demonstrates that machine perfusion significantly reduces 7-day early allograft dysfunction (EAD) compared to SCS. Individual studies also report improvements in non-anastomotic biliary strictures and graft survival at 1- and 5-year intervals. However, the data remains inconclusive for overall survival and re-transplantation rates, where researchers observed no significant differences.

7 studies focused on normothermic perfusion, primarily utilising the *metra* system. While some cohort studies indicate benefits for EAD and peak laboratory markers, the results lack the consistency found in hypothermic trials. Currently, no statistically significant findings support improvements in non-anastomotic biliary strictures, overall survival or graft survival for normothermic perfusion.

The evidence suggests that machine perfusion does not increase adverse events compared to SCS. Multiple trials actually report significantly lower rates of serious adverse events up to 48 months post-transplant. Regarding high-risk grafts, such as those from donors after circulatory death (DCD), limited evidence suggests machine perfusion improves complication rates and reduces EAD.

Key areas for evidence generation

Several limitations in the current evidence base were identified, and these were identified as key areas for evidence generation.

No evidence was found on the efficacy and safety of the PerLifePRO device, although an ongoing study may provide evidence when results are posted.

Long-term evidence exceeding one year was available, particularly for LiverAssist HOPE (3 RCTs). However, further long-term studies exceeding one year are essential to confirm the sustained benefits of machine perfusion over static cold storage, particularly in normothermic perfusion. Limited evidence from non-randomised studies was found in the perfusion initiated at the recipient centre pathway for *metra*. More robust evidence from randomised trials in this scenario is needed for this device.

Although studies on the sequential use of NRP and ex-situ machine perfusion were identified, none were prioritised and included in the review. Data from larger studies in a UK setting would be beneficial. Significant gaps also remain regarding paediatric populations and populations undergoing extended perfusion; however, a clear clinical consensus on the definition of 'prolonged' perfusion would facilitate better data collection. Investigators should also

prioritise the utilisation of high-risk and DCD grafts to measure how this technology impacts overall organ acceptance rates. Finally, adding patient-reported outcomes and staff surveys will address the current lack of data on quality of life and healthcare professional satisfaction.

Economic Evidence

A total of 15 studies reporting economic evidence were identified, of which four were prioritised for detailed review based on relevance to the decision problem and applicability to UK or European practice. The prioritised studies evaluated Liver Assist, *metra* (OrganOx), VitaSmart and combinations of machine perfusion with SCS. No economic evaluations were identified for PerLifePRO

Time horizons for these analyses ranged from one-year post-transplant to lifetime. Three studies employed a Markov modelling framework; one was a trial-based cost-effectiveness analysis. Results were heterogeneous across settings and headline results were mixed. Differences in conclusions appeared to reflect variation in structural assumptions (such as differences in clinical pathways), utilisation rates, and long-term survival.

One company, OrganOx (*metra*), submitted a *de novo* economic model for consideration. This model demonstrated machine perfusion to be cost-effective however the model structure was associated with some moderate limitations.

Overall, no existing model was considered fully suitable for direct adaptation to the NICE decision problem, and the external assessment group (EAG) developed a *de novo* economic model. The model structure was designed to explicitly capture:

- Liver transplant waitlist, and waitlist mortality.
- Short-term post-transplant complications.
- Re-transplantations and long-term survival.

A cohort-based Markov model with an initial decision tree component was selected as the most appropriate structure, given the available evidence base, the value proposition of machine perfusion, and the need to represent both short- and long-term outcomes.

Many of the device-specific inputs, particularly concerning complications, were not statistically significant. Key structural and parameter uncertainties were explored through extensive sensitivity and scenario analyses. Anticipated benefits of machine perfusion were limited to only being applicable over the time horizon for which robust data was available. This represents a key conservative assumption and may, therefore, underestimate the potential longer-term benefits of machine perfusion.

In the base case deterministic analysis, all machine perfusion technologies were cost-effective compared with SCS alone. Incremental cost-effectiveness ratios (ICERs) ranged from approximately £5,600 (Liver Assist; HMP) to £19,400 (PerLifePRO; NMP) per quality-adjusted life year (QALY) gained. Total costs were higher with machine perfusion due to device costs and an increase in the number of transplants, which were partially offset by fewer re-transplantations and reduced time on the waitlist. Incremental QALY gains were driven primarily by:

- Increased numbers of transplants performed
- Reductions in primary non-function (PNF) and associated mortality
- Improvements in long-term survival

Probabilistic sensitivity analysis (PSA) showed mean probabilistic ICERs ranging range from £6,300 to £20,900 (only up to £12,200 when PerLifePRO excluded) per QALY gained and the probability of machine perfusion being cost-effective ranged from 61% to 100% (or 93% to 100% when PerLifePRO is excluded. PerLifePRO was associated with considerably higher data uncertainties due to a lack of device-specific data. Device-specific differences in ICERs were driven by small differences in complication rates and inconsistently reported device costs. These differences were associated with

considerable uncertainty. Therefore, the results of this analysis should not be used to make conclusions regarding relative benefits of different machine perfusion devices.

One-way and two-way sensitivity analyses demonstrate that the model results are most sensitive to assumptions regarding long-term mortality and organ utilisation rates. Two-way sensitivity analysis further confirmed that the DBD HR for mortality is a more significant driver of results than the DCD HR, because the better baseline survival of DBD recipients allows for the accumulation of more QALYs over time.

The analysis also highlighted differences between modalities, with NMP devices generally associated with higher ICERs than HMP devices due to a higher reported frequency of complications in the NMP clinical data. However, it is important to note that these differences are statistically insignificant.

Scenario analysis testing key structural assumptions and parameters indicated results were broadly robust to uncertainty within the model. When assuming no long-term mortality benefit, ICERs increased to between £9,800 and £23,600, with the *metra* device being the only intervention to exceed the £20,000 threshold. In an additional scenario assuming neither mortality benefits nor increased organ utilisation, ICERs reached £115,000 to £6,000,000 due to negligible incremental QALY gains. These results demonstrate the model's sensitivity to these primary drivers, though clinical feedback suggest such scenarios are unlikely to reflect real-world outcomes.

Very limited data were identified on the use of machine perfusion in the paediatric population. Some data were available for extended donor criteria (ECD) subpopulations however the results of this analysis are not presented in this report as the data were highly inconsistent. Presenting separate ECD results could therefore give the impression of differences (relative to the base case population) that are not supported by the evidence.

Key economic considerations

<u>Regarding the economic evidence:</u>

- Existing identified economic evaluations use heterogeneous approaches and as such, results are mixed across populations and clinical settings.
- Within the EAG model, evidence used to inform short-term complications were mostly statistically insignificant, and machine perfusion device costs were inconsistently reported by device companies. This means that differences between individual devices are subject to substantial parameter uncertainty and limits the extent to which results between devices can be compared.
- There is very limited evidence on the use of machine perfusion on paediatric and ECD populations.
- Results are most sensitive to the long-term mortality and re-transplantation benefits of machine perfusion. When this benefit is removed, ICERs increase, with some results exceeding the £20,000 per QALY threshold.
- While most scenario and sensitivity analyses around key areas of parameter and structural uncertainty align with the base-case modelling, very specific scenarios, such as the combined removal of both mortality and utilisation benefits, can lead to high ICERs due to negligible incremental QALY gains. Clinical consultation indicated that this scenario is unlikely to reflect real-world outcomes.

1. Decision problem

The decision problem for this evaluation is as described in the Final Scope and EAG comments are included in Final Protocol. The EAG made no further changes or comments.

2. Technologies

A brief description of the technologies can be found in Table 2.1. Please see the Final Scope for further details.

TransMedics have subsequently advised NICE that they will not be making OCS Liver available to the NHS for the use cases outlined in this scope and therefore have been withdrawn from this assessment.

Table 2.1: Description of technologies

Technology (company)	Population	Component and CE mark	Perfusion temperature (time length of perfusion)	Device functionality and use	Current use in the NHS
Liver Assist (XVIVO V.V)	Adult and paediatric	Class IIb – reusable Liver Assist device Class IIa – single use sterile perfusion set	Hypothermic (up to 24 hours) Normothermic (up to 6 hours)	Intended to be used at the recipient hospital Able to perform controlled oxygenated rewarming Able to be used as a platform for liver splitting during machine perfusion Able to conduct liver viability testing (during normothermic perfusion)	Used in several NHS transplant centres

Technology (company)	Population	Component and CE mark	Perfusion temperature (time length of perfusion)	Device functionality and use	Current use in the NHS
metra (OrganOx Ltd)	Adult (excluding acute/fulminant liver failure)	CE class IIb – *metra* device CE class IIa) – disposable solution perfusion set CE class III – bile salt	Normothermic (up to 24 hours)	Can be initiated at the donor hospital or on arrival at the recipient hospital Able to conduct liver viability testing	Used in several NHS transplant centres
PerLifePRO (Aferetica S.R.L)	Adults and paediatric	CE class IIa – PerLifePRO machine unit CE class IIa – disposable liver perfusion kit	Hypothermic (up to 24 hours) Normothermic (up to 24 hours)	Intended to be initiated at the recipient hospital Able to perform controlled oxygenated rewarming	Not currently in use within the NHS
VitaSmart (Bridge to Life Ltd)	Adults and paediatric	CE class IIb – machine unit CE class IIa – disposables CE class IIa – oxygenators	Hypothermic (time length not provided)	Intended to be initiated at the recipient hospital	Used in several NHS transplant centres

Table abbreviations: CE, Conformité Européene; NHS, National Health Service.

3. Clinical context

Liver transplantation is the standard treatment for people with end-stage liver disease in the UK. People who are identified as in need of a transplant are referred to a transplant centre. There are 7 transplant centres for adults in the UK and 3 centres for children, as outlined in the Final Scope. People can be referred immediately as a super urgent referral if they require emergency transplantation (Transplant 2025a). Otherwise, they are placed on a waiting list. They are then matched with a suitable donated liver as one becomes available. Between 1 April 2022 and 31 March 2024, the median wait time for elective liver transplant in the UK was 144 days for adults and 183 days for children, although there was wide variation in wait times across the UK transplant centres (Transplant 2025a)

Livers are usually transplanted as a whole organ into adults, but they may be split after retrieval for transplant into children or smaller adults. The smaller left-lobe of the liver is transplanted into the child or smaller adult, and the larger right-lobe may be transplanted into an adult patient.

Livers are donated from deceased donors after either brain stem death (DBD) or circulatory death (DCD). Livers retrieved from donors after circulatory death are more likely to be discarded and not transplanted, in the UK in 2023/24 35% of DCD were not transplanted, compared to 18% of DBD livers (see final scope). DCD liver transplantation has been seen as challenging compared with DBD liver transplantation, with an increased chance of post-operative complications due to the damage caused to the graft from warm ischaemia (Tingle et al. 2023).

Clinical pathway

As outlined in the final scope, in the current standard of care pathway, the liver is flushed with cold fluids after retrieval and then stored in ice (static cold storage or SCS) and transported to the transplant centre. Retrieval and preservation are undertaken by a specialised surgical team prior to transfer to the designated transplant centre. The interval between procurement and

implantation is kept as short as possible to limit ischaemic injury, with cold ischaemia times typically not exceeding 8 to 12 hours (see the final scope for information). Storage in SCS until transplant is standard of care for liver transplantation [2], and it is used as the comparator in this review.

In the UK, ex-situ machine perfusion is also used in practice in transplant centres. This is usually end-ischaemic perfusion, where the liver undergoes ex-situ machine perfusion initiated at the transplant centre. Donor livers are placed in a perfusion machine, which generally comprises a reservoir, a pump, an oxygenator and a warming or a cooling unit (Excellence 2019b). Fluid is then circulated through the liver. Ex-situ perfusion of the liver during transportation is also possible with some perfusion devices, but this is not standard practice in the UK. Following perfusion, the liver is removed from the device, prepared for surgery and transplanted into the recipient.

Both hypothermic (HOPE) and normothermic (NMP) ex-situ perfusion are used in the UK. In HOPE, the liver is perfused ex-situ with oxygenated fluids at low temperatures (4 to 10˚C). HOPE can be done only via the portal vein, or via the hepatic vein and portal vein at the same time (known as DHOPE). The aim of HOPE or DHOPE perfusion is to reduce ischaemic injury to the donated liver (Mugaanyi et al. 2022), as ischemia re-perfusion injury is one of the main concerns with SCS (Mugaanyi et al. 2022). A Cochrane review found that compared with SCS, HOPE was associated with improved graft survival, and a reduction in serious adverse events (Tingle et al. 2023). The review also found that there were reduced complications compared with SCS when HOPE was used for livers that were donated after circulatory death.

In normothermic ex-situ perfusion, the liver is perfused with warmer fluids, generally at body temperature (i.e. 37˚C). NMP aims to keep the liver metabolically active by providing oxygen and nutrients during perfusion (Tingle et al. 2023). The aim of normothermic perfusion is also to reduce ischaemic reperfusion injury {Liu, 2021 #2626}. Further, NMP aims to allow viability assessment of the liver prior to transplant.”

In-situ normothermic perfusion of the liver before retrieval (normothermic regional perfusion or NRP) is also possible, using a different device to that used in ex-situ machine perfusion. NRP allows assessment of liver viability prior to retrieval whilst the liver is situated in the donor body. It has only been used for DCD donated livers in the UK. Studies have shown that NRP has high graft utilisation rates following DCD donation. These studies report favourable outcomes regarding ischemia re-perfusion injury, early graft function, and one-year survival (Czigany et al. 2019). Although NRP is not routinely practiced across all liver transplant centres in the UK, in-situ NRP is part of the NHS Blood and Transplant framework (Transplant 2026), and a review is currently in process as part of NICE's interventional procedures guidance (National Institute for Health and Care Excellence 2026). It has been piloted in several UK transplant centres (NHS Blood and Transplant 2025b).

Unmet need

The scope outlines the shortage of high-quality organs available for transplant in the UK, and the rise in demand due to the increasing prevalence of chronic liver disease. This is coupled with the fact that the average age of donors is rising and that donors increasingly have co-morbidities that may affect liver function. Ex-situ machine perfusion aims to increase liver availability by enabling the safe use of marginal organs, including those from older donors, steatotic livers, and donations after circulatory death. Increasing the availability of viable livers has the potential to reduce transplant waiting lists and mortality rates. Ex-situ machine perfusion may also reduce graft failure rates and the subsequent need for emergency re-transplantation.

Donor and recipient characteristics

We have extracted the Model for End-Stage Liver Disease (MELD) score as an indicator of recipient condition and Donor Risk Index (DRI) score as an indicator of graft liver quality. The MELD score is a numerical scale that assesses the 90-day mortality risk for patients with chronic liver disease. It ranges from 6 to 40, with a higher score indicating a greater risk of mortality and more urgent need for transplant (Singal and Kamath 2013). The DRI is a

scoring system that assesses the risk of post-operative complications or graft failure based on donor characteristics, with higher scores indicating greater risk (Feng et al. 2006). However, the DRI was devised prior to the introduction of machine perfusion and does not account for how this can mitigate risk, leading some authors to devise updated versions (Tanaka and Sewell 2026)

Prioritised outcomes

Clinical experts consulted for this assessment advised on which of the scoped outcomes should be considered most important. There was agreement that transplant utilisation (proportion of donor organs that proceeded to transplant) was the most important outcome. The size and duration of the transplant waiting list, and mortality whilst on the waiting list were also regarded as key.

The number of biliary complications was also prioritised as an outcome. Biliary complications after a liver transplant occur in 5% to 32% of cases (Fasullo M 2022). They are issues with the bile ducts that can cause severe morbidity or graft failure. These can include anastomotic strictures (narrowing at the site where the donor and recipient bile ducts are joined) or non-anastomotic strictures (bile duct damage caused by the lack of blood supply). Bile leakage is also regarded as an important biliary complication (Fasullo M 2022).

Other prioritised outcomes were device-related adverse events, overall patient survival, early allograft dysfunction, mechanical failure, re-transplantation, graft survival, primary non-function of the graft, patient/carer quality of life and healthcare professional satisfaction/wellbeing.

NICE Guidance

NICE interventional procedures guidance, published in 2019 (Excellence 2019a), acknowledged that there were no major safety concerns associated with ex-situ machine perfusion. However, the guidance stated that there was limited evidence on efficacy. It was recommended that ex-situ machine perfusion should only be used with special arrangements for clinical governance, consent, and audit or research. Graft survival and the use of marginal grafts were identified as key outcomes in any further research.

3.1 Equality issues

Equalities issues and considerations for this assessment are described in the equalities impact assessment alongside the Final Scope. No additional equality issues have been identified during the assessment.

4. Clinical evidence

4.1 Search strategies and study selection

Searches were conducted by the EAG to identify studies of the 4 technologies (Liver Assist, *metra*, PerLifePRO and VitaSmart) named in the Final Scope. The original scope also included the TransMedics OCS system, but TransMedics subsequently advised NICE that they will not be making OCS Liver available to the NHS for the use cases outlined in this scope and therefore requested to be withdrawn from this assessment. The searches were designed to identify both clinical and economic evidence. They were conducted on 15 September 2025, in a range of resources. Full details of the search methods are provided in Appendix A.

The EAG searches retrieved a total of 5,262 records after elimination of 1,687 duplicates. Titles and abstracts were screened by 2 reviewers. 448 of these records were identified from the trial registry searches. A total of 669 full texts were retrieved and examined by two reviewers to select those meeting the scope.

4.2 Included and excluded studies

A total of 168 studies (reported in 248 papers or trial records) were identified for the clinical review. Of these studies, 15 were prioritised for further data extraction. Key study characteristics are summarised in Table 4.1 and a detailed description of the studies is presented in Appendix G. Studies were first prioritised on the basis of evidence quality, such that RCT evidence was prioritised over non-RCT evidence. If RCT evidence was not available in the perfusion initiated at the recipient centre pathway for a device type, further evidence for this device in this pathway was sought in the non-RCT studies (first prioritizing non-randomised comparative evidence, then single-arm evidence, etc.) in a European setting. It is therefore possible that there is further evidence on the relevant outcomes in the deprioritised studies that has not been extracted and summarized in this report.

The 15 prioritised studies are as follows:

- Liver Assist: 7 RCTs
- *metra*: 3 matched-case studies and 3 cohort studies in a European setting (3 *metra* RCTs were identified which were not in the perfusion initiated at the recipient centre pathway, and were therefore deprioritised (University of Oxford (UK) 2014, University Health Network 2015, OrganOx Ltd. 2016)).
- VitaSmart: 2 RCTs
- No studies were identified that evaluated PerLifePRO.

Patients

All studies aligned with the decision problem population criteria, including patients undergoing liver transplantation. No comparative evidence was found in children or young people (< 18 years old).

MELD

2 studies (1 Liver Assist RCT (Schlegel et al. 2023) and 1 *metra* matched-case study (Hann et al. 2022)) included patients with a severe MELD score (>20 points) in the machine perfusion arm. In the SCS arms of these studies and in all other studies, patients in all treatment arms had a median MELD score below 20.

DRI

10 studies reported the median donor risk index (DRI), of which 7 reported a severe median DRI (>1.7) in both treatment arms:

- 4 Liver Assist RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Minor et al. 2022, Lesurtel et al. 2025)
- 1 VitaSmart RCT (Ravaioli et al. 2022)
- 2 *metra* non-randomised comparative studies (Fodor et al. 2021, Puttappa et al. 2025)

1 Liver Assist RCT reported a severe DRI in the machine perfusion arm only (Schlegel et al. 2023), and 2 *metra* non-randomised comparative studies

reported DRI scores below 1.7 in both arms (Vogt et al. 2024, Hann et al. 2022).

DBD and DCD livers

15 studies reported whether donor livers were DCD or DBD. 8 studies included only DBD livers:

- 6 Liver Assist RCTs (Czigany et al. 2021, Lesurtel et al. 2025, Ghinolfi et al. 2019, Grat et al. 2023, Schlegel et al. 2023, Minor et al. 2022)
- 1 VitaSmart RCT (Ravaioli et al. 2022)
- 2 *metra* non-randomised comparative studies (Vogt et al. 2024, Hann et al. 2022))

2 studies included only DCD livers:

- 1 Liver Assist RCT (van Rijn et al. 2021c)
- 1 *metra* retrospective cohort study (Puttappa et al. 2025)

1 VitaSmart RCT and 3 *metra* non-randomised comparative studies included mixed DCD/DBD livers (<30% DCD) (Reich et al. 2024b, Krendl et al. 2025, Fodor et al. 2021, Mathis et al. 2024).

Extended Criteria Donor (ECD) livers

The definition of ECD livers varied across studies. Some studies cited criteria such as the German Medical Chambers ECD liver criteria [21] and United Network for Organ Sharing criteria (Ravaioli et al. 2022), while others specified criteria (e.g. including only livers from donors >70 years old or only DCD livers, other biomarker characteristics, etc.).

6 studies included only extended criteria donor (ECD) grafts, either according to ECD criteria such as the German Medical Chambers ECD liver criteria (Schrem H 2012) or due to other liver criteria (e.g. including only livers from donors >70 years old):

- 4 Liver Assist RCTs (Czigany et al. 2021, Minor et al. 2022, Lesurtel et al. 2025, Ghinolfi et al. 2019)

- 2 VitaSmart RCTs (Reich et al. 2024b, Ravaioli et al. 2022)(Puttappa et al. 2025)

2 studies included only ECD livers as a result of including only DCD livers, with no further ECD criteria being reported:

- 1 LiverAssist RCT (van Rijn et al. 2021c)
- 1 *metra* non-randomised comparative studies (Puttappa et al. 2025)

4 studies included both ECD and non-ECD livers in both the experimental and control arms:

- 1 Liver Assist RCT (Grat et al. 2023)
- 3 *metra* non-randomised comparative studies (Krendl et al. 2025, Fodor et al. 2021, Mathis et al. 2024)

1 *metra* matched case study included ECD livers in the machine perfusion arm only (Hann et al. 2022).

Two studies (1 Liver Assist RCT (Schlegel et al. 2023) and 1 *metra* retrospective cohort study (Vogt et al. 2024)) did not report any information on the use of ECD livers.

Transplant history

1 *metra* matched-case study included only patients undergoing repeat liver transplantation {Hann, 2022 #741}. In 1 LiverAssist RCT {Grat, 2023 #426} and 1 *metra* cohort study {Puttappa, 2025 #178} retransplant patients were included and were a minority of participants (<10%).

1 LiverAssist RCT {Lesurtel, 2025 #4063} and 2 *metra* matched-case studies {Mathis, 2024 #462}{Krendl, 2025 #163} reported that patients with prior liver transplantations were excluded.

Transplant history was not reported by any other study.

Interventions

All 15 prioritised studies included one of the machine perfusion devices in the scope initiated at the transplant centre following transport in SCS. All compared machine perfusion to SCS.

In 8 RCTs hypothermic machine perfusion was used:

- 6 Liver Assist (van Rijn et al. 2021c, Czigany et al. 2021, Minor et al. 2022, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)
- 2 VitaSmart (Reich et al. 2024b, Ravaioli et al. 2022).

5 of these studies investigated single-perfusion and 3 investigated dual-perfusion (Liver Assist RCTs (van Rijn et al. 2021c, Minor et al. 2022, Grat et al. 2023)). 1 Liver Assist RCT also reported that hypothermic perfusion was followed by controlled oxygenated re-warming and then transplant (the mean duration of warm perfusion across arms was 28.3 (SD 5.9) minutes, and testing of perfusate samples for metabolic parameters was conducted at regular intervals) (Minor et al. 2022).

In 7 studies normothermic dual perfusion was used:

- 1 Liver Assist RCT (Ghinolfi et al. 2019)
- 6 *metra* non-randomised comparative studies (Vogt et al. 2024, Krendl et al. 2025, Fodor et al. 2021, Mathis et al. 2024, Hann et al. 2022, Puttappa et al. 2025).

The scope identified NRP following DCD in the context of a machine perfusion study as a subgroup of interest. 1 *metra* retrospective cohort study using DCD livers included a cohort of livers which underwent NRP followed by SCS in addition to the *metra* and SCS cohorts (Puttappa et al. 2025).

Table 4.1: Summary of salient study characteristics of prioritised studies

Study ID	Study design	Perfusion type	UK/non-UK	Donor type
Liver Assist				
van Rijn et al 2021 (van Rijn et al. 2021c)	RCT	Hypothermic; dual perfusion	UK centres among other international centres	DCD; ECD (all DCD, further ECD criteria NR)
Czigany et al 2021 (Czigany et al. 2021)	RCT	Hypothermic; single perfusion	Non-UK	DBD; ECD
Minor et al 2021 (Minor et al. 2022)	RCT	Hypothermic with controlled re-warming; dual perfusion	Non-UK	DBD; ECD
Lesurtel et al 2025 (Lesurtel et al. 2025)	RCT	Hypothermic; single perfusion	Non-UK	DBD; ECD
Ghinolfi et al 2019 (Ghinolfi et al. 2019)	RCT	Normothermic; dual perfusion	Non-UK	DBD; ECD (all donors >70 years, further criteria NR).
Grat et al 2023 (Grat et al. 2023)	RCT	Hypothermic; dual perfusion	Non-UK	DBD; 54% ECD
Schlegel et al 2023 (Schlegel et al. 2023)	RCT	Hypothermic; single perfusion	UK centres among other international centres	DBD; ECD not reported
metra				

Study ID	Study design	Perfusion type	UK/non-UK	Donor type
Vogt 2024 (Vogt et al. 2024)	Prospective cohort study	Normothermic; dual perfusion	Non-UK	DBD; NR if ECD
Krendl 2025 (Krendl et al. 2025)	Retrospective cohort study	Normothermic; dual perfusion	Non-UK	Mixed, <20% DCD; mixed, >60% ECD
Fodor 2021 (Fodor et al. 2021)	Matched case study	Normothermic; dual perfusion	Non-UK	Mixed, <20% DCD; mixed >70% ECD
Mathis 2024 (Mathis et al. 2024)	Matched case study	Normothermic; dual perfusion	Non-UK	Mixed, <20% DCD; mixed ECD, NR
Hann 2022 (Hann et al. 2022)	Matched case study	Normothermic; dual perfusion	UK	DBD; ECD in the *metra* arm only.
Puttappa et al, 2025 (Puttappa et al. 2025)	Retrospective cohort	Normothermic; dual perfusion	UK	DCD; ECD (all DCD, further ECD criteria NR)
VitaSmart				
Reich et al (Reich et al. 2024b)	RCT	Hypothermic; single perfusion	Non-UK	Mixed, <30% DCD; ECD
Ravaioli et al 2022 (Ravaioli et al. 2022)	RCT	Hypothermic; single perfusion	Non-UK	DBD; ECD

Table abbreviations: DBD, donation after brainstem death; DCD, donation after circulatory death; ECD, extended criteria donor; NR, not reported.

5. Clinical evidence review

The EAG explored the possibility of a pairwise meta-analysis but this was ultimately not considered to be valuable due to heterogeneity across studies reporting similar outcomes. In particular, clinical experts advised that pooling together studies using normothermic and hypothermic perfusion would not be appropriate.

5.1 Quality appraisal of studies

The 9 RCTs were assessed for risk of bias with the Cochrane Risk of Bias version 1 tool (Higgins et al. 2011). 1 RCT (Liver Assist) was judged to be at a moderate risk of bias due to lack of clarity in the handling of missing data (multiple imputation was used in sensitivity analyses of the primary outcome due to some missing data in co-variates, though it was unclear if data was missing for the secondary outcomes) (Schlegel et al. 2023). All other RCTs were judged to be at a low risk of bias. All RCTs were either open-label or single-blind; surgeons and healthcare personnel were unavoidably aware of the perfusion method used and blinding of outcome assessors was not clearly reported by most trials. However, because the reported outcomes are all objectively measured outcomes this was not considered to be a risk of bias concern in this context.

4 of the 6 non-randomised studies (all investigating *metra*) were judged to be at a moderate risk of bias using the ROBINS-I tool (Sterne et al. 2016), all due to potential imbalance in confounding factors between treatment arms (2 matched- case studies (Hann et al. 2022, Mathis et al. 2024) and 2 cohort studies (Krendl et al. 2025, Puttappa et al. 2025)). The other two non-randomised studies were judged to be at a low risk of bias.

Relevance to decision problem

All prioritised studies were in the perfusion initiated at transplant centre pathway. However, the relevance of the evidence base to some aspects of the decision problem was more limited.

A key use case for machine perfusion is the potential to increase the utilisation of high risk ECD livers, and DCD livers in particular, as outlined in the scope. Most of the prioritised studies included ECD livers (though the ECD criteria varied and it was not clearly reported how many liver grafts met which criteria). However, evidence in DCD livers was more limited as only 3 of 15 prioritised studies included DCD livers specifically (in a further 3 studies a minority of grafts were DCD, <20%). Therefore it is difficult to assess how effective machine perfusion is in improving the viability of DCD liver grafts.

In most studies using ECD and/or DCD livers similar numbers of these livers were used in both the machine perfusion and control arm. 1 *metra* matched case series reported that ECD livers were used in the *metra* cases only, 1 retrospective cohort study reported that significantly more ECD and DCD livers were used in the *metra* cohort than the SCS cohort (both p<0.001) (Krendl et al. 2025) and 1 matched-case study reported that there were significantly more DCD livers in the *metra* cases (p=0.048) (Mathis et al. 2024). Where these studies reported no significant differences in any outcome measure therefore may reflect greater efficacy of *metra* as a preservation method relative to SCS (in that similar results were achieved even when using more suboptimal livers in *metra* compared to those used in SCS).

Generalisability

The EAG had the following concerns about the generalisability of the evidence base to the UK setting:

- Evidence in a UK setting was available in 4 studies: 2 Liver Assist RCTs included UK centres among other international centres, and 2 *metra* non-randomised comparative studies were conducted in the UK alone (Hann et al. 2022, Puttappa et al. 2025). No UK evidence was available for VitaSmart. Although not all studies were conducted in a UK setting, all were conducted in the pathway with perfusion initiated at the recipient centre. Advice from clinical experts suggested that these studies would therefore be broadly applicable to the UK setting, with caveats around possible

differences in donor case-mix, logistics, cold ischaemia times, allocations and peri-operative pathways.

5.2 Results from the evidence base

The following sections summarise the results extracted from the prioritised studies.

All RCTs randomised patients to receive livers preserved by machine perfusion or SCS, except 2 RCTs in which the liver grafts were randomised to a preservation method at point of arrival to the transplant centre (Schlegel et al. 2023, Grat et al. 2023). All RCTs conducted intent-to-treat (ITT, including all randomised patients according to their allocated preservation method) or modified ITT (including all patients who underwent transplant according to their allocated preservation method) analyses, with the exception of 1 VitaSmart RCT in which per protocol (PP, patients were analysed according to the preservation method used during their transplant) analyses were conducted and 1 Liver Assist RCT in which complete case analyses were conducted for post-reperfusion syndrome (PRS) and EAD (van Rijn et al. 2021c).

The outcomes have been reported in alignment with how they were prioritised by the clinical experts (see section 3). A summary of the prioritised outcomes is presented in Table 5.1.

The EAG is aware that there is debate among experts around the relevance of surrogate markers like EAD and transaminase release, and inconsistent definitions of outcomes such as PNF and PRS in the literature. During scoping feedback one clinical expert advised that transaminase release in the first week post-transplant has significant limitations as an outcome in machine perfusion, as much transaminase is released into the perfusate during perfusion (the “wash-out effect” (Melandro et al. 2022)), which is discarded. Thus recipient transaminases in machine perfused versus SCS livers may not be a good measure of damage or function. The same concern undermines the validity of EAD which is defined using transaminase release levels; experts

noted that the Olthoff et al 2010 criteria for EAD was validated through the correlation of EAD with 1-year survival prior to the era of machine perfusion, and that recent studies including a Cochrane systematic review have shown that this correlation does not hold when using machine perfusion (Nasralla et al. 2018, Tingle et al. 2023). The evidence for these outcomes should therefore be interpreted with caution.

Table 5.1: Summary of key outcome results

Study	Study design	Donor type	Quality appraisal	Outcome	Result
Hypothermic perfusion					
LiverAssist (HMP)					
van Rijn et al 2021 (van Rijn et al. 2021c)	RCT Location: Belgium; UK; Netherlands	DCD; ECD (all DCD, further ECD criteria NR)	Low risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	<u>Non-anastomotic biliary strictures</u> 6 months adjusted HR: 0.32 (95% CI 0.11 to 0.89) p=0.03 5 year adjusted HR: 0.4 (95% CI 0.23 to 0.99) p=0.048 <u>Anastomotic biliary strictures</u> 6 months adjusted HR: 1.07 (95% CI 0.52 to 2.20) 5 year LiverAssist vs SCS: 45% vs 47% p=0.748 <u>Biliary anastomotic leakage</u> 6 month RR: 0.69 (95% CI 0.22 to 2.13)
				Device-related AE	NR
				Overall survival	1 year HR: 2.45 (95% CI 0.77 to 7.85) 5 year HR: 1.30 (95% CI 0.75 to 2.26) p=0.35
				Graft survival	1 year HR: 0.65 (95% CI 0.18 to 2.29) 5 year HR: 0.91 (95% CI 0.45 to 1.87) p=0.806

Study	Study design	Donor type	Quality appraisal	Outcome	Result
				EAD	Adjusted RR: 0.61 (95% CI 0.39 to 0.96)
				PNF	LiverAssist vs SCS: 0 vs 1%
				Mechanical failure	6 months LiverAssist vs SCS: 1/78 vs 0/78
				Re-transplantation	6 months adjusted HR: 0.49 (95% CI 0.12 to 1.94) 5 years (LiverAssist vs SCS): 13% vs 15% p=0.753
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Czigany et al, 2021 (Czigany et al. 2021)	RCT Location: Czech Republic; Germany	DBD; ECD	Low risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	1 year LiverAssist vs SCS: 17% vs 26% p=0.722
				Device-related AE	NR
				Overall survival	1 year LiverAssist vs SCS: 91% vs 83% p=0.442 3 year LiverAssist vs SCS: 86.9% vs 64.9% 5 year LiverAssist vs SCS: 86.9% vs 64.9% p=0.107
				Graft survival	1 year LiverAssist vs SCS: 91% vs 78% p=0.253 3 year LiverAssist vs SCS: 86.9% vs 60.6% 5 year LiverAssist vs SCS: 86.9% vs 51.9% p=0.029

Study	Study design	Donor type	Quality appraisal	Outcome	Result
				EAD	LiverAssist vs SCS: 17% vs 35% p=0.314
				PNF	LiverAssist vs SCS: 4% vs 4% p>0.999
				Mechanical failure	NR
				Re-transplantation	1 year LiverAssist vs SCS: 4% vs 9% p>0.999 Median 48 months LiverAssist vs SCS: 0% vs 10% p=0.232
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Minor et al 2021 (Minor et al. 2022)	RCT Location: France	DBD; ECD	Low risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	NR
				Device-related AE	NR
				Overall survival	NR
				Graft survival	3 months LiverAssist vs SCS: 100% vs 95% p>0.999
				EAD	LiverAssist vs SCS: 20% vs 30% p=0.48
				PNF	NR
				Mechanical failure	NR
				Re-transplantation	3 months LiverAssist vs SCS: 0% vs 5% p>0.999
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
	RCT	DBD; ECD		Organ utilisation	NR

Study	Study design	Donor type	Quality appraisal	Outcome	Result
Lesurtel, 2025 (Lesurtel et al. 2025)	Location: France		Low risk of bias	Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	90 days LiverAssist vs SCS: 9.9% vs 16.8% p=0.1
				Device-related AE	NR
				Overall survival	1 year HR: 1.07 (95% CI 0.49 to 2.34)
				Graft survival	1 year HR: 0.92 (95% CI 0.46 to 1.81)
				EAD	LiverAssist vs SCS: 20% vs 30% p=0.48
				PNF	LiverAssist vs SCS: 0.76% vs 4.58% p=0.12
				Mechanical failure	NR
				Re-transplantation	1 year LiverAssist vs SCS: 2.3% vs 4.6% p=0.5
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Grat et al, 2023 (Grat et al. 2023)	RCT Location: Poland	DBD; 54% ECD	Low risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	Biliary complications 90 days LiverAssist vs SCS: 23.7% vs 43.4% p=0.11 Anastomotic strictures 90 days LiverAssist vs SCS: 19.9% vs 33.7% p=0.2
				Device-related AE	NR
				Overall survival	2 years LiverAssist vs SCS: 92.3% vs 83.9% p=0.23

Study	Study design	Donor type	Quality appraisal	Outcome	Result
				Graft survival	2 years LiverAssist vs SCS: 92.3% vs 81.4% p=0.23
				EAD	Model for Early Allograft Function LiverAssist vs SCS (mean, SD): 4.94 (1.72) vs 5.49 (2.14) p=0.24
				PNF	LiverAssist vs SCS: 0% vs 3.8% p=0.57
				Mechanical failure	NR
				Re-transplantation	NR
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Schlegel et al 2023 (Schlegel et al. 2023)	RCT Location: UK, Belgium, Netherlands, France, Austria, Switzerland	DBD; ECD not reported	Moderate risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	Biliary complications: 1 year OR: 0.744 (95% CI 0.35 to 1.58), p=0.44 Anastomotic biliary strictures 1 year LiverAssist vs SCS: 16.5% vs 21.2% Non-anastomotic biliary strictures 1 year LiverAssist vs SCS: 1.2% vs 3.5%
				Device-related AE	NR
				Overall survival	1 year OR: 1 (95% CI 0.229 to 4.359), p=1

Study	Study design	Donor type	Quality appraisal	Outcome	Result
				Graft survival	1 year OR: 0.55 (95% CI 0.14 to 1.896), p=0.36
				EAD	LiverAssist vs SCS: 16.5% vs 45.9%
				PNF	Graft loss due to PNF LiverAssist vs SCS: 0% vs 3.5% p=0.015
				Mechanical failure	LiverAssist vs SCS: 4.5% vs 0%
				Re-transplantation	1 year LiverAssist vs SCS: 0% vs 3.5%
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
VitaSmart					
Reich et al 2024 (Reich et al. 2024b)	RCT Location: USA	Mixed, <30% DCD; ECD	Low risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	NR
				Device-related AE	NR
				Overall survival	6 months VitaSmart vs SCS: 95% (95% CI 93.6 to 99.5%) vs 97% 95% CI 92.3% vs 99.1%) p=non-significant
				Graft survival	6 months VitaSmart vs SCS: 96% (95% CI 90.9% to 98.6%) vs 94% (95% CI 87.4% to 96.9%)
				EAD	RR: 0.54 (95% CI 0.35 to 0.85)
				PNF	VitaSmart vs SCS: 0% vs 0.9%
				Mechanical failure	NR
				Re-transplantation	NR

Study	Study design	Donor type	Quality appraisal	Outcome	Result
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Ravaioli et al 2022 (Ravaioli et al. 2022)	RCT Location: Italy	DBD; ECD	Low risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	Hepatic biliary or vascular complications: 6 months VitaSmart vs SCS: 16% vs 22% p=0.47 Biliary strictures (not specified as anastomotic/non-anastomotic) 6 months VitaSmart vs SCS: 4% vs 4% p= non-significant Biliary leak 6 months VitaSmart vs SCS: 4% vs 2% p=non-significant
				Device-related AE	NR
				Overall survival	1 year VitaSmart vs SCS: p=0.52
				Graft survival	1 year adjusted RD: 0.109 (95% CI 0.014 to 0.204) p=0.03
				EAD	Adjusted RD: 0.218 (0.065 to 0.372), p=0.005
				PNF	VitaSmart vs SCS: 0% vs 4% p=0.49
				Mechanical failure	NR
				Re-transplantation	Day 7 VitaSmart vs SCS: 0% vs 11% p=0.027

Study	Study design	Donor type	Quality appraisal	Outcome	Result
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Normothermic perfusion					
LiverAssist (NMP)					
Ghinolfi et al 2019 (Ghinolfi et al. 2019)	RCT Location: Italy	DBD; ECD (all donors >70 years, further criteria NR).	Low risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	6 months LiverAssist vs SCS: 1% vs 0% p=1
				Device-related AE	NR
				Overall survival	6 months LiverAssist vs SCS: 100% vs 90% p=1
				Graft survival	6 months LiverAssist vs SCS: 90% vs 100% p=1
				EAD	LiverAssist vs SCS: 20% vs 10% p=1
				PNF	LiverAssist vs SCS: 0% vs 0%, p=1
				Mechanical failure	NR
				Re-transplantation	6 months LiverAssist vs SCS: 10% vs 0%
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
metra					
		DBD; NR if ECD		Organ utilisation	NR

Study	Study design	Donor type	Quality appraisal	Outcome	Result
Vogt et al, 2024 (Vogt et al. 2024)	Prospective cohort study Location: Germany		Low risk of bias	Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	NR
				Device-related AE	NR
				Overall survival	NR
				Graft survival	NR
				EAD	*metra* vs SCS: 35.5% vs 50% p=0.6534
				PNF	NR
				Mechanical failure	NR
				Re-transplantation	NR
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Krendl et al, 2025 (Krendl et al. 2025)	Retrospective cohort study Location: Austria	Mixed, <20% DCD; mixed, >60% ECD	Moderate risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	Overall biliary complications 1 year *metra* vs SCS: 42% vs 36.7% p =0.329 Anastomotic strictures 1 year *metra* vs SCS: 23.6% vs 18.4% p=0.245 Non-anastomotic strictures 1 year *metra* vs SCS: 10.9% vs 8.9% p=0.531

Study	Study design	Donor type	Quality appraisal	Outcome	Result
					Bile duct leak 1 year *metra* vs SCS: 11.5% vs 12% p=0.881
				Device-related AE	NR
				Overall survival	NR
				Graft survival	1 year *metra* vs SCS: 83.8% vs 81.3% 36 months *metra* vs SCS: 73.1% vs 73.9%
				EAD	*metra* vs SCS: 29.9% vs 36.1% p=0.230
				PNF	*metra* vs SCS: 0% vs 2.5% p=0.05
				Mechanical failure	NR
				Re-transplantation	NR
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Fodor et al, 2021 (Fodor et al. 2021)	Matched case study Location: Austria	Mixed, <20% DCD; mixed >70% ECD	Low risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	Bile duct complications >30 days *metra* vs SCS: 27% vs 36% p=0.321 Anastomotic strictures *metra* vs SCS (timepoint unclear): 36% vs 39% p=0.703 Non-anastomotic strictures

Study	Study design	Donor type	Quality appraisal	Outcome	Result
					metra vs SCS (timepoint unclear): 8% vs 17% p=0.167 Bile duct leak *metra* vs SCS (timepoint unclear): 17% vs 19% p=0.81
				Device-related AE	NR
				Overall survival	1 year *metra* vs SCS: 81% vs 82% p=0.347
				Graft survival	1 year *metra* vs SCS: 81% vs 79% p=0.784
				EAD	*metra* vs SCS: 32% vs 34% p=0.794
				PNF	*metra* vs SCS: 0% vs 0%
				Mechanical failure	NR
				Re-transplantation	NR
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Mathis et al, 2024 (Mathis et al. 2024)	Matched case study Location: Austria	Mixed, <20% DCD; mixed ECD, NR	Moderate risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	NR
				Device-related AE	NR
				Overall survival	Mortality at median 18 days, metra vs SCS: 0% vs 3%
				Graft survival	NR
				EAD	NR
				PNF	NR
				Mechanical failure	NR

Study	Study design	Donor type	Quality appraisal	Outcome	Result
				Re-transplantation	NR
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Hann et al, 2022 (Hann et al. 2022)	Matched case study Location: UK	DBD; ECD in the *metra* arm only.	Moderate risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	Anastomotic stricture *metra* vs SCS retrospective vs SCS prospective (timepoint unclear): 3.8% vs 9.6% vs 8% p=0.693 Non-anastomotic stricture *metra* vs SCS retrospective vs SCS prospective (timepoint unclear): 3.8% vs 12% vs 8% p=0.473 Bile leak *metra* vs SCS retrospective vs SCS prospective (timepoint unclear): 0% vs 6.4% vs 0% p=0.185
				Device-related AE	NR
				Overall survival	6 month *metra* vs SCS retrospective vs SCS prospective: 88% vs 87% vs 92% p=0.837
				Graft survival	6 month *metra* vs SCS retrospective vs SCS prospective: 84% vs 87% vs 88% p=0.934

Study	Study design	Donor type	Quality appraisal	Outcome	Result
				EAD	*metra* vs SCS retrospective vs SCS prospective: 46% vs 38% vs 36% p=0.743
				PNF	*metra* vs SCS retrospective vs SCS prospective: 0% vs 3.2% vs 0% p=0.423
				Mechanical failure	NR
				Re-transplantation	NR
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR
Puttappa et al, 2025 (Puttappa et al. 2025)	Retrospective cohort Location: UK	DCD; ECD (all DCD, further ECD criteria NR)	Moderate risk of bias	Organ utilisation	NR
				Size and duration of waitlist and waitlist mortality	NR
				Biliary complications	NR
				Device-related AE	NR
				Overall survival	NR
				Graft survival	1 year *metra* vs SCS vs NRP then SCS: 94% vs 90% vs 94% 5 year HR SCS vs *metra*: 2.0 (95% CI 0.9 to 4.4) p=0.089
				EAD	Model for Early Allograft Dysfunction score *metra* vs SCS vs NRP then SCS (median, IQR): 3.3 (2.1 to 5.2) vs 5.8 (4.8 to 7.0) vs 4.1 (2.8 to 5.4) p<0.001
				PNF	*metra* vs SCS vs NRP then SCS: 1% vs 3% vs 0%
				Mechanical failure	NR
				Re-transplantation	NR

Study	Study design	Donor type	Quality appraisal	Outcome	Result
				Patient/caregiver HRQoL	NR
				HCP satisfaction	NR

Table abbreviations: AE, adverse event; CI, confidence interval; DBD, donation after brain death; DCD, donation after circulatory death; EAD, early allograft dysfunction; ECD, extended criteria donor; HCP, healthcare practitioner, HMP, hypothermic machine perfusion; HR, hazard ratio; HRQoL, health-related quality of life; IQR, interquartile range; NMP, normothermic machine perfusion; NR, not reported; NRP, normothermic regional perfusion; OR, odds ratio; RR, risk ratio; RD, risk difference; SCS, static cold storage.

Key outcomes as identified by clinical experts

Waitlists and utilisation

Transplant utilisation, the size and duration of liver transplant waitlist and liver transplant waitlist mortality were outcomes of interest in the decision problem.

None of the prioritised studies reported data relating to liver transplant waitlists.

2 *metra* matched case studies reported some information on utilisation. 1 reported that of the 174 grafts in the *metra* arm, 67 were considered to only be viable if preserved with machine perfusion These livers had a significantly higher DRI compared with livers that would have been accepted regardless of machine perfusion availability (median 2.13 (range 1.67 to 2.55) vs 1.70 (1.30 to 1.95) p< 0.001), and included significantly more DCD livers (25 (37.3%) vs 9 (8.4%) p<0.001) (Krendl et al. 2025).1 reported that of 75 livers that were machine perfused during the study period, 59 were ultimately considered suitable for transplantation(Fodor et al. 2021).

Overall biliary complications

2 RCTs reported overall biliary complications at 6 months. 1 VitaSmart RCT (DBD) investigated hypothermic perfusion and reported no significant difference in overall biliary complications at 6 months (Ravaioli et al. 2022). The other RCT investigated normothermic LiverAssist (DBD) and reported no significant differences at 6 months (Ghinolfi et al. 2019).

3 studies (2 LiverAssist RCTs and 1 *metra* cohort study) reported overall biliary complications at 1 year. The 2 Liver Assist RCTs (DBD) investigated hypothermic perfusion and reported no significant difference, though rates were lower in the Liver Assist arm in both trials (17% vs 26% p=0.722 (Czigany et al. 2021); odds ratio: 0.744, 95% CI 0.35 to 1.58 (Schlegel et al. 2023)).

The *metra* cohort study (mixed DBD/DCD) investigated normothermic perfusion and reported no statistically significant difference between arms, with a higher rate of complications in the *metra* arm (42% vs 36.7% p=0.329 (Krendl et al. 2025)). Full outcome data is presented in Appendix D in Table D.1.

Non-anastomotic biliary strictures

Regarding biliary strictures, the EAG was advised by clinical experts on the importance of distinguishing anastomotic (surgery-related) and non-anastomotic strictures, as only the latter relate to graft preservation. This expert also advised that livers donated after circulatory death (DCD) are significantly more prone to non-anastomotic biliary strictures (NAS), data should be assessed based on donor type (i.e. DCD vs DBD). We have accordingly summarised studies of DCD and DBD livers separately.

2 Liver Assist RCTs (DBD) investigated hypothermic perfusion and reported the rate of non-anastomotic biliary strictures up to 1 year. 1 reported a significantly lower rate in the Liver Assist arm (adjusted hazard ratio (HR): 0.32, 95% CI 0.11 to 0.89, p=0.03 (van Rijn et al. 2021c)); more patients in the SCS arm than LiverAssist arm were indicated for transplant due to primary slecorising cholangitis (PCS; LiverAssist 7/78 vs SCS 13/78) which may affect the rate of NAS, however the hazard ratio was adjusted for numerous prognostic factors including PSC and therefore represents the treatment effect after accounting for any potential impact of PSC on NAS {van Rijn, 2025 #4062}. The other trial reported the rate at 1 year. Rates were lower in the Liver Assist arm, although no statistical comparison between groups was reported (Liver Assist 1.2% vs SCS 3.5% (Schlegel et al. 2023)).

1 *metra* retrospective cohort study (mixed DBD/DCD with 10.8% DCD) investigated normothermic perfusion and reported no significant difference between arms in non-anastomotic stenosis at 1 year, with a higher rate in the *metra* arm (10.9% vs. 8.9% p=0.531 (Krendl et al. 2025)).

2 other *metra* matched case studies reported non-anastomotic strictures at unclear timepoints, both of which reported no significant difference between arms in the rate of non-anastomotic strictures (3.8% vs 12% vs 8% p=0.473 {Hann, 2022 #741}; 8% vs 17% p=0.167 {Fodor, 2021 #842}).

Anastomotic biliary strictures

Biliary strictures not clearly specified as non-anastomotic or anastomotic are synthesised below with anastomotic strictures. All studies used only ECD livers except one which used both ECD and non-ECD (>60% ECD) (Krendl et al. 2025) and one which did not report this (Schlegel et al. 2023). Full results are presented in Table 4.1.

3RCTs reported rates at 6 months, all investigating hypothermic perfusion. 2 Liver Assist RCTs (1 DBD, 1 DCD) reported no statistically significant difference between arms, with inconsistent direction of effect (van Rijn et al. 2021c, Schlegel et al. 2023). 1 VitaSmart RCT (DBD) did not specify whether strictures were non-anastomotic or anastomotic. At 6 months, the rate of strictures was 4% in both arms (Ravaioli et al. 2022)).

2 studies reported rates at 1 year. 1 Liver Assist RCT (DBD) investigated hypothermic perfusion and reported a lower rate in the Liver Assist arm, though no statistical comparison was reported (16.5% vs 21.2% (Schlegel et al. 2023)). 1 *metra* retrospective cohort study (mixed DBD/DCD) investigated normothermic perfusion and reported no statistically significant difference, with a slightly higher rate in the *metra* arm (23.6% vs 18.4% p=0.245 (Krendl et al. 2025)).

Biliary leakage

3 studies (1 Liver Assist RCT, 1 VitaSmart RCT and 1 *metra* retrospective cohort study) reported the rate of biliary leakage. All studies used only ECD livers except the *metra* cohort study which used >60% ECD livers (Krendl et al. 2025).

The RCTs investigated hypothermic perfusion reported rates at 6 months. The Liver Assist RCT (DCD) reported no statistically significant difference between arms, although the rate was lower in the Liver Assist arm (risk ratio 0.69, 95% CI 0.22 to 2.13) (van Rijn et al. 2021c). The VitaSmart RCT (DBD) reported no significant difference, with a slightly higher rate in the VitaSmart arm (4% vs 2%, p=n.s.) (Ravaioli et al. 2022).

The *metra* retrospective cohort study (mixed DBD/DCD) investigated normothermic perfusion and reported similar rates of biliary leakage at 1 year (*metra* 11.5% vs SCS 12% p=0.881 (Krendl et al. 2025)).

Overall survival up to 1 year

6 studies (4 Liver Assist RCTs, 1 VitaSmart RCT and 1 *metra* matched case study) reported overall survival at 1 year. All RCTs included ECD livers except 1 (which did not report this (Schlegel et al. 2023)) and all investigated hypothermic perfusion. Full results are presented in Appendix D in Table D.1 .

None of the 4 Liver Assist RCTs (1 DCD and 3 DBD) reported a statistically significant difference between treatment arms and confidence intervals (CIs) were wide (van Rijn et al. 2021c, Lesurtel et al. 2025, Schlegel et al. 2023, Czigany et al. 2021).The VitaSmart RCT (DBD) reported no statistically significant difference between groups at 1 year (p=0.52, survival estimates not reported (NR)) (Ravaioli et al. 2022).

The *metra* matched-case study (mixed DBD/DCD and ECD/non-ECD) investigated normothermic perfusion and reported no significant difference between arms at 1 year (Fodor et al. 2021).

Among the studies that did not report data on overall survival there were 2 normothermic *metra* non-randomised comparative studies that reported absolute mortality data. 1 prospective cohort study (DBD, ECD NR) reported that 4 patients died due to graft failure by post-operative day 69, and that 3 patients died due to non-graft related reasons by 6 months (not reported separately by treatment cohort) (Vogt et al. 2024). 1 matched case study (mixed DBD/DCD, mixed ECD) reported that at median 18 days 1 (2.8%)

patient in the SCS arm died of sepsis, with no deaths occurring in the *metra* group (Mathis et al. 2024).

Overall survival at >1 year

Long term survival data (timepoints beyond 1 year) was reported by 3 Liver Assist RCTs (2 DBD and 1 DCD), all investigating hypothermic perfusion. Again, no statistically significant differences were reported between treatment arms, and the direction of effect was inconsistent across studies (van Rijn et al. 2021c, Grat et al. 2023, Czigany et al. 2021).

Graft survival up to 1 year

5 RCTs (4 Liver Assist and 1 VitaSmart) and 3 non-randomised comparative studies (*metra*) reported 1-year graft survival. All RCTs included ECD livers..

The 5 RCTs investigated hypothermic perfusion. The 4 Liver Assist RCTs (1 including DCD livers and 3 DBD livers) reported no statistically significant differences in graft survival, though graft survival was generally higher in the Liver Assist arm than the SCS arm in all trials (Lesurtel et al. 2025, van Rijn et al. 2021c, Schlegel et al. 2023, Czigany et al. 2021, Minor et al. 2022) (full outcome data is presented in Table 5.1). The VitaSmart RCT (DBD livers) reported statistically significantly improved graft survival at 1 year with VitaSmart compared with SCS (adjusted risk difference for graft failure 0.109 (95% CI 0.014 to 0.204) p=0.03) (Ravaioli et al. 2022).

The 3 *metra* non-randomised studies investigated normothermic perfusion included 2 cohort studies (1 using DCD livers, 1 using >80% DBD livers) and 1 matched-case study (using >80% DBD livers). None reported a statistically significant difference in graft survival at 1 year (Krendl et al. 2025, Fodor et al. 2021, Puttappa et al. 2025).

Graft survival at >1 year

5 studies (3 Liver Assist RCTs and 2 *metra* non-randomised comparative studies) reported graft survival at long term timepoints.

The 3 LiverAssist RCTs investigated hypothermic perfusion; 2 included ECD livers and 1 included mixed ECD and non-ECD livers (54% ECD) (Grat et al. 2023). Of 3 Liver Assist RCTs (1 DCD and 2 DBD), 1 RCT (DBD) reported a statistically significant difference in graft survival at 5 years in favour of Liver Assist (86.9% vs 51.9%, p=0.029 (Czigany et al. 2021)). No statistically significant findings were reported at any other timepoint or in the other trials, though survival was consistently higher in the Liver Assist arm (Grat et al. 2023, Czigany et al. 2021, van Rijn et al. 2021c).

The 2 *metra* non-randomised comparative studies (1 using DCD, 1 which did not report whether DCD or DBD livers were used) investigated normothermic perfusion and reported no statistically significant differences in graft survival at 3- (*metra* 73.1% vs SCS 73.9% (Krendl et al. 2025)) or 5- years (HR SCS vs *metra* 2.0, 95% CI 0.9 to 4.4 (Puttappa et al. 2025)).

Re-transplantation

Re-transplantation was reported only by RCTs investigating hypothermic perfusion. Re-transplantation at 1 year was reported by 3 Liver Assist RCTs (all DBD livers). None reported a statistically significant difference between treatment arms, though the rate of re-transplantation was consistently lower in the Liver Assist arms (Czigany et al. 2021, Lesurtel et al. 2025, Schlegel et al. 2023).

2 Liver Assist RCTs reported long term re-transplantation data (both hypothermic; 1 DCD and 1 DBD). Neither reported a statistically significant difference between treatment arms (Czigany et al. 2021, van Rijn et al. 2021c).

Acute Kidney Injury

1 *metra* matched case study (normothermic perfusion; mixed DBD/DCD and ECD/non-ECD liver) reported no statistically significant difference in the rate

of acute kidney failure, though rates were lower in the *metra* arm (8% vs 14% p=0.378) (Fodor et al. 2021).

Early allograft dysfunction

12 studies (6 Liver Assist RCTs, 2 VitaSmart RCTs and 4 *metra* non-comparative studies) reported early allograft dysfunction (EAD) defined according to the Olthof criteria (Olthoff et al. 2010). This criteria defines EAD as the presence of at least one of: serum bilirubin >10 mg/dl on postoperative day 7; international normalized ratio (INR) >1.6 on postoperative day 7; or AST or ALT >2.000 UI/ml with 7 postoperative days.

7 RCTs investigated hypothermic perfusion and all used ECD livers except 1 trial which did not report this (Schlegel et al. 2023). 5 LiverAssist RCTs investigated hypothermic perfusion of which 2 RCTs reported statistically significantly lower rates of EAD in Liver Assist arm compared with SCS: 1 (DCD) reported an adjusted risk ratio of 0.61 (95% CI 0.39 to 0.96) (van Rijn et al. 2021c) and 1 (DBD) reported a rate of 17.6% vs 30.5% (p=0.014) (Lesurtel et al. 2025). The other 3 trials reported no statistically significant difference, rates were lower in the Liver Assist arms (Minor et al. 2022, Schlegel et al. 2023, Czigany et al. 2021).

2 VitaSmart RCTs, both investigating hypothermic perfusion of ECD livers, reported statistically significantly lower rates of EAD with VitaSmart. 1 RCT (DCD) reported a risk difference of 0.54 (95% CI 0.35 to 0.85, p=0.007) and the other trial (DBD) reported an adjusted risk difference of 0.218 (95% CI 0.065 to 0.372, p=0.005) (Ravaioli et al. 2022).

5 studies (1 LiverAssist RCT and 4 *metra* non-randomised comparative studies) investigated normothermic perfusion. 1 LiverAssist RCT did not report a statistical comparison of the rate of EAD, though the rate was higher in the Liver Assist arm (20% vs 10%) (Ghinolfi et al. 2019).

4 *metra* non-randomised comparative studies reported EAD, all including a mix of ECD/non-ECD livers except 1 study which did not report this (Vogt et al. 2024). None reported a statistically significant difference between arms. In

3 studies (1 DBD and 2 mixed DCD/DBD) the rates were lower in the *metra* arm (Vogt et al. 2024, Krendl et al. 2025, Fodor et al. 2021)) and in 1 matched case study (DBD) rates were higher in the *metra* arm (Hann et al. 2022).

Model for Early Allograft Function (MEAF)

The Model of Early Allograft Function (MEAF) score is a continuous 0–10 grading system used to assess the severity of EAD within the first 3 days post-liver transplant, and is calculated using bilirubin, International Normalised Ratio and ALT levels (Pareja et al. 2015). 1 Liver Assist RCT (hypothermic; DBD; mixed ECD/non-ECD livers) reported no significant difference in MEAF score (Liver Assist mean 4.94 standard deviation (SD) 1.72 vs SCS mean 5.49 SD 2.14, p=0.24) (Grat et al. 2023).

1 *metra* retrospective cohort study (normothermic; DCD and ECD livers) reported a significantly higher (indicating worse symptoms of EAD) score in the SCS arm compared with both the *metra* and regional perfusion followed by SCS arm (SCS median 5.8 IQR 4.8 to 7, *metra* 3.3, 2.1 to 5.2, NRP then SCS 4.1, 2.8 to 5.4, p<0.001) (Puttappa et al. 2025).

Primary non-function

13 studies (6 Liver Assist RCTs, 2 VitaSmart RCTs and 4 *metra* non-randomised comparative studies) reported primary non-function (PNF) of the liver graft. The clinical experts noted that the definition of PNF can be inconsistent in the literature. Among the prioritised studies the definition varied; in 4 RCTs (2 LiverAssist, 2 VitaSmart) PNF was defined as graft loss or patient death within 7 days and in 1 *metra* matched case study it was defined as peak AST ≥ 3000 IU/L plus at least one of either International Normalised Ratio ≥2.5, serum lactate ≥4 mmol/L, and total bilirubin ≥ 10 mg/dL on day 3 post-transplant (Krendl et al. 2025). The remaining studies did not report how PNF was defined. It is therefore difficult to interpret the PNF results across studies.

7 RCTs used hypothermic perfusion, of which all used ECD livers except 1 trial that used both ECD and non-ECD livers (Grat et al. 2023) and 1 trial that

did not report this (Schlegel et al. 2023). Full outcome data is presented in in Appendix D Table D.2.

5 LiverAssist trials investigated hypothermic perfusion (4 DBD, 1 DCD), of which 1 RCT (DBD) reported significantly lower liver graft loss due to PNF in the Liver Assist arm (0% vs 2.5%, p=0.015 (Schlegel et al. 2023)). The other RCTs reported no significant differences between arms, though rates were either equal across arms or lower in the Liver Assist arm (van Rijn et al. 2021c, Czigany et al. 2021, Lesurtel et al. 2025, Ghinolfi et al. 2019, Grat et al. 2023)).

Neither VitaSmart RCT (1 mixed <30% DCD, 1 DBD) reported significant differences between arms, though rates were lower for VitaSmart (0% vs 0.9% (Reich et al. 2024b), 0% vs 4% p=0.49 (Ravaioli et al. 2022)).

5 studies investigated normothermic perfusion (1 LiverAssist RCT and *metra* 4 non-randomised comparative studies). The LiverAssist RCT (DBD, ECD livers) reported no occurrence of PNF in either arm (Ghinolfi et al. 2019).

Of the 4 *metra* non-randomised comparative studies (1 DCD, 1 DBD and 2 mixed DBD/DCD) 1 study included ECD livers (Puttappa et al. 2025) and 3 studies (Fodor et al. 2021, Hann et al. 2022, Krendl et al. 2025) included both ECD and non-ECD livers. 1 cohort study (mixed DCD/DBD) reported a significantly lower rate of PNF in the *metra* arm compared with SCS (0% vs 2.5%, p=0.05 (Krendl et al. 2025)); notably this study included significantly more DCD and ECD livers in the *metra* arm than SCS arm (both p<0.001). None of the other *metra* studies reported a significant result, though rates were either equal or lower in the *metra* arm (Fodor et al. 2021, Hann et al. 2022, Puttappa et al. 2025)).

Patient and caregiver health-related quality of life and healthcare professional satisfaction/wellbeing

None of the prioritised studies reported data relating to liver transplant patient and caregiver health-related quality of life or healthcare professional satisfaction or wellbeing.

Other outcomes

Hepatic artery thrombosis

11 studies reported rates of HAT (7 Liver Assist RCTs, 1 VitaSmart RCT and 3 *metra* non-randomised comparative studies). 7 studies investigated hypothermic perfusion (6 LiverAssist RCTs and 1 VitaSmart RCT). The timepoint at which HAT was reported was not clear across studies; 2 RCTs reported HAT among other complications reported as having occurred by 90 days (Czigany et al. 2021, Lesurtel et al. 2025), 2 among complications having occurred by 6 months (van Rijn et al. 2021c, Ravaioli et al. 2022), 1 within overall outcomes having measured by 12 months(Schlegel et al. 2023), and 1 did not report the timepoint (Grat et al. 2023). 1 reported that 1 individual experience HAT at post-operative day 1 (Minor et al. 2022). Of 6 Liver Assist RCTs (6 DBD, 1 DCD,) 5 included ECD livers, 1 included mixed ECD and non-ECD livers (Grat et al. 2023) and 1 did not report this (Schlegel et al. 2023). None reported a statistically significant difference between arms. The direction of effect was inconsistent across the trials and rates were generally low (van Rijn et al. 2021c, Czigany et al. 2021, Minor et al. 2022, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)).

The VitaSmart RCT (ECD livers; hypothermic perfusion; DBD) reported slightly higher rates in the VitaSmart arm but found no statistically significant difference between arms (VitaSmart 2% vs SCS 0% p=n.s.) (Ravaioli et al. 2022).

4 studies (1 LiverAssist RCT and 3 *metra* non-randomised comparative studies) investigated normothermic perfusion. The timepoint at which HAT was reported was not clear across studies; 1 cohort study reported HAT among other complications having occurred by 30 days (Krendl et al. 2025), 1 matched case series reported HAT among outcomes experienced during the hospital stay (mean 17 to 23 days) (Fodor et al. 2021) and 1 matched-case

study did not report the timepoint. The LiverAssist RCT (DBD, non-UK setting, ECD livers) reported that 1 patient experienced HAT on post-operative day 9 and did not test the statistical significance of the difference in rate of HAT between arms (Ghinolfi et al. 2019).

The 3 *metra* studies all included both ECD and non-ECD livers (1 DBD, 2 mixed DCD/DBD). 1 study reported a significantly lower rate of arterial thrombosis in the *metra* arm (0% vs 7%, p=0.042 (Fodor et al. 2021)). Results were not statistically significant in the other 2 studies and did not have a consistent direction of effect (Krendl et al. 2025, Hann et al. 2022)).

Post-reperfusion syndrome

7 studies (4 Liver Assist RCTs, 1 VitaSmart RCT and 2 *metra* non-randomised comparative studies) reported in-hospital PRS. The clinical experts noted that the definition of PRS can be inconsistent in the literature. The definition varied across studies; 4 studies (2 LiverAssist RCTs and 2 *metra* non-randomised comparative studies) defined PRS as ≥30% decrease in mean arterial pressure in the first 5 minutes after reperfusion (van Rijn et al. 2021c, Grat et al. 2023, Mathis et al. 2024, Puttappa et al. 2025), 1 LiverAssist RCT defined it as a ≥50% decrease in median arterial pressure in the first 5 minutes after reperfusion and 1 VitaSmart RCT defined it as a decrease of ≥30% in the mean arterial blood pressure post-reperfusion or the need for aminic support to maintain hemodynamic stability (Ravaioli et al. 2022). It is therefore difficult to interpret PRS results across studies.

6 studies investigated hypothermic (3 LiverAssist, 1 VitaSmart RCT and 2 *metra* non-randomised comparative studies). The 3 Liver Assist trials included DBD livers and all used ECD livers except 1 trial that used both non-ECD and ECD livers (Grat et al. 2023). 1 RCT (DCD) reported a statistically significantly lower rate of PRS in the Liver Assist arm (adjusted risk ratio 0.43, 95% CI 0.20 to 0.91 (van Rijn et al. 2021c)). The other trials reported no statistically significant differences and inconsistent effect directions (Lesurtel et al. 2025, Grat et al. 2023)).

The VitaSmart RCT (hypothermic perfusion; ECD livers; DBD) reported no statistically significant difference, with a higher rate in the VitaSmart arm (55% vs 47% p=0.45) (Ravaioli et al. 2022).

3 studies (1 LiverAssist RCT and 2 *metra* non-randomised comparative studies) investigated normothermic perfusion. The LiverAssist RCT (DBD, ECD livers) reported no statistically significant difference in the rate of PRS (Ghinolfi et al. 2019).

Of the 2 *metra* non-randomised comparative studies, 1 retrospective cohort study (ECD and DCD livers) reported a significantly lower rate of PRS in the *metra* arm (odds ratio SCS vs *metra*: 3.3, 95% CI 1.5 to 7.6, p=0.004 (Puttappa et al. 2025)). The other study, a retrospective cohort study (mixed DCD/DBD and ECD/non-ECD livers) reported no significant difference, though rates were lower in the *metra* arm (5.6% vs 13.9%, p=0.651) (Mathis et al. 2024).

Post-operative requirement for renal replacement therapy

7 studies (3 LiverAssist RCTs, 1 VitaSmart RCT and 3 *metra* matched-case studies) reported the requirement for renal replacement, with timepoints ranging from 90 days to 6 months.

All 4 RCTs investigated hypothermic perfusion (van Rijn et al. 2021c). Reported timepoints ranged from 90 days to 6 months. None reported a significant difference in the requirement for renal replacement (van Rijn et al. 2021c, Czigany et al. 2021, Lesurtel et al. 2025, Ravaioli et al. 2022)The 3 *metra* matched-case studies were all conducted in the UK and investigated normothermic perfusion. None reported significant differences in the need for renal replacement therapy (Mathis et al. 2024, Hann et al. 2022, Puttappa et al. 2025). The reported timepoints were unclear.

Alanine Transaminase Levels

7 studies (5 Liver Assist RCTs and 2 *metra* non-randomised comparative studies) reported peak alanine transaminase levels within 7 days of transplant.

4 Liver Assist RCTs investigated hypothermic perfusion, all of which included DBD livers2 included ECD livers, 2 included mixed ECD and non-ECD livers and 1 did not report this. 2 trials (both DBD) reported significantly lower levels (indicating better condition) in the Liver Assist arm (median 418 IU/L IQR 221 to 828 vs median 796 IU/L IQR 1195, p=0.03 (Czigany et al. 2021) and median difference -21% p=0.021 (Lesurtel et al. 2025)). The other trials reported no statistically significant difference between arms, (Schlegel et al. 2023, Grat et al. 2023).

3 studies (1 LiverAssist RCT and 2 *metra* non-randomised comparative studies) investigated normothermic perfusion. The LiverAssist RCT (DBD, ECD livers) reported no statistically significant difference in alanine transaminase levels (Ghinolfi et al. 2019). The 2 *metra* non-randomised comparative studies investigated normothermic perfusion. 1 retrospective cohort study (DCD) reported that levels were statistically significantly higher in the SCS arm compared with both *metra* and NRP followed by SCS arms (p<0.001) (Puttappa et al. 2025). 1 matched case study (DBD) reported no statistically significant difference, though the level was lower in the *metra* arm compared with both SCS arms (Hann et al. 2022).

Aspartate transaminase level

6 Liver Assist RCTs reported peak aspartate transaminase levels within 7 days of transplant.

5 LiverAssist RCTs investigated hypothermic perfusion, of which 3 trials included ECD livers (Czigany et al. 2021, Minor et al. 2022, Lesurtel et al. 2025), 1 included both ECD and non-ECD livers (Ghinolfi et al. 2019, Grat et al. 2023) and one did not report whether livers were ECD or not (Schlegel et al. al. 2023).

1 RCT (DBD) reported statistically significantly lower peak levels in the Liver Assist arm (median difference: -24%, 0.009) (Lesurtel et al. 2025). None of the other trials reported a statistically significant difference. Where reported, peak levels were lower in the Liver Assist arm in all trials investigating hypothermic perfusion (Czigany et al. 2021, Minor et al. 2022, Schlegel et al. 2023)) (full outcome data is presented in Table D.3). 1 trial did not report the endpoint data, reporting only that there was no significant difference (p=0.5) (Grat et al. 2023).

1 LiverAssist RCT (DBD, ECD livers) investigated normothermic perfusion and reported no statistically significant difference in aspartate transaminase levels (Ghinolfi et al. 2019).

5.3 Adverse events and clinical risk

Serious Adverse Events (Clavien-Dindo grade ≥3)

2 Liver Assist RCTs (both hypothermic, 1 DCD, ECD livers and 1 DBD livers, NR if ECD;) reported serious adverse events (SAEs) at 1 year. Both reported no significant difference in the rate of SAEs (50% vs 53% p=0.749 (van Rijn et al. 2021c); adjusted odds ratio 0.874, 95% CI 0.46 to 1.67, p=0.68 (Schlegel et al. 2023)).

1 VitaSmart RCT (hypothermic; ECD; mixed <30% DCD) reported no significant difference in SAEs at 6 months (44% vs 54%, p=not significant (Reich et al. 2024b)).

4 Liver Assist RCTs (all hypothermic; 3 DBD livers, 1 NR; 3 ECD livers, 1 mixed ECD/non-ECD) reported SAEs at 3 months post-transplant. 1 trial (DBD) reported a statistically significantly lower rate of SAEs in the Liver Assist arm (44% vs. 74% p=0.036 (Czigany et al. 2021)). None of the other trials reported a statistically significant difference, though SAE rates were consistently lower in the Liver Assist arm Liver Assist: 40% vs 75% (Minor et al. 2022); 52.4% vs. 61.5% p=0.15 (Lesurtel et al. 2025); 30.8% vs. 46.2% p=0.25 (Grat et al. 2023)).

Only 1 study reported long-term SAE rates. This Liver Assist RCT (hypothermic; DBD; ECD) reported a statistically significantly lower rate of SAEs in the Liver Assist arm at a median 48-month follow-up (43% vs 85% p=0.009 (Czigany et al. 2021)).

Device-related adverse events

None of the prioritised studies reported device-related adverse events.

Mechanical failure of machine perfusion technology

2 Liver Assist RCTs reported the rate of machine failure. 1 RCT (hypothermic; ECD; DCD) reported that in 1/78 perfusions in the Liver Assist arm there was a malfunctioning pressure sensor due to user error, with no injury to the liver (van Rijn et al. 2021c). 1 RCT (hypothermic; NR if ECD/non-ECD; DBD) reported 4 device malfunctions in 88 machine perfusions, resulting in insufficient portal perfusion flow in 3 cases and excessive perfusion (>400 ml/min) in 1 case; no injury to the livers was reported (Schlegel et al. 2023).

5.4 Subgroup data

The decision problem included children and young people (CYP), sequential use of normothermic regional and ex situ machine perfusion and patients undergoing transplants with logistical considerations that may require cold ischemia times in excess of acceptable limits in the absence of the use of machine perfusion (e.g. split liver surgeries, prolonged preservation to allow daylight hour surgery, multi-organ transplants etc.) as subgroups of interest. 1 prioritised study reported evidence on normothermic regional perfusion. No evidence in CYP patients or patients undergoing extended perfusion was identified in the prioritised studies. The deprioritised included studies were re-screened for any evidence on these subgroups, but only limited evidence was identified.

Sequential use of normothermic regional and ex-situ machine perfusion

2 studies on the use of sequential NRP and ex situ machine perfusion were identified among the deprioritised studies. This included a LiverAssist RCT which randomised DCD ECD livers (all donors aged >70 years) to either NRP followed by DHOPE (n=6) or NRP followed by NMP (n=5) (Torri et al. 2024). The trial reported no significant differences in the rate of EAD, PNF, grade ≥3 adverse events or 3 month graft survival. 1 LiverAssist retrospective case series was also identified in which 34 DCD livers underwent NRP followed by ex situ machine perfusion, of which 20 were considered eligible following NRP and perfused ex situ (Ghinolfi et al. 2021). 18 livers were ultimately transplanted. No recipients experienced PNF, 4 (44%) experienced PRS, 5 (28%) experienced EAD and 5 (28%) experienced acute kidney injury. There was one patient death within the median follow-up of 15.1 months.

Normothermic regional perfusion without sequential machine perfusion

1 prioritised *metra* retrospective cohort study (UK, DCD livers) included 3 cohorts of livers preserved by *metra*, SCS and NRP followed by SCS. This study reported statistically significantly greater graft survival at 5 years in the NRP SCS cohort compared to the SCS cohort (hazard ratio 2.4, 95% CI 1.1 to 5.4, p=0.028) (Puttappa et al. 2025). In hospital PRS was statistically significantly higher in the SCS cohort compared to the NRP then SCS cohort (hazard ratio 4.9, 95% CI 2.2 to 11.4, p<0.001). The SCS cohort had statistically significantly higher median alanine transaminase levels (*metra* 360, SCS 697, NRP SCS 508 units per litre) and median MEAF scores (*metra* 3.3, SCS 5.8, NRP SCS 4.1) within 7 days, and rates of acute kidney injury (*metra* 28%, SCS 47%, NRP SCS 29%) compared to both the *metra* and NRP SCS cohorts. No significant difference was reported for PNF or requirement for renal replacement therapy (Puttappa et al. 2025).

Among the deprioritised studies, 8 studies were identified which examined NRP. These studies were not prioritised because they were either smaller, non-comparative studies or because it was not clear that the comparator arm ex-situ machine perfusion was used after SCS initiated at the recipient centre.

Studies took place in Italy and France, but one study on *metra* (Hunt et al. 2022) took place in the UK, this was a non-comparative cohort study including 57 livers. A further study was a multicentre retrospective study including some UK centres (Mohkam et al. 2021) which compared NRP with subsequent SCS to continuous machine perfusion following only short-term SCS at the donor centre.. Prospective, comparative studies in a UK context with NRP included in the end-ischaemic pathway would be beneficial, as NRP becomes more commonly used in transplant centres in the UK.

Paediatric patients

2 studies reported on machine perfusion in paediatric patients. 1 Liver Assist cohort study assessed 16 split liver transplantations in which 1 cohort received grafts split conventionally in cold storage and 1 cohort received grafts split concurrently with DHOPE perfusion (Rossignol et al. 2022). The study included 20 paediatric patients, 12 of whom received livers split during SCS and 8 of whom received livers split during HOPE. Baseline patient characteristics were similar. The study reported no significant differences between groups in: EAD, PNF and alanine or aspartate transaminase levels at 7 days; grade ≥3 complications, biliary complications (including non-anastomotic and anastomotic strictures), acute kidney injury and HAT at 90 days; patient survival and graft survival at 90 days and median 7.5 months. Other outcomes such as organ utilisation, waitlist duration, waitlist mortality and health-related quality of life were not reported.

1 case series was reported only in a conference abstract that included a single paediatric patient. The patient underwent complex transplantation with re-operation for planned delayed completion of the biliary anastomosis, hematoma evacuation, and subsequent duodenal and colonic repair and did

not experience PNF, EAD or biliary complications (Todd et al. 2023).(Krendl et al. 2024)

Transplantations with complex logistical considerations and involving extended perfusion

6 studies were identified evaluating machine perfusion using named devices in extended preservation scenarios, either with extended perfusion durations or extended total preservation with longer SCS duration enabled by the subsequent use of machine perfusion (Calderon et al. 2024b, Calderon et al. 2024a, Cardini et al. 2020, De Carlis et al. 2025, Bruggenwirth et al. 2024, Rossignol et al. 2022). Of these, 4 studies were in the perfusion initiated at the recipient centre pathway (Cardini et al. 2020, De Carlis et al. 2025, Bruggenwirth et al. 2024, Rossignol et al. 2022) and are summarised below.

2 were comparative Liver Assist studies comparing cohorts of patients undergoing different durations of perfusion:

1 non-randomised trial (n=24) compared DHOPE in which donor hepatectomy finished between 16:00 and 03:59 the day prior to transplant (median 9.3, range 8.0 to 10.1 hours) to DHOPE in which donor hepatectomy was finished between 04:00 and 15:59 the day of the transplant (median 2.2, range 2.0 to 2.4 hours), and reported no differences in efficacy (no EAD, death or graft failure occurred or non-anastomotic biliary strictures occurred in either group) or safety (serious device-related AE: 3/12 control vs 3/12 prolonged p=1, Clavien-Dindo grade >IIIb 5/12 control vs 4/12 prolonged, p=NR) (Bruggenwirth et al. 2024).

1 retrospective cohort study (n=354) compared one cohort with <4 hours of DHOPE to another with >4 hours of DHOPE, and reported no significant differences between groups in efficacy (EAD, PNF, PRS, biliary complications, overall survival or graft survival at 3 months) with the exception of acute kidney injury (30.5% prolonged vs 44.6% short, p=0.008) (De Carlis et al. 2025).

1 was a Liver Assist cohort study assessing 16 split liver transplantations in which 1 cohort received grafts split conventionally in cold storage and 1 cohort received grafts split concurrently with DHOPE perfusion (Rossignol et al. 2022). This study reported that splitting the liver graft within DHOPE allowed a significant reduction of SCS time (median 472 IQR 410 to 516 minutes vs. 544 IQR 508 to 581 minutes, p=0.001) and a significant increase in total ex vivo preservation time (median 595 IQR 562 to 639 minutes vs 544 IQR 508 to 581 minutes p=0.007), with no differences in efficacy (no significant differences in EAD, PNF, transaminase levels, acute kidney injury or overall or graft survival) or safety (no difference in liver graft–related adverse event per recipient or Clavien-Dindo grade >III AEs).

1 study was a *metra* case series reporting 25 cases of *metra* in an Austrian centre. 9 of these cases underwent prolonged perfusion due to a marginal liver graft, while 16 underwent prolonged perfusion due to logistical considerations (such as multiple-organ transplant) and/or surgical complexity in the recipient (in some cases also with marginal liver grafts). Mean machine perfusion time was 816.4 minutes (SD 386) and mean total preservation time was 1213.3 minutes (426.5) {Cardini, 2020 #971}. No comparative data was reported.

5.5 Clinical evidence summary and interpretation

15 studies that provided clinical evidence for machine perfusion of liver grafts were prioritised. Studies were prioritised for extraction on the basis of evidence quality for each device (RCT evidence was prioritised over non-randomised evidence if available, then non-randomised comparative evidence over single-arm evidence if available, etc.). Therefore there may be further evidence on the relevant outcomes in the deprioritised studies that has not been extracted and summarized in this report.

There was limited evidence for a number of the key outcomes identified by the clinicians among the prioritised studies. Notably no or limited evidence was

identified for organ utilisation, waitlist size and duration, waitlist mortality, healthcare practitioner satisfaction, patient and caregiver health-related quality of life, and device-related adverse events.

Evidence was identified for overall survival, graft survival, biliary complications, EAD and re-transplantation.

8 studies investigated hypothermic perfusion (6 LiverAssist RCTs and 2 VitaSmart RCTs). The hypothermic perfusion evidence base consistently shows statistically significant differences favouring machine perfusion over SCS in 7 day EAD (3 RCTs (van Rijn et al. 2021c, Lesurtel et al. 2025, Reich et al. 2024b), 2 of which were powered for this outcome (Lesurtel et al. 2025, Reich et al. 2024b)). The evidence was less conclusive, with only 1 or 2 studies reporting a significant finding among non-significant findings mostly favouring machine perfusion, for PNF (1 RCT (Schlegel et al. 2023)), aspartate aminotransferase levels (1 RCT (Lesurtel et al. 2025)), non-anastomotic biliary strictures (1 LiverAssist RCT at 6 months and 5 years) (van Rijn et al. 2021c), and graft survival (1 VitaSmart RCT at 1 year (Ravaioli et al. 2022) and 1 Liver Assist RCT at 5 years, (Czigany et al. 2021)). No significant differences were reported for overall survival or re-transplantation in the studies investigating hypothermic perfusion.

7 studies investigated normothermic perfusion (1 LiverAssist RCT and 6 *metra* non-randomised comparative studies). 1 cohort study reported a significant difference for each of EAD and alanine transaminase levels (Puttappa et al. 2025) and PNF (Krendl et al. 2025). No statistically significant findings were reported for non-anastomotic biliary strictures, overall survival, graft survival, re-transplantation or EAD in the studies investigating normothermic perfusion.

Evidence was identified for other outcomes than those identified as key by clinicians.

Among the hypothermic perfusion studies 2 RCTs reported significant differences in alanine transaminase levels favouring machine perfusion (2 RCTs (Lesurtel et al. 2025, Czigany et al. 2021), 1 of which was powered for

this outcome (Czigany et al. 2021), with non-significant findings in the other RCTs generally favouring machine perfusion. 1 RCT reported a statistically significant finding in favour of machine perfusion for PNF (Schlegel et al. 2023), aspartate aminotransferase levels (Lesurtel et al. 2025) and PRS (van Rijn et al. 2021c), though non-significant findings in the other trials did not have a consistent direction of effect. Among the normothermic perfusion studies 1 cohort study reported statistically significantly lower alanine transaminase levels (Puttappa et al. 2025) in the *metra* arm, with non-significant findings in the other studies generally favouring machine perfusion. Statistically significant findings favouring *metra* were reported for HAT (Fodor et al. 2021) by a matched case study and PRS (Puttappa et al. 2025) by a retrospective cohort study, though non-significant findings across other studies did not have a consistent direction of effect.

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The evidence suggests that machine perfusion is not associated with more AEs than SCS. 2 Liver Assist RCTs reported a statistically significantly lower rate of serious adverse events, 1 at 3 months (Czigany et al. 2021) and 1 at median 48 months post-transplant (Czigany et al. 2021). Findings in other studies and at other timepoints were non-significant, though the rate of SAEs was consistently lower in the machine perfusion arm.

One of the use cases for machine perfusion is the potential to increase the utilisation of high risk ECD livers, and DCD livers in particular. A majority of studies included ECD livers. However, the ECD criteria varied and evidence in DCD livers specifically was more limited. Only 2 of 15 prioritised studies included DCD livers specifically (in a further 3 studies a minority of grafts were DCD, <20%), though their findings suggest that machine perfusion may improve rates of graft-related complications compared with SCS. These comprised 1 Liver Assist RCT (van Rijn et al. 2021c) and 1 *metra* retrospective cohort study (Puttappa et al. 2025), all of which reported statistically significantly lower rates of EAD with perfusion compared with SCS. The Liver Assist RCT also reported significantly lower rates of PRS (as

did the *metra* cohort study (Puttappa et al. 2025)) and non-anastomotic strictures (van Rijn et al. 2021c).

metra is designed for normothermic perfusion and VitaSmart is designed for hypothermic perfusion, and thus all studies of these technologies assessed perfusion in their respective modes. Liver Assist and PerLifePRO are the only technologies that allows both modes of perfusion (though no studies assessing PerLifePRO were identified); all Liver Assist RCTs assessed hypothermic perfusion except 1 which assessed normothermic perfusion (Ghinolfi et al. 2019). The evidence in favour of machine perfusion was more robust for hypothermic perfusion specifically. There were more statistically significant findings in favour of machine perfusion in the hypothermic trials and 2 outcomes (EAD and alanine transaminase levels) with such findings across multiple trials; however, the clinical experts have noted that transaminase level (and EAD as an outcome partly defined by transaminase levels) is less useful as an outcome in the era of machine perfusion and particular in normothermic machine perfusion. Therefore these results may not be clinically meaningful. For normothermic perfusion all statistically significant findings were reported in single, non-RCT studies.

The EAG identified the following concerns around the clinical evidence.

- Only 4 studies were conducted in the UK, with 2 of these studies being RCTs only partly conducted in UK settings among others across Europe. Although not all studies were conducted in a UK setting, all were conducted in the pathway with perfusion initiated at the recipient centre. Advice from clinical experts suggested that these studies would therefore be broadly applicable to the UK setting, with caveats around possible differences in donor case-mix, logistics, cold ischaemia times, allocations and peri-operative pathways.
- Long-term evidence (outcomes reported at >2-year timepoints) was limited.
- The decision problem included children and young people (CYP) and patients undergoing extended perfusion as subgroups of interest. No evidence in these subgroups was identified in the prioritised studies. The

deprioritised included studies were re-screened for any evidence on these subgroups, but only limited evidence (case series and retrospective cohort studies, much of which was not in the perfusion initiated at the recipient centre pathway) was identified. Some evidence was identified in 2 comparative studies that prolonged perfusion in Liver Assist is not inferior to conventional perfusion in efficacy or safety, though further evidence generation would be required to demonstrate this conclusively.

- Transplant utilisation rate was reported by only 2 studies (Krendl et al. 2025, Fodor et al. 2021). This is likely because the prioritisation of interventional studies, and randomised controlled trials (RCTs) in particular, as livers were allocated to a perfusion method after having been assessed and accepted at the transplant centre in all trials.

6. Economic evidence

6.1 Existing economic evidence

A single set of searches was conducted to identify both clinical and economic evidence (see Section 4.1). Search methods are reported in Appendix A Search strategies.

Studies were screened using the methods and eligibility criteria described in the published protocol.

6.1.1 Relevant economic models

A total of 15 studies were identified as reporting economic evidence. Of these studies, 4 were prioritised for further data extraction (Table 6.1). The studies assessed Liver Assist, *metra* and VitaSmart and are summarised in Table 6.2. No studies were identified that evaluated PerLifePRO. For each intervention, studies were prioritised on the basis of evaluation type such that full economic evaluations were prioritised over partial economic evaluations. Evaluations in a UK and/or European setting were prioritised where possible.

Table 6.1: Summary of prioritised studies

Study ID	Perfusion type	Device use	Setting	Analysis
Liver Assist				
Endo et al 2025 (Endo et al. 2025)	HMP (DHOPE)	Intended to be used at the recipient hospital	Netherlands	Cost effectiveness analysis
metra				

Webb et al 2022 (Webb et al. 2022)	NMP	Assumed to be initiated at the recipient hospital	Canada	Cost utility analysis
Liver Assist and *metra*				
Zimmerman et al 2022 (Zimmermann and Carter 2022)	HMP (Liver Assist) NMP (*metra*)	Liver Assist is intended to be used at the recipient hospital *metra* was assumed to be initiated at the recipient hospital	UK	Cost utility analysis
VitaSmart				
Axelrod et al 2025 (Axelrod et al. 2025)	HMP (HOPE)	Intended to be initiated at the recipient hospital	US	Cost consequence analysis

The prioritised studies comprised 4 papers (Axelrod 2025 (Axelrod et al. 2025), Endo 2025 (Endo et al. 2025), Webb 2022 (Webb et al. 2022) and Zimmerman 2022 (Zimmermann and Carter 2022)), 1 of which was a Letter where the results and interpretation were limited and the peer review process was unclear (Zimmerman 2022) and 1 a conference abstract (Axelrod 2025) where all details of the study were very limited. One company, *metra*, provided an economic model as part of their company submission which is critiqued in Section 6.1.2. A paper was published on a previous version of this model (Javabakht 2020), however, the paper was excluded from the review due to being out of scope. None of the other companies submitted their own economic evidence.

3 economic evaluations used a Markov model structure (Endo 2025, Webb 2022, Zimmerman 2022) and 1 study used was a trial-based cost effectiveness analysis. The time horizon used across the selected studies ranged from 1 year post transplant to lifetime. The cycle length used in the studies employing a Markov model structure varied from monthly to yearly.

Axelrod 2025 did not explicitly state a time horizon; the reported evidence suggested a 1-year time horizon. Similarly, Axelrod 2025 did not report the cycle length. The sub-group analyses within these papers were varied. Axelrod 2025 stratified its analysis by DCD and DBD donors. The Endo 2025 analysis was for DCD only. Zimmerman 2022 stated that due to a paucity in data, subgroup analysis of DCD, DBD and ECD livers was not possible. Webb 2022 did not explicitly assess livers by DCD or DBD categories, however the analysis was focused on ECD livers.

Endo 2025 conducted a trial-based cost-effectiveness analysis (hospital perspective) using Dutch data from the DHOPE-DCD trial comparing DHOPE (using Liver Assist) versus SCS in DCD liver transplantation. DHOPE was dominant: it was less costly than SCS (approximately €15,000 lower overall per patient) and slightly more effective (an incremental 0.4 graft survival years per patient). The cost savings were driven by a 12.2% reduction in downstream healthcare consumption. The minimal number of annual procedures required for DHOPE to be cost-effective ranged from 1 (in the basic cost scenario) to 30 (when including all personnel and dedicated unit costs).

Webb 2022 was a cost utility analysis (public healthcare payer perspective) of incorporating OrganOx (*metra*), a NMP device, into a Canadian liver transplant program alongside SCS. The study compared NMP after SCS versus SCS alone, where NMP was assumed to be initiated at the recipient hospital. NMP was used was at the discretion of the surgeon for ECDs (the base case health state transition probability for transplant by NMP in the NMP strategy in the model was 0.15). The authors concluded that NMP plus SCS dominated SCS alone, i.e. was both more effective and cost less (ICER for SCS vs NMP plus SCS: $-198,577 per QALY gained). This was driven by additional livers being transplanted (meaning less time on the liver transplant list and a decrease in deaths whilst on the waitlist).

Zimmerman 2022 conducted a cost utility analysis (public healthcare payer perspective) of NMP (*metra*) and HMP (Liver Assist) ex-situ machine

perfusion, each compared with current practice (SCS) for liver transplantation in the NHS in the UK. Both technologies were modelled as being initiated at the recipient hospital. The study concluded that, in the base case, both machine perfusion devices were more costly and less effective than SCS. The ICER for NMP (*metra*) vs SCS was £204,059.25 per QALY gained; the ICER for HMP (Liver Assist) vs SCS was £1,089,783.06 per QALY gained. The high ICER value was attributable to marginal QALY difference. Deterministic sensitivity analysis (DSA) was used to explore the results further: alternate data for long-term outcomes (EAD and PNF), varying discount rates (using the NICE reference case), and varying the time horizon (unspecified). High and low estimates for parameters were sourced from the 95% confidence interval (95% CI) where available, or were varied by +/-10% where 95% CI was not available. DSA determined that neither interventions achieved cost effectiveness in any of the scenarios. DSA demonstrated that NMP (*metra*) and HMP (Liver Assist) were dominated by SCS when organ utilisation using each intervention was decreased. The variables that had the most impact on the ICER were the risk ratios of EAD (increased by 80% and decreased by 45% based on a SR and meta-analysis Jia 2020), probability of organ utilisation (+/-10%) and the data source for the long-term outcomes (Lee 2016, 1 year and 5 year outcomes). The authors noted the findings were different to an evaluation (Javanbakht 2020) that reported *metra* to be cost-effective vs current practice in a UK setting. The authors outlined a key difference between the analyses as where Javanbakht was a trial-based assessment (including using organ utilisation data from a publication assessed as having a high risk of bias by Zimmerman), Zimmerman drew effectiveness data from a systematic review (though did also state a limitation of their analysis was the availability of data inputs). The authors identified the following as key model inputs that might enable a future re-evaluation: organ utilisation and long-term outcomes and costs. A comparison of Zimmerman 2022 with the modelling approach for this assessment is detailed in Section 6.4.1.

Axelrod 2025 reported a cost consequence analysis of HOPE (VitaSmart) vs SCS in liver transplantation in the US. It reported HOPE resulted in a total

estimated 1-year cost reduction of $28,565 vs SCS per liver transported due to reduced hospitalisation stay and decreasing late complications (biliary complications, graft failure and death) and possibly increased utilisation of organs, reduced staff overtime and fewer end-stage disease transplants. Savings were greater for DCD donors than DBD donors. No specific factor was attributed to this.

Table 6.2: Included economic evaluations

Study author, design, location, cost year/currency	Intervention(s), comparator(s), DCD/DBD, ECD, extended perfusion	Population and key data sources	Model structure	Relevant outcomes	EAG comments
Liver Assist					
Author, year: Endo, 2025 Design: Cost effectiveness analysis Modelled location: The Netherlands Cost year and currency: 2019 EUR	Intervention: DHOPE (Liver Assist) Comparator: SCS DCD/DBD: DCD Cost scenarios: Scenario 1 - Basic machine perfusion and disposable costs. Scenario 2 - Scenario 1 plus personnel costs. Scenario 3 - Scenario 2 plus dedicated organ preservation and resuscitation unit. ECD: N/A Extended perfusion: N/A	Population: Patients undergoing transplantation of a liver from DCD donor. Data sources: This was a trial-based economic evaluation of the DHOPE-DCD trial (NCT02584283). Healthcare activity and machine perfusion costs were from University Medican Center Groningen (UMCG).	Model structure: Trial-based cost effectiveness analysis Time horizon: up to 1 year post transplant	DHOPE costs were approximately €15,000 lower per patient vs SCS (€110,794 vs €126,221). DHOPE provided slightly more graft survival years (53.0 years for 60 patients) vs SCS (52.6 years for 59 patients) (non-significant difference). DHOPE was cost effective compared with SCS: Scenario 1: after 1 procedure. Scenario 2: after 25 annual procedures. Scenario 3: after 30 annual procedures.	Bootstrap analysis (3000 replications) of cost per graft against graft survival indicated cost and effect differences were statistically insignificant. Aligns with trial findings that suggest reductions in complications are reduced but not 1-year graft and patient survival. The trial was multinational (Belgium, the Netherlands, UK) but economic evaluation only included data from 3 Dutch centres. Limitations include one year follow-up as complications presenting later may not be captured. Costs were 12.2% less for DHOPE vs SCS. The highest costs reductions were in: intensive care costs (28.4%); nonsurgical interventions (24.3%); ward stay (20.2%); outpatient and day treatment (19.3%); surgical interventions (19.2%); imaging diagnostics (17.2%); other diagnostics (15.1%); and laboratory diagnostics (14.0%).

Study author, design, location, cost year/currency	Intervention(s), comparator(s), DCD/DBD, ECD, extended perfusion	Population and key data sources	Model structure	Relevant outcomes	EAG comments
metra					
Author, year: Webb, 2022 Design: Cost utility analysis Modelled location: Canada Cost year and currency: 2021 USD	Intervention: Ex-situ NMP (*metra*) plus SCS Comparator: SCS DCD/DBD: N/A ECD: NMP was modelled to primarily be for ECDs. Extended perfusion: N/A	Population: Patients on the Canadian liver transplantation waiting list. Data sources: Transition probabilities were from the Alberta liver transplant database. Utilities were from Ratcliffe et al. 2002. Costs were from Data Integration, Measurement and Reporting (DIMR) from Alberta health services.	Model structure: Markov model Time horizon: 5 years Cycle length: Yearly	Primary outcomes: ICER - SCS vs NMP plus SCS: $-198,577 per QALY gained SCS was less effective and more costly than NMP plus SCS at a willingness-to-pay threshold of $40,941 (CAD$50,000). Uncertainty: NMP plus SCS dominated SCS in all PSA scenario analyses except when replacing survival cost beyond one year with waitlist cost. In this case, NMP was cost-effective against but not dominant.	The study's transferability to a UK setting is limited due to being conducted in Canada where the healthcare perspective differs to that of the UK. The case mix approach of using NMP as well as SCS in the intervention arm means that the results are unable to be fully attributable to NMP alone. The one-year life cycle is limiting, given that the condition may deteriorate or develop complications at any time during both the waitlist period and the post-transplant phase.

Study author, design, location, cost year/currency	Intervention(s), comparator(s), DCD/DBD, ECD, extended perfusion	Population and key data sources	Model structure	Relevant outcomes	EAG comments
Liver Assist and *metra*					
Author, year: Zimmerman, 2022 Design: Cost utility analysis (published as a research letter) Modelled location: UK Cost year and currency: 2018/19 GBP	Intervention: Ex-situ NMP (*metra*); Ex-situ HMP (Liver Assist) Comparator: Current practice (SCS) DCD/DBD: N/A (due to paucity of data, subgroup analyses of DBD and DCD donor types were not possible) ECD: N/A (due to paucity of data, subgroup analyses of ECD was not possible) Extended perfusion: N/A	Population: Patients on the adult elective deceased donor transplant list. Data sources: Patient characteristics were from National Health Services Blood and Transplant (NHSBT). Staff costs were from PSSRU. Device costs were provided by the manufacturer.	Model structure: Markov model Time horizon: Lifetime Cycle length: One month	Primary outcomes: ICER NMP vs SCS: €241,300.07 (£204,059.25) per QALY gained HMP vs SCS: €1,288,668.47 (£1,089,783.06) per QALY gained Uncertainty: DSA showed that neither NMP or HMP achieved cost-effectiveness in any scenario.	DSA showed that NMP and HMP were each dominated by SCS when organ utilisation (+/- 10%) using the intervention was decreased. The ICER results were most impacted by: risk ratio of EAD; probability of organ utilisation; and the data source for the long-term outcomes. The study reported high risk of bias in organ utilisation rate. It was noted that the model was limited by availability of the data inputs. This analysis was published as a research letter; the peer review process was unclear.

Study author, design, location, cost year/currency	Intervention(s), comparator(s), DCD/DBD, ECD, extended perfusion	Population and key data sources	Model structure	Relevant outcomes	EAG comments
VitaSmart					
Author, year: Axelrod, 2025 Design: Cost consequence (published as a conference abstract) Modelled location: US Cost year and currency: USD, year NR	Intervention: HOPE with SCS Comparator: SCS DCD/DBD: Both were analysed ECD: NR Extended perfusion: NR	Population: Liver transplant recipients receiving from DCD or DBD donors. Data sources: Costs were from national hospital cost accounting data and Medicare payment data.	Model structure: Markov model Time horizon: It seems to be 1-year (this is not explicitly stated) Cycle length: NR	Primary outcomes: Total estimated 1-year cost reduction HOPE vs SCS: $28,565 (credible interval: $23,027 to $34,541) Length of initial hospital stay post-transplant was reduced from 12.9 days (SCS) to 10.8 days (HOPE). Biliary complications reduced from 24.6% (SCS) to 20.2% (HOPE). Subgroups: Savings reported by donor DCD: $64,370 DBD: $16,929	This study's outcomes are not transferable to a UK setting due to being based in the US. Due to being published as a conference abstract, there is very limited detail on the modelling approach and data used to inform the analysis.

Table abbreviations: CAD, Canadian Dollars; DBD, Donation after brain death; DCD, Donation after circulatory death; ECD, Extended criteria donor; HMP, hypothermic machine perfusion; DHOPE, dual hypothermic oxygenated machine perfusion; DSA, deterministic sensitivity analysis; HOPE, Hypothermic

oxygenated machine perfusion; ICER, incremental cost-effectiveness ratio; NA, not applicable; NMP, normothermic machine perfusion; NR, not reported; PSA, probabilistic sensitivity analyses; PSSRU, Personal Social Services Research Unit; QALY, quality adjusted life year; SCS, static cold storage; UK, United Kingdom; US, United States; USD, United States Dollars.

6.1.2 Critique of OrganOx *metra* model

The following economic evaluation was received as part of company submission for this assessment: “Cost–Utility Analysis of Normothermic Machine Perfusion (OrganOx *metra*) versus Static Cold Storage (SCS) and Hypothermic Machine Perfusion (Liver Assist).”

This cost-utility analysis compared the use of SCS with OrganOx *metra* and Liver Assist separately (both without the use of SCS). This took a hybrid modelling approach, incorporating a decision tree linked to a Markov model structure. The initial decision tree captured short-term outcomes, including whether individuals received a transplant, remained on the waitlist based on the organ utilisation rate, and any clinical outcomes one-year post-transplant. For the transplanted cohort, the model applied the probability of developing specific complications and the probability of re-transplantation linked to those complications.

Following the first year, patients transitioned into the Markov model and were stratified into the following health states: alive on the waitlist, alive without EAD (including those who recovered from other complications), alive with (or with history of) EAD, and dead. The Markov model followed a lifetime time horizon with annual cycles. The overall model structure aligned with previous economic evaluations on the use of machine perfusion for liver transplantation (Webb et al. 2022, Zimmermann and Carter 2022). The model structure remained the same across livers of DBD and DCD origin and was consistent with the liver transplant clinical pathways. However, the following elements were noted:

- The decision tree structure assumed patients remain in a fixed complication state for a full one-year duration. This is clinically unrepresentative because it fails to account for patients who may recover earlier.
- The transition probabilities in the Markov model for movement to and from the waitlist are applied annually, and theoretically, individuals can remain on the waitlist for many years or can move

between the waitlist and post-transplant health state multiple times. This means that patients may be receiving more re-transplantation, than are clinically plausible.

- Mortality is higher for those with a single transplant and a history of EAD than those on the waitlist. Waitlisted populations can include those with a transplant and a history of EAD and therefore this does not hold face validity.
- The impact of machine perfusion on re-transplantation rates and mortality are applied each year, and for an individual's entire life. This means that the incremental benefits associated with machine perfusion are assumed to apply for a person's lifetime. Data sources used to inform these parameters were not obtained from life-time studies and so this introduced the assumption that these benefits are directly applicable to a person's entire life. The annual cost of being on the waitlist is assumed to be equivalent to the annual cost of end stage liver disease (£35,000)

The base case results indicated that the OrganOx *metra* device is cost-effective over a lifetime time horizon with an (ICER of £12,402). The PSA estimated that *metra* is cost-effective in 100% of the 2,000 iterations. However, because some inputs could not be independently validated, the robustness of this remains uncertain when considered alongside the aforementioned structural limitations. The DSA indicated that the key drivers of the net monetary benefit (NMB) included the probability of developing EAD (in the intervention arm of the model) and re-transplantation rates, applicable to subsequent cycles of the model. Data to inform the probability of developing EAD was sourced from NHSBT registry data, however, we were unable to validate the quoted re-transplantation values. As above, these values are not stratified by year and hence likely misrepresent the total number of re-transplantations that occur in the long-term.

Expert clinical validation was sought to address this, and feedback suggests that the modelled re-transplantation rates for those with EAD may be over-estimated. Specifically, one clinician noted that a majority of EAD patients requiring re-transplantation at 10 years is not plausible, while another

highlighted recent data suggesting that EAD may not have a significant long-term impact on overall patient survival.

6.2 *De novo* model

No suitable models relevant to the decision problem were identified during the review of available published economic evidence as:

- There were unclear or unreported details on the specific modelling approach.
- Outcomes of interest (such as re-transplantations or complications) were not captured in sufficient detail.
- The impact of machine perfusion on waitlists was not captured.

Therefore, a *de novo* economic model was developed to explore the impact of machine perfusion for the decision problem outlined in the scope.

6.2.1 Model conceptualisation

Based on the value proposition of machine perfusion and their impact on outcomes, the following were key considerations:

- The impact of machine perfusion on waitlists.
- The incremental number of short-term complications.
- Differences in overall mortality and number of re-transplantations.

The liver transplant waitlist was considered a critical component of the model structure. Individuals can spend a considerable period on the waiting list, during which they incur ongoing healthcare costs and experience reduced health-related quality of life (HRQoL). Machine perfusion may have an impact on this by increasing the number of livers that can be utilised through longer and more effective preservation. It may also allow for more robust liver viability assessment, thereby increasing clinician confidence in suitability of high-risk organs. As a result, mortality rates may be lower by reducing waiting list.

Short-term post-transplant complications were also considered to be important as these events can lead to additional procedures, prolonged hospital stay, increased healthcare costs, and temporary or permanent reductions in HRQoL. Data indicates that an increase in short-term complications leads to a reduction in long-term survival (S J Tingle 2021). However, it was not possible to explicitly model the extent to which mortality is driven by each individual complication. Therefore, long-term mortality is represented through survival estimates which vary based on whether a person has received a transplant via machine perfusion or SCS. This approach will indirectly capture the impact on long-term survival associated with the specific preservation method used (and any complications that may arise). This is applicable to all complications except for PNF. PNF mortality is explicitly included as it occurs immediately post-transplantation. It is a limitation that this may lead to double counting of mortality, however, given the relatively low incidence of PNF, this is unlikely to have a meaningful impact on model results.

Long-term re-transplantation and mortality were also expected to be key drivers of model outcomes. Graft failure requiring re-transplantation is associated with substantial additional costs. Mortality directly determines the duration over which costs and QALYs are accrued. Differences in these long-term outcomes can therefore have a material impact on cost-effectiveness, particularly given the lifetime time horizon of the analysis.

Model type

Different modelling approaches were considered to represent outcomes following liver transplantation.

A patient level simulation (PLS) was considered as this would allow individual-level pathways to be tracked, including variation in time spent on the waitlist and timing of post-transplant events. This would provide greater flexibility in modelling heterogeneity in donor type, recipient characteristics, and timing of complications. However, implementation of a PLS requires granular patient-level data to inform transitions and resource use. Available evidence,

particularly for post-transplant survival and re-transplantation, was reported as aggregate cohort-level values.

A cohort-based approach was also considered.

With this approach, it would be necessary to assume that individuals transition from the waitlist at the same time, based on the average time to transplantation. This assumption ensures that the application of post-transplant mortality and re-transplantation risks is coherent and consistent across the cohort. Without this simplifying assumption, it would not be possible to apply post-transplant survival appropriately within a cohort-based model, given this varies based on the time since transplant.

It is worth noting that, in general, modelling the liver transplant waitlists is inherently uncertain due to the large number of interacting factors that influence organ availability, listing practices, and transplant activity, all of which change over time. These changes are further affected by varied clinical practices and annual fluctuations in the availability of appropriate transplant organs, which can alter liver utilisation rates and waiting times in ways that are difficult to predict.

Within a cohort-based approach, Markov models using annual, monthly, and hybrid cycle lengths (e.g. monthly for the first year, transitioning to annual from year two onwards) were considered. Monthly cycle lengths would allow post-transplant survival and the rate of re-transplantations to be tracked in greater detail, particularly in the first year following transplantation. However, available data informing these parameters were reported at one-year post-transplantation or over longer time horizons, rather than at monthly intervals. Therefore, implementing monthly cycles would require additional assumptions regarding the timing and distribution of events within the first year. This would not introduce any additional granularity into the model results.

If a Markov-only approach with annual cycle lengths were selected, however, this would require the assumption that transplantations either occur instantly, or after one year.

Given the above, the use of a decision-tree to represent the wait list and short-term post-transplant outcomes was considered. In a decision tree, short-term complications occurring within the first-year post-transplant could be applied as one-off payoffs at the point of transplantation. This could allow for the costs and utility payoffs associated with these to be applied but would require the assumption that their impact on survival is inherently captured within underlying post-transplant survival data. The timeline of the decision tree could capture all waitlist outcomes and allow for the cohort to transition into the long-term Markov model once a transplant is received.

Overall, a Markov-based cohort approach was selected, with scenario analysis conducted around key structural elements of the model.

Within the cohort-based approach, a decision tree was also selected. This was done to allow more transparent representation of the waitlists and short-term complications, while allowing for a long-term Markov model that uses annual cycle lengths, which better reflected the nature of the available long-term survival and re-transplantation data.

6.2.2 Model structure

The final model structure is presented in Figure 1.1. The model captures a cohort of people eligible for a liver transplant and is divided into a short-term component, capturing waitlist and short-term post-transplant outcomes (represented as pay-offs), and a long-term component, capturing post-transplant survival and re-transplantations over the lifetime time horizon.

The cohort begins on the liver transplant waiting list. Time spent on the waiting list is informed by NHS Blood and Transplant (NHSBT) activity data and reflects the average duration until transplantation. In the base case, the utilisation rate of donated livers directly affects the total proportion of people who eventually receive a transplant, but does not change the average time to

transplant, such that higher utilisation results in more transplants received. This is varied in scenario analysis as described in Section 6.2.3

Once a transplant is received, the model applies the transplant procedure cost, which, in the intervention arm of the model, includes the cost of machine perfusion as well as SCS. Device-specific costing evidence supplied by companies was reported inconsistently, which reflects a range of costing approaches offered to the NHS by technology companies. As a result, different costing approaches were applied to the devices dependent on available cost data. Whilst these prices are reflective, any impact on results that these costing inputs have may be associated with considerable uncertainty. As a result, we have included additional threshold analyses for each device where the total per-procedure cost of machine perfusion is varied. Specific costs are detailed and discussed in Section 6.2.3.

Incidence of short-term post-transplant complications as one-off events are also applied at this point in the model. Complications are only captured within the first year. Clinical feedback suggested that while most complications occur in the first year, some do occur later. An assumption is made in the evaluation that that any complication costs beyond this are assumed to be inherently captured by the ongoing annual cost of living with a transplant. Complications included within the evaluation include:

- PNF
- EAD
- PRS
- biliary leaks
- anastomotic strictures
- non-anastomotic biliary strictures
- HAT
- renal replacement therapy (RRT).

PNF is assumed to lead either to immediate re-transplantation or death. For all other complications, associated costs are applied. Robust data on long-term mortality conditional on a history of the modelled conditions was not

available. Furthermore, mortality associated with these conditions are likely to be indirectly captured with the long-term post-transplant survival estimates for SCS and machine perfusion. Capturing mortality outcomes independently require additional assumptions about how these datasets interact and would have likely led to double counting of mortality, adding structural uncertainties into the model. An exception to this is made in the case of PNF, where mortality is more explicitly captured. This represents the fact that PNF-related mortality occurs within the first few days and is associated with significant QALY losses.

Following the first-year post-transplant, people enter the long-term component of the model, which is structured as a three-state Markov model comprising post-transplantation, post-re-transplantation, and death. An additional tunnel state is included to capture re-transplantations, and all outcomes within the first year of having a re-transplantation (including death). The long-term model applies survival and re-transplantation risks over a lifetime horizon, with outcomes accrued until the entire cohort has transitioned to death.

People who have a re-transplantation have an increased risk of mortality, with clinical consultation confirming that mortality can be up to 50% higher in these cases (René Adam 2018). As with short-term complications, this is assumed to be inherently captured in the differences in long-term survival between SCS and machine perfusion and were not modelled separately to avoid double-counting. The impact of machine perfusion on mortality and re-transplantations is assumed applicable for the first five-years post-transplantation only. This is driven by the availability of data, which only spans this period. This represents a conservative assumption and therefore long-term impacts of machine perfusion are likely to be underestimated within the modelling. This is tested in scenario analysis.

There was no data identified on the proportion of people who receive a third transplantation, or how this may impact long-term outcomes. The long-term

outcomes of additional re-transplantation are therefore assumed to be captured indirectly through the long-term outcome data.

Data on complications was only available for those who receive an initial transplant; no data was identified on how this might vary between the first and second transplant. While re-transplants are widely anticipated to have higher complication rates, clinicians noted this may be more related to the inherent complexity of the donor operation and surgical history than the storage method itself. In order to avoid misrepresenting the data available, complications following re-transplantation were not explicitly modelled and were instead assumed to be captured in the overarching cost of re-transplantation, mortality, and QALY outcomes.

Figure 6.1: Liver perfusion model structure

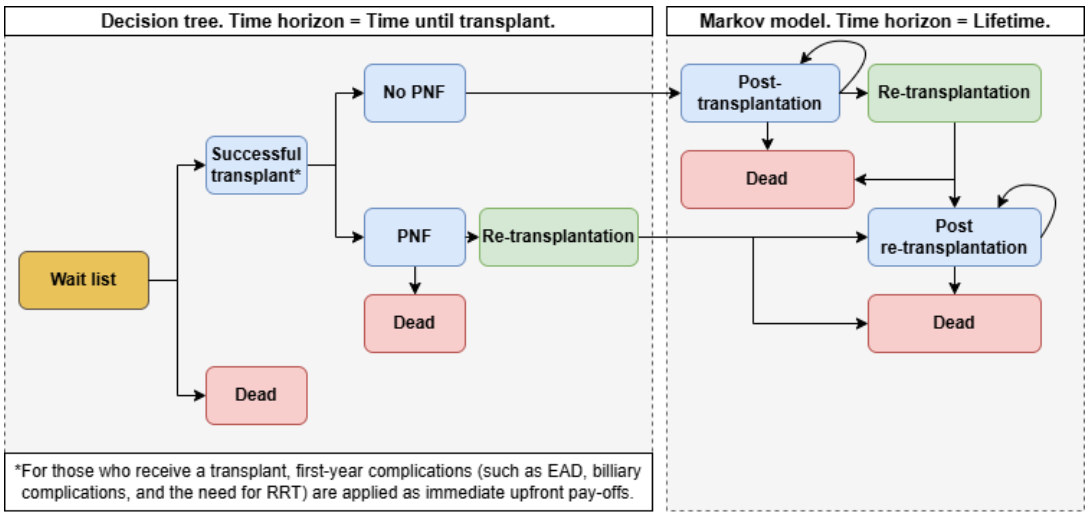

Figure abbreviations: PNF, primary non-function; EAD, early allograft dysfunction; RRT, renal replacement therapy

Machine perfusion and additional storage techniques

Each machine perfusion device in scope is included as separate interventions within the model. Table 6.3 details the functionality of each machine perfusion device and how this is captured within the model. Further information on specific inputs is included in Section 6.2.3

Specific clinical evidence regarding the use of NRP (DCD organs only) was sparse and was only explicitly referenced in Puttappa et al. (2025) [14] where

SCS with NRP was compared against SCS alone. Given that this evidence was specific to SCS, and the primary comparator for this evaluation is conventional SCS (as defined in the NICE final scope), NRP was excluded as a distinct component of the evaluation.

In addition, no evidence was identified to stratify outcomes associated with subtypes of NMP and HMP (including sequential HMP and NMP with rewarming). As with NRP, marginal impacts are therefore excluded from the evaluation.

It is worth noting that, while we are unable to directly stratify the impact of these additional techniques, where data is sourced from NHSBT, it is likely the case that any associated benefits of NRP or modality sub-types are implicitly captured within the reported clinical outcomes. Clinical evidence on complications may also indirectly incoporate these impacts, as these additional procedures may have been conducted even where not specifically detailed in the evidence base.

Table 6.3: Machine perfusion modelling approach

Intervention	Perfusion method	Model
LiverAssist	NMP (moderate availability of data) and HMP (good availability of data)	Only one study was identified on the use of LiverAssist as a NMP device (Ghinolfi et al. 2019). The relevant outcomes of this study were limited to 6-month survival, re-transplantation rate at one-year, biliary complications (unspecified), HAT (9=day follow-up) PRS, and EAD. Furthermore, this study had an intervention sample size of 10 and was based in Italy. No outcomes from this study were deemed statistically significant and so they were not included. Given that this was the only available evidence on the use of Liver Assist as a NMP device, Liver Assist when used as an NMP device used data relating to *metra*.
PerLifePRO	NMP and HMP (poor availability of data)	Although costing evidence was submitted to NICE, we were unable to identify any device-specific evidence for the use of PerLifePRO Within the model, the outcomes of PerLifePRO when used as a HMP and NMP device are assumed to be the same as Liver Assist and *metra*, respectively.

Intervention	Perfusion method	Model
		Given this, model results relating to PerLifePRO reflected the next most applicable device and not the device itself. Therefore, the results of this analysis are highly uncertain and should be interpreted with caution. Only key results on the use of this device are included within this report..
OrganOx *metra*	NMP (good availability of data)	Data to inform this device were available for all parameters except re-transplantation rate (at both 1- and 5-year) and RRT. No data was available to inform NMP-specific re-transplantation rate or rate of RRT and so these are assumed the same as Liver Assist.
VitaSmart	HMP (good availability of data	Data were available to inform all parameters except for HAT, non-anastomotic biliary strictures, PNF, and re-transplantation rate. These inputs are assumed to be the same as those relating to Liver Assist when used as a HMP device.

Outcomes

The model captures outcomes across the waitlist, short-term post-transplant period, and long-term post-transplant time horizon as follows:

- Waitlist outcomes: time-to-transplantation, waitlist mortality, and the cost of being on the waitlist.
- Short-term post-transplant outcomes: incidence of key complications occurring within the first year following transplantation (as described above) and the associated costs.
- Long-term outcomes: overall survival, re-transplantation, ongoing post-transplant healthcare costs, and QALYs.

For all outcomes, the number of events which occur and the associated costs are explicitly reported. In the long-term model, costs and QALYs are accrued according to health states that represent living with a functioning transplant, having a re-transplant, and living following re-transplantation.

Model assumptions

Select structural and parameter assumptions were applied to address limitations in the available evidence. Where possible, the assumptions were informed by published sources and clinical consultation and were explored further through scenario and sensitivity analyses.

Table 6.4: Key modelling assumptions

Assumption	Rationale
Baseline inputs derived from NHSBT registry data, specifically organ utilisation and short-term complications, are assumed to reflect the outcomes associated with SCS.	NHSBT registry data are not stratified by preservation method. As machine perfusion is currently utilised within UK practice, the baseline data likely incorporate its associated benefits. This lack of stratification results in a misrepresentation of the true SCS outcomes. While this means that the current model results likely represent an underestimation of the incremental benefit by narrowing the gap between arms, it also introduces the risk that results are skewed if improvement factors are applied to a baseline that already includes these gains. This uncertainty is explored through scenario analyses where complications are equalised and the link between utilisation and waitlist mortality is removed.
Long-term mortality rates for all machine perfusion devices are informed by 5-year data from a single device (Liver Assist) in a DBD population.	Evidence for long-term survival is limited, with only two studies (Czigany et al. 2024, (van Rijn et al. 2025) providing consistent 1- and 5-year outcomes (both HMP). Czigany et al (2024) was used in this analysis because, while both studies reported mortality to not be statistically significant, data from the van Rijn trial had a higher p value (p=0.35] versus p=0.105). 2-year data was identified for Liver Assist (HMP; DBD), 1-year data was identified for *metra* (NMP; mixed donor origin) and 6-month data was identified for VitaSmart (HMP; mixed donor origin). These were excluded from the base case analysis due to heterogeneity between the populations. Given uncertainty around the HR of mortality associated with machine perfusion, scenario analysis was includes where mortality was the same between each arm of the model. Furthermore, two-way threshold analysis was also conducted for each device where mortality was varied across both DBD and DCD populations. .
Long-term re-transplantation rates are based on 5-year data from a single study using Liver Assist with DCD organs.	Only one study was identified that provided re-transplantation data up to the 5-year mark. Due to this paucity of data, these rates are assumed to be representative of all machine perfusion devices in scope. Given that re-transplantation is a significant driver of both cost and clinical outcomes, this assumption is tested through scenario analysis to test for potential variations between technologies and organ types.
Outcomes were assumed to be equivalent within machine perfusion modality where device-specific evidence was lacking (e.g.	There was limited evidence to differentiate outcomes between individual devices operating under the same modality. Applying modality-level estimates avoided introducing unsupported between-device differences and reduced structural uncertainty.

Assumption	Rationale
re-transplantation rates, long-term mortality, and short-term complication RRs within NMP and HMP modalities).	
Re-transplantation beyond five years post-transplantation was assumed to be zero.	Robust evidence informing re-transplantation rates beyond five years was not identified. Any re-transplantation occurring after this point was assumed unlikely to differ materially between arms and therefore unlikely to affect incremental outcomes. Excluding re-transplantation beyond five years reduced reliance on unsupported extrapolation. This is tested in scenario analysis and specific inputs for which this is applicable are described above.
The HR for mortality associated with machine perfusion was applied for the first five years post-transplant only.	No evidence was identified to support a sustained mortality effect beyond five years. Applying the HR beyond the observed data period would require strong assumptions regarding durability of effect. Limiting the effect to five years represents a conservative and evidence-aligned approach. This is tested in scenario analysis
A single aggregate utilisation rate was applied across all machine perfusion devices.	Device-specific utilisation data were only available for OrganOx *metra*. Applying this value across devices avoided introducing additional uncertainty through unsupported assumptions and ensured consistency across analyses. Utilisation was explored in DSA, PSA, and scenario analysis.
Of newly utilised livers, 70% were assumed to be DCD in origin.	Utilisation rate for newly utilised livers was not stratified by donor type in available data. Clinical expert input indicated that increased utilisation is more likely to occur in DCD organs. The 70% estimate reflects expert opinion and was explored in one-way sensitivity analyses. See Section 6.2.3 for more information on these inputs.
Costs of short-term complications were applied as point estimates from the NHS National Cost Collection and are based on the cost of the most commonly delivered treatment option for each complication.	While patient-level costs may vary, use of standardised national estimates improves consistency and transparency. These were validated with clinicians as broadly reflective of current practice.
Post-retransplant HRQoL was assumed to be equal to post-first transplant HRQoL.	Utility data specific to re-transplantation were not identified. In the absence of robust evidence differentiating these health states, equivalent utilities were applied as a pragmatic assumption to avoid introducing unsupported differences.

Assumption	Rationale
Individuals remaining on the waitlist beyond 42 months were assumed to die before the end of year four.	Long-term waitlist outcome data up to 42 months was provided by NHSBT, and this indicated that the number of additional transplantations drops sharply after waiting for more than two years. This assumption avoids overstating prolonged waiting times and was tested in scenario analyses. See Section 6.2.3 for more information on these inputs.
In the base case, improved utilisation was assumed to increase the total number of transplants performed, without affecting the average time to transplant for those transplanted (unless organ availability exceeded waitlist demand).	This reflects the assumption that the primary effect of increased organ utilisation is to expand transplant capacity rather than shortening waiting times. Two alternative structural assumptions regarding utilisation and time to transplant were explored in scenario analyses.
The potential impacts of NRP, and additional machine perfusion subtypes (such as sequential HMP or NMP with rewarming) are not captured in the model	Very limited evidence was identified to inform the use of machine perfusion with NRP, or for machine perfusion modality sub-types and so the direct impact pf this was excluded. The modelling may still implicitly capture some of the impacts of these techniques as detailed in Section 6.2.2. Potential additional benefits associated with this are discussed qualitatively in Section 6.4.2.

Figure abbreviations: DCD, donation after circulatory death; HR, hazard ratio; HRQoL, health-related quality-of-life; NHS, National Health Service; NRP, normothermic regional perfusion.

Comparison to existing UK-based economic analyses

OrganOx *metra* model

As with our evaluation, the OrganOx *metra* model (see Section 6.1.1) incorporates a decision tree to capture short-term outcomes followed by a Markov model to estimate lifetime costs and benefits.

Key differences between the two models include the following:

- In the EAG's evaluation, overarching HRs were applied to the entire machine perfusion cohort to reflect long-term survival. This differs from the *metra* model, which used distinct health states for "history of EAD" and "no history of EAD" as the primary drivers for mortality. This decision was based on the lack of robust evidence to explicitly quantify how a history of

EAD impacts survival over a lifetime. This approach assumes that the impact of EAD, alongside other complications, is implicitly captured within long-term survival estimates.

- This model conservatively assumes that the impact of machine perfusion on mortality and re-transplantation is applicable for the first five years only, as this is the timepoint across which clinical evidence was identified. Conversely, the *metra* model assumed that these benefits remain for a person's lifetime.
- The decision tree time horizon in the EAG model is the time until transplant, with short-term complications applied as one-off events at the point of transplant. The *metra* model used a decision tree time horizon of one-year, which captures all transplants, first-year complications, and any re-transplantations associated with complications.
- This evaluation incorporates a tunnel state for re-transplantation and stratifies post-transplant costs by year to reflect an increased early resource use required in the initial period post-surgery. All elements of the re-transplantation process (including being on the waitlist, having a re-transplantation, or death) are assumed to be captured in the long-term survival and clinical outcomes data. There was limited evidence on the outcomes of second transplants, and so this assumption avoids the introduction of additional uncertainty associated with this. In the *metra* model, individuals could remain on the waitlist for multiple annual cycles. Costs applied to those on the waitlist were assumed equivalent to those with end-stage liver disease (£35,000)

Zimmermann et al (2022) model

In addition to the *metra* submission, this evaluation was compared with the UK cost-effectiveness study by Zimmermann et al. (2022) (Zimmermann and Carter 2022). While both analyses applied a lifetime time horizon and a UK NHS perspective, several methodological differences exist which are likely to contribute to the different outcomes observed.

Key differences between the two models include the following:

- The model by Zimmermann used a Markov-only structure with monthly cycles to capture costs and outcomes for current practice and two comparator devices. In contrast, this evaluation uses a decision tree to capture acute post-transplant outcomes and complications as one-off events, followed by a Markov model for long-term health states.
- In this evaluation, the impact of machine perfusion on organ utilisation is a key driver, affecting the total proportion of people receiving a transplant. The Zimmermann et al. (2022) model assumes no difference in organ utilisation between SCS and machine perfusion.
- Health states included in the Zimmermann model relied on tunnel states for specific complications, including biliary complications, EAD, and PNF. Following these states, patients transitioned into long-term states based on whether they had a history of dysfunction (i.e. EAD or PNF) or not. The EAG evaluation instead used overarching survival estimates and HRs to reflect long-term outcomes for the entire machine perfusion cohort.
- The treatment of re-transplantation also differs between the two evaluations. The Zimmermann model allowed for multiple re-transplantations to occur, with each subsequent procedure incurring high associated costs. These rates were stratified by complication history, with a 4.35% risk for those with a history of EAD or PNF compared with 0.05% for those without. In contrast, this analysis uses a tunnel state to capture the impact of a second transplant and assumes further re-transplantations are captured indirectly through long-term clinical data to avoid the introduction of additional uncertainty.
- The cost of the *metra* device used in the Zimmermann model was lower than the one-off per-procedure cost provided by the company for this evaluation. Costs for Liver Assist were broadly consistent across both analyses.

6.2.3 Model parameters

The model compares each machine perfusion device with SCS over a lifetime horizon across three populations: adult, paediatric, and ECD. Evidence on the

use of ECD livers was limited and definitions of this varied. Three clinical papers on the use of ECD organs were identified (where ECD was defined as anything other than just DCD organs). The definitions of ECD across each of these are as follows:

- Grat et al: DRI > 1.7 (Grat et al. 2023)
- Fodor et al: Criteria and number NR, but results were reported separately (Fodor et al. 2021)
- Puttappa et al: MEAF > 7 (Puttappa et al. 2025)

DCD and DBD livers were modelled separately and, where possible, differences in clinical outcomes associated with the use of these livers were applied. The discount rates for costs and benefits and the cost-effectiveness threshold were set at 3.5% and £20,000/QALY, respectively though PSA results also include the probability of cost-effectiveness at a threshold of £30,000/QALY.

Population parameters

Population characteristics are detailed in Table 6.5. For the adult population, the sex distributions and cohort age at the time of transplant were sourced from the NHS Blood and Transport (NHSBT) liver activity report 2024/25 (Transplant 2025c) . The reported data originally included both adult and paediatric recipients. The total adult age was calculated by adjusting the total average age to remove paediatric cases. Due to limited available data on the ECD population, both the cohort age and sex distributions were assumed to be the same as those for the adult population.

Table 6.5: Population characteristics parameters

Parameter	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
Cohort age at transplant (years)	Adult / ECD population: 59.85 Paediatric: 5.02	NHSBT liver transplant activity report 2024/25 (Transplant 2025c)	Calculated from registry data, which is representative of the population. Cohort age is included in DSA which suggests only minimal

Parameter	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
			impact on the magnitude of results.
Proportion male	Adult / ECD: 63.00% Paediatric: 55.00%	NHSBT liver transplant activity report 2024/25 (Transplant 2025c)	Registry data source hence considered representative of those on the transplant waiting list. DSA suggests this input has very limited impact on model results.

Table abbreviations: DSA, deterministic sensitivity analysis; EAG, external assessment group; ECD, extended donor criteria; NHSBT, National Health Service Blood and Transplant.

Organ utilisation and waitlist parameters

There was limited available evidence on organ utilisation for each machine perfusion device in the identified and prioritised studies. As noted in Section 5.2, only two studies details information on organ utilisation. These were as follows:

- Fodor et al (2021) (Fodor et al. 2021): 59 of 75 machine perfusion cases resulted in transplantation (utilisation rate of 78.7%). This is a matched study that compared the use of machine perfusion with successful SCS transplants and therefore cannot be used to inform the relative difference in organ utilisation rate.
- Krendl et al (2025) (Krendl et al. 2025): This study stated “NLMP use permitted us to accept 67 additional liver grafts which we would not have accepted before the introduction of NLMP”. This statement is provided with no context as to the number of additional organs that were rejected and therefore did not allow for relative comparison of organ utilisation rates between SCS and NMP.

In addition to the above, a single systematic literature review was identified that included organ utilisation rate from three papers, including two on the use of OrganOx *metra*) (Viana et al. 2025). (NMP). These individual studies were

originally excluded from the analysis as they both used *metra* initiated at donor hospital during transport and hence were out of scope. Utilisation rates cited by this paper may therefore not be reflective. These studies were as follows:

- Chapman et al. 2023: RR of organ utilisation = 1.04 (0.91-1.19)
- Nasralla et al. 2018: RR of organ utilisation = 1.16 (1.04-1.30)

This study reported a pooled average organ utilisation rate of 1.1, which in the absence of alternative identified evidence, was used in this evaluation. There was no identified evidence to inform organ utilisation for any of the other scoped devices, or for HMP in general. Therefore, an assumption is made that this value is applicable to HMP and NMP devices. Although it is anticipated that machine perfusion leads to a higher proportion of DCD organs being utilised, evidence to inform specific differences in organ utilisation across DBD and DCD organs were also not available. This impact was therefore modelled through a separate parameter, which defined the number of newly utilised organs that were DCD in origin. In the base case, this was set to 70%, informed by clinical consultation.

Organ utilisation was demonstrated to be a key driver of model results and therefore additional threshold analysis where the total utilisation rate is varied across each device and organ type is included within this analysis (See section 6.3.4). The value used in the analysis (1.1) was cross-checked with clinicians who stated that a 10% increase is likely appropriate, though the specific impact of different technologies remains uncertain. While one clinician noted that NMP likely provides superior functionality data that could improve results, they felt this impact is not yet fully demonstrated. Another suggested that NMP might achieve even higher utilisation rates due to extended perfusion times and viability testing, though they cautioned that some observed effects could be a placebo. Conversely, a third clinician highlighted that the rigorous viability assessments possible with NMP could reduce utilisation by leading to more frequent organ rejections.

In the base case, an increased organ utilisation is assumed to be directly proportional to an increase in the number of successful transplants carried out (for example, a utilisation rate factor of 1.1 would result in 10% more successful liver transplants, given there is sufficient demand). This is assumed to not impact the average time-to-transplant.
Scenario analysis was conducted to explore this structural assumption using other approaches. In the first approach we assume that an increase in organ utilisation reduces the time-to-transplant but has no impact on the total number of transplants conducted. The second approach combined the above with the base case, assuming that organ utilisation directly correlates to the number of transplants as well as the average time-to-transplant. This combined scenario may overestimate the impact of machine perfusion, as it assumes that improvements in utilisation simultaneously expand overall transplant capacity and accelerate access for individuals already on the waiting list. In practice, these effects are likely to be partially overlapping, with increases in utilisation primarily affecting marginal organs or specific donor types, rather than delivering independent linear gains in both transplant volume and waiting time reductions.

The calculations for the number of successful transplants, which were used in the base case and in the second approach, are as follows:

$$tMP = \frac{uMP}{uSCS} \times trSCS$$

The calculations for the number of successful transplants, which were used in the base case and in scenario two, are as follows:

$$tttMP = \frac{tttSCS}{(\frac{uMP}{uSCS})}$$

Equation abbreviations: MP, machine perfusion; SCS, static cold storage; ttt, time-to-transplant; t, transplant rate; u, utilisation rate.

The full dataset used to calculate waitlist inputs are detailed in Appendix E.

Table 6.6: Organ utilisation and waitlist parameters

Parameter	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
SCS			
Proportion of DBD livers that are utilised	77.90%	NHSBT Organ Utilisation Annual Report 2024/25 (NHS Blood and Transplant 2025a)	Values are sourced from NHSBT organ utilisation annual report (registry data) and are considered the best available evidence. This data is not stratified by SCS and machine perfusion, meaning this value likely includes data relating to machine perfusion. This is a limitation of the data and is tested in scenario analysis.
Proportion of utilised DCD livers with SCS	34.50%		
Total number of donated DBD livers per annum	675		
Total number of donated DCD livers per annum	898		
Calculated weighted average utilisation	53.12%	Calculation	Weighted average calculated using the proportion of livers utilised with SCS and total number of donated livers per annum.
Machine perfusion			
Utilisation rate factor (DBD and DCD)	1.10	Viana et al. (2025) (Viana et al. 2025)	The systematic review was inclusive of 1295 patients from RCTs and observational studies using NMP with SCS. 95% CIs 1.02, 1.18, p value - 0.011088, I2 – 0%. This input is a key driver of results, and a key limitation of this input is that the evidence base is primarily derived from NMP data, which has been assumed applicable to HMP devices in the model. The magnitude of this effect remains a source of uncertainty. Clinician opinion on the applicability of this assumption is detailed above.

Parameter	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
Calculated average utilisation	58.44%	Calculation	Calculated using the weight average utilisation for SCS and multiplying by the utilisation rate factor (DBD and DCD) for machine perfusion. Capped in the model at 100% to avoid assigning more livers than are available. Scenario analysis is included on this parameter.
Proportion of newly utilised livers which are DCD	70%	Assumption	This value was based on clinical consultation. One-way scenario analysis is included around this, which indicates it is not a key driver of model results.

Table abbreviations: DBD, donation after brainstem death; DCD, donation after circulatory death; EAG, external assessment group; RCT, randomised control trial; SCS, static cold storage.

Clinical parameters

The key clinical parameters used in the model were informed by published literature where available. Clinical parameters used in the model included:

- Complication rates
- Re-transplantation rates

Complications rates

SCS complication rates were primarily sourced from NHSBT and stratified by DCD/DBD where possible. It is worth noting that NHSBT data may indirectly include some of the impacts of machine perfusion.

Per-procedure complication rates for each machine perfusion device could not be identified from a single source because no individual study reported on the full range of complications listed. Therefore, the complication rates were identified from the most robust available data. Due to limited data on specific machine perfusion devices, , some input values were assumed equivalent to other machine perfusion devices where devices shared operational capabilities (e.g., where data is reported from a HMP/NMP modality of one device, this may be applied to another device that use the same perfusion method.). This was done where data were unavailable for specific parameters and is detailed in section 6.2.2. Where it is the case that non-device-specific values are used, this is detailed in Table 6.7. It is also worth noting that all machine perfusion RR values were found to be statistically non-significant, except the RR of EAD for VitaSmart. Therefore, the impact of machine perfusion on short-term complications are highly uncertain. A scenario analysis is included where the impact of machine perfusion on complications is assumed to be unchanged. Some data to inform the rate of complications is taken from European studies however clinical feedback suggested that it is broadly appropriate to generalise from non-UK settings to the UK.

Table 6.7: Complications parameters

Parameter	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
Complication rates (per-procedure): SCS			
RRT	DBD: 17.19% DCD: 15.51%	Provided by NHSBT statistician (Rhiannon Taylor) via email on 03.02.26	NHBT registry data generally considered the best available evidence. However, a limitation of this data is that it is not stratified by SCS and machine perfusion, meaning this value may inherently include data relating to machine perfusion. This is tested in scenario analysis
Anastomotic biliary strictures	DBD/DCD: 18.61%	Risbey et al. (2024) (Risbey et al. 2024)	This systematic review was inclusive of ten records from various European countries including the UK. There is noted heterogeneity within the quality of evidence. However, upon review, were deemed to be the best available evidence. Scenario analysis assuming no incremental impact in complications is conducted and suggest a limited impact on long-term results.
Non-anastomotic biliary strictures	DBD/DCD: 14.83%		
Post reperfusion syndrome	DBD/DCD: 44.36%		
EAD	DBD/DCD: 34.12%		
PNF	DBD: 0.82% DCD: 1.30%	Provided by NHSBT statistician (Rhiannon Taylor) via email 03.02.26 Provided by NNSBT statistician (Rhiannon Taylor) via email 03.02.26	
HAT	DBD: 1.46% DCD: 3.10%		
Biliary leaks	DBD: 3.41% DCD: 4.09%		NHBT registry data is considered the best available evidence. This data is not stratified by SCS and machine perfusion, meaning this value may inherently include data relating to machine perfusion. This is tested in scenario analysis.

Parameter	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
			Where relevant, these outcomes only include those which require treating and hence may underestimate the true number of events recorded. This does not impact model results as those which do not require treatment are assumed to not incur any additional resource use.
Risk ratio of complications (machine perfusion; Liver Assist; HMP))			
RRT	DBD and DCD: 0.79	Van Rijn et al (2021) (van Rijn et al. 2021c)	This European RCT, conducted across 3 countries (including the UK) reported the RR of biliary leaks, RRT, anastomotic biliary strictures, and non-anastomotic biliary strictures for DCD organs only, which therefore may limit its applicability across DBD organs or in a UK-only population. This outcome was noted as statistically non-significant. This study was specific to Liver Assist using HMP modality.
Anastomotic biliary strictures	DBD and DCD: 1.07		
Non-anastomotic biliary strictures	DBD and DCD: 0.36		
PRS	DBD and DCD: 0.96	Lesurtel et al (2025) (Lesurtel et al. 2025)	This French RCT study reported the RR of PRS, PNF, and HAT for DBD organs only, which therefore may limit its applicability across DCD organs, or in a UK population. This outcome was also noted as statistically non-significant. This study was specific to Liver Assist using HMP modality.
EAD	DBD and DCD: 0.36	Schlegel et al (2023) (Schlegel et al. 2023)	This European RCT, conducted across 6 European countries (including the UK), reported the RR of EAD for DBD organs only, which therefore may limit its applicability across DCD organs or in a UK-only population. This outcome was noted as statistically non-significant. This study was specific to Liver Assist using HMP modality.
PNF	DBD and DCD: 0.17	Lesurtel et al. (2025) (Lesurtel et al. 2025)	This French RCT study reported the RR of PRS for DBD organs only, which therefore may limit its applicability across DCD organs, or in a UK population. This outcome was also noted as statistically non-significant. This study was specific to Liver Assist using HMP modality.
HAT	DBD and DCD: 0.25		

Parameter	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
Biliary leaks	DBD and DCD: 0.75	Van Rijn et al (2021) (van Rijn et al. 2021c)	This European RCT, conducted across 3 countries (including the UK) reported the RR of biliary leaks, RRT, anastomotic biliary strictures, and non-anastomotic biliary strictures for DCD organs only, which therefore may limit its applicability across DBD organs or in a UK-only population. This outcome was noted as statistically non-significant. This study was specific to Liver Assist using HMP modality.
Risk ratio of complications (machine perfusion; *metra* [NMP], assumed applicable to Liver Assist [NMP])			
RRT	DBD and DCD: 0.79	Assumed the same as Liver Assist	No data was available on the RR of RRT for *metra*, or any NMP device. Data from the use of Liver Assist in NMP modality is therefore used. This may limit its applicability to this specific device and modality.
Anastomotic biliary strictures	DBD and DCD: 1.28	Krendl et al. (2025) (Krendl et al. 2025)	This retrospective cohort study conducted in Austria reported the RR of biliary leaks, EAD, HAT, anastomotic biliary strictures, and non-anastomotic biliary strictures across a mixed donor pool (i.e. DBD and DBD organs). The applicability of this study may be limited in a UK-only population. This outcome was noted as statistically non-significant. This study was specific to *metra* using NMP modality.
Non-anastomotic biliary strictures	DBD and DCD: 1.22		

Parameter	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
Post reperfusion syndrome	DBD and DCD: 0.41	Puttappa et al (2025) (Puttappa et al. 2025)	This retrospective cohort study conducted in the UK reported the RR of PRS and PNF for DCD organs only, which therefore may limit its applicability across DBD organs. This outcome was noted as statistically non-significant. This study was specific to *metra* using NMP modality.
EAD	DBD and DCD: 0.83	Krendl et al. (2025) (Krendl et al. 2025)	This retrospective cohort study conducted in Austria reported the RR of biliary leaks, EAD, HAT, anastomotic biliary strictures, and non-anastomotic biliary strictures across a mixed donor pool (i.e. DBD and DBD organs). The applicability of this study may be limited in a UK-only population. This outcome was noted as statistically non-significant. This study was specific to *metra* using NMP modality.
PNF	DBD and DCD: 0.38	Puttappa et al (2025) (Puttappa et al. 2025)	This retrospective cohort study conducted in the UK reported the RR of PRS and PNF for DCD organs only, which therefore may limit its applicability across DBD organs. This outcome was noted as statistically non-significant. This study was specific to *metra* using NMP modality.
HAT	DBD and DCD: 0.57	Krendl et al. (2025) (Krendl et al. 2025)	This retrospective cohort study conducted in Austria reported the RR of biliary leaks, EAD, HAT, anastomotic biliary strictures, and non-anastomotic biliary strictures across a mixed donor pool (i.e. DBD and DBD organs). The applicability of this study may be limited in a UK-only population. This outcome was noted as statistically non-significant. This study was specific to *metra* using NMP modality.
Biliary leaks	DBD and DCD :1.14		
Risk ratio of complications (machine perfusion; VitaSmart)			
RRT	DBD and DCD: 0.75	Ravaioli et al (2022) (Ravaioli et al. 2022)	
Anastomotic biliary strictures	DBD and DCD: 1.00		This Italian RCT reported the RR of RRT, biliary leaks, anastomotic biliary strictures, and PRS within the DBD population. The applicability of this study may therefore be limited in a DCD population. This outcome was

Parameter	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
			noted as statistically non-significant. This study was specific to VitaSmart using HMP modality.
Non-anastomotic biliary strictures	DBD and DCD: 0.3600	Assumption	No data was available on the RR of non-anastomotic biliary structures for VitaSmart. This is therefore assumed applicable to Liver Assist when in HMP modality. While this data is still relevant for HMP devices, it may not be specifically applicable to VitaSmart
Post reperfusion syndrome	DBD and DCD: 1.17	Ravaioli et al (2022) (Ravaioli et al. 2022)	This Italian RCT reported the RR of RRT, biliary leaks, anastomotic biliary strictures, and PRS within the DBD population. The applicability of this study may therefore be limited in a DCD population. This outcome was noted as statistically non-significant. This study was specific to VitaSmart using HMP modality.
EAD	DBD and DCD: 0.54	Reich et al (2024) (Reich et al. 2023a)	This US-based RCT reported the RR of EAD in a mixed donor pool. This parameter was deemed to be statistically significant, however may not be applicable to a UK-based population. This study was specific to VitaSmart using HMP modality.
PNF	DBD and DCD: 0.17	Assumption	No data was available on the RR of PNF or HAT for VitaSmart. This is therefore assumed applicable to Liver Assist when in HMP modality. While this data is still relevant for HMP devices, it may not be specifically applicable to VitaSmart
HAT	DBD and DCD: 0.25		
Biliary leaks	DBD and DCD: 2.00	Ravaioli et al (2022) (Ravaioli et al. 2022)	This Italian RCT reported the RR of RRT, biliary leaks, anastomotic biliary strictures, and PRS within the DBD population. The applicability of this study may therefore be limited in a DCD population. This outcome was noted as statistically non-significant. This study was specific to VitaSmart using HMP modality.

Table abbreviations: DBD, Donor after brainstem death; DCD, donation after circulatory death; EAD, early allograft dysfunction; EAG, external assessment group; ECD, extended criteria donor; HAT, hepatic artery thrombosis; HMP, hypothermic machine perfusion; NMP, normothermic machine perfusion; PNF, primary non-function; SCS, static cold storage; RCT, randomised control trial; RRT, renal replacement therapy.

Re-transplantation rate

The PNF re-transplantation rate was informed by NHSBT registry data, received via email consultation. The re-transplantation rate for SCS and the RR of re-transplantation with machine perfusion within one and five years were sourced from Van Rijn (2021) (van Rijn et al. 2021c) and Van Rijn (2025) (van Rijn et al. 2025), respectively. One-year data was not presented in the former source; therefore, it was assumed that the reported six-month values are applicable for year one for both SCS and machine perfusion. Year one data was not extrapolated because re-transplantations are generally more prevalent within the initial months post-transplant. Therefore, extrapolation was avoided to prevent overestimating the number of re-transplantations.

The annual re-transplantation rates for years 2 to 4 were calculated using one- and five-year data. Notably, these long-term rates are based on a single study using Liver Assist with DCD organs, as this was the only available evidence for re-transplantation up to five years. The annual re-transplantation rate for year five onwards in both arms of the model is assumed to be 0%. This was done because no data were identified to inform the impact of machine perfusion beyond five years post-transplant. These assumptions are tested in in scenario analysis.

Table 6.8: Re-transplantation rate parameters

Parameters	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
Proportion who receive re-transplantation due to PNF	76.47%	Provided by NHSBT via email consultation (Rhiannon Taylor; 03.04.26)	NHSBT registry data generally considered the best available evidence. This data is not stratified by SCS and machine perfusion, meaning this value may inherently include data relating to machine perfusion. This is tested in scenario analysis.
Re-transplantation rate within year one (excluding PNF)	7.69%	Van Rijn et al. (2021) (van Rijn et al. 2021c)	Clinical trial data on the use of hypothermic machine perfusion compared with SCS. The clinical trial was based in the Europe with a sample size of 160. The trial location is not likely to impact the value and is considered generalisable to the model population.
Re-transplantation rate within year five (excluding PNF)	15.38%	Van Rijn et al. (2025) (van Rijn et al. 2025)	
Risk ratio of re-transplantation (machine perfusion; applicable to all devices and modalities)			
Re-transplantation rate within year one (excluding PNF)	0.50	Van Rijn et al. (2021) (van Rijn et al. 2021c)	Data to inform the risk of re-transplantation was only available on the use of Liver Assist in HMP modality, and across DCD organs only. In this study, HMP was compared against SCS. The clinical trial was based in the Europe with a sample size of 160. The trial location is not likely to impact the value, however, given this is HMP and DCD-only data, it may not be fully representative of the full population. Additional two-way sensitivity analysis is included where the impact of varying this parameter across DBD/DCD organs is included.
Re-transplantation rate within year five (excluding PNF)	0.83	Van Rijn et al. (2025) (van Rijn et al. 2025)	

Table abbreviations: EAG, external assessment group; PNF, primary non-function; SCS, static cold storage.

Cost parameters

The key cost parameters used to inform the model were:

- Procedure and post-transplant costs
- Technology costs
- Complication costs

Procedure and post-transplant costs

The procedure costs of liver transplant and re-transplantation were sourced from the National Cost Collection (NCC) (Service 2024/25), see Table 6.9. The monthly cost of being on the waitlist was sourced from Zimmerman et al. (2022) (Zimmermann and Carter 2022). The annual cost post-transplant for the first two years was sourced from [redacted]. Both costs were inflated to the 2023/24 costing year using Personal Social Services Research Unit (PSSRU) inflation indices (Unit 2024).

The annual cost post-transplant for year three and beyond was [redacted]

Clinical consultation determined that a dedicated perfusion team may be required for the machine perfusion procedure, though this will likely vary by NHS trust and evolve over time. Expert feedback indicates that a typical centre requires between 3 and 7 whole time equivalent staff members, with a starting pay grade of Band 6 (which can increase to Band 8 or beyond).

Attributing a specific cost to this staff time is complex, clinical feedback indicates the time commitment is often difficult to determine and these staff members likely perform other clinical roles, meaning a full salary attribution would result in a significant overestimation of the per-procedure cost.

Due to these uncertainties, perfusion costs are excluded from the base case and instead addressed through two distinct scenario analyses:

- A one-off cost based on four staff members contributing an assumed two hours of time each per procedure, totalling £500 per transplant.
- The total annual cost of a dedicated perfusion team is divided by the estimated number of transplants conducted per site (125 procedures, derived from NHSBT data (Transplant 2025c) by dividing total annual procedures by the number of UK transplant sites). This results in an additional £3,400 per transplant.

The latter scenario likely represents an upper-bound estimate, as it does not account for the time these staff members spend on work already completed under standard care or roles within the wider clinician team unrelated to perfusion. It is not possible to determine the exact extent of this overlap.

Table 6.9: Procedure and post-transplant costs

Parameter	Cost	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
Cost of liver transplant (adults)	£27,206	NCC (Service 2024/25)	Values were sourced from the NCC which is representative data source from the healthcare payer perspective. Costs for the annual post-transplant cost (year two plus) were sourced from NCC and BNF. The BNF provides indicative NHS prices of drugs. This value is based on NHS guidance that suggest three annual appointments are required, obtained from NHS liver transplant guidance. This conservatively assumed no further complications occur beyond two years (unless resulting in re-transplantation).
Cost of liver transplant (paediatrics)	£58,138		
Cost of liver re-transplantation	£39,587		
Cost of liver re-transplantation	£63,906		
[redacted]	[redacted]	[redacted]	[redacted]
Cost of waitlist (monthly)	£1,469	Zimmermann et al. (2022) (Zimmermann and Carter 2022)	The specific breakdown of the waitlist cost was not detailed in the source. However, this was the best identified evidence. Values were inflated to the current costing year therefore is associated with a degree of uncertainty. DSA indicates this is not a key driver of results.
[redacted]	[redacted]	[redacted]	[redacted]

Parameter	Cost	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
			[redacted]

Table abbreviations: BNF, British national formulary; DSA, deterministic sensitivity analysis; NCC, National cost collection; NHS, National Health Service.

Table 6.10: Machine perfusion team costs

Parameter	Cost	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
Band 6 clinician (per hour)	£55.00	PSSRU (Unit 2024)	Values sourced from the 2024 PSSRU manual. These values are mid-band estimates, however, this is widely accepted as representative of the healthcare payer perspective.
Band 7 clinician (per hour)	£66.00		
Band 8 clinician (per hour)	£74.00		
Total cost of machine perfusion team	Existing staff time scenario: £500 Whole team scenario: £3,364	Calculation from above inputs	Staff time scenario: Calculated as described above, assuming two hours of additional staff time for two Band 6, one Band 7, and one Band 8 clinician per procedure. This is associated with considerable uncertainty and is, therefore, only used in scenario analysis. Whole team scenario: FTE costs for two Band 6, one Band 7, and one Band 8 clinician, divided by the calculated number of procedures per NHS site (where the total number of procedures is a product of the total organs available for transplant and the utilisation rate of SCS).

Table abbreviations: EAG, External assessment group; PSSRU, Personal Social Services Research Unit.

Technology costs

The cost of SCS (per procedure) comprises the cost of an icebox (£45.80), sourced from Bond et al (2009) (Bond M 2009), as well as a solution cost (£665.00), sourced from Javanbakht et al (2020) (Javanbakht et al. 2020). Both these costs were inflated to the 2023/24 costing year using PSSRU inflation indices (Unit 2024) (see Table 6.9). This cost is applicable to both arms of the model, as SCS is used in conjunction with machine perfusion.

Device cost values were provided by NICE via information submitted by companies and detailed in Table 6.10. In general, costing data was reported sporadically and inconsistently.

[redacted]

Costs provided by Liver Assist, PerLifePRO and VitaSmart varied as follows:

[redacted]

Inconsistencies between device costs represent the inherently varied nature of company-specific pricing approaches. Some companies opt to charge higher up-front prices, while others charge more for ongoing and consumable

components. There was a significant lack of clarity regarding exactly which consumables and maintenance services were included within each company's reported costs.

The expected lifetime of a machine perfusion device was [redacted]

[redacted] Two costing approaches were included in the model as follows:

- Annutised costing approach: it is assumed that the cost of machine perfusion is spread across the total number of expected perfusion procedures, taking into consideration both the number of procedures per year, and the expected lifetime of the device.
- Upfront costing approach: it is assumed that the total cost of the perfusion devices is incurred upfront upon first use of the machine perfusion device. This does not consider the expected lifetime of a machine perfusion device.

The annutised costing approach better reflects the average per-procedure cost of machine perfusion over a long period of time, while the upfront costing approach will better reflect the actual and immediate costs incurred by the NHS as a result of purchasing a machine perfusion device. In the base case analysis, the upfront costing approach, which represents a higher value, is conservatively assumed more applicable, though additional scenario analysis, which is not detailed in this report, suggests the annutised costing approach has negligible impact on model results.

The annual number of procedures conducted per device was assumed to be 60 based on clinical consultation.

Table 6.11: Base cost parameters

Parameter	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
Cost of SCS (per procedure)	£827.35	Bond et al. (2009) (Bond M 2009) Javanbakht et al. (2020) (Javanbakht et al. 2020)	Both associated costs were inflated to the current costing year. Uncertainty remains around the icebox cost given this value was originally published in 2007. DSA suggests this cost has limited impact on model results due to the fact it is applied in both arms of the model as well as its relative magnitude when compared with machine perfusion.

Table abbreviations: DSA, deterministic sensitivity analysis; EAG, external assessment group; SCS, static cold storage.

Table 6.12: Technology costs

Parameter	Liver Assist	VitaSmart	*metra*	PerLifePRO	Comment
Cost of device including staff training (upfront)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost of maintenance	[redacted]	[redacted]	[redacted]	[redacted]	
Cost of consumables	[redacted]	[redacted]	[redacted]	[redacted]	
Single unit cost of machine perfusion	[redacted]	[redacted]	[redacted]	[redacted]	

Complication costs

The costs for short-term complications were applied as one-off costs at the point of transplant. All costs, except for EAD, were sourced from NCC 2024/25 (Service 2024/25), BNF 2025 (National Institute for Health and Care Excellence 2025) and NHSBT 2025 (Transplant 2025b); see Table 6.13. These costs have been selected as they represent the most commonly delivered treatments for each complication. For all inputs, except EAD, these values are calculated as weighted averages based on all NHS activity for the specified treatment for each complication. Subpopulation-specific data was only available for the cost of RRT, which was broken down by paediatric and adult populations. Other costs are assumed applicable across adult and paediatric populations. It was also not possible to stratify complication costs by adult and ECD populations, and so these are assumed to be the same. The additional cost of EAD was calculated using cost of additional general ward and ICU stay due to EAD. However, the values may underestimate or overestimate the cost of complications, as the case mix of treatments is likely to vary by severity and population. See Appendix E for additional data used.

Table 6.13: Unit cost of complications

Parameter	Unit cost	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
RRT (adults)	£903	NCC (Service 2024/25)	Values were sourced from the NCC which is representative data source from the healthcare payer perspective.
RRT (paediatrics)	£1,133		
HAT	£11,764		
Biliary leaks	£4,586		
Anastomotic strictures	£9,588	NCC (Service 2024/25)	Values were sourced from the NCC, which provides a representative data source from the healthcare payer perspective. This cost is assumed to be equivalent for both non-anastomotic and anastomotic biliary strictures. During consultation, most experts agreed that this grouping was a reasonable assumption for the modelling approach. While one expert highlighted that anastomotic strictures may involve more complex management, such as surgery and a Roux-en-Y loop leading to a prolonged hospital stay, a paucity in data suggesting the sub proportions this is applicable to, as well as a lack in granular NCC data, prevented the explicit separation of these costs. This simplification was considered appropriate as these complication costs were not identified as primary drivers of the model outcomes.
Non-anastomotic biliary strictures	£9,588	Assumption	
PRS	£378	BNF (Ltd.), NHSBT (Transplant 2025b)	It is assumed that PRS requires treatment with vasopressors and one additional blood transfusion. Vasopressor costs assume to equate two pack of Noradrenaline (base) 4mg/50ml solution for infusion vials. Guidance on dosage states this varies by response hence a conservative estimate assuming one pack of 10 vials per person is used. DSA demonstrated this to have very little impact on model results.
EAD	£7,587.72	Calculation	This value was calculated based on the increased stay in both general and ICU wards. Incremental change (%) in LoS is sourced from a Canadian study (Croome KP 2013) and applied to UK data on actual LoS (Limbu Y 2025). Costs are obtained from NHS Cost Collection. Calculations are provided in more detail in Appendix E.

Table abbreviations: EAD, early allograft dysfunction; HAT, hepatic artery thrombosis; ICU, intensive care unit; LoS, length of stay; NCC, national cost collection; PRS, post-reperfusion syndrome; RRT, renal replacement therapy.

Health state utilities

Annual utilities for being on the waitlist and living with a transplant were sourced from Ratcliffe et al, 2002 (Ratcliffe J 2002). This source is also used in the OrganOx *metra*, and Zimmerman et al (2021) economic evaluations, which are described in Section 6.1. This study is dated and, as such, the utility estimates may not be fully reflective of current outcomes. However, in light of no other data identified, we have used the best available evidence. This study included 382 people across three UK transplant centres, which provides data estimated that are relevant to the population. The impact that these values have on model results is explored in the sensitivity analysis.

The reported EQ-5D listing mean score of 0.53 was used as the waitlist utility score. This value is considered representative of the pre-transplant utility. The post-transplant utility for the first year was calculated as 0.71. The post-transplant utility for the second year and beyond was 0.78. The utilities experienced after a second transplant (re-transplantation) are assumed to be equal to those experienced after the initial transplant, due to a lack of data to inform this specific parameter. Utilities in the model were applied multiplicatively to UK population EQ-5D-3L background utilities sourced from NICE Decision Support Unit (DSU) (2022).

Utilities were applied multiplicatively as this better represents how the true HRQoL experiences by populations on the waitlist, or with a transplant, will vary with age. Applying utilities multiplicatively is considered more representative because it treats a health condition as a proportionate reduction in QALYs, rather than a fixed penalty. Since background population health naturally declines with age, this approach ensures that the utility of a transplant recipient remains proportionate over time. If fixed values were applied, it could lead to unrealistic scenarios where an older patient is modelled to have better health than a healthy individual of the same age.

The model includes the functionality to include one-off complication and surgery disutilities. However, due to limited available evidence, these parameters have not been included in the base case analysis.

Mortality

Survival data for people living with a liver transplant were sourced from NHSBT 2024/25 (Transplant 2025d); the impact of machine perfusion on survival outcomes was captured by calculating a HR (0.32). This was sourced from Czigany et al., (2024) (Czigany et al. 2024) and applied over the first five years of the model. This study reported 5-year mortality Liver Assist (HMP) in a DBD population compared with SCS.

Additional data were identified for other devices and donor types, though these were restricted to shorter follow-up periods. This included 2-year mortality for Liver Assist in a DBD population, 1-year data for *metra* (HMP; mixed DBD/DCD) and 6-month data for VitaSmart. To account for the lack of long-term evidence for these specific cohorts, these values were extrapolated to the 5-year mark and tested in scenario analyses. Furthermore, a two-way sensitivity analysis was conducted to vary mortality across both DBD and DCD populations.

The impact of living with a second transplant was not captured in the analysis, as it is likely that this is captured indirectly through existing survival data HR. A separate parameter to capture mortality associated with re-transplantations risks double counting the mortality. General population mortality was included using data from the Office for National Statistics (2021) and applied in the model if post-transplant survival exceeded overall background mortality.

6.2.4 Presentation of results

Base case deterministic analysis was conducted for an adult population on the liver transplant wait list. Results comparing the use of each machine perfusion

device with SCS are presented. Results across perfusion methods are also presented where there is sufficient evidence, as described in Section 6.2.2.

Key outcomes across all deterministic analyses include:

- Total and incremental costs and QALYS
- ICER
- NHB
- NMB
- Total and incremental number of events, including transplantations, re-transplantations, deaths on the waitlist, and short-term complications.

DSA was conducted for the scenario where best available machine perfusion data is used, and results are presented in the form of a tornado diagram. Additional one-way analysis evaluated results when:

- The cost of machine perfusion was varied from £0 to £50,000 per procedure
- The proportion of newly utilised livers which are DCD was varied from 0% to 100%
- The HR of mortality associated with machine perfusion is varied from 0 to 1 (base case calculated value 0.32)
- The organ utilisation was varied from 1 to 1.88 (where 1.88 is the theoretical maximum organ utilisation increase without utilising more organs than there are available).

Two-way scenario analysis is also carried out where:

- The long-term impact of mortality associated with DBD/DCD organs is varied.
- The long-term rate of re-transplantation rate associated with DBD/DCD organs is varied.

PSA was also conducted, results across each machine perfusion device are presented and include:

- Total intervention and incremental costs and QALYs
- The probability of machine perfusion being cost-effective at cost-effectiveness threshold of £20,000/QALY
- The probability of machine perfusion being cost-effective at cost-effectiveness threshold of £30,000/QALY
- The probability of machine perfusion being cost-saving.
- Cost-effectiveness plane

An additional PSA was included where the long-term impact machine perfusion has on survival was excluded as this was determined to be a key driver of model results.

Scenario analyses

Additional scenario analyses carried out include:

- Applying the median time to transplant, as opposed to the mean, to reflect the experience of a typical patient and account for the skewed nature of waitlist data.
- Assuming changes in organ utilisation reduces time to transplant but does not change the number of organs transplanted.
- Assuming long-term mortality does not change, changes in organ utilisation reduces time to transplant, and changes in organ utilisation do not change the number of organs utilised
- Assuming change in organ utilisation affects both the number of transplants performed and time-to-transplant.
- Assuming that 50% of those who do not receive a transplant by 42 months instead go on to receive a transplant by the end of the fourth year (48 months).
- Extending mortality HRs associated with machine perfusion to 10 years
- Excluding the impact of machine perfusion on all mortality

- Assuming that, after five years, the rate of re-transplantation is 1% (as opposed to 0% in the base case) and maintaining the RR of re-transplantation for machine perfusion.
- Excluding differences in complications to explore the impact of machine perfusion when the rate of complications are the same between each arm of the model.
- Including an additional cost relating to perfusionist staff time, assuming 8 cumulative hours of clinician time (See Section 6.2.3). Including an additional cost relating to a standalone perfusionist team, assuming four dedicated clinicians (See Section 6.2.3).

In the base case analysis, the cost and QALYs accrued in the post-transplant and post-re-transplantation health states are assumed to be the same. Therefore, in the DSA, PSA, and all additional scenario analyses, these are varied codependently such that, when one is varied, they both are (and by the same margin). This reflects limitations in the available evidence, as robust data describing differences in long-term healthcare costs and QALYs according to the number of prior transplantations were not identified. While it is clinically plausible that outcomes following re-transplantation may differ from those following a first transplant, available published data are insufficient to parameterise these differences. The assumption of equal post-transplant costs and utilities, therefore, represents a pragmatic and conservative approach.

6.3 Results from the economic modelling

6.3.1 Deterministic results

Base case deterministic results indicate that machine perfusion, plus SCS, is cost-effective compared with SCS alone across all device types considered. ICERs range from approximately £5,600 (Liver Assist; HMP) to £19,400 (PerLifePRO; NMP) per QALY gained. Incremental QALYs are the same (to

two decimal places) across interventions, driven only by minor and statistically insignificant changes in the rates of PNF and associated mortality as well as from re-transplantations. Differences in ICERs are primarily driven by variation in device costs, with other contributors comprising statistically insignificant differences in complications, as well as PNF-related re-transplantations and mortality.

Results across the various interventions indicated that devices using the NMP modality generally led to higher ICERs than those using HMP. This trend is primarily driven by the NMP clinical data, which estimated a higher frequency of complications, thereby increasing the overall costs associated with these procedures. However, it is important to note that these differences in complication rates were statistically insignificant. Consequently, it is not possible to definitively conclude whether this cost increase reflects real-world clinical outcomes or is a product of data variability. The robustness of the results for NMP devices is further limited by the available evidence base. Many of the key drivers in the model, specifically long-term mortality and re-transplantation rates, were sourced from studies evaluating HMP devices. Applying these parameters to NMP devices assumes equivalence that may not be present. As a result, the findings for HMP-based devices may be considered more robust.

Machine perfusion costs were sourced from company submissions provided to NICE, with inconsistent reporting across companies on costing structure and format, as detailed in Section 6.2.2 and 6.2.3. It should also be noted that several device-specific complication probabilities were not statistically significant. Because these are both key drivers of the differences in ICER between devices, given the evidence available, the model results from this analysis should not be used to compare impact between devices. Furthermore, there was very limited clinical data to inform Liver Assist in NMP modality and PerLifePRO, so all results relating to these are subject to additional uncertainty.

A breakdown of costs, QALYs, and event counts are supplied in Appendix F. These results suggest that on average, life expectancy is extended by approximately 2 years with machine perfusion compared with SCS alone. Fewer QALYs are accrued in the machine perfusion arm within the waitlist and post-re-transplantation health states. This reflects an increase in the number of people spending less time on the waitlist because they are having transplants as well as a reduction in the number of re-transplantations because of using machine perfusion.

From a cost perspective, total costs are higher with machine perfusion. This is driven by the additional cost of the perfusion device and the higher proportion of patients undergoing transplantation and subsequently receiving additional care post-transplant. These increased costs are partially offset by marginal cost savings associated with fewer re-transplantations and reduced time spent on the waitlist because a greater proportion of the cohort proceed to transplant rather than remaining on the waitlist until death.

Event breakdowns indicate that machine perfusion increases the number of initial transplants performed and reduces the number of re-transplantations. Fewer deaths occur on the waitlist and fewer deaths are attributable to PNF. Across all devices, machine perfusion is associated with fewer cases of EAD, HAT, RRT, and PNF. Increases (or no change) are observed across all devices in anastomotic biliary strictures. This is due to data on the direction of effect being mixed for biliary leaks, non-anastomotic biliary strictures, and PRS. The incremental differences in complication rates across devices are small and associated with considerable uncertainty due to the statistical insignificance of the data used to inform them, as noted in the original studies.

Overall, Liver Assist (NMP modality), PerLifePRO (NMP modality), and *metra* are associated with higher overall complication costs. As above, this is affected by the statistical insignificance of the data. The prevalence and cost of complications are demonstrated not to be a key driver of model results. The cost of PNF was not explicitly modelled to avoid double counting because this

was assumed to be captured through the cost of additional re-transplantations.

Two subpopulations were explored: paediatric recipients and recipients of ECD livers (see Section 6.2.3 for modelled definition). Due to limited subgroup-specific evidence, most model parameters remained consistent with the adult population. Deviations are described in Section 6.2.3.

Results for these analyses were broadly consistent with the base case; Results for the paediatric population are displayed in Table 6.15. The use of machine perfusion is estimated to generally yield lower ICERs in a paediatric population. Due to an absence of data, this result is primarily driven by the age of the cohort, as a paediatric population has a higher average life-expectancy and so each additional liver transplant leads to higher QALY gains. Nuances in the long-term costs of treating paediatric patients, as well as the specific impact on key drivers such as the re-transplantations and mortality however, is not well understood The results of the ECD population are not detailed in this report as the results of this analysis they are associated with considerable uncertainty and only marginal differences in ICERs compared to the adult population.

Device-specific data were sporadically reported across devices. Results for Liver Assist (HMP), *metra*, and VitaSmart are deemed to be associated with higher significance. Results for Liver Assist (NMP) are of moderate quality, due to the assumption that all complication data is equivalent to that of *metra*. Results for PerLifePRO are associated with low significance, as no device-specific inputs could be identified. Specific inputs assumed applicable across devices and perfusion modalities are described in more detail in Table 6.6 to Table 6.8.

Table 6.14: Deterministic base case results: Adult population

Technology	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER*	NMB	NHB
SCS alone	£72,733	6.44	-	-	-	-	-
Liver Assist (NMP)	£82,986	7.84	£10,253	1.41	£7,289	£17,880	0.89
Liver Assist (HMP)	£80,686	7.85	£7,953	1.41	£5,639	£20,257	1.01
PerLifePRO (NMP)	£100,046	7.84	£27,313	1.41	£19,417	£820	0.04
PerLifePRO (HMP)	£97,709	7.85	£24,975	1.41	£17,706	£3,235	0.16
metra (NMP)	£88,540	7.84	£15,806	1.41	£11,237	£12,326	0.62
VitaSmart (HMP)	£81,057	7.85	£8,324	1.41	£5,902	£19,885	0.99

Table abbreviations: ICER, incremental cost-effectiveness ratio; MP, machine perfusion; NMB, net monetary benefit; NHB, net health benefit; QALY, quality-adjusted life year; SCS, static cold storage.

* The evidence to inform the model does not support comparisons to be made between different perfusion devices.

Table 6.15: Deterministic base case results: Paediatric population

Technology	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER	NMB	NHB
SCS alone	£107,015	12.95	-	-	-	-	-
Liver Assist (NMP)	£120,191	15.00	£13,176	2.05	£6,422	£27,860	1.39
Liver Assist (HMP)	£117,831	15.00	£10,816	2.05	£5,265	£30,271	1.51
PerLifePRO (NMP)	£137,147	15.00	£30,132	2.05	£14,686	£10,904	0.55
PerLifePRO (HMP)	£134,774	15.00	£27,759	2.05	£13,512	£13,328	0.67
metra (NMP)	£125,711	15.00	£18,695	2.05	£9,112	£22,340	1.12
VitaSmart (HMP)	£118,631	15.00	£11,616	2.06	£5,649	£29,509	1.48

Table abbreviations: ICER, incremental cost-effectiveness ratio; MP, machine perfusion; NMB, net monetary benefit; NHB, net health benefit; QALY, quality-adjusted life year; SCS, static cold storage.

6.3.2 Probabilistic results

PSA results are consistent with the deterministic findings. At a cost-effectiveness threshold of £20,000 per QALY gained, the probability of machine perfusion being cost-effective ranges from 61% to 100% (or 93% to 100% when PerLifePRO is excluded). The probability of cost-effectiveness at a threshold of £30,000 per QALY ranges from 87% to 100% (or 99% to 100% when PerLifePRO is excluded ICERs range from £6,300 to £20,900 (only up to £12,200 when PerLifePRO excluded). 95% confidence intervals indicate ICERs range from £5,200 to £26,200. PerLifePRO consistently demonstrated higher ICERs driven by the incremental difference in the device cost. As with the deterministic results, given the lack of device-specific data for PerLifePRO, results relating to this device are associated with considerable uncertainty.

The cost-effectiveness planes (See Appendix F) demonstrate that for all technologies, the majority of simulations lie in the north-east quadrant, reflecting higher costs and higher QALYs compared with SCS alone, with a small number of iterations indicating cost savings. Variation in QALYs across iterations is greater than variation in costs, reflecting the fact that QALY gains are driven by a limited number of clinical parameters, including mortality and re-transplantation risks, which are associated with greater uncertainty. Utility estimates themselves are also subject to uncertainty, as discussed in Section 6.2.3.

An additional PSA was conducted in which the mortality benefit associated with machine perfusion was removed (i.e. the HR for mortality was set to 1). This analysis was undertaken to explore a key structural assumption, identified in the scenario analyses (see Section 6.3.4) as an important driver of results. The HR informing the mortality benefit of machine perfusion was derived from evidence that was statistically non-significant and, therefore, subject to uncertainty. Removing the mortality effect represents a conservative scenario in which machine perfusion results in no long-term survival differences.

Under this assumption, at a willingness-to-pay threshold of £20,000 per QALY, Liver Assist (both HMP and NMP), as well as VitaSmart, remained cost-effective; PerLifePRO (NMP), PerLifePRO (HMP), and *metra* demonstrated ICERs of £46,000, £41,500, and £26,200, respectively. These increases were driven by the higher estimated per-device cost of machine perfusion and are therefore associated with uncertainty. As with the deterministic results, incremental ICER differences between individual devices are subject to considerable uncertainty due to the nature of the reported costing data. Therefore, these results should not be interpreted as reflecting higher certainty with one device over another. It is important to note that clinical expert feedback indicated that a reduction in mortality associated with machine perfusion is highly plausible. This is expected to be driven by reductions in complication-related mortality, as well as improved graft viability and longer-term transplant outcomes.

Table 6.16: Probabilistic base case results (Liver Assist; NMP)

Technology	Incremental costs	Incremental QALYs	ICER	NMB	NHB	Probability of CE at £20k/QALY	Probability of CE at £30k/QALY	Probability that the intervention is dominant
Average	£11,386	1.40	£8,124	£16,644	0.83	98.20%	99.70%	5.40%
Lower CI	£8,686	0.93	£9,310	£9,973	0.50			
Upper CI	£13,416	1.83	£7,314	£23,268	1.16			

Table abbreviations: CE, cost-effectiveness; ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year.

Table 6.17: Probabilistic base case results (Liver Assist; HMP)

Technology	Incremental costs	Incremental QALYs	ICER	NMB	NHB	Probability of CE at £20k/QALY	Probability of CE at £30k/QALY	Probability that the intervention is dominant
Average	£8,815	1.41	£6,262	£19,340	0.97	99.00%	99.90%	10.00%
Lower CI	£7,184	0.89	£8,069	£10,622	0.53			
Upper CI	£10,886	1.77	£6,133	£24,614	1.23			

Table abbreviations: CE, cost-effectiveness; ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year.

Table 6.18: Probabilistic base case results (PerLifePRO; NMP)

Technology	Incremental costs	Incremental QALYs	ICER	NMB	NHB	Probability of CE at £20k/QALY	Probability of CE at £30k/QALY	Probability that the intervention is dominant
Average	£29,239	1.40	£20,903	-£1,263	-0.06	44.10%	88.60%	0.00%
Lower CI	£25,193	0.96	£26,214	-£5,972	-0.30			
Upper CI	£34,073	1.80	£18,933	£1,919	0.10			

Table abbreviations: CE, cost-effectiveness; ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year.

Table 6.19: Probabilistic base case results (PerLifePRO; HMP)

Technology	Incremental costs	Incremental QALYs	ICER	NMB	NHB	Probability of CE at £20k/QALY	Probability of CE at £30k/QALY	Probability that the intervention is dominant
Average	£26,119	1.40	£18,696	£1,822	0.09	61.60%	93.90%	0.00%
Lower CI	£23,122	0.92	£25,236	-£4,797	-0.24			
Upper CI	£27,985	1.74	£16,106	£6,766	0.34			

Table abbreviations: CE, cost-effectiveness; ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year.

Table 6.20: Probabilistic base case results (*metra*; NMP)

Technology	Incremental costs	Incremental QALYs	ICER	NMB	NHB	Probability of CE at £20k/QALY	Probability of CE at £30k/QALY	Probability that the intervention is dominant
Average	£17,134	1.40	£12,219	£10,912	0.55	93.00%	99.00%	1.00%
Lower CI	£15,674	0.94	£16,734	£3,059	0.15			
Upper CI	£18,907	1.81	£10,437	£17,322	0.87			

Table abbreviations: CE, cost-effectiveness; ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year.

Table 6.21: Probabilistic base case results (VitaSmart; HMP)

Technology	Incremental costs	Incremental QALYs	ICER	NMB	NHB	Probability of CE at £20k/QALY	Probability of CE at £30k/QALY	Probability that the intervention is dominant
Average	£9,150	1.41	£6,500	£19,005	0.95	99.40%	99.80%	7.50%
Lower CI	£7,804	0.95	£8,247	£11,121	0.56			
Upper CI	£9,378	1.79	£5,235	£26,452	1.32			

Table abbreviations: CE, cost-effectiveness; ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year.

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6.3.3 Sensitivity analysis results

One-way threshold analysis

Three additional one-way threshold analyses have been included for all devices (except PerLifePRO because no evidence specific to PerLifePRO was used to inform this analysis). The full results of these analyses are displayed in Appendix F. Threshold analysis conducted to determine the per-procedure cost of machine perfusion at which the ICER would reach £20,000 per QALY gained. This analysis indicated that machine perfusion would remain cost-effective up to a device cost of approximately [redacted] (Liver Assist (NMP) and *metra*) to [redacted] (Liver Assist (HMP)). For the devices included in this analysis, machine perfusion costs were estimated to range between [redacted] per procedure[redacted].

Additional one-way sensitivity analysis varied the proportion of newly utilised livers assumed to be DCD in origin. Across all included devices, NMB ranged from approximately £12,200 to £20,500 as this value was varied from [redacted]

As DCD livers are traditionally associated with poorer long-term survival outcomes compared with DBD livers, increasing the proportion of newly utilised DCD livers resulted in smaller incremental health gains. While the benefits of machine perfusion are anticipated to have a larger impact on long-term outcomes of DCD organs, data limitations required the modelling to assume that key inputs regarding mortality and re-transplantation outcomes are the same across both DBD and DCD organs. Consequently, this analysis may underestimate the potential impact of donor origin on incremental outcomes.

One-way sensitivity analysis was also conducted on the HR for mortality associated with machine perfusion. In this scenario, cost-effectiveness was primarily driven by the increased number of transplants performed and reductions in costly complications, including PNF and subsequent re-transplantation.

Additional threshold analysis was conducted to explore how the NMB changed as the machine perfusion utilisation rate was varied between 1 and 1.88. A ceiling value of 1.88 was selected because this represents a device which is able to utilise all organs eligible for donation (given all additional known base case inputs). This analysis demonstrated that, when machine perfusion was assumed to lead to no additional livers being utilised, the NMB was approximately £5,000 to £12,000 (depending on device selected). This increased to between £34,000 and £44,000 when the utilisation rate was approximately 1.4. This indicates that machine perfusion is still cost-effective, even when no new livres are utilised and is driven by the reduction in long-term mortality and re-transplantations.

Clinical consultation indicated that experts broadly anticipate utilisation rates to be positive (i.e. above 1). However, there remains significant uncertainty regarding the exact magnitude of this increase. Furthermore, it is not well understood whether these gains will be more pronounced for DCD versus DBD organs, or if specific device types, such as NMP or HMP, will drive higher utilisation. Due to this uncertainty, the base-case assumption relies on NMP data which has been extrapolated across all machine perfusion modalities.

The NMB results plateaued beyond a utilisation rate of 1.4 because at this point, the health gains were constrained by the size of the recipient cohort. This occurs because the model can only assign a transplant to patients on the waitlist. Once the supply of viable organs is sufficient to treat the entire population on the waitlist, further increases in organ availability do not yield additional incremental benefits, as there are no remaining patients within the model to receive these additional organs. In reality the waitlist will be dynamic with additional people entering the waitlist, however, we have not accounted for this in the currently analysis due to paucity of evidence.

Two-way threshold analysis

Two two-way sensitivity analyses were conducted for all devices, except PerLifePRO. The full results of these analyses are displayed in Appendix F.

Two-way sensitivity analysis was performed to explore the relationship between the mortality HRs for DBD and DCD organs. These were varied co-dependently from 1 (representing no mortality benefit over SCS alone) to 0 (representing the elimination of transplant-related mortality).

The results indicated that when both HRs were set to 1, the NMB for the *metra* device was -£2,000, increasing to £15,300 as the HRs approached 0. For all other devices, including Liver Assist (HMP and NMP modalities) and VitaSmart, the NMB remained positive, ranging from £3,500 to £23,300. This suggests that for these three devices, the intervention remains cost-effective even in a scenario where no mortality benefit is assumed, primarily due to the offsets provided by improved organ utilisation and reduced short-term complications. However, these results highlight that HRs for mortality are key drivers of QALY gains within the model. In scenarios where these HRs are set to 1 (indicating no mortality benefit), the incremental QALYs are significantly reduced and move much closer to 0. When the health gain is this marginal, the additional upfront costs of the machine perfusion devices have a far larger impact on the ICER.

[redacted].

The range of results produced by this analysis demonstrates that the impact of machine perfusion on long-term survival is a key driver of the model results. Further analysis suggests that the DBD HR of mortality is a more significant driver of the NMB than the corresponding HR for DCD organs. This trend is explained by the fact that recipients of DBD organs generally experience better survival outcomes. Consequently, any incremental survival benefits incurred by machine perfusion are experienced over a longer period compared with the DCD cohort.

A second two-way sensitivity analysis was conducted to explore the impact of re-transplantation RRs within the first-year post-transplant, and years 2 to 5. These RRs were varied co-dependently from 0 (representing the total avoidance of re-transplantation) to 1 (representing no difference between SCS and machine perfusion). As these values were varied, the NMB across all included devices ranged from £10,900 (*metra*, when both RRs are 1) to £25,000 (Liver Assist (HMP), when both RRs are 0). These findings indicate that even in a scenario where re-transplantation rate differences are assumed to be zero across both time periods, machine perfusion remains a cost-effective intervention.

Further analysis suggests that the RR for the 2- to 5-year post-transplantation period is a larger driver of model results than the RR for the first year. This trend occurs because the 2- to 5-year window represents a significantly longer duration of the model's time horizon. Consequently, any incremental differences associated with machine perfusion are experienced over a more prolonged period, leading to a greater cumulative impact on both total costs and QALYs compared with those arising from the first year

6.3.4 Scenario analysis results

Scenario analyses are not conducted for PERLIFEPRO, given the limited availability of clinical evidence. Results from scenario analyses (see Section 0.4) were broadly aligned with the base case findings. In most scenarios, variation in ICERs was modest, suggesting that the model results are relatively robust to plausible changes in structural and parameter assumptions.

One of two notable exceptions was the scenario in which machine perfusion was assumed to have no impact on long-term mortality (HR = 1). Under this assumption, the ICER increased to between £9,800 (Liver Assist; HMP) and £23,600 (*metra*) per QALY gained. The increase relative to the base case reflects the removal of incremental survival benefits, such that cost-effectiveness is driven solely by changes in complication rates, re-

transplantations, and transplant volume. Notably, within this scenario, the *metra* was the only device that led to an ICER above the £20,000 per QALY threshold.

Long-term mortality is assumed to capture any complication-related mortality (with the exception of PNF and waitlist mortality). Consequently, this scenario indirectly assumes that complications remain unchanged from a survival perspective. Clinical consultation indicated that the use of machine perfusion is widely understood to reduce complications and associated complication-related mortality. As such, this specific scenario may not fully reflect real-world outcomes but instead illustrates the model's sensitivity to the long-term survival assumptions.

The second notable exception is the scenario in which machine perfusion is assumed to have no impact on long-term mortality (HR = 1) while simultaneously failing to increase the uptake of organs. In this scenario, the ICERs ranged from £115,000 to £6,000,000 per QALY gained.

These high values are driven by the fact that, with mortality and utilisation benefits removed, the only remaining outcomes impacting QALYs are the rate of PNF and the rate of re-transplantation. Given that the incidence of PNF is very low, and re-transplantation only leads to a temporary decrease in QALYs within the first year, the resulting incremental QALY gain is negligible and therefore even a marginal change in costs can lead to disproportionately large ICERs.

It is worth noting that, as previously discussed, it is unlikely that machine perfusion would have zero impact on mortality. Furthermore, clinical feedback suggested that while the exact utilisation rate remains unknown, it is generally expected to be positive. It is also important to highlight that the scenario in which organ utilisation is assumed not to change does not alter the direction of the results and only leads to marginal increases in the ICER. This confirms that the extreme results in this specific scenario are a product of the combined removal of both primary drivers of clinical benefits.

Table 6.22: Deterministic scenario analysis results (Liver Assist; NMP)

Scenario	Incremental costs	Incremental QALYs	ICER	NMB	NHB
Base case	£10,253	1.41	£7,289	£17,880	0.89
Median wait time used	£10,575	1.42	£7,428	£17,897	0.89
Organ utilisation reduced time to transplant but does not impact number of transplants	£4,768	0.76	£6,235	£10,526	0.53
Organ utilisation increased transplants and reduced wait times	£9,639	1.40	£6,890	£18,342	0.92
Machine perfusion has no impact on mortality and organ utilisation reduced time to transplant but does not impact number of transplants	£2,600	0.00	£2,067,783	-£2,575	-0.13
50% of individuals waiting longer than 42 months receive transplant	£11,044	1.47	£7,524	£18,312	0.92
Mortality RRs are applied for 10 years	£11,263	1.86	£6,070	£25,848	1.29
Machine perfusion has no impact on mortality	£7,869	0.57	£13,872	£3,476	0.17
1% probability of re-transplantation applied for lifetime	£10,852	1.41	£7,717	£17,274	0.86
Post-transplant complications set equal across SCS and machine perfusion	£10,307	1.40	£7,387	£17,597	0.88
Perfusionist staff time is includes (8 cumulative hours per procedure)	£10,678	1.41	£7,591	£17,455	0.87
A full perfusionist team is costed for and included in the model	£13,113	1.41	£9,322	£15,020	0.75

Table abbreviations: ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year; RR, risk ratio; SCS, static cold storage.

Table 6.23: Deterministic scenario analysis results (Liver Assist; HMP)

Scenario	Incremental costs	Incremental QALYs	ICER	NMB	NHB
Base case	£7,953	1.41	£5,639	£20,257	1.01
Median wait time used	£8,260	1.43	£5,786	£20,291	1.01
Organ utilisation reduced time to transplant but does not impact number of transplants	£2,675	0.77	£3,482	£12,690	0.63
Organ utilisation increased transplants and reduced wait times	£7,335	1.40	£5,228	£20,724	1.04
Machine perfusion has no impact on mortality and organ utilisation reduced time to transplant but does not impact number of transplants	£506	0.00	£115,218	-£418	-0.02
50% of individuals waiting longer than 42 months receive transplant	£8,665	1.47	£5,887	£20,772	1.04
Mortality RRs are applied for 10 years	£8,964	1.86	£4,820	£28,230	1.41
Machine perfusion has no impact on mortality	£5,568	0.57	£9,756	£5,846	0.29
1% probability of re-transplantation applied for lifetime	£8,561	1.41	£6,071	£19,644	0.98
Post-transplant complications set equal across SCS and machine perfusion	£10,307	1.40	£7,387	£17,597	0.88
Perfusionist staff time is includes (8 cumulative hours per procedure)	£8,378	1.41	£5,939	£19,833	0.99
A full perfusionist team is costed for and included in the model	£10,807	1.41	£7,662	£17,404	0.87

Table abbreviations: ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year; RR, risk ratio; SCS, static cold storage.

Table 6.24: Deterministic scenario analysis results (*metra*; NMP)

Scenario	Incremental costs	Incremental QALYs	ICER	NMB	NHB
Base case	£15,806	1.41	£11,237	£12,326	0.62
Median wait time used	£16,167	1.42	£11,356	£12,305	0.62
Organ utilisation reduced time to transplant but does not impact number of transplants	£9,827	0.76	£12,850	£5,468	0.27
Organ utilisation increased transplants and reduced wait times	£15,203	1.40	£10,867	£12,778	0.64
Machine perfusion has no impact on mortality and organ utilisation reduced time to transplant but does not impact number of transplants	£7,627	0.00	£6,065,214	-£7,602	-0.38
50% of individuals waiting longer than 42 months receive transplant	£16,789	1.47	£11,438	£12,567	0.63
Mortality RRs are applied for 10 years	£16,817	1.86	£9,063	£20,295	1.01
Machine perfusion has no impact on mortality	£13,388	0.57	£23,602	-£2,043	-0.10
1% probability of re-transplantation applied for lifetime	£16,742	1.41	£11,905	£11,385	0.57
Post-transplant complications set equal across SCS and machine perfusion	£15,897	1.40	£11,394	£12,007	0.60
Perfusionist staff time is includes (8 cumulative hours per procedure)	£16,232	1.41	£11,539	£11,901	0.60
A full perfusionist team is costed for and included in the model	£18,666	1.41	£13,270	£9,466	0.47

Table abbreviations: ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year; RR, risk ratio; SCS, static cold storage.

Table 6.25: Deterministic scenario analysis results (VitaSmart; HMP)

Scenario	Incremental costs	Incremental QALYs	ICER	NMB	NHB
Base case	£8,324	1.41	£5,902	£19,885	0.99
Median wait time used	£8,633	1.43	£6,048	£19,916	1.00
Organ utilisation reduced time to transplant but does not impact number of transplants	£3,012	0.77	£3,921	£12,352	0.62
Organ utilisation increased transplants and reduced wait times	£7,707	1.40	£5,494	£20,351	1.02
Machine perfusion has no impact on mortality and organ utilisation reduced time to transplant but does not impact number of transplants	£844	0.00	£194,923	-£757	-0.04
50% of individuals waiting longer than 42 months receive transplant	£9,049	1.47	£6,148	£20,386	1.02
Mortality RRs are applied for 10 years	£9,335	1.86	£5,020	£27,858	1.39
Machine perfusion has no impact on mortality	£5,939	0.57	£10,408	£5,473	0.27
1% probability of re-transplantation applied for lifetime	£8,926	1.41	£6,330	£19,277	0.96
Post-transplant complications set equal across SCS and machine perfusion	£10,218	1.40	£7,324	£17,685	0.88
Perfusionist staff time is includes (8 cumulative hours per procedure)	£8,748	1.41	£6,203	£19,461	0.97
A full perfusionist team is costed for and included in the model	£11,178	1.41	£7,925	£17,031	0.85

Table abbreviations: ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year; RR, risk ratio; SCS, static cold storage.

6.4 Summary and interpretation of the economic evidence

6.4.1 Discussion of results

A total of 15 studies reporting economic evidence were identified, of which four were prioritised for detailed review based on evaluation type and relevance to UK or European practice. The majority used a Markov modelling framework, although time horizons and structural assumptions varied. No economic evaluations were identified for PerLifePRO. Of the companies, only *metra* submitted its own de novo economic model for consideration; no other manufacturer submissions included original economic analyses. The direction of results across the prioritised studies was mixed. Economic evaluations conducted in the Netherlands and Canada suggested that machine perfusion may be cost saving or dominant compared with SCS, whereas a UK-based analysis concluded that machine perfusion was more costly and less effective than SCS. This heterogeneity likely reflects differences in healthcare setting, modelling assumptions, utilisation rates, and the data sources used to inform long-term outcomes. Specific differences between these models are discussed in Section 6.1.1 and a comparison of our model results to the Zimmerman et al (2022) model is included below.

In the EAG's economic modelling, all machine perfusion technologies were estimated to be cost-effective compared with SCS alone in the base case, with ICERs ranging from approximately £5,600 to £19,400 per QALY gained. Results were most sensitive to assumptions regarding organ utilisation, re-transplantation rates, and mortality HR associated with machine perfusion.

Overall, results of the modelling suggests that the use of any of the included devices (and across all modalities) are likely to represent a cost-effective use of NHS resources within the decision context considered. PerLifePRO was modelled but given an absence of available evidence, results are likely associated with a considerable level of uncertainty. Equally, results relating to Liver Assist (when used in NMP modality only) utilise complication data from *metra* studies and therefore may not be fully applicable. More generally, due

to limitations relating to the statistical significance of device-specific data as well as inconsistencies in the company-reported device costs, the relative difference in ICER values may not be reflective and should be interpreted with caution. Key uncertainties remain around the magnitude of machine perfusion survival benefit and the liver utilisation rates of machine perfusion devices, particularly across modalities and organ types. However, scenario analysis demonstrate that the results of the modelling remain broadly robust to these structural assumptions.

The primary conclusion from the evaluation is that there is likely to be a price point and clinical effectiveness threshold at which machine perfusion, adjunct to SCS, can be cost-effective against SCS alone.

6.4.2 Comparison to Zimmermann model

The findings of this evaluation contrast with those reported by Zimmermann et al. (2022) (Zimmermann and Carter 2022), which indicated that machine perfusion was not a cost-effective intervention. While incremental costs are similar between this study and the EAG evaluation, the QALY differences are wider. The marginal QALY impact in the Zimmermann model contributes to a high ICER. Differences between QALYs appear to be driven by structural assumptions regarding organ utilisation and re-transplantations.

In the Zimmermann model, no difference in organ utilisation was assumed between SCS and machine perfusion, effectively removing one of the most significant clinical and economic benefits of the technology. In contrast, this evaluation captures how improved preservation increase the total proportion of people receiving a transplant. This shifts the results by accounting for the reduced mortality and health gains associated with successful transplantation for those who would otherwise remain on the waiting list.

Furthermore, in the Zimmermann evaluation, QALY gains are only driven by a reduction in the incidence of EAD and PNF, as these complications lead to fewer people transitioning into a "history of dysfunction" state associated with higher mortality. The EAG model instead uses overarching survival estimates,

which capture these impacts, which are further driven by changes in organ utilisation and fewer waitlist deaths.

The Zimmermann model reported overall costs of £321,000 for SCS, compared with approximately [redacted] for SCS in our analysis, though the incremental costs remained broadly the same. This increase in baseline cost estimates is likely due to the model allowing for multiple, high-cost re-transplantations to occur over a lifetime, with risks as high as 4.35% for those with a history of dysfunction. By applying a tunnel state and assuming that the impact of additional re-transplantations is captured indirectly through long-term survival data, the EAG model avoids the compounding costs and structural uncertainties that likely drive the high ICER observed in the Zimmermann study.

Finally, while a detailed DSA was not presented, a review of scenario analysis results, presented in the form of a percentage change in ICER, indicated that varying key drivers of results had large impacts on the results. ICERs in scenario analysis ranged from £93,000/QALY to £490,000/QALY (SCS versus Liver Assist), and £45,000/QALY to £3,200,000/QALY (SCS versus *metra*), with some scenarios indicating that SCS was dominant. Key drivers of results were the relative risk of organ utilisation, the use of alternative long-term outcome data, and the cost of perfusion theatre space. It is plausible that the organ utilisation rate impacts results significantly however, the nature of the alternative long-term data sources were not reported in detail, and it is therefore unclear which parameters were changed. The impact on results that a change in theatre space costs is not discussed in the study and without full access to the model, it is not possible to determine why this has such a large impact on model results.

6.4.3 Qualitative discussion of additional benefits

The exclusion of NRP from the economic evaluation represents a limitation of the data, because emerging evidence suggests it may offer significant clinical benefits that were not fully captured in the primary analysis. Findings from Puttappa et al. (2025) (Puttappa et al. 2025) highlighted that NRP combined

with SCS resulted in a HR of 2.4 for long-term graft survival compared with SCS alone. Additional clinical studies in the UK have indicated that NRP can improve the viability assessment of livers from DCD donors, and enable them to withstand hypothermic storage conditions better, leading to increased organ utilisation and a reduction in the incidence of biliary complications (Watson et al., 2019) (Watson et al. 2019). Furthermore, the use of NRP has been shown to potentially increase the number of viable organs retrieved from ECD donors, which aligns with the broader objectives of increasing transplant capacity within the NHS (Williams et al., 2025) (Williams L J L 2025).

While NRP is not explicitly modelled in this analysis. It is highly likely that data already included implicitly capture the impact of NRP. This is particularly likely to be the case where NHSBT registry data is used(Puttappa et al. 2025)(Watson et al. 2019)(Williams L J L 2025)

Beyond the benefits of NRP, several other advantages of ex-situ machine perfusion may be underrepresented within the model due to data limitations. Logistical flexibility is another potential benefit of machine perfusion, as it allows for the conversion of emergency overnight procedures into scheduled daytime operations, which may improve surgical performance and reduce staff fatigue (Nasralla et al., 2018) (Nasralla et al. 2018). There is also evidence to suggest that the ability to perform viability assessments on ECD organs that would otherwise be discarded can reduce the psychological burden and anxiety for individuals on the waitlist who might otherwise experience the cancellation of a transplant operation (Mergental et al., 2020) (Mergental et al. 2020).

While these factors were not explicitly quantified, they suggest that the clinical and economic value of machine perfusion may be higher than what is reflected in the base case results.

6.5 Ongoing studies

The search identified a total of 14 ongoing studies at full text screening, however only 4 of these are fully aligned with the scope.

Two of the studies are on Liver Assist (University Medical Center Groningen 2014) (XVIVO Perfusion 2025b, XVIVO Perfusion), one is on *metra* (Washington University School of Medicine 2020) and one ongoing study includes three of the technologies: Liver Assist, VitaSmart and PerLifePRO (Philipp Dutkowski 2025, Philipp Dutkowski).

The Liver Assist studies are both single-arm, one is based in the Netherlands, the other includes ECDs but the location is unclear (XVIVO Perfusion 2025b, XVIVO Perfusion). The *metra* study is the RESTORE trial (Washington University School of Medicine 2020), a prospective, case-matched study based in the US. This study has produced interim results for the perfusion arm to date, but not for the case-controlled arm.

The ongoing study which will report on Liver Assist, VitaSmart and PerLifePRO together is a RCT based in multiple centres across Europe, including the UK (Philipp Dutkowski 2025, Philipp Dutkowski). It aims to compare hypothermic perfusion to SCS and only includes participants with hepatocellular cancer. The study will complete in 2028. When complete, it may provide RCT evidence on PerLifePRO and may therefore meet one of the evidence gaps identified by this review.

We identified a further 10 studies that were on named technologies, but these were either not in the pathway where perfusion was initiated at the recipient centre, or it was unclear whether they were fully aligned with the scope. Again, it is possible that when full details of the study are reported on publication, one or more of these studies may meet the decision problem.

41 other ongoing studies were identified, but these studies did not meet the scope for inclusion in this review. In most cases, this was because they do not mention one of the named technologies in the trial registry records or protocols. Future publications may include this information, therefore there

may be more ongoing studies which could align with the scope when full results are published (see Appendix B). Other ongoing studies did not meet the eligibility criteria because they did not compare perfusion with SCS, or it was unclear whether SCS was used in the pathway at all. One ongoing RCT on VitaSmart (King's College Hospital NHS Trust) compares HOPE, NRP and SCS, but in all three arms, ex-situ normothermic machine perfusion will also be used, therefore this study does not fully meet the scope either.

Table 6.26: Ongoing studies and their relevance to the decision problem (n = 14)

Ongoing study	Alignment with scope	Indicated study end date	EAG comments
Liver Assist (6 studies)			
Clinical trial (XVIVO Perfusion) Clinical trial (XVIVO Perfusion 2025b)	Fully aligned	2032-01	Single-arm trial with ECDs.
Clinical trial (Medical University of Vienna)	Unclear – we do not know if the perfused liver was subject to cold static storage prior to perfusion.	2038-12-31	Retrospective cohort study.
Clinical trial (University Medical Center Groningen 2014)	Fully aligned	NR	Single-arm trial, with DCD donors.
Clinical trial (Universitair Medisch Centrum Groningen 2020)	Unclear – we do not know if the perfused liver was subject to cold static storage prior to perfusion.	NR	Non-randomised trial.
Clinical trial (University Hospital Duisburg-Essen 2017)	Unclear – we do not know if the perfused liver was subject to cold static storage prior to perfusion.	NR	RCT with ECDs.
Clinical trial (University of Bologna)	Not aligned – livers in the intervention group are not subject to cold storage but are continuously perfused.	2025-05	RCT limited to recipients with hepatocellular carcinoma.

Ongoing study	Alignment with scope	Indicated study end date	EAG comments
***metra* (6 studies)**			
Clinical trial (University of Oxford 2022)	Not aligned – compares normothermic perfusion with normothermic perfusion plus liver defatting.	NR	RCT.
Clinical trial (Cambridge University Hospitals NHS Foundation Trust 2021)	Not aligned – studying the effects of adding thrombolysis to livers whilst on perfusion machine.	NR	Single-arm study.
Clinical trial (University of Oxford 2021)	Not aligned – livers in the intervention group are not subject to cold storage but are continuously perfused.	NR	Cohort study with retrospective control.
Clinical trial (Charite University)	Unclear – we do not know if the perfused liver was subject to cold static storage prior to perfusion.	2024-12	RCT comparing hypothermic and normothermic perfusion, and there is a SCS comparator arm.
Clinical trial (OrganOx Ltd. 2022b) Clinical trial (OrganOx Ltd.)	Unclear – we do not know if the perfused liver was subject to cold static storage prior to perfusion.	2025-02-05	Cohort study.
RESTORE, NCT04483102 Clinical trial record (Washington University School of Medicine 2020)	Fully aligned	NR	Prospective matched-case study. Interim results published but only for the *metra* arm, matched SCS case comparison not yet reported.

Ongoing study	Alignment with scope	Indicated study end date	EAG comments
Interim results (non-comparative) (Olumba et al. 2023)			
VitaSmart (1 study)			
Clinical trial (King's College Hospital NHS Trust)	Partially: there are three arms: hypothermic perfusion, NRP and SCS. All three arms will also undergo normothermic perfusion to allow clinical assessment.	2026-05-31	RCT.
Liver Assist, VitaSmart, and PerLifePRO (1 study)			
Clinical trial (Philipp Dutkowski 2025) Clinical trial (Philipp Dutkowski)	Fully aligned.	2028-01-31	RCT comparing hypothermic perfusion with SCS.

Table abbreviations: EAG, external assessment group; DCD, donation after circulatory death; NR, not reported; SCS, static cold storage.

7. Evidence gaps

Please note that objectives and scope of the routine use assessment process does not include exhaustive consideration of all studies identified in the review. The evidence gap analysis is therefore based on the prioritised studies only. The EAG notes that the deprioritised studies may include evidence for some of the areas identified in the evidence gap analysis. The evidence gaps are presented in a table Appendix H.

Comparative clinical evidence meeting the scope was available for 3 of the scoped technologies (Liver Assist, *metra* and VitaSmart). No evidence was identified for PerLifePRO. Of 15 prioritised studies, 7 RCTs reported on Liver Assist, 2 RCTs reported on VitaSmart and 6 non-randomised comparative studies conducted in Europe reported on *metra*. Some RCT evidence was identified for *metra* but was not in the perfusion initiated at the recipient centre pathway; therefore, non-randomised comparative evidence in the correct pathway was prioritised. Of the 2 VitaSmart RCTs, 1 had yet to be published in full and thus results were only available in a number of conference abstracts (Reich et al. 2024b).

All RCTs were considered to have a low risk of bias except 1 moderate risk trial (Liver Assist (Schlegel et al. 2023)). Most *metra* studies were considered to have a moderate risk of bias; 2 non-randomised studies were rated at a low risk of bias, and 4 at a moderate risk of bias.

Although studies on the sequential use of NRP and ex-situ machine perfusion were identified, none were prioritised and included in the review. Most of the studies we identified were either not in the perfusion initiated at the recipient centre pathway or were relatively small-scale and non-comparative.

A majority of studies included ECD livers, though the ECD criteria varied. Only 3 of 15 prioritised studies included DCD livers specifically, and in 3 a minority (<20%) of grafts were DCD. Evidence on the use of machine perfusion in DCD livers is thus limited.

7.1 Key areas for evidence generation

Suggestions for future evidence generation are summarised below.

As no evidence was found on the PerLifePRO device, future studies should assess this technology for efficacy and safety. There is one ongoing study (Philipp Dutkowski 2025, Philipp Dutkowski) which may provide evidence on this device when results are posted. Limited evidence from non-randomised studies was found in the perfusion initiated at the recipient centre pathway for *metra* (3 *metra* RCTs were identified which were not in the perfusion initiated at the recipient centre pathway, and were therefore deprioritised (University of Oxford (UK) 2014, University Health Network 2015, OrganOx Ltd. 2016)). More robust evidence from randomised trials in this scenario is needed for this device.

Long term clinical evidence (at timepoints longer than 1 year) was limited. To understand the possible long-term benefit of machine perfusion it is important to generate evidence on long-term outcomes in transplant recipients associated with machine perfusion compared with SCS. Long-term results may be reported from trials included in the review in the coming years.

The decision problem included children and young people (CYP) and patients undergoing extended perfusion as subgroups of interest. No evidence in these subgroups was identified in the prioritised studies. The deprioritised included studies were re-screened for any evidence on these subgroups, but only limited evidence (case series and retrospective or prospective cohort studies, much of which was not in the perfusion initiated at the recipient centre pathway) was identified. Some evidence was identified in 2 comparative studies that prolonged perfusion in Liver Assist is not inferior to conventional perfusion in efficacy or safety, though further evidence generation would be required to demonstrate this conclusively. Future studies should include subgroup data for these patients, where feasible. We understand from clinical feedback that there is no cross-centre agreed-upon definition of what perfusion duration would be considered extended or prolonged. The development of a clinical consensus would facilitate evidence generation in

this area. Evidence in paediatric patients was identified in 1 prospective cohort study and 1 case series. The cohort study investigated split livers, included 20 paediatric patients and reported no statistically significant differences between the SCS and HOPE cohorts.

The deprioritised studies were also re-screened for evidence in the use of NRP with sequential ex situ machine perfusion, though limited information was identified. 2 studies were identified, of which 1 study was a retrospective case series. The other was an RCT, though the sample size was small (n=11) and the comparison was between HOPE and NMP following NRP, rather than sequential NRP and ex situ machine perfusion compared to ex situ machine perfusion alone.

There was evidence on the use of higher-risk donor livers, as most prioritised studies used ECD livers according to various criteria. However, there was limited evidence in the use of DCD livers specifically. Future research in the utilisation of DCD livers would therefore be valuable.

The EAG understands that machine perfusion could increase the utilisation of donated organs, and transplant utilisation was an outcome of interest in the final scope. However, the transplant utilisation rate was reported by only 2 studies (Krendl et al. 2025, Fodor et al. 2021). This is likely due to the prioritisation of interventional studies, and RCTs in particular, as livers were allocated to a perfusion method after having been assessed and accepted at the transplant centre in most studies. Further evidence on transplant utilisation may be found in observational studies that were deprioritised in this review on the basis of evidence quality.

No evidence was identified in the prioritised studies on patient quality of life or healthcare professional satisfaction. Future studies could include patient-reported outcome measures for quality of life and user satisfaction surveys.

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9. Appendices

9.1 Appendix A Search strategies

A MEDLINE (OvidSP) search strategy was designed to identify studies of the four eligible technologies for machine perfusion of the liver prior to transplant. It is presented below (see Section 4.1).

The strategy comprised search terms for liver transplantation (search lines 1 to 4), machine perfusion (search lines 5 to 14) and the eligible technologies (search line 15).

The search concepts were combined as follows: (liver transplantation AND machine perfusion) OR eligible technologies.

The strategy excluded animal studies from MEDLINE using a standard algorithm (search line 17). The strategy also excluded some ineligible publication types which were 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 was restricted to studies published in English (search line 20) from 2010 to the search date (search line 21).

Searches were not restricted by study design or outcome so were appropriate to retrieve both clinical and economic evidence.

The final Ovid MEDLINE strategy was peer-reviewed before execution by a second Information Specialist. Peer review considered 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.

Note that Organ Care System or OCS Liver was initially included in the scope for this review, so the technology was included in the search strategy in line 15. However, the technology was subsequently excluded from the amended, finalised scope. Any retrieved studies on Organ Care System devices were excluded during record screening.

Resources searched

We conducted the literature search in the databases and information resources shown in Table A.1.

Table A.1: Databases and information sources 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/
Other	
Reference list checking	n/a
Company submissions	n/a

The trials register sources listed above (ClinicalTrials.gov and ICTRP) were searched to identify information on studies in progress.

Embase and CPCI-S were searched for conference abstracts. Reflecting the eligibility criteria, searches for conference abstracts were limited to abstracts published after 2022.

We also checked included studies lists of any industry submissions to NICE as well as retrieved relevant systematic reviews for additional eligible studies.

Running the search strategies and downloading results

Where possible, we conducted searches using each database or resource listed above, translating the agreed Ovid MEDLINE strategy appropriately. Translation included consideration of differences in database interfaces and functionality, in addition to variation in indexing languages and thesauri. The final translated database strategies were peer-reviewed by a second Information Specialist. Peer review considered the appropriateness of the

translation for the database being searched, errors in syntax and line combinations, and application of exclusions.

Where possible, we downloaded the results of searches in a tagged format and loaded them into bibliographic software (EndNote)(Clarivate 2021). The results were deduplicated using several algorithms and the duplicate references held in a separate EndNote database for checking if required. Results from resources that did not allow export in a format compatible with EndNote were saved in Word or Excel documents as appropriate and manually deduplicated.

A.1: Source: MEDLINE ALL

Interface / URL: OvidSP

Database coverage dates: 1946 to September 12, 2025

Search date: 15/09/2025

Retrieved records: 1,399

Search strategy:

1 liver transplantation/ (68408)

2 ((liver* or hepat*) adj5 (transplant* or allograft* or graft* or replac*)).ti,ab,kf. (98623)

3 ((liver* or hepat*) adj5 (donat* or donor*)).ti,ab,kf. (20977)

4 or/1-3 (112429)

5 organ preservation/ (10630)

6 perfusion/ (54462)

7 (machine* or oxygen* or hypotherm* or normotherm* or subnormotherm* or "ex vivo" or "ex situ").ti,ab,kf. (1279888)

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. (5026)

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 (22129)

14 4 and 13 (2097)

15 (bridge to life or vitasmart* or vita smart* or organox or organ ox or *metra* or *metra*tm or *metra*r 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/ (5375110)

18 (news or editorial or case reports).pt. or case report.ti. (3521106)

19 16 not (17 or 18) (1747)

20 limit 19 to english language (1669)

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

A.2: Source: Embase

Interface / URL: OvidSP

Database coverage dates: 1974 to 2025 September 11

Search date: 15/09/2025

Retrieved records: 2,534

Search strategy:

1 exp liver transplantation/ (158776)

2 ((liver* or hepat*) adj5 (transplant* or allograft* or graft* or replac*)).ti,ab,kf,dq. (168266)

3 ((liver* or hepat*) adj5 (donat* or donor*)).ti,ab,kf,dq. (36702)

4 or/1-3 (201409)

5 organ preservation/ (12207)

6 perfusion/ (67585)

7 liver perfusion/ (9898)

8 liver preservation/ (1794)

9 (machine* or oxygen* or hypotherm* or normotherm* or subnormotherm* or "ex vivo" or "ex situ").ti,ab,kf,dq. (1593012)

10 (5 or 6 or 7 or 8) and 9 (17309)

11 ((machine* or oxygen*) adj5 perfus*).ti,ab,kf,dq. (14033)

12 ((hypotherm* or normotherm* or subnormotherm*) adj5 perfus*).ti,ab,kf,dq. (8038)

13 (("ex vivo" or "ex situ") adj5 perfus*).ti,ab,kf,dq. (7354)

14 ((back to base or end ischemic or end ischaemic or device to donor* or transport*) adj5 perfus*).ti,ab,kf,dq. (1525)

15 or/10-14 (34056)

16 4 and 15 (3963)

17 (bridge to life or vitasmart* or vita smart* or organox or organ ox or *metra* or *metra*tm or *metra*r 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,dq,dv,my,ot. (1599)

18 16 or 17 (5233)

19 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (7369095)

20 editorial.pt. or case report.ti. (1293931)

21 conference abstract.pt. (5600584)

22 or/19-21 (13856764)

23 18 not 22 (2146)

24 limit 23 to yr="2010 -Current" (1716)

25 18 and 21 (2148)

26 limit 25 to yr="2022 -Current" (875)

27 24 or 26 (2591)

28 limit 27 to english language (2534)

A.3: Source: Cochrane Database of Systematic Reviews (CDSR)

Interface / URL: Cochrane Library / Wiley

Database coverage dates: Information not found. Issue searched: Issue 9 of 12, September 2025

Search date: 15/09/2025

Retrieved records: 2 (2 reviews, 0 protocols)

Search strategy:

#1 MeSH descriptor: [Liver Transplantation] this term only 1716

#2 ((liver* or hepat*) NEAR/5 (transplant* or allograft* or graft* or replac*)):ti,ab,kw 6459

#3 ((liver* or hepat*) NEAR/5 (donat* or donor*)):ti,ab,kw 1115

#4 #1 or #2 or #3 6625

#5 MeSH descriptor: [Organ Preservation] this term only 292

#6 MeSH descriptor: [Perfusion] this term only 673

#7 (machine* or oxygen* or hypotherm* or normotherm* or subnormotherm* or "ex vivo" or "ex situ"):ti,ab,kw 92683

#8 #5 or #6 851

#9 #7 and #8 287

#10 ((machine* or oxygen*) NEAR/5 perfus*):ti,ab,kw 1100

#11 ((hypotherm* or normotherm* or subnormotherm*) NEAR/5 perfus*):ti,ab,kw 387

#12 (("ex vivo" or "ex situ") NEAR/5 perfus*):ti,ab,kw 165

#13 (("back to base" or "end ischemic" or "end ischaemic" or "device to donor" or "device to donors" or transport*) NEAR/5 perfus*):ti,ab,kw 35

#14 #9 or #10 or #11 or #12 or #13 1453

#15 #4 and #14 179

#16 ("bridge to life" or vitasmart* or (vita NEXT smart*) or organox or "organ ox" or *metra* or *metra*tm or *metra*r 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 "PerLife Protm" or "PerLife Pror" or

transmedics or "trans medics" or "organ care system" or "organ care systemtm" or "organ care systemr" or (OCS NEXT Liver*)):ti,ab,kw 167

#17 #15 or #16 with Cochrane Library publication date Between Jan 2010 and Sep 2025, in Cochrane Reviews, Cochrane Protocols 2

A.4: Source: Cochrane Central Register of Controlled Trials (CENTRAL)

Interface / URL: Cochrane Library / Wiley

Database coverage dates: Information not found. Issue searched: Issue 8 of 12, August 2025

Search date: 15/09/2025

Retrieved records: 554

Search strategy:

#1 MeSH descriptor: [Liver Transplantation] this term only 1716

#2 ((liver* or hepat*) NEAR/5 (transplant* or allograft* or graft* or replac*)) 7100

#3 ((liver* or hepat*) NEAR/5 (donat* or donor*)) 1213

#4 #1 or #2 or #3 7287

#5 MeSH descriptor: [Organ Preservation] this term only 292

#6 MeSH descriptor: [Perfusion] this term only 673

#7 (machine* or oxygen* or hypotherm* or normotherm* or subnormotherm* or "ex vivo" or "ex situ") 95146

#8 #5 or #6 851

#9 #7 and #8 287

#10 ((machine* or oxygen*) NEAR/5 perfus*) 1187

#11 ((hypotherm* or normotherm* or subnormotherm*) NEAR/5 perfus*) 408

#12 (("ex vivo" or "ex situ") NEAR/5 perfus*) 170

#13 (("back to base" or "end ischemic" or "end ischaemic" or "device to donor" or "device to donors" or transport*) NEAR/5 perfus*) 36

#14 #9 or #10 or #11 or #12 or #13 1524

#15 #4 and #14 188

#16 ("bridge to life" or vitasmart* or (vita NEXT smart*) or organox or "organ ox" or *metra* or *metra*tm or *metra*r 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 "PerLife Protm" or "PerLife Pror" or transmedics or "trans medics" or "organ care system" or "organ care systemtm" or "organ care systemr" or (OCS NEXT Liver*)) 486

#17 #15 or #16 with Publication Year from 2010 to 2025, in Trials 554

A.5: Source: HTA database

Interface / URL: https://database.inahta.org/

Database coverage dates: Information not found. The former database was produced by the CRD until March 2018, at which time the addition of records was stopped as INAHTA was in the process of rebuilding the new database platform. In July 2019, the database records were exported from the CRD platform and imported into the new platform that was developed by INAHTA. The rebuild of the new platform was launched in June 2020.

Search date: 15/09/2025

Retrieved records: 27

Search strategy:

14 #13 OR #12 27

13 ((bridge AND life) OR vitasmart* OR "vita smart" OR "vita smarttm" OR "vita smartr" OR "vita-smart" OR "vita-smarttm" OR "vita-smartr" OR organox OR *metra** 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 "PerLife Protm" OR "PerLife Pror" OR transmedics OR "trans medics" OR "trans-medics" OR "organ care system" OR "organ care systemtm" OR "organ care systemr" OR "ocs liver" OR "ocs livertm" OR "ocs liverr") 23

12 #11 AND #4 4

11 #10 OR #9 76

10 perfus* 73

9 #8 AND #7 14

8 #6 OR #5 44

7 (machine* OR oxygen* OR hypotherm* OR normotherm* OR subnormotherm* OR vivo OR situ) 434

6 "Perfusion"[mh] 36

5 "Organ Preservation"[mh] 15

4 #3 OR #2 OR #1 128 September 15 2025 2:16 PM

3 ((liver* OR hepat*) AND (donat* OR donor*)) 28

2 ((liver* OR hepat*) AND (transplant* OR allograft* OR graft* OR replac*)) 121

1 "Liver Transplantation"[mh] 47

A.6: Source: Conference Proceedings Citation Index – Sciences (CPCI-S)

Interface / URL: Web of Science

Database coverage dates: 1990 to 15/09/2025

Search date: 15/09/2025

Retrieved records: 278

Search strategy:

1 TS=((liver* OR hepat*) NEAR/5 (transplant* OR allograft* OR graft* OR replac*)) 35276

2 TS=((liver* OR hepat*) NEAR/5 (donat* OR donor*)) 8,000

3 #1 OR #2 36,981

4 TS=((machine* OR oxygen*) NEAR/5 perfus*) 1,673

5 TS=((hypotherm* OR normotherm* OR subnormotherm*) NEAR/5 perfus*) 1,357

6 TS=(("ex vivo" OR "ex situ" OR ex-vivo OR ex-situ) NEAR/5 perfus*) 1,100

7 TS=(("back to base" OR back-to-base OR "end ischemic" OR end-ischemic OR "end ischaemic" OR end-ischaemic OR "device to donor*" OR device-to-donor* OR transport*) NEAR/5 perfus*) 129

8 #4 OR #5 OR #6 OR #7 3,179

9 #3 AND #8 532

10 TS=("bridge to life" OR bridge-to-life OR vitasmart* OR vita-smart* OR "vita smart*" OR organox OR "organ ox" OR organ-ox OR *metra* OR *metra*tm OR *metra*r OR xvivo OR "liver assist*" OR "organ assist*" OR aferetica OR perlife* OR "PerLife Pro*" OR transmedics OR "trans medics" OR trans-medics OR "organ care system" OR "organ care systemtm" OR "organ care systemr" OR "OCS liver*") 178

11 #9 OR #10 278 Limited to timespan: 2022-01-01 to 2025-09-15

A.7: Source: NHS Economic Evaluation Database (NHS EED)

Interface / URL: https://www.crd.york.ac.uk/CRDWeb

Database coverage dates: Information not found. Bibliographic records were published on NHS EED until 31st March 2015. Searches of MEDLINE, Embase, CINAHL, PsycINFO and PubMed were continued until the end of the 2014.

Search date: 15/09/2025

Retrieved records: 0

Search strategy:

1 MeSH DESCRIPTOR liver transplantation IN NHSEED 78

2 (((liver* OR hepat*) ADJ5 (transplant* OR allograft* OR graft* OR replac*))) IN NHSEED 201

3 (((transplant* OR allograft* OR graft* OR replac*) ADJ5 (liver* OR hepat*))) IN NHSEED 60

4 (((liver* OR hepat*) ADJ5 (donat* OR donor*))) IN NHSEED 11

5 (((donat* OR donor*) ADJ5 (liver* OR hepat*))) IN NHSEED 22

6 #1 OR #2 OR #3 OR #4 OR #5 218

7 MeSH DESCRIPTOR organ preservation IN NHSEED 3

8 MeSH DESCRIPTOR perfusion IN NHSEED 3

9 ((machine* OR oxygen* OR hypotherm* OR normotherm* OR subnormotherm* OR ex vivo OR ex-vivo OR ex situ OR ex-situ)) IN NHSEED 290

10 #7 OR #8 5

11 #9 AND #10 4

12 (((machine* OR oxygen*) ADJ5 perfus*)) IN NHSEED 3

13 ((perfus* ADJ5 (machine* OR oxygen*))) IN NHSEED 1

14 (((hypotherm* OR normotherm* OR subnormotherm*) ADJ5 perfus*)) IN NHSEED 0

15 ((perfus* ADJ5 (hypotherm* OR normotherm* OR subnormotherm*))) IN NHSEED 0

16 (((ex vivo OR ex-vivo OR ex situ OR ex-situ) ADJ5 perfus*)) IN NHSEED 0

17 ((perfus* ADJ5 (ex vivo OR ex-vivo OR ex situ OR ex-situ))) IN NHSEED 0

18 (((back to base OR back-to-base OR end ischemic OR end-ischemic OR end ischaemic OR end-ischaemic OR device to donor* OR device-to-donor* OR transport*) ADJ5 perfus*)) IN NHSEED 0

19 ((perfus* ADJ5 (back to base OR back-to-base OR end ischemic OR end-ischemic OR end ischaemic OR end-ischaemic OR device to donor* OR device-to-donor*))) IN NHSEED 0

20 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 4

21 #6 AND #20 1

22 * IN NHSEED FROM 2010 TO 2025 7196

23 #21 AND #22 0

A.8: Source: EconLit

Interface / URL: OvidSP

Database coverage dates: 1886 to September 04, 2025

Search date: 16/09/2025

Retrieved records: 4

Search strategy:

1 ((liver* or hepat*) adj5 (transplant* or allograft* or graft* or replac*)).af. (43)

2 ((liver* or hepat*) adj5 (donat* or donor*)).af. (13)

3 1 or 2 (45)

4 ((machine* or oxygen*) adj5 perfus*).af. (0)

5 ((hypotherm* or normotherm* or subnormotherm*) adj5 perfus*).af. (0)

6 (("ex vivo" or "ex situ") adj5 perfus*).af. (0)

7 ((back to base or end ischemic or end ischaemic or device to donor* or transport*) adj5 perfus*).af. (0)

8 or/4-7 (0)

9 3 and 8 (0)

10 (bridge to life or vitasmart* or vita smart* or organox or organ ox or *metra* or *metra*tm or *metra*r 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*).af. (4)

11 9 or 10 (4)

12 limit 11 to yr="2010 -Current" (4)

A.9: Source: ClinicalTrials.gov

Interface / URL: https://clinicaltrials.gov/ct2/home

Database coverage dates: Information not found. ClinicalTrials.gov was created as a result of the Food and Drug Administration Modernization Act of 1997 (FDAMA). The site was made available to the public in February 2000.

Search date: 16/09/2025

Retrieved records: 257

Search strategy:

The following 2 searches were conducted separately. All search terms were entered using the Expert search interface.

The results from each search were downloaded as an individual set. The total number of records retrieved represents the sum of all searches, and includes duplicates caused by the same record being retrieved in each search.

Search 1: ((liver OR livers OR hepatic OR hepato OR hepatocellular) AND (transplant OR transplanted OR transplants OR transplanting OR transplantation OR transplantations OR allograft OR allografts OR allografted OR allografting OR graft OR grafts OR grafting OR grafted OR replace OR replaces OR replacing OR replaced OR replacement OR replacements OR donate OR donator OR donators OR donates OR donation OR donations OR donating OR donated OR donor OR donors) AND (perfuse OR perfusing OR perfused OR perfusion OR perfusions)) = 172 studies

Search 2: ("bridge to life" OR "bridge-to-life" OR vitasmart OR vitasmarttm OR vitasmartr OR "vita smart" OR "vita smarttm" OR "vita smartr" OR "vita-smart" OR "vita-smarttm" OR "vita-smartr" OR organox OR "organ ox" OR "organ-ox" OR *metra* OR *metra*tm OR *metra*r 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 perlifetm OR perlifer OR "PerLife Pro" OR "PerLife Protm" OR "PerLife Pror" OR transmedics OR "trans medics" OR

"trans-medics" OR "organ care system" OR "organ care systemtm" OR "organ care systemr" OR "ocs liver" OR "ocs livertm" OR "ocs liverr") = 85 studies

A.10: Source: WHO International Clinical Trials Registry Portal (ICTRP)

Interface / URL: https://trialsearch.who.int/

Database coverage dates: Information not found. On the date of search, files had been imported from data providers between October 2024 and September 2025.

Search date: 16/09/2025

Retrieved records: 191

Search strategy:

The following 3 searches were conducted separately using the search interface at the above URL. 'Without Synonyms' was selected for all searches.

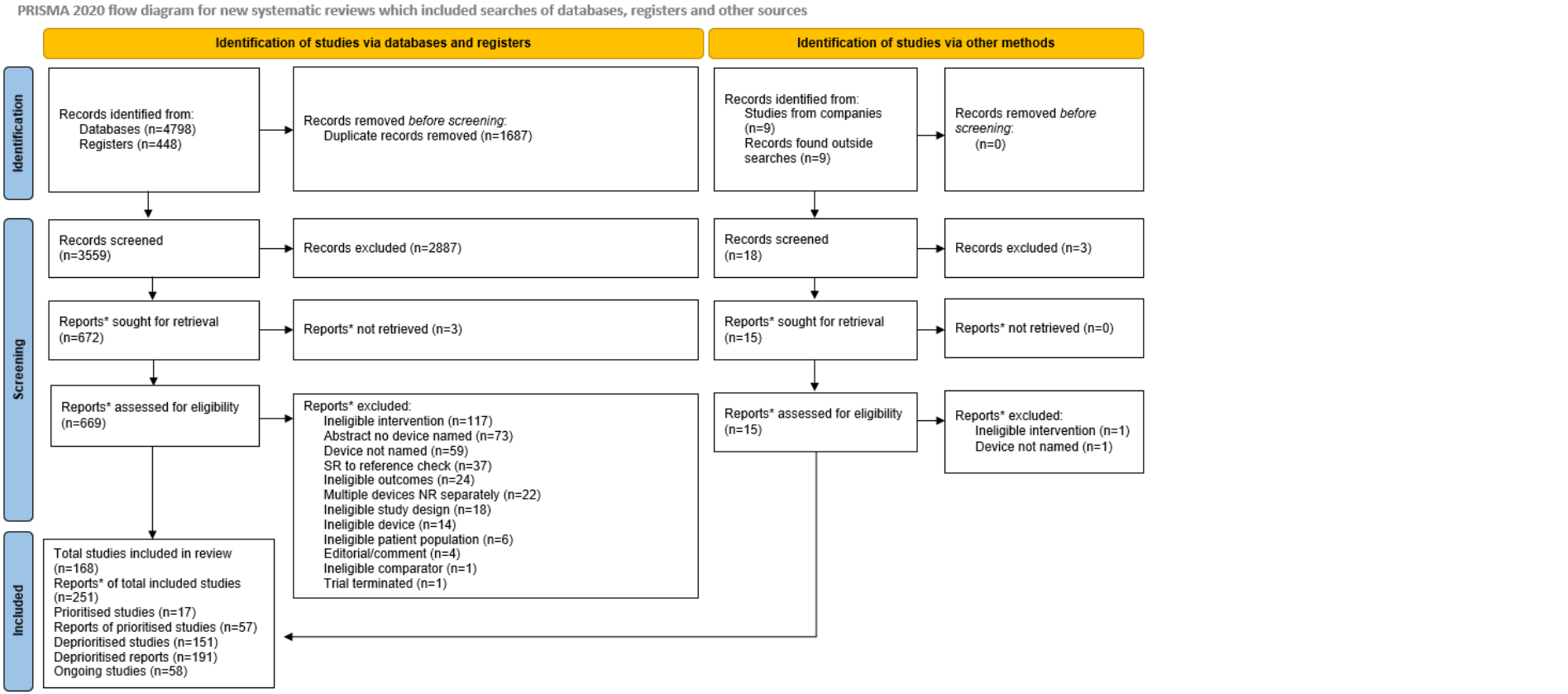
The results from each search were downloaded as an individual set. The total number of records retrieved represents the sum of all searches, and includes duplicates caused by the same record being retrieved in each search.

(((liver* OR hepat*) AND (transplant* OR allograft* OR graft* OR replac* OR donat* OR donor*) AND perfus*)) = 125 records for 119 trials

("bridge to life" OR vitasmart* OR "vita smart*" OR organox OR "organ ox" OR *metra* OR *metra*tm OR *metra*r OR xvivo OR "liver assist" OR "liver assisttm" OR "liver assistr" OR "organ assist" OR "organ assisttm" OR "organ assistr") = 48 records for 45 trials found

(aferetica OR perlife* OR "PerLife Pro" OR "PerLife Protm" OR "PerLife Pror" OR transmedics OR "trans medics" OR "organ care system" OR "organ care systemtm" OR "organ care systemr" OR "OCS liver*") = 27 records for 27 trials found

Figure A.1: PRISMA flow diagram



*"Note that a "report" could be a journal article, preprint, conference abstract, study register entry, clinical study report, dissertation, unpublished manuscript, government report or any other document providing relevant information": https://www.bmj.com/content/372/bmj.n71.

Adapted from: 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. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

9.2 Appendix B Excluded studies

Include a list of excluded studies at full text review stage with reasons for exclusion. If there is a large number of studies, discuss the approach to present these with the NICE team.

Table B.1: Excluded studies list (n = 377)

Reference	Exclusion reason
Abudhaise H, Davidson BR, DeMuylder P, Luong TV, Fuller B. Evolution of dynamic, biochemical, and morphological parameters in hypothermic machine perfusion of human livers: A proof-of-concept study. PLoS ONE. 2018.13(9):e0203803. doi: https://dx.doi.org/10.1371/journal.pone.0203803	Ineligible device
Abu-Gazala S, Tang H, Abt P, Mahmud N. National trends in utilization of normothermic machine perfusion in DCD liver transplantation. Transplant Direct. 2024.10(5):e1596. doi: https://dx.doi.org/10.1097/TXD.0000000000001596	Device not named
Akabane M, Bekki Y, Kwong AJ, Esquivel CO, Kim WR, Melcher ML, et al. Navigating new frontiers: Onsite machine perfusion in us liver transplantation. Hpb. 2025.27(6):780-88. doi: https://dx.doi.org/10.1016/j.hpb.2025.02.011	Device not named
Akabane M, Imaoka Y, Melcher ML, Sasaki K. The current situation of onsite normothermic machine perfusion in the us liver transplantation. Hpb. 2024.26(Suppl 2):S637. doi: https://dx.doi.org/10.1016/j.hpb.2024.04.080	Abstract - device not named
Al-Ameri A, Zheng S. Outcomes of liver transplantation for hepatocellular carcinoma in donation after circulatory death compared with donation after brain death. Hpb. 2024.26(Suppl 1):S75. doi: https://dx.doi.org/10.1016/j.hpb.2024.03.125	Ineligible study design
Alderete IS, Gao Q, Samy K, Nauser C, Abraham N, Vikraman D, et al. Clinical outcomes and cost analysis following normothermic machine perfusion versus static cold storage for liver transplantation: A single center analysis. Am J Transplant. 2023.23(6):S727-S27.	Ineligible intervention

Reference	Exclusion reason
Ali K, Cazzaniga B, Liu Q, Miyazaki Y, Tuul M, Raj R, et al. Machine perfusion or straight to transplant? Predictive value of flavin mononucleotide levels in flush solution of human liver allograft. Ann Surg. 2024.25:25. doi: https://dx.doi.org/10.1097/SLA.0000000000006576	Ineligible intervention
Allen ES, Stephens LD, Weber N, Brubaker AL, Hudson K, Pretorius V, et al. Providing red blood cells to facilitate organ transplant via normothermic perfusion techniques: A single-center experience. Transfusion. 2024.64(10):1899-908. doi: https://dx.doi.org/10.1111/trf.17994	Ineligible intervention
Alomar O, Vachharajani N, Chapman W, Doyle M. Revolutionizing DCD liver transplantation: Expanding donor criteria with normothermic machine and regional perfusion. Am J Transplant. 2025.25(1 Suppl 1):S45. doi: https://dx.doi.org/10.1016/j.ajt.2024.12.095	Abstract - device not named
Amara D, Melehy A, Ebaid S, Kaldas FM, Farmer DG, Stock P, et al. Impact of normothermic machine perfusion on access to liver transplantation in patients with primary hepatic malignancies. Clin Transplant. 2025.39(8):e70254. doi: https://dx.doi.org/10.1111/ctr.70254	Device not named
Amaral MJOSB, Duque M, Constantino J, Martins R, Oliveira P, Simoes J, et al. Results of the first 100 cases of hypothermic oxygenated perfusion in liver transplantation in a portuguese liver transplant center. J Am Coll Surg. 2024.239(5 Suppl 1):S504. doi: https://dx.doi.org/10.1097/XCS.0000000000001180	Abstract - device not named
Angelico R, Sensi B, Quaranta C, Orsi M, Parente A, Schlegel A, et al. The impact of center volume on the utilization and outcomes of machine perfusion technology in liver transplantation: An international survey. Artif Organs. 2023.47(11):1773-85. doi: https://dx.doi.org/10.1111/aor.14635	Device not named
Anouti A, Dahshi H, Cotter T, Aqul A, Lee W, Hwang C, et al. The impact of machine perfusion on transplanted liver grafts with macrosteatosis. Hepatology. 2024.80(Suppl 1):S1016. doi: https://dx.doi.org/10.1097/HEP.0000000000001076	Abstract - device not named
Anouti A, Dahshi H, Cotter T, Aqul A, Lee W, Hwang C, et al. The impact of machine perfusion on transplanted liver grafts with macro-steatosis. Hepatology. 2024.80:S1016-S16.	Abstract - device not named

Reference	Exclusion reason
Anouti A, Dakroub AH, Krayem H, Matevish LE, Dahshi H, Hassan S, et al. The current state of simultaneous heart-liver transplantation in the United States. Am J Transplant. 2025.05:05. doi: https://dx.doi.org/10.1016/j.ajt.2025.07.001	Abstract - device not named
Antoine C, Jasseron C, Dondero F, Savier E. Liver transplantation from controlled donors after circulatory death using normothermic regional perfusion: An initial French experience. Liver Transpl. 2020.26(11):1516-21. doi: https://dx.doi.org/10.1002/lt.25818	Device not named
Aqel B, Nguyen M, Reddy K, Luque Villa E, Katariya N, Moss A, et al. Normothermic mechanical perfusion (NMP) significantly reduces the risk of ischemic cholangiopathy in recipients of donation after cardiac death (DCD) liver transplants. Transplantation. 2023.107(9 Suppl 1):97 EP - 98.	Ineligible intervention
Aqel B, Nguyen M, Reddy K, Moss A, Hewitt W, Jadlowiec C, et al. Normothermic mechanical perfusion (NMP) significantly reduces the risk of ischemic cholangiopathy in recipients of donation after cardiac death (DCD) liver transplants. Am J Transplant. 2023.23(6):S457-S57.	Ineligible intervention
Aragon Health Science Institute (Spain). Celsior versus university of wisconsin preserving solutions for liver transplantation. Identifier: ISRCTN82547607. In: ISRCTN Registry [internet]. London: BioMed Central Limited: 2009. Available from http://isrctn.com/ISRCTN82547607.	Ineligible intervention
Archie W, Mantha R, Janusek C, Peterson K, Huckleberry D, Eskind L, et al. Patients who received DCD grafts preserved with normothermic machine perfusion had better 90-day outcomes than those who received DBD grafts preserved with ischemic cold storage. Am J Transplant. 2025.25(8 Suppl 1):S748. doi: https://dx.doi.org/10.1016/j.ajt.2025.07.1765	Abstract - device not named
Archie W, Mantha R, Peterson K, Adlakha N, deLemos A, Russo M, et al. Extension of liver graft preservation times using normothermic machine perfusion in simultaneous liver-kidney transplantation may indirectly lead to increase in ureteral complication rates. Am J Transplant. 2025.25(8 Suppl 1):S475. doi: https://dx.doi.org/10.1016/j.ajt.2025.07.1087	Abstract - device not named
Archie W, Mantha R, Stephens B, Peterson K, Janusek C, Casingal V, et al. Normothermic machine perfusion of DCD liver grafts is associated with increased 90-day acute cellular rejection rates and continues in a time	Abstract - device not named

Reference	Exclusion reason
dependent manner. Am J Transplant. 2025.25(8 Suppl 1):S486. doi: https://dx.doi.org/10.1016/j.ajt.2025.07.1117	
Archie WH, Baimas-George M, Haynes N, Kundu S, Peterson K, Wehrle CJ, et al. Upper limit of normothermic machine preservation of liver grafts from donation after circulatory death yet to be defined. World j. 2025.15(2):99170. doi: https://dx.doi.org/10.5500/wjt.v15.i2.99170	Device not named
Aspord C, Macek Jilkova Z, Bonadona A, Gerster T, Lesurtel M, Girard E, et al. Hypothermic oxygenated machine perfusion and static cold storage drive distinct immunomodulation during liver transplantation: A pilot study. Transplantation. 2025.109(4):658-70. doi: https://dx.doi.org/10.1097/TP.0000000000005274	Device not named
Avolio AW, Pascale MM, Barbier L, Braun F, Boin I, Caccamo L, et al. Report of the global liver transplant activity. Preliminary analysis of the improvement project (ongoing international study). Hpb. 2024.26(Suppl 1):S18 EP - S19. doi: https://dx.doi.org/10.1016/j.hpb.2024.03.034	Abstract - device not named
Avruch J, Goussous N, Malik S, Pinedo M, Meier R, Bhati C, et al. A multicenter randomized controlled trial to compare the efficacy of ex-vivo machine perfusion with static cold storage in human liver transplantation: The University of Maryland experience. Am J Transplant. 2022.22(Suppl 3):737. doi: https://dx.doi.org/10.1111/ajt.17073	Ineligible outcomes
Azar F, Margolin E, Reddy N, Birs A, Brubaker A, Schnickel G, et al. Rise of the machines: The utilization of technology for triple-organ transplantation. Journal of Heart and Lung Transplantation. 2024.43(4 Suppl):S532 EP - S33. doi: https://dx.doi.org/10.1016/j.healun.2024.02.765	Ineligible intervention
Bababekov Y, Hoffman J, Shinsako J, Nydam T, Pomposelli S, Moore H, et al. Thoracoabdominal normothermic regional perfusion (TA-NRP) reduces resource utilization after DCD liver transplant (DCD LT). Am J Transplant. 2024.24(1):S83-S83.	Abstract - device not named
Bababekov Y, Nydam T, Hoffman J, Goncalves C, Shinsako J, Ha A, et al. Normothermic regional perfusion: Challenging futility in DCD liver transplantation. Liver Transpl. 2024.30:258-58.	Abstract - device not named
Bababekov Y, Nydam T, Hoffman J, Moore H, Shinsako J, Pomposelli S, et al. Thoracoabdominal normothermic regional perfusion (TA-NRP): Challenging futility in DCD liver transplantation (LT). Am J Transplant. 2024.24(1):S35-S35.	Abstract - device not named

Reference	Exclusion reason
Bababekov Y, Pomposelli J, Moore H, Hoffman J, Pomposelli S, Shinsako J, et al. Early allograft survival after DCD liver transplant: Thoracoabdominal normothermic regional perfusion (NRP) versus static cold storage (SCS). Am J Transplant. 2024.24(1):S35-S36.	Abstract - device not named
Bababekov Y, Shinsako J, Goncalves C, Ha A, Hoffman J, Pomposelli S, et al. Normothermic regional perfusion reduces resource utilization after DCD liver transplantation. Liver Transpl. 2024.30:74-74.	Abstract - device not named
Bababekov YJ, Ha AH, Nydam TL, Goncalves C, Choudhury R, Shinsako J, et al. Thoracoabdominal normothermic regional perfusion: Real-world experience and outcomes of DCD liver transplantation. Transplant Direct. 2025.11(3):e1767. doi: https://dx.doi.org/10.1097/TXD.0000000000001767	Ineligible intervention
Bahadori K, Lee CYC, Ferdinand JR, Cabantous M, Butler AJ, Rouhani FJ, et al. Inflammatory gene expression in livers undergoing ex situ normothermic perfusion is attenuated by leukocyte removal from the perfusate. Transplantation. 2025.109(2):332-45. doi: https://dx.doi.org/10.1097/TP.0000000000005214	Ineligible outcomes
Banan B, Watson R, Xu M, Lin Y, Chapman W. Development of a normothermic extracorporeal liver perfusion system toward improving viability and function of human extended criteria donor livers. Liver Transpl. 2016.22(7):979-93. doi: https://dx.doi.org/10.1002/lt.24451	Ineligible device
Baptista PM, Moran EC, Vyas D, Ribeiro MH, Atala A, Sparks JL, et al. Fluid flow regulation of revascularization and cellular organization in a bioengineered liver platform. Tissue Eng Part C Methods. 2016.22(3):199-207. doi: https://dx.doi.org/10.1089/ten.TEC.2015.0334	Ineligible device
Barbas A, Gao Q, Alderete I, Aykun N, Samy K, Nauser C, et al. Transforming the logistics of liver transplantation with normothermic machine perfusion: Clinical impact versus cost. Am J Transplant. 2025.25(1 Suppl 1):S12 EP - S13. doi: https://dx.doi.org/10.1016/j.ajt.2024.12.031	Ineligible intervention
Barbier L, Guillem T, Savier E, Scatton O, Dondero F, Si Larbi A-G, et al. Impact of the duration of normothermic regional perfusion on the results of liver transplant from controlled circulatory death donors: A retrospective, multicentric study. Clin Transplant. 2022.36(2):e14536. doi: https://dx.doi.org/10.1111/ctr.14536	Ineligible intervention

Reference	Exclusion reason
Baroni S, Marudi A, Rinaldi S, Ghedini S, Magistri P, Guerrini GP, et al. Cytokine mass balance levels in donation after circulatory death donors using hemoadsorption: Case series report. Blood Purif. 2022.51(Suppl 3):17 EP - 18. doi: https://dx.doi.org/10.1159/000528706	Abstract - device not named
Baroni S, Marudi A, Rinaldi S, Ghedini S, Magistri P, Piero Guerrini G, et al. Cytokine mass balance levels in donation after circulatory death donors using hemoadsorption: Case series report. Int J Artif Organs. 2022.45(7):642-46. doi: https://dx.doi.org/10.1177/03913988221091288	Device not named
Baskin R, Alderete IS, Gao Q, Samy K, Nauser C, Abraham N, et al. Clinical outcomes and cost analysis following normothermic machine perfusion versus static cold storage for liver transplantation: A single center analysis. Am J Transplant. 2023.23(6 Suppl 1):S727. doi: https://dx.doi.org/10.1016/j.ajt.2023.05.014	Ineligible intervention
Basta G, Babboni S, Pezzati D, Del Turco S, Balzano E, Catalano G, et al. Perfusate liver arginase 1 levels after end-ischemic machine perfusion are associated with early allograft dysfunction. Biomedicines. 2025.13(1):20. doi: https://dx.doi.org/10.3390/biomedicines13010244	Device not named
Basta G, Del Turco S, Babboni S, Patrono D, De Stefano N, Trizzino A, et al. Bile levels of keratin 19 from donations after circulatory death are associated with early graft dysfunction. Transplantation. 2024.108(9 Suppl):329. doi: https://dx.doi.org/10.1097/01.tp.0001066220.16750.c1	Abstract - device not named
Bekki Y, Croome KP, Myers B, Sasaki K, Tomiyama K. Normothermic regional perfusion can improve both utilization and outcomes in DCD liver, kidney, and pancreas transplantation. Transplant Direct. 2023.9(3):e1450. doi: https://dx.doi.org/10.1097/TXD.0000000000001450	Device not named
Bluhme E, Gabel M, Martinez de la Maza L, Nilsen V, Hildebrand K, Jarsater J, et al. Normothermic regional perfusion in controlled DCD liver procurement: Outcomes of the Swedish national implementation protocol. Liver Transpl. 2024.30(11):1132-44. doi: https://dx.doi.org/10.1097/LVT.0000000000000434	Ineligible device
Bodewes SB, Lascaris B, Adelmeijer J, de Meijer VE, Porte RJ, Lisman T. Normothermic machine-perfused human donor livers produce functional hemostatic proteins. Transplantation. 2023.107(11):2377-83. doi: https://dx.doi.org/10.1097/TP.0000000000004670	Ineligible outcomes

Reference	Exclusion reason
Bodzin AS, MacConmara MP, Attia M, Perry DK, Shah AP. Assessing hepatic arterial injuries in the setting of normothermic machine perfusion in liver transplantation: A noninvasive approach. Liver Transpl. 2025.25:25. doi: https://dx.doi.org/10.1097/LVT.0000000000000610	Ineligible study design
Boerger L, Hillebrandt KH, Czigany Z, Lurje G, Gassner JMGV, Patel MS, et al. Ex vivo liver machine perfusion reduces the length of hospital stay in recipients of allografts from elderly donors: A systematic review. Advanced Therapeutics. 2023.6(6):2200291. doi: https://dx.doi.org/10.1002/adtp.202200291	Systematic review to check
Boteon Y, Attard J, Laing R, Boteon A, Bhogal R, Reynold G, et al. Pharmacological defatting of steatotic human livers using a novel perfusion solution during normothermic machine perfusion. Am J Transplant. 2018: 324. Available from: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01605103/full	Abstract - device not named
Boteon Y, Attard J, Laing R, Boteon APCS, Wallace L, Bhogal R, et al. Pharmacological defatting of steatotic human livers using a novel perfusion solution during normothermic machine perfusion. Transplantation. 2018	Abstract - device not named
Boteon YL, Hessheimer AJ, Bruggenwirth IMA, Boteon APCS, Padilla M, de Meijer VE, et al. The economic impact of machine perfusion technology in liver transplantation. Artif Organs. 2022.46(2):191-200. doi: https://dx.doi.org/10.1111/aor.14131	Ineligible study design
Botha JF, Paci P, Contreras A, Zendejas I, Cook B. One hundred abdominal normothermic regional perfusion (NRP) DCD liver transplants: Zero ischemic cholangiopathy. Am J Transplant. 2025.25(8 Suppl 1):S209. doi: https://dx.doi.org/10.1016/j.ajt.2025.07.459	Abstract - device not named
Brubaker A, Mathur A, Lee D, Hobeika M, Nassar A, Sudan D, et al. OCS liver enables better recipient outcomes when donors are located over 250nm from recipient. Liver Transpl. 2024.30:192-92.	Ineligible intervention
Brubaker AL, Sellers MT, Abt PL, Croome KP, Merani S, Wall A, et al. US liver transplant outcomes after normothermic regional perfusion vs standard super rapid recovery. JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION Surgery. 2024.159(6):677-85. doi: https://dx.doi.org/10.1001/jamasurg.2024.0520	Ineligible intervention
Brubaker AL, Taj R, Jackson B, Lee A, Tsai C, Berumen J, et al. Early patient and liver allograft outcomes from donation after circulatory death donors using thoracoabdominal normothermic regional: A multi-center	Ineligible intervention

Reference	Exclusion reason
observational experience. Front Transplant. 2023.2:1184620. doi: https://dx.doi.org/10.3389/frtra.2023.1184620	
Butler AJ, Randle LV, Watson CJ. Normothermic regional perfusion for donation after circulatory death without prior heparinization. Transplantation. 2014.97(12):1272-8. doi: https://dx.doi.org/10.1097/TP.0000000000000082	Ineligible intervention
Calleja R, Rivera M, Guijo-Rubio D, Hessheimer AJ, de la Rosa G, Gastaca M, et al. Machine learning algorithms in controlled donation after circulatory death under normothermic regional perfusion: A graft survival prediction model. Transplantation. 2025.109(7):e362-e70. doi: https://dx.doi.org/10.1097/TP.0000000000005312	Ineligible intervention
Campo-Canaveral de la Cruz JL, Minambres E, Coll E, Padilla M, Antolin GS, de la Rosa G, et al. Outcomes of lung and liver transplantation after simultaneous recovery using abdominal normothermic regional perfusion in donors after the circulatory determination of death versus donors after brain death. Am J Transplant. 2023.23(7):996-1008. doi: https://dx.doi.org/10.1016/j.ajt.2023.04.016	Ineligible intervention
Canizares S, Montalvan A, Chumdermpadetsuk R, Modest A, Eckhoff D, Lee DD. Liver machine perfusion technology: Expanding the donor pool to improve access to liver transplantation. Am J Transplant. 2024.24(9):1664-74. doi: https://dx.doi.org/10.1016/j.ajt.2024.03.013	Multiple devices not reported seperately
Canizares S, Montalvan A, Chumdermpadetsuk R, Modest A, Eckhoff D. Machine perfusion technology drives a major growth surge in liver transplantation. J Surg Res. 2024.302:454-62. doi: https://dx.doi.org/10.1016/j.jss.2024.07.077	Device not named
Caralt M, Bello I, Sandiumenge A, Dopazo C, Pando E, Molino JA, et al. "Non-touch" vena cava technique as an improvement in combined lung and liver procurement in controlled donation after circulatory death. Transplant Proc. 2019.51(1):9-11. doi: https://dx.doi.org/10.1016/j.transproceed.2018.02.216	Ineligible intervention
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Matteo Ravaioli. Hypothermic oxygenated perfusion versus static cold storage for marginal graft (PIO). Identifier: NCT03031067. In: ClinicalTrials.gov [internet]. Bethesda (MD): National Library of Medicine (US): 2016. Available from https://clinicaltrials.gov/study/NCT03031067.	Device not named

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Melandro F, Basta G, Torri F, Biancofiore G, Del Turco S, Orlando F, et al. Normothermic regional perfusion in liver transplantation from donation after cardiocirculatory death: Technical, biochemical, and regulatory aspects and review of literature. Artif Organs. 2022.46(9):1727-40. doi: https://dx.doi.org/10.1111/aor.14330	Systematic review to check
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Nauser C, Alderete I, Aykun N, Gao QM, Samy K, Vikraman D, et al. Clinical outcomes following normothermic machine perfusion versus static cold storage for donation after circulatory death liver transplantation: A single center analysis. Am J Transplant. 2024.24(1):S47-S47.	Multiple devices not reported seperately
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Nguyen MC, Aqel B, Zhang C, Villa EL, Douglas D, Hewitt W, et al. Early outcomes and hospital resource utilization after liver transplantation: Impact of normothermic mechanical perfusion in a high volume us DCD liver transplant center. Am J Transplant. 2023.23(6):S419-S20.	Ineligible intervention
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Niu A, Lau NS, Ly M, Yousif P, Risbey C, Babekuhl D, et al. Is it time to introduce ex-situ normothermic machine perfusion in paediatric liver transplantation? Liver Transpl. 2024.30:57-57.	Abstract - device not named
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Shuja MH, Abdalkarim M, Shahzad A, Abbasi AF, Shakil F, Jameel K, et al. Normothermic regional perfusion vs. Non-normothermic techniques in CDCD liver transplantation: A systematic review and meta-analysis. Gastroenterology. 2025.169(1)	Systematic review to check
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Sneiders D, Lembach H, Hann A, Nutu A, Hodson J, Isaac J, et al. Normothermic machine perfusion (NMP) improves access to transplantation for late liver re-transplant candidates. Transplantation. 2022.106(9 Suppl):S206.	Abstract - device not named
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Reference	Exclusion reason
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Takido N, Miyagi S, Kashiwadate T, Nishimaki H, Miyazawa K, Tokodai K, et al. Investigation of optimal temperature for machine perfusion of liver transplantation in donors after cardiac death. Transplantation. 2022.106(9):S689-S89.	Ineligible patient population
Tang G, Zhang L, Xia L, Zhang J, Wei Z, Zhou R. Hypothermic oxygenated perfusion in liver transplantation: A meta-analysis of randomized controlled trials and matched studies. Int J Surg. 2024.110(1):464-77. doi: https://dx.doi.org/10.1097/JS9.0000000000000784	Systematic review to check
Tang H, Abu-Gazala S, Mahmud N, Abt P. National trends in utilization of normothermic machine perfusion in DCD liver transplantation. Hepatology. 2023.78(Suppl 1):S281. doi: https://dx.doi.org/10.1097/HEP.0000000000000580	Abstract - device not named
Tarigoppula H, Prem kumar GV, Amita S. The first series of normothermic machine perfusion in India - the way ahead. Int J Surg. 2022.100(Suppl):106471. doi: https://dx.doi.org/10.1016/j.ijsu.2022.106471	Ineligible study design
Thomas J, Chen Q, Roach A, Wolfe S, Osho AA, Sundaram V, et al. Donation after circulatory death heart procurement strategy impacts utilization and outcomes of concurrently procured abdominal organs. Journal of Heart AND Lung Transplantation. 2023.42(7):993-1001. doi: https://dx.doi.org/10.1016/j.healun.2023.02.1497	Device not named
Thorne AM, Geng Y, Lantinga VA, Smit M, Kuivenhoven JA, Porte RJ, et al. Therapeutic hyperthermia promotes lipid export and HSP70/90 during machine perfusion of human livers. Physiol Rep. 2025.13(9):e70348. doi: https://dx.doi.org/10.14814/phy2.70348	Ineligible outcomes
Thorne AM, Lantinga V, Bodewes S, de Kleine RHJ, Nijkamp MW, Sprakel J, et al. Ex situ dual hypothermic oxygenated machine perfusion for human split liver transplantation. Transplant Direct. 2021.7(3):e666. doi: https://dx.doi.org/10.1097/TXD.0000000000001116	Ineligible study design
Tingle S, Dobbins J, Thompson E, Figueiredo R, Mahendran B, White S, et al. Machine perfusion in liver transplantation	Systematic review to check

Reference	Exclusion reason
Tingle S, Kourounis G, Dobbins J, Thompson E, Figueiredo R, Mahendran B, et al. Machine perfusion in liver transplantation: Cochrane review and meta-analysis. Liver Transpl. 2024.30:266-66.	Systematic review to check
Tingle SJ, Dobbins JJ, Thompson ER, Figueiredo RS, Mahendran B, Pandanaboyana S, et al. Machine perfusion in liver transplantation. Cochrane Database Syst Rev. 2023.9:CD014685. doi: https://dx.doi.org/10.1002/14651858.CD014685.pub2	Systematic review to check
Tingle SJ, Ibrahim I, Thompson ER, Bates L, Sivaharan A, Bury Y, et al. Methaemoglobinaemia can complicate normothermic machine perfusion of human livers. Front. 2021.8:634777. doi: https://dx.doi.org/10.3389/fsurg.2021.634777	Ineligible outcomes
Todd R, Rosowicz A, Holzner M, Meyerovich G, Tabrizian P, Rocha C, et al. Using normothermic machine perfusion (NMP) to assess, resuscitate and rescue livers for transplantation: First 50 cases of a US single center. Hepatology. 2023.78:S294-S94.	Device not named
Todd R, van Leeuwen LL, Holzner M, Kim-Schluger L, Fiel MI, Puleston D, et al. Normothermic machine perfusion of explanted livers: Exploratory study of an alternative translational model for end-stage liver disease. Artif Organs. 2025.49(3):431-40. doi: https://dx.doi.org/10.1111/aor.14905	Ineligible outcomes
TransMedics. Continued access protocol to evaluate the effectiveness of the portable organ care system (OCS) liver for preserving and assessing donor livers for transplantation A1 - anonymous. Identifier: NCT04186221. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2019. Available from https://clinicaltrials.gov/study/NCT04186221.	Ineligible intervention
TransMedics. International randomized trial to evaluate the effectiveness of the portable organ care system (OCSTM) liver for preserving and assessing donor livers for transplantation (OCS liver protect trial) A1 - anonymous. Identifier: NCT02522871. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2015. Available from https://clinicaltrials.gov/study/NCT02522871.	Ineligible intervention
TransMedics. OCS liver DCD trial. Identifier: NCT04194437. In: ClinicalTrials.gov [internet]. Bethesda (MD): National Library of Medicine (US): 2020. Available from https://clinicaltrials.gov/study/NCT04194437.	Ineligible intervention

Reference	Exclusion reason
TransMedics. OCS liver perfusion (OLP) post-approval registry A1 - anonymous. Identifier: NCT05074160. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2021. Available from https://clinicaltrials.gov/study/NCT05074160.	Ineligible intervention
TransMedics. OCS liver protect continuation post-approval study A1 - anonymous. Identifier: NCT05096741. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2021. Available from https://clinicaltrials.gov/study/NCT05096741.	Ineligible intervention
TransMedics. OCS liver protect continued access protocol (CAP) continuation post-approval study A1 - anonymous. Identifier: NCT05096754. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2021. Available from https://clinicaltrials.gov/study/NCT05096754.	Ineligible intervention
TransMedics. OCS liver protect continued access protocol. Identifier: NCT04186221. In: ClinicalTrials.gov [internet]. Bethesda (MD): National Library of Medicine (US): 2020. Available from https://clinicaltrials.gov/study/NCT04186221.	Ineligible intervention
TransMedics. Prospective trial to evaluate the effectiveness of the portable organ care system (OCS) liver for preserving, optimizing and assessing currently seldom utilized DCD donor livers for transplantation A1 - anonymous. Identifier: NCT04194437. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2019. Available from https://clinicaltrials.gov/study/NCT04194437.	Ineligible intervention
TransMedics. Single-arm prospective trial to evaluate the safety and performance of the portable organ care system (OCSTM) liver for preserving and assessing donor livers for transplantation A1 - anonymous. Identifier: NCT02449694. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2015. Available from https://clinicaltrials.gov/study/NCT02449694.	Ineligible intervention
TransMedics. US national OCS liver perfusion (OLP) registry A1 - anonymous. Identifier: NCT05940857. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2023. Available from https://clinicaltrials.gov/study/NCT05940857.	Ineligible intervention
Universitätsklinikum Tübingen R, Abteilung für Diagnostische und Interventionelle Radiologie,. Non-invasive ultrasound-based quantification of perfusion parameters, fibrosis, inflammation and steatosis in paediatric patients after liver transplantation. Identifier: DRKS00034751. In: German Clinical Trials Register [internet].	Ineligible intervention

Reference	Exclusion reason
Freiburg: Institute for Medical Biometry and Statistics - University of Freiburg: 2024. Available from http://drks.de/search/en/trial/DRKS00034751.	
University Health Network T. A single centre study of the feasibility and safety of using ex-vivo normothermic machine perfusion with the organox *metra*tm device to store human livers for transplantation A1 - anonymous. Identifier: NCT02478151. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2014. Available from https://clinicaltrials.gov/study/NCT02478151.	Ineligible intervention
University Medical Center Groningen. Assessment of long-term outcomes after transplantation of donor livers preserved by hypothermic oxygenated machine perfusion (HOPE): A retrospective cohort analysis of real-world data (ideal-d stage 4) A1 - anonymous. Identifier: NCT05520320. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2022. Available from https://clinicaltrials.gov/study/NCT05520320.	Multiple devices not reported seperately
van den Boom BP, Bodewes SB, Lascaris B, Adelmeijer J, Porte RJ, de Meijer VE, et al. The international normalised ratio to monitor coagulation factor production during normothermic machine perfusion of human donor livers. Thromb Res. 2023.228:64-71. doi: https://dx.doi.org/10.1016/j.thromres.2023.05.025	Device not named
van Leeuwen OB, van Reeven M, van der Helm D, Ijzermans JNM, de Meijer VE, van den Berg AP, et al. Donor hepatectomy time influences ischemia-reperfusion injury of the biliary tree in donation after circulatory death liver transplantation. Surgery. 2020.168(1):160-66. doi: https://dx.doi.org/10.1016/j.surg.2020.02.005	Ineligible intervention
Vargas P, Robinson T, Patel K, Oberholzer J, Goldaracena N, Pelletier S. Impact of machine perfusion preservation on discard rates of liver grafts since its implementation in the us. Am J Transplant. 2023.23(1):S41-S41.	Abstract - device not named
Vasuri F, Germinario G, Ciavarella C, Carroli M, Motta I, Valente S, et al. Trophism and homeostasis of liver sinusoidal endothelial graft cells during preservation, with and without hypothermic oxygenated perfusion. Biology (Basel). 2022.11(9):08. doi: https://dx.doi.org/10.3390/biology11091329	Device not named
Vella I, De Carlis R, Lauterio A, Cerchione R, Migliorini M, Centonze L, et al. Preliminary experience with perlife system for ex-situ liver perfusion and purification. Blood Purif. 2022.51(Suppl 3):15. doi: https://dx.doi.org/10.1159/000528706	Ineligible study design

Reference	Exclusion reason
Vendrell M, Hessheimer AJ, Ruiz A, de Sousa E, Paredes D, Rodriguez C, et al. Coagulation profiles of unexpected DCDD donors do not indicate a role for exogenous fibrinolysis. Am J Transplant. 2015.15(3):764-71. doi: https://dx.doi.org/10.1111/ajt.13058	Ineligible device
Venezian FMM, Rivas E, Galaz V, Castillo V, Benitez J, Martinez E, et al. P-4 hypothermic oxygenated perfusion using an ecmo device in liver transplantation: An analysis of the first 100 cases at a Chilean public hospital. Ann Hepatol. 2024.29(Suppl 3):101618. doi: https://dx.doi.org/10.1016/j.aohep.2024.101618	Abstract - device not named
Viana P, Castillo-Flores S, Mora MMR, Cabral TDD, Martins PN, Kueht M, 2nd, et al. Normothermic machine perfusion vs. Static cold storage in liver transplantation: A systematic review and meta-analysis. Artif Organs. 2025.49(6):945-54. doi: https://dx.doi.org/10.1111/aor.14960	Systematic review to check
Viguera L, Blasi A, Reverter E, Arjona B, Caballero M, Chocron I, et al. Liver transplant with controlled donors after circulatory death with normothermic regional perfusion and brain dead donors: A multicenter cohort study of transfusion, one-year graft survival and mortality. Int J Surg. 2021.96:106169. doi: https://dx.doi.org/10.1016/j.ijsu.2021.106169	Ineligible intervention
Vivaldi JAS, Kadakia Y, MacConmara M, Patel M, Shah J, Hanish S, et al. Utilization of normothermic machine perfusion in pediatric donor livers. Am J Transplant. 2023.23(6):S348-S48.	Abstract - device not named
Vyas F, Cederquist K, Abu-Gazala S, Levine M, Olthoff K, Shaked A, et al. Liver transplant after normothermic regional perfusion from controlled donation after cardiac death: Early experience. Am J Transplant. 2023.23(1):S66-S66.	Abstract - device not named
Wakam G, Keslar K, Baldwin W, Miller C, Quintini C, Hashimoto K, et al. Pretransplant normothermic perfusion affects inflammatory transcripts following perfusion and implantation in both DCD and DBD liver grafts. Am J Transplant. 2024.24(1):S14-S14.	Abstract - device not named
Walcott J, Logue J, Bell R, Hakeem A, Farid S, Upasani V, et al. Favourable outcomes with hypothermic oxygenated machine perfusion in donation after circulatory death liver transplants - a single centre experience. Transplantation. 2023.107(9):184-84.	Abstract - device not named

Reference	Exclusion reason
Wall A, Snoddy M, Du J, Bayer J, Danobeitia S, Lee SH, et al. The current landscape of in situ and ex situ machine perfusion utilization for liver grafts from cardiac donation after circulatory death donors in the us. Am J Transplant. 2025.25(3):574-82. doi: https://dx.doi.org/10.1016/j.ajt.2024.09.012	Multiple devices not reported seperately
Wang BK, Shubin AD, Harvey JA, MacConmara MM, Hwang CS, Patel MS, et al. From patients to providers: Assessing impact of normothermic machine perfusion on liver transplant practices in the us. J Am Coll Surg. 2024.238(5):844-52. doi: https://dx.doi.org/10.1097/XCS.0000000000000924	Multiple devices not reported seperately
Watson CJE, Hunt F, Messer S, Currie I, Large S, Sutherland A, et al. In situ normothermic perfusion of livers in controlled circulatory death donation may prevent ischemic cholangiopathy and improve graft survival. Am J Transplant. 2019.19(6):1745-58. doi: https://dx.doi.org/10.1111/ajt.15241	Ineligible intervention
Wehrle C, Keslar K, Liu Q, Baldwin W, Miller C, Schlegel A, et al. Normothermic perfusion compared to static cold storage attenuates inflammatory transcript expression in standard criterion donated after brain death livers. Liver Transpl. 2024.30:262-63.	Abstract - device not named
Wehrle C, Kusakabe J, Gross A, Zhang MC, Wakam G, Shanmugarajah K, et al. Programmatic normothermic machine perfusion improves liver transplant waitlist outcomes for patients with lower meld scores: A multi-center study. Am J Transplant. 2025.25(1 Suppl 1):S4 EP - S5. doi: https://dx.doi.org/10.1016/j.ajt.2024.12.018	Abstract - device not named
Wehrle CJ, Dewey E, Nadeem MA, Batista de Oliveira L, Jiao C, Sun K, et al. Cost effectiveness analysis and clinical outcomes of back-to-base normothermic machine perfusion with and without FMN: A multi-center risk-matched study of 967 patients. Am J Transplant. 2025.25(8 Suppl 1):S183. doi: https://dx.doi.org/10.1016/j.ajt.2025.07.403	Abstract - device not named
Wehrle CJ, Hong H, Ali K, Cazzaniga B, Miyazaki Y, Tuul M, et al. Integration of normothermic machine perfusion in a liver transplant program reduces waitlist time and mortality: A two-center/one enterprise modern experience. Gastroenterology. 2024.166(5 Suppl):S EP - 1748. doi: https://dx.doi.org/10.1016/S0016-5085%2824%2904486-X	Abstract - device not named

Reference	Exclusion reason
Wehrle CJ, Hong H, Gross A, Liu Q, Ali K, Cazzaniga B, et al. Integration of machine perfusion in a liver transplant program reduces waitlist time and mortality. Hpb. 2024.26(Suppl 2):S617. doi: https://dx.doi.org/10.1016/j.hpb.2024.04.044	Abstract - device not named
Wehrle CJ, Kusakabe J, Gross A, Modaresi J, Fujiki M, Schlegel A, et al. Routine normothermic perfusion improves liver transplant waitlist outcomes for lower meld patients. Hpb. 2025.27(Suppl 1):S63. doi: https://dx.doi.org/10.1016/j.hpb.2025.03.120	Abstract - device not named
Wisel SA, Steggerda JA, Kim IK. Use of machine perfusion in the United States increases organ utilization and improves DCD graft survival in liver transplantation. Transplant Direct. 2024.10(12):e1726. doi: https://dx.doi.org/10.1097/TXD.0000000000001726	Multiple devices not reported seperately
Wisel SA, Steggerda JA, Thiessen C, Roll GR, Chen Q, Thomas J, et al. Preserved 2-y liver transplant outcomes following simultaneous thoracoabdominal DCD organ procurement despite effects on liver utilization rate. Transplant Direct. 2023.9(11):e1528. doi: https://dx.doi.org/10.1097/TXD.0000000000001528	Device not named
Xie X, Zheng Q, Li K, Xiang B. Hypothermic oxygenated perfusion in human liver transplantation: Meta-analysis of randomized clinical trials. Br J Surg. 2024.111(1):03. doi: https://dx.doi.org/10.1093/bjs/znad403	Systematic review to check
Xu M, Zhou F, Ahmed O, Randle LV, Shin J-K, Zhu Y, et al. Dual lactate clearance in the viability assessment of livers donated after circulatory death with ex situ normothermic machine perfusion. Transplant Direct. 2021.7(12):e789. doi: https://dx.doi.org/10.1097/TXD.0000000000001243	Ineligible outcomes
Yamamoto T, Atthota S, Agarwal D, Crisalli K, MacConmara M, Nakamura T, et al. Impact of portable normothermic machine perfusion for liver transplantation from adult deceased donors. Ann Surg. 2023.278(5):e922-e29. doi: https://dx.doi.org/10.1097/SLA.0000000000006032	Ineligible intervention
Yamamoto T, Atthota S, Crisalli K, MacConmara M, Nakamura T, Teo R, et al. Expansion of the liver donor pool by portable normothermic machine perfusion (NMP) - single center experience of 108 donor livers preserved with NMP. Am J Transplant. 2023.23(6):S456-S56.	Ineligible intervention

Reference	Exclusion reason
Yamamoto T, Koizumi N, Markmann JF. The impact of over three years commercial use of ex vivo normothermic machine perfusion for liver transplantation in the USA: A UNOS/OPTN database analysis. Artif Organs. 2025.49(6):1030-45. doi: https://dx.doi.org/10.1111/aor.14975	Multiple devices not reported seperately
Yamamoto T, Nakamura T, Teo R, Dageforde L, Kimura S, Elias N, et al. Normothermic machine perfusion (NMP) could prevent discarding livers from older (>60yo) DBD donors. Am J Transplant. 2023.23(6 Suppl 1):S723 EP - S24. doi: https://dx.doi.org/10.1016/j.ajt.2023.05.014	Abstract - device not named
Yamamoto T, Nakamura T, Teo R, Dageforde L, Kimura S, Elias N, et al. The impact of normothermic machine perfusion (NMP) in deceased donor liver transplantation in the USA. Am J Transplant. 2023.23(6 Suppl 1):S858 EP - S59. doi: https://dx.doi.org/10.1016/j.ajt.2023.05.014	Multiple devices not reported seperately
Yamamoto T, Ruch B, Wagler J, Kumm K, Zhang C, Nguyen MC, et al. Normothermic machine perfusion: Reducing preoperative admissions and increasing organ offers. Am J Transplant. 2023.23(6 Suppl 1):S724. doi: https://dx.doi.org/10.1016/j.ajt.2023.05.014	Multiple devices not reported seperately
Yang X, Guo Q, Li Y, Zhong X. Effectiveness of machine perfusion in liver transplantation: A meta-analysis of randomized controlled trials. J Liver Transpl. 2023.12((Yang, Li, Guo, Li, Zhong) Department of Hepatopancreatobiliary Surgery, The Second Affiliated Hospital of Harbin Medical University, China):100176. doi: https://dx.doi.org/10.1016/j.liver.2023.100176	Systematic review to check
Yue P, Lv X, Cao H, Zou Y, You J, Luo J, et al. Hypothermic oxygenated perfusion inhibits CLIP1-mediated TIRAP ubiquitination via TFPI2 to reduce ischemia-reperfusion injury of the fatty liver. Experimental AND Molecular Medicine. 2024.56(12):2588-601. doi: https://dx.doi.org/10.1038/s12276-024-01350-8	Ineligible patient population
Zhang C, Kumm K, Ruch B, Harbell J, Hewitt W, Jadlowiec C, et al. Machine perfusion impact on liver transplant operative start times. Am J Transplant. 2024.24(1):S103-S03.	Abstract - device not named
Zhou AL, Akbar AF, Ruck JM, Weeks SR, Wesson R, Ottmann SE, et al. Use of ex situ machine perfusion for liver transplantation: The national experience. Transplantation. 2025.109(6):967-75. doi: https://dx.doi.org/10.1097/TP.0000000000005290	Multiple devices not reported seperately

Table B.2: Deprioritised studies (n = 191)

Technology	Study	Publication type	Reasons for exclusion
metra (OrganOx Ltd)	Ali K, Sun K, Jiao C, et al. (2024) Mitochondrial injury during normothermic machine perfusion predicts outcomes and costs after liver transplantation - the first analysis in 200 human livers. Liver Transplantation 30: 36-37	Abstract	Not back-to-base pathway
metra (OrganOx Ltd)	Angelico R, Perera MTPR, Ravikumar R, et al. (2016) Normothermic machine perfusion of deceased donor liver grafts is associated with improved postreperfusion hemodynamics. Transplantation Direct 2(9): e97	Journal article	Not back-to-base pathway
Liver Assist (XVIVO B.V.)	Arend J, Bollensdorf A, Stelter F, et al. (2025) Dual hypothermic oxygenated machine perfusion (DHOPE) improves extended allocation graft function in liver transplantation. Journal of Liver Transplantation 18((Arend, Bollensdorf, Stelter, Rahimli, Croner, Franz) Department of General, Visceral, Vascular and Transplant Surgery, University Hospital Magdeburg, Magdeburg, Germany): 100271	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Blondeel J, van Leeuwen OB, Schurink IJ, et al. (2025) Dynamic preservation of donation after circulatory death liver grafts from donors aged 60 y and older. Transplantation 109(5): 844-852	Abstract	Non-RCT
metra (OrganOx Ltd)	Bohils M and Albiol J (2025) Hypothermic liver perfusion: A retrospective analysis of its implementation and procedural impact. American Journal of Transplantation 25(8 Suppl 1): S972 EP - S973	Abstract	Non-RCT
metra (OrganOx Ltd)	Bral M, Gala-Lopez B, Bigam D, et al. (2017) Preliminary single-center canadian experience of human normothermic ex vivo liver perfusion:	Journal article	Not back-to-base pathway

Technology	Study	Publication type	Reasons for exclusion
	Results of a clinical trial. American Journal of Transplantation 17(4): 1071-1080		
metra (OrganOx Ltd)	Bral M, Gala-Lopez B, Bigam D, et al. 2017. (Preliminary results of clinical normothermic ex vivo liver perfusion in a North American setting) American journal of transplantation [Online]. Available: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01378600/full	Abstract	Not back-to-base pathway
Liver Assist (XVIVO B.V.)	Burlage LC, Hessels L, van Rijn R, et al. (2019) Opposite acute potassium and sodium shifts during transplantation of hypothermic machine perfused donor livers. American Journal of Transplantation 19(4): 1061-1071	Journal article	Non-RCT
metra (OrganOx Ltd)	Caballero-Marcos A, Rodriguez-Bachiller L, Baroja-Mazo A, et al. (2024) Dynamics of ischemia/reperfusion injury markers during normothermic liver machine perfusion. Transplantation Direct 10(12): e1728	Journal article	Not back-to-base pathway
metra (OrganOx Ltd)	Calderon E, Ali K, Cazzaniga B, et al. (2024) Is duration of normothermic machine perfusion a predictor of early allograft disfunction in liver transplantation? American Journal of Transplantation 24(1): S85-S85	Abstract	Not back-to-base pathway
metra (OrganOx Ltd)	Calderon E, Shanmugarajah K, Ali K, et al. (2024) Is duration of normothermic machine perfusion a predictor of early allograft dysfunction in liver transplantation? Liver Transplantation 30: 84-85	Abstract	Not back-to-base pathway
Liver Assist (XVIVO B.V.)	Caracciolo D, Magistri P, Olivieri T, et al. (2022) Use of machine perfusion in extended criteria DBD donors. Transplantation 106(8): 120 EP - 121	Abstract	Non-RCT

Technology	Study	Publication type	Reasons for exclusion
metra (OrganOx Ltd)	Cardini B, Oberhuber R, Fodor M, et al. (2020) Clinical implementation of prolonged liver preservation and monitoring through normothermic machine perfusion in liver transplantation. Transplantation 104(9): 1917-1928	Journal article	Not back-to-base pathway
metra (OrganOx Ltd)	Cazzaniga B, Ali K, Kusakabe J, et al. (2025) Transforming transplant oversight: Enhancing combined cardiothoracic surgery and liver transplantation with normothermic machine perfusion. Transplantation Direct 11(6): e1810	Journal article	Not back-to-base pathway
metra (OrganOx Ltd)	Cazzaniga B, Ali K, Liu Q, et al. (2024) Transforming transplant oversight: Enhancing combined cardiothoracic surgery and liver transplantation with normothermic machine perfusion. American Journal of Transplantation 24(1): S37-S37	Abstract	Not back-to-base pathway
metra (OrganOx Ltd)	Cazzaniga B, Ali K, Liu Q, et al. (2024) Optimizing combined cardiothoracic surgery and liver transplantation through normothermic machine perfusion: A paradigm shift in liver transplant. Liver Transplantation 30: 186-186	Abstract	Not back-to-base pathway
Liver Assist (XVIVO B.V.)	Chen M, Chen Z, Lin X, et al. (2021) Application of ischaemia-free liver transplantation improves prognosis of patients with steatotic donor livers - a retrospective study. Transpl Int 34(7): 1261-1270	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Chen Z, Wang T, Chen C, et al. (2022) Transplantation of extended criteria donor livers following continuous normothermic machine perfusion without recooling. Transplantation 106(6): 1193-1200	Journal article	Non-RCT
Liver Assist (XVIVO B.V.); ChiCTR-OPN-17012090	Guo Z, Zhao Q, Huang S, et al. (2021) Ischaemia-free liver transplantation in humans: A first-in-human trial. The Lancet Regional Health. Western Pacific 16: 100260	Journal article	Non-RCT

Technology	Study	Publication type	Reasons for exclusion
	Guo Z, Xu J, Huang S, et al. (2022) Abrogation of graft ischemia-reperfusion injury in ischemia-free liver transplantation. Clin Transl Med 12(4): e546	Journal article	
	Jia Z, Zhu J, Zhang J, et al. (2025) Ischemia-free liver transplantation improves long-term outcomes in a 5-year follow-up study. JHEP Reports 7(7): 101393	Journal article	
Liver Assist (XVIVO B.V.); ChiCTR1900021158	Huang C, Huang S, Tang Y, et al. (2020) Prospective, single-centre, randomised controlled trial to evaluate the efficacy and safety of ischaemia-free liver transplantation (IFLT) in the treatment of end-stage liver disease. BRITISH JOURNAL MEDICINE Open 10(5): e035374	Journal article	Not back-to-base pathway
	Guo Z, Zhao Q, Jia Z, et al. (2023) A randomized-controlled trial of ischemia-free liver transplantation for end-stage liver disease. Journal of Hepatology 79(2): 394-402	Journal article	
	Lin J, Li Y, Fang T, et al. (2024) Substantial decline of organ preservation fluid contamination following adoption of ischemia-free liver transplantation: A post-hoc analysis. Int J Surg 110(5): 2855-2864	Journal article	
metra (OrganOx Ltd); COPE trial, ISRCTN39731134	Nasralla D, Coussios CC, Mergental H, et al. (2018) A randomized trial of normothermic preservation in liver transplantation. Nature 557(7703): 50-56	Journal article	Not back-to-base pathway
	University of Oxford (UK). Work package 2 (WP2) - normothermic liver perfusion vs cold storage in liver transplants. Identifier: ISRCTN39731134. In: ISRCTN Registry [internet]. London: BioMed Central Limited: 2014. Available from http://isrctn.com/ISRCTN39731134	Clinical trial record	

Technology	Study	Publication type	Reasons for exclusion
	Chiocchia V, Nasralla D, Bradley A, et al. 2017. (Machine perfusion in liver transplantation: Practical issues to consider in the design and conduct of a complex multinational interventional trial and the potential impact on the analysis) Trials [Online]. Available: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01470666/full	Abstract	
	David N, Rutger P and Peter F. 2017. (Normothermic machine perfusion vs static cold storage in liver transplantation: Outcomes from a randomised controlled trial) Transplant international [Online]. Available: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01421459/full	Journal article	
	Gilbo N, Neil D, Brais R, et al. (2023) The effect of continuous liver normothermic machine perfusion on the severity of histological bile duct injury. Transplant International 36: 11645	Journal article	
	Mohkam K, Nasralla D, Mergental H, et al. 2021. (Normothermic regional perfusion or normothermic machine perfusion in liver transplantation from donation after circulatory death: A first comparative study) Hpb [Online]. Available: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02343569/full	Abstract	
	Nasralla D, Mergental H, Jassem W, et al. 2015. (A randomised controlled trial of normothermic liver perfusion versus cold storage in human liver transplantation) Transplant international [Online]. Available: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01126596/full	Abstract	

Technology	Study	Publication type	Reasons for exclusion
	Nasralla D, Ploeg R, Coussios C, et al. 2017. (Outcomes from a multinational randomised controlled trial comparing normothermic machine perfusion with static cold storage in human liver transplantation) American journal of transplantation [Online]. Available: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01378566/full	Abstract	
	Nasralla D, Lembach H, Mergental H, et al. (2020) Ex situ arterial reconstruction during normothermic perfusion of the liver. Transplantation Direct 6(9): e596	Journal article	
Liver Assist (XVIVO B.V.)	Corcione S, Patrono D, Shbaklo N, et al. (2025) Hypothermic oxygenated machine perfusion does not increase the risk of infection after liver transplantation: A retrospective cohort study. Hepatobiliary Surgery and Nutrition 14(4): 562-574	Journal article	Non-RCT
metra (OrganOx Ltd)	Datta M, Sambommatsu Y, Imai D, et al. (2025) Impact of implementing routine normothermic machine perfusion in liver transplantation: A single-center retrospective study. American Journal of Transplantation 25(8 Suppl 1): S736	Abstract	Unclear pathway
Liver Assist (XVIVO B.V.) DCDNet; NCT04744389	Azienda Ospedaliero UP. Comparison of hypothermic versus normothermic ex-vivo preservation. Identifier: NCT04744389. In: ClinicalTrials.gov [internet]. 2021. Available from https://clinicaltrials.gov/study/NCT04744389	Clinical trial record	Comparison not relevant to decision problem (compared LiverAssist in hyporthermic and normothermic modes, not to SCS)
	Bronzoni J, Pezzati D, Carrai P, et al. (2024) Pilot, open, randomized, multicenter trial for the comparison of hypothermic versus normothermic ex-situ liver preservation in DCD liver transplantation with extended ischemia time (DCDNet trial). Digestive and Liver Disease 56(Suppl 1): S38 EP - S39	Abstract	

Technology	Study	Publication type	Reasons for exclusion
	Catalano G, Patrono D, Pezzati D, et al. (2024) Pilot, open, randomized, multicenter trial for the comparison of hypothermic versus normothermic ex-situ liver preservation in DCD liver transplantation with extended ischemia time (DCDNet trial). Transplantation 108(9 Suppl): 125	Abstract	
	Catalano G, Vacca PG, Pezzati D, et al. (2024) Sequential normothermic regional and end-ischemic ex-situ machine perfusion allows the safe use of very old DCD donors in liver transplantation (DCDNet trial). Transplantation 108(9 Suppl): 125	Abstract	
	Ghinolfi D, Melandro F, Torri F, et al. (2023) The role of sequential normothermic regional perfusion and end-ischemic normothermic machine perfusion in liver transplantation from very extended uncontrolled donation after cardiocirculatory death. Artificial Organs 47(2): 432 EP - 440	Journal article	
	Martinelli C, Ghinolfi D, Pezzati D, et al. (2024) Sequential normothermic regional and end-ischemic ex-situ machine perfusion allows the safe use of very old DCD donors in liver transplantation (DCDNet trial). Journal of Hepatology 80(Suppl 1): S370 EP - S371	Abstract	
	Torri F, Balzano E, Melandro F, et al. (2024) Sequential normothermic regional perfusion and end-ischemic ex situ machine perfusion allow the safe use of very old DCD donors in liver transplantation. Transplantation 108(6): 1394-1402	Journal article	
	Torri F, Martinelli C, Bronzoni J, et al. (2023) Perfusate cytokines concentrations during liver grafts ex-situ normothermic perfusion (DCDNet study). Transplantation 107(9 Suppl 1): 137 EP - 138	Conference poster	

Technology	Study	Publication type	Reasons for exclusion
	Torri F, Melandro F, Balzano E, et al. (2023) Pilot, open, randomized, multicenter trial for the comparison of hypothermic versus normothermic ex-situ liver preservation in DCD liver transplantation with extended ischemia time (DCDNet trial). Transplantation 107(9 Suppl 1): 21 EP - 22	Abstract	
	Vacca PG, Pezzati D, Bronzoni J, et al. (2024) Sequential normothermic regional and end-ischemic ex-situ machine perfusion allows the safe use of very old DCD donors in liver transplantation (DCDNet trial). Liver Transplantation 30: 39-39	Abstract	
	Vacca PG, Pezzati D, Bronzoni J, et al. (2024) Perfusate cytokines concentrations during liver grafts ex-situ normothermic perfusion (DCDNet study). Digestive and Liver Disease 56(Suppl 1): S42 EP - S43	Abstract	
Liver Assist (XVIVO B.V.)	De Carlis R, Di Sandro S, Lauterio A, et al. (2018) Liver grafts from donors after circulatory death on regional perfusion with extended warm ischemia compared with donors after brain death. Liver Transplantation 24(11): 1523-1535	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	De Carlis R, Di Sandro S, Lauterio A, et al. (2017) Successful donation after cardiac death liver transplants with prolonged warm ischemia time using normothermic regional perfusion. Liver Transplantation 23(2): 166-173	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	De Carlis R, Lauterio A, Schlegel A, et al. (2025) Are there any benefits of prolonged hypothermic oxygenated perfusion?: Results from a national retrospective study. Liver Transplantation 31(1): 70-84	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	De Carlis R, Schlegel A, Frassoni S, et al. (2021) How to preserve liver grafts from circulatory death with long warm ischemia? A	Journal article	Non-RCT

Technology	Study	Publication type	Reasons for exclusion
	retrospective Italian cohort study with normothermic regional perfusion and hypothermic oxygenated perfusion. Transplantation 105(11): 2385-2396		
Liver Assist (XVIVO B.V.)	De Jong IE, Bodewes SB, Overi D, et al. (2022) Assessment of bile duct injury of donor livers during ex situ normothermic machine perfusion. Transplantation 106(8): 87	Abstract	Non-RCT
Liver Assist (XVIVO B.V.)	de Jong IEM, Bodewes SB, van Leeuwen OB, et al. (2023) Restoration of bile duct injury of donor livers during ex situ normothermic machine perfusion. Transplantation 107(6): e161-e172	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Dingfelder J, Kollmann D, Rauter L, et al. (2025) Validation of mitochondrial FMN as a predictor for early allograft dysfunction and patient survival measured during hypothermic oxygenated perfusion. Liver Transplantation 31(4): 476-488	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Dondossola D, Lonati C, Zanella A, et al. (2019) Preliminary experience with hypothermic oxygenated machine perfusion in an Italian liver transplant center. Transplantation Proceedings 51(1): 111-116	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Dutkowski P, Polak WG, Muiesan P, et al. (2015) First comparison of hypothermic oxygenated perfusion versus static cold storage of human donation after cardiac death liver transplants. Annals of Surgery 262(5): 764 EP - 771	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Dutkowski P, Schlegel A, de Oliveira M, et al. (2014) HOPE for human liver grafts obtained from donors after cardiac death. Journal of Hepatology 60(4): 765-72	Journal article	Non-RCT

Technology	Study	Publication type	Reasons for exclusion
Liver Assist (XVIVO B.V.)	Elgosbi M, Kurt AS, Londono M-C, et al. (2025) Hypothermic oxygenated machine perfusion influences the immunogenicity of donor livers in humans. Liver Transplantation 31(3): 311-322	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Endo C, Lascaris B, Bruggenwirth IMA, et al. (2024) The risk of microbial transmission in recipients of donor livers that underwent hypothermic or normothermic machine perfusion. Transplantation Direct 10(7): e1664	Journal article	Non-RCT
metra (OrganOx Ltd)	Fagenson A, Brown C, Todd R, et al. (2025) Simultaneous liver kidney transplantation in the era of machine perfusion: To pump or not to pump? American Journal of Transplantation 25(1 Suppl 1): S112	Abstract	Non-comparative study
metra (OrganOx Ltd)	Flynn B, Muralidaran V, McDeed A, et al. (2025) Determinants of early allograft dysfunction in liver transplantation using normothermic machine perfusion. American Journal of Transplantation 25(8 Suppl 1): S969	Abstract	Non-comparative study
Liver Assist (XVIVO B.V.)	Ghinolfi D, Dondossola D, Rreka E, et al. (2021) Sequential use of normothermic regional and ex situ machine perfusion in donation after circulatory death liver transplant. Liver Transplantation 27(3): 385-402	Journal article	Non-RCT
Liver Assist (XVIVO B.V.), *metra* (OrganOx Ltd)	Gruttadauria S, Vella I, Li Petri S, et al. (2025) Liver transplantation after ex vivo normothermic machine preservation without recooling the graft: A clinical series from a single center. Liver Transplantation 31(9): 1190 EP - 1194	Brief report	Non-RCT
metra (OrganOx Ltd)	Habbouche J, Zhang K, Bachul PJ, et al. (2025) Initial experience with normothermic machine liver perfusion for combined liver and thoracic transplantation. American Journal of Transplantation 25(8 Suppl 1): S716	Abstract	Non-comparative study

Technology	Study	Publication type	Reasons for exclusion
metra (OrganOx Ltd)	Hann A, Alfarah J, Clarke G, et al. (2023) Normothermic machine preservation of large DBD liver grafts is associated with early allograft dysfunction. Transplantation 107(9 Suppl 1): 22 EP - 23	Abstract	Unclear pathway
metra (OrganOx Ltd); Hofmann et al 2024	Hofmann J, Meszaros AT, Butler A, et al. (2024) Predictive value of early postoperative lactate (<6 h) during normothermic machine perfusion and outcome after liver transplantation: Results from a multicentre study. British Journal of Surgery 111(6): 12	Journal article	Non-comparative study
	Hofmann J, Meszaros AT, Butler A, et al. (2022) Lactate auc of 0-6h during normothermic machine perfusion has strong predictive value towards the outcome after liver transplantation: Results from a multicenter study. Transplantation 106(8): 66	Abstract	
Liver Assist (XVIVO B.V.), VitaSmart (Bridge to Life Ltd); HOPE-REAL NCT05520320	Eden J, Brüggenwirth IM, Berlakovich G, et al. (2024) Long-term outcomes after hypothermic oxygenated machine perfusion and transplantation of 1,202 donor livers using realworld data. Liver Transplantation 30: 8-8	Abstract	Non-RCT
	Eden J, Bruggenwirth IMA, Berlakovich G, et al. (2025) Long-term outcomes after hypothermic oxygenated machine perfusion and transplantation of 1,202 donor livers in a real-world setting (HOPE-real study). Journal of Hepatology 82(1): 97-106	Journal article	
	Eden J, Muller PC, Kuemmerli C, et al. (2025) Life expectancy of transplanted livers - HOPE against aging? Annals of Surgery 07: 07	Journal article	
	University Medical Center Groningen. Long-term outcomes after hypothermic oxygenated machine perfusion of donor livers using real-world data (HOPE-real). Identifier: NCT05520320. In: ClinicalTrials.gov [internet]. Bethesda (MD): National Library of	Clinical trial record	

Technology	Study	Publication type	Reasons for exclusion
	Medicine (US): 2022. Available from https://clinicaltrials.gov/study/NCT05520320		
Liver Assist (XVIVO B.V.)	Horne F, Drefs M, Schirren MJ, et al. (2022) Hypothermic oxygenated machine perfusion (HOPE) prior to liver transplantation mitigates PRS and perioperative electrolyte shifts. Journal of Clinical Medicine 11(24): 12	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Hoyer DP, Benkö T, Manka P, et al. (2020) Long-term outcomes after controlled oxygenated rewarming of human livers before transplantation. Transplant Direct 6(4): e542	Journal article	Non-RCT
metra (OrganOx Ltd)	Hu A, Akhtar MZ, Bekki Y, et al. (2023) Using normormothermic machine perfusion (NMP) to assess, resuscitate and rescue livers for transplantation: Initial success from a us single center. American Journal of Transplantation 23(6 Suppl 1): S1060	Abstract	Non-comparative study
metra (OrganOx Ltd)	Hunt F, Johnston CJC, Coutts L, et al. (2022) From haphazard to a sustainable normothermic regional perfusion service: A blueprint for the introduction of novel perfusion technologies. Transplant International 35: 10493	Journal article	Non-comparative study
metra (OrganOx Ltd)	Idrees MT, Land G, Kathuria N, et al. (2025) Enhancing organ availability: Increased DCD liver utilization following implementation of a normothermic machine perfusion program. ANZ Journal of Surgery 19: 19	Abstract	Unclear pathway
metra (OrganOx Ltd); ISRCTN14355416	Jassem W, Xystrakis E, Ghnewa YG, et al. (2019) Normothermic machine perfusion (NMP) inhibits proinflammatory responses in the liver and promotes regeneration. Hepatology 70(2): 682-695	Abstract	Not back-to-base pathway
	OrganOx Ltd (UK). Clinical investigation to assess the safety and performance of the organox *metra*, for normothermic perfusion of	Clinical trial record	

Technology	Study	Publication type	Reasons for exclusion
	livers, prior to transplantation and to compare with retrospective data from matched controls. Identifier: ISRCTN14355416. In: ISRCTN Registry [internet]. London: BioMed Central Limited: 2012. Available from http://isrctn.com/ISRCTN14355416		
	Ravikumar R, Jassem W, Mergental H, et al. (2016) Liver transplantation after ex vivo normothermic machine preservation: A Phase 1 (first-in-man) clinical trial. American Journal of Transplantation 16(6): 1779-87	Journal article	
metra (OrganOx Ltd)	Iype S, Ceresa C, Kostakis I, et al. (2024) Improving utilisation of marginal liver grafts with normothermic perfusion. Liver Transplantation 30: 177-177	Abstract	Non-comparative study
metra (OrganOx Ltd)	Iype S, Kostakis I, Ceresa C, et al. (2024) Early allograft outcomes in liver transplants after normothermic machine perfusion. Liver Transplantation 30: 177-177	Abstract	Non-comparative study
metra (OrganOx Ltd)	Javanbakht M, Mashayekhi A, Trevor M, et al. (2020) Cost-utility analysis of normothermic liver perfusion with the organox *metra* compared to static cold storage in the United Kingdom. Journal of Medical Economics 23(11): 1284-1292	Journal article	Non-comparative study
metra (OrganOx Ltd)	Kneifel F, Wagner T, Flammang I, et al. (2022) Hyperspectral imaging for viability assessment of human liver allografts during normothermic machine perfusion. Transplantation Direct 8(12): e1420	Journal article	Non-comparative study
Liver Assist (XVIVO B.V.)	Koch DT, Tamai M, Schirren M, et al. (2025) Mono-HOPE versus dual-HOPE in liver transplantation: A propensity score-matched evaluation of early graft outcome. Transplant International 38: 13891	Journal article	Non-RCT

Technology	Study	Publication type	Reasons for exclusion
metra (OrganOx Ltd)	Krendl FJ, Cardini B, Laimer G, et al. (2024) Normothermic liver machine perfusion and successful transplantation of split liver grafts: From proof of concept to clinical implementation. Transplantation 108(6): 1410-1416	Journal article	Non-comparative study
Liver Assist (XVIVO B.V.)	Lascaris B, Bodewes SB, Thorne AM, et al. (2025) Perfusion pressures and weight loss during normothermic machine perfusion of human donor livers. Artificial Organs 49(5): 820-830	Journal article	Non-RCT
metra (OrganOx Ltd)	Li S, Squires RA, Cook CC, et al. (2025) Large liver could be at risk for liver graft failure during normothermic machine perfusion. American Journal of Transplantation 25(8 Suppl 1): S710	Abstract	Non-comparative study
metra (OrganOx Ltd)	Liu Q, Ali K, Cazzaniga B, et al. (2023) A pilot comparison of two devices for liver normothermic machine perfusion in clinical transplantation. Transplantation 107(9 Suppl 1): 187 EP - 188	Abstract	Unclear pathway
metra (OrganOx Ltd)	Liu Q, Ali K, Cazzaniga B, et al. (2024) Programmatic implementation of normothermic machine perfusion in liver transplantation: Short-term outcome analysis in the first 150 cases. American Journal of Transplantation 24(1): S44-S44	Abstract	Non-comparative study
metra (OrganOx Ltd)	Liu Q, Ali K, Cazzaniga B, et al. (2024) Does hypo- or hyper-perfusion affect metabolism during liver normothermic machine perfusion and post-transplant outcomes? Liver Transplantation 30: 185-185	Abstract	Non-comparative study
Liver Assist (XVIVO B.V.)	Lonati C, Schlegel A, Battistin M, et al. (2021) Effluent molecular analysis guides liver graft allocation to clinical hypothermic oxygenated machine perfusion. Biomedicines 9(10): 11	Journal article	Non-RCT

Technology	Study	Publication type	Reasons for exclusion
metra (OrganOx Ltd)	Loughnan A, Jabri Y, Dancy L, et al. (2023) Post reperfusion syndrome in liver transplant after normothermic perfusion. HPB 25(Suppl 2): S566 EP - S567	Abstract	Unclear pathway
metra (OrganOx Ltd)	Loughnan A, Schwartz F, Dancy L, et al. (2022) Reperfusion syndrome in liver transplant after normothermic perfusion. Transplantation 106(8): 82 EP - 83	Abstract	Unclear pathway
metra (OrganOx Ltd)	Maeda A, Starkey G, Spano S, et al. (2025) Perfusate hemoglobin during normothermic liver machine perfusion as biomarker of early allograft dysfunction: A pilot study. Artificial Organs 49(1): 108-118	Journal article	Comparison not relevant to the decision problem (compared low and high hemoglobin livers)
Liver Assist (XVIVO B.V.)	Maroni L, Musa N, Ravaioli M, et al. (2021) Normothermic with or without hypothermic oxygenated perfusion for DCD before liver transplantation: European multicentric experience. Clinical Transplantation 35(11): e14448	Journal article	Non-RCT
metra (OrganOx Ltd)	Martin JL, Rhodes F, Upponi S, et al. (2024) Localized liver injury during normothermic ex situ liver perfusion has no impact on short-term liver transplant outcomes. Transplantation 108(6): 1403-1409	Journal article	Non-comparative study
PerLife (Aferetica Srl)	Martinelli C, Melandro F, Torri F, et al. (2022) Hypothermic oxygenated machine perfusion for liver transplantation: An initial experience with a new device. Blood Purification 51(Suppl 3): 4	Abstract	Comparison not relevant to the decision problem (compared different perfusion fluids)

Technology	Study	Publication type	Reasons for exclusion
Liver Assist (XVIVO B.V.); *metra* (OrganOx Ltd)	Martini S, Saracco M, Cocchis D, et al. (2023) Favorable experience of transplant strategy including liver grafts from covid-19 donors: One-year follow-up results. Transplant Infectious Disease 25(5): e14126	Journal article	Non-comparative study
metra (OrganOx Ltd)	Mathis S, Weissenbacher A, Putzer G, et al. (2024) Interleukin-6 levels during normothermic machine perfusion impact postreperfusion hemodynamics of liver graft recipients: A prospective single-center observational study. Transplantation 108(5): 1166-1171	Journal article	Non-comparative study
Liver Assist (XVIVO B.V.)	Matton APM, de Vries Y, Burlage LC, et al. (2019) Biliary bicarbonate, ph, and glucose are suitable biomarkers of biliary viability during ex situ normothermic machine perfusion of human donor livers. Transplantation 103(7): 1405-1413	Journal article	Non-RCT
Liver Assist (XVIVO B.V.); *metra* (OrganOx Ltd)	Mergental H, Perera MTPR, Laing RW, et al. (2016) Transplantation of declined liver allografts following normothermic ex-situ evaluation. American Journal of Transplantation 16(11): 3235-3245	Journal article	Non-comparative study
metra (OrganOx Ltd)	Meszaros AT, Hofmann J, Buch ML, et al. (2022) Mitochondrial respiration during normothermic liver machine perfusion predicts clinical outcome. EBioMedicine 85: 104311	Journal article	Non-comparative study
metra (OrganOx Ltd); Mohkam et al 2022	Mohkam K, Nasralla D, Mergental H, et al. (2022) In situ normothermic regional perfusion versus ex situ normothermic machine perfusion in liver transplantation from donation after circulatory death. Liver Transplantation 28(11): 1716-1725	Journal article	Not back-to-base pathway
	Mohkam K, Nasralla D, Mergental H, et al. 2021. (Normothermic regional perfusion or normothermic machine perfusion in liver transplantation from donation after circulatory death) Transplant international [Online]. Available:	Abstract	

Technology	Study	Publication type	Reasons for exclusion
	https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02324443/full		
Liver Assist (XVIVO B.V.)	Morawski M, Zhylko A, Kubiszewski H, et al. (2025) Normothermic machine perfusion in orphan liver graft viability assessment. Journal of Clinical Medicine 14(3): 24	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Muller X, Mohkam K, Mueller M, et al. (2020) Hypothermic oxygenated perfusion versus normothermic regional perfusion in liver transplantation from controlled donation after circulatory death: First international comparative study. Annals of Surgery 272(5): 751-758	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Muller X, Schlegel A, Kron P, et al. (2019) Novel real-time prediction of liver graft function during hypothermic oxygenated machine perfusion before liver transplantation. Annals of Surgery 270(5): 783-790	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Muller X, Schlegel A, Wurdinger M, et al. (2019) Can hypothermic oxygenated perfusion (HOPE) rescue futile DCD liver grafts? HPB 21(9): 1156-1165	Journal article	Non-RCT
metra (OrganOx Ltd)	Muralidaran V, Flynn B, McDeed A, et al. (2025) Expanding viability criteria for extended criteria grafts in liver transplantation using normothermic machine perfusion: To transplant or to discard? American Journal of Transplantation 25(8 Suppl 1): S744	Abstract	Non-comparative study
metra (OrganOx Ltd)	Nasralla D, Ploeg R and Friend P. 2016. (A multicentre randomised controlled trial to compare the efficacy of normothermic machine perfusion with static cold storage in human liver transplantation: Early outcomes) Transplantation [Online]. Available: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01252582/full	Abstract	Non-comparative study

Technology	Study	Publication type	Reasons for exclusion
Liver Assist (XVIVO B.V.)	Nastase AG, Vasilescu AM, Trofin AM, et al. (2025) Hypothermic machine perfusion is associated with improved short-term outcomes in liver transplantation: A retrospective cohort study. Life 15(7): 16	Journal article	Non-RCT
metra (OrganOx Ltd); NCT02478151	Chapman WC, Barbas AS, D'Alessandro AM, et al. (2023) Normothermic machine perfusion of donor livers for transplantation in the United States: A randomized controlled trial. Annals of Surgery 278(5): e912-e921	Abstract	Not back-to-base pathway
	University Health Network T. Using ex-vivo normothermic machine perfusion with the organox *metra*™ device to store human livers for transplantation. Identifier: NCT02478151. In: ClinicalTrials.gov [internet]. Bethesda (MD): National Library of Medicine (US): 2015. Available from https://clinicaltrials.gov/study/NCT02478151	Clinical trial record	
metra (OrganOx Ltd); NCT03089840	Bral M, Dajani K, Leon Izquierdo D, et al. (2019) A back-to-base experience of human normothermic ex situ liver perfusion: Does the chill kill? Liver Transplantation 25(6): 848-858	Journal article	Comparison not aligned with decision problem (compared back-to-base procedure to immediate NMP)
	Hefler J, Izuierdo DL, Meeberg G, et al. (2022) Normothermic machine perfusion in liver transplantation - seven year experience at a single North American centre. American Journal of Transplantation 22(Suppl 3): 392	Abstract	
	Hefler J, Leon-Izquierdo D, Marfil-Garza BA, et al. (2023) Long-term outcomes after normothermic machine perfusion in liver transplantation-experience at a single North American center. American Journal of Transplantation 23(7): 976-986	Journal article	
	University of Alberta. Normothermic liver preservation trial. Identifier: NCT03089840. In: ClinicalTrials.gov [internet]. Bethesda (MD):	Clinical trial record	

Technology	Study	Publication type	Reasons for exclusion
	National Library of Medicine (US): 2017. Available from https://clinicaltrials.gov/study/NCT03089840		
metra (OrganOx Ltd); NCT03176433	Ceresa CDL, Nasralla D, Watson CJE, et al. (2019) Transient cold storage prior to normothermic liver perfusion may facilitate adoption of a novel technology. Liver Transplantation 25(10): 1503-1513	Journal article	Non-comparative study
	University of Oxford. Post static cold storage normothermic machine liver perfusion. Identifier: NCT03176433. In: ClinicalTrials.gov [internet]. Bethesda (MD): National Library of Medicine (US): 2017. Available from https://clinicaltrials.gov/study/NCT03176433	Clinical trial record	
Liver Assist (XVIVO B.V.); NCT03376074	Rayar M, Beaurepaire J-M, Bajeux E, et al. (2021) Hypothermic oxygenated perfusion improves extended criteria donor liver graft function and reduces duration of hospitalization without extra cost: The PERPHO study. Liver Transplantation 27(3): 349-362	Journal article	Non-RCT
	Rennes University Hospital. Interest of oxygenated hypothermic perfusion (PHO) in preservation of hepatic grafts from expanded criteria donors (PERPHO). Identifier: NCT03376074. In: ClinicalTrials.gov [internet]. Bethesda (MD): National Library of Medicine (US): 2018. Available from https://clinicaltrials.gov/study/NCT03376074	Clinical trial record	
Liver Assist (XVIVO B.V.); NCT06418165	Medical University of Vienna. Vienna hypothermic oxygenated machine perfusion study (vihomps). Identifier: NCT06418165. In: ClinicalTrials.gov [internet]. Bethesda (MD): National Library of Medicine (US): 2018. Available from https://clinicaltrials.gov/study/NCT06418165	Clinical trial record	Non-RCT
	Pereyra D, Dingfelder J, Riha M, et al. (2024) Dual hypothermic oxygenated machine perfusion of the liver reduces post-transplant	Journal article	

Technology	Study	Publication type	Reasons for exclusion
	biliary complications: A retrospective cohort study. International Journal Of Surgery 110(12): 7909-7918		
	Pereyra D, Dingfelder J, Riha M, et al. (2025) Sodium and lactate levels during hypothermic oxygenated machine perfusion as predictive biomarkers for early allograft dysfunction in liver transplantation. Journal of Hepatology 82	Abstract	
Liver Assist (XVIVO B.V.), VitaSmart (Bridge to Life Ltd); NL8740	Bruggenwirth IM, Lantinga VA, Lascaris B, et al. (2023) Prolonged hypothermic machine perfusion to enable daytime liver transplantation - a randomized clinical trial. Transplantation 107(9 Suppl 1): 20	Abstract	Non-RCT
	Bruggenwirth IMA, Lantinga VA, Rayar M, et al. (2022) Prolonged dual hypothermic oxygenated machine preservation (DHOPE-PRO) in liver transplantation: Study protocol for a stage 2, prospective, dual-arm, safety and feasibility clinical trial. BRITISH JOURNAL MEDICINE Open Gastroenterology 9(1)	Journal article	
	Bruggenwirth IMA, Mueller M, Lantinga VA, et al. (2022) Prolonged preservation by hypothermic machine perfusion facilitates logistics in liver transplantation: A European observational cohort study. American Journal of Transplantation 22(7): 1842-1851	Journal article	
Liver Assist (XVIVO B.V.)	Bruggenwirth IMA, Lantinga VA, Lascaris B, et al. (2024) Prolonged hypothermic machine perfusion enables daytime liver transplantation - an ideal stage 2 prospective clinical trial. EClinicalMedicine 68: 102411	Journal article	Non-RCT

Technology	Study	Publication type	Reasons for exclusion
VitaSmart (Bridge to Life Ltd)	Noren A, Molne J, Bennet W, et al. (2023) End-ischemic hypothermic oxygenated machine perfusion does not improve renal outcome following liver transplantation from aged donors: A single-center retrospective report. Artificial Organs 47(12): 1854-1864	Journal article	Non-RCT
metra (OrganOx Ltd)	Obana A, Akabane M, Chi H, et al. (2025) Dynamic lactate clearance patterns during normothermic machine perfusion predict posttransplant biliary complications in donation after circulatory death liver transplantation. Transplantation Direct 11(8): e1823	Journal article	Comparison not relevant to decision problem (compared DCD and DBD livers)
Liver Assist (XVIVO B.V.)	Olivieri T, Magistri P, Guidetti C, et al. (2019) University of modena experience with liver grafts from donation after circulatory death: What really matters in organ selection? Transplantation Proceedings 51(9): 2967-2970	Journal article	Non-RCT
metra (OrganOx Ltd)	OrganOx Ltd. WP01 - normothermic liver preservation. Identifier: NCT02775162. In: ClinicalTrials.gov [internet]. 2016. Available from https://clinicaltrials.gov/study/NCT02775162	Clinical trial record	Not back-to-base pathway
metra (OrganOx Ltd)	OrganOx Ltd. Continued access protocol study for the use of the organox *metra* normothermic machine perfusion device in human liver transplantation A1 - anonymous. Identifier: NCT04862156. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2021. Available from https://clinicaltrials.gov/study/NCT04862156	Clinical trial record	Non-comparative study
Liver Assist (XVIVO B.V.)	Patrono D, Catalano G, Rizza G, et al. (2020) Perfusate analysis during dual hypothermic oxygenated machine perfusion of liver grafts: Correlations with donor factors and early outcomes. Transplantation 104(9): 1929-1942	Journal article	Non-RCT

Technology	Study	Publication type	Reasons for exclusion
Liver Assist (XVIVO B.V.)	Patrono D, Cussa D, Sciannameo V, et al. (2022) Outcome of liver transplantation with grafts from brain-dead donors treated with dual hypothermic oxygenated machine perfusion, with particular reference to elderly donors. American Journal of Transplantation 22(5): 1382-1395	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Patrono D, Lavezzo B, Molinaro L, et al. (2018) Hypothermic oxygenated machine perfusion for liver transplantation: An initial experience. Experimental AND Clinical Transplantation: Official Journal of the Middle East Society for Organ Transplantation 16(2): 172-176	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Patrono D, Roggio D, Mazzeo AT, et al. (2022) Clinical assessment of liver metabolism during hypothermic oxygenated machine perfusion using microdialysis. Artificial Organs 46(2): 281-295	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Patrono D, Surra A, Catalano G, et al. (2019) Hypothermic oxygenated machine perfusion of liver grafts from brain-dead donors. Scientific Reports 9(1): 9337	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Patrono D, Zanierato M, Vergano M, et al. (2022) Normothermic regional perfusion and hypothermic oxygenated machine perfusion for livers donated after controlled circulatory death with prolonged warm ischemia time: A matched comparison with livers from brain-dead donors. Transplant International 35: 10390	Journal article	Non-RCT
VitaSmart (Bridge to Life Ltd)	Pavicevic S, Uluk D, Reichelt S, et al. (2022) Hypothermic oxygenated machine perfusion for extended criteria donor allografts: Preliminary experience with extended organ preservation times in the setting of organ reallocation. Artificial Organs 46(2): 306-311	Journal article	Non-RCT

Technology	Study	Publication type	Reasons for exclusion
metra (OrganOx Ltd)	Pereira LB, Loughnan A, Jabri Y, et al. (2023) Post reperfusion syndrome in liver transplant after normothermic perfusion: Experience of a reference center. Journal of Hepatology 78(Suppl 1): 483 EP - 484	Abstract	Unclear pathway
Liver Assist (XVIVO B.V.)	Pezzati D, Torri F, Franzini M, et al. (2025) Association of perfusate cytokine concentrations during liver graft ex situ normothermic perfusion to donor type and postoperative outcomes. Liver Transplantation 31(7): 877-889	Journal article	Non-RCT
metra (OrganOx Ltd)	Punjala SR, Logan AJ, Iyer M, et al. (2025) Posttransplant health-economic impact of normothermic machine perfusion (back-to-base model): Advancing donation after circulatory death liver transplants with improved outcomes and reduced wait times. Transplant Direct 11(10): e1861	Journal article	Not in the EU or the UK
Liver Assist (XVIVO B.V.)	Rauter L, Kollmann D, Schiefer J, et al. (2025) Endothelial glycocalyx damage marker syndecan-1 during hypothermic oxygenated machine perfusion of donor grafts facilitates prediction of early allograft dysfunction after liver transplantation. Hepatobiliary Surgery and Nutrition 14(2): 233-245	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Rauter L, Schiefer J, Raeven P, et al. (2022) Glycocalyx damage marker syndecan-1 correlates with early allograft dysfunction during hypothermic liver machine perfusion. Transplantation 106(9 Suppl): S221	Abstract	Non-RCT
metra (OrganOx Ltd)	Reiling J, Butler N, Simpson A, et al. (2020) Assessment and transplantation of orphan donor livers: A back-to-base approach to normothermic machine perfusion. Liver Transplantation 26(12): 1618-1628	Journal article	Non-comparative study

Technology	Study	Publication type	Reasons for exclusion
Liver Assist (XVIVO B.V.)	Rigo F, De Stefano N, Patrono D, et al. (2023) Impact of hypothermic oxygenated machine perfusion on hepatocellular carcinoma recurrence after liver transplantation. Journal of Personalized Medicine 13(5): 22	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Rossignol G, Muller X, Hervieu V, et al. (2022) Liver transplantation of partial grafts after ex situ splitting during hypothermic oxygenated perfusion-the HOPE-Split pilot study. Liver Transplantation 28(10): 1576-1587	Journal article	Non-RCT
metra (OrganOx Ltd), Sambommatsu et al 2025	Sambommatsu Y, Imai D, Savsani K, et al. (2025) Establishing a normothermic machine perfusion program for liver transplantation: Lessons learned and early outcomes in the United States. Clinical Transplantation 39(5): e70170	Journal article	Non-comparative study
	Sambommatsu YUZURU, Imai D, Khan A, et al. (2025) Implementing normothermic machine perfusion of the liver: Lessons learned and initial outcomes from 100 cases. American Journal of Transplantation 25(1 Suppl 1): S69	Abstract	
Liver Assist (XVIVO B.V.)	Schlegel A, Muller X, Kalisvaart M, et al. (2019) Outcomes of DCD liver transplantation using organs treated by hypothermic oxygenated perfusion before implantation. Journal of Hepatology 70(1): 50-57	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Schurink IJ, Luijmes SH, Willemse J, et al. (2025) Assessment of ex situ liver function by indocyanine green clearance during clinical normothermic machine perfusion of extended criteria grafts. Transplantation 109(9): e484-e493	Journal article	Non-RCT
metra (OrganOx Ltd)	Selzner M, Goldaracena N, Echeverri J, et al. (2016) Normothermic ex vivo liver perfusion using steen solution as perfusate for human liver	Journal article	Not back-to-base pathway

Technology	Study	Publication type	Reasons for exclusion
	transplantation: First North American results. Liver Transplantation 22(11): 1501-1508		
Liver Assist (XVIVO B.V.) ; *metra* (OrganOx Ltd)	Sorbini M, Carradori T, Patrono D, et al. (2025) Circulating cell-free DNA in liver transplantation: A pre- and post-transplant biomarker of graft dysfunction. Artificial Organs 49(4): 649-662	Journal article	Non-comparative study
metra (OrganOx Ltd)	Subramanian V, Hogen R, Singhal A, et al. (2025) Controlled hypothermic preservation of donor livers with back-to-base normothermic machine perfusion facilitates expansion of the donor pool. American Journal of Transplantation 25(8 Suppl 1): S967	Abstract	Comparison not relevant to the decision problem
metra (OrganOx Ltd)	Subramanian V, Messeha P, Walter O, et al. (2025) Using lactate clearance at 6 hours and glucose metabolism as a marker for usability of liver following normothermic machine perfusion. American Journal of Transplantation 25(1 Suppl 1): S132 EP - S133	Abstract	Non-comparative study
metra (OrganOx Ltd)	Subramanian V, Messeha P, Walter O, et al. (2025) Give it some time - the six hour threshold to determine usability of livers following normothermic machine perfusion. American Journal of Transplantation 25(8 Suppl 1): S797 EP - S798	Abstract	Non-comparative study
metra (OrganOx Ltd)	Subramanian V, Nguyen N, Berry J, et al. (2025) Reducing costs and post liver transplant complications associated with donation after circulatory death grafts using normothermic machine perfusion. American Journal of Transplantation 25(8 Suppl 1): S745	Abstract	Non-comparative study
metra (OrganOx Ltd)	Subramanian V, Witt M, Hogen R, et al. (2025) Flip the liver: Preventing perfusion related liver graft injury in normothermic machine preservation. American Journal of Transplantation 25(8 Suppl 1): S210	Abstract	Non-comparative study

Technology	Study	Publication type	Reasons for exclusion
metra (OrganOx Ltd)	Sun K, Jiao C, Zhang M, et al. (2024) Mitochondrial injury assessed in bile during normothermic machine perfusion predicts biliary complications after liver transplantation. Biochimica et Biophysica Acta - Bioenergetics 1865(Suppl): 149463	Abstract	Non-comparative study
VitaSmart (Bridge to Life Ltd)	Tamayo BV, Valero AP, Ordorica PR, et al. (2025) Preservation of liver graft using the hypothermic oxygenated perfusion (HOPE) system: A single-center experience. Transplantation Proceedings 57(1): 55-58	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Tang Y, Wang T, Ju W, et al. (2021) Ischemic-free liver transplantation reduces the recurrence of hepatocellular carcinoma after liver transplantation. Front Oncol 11: 773535	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Thorne AM, Wolters JC, Lascaris B, et al. (2023) Bile proteome reveals biliary regeneration during normothermic preservation of human donor livers. Nature communications 14(1): 7880	Journal article	Non-RCT
metra (OrganOx Ltd)	Todd R, Gamboa S, Sacks B, et al. (2024) Normothermic machine perfusion versus static cold storage in simultaneous liver kidney transplantation. American Journal of Transplantation 24(1): S100-S101	Abstract	Non-comparative study
metra (OrganOx Ltd)	Todd R, Rosowicz A, Holzner M, et al. (2024) Normothermic machine perfusion of marginal grafts in high meld recipients: A NY center experience. HPB 26(Suppl 2): S729 EP - S730	Abstract	Non-comparative study
metra (OrganOx Ltd)	Todd R, Rosowicz A, Kressel A, et al. (2023) Novel indications for normothermic machine perfusion: A case series. Hepatology 78(Suppl 1): S282	Abstract	Non-comparative study

Technology	Study	Publication type	Reasons for exclusion
metra (OrganOx Ltd)	Todd R, Rosowicz A, van Leeuwen L, et al. (2024) Initial year of normothermic machine perfusion of a new york center: Risk assessment strategies and outcomes in liver transplantation. Liver Transplantation 30: 189-190	Abstract	Non-comparative study
metra (OrganOx Ltd)	Todd R, van Leeuwen L, Rosowicz A, et al. (2025) Treating donation after circulatory death liver grafts with alteplase during ex situ normothermic machine perfusion. Clinical Transplantation 39(8): e70282	Journal article	Non-comparative study
Liver Assist (XVIVO B.V.)	van Rijn R, Karimian N, Matton APM, et al. (2017) Dual hypothermic oxygenated machine perfusion in liver transplants donated after circulatory death. British Journal of Surgery 104(7): 907-917	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	van Rijn R, van Leeuwen OB, Matton APM, et al. (2018) Hypothermic oxygenated machine perfusion reduces bile duct reperfusion injury after transplantation of donation after circulatory death livers. Liver Transplantation 24(5): 655-664	Journal article	Non-RCT
VitaSmart (Bridge to Life Ltd)	Vasuri F, Riefolo M, Ravaioli M, et al. (2023) Predictive value of portal fibrosis and inflammation in transplanted liver grafts treated with hypothermic oxygenated perfusion. Pathology, Research AND Practice 243: 154361	Journal article	Non-RCT
metra (OrganOx Ltd); VITTAL, NCT02740608	Laing RW, Mergental H, Yap C, et al. (2017) Viability testing and transplantation of marginal livers (VITTAL) using normothermic machine perfusion: Study protocol for an open-label, non-randomised, prospective, single-arm trial. BRITISH JOURNAL MEDICINE Open 7(11): e017733	Protocol	Non-comparative study
	Mergental H, Laing RW, Kirkham AJ, et al. (2024) Discarded livers tested by normothermic machine perfusion in the VITTAL trial:	Journal article	

Technology	Study	Publication type	Reasons for exclusion
	Secondary end points and 5-year outcomes. Liver Transplantation 30(1): 30-45		
	Mergental H, Laing RW, Hodson J, et al. (2022) Introduction of the concept of diagnostic sensitivity and specificity of normothermic perfusion protocols to assess high-risk donor livers. Liver Transplantation 28(5): 794-806	Journal article	
	Mergental H, Laing RW, Kirkham AJ, et al. (2020) Transplantation of discarded livers following viability testing with normothermic machine perfusion. Nature communications 11(1): 2939	Journal article	
	University of Birmingham. Viability testing and transplantation of marginal livers (VITTAL). Identifier: NCT02740608. In: ClinicalTrials.gov [internet]. Bethesda (MD): National Library of Medicine (US): 2016. Available from https://clinicaltrials.gov/study/NCT02740608	Clinical trial record	
metra (OrganOx Ltd)	Vogel T, Szardenings C, Becker F, et al. (2024) Viability assessment and transplantation of extended criteria donor liver grafts using normothermic machine perfusion. Surgery 176(3): 934-941	Journal article	Comparison not relevant to decision problem (compares scores of DRI cohorts)
metra (OrganOx Ltd)	Wagner T, Katou S, Wahl P, et al. (2022) Hyperspectral imaging for quantitative assessment of hepatic steatosis in human liver allografts. Clinical Transplantation 36(8): e14736	Journal article	Non-comparative study
metra (OrganOx Ltd)	Watson CJE, Gaurav R, Swift L, et al. (2024) Bile chemistry during ex situ normothermic liver perfusion does not always predict cholangiopathy. Transplantation 108(6): 1383-1393	Journal article	Non-comparative study

Technology	Study	Publication type	Reasons for exclusion
Liver Assist (XVIVO B.V.)	Watson CJE, Kosmoliaptsis V, Pley C, et al. (2018) Observations on the ex situ perfusion of livers for transplantation. American Journal of Transplantation 18(8): 2005-2020	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Watson CJE, Kosmoliaptsis V, Randle LV, et al. (2017) Normothermic perfusion in the assessment and preservation of declined livers before transplantation: Hyperoxia and vasoplegia-important lessons from the first 12 cases. Transplantation 101(5): 1084-1098	Journal article	Non-RCT
metra (OrganOx Ltd)	Webb AN, Izquierdo DL, Eurich DT, et al. (2021) The actual operative costs of liver transplantation and normothermic machine perfusion in a canadian setting. PharmacoEconomics Open 5(2): 311-318	Journal article	Non-comparative study
metra (OrganOx Ltd)	Wehrle C, Gross A, Fares S, et al. (2024) Changing landscape of open offers in liver transplantation with machine perfusion: Exposure, equity and economics. Liver Transplantation 30: 81-82	Abstract	Non-comparative study
metra (OrganOx Ltd)	Wehrle C, Zhang M, Miyazaki Y, et al. (2024) Ninety-day complications and costs of liver transplantation with normothermic machine perfusion: A multi-center, real-world riskmatched analysis. Liver Transplantation 30: 87-87	Abstract	Unclear pathway
metra (OrganOx Ltd)	Wehrle CJ, Gross A, Fares S, et al. (2024) Changing landscape of open offers in liver transplantation in the machine perfusion era: Exposure, equity, and economics. Clinical Transplantation 38(10): e70012	Journal article	Non-comparative study
metra (OrganOx Ltd)	Wehrle CJ, Hong H, Gross A, et al. (2025) The impact of normothermic machine perfusion and acuity circles on waitlist time, mortality, and cost in liver transplantation: A multicenter experience. Liver Transplantation 31(4): 438-449	Journal article	Not in the EU or the UK

Technology	Study	Publication type	Reasons for exclusion
metra (OrganOx Ltd)	Wehrle CJ, Kusakabe J, Gross A, et al. (2025) Programmatic normothermic machine perfusion and association with liver transplant waitlist outcomes for patients with lower model for end-stage liver disease score. Journal of the American College of Surgeons 241(3): 486-496	Journal article	Non-comparative study
metra (OrganOx Ltd)	Wehrle CJ, Satish S, Dewey E, et al. (2025) A new era of decision-making in liver transplantation: A prospective validation and cost-effectiveness analysis of FMN-guided liver viability assessment during normothermic machine perfusion. Annals of Surgery 282(3): 479-493	Journal article	Not in the EU or the UK
metra (OrganOx Ltd)	Wehrle CJ, Zhang M, Khalil M, et al. (2024) Impact of back-to-base normothermic machine perfusion on complications and costs: A multicenter, real-world risk-matched analysis. Annals of Surgery 280(2): 300-310	Journal article	Not in the EU or the UK
metra (OrganOx Ltd)	Weissenbacher A, Bogensperger C, Oberhuber R, et al. (2022) Perfusate enzymes and platelets indicate early allograft dysfunction after transplantation of normothermically preserved livers. Transplantation 106(4): 792-805	Journal article	Non-comparative study
Liver Assist (XVIVO B.V.)	Zhang Z, Ju W, Tang Y, et al. (2020) First preliminary experience with preservation of liver grafts from extended-criteria donors by normothermic machine perfusion in asia. Annals of Transplantation 25: e921529	Journal article	Non-RCT
Liver Assist (XVIVO B.V.)	Zhang Z, Tang Y, Zhao Q, et al. (2020) Association of perfusion characteristics and posttransplant liver function in ischemia-free liver transplantation. Liver Transplantation 26(11): 1441-1454	Journal article	Non-RCT

Table B.3: Ongoing studies with no device named (n = 41)

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Abbas SH, Ceresa CDL, Hodson L, Nasralla D, Watson CJE, Mergental H*, et al.* Defatting of donor transplant livers during normothermic perfusion - a randomised clinical trial: Study protocol for the DeFat study. Trials. 2024.25(1):386. doi: https://dx.doi.org/10.1186/s13063-024-08189-4
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Azienda Ospedaliero-Universitaria di Modena. Impact of graft reconditioning with hypothermic machine perfusion on HCC recurrence after liver transplantation A1 - anonymous. Identifier: NCT06236568. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2024. Available from https://clinicaltrials.gov/study/NCT06236568.
Centre hospitalier de l'Université de Montréal (CHUM). Intraoperative hemodynamic management and postoperative outcomes in liver transplantation: A multicenter prospective cohort study A1 - anonymous. Identifier: NCT04732689. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2021. Available from https://clinicaltrials.gov/study/NCT04732689.
Charite University B, Germany,. Hypothermic oxygenated (HOPE) versus normothermic machine perfusion (NMP) in human liver transplantation. Identifier: NCT04644744. In: ClinicalTrials.gov [internet]. 2020. Available from https://clinicaltrials.gov/study/NCT04644744.
Charite University B, Germany,. Pilot, open, prospective, randomized, multicenter trial on quality assessment of declined liver grafts by normothermic ex vivo machine perfusion for decreasing time to transplantation A1 - anonymous. Identifier: NCT06874296. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2025. Available from https://clinicaltrials.gov/study/NCT06874296.
Cristiano Quintini. A Phase I pilot study to assess safety and feasibility of normothermic machine preservation in human liver transplantation A1 - anonymous. Identifier: NCT02515708. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2015. Available from https://clinicaltrials.gov/study/NCT02515708.

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Erasmus Medical Center. Direct comparison of NRP with DHOPE and COR-NMP to maximize the use of ECD after DCD donation in the netherlands A1 - anonymous. Identifier: NCT05327478. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2022. Available from https://clinicaltrials.gov/study/NCT05327478.
Erasmus Medical Center. Safe transplantation of extended criteria donor livers: Two-center experience with resuscitation and viability assessment of 206 livers using sequential hypo- and normothermic machine perfusion A1 - anonymous. Identifier: NCT06804746. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2025. Available from https://clinicaltrials.gov/study/NCT06804746.
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Papa Giovanni XXIII Hospital. Hypothermic oxygenated perfusion with cytokine filtration in clinical liver transplantation: A randomised controlled trial A1 - anonymous. Identifier: NCT04203004. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2019. Available from https://clinicaltrials.gov/study/NCT04203004.
Papa Giovanni XXIII Hospital. Post-static cold storage hypothermic oxygenated perfusion in bergamo liver transplant program: A prospective observational study A1 - anonymous. Identifier: NCT03098043. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2017. Available from https://clinicaltrials.gov/study/NCT03098043.
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Roberta Angelico. Machine-perfusion for liver transplantation in high versus low/mid-volume centres: An international multicentre survey A1 - anonymous. Identifier: NCT05662969. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2022. Available from https://clinicaltrials.gov/study/NCT05662969.
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The First Affiliated Hospital of Sun Yat-sen University. Pilot study to assess safety and feasibility of normothermic machine perfusion in liver transplantation. Identifier: ChiCTR-OPN-17012090. In: Chinese Clinical Trial Register [internet]. Chengdu: Chinese University of Hong Kong: 2017. Available from http://www.chictr.org.cn/showproj.aspx?proj=20665.
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UniversitätsSpital Zürich. Hypothermic oxygenated perfusion (HOPE) of human liver grafts before transplantation - a multicenter, randomized controlled trial. Identifier: NL-OMON47605. In: Overview of Medical Research in the Netherlands [internet]. Netherlands: Central Committee on Research Involving Human Subjects: 2019. Available from https://onderzoekmetmensen.nl/en/trial/47605.

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9.3 Appendix C Critical appraisal

Table C.1: Quality appraisal of the prioritised studies included in the economic evidence review

	Endo 2025	Webb 2022	Zimmerman 2022	Axelrod 2025
1. Was the research question stated?	Yes	Yes	Yes	Yes
2. Was the economic importance of the research question stated?	Yes	Yes	Yes	Yes
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	Yes	Yes	Yes	Yes
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Unclear - No rationale is given for excluding other forms of the devices or other preservation methods such as NMP. It is noted in the discussion that NMP serves a different clinical goal but it is still a method of liver DCD preservation. This can be attributed to the clinical trial.	Yes	Yes	Yes

	Endo 2025	Webb 2022	Zimmerman 2022	Axelrod 2025
5. Were the alternatives being compared clearly described?	Yes	Yes	Yes	Unclear - It is not clearly detailed how HOPE is used.
6. Was the form of economic evaluation stated?	Yes	Yes	Yes	No - It does not explicitly state the form of evaluation.
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	Yes	Yes	Yes	No - It does not explicitly state the form of evaluation.
8. Was/were the source(s) of effectiveness estimates used stated?	Yes	Yes	Yes	Yes
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	Yes	N/A – Not based on a single study.	N/A – Not based on a single study.	Yes
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	N/A	N/A	N/A	N/A

	Endo 2025	Webb 2022	Zimmerman 2022	Axelrod 2025
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	Yes	Yes	Yes	Yes
12. Were the methods used to value health states and other benefits stated?	N/A	Yes	Yes	N/A
13. Were the details of the subjects from whom valuations were obtained given?	N/A	Unclear - The utility values were sourced from a cost utility analysis based in the UK, specific details of the population were not included.	Yes	N/A
14. Were productivity changes (if included) reported separately?	N/A - Hospital perspective, not included.	N/A - Not included, conducted from a public payer perspective.	N/A - Not included, conducted from NHS and PSSRU perspective.	N/A - Not included.
15. Was the relevance of productivity changes to the study question discussed?	N/A	N/A - Productivity changes were not incorporated.	N/A - Productivity changes were not incorporated.	N/A - Productivity changes were not incorporated.
16. Were quantities of resources reported separately from their unit cost?	Yes	Yes	Yes	No - Detail was not provided in this conference abstract.

	Endo 2025	Webb 2022	Zimmerman 2022	Axelrod 2025
17. Were the methods for the estimation of quantities and unit costs described?	Yes	Yes	Yes	Unclear - Individual quantities were not reported.
18. Were currency and price data recorded?	Yes	Yes	Yes	Yes
19. Were details of price adjustments for inflation or currency conversion given?	Yes	Yes	Yes	No – This was not stated.
20. Were details of any model used given?	Yes	Yes	Yes	Yes
21. Was there a justification for the choice of model used and the key parameters on which it was based?	Yes	Yes	Yes	Unclear – No justification was given.
22. Was the time horizon of cost and benefits stated?	Yes	Yes	Yes	Unclear - A 1-year cost reduction was stated but the time horizon as not explicitly noted.
23. Was the discount rate stated?	No - This was not stated.	Yes	Yes	No - This was not stated.
24. Was the choice of rate justified?	N/A	Yes	Yes	N/A

	Endo 2025	Webb 2022	Zimmerman 2022	Axelrod 2025
25. Was an explanation given if cost or benefits were not discounted?	No - This was not stated or justified. Due to the focus of the analysis being on economic viability and 1 year follow up period, this was not considered as it is was early approach.	N/A	N/A - Discount was applied to both.	No - No explanation was given.
26. Were the details of statistical test(s) and CIs given for stochastic data?	Yes	Yes	Yes	Yes
27. Was the approach to sensitivity analysis described?	Yes	Yes	Yes	Unclear - The type or details were not reported.
28. Was the choice of variables for sensitivity analysis justified?	Yes	Yes	Yes	No - The type or details were not reported.
29. Were the ranges over which the parameters were varied stated?	Yes	Yes	Yes	Yes - The type or details were not reported.
30. Were relevant alternatives compared? (That is, were appropriate comparisons made	Yes	Yes	Yes	Yes

	Endo 2025	Webb 2022	Zimmerman 2022	Axelrod 2025
when conducting the incremental analysis?)				
31. Was an incremental analysis reported?	Yes	Yes	Yes	Yes
32. Were major outcomes presented in a disaggregated as well as aggregated form?	Yes	Yes	Yes	Yes
33. Was the answer to the study question given?	Yes	Yes	Yes	Yes
34. Did conclusions follow from the data reported?	Yes	Yes	Yes	Yes
35. Were conclusions accompanied by the appropriate caveats?	Yes	Yes	Yes	No – No caveats were reported.
36. Were generalisability issues addressed?	Yes	Yes	Yes	No – They were not addressed.

9.4 Appendix D Outcome data

Table D.1: Long-term transplant outcomes

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: van Rijn et al 2021 (van Rijn et al. 2021c) **Design: RCT** **Location:** Belgium; UK; Netherlands **Status of study: (published, unpublished, abstract etc.)** **Associated records**: 5 year data from van Rijn et al 2025 (van Rijn et al. 2025)	**Intervention**: Liver Assist (n=78) **Comparator**: SCS (n=78) **Analysis population**: mITT (included all patients who received allocated intervention)	**1 year:** Liver Assist: NR SCS: NR **HR (patient death)**: 2.45 (95% CI 0.77 to 7.85) **5 years**: Liver Assist: 63% SCS: 70% **HR (patient death):** 1.30 (95% CI 0.75 to 2.26) p=0.35	**1 year:** Liver Assist: NR SCS: NR **HR (graft failure)**: 0.65 (95% CI 0.18 to 2.29) **5 years**: Liver Assist: 82% SCS: 79% **HR (graft failure)**: 0.91 (95% CI 0.45 to 1.87) p=0.806	**6 months:** Liver Assist**:** 3 (4%) SCS**:** 6 (8%) **Adjusted HR (re-transplantation):** 0.49 (95% CI 0.12 to 1.94) **5 years**: Liver Assist: 10 (13%) SCS: 12 (15%) **P value:** 0.753	**<u>Non-anastomotic biliary strictures</u>** **6 months:** Liver Assist: 5 (6%) SCS: 14 (18%) **P value:** 0.03 **Adjusted HR:** 0.32 (95% CI 0.11 to 0.89) p=0.03 **5 years:** Liver Assist: 11/78 (14%) SCS: 20/78 (26%) **Adjusted HR:** 0.4 (95% CI 0.23 to 0.99) p=0.048 **<u>Anastomotic biliary strictures</u>** **6 months:** Liver Assist: 23/78 (29%) SCS: 22/78 (28%) **RR:** 1.07 (95% CI 0.52 to 2.20) **5 years:** Liver Assist: 35/78 (45%)

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
					SCS: 37/78 (47%) **P value**: 0.748 **<u>Biliary anastomotic leakage</u>** **6 months** Liver Assist: 6/78 (8%) SCS: 8/78 (10%) **RR:** 0.69 (95% CI 0.22 to 2.13)
Primary publication: Czigany et al 2021 (Czigany et al. 2021) **Design:** RCT **Location:** Czech Republic; Germany **Status of study:** Published **Associated records**: Long term (median 48 months and 5 years) data from Czigany et al 2024 (Czigany et al. 2024)	**Intervention**: Liver Assist (n=23) **Comparator**: SCS (n=23) **Analysis population**: survival and biliary complication data is ITT; re-transplantation at median 48 months is complete case	**1 year:** Liver Assist: 91% SCS: 83% **P value:** 0.442 **3 year:** Liver Assist: 86.9% SCS: 64.9% **5 years:** Liver Assist: 86.9% SCS: 64.9% **P value:** 0.107	**1 year:** Liver Assist: 91% SCS: 78% **P value:** 0.253 **3 year:** Liver Assist: 86.9% SCS: 60.6% **5 years:** Liver Assist: 86.9% SCS: 51.9% **P value:** 0.029	**1 year:** Liver Assist: 1 (4%) SCS: 2 (9%) **P value:** >0.999 **Median 48 months** Liver Assist: 0/21 (0%) SCS: 2/20 (10%) **P value:** 0.232	**<u>Biliary complications (clinical, radiological):</u>** **1 year:** Liver Assist: 4 (17%) SCS: 6 (26%) **P value:** 0.722 **<u>Biliary stenosis</u>** **Median 48 months** Liver Assist: 7 (30%) SCS: 8 (35) **P value:** 0.751

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: Minor et al 2021 (Minor et al. 2022) **Design: RCT** **Location:** France **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=20) **Comparator**: SCS (n=20) **Analysis population**: ITT	NR	**3 months:** Liver Assist: 20 (100%) SCS: 19 (95%) **P value:** >0.999	**3 months:** Liver Assist: 0 (0%) SCS: 1 (5*%) **P value:** >0.999	NR
Primary publication: Lesurtel et al 2025 (Lesurtel et al. 2025) **Design:** RCT **Location:** France **Associated records**: None in these columns	**Intervention**: Liver Assist (n=131) **Comparator**: SCS (n=131) **Analysis population**: mITT	**1 year:** Liver Assist: 118 (90.1%) SCS: 119 (90.8%) **P value:** 0.873 **HR (patient death)**: 1.07 (95% CI 0.49 to 2.34)	**1 year:** Liver Assist: 115 (87.8%) SCS: 114 (87.0%) **P value:** 0.803 **HR (graft failure)**: 0.92 (95% CI 0.46 to 1.81)	**1 year:** Liver Assist: 3 (2.3%) SCS: 6 (4.6%) **P value:** 0.5	**Any biliary complications:** **90 days**: Liver Assist: 13 (9.9%) SCS: 22 (16.8%) **P value:** 0.1 **Biliary stenosis** **90 day**: Liver Assist: 10 (7.6%) SCS: 14 (10.7%) **P value:** 0.39 **Biliary fistula:** **90 days**: Liver Assist: 5 (3.8%) SCS: 10 (7.6%) **P value:** 0.18

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: Ghinolfi et al 2019 (Ghinolfi et al. 2019) **Design:** RCT **Location:** Italy **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=10) **Comparator**: SCS (n=10) **Analysis population**: ITT	**6 months** Liver Assist: 10 (100%) SCS:-9 (90%) **P value (patient death):** 1	**Graft loss at 6 months:** Liver Assist: 1 (10%) SCS: 0 P value**:** 1.000	**6 months:** Liver Assist: 1 (10%) SCS: 0 **P value:** NR	**6 months:** Liver Assist: 1 (10%) SCS: 0 **P value :** 1

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: Grat et al 2023 (Grat et al. 2023) **Design:** RCT **Location:** Poland **Status of study:** Published **Associated records**: All data from Morawski et al 2024 (Morawski et al. 2024)	**Intervention**: Liver Assist (n=26) **Comparator**: SCS (n=78) **Analysis population**: ITT	**Overall survival** **2 years:** Liver Assist: 92.3% SCS: 83.9% **P value:** 0.35 **High-risk donor (DRI >1.7) subgroup** Liver Assist (n=14): 100% SCS (n=26): 76.9% **P value:** 0.06 **Mean survival time (months)** **2 years** Liver Assist: Mean 22.2 (SD 1.2) SCS: Mean 21.2 (SD 0.8) P value: 0.47 **High-risk donor (DRI >1.7) subgroup** Liver Assist (n=14): Mean 24 (SD 0) SCS (n=26): Mean 19.2 (SD 1.7) **P value**: 0.006	**2 years:** Liver Assist: 92.3% SCS: 81.4% **P value:** 0.23 **High-risk donor (DRI >1.7) subgroup** Liver Assist: 100% SCS (n=14): 73.1% P value (n=26): 0.038 **Mean graft survival time (months)** **2 years** Liver Assist: Mean 22.2 (SD 1.2) SCS: Mean 20.5 (SD 0.9) P value: 0.26 **High-risk donor (DRI >1.7) subgroup** Liver Assist (n=14): Mean 24 (SD 0) SCS (n=26): Mean 18.2 (SD 1.9) P value (n=26): 0.002	NR	**Overall biliary complications** **90 days:** Liver Assist: 6 (23.7%) SCS: 30 (43.4%) **P value:** 0.11 **High-risk donor (DRI >1.7) subgroup** Liver Assist (n=14): 3 (21.4%) SCS (n=26): 8 (34.9%) P value: 0.34 **Anastomotic strictures** **90 days:** Liver Assist: 5 (19.9%) SCS: 23 (33.7%) **P value** = 0.2 **High-risk donor (DRI >1.7) subgroup** Liver Assist (n=14): 3 (21.4%) SCS (n=26): 6 (27.4%) P value: 0.61 **Non-anastomotic strictures**

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
					90 days: Liver Assist: 0% SCS: 7 (11%) **P value:** 0.1 **High-risk donor (DRI >1.7) subgroup** Liver Assist (n=14): 0 SCS (n=26): 1 (2.8%) P value: NR **<u>Biliary fistulas</u>** **90 days:** Liver Assist: 3 (11.7%) SCS: 9 (12.2%) **P value:** 0.93 **High-risk donor (DRI >1.7) subgroup** Liver Assist (n=14): 1 (7.1%) SCS (n=26): 3 (12.7%) P value: 0.58

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: Schlegel et al 2023 (Schlegel et al. 2023) **Design:** RCT **Location:** UK, Belgium, Netherlands, France, Austria, Switzerland **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=85) **Comparator**: SCS (n=85) **Analysis population**: mITT	**Patient death:** **1 year:** Liver Assist: 4 (4.7%) SCS: 4 (4.7%) **OR:** 1 (95% CI 0.229 to 4.359), p = 1	**Graft loss:** **1 year:** Liver Assist: 4 (4.7%) SCS: 7 (8.2%) **OR:** 0.55 (95% CI 0.14 to 1.896), p = 0.36	**1 year:** Liver Assist: 0 SCS: 3 (3.5%) **Difference between interventions:** NR	**Any biliary complications** **1 year:** Liver Assist: 15 (17.6%) SCS: 19 (22.4%) **OR:** 0.744 (95% CI 0.35 to 1.58), p = 0.44 **Anastomotic biliary complications** **1 year:** Liver Assist: 14 (16.5%) SCS: 18 (21.2%) **Difference between interventions:** NR **Non-anastomotic biliary complications** **1 year:** Liver Assist: 1 (1.2%) SCS: 3 (3.5%) **Difference between interventions**: NR

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: Vogt et al 2024 (Vogt et al. 2024) **Design:** Prospective cohort study **Location:** Germany **Status of study:** Published **Associated records**: NA	**Intervention**: *metra* (n=31) **Comparator**: SCS (n=6) **Analysis population**: All included participants	NR	NR	NR	NR
Primary publication: Krendl et al 2025 (Krendl et al. 2025) **Design:** Retrospective cohort study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention**: *metra* (n=174) **Comparator**: SCS (n=158) **Analysis population**: All included participants	NR	**Graft survival (%)** **1 year:** *metra*: 83.8% SCS: 81.3% Non-benchmark *metra*: 74.6% Non-benchmark SCS: 74.3% **Difference between interventions:** NR **36 months:** *metra*: 73.1% SCS: 73.9% **P value**: 0.933 Non-benchmark	NR	**Biliary complications:** **1 year:** *metra*: 73 (42%) SCS: 58 (36.7%) **P value:** 0.329 Non-benchmark *metra*: 49 (44.1%) Non-benchmark SCS: 30 (37%) **P value:** 0.323 **Bile duct leaks** **1 year** *metra*: 20 (11.5%) SCS: 19 (12%) **P value:** 0.881

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
			metra: 65.3% Non-benchmark SCS: 66.1% **Difference between interventions**: NR		Non-benchmark *metra*: 12 (10.8%) Non-benchmark SCS: 12 (14.8%) **P value:** 0.407 **<u>Anastomotic stricture</u>** **1 year:** *metra*: 41 (23.6%) SCS: 29 (18.4%) **P value:** 0.245 Non-benchmark *metra*: 29 (26.1%) Non-benchmark SCS: 14 (17.3%) **P value:** 0.147 **<u>Non-anastomotic stenosis</u>** **1 year** *metra*: 19 (10.9%) SCS: 14 (8.9%) **P value:** 0.531 Non-benchmark *metra*: 17 (15.3%) Non-Benchmark SCS: 3

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
					(3.7%) **P value:** 0.009
Primary publication: Fodor et al 2021 (Fodor et al. 2021) **Design:** Matched case study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=59) **Comparator:** SCS (n=59) **Analysis population:** All included participants	**30 days:** *metra*: 97% SCS: 98% **90 days:** *metra*: 89% SCS: 93% **1 year:** *metra*: 81% SCS: 82% **P value**: 0.347 **Subgroup predominant donor**	**30 days:** *metra*: 95% SCS: 95% **90 days:** *metra*: 89% SCS: 91% **1 year:** *metra*: 81% SCS: 79% **P value**: 0.784 **Subgroup predominant donor**	NR	**<u>Bile duct complications</u>** **≤ 30 days:** *metra*: 13 (22%) SCS: 11 (19%) **P value:** 0.647 **>30 days:** *metra*: 16 (27%) SCS: 21 (36%) **P value:** 0.321 **<u>Bile duct leak</u>** **Timepoint:** NR *metra*: 10 (17%) SCS: 11 (19%)

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
		characteristics for NMP (extended criteria livers) **30 days**: *metra* (n=42, 2 deaths): 95% (95% CI 89% to 100%) SCS (n=42, 1 death): 98% (95% CI 93% to 100%) **90 days**: *metra* (n=42, 3 deaths): 86% (95% CI 76% to 98%) SCS (n=42, 2 deaths): 93% (95% CI 85% to 100%) **1 year**: *metra* (n=42): 86% (95% CI 76% to 98%) SCS (n=42, 5 deaths): 80% (95% CI 68% to 93%) **P value:** 0.942	**characteristics for NMP (extended criteria livers)** **30 days**: *metra* (n=42, 2 graft failures): 95% (95% CI 89% to 100%) SCS (n=42, 3 graft failures): 93% (95% CI 85% to 100%) **90 days**: *metra* (n=42, 3 graft failures): 86% (95% CI 76% to 98%) SCS (n=42, 1 graft failures): 90% (95% CI 82% to 100%) **1 year**: *metra* (n=42): 86% (95% CI 76% to 98%) SCS (n=42, 6 graft failures): 75% (95% CI 62% to 90%) **P value**: 0.586		**P value:** 0.810 **<u>Anastomotic strictures</u>** **Timepoint:** NR *metra*: 21 (36%) SCS: 23 (39%) P value: 0.703 **<u>Non-anastomotic strictures</u>** **Timepoint:** NR *metra*: 5 (8%) SCS: 10 (17%) **P value:** 0.167

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: Mathis et al, 2024 (Mathis et al. 2024) **Design:** Matched case study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=18) **Comparator:** SCS (n=36) **Analysis population:** All included participants	NR	NR	NR	NR

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: Hann et al, 2022 (Hann et al. 2022) **Design:** Matched case study **Location:** UK **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=26) **Comparator:** SCS group 1, retrospective (n=31), SCS group 2, prospective (n=25) **Analysis population:** All included participants	**Patient survival** **90 day:** *metra*: 25 (96%) SCS1: 28 (90%) SCS2: 24 (96%) **P value:** 0.572 **6 month:** *metra*: 23 (88%) SCS1: 27 (87%) SCS2: 22 (92%) **P value:** 0.837	**Graft survival** **90 day:** *metra*: 24 (92%) SCS1: 27 (87%) SCS2: 24 (96%) **P value:** 0.318 **6 month:** *metra*: 22 (84%) SCS1: 27 (87%) SCS2: 22 (88%) **P value:** 0.934	NR	**Anastomotic stricture** **Timepoint:** NR *metra*: 1 (3.8%) SCS1: 3 (9.6%) SCS2: 2 (8%) **P value:** 0.693 **Non-anastomotic stricture** **Timepoint:** NR *metra*: 1 (3.8%) SCS1: 4 (12%) SCS2: 2 (8%) **P value:** 0.473 **Bile leak** **Timepoint:** NR *metra*: 0 SCS1: 2 (6.4%) SCS2: 0 **P value**: 0.185

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: Puttappa et al, 2025 (Puttappa et al. 2025) **Design:** Retrospective cohort **Location:** UK **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=78) **Comparator:** SCS (n=59), NRP then SCS (n=101) **Analysis population:** All included participants	NR	**1 year**: *metra*: 94% SCS: 90% NRP then SCS: 94% **5 years**: *metra*: 84% SCS: 69% NRP then SCS: 85% **HR (SCS vs NRP then SCS)**: 2.4 (95% CI 1.1 to 5.4) p=0.028 **HR (SCS vs *metra*)**: 2.0 (95% CI 0.9 to 4.4) p=0.089	NR	NR

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: Ravaioli et al 2022 (Ravaioli et al. 2022) **Design:** RCT **Location:** Italy **Status of study:** Published **Associated records**: None in these columns	**Intervention**: VitaSmart (n=55) **Comparator**: SCS (n=55) **Analysis population**: PP	**1 year:** VitaSmart: NR SCS: NR **P value:** 0.52	**Graft failure at 1 year:** VitaSmart: 1 (2%) SCS: 7 (13%) **P value:** 0.03 **Adjusted RD (graft failure)**: 0.109 (95% CI 0.014 to 0.204) p=0.03	**Day 7:** VitaSmart: 0 SCS: 6 (11%) **P value:** 0.027	**Hepatic biliary or vascular complications** **6 months:** **VitaSmart:** 9 (16%) **SCS:** 12 (22%) **P value**: 0.47 **Biliary stricture:** **6 months:** VitaSmart: 2 (4%) SCS: 2 (4%) **P value:** Not significant **Biliary leak:** **6 months:** VitaSmart: 2 (4%) SCS: 1 (2%) **P value:** Not significant **Biliary other:** **6 months:** VitaSmart: 2 (4%) SCS: 2 (4%) **P value**: Not significant

Study	Interventions	Overall participant survival at 1 year	Graft survival at 1 year	Re-transplantation at 1 year/maximum follow-up	Biliary complications at 6 months, 1 year and maximum follow-up
Primary publication: Reich et al 2024 (Reich et al. 2024b) **Design: RCT** **Location:** USA **Status of study:** Unpublished, conference abstract only **Associated records**: None in these columns	**Intervention**: VitaSmart (n=109) **Comparator**: SCS (n=110) **Analysis population**: ITT	**6 month:** VitaSmart: 107 (98%, 95% CI 93.6% to 99.5%) SCS: 107 (97%, 95% CI 92.3% to 99.1%) **P value:** not significant	**6 month:** VitaSmart: 105 (96%, 95% CI 90.9% to 98.6%) SCS: 103 (94%, 95% CI 87.4% to 96.9) **P value:** not significant **DCD subgroup** **6 month:** VitaSmart (n=28): 26 (93%, 95% CI 77.4% to 98.0%) SCS (n=27): 22 (81%, 95% CI 63.3% to 91.8%) **P value:** not significant	NR	NR

CI: confidence interval; DCD: donation after circulatory death; DRI: Donor Risk Index; HR: hazard ratio; ITT: intent to treat; NA: not applicable; NMP: normothermic machine perfusion; NR: not reported; NRP: normothermic regional perfusion; OR: odds ratio; PP: per protocol; RCT: randomised controlled trial; RD: risk difference; RR: risk ratio; SCS: standard cold storage; SD: standard deviation

Table D.2: Graft-related complications

Study	Interventions	PNF of the graft	HAT within 28 days	In hospital incidence of post reperfusion syndrome	Early allograft function, measured with a validated model
Primary publication: van Rijn et al 2021 (van Rijn et al. 2021c) **Design:** RCT **Location:** Belgium; UK; Netherlands **Associated records**: 5 year data from van Rijn et al 2025 (van Rijn et al. 2025)	**Intervention**: Liver Assist (n=78) **Comparator**: SCS (n=78) **Analysis population**: mITT (included all patients who received allocated intervention), except PRS and EAD data which is complete case	Liver Assist: 0 SCS: 1 (1%)	**6 months:** Liver Assist: 2 (3%) SCS: 2 (3%) **Adjusted RR:** 0.94 (0.12 to 7.19)	**Patients with intraoperative PRS (>30% decrease in systemic mean arterial pressure)** Liver Assist: 9/72 (12%) SCS: 19/70 (27%) **Adjusted RR:** 0.43 (95% CI 0.20 to 0.91) **Patients with intraoperative >30% decrease in systemic mean arterial pressure *or* >100% increase in norepinephrine dose:** Liver Assist: 20/72 (28%) SCS: 33/72 (46%) **Adjusted RR:**-0.59 (0.38 to 0.92)	Liver Assist: 20/78 (26%) SCS: 31/72 (40%) **Adjusted RR:** 0.61 (95% CI 0.39 to 0.96)
Primary publication: Czigany et al 2021 (Czigany et al. 2021) **Design:** RCT **Location:** Czech Republic; Germany **Status of study:** Published **Associated**	**Intervention**: Liver Assist (n=23) **Comparator**: SCS (n=23) **Analysis population**: ITT	Liver Assist: 1 (4%) SCS: 1 (4%) **P value:** >0.999	**1 year:** Liver Assist: 0 (0%) SCS: 2 (9%) **P value:** 0.489	NR	Liver Assist: 4 (17%) SCS: 8 (35%) **P value:** 0.314

Study	Interventions	PNF of the graft	HAT within 28 days	In hospital incidence of post reperfusion syndrome	Early allograft function, measured with a validated model
records: None in these columns.					
Primary publication: Minor et al 2021 (Minor et al. 2022) **Design:** RCT **Location:** France **Status of study:** Published **Associated records**: None in these columns.	**Intervention**: Liver Assist (n=20) **Comparator**: SCS (n=20) **Analysis population**: ITT	NR	**3 months:** Liver Assist: 0 (0%) SCS: 1 (5*%)	NR	Liver Assist: 4 (20%) SCS: 6 (30%) **P value:** 0.48
Primary publication: Lesurtel et al 2025 (Lesurtel et al. 2025) **Design:** RCT **Location:** France **Associated records**: None in these columns.	**Intervention**: Liver Assist (n=131) **Comparator**: SCS (n=131) **Analysis population**: mITT	Liver Assist: 1 (0.76%) SCS: 6 (4.58%) **P value:** 0.12	**1 year:** Liver Assist: 1 (0.8%) SCS: 4 (3.1%) **P value:** 0.37	Liver Assist: 44 (33.6%) SCS: 46 (35.1%) **P value:** 0.79	Liver Assist: 23 (17.6%) SCS: 40 (30.5%) **P value:** 0.014

Study	Interventions	PNF of the graft	HAT within 28 days	In hospital incidence of post reperfusion syndrome	Early allograft function, measured with a validated model
Primary publication: Ghinolfi et al 2019 (Ghinolfi et al. 2019) **Design:** RCT **Location:** Italy **Status of study:** Published **Associated records**: None in these columns.	**Intervention**: Liver Assist (n=10) **Comparator**: SCS (n=10) **Analysis population**: ITT	Liver Assist: 0 SCS: 0 **P value:** 1	**HAT leading to graft loss and retransplant** **Day 9:** Liver Assist: 1 (10%) SCS: 0 **Difference between interventions:** NR	Liver Assist: 3 (30%) SCS: 1 (10%) **P value:** 0.576	Liver Assist: 2 (20%) Cold storage: 1 (10%) **P value:** 1
Primary publication: Grat et al 2023 (Grat et al. 2023) **Design:** RCT **Location:** Poland **Status of study:** Published **Associated records**: None in these columns.	**Intervention**: Liver Assist (n=26) **Comparator**: SCS (n=78) **Analysis population**: ITT	Liver Assist: 0 SCS: 3 (3.8) **P value:** 0.57	**HAT leading to retransplant** **90 days:** Liver Assist:0 SCS: 1 **Difference between interventions:** NR	Liver Assist: 6 (23.1) SCS: 15 (19.2) **P value:** 0.78	**Model for early allograft function (MEAF, 0 to 10, higher is more severe))** Liver Assist: Mean 4.94 (SD 1.72) SCS: Mean 5.49 (SD 2.14) **P value:** 0.24 **Patients with MEAF score ≥ 8** Liver Assist: 1 (3.8%) SCS: 12 (15.4%) **P value:** 0.18

Study	Interventions	PNF of the graft	HAT within 28 days	In hospital incidence of post reperfusion syndrome	Early allograft function, measured with a validated model
Primary publication: Schlegel et al 2023 (Schlegel et al. 2023) **Design:** RCT **Location:** UK, Belgium, Netherlands, France, Austria, Switzerland **Status of study:** Published **Associated records**: None in these columns.	**Intervention**: Liver Assist (n=85) **Comparator**: SCS (n=85) **Analysis population**: mITT	**Liver-related graft loss due to PNF** Liver Assist: 0 SCS: 3 (3.5%) **P value:** 0.015	**1 year:** Liver Assist: 2 (2.4%) SCS: 0 **Difference between interventions:** NR	NR	Liver Assist: 14 (16.5%) CS: 39 (45.9%) **Difference between interventions:** NR
Primary publication: Vogt et al 2024 (Vogt et al. 2024) **Design:** Prospective cohort study **Location:** Germany **Status of study:** Published **Associated records**: NA	**Intervention**: *metra* (n=31) **Comparator**: SCS (n=6) **Analysis population**: All included participants	NR	NR	NR	*metra*: 11 (35.5%) SCS: 3 (50%) **P value:** 0.6534

Study	Interventions	PNF of the graft	HAT within 28 days	In hospital incidence of post reperfusion syndrome	Early allograft function, measured with a validated model
Primary publication: Krendl et al 2025 (Krendl et al. 2025) **Design:** Retrospective cohort study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention**: *metra* (n=174) **Comparator**: SCS (n=158) **Analysis population**: All included participants	*metra*: 0 (0%) SCS: 4 (2.5%) **P value:** 0.05 Non-benchmark *metra*: 0 (0)%) Non-benchmark SCS: 3 (3.7%) **P value:** 0.073	**1 year:** *metra*: 5 (2.9%) SCS: 8 (5.1%) **P value:** 0.304 Non-benchmark *metra*: 5 (4.5%) Non-benchmark SCS: 5 (6.2%) **P value:** 0.745	NR	*metra*: 52 (29.9%) SCS: 57 (36.1%) **P value**: 0.230 Non-benchmark *metra*: 35 (31.5%) Non-benchmark SCS: 27 (33.3%) **P value:** 0.792
Primary publication: Fodor et al 2021 (Fodor et al. 2021) **Design:** Matched case study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=59) **Comparator:** SCS (n=59) **Analysis population:** All included participants	*metra*: 0 (0%) SCS: 0 (0%)	**Arterial thrombosis** **Timepoint NR**: *metra*: 0 (0%) SCS: 4 (7%) **P value**: 0.042	NR	*metra*: 32% SCS (n=58): 34% **P value:** 0.794
Primary publication: Mathis et al, 2024 (Mathis et al. 2024) **Design:** Matched case study	**Intervention:** *metra* (n=18) **Comparator:** SCS (n=36) **Analysis population:** All included participants	NR	NR	*metra*: 1 (5.6%) SCS: 5 (13.9%) **P value:** 0.651	NR

Study	Interventions	PNF of the graft	HAT within 28 days	In hospital incidence of post reperfusion syndrome	Early allograft function, measured with a validated model
Location: Austria **Status of study:** Published **Associated records**: NA					
Primary publication: Hann et al, 2022 (Hann et al. 2022) **Design:** Matched case study **Location:** UK **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=26) **Comparator:** SCS group 1, retrospective (n=31), SCS group 2, prospective (n=25) **Analysis population:** All included participants	*metra*: 0 (0%) SCS1: 1 (3.2%) SCS2: 0 (0%) **P value:** 0.423	**Timepoint:** NR *metra*: 3 (11%) SCS1: 1 (3.2%) SCS2: 2 (8%) **P value:** 0.481	NR	*metra*: 12 (46%) SCS1: 12 (38%) SCS2: 9 (36%) **P value:** 0.743
Primary publication: Puttappa et al, 2025 (Puttappa et al. 2025) **Design:** Retrospective cohort **Location:** UK **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=78) **Comparator:** SCS (n=59), NRP then SCS (n=101) **Analysis population:** All included participants	*metra*: 1 (1%) SCS: 2 (3%) NRP then SCS: 0	NR	*metra*: 12 (15%) SCS: 22 (37%) NRP then SCS: 11 (11%) **Odds ratio SCS vs *metra***: 3.3 (95% CI 1.5 to7.6) p=0.004 **Odds ratio SCS vs NRP SCS:** 4.9, (95% CI 2.2 to 11.4) p<.001	**MEAF score (median, IQR)** *metra*: 3.3 (2.1 to 5.2) SCS: 5.8 (4.8 to 7.0) NRP then SCS: 4.1 (2.8 to 5.4) **P value**: <.001

Study	Interventions	PNF of the graft	HAT within 28 days	In hospital incidence of post reperfusion syndrome	Early allograft function, measured with a validated model
Primary publication: Reich et al 2024 (Reich et al. 2024b) **Design: RCT** **Location: USA** **Status of study:** Unpublished, conference abstract only **Associated records**: None in these columns.	**Intervention**: VitaSmart (n=109) **Comparator**: SCS (n=110) **Analysis population**: ITT	VitaSmart: 0 (0%) SCS: 1 (0.9*%)	NR	NR	VitaSmart: 22 (20%) SCS: 41 (37%) **RR:** 0.54 (95% CI 0.35 to 0.85) p=0.007
Primary publication: Ravaioli et al 2022 (Ravaioli et al. 2022) **Design:** RCT **Location:** Italy **Status of study:** Published **Associated records**: None in these columns	**Intervention**: VitaSmart (n=55) **Comparator**: SCS (n=55) **Analysis population**: PP	VitaSmart: 0 (0%) SCS: 2 (4%) **P value:** 0.49	**HAT** **6 months:** VitaSmart: 1 (2%) SCS: 0 (0%) **P value:** not significant	VitaSmart: 30 (55%) SCS: 26 (47%) **P value:** 0.45	VitaSmart: 7 (13%) SCS: 19 (35%) **P value:** 0.007 **Adjusted RD:** 0.218 (0.065 to 0.372), p=0.005

CI: confidence interval; EAD: early allograft dysfunction; IQR: interquartile range; ITT: intent to treat; MEAF: Model for Early Allograft Function; NA: not applicable; NR: not reported; NRP: normothermic regional perfusion; PP: per protocol; PRS: post-reperfusion syndrome; RCT: randomised controlled trial; RD: risk difference; RR: risk ratio; SCS: standard cold storage; SD: standard deviation

Table D.3: Graft-related complications 2

Study	Interventions	Acute kidney injury post transplantation	Post-operative requirement for RRT	Transaminase/aminotransferase release during the first week posttransplant
Primary publication: van Rijn et al, 2021 (van Rijn et al. 2021c) **Design:** RCT **Location:** Belgium; UK; Netherlands **Associated records**: None in these columns	**Intervention**: Liver Assist (n=78) **Comparator**: SCS (n=78) **Analysis population**: mITT (included all patients who received allocated intervention), except PRS and EAD data which is complete case	NR	**Renal replacement during transplant:** Liver Assist: 3 (4%) SCS: 2 (3%) **Renal failure leading to dialysis**: **6 months:** Liver Assist: 7 (9%) SCS: 7 (9%) **Adjusted RR:** 0.79 (95% CI 0.27 to 2.34)	NR
Primary publication: Czigany et al, 2021 (Czigany et al. 2021) **Design:** RCT **Location:** Czech Republic; Germany **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=23) **Comparator**: SCS (n=23) **Analysis population**: ITT	NR	**90 days:** Liver Assist: 5 (22%) SCS: 9 (39%) **P value: 0.337**	**Peak serum alanine aminotransferase** Liver Assist: Median 418 IU/L (IQR 221 to 828) SCS: Median 796 IU/L (IQR 477 to 1195) **P value:** 0.030 **Peak aspartate aminotransferase** Liver Assist: Median 652 IU/L (IQR 415 to 1332) SCS: Median 1312 IU/L (IQR 576 to

Study	Interventions	Acute kidney injury post transplantation	Post-operative requirement for RRT	Transaminase/aminotransferase release during the first week posttransplant
				2514) **P value**: 0.091
Primary publication: Minor et al, 2021 (Minor et al. 2022) **Design: RCT** **Location: France** **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=20) **Comparator**: SCS (n=20) **Analysis population**: ITT	NR	NR	**<u>Peak aspartate aminotransferase</u>** **3 days:** **Liver Assist:** Mean 767 U/L (SD 1,157) **SCS:** Mean 1,371 U/L (SD 2,871) **P value:** 0.273 **3 to 7 days:** Liver Assist: Mean 48 U/L (SD 62) SCS: Mean 90 U/L (SD 134) **P value:** 0.058

Study	Interventions	Acute kidney injury post transplantation	Post-operative requirement for RRT	Transaminase/aminotransferase release during the first week posttransplant
Primary publication: Lesurtel et al, 2025 (Lesurtel et al. 2025) **Design:** RCT **Location:** France **Associated records**: None in these columns	**Intervention**: Liver Assist (n=131) **Comparator**: SCS (n=131) **Analysis population**: mITT	NR	**Renal insufficiency:** **90 days:** Liver Assist: 24 (18.3%) SCS: 20 (15.3%) **P value:** 0.51	**Peak serum alanine aminotransferase** Liver Assist: Median 593 IU/L (IQR 346 to 905) SCS: Median 756 IU/L (IQR 428 to 1,424) Difference between arms**:** -21%, 0.021 **Peak aspartate aminotransferase** **Liver Assist:** Median 777 IU/L (IQR 528 to 1,462) **SCS:** Median 1,027 IU/L (IQR 573 to 2,137) **Difference between arms:** -24%, 0.009
Primary publication: Ghinolfi et al, 2019 (Ghinolfi et al. 2019) **Design:** RCT **Location:** Italy **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=10) **Comparator**: SCS (n=10) **Analysis population**: ITT	NR	NR	**Peak aspartate aminotransferase, units per litre:** Liver Assist: median 709 (IQR 371 to 1575) SCS: median 574 (IQR 377 to 1162) **P value:** 0.597 **Peak alanine aminotransferase, units per litre:** Liver Assist: median 332 (IQR 263 to 610) SCS: median 428 (IQR 303 to 616) **P value:** 0.821

Study	Interventions	Acute kidney injury post transplantation	Post-operative requirement for RRT	Transaminase/aminotransferase release during the first week posttransplant
Primary publication: Grat et al, 2023 (Grat et al. 2023) **Design:** RCT **Location:** Poland **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=26) **Comparator**: SCS (n=78) **Analysis population**: ITT	NR	NR	**Alanine transaminase activity** P value (difference between treatments): 0.81 **Aspartate transaminase activity** P value (difference between treatments): 0.5
Primary publication: Schlegel et al, 2023 (Schlegel et al. 2023) **Design:** RCT **Location:** UK, Belgium, Netherlands, France, Austria, Switzerland **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=85) **Comparator**: SCS (n=85) **Analysis population**: mITT	NR	NR	**Peak alanine aminotransferase, units per litre** Liver Assist: median 636 (IQR 341 to 1,055) SCS: median 695 (IQR 379 to 1,575) **Difference between interventions:** NR **Alanine aminotransferase AUC, units per litre** Liver Assist: median 2,048 (IQR 1,252 to 3,475) CS: median 1,978 (IQR 1,232 to 4,128) **Mean difference:** -0.089 (95% CI −0.34 to 0.16), p = 0.49 **Peak aspartate aminotransferase,**

Study	Interventions	Acute kidney injury post transplantation	Post-operative requirement for RRT	Transaminase/aminotransferase release during the first week posttransplant
				<u>units per litre</u> Liver Assist: median 803 (IQR 435 to 1,303) SCS: median 896 (IQR 409 to 2,478) **Difference between interventions:** NR **<u>Aspartate aminotransferase AUC, units per litre</u>** Liver Assist: median 1,149 (IQR 693 to 1,856) SCS: median 1,147 (IQR 683 to 2,752) **Mean difference:** -0.157 (95% CI −0.42 to 0.11), p = 0.25 **Population:** 1.8% missing data
Primary publication: Vogt et al, 2024 (Vogt et al. 2024) **Design:** Prospective cohort study **Location:** Germany **Status of study:** Published **Associated records**: NA	**Intervention**: *metra* (n=31) **Comparator**: SCS (n=6) **Analysis population**: All included participants	NR	NR	NR

Study	Interventions	Acute kidney injury post transplantation	Post-operative requirement for RRT	Transaminase/aminotransferase release during the first week posttransplant
Primary publication: Krendl et al, 2025 (Krendl et al. 2025) **Design:** Retrospective cohort study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention**: *metra* (n=174) **Comparator**: SCS (n=158) **Analysis population**: All included participants	NR	NR	NR
Primary publication: Fodor et al, 2021 (Fodor et al. 2021) **Design:** Matched case study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=59) **Comparator:** SCS (n=59) **Analysis population:** All included participants	**Acute kidney failure** **Time point:** NR *metra*: 5 (8%) SCS: 8 (14%) **P value**: 0.378	NR	NR

Study	Interventions	Acute kidney injury post transplantation	Post-operative requirement for RRT	Transaminase/aminotransferase release during the first week posttransplant
Primary publication: Mathis et al, 2024 (Mathis et al. 2024) **Design:** Matched case study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=18) **Comparator:** SCS (n=36) **Analysis population:** All included participants	NR	Both the incidence of dialysis and the length of time on dialysis were comparable between the 2 groups.	Post operative day 4 onward *metra* patients had significantly lower aspartate aminotransferase values than SCS patients
Primary publication: Hann et al, 2022 (Hann et al. 2022) **Design:** Matched case study **Location:** UK **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=26) **Comparator:** SCS group 1, retrospective (n=31), SCS group 2, prospective (n=25) **Analysis population:** All included participants	NR	**Short-term postoperative renal replacement therapy** *metra*: 15 (57.7%) SCS group 1: 11 (35.5%) SCS group 2: 9 (36%) **P value:** 0.194	**Peak alanine aminotransferase, units per litre** *metra*: median 545 (IQR 287 to 1166) SCS1: median 737 (IQR 448 to 1582) SCS2: median 825 (IQR 525 to 1401) **P value:** 0.281

Study	Interventions	Acute kidney injury post transplantation	Post-operative requirement for RRT	Transaminase/aminotransferase release during the first week posttransplant
Primary publication: Puttappa et al, 2025 (Puttappa et al. 2025) **Design:** Retrospective cohort **Location:** UK **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=78) **Comparator:** SCS (n=59), NRP then SCS (n=101) **Analysis population:** All included participants	**Acute kidney injury stage ≥2** *metra*: 22 (28%) SCS: 28 (47%) NRP then SCS: 29 (29%) **P value**: 0.033	**Day 7**: *metra*: 12 (15%) SCS: 9 (15%) NRP then SCS: 16 (16%) **P value**: >0.999	**Peak alanine aminotransferase, units per litre** *metra*: median 360 (IQR 208 to 621) SCS: median 697 (IQR 451 to 1277) NRP then SCS: median 508 (IQR 328 to 970) **P value**: <0.001
Primary publication: Reich et al, 2024 (Reich et al. 2024b) **Design: RCT** **Location: USA** **Status of study:** Unpublished, conference abstract only **Associated records**: None in these columns	**Intervention**: VitaSmart (n=109) **Comparator**: SCS (n=110) **Analysis population**: ITT	NR	NR	NR
Primary publication: Ravaioli et al, 2022 (Ravaioli et al. 2022) **Design:** RCT **Location:** Italy **Status of study:** Published **Associated records**: None in these columns	**Intervention**: VitaSmart (n=55) **Comparator**: SCS (n=55) **Analysis population**: PP	NR	**Renal insufficiency:** **6 months:** VitaSmart: 15 (27%) SCS: 20 (37%)	NR

AUC: area under the curve; CI: confidence interval; EAD: early allograft dysfunction; IQR: interquartile range; ITT: intent-to-treat; IU: international unit; NA: not applicable; NR: not reported; NRP: normothermic regional perfusion; PP: per protocol; PRS: post-reperfusion syndrome; RCT: randomised controlled trial; RR: risk ratio; SCS: standard cold storage; SD: standard deviation

Table D.4: Safety outcomes

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
Primary publication: van Rijn et al, 2021 (van Rijn et al. 2021c) **Design: RCT** **Location:** Belgium; UK; Netherlands **Associated records**: 1 year SAE data is from van Rijn et al 2025 (van Rijn et al. 2025)	**Intervention**: Liver Assist (n=78) **Comparator**: SCS (n=78) **Analysis population**: mITT (included all patients who received allocated intervention)	**6 months:** Liver Assist: 1/78 (malfunctioning pressure sensor due to user error, no injury to liver) SCS: 0	**1 year:** Liver Assist: 39 (50%) SCS: 41 (53%) **P value:** 0.749	NR	**6 months:** Liver Assist: 6 SCS: 2
Primary publication: Czigany et al, 2021 (Czigany et al. 2021) **Design:** RCT **Location:** Czech Republic; Germany **Status of study:** Published **Associated records**: Czigany et al 2024 (Czigany et al. 2024) (long term outcome data)	**Intervention**: Liver Assist (n=23) **Comparator**: SCS (n=23) **Analysis population**: ITT; long term (median 48 months) serious adverse event and mortality data is complete case	NR	**90 days:** Liver Assist: 10 (44%) SCS: 17 (74%) **P value:** 0.036 **Late onset (occurring >6 months after surgery), Clavien-Dindo ≥3:** **Median 48 months:** Liver Assist: 9/21 (43%) SCS: 17/20 (85%) **P value:** 0.009	NR	**Deaths with/due to graft failure** **1 year:** Liver Assist: 1 (septic complications after re-transplantation due to PNF) SCS: 1 (hepatic arterial thrombosis followed by candida sepsis, ineligible for re-transplantation with multiple organ failure at 2 months) **Deaths with functional grafts** **1 year:** Liver Assist: 1 (cardiac

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
					complications) SCS: 3 (1 recurrent hepatocellular carcinoma with rapid metastases; 1 unclear domestic death after discharge; 1 septic complications) **<u>Deaths later than 6 months due to graft failure:</u>** **Median 48 months** Liver Assist: 1/21 (5%) SCS: 1/20 (5%) **<u>Deaths later than 6 months with functional grafts:</u>** **Median 48 months** Liver Assist: 0/21 (0%) SCS: 4/20 (20%)
Primary publication: Minor et al, 2021 (Minor et al. 2022) **Design: RCT** **Location:** France **Status of study:** Published **Associated**	**Intervention**: Liver Assist (n=20) **Comparator**: SCS (n=20) **Analysis population**: ITT	NR	**<u>Clavien-Dindo Grade >IIIb AE</u>** 3 months: Liver Assist: 8 (40*%) SCS: 15 (75*%) **<u>Clavien-Dindo Grade IIIa AE</u>** **3 months:** Liver Assist: 3 (15*%)	NR	NR

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
records: None in these columns			SCS: 3 (15*%) **<u>Clavien-Dindo Grade IIIb AE</u>** **3 months:** Liver Assist: 2 (10*%) SCS: 7 (35*%) **<u>Clavien-Dindo Grade IVa AE</u>** **3 months:** Liver Assist: 2 (10*%) SCS: 5 (25*%) **<u>Clavien-Dindo Grade IVb AE</u>** **3 months:** Liver Assist: 0 (0%) SCS: 0 (0%) **<u>Clavien-Dindo Grade V AE</u>** **3 months:** Liver Assist: 4 (20*%) SCS: 3 (15*%)		

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
Primary publication: Lesurtel et al, 2025 (Lesurtel et al. 2025) **Design:** RCT **Location:** France **Associated records**: None in these columns	**Intervention**: Liver Assist (n=131) **Comparator**: SCS (n=131) **Analysis population**: mITT	NR	**90 days:** Liver Assist: 66 (52.4%) SCS: 75 (61.5%) **P value:** 0.15	NR	**90 days:** Liver Assist: 3 (2.3%) SCS: 7 (5.3%) **P value:** 0.2
Primary publication: Ghinolfi et al, 2019 (Ghinolfi et al. 2019) **Design:** RCT **Location:** Italy **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=10) **Comparator**: SCS (n=10) **Analysis population**: ITT	NR	NR	NR	**6 months** Liver Assist: 0 (0%) SCS: 1 (10%) **P value:** 1.0

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
Primary publication: Grat et al, 2023 (Grat et al. 2023) **Design:** RCT **Location:** Poland **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=26) **Comparator**: SCS (n=78) **Analysis population**: ITT	NR	**Grade ≥3** **90 days:** Liver Assist: 8 (30.8%) SCS: 36 (46.2%) **P value:** 0.25 **Grade ≥4** **90 days:** Liver Assist: 4 (15.4%) SCS: 18 (23.1%) **P value:** 0.58	NR	**90 days:** Liver Assist: 1 (3.8%) Comparator: 6 (7.7%) **P value:** 0.68
Primary publication: Schlegel et al, 2023 (Schlegel et al. 2023) **Design:** RCT **Location:** UK, Belgium, Netherlands, France, Austria, Switzerland **Status of study:** Published **Associated records**: None in these columns	**Intervention**: Liver Assist (n=85) **Comparator**: SCS (n=85) **Analysis population**: mITT	Four device malfunctions occurred in 88 machine liver perfusions (4.5%), which resulted in insufficient perfusion flow through the portal vein in three cases, and in excessive perfusion (>400 ml/min) despite low portal pressure in one case. In one of these cases, an unexpected peritoneal metastasis	**Proportion of patients with at least 1 Clavien ≥ IIIa complication** **1 year:** Liver Assist: 44 (51.8%) SCS: 46 (54.1%) **Adjusted OR (sensitivity analysis 1)**: 0.874 (95% CI 0.46–1.67) p = 0.68 **Adjusted OR (sensitivity analysis 2**): 0.91 (95% CI 0.47–1.78) p = 0.787 **Number of Clavien ≥ IIIb complications**	NR	**Recipient death** **1 year:** Liver Assist: 4 (4.7%) SCS: 4 (4.7%) **OR:** 1.000 (95% CI 0.229 to 4.359)

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
		in the recipient was confirmed through histology, with consecutive cancelled transplantation. This case was therefore excluded from the analysis. The other three device malfunctions were included	**1 year:** Liver Assist**:** 25 (29.4%) SCS: 46 (54.1%) **Difference between interventions:** NR **<u>Number of Clavien ≥ IV complications</u>** **1 year:** Liver Assist: 12 (14.1%) SCS: 19 (22.4%) **Difference between interventions:** NR **<u>Number of Clavien ≥ V complications</u>** **1 year:** Liver Assist: 4 (4.7%) SCS: 4 (4.7%) **Difference between interventions:** NR		

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
Primary publication: Vogt et al, 2024 (Vogt et al. 2024) **Design:** Prospective cohort study **Location:** Germany **Status of study:** Published **Associated records**: NA	**Intervention**: *metra* (n=31) **Comparator**: SCS (n=6) **Analysis population**: All included participants	NR	NR	NR	**<u>Patient death due to graft failure (NR by treatment arm)</u>** **Post operative day 4:** 1 (2.7*%) **Post operative day 23 (n=36):** 1 (2.8*%) **Post operative day 53 (n=35):** 1 (2.9*%) **Post operative day 69 (n=34)**: 1 (2.9*%) **<u>Patient death due other reasons (NR by treatment arm)</u>** **3 months** Invasive tuberculosis: 2 (5.9*%) **6 months** Recurrent hepatocellular carcinoma: 1 (2.7*%)

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
Primary publication: Krendl et al, 2025 (Krendl et al. 2025) **Design:** Retrospective cohort study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention**: *metra* (n=174) **Comparator**: SCS (n=158) **Analysis population**: All included participants	NR	NR	NR	NR

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
Primary publication: Fodor et al, 2021 (Fodor et al. 2021) **Design:** Matched case study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=57) **Comparator:** SCS (n=59) **Analysis population: Safety population**	NR	**Clavien-Dindo stage IIIb or above** **Timepoint:** NR *metra*: 37% SCS: 34% **Clavien-Dindo stage IIIa** **Timepoint:** NR *metra*: 5 (9%) SCS: 0 (0*%) **Clavien-Dindo stage IIIb** **Timepoint**: NR *metra*: 12 (21%) SCS: 12 (20%) **Clavien-Dindo stage IVa** **Timepoint**: NR *metra*: 18 (32%) SCS: 17 (29%) **Clavien-Dindo stage V** **Timepoint:** NR *metra*: 7 (12%) SCS: 5 (8%) **Difference between interventions:** p=0.086	NR	NR

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
Primary publication: Mathis et al, 2024 (Mathis et al. 2024) **Design:** Matched case study **Location:** Austria **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=18) **Comparator:** SCS (n=36) **Analysis population:** All included participants	NR	NR	NR	**Median 18 days (before discharge)** *metra*: 0 (0%) SCS: 1 (2.8*%) sepsis
Primary publication: Hann et al, 2022 (Hann et al. 2022) **Design:** Matched case study **Location:** UK **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=26) **Comparator:** SCS group 1, retrospective (n=31), SCS group 2, prospective (n=25) **Analysis population:** All included participants	NR	NR	NR	**3 months** *metra*: 1 (3.8*%; COVID-19) SCS group 1: 3 (9.7*%; 1 bleeding, 1 enteric perforation and 1 portal vein thrombosis) SCS group 2: 1 (4*%; bleeding)

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
Primary publication: Puttappa et al, 2025 (Puttappa et al. 2025) **Design:** Retrospective cohort **Location:** UK **Status of study:** Published **Associated records**: NA	**Intervention:** *metra* (n=78) **Comparator:** SCS (n=59), NRP then SCS (n=101) **Analysis population:** All included participants	NR	NR	NR	NR
Primary publication: Reich et al, 2024 (Reich et al. 2024b) **Design: RCT** **Location: USA** **Status of study:** Unpublished, conference abstract only **Associated records**: None in these columns	**Intervention**: Liver Assist (n=109) **Comparator**: SCS (n=110) **Analysis population**: ITT	NR	**6 months:** VitaSmart: 48 (44%, 95% CI 35.1% to 53.4%) SCS: 59 (54%, 95% CI, 44.4% to 62.7%) **P value:** not significant	NR	**6 months:** VitaSmart: 2 (1.8*%; hepatopulmonary syndrome & cerebral arteriovenous malformation) SCS: 3 (1.8*%; cholangiopathy 2, hepatocellular carcinoma 1)

Study	Interventions	Mechanical failure of machine perfusion technology	Serious adverse events (e.g., Clavien-Dindo classification, grade III or higher)	Device related adverse events	Mortality
Primary publication: Ravaioli et al, 2022 (Ravaioli et al. 2022) **Design:** RCT **Location:** Italy **Status of study:** Published **Associated records**: None in these columns	**Intervention**: VitaSmart (n=55) **Comparator**: SCS (n=55) **Analysis population**: PP	NR	NR	NR	NR

AE: adverse event; CI: confidence interval; ITT: intent-to-treat; NA: not applicable; NR: not reported; NRP: normothermic regional perfusion; OR: odds ratio; PNF: primary non-function; PP: per protocol; RCT: randomised controlled trial; SAE: serious adverse events; SCS: standard cold storage

9.5 Appendix E Model inputs

Table E.1: Baseline waitlist populations over time

Time point (months)	Transplanted	Waitlist	Removed/died	Source
0	0.00%	100.00%	0	Provided by NHSBT from registry data
6	52.20%	40.25%	6	
12	60.38%	27.40%	12	
24	69.00%	11.95%	24	
36	71.07%	7.37%	36	
42	71.88%	5.57%	42	
48	71.88%	0.00%	48	Assumption

Table E.2: Device specific risk ratios of complications and re-transplantation

Variable	Liver Assist	Source	*metra*	Source	VitaSmart	Source
RRT	0.79	Van Rijn et al. (2021) (van Rijn et al. 2021c)	0.79	Assumption	0.75	Ravaioli et al. (2022) (Ravaioli et al. 2022)
HAT	0.25	Lesurtel et al. (2025) (Lesurtel et al. 2025)	0.57	Krendl et al. (2025) (Krendl et al. 2025)	0.25	Assumption
Biliary leaks	0.75	Van Rijn et al. (2021) (van Rijn et al. 2021c)	1.14	Krendl et al. (2025) (Krendl et al. 2025)	2.00	Ravaioli et al. (2022) (Ravaioli et al. 2022)
Anastomotic biliary strictures	1.07	Van Rijn et al. (2021) (van Rijn et al. 2021c)	1.28	Krendl et al. (2025) (Krendl et al. 2025)	1.00	Ravaioli et al. (2022) (Ravaioli et al. 2022)

Non-anastomotic biliary strictures	0.36	Van Rijn et al. (2021) (van Rijn et al. 2021c)	1.22	Krendl et al. (2025) (Krendl et al. 2025)	1.00	Assumption
PRS	0.96	Lesurtel et al. (2025) (Lesurtel et al. 2025)	0.41	Puttappa et al. (2025) (Puttappa et al. 2025)	1.17	Ravaioli et al. (2022) (Ravaioli et al. 2022)
EAD	0.36	Schlegel et al. (2023) (Schlegel et al. 2023)	0.83	Krendl et al. (2025) (Krendl et al. 2025)	0.54	Reich et al. (2024) (Reich et al. 2024b)
PNF	0.17	Lesurtel et al. (2025) (Lesurtel et al. 2025)	0.38	Puttappa et al. (2025) (Puttappa et al. 2025)	0.17	Assumption

Table E.3: Breakdown cost of EAD

Variable	Value	Source
Total ICU stay without EAD	3.0	Limbu et al. (2025) (Limbu Y 2025)
Total general ward stay without EAD	13.0	
Increase in ICU stay with EAD	58%	Croome et al. (2013) (Croome KP 2013)
Increase in general ward with EAD	55%	
Cost of ICU bed day	£1,979	NCC (Service 2024/25)
Cost of general ward bed day	£579	
Total additional cost of EAD	£7,588	

9.6 Appendix F Additional economic model results

Table F.1: Deterministic cost breakdown per person (Liver Assist; NMP)

Cost breakdown by health state	Intervention	Standard care	Incremental
Waitlist	£14,257	£15,574	-£1,317
Cost of transplants (procedure)	[redacted]	[redacted]	[redacted]
Post-transplantation annual costs	[redacted]	[redacted]	[redacted]
Cost of retransplants (procedure + first year)	[redacted]	[redacted]	[redacted]
Post-re-transplantation annual costs	[redacted]	[redacted]	[redacted]
Complications	£5,204	£4,623	£581
Total	**£82,986**	**£72,733**	**£10,253**

Table F.2: Deterministic complication cost breakdown (Liver Assist; NMP)

Complications cost breakdown	Intervention	Standard care	Incremental
EAD	£1,661	£1,823	-£162
RRT	£90	£103	-£14
HAT	£125	£199	-£74
Biliary leaks	£155	£123	£32
Anastomotic strictures	£1,773	£1,257	£516
Non-anastomotic biliary stricture	£1,349	£1,001	£348
PRS	£53	£118	-£65
Complications subtotal	£5,204	£4,623	£581

Table abbreviations: EAD, early allograft dysfunction; HAT, hepatic artery thrombosis; PNF, primary non-function; PRS, post-reperfusion syndrome; RRT, renal replacement therapy.

Table F.3: Deterministic quality-adjusted life year breakdown by health state (Liver Assist; NMP)

QALY breakdown by health state	Intervention	Standard care	Incremental
Waitlist	0.41	0.45	-0.04
Transplanted	6.72	5.22	1.50
Re-transplantation	0.71	0.77	-0.06
Total	**7.84**	**6.44**	**1.41**

Table abbreviations: QALY, quality-adjusted life year.

Table F.4: Deterministic base case event counts (Liver Assist; NMP)

Outcome	Intervention	Comparator	Incremental
Transplantations	0.79	0.72	0.07
Re-transplantations	0.09	0.10	-0.01
Subtotal	0.88	0.82	0.06
Cases of:			
EAD	0.22	0.25	-0.02
RRT	0.10	0.12	-0.02
HAT	0.01	0.02	-0.01
Biliary leaks	0.03	0.03	0.01
Anastomotic strictures	0.19	0.13	0.05
Non-anastomotic biliary stricture	0.14	0.11	0.04
PRS	0.14	0.32	-0.18
PNF	0.00	0.01	0.00
Mortality outcomes			
Deaths on the waitlist	209	281	-72
Deaths post-PNF	1	2	-1
Mean time-to mortality (years)	11.32	9.35	1.97

Table abbreviations: EAD, early allograft dysfunction; RRT, renal replacement therapy; HAT, hepatic artery thrombosis; PRS, post-reperfusion syndrome; PNF, primary non function. .

Table F.5: Deterministic cost breakdown per person (Liver Assist; HMP)

Cost breakdown by health state	Intervention	Standard care	Incremental
Waitlist	£14,257	£15,574	-£1,317
Cost of transplants (procedure)	[redacted]	[redacted]	[redacted]
Post-transplantation annual costs	[redacted]	[redacted]	[redacted]
Cost of retransplants (procedure + first year)	[redacted]	[redacted]	[redacted]
Post-re-transplantation annual costs	[redacted]	[redacted]	[redacted]
Complications	£2,963	£4,623	-£1,660
Total	**£80,686**	**£72,733**	**£7,953**

Table F.6: Deterministic complication cost breakdown (Liver Assist; HMP)

Complications cost breakdown	Intervention	Standard care	Incremental
EAD	£721	£1,823	-£1,102
RRT	£90	£103	-£14
HAT	£55	£199	-£143
Biliary leaks	£101	£123	-£21
Anastomotic strictures	£1,479	£1,257	£222
Non-anastomotic biliary stricture	£393	£1,001	-£608
PRS	£124	£118	£6
Complications subtotal	£2,963	£4,623	-£1,660

Table abbreviations: EAD, early allograft dysfunction; HAT, hepatic artery thrombosis; PNF, primary non-function; PRS, post-reperfusion syndrome; RRT, renal replacement therapy.

Table F.7: Deterministic quality-adjusted life year breakdown by health state (Liver Assist; HMP)

QALY breakdown by health state	Intervention	Standard care	Incremental
Waitlist	0.41	0.45	-0.04
Transplanted	6.73	5.22	1.52
Re-transplantation	0.70	0.77	-0.07
Total	**7.85**	**6.44**	**1.41**

Table abbreviations: QALY, quality-adjusted life year.

Table F.8: Deterministic base case event counts (Liver Assist; HMP)

Outcome	Intervention	Comparator	Incremental
Transplantations	0.79	0.72	0.07
Re-transplantations	0.08	0.10	-0.02
Subtotal	0.87	0.82	0.06
Cases of:			
EAD	0.10	0.25	-0.15
RRT	0.10	0.12	-0.02
HAT	0.00	0.02	-0.01
Biliary leaks	0.02	0.03	0.00
Anastomotic strictures	0.16	0.13	0.02
Non-anastomotic biliary stricture	0.04	0.11	-0.06
PRS	0.34	0.32	0.02
PNF	0.00	0.01	-0.01
Mortality outcomes			
Deaths on the waitlist	209	281	-72
Deaths post-PNF	0	2	-1
Mean time-to mortality (years)	11.33	9.35	1.98

Table abbreviations: EAD, early allograft dysfunction; RRT, renal replacement therapy; HAT, hepatic artery thrombosis; PRS, post-reperfusion syndrome; PNF, primary non function. .

Table F.9: Deterministic cost breakdown per person (PerLifePRO; NMP)

Cost breakdown by health state	Intervention	Standard care	Incremental
Waitlist	£14,257	£15,574	-£1,317
Cost of transplants (procedure)	[redacted]	[redacted]	[redacted]
Post-transplantation annual costs	[redacted]	[redacted]	[redacted]
Cost of retransplants (procedure + first year)	[redacted]	[redacted]	[redacted]
Post-re-transplantation annual costs	[redacted]	[redacted]	[redacted]
Complications	£5,204	£4,623	£581
Total	**£100,046**	**£72,733**	**£27,313**

Table F.10: Deterministic complication cost breakdown (PerLifePRO; NMP)

Complications cost breakdown	Intervention	Standard care	Incremental
EAD	£1,661	£1,823	-£162
RRT	£90	£103	-£14
HAT	£125	£199	-£74
Biliary leaks	£155	£123	£32
Anastomotic strictures	£1,773	£1,257	£516
Non-anastomotic biliary stricture	£1,349	£1,001	£348
PRS	£53	£118	-£65
Complications subtotal	£5,204	£4,623	£581

Table abbreviations: EAD, early allograft dysfunction; HAT, hepatic artery thrombosis; PNF, primary non-function; PRS, post-reperfusion syndrome; RRT, renal replacement therapy.

Table F.11: Deterministic quality-adjusted life year breakdown by health state (PerLifePRO; NMP)

QALY breakdown by health state	Intervention	Standard care	Incremental
Waitlist	0.41	0.45	-0.04
Transplanted	6.72	5.22	1.50
Re-transplantation	0.71	0.77	-0.06
Total	**7.84**	**6.44**	**1.41**

Table abbreviations: QALY, quality-adjusted life year.

Table F.12: Deterministic base case event counts (PerLifePRO; NMP)

Outcome	Intervention	Comparator	Incremental
Transplantations	0.79	0.72	0.07
Re-transplantations	0.09	0.10	-0.01
Subtotal	0.88	0.82	0.06
Cases of:			
EAD	0.22	0.25	-0.02
RRT	0.10	0.12	-0.02
HAT	0.01	0.02	-0.01
Biliary leaks	0.03	0.03	0.01
Anastomotic strictures	0.19	0.13	0.05
Non-anastomotic biliary stricture	0.14	0.11	0.04
PRS	0.14	0.32	-0.18
PNF	0.00	0.01	0.00
Mortality outcomes			
Deaths on the waitlist	209	281	-72
Deaths post-PNF	1	2	-1
Mean time-to mortality (years)	11.32	9.35	1.97

Table abbreviations: EAD, early allograft dysfunction; RRT, renal replacement therapy; HAT, hepatic artery thrombosis; PRS, post-reperfusion syndrome; PNF, primary non function.

Table F.13: Deterministic cost breakdown per person (PerLifePRO; HMP)

Cost breakdown by health state	Intervention	Standard care	Incremental
Waitlist	£14,257	£15,574	-£1,317
Cost of transplants (procedure)	[redacted]	[redacted]	[redacted]
Post-transplantation annual costs	[redacted]	[redacted]	[redacted]
Cost of retransplants (procedure + first year)	[redacted]	[redacted]	[redacted]
Post-re-transplantation annual costs	[redacted]	[redacted]	[redacted]
Complications	£2,963	£4,623	-£1,660
Total	**£97,709**	**£72,733**	**£24,975**

Table F.14: Deterministic complication cost breakdown (PerLifePRO; HMP)

Complications cost breakdown	Intervention	Standard care	Incremental
EAD	£721	£1,823	-£1,102
RRT	£90	£103	-£14
HAT	£55	£199	-£143
Biliary leaks	£101	£123	-£21
Anastomotic strictures	£1,479	£1,257	£222
Non-anastomotic biliary stricture	£393	£1,001	-£608
PRS	£124	£118	£6
Complications subtotal	£2,963	£4,623	-£1,660

Table abbreviations: EAD, early allograft dysfunction; HAT, hepatic artery thrombosis; PNF, primary non-function; PRS, post-reperfusion syndrome; RRT, renal replacement therapy.

Table F.15: Deterministic quality-adjusted life year breakdown by health state (PerLifePRO; HMP)

QALY breakdown by health state	Intervention	Standard care	Incremental
Waitlist	0.41	0.45	-0.04
Transplanted	6.73	5.22	1.52
Re-transplantation	0.70	0.77	-0.07
Total	**7.85**	**6.44**	**1.41**

Table abbreviations: QALY, quality-adjusted life year.

Table F.16: Deterministic base case event counts (PerLifePRO; HMP)

Outcome	Intervention	Comparator	Incremental
Transplantations	0.79	0.72	0.07
Re-transplantations	0.08	0.10	-0.02
Subtotal	0.87	0.82	0.06
Cases of:			
EAD	0.10	0.25	-0.15
RRT	0.10	0.12	-0.02
HAT	0.00	0.02	-0.01
Biliary leaks	0.02	0.03	0.00
Anastomotic strictures	0.16	0.13	0.02
Non-anastomotic biliary stricture	0.04	0.11	-0.06
PRS	0.34	0.32	0.02
PNF	0.00	0.01	-0.01
Mortality outcomes			
Deaths on the waitlist	209	281	-72
Deaths post-PNF	0	2	-1
Mean time-to mortality (years)	11.33	9.35	1.98

Table abbreviations: EAD, early allograft dysfunction; RRT, renal replacement therapy; HAT, hepatic artery thrombosis; PRS, post-reperfusion syndrome; PNF, primary non function.

Table F.17: Deterministic cost breakdown per person (*metra*; NMP)

Cost breakdown by health state	Intervention	Standard care	Incremental
Waitlist	£14,257	£15,574	-£1,317
Cost of transplants (procedure)	[redacted]	[redacted]	[redacted]
Post-transplantation annual costs	[redacted]	[redacted]	[redacted]
Cost of retransplants (procedure + first year)	[redacted]	[redacted]	[redacted]
Post-re-transplantation annual costs	[redacted]	[redacted]	[redacted]
Complications	£5,204	£4,623	£581
Total	**£88,540**	**£72,733**	**£15,806**

Table F.18: Deterministic complication cost breakdown (*metra*; NMP)

Complications cost breakdown	Intervention	Standard care	Incremental
EAD	£1,661	£1,823	-£162
RRT	£90	£103	-£14
HAT	£125	£199	-£74
Biliary leaks	£155	£123	£32
Anastomotic strictures	£1,773	£1,257	£516
Non-anastomotic biliary stricture	£1,349	£1,001	£348
PRS	£53	£118	-£65
Complications subtotal	£5,204	£4,623	£581

Table abbreviations: EAD, early allograft dysfunction; HAT, hepatic artery thrombosis; PNF, primary non-function; PRS, post-reperfusion syndrome; RRT, renal replacement therapy.

Table F.19: Deterministic quality-adjusted life year breakdown by health state (*metra*; NMP)

QALY breakdown by health state	Intervention	Standard care	Incremental
Waitlist	0.41	0.45	-0.04
Transplanted	6.72	5.22	1.50
Re-transplantation	0.71	0.77	-0.06
Total	**7.84**	**6.44**	**1.41**

Table abbreviations: QALY, quality-adjusted life year.

Table F.20: Deterministic base case event counts (*metra*; NMP)

Outcome	Intervention	Comparator	Incremental
Transplantations	0.79	0.72	0.07
Re-transplantations	0.09	0.10	-0.01
Subtotal	0.88	0.82	0.06
Cases of:			
EAD	0.22	0.25	-0.02
RRT	0.10	0.12	-0.02
HAT	0.01	0.02	-0.01
Biliary leaks	0.03	0.03	0.01
Anastomotic strictures	0.19	0.13	0.05
Non-anastomotic biliary stricture	0.14	0.11	0.04
PRS	0.14	0.32	-0.18
PNF	0.00	0.01	0.00
Mortality outcomes			
Deaths on the waitlist	209	281	-72
Deaths post-PNF	1	2	-1
Mean time-to mortality (years)	11.32	9.35	1.97

Table abbreviations: EAD, early allograft dysfunction; RRT, renal replacement therapy; HAT, hepatic artery thrombosis; PRS, post-reperfusion syndrome; PNF, primary non function.

Table F.21: Deterministic cost breakdown per person (VitaSmart; HMP)

Cost breakdown by health state	Intervention	Standard care	Incremental
Waitlist	£14,257	£15,574	-£1,317
Cost of transplants (procedure)	[redacted]	[redacted]	[redacted]
Post-transplantation annual costs	[redacted]	[redacted]	[redacted]
Cost of retransplants (procedure + first year)	[redacted]	[redacted]	[redacted]
Post-re-transplantation annual costs	[redacted]	[redacted]	[redacted]
Complications	£3,421	£4,623	-£1,202
Total	**£81,057**	**£72,733**	**£8,324**

Table F.22: Deterministic complication cost breakdown (VitaSmart; HMP)

Complications cost breakdown	Intervention	Standard care	Incremental
EAD	£1,083	£1,823	-£740
RRT	£85	£103	-£18
HAT	£55	£199	-£143
Biliary leaks	£270	£123	£148
Anastomotic strictures	£1,382	£1,257	£126
Non-anastomotic biliary stricture	£393	£1,001	-£608
PRS	£152	£118	£34
Complications subtotal	£3,421	£4,623	-£1,202

Table abbreviations: EAD, early allograft dysfunction; HAT, hepatic artery thrombosis; PNF, primary non-function; PRS, post-reperfusion syndrome; RRT, renal replacement therapy.

Table F.23: Deterministic quality-adjusted life year breakdown by health state (VitaSmart; HMP)

QALY breakdown by health state	Intervention	Standard care	Incremental
Waitlist	0.41	0.45	-0.04
Transplanted	6.73	5.22	1.52
Re-transplantation	0.70	0.77	-0.07
Total	**7.85**	**6.44**	**1.41**

Table abbreviations: QALY, quality-adjusted life year.

Table F.24: Deterministic base case event counts (VitaSmart; HMP)

Outcome	Intervention	Comparator	Incremental
Transplantations	0.79	0.72	0.07
Re-transplantations	0.08	0.09	-0.01
Subtotal	0.87	0.81	0.06
Cases of:			
EAD	0.10	0.25	-0.15
RRT	0.03	0.04	-0.01
HAT	0.01	0.03	-0.02
Biliary leaks	0.08	0.04	0.04
Anastomotic strictures	0.15	0.13	0.01
Non-anastomotic biliary stricture	0.12	0.11	0.01
PRS	0.41	0.32	0.09
PNF	0.00	0.00	0.00
Mortality outcomes			
Deaths on the waitlist	209	281	-72
Deaths post-PNF	0	1	-1
Mean time-to mortality (years)	18.82	16.30	2.52

Table abbreviations: EAD, early allograft dysfunction; RRT, renal replacement therapy; HAT, hepatic artery thrombosis; PRS, post-reperfusion syndrome; PNF, primary non function. .

Figure F.1: Probabilistic sensitivity analysis cost-effectiveness plane (Liver Assist; NMP)

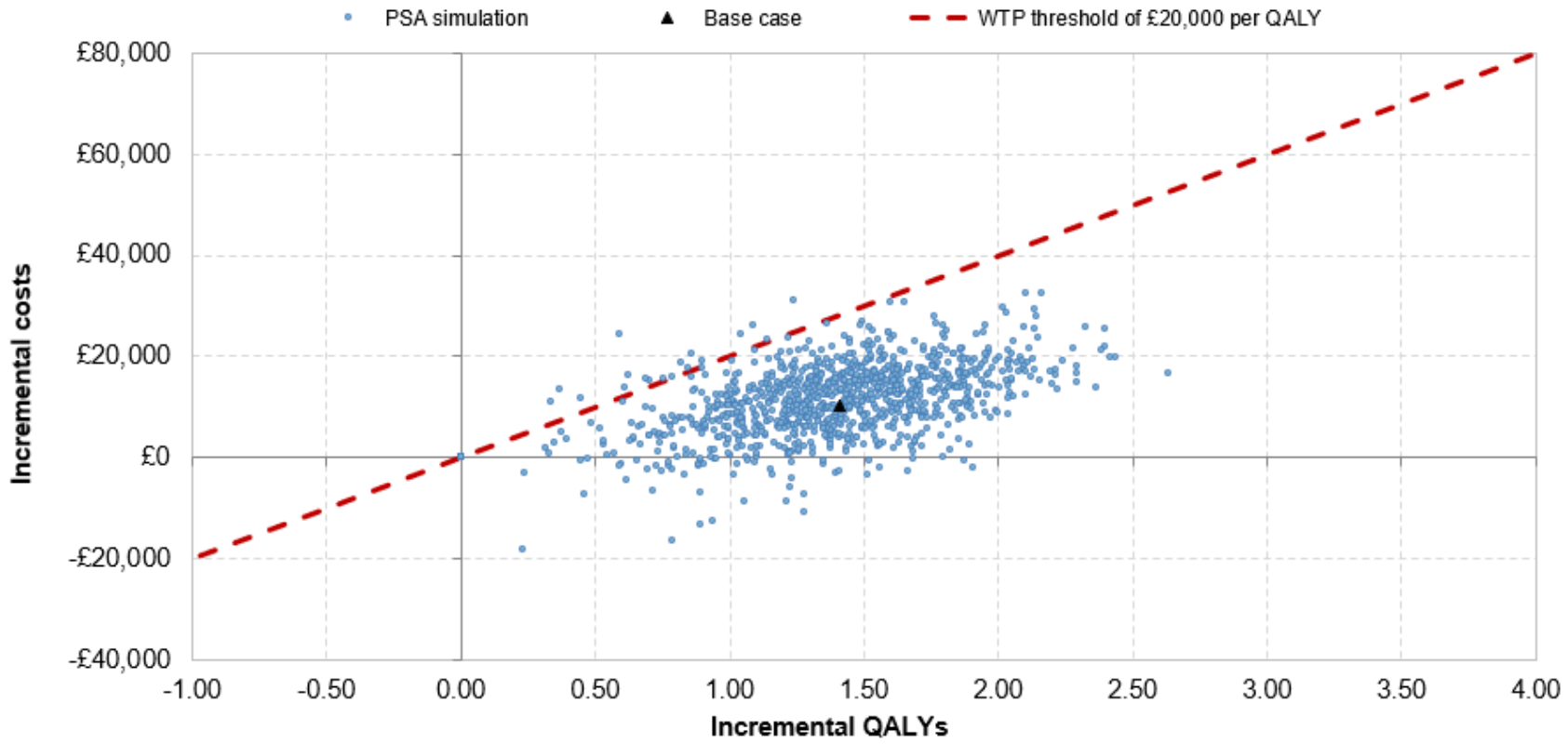

Figure abbreviations: QALY, quality-adjusted life year; WTP, willingness-to-pay.

Figure F.2: Probabilistic sensitivity analysis cost-effectiveness plane (Liver Assist; HMP)

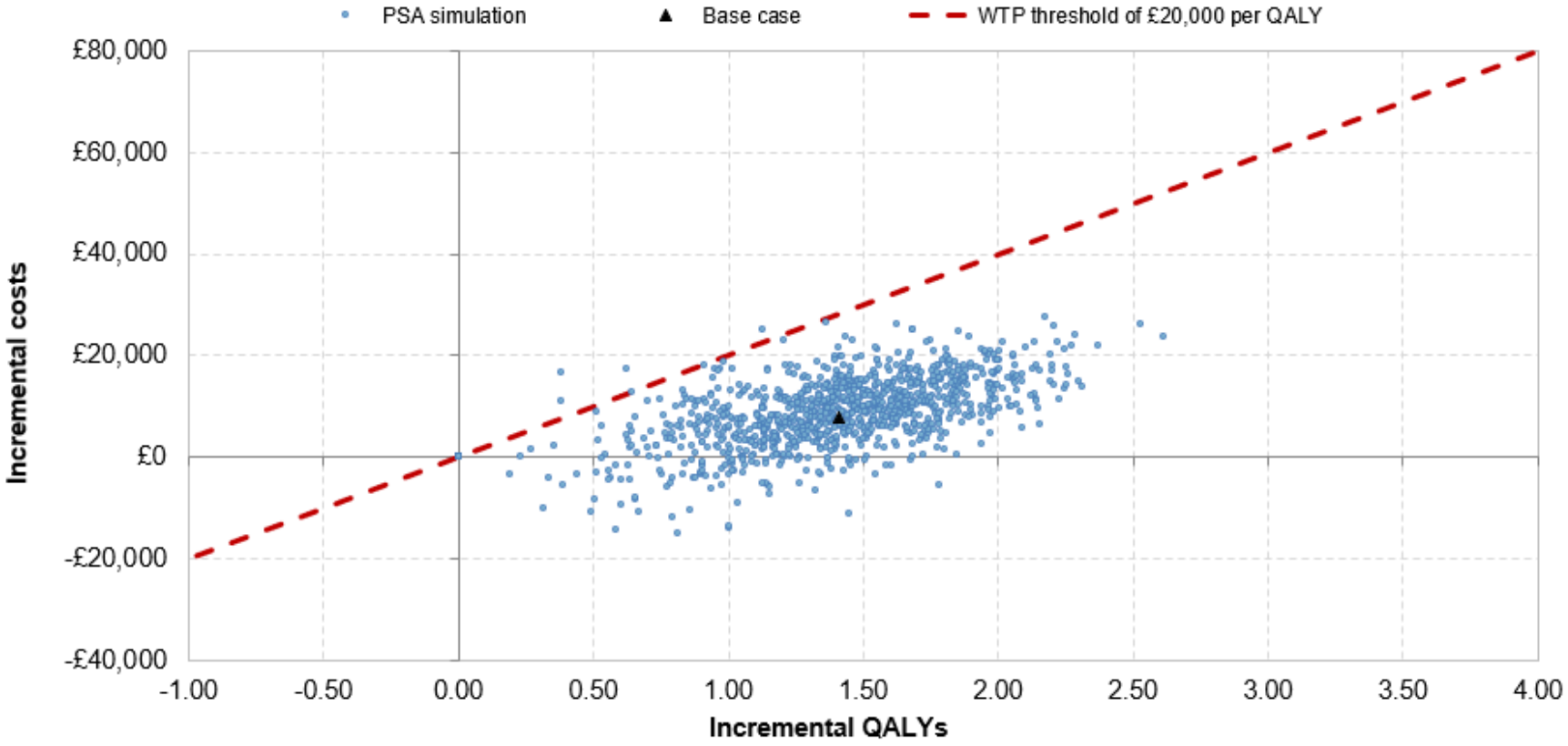

Figure abbreviations: QALY, quality-adjusted life year; WTP, willingness-to-pay.

Figure F.3: Probabilistic sensitivity analysis cost-effectiveness plane (*metra*; NMP)

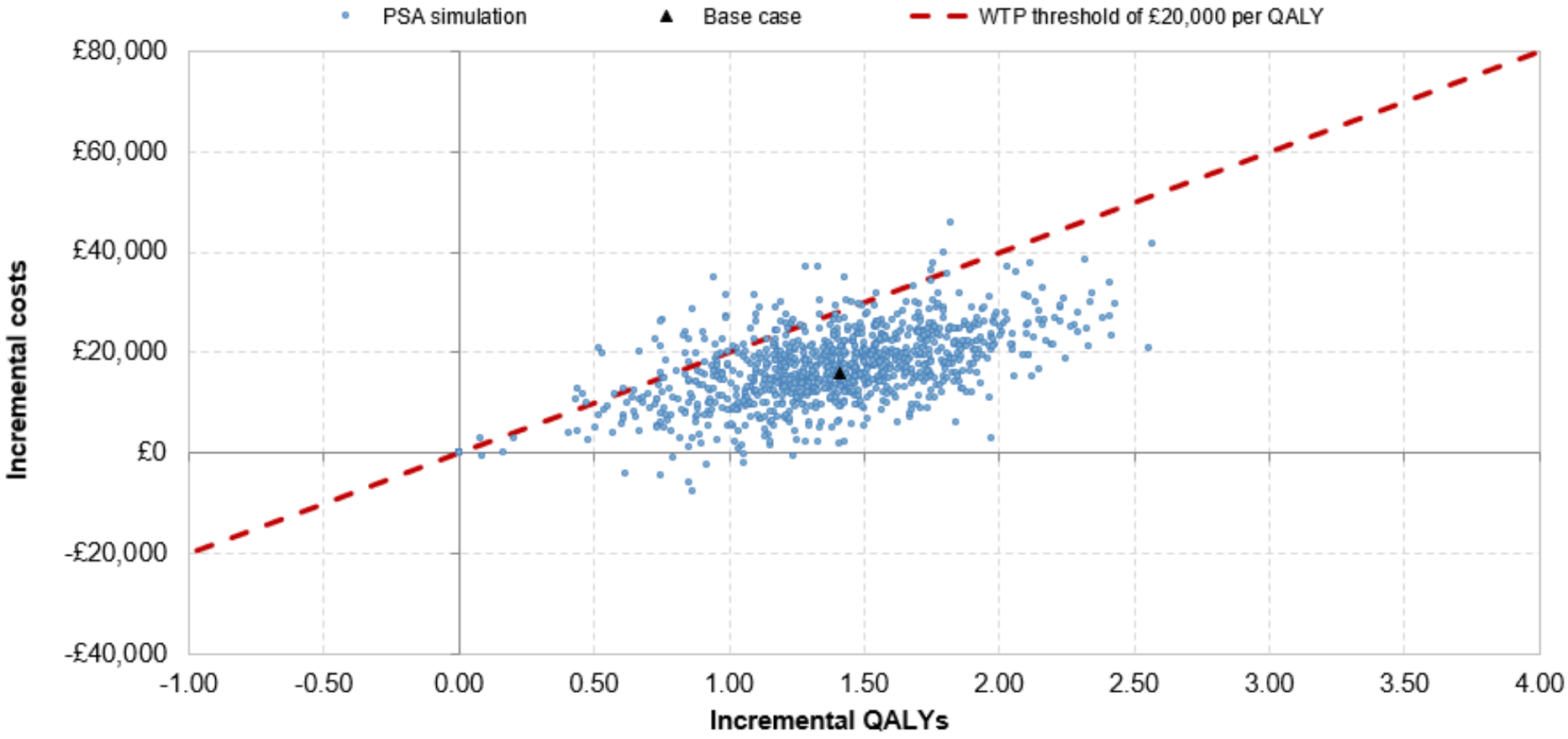

Figure abbreviations: QALY, quality-adjusted life year; WTP, willingness-to-pay.

Figure F.4: Probabilistic sensitivity analysis cost-effectiveness plane (VitaSmart; HMP)

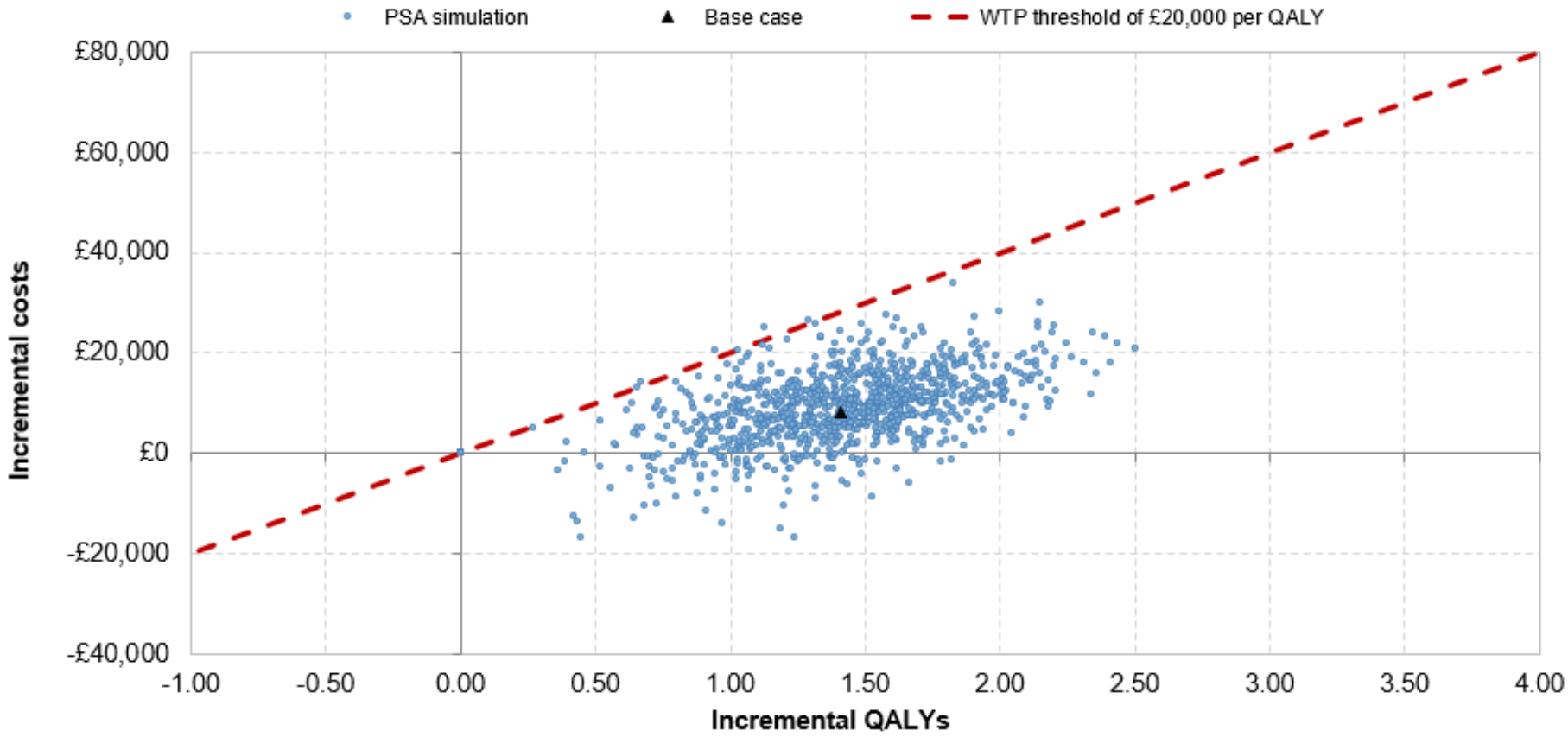

Figure abbreviations: QALY, quality-adjusted life year; WTP, willingness-to-pay.

Table F.25: Probabilistic base case results (Machine perfusion assumed to have no impact on mortality)

Technology	Incremental costs	Incremental QALYs	ICER	NMB	NHB	Probability of CE at £20k/QALY	Probability of CE at £30k/QALY	Probability that the intervention is dominant
Liver Assist (NMP)								
Average	£8,960	0.56	£16,016	£2,229	0.11	66.60%	89.00%	7.60%
Lower CI	£7,744	0.42	£18,547	£607	0.03	-	-	-
Upper CI	£10,743	0.77	£13,972	£4,635	0.23	-	-	-
Liver Assist (HMP)								
Average	£6,389	0.57	£11,160	£5,061	0.25	84.30%	95.20%	13.80%
Lower CI	£5,674	0.43	£13,122	£2,974	0.15	-	-	-
Upper CI	£7,040	0.76	£9,285	£8,124	0.41	-	-	-
PerLifePRO (NMP)								
Average	£26,197	0.57	£46,010	-£14,810	-0.74	1.20%	11.50%	0.10%
Lower CI	£23,278	0.41	£56,400	-£15,024	-0.75	-	-	-
Upper CI	£29,092	0.77	£37,587	-£13,612	-0.68	-	-	-
PerLifePRO (HMP)								
Average	£23,342	0.56	£41,536	-£12,103	-0.61	2.30%	18.20%	0.00%
Lower CI	£20,909	0.38	£55,149	-£13,326	-0.67	-	-	-
Upper CI	£25,038	0.75	£33,414	-£10,052	-0.50	-	-	-

***metra* (NMP)**								
Average	£14,948	0.57	£26,163	-£3,521	-0.18	26.80%	61.40%	1.20%
Lower CI	£13,132	0.45	£29,170	-£4,128	-0.21	-	-	-
Upper CI	£17,194	0.77	£22,383	-£1,830	-0.09	-	-	-
VitaSmart (HMP)								
Average	£6,742	0.56	£11,956	£4,536	0.23	82.00%	94.20%	11.70%
Lower CI	£5,312	0.35	£15,392	£1,590	0.08	-	-	-
Upper CI	£6,553	0.86	£7,662	£10,551	0.53	-	-	-

Table abbreviations: CE, cost-effectiveness; HMP, hypothermic machine perfusion; ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; NMP, normothermic machine perfusion; QALY, quality-adjusted life year.

Figure F.5: Deterministic sensitivity analysis tornado diagram (Liver Assist; NMP)

Figure abbreviations: HR, hazard ratio; MP, machine perfusion; PNF, primary non-function; RR, risk ratio; SCS, static cold storage.

Figure F.6: Deterministic sensitivity analysis tornado diagram (Liver Assist; HMP)

Figure abbreviations: DSA, deterministic sensitivity analysis; HR, hazard ratio; MP, machine perfusion; PNF, primary non-function; RR, risk ratio; SCS, static cold storage.

Figure F.7: Deterministic sensitivity analysis tornado diagram (*metra*; NMP)

Figure abbreviations: DSA, deterministic sensitivity analysis; HR, hazard ratio; MP, machine perfusion; PNF, primary non-function; RR, risk ratio; SCS, static cold storage.

Figure F.8: Deterministic sensitivity analysis tornado diagram (VitaSmart; HMP)

Figure abbreviations: DSA, deterministic sensitivity analysis; HR, hazard ratio; MP, machine perfusion; PNF, primary non-function; RR, risk ratio; SCS, static cold storage.

Figure F.9: Net monetary benefit as per-procedure cost of machine perfusion is varied (Liver Assist; NMP)

Figure abbreviations: NMB, net monetary benefit

Figure F.10: Net monetary benefit as per-procedure cost of machine perfusion is varied (Liver Assist; HMP)

Figure abbreviations: NMB, net monetary benefit

Figure F.11: Net monetary benefit as per-procedure cost of machine perfusion is varied (*metra*; NMP)

Figure abbreviations: NMB, net monetary benefit

Figure F.12: Net monetary benefit as per-procedure cost of machine perfusion is varied (VitaSmart; HMP)

Figure abbreviations: NMB, net monetary benefit

Figure F.13: Net monetary benefit as machine perfusion organ utilisation factor is varied (Liver Assist; NMP)

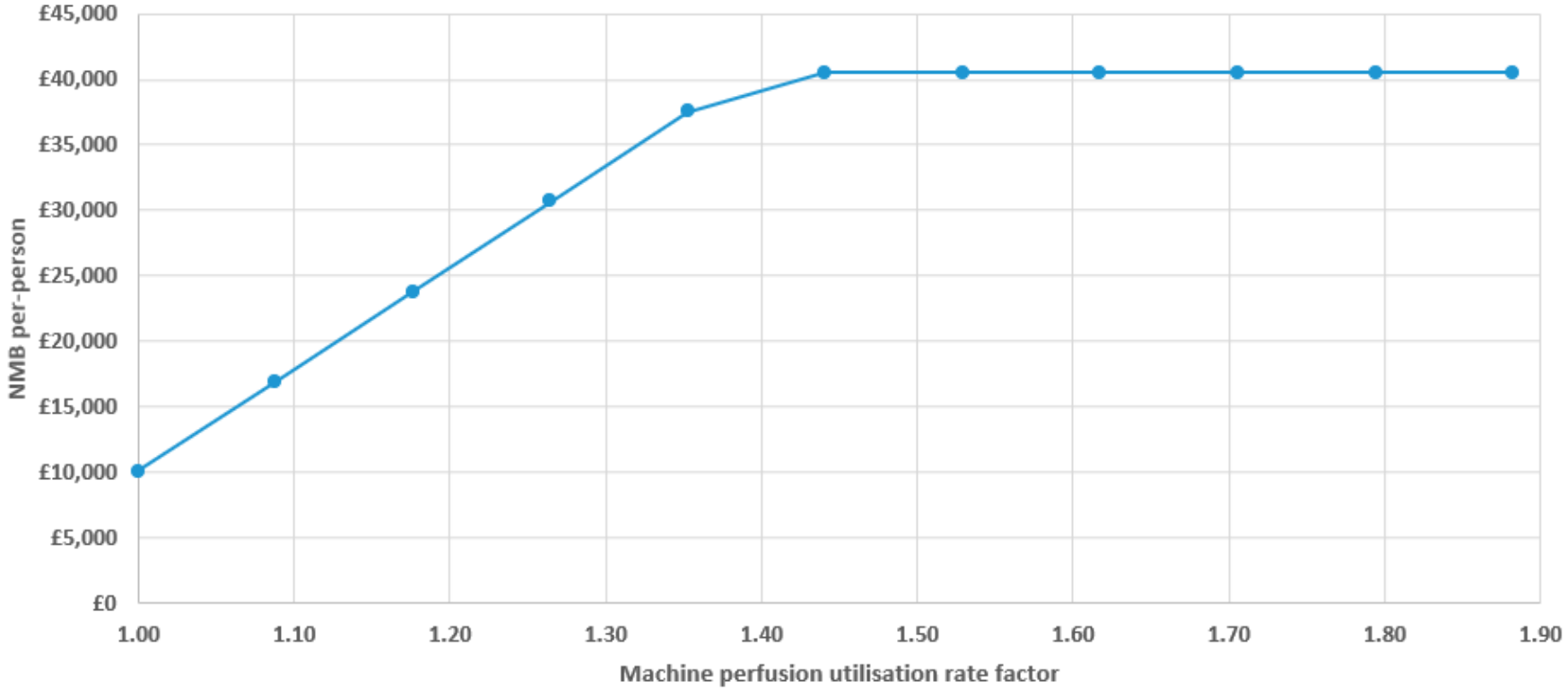

Figure abbreviations: MP, machine perfusion; NMB, net monetary benefit

Figure F.14: Net monetary benefit as machine perfusion organ utilisation factor is varied (Liver Assist; HMP)

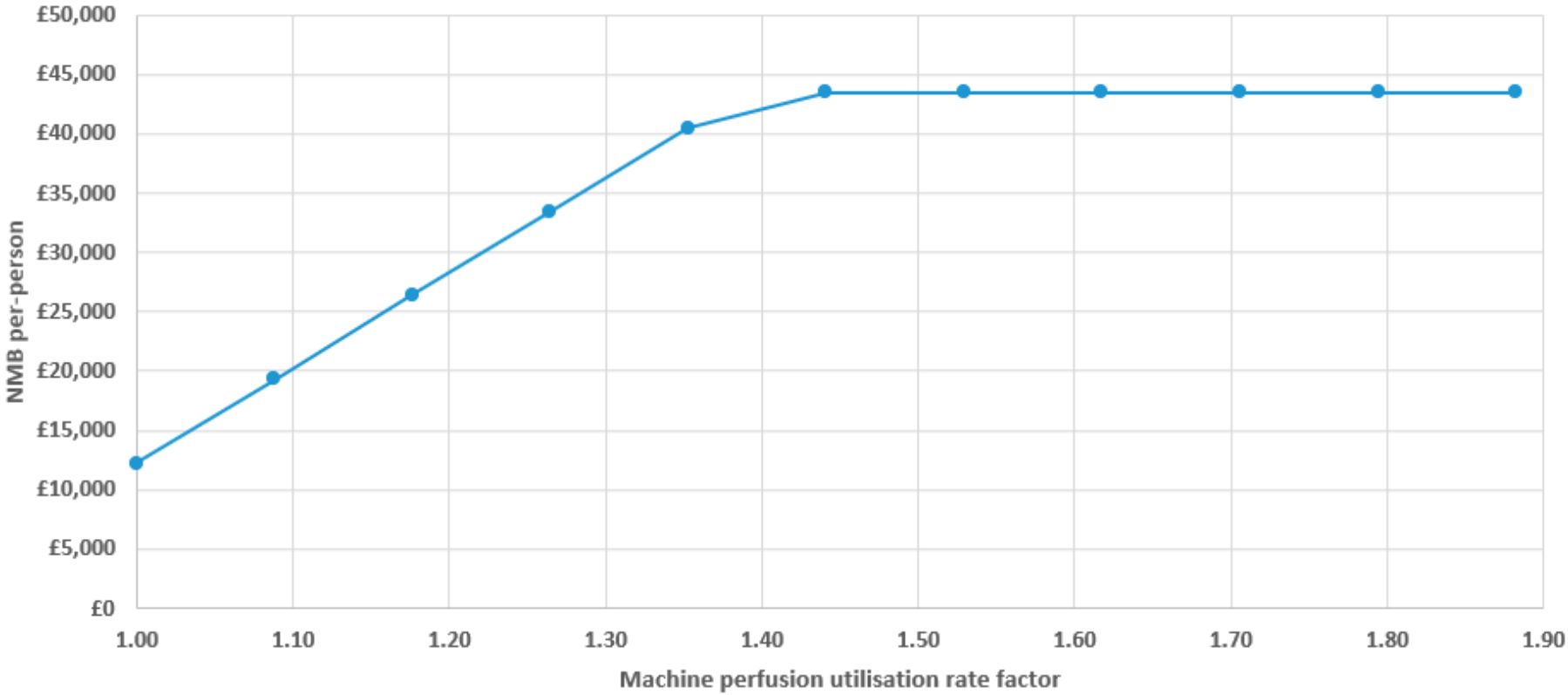

Figure abbreviations: MP, machine perfusion; NMB, net monetary benefit

Figure F.15: Net monetary benefit as machine perfusion organ utilisation factor is varied (*metra*; NMP)

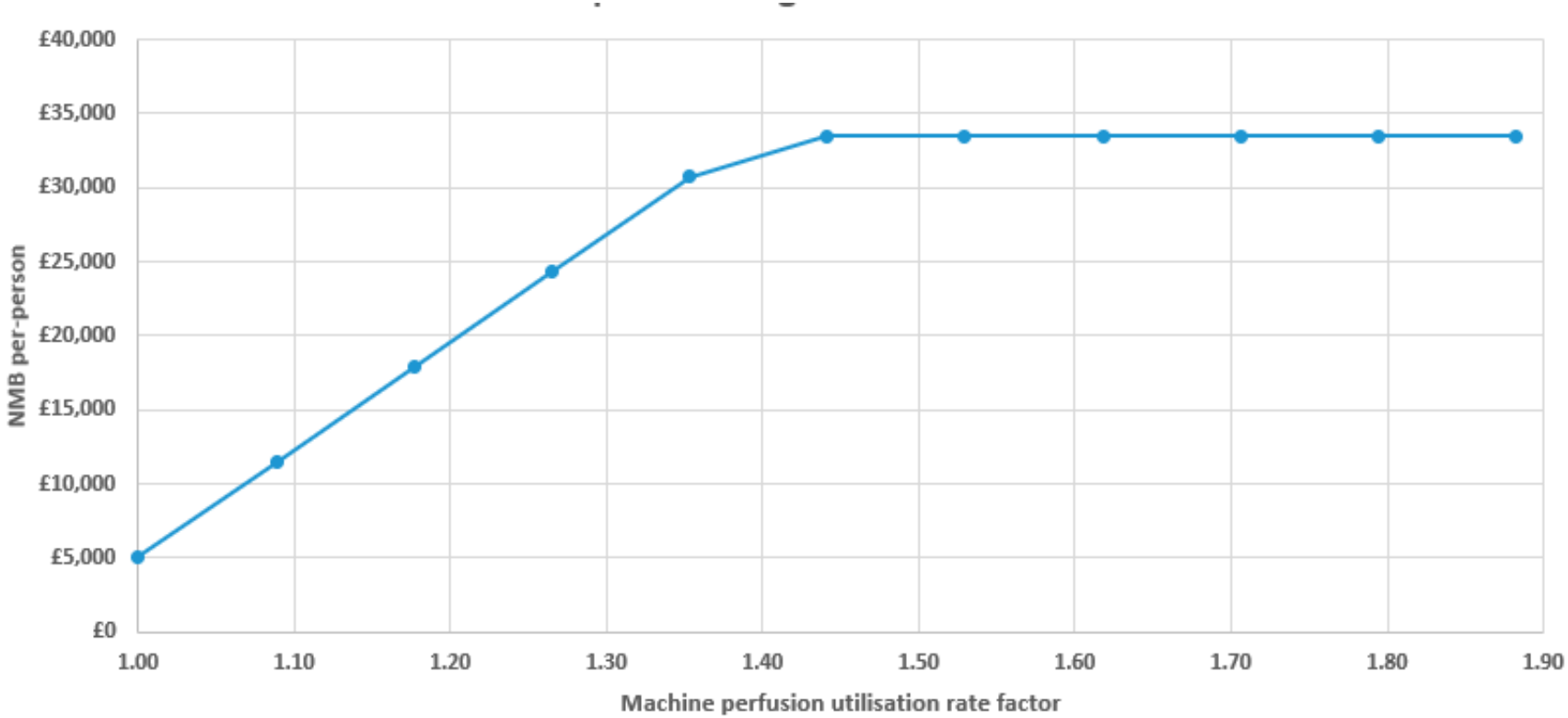

Figure abbreviations: MP, machine perfusion; NMB, net monetary benefit

Figure F.16: Net monetary benefit as machine perfusion organ utilisation factor is varied (VitaSmart; HMP)

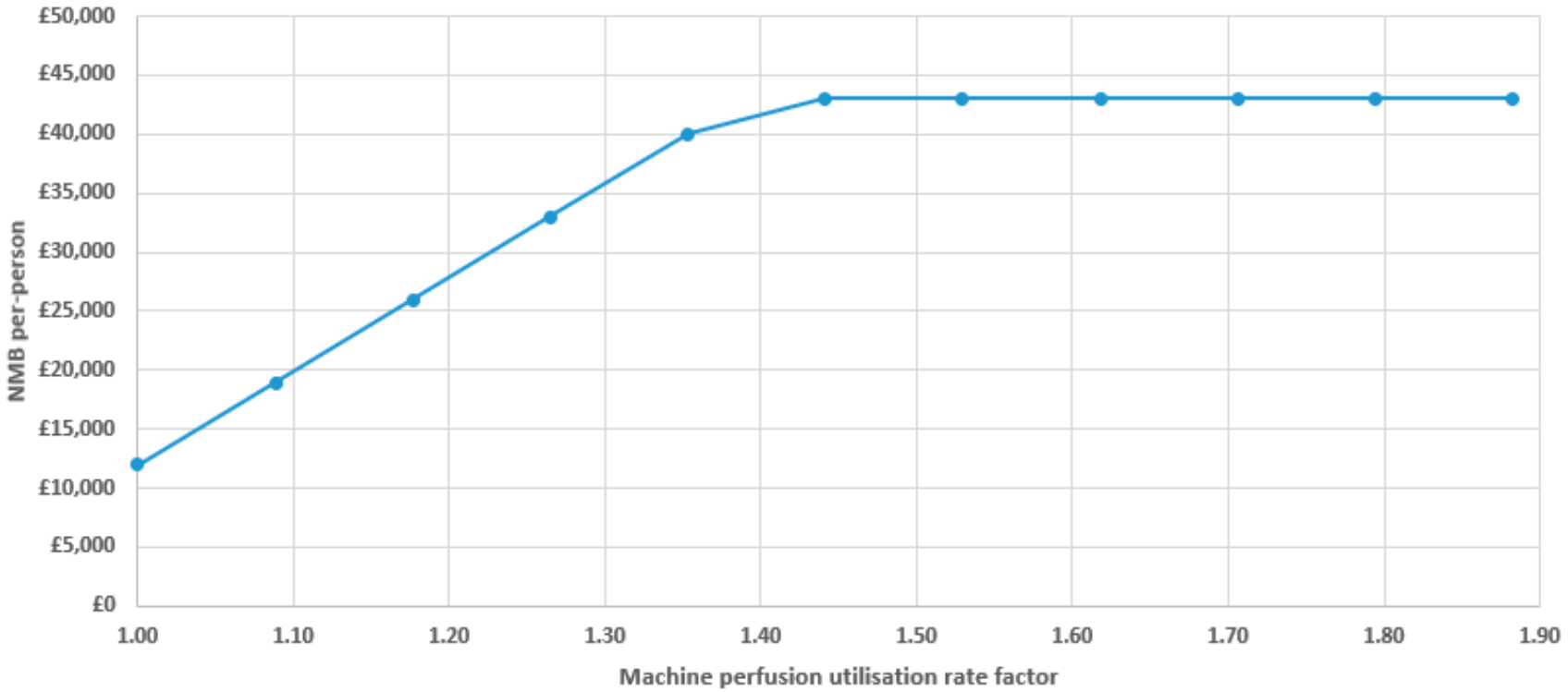

Figure abbreviations: MP, machine perfusion; NMB, net monetary benefit

Table F.26: Net monetary benefit as mortality HRs associated with machine perfusion in DBD and DCD organs are varied (Liver Assist; HMP)

DCD organ MP HRs	DBD organ MP HRs										
	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
0	£23,278	£23,278	£22,976	£22,452	£21,582	£20,718	£19,870	£19,037	£18,219	£17,416	£16,626
0.1	£23,214	£23,214	£22,911	£22,387	£21,518	£20,654	£19,806	£18,973	£18,155	£17,351	£16,562
0.2	£22,673	£22,673	£22,371	£21,847	£20,977	£20,114	£19,265	£18,432	£17,614	£16,811	£16,022
0.3	£21,572	£21,572	£21,269	£20,745	£19,876	£19,012	£18,164	£17,331	£16,513	£15,709	£14,920
0.4	£20,192	£20,192	£19,890	£19,366	£18,496	£17,633	£16,785	£15,952	£15,133	£14,330	£13,541
0.5	£18,842	£18,842	£18,539	£18,015	£17,146	£16,282	£15,434	£14,601	£13,783	£12,979	£12,190
0.6	£17,519	£17,519	£17,217	£16,693	£15,823	£14,960	£14,112	£13,278	£12,460	£11,657	£10,868
0.7	£16,224	£16,224	£15,922	£15,398	£14,528	£13,665	£12,816	£11,983	£11,165	£10,362	£9,573
0.8	£14,956	£14,956	£14,654	£14,130	£13,260	£12,396	£11,548	£10,715	£9,897	£9,093	£8,304
0.9	£13,714	£13,714	£13,412	£12,888	£12,018	£11,154	£10,306	£9,473	£8,655	£7,851	£7,062
1	£12,498	£12,498	£12,195	£11,671	£10,802	£9,938	£9,090	£8,257	£7,439	£6,635	£5,846

Table abbreviations: DBD, donation after brainstem death; DCD, donation after circulatory death; HR, hazard ratio; MP, machine perfusion.

Table F.27: Net monetary benefit as mortality HRs associated with machine perfusion in DBD and DCD organs are varied (Liver Assist; NMP)

DCD organ MP HRs	DBD organ MP HRs										
	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
0	£20,899	£20,899	£20,597	£20,073	£19,204	£18,340	£17,492	£16,660	£15,842	£15,038	£14,250
0.1	£20,834	£20,834	£20,532	£20,008	£19,139	£18,276	£17,428	£16,595	£15,777	£14,974	£14,185
0.2	£20,294	£20,294	£19,992	£19,468	£18,599	£17,736	£16,888	£16,055	£15,237	£14,434	£13,645
0.3	£19,193	£19,193	£18,891	£18,367	£17,498	£16,635	£15,787	£14,954	£14,136	£13,333	£12,544
0.4	£17,815	£17,815	£17,513	£16,989	£16,120	£15,256	£14,409	£13,576	£12,758	£11,955	£11,166
0.5	£16,465	£16,465	£16,163	£15,639	£14,770	£13,907	£13,059	£12,226	£11,408	£10,605	£9,816
0.6	£15,144	£15,144	£14,841	£14,318	£13,448	£12,585	£11,737	£10,904	£10,087	£9,283	£8,494
0.7	£13,850	£13,850	£13,547	£13,023	£12,154	£11,291	£10,443	£9,610	£8,792	£7,989	£7,200
0.8	£12,582	£12,582	£12,280	£11,756	£10,887	£10,023	£9,175	£8,343	£7,525	£6,722	£5,933
0.9	£11,341	£11,341	£11,039	£10,515	£9,646	£8,782	£7,934	£7,102	£6,284	£5,480	£4,692
1	£10,125	£10,125	£9,823	£9,299	£8,430	£7,567	£6,719	£5,886	£5,068	£4,265	£3,476

Table abbreviations: DBD, donation after brainstem death; DCD, donation after circulatory death; HR, hazard ratio; MP, machine perfusion.

Table F.28: Net monetary benefit as mortality HRs associated with machine perfusion in DBD and DCD organs are varied (*metra*; NMP)

DCD organ MP HRs	DBD organ MP HRs										
	0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
0	£15,336	£15,336	£15,035	£14,512	£13,645	£12,784	£11,938	£11,107	£10,291	£9,490	£8,703
0.1	£15,271	£15,271	£14,970	£14,448	£13,581	£12,720	£11,874	£11,043	£10,227	£9,426	£8,639
0.2	£14,734	£14,734	£14,432	£13,910	£13,043	£12,182	£11,336	£10,505	£9,689	£8,888	£8,101
0.3	£13,636	£13,636	£13,335	£12,812	£11,945	£11,084	£10,238	£9,407	£8,591	£7,790	£7,003
0.4	£12,261	£12,261	£11,960	£11,437	£10,570	£9,709	£8,863	£8,032	£7,216	£6,415	£5,628
0.5	£10,914	£10,914	£10,613	£10,091	£9,224	£8,362	£7,516	£6,686	£5,870	£5,068	£4,281
0.6	£9,596	£9,596	£9,295	£8,773	£7,905	£7,044	£6,198	£5,367	£4,551	£3,750	£2,963
0.7	£8,305	£8,305	£8,004	£7,481	£6,614	£5,753	£4,907	£4,076	£3,260	£2,459	£1,672
0.8	£7,040	£7,040	£6,739	£6,217	£5,350	£4,488	£3,643	£2,812	£1,996	£1,194	£407
0.9	£5,802	£5,802	£5,501	£4,979	£4,112	£3,250	£2,404	£1,574	£758	-£44	-£831
1	£4,590	£4,590	£4,289	£3,767	£2,899	£2,038	£1,192	£361	-£455	-£1,256	-£2,043

Table abbreviations: DBD, donation after brainstem death; DCD, donation after circulatory death; HR, hazard ratio; MP, machine perfusion.

Table F.29: Net monetary benefit as mortality HRs associated with machine perfusion in DBD and DCD organs are varied (VitaSmart; HMP)

DCD organ MP HRs	DBD organ MP HRs										
	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
0	£22,906	£22,906	£22,603	£22,079	£21,210	£20,346	£19,498	£18,665	£17,847	£17,043	£16,254
0.1	£22,841	£22,841	£22,539	£22,015	£21,145	£20,282	£19,433	£18,600	£17,782	£16,978	£16,189
0.2	£22,301	£22,301	£21,998	£21,474	£20,605	£19,741	£18,893	£18,060	£17,242	£16,438	£15,649
0.3	£21,199	£21,199	£20,897	£20,373	£19,503	£18,639	£17,791	£16,958	£16,140	£15,336	£14,547
0.4	£19,820	£19,820	£19,518	£18,994	£18,124	£17,260	£16,412	£15,579	£14,761	£13,957	£13,168
0.5	£18,469	£18,469	£18,167	£17,643	£16,773	£15,910	£15,061	£14,228	£13,410	£12,607	£11,817
0.6	£17,147	£17,147	£16,844	£16,320	£15,451	£14,587	£13,739	£12,906	£12,088	£11,284	£10,495
0.7	£15,852	£15,852	£15,549	£15,025	£14,156	£13,292	£12,444	£11,611	£10,793	£9,989	£9,200
0.8	£14,583	£14,583	£14,281	£13,757	£12,887	£12,024	£11,176	£10,342	£9,524	£8,721	£7,932
0.9	£13,341	£13,341	£13,039	£12,515	£11,645	£10,782	£9,933	£9,100	£8,282	£7,479	£6,690
1	£12,125	£12,125	£11,823	£11,299	£10,429	£9,565	£8,717	£7,884	£7,066	£6,262	£5,473

Table abbreviations: DBD, donation after brainstem death; DCD, donation after circulatory death; HR, hazard ratio; MP, machine perfusion.

Table F.30: Net monetary benefit as re-transplantation RRs associated with machine perfusion in year 1 and year 2 to 5 are varied (Liver Assist; NMP)

5-year re-transplantation RR	1-year re-transplantation RR										
	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
0	£22,639	£22,552	£22,464	£22,376	£22,287	£22,198	£22,108	£22,018	£21,927	£21,835	£21,743
0.1	£22,122	£22,036	£21,950	£21,863	£21,775	£21,687	£21,598	£21,509	£21,419	£21,328	£21,237
0.2	£21,604	£21,519	£21,433	£21,347	£21,261	£21,174	£21,086	£20,998	£20,909	£20,820	£20,730
0.3	£21,083	£20,999	£20,915	£20,830	£20,744	£20,658	£20,572	£20,485	£20,397	£20,309	£20,220
0.4	£20,560	£20,478	£20,394	£20,310	£20,226	£20,141	£20,056	£19,970	£19,883	£19,796	£19,708
0.5	£20,035	£19,953	£19,871	£19,788	£19,705	£19,621	£19,537	£19,452	£19,367	£19,281	£19,194
0.6	£19,508	£19,427	£19,346	£19,264	£19,182	£19,099	£19,016	£18,932	£18,848	£18,763	£18,678
0.7	£18,978	£18,898	£18,818	£18,738	£18,656	£18,575	£18,493	£18,410	£18,327	£18,243	£18,159
0.8	£18,446	£18,367	£18,288	£18,209	£18,129	£18,048	£17,967	£17,886	£17,803	£17,721	£17,638
0.9	£17,911	£17,833	£17,755	£17,677	£17,598	£17,519	£17,439	£17,359	£17,278	£17,196	£17,114
1	£17,373	£17,297	£17,220	£17,143	£17,065	£16,987	£16,908	£16,829	£16,749	£16,669	£16,588

Table abbreviations: RR, relative risk.

Table F.31 Net monetary benefit as re-transplantation RRs associated with machine perfusion in year 1 and year 2 to 5 are varied (Liver Assist; HMP)

5-year re-transplantation RR	1-year re-transplantation RR										
	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
0	£25,027	£24,940	£24,852	£24,764	£24,675	£24,585	£24,495	£24,405	£24,314	£24,222	£24,129
0.1	£24,510	£24,424	£24,337	£24,250	£24,162	£24,073	£23,984	£23,895	£23,805	£23,714	£23,623
0.2	£23,990	£23,905	£23,819	£23,733	£23,646	£23,559	£23,471	£23,383	£23,294	£23,204	£23,114
0.3	£23,468	£23,384	£23,300	£23,214	£23,129	£23,043	£22,956	£22,868	£22,781	£22,692	£22,603
0.4	£22,944	£22,861	£22,778	£22,694	£22,609	£22,524	£22,438	£22,352	£22,265	£22,178	£22,090
0.5	£22,418	£22,336	£22,253	£22,170	£22,087	£22,003	£21,918	£21,833	£21,748	£21,661	£21,575
0.6	£21,889	£21,808	£21,727	£21,645	£21,563	£21,480	£21,396	£21,312	£21,228	£21,143	£21,057
0.7	£21,358	£21,278	£21,198	£21,117	£21,036	£20,954	£20,872	£20,789	£20,705	£20,622	£20,537
0.8	£20,824	£20,746	£20,666	£20,587	£20,507	£20,426	£20,345	£20,263	£20,181	£20,098	£20,015
0.9	£20,288	£20,211	£20,133	£20,054	£19,975	£19,895	£19,815	£19,735	£19,654	£19,572	£19,490
1	£19,750	£19,673	£19,596	£19,519	£19,441	£19,362	£19,284	£19,204	£19,124	£19,044	£18,963

Table abbreviations: RR, relative risk.

Table F.32 Net monetary benefit as re-transplantation RRs associated with machine perfusion in year 1 and year 2 to 5 are varied (*metra*; NMP)

5-year re-transplantation RR	1-year re-transplantation RR										
	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
0	£17,555	£17,457	£17,358	£17,258	£17,158	£17,057	£16,956	£16,854	£16,751	£16,647	£16,543
0.1	£16,989	£16,892	£16,794	£16,696	£16,597	£16,497	£16,397	£16,296	£16,195	£16,092	£15,990
0.2	£16,421	£16,325	£16,229	£16,131	£16,033	£15,935	£15,836	£15,736	£15,636	£15,535	£15,433
0.3	£15,851	£15,756	£15,660	£15,564	£15,468	£15,370	£15,273	£15,174	£15,075	£14,975	£14,875
0.4	£15,278	£15,184	£15,090	£14,995	£14,899	£14,803	£14,707	£14,609	£14,512	£14,413	£14,314
0.5	£14,703	£14,610	£14,517	£14,423	£14,329	£14,234	£14,138	£14,042	£13,946	£13,849	£13,751
0.6	£14,125	£14,033	£13,941	£13,849	£13,756	£13,662	£13,568	£13,473	£13,377	£13,281	£13,185
0.7	£13,544	£13,454	£13,363	£13,272	£13,180	£13,087	£12,994	£12,901	£12,807	£12,712	£12,616
0.8	£12,961	£12,872	£12,782	£12,692	£12,601	£12,510	£12,418	£12,326	£12,233	£12,140	£12,045
0.9	£12,375	£12,287	£12,198	£12,110	£12,020	£11,930	£11,840	£11,749	£11,657	£11,565	£11,472
1	£11,786	£11,699	£11,612	£11,524	£11,436	£11,347	£11,258	£11,168	£11,078	£10,987	£10,895

Table abbreviations: RR, relative risk.

Table F.33 Net monetary benefit as re-transplantation RRs associated with machine perfusion in year 1 and year 2 to 5 are varied (VitaSmart; HMP)

5-year re-transplantation RR	1-year re-transplantation RR										
	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
0	£24,647	£24,560	£24,473	£24,384	£24,296	£24,206	£24,116	£24,026	£23,935	£23,843	£23,751
0.1	£24,131	£24,045	£23,958	£23,871	£23,783	£23,695	£23,606	£23,517	£23,427	£23,336	£23,245
0.2	£23,612	£23,527	£23,441	£23,355	£23,269	£23,181	£23,094	£23,006	£22,917	£22,827	£22,737
0.3	£23,091	£23,007	£22,922	£22,837	£22,752	£22,666	£22,579	£22,492	£22,404	£22,316	£22,227
0.4	£22,567	£22,484	£22,401	£22,317	£22,233	£22,148	£22,062	£21,976	£21,890	£21,803	£21,715
0.5	£22,042	£21,960	£21,878	£21,795	£21,712	£21,628	£21,543	£21,458	£21,373	£21,287	£21,200
0.6	£21,514	£21,433	£21,352	£21,270	£21,188	£21,105	£21,022	£20,938	£20,854	£20,769	£20,684
0.7	£20,984	£20,904	£20,824	£20,743	£20,662	£20,580	£20,498	£20,416	£20,332	£20,249	£20,164
0.8	£20,451	£20,372	£20,293	£20,214	£20,134	£20,053	£19,972	£19,891	£19,809	£19,726	£19,643
0.9	£19,916	£19,838	£19,760	£19,682	£19,603	£19,524	£19,444	£19,363	£19,282	£19,201	£19,119
1	£19,378	£19,301	£19,225	£19,147	£19,070	£18,991	£18,913	£18,833	£18,754	£18,673	£18,593

Table abbreviations: RR, relative risk.

9.7 Appendix G Description of key studies in the evidence base

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
Liver Assist (XVIVO Perfusion AB)				
Primary publication: van Rijn et al 2021 (van Rijn et al. 2021c) **Design:** RCT **Location:** Belgium; UK; Netherlands **Status of study:** Published **Associated records**: Robert J. Porte (clinical trial registry record) (Robert J. Porte 2015) van Rijn et al 2021 (conference abstract) (Van Rijn et al. 2021a) van Rijn et al 2021 (conference	160 adult (>18 years) liver transplant recipients were randomised; 4 (1 NMP, 3 SCS) had procedures cancelled (3 livers were declined and 1 recipient had an infection preventing transplant) and were not included in the analysis. **Liver Assist:** 78 **Recipient age (years, median IQR):** 60 (52 to 65) **Recipient male gender n (%):** 55 (71) **Recipient Laboratory MELD score** (median IQR): 14 (10 to 19) **Reason for transplant:** NR **Donor age (years, median IQR)**: 52 (43 to 57) **Donor male gender**: 52 (67) **Donor DRI (median IQR)**: 2.12 (1.84 to 2.38) **SCS**: 78 **Age (years, median IQR**): 60 (52 to	**Intervention**: Liver Assist **Comparator**: Standard cold storage **Hypothermic/Normothermic**: Hypothermic **Single/dual perfusion**: Dual **Pathway**: Perfusion initiated at the recipient centre **DCD/DBD**: DCD **ECD**: Yes (all DCD) **Extended perfusion**: None **GREEN**	Overall survival Graft survival Re-transplantation Biliary complications PNF HAT PRS EAD Post-operative requirement for renal replacement Mechanical failure of deice Serious adverse events Costs Statistical methods: Primary endpoint (non-anastomotic biliary stricture) analysed with Chi-square test as well as	Population: Adult patients undergoing liver transplant, relevant to decision problem **GREEN** Intervention: Machine perfusion using a device relevant to decision problem **GREEN** Outcomes: Reported outcomes relevant to decision problem **GREEN** Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem **GREEN** Authors report that while adequate to detect differences in the primary outcomes (non-

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
abstract) (van Rijn et al. 2021b) van Rijn et al 2019 (protocol) (van Rijn et al. 2019) van Rijn et al 2025 (van Rijn et al. 2025) (long term 5 year results paper) **GREEN**	65) **Male gender n** (%): 52 (67) **MELD score (median IQR**): 16 (10 to 22) **Reason for transplant**: NR **Donor age (years, median IQR)**: 49 (37 to 59) **Donor male gender**: 51 (65) **Donor DRI (median IQR)**: 2.12 (1.86 to 2.42) **Subgroups:** NR **GREEN**		log-binomial regression model with risk ratios Secondary binary end points were assessed by means of a chi-square test or log-binomial regression to adjust for stratification factors Time-to-event outcomes analysed with Kaplan Meier curves with log-rank test and Cox proportional hazards regression model with HR. Continuous outcomes compared with independent Student's t-test No adjustment for multiplicity in analyses of secondary endpoints Prespecified covariates included stratification factors	anastomotic biliary strictures), the sample size is inadequate to detect significant differences in overall survival and graft survival as events are rare in these outcomes. Randomisation was stratified for primary sclerosing cholangitis as an indiciation, though the rate was higher in the SCS arm (LiverAssist 7/78 vs SCS 13/78).

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
			(trial site and primary sclerosing cholangitis) and donor-specific risk factors (donor risk index and donor warm-ischemia time, defined as the time period between circulatory arrest and in situ cold flush-out in the donor).	
Primary publication: Czigany et al 2021 (Czigany et al. 2021) **Design:** RCT **Location:** Czech Republic; Germany **Status of study:** Published **Associated records**: University Hospital Aachen 2017 (University Hospital Aachen	**Liver Assist:** 23 **Recipient age (years, median IQR):** 60 (52 to 64) **Recipient male gender n (%):** 18 (78%) **Recipient Laboratory MELD score** (median IQR): 13 (9 to 18) **Reason for transplant:** Alcohol-related cirrhosis 4 (17); Viral hepatitis 3 (13); hepatocellular carcinoma in cirrhosis 11 (48); primary biliary/sclerosing cholangitis 1 (4); other 4 (17). **Donor age (years, median IQR)**: 73 (60 to 78) **Donor male gender**: 12 (52) **Donor DRI (median IQR)**: 2.08	**Intervention:** Liver Assist **Comparator:** Standard cold storage **Hypothermic/Normothermic**: Hypothermic **Single/dual perfusion**: Single (portal vein) **Pathway:** Perfusion initiated at the recipient centre **DCD/DBD:** DBD **ECD**: Yes, based on recommendations of the German Medical Chamber (donors 65 years of age and older, intensive care therapy of the donor was required before donation for at least 7 days,	Renal replacement, EAD, survival, graft survival, aminotransferase levels, serious adverse events, mortality Statistical methods: Patient/graft survival: Kaplan-Meier estimates of survival and log-rank p value (patients yet to complete 1 year follow up were censored at	Population: Adult patients undergoing liver transplant, relevant to decision problem **GREEN** Intervention: Machine perfusion using a device relevant to decision problem **GREEN** Outcomes: Reported outcomes relevant to decision problem **GREEN** Setting: Perfusion initiated at the recipient centre pathway,

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
2017) (clinical trial registry record) Czigany et al 2024 (long term outcome data) (Czigany et al. 2024) GREEN	(1.910 to 2.210) **SCS**: 23 **Recipient age (years, median IQR)**: 63 (56 to 67) **Recipient male gender n(%):** 20 (87) **Recipient MELD score (median IQR):** 17 (8 to 25) **Reason for transplant:** Alcohol-related cirrhosis 7 (31); viral hepatitis 0 (0); hepatocellular carcinoma in cirrhosis 9 (39); primary biliary/sclerosing cholangitis 1 (4); other 6 (26). **Donor age (years, median IQR)**: 71 (59 to 78) **Donor male gender**: 13 (56) **Donor DRI (median IQR)**: 1.96 (1.83 to 2.24) **Subgroups:** NR GREEN	obesity of the donor with a body mass index >30kg/m², fatty liver (with histology) >40%, serum sodium >165mmol/L, serum AST or ALT >3 times the upper limits of normal, serum bilirubin>2mg/dL) **Extended perfusion**: NR GREEN	last study visit at 6 months, n=4).	relevant to decision problem GREEN Authors note that a number of patients in all participating hospitals were not assessed for eligibility, mostly due to limited availability of perfusion staff and logistics; this also resulted in prolonged interval for recruitment into the trial. Authors also observe that national allocation policies had an indirect selection effect, resulting in a higher donor risk status in the trial when compared to other liver perfusion trials (e.g. average DRI of 2.05 vs 1.71 in Nasralla et al 2018 (Nasralla et al. 2018)
Primary publication: Minor et al 2021	**Liver Assist:** 20 **Recipient age (years, median IQR):** Mean 57.50 (SD 6.97)	**Intervention**: Liver Assist **Comparator**: SCS **Hypothermic/Normothermic**:	Aminotransferase levels EAD	Population: Adult patients undergoing liver transplant, relevant

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
(Minor et al. 2022) **Design:** RCT **Location:** France **Status of study:** Published **Associated records**: University Hospital Duisberg-Essen 2018 (University Hospital Duisberg-Essen 2018) (clinical trial registry record) Minor at al 2023 (conference abstract) (Minor et al. 2023) GREEN	**Recipient male gender n (%):** 14 (70%) **Recipient Laboratory MELD score** (median IQR): Mean 16.2 (SD 8.3) **Reason for transplant:** viral hepatitis 3 (15); cholestatic disease 3 (15); alcohol-related steatohepatitis 3 (15); non-alcohol-related steatohepatitis 3 (15); other 8 (40). **Donor age (years, median IQR)**: Mean 63.65 (SD 12.75) **Donor male gender**: 9 (45%) **Donor DRI (median IQR)**: Mean 1.8 (SD 0.31) **SCS**: 20 **Recipient age (years, median IQR):** Mean 48.65 (SD 14.47) **Recipient male gender n(%):** 15 (75%) **Recipient MELD score (median IQR): Mean** 18.7 (SD 8.12) **Reason for transplant:** viral hepatitis 4 (20); cholestatic disease 5 (25); alcohol-related steatohepatitis 3 (15); non-alcohol-related steatohepatitis 1 (5); other 7 (35).	Hypothermic with controlled re-warming **Single/dual perfusion**: Dual **Pathway**: Perfusion initiated at the recipient centre; controlled oxygenated re-warming prior to surgery **DCD/DBD**: DBD **ECD:** Donor livers fulfilling the extended criteria as defined by the German Medical Chamber (at least one of: age >65 years; intensive therapy including assisted ventilation >7 days; obesity of donor [BMI >30]; serum sodium >165Mol/L; aspartate aminotransferase or alanine aminotransferase >3x of normal; serum bilirubin >3mg/dl; liver steatosis [histologically proven] >40%) **Extended perfusion**: NR	Adverse events ICU stay Statistical methods: Aminotransferase levels were analysed with two-sided exact Mann–Whitney U test (a nonparametric procedure was used due to this data being highly skewed). Secondary end points were analysed with Mann– Whitney U test for independent categorial variables and Fisher's exact test for categorial variables. Secondary analyses were not adjusted for multiplicity.	to decision problem GREEN Intervention: Machine perfusion using a device relevant to decision problem GREEN Outcomes: Reported outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN Pilot study with limited sample size (though met target size to detect difference in AST levels with 80% power).

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
	Donor age (years, median IQR): Mean 63.50 (SD 16.18) **Donor male gender**: 5 (25%) **Donor DRI (median IQR)**: Mean 1.9 (SD 0.29) **Subgroups:** NR			
Primary publication: Lesurtel, 2025 (Lesurtel et al. 2025) **Design:** RCT **Location:** France **Status of study:** Unpublished (preprint) **Associated records**: Pradat et al 2023 (protocol) (Pradat et al. 2023) Lesurtel et al 2024 (conference abstract, no further results) (Lesurtel et al. 2024)	**Liver Assist:** 131 **Recipient age (years, median IQR):** 60 (53 to 65) **Recipient male gender n (%):** 80.9% **Recipient Laboratory MELD score** (median IQR): 17 (11 to 23) **Reason for transplant:** hepatitis B virus 13 (9.9); hepatitis C virus 18 (13.7); alcohol 86 (65.6); non-alcohol-related steatohepatitis 28 (21.4); autoimmune hepatitis 2 (1.5); other 0 (0.0) **Donor age (years, median IQR)**: 68 (57 to 76) **Donor male gender**: 58.8% **Donor DRI (median IQR)**: 1.70 (1.43 to 1.89) **SCS**: 131 **Recipient age (years, median IQR):** 60 (54 to 65)	**Intervention:** Liver Assist **Comparator:** SCS **Hypothermic/normothermic**: Hypothermic **Single/dual perfusion:** Single (portal vein) **Pathway**: Perfusion initiated at the recipient centre **DCD/DBD**: DBD **ECD**: Yes, defined as the presence of at least 1 of the following published criteria: donor age >65 years, ICU stay >7 days, body mass index >30 kg/m2, proven biopsy macro-steatosis ≥30%, natremia >155 mmol/L at any time, serum aspartate aminotransferase (AST) levels >150 IU/L at any time, and serum alanine aminotransferase (ALT) levels	Overall survival Graft survival Re-transplantation PNF Hepatic thrombosis PRS EAD Aminotransferase levels SAEs Mortality Statistical methods: Categorical variables were compared between study arms using the chi-square test or the Fisher exact test. Continuous variables were compared using the Student t-test in the	Population: Adult patients undergoing liver transplant, relevant to decision problem **GREEN** Intervention: Machine perfusion using a device relevant to decision problem **GREEN** Outcomes: Reported outcomes relevant to decision problem **GREEN** Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem **GREEN** A centre effect on outcomes cannot be

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
Hospices Civils de Lyon 2025 (clinical trial registration) (Hospices Civils de Lyon 2019) GREEN	**Recipient male gender n(%):** 80.2% **Recipient Laboratory MELD score (median IQR):** 14 (9 to 22) **Reason for transplant:** hepatitis B virus 7 (5.3); hepatitis C virus 13 (9.9); alcohol 86 (65.6); non-alcohol-related steatohepatitis 27 (20.6); autoimmune hepatitis 1 (0.8); other 2 (1.5) **Donor age (years, median IQR)**: 70 (55 to 76) **Donor male gender**: 55% **Donor DRI (median IQR)**: 1.76 (1.38 to 1.90) **Subgroups:** NR GREEN	>170 IU/L at any time **Extended perfusion**: NR GREEN	case of normal distribution or the Mann-Whitney U-test otherwise. Normality was tested using the Shapiro-Wilk test. Graft and patient survival were estimated using the Kaplan-Meier method and survival curves were compared using the log-rank test. A Cox proportional hazard model was used to assess the effect of HOPE (vs control) on survival.	ruled out since the volume of liver transplants was heterogeneous among centres.
Primary publication: Ghinolfi et al, 2019 (Ghinolfi et al. 2019) **Design:** RCT **Location:** Italy **Status of study:** Published **Associated**	**Liver Assist** 10 **Recipient age (years, median IQR):** 57 (46 to 61) **Recipient male gender n(%):** 9 (90) **Recipient laboratory MELD score (median IQR):** 12.5 (9 to 16) (D-MELD 1016 (711 to 1392)) **Reason for transplant:** Hepatitis C virus 6 (60); hepatocellular	**Intervention**: Liver Assist **Comparator**: Cold storage **Hypothermic/normothermic**: Normothermic **Single/dual perfusion**: Dual **Pathway**: Perfusion initiated at the recipient centre (grafts were stored at 4°C and shipped to institution for back-table preparation)	Graft survival, patient survival, transaminases, biliary complications Statistical methods: The 2-tailed Student t test was used to compare continuous variables	Population: Adult patients undergoing liver transplant, relevant to decision problem GREEN Intervention: Machine perfusion using a device relevant to decision problem GREEN

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
records: (Ghinolfi et al. 2017) (conference abstract) Ghinolfi et al 2018 (conference abstract) (Ghinolfi et al. 2018) University Hospital of Pisa (clinical trial registry record) (Azienda Ospedaliero 2016) GREEN	carcinoma 2 (20); hepatitis b virus 3 (30); alcohol-related cirrhosis 2 (20); biliary cirrhosis 1 (10), other 1 (10) **Donor age (years, median IQR)**: 81 (77.5 to 87.2) **Donor male gender**: 7 (70) **Donor DRI (median IQR)**: NR **Cold storage** 10 **Recipient age (years, median IQR):** 55 (43 to 61) **Recipient male gender n (%):** 8 (80) **Recipient MELD score (median IQR):** 9.5 (8 to 15). (D-MELD 778.5 (637 to 1200)) **Reason for transplant: Hepatitis C virus** 3 (30); hepatocellular carcinoma 6 (60); hepatitis b virus 5 (50); alcohol-related cirrhosis 3 (30); other 2 (20) **Donor age (years, median IQR)**: 80 (72 to 87.2) **Donor male gender**: 3 (30) **Donor DRI (median IQR)**: NR **Subgroups:** NR GREEN	**DCD/DBD:** DBD **ECD:** Yes, aged ≥70 years **Extended perfusion**: NR GREEN	across independent samples and paired data 2-proportion z test was used to compare categorical variables	Outcomes: Reported outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN This LiverAssist study uses normothermic perfusion and provides the only RCT evidence on normothermic perfusion in the review.

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
Primary publication: Grat et al, 2023 (Grat et al. 2023) **Design:** RCT **Location:** Poland **Status of study:** Published **Associated records**: (Medical University of Warsaw 2021) (Clinical trial record) Zhylko et al 2025 (Biomarker outcomes) (Zhylko et al. 2025) Morawski et al 2024 (2 year follow-up data) (Morawski et al. 2024) GREEN	**Liver Assist:** 26 **Recipient age (years, median IQR):** 46 (39 to 62) **Recipient male gender n(%):** 18 (69.2) **Recipient MELD score** (median IQR): 12 (8 to 21) **Reason for transplant:** hepatitis C 5 (19.2); hepatitis B 1 (3.8); alcohol-related liver disease 6 (23.1); autoimmune hepatitis 3 (11.5); primary sclerosing cholangitis 6 (23.1); primary biliary cirrhosis 1 (3.8); non-alcohol-related steatohepatitis 1 (3.8); hepatocellular carcinoma 5 (19.2) **Donor age (years, median IQR)**: 53 (40 to 60) **Donor male gender**: NR **Donor DRI (median IQR)**: 1.74 (1.41 to 1.98) **Cold storage**: 78 **Recipient age (years, median IQR):** 51 (41 to 60) **Recipient male gender n(%):** 50 (64.1) **Recipient MELD score (median IQR):** 14 (10 to 21)	**Intervention**: Liver Assist **Comparator**: SCS **Hypothermic/normothermic:** Hypothermic **Single/dual perfusion**: Dual **Pathway**: Perfusion initiated at the recipient centre (liver grafts were procured following the standard procurement protocol, including a cold in situ flush; upon arrival at the transplant centre, livers underwent final assessments to determine suitability for transplantation) **ECD**: Liver Assist: 17 (65.4%) SCS: 39 (50%) **DCD/DBD:** DBD **Extended perfusion**: Perfusion was prolonged due to ongoing hepatectomy in 12 patients (46.2%) up to 135 to 220 minutes GREEN	Patient and graft survival Biliary complications Graft function 90-day complications Post reperfusion syndrome	Population: Adult patients undergoing liver transplant, relevant to decision problem GREEN Intervention: Machine perfusion using a device relevant to decision problem GREEN Outcomes: Reported outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN Uneven numbers of patients between groups (78 in SCS group and 26 in Liver Assist. The Liver Assist group also had a significantly higher donor BMI and lower Child Turcotte-Pugh

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
	Reason for transplant: hepatitis C 12 (15.4); hepatitis B 14 (17.9); alcohol-related liver disease 18 (23.1); autoimmune hepatitis 11 (14.1); primary sclerosing cholangitis 13 (16.7); primary biliary cirrhosis 4 (5.1); non-alcohol-related steatohepatitis 3 (3.8); hepatocellular carcinoma 11 (14.1) **Donor age (years, median IQR)**: 44 (35 to 56) **Donor male gender**: NR **Donor DRI (median IQR)**: 1.52 (1.26 to 1.79) **Subgroups:** NR GREEN			class and in the high DRI subgroup Liver Assist patients had significantly higher BMI (though this would bias results in favour of SCS). The study was adequately powered for primary and not for secondary outcome measures.
Primary publication: Schlegel et al, 2023 (Schlegel et al. 2023) **Design:** RCT **Location:** UK, Belgium, Netherlands, France, Austria, Switzerland	**Liver Assist:** 85 **Recipient age (years, median IQR):** 60 (51 to 64) **Recipient male gender n(%):** 55 (64.7) **Recipient MELD score** (median IQR): 20 (11 to 28) **Reason for transplant:** Acute liver failure 0; Cirrhosis Child-Pugh A 26 (30.6); Cirrhosis Child-Pugh B,C 43 (50.6); Other 16 (18.8)	**Intervention:** Liver Assist **Comparator:** Cold storage **Hypothermic/normothermic**: Hypothermic **Single/dual perfusion**: Single (portal vein) **Pathway**: Perfusion initiated at the recipient centre **DCD/DBD:** DBD **ECD**: NR **Extended perfusion**: NR	Post operative complications Aminotransferase Biliary complications Patient survival Graft survival Statistical methods: Primary outcomes (SAEs) analysed by generalized linear	Population: Adult patients undergoing liver transplant, relevant to decision problem GREEN Intervention: Machine perfusion using a device relevant to decision problem GREEN Outcomes: Reported

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
Status of study: Published **Associated records**: University of Zurich 2011 (clinical trial registry record) (University of Zurich 2011) GREEN	**Donor age (years, median IQR)**: 59 (48 to 72) **Donor male gender n (%)**: 45 (52.9) **Donor DRI (median IQR)**: NR **Cold storage**: 85 **Recipient age (years, median IQR):** 7 (49 to 64) **Recipient male gender n (%):** 67 (78.8) **Recipient MELD score (median IQR):** 19 (12 to 26) **Reason for transplant:** Acute liver failure 1 (1.2); Cirrhosis Child-Pugh A 23 (27.1); Cirrhosis Child-Pugh B,C 50 (58.8); Other 11 (12.9) **Donor age (years, median IQR)**: 62 (44 to 71) **Donor male gender**: 43 (50.6) **Donor DRI (median IQR)**: NR **Subgroups:** NR GREEN	GREEN	model with binomial error and logit link and treatment as an explanatory variable to estimate an odds ratio with 95% CIs. Two pre-specified sensitivity analyses were performed: in sensitivity analysis 1 a generalized linear mixed-effects model, with a random intercept for centre, for which the randomization was stratified; sensitivity analysis 2 added covariates (MELD score, cold storage time, recipient and donor age, previous transplantation) as fixed exploratory variables - due to some missing data in these variables, multiple imputation (50 imputations) was	outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN There are some differences in baseline characteristics between groups such as liver weight, cold storage time, proportion of female participants and reasons for transplant. Modified intention to treat population, as only 170/177 recipients were actually transplanted (though this is only 3.9%, and similar across groups).

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
			used. Results were pooled according to Rubin's rules. Secondary outcome (comprehensive complication index) was compared between groups by a linear regression model with treatment as an explanatory variable. The same two sensitivity analyses were performed as described for the primary outcome but using a linear mixed-effects model instead of a generalized linear mixed model. Binary secondary outcomes were analysed by generalized linear model with binomial error and logit link. Length of hospital stay and length of ICU stay	

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
			were analysed by cause-specific Cox proportional hazards models on time to discharge alive, accounting for death during hospital or ICU stay as a competing risk. Number of major complications (per patient) was analysed post hoc using a generalized linear model with log link and quasi-Poisson error. Survival outcomes comparisons used Cox proportional hazards models	
***metra* (OrganOx Ltd.)**				
Primary publication: Vogt et al, 2024 (Vogt et al. 2024) **Design:** Prospective cohort study	***metra*:** 31 **Recipient age (years, median IQR):** 54 (40 to 62) **Recipient male gender n(%):** 17 (54.8%) **Recipient MELD score (median IQR):** 21 (9 to 32)	**Intervention:** *metra* **Comparator:** SCS **Hypothermic/normothermic**: Normothermic **Single/dual perfusion:** Dual **Pathway**: Perfusion initiated at the recipient centre	EAD Patient survival Graft survival Statistical methods: Differences between groups were tested	Population: Adult patients undergoing liver transplant, relevant to decision problem **GREEN** Intervention: Machine perfusion using a

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
Location: Germany **Status of study:** Published **Associated records**: NA GREEN	**Reason for transplant:** alcohol-related cirrhosis 4 (12.9%); hepatitis B 3 (9.7%); hepatitis C 0; hepatocellular carcinoma 7 (22.6%); non-alcohol-related steatohepatitis 2 (6.4%); other 15 (48.4%) **Donor age (median IQR)**: NR **Donor male gender**: NR **Donor DRI (median IQR)**: 1.560 (1.366 to 1.779) **SCS**: 6 **Recipient age (years, median IQR)**: 57 (51 to 68) **Recipient male gender n (%):** 5 (83.3%) **Recipient MELD score (median IQR):** 17 (10 to 40) **Reason for transplant:** hepatocellular carcinoma 2 (33.3%); other 4 (66.7%) **Donor age (median IQR)**: NR **Donor male gender**: NR **Donor DRI (median IQR)**: 1.656 (1.349 to 1.961) **Subgroups:** NR GREEN	**DCD/DBD:** DBD **ECD**: NR **Extended perfusion**: NR GREEN	using Fisher's exact test or chi-square test for categorical variables, and unpaired t test or Mann-Whitney test for continuous variables Graft and patient survival were evaluated using the Kaplan-Meier method and compared with the log-rank test	device relevant to decision problem GREEN Outcomes: Reported outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN Large difference in population sizes between groups, 31 for *metra* and 6 for SCS.

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
Primary publication: Krendl et al, 2025 (Krendl et al. 2025) **Design:** Retrospective cohort study **Location:** Austria **Status of study:** Published **Associated records**: NA GREEN	***metra*:** 174 **Recipient age (years, median IQR):** 60 (53 to 66.3) **Recipient male gender n (%):** 127 (73%) **Recipient MELD score (median IQR):** 14.0 (10 to 19.3) **Reason for transplant:** metabolic dysfunction-associated steatotic liver disease 36 (20.7%); alcohol-associated liver disease 23 (13.2%); metabolic dysfunction-associated liver disease 12 (6.9%); hepatitis B virus 8 (4.6%); hepatitis C virus 16 (9.2); hepatocellular carcinoma 54 (31%); acute liver failure 12 (6.9%) **Donor age (median IQR)**: 57.0 (44.8 to 67.0) **Donor male gender**: 98 (56.3%) **Donor DRI (median IQR)**: NR **SCS**: 158 **Recipient age (years, median IQR)**: 58.5 (50 to 64) **Recipient male gender n(%):** 120 (75.9%) **Recipient MELD score (median IQR):** 15 (10.8 to 20.0) **Reason for transplant**: metabolic	**Intervention:** *metra* **Comparator:** SCS **Hypothermic/normothermic**: Normothermic **Single/dual perfusion**: Dual **Pathway**: Perfusion initiated at the recipient centre **DCD/DBD**: Mixed DCD, *metra*: 34 (19.5%) DCD, SCS: 2 (1.3%) **ECD:** Eurotransplant Manual Chapter 9 criteria: Total: 245 (73.8%) ECD criteria ≥ 2: 121 (36.4%) **Extended perfusion**: NR GREEN	Graft survival MP utilisation rate EAD Post-transplant complications Biliary complications Statistical methods: Comparative analysis of categorical variables was conducted using the χ2 or Fisher exact test (if one or more cells had an expected count of < 5). The MannWhitney U and Kruskal-Wallis test were used to compare continuous, not normally distributed variables. Univariate and multivariate binary logistic regression analyses were performed for selected study endpoints, starting with a	Population: Adult patients undergoing liver transplant, relevant to decision problem GREEN Intervention: Machine perfusion using a device relevant to decision problem GREEN Outcomes: Reported outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN Uneven split of patients between groups but this was due to the consecutive allocation of patients. Authors note that, due to centre policy, almost all DCD grafts were normothermically

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
	dysfunction-associated steatotic liver disease 29 (18.4%); alcohol-associated liver disease 29 (18.4%); metabolic dysfunction-associated liver disease 6 (3.8%); hepatitis B virus 7 (4.4%); hepatitis C virus 9 (5.7%); hepatocellular carcinoma 49 (31%); acute liver failure 18 (11.4%) **Donor age (median IQR)**: 52.5 (40 to 60.0) **Donor male gender**: 93 (58.9%) **Donor DRI (median IQR)**: NR **Subgroups:** Benchmark cases: 140 (donor / recipient meet the following characteristics: MELD score ≤20, Balance of Risk score ≤9, absence of acute liver failure, absence of mechanical ventilation support before liver transplant, absence of portal vein thrombosis, absence of previous major abdominal surgery, and a full-size graft from a DBD donor) **GREEN**		univariate analysis of each variable. Any variable with a univariate P value <0.1 was selected as a candidate for the multivariate regression model. Kaplan-Meier survival curves and the log-rank test were used to analyse and compare graft and patient survival.	perfused, limiting comparison of DCD-NMP to DCD-SCS. Complications were reported but not using the Clavien Dindo classifications. Authors note that they did not find a significant reduction of EAD in the NMP group and speculate that this may be due to limited statistical power as the EAD rate was 30% in the NMP group versus 36% in the SCS group and 27% versus 39% when comparing benchmark NMP to benchmark SCS.
Primary publication:	***metra*: 59** **Recipient age (years, median**	**Intervention:** *metra* **Comparator:** SCS	Patient survival Graft survival	Population: Adult patients undergoing

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
Fodor et al, 2021 (Fodor et al. 2021) **Design:** Matched case study **Location:** Austria **Status of study:** Published **Associated records**: NA GREEN	**IQR):** 63.4 (12.7) **Recipient male gender n (%):** 52 (88%) **Recipient MELD score (reported for 58 patients, median IQR):** 15 (12) **Reason for transplant:** alcohol-related steatohepatitis 14 (24%); non-alcohol-related steatohepatitis 9 (15%); PNF 0; polycystic liver disease 0; Budd Chiari syndrome 2 (3%); primary biliary cirrhosis 1 (2%); primary sclerosing cholangitis 3 (5%); cryptogenic liver cirrhosis 3 (5%); hepatitis virus infection 3 (5%); cholangitic abscess formation 6 (10%); alpha 1-antitrypsin deficiency 3 (5%); acute liver failure 7 (12%); tumour 20 (34%) **Donor age (median IQR)**: 57 (22) **Donor male gender**: 30 (51%) **Donor DRI (median IQR)**: 2 (1; Eurotransplant DRI) **SCS**: 59 **Recipient age (years, median IQR)**: 60.6 (10.5) **Recipient male gender n(%):** 48 (81%)	**Hypothermic/normothermic**: Normothermic **Single/dual perfusion**: Dual **Pathway**: Perfusion initiated at the recipient centre **DCD/DBD:** Mixed DCD, *metra*: 9/58 (16%) SCS: 4 (7%) **ECD**: Some, criteria and number NR. *metra* was used in these cases. **Extended perfusion**: NR GREEN	EAD Biliary complications Statistical methods: X^2 and Fisher's exact test for categorical variables Mann–Whitney U test for continuous variables. Patient and graft survival rates were compared using the Kaplan–Meier method and the log rank test.	liver transplant, relevant to decision problem GREEN Intervention: Machine perfusion using a device relevant to decision problem GREEN Outcomes: Reported outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN Mixture of DCD and DBD patients included and NR separately which may impact the results. Authors note that despite an optimized matching process, residual confounders cannot be ruled out.

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
	Recipient MELD score (median IQR): 17 (10) **Reason for transplant**: alcohol-related steaohepatisis 12 (20%); non-alcohol-related steatohepatitis 6 (10%); PNF 1 (2%); polycystic liver disease 2 (3%); Budd Chiari syndrome 0; primary biliary cirrhosis 3 (5%); primary sclerosing cholangitis 0; cryptogenic liver cirrhosis 5 (8%); hepatitis virus infection 3 (5%); cholangitic abscess formation 9 (15%); alpha 1-antitrypsin deficiency 1(2%); acute liver failure 7 (12%); tumour 21 (36%) **Donor age (median IQR)**: 56 (16.5) **Donor male gender**: 36 (61%) **Donor DRI (median IQR)**: 2 (0; Eurotransplant DRI) **Subgroups:** NR **GREEN**			
Primary publication: Mathis et al, 2024 (Mathis et al. 2024)	***metra*:** 18 **Recipient age (years, median IQR):** 65 (56.5 to 67) **Recipient male gender n (%):** 17 (94.4)	**Intervention:** *metra* **Comparator:** SCS **Hypothermic/normothermic**: Normothermic **Single/dual perfusion**: Dual	Liver function (aminotransferase) Incidence and duration of RRT	Population: Adult patients undergoing liver transplant, relevant to decision problem **GREEN**

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
Design: Matched case study **Location:** Austria **Status of study:** Published **Associated records**: NA GREEN	**Recipient MELD score (median IQR):** NR **Reason for transplant:** alcohol-related 6 (33.3%); hepatitis B 1 (5.56%); hepatitis C 1 (5.56%); hepatocellular carcinoma 5 (27.78%); non-alcohol-related steatohepatitis 2 (11.11%); alpha 1 antitrypsin 2 (11.11%); Budd Chiari syndrome 1 (5.56%). **Donor age (years, median IQR)**: 64.5 (55.75 to 68) **Donor male gender**: 9 (48.1) **Donor DRI (median IQR)**: NR **SCS**: 36 **Recipient age (years, median IQR)**: 63 (56.5 to 66) **Recipient male gender n (%):** 26 (82.2) **Recipient MELD score (median IQR):** NR **Reason for transplant**: alcohol-related 12 (33.33%); hepatitis B 1 (2.78%); hepatitis C 11 (30.56%); hepatocellular carcinoma 8 (22.22%); non-alcohol-related steatohepatitis 3 (8.33%); primary sclerosis cholangitis 1 (2.78%);	**Pathway**: Perfusion initiated at the recipient centre **DCD/DBD**: Mixed *metra*: 4 (22.2%) SCS: DCD 1 (2.78%) **ECD**: Mixed (some DCD) **Extended perfusion**: NR GREEN	Statistical methods: Wilcoxon rank-sum test was used to analyse continuous variables Fisher exact test was used to analyse categorical variables	Intervention: Machine perfusion using a device relevant to decision problem GREEN Outcomes: Reported outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN Uneven population split between intervention groups despite creation of a matched pair control group. Authors note insufficient statistical power could explain why the higher occurrence of PRS in the SCS group did not reach statistical significance.

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
	Budd Chiari syndrome 1 (2.78%). **Donor age (years, median IQR)**: 64 (54.5 to 69) **Donor male gender**: 17 (47.2) **Donor DRI (median IQR)**: NR **Subgroups:** NR GREEN			
Primary publication: Hann et al, 2022 (Hann et al. 2022) **Design:** Matched case study **Location:** UK **Status of study:** Published **Associated records**: NA GREEN	***metra*:** 26 **Recipient age (years, median IQR):** 39 (26 to 52) **Recipient male gender n(%):** 13 (50) **Recipient MELD score (median IQR):** 21 (13 to 25) **Reason for transplant:** HAT 8/26 (biliary strictures 5/8, bilomas 5/8, biliary sepris 6/8); chronic rejection 6/26; biliary complications 6/26 (ischaemic-type biliary lesions 6/6, biliary sepsis 4/6); disease recurrence 4/26; other 2/26 **Donor age (years, median IQR)**: 51 (40 to 63) **Donor male gender:** 8 (30%) **Donor DRI (median IQR)**: 1.63 (1.43 to 1.95)	**Intervention:** *metra* **Comparator:** SCS Hypothermic/normothermic: Normothermic **Single/dual perfusion**: Dual **Pathway**: Perfusion initiated at the recipient centre **DCD/DBD**: DBD **ECD**: *metra*: All "suboptimal grafts" either declined by at least one other transplant centre or assessed as having suboptimal features that would preclude its use in a high-risk recipient SCS: NR **Extended perfusion**: NR GREEN	Graft survival Patient survival Post operative morbidity RRT Graft rejection EAD Statistical methods: Continuous variables that did not follow a normal distribution were compared using the Kruskal–Wallis test, and post hoc analysis for direction of association was assessed by means of the Mann–Whitney U test. One-way ANOVA	Population: Adult patients undergoing liver transplant, relevant to decision problem GREEN Intervention: Machine perfusion using a device relevant to decision problem GREEN Outcomes: Reported outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
	SCS group 1: 31 Historical comparison group of patients who underwent re-transplantation between January 2015 and March 2018 **Recipient age (years, median IQR)**: 42 (28 to 54) **Recipient male gender n(%):** 16 (51%) **Recipient MELD score (median IQR):** 18 (14 to 24) **Reason for transplant**: HAT 11/31 (biliary strictures 5/11, bilomas 8/11, biliary sepris 9/11); chronic rejection 2/31; biliary complications 10/31 (ischaemic-type biliary lesions 10/10, biliary sepsis 8/10); disease recurrence 6/31; other 2/31. **Donor age (years, median IQR)**: 53 (44 to 58) **Donor male gender**: 15 (48) **Donor DRI (median IQR)**: 1.58 (1.40 to 1.74) **SCS group 2**: 25 Contemporaneous comparison group of patients undergoing re-transplantation between April 2018 and November 2020		was used for multigroup comparison of normally distributed continuous variables, and post hoc analysis for direction of association done using the Games–Howell test. Survival curves in the Kaplan–Meier analysis were compared using the log rank test.	Retransplant patients only so not generalisable to patients receiving their first liver transplant .

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
	Recipient age (years, median IQR): 50 (31 to 58) **Recipient male gender n(%):** 12 (48) **Recipient MELD score (median IQR):** 19 (15 to 25) **Reason for transplant:** HAT 8/25 (biliary strictures 5/8, bilomas 5/8, biliary sepris 6/8); chronic rejection 4/25; biliary complications 4/25 (ischaemic-type biliary lesions 4/4, biliary sepsis 3/4) disease recurrence 8/25; other 1/25. **Donor age (years, median IQR):** 49 (44 to 63) **Donor male gender:** 14 (56) **Donor DRI (median IQR):** 1.51 (1.41 to 1.71) **Subgroups:** NR **GREEN**			
Primary publication: Puttappa et al, 2025 (Puttappa et al. 2025) **Design:** Retrospective	***metra*:** 78 **Recipient age (years, median IQR):** 56 (49 to 61) **Recipient male gender n (%):** 56 (72) **Recipient MELD score (median IQR):** 14 (11 to 16)	**Intervention:** *metra* **Comparator:** SCS; NRP (Maquet Cardiohelp) followed by SCS **Hypothermic/normothermic:** Normothermic **Single/dual perfusion**: Dual	Graft survival PNF PRS Kidney injury Renal replacement Aminotransferase levels	Population: Adult patients undergoing liver transplant, relevant to decision problem **GREEN** Intervention: Machine perfusion using a

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
cohort **Location:** UK **Status of study:** Published **Associated records**: NA GREEN	**Reason for transplant:** Alcohol-related liver disease: 22 (28%); MASLD: 17 (22%); primary sclerosing cholangitis: 7 (9%); primary biliary cholangitis: 4 (5%); hepatitis C cirrhosis: 12 (15%); retransplant: 3 (4%); others: 13 (17%) **Donor age (years, median IQR)**: 46 (28 to 59) **Donor male gender: NR** **Donor DRI (median IQR)**: 2.4 (2.0 to 2.8) **SCS**: 59 **Recipient age (years, median IQR)**: 56 (49 to 62) **Recipient male gender n(%):** 31 (53) **Recipient MELD score (median IQR): 16 (13 to 20)** **Reason for transplant**: Alcohol-related liver Disease: 18 (31%); MASLD: 8 (14%); primary sclerosing Cholangitis: 9 (15%); primary biliary cholangitis: 10 (17%); hepatitis C cirrhosis: 9 (15%); retransplant: 1 (2%); others: 4 (7%) **Donor age (years, median IQR)**:	**Pathway**: Perfusion initiated at the recipient centre **DCD/DBD**: DCD **ECD**: Yes (all DCD) **Extended perfusion**: NR GREEN	**Statistical methods:** Comparison of continuous variables was performed using Kruskal-Wallis with Dunn's test for multiple pairwise comparisons. Categorical variables were compared using chi-square or Fisher exact tests as appropriate. Transplant survival, estimated using the Kaplan-Meier method, was compared between groups by log-rank analysis.	device relevant to decision problem GREEN Outcomes: Reported outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN Authors note that non-use of some organs on the basis of biochemical testing during NMP and NRP may have improved graft selection in these groups, a potential benefit of machine perfusion not addressed in this study. There was an overrepresentation of female patients and patients with primary biliary cholangitis and

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
	50 (36 to 58) **Donor male gender**: NR **Donor DRI (median IQR)**: 2.5 (2.0 to 3.0) **NRP then SCS**: 101 **Recipient age (years, median IQR)**: 57 (48 to 62) **Recipient male gender n(%): 73 (72)** **Recipient MELD score (median IQR): 14 (10 to 18)** **Reason for transplant:** Alcohol-related liver Disease 32: (32%); MASLD: 23 (23%); primary sclerosing Cholangitis: 15 (15%); primary biliary cholangitis: 4 (4%); hepatitis C cirrhosis: 7 (7%); retransplant: 7 (7%); others: 13 (13%) **Donor age (years, median IQR): 55 (42 to 60)** **Donor male gender: NR** **Donor DRI (median IQR): 2.3 (2.1 to 2.5)** **Subgroups:** NR **GREEN**			others with low surgical risk in the SCS-only group, which authors suggest as a possible result of the imperative to minimize ischemia time in DCD livers encouraging the use of direct procurement DCD-SCS organs in recipients with short predicted explant times when NRP and NMP were unavailable. However, this bias would favour the intervention arms.

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
VitaSmart (Bridge to Life Ltd)				
Primary publication: Reich et al 2024 (Reich et al. 2024b) **Design: RCT** **Location:** USA **Status of study: Unpublished, conference abstract only** **Associated records**: Bridge to Life Ltd. 2021 (clinical trial registry record) (Bridge to Life Ltd. 2021) Reich et al 2025 (conference abstract, full cohort rejection results) (Reich et al. 2025) Reich et al 2023 (conference abstract, interim	**VitaSmart:** 109 **Recipient age (years, median IQR):** 59 (49 to 64) **Recipient male gender n(%):** NR **Recipient Laboratory MELD score** (median IQR): 17 (12 to 24) **Reason for transplant:** NR **Donor age (years, median IQR)**: DBD: 61 (51 to 65) DCD: 46 (34 to 55) **Donor male gender**: NR **Donor DRI (median IQR)**: NR **SCS**: 110 **Recipient age (years, median IQR):** 58 (51 to 65) **Recipient male gender n(%):** NR **Recipient Laboratory MELD score (median IQR):** 17 (12 to 22) **Reason for transplant:** NR **Donor age (years, median IQR)**: DBD: 58 (50 to 65) DCD: 40 (34 to 46) **Donor male gender**: NR **Donor DRI (median IQR)**: NR **Subgroups:** DCD donor livers	**Intervention**: VitaSmart **Comparator**: SCS **Hypothermic/normothermic**: Hypothermic **Single/dual perfusion**: Single (portal vein) **Pathway**: Perfusion initiated at the recipient centre **DCD/DBD**: VitaSmart: Mixed, 28 (26%) DCD SCS: Mixed, 27 (25%) DCD **ECD**: Trial webpage (https://bridgetolife.com/bridge-to-hope/) states that ≥1 of the extended risk criteria for DBD grafts had to be met for inclusion: donor age 50 to 85 years, anticipated cold ischemia time 10 to 15h (excl. HOPE duration), macrosteatosis 10 to 40 %, terminal ALT 250 to 1,500 IU/L, peak ALT within 3 days 1,000 to 3,000 IU/L, terminal total bilirubin 2 to 4 mg/dl **Extended perfusion**: NR	Patient and graft survival PNF EAD SAEs Mortality Statistical methods: NR (conference abstract only, limited reporting).	Population: Adult patients undergoing liver transplant, relevant to decision problem **GREEN** Intervention: Machine perfusion using a device relevant to decision problem **GREEN** Outcomes: Reported outcomes relevant to decision problem **GREEN** Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem **GREEN** Trial was terminated in mid-2023 for 10 endpoint superiority (P=0.003) at interim analysis; follow-up data for full patient cohort is at the 6 month

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
results at 25% enrolment) (Reich et al. 2023a) Reich et al 2023 (conference abstract, interim results at 25% enrolment) (Reich et al. 2023c) Reich et al 2023 (conference abstract, interim results at 50% enrolment) (Reich et al. 2023b) Reich et al 2024 (conference abstract, analysis of correlation of EAD with other clinical outcomes) (Reich et al. 2024a) Reich et al 2024 (conference abstract, DCD	GREEN	GREEN		endpoint. Study is not yet published. All available information is from conference abstracts, thus limited information available.

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
livers) (Reich et al. 2024c) Reich et al 2022 (conference abstract, protocol) (Reich et al. 2022) Axelrod et al 2024 (conference abstract, economic analysis) (Axelrod et al. 2024) Axelrod et al 2025 (conference abstract, economic analysis) (Axelrod et al. 2025) GREEN				
Primary publication: Ravaioli et al 2022 (Ravaioli et al. 2022) **Design:** RCT	**VitaSmart:** 66 allocated, 55 included **Recipient age (years, median IQR):** 57 (47 to 65) **Recipient male gender n(%):** 41 (74%)	**Intervention**: VitaSmart **Comparator**: SCS **Hypothermic/normothermic**: Hypothermic **Single/dual perfusion**: Single (portal vein)	List eligible outcomes reported EAD PNF Postreperfusion syndrome	Population: Adult patients undergoing liver transplant, relevant to decision problem GREEN Intervention: Machine

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
Location: Italy **Status of study:** Published **Associated records**: University of Bologna 2019 (clinical trial registration) (University of Bologna 2019) Ravaioli et al 2020 (conference abstract, interim analysis of first 70 patients) (Ravaioli et al. 2020) Ravaioli et al 2021 (conference abstract) (Ravaioli et al. 2021) GREEN	**Recipient Laboratory MELD score** (median IQR): 15 (10 to 18) **Reason for transplant:** Cholestatic disease 7; viral 7; alcohol-related 2; metabolic 3; autoimmune 2; tumours 30; hepatocellular carcinoma and cirrhosis 2; other 2 **Donor age (years, median IQR)**: 76 (64 to 81) **Donor male gender**: 31 (56%) **Donor DRI (median IQR)**: 1.846 (1.719 to 1.908) **SCS**: 69 allocated, 55 included **Recipient age (years, median IQR):** 60 (53 to 66) **Recipient male gender n (%):** 39 (71%) **Recipient Laboratory MELD score (median IQR):** 14 (9 to 20) **Reason for transplant:** Cholestatic disease 2; viral 10; alcohol-related 5; metabolic 0; autoimmune 1; tumours 35; hepatocellular carcinoma and cirrhosis 0; other 2 **Donor age (years, median IQR)**: 72 (59 to 77) **Donor male gender**: 33 (60%) **Donor DRI (median IQR)**: 1.766	**Pathway**: Perfusion initiated at the recipient centre **DCD/DBD:** DBD (DCD livers were excluded) **ECD**: All ECD According to United Network for Organ Sharing criteria - hemodynamic deterioration, donor age >65 years, donor BMI >30 kg/m2, serum bilirubin >3 mg/dL, aspartate aminotransferase or alanine aminotransferase >3 times the upper reference threshold, sodium >165 mmol/L, intensive care unit stay >7 days, steatosis >40%, or cold ischemia time >12 hours. **Extended perfusion**: None GREEN	Length of hospital stay Biliary and vascular complications Graft survival Patient death due to liver failure Patient overall survival Statistical methods: Chi-square and Fisher's exact tests were used to compare categorical variables, while parametric (ANOVA) or non-parametric (Kruskal Wallis) tests were used for continuous variables. Graft survival outcomes were evaluated with the use of the Kaplan–Meier method with a log-rank test.	perfusion using a device relevant to decision problem GREEN Outcomes: Reported outcomes relevant to decision problem GREEN Setting: Perfusion initiated at the recipient centre pathway, relevant to decision problem GREEN Authors note that recipients had relatively low MELD scores because matching ECD and very sick patients is usually avoided to reduce the risk of transplant failure. They also note that median DRI was higher than in other similar randomized studies (citing van Rijn et al 2021 (van Rijn et al. 2021c)). Perfusion

Study name, design and location	Participants and setting	Interventions and comparators	Outcomes	EAG comments
	(1.545 to 1.908) **Subgroups:** NR **GREEN**			strategy was somewhat particular (described as a simple oxygenated machine perfusion system through only the portal vein applied after a period of conventional SCS, characterized by a period of graft flushing during the back-table preparation first and then conventional recirculation strategy), with intention of reducing the cold ischemic time by starting with HOPE at the time of back table to increase the time of HOPE and shorten time of cold ischemia.

Table abbreviations: ALT, alanine transaminase; ANOVA, analysis of variance; AST, aspartate transaminase; BMI, body mass index; DBD, donation after brain death; DCD, donation after circulatory death; DRI, Donor Risk Index; EAD, early allograft dysfunction; EAG, external assessment group; ECD, extended criteria donor; HAT, hepatic artery thrombosis; HOPE, Hypothermic oxygenated machine perfusion; HR, hazard ratio; ICU, intensive care unit; IQR, interquartile range; IU/L, international unit/litre; MASLD, metabolic dysfunction-associated steatotic liver disease; MELD, Model for End-Stage Liver Disease; MP, machine perfusion; NA, not applicable; NMP, normothermic machine perfusion; NR, not reported; NRP, normothermic regional perfusion;

PNF, primary non-function; PRS, post-reperfusion syndrome; RCT, randomised controlled trial; RR, risk ratio; SCS, static cold storage; SD, standard deviation.

9.8 Appendix H Evidence gaps

Outcomes	Liver Assist (HMP)	LiverAssist (NMP)	*metra*	PerLife	VitaSmart
Long-term outcomes					
Overall survival	5 RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)	1 RCT (Ghinolfi et al. 2019)	2 matched-case studies (Fodor et al. 2021, Hann et al. 2022) **AMBER**	None **RED**	1 RCT (Reich et al. 2024b)
Graft survival	6 RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Minor et al. 2022, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)	1 RCT (Ghinolfi et al. 2019)	2 retrospective cohort studies (Krendl et al. 2025, Puttappa et al. 2025) and 2 matched-case studies (Fodor et al. 2021, Hann et al. 2022) **AMBER**	None **RED**	2 RCTs (Reich et al. 2024b, Ravaioli et al. 2022)
Re-transplantation	5 RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Minor et al. 2022, Lesurtel et al. 2025, Schlegel et al. 2023)	1 RCT (Ghinolfi et al. 2019)	None **RED**	None **RED**	1 RCT (Ravaioli et al. 2022)
Biliary complications	4 RCTs (Czigany et al. 2021, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)	1 RCT (Ghinolfi et al. 2019)	1 retrospective cohort study (Krendl et al. 2025) and 1 matched case study (Fodor et al. 2021) **AMBER**	None **RED**	1 RCT (Ravaioli et al. 2022)

Outcomes	Liver Assist (HMP)	LiverAssist (NMP)	*metra*	PerLife	VitaSmart
Non-anastomotic strictures	4 RCTs (van Rijn et al. 2021c, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)	None **RED**	2 matched case studies (Fodor et al. 2021, Hann et al. 2022) **AMBER**	None **RED**	None **RED**
Anastomotic strictures	4 RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Grat et al. 2023, Schlegel et al. 2023)	None **RED**	1 retrospective cohort study (Krendl et al. 2025) and 2 matched-case studies (Fodor et al. 2021, Hann et al. 2022) **AMBER**	None **RED**	1 RCT (Ravaioli et al. 2022)
Biliary leakages	1 RCT (van Rijn et al. 2021c)	None **RED**	1 retrospective cohort study (Krendl et al. 2025) and 2 matched-case studies (Fodor et al. 2021, Hann et al. 2022) **AMBER**	None **RED**	1 RCT (Ravaioli et al. 2022)
Graft-related complications					
PNF	5 RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)	1 RCT (Ghinolfi et al. 2019)	1 retrospective cohort study (Krendl et al. 2025) and 2 matched-case studies (Fodor et al. 2021, Hann et al. 2022) **AMBER**	None **RED**	2 RCTs (Reich et al. 2024b, Ravaioli et al. 2022)
HAT	6 RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Minor et al. 2022, Lesurtel et al.	1 RCT {Ghinolfi, 2019 #1048	1 retrospective cohort study (Krendl et al. 2025) and 2 matched-case studies (Fodor et al.	None **RED**	1 RCT (Ravaioli et al. 2022)

Outcomes	Liver Assist (HMP)	LiverAssist (NMP)	*metra*	PerLife	VitaSmart
	2025, Grat et al. 2023, Schlegel et al. 2023)		2021, Hann et al. 2022) **AMBER**		
PRS	3 RCTs (van Rijn et al. 2021c, Lesurtel et al. 2025, Grat et al. 2023)	1 RCT {Ghinolfi, 2019 #1048	1 retrospective cohort study (Puttappa et al. 2025) and 1 matched case study (Mathis et al. 2024) **AMBER**	None **RED**	1 RCT (Ravaioli et al. 2022)
EAD	6 RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Minor et al. 2022, Lesurtel et al. 2025, Ghinolfi et al. 2019, Schlegel et al. 2023)	None **RED**	1 prospective cohort study (Vogt et al. 2024), 1 retrospective cohort study (Krendl et al. 2025) and 2 matched case studies (Fodor et al. 2021, Hann et al. 2022) **AMBER**	None **RED**	2 RCTs (Reich et al. 2024b, Ravaioli et al. 2022)
Acute kidney injury post-transplantation	None **RED**	None **RED**	1 retrospective cohort study (Puttappa et al. 2025) and 1 matched-case study (Fodor et al. 2021) **AMBER**	None **RED**	None **RED**
Post-operative requirement for renal replacement	3 RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Lesurtel et al. 2025)	None **RED**	1 retrospective cohort study (Puttappa et al. 2025) 2 matched case studies (Mathis et al. 2024, Hann et al. 2022) **AMBER**	None **RED**	1 RCT (Ravaioli et al. 2022)

Outcomes	Liver Assist (HMP)	LiverAssist (NMP)	*metra*	PerLife	VitaSmart
Transaminase release during first week post-transplant (alanine)	4 RCTs (Czigany et al. 2021, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)	1 RCT (Ghinolfi et al. 2019)	1 retrospective cohort study (Puttappa et al. 2025) and 1 matched-case study (Hann et al. 2022) **AMBER**	None **RED**	None **RED**
Transaminase release during first week post-transplant (aspartate)	5 RCTs (Czigany et al. 2021, Minor et al. 2022, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)	1 RCT (Ghinolfi et al. 2019)	None **RED**	None **RED**	None **RED**
Adverse events					
Mechanical failure of machine perfusion technology	1 RCT (van Rijn et al. 2021c, Schlegel et al. 2023)	None **RED**	None **RED**	None **RED**	None **RED**
Serious adverse events (Clavien-Dindo grade >III)	6 RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Minor et al. 2022, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)	None **RED**	1 matched case study (Fodor et al. 2021) **AMBER**	None **RED**	1 RCT (Reich et al. 2024b)
Device-related adverse events	None **RED**	None **RED**	None **RED**	None **RED**	None **RED**

Outcomes	Liver Assist (HMP)	LiverAssist (NMP)	*metra*	PerLife	VitaSmart
Mortality	5 RCTs (van Rijn et al. 2021c, Czigany et al. 2021, Lesurtel et al. 2025, Grat et al. 2023, Schlegel et al. 2023)	1 RCT (Ghinolfi et al. 2019)	2 matched case studies (Mathis et al. 2024, Hann et al. 2022) **AMBER**	None **RED**	1 RCT (Reich et al. 2024b)
Quality of life and staff satisfaction					
Patient-reported HRQoL	None **RED**	None **RED**	None **RED**	None **RED**	None **RED**
Healthcare professional satisfaction and/or wellbeing	None **RED**	None **RED**	None **RED**	None **RED**	None **RED**

Table abbreviations: EAD, early allograft dysfunction; HAT, hepatic artery thrombosis; HRQoL, health-related quality of life; PNF, primary non-function; PRS, post-reperfusion syndrome; RCT, randomised controlled trial.

HealthTech Programme

HTE10066 Ex-situ machine perfusion devices for deceased donor liver transplants

External Assessment Report - Comments collated table

Any confidential sections of the information provided should be underlined and highlighted. Please underline all confidential information, and separately highlight information that is 'commercial in confidence' in blue and all that is 'academic in confidence' in yellow

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
1	Bridge to Life			We anticipate multi peer reviewed journal articles to come out in the next few months on VitaSmart and HOPE which may affect some of the default values in the model. What is the mechanism to provide those updates? For example, our US RCT publication is under review and we expect will be published in the next few weeks.	Thank you for your comment. The searches were conducted 15 September 2025 and company evidence submissions were received in September 2025. The EAG can't include data published beyond this time without conducting a full update review. Evidence published after this date can be brought to the attention of NICE during consultation on the draft guidance.
2	Bridge To Life			There are several instances in the EAR to VitaSmart as HMP. Our system is a hypothermic oxygenated perfusion system (HOPE) which is distinct from a Hypothermic Machine Perfusion (HMP). HMP does not have active oxygenation.	Thank you for your comment. We have used "HMP" to distinguish the temperature mode of the included devices; the term "HMP" is not exclusive of oxygenated perfusion. All the devices included in the scope of this assessment (both normothermic and hypothermic) use oxygenated perfusion.
3	Bridge To Life	10,122		VitaSmart is listed in parenthesis with NMP. We are a HOPE system.	Thank you for your comment, this has been corrected.
4	Aferetica	7	Clinical evidence	The report states that no eligible clinical studies were identified for PerLifePRO. However, this conclusion appears to be based	Thank you for your comment. Studies were included where they referred to the Perlife device and not solely PerLifePRO. Only 1

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				on a narrow interpretation of device naming rather than underlying technology. A substantial proportion of the available literature refers to the PerLife system, which represents the same technological platform as PerLifePRO, with no material differences in hardware, perfusion principles, or clinical application. The PerLifePRO version reflects a software evolution of the same device rather than a distinct technology. Therefore, studies conducted using the PerLife system should be considered directly relevant and transferable to PerLifePRO. Excluding these studies may have led to an underestimation of the available clinical evidence.	published study was identified (Martinelli et al 2022), which was not prioritised for extraction because the pathway was unclear and the comparison made was between different perfusion fluids and not Perlife vs static cold storage.
5	Aferetica	7–8	Clinical evidence review	The identification of “no evidence” for PerLifePRO does not reflect the actual evidence base when considering the broader PerLife platform. Multiple published studies, including prospective investigations, clinical series, and early randomized data, have evaluated the PerLife system in liver and kidney transplantation settings. Given that PerLifePRO shares the same hardware and perfusion technology, these data are directly applicable and should be considered in the clinical evaluation.	Thank you for your comment. The search strategies included “Perlife” as a search term (see Appendix A) and we did not exclude records that referred only to “Perlife” during study selection. If there are records that are in scope and have been missed in the searches we are happy to review them, please provide references.
6	Aferetica	8	Key areas for evidence generation	The reported lack of evidence for PerLifePRO appears to be influenced by the exclusion of studies referring to the PerLife system. A large number of real-world clinical experiences, feasibility studies, and conference presentations are available for PerLife, demonstrating its use in liver transplantation and organ perfusion strategies. These data reflect the same device platform and should be considered as valid real-world evidence for PerLifePRO.	Thank you for your comment, please see response to comment 5.
7	Aferetica	9	Economic evidence	The absence of economic evidence for PerLifePRO may be a direct consequence of excluding studies conducted with the PerLife system. Since PerLife and PerLifePRO are based on the same technological platform, clinical data generated with PerLife could reasonably inform economic modelling assumptions for PerLifePRO. The current approach may therefore overestimate uncertainty and limit the validity of the model outputs for this technology.	Thank you for your comment, please see response to comment 5.

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8	Aferetica	10–11	Economic modelling results	The report attributes higher uncertainty to PerLifePRO due to lack of device-specific data. However, this uncertainty may be artificially inflated due to the exclusion of relevant studies conducted with the PerLife system. Considering the equivalence between PerLife and PerLifePRO in terms of hardware and clinical application, incorporating these data would likely reduce uncertainty and provide a more accurate estimate of clinical effectiveness.	Thank you for your comment, please see response to comment 5.
9	Aferetica	7–12	Overall	Across the report, the absence of evidence for PerLifePRO is repeatedly highlighted. However, this appears to be primarily due to the exclusion of studies referring to the PerLife system, which represents the same underlying technology. PerLifePRO should be considered an updated version of the PerLife platform, with no fundamental differences in device structure or mechanism of action. Therefore, the available body of evidence for PerLife constitutes a relevant and important evidence base for PerLifePRO and should be included in the assessment to ensure a fair and comprehensive evaluation.	Thank you for your comment, please see response to comment 5.
10	XVIVO	21, 151	4.2	Section 4.2 (page 21) states: *"If RCT evidence was not available in the perfusion initiated at the recipient centre pathway for a device type, further evidence for this device in this pathway was sought in the non-RCT studies (first prioritizing non-randomised comparative evidence, then single-arm evidence, etc.) in a European setting. It is therefore possible that there is further evidence on the relevant outcomes in the deprioritised studies that has not been extracted and summarized in this report."* The use of a tiered evidence selection and prioritization strategy, while common for HTAs, comes with important methodological limitations that should be addressed. This is particularly important when there are inconsistencies in evidence treatment across interventions. A common limitation is asymmetric application of the tiered logic, e.g., when lower-level evidence is accepted as sufficient for one device (in this case Metra), and the same evidence type is dismissed for another device (in this case Liver Assist – HOPE). This creates methodological inconsistency and violates HTA	Thank you for your comment. The EAG appreciates the methodological issues around prioritising studies at different levels of evidence according to the evidence available for each device. However, this approach was agreed with NICE as necessary to assess the within-scope devices in an efficient way within the scope of the assessment. The risk of bias assessments were conducted using tools appropriate to each study design, i.e. cohort studies were assessed with the ROBINS-I tool and RCTs with the Cochrane RoB v1 tool. This is explained in the EAR, thus committee members will be aware that a "Low RoB" judgement for a cohort study does not imply parity in overall evidence quality with a "Low RoB" RCT. The approach is detailed in the EAR, and the different levels of evidence available across different devices is discussed in the results and evidence gaps sections (in the latter of which the absence of metra RCT

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				principles that require equivalent evidentiary standards across technologies. One example of this inconsistency is shown on page 145, where logistical flexibility is ascribed explicitly as a significant benefit of NMP – a conclusion that cannot, and should not, be drawn based on the prioritized studies, especially since evidence supporting the same benefit of HOPE with Liver Assist have were disregarded. Also, while the tiered evidence-selection strategy is methodologically sound in isolation; its interpretation is critically dependent on a correct assessment of internal validity. The prioritized studies are rated as follows (page 151): • Liver Assist: 5 RCTs (Low1 RCT (moderate RoB) • VitaSmart: 2 RCTs (Low RoB) • Metra: 2 non-RCTs (low RoB); 4 non-RCTs (moderate RoB) Rating non-randomized studies as 'low' RoB (the same as for RCTs) results in a flattening of the evidence hierarchy, where evidence derived exclusively from non-randomized designs is treated as comparable to randomized evidence. This is not consistent with NICE methods, which require that non-randomized evidence be considered intrinsically more susceptible to bias, irrespective of analytical adjustment. In this context, assigning 'low' RoB to non-randomized studies, while methodologically incorrect in itself, becomes particularly problematic when those studies later form the sole basis for device-specific conclusions. When assessing RCTs, low RoB is achievable *provided adequate reporting*. NICE guidance states that incomplete reporting should be judged conservatively, with a moderate RoB at best, rather than low. As such, relying on evidence like the RCTS by Reich 2024 (VitaSmart), which is based only on abstracts, further skews comparisons between devices.	evidence in the end-ischaemic pathway is explicitly stated) The EAG has also noted the possibility that relevant evidence may have been deprioritised as a result. Regarding the comment on page 145 [now page 151], the statement regarding logistical flexibility is presented as part of a qualitative discussion of additional potential benefits and is not incorporated into the economic model or the cost-effectiveness results. However, we acknowledge that the previous wording may have been interpreted as attributing this benefit specifically to NMP and have revised the wording to refer more broadly to machine perfusion in general. Furthermore, given the lack of quantitative evidence for this (and hence, it's exclusion from the quantitative model), this is worded more neutrally.

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				Taken together, the combination of a tiered evidence selection approach and a methodologically inappropriate RoB assessment - which fails to differentiate between study designs – can lead to misinterpretations of data and iaccrate conclusions. Please consider these issues when moving forward.	
11	XVIVO	8 and 11	Executive summary	Page 8 states that “more long-term studies exceeding one year are essential to confirm the sustained benefits of machine perfusion over static cold storage”. Although this applies to NMP, it is also important to note the considerable amount of high quality, long-term, confirmative evidence on HOPE with Liver Assist. This includes three RCTs[1], two non-randomized comparative studies[2], and one large-scale, multicenter, observational, IDEAL-D stage 4 study[3], all of which report outcomes up to 5-years post-Tx apart from one (Morawski 2024) which includes data up to 2-years. With think this should be clearly stated in the report to accurately reflect the level of evidence for HOPE with Liver Assist. Since NICE guidance informs healthcare providers, a concise summary of the available evidence is essential. The same reasoning applies to the statement on page 11 that ECD results are omitted because of insufficient data. We consider this inaccurate as two of the prioritized studies on HOPE with Liver Assist, including their respective long-term follow-up, focus on or include analyses of ECD-DBD (Czigany 2021 and Czigany 2024; Grat 2023 and Morawski 2024). Several non-randomized comparative studies[4] and systematic reviews (e.g., Tingle 2023) also provide data on ECD-DBD LT. Overall, these sources show clear benefits of HOPE with Liver Assist in ECD-DBD LT compared to SCS.	Thank you for your comment, we agree that it is useful to note that more long-term evidence is available for LiverAssist hope and have edited these sentences accordingly. Regarding the point on page 11 [now page 15], we acknowledge that evidence is available for HOPE in ECD populations and have updated the language in the report to reflect this. However, separate ECD-specific model results have not been presented. The relevant inputs relating to ECD organs are already incorporated within the baseline model population if specifically relating to all DCD organs (as described in Section 6.2.3), and where additional ECD-specific data exist, they do not show statistically significant differences in outcomes. Presenting separate ECD results could be interpreted that there are clinical differences beyond those that are supported by the evidence.

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				[1] van Rijn 2025 (RCT; 5-year follow-up of van Rijn 2021); Czigany 2024 (RCT; 5-year follow-up of Czigany 2021); Morawski 2024 (RCT; 2-year follow-up of Graft 2023). [2] Coquelle 2025 (prospective comparative study; 5-year follow-up of Rayar 2021); Schlegel 2018 (prospective comparative study; 5-years follow-up) [3] Eden et al 2024 (HOPE-REAL study; long-term (up to 5-years) confirmative evidence of HOPE in a real-world setting) [4] Rayar 2021; Coquelle 2025; Arend 2025; Patrono 2022; Hoyer 2020; Patrono 2019; Corcione 2025; Eden 2024	
12	XVIVO	124	6.3.1	Page 124 states: "Overall, Liver Assist (NMP modality), PerLifePRO (NMP modality), and VitaSmart are associated with higher overall complication costs". How can this be limited to Liver Assist (NMP) and PerLife (NMP) and not OrganOx, since the data on which the costs are based are the same for all three devices?	Thank you for your comment, this has been corrected.
13	XVIVO	12	Executive summary	Page 12 states: "machine perfusion device costs were inconsistently reported by device companies". We believe this to be untrue for Liver Assist and would like this to be reflected in the report. Also, page 93 states: "Costs for Liver Assist were broadly consistent across both analyses".	Thank you for your comment. The statement on page 12 [now page 16] refers to differences in how cost components were reported across technologies, rather than the consistency of reporting from any single company. Specifically, some submissions provided more granular breakdowns of individual cost elements, whereas others presented costs in a more aggregated form. This point is not intended to reflect an issue with the costing evidence provided for Liver Assist. As noted on page 93 [now page 99], the costs for Liver Assist were broadly consistent across both our analyses and the Zimmerman model hence we do not have concerns that these are misrepresented.
14	XVIVO	89	6.4	Table 6.4 (page 89) states that "Long-term mortality rates for all machine perfusion devices are informed by 5- year data from a single device (Liver Assist) in a DCD population".	Thank you for alerting us to this typo, this has been corrected.

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				However, the rationale correctly includes Czigany 2021 which assesses HOPE in ECD-DBD.	
15	XVIVO	119	6.2.3	Page 119 states that Czigany 2024 reported 5-year mortality Liver Assist (NMP) in a DCD population compared with SCS. This is incorrect as Czigany 2024 (long-term follow-up of Czigany 2021) is on HOPE in ECD-DBD (with Liver Assist).	Thank you for alerting us to this typo, this has been corrected.
16	XVIVO	250	Table B.2	Page 250 (Table B.2) lists Brüggenwirth 2022 and Brüggenwirth 2024 as the same trial (NL8740); however, there is no overlap between the two trials. The latter trial (DHOPE-PRO trial) is a single-center prospective, pseudo-RCT trial including only Liver Assist, while the first trial is a multicenter observational cohort study including both Liver Assist and VitaSmart.	Thank you for alerting us to this error, this has now been corrected.
17	XVIVO	104	Table 6.7	Table 6.7 (page 104): RR for RRT is 0.75 for VitaSmart while RR is 0.79 for Liver Assist despite data on Liver Assist is used also for VitaSmart.	Thank you for alerting us to this error, this has been corrected.
18	XVIVO	105-106	Table 6.7	Table 6.7 (page 105-106): For parameter HAT – the table states that Lesurtel 2025 is “specific to VitaSmart using HMP modality”. This is incorrect as the study uses Liver Assist (HOPE).	Thank you for alerting us to this error, this has been corrected.
19	XVIVO	86, 106, 117, 404	Fig 6.1, Table 6.7, 6.13, Appendix H	The definition of EAD is incorrect – should be Early allograft dysfunction not ‘disorder’. Add EAD to list of definitions.	Thank you for alerting us to these errors, this has been corrected and EAD has been added to the abbreviations list.
20	XVIVO	390	Appendix D	Appendix D (page 390) refers to re-Tx of Lungs instead of Liver	Thank you for alerting us to this error, this has now been corrected.
21	XVIVO	390	Table D.1	Table D.1 ‘Long-term outcomes’ includes studies that have a follow-up of 1 year or shorter	Thank you for your comment – in this context “Long term outcomes” is used to distinguish the outcomes discussed in table D.1 from the graft-related outcomes in the immediate post-operative period (discussed in table 2). We have changed this to “Long term transplant outcomes” for clarity.
22	XVIVO	17	Clinical context	Page 17 states that “NMP reduces ischemic reperfusion injury”. Please clarify the reasoning behind this statement and what data is used to support it.	Thank you for your comment, this has been actioned.

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23	XVIVO	N/A	N/A	General comment: Consider including references in the text to improve readability and traceability of the report	Thank you for your comment. Study citations are provided throughout the report in the format required by the NICE report template. We have added further background references as suggested in the previous comments.
24	OrganOx	7		The decision to only use data from studies where perfusion begins at the transplant centre removes a large UK RCT of the *metra* from analysis; lack of UK data is subsequently (p29) expressed by EAG as a concern. There is no evidence that taking the device to the donor is worse than bringing the liver back to the device in the recipient centre. The rare use of machines at the donor centre reflects both the inability of most of the devices to allow transport of the liver and lack of an infrastructure that allows personnel to travel to place livers on the device at the donor hospital. By keeping cold ischaemic time to a minimum it is likely that device to donor is superior to back to base perfusions. For cardiac retrievals from DCD donors, the perfusion device is taken to the donor hospital for this reason.	Thank you for your comment. The decision to focus the assessment on the end-ischemic pathway was made by NICE during the scoping process, as this pathway is most relevant to the UK clinical context. We appreciate that this metra RCT has been deprioritised as a result.
25	OrganOx	19	3	Transplant utilisation is an important outcome, but only if the additional livers utilised provide life sustaining function. Hence “functional utilisation”, where the increase is only counted if the additional livers provide life sustaining function, should be the metric used. This is where the ability to estimate viability, both to ensure function of transplanted organs and avoid organs which would go on to suffer primary or early non function, is so important, something not adequately stressed as benefits in the report	Thank you for your comment, we understand that the ability to directly test liver function at body temperature during viability testing is one of the purported advantages of normothermic perfusion. This has been noted in the Clinical Context section. This possible advantage has not been explored further in the EAR due to the lack of evidence on utilisation in the prioritised studies.
26	OrganOx	30	5	Transaminase enzymes are released during cold storage as a result of ischaemia. These enzymes are washed out of livers both during hypothermic perfusion and normothermic perfusion; this “wash-out effect” is not a phenomenon limited to normothermic perfusion, contrary to what the clinical expert referred to by the EAG states.	Thank you for your comment. We have reviewed the expert’s comment and found that their reference to NMP specifically when discussing the “wash-out” effect related specifically to the use of transaminase enzymes in NMP viability assessment, and did not suggest that the “wash-out” effect was limited to NMP. We have edited the report to reflect that the wash-out effect is not limited to NMP perfusion.

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27	OrganOx	32	5	Table 5.1 highlights the van Rijn study of 2021 and the 5-year follow up published in 2025. In the 5-year follow up paper the authors reveal that 7/78 DHOPE subjects and 13/78 SCS subjects had primary sclerosing cholangitis as their indication for transplantation. These patients develop recurrent disease, often quite early, which causes non-anastomotic strictures (NAS) which are indistinguishable from those on the cholangiograms of patients without primary sclerosing cholangitis. Nowhere in either paper is this considered and the incidence of non-anastomotic strictures in the subgroup with primary sclerosing cholangitis is not reported, but it is likely to have skewed the outcome data on the incidence of NAS differently in each half of the study, benefitting the intervention rather than the SCS control group. This is a major flaw with the reporting of that study.	Thank you for your comment, we have added detail of this to the results section of the report.
28	OrganOx	48	5	Anastomotic biliary strictures can be defined as those requiring surgical, endoscopic or radiological intervention, or as a finding on cholangiography. The problem with the latter is that when different diameter donor and recipient bile ducts are anastomosed there can be an apparent stricture which is not a real stricture when further investigated, and does not need intervention. Therefore the criteria used for defining anastomotic strictures are crucial for comparing across series.	We acknowledge the reviewer's valid concern regarding the definition of anastomotic biliary strictures. We have reported the data as presented in the prioritised studies
29	OrganOx	98	6	The organ utilisation numbers in Table 6.6 are not accurately reported. The NHSBT Annual Report for 2024/25 says that there were 676 DBD and 727 DCD **actual** organ donors. The utilisation report refers to liver **offers**, which is similar to actual donors for DBDs but not for DCDs, where many potential donors do not die in a time frame to permit organ recovery. Hence the number of offered DCD livers in 2024/25 is more (898) than the actual number of donors (727) from whom only 438 livers were retrieved, and only 310 livers used. It is also important to distinguish between organ donors and retrieved organs. Many livers are not retrieved from DCD donors because of the time it has taken the donor to die increases the risk that the liver may not work. If you are unable to test viability then safety dictates that those livers go unused. The true potential of utilisation by testing viability is to increase the use of not only retrieved livers, but also DCD donor livers that are currently not even retrieved because the donor took "too long" to	Thank you for your comment. We agree that organ utilisation can be defined at multiple stages of the transplant pathway, including organ offer, retrieval, and transplantation, and that these distinctions are particularly important for DCD donors where non-retrieval is relatively common. In the current model, utilisation is applied at the point of organ offer. As such, the values used (Table 6.6, based on Table 3.3) reflect the proportion of offered livers that are ultimately transplanted. This approach is consistent with the available data used to inform the model and aligns with the NICE scope, which focuses on the use of machine perfusion once organs have been offered and are available at the donor hospital. We acknowledge that this approach may not fully capture potential upstream effects of machine

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				die. The definition of “too long” is becoming irrelevant with the advent of NMP and NRP.	perfusion technologies, particularly the impact on retrieval decisions for DCD donors or the potential to increase the pool of organs that are retrieved in the first instance. These broader pathway effects are important but fall outside the scope of the current analysis.
30	OrganOx	9	Executive summary Economic Evidence	It should read one not Ome	Thank you for alerting us to this error, this has been corrected.
31	OrganOx	96	Organ utilisation and waitlist parameters	The reported confidence interval is incorrect. Nasralla et al. (2018) report a relative risk of organ utilisation of 1.16 with a 95% CI of (1.04–1.30).	Thank you for alerting us to this error, this has been corrected.
32	OrganOx	102	Table 6.7: Complications parameters	The risk ratio of complications (machine perfusion; Liver Assist; HMP) for PNF is not reported in Schlegel et al. It would be helpful to clarify the source of this value.	Thank you for alerting us to this error, this has been corrected.
33	OrganOx	103	Table 6.7: Complications parameters	**Risk ratio of complications (machine perfusion; *metra* [NMP], assumed applicable to Liver Assist [NMP])** Although not all studies in the Lai (2025) meta-analysis used a strict back-to-base approach, this analysis provides the most reliable overall estimate. Across all included studies, the pooled relative risk of post-LT ischemic cholangiopathy with NMP was 0.68 (95% CI: 0.41–1.13; p = 0.14), indicating no statistically significant difference in risk compared with SCS.	Thank you for your comment. Systematic reviews and meta-analyses were not eligible for inclusion in the review according to the eligibility criteria in the review protocol agreed with NICE.
34	OrganOx	104	Table 6.7: Complications parameters	Risk ratio of complications (machine perfusion; VitaSmart) should be 0.79	Thank you for alerting us to this typo, this has been corrected.
35	OrganOx	111	Table 6.9: Procedure and post-transplant costs	The waitlist cost applied in the model (£1,469 per month; ~£17,628 per year), sourced from Zimmermann et al. (2022), is not aligned with NHSBT-based evidence. The source does not provide a transparent breakdown and acknowledges uncertainty. In contrast, UK-specific data derived from NHSBT-linked analysis (Riley et al., 2026, DHSC/NHSBT) indicates that the annual	Thank you for your comment. The study by Riley et al. (2026) was not identified in our literature search as it was published after the search cut-off date and is currently only available as a pre-print.

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				secondary care cost for liver patients on the waiting list is approximately **£34,982 per year**, which is almost double the value used in the model. This reflects the real-world cost of managing patients with end-stage liver disease, including hospital admissions, monitoring, and complications. Therefore, the current assumption significantly underestimates the true cost of remaining on the waitlist and may bias the model against technologies that increase transplant rates and reduce waiting time. A revised, UK-specific estimate consistent with NHSBT data should be applied. medrxiv.org/content/10.64898/2026.03.18.26348687v1.full.pdf+html	The waitlist cost used in the model was based on the best available evidence at the time of analysis. While we acknowledge that UK-specific NHSBT-linked estimates may better reflect real-world costs, DSA did not identify waitlist cost as a key driver of model results. Additional internal analyses suggest that applying this higher waitlist cost does not change the direction of results.
36	OrganOx	111	Table 6.9: Procedure and post-transplant costs	The model does not account for differences between overnight and daytime procedures. Available data indicate that daytime procedures are associated with lower costs. This distinction should be incorporated to better reflect variation in resource use and overall costs.	Thank you for your comment. The National Cost Collection values used in the model represent average costs across all procedures and therefore implicitly capture variation in resource use, including differences between daytime and overnight procedures. As such, these distinctions are already reflected in the applied unit costs.
37	OrganOx	111	Table 6.9: Procedure and post-transplant costs	**Cost of liver transplant (adults)** In Table 6.9 (Procedure and post-transplant costs), the unit costs for liver transplantation appear to reflect elective inpatient cases only, which represent a subset of the total transplant population. This approach may not capture the full range of resource use across all patients undergoing transplantation. Using an average cost would be more appropriate, estimated at £36,331, to better capture overall resource use.	Thank you for your comment. It is assumed in the model that primary (i.e. first) transplants are undertaken on an elective basis, reflecting that these procedures are more commonly planned. In contrast, subsequent transplantations (e.g. re-transplantation) are more likely to occur under urgent or non-elective circumstances due to graft failure or clinical deterioration. As such, different cost inputs are applied to reflect these differences in resource use. We acknowledge that applying an average cost across all transplant types is an alternative approach; however, the current method was selected to better capture variation between planned and urgent procedures. Deterministic sensitivity analysis indicates that this assumption is not a key driver of model results.

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38	OrganOx	111	Table 6.9: Procedure and post-transplant costs	**Cost of liver transplant (paediatrics)** The average paediatric cost is £57,588 per case	Thank you for your comment. Upon review, we confirm that the paediatric cost used in the model was calculated using a weighted average of procedures across age groups 0-1 and 2-17 years. The value cited (£57,588) relates to the 2-17 age group only and therefore does not reflect the full paediatric population included in the model.
39	OrganOx	98	Table 6.6: Organ utilisation and waitlist parameters	The organ utilization rate for DCD appears to be underestimated. Based on NHSBT data, 310 out of 438 retrieved organs were transplanted, corresponding to a utilization rate of 70.8%.	Thank you for your comment. As noted above, organ utilisation in the model is defined at the point of organ offer rather than retrieval. As such, the utilisation rates applied reflect the proportion of offered organs that are ultimately transplanted, rather than the proportion of retrieved organs used. We acknowledge that defining utilisation at the point of retrieval would result in higher estimated utilisation rates (e.g. 310/438); however, the current approach was selected to maintain consistency with the model structure and available data inputs.
40	OrganOx	98	Table 6.6: Organ utilisation and waitlist parameters	For DBD, 512 out of 612 retrieved organs were transplanted, giving an organ utilization rate of **83.7%**.	See above comment
41	OrganOx	98	Table 6.6: Organ utilisation and waitlist parameters	The same relative risk (RR = 1.1 vs static cold storage) has been applied to both HMP and NMP, which is not justified. These technologies differ fundamentally in both mechanism and clinical application: HMP preserves the organ under hypothermic conditions and may provide modest improvements in outcomes, but it does not enable real-time functional assessment. NMP, by contrast, maintains the organ in a near-physiological state, allowing	Thank you for your comment and for highlighting the relevant clinical evidence. We acknowledge that HMP and NMP differ in their mechanisms and that there is evidence suggesting NMP may have a greater impact on organ utilisation. However, there was limited consistent and comparable evidence available to quantify

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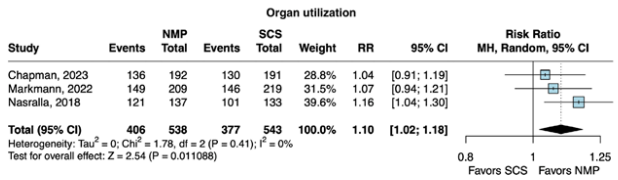
				viability assessment, monitoring of metabolic activity, and potential resuscitation of marginal or previously declined organs. This capability directly supports higher organ acceptance and utilization rates by NMP. This distinction is supported by clinical evidence. Multiple randomized controlled trials of HMP have failed to show any evidence of improvement in organ utilization compared with SCS, including: van Rijn et al., NEJM 2021 Czigany et al., Annals of Surgery 2021 Ravaioli, American Journal of Transplantation 2022 Schlegel et al., Journal of Hepatology 2023 Panayotova et al., Hepatology 2024 In contrast, evidence from Nasralla et al. (2018) and the Viana (2025) meta-analysis shows that NMP is linked to a statistically significant increase in organ utilization (see below please). Therefore, assigning the same relative risk to both technologies is not supported by the evidence or by the observed data from the previous RCT analysis. **Based on this evidence, the appropriate assumption is that the relative risk for HMP should be 1.0, reflecting no improvement in organ utilization compared with static cold storage.**  Organ utilization Study / NMP Events Total / SCS Events Total / Weight / RR / 95% CI / Risk Ratio MH, Random, 95% CI Chapman, 2023 136 192 130 191 28.8% 1.04 [0.91; 1.19] Markmann, 2022 149 209 146 219 31.5% 1.07 [0.94; 1.21] Nasralla, 2018 121 137 101 133 39.6% 1.16 [1.04; 1.30] Total (95% CI) 406 538 377 543 100.0% 1.10 [1.02; 1.18] Heterogeneity: Tau² = 0; Chi² = 1.78, df = 2 (P = 0.41); I² = 0% Test for overall effect: Z = 2.54 (P = 0.011088) 0.8 1 1.25 Favors SCS Favors NMP FIGURE 5 | Organ utilization rates were significantly higher in the NMP group when compared to SCS. [Color figure can be viewed at wileyonlinelibrary.com]	differential effects on utilisation across technologies in a way that could be robustly incorporated into the model. As such, a common relative risk was applied across device types to avoid introducing additional uncertainty or bias based on heterogeneous data sources. To explore this uncertainty, threshold analyses were conducted in which organ utilisation rates were varied independently for each technology. These analyses allow assessment of the extent to which differential utilisation effects, including scenarios where HMP has no impact (RR = 1.0) and NMP has a greater effect, would influence the model results.
42	OrganOx			Throughout the report, the *metra* device should be written in lowercase and italicized.	Thank you for your comment, this has been actioned.

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Section B Economic model - Comments

Stakeholder	Comment	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
XVIVO	1	**Inaccurate transferal of data from HOPE to NMP** Using HOPE data to fill evidence gaps for NMP is not appropriate as it introduces a risk of biased or misleading conclusions, such as: - Overestimation of treatment effect - Misleading comparative effectiveness conclusions - Inappropriate weighting of non-equivalent evidence. Several published systematic reviews on machine perfusion in LT, including the Cochrane review by Tingle 2023, provide high certainty evidence of the superiority of end-ischemic HOPE over SCS for clinically relevant outcomes such as graft survival, ischemic cholangiopathy, and severe post-operative complications. In contrast, NMP is reportedly not associated with improvement in any of these outcomes. Extrapolating clinical effectiveness data from HOPE to NMP may not accurately represent clinical reality and is likely to result in an overestimation of NMP's benefits.	Due to the fundamental differences between HOPE and NMP, we propose using data from high-quality systematic reviews to inform survival rates with NMP instead of assuming similar post-transplant outcomes across modalities. e.g., Tingle 2023 - Patient survival: HR 1.08 - Graft survival: HR 1.2	This is expected to more accurately reflect the real-world outcomes and costs.	Thank you for your comment. We acknowledge that HOPE and NMP differ in their mechanisms and clinical effects, and that extrapolating evidence between modalities introduces uncertainty. However, there was limited consistent evidence available to inform post-transplant survival outcomes separately for each perfusion modality in a way that could be robustly incorporated into the model. As such, a simplifying assumption was applied to ensure a complete and internally consistent evidence base across outcomes. This assumption was explicitly acknowledged

		This is particularly problematic in NICE HTAs, where such interpretations may directly influence recommendations and resource allocation. As mortality is one of the main outcomes assessed in the HTE, using a RR of 0.32 across all devices and perfusion modalities introduces significant risks of overestimation of treatment effect with NMP.			in the methods and tested extensively through scenario analyses, including the use of alternative effect estimates. These analyses did not materially alter the overall conclusions.
XVIVO	2	**Issues relating to reporting of non-anastomotic stricture (NAS)** Table 6.7 presents a combined incidence of NAS for both DBD and DCD with SCS: 14.83%. Combining NAS data for DBD and DCD is not relevant as NAS is mainly an issue in DCD LT. A recent consensus report on biliary complications in LT states that the incidence of NAS following SCS is ~5% in DBD and up to 44% in DCD[1]. As the report rates NAS as the second highest complication cost (£9,588), underestimating the prevalence of NAS in SCS may not accurately reflect the true cost savings achieved through the reduction of NAS following HOPE in DCD LT (as demonstrated by van Rijn 2021 and 2025). The incidence of NAS should therefore be reported separately for DBD and DCD for all preservation methods (SCS, HOPE, and NMP). The following rates of NAS are recommended for DBD + SCS: 5% and DCD+SCS: ~20% (18-26%; based on van Rijn 2021 and 2025 data, respectively). [1] Esser et al 205 Consensus classification of biliary complications after liver transplantation: guidelines from the BileducTx meeting; doi: 10.1093/bjs/znae321	We therefore propose that the incidence of NAS should be reported separately for DBD and DCD for all preservation methods (SCS, HOPE, and NMP). And that the following rates of NAS are used for SCS in the different donor types: - DBD: 5% (*based on consensus paper by Esser 2025)* - DCD: ~20% *(18-26%; based on van Rijn 2021 and 2025 data, respectively.*	This amendment is expected to more accurately reflect the true cost savings achieved through the reduction of NAS in DCD LT with the use of machine perfusion.	Thank you for your comment. We agree that the incidence of NAS differs between DBD and DCD donors, with higher rates typically observed in DCD transplantation. However, there was limited consistent evidence identified that would allow robust stratification of NAS rates by donor type and preservation method within the model framework. As such, a pooled estimate was applied to maintain consistency across inputs. We acknowledge that this approach may not fully capture differences in NAS incidence between DBD and DCD pathways. Scenario analyses were conducted to explore the impact of NAS on costs and outcomes; these indicated that variation in NAS incidence has a

					limited impact on overall model results.
OrganOx	3	The model uses an initial patient population of 1,000, while the actual number of patients on the waiting list is 1,148. This leads to inconsistency between the modelled population and real-world data. In addition, device costs and staff time are allocated by dividing total costs by the number of transplants. Since the model underestimates transplant volumes compared to NHSBT 2024–25 data, this inflates the cost per device and per procedure.	Update the model to reflect the actual waiting list population of 1,148 patients. Revise transplant volume assumptions to align with NHSBT 2024–25 data. Recalculate per-device and staff costs using the corrected number of transplants to ensure accurate cost allocation.	This amendment is expected to reduce the cost per device and per procedure due to higher transplant volumes spreading fixed costs more appropriately. As a result, total cost estimates per patient may decrease, which could improve the ICER if outcomes remain unchanged.	The calculation for cost per procedure within the model is based on the total expected volume of procedures carried out per year and results produced are on a per-person basis. Annual fluctuations in the total number of procedures completed would reduce the applicability of this alternative proposed method
OrganOx	4	There is an inconsistency between the EAG report and the economic model. The EAG report states (page 114) that each device performs 60 procedures per year, whereas the cost-effectiveness model (costs tab) uses 50 procedures per year. This discrepancy creates inconsistency in cost calculations and assumptions..	Align the number of procedures per device across the report and the model. A single, justified value (based on UK practice) should be applied consistently throughout.	Ensuring consistency will improve transparency and reliability of the model. Depending on the value used, this may increase or decrease cost per procedure and impact the ICER.	Thank you for your comment. The discrepancy reflects redaction and rounding applied to certain model inputs to prevent back-calculation of other companies confidential costing data. As such, the value presented in the report does not exactly match the value implemented in the model. This does not affect the internal consistency of the model or the cost-effectiveness results, as the model itself uses a single consistent set of inputs throughout.
OrganOx	5	We attempted to replicate the reported ICERs in the EAG report. For example, for liver assist HMP, even when a device cost of £0 is applied, the ICER remains higher than the reported ICER of £5,639,	We are raising this issue for checking. It would be helpful to confirm whether there	Clarification will help confirm whether the model is working as intended and ensure	Thank you for your comment. The discrepancy reflects redaction and rounding applied to certain

		which suggests that the results cannot be reproduced from the available inputs. It appears that device costs are calculated in the DT-intervention tab, then carried through to the MM-intervention tab, and from there into the summary tab, which seems logical and transparent. However, the ICERs remain non-reproducible, even when device costs are set to zero. Unless additional changes have been made to the model that prevent back-calculation of the device cost, this discrepancy remains unclear.	are any additional assumptions, adjustments, or structural elements in the model that explain this difference.	consistency across technologies.	model inputs to prevent back-calculation of other companies confidential costing data. As such, the value presented in the report does not exactly match the value implemented in the model. This does not affect the internal consistency of the model or the cost-effectiveness results, as the model itself uses a single consistent set of inputs throughout.
OrganOx	6	When applying device cost input for Liver assist (HMP) from Zimmermann et al. (2022), the resulting ICER is substantially higher than that reported in the EAG analysis.  Intervention Select overall costing approach Select micro costed device cost approach Include perfusionist staff time costs? Select perfusionist cost scenario Inputs all correct Machine perfusion cost: Micro costed approach / Base case / User defined / Live Cost of device including staff training (upfront) £0.00 £0.00 Lifetime of device (years) 5 5 Number of procedures conducted per year 50 50 Per-procedure cost of device £0.00 £0.00 Cost of consumables (per procedure) £0.00 £0.00 Cost of annual maintenance £0.00 £0.00 Cost of annual maintenance per procedure £0.00 £0.00 Total per-procedure cost of machine perfusion £0.00 £0.00 Machine perfusion cost: One-off unit cost approa / Base case / User defined / Live Total per-procedure cost of machine perfusion £10,000 £4,508 £4,508 Total calculated cost (excluding perfusionist tear £4,508	Double-check that the ICERs have been reported correctly across all devices	Applying these inputs results in an ICER of approximately £11,520 and £13,103 per QALY for HMP and NMP among adult population, which is higher than the ICER reported in the EAG deterministic base case.	Thank you for your comment. The discrepancy reflects redaction and rounding applied to certain model inputs to prevent back-calculation of other companies confidential costing data. As such, the value presented in the report does not exactly match the value implemented in the model. This does not affect the internal consistency of the model or the cost-effectiveness results, as the model itself uses a single consistent set of inputs throughout.