Indications for LDLT in paediatrics; Do we need to rethink

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KING'S HEALTH PARTNERS

Living Donor Liver Allocation Policy

Claude content

🎯 Non-Directed Altruistic (NDAD)

- Donation to UK transplant list
- No genetic/emotional relationship
- Offered to local centre first
- Anonymity required pre-surgery
- Can break anonymity post-surgery with consent

🤝 Directed Altruistic (DAD)

- Genetic relationship, no emotional bond
- No pre-existing relationship before need identified
- Requires HTA approval
- No evidence of coercion or reward

👨‍👩‍👧‍👦 Directed Living Donation

- Blood relative of recipient
- Emotional relationship (spouse, partner, friend)
- If recipient unavailable, redirected to list
- Private sector considerations apply

🔄 Domino Liver

- Currently in development
- Outside formal allocation process
- May use for patients outside standard criteria
- Recorded as 'Domino Donor' with NHSBT

1st Paed LRLT
Sir Roy Calne, 1984

Indications for LT 2020

- • **Chronic liver disease**

  •-Biliary atresia
  -α-1-antitrypsin deficiency
  -Autoimmune liver disease
  -Sclerosing cholangitis (neonatal, primary, autoimmune)
  -Caroli's syndrome and other liver ciliopathies
  -Wilson's disease
  -Cystic fibrosis
  -Progressive familial intrahepatic cholestasis (all types)

  •-Bile acid synthesis disorders

  •-Alagille syndrome
  -Glycogen storage disease types 1, 3 and 4
  -Tyrosinaemia type 1

  •-Graft versus host disease

  •-Sickle cell disease

  •-Sinusoidal obstruction syndrome
  -Budd-Chiari syndrome

  •-Cryptogenic cirrhosis

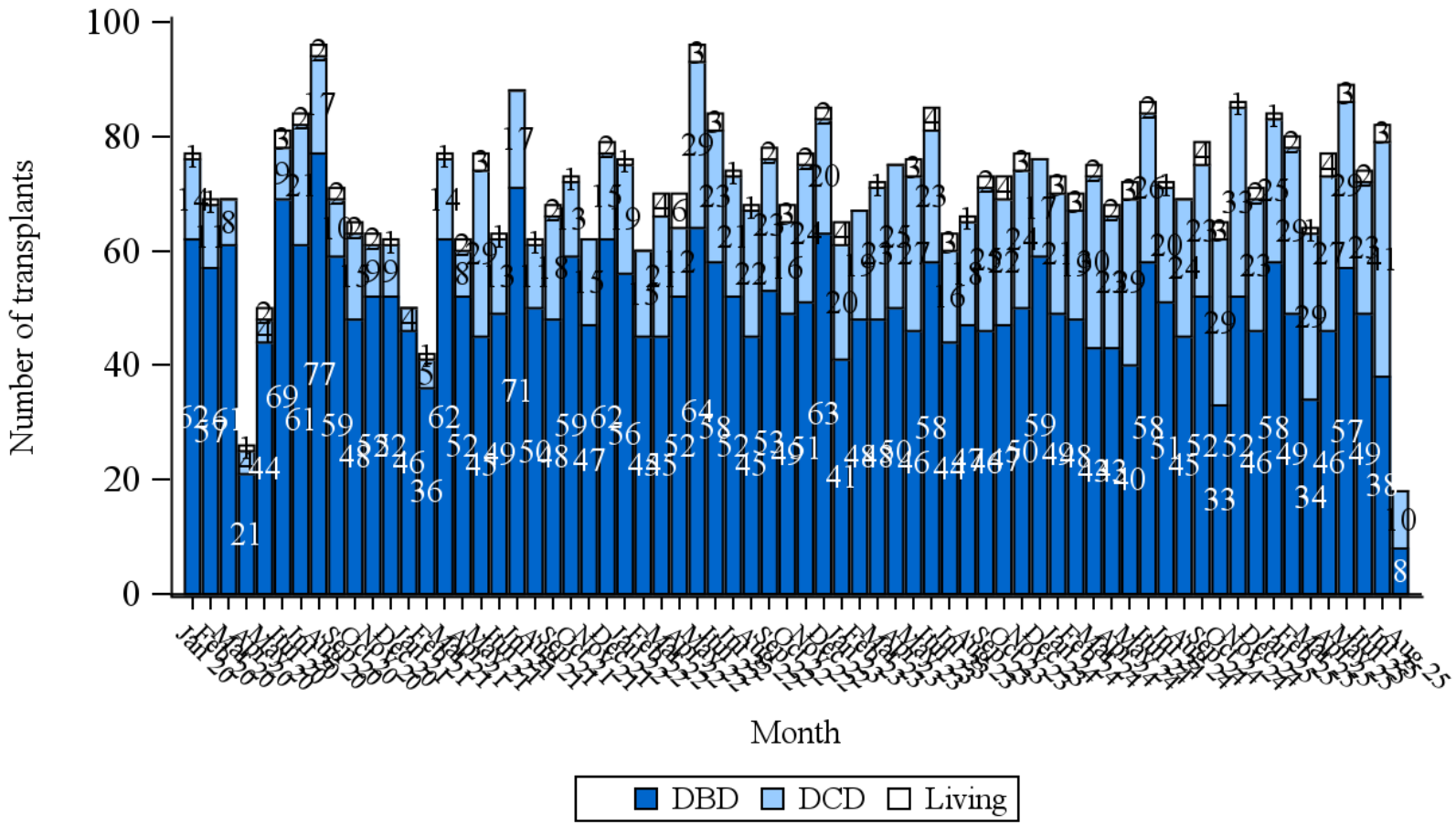
  •-Intestinal Failure Associated Liver Disease

  •-Any aetiology leading to portal hypertension, hepatopulmonary syndrome or portopulmonary hypertension

- • **Liver tumours**
- -Unresectable hepatoblastoma (without active extrahepatic disease)
- -Unresectable benign liver tumours with disabling symptoms

- • **Metabolic liver disease with life-threatening extra-hepatic complications**
- Citrullinemia
- Transaldolase deficiency
- Arthrogryposis-renal dysfunction-cholestasis syndrome
- Crigler-Najjar syndrome type 1
- Urea cycle defects
- Hypercholesterolaemia
- Organic acidaemias
- Primary hyperoxaluria
- Fatty acid oxidation defects
- Congenital Disorders of Glycosylation (CDG)
- Inherited disorders of complement causing atypical haemolytic uraemic syndrome
- Molybdenum cofactor deficiency
- **Congenital liver vascular malformations**

Figure 3 Number of liver transplants performed in the UK, by donor type, 1 January 2020 to 11 August 2025



UK Liver Transplant list

UK Liver Tx list

Figure 14 **Number of paediatric patients on the liver transplant list at the end of each month, January 2020 - 14 August 2025**

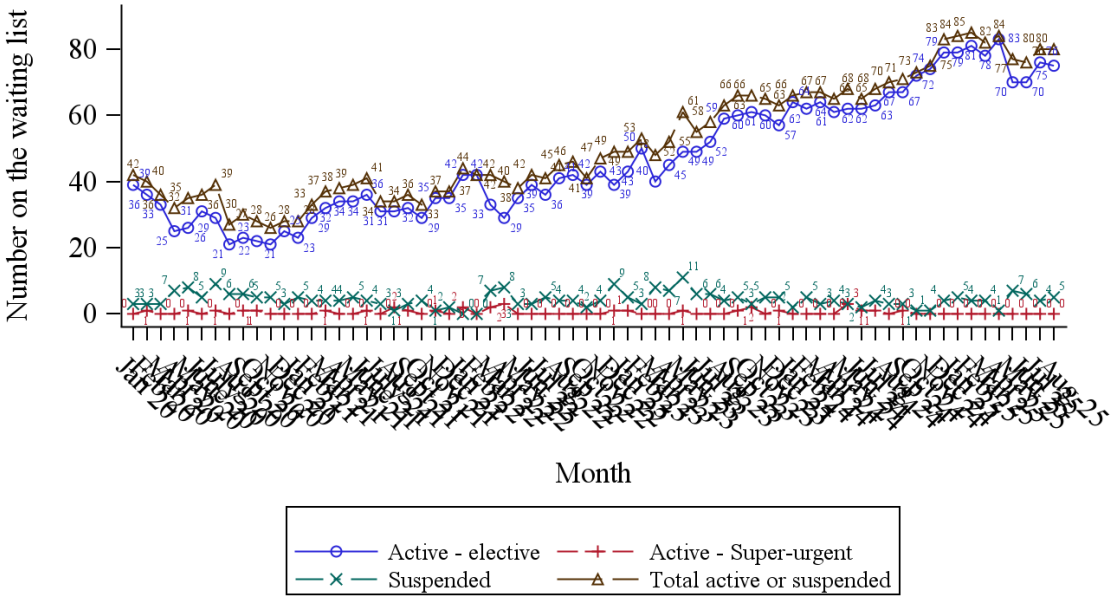


Figure 16 **Total number of paediatric patients on the elective UK liver transplant list on 14 August 2025, by registration status**

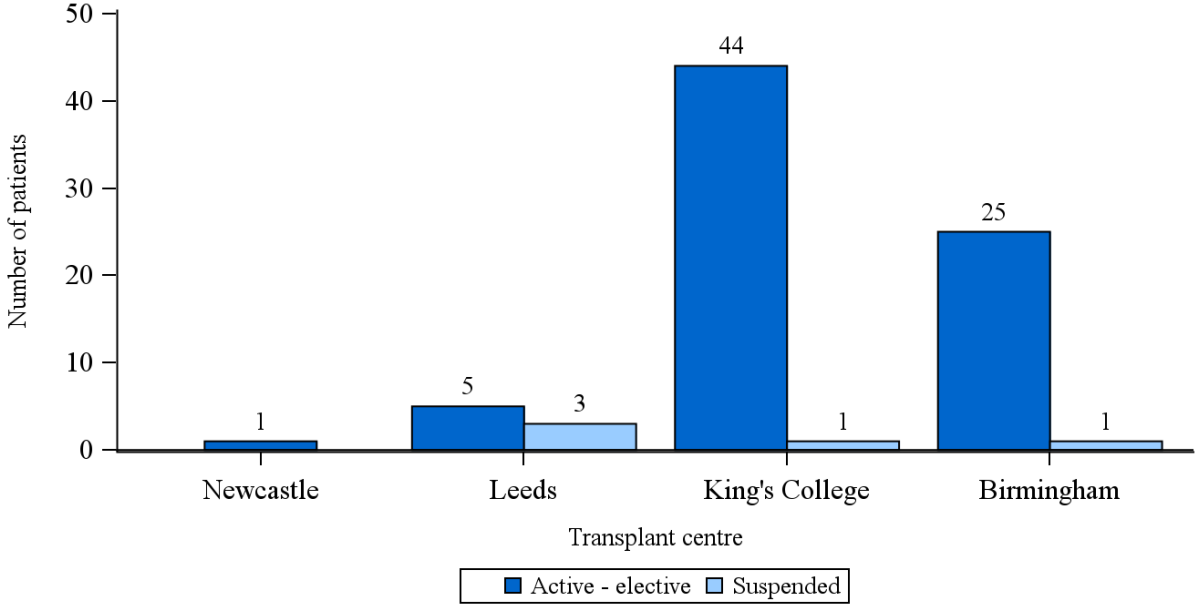


Table 2 Clinical outcomes.

Variable	Result
Survival, %	
Patient	
Absolute	95.7
1-yr actuarial	97.8
5-yr actuarial	95.1
10-yr actuarial	95.1
Graft	
Absolute	93.2
1-yr actuarial	100
5-yr actuarial	97.0
10-yr actuarial	77.6

Clinical and histological outcomes following living-related liver transplantation in children

Nikesh Dattani[a], Alastair Baker[a,*], Alberto Quaglia[b], Hector Vilca Melendez[b], Mohamed Rela[b], Nigel Heaton[b]

Table 1 Recipient and donor demographics.

Variable	Result
Recipient	
Sex (M/F)	30/16
Age (yr), mean (range)	2.4 (0.5–11)
Weight (kg), mean (range)	11.0 (3.7–32.3)
Primary liver disease, *n* (%)	
BA	24 (52.1)
Metabolic	6 (13.0)
Hepatoblastoma	6 (13.0)
PFIC	5 (10.9)
Other	5 (10.9)
Presentation, *n*	
Chronic liver disease	41 (89.1)
Fulminant hepatic failure	3 (6.5)
Re-transplantation	2 (4.3)
Pre-transplant condition, *n* (%)	
At Home	26 (56.5)
At Hospital	12 (26.1)
In ICU	4 (8.7)
Missing	4 (8.7)

Review

JOURNAL
OF HEPATOLOGY

LDLT
CONTRAINDICATED CONDITIONS (High Risk)

Evaluation of living donors for hereditary liver disease (siblings, heterozygotes)

Mureo Kasahara[1,*], Johnny C. Hong[2], Anil Dhawan[3]

Disease	Inheritance	Prevalence	Indication for LT	Donor Risk	Outcome	Limitation
Ornithine Transcarbamylase Deficiency (OTCD)	X-linked	1 in 50,000	Most common metabolic indication; refractory hyperammonemia	Heterozygous mothers: 18% risk hyperammonemia from skewed X-inactivation	Recipients may have post-transplant hyperammonemia due to low OTC activity	CONTRAINDICATED: Heterozygous mothers unsuitable donors
Protein C Deficiency	Autosomal recessive	1 in 20,000	Life-threatening thrombosis/hemorrhage in neonates	Heterozygous parents have borderline low protein C activity	Case report required aggressive thromboprophylaxis and protein C concentrate	CONTRAINDICATED: Significant thromboembolic risk
Familial Hypercholesterolemia	Autosomal dominant	1 in 160,000-300,000	Severe cardiovascular risk, poor response to statins	Long-term cardiovascular disease risk in heterozygous donors	3 cases reported; both donors and recipients need ongoing cholesterol drugs	MARGINAL: May induce premature atherosclerosis
Acute Intermittent Porphyria	Autosomal recessive	1 in 20,000	Life-threatening acute attacks, liver failure	50% reduction in porphobilinogen deaminase activity	One case had recurrence 4 years post-transplant	CONTRAINDICATED: Genetic testing mandatory
Erythropoietic Protoporphyria	Autosomal recessive	1 in 50,000-75,000	Liver failure, photosensitivity	Decreased ferrochelatase activity in heterozygotes	3 cases reported, 1 death from cerebral herniation	CONTRAINDICATED: Heterozygous relatives unsuitable
Alagille Syndrome	Autosomal dominant	1 in 100,000	End-stage liver disease from bile duct paucity	Asymptomatic parents may have intrahepatic bile duct abnormalities	Poor prognosis if insufficient biliary drainage	REQUIRES: MRCP, liver biopsy, genetic studies
HLA Homozygous Donors	-	3.2% in Japan	Any indication	Significantly increased graft-versus-host disease risk	Poor prognosis with GVHD	ABSOLUTE CONTRAINDICATION

LDLT
INDICATED CONDITIONS (Low Risk)

Disease	Inheritance	Prevalence	Indication for LT	Donor Considerations	Outcome	Genetic Testing Required
Wilson's Disease	Autosomal recessive	1 in 40,000	Acute liver failure, decompensated chronic disease	Heterozygous carriers asymptomatic; 50% have low ceruloplasmin	Excellent: 75.8% survival at 30 years	NO
Methylmalonic Acidemia (MMA)	Autosomal recessive	1 in 69,000	Metabolic decompensation, poor quality of life	Heterozygous donors have acceptable enzyme activity	85.2% survival at 10 years; metabolic improvement	NO
Propionic Acidemia (PA)	Autosomal recessive	1 in 240,000	Recurrent metabolic crises	Partial enzyme correction sufficient	Stabilized metabolite levels, improved protein tolerance	NO
Alpha-1 Antitrypsin Deficiency	Autosomal recessive	1 in 5,000	Progressive liver disease, risk of cirrhosis	May have complicated post-transplant course	Normal A1AT levels achieved; 89.1% survival at 20 years	NO
Crigler-Najjar Syndrome Type 1	Autosomal recessive	1 in 1,000,000	Risk of kernicterus from unconjugated bilirubin	Heterozygotes have low but sufficient UDP-glucuronyl transferase	8 cases reported, 7 excellent outcomes (1 aspiration death)	NO
Primary Hyperoxaluria Type 1	Autosomal recessive	1 in 120,000	Progressive renal failure from oxalate stones	AGT activity 30-77% of normal in heterozygotes	Excellent recipient survival, no donor symptoms	NO
Maple Syrup Urine Disease	Autosomal recessive	1 in 185,000	Poor metabolic control, recurrent crises	Parents inevitably carriers; normal BCKDH activity sufficient	22/24 patients well; unrestricted diet possible	NO

Living Donor Liver Transplantation for Pediatric Wilson's Disease-related Acute Liver Failure—Hard Work With High Rewards

Somashekara H. Ramakrishna [*,†], Vellaichamy Katheresan [‡], Mohan B. Kasala [§], Karnan Perumal [§], Selvakumar Malleeswaran [¦], Joy Varghese [¶], Rajanikanth V. Patcha [‡], Prashant Bachina [#], Poushya S. Madhavapeddy [#], Mettu S. Reddy [‡,**]

- **Patient Characteristics**
- 53 children studied: 28 with Wilson's Disease Acute Liver Failure (WD-ALF), 25 with chronic presentation (WD-CLD)
- WD-ALF patients were younger (8.5 vs 10.5 years), had higher PELD scores (35 vs 20), and higher King's New Wilson Index (15 vs 9)
- **2. Clinical Presentation Differences**
- WD-ALF patients
- 86% had ongoing hemolysis vs 28% in chronic cases
- 64% were encephalopathic vs 4%
- required more intensive pre-transplant support

- **Benefits & Indications**
- **3. Curative Treatment**
- LDLT provides complete cure for Wilson's disease with excellent long-term outcomes
- All survivors had good graft function without neurological sequelae at follow-up
- **4. Emergency Life-Saving Option**
- For WD-ALF patients, liver transplantation is often the only life-saving option as medical therapy (including therapeutic plasma exchange) alone has limited success

Hepatology International
https://doi.org/10.1007/s12072-025-10851-1

ORIGINAL ARTICLE

Outcomes of pediatric living donor liver transplantation using steatotic grafts: expanding the donor pool for rising MASLD prevalence

Jie Li[1] · Yixiao Pan[1] · Yefeng Lu[1] · Xinye Zhu[1] · Jiahao Ge[1] · Siyuan Tang[1] · Jie Zhao[1] · Mei Long[1] · Xiaochen Bo[1] · Yiqing Zhang[1] · Ping Wan[1] · Kang He[1] · Taihua Yang[1] · Qiang Xia[1,2,3]

- **Study Overview**
- **Large cohort**: 151 pediatric recipients analyzed from 905 total cases (2019-2021)
- **Classification**: Donors grouped by steatosis severity - Normal (<5%), Mild (5-33%), Moderate-to-severe (>33%)
- **Rationale**: Rising MASLD prevalence necessitates expanding donor pool

Hepatology International
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- **Early Outcomes - Generally Safe:**
- No primary non-function (PNF) cases in any group
- No significant differences in liver function markers (ALT, AST, bilirubin, INR)
- Similar ICU stay and hospitalization duration across groups
- Initial poor function rates not significantly different

- **Survival Outcomes:**
- 1-year survival: Normal 94.1%, Mild 95.9%, Moderate-severe 77.8%
- 3-year survival: Normal 92.6%, Mild 95.9%, Moderate-severe 77.8%
- While numerically lower for severe steatosis, differences not statistically significant

Outcomes

Significant Complications

Higher Rejection Risk:

Rejection rates: Normal 1.5%, Mild 9.5%, Moderate-severe 22.2% (p=0.018)

Most concerning finding - significantly elevated despite comparable immunosuppression levels

Other Complications:

Increased gastrointestinal bleeding in moderate-severe group

Higher CMV infection rates in steatotic graft recipients

No significant differences in biliary or vascular complications

- **Clinical Implications**
- **Feasibility:**
- Steatotic grafts can be used successfully in pediatric transplantation
- Careful donor selection and enhanced monitoring essential
- Particularly valuable given organ shortage
- **Management Considerations:**
- Enhanced immunosuppressive monitoring required
- Vigilant postoperative surveillance for rejection
- Risk-benefit evaluation crucial for each case

LONG-TERM OUTCOME OF LIVING RELATED LIVER TRANSPLANTATION FOR PATIENTS WITH INTRAPULMONARY SHUNTING AND STRATEGY FOR COMPLICATIONS[1,2]

Egawa, Hiroto[3,7]; Kasahara, Mureo[3]; Inomata, Yukihiro[3]; Uemoto, Shinji[3]; Asonuma, Katsuhiko[3]; Fujita, Siro[3]; Kiuchi, Tetsuya[3]; Hayashi, Michihiro[3]; Yonemura, Toshiya[4]; Yoshibayashi, Muneo[4]; Adachi, Yasuhiko[5]; Shapiro, James A. M.[6]; Tanaka, Koichi[3]

- **Benefits**
- **Reduced waiting time** - No need for deceased donor
- **Timing flexibility** - Can schedule when recipient is optimal
- **Better organ quality** - Fresh, healthy liver tissue
- **Improved outcomes** - Shorter ischemia time
- **HPS resolution**- All survivors showed improvement
- **Long-term survival** - 62% survival rate in HPS patients

- **Risks & Complications**
- **Wound infection** - 66-80% incidence (higher in severe HPS)
- **Biliary complications** - 33% rate (vs 13.9% overall)
- **Portal vein thrombosis** - 20% in severe HPS
- **Intracranial complications** - 20% in severe HPS
- **Donor morbidity** - Risk to healthy donor
- **Technical complexity** - Requires expertise

- **1yr Survival Outcomes by HPS Severity**
- **Mild HPS:**80%
- **Moderate HPS:** 66.7%
- **Severe HPS:**48%

Domino LT

Domino donor disease	Primary defect	Description of defect	De novo disease in domino recipient
Familial Amyloidotic Polyneuropathy	Transthyretin (TTR)[6]	Abnormal transthyretin production resulting in systemic toxic accumulation[6]	Yes, as early as 8–9 years after transplant[8-10]
Maple Syrup Urine Disease	Branched chain ketoacid dehydrogenase (BCKDH) complex[11]	Abnormal systemic BCKDH activity results in toxic accumulation of branched chain amino acids[11-13]	Not reported[13,21]
Familial Hypercholesterolemia	Low density lipoprotein (LDL) receptor[27]	Abnormal LDL receptor function leads to high circulating cholesterol and subsequent deposition[27-29]	Yes, potentially rapidly progressive[30-33]
Primary Hyperoxaluria	Alanine:glycoxylate aminotransferase[22]	Hepatic oxalate production leads to progressive renal insufficiency[22]	Yes, renal failure within the first year[23-25]
Methylmalonic acidemia	Methylmalonyl-CoA Mutase[34]	Toxic accumulation of valine, isoleucine, threonine, methionine, cholesterol, and certain fatty acids resulting in mitochondrial dysfunction[34]	Not reported[34]
Propionic acidemia	Propionyl-CoA carboxylase[37]	Toxic accumulation of valine, isoleucine, threonine, methionine, cholesterol, and certain fatty acids resulting in mitochondrial dysfunction[37]	Not reported on altered diet[37]
Ornithine Transcarbamylase Deficiency	Ornithine transcarbamylase[35,36]	Inability to convert nitrogenous waste into urea[35,36]	Yes, unless used as an auxiliary graft[35,36]
Crigler-Najjar syndrome	UDP-glucuronosyltransferase 1[36]	Inability to conjugate bilirubin for excretion[36]	Not reported in auxiliary graft[36]

Domino transplantation for pediatric liver recipients: Obstacles, challenges, and successes

Vikram K. Raghu[1] | Peter D. Carr-Boyd[2] | James E. Squires[1] | Jerry Vockley[3]
Nicolas Goldaracena[4] | George V. Mazariegos[2]

Domino LT-Future directions

Expanding applications

- **Cross-center sharing**
- **Novel approaches** - Cross-auxiliary domino transplantation and hepatocyte transplantation using explanted metabolic livers
- **Broader indications**

Gene Therapy Impact

- **Future competition**

gene therapy

- **Cost-effectiveness considerations**

Research Priorities

- Long-term outcome studies
- Registry development

Commissioning Policy: Reimbursement of Expenses for Living Donors

Reference: NHS England A06/P/a

6 Living Organ Donors who are non-resident in the UK

There are cases when the individual wishing to donate is non-resident in the UK.

There are two categories of donors who live overseas:

1. Full-time residents (non-UK residents)
2. UK residents living temporarily overseas (e.g. for work or personal reasons)

Future perspectives

- Expanding indications
- NAFLD
- Living related LT or LKTx
- Domino
- Genotype-phenotype associations
- It does NOT have to be a parent!
- Need to work collectively with professionals, charities, patient groups and NHS

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Thank you