Changes in this version

Adding sickle cell hepatopathy
Updated Appendices following FTWU recommendations
Updated wording for SLK patients in 3.6.1

Policy

This policy has been created by the Liver Advisory Group on behalf of NHSBT.

This policy previously received approval from the Transplant Policy Review Committee (TPRC). This committee was disbanded in 2020 and the current governance for approval of policies is now from Organ and Tissue Donation and Transplantation Clinical Audit Risk and Effectiveness Group (OTDT CARE), which will be responsible for annual review of the guidance herein.

Last updated: July 2025

Approved by OTDT CARE: August 2025

Purpose

The aim of this document is to provide a policy for the selection of adult and paediatric patients on to the UK national transplant list and, where necessary, criteria for their de-selection. These criteria apply to all proposed recipients of organs from deceased donors.

In the interests of equity and justice all centres should work to the same selection criteria.
Non-compliance to these guidelines will be handled directly by NHSBT, in accordance with the policy on Non-Compliance with Selection and Allocation Policies. **POL198**

It is acknowledged that these guidelines will require regular review and refreshment. Where they do not cover specific individual cases, mechanisms are in place for selection of exceptional cases (see section 4).

Liver transplantation is an established treatment in patients who have a likelihood of poor survival or impaired quality of life secondary to acute or chronic liver disease.

Selection criteria for adult transplantation are largely based on outcome measures. While the same general principles apply to children there are notable differences:

- The success of liver splitting allows many children to benefit from liver transplantation with little net effect on the overall donor organ pool
- In some circumstances a smaller probability of long-term success may be a very worthwhile outcome for some children and their families

Applicable Documents

- **POL191** – Guidelines for consent for solid organ transplantation in adults
- **POL193** – Intestinal transplantation: Organ Allocation
- **POL194** – Intestinal transplantation: Patient Selection
- **POL196** – Deceased Donor Liver Distribution and Allocation
- **POL198** – Non-compliance with Selection and Allocation Policies
- **POL228** – Heart Transplantation: Organ Allocation
- **POL229** – Heart Transplantation: Selection Criteria and Recipient Registration
- **POL230** – Donor Lung Distribution and Allocation
- **POL231** – Lung Candidate Selection Criteria
- **SOP5907** – Registration process for liver indications requiring additional waiting time
- The NHS Blood and Transplant (Gwaed a Thrawsblaniadau'r GIG) (England) Directions 2005

1. Conditions that are considered for transplantation

1.1. *Adult patients*

Most adult patients with liver disease are not managed in transplant centres. Patients referred for assessment for liver transplant will include those with the following broad categories of conditions:

- Acute liver failure
  - Multi-system disorder in which severe acute impairment of liver function with encephalopathy occurs within 8 weeks of the onset of symptoms and no recognised underlying chronic liver disease
- Acute on Chronic liver failure (see **SOP5907 for the process to register ACLF patients)**
- Chronic liver disease: any cirrhosis which may be due to:
  - Fatty liver disease: alcohol or non-alcohol related
  - Chronic viral hepatitis B, C, D
  - Autoimmune liver diseases: primary biliary cirrhosis, primary sclerosing cholangitis, chronic active liver disease and overlap syndromes
  - Genetic haemochromatosis
  - Wilson's disease
  - α-1 antitrypsin deficiency
  - Congenital hepatic fibrosis and other congenital or hereditary liver diseases
  - Secondary biliary cirrhosis
- Sickle cell disease (see Appendix E for information)
- Liver tumours
  - Hepatocellular carcinoma (including patients downstaged (see Appendix A))
  - Neuroendocrine tumours (see Appendix B)
  - Colorectal Metastases (see Appendix C)
  - Intrahepatic Cholangiocarcinoma (see Appendix D)
  - Adenoma (see flow diagram in **Appendix F**)
- Variant syndromes
  - Intractable pruritus
  - Hepatopulmonary syndrome
  - Familial amyloidosis
  - Primary hypercholesterolaemia
  - Polycystic liver disease
  - Hepatic epithelioid haemangioendothelioma
  - Recurrent cholangitis
  - Nodular regenerative hyperplasia
  - Hereditary haemorrhagic telangiectasia
  - Glycogen storage disease
  - Ornithine transcarbamylase deficiency

- Primary hyperoxaluria
- Maple syrup urine disease
- Porphyria
- Amyloidosis - other

Patients not falling within these categories may be considered through the National Appeals Panel route (see section 4).

1.2. *Paediatric patients*

- Acute liver failure
  - Multi-system disorder in which severe acute impairment of liver function with encephalopathy occurs within 8 weeks of the onset of symptoms and no recognised underlying chronic liver disease
- 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

Please refer to SOP5907 for the process to register either genuine hepatoblastoma patients, prioritised paediatric patients, or Acute on Chronic Liver Failure patients.

2. Assessment of patients

2.1. *Adult patients*

Adults are assessed and reviewed by the multi-disciplinary team, as outlined in the Introduction.

2.1.1. *Illicit drug use*

2.1.1.1. *Assessment*

Due to the potential risk of recurrent disease or poor adherence leading to graft loss, and with the increasing number of assessments for patients with viral hepatitis C (HCV) secondary to intravenous drug use (IVDU) there is a growing requirement for careful assessment of illicit drug use and potential impact on outcomes after organ transplantation. In particular, it is important to consider poly-substance use and drug dependence due to the potential for both a direct effect upon the liver and also indirect consequences such as poor programme adherence or initiation/resumption of harmful alcohol use. These guidelines are complementary to those for patients with harmful alcohol consumption. Illicit drug use is not a contraindication to transplantation if the patient will comply with the required management schedules. However, continued intravenous drug use is considered a contraindication owing to the possible risk of infection in an immune-suppressed patient.

Patients admitted for a transplant assessment irrespective of diagnosis should be screened for current and past illicit substance use as part of the clinical interview. This should include misuse of over-the-counter medications and apparent misuse of pain relief medication.

- Any patient considered to have a significant drug-taking history should be assessed by a specialist in substance misuse; the term 'significant' must be interpreted by the clinical multidisciplinary team
- Adequate time and resources should be made available to allow this specialist to undertake this process
- Assessment should include problematic or dependent use as well as recent use. It should also identify substance use and stability within the patient's wider social support network, and take into account mental health and criminal justice issues as appropriate
- Services should endeavour to develop and implement joint screening and assessment protocols between hepatology and substance misuse services to ensure effective care pathways are in place

2.1.1.2. *Illicit drug use and substitute prescribing*

The recommendations regarding this area are given in the context of limited research data. Small studies are favourable to consideration of transplantation whilst on a substitute prescription, e.g. methadone maintenance therapy (MMT).

In such patients, analgesia post transplantation will need careful consideration and will require an agreed plan between the anaesthetist, pain team and substance misuse specialist.

Awareness of potential issues relating to patient-controlled analgesia will also be required, and risk factors should be assessed, and a local management plan effected accordingly

The potential for misuse should be balanced with the knowledge that opiate-tolerant patients are likely to need higher doses than an opiate-naive patient.

a. Methadone maintenance therapy (MMT)

MMT is a safe, well-evidenced treatment for patients unable to become opiate-free. It is commonly a long-term treatment. Patients on a stable MMT should be offered assessment for transplantation where medically indicated. Stability (individually measured as a continuum, not an absolute) indicates abstinence from other illicit drug use (predominantly other opiates and stimulants – including cocaine and crack cocaine).

There should be engagement with a drug treatment service and the patient should have an agreed care plan and a named key worker (though it should be acknowledged that it is now common practice to transfer stable patients to GP management). MMT patients should not be asked to reduce their methadone simply for the purpose of transplantation as this has the potential to destabilise them and provoke a relapse to other drug use.
Evidence suggests the likelihood of a prolonged ITU stay post-transplant and the requirement for larger doses and longer treatment for post-operative analgesia.

b. Buprenorphine

The same requirements apply in the context of substitute prescribing as for MMT. Due to its method of action as a partial opioid agonist antagonist there will be issues around peri-operative analgesia. Where possible, conversion to methadone peri-transplant will assist with this issue. This should be undertaken in consultation with a substance misuse specialist.

c. Prescribed IV diamorphine or physeptone

Where clinically possible, conversion to oral substitution therapy should be considered, in view of concerns including venous access and sepsis. This decision needs consideration and team discussion incorporating the patient and substance misuse specialist.

d. Benzodiazepines

Careful assessment should be made where there is past or current significant use of benzodiazepines – whether prescribed or illicit – and the context of this use. Replacement of opioids and alcohol with benzodiazepines can occur, and thus their use might mask a relative risk to relapse. It is worth noting that benzodiazepines are also associated with high risk behaviours and cognitive and memory impairment, and so their use may actively trigger relapse

2.1.1.3. *Drug screening*

Drug screening should be arranged where there is concern about concurrent illicit drug use. Where a patient is on MMT they should be undergoing drug screening as part of their programme with the substance misuse team, and consent to obtain drug test results from the substance misuse team should be given. A positive screen for illicit drugs (except cannabis) prior to transplant is a contraindication to listing. Post-transplant, a positive screen is a clear prompt for intervention and

support. Whether drug testing is via mouth swab or urinalysis, and whether it is a supervised process or not will depend on the practice of individual centres.

2.1.1.4. *Drug screening and alcohol agreements*

These should be undertaken on the basis of past history or where there is perceived risk of alcohol being used to substitute for other drugs (commonly opioids). This approach to testing requires each centre to consider its approach to the process of screening questions for alcohol and drug use and referral to the substance misuse specialist. Blood alcohol levels can be taken during blood tests or randomly requested. A “drugs of abuse” screen can be undertaken with a urine sample via the toxicology laboratory. All patients assessed for transplant listing should give explicit consent to future drug and alcohol testing from this period onward, as considered appropriate by the centre.

2.1.1.5. *Treatment agreement*

If the opinion of the multidisciplinary team is that the patient should be listed, then the patient may be asked to sign an agreement that they will not drink alcohol post-transplant and will comply with follow-up if the team feel that will promote long-term abstinence. A treatment agreement is recommended as a useful process for a number of reasons; it can outline a statement of intent including treatment engagement, commitment to the programme and consent to share appropriate information with relevant agencies. Any potential consequences to non-concordance with the treatment agreement (e.g. non-attendance, refusal of, or positive, drug screens) should be made clear in the agreement. Past behaviour documented in a comprehensive assessment is a better guide to stability and engagement than the signing of a treatment agreement. Consent should be part of a treatment plan.

It is recommended that follow-up with the local drug/support services, where required, is explicit in the agreement and should also form part of the care plan at the substance misuse service. Follow-up within the transplant programme should also clearly monitor and document substance use – preferably with monitoring by a substance misuse specialist – and the transplant team should actively encourage referral to and engagement with substance misuse services in the event of a relapse. This is likely to be expedited more successfully where contact with local substance misuse services has already occurred. As stated above, good data collection for the purpose of clinical audit is necessary to inform this area of transplantation.

2.1.1.6. *Predictors of relapse*

Research data in this field is currently limited. Guiding principles require referring to good practice and clinical "common sense". Dependence on substances such as opioids and alcohol are a relapsing condition and harmful patterns of drug use may be repeated. However, behaviour change can occur and be sustained though may take many years and numerous treatment attempts. Reasons for abstinence as well as relapse are numerous and individual.

2.1.2. *Alcohol consumption*

2.1.2.1. *Assessment process*

A history of excess alcohol is relevant in regard to potential or actual significant damage to cardiovascular and neurological tissue, to the risk that patients might revert to alcohol abuse or might not comply with medication or follow-up schedules and thus damage the new liver. A multidisciplinary approach is required to select patients who are likely to comply with follow-up and not return to a damaging pattern of alcohol consumption after transplantation and may include psychological/psychiatric assessment.

Patients admitted for assessment where alcohol has contributed to their liver disease should be assessed by a specialist team in substance misuse. This team should have dedicated time for this purpose. This assessment should include careful attention to risk factors associated with predicting a relapse to drinking and advising the transplant team on follow-up requirements to prevent this.

2.1.2.2. *Factors to be considered in assessment*

At present, there is conflicting evidence that a fixed period of abstinence will predict adherence post-transplant. However, it is important to recognise that with abstinence, many possible candidates will improve to such an extent that transplantation is no longer indicated. A period of abstinence is also required to allow the addiction team to assess the patient and organise any support measures that may be required. Those factors that have been identified in meta-analyses as being associated with relapse include:

- A shorter period of abstinence
- A family history of alcoholism
- Absence of social back-up
- Repeated behavioural lapses to harmful drinking

The presence of one of these is not a veto to transplantation. Use of single

predictors to identify patients who are liable to drink following transplant should be used with caution because of the weak inconsistent evidence base and the fact that most patients who drink following transplantation do so without harm. Robust criteria for predicting a return to heavy drinking (and its consequences on graft function and with adherence) must:

- Discriminate consistently and be clinically meaningful
- Be objective, measurable, and fair
- Cannot be, or unlikely to be, modified

2.1.2.3. *Alcohol as a co-factor*

The same process of assessment and listing should be applied to patients where alcohol has contributed to the progression of another chronic liver disease. This is definitely the case if alcohol consumption is >100 units per week and very likely to be the case if consumption lies between 50–100 units. A separate agreement indicating alcohol as a co-factor should be used.

2.1.2.4. *Living-related liver transplantation*

These considerations should be applied to all potential liver transplant recipients regardless of the type of donor, living or cadaveric.

2.1.2.5. *Advice to recipients with hepatitis B or C*

As alcohol contributes to the progression of hepatitis C recurrence it is expected that all recipients with chronic hepatitis C, irrespective of whether they have misused alcohol or drunk normally, should ensure that their alcohol consumption remains within safe limits. As these limits are unknown, the safest approach is to advise all such patients to abstain totally from alcohol.

2.1.2.6. *Alcohol advice to other transplant recipients*

Available evidence and clinical experience suggest that a liver allograft is more susceptible to alcohol injury and therefore the following recommendations are given for recipients not transplanted for alcohol-related liver disease or those with hepatitis C infection.

Male recipients – a maximum of 3–4 units on one day, two alcohol free days per week

Female recipients – a maximum of 2–3 units on one day, two alcohol free days per week

2.1.3. *Paracetamol hepatotoxicity*

Self-inflicted conditions such as resulting from an overdose of paracetamol would only be contraindicated if there were good reason to believe that the patient would, despite appropriate support, return to a behavioural pattern that would lead to liver failure or result in a quality of life unacceptable to the patient. The views of the family doctor and other support agencies and the family may have to be taken into account.

2.1.4. *Medical and psychiatric comorbidity*

Concurrent extra-hepatic comorbid medical or psychiatric conditions are relevant if they will affect the patient's quality of life, prospect for survival post-transplant or likelihood of compliance with medical treatments and clinic follow up. The comorbidities that should be considered will include prior cardiac, peripheral, or cerebral vascular disease, chronic lung disease and diabetes mellitus, although this list is not exhaustive. If there is a history of prior psychiatric disease, albeit without illicit drug or alcohol use, the advice of a psychiatric team, preferably the patient's own team, should be sought to assess the potential impact of such diagnoses on compliance and outcomes. Where uncertainty remains, evaluation should be considered in discussion with other transplant centres and, where appropriate, the Chairman of NHSBT Liver Advisory Group.

2.1.5. *Age*

Age itself is not a contraindication to liver transplantation, although the survival rate in the over 65s is significantly worse than that of younger patients.

2.1.6. *Re-transplants*

Re-transplants will need special consideration dependent on the circumstances that gave rise to the need for re-transplant, as results after re-transplant are worse than for first transplants and only limited benefit may be achieved. However, the principles for listing that apply to primary grafts should also apply to re-transplants.

2.1.7. *Prior non-hepatic malignancy*

Where potential liver allograft recipients have suffered from prior non-hepatic malignancy, the decision to proceed for liver transplantation should depend, in part, on the probability of malignancy recurring and failing to respond to treatment following liver transplantation. Some immunosuppressive agents may encourage the growth of malignancy. Patients should be considered in the light of their anticipated quality and length of life.

Selection criteria for patients with primary hepatic malignancy are considered in section 3, below. Secondary hepatic malignancy is not an appropriate indications for transplantation. Please see the appendices for details on new cancer indication service evaluations.

2.2. *Paediatric recipients*

Most children with liver disease who are candidates for transplant will have already been referred to one of the three paediatric liver transplant centres: King's College Hospital, London, The Children's Hospital Birmingham, and Leeds General Infirmary. Well established referral pathways exist for this. For the more frequent indications listed in the selection criteria (see section 3.3) it is usually clear whether these criteria are met, and if so, they should be offered transplantation if there is an expectation that they have a >50% probability of survival at 5 years after transplantation with a quality of life acceptable to them and their families.

Assessment is carried out by the transplant multidisciplinary team and will involve the patient and their family. These initial procedures often follow outpatient review and are usually undertaken over 4–5 working days.

The decision whether or not to register a patient on the transplant list will be made after discussion with the multidisciplinary team, the patient's family and, with age-appropriate language, the patient themselves. This should allow informed consent to be given by the patient's family and where appropriate the patient themselves.

The ability of the child's family to comply with instructions and follow-up plans are relevant factors that must be considered in the transplant assessment process. However, the aim of the process is to identify support required to enable successful transplantation. Children should not be disadvantaged by family factors beyond their control.

Age is not itself a contraindication, but the outcome of transplantation in the neonatal period is inferior to transplantation later in childhood.

3. Selection criteria

Eligible patients can be placed on the UK national transplant list only following registration with NHSBT. Guidelines for consent for solid organ transplantation in adults are laid down in **POL191**. Patients who have not been registered with NHSBT will not be offered an organ. Patients will be placed on the national transplant list on the day on which all required details are received by NHSBT. Discrepancies or missing information will be followed up with the local centre and might cause a delay. Only waiting list registrations with an 'active' (rather than 'suspended') status will be accepted.

In an emergency, as defined in section 3.4, a super-urgent recipient registration can be made by telephone and a temporary form will be completed at NHSBT. Centres must ensure that a replacement form is completed and sent to NHSBT at the first opportunity following the telephoned registration.

Recipients are categorised as Group 1 or Group 2 (as defined by The NHS Blood and Transplant (Gwaed a Thrawsblaniadau'r GIG) (England) Directions 2005). It should nevertheless be noted that nationals of a non-UK country may only be registered on a transplant list after they have been accepted by a consultant as suitable for treatment. It is the responsibility of the consultant registering such a patient on the transplant list to confirm that they have been accepted under the appropriate relevant healthcare agreement.

3.1. *Rationale for two different types of selection criteria*

Separate selection criteria have been devised for those cases requiring emergency transplantation (super-urgent transplantation criteria, section 3.4) compared to those who require an elective procedure. The two groups have a different range of aetiologies with markedly different short-term prognoses; different criteria are required to define that prognosis. Similarly, allocation processes are different for super-urgent and elective transplantation, reflecting those patient groups with a different risk of death without transplantation.

3.2. *Selection criteria for adult elective transplantation*

- Selection will be based primarily on risk of death without a transplant. Patients can be considered for elective transplantation if they have an anticipated length of life or survival in the absence of transplantation that is less than that obtained with a liver transplant
- All patients selected for the elective adult liver transplant list must have a projected 5-year survival after transplantation of >50%. That figure may change in the future if/when donor numbers alter
- Selection will be assessed secondarily on ability of transplantation to improve quality of life
- All patients will need to be regularly reviewed to ensure that they continue to meet criteria and have not improved or become too sick to benefit from transplantation

- When the clinical situation alters such that a patient no longer meets these criteria, the patient's name must be removed from the national list

3.2.1. *Criteria for selection*

Patients can be selected if they fulfil one of the following criteria:

- Chronic liver disease or failure
  - Projected 1-year liver disease mortality without transplantation of >9%, predicted by a United Kingdom Model for End-Stage Liver Disease (UKELD) score of ≥49. The UKELD score is derived from the patient's serum sodium, creatinine and bilirubin and International Normalised Ratio (INR) of the prothrombin time
  - Patients with porto-pulmonary hypertension (mean PAP ≥25 mmHg, <50 mmHg; PVR ≥120 dynes/s/cm^{-5}; PCWP <15 mmHg) should have had a clinically significant response to one of long-acting prostacyclin (or analogues), sildenafil, or bosentan.
- Sickle cell disease (see **Appendix E for information)**
- Hepatocellular carcinoma (HCC)
  - Radiological assessment should include both MDCT and MRI with size being assessed by the widest dimensions on either scan. A tumour (for the purposes of counting numbers) will require to be identified as an arterialised focal abnormality with portal phase washout on MDCT or Gd enhanced MR. Other tumours are considered indeterminate and do not count. Tumour rupture and an α-fetoprotein (AFP) >1,000 iu/ml are absolute contraindications to transplantation, as are extra-hepatic spread and macroscopic vascular invasion. The following are criteria for transplantation listing:
  - A single tumour ≤5cm diameter (Patients with very early stage HCC (solitary nodule < 2cm, compensated cirrhosis; BCLC Stage 0) should be referred and reviewed to the national HCC and adenoma appeals panel as detailed below before registration) or
  - Up to 5 tumours all ≤3cm or
  - Single tumour >5cm and ≤7cm diameter where there has been no evidence of tumour progression, no extra-hepatic spread, and no new nodule formation over a 6-month period. Locoregional therapy +/- chemotherapy may be given during that time. Their transplant list place may be considered from the time of their first staging scan
  - HCC patients undergoing downstaging (see **Appendix A**)
  - Locoregional therapy should be considered for all transplant list patients who have a hepatocellular carcinoma
  - It is recognised that different imaging modalities may identify differences both in number and size of tumour, but to qualify as an HCC will require a congruent lesion

to be seen on a minimum of two different radiological modalities. There must be no radiological evidence of vascular invasion and no distant metastasis

- Unresectable liver metastatic Neuroendocrine Tumours (NETs) (see **Appendix B**)
- Unresectable Colorectal Liver Metastases (CRC) (see **Appendix C)**
- Intrahepatic Cholangiocarcinoma (**see Appendix D**)
- Adenoma (see Appendix F)
- A variant syndrome
    - Hepatopulmonary syndrome*:
    - Arterial pO2 <7.8, alveolar arterial oxygen gradient >20 mmHg, calculated shunt fraction >8% (brain uptake following TC macroaggregated albumen), pulmonary vascular dilatation documented by positive contrast enhanced transthoracic echo, in the absence of overt chronic lung disease
    - Persistent and intractable pruritus*:
    - Pruritus consequent on cholestastic liver disease, which is intractable after therapeutic trials. Exclude psychiatric co-morbidity that might contribute to the itch.
    - Lethargy is not an accepted primary indication for orthotopic liver transplantation
    - Familial amyloidosis:
    - Confirmed transthyretin gene mutation in the absence of significant debilitating cardiac involvement, or autonomic neuropathy
    - Primary hypercholesterolaemia:
    - Homozygous familial hypercholesterolaemia
    - Polycystic liver disease:
    - Intractable symptom due to mass of liver or pain unresponsive to cystectomy, or severe complications secondary to portal hypertension
    - Recurrent cholangitis*:
    - Recurrent significant cholangitis not responsive to medical, surgical, or endoscopic therapy
    - Hepatic epithelioid haemangioendothelioma:
        - Considered for listing for transplantation with:
            - 1) Histological confirmation
            - 2) Two or more lesions not amenable to resection
            - 3) Local, low volume lymph node involvement does not necessarily preclude transplantation
            - 4) Minimum observation period of three months
    - Nodular regenerative hyperplasia:
    - Indications similar to end-stage cirrhotic liver disease
    - Hereditary haemorrhagic telangiectasia

- Glycogen storage disease
- Primary hyperoxaluria
- Ornithine transcarbamylase deficiency
- Maple syrup urine disease
- Porphyria
- Amyloidosis – other

* UKELD score less than 49 is required *unless patient has severe or very severe Hepatopulmonary syndrome based on PaO2 on air*.

- A variant syndrome in the context of chronic liver disease. Patients with diuretic resistant ascites (DRA) and/or chronic hepatic encephalopathy (CHE), for whom their UKELD score at registration may be < 49. These cases will be registered under the chronic liver disease criterion in the elective liver patient registration form.
  - DRA. Ascites unresponsive to or intolerant of maximum diuretic dosage and non-responsive to TIPS or where TIPS deemed impossible or contraindicated
  - CHE. Confirmed by EEG or trail-making tests, with at least two admissions in one year due to exacerbations in encephalopathy, not manageable by standard therapy. Structural neurological disease must be excluded by appropriate imaging and, if necessary, psychometric testing

Any cases not falling within these criteria may be referred to the National Appeals Panel (see section 4).

Please refer to SOP5907 for the process to register either genuine hepatoblastoma patients, prioritised paediatric patients, Acute on Chronic Liver Failure patients or patients with NETs, CRC liver Metastases or Intrahepatic Cholangiocarcinoma.

Please also refer to SOP5907 for the appeal and registration process for patients with Hepatopulmonary Syndrome with a PaO2 on air of less 8kPa.

3.3. *Selection criteria for paediatric elective transplantation*

3.3.1. *Criteria for selection*

Indications for elective liver transplantation in children are:

- Chronic liver disease
  - Life expectancy: anticipated length of life <18 months (because of liver disease)
  - Unacceptable quality of life (because of liver disease)
  - Growth failure or impairment due to liver disease
  - Reversible neuro-developmental impairment due to liver disease
  - Likelihood of irreversible end organ damage (which may be renal, respiratory, or cardiovascular depending on the underlying disorder)
- Rarer indications:

  A complicating factor in paediatric practice is that many of the conditions affecting children are individually rare and decisions have to be based on general principles rather than condition-specific data. Particular rare indications for liver transplantation that paediatric centres would feel are reasonable, but for which there is limited outcome data, would include the following conditions:
  - Liver transplantation for organic acidaemia
  - Unresectable hepatic malignancies without extra-hepatic spread (to include selected hepatocellular carcinoma and epithelioid haemangioendothelioma)
  - Diffuse hepatic haemangioendothelioma unresponsive to alternative treatments
  - Langerhans cell histiocytosis
  - Mitochondrial respiratory chain disorders with chronic liver disease (selected) but without discernible disabling extrahepatic disease
  - Intestinal failure associated liver disease
  - Hepatoblastoma: children hepatoblastoma should be discussed at a Multi-Disciplinary Team which should include a paediatrician with an interest in liver disease, a paediatric oncologist, a hepatobiliary surgeon, and liver transplant surgeon.

The use of transplantation for the rarer indications should be audited regularly and new indications should in general be developed by consensus.

Patients can be placed on the UK national transplant list only following registration with NHSBT. Patients who have not been registered should not be offered an organ.

A patient registered as paediatric, who reaches their 17th birthday while on the elective liver waiting list, shall retain their paediatric status until their registration reaches an outcome (transplanted, removed or died). Patients will not automatically receive adult and paediatric donor offers when they turn 17 years.

Patients registered before their 17th birthday and weighing less than 40kg after they reach their 17th birthday will continue to be classified as paediatric only and will NOT receive adult and paediatric donor offers. Such patients should be suspended pending transfer and reregistered as a small adult (see **section 7.2.3** for details) in order to receive named patient offers. Time on the transplant list will be carried forward and not reset.

Patients registered before their 17th birthday and weighing 40kg or more after they reach their 17th birthday should be dual-listed as a large paediatric (see **section 7.2.2** for details) in order to receive named patient offers.

Age at registration	Weight on latest sequential update	Dual-listing recorded on latest sequential update	Offering pathway
<17 years	<40kg	-	Paediatric only unless transferred and reregistered as small adult when patient turns 17 years (small adult defined as aged 17 years or over and weigh<40kg and dual-listed recorded)
<17 years	≥40kg	No	Paediatric only (no named patient offers)
<17 years	≥40kg	Yes	Paediatric and named patient (classed as large paediatric)
≥17 years	<40kg	No	Named patient only
≥17 years	<40kg	Yes	Paediatric and named patient (classed as small adult)
≥17 years	≥40kg	-	Named patient only

3.4. *Selection criteria for Acute on Chronic Liver Failure (ACLF) patients*

3.4.1. The inclusion criteria for consideration under the ACLF process include:

- Requirement for care in ICU or HDU setting for organ support.
- Cirrhotic Chronic Liver Disease
- ACLF with 28-day survival <50%, likely grade of 3 or higher

3.4.2. The exclusion criteria include:

- Age >60 years
- Active bacterial or fungal sepsis
- Multi-organ failure overwhelming or with adverse trajectory
- Excessive comorbidity
- Frailty likely to preclude rehabilitation.

Please refer to SOP5907 regarding how to register ACLF patients.

It has been agreed that ACLF patients should be active on the liver only transplant list and it is the responsibility of the transplant centre to promptly remove patients from other organ transplant lists (e.g kidney). The transplant centre also maintains responsibility to reregister the patient on the original organ list when appropriate and the waiting time should continue from a relevant point (e.g. dialysis start date or original registration date for kidney patients).

ACLF patients should also be registered for whole liver offers only.

3.5. *Selection criteria for adult and paediatric super-urgent transplantation*

3.5.1. *Process for super-urgent registration*

Initial registration on the super-urgent liver scheme must be made by telephone to Hub Operations, who will then place the recipient on the national super-urgent liver waiting list upon receipt of completed registration form. The recipient centre must immediately complete a super-urgent registration form that must be counter-signed by the clinician and sent to Hub Operations by facsimile or email. The recipient centre must call Hub Operations immediately after sending the form to confirm receipt and go through the details on the form to ensure correct. On receipt, Hub Operations will notify all designated liver transplant centres in the UK and the European Organ Exchange Organisations of the new registration.

Centres wishing to seek clarification of the details of a recipient on the super-urgent liver scheme will be able to do so via the national super-urgent liver/intestinal list electronic system. The clinician from the centre seeking clarification should make direct contact at the earliest opportunity with the registering centre and discuss the case clinician to clinician. If questions remain following discussion with the registering centre, the centre should raise concerns at the earliest opportunity with either the Chair of the Liver Advisory Group or Deputy. The Chair of the Liver Advisory Group will notify ODT Hub Operations whether the patient should be suspended pending discussion between the Chair and the registering

centre as well as the outcome of the discussion.

Real time anonymised data on super-urgent liver patients' statuses can be accessed by all designated liver transplant centres, plus St Vincent's Hospital Dublin, via the national super-urgent liver list electronic system. The system will show data such as the date and time of registration on the super-urgent liver scheme.

A patient suspended from the super-urgent list can be reactivated within 5 days and maintain their position on the list. If a patient is suspended from the super-urgent list for more than 5 days, the centre should remove them from the transplant list. Note that the patient will not be automatically moved to the elective list. If the patient needs to be reactivated after 5 days then a new registration form will be required and their waiting time will restart from zero. Centres are responsible for informing ODT Hub Operations when a patient is to be reactivated or has been removed. If the patient is removed from the super-urgent list and needs to be registered on the elective list, then an elective registration form must be completed.

3.5.2. *Adult and paediatric super-urgent selection criteria*

The super-urgent liver scheme is available to Group 1 patients only in the UK and Republic of Ireland. To be registered on the super-urgent liver scheme, at least one of the following criteria must be met:

- Category 1
  Aetiology: Paracetamol poisoning: pH <7.25 more than 24 hours after overdose and after fluid resuscitation
- Category 2
  Aetiology: Paracetamol poisoning: Co-existing prothrombin time >100 seconds or INR >6.5, and serum creatinine >300 µmol/l or anuria, and grade 3–4 encephalopathy
- Category 3
  Aetiology: Paracetamol poisoning: Significant liver injury and coagulopathy following exclusion of other causes of hyperlactatemia (e.g. pancreatitis, intestinal ischemia) after adequate fluid resuscitation: arterial lactate >5 mmol/l on admission and >4 mmol/l 24 hours later in the presence of clinical hepatic encephalopathy.
- Category 4
  Aetiology: Paracetamol poisoning: Two of the three criteria from category 2 with clinical evidence of deterioration (e.g. increased ICP, FiO2 >50%, increasing inotrope requirements) in the absence of clinical sepsis

- Category 5
  Aetiology: Favourable non-paracetamol aetiologies such as acute viral hepatitis or ecstasy/cocaine induced ALF: the presence of clinical hepatic encephalopathy is mandatory and: prothrombin time >100 seconds, or INR >6.5, or any three from the following: age >40 or <10 years; prothrombin time >50 seconds or INR >3.5; any grade of hepatic encephalopathy with jaundice to encephalopathy time >7 days; serum bilirubin >300 μmol/l.
- Category 6
  Aetiology: Unfavourable non-paracetamol aetiologies such as seronegative or idiosyncratic drug reactions: a) prothrombin time >100 seconds, or INR >6.5, or b) in the absence of clinical hepatic encephalopathy then INR >2 after vitamin K repletion is mandatory and any two from the following: age >40 or <10 years; prothrombin time >50 seconds or INR >3.5; if hepatic encephalopathy is present then jaundice to encephalopathy time >7 days; serum bilirubin >300 μmol/l.
- Category 7
  Aetiology: Acute presentation of Wilson's disease, or Budd-Chiari syndrome. A combination of coagulopathy, and any grade of encephalopathy
- Category 8
  Hepatic artery thrombosis on days 0 to 21 after liver transplantation
- Category 9
  Early graft dysfunction on days 0 to 7 after liver transplantation with at least two of the following: AST >10,000, INR >3.0, arterial lactate >3 mmol/l, absence of bile production
- Category 10
  The total absence of liver function (e.g. after total hepatectomy)
- Category 11
  Any patient who has been a live liver donor (NHS entitled) who develops severe liver failure within 4 weeks of the donor operation
- Category 20
  Acute liver failure in children under two years of age: INR >4 or grade 3-4 encephalopathy. Definition: Multisystem disorder in which severe acute impairment of liver function with or without encephalopathy occurs in association with hepatocellular necrosis in a child with no recognised underlying chronic liver disease. Children with leukaemia/lymphoma, haemophagocytosis and disseminated intra-vascular coagulopathy are excluded

  No other causes of liver failure may be considered appropriate for registration on the super-urgent liver scheme.

A patient registered as paediatric, who reaches their 17th birthday while on the super-urgent liver waiting list, shall retain their paediatric status until their registration reaches an outcome (transplanted, removed or died).

3.6. *Multiple organ transplants*

3.6.1. *Simultaneous liver and kidney (SLK) transplantation*

Simultaneous liver and kidney transplantation are only undertaken when there is evidence of kidney failure that will not recover with a liver transplant alone.

The indications for SLK are:

- Genetic liver kidney syndromes: primary hyperoxaluria type 1 or glycogen storage disease type 1 (UKELD score does not apply)
- Patient meeting at least one of the criteria for chronic liver disease or failure transplant selection, and end-stage renal disease on long-term renal support (UKELD≥49 required)
- Patient meeting at least one of the criteria for chronic liver disease or failure transplant selection, and hepato-renal syndrome with serum creatinine >200 µmol/l and dialysis >6 weeks (UKELD≥49 required)

- Patient meeting at least one of the criteria for chronic liver disease or failure transplant selection, and GFR <30 ml/min (isotope or MDRD v6) or renal biopsy showing >30% fibrosis and/or glomerulosclerosis (UKELD≥49 required)

  All other cases should be referred to the National Appeals Panel.

Waiting time for elective combined liver and kidney patients registered with a Variant syndrome who require a SIMULTANEOUS liver and kidney will be calculated from the earliest of liver registration, kidney registration or dialysis start date at a UK centre as appropriate. Transplant centres should email ODT Hub Information services (ODTRegistrationTeamManagers@nhsbt.nhs.uk) and the lead statistician for liver transplantation confirming the date of kidney registration or dialysis start date.

Waiting time for elective combined liver and kidney patients registered with a Variant syndrome who require a SEQUENTIAL kidney after liver transplant will be calculated from date of liver registration only. Transplant centres should email ODT Hub Information services (ODTRegistrationTeamManagers@nhsbt.nhs.uk) confirming the transplant type required.

Waiting time for elective combined liver and kidney patients registered with either CLD or HCC and not VS will be calculated from the date of liver registration only.

3.6.2. *Combined lung/liver or heart/liver patient transplantation*

Patients requiring a combined liver and cardiothoracic organ transplant should meet minimal listing criteria for the required organs. Minimal listing criteria for cardiothoracic organs are specified in **POL231** (Lung) and **POL229** (Heart). If they do not meet minimal listing criteria for either liver or the required cardiothoracic organ, the patient should be referred to the National Liver Appeals Panel (Section 4) and/or the relevant cardiothoracic organ Adjudication Panel(s) for approval as appropriate before listing. A patient can be registered on the relevant cardiothoracic organ urgent or non-urgent scheme while also requiring a liver but must be referred to the relevant cardiothoracic organ Adjudication Panel for urgent listing if urgent criteria are not met. Patients requiring a combined liver and cardiothoracic organ transplant cannot be registered on the relevant cardiothoracic organ super-urgent scheme.

3.7. *Multi-visceral transplantation*

Please refer to **POL194**.

3.8. *Contraindications to selection*

Any patient who does not fulfil the criteria listed in section 3 is contraindicated for selection. This is also the case for paediatric patients.

3.8.1. *Absolute contraindications*

3.8.1.1. *Alcohol-related liver disease*

Some factors have been accepted, currently, as a contraindication to registration on the transplant list:

- Alcoholic hepatitis
- More than two episodes (within 2 years) of non-adherence with medical care where there was not a satisfactory explanation. Non-adherence with medical care should not be confined to management of their liver disease, but includes management of their alcohol abuse as well
- More than two episodes (within 2 years) of return to drinking following full professional assessment and advice
- Concurrent or consecutive illicit drug use (except occasional cannabis use)
- Evidence of drinking whilst on the transplant list will result in permanent removal from the list. Patients should be informed on entry to the list that this will occur if they drink whilst waiting for their transplant

3.8.1.2. *Illicit drug use*

Contraindications to listing for transplantation include the following:

- Current ongoing intravenous use of illicit or non-prescribed substances
- More than two recent incidences of unexplained and significant non-adherence with treatment – not necessarily confined to the management of liver disease
- Current failure to comply with the assessment and treatment process for transplantation, including refusal to provide consent for gaining access to information pertaining to drug treatment and prescribing
- Recent history of cross dependency (substituting from one drug to harmful/problematic use of another), within the last 2 years; this requirement could be relaxed for patients who have switched drugs within 2 years but have been stable since maintaining engagement in substance misuse services

3.8.2. *Relative contraindications*

Relative contraindications are those which, while not absolute contra-indications, may preclude transplantation in individual cases and allow issues of concern to be factored in without necessarily attempting to weigh issues against one another in the absence of good evidence. The importance of potential contraindications should be discussed between the transplant team and substance misuse specialist and interpreted with clinical judgement on a case by case basis:

- Current legally prescribed intravenous drug use (i.e. diamorphine or physeptone). Some patients are long term yet stable IVDUs and their use of prescribed IVDU opiates is as part of a long term agreed treatment plan. Others may be more recent presentations who have failed on an optimum treatment programme but are a high-risk group. Assessment here needs to be undertaken by a specialist
- Insufficient social support network to remain abstinent from illicit drugs, and where it is not possible to work with the patient to facilitate a suitable and acceptable social support package
- Lack of motivation to move away from drug using culture/area, within the confines of opportunity
- Current illegal drug use
- Past history of cross dependency (substituting from one drug to harmful or problematic use of another) within the last 2–5 years
- Reluctance to agree to drug treatment and after-care or to sign a treatment agreement
- Active ongoing alcohol use in the presence of HCV, where there is clear evidence of medical advice to become abstinent

3.9. *De-selection criteria*

Following selection, certain criteria are indications for de-selection:

- In the category of chronic liver disease, sodium, creatinine, bilirubin, and INR present and UKELD score <49
- Tumour rupture occurred
- α-fetoprotein (AFP) greater than 1,000 iu/ml
- A single tumour >7 cm diameter, more than 5 tumours, between 2 to 5 tumours any one >3 cm diameter or a single tumour >5 cm and ≤7 cm diameter and evidence of tumour progression within a 6-month time period, all judged by USS or CT scan, radiological evidence of vascular invasion, extra-hepatic tumour spread. Tumour size will be assessed by serial scanning 3-monthly using the scan, which demonstrates the largest diameter
- Failure of adherence with guidelines relating to alcoholic liver disease and illicit drug use
- The development of comorbidities sufficient to impact on expected 50% probability of survival at 5 years

It has not been possible to define other universally acceptable de-selection criteria either for super-urgent or electively listed candidates. The ODT Directorate of NHSBT will continue to collate clinical and laboratory data on all patients that are de-selected to try to identify common themes within the separate centres.

3.10. *Selection for re-transplant*

Registrations for second or subsequent transplants will require a different set of criteria as different factors affect risk and outcome and so are not subject to these criteria. Decisions are, therefore, left, at present, to the discretion of each transplant centre. Re-transplants are only undertaken when there is evidence of irreversible graft failure and the risk of mortality from that exceeds the increased post-operative mortality after re-transplantation.

Re-transplant patients are also expected to achieve a 50% probability of an acceptable survival and quality of life 5 years after transplant.

4. Appeals process

The above criteria have been agreed by the Liver Advisory Group in order to be placed on the national transplant list. It is recognised that these criteria may exclude a small group of patients who would otherwise be appropriate candidates; the purpose of the National Appeals Panel is to determine whether such excluded patients should be placed on the national transplant list.

If a centre wishes to register a patient, adult or paediatric for an elective first or subsequent liver transplant who does not satisfy any of the above criteria, a request should be made in writing/electronically to the Chair of the Liver Advisory Group. The process for an appeal to register a super-urgent patient is described in Section 4.3.3.

It has been agreed that patients with either very early stage HCC (solitary nodule < 2cm, compensated cirrhosis; BCLC Stage 0) or adenomas should be referred and reviewed by the National HCC and adenoma Appeals Panel. The process for an appeal is described in **Section 4.3.2**.

4.1. *Composition of the National Appeals Panels*

4.1.1. *National Appeals Panel for elective patients*

4.1.1.1. The panel will consist of an independent non-voting Chair and two representatives from each of the seven UK Liver Transplant Centres. Only one vote will be allowed per centre. The centre proposing a case may not vote but the appeal will be allowed if four or more centres are in favour.

4.1.1.2. The chair of the Appeals Panel will be the Chair of the Liver Advisory Group. The centres will nominate one representative and one substitute.

4.1.2. *National Appeals Panel for patients with either very early stage HCC or adenomas*

4.1.2.1. The panel will consist of a Chair, a liver transplant surgeon, a Hepatobiliary surgeon, hepatologist and a radiologist. The National panel will ordinarily meet on a monthly basis to consider appeals that have been submitted but may meet on an adhoc bases to review urgent cases.

4.2. *Criteria for acceptance*

4.2.1. *Criteria*

The Panel may place a patient on the transplant list if they do not meet any of the current criteria and, on the evidence provided to them, one or more of the following conditions are met:

- Greater than 50% probability that the patient will be alive and with an acceptable quality of life 5 years after transplant
- ***and*** probability of death from liver disease of >9 % at 1 year

  or
- Unacceptable quality of life because of the liver disease that would be corrected by transplantation that occurs despite full therapeutic intervention

4.2.2. *Hepatocellular carcinoma*

The panel will not allow exceptions purely on the basis of cases being outside number or size criteria. Nevertheless, if a unit believes that it can make a case that the specific circumstances of their candidate demonstrates tumour biology that meets the criteria in 4.2.1 then the Appeal Panel will consider the appeal. The flow diagram below should be used fot patients with adenoma.

4.2.3. *Paediatric candidates*

Paediatric candidates for the transplant list outside current criteria may be referred to the Appeals Panel, where the two other paediatric transplant centres will give their opinion.

4.2.4. *Live Donor Liver Transplantation (LDLT)*

NHSBT is responsible under its Directions for criteria for deceased organ transplantation but is not responsible for national criteria for LDLT, which are laid down by commissioners at NHS England and the devolved Health administrations. Current criteria are that LDLT criteria are the same as for deceased donor transplantation. Units wishing to undertake LDLT outside of deceased liver transplantation criteria should seek the advice/ permission of their commissioners and use this Appeals Panel process as a means of external peer review of their decision. Emergency deceased re-transplantation, should that be required, would not be possible after “out of criteria” LDLT.

4.3. *Process*

- Any clinician working in a designated transplant centre may apply to the Panel for a patient to be considered for either a super-urgent or an elective transplant listing
- There will be no appeal from the Panel's decision
- NHSBT Statistics and Clinical Studies will maintain records of all proposals, decisions and the proportion of each centre's transplant list that are referred to the National Appeals Panel and National Cancer and Adenoma Appeals Panel, and the outcome of all applications will be tabled at the next LAG meeting
- The Panel may make recommendations to the Core Group of the Liver Advisory Group to revise the agreed criteria. The terms of reference of the Panel will be reviewed annually.
- As far as possible, the Panel will conduct its business electronically and by telephone
- The physician responsible for the patient may present the case to the Panel, but the representative(s) of the region where the application is from will not vote.

4.3.1. *Elective cases*

- The process will be managed and overseen by the Chair of the National Appeals Panel, who will provide the Panel with the information required.
- The Panel should reach a decision within 5 working days of receipt of all relevant information. The appeal will be allowed if four or more centres are in favour. If a decision has not been reached by members of the Panel after 7 working days, an executive decision will be made by the Chair (or his deputy if the Chair is away or if there is a potential conflict of interest).
- The Chair will notify the applicant's clinician of the decision.

4.3.2. *Elective patients with very early HCC or adenoma*

- Centres wishing to refer patients to the National HCC and adenoma Appeals Panel should complete the HCC proforma and email the completed form to the Chair of the National HCC Appeals Panel.
- Summative radiological imaging studies, with reports, should be IEP'ed for the attention of the nominated radiologist.
- The process will be managed and overseen by the Chair of the National HCC Appeals Panel, who will provide the Panel with the required information.
- The National panel will plan to meet on a monthly basis to consider appeals that have been submitted.
- It is understood that there will be a few cases which require more urgent decision making is required and the Chair should be contacted wither by email or telephone. Under these circumstances, an urgent ad hoc panel meeting will be scheduled.

- The Chair will notify the applicant's clinician of the decision copying in the Chair and Deputy Chair of Liver Advisory Group and NHSBT Lead statistician for liver transplantation.

4.3.3. *Super-urgent cases*

- A case will be submitted by the centre, in writing, to the Chair of the National Appeals Panel.
- The Chair will respond to as a go/no-go. If Chair deems it as a valid appeal case, the centre will submit to Hub Operations a Super-Urgent Liver Recipient Registration, including the details of the appeal spelled out at the form Appendix on the 'Super-Urgent Liver Recipient Registration form'.
- Hub Operations will circulate the Appendix with the appeal details by the agreed methods to each centre. The centres will be responsible for seeking a response from their appeal panel representatives.
- Centres will be expected to respond to Hub Operations within 12 hours.
- A super-urgent appeal case will be deemed as approved if four positive responses are obtained.
- Hub Operations will inform centre of the outcome.

4.4. *Second opinion for patients with alcohol-related liver disease*

As with all potential transplant candidates, if a potential recipient is deemed not to be a suitable candidate by the multidisciplinary team then the opportunity for a second opinion from a different liver transplant centre can be considered and should not be refused. This may initially be in the form of a case notes review with full reassessment to follow if appropriate.

4.5. *Prioritisation for paediatric patients*

Requests to formally prioritise paediatric patients who are clinically deteriorating will be managed and overseen by the requesting transplant centre who will provide the agreed representatives from the other UK paediatric transplant centres and the chair of the National Appeals Panel with the information required. If formal prioritisation is agreed by the other paediatric centres, the recipient centre should email ODT Hub Information Services with the agreement and the registration should be updated with

- Hepatoblastoma as the primary indication
- Original primary indication as the secondary indication
- Other please specify as the tertiary indication with "PRIORITISED PAEDIATRIC PATIENT" added in the free text other indication.

It has been agreed that approval for blood group incompatible offers is only required for prioritised paediatric patients aged one year or over. Centres wishing to receive blood group incompatible

offers for patients aged less than one year should record blood group AB on the registration form and inform ODT Hub Information Services of the true blood group when registering an agreed patient.

Transplant centres maintain responsibility of updating the blood group to the true blood group if they would like to receive blood group compatible offers only at any point during the patients registration.

Please refer to SOP5907 for the process to register prioritised paediatric patients.

5. Follow-up while on the transplant list and post transplantation

All patients undergoing organ transplantation require lifelong follow-up and should have that explained at the start of their assessment process (refer to **POL191**).

5.1. Liver recipient registration sequential data collection – follow-up while on the list

Transplant centres are required to submit sequential updates on the clinical status of their patients on the waiting list at least once every three months but centres may decide to submit more often than this if, for instance, the clinical status of a patient deteriorates. All out of hours' registrations and sequential updates must be submitted to NHSBT via the ODT Online system and then confirmed with ODT Hub Operations via telephone (0117 975 7580). The sequential data collection process allows the patient to update their preferences about donor type, donor virology and dual-listing status (see section 7.2). The sequential updates are used to calculate the Transplant Benefit Score (TBS; see section 4.3 in POL196) of the majority of patients, which determines the priority order for liver offering; hence data that reflect the up to date condition of a patient are required.

Sequential updates are mandatory for the following liver elective recipients; adult, small adult and large paediatric patients with chronic liver disease, hepatocellular carcinoma or a variant syndrome in the context of chronic liver disease (DRA and/or CHE), and who require the liver only or a combined liver kidney transplant.
If centres wish to submit a sequential update to be processed at the weekend (between 17:00 on Friday and 09:00 on Monday, or 09:00 on Tuesday for bank holiday weekends), the details will be sent to odthub.operations@nhsbt.nhs.uk.

Sequential data updates received between 09:00 on Monday to 17:00 on Friday will be processed by ODT Hub: Information Services.

5.2. *Re-assessment on list*

It has to be recognised that patients awaiting a liver transplant are, by definition, ill and their condition may deteriorate to the extent that the probability of a 5-year survival may fall below 50%. In these circumstances, the patient will be removed from the transplant list but only after full discussion with them. Such patients, although in greatest need, are at greatest risk of not benefiting after transplantation.

Paediatric patients should be kept under review while on the transplant list as their condition may deteriorate to the point that transplantation becomes inappropriate or unnecessary. In these circumstances the patient would be removed from the transplant list only after discussion with their family and, where appropriate, the child themselves.

One of the three selection criteria for adult elective transplantation is one or more variant syndromes. These patients will be offered donor organs equal to the proportion of variant syndrome registrations each year and, therefore, will be prioritised for transplantation outside the TBS-based offering system (see section 4.3 in POL196). There will be instances where a patient, originally registered with chronic liver disease, develops an HCC while on the waiting list. The TBS-based offering system treats patients with an HCC and those without differently (in line with the differences in expected survival with and without a transplant between these two types of patients). At present, the offering system is able to identify an HCC patient only from registration data, meaning that the development of an HCC while on the list, as reported at sequential data collection, is not taken into account for offering purposes.

5.3. *Post-transplant monitoring of alcohol consumption*

The expectation is that all patients who are transplanted for alcoholic liver disease will remain abstinent following liver transplantation. To encourage this, follow-up for alcohol use will be separate from and additional to the transplant follow-up and should be carried out by specialists in substance misuse. Ideally this would be the same individual/s that were involved in the initial assessment. It is anticipated that as time from the liver transplant increases, frequency of follow-up will decrease, and that shared care arrangements with alcohol services in the patient's locality will often be appropriate. The type and frequency of follow-up will depend on the patient's needs.

In order to monitor the outcome of transplant listed patients with a significant illicit drug history, appropriate clinical data should be recorded. Consent for this to occur should be given at the same time as the drug and alcohol screening.

6. Audit

6.1. *Policy audit and updates*

The details of any policy concerning selection and allocation will inevitably change with time. Any new versions of protocols will be updated and published only twice per year in April and October following ratification at Liver Advisory Group Meetings. All changes to the guidance must first be agreed with the Liver Advisory Group, usually after discussion within the Core Group. Regular reports will need to be produced to assess the success or failure of any new selection, allocation, and distribution policy.

6.2. *Policy outcomes*

The purpose of all liver transplant policies and guidelines is to ensure equitable access to organ transplantation in all transplant centres in the UK and the best possible outcomes when judged from the point of registration. All policies will be judged against those standards. Six monthly audits of outcomes will be undertaken by the Statistics and Clinical Studies department at NHSBT. The Liver Advisory Group will decide which additional topics are to be included in the Interim and Annual Report.

7. Recipient registration

7.1. All patients awaiting a transplant must be registered on the National liver transplant list at NHSBT. A standard registration form must be completed and sent to NHSBT via ODT online or by post. Patients will be placed on the National liver transplant list on the day on which details are received at NHSBT. Discrepancies or missing information will be followed up with the local centre and might cause a delay.

7.2. *Patient preferences: donor type, donor virology and dual-listing status*

7.2.1. *Donor type and donor virology*

All elective liver patients may state their preference, at the point of registration or sequential data update, for donor type (e.g. would the recipient consider a liver offer from a donor after circulatory death or a split liver) and donor virology (e.g. would the recipient consider a liver offer from a donor with an HIV positive test result). The donor type questions default to ‘yes’ on both the registration and sequential data update forms whilst the donor virology questions default to ‘null’ (subject to I.T. change) on both the registration and sequential data update forms.

7.2.2. *Large paediatric recipient*

An elective liver patient aged less than 17 years at time of registration with a body weight of 40kg or more and dual-listing option currently specified (either at registration or subsequently via sequential data collection), will be deemed as a large paediatric and receive both adult and paediatric donor offers.

7.2.3. *Small adult recipient*

An elective liver patient aged 17 years or over at time of registration with a body weight of 40kg or less and dual-listing option currently specified (either at registration or subsequently via sequential data collection), will be deemed as a small adult and receive both adult and paediatric donor offers.

7.3. *Multivisceral grafts*

7.3.1. For recipients awaiting composite liver and small intestine grafts, paediatric recipients will be given, in general, priority when offering a paediatric donor organ. Offering criteria are defined in **POL193**.

7.3.2. For recipients awaiting composite liver and small intestine grafts, offering will be made following offers to the national super-urgent liver/intestinal and the national hepatoblastoma waiting lists, in line with both **POL193** and **POL196**.

7.4. *Combined lung/liver and heart/liver patient transplantation*

7.4.1. If a suitable combined lung/liver or heart/liver patient is identified, the liver (if suitable and not required by a super-urgent, hepatoblastoma or multivisceral patient) will be offered with the lung and/or heart, according to **POL228** and **POL230**.

7.5. *NHS Group*

7.5.1. Recipients are categorised as Group 1 or Group 2 (as defined by The NHS Blood and Transplant (Gwaed a Thrawsblaniadau'r GIG) (England) Directions 2005). Group 1 include those who are ordinarily resident in the UK; members of UK HM Forces serving abroad, their spouse, civil partner, and children under the age of 19 years; persons entitled under EU Regulations and reciprocal health agreements. Group 2 patients are all those who are not included as Group 1.

7.5.2. Nationals of a non-UK country may only be registered on a transplant list after they have been accepted by a consultant as suitable for treatment. It is the responsibility of the consultant registering such a patient on the waiting list to confirm that they have been accepted under E112 or similar arrangements.

7.5.3. Group 1 patients have priority for available organs above Group 2 patients. Group 2 patients registered in the UK and Republic of Ireland will be offered liver or liver and other organs before offers are made to European Organ Exchange Organisations or Group 2 countries abroad. No organ should be offered to a Group 2 patient in the UK or elsewhere if there is a clinically suitable Group 1 patient.

7.6. *Super-Urgent liver scheme*

7.6.1. Initial registration on the super-urgent liver scheme can be made by telephone to Hub Operations or a form may be emailed to ODT Hub Operations. Centres must ensure that a super-urgent registration form is counter-signed by the clinician and sent to Hub Operations at the first opportunity following the telephoned registration. On receipt, Hub Operations will notify all designated liver transplant centres in the UK and the European Organ Exchange Organisations.

7.6.2. Centres wishing to seek clarification of the details of a recipient on the super-urgent liver scheme will be able to do so via the national super-urgent liver/intestinal list electronic system. The clinician from the centre seeking clarification should make direct contact at the earliest opportunity with the registering centre and discuss the case clinician to clinician. If questions remain following discussion with the registering centre, the centre should raise concerns at the earliest opportunity with either the Chair of the Liver Advisory Group or Deputy. The Chair of the Liver Advisory Group will notify ODT Hub Operations whether the patient should be suspended pending discussion between the Chair and the registering centre as well as the outcome of the discussion.

7.6.3. Real time anonymised data on super-urgent liver patients' statuses can be accessed by all designated liver transplant centres, plus St Vincent's Hospital Dublin, via the national super-urgent liver list electronic system. The system will show data such as the date and time of registration on the super-urgent liver scheme.

7.6.4. A patient suspended from the super-urgent list can be reactivated within 5 days and maintain their position on the list. Once the patient is suspended for over the 5 days, the patient will then be removed from the super-urgent list and will not automatically by moved to the elective list. If the patient is removed from the super-urgent list and needs to be registered on the elective list, then an elective registration form must be completed.

APPENDIX A
Patients undergoing "down-staging" of Hepatocellular Carcinoma

Background

Current UK selection criteria for patients with hepatocellular carcinoma (HCC) are a modification of the Milan Criteria[1]. Using size and number of HCC on pre-transplant imaging, these criteria aim to select at time of presentation patients that have HCC with favourable tumour biology and hence good outcome following liver transplantation. However, it is recognised that some patients out with standard selection criteria based on size and number of HCC at the time of initial presentation have good biology disease and would benefit from liver transplantation. This recognition has led to the development of expanded criteria for listing of patients at presentation and the listing of patients who have undergone specific anti-cancer therapies resulting in apparent good response. This latter approach has been called "down-staging". A service evaluation was undertaken between 2015 and 2023 and it was agreed in November 2023 that downstaging of HCC utilising the selection criteria as developed by Duvoux and colleagues should become an agreed indication for liver transplantation in the UK.

Inclusion criteria

- Not eligible for elective listing for under standard UK listing criteria for HCC
- Within Duvoux criteria for down-staged HCC[3]
- Interval of ≥6 months from down-staging treatment to imaging upon which registration based
- Interval of ≥3 months from first imaging demonstrating patient within criteria to registration

Duvoux criteria for listing for HCC

Criteria for listing following "down-staging" treatment will be consistent with that detailed in Duvoux et al[3].

Variable	Points
Largest diameter (cm)	
≤3	0
3-6	1
>6	4
Number of nodules	
1-3	0
≥4	2
AFP (ng/mL)	
≤100	0
100-1000	2
>1000	3

Patients with a score ≤2 points following down-staging treatment will be eligible for registration for liver transplantation.

Either local or systemic anti-cancer therapies may be undertaken in order to achieve down-staging of HCC, but that for patients who have undergone either surgical resection or ablative therapies within 1 year of registration the resected or ablated lesions will continue to be counted with diameter of lesions as determined by the resection pathology or the pre-intervention imaging with the greatest diameter being used.

Exclusion criteria

- Macrovascular invasion – identified at any time on radiological imaging or liver resection pathology
- Nodal metastases at any time
- Extrahepatic metastases at any time
- Ruptured HCC at any time
- Absence of an absolute contra-indication to liver transplantation as defined in the current UK selection assessment and selection criteria for liver transplantation.

[1]Mazzaferro et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med. 1996 Mar 14;334(11):693-9.

Radiological imaging

Patients with presumed HCC should undergo the following imaging modalities during assessment for liver transplantation

1. Contrast-enhanced CT of chest, abdomen, and pelvis
2. Contrast-enhanced MRI liver

Imaging for the purpose of diagnosis and assessment must be undertaken within 4 weeks of listing.

Two independent radiologists will review all imaging undertaken prior to listing in order to confirm that imaging demonstrates HCC within the Duvoux criteria with regard to size and number.

For any given lesion the longest axis will be determined and used for assessment purposes. Measurements will be determined from the imaging modality that provides the best definition of the lesions under investigation

Waiting list management of patients

Local or systemic therapy for HCC is allowed whilst the patient is on the waiting list.

The maximum interval between repeat radiological imaging/AFP estimations will be 3 months.

Repeat imaging for estimation of HCC size and number will be with the modality (CT or MRI) that provides the best definition of identified liver lesions. The independent radiologists reviewing the initial imaging will determine the imaging modality to be used during follow up imaging.

CT chest, abdomen and pelvis will be required at 3 monthly intervals to assess the presence or absence of extra-hepatic disease.

Date of repeat imaging and lesion measurements will be provided to NHSBT along with other required variables.

Removal from waiting list

Patients will be removed from the waiting list if they progress beyond the Duvoux criteria or develop an exclusion criterion as listed above.

APPENDIX B
A service development evaluation of orthotopic liver transplantation for patients with Grade 1 and 2 Well Differentiated Unresectable Liver Metastatic Neuroendocrine Tumours (NETs)

Background
The incidence of neuroendocrine tumours has increased more than six-fold over the past four decades to almost 9 per 100,000 probably due to improved diagnostic methods[1] These tumours can originate at various sites in the body and generally behave better than high grade cancers
A large proportion of NET primaries are early and benign; incidentally found in the stomach, duodenum, appendix or rectum at an early stage and easily managed with curative local resections. About 40-50% of newly diagnosed cases present with distant metastases, commonly to the liver[2].
Liver metastases are most common in patients with small bowel or pancreatic NETs[3]. The presence of liver metastases has a negative effect on survival, with 5-year overall survival rates reducing dramatically from 75-99% in localised disease to 13-54% in the presence of liver metastases [4].

Aims of evaluation
To assess the criteria and role of liver transplantation for patients with NETs

Inclusion criteria
- Histology grades 1-2
- Primary site is Bowel or pancreas
- Primary and associated lymph nodes are completely removed before liver transplant surgery
- Primary tumour site drained by the portal system
- Tumour is less than 50% of the liver volume
- Interval of ≥6 months from resection of primary tumour to consideration for listing
- Stable disease/response to therapies for at least 6 months prior to transplant consideration

Exclusion criteria
- Any patient not fufilling inclusion criteria
- Patients requiring multiple organs (e.g. simultaneous liver and kidney patients)

Waiting list management of patients

Patients accepted on to the wait list will likely wait 6-12 months for a suitable liver to become available for them and will be offered through the variant syndrome pathway. During this time, they will be regularly seen by their NET team as well as 3 monthly by their liver transplant team. Patients' cancers will continue to be actively managed on the waiting list. They will remain on their treatments and will have any extra treatments as needed.

Patients will require the following reassessments in the following manner:
- ***Clinical assessment*** [3 monthly] to ensure remains in adequate physiological condition without rapid, unmanageable changes in health
- ***Biochemical assessment*** [3 monthly] to monitor for fluctuations in hormone symptoms, liver and renal function, and development of carcinoid heart disease.
- ***Radiological assessment*** [6 monthly since relatively slow growing cancers] using CT TAP, MRI liver and Ga-68 DOTA SSTA PET to look for disease progression.

Removal from waiting list

Patients will be removed from the waiting list if

- Overall deterioration in patient's condition makes transplantation unsafe.

- Rapid radiological disease progression within liver [slow progression may be acceptable for remaining on the list].
- Recurrence of extra-hepatic disease.

Cohort Size: a maximum of 50 patients will be listed for transplantation but outcomes will be assessed after 10 patients have been registered. The cohort size will be routinely monitored and reported at the six-monthly Liver Advisory Group meetings.

Outcome measures:
Participating Centres [ENETS Centres of Excellence and Transplant Centres] shall provide data in order to remain within the pilot programme.

- There will need to be robust data capture on ***all*** patients from when they are referred by the NET specialist to the National Board for an opinion on suitability for the liver transplant pathway. Since this is a single arm evaluation and there are so many points at which patients can drop out, a comprehensive database, ***that includes patients not transplanted***, will add to evidence for best management of patients with NETs. Need funding to be able to do this proactively – using a part-time data manager.
- Overall survival (from listing?) : 3 months, 1 year, 5 years, 10 years
- Disease Free Survival in transplanted: 3 months, 1 year, 5 years, 10 years
- Survival of 'not transplanted': 3 months, 1 year, 5 years, 10 years
- QoL measures: CLQ C30, GINET Q21, psychological wellbeing GHQ9 [possibly other tools to be decided], and EQ5D for health economics. These measures will be assessed for all patients referred to the advisory group so that we have data for an intention to treat analysis.

Evaluation monitoring

An independent Oversight Committee will be responsible for the running of the evaluation. This committee will consist of both clinicians and lay members.

The Oversight Committee will provide reports to the Liver Advisory Core Group.

The LAG Core Group will report and be responsible to the Liver Advisory Wider Group at the 6 monthly meetings.

Termination of service development evaluation

The evaluation will be terminated if there is

1. Evidence of poor outcome following liver transplantation.
2. Evidence of poor recruitment to the service development evaluation.

Dissemination of details of planned service development evaluation

Patients eligible for inclusion in the present evaluation may not have traditionally been managed within a liver transplant centre raising the possibility of inequity of access to a potentially curative treatment if referring centres are unaware of the proposed evaluation. Consequently, details of the evaluation will be circulated to all cancer networks, gastroenterologists, and hepatobiliary surgeons. Where possible information will be circulated through relevant professional bodies e.g. British Association for the Study of the Liver (BASL), GB and Ireland HepatoPancreaticoBiliary Association (GBIHPBA).

[1] White B E BC, Genus T, Rous B, Srirajaskanthan R, Chandrakumaran K, Ramage J. Incidence of Neuroendocrine Neoplasms Reported in England 2015-2017. *Abstract #3046 ENETS - The European Neuroendocrine Tumor Society Conference 2020* 2020.
[2] Pavel M, O'Toole D, Costa F, et al. ENETS Consensus Guidelines Update for the Management of Distant Metastatic Disease of Intestinal, Pancreatic, Bronchial Neuroendocrine Neoplasms (NEN) and NEN of Unknown Primary Site. *Neuroendocrinology* 2016; **103**(2): 172-85.
[3] Frilling A, Clift AK. Surgical Approaches to the Management of Neuroendocrine Liver Metastases. *Endocrinol Metab Clin North Am* 2018; **47**(3): 627-43.
[4] Eghtesad B, Aucejo F. Liver transplantation for malignancies. *J Gastrointest Cancer* 2014; **45**(3): 353-62.

APPENDIX C
A service development evaluation of orthotopic liver transplantation for patients with Unresectable Colorectal Liver Metastases

Background

Colorectal cancer (CRC) is the third most common cancer and cause of cancer-related deaths in Europe(1). Despite significant progress in management strategies for colorectal cancer over the years, metastatic disease is a difficult conundrum and can often be incurable. For Isolated CRCLM, liver resection is currently the only potential curative therapy, However, only 20% patients undergo resection with curative intent and there is considerable discrepancy between centres with regards to eligibility, treatment, and subsequent outcomes. For most unresectable metastases, palliative chemotherapy is the only option with 5- year overall survival between 8 to 15% (9). The use of liver transplantation to treat metastatic disease has been controversial, primarily due to fear of disease recurrence or progression, or de novo malignancies in the context of immunosuppression. The first of prospective series documenting a potential role for LT in this setting came in 2013 from a Norwegian group in their SEcondary CArcinoma (SECA-I) study which reported that survival of 10 years or more was possible in carefully selected patients with liver- only disease. Their cohort of 21 patients demonstrated a 5-year survival of 60%, and included those who had undergone prior total resection of their lymph node- negative primary CRC tumour, with ECOG score 0 or 1, and received at least 6 weeks of neoadjuvant chemotherapy (1). However, more stringent patient selection criteria were adopted in their subsequent study, SECA- II, finally comprising a cohort of 15 patients with Oslo score between 0 and 2 who underwent LT between 2012-2016. The estimated 1- and 5-year OS in this group was 100% and 83%, with 1- and 3-year DFS of 53% and 35%(2). In view of the recent prospective evidence and consensus guidelines from IHPBA supporting the utility of LT in CRCLM (3), the Liver Advisory Group (LAG) of NHS Blood and Transplant (NHSBT), the regulatory authority overseeing all donation and transplant related activity in the United Kingdom, established a Fixed Term Working Unit (FTWU) to explore the feasibility and formulate a protocol for LT for isolated, unresectable CRCLM in the United Kingdom.

Between July 2024 and May 2025, the original CRC Mets working group were asked to consider three Questions in relation to the new service evaluation as part of a new transplant indications FTWG on behalf of the LAG:
1. Are all inclusion and exclusion criteria appropriate based on current evidence?
2. Do we have sufficient stake holder engagement to maximise referral of appropriate patients who may benefit from transplant and if not, how do we address this?
3. Is offering as currently set for these indications working in offering organs in a timely manner? If not, what has to change?

Addressing these questions were considered and led to updated recommendations which were approved by the LAG at the meeting in May 2025. These recommendations were:

1. ***Are all inclusion and exclusion criteria appropriate based on current evidence?***
   Recommendation:
   - The primary resection will be mandatory, as there is risk of progression of primary cancer or recurrence in the primary site after liver transplant.
   - Patients with synchronous colorectal liver metastases who are deemed suitable from an inclusion criteria point of view for LT at the time of diagnosis should have their primary tumour removed at the earliest after 6 months of commencing chemotherapy. This would allow patients to proceed to start the process for listing around 22 months as they approach the 2 year period.
   - Chemotherapy to continue all the way up to coming in for the LT has already been agreed with the understanding that patients are aware that if they have 'chemotherapy related complications or low counts that may preclude them from proceeding to LT
   - Time to transplant will remain at 24 months
   - BMI>30 no longer an exclusion criteria

- With regards to tumour progression if chemotherapy is paused for surgery of the primary or a break in treatment the following will apply:
    - If there is progression in the previously known metastases then the clock will not be 'reset' and if there is stability in the tumours with either same line of chemotherapy or switch to second line for a '3 month period' they can proceed to listing
    - If however there are new metastases and there is a switch to 'second or third line chemotherapy' then a stability over at least a '6 month period' to get them to 2 years would need to be demonstrated prior to consider listing for LT. In other word, although stability over 6 months would be accepted the 2 year waiting time would still apply.
    - Patients will no longer be considered for LT in this service evaluation If there is any evidence of extra hepatic disease.
- Post LT Chemotherapy – the risk benefits can be discussed with the patients on an individual case basis, as globally there is no agreement. However, the view from the UK Oncology experts was that there is no evidence to give this routinely.
- Post-transplant imaging will change from 2 monthly CT scans to 3 monthly CT scan with PET-CT as additional imaging
- Post-transplant Sirolimus based immunosuppression to be used – switch to be done at 3 months post LT

2. Do we have sufficient stakeholder engagement to maximise referral of appropriate patients who may benefit form transplant and of not how do we address this?

Although referral of patients with CRLM as possible transplant candidates was initially low, this number has now increased. It was however recognised that more engagement would be helpful to ensure equity of access for all potentially eligible patients and meetings will be arranged.

3. Is offering as currently set for these indications (and in this case also including HPS) working in offering organs in a timely manner? If not what has to change?

It was agreed that patients with colorectal liver metastases should receive a named patient offer within 3 months of listing.

Recommendations:

- To ensure equity of access to all donor groups for all patients on the waiting list for liver transplant it was felt important to consider both DCD and LDLT grafts for CRC met patients.
- As with all the new indications, the current review of the National Liver offering system (NLOS) may impact on allocation for these patients and we await the final recommendations.

These refinements have been edited into the document

Inclusion criteria (Patient selection criteria for UKCoMET Service Evaluation)

1. Histologically verified primary adenocarcinoma in colon or rectum that has been fully resected at least 3 months before listing, with microscopically negative resection margins, including CRM of ≥ 2mm for rectal cancer patients.
2. Isolated synchronous/ metachronous CRCLM on chemotherapy and liver MR with no liver resection option, based on the outcome of local MDT and in case of doubt sanctioned by National Review Panel.
3. At least 30% sustained response to induction chemotherapy over a 2- year period, based on RECIST criteria; Disease progression/ second line therapy will lead to 'reset' of clock
4. No signs of extra hepatic metastatic disease or local recurrence in PET- CT within 4 weeks of listing meet.
5. No signs of extra- hepatic metastatic disease or local recurrence according to CT and MR (thorax/abdomen/pelvis) scan within 4 weeks prior to the listing meet
6. No signs of local recurrence on colonoscopy / CT colonography within 12 months prior to listing meet
7. No evidence of peritoneal recurrence on diagnostic laparoscopy and/ or MR abdomen and pelvis with DWI in two planes, in case of T3 or more tumours, within 4 weeks of listing meet.

8. Good performance status, ECOG 0 or 1.
9. Hb >10g/dl, Serum Bilirubin < 5 x upper normal level, Serum Creatinine < 1.25 times ULN, albumin above lower range of normal at assessment/registration
10. Signed, informed consent as per GCP

Exclusion Criteria

1. Weight loss >10% the last 6 months
2. Any second primary malignancies, except non-melanoma skin cancers
3. Prior extra hepatic metastatic disease or local relapse.
4. Sequentially increasing serum CEA assays
5. Patients who have not received standard operative treatment for the primary CRC.
6. Patients who have undergone palliative resection of primary CRC tumour
7. Patients with complete clinical response of primary tumours, without radical resection.
8. Patients requiring multiple organs (e.g. simultaneous liver and kidney patients)

Special considerations

1. Following morpho- pathological factors will ***not*** be used as exclusion criteria
    - Mucinous differentiation
    - Signet- ring cell morphology
    - Tumour differentiation status
    - Nodal metastases, extramural/ lymphovascular/ perineural invasion
    - BRAF V600R, KRAS, mismatch repair protein status, or right sided tumours
2. Patients requiring salvage transplantation and previously resected liver metastases will be excluded for the study, however the decision may be reviewed by the National Expert Panel following at commencement of the study and after assessing initial recruitment.

'The FTWU considered that given the requirement for a ≥30% reduction in disease volume followed by disease stability during a two-year period before being eligible for transplant assessment allowed for the biology of the cancer to be time tested'

Workflow for LTx for Unresectable CRLM

All referrals of patients from Colorectal Centres must feed into their referring HPB or HPB+ Liver Transplant Centre

Referral to HPB Centre

1. Centre assesses patient and eligibility as per defined inclusion criteria
2. If deemed appropriate, then Collation of all information as below

i) Imaging – CTCAP, MRI, FDG PET
ii) Relevant Histology
iii) Relevant MDT information/letters re primary and Unresectable Colorectal Liver Metastases

Referral to Liver Transplant HPB centre with all collated information

Liver Transplant and HPB Centre

1. Referral from non-transplant HPB centre – Liver Transplant HPB Centre assesses patient and eligibility as per defined inclusion criteria
2. Centre presents the patient to the HPB MDT at the Liver Transplant Centre
3. If the patient is local to the Liver Transplant HPB Unit then the case is first presented to the HPB MDM to confirm eligibility
4. HPB MDM - decision to proceed with liver transplant then patient is formally assessed for transplant and discussed in the Liver Transplant Listing Meeting and the decision is made to list or not to list
5. Patient is informed of listing outcome and prepared for listing on the Transplant assessment pathway as per the local liver transplant centre protocol
6. Patient is activated on the National waiting list
7. In case of uncertainty the case will be referred to a **National Expert Panel** (some members from FTWG and Chair of LAG – exact structure to be finalised) for review and the decision will be made and conveyed to the referring Unit.

Waiting list management:

The centres will be told to refer patients at the 18 month time point – allowing 4 months of assessment and work up and treatment of the primary.

If there is any concern with regards to candidacy of the patient being listed the case will be reviewed by the National Expert Review Panel. Once on the waitlist, all systemic treatment will be stopped, and it is anticipated that transplantation will occur within a three- month period. Deterioration in performance status, disease progression either within the liver or extrahepatically while on the waiting list and development of additional malignancies will lead to de-listing of the patient.

Assessments while on the waiting list:

Therefore, from the time of listing to transplantation, FTWU recommends CT Chest Abdomen and Pelvis scan every 6 weeks, or earlier if clinically indicated.

Cohort size:

It is estimated that 20 patients would be transplanted over a 2 year period as part of the service evaluation. The cohort size will be routinely monitored and reported at the six-monthly Liver Advisory Group meetings.

Outcome measures:

1. Overall survival
2. Progression- free survival
3. Disease recurrence sites and volume
4. The number and type of oncological interventions post-transplant will be recorded.
5. Quality of life will be measured using validated questionnaires (SF-36 Health Survey) at specific time points throughout the evaluation.
6. Recorded variables will be compared with patients considered for listing but found unfit for surgery.
7. A national registry will be maintained to record graft and oncological outcomes for the purpose of audit and research.

Follow up:

As per the SECA I and II study, the FTWU recommendation would be that patients are seen every month for the first year, thereafter every 3 months for the second year, and every 6 months from the third year.
CT scan of the chest, abdomen and pelvis is recommended every 2 months in the first year, every 3 months the second year and every six months thereafter.

The FTWU recommends although the schedule may be too elaborate for a service evaluation, it must be adapted to have consistency in monitoring outcomes.

Service Evaluation:

The National Expert review Panel with the LAG will monitor recruitment and outcomes at 3 monthly intervals to evaluate any need to alter protocol or interrupt the study.

Dissemination of results:

1. National Groups – Special Interest Group- Transplant Oncology (SIG -TO), BTS, BASL, BLTG, GBIHPBA, Local Referring Network Groups
2. Publication in peer reviewed journals

References:

1. Hagness M, Foss A, Line P-D, Scholz T, Jørgensen PF, Fosby B, et al. Liver transplantation for nonresectable liver metastases from colorectal cancer. Ann Surg. 2013 May;257(5):800–6.
2. Dueland S, Syversveen T, Solheim JM, Solberg S, Grut H, Bjørnbeth BA, et al. Survival Following Liver Transplantation for Patients With Nonresectable Liver-only Colorectal Metastases. Ann Surg. 2020 Feb;271(2):212–8.
3. Bonney GK, Chew CA, Lodge P, Hubbard J, Halazun KJ, Trunecka P, et al. Liver transplantation for non-resectable colorectal liver metastases: the International Hepato-Pancreato-Biliary Association consensus guidelines. Lancet Gastroenterol Hepatol. 2021 Nov 1;6(11):933–46.

Appendix D: A service development evaluation of orthotopic liver transplantation for patients with Intrahepatic Cholangiocarcinoma

Background

Intrahepatic cholangiocarcinoma (iCCA), whilst rare, is increasingly diagnosed in patients with background chronic liver disease. Where feasible, liver resection remains the gold standard for curative attempts in management of iCCA. The associated chronic liver disease, location of tumour, portal hypertension and liver failure limits applicability of liver resection even in patients with small iCCA.

iCCA remains a contraindication for listing for liver transplantation in most programmes across the world. However, recent multicentre studies show encouraging outcomes in a select group of patients with these cancers that prompted reassessment of iCCA as an indication for liver transplantation. In a significant number of these liver transplant recipients with iCCA, the diagnosis was incidental at explant, of either a previously unknown lesion not seen on pre-transplant radiology or a lesion misdiagnosed as HCC on radiology.

A single centre study from United States of 13 patients with iCCA, 4 patients with well differentiated tumours showed no recurrence compared to 78% recurrence with moderately differentiated tumours, indicating the importance of tumour biology for post-transplant outcomes. A multicentre study from Spain showed that patients with very early iCCA (defined by tumours that are solitary and less than 2 cm in size) had a 73% 5-year survival rate in 8 patients. An international multicentre study again demonstrated a favourable impact of the number and size of tumours in long term outcomes. 15 patients with very early iCCA had a 5-year 65% survival with recurrence rates comparable to HCC within Milan criteria. Jung et al investigated the outcome of liver transplantation for 16 patients with incidental iCCA and compared their outcomes with a propensity score matched 100 iCCA patients who underwent liver resection. Three patients with very early iCCA who underwent liver transplantation had no recurrence at a mean follow up of 39.1 +/- 29.9 months. 26 patients who underwent liver resection had very early iCCA and 6 (24.2%) developed recurrence. Half of the recurrences were intra-hepatic and the authors argued that these patients would have potentially benefited if they had transplant as a treatment for very early iCCA.

A recent multicentre French study suggests a more liberal approach towards size of the tumour. A retrospective three centre study compared outcomes of patients who underwent liver transplantation with incidentally iCCA at explants (n=49) with patients who underwent liver resection for iCCA and background chronic liver disease (n=26). The incidence of incidental iCCA and mixed Hepatocellular-cholangiocarcinoma (cHCC-CCA) increased from 0.6% of transplants in 2002 to 2% by 2015. At a median follow up of 25 months, the 1,3- and 5-year survival of patients who underwent LT was 90,76 and 67% respectively compared to 92,59 and 40% for patients who had resection. The recurrence free survival was 75% at 5 years post transplantation compared to 36% for resection. Independent risk factors for recurrence were the size of the largest tumour and differentiation. The 1,3- and 5-year survival for tumours <2cm after transplantation was 92,87 and 69% compared to 87,65 and 65% for tumours 2-5 cm in size. cHCC-CCA had similar outcomes to iCCA. 55% of patients who underwent liver transplantation had TACE as bridging therapy and five patients had adjuvant chemotherapy with Gemcitabine and Oxaliplatin. Two recent studies investigated the role of neoadjuvant therapy prior to liver transplantation for large unresectable iCCA. Systemic therapy and locoregional approach with radioembolization have been used in these studies. These studies indicate potential benefit of neoadjuvant and adjuvant therapies that need to be investigated as larger clinical trials.

Between July 2024 and May 2025, the original CCa working group were asked to consider three Questions in relation to the new service evaluation as part of a new transplant indications FTWG on behalf of the LAG:
1. Are all inclusion and exclusion criteria appropriate based on current evidence?
2. Do we have sufficient stake holder engagement to maximise referral of appropriate patients who may benefit from transplant and if not, how do we address this?
3. Is offering as currently set for these indications working in offering organs in a timely manner? If not, what has to change?

Addressing these questions were considered and led to updated recommendations which were approved by the LAG at the meeting in May 2025. These recommendations were:

2. Are all inclusion and exclusion criteria appropriate based on current evidence?

To summarise the current criteria of 2cm was felt to be too tight.
We discussed extending to </=3cm (as per the EASL_ILCA guidance https://www.journal-of-hepatology.eu/action/showPdf?pii=S0168-8278%2823%2900185-X) or even up to 5cm T1a <5cm with no vascular invasion avoiding poorly differentiated and consideration of lymphadenectomy. The consensus was to increase in a staged way to 3cm. External input was received from Gonzalo Sapisochin (Canada) who supported expanding to 3cm with lymphadenectomy and exclusion of poorly differentiated tumours and macrovascular invasion.

Recommendation:

a. Expand criteria to 3cm
b. Recommend lymphadenectomy
c. Exclude macrovascular and poorly differentiated tumour
d. Cholangiocellular HCC should be excluded initially and consideration given to including later depending on progress of the pilot
e. Neoadjuvant locoregional therapy could be employed for bridging with local discretion provided it was in alignment with national guidance
f. Prior systemic therapy does not preclude entry to the pilot provided it is discontinued in advance of listing

2. Do we have sufficient stakeholder engagement to maximise referral of appropriate patients who may benefit form transplant and of not how do we address this?

It wasn't felt this was the primary reason for the poor accrual into the programme but could be contributing. That said the general feeling was for the existing new indications this was likely better than the others as such lesions find their way through HPB MDTs. Still a concern that in HPB MDTs not in transplant centres awareness could be improved.

Recommendation:
a. Should be a part of a drive to increase awareness generally of the new cancer indications
b. Re-advertise expanded criteria if these are implemented
c. Present amendments at HPB meetings i.e.GBHPBA
d. ILTS supported symposium on non-HCC indications in Autumn 2025

3. Is offering as currently set for these indications (and in this case also including HPS) working in offering organs in a timely manner? If not what has to change?

Too few to determine if the current offering process was meeting the needs of recipients (75% of those listed should have a named transplantable offer within 3 months of listing). *Both patients listed and transplanted so far were transplanted with a DCD NRP graft within 92 days of registration*

Recommendation:
a. Consider a broader range of donors for patients with this indication given concerns about non recovery of DBD donation
b. No adjustment currently to DBD offering as not proven to have failed as an offering process.
c. As with all the new indications the current review of the National Liver Offering Scheme (NLOS) may impact offering for these patients and we await the final recommendations from this.

These refinements have been edited into the document

Aims of evaluation

To assess the criteria and role of liver transplantation for patients with

- Very early intrahepatic cholangiocarcinoma in the background of cirrhosis

Inclusion criteria

- < 3 cm tumours with background chronic liver disease
- resection is precluded because of underlying liver function or the position of the tumour.
- biopsy proven
- Prior systemic therapy does not preclude entry to the pilot provided it is discontinued in advance of listing

Exclusion criteria

- Inability to consent
- Poor performance status
- Failed fitness assessment
- Macrovascular invasion
- Poorly differentiated tumour
- Patients with mixed cholangiocellular/hepatocellular carcinoma.
- Extrahepatic disease at any stage of presentation, assessment and treatment
- Patients requiring multiple organs (e.g. simultaneous liver and kidney patients)

Study pathway

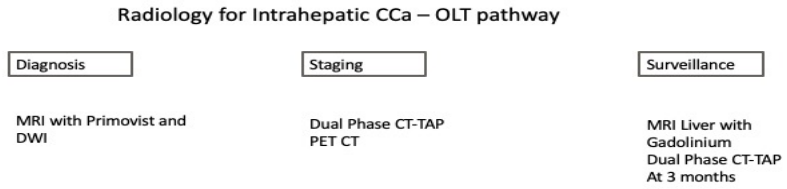
1. Referrer assesses eligibility according to the eligibility criteria for
    a. suspected ICCa in patients with CLD
    b. often this is at Hepatology units (Secondary care)/Hepatology Centres (Teaching Hospitals) or HPB Units (Teaching Hospitals)
2. Referral to Liver Transplant Centre for opinion – All clinical information and imaging transferred
3. Discussion in Cancer MDT to confirm diagnosis, arrange investigations to confirm diagnosis and staging.
4. Discussion in Transplant MDT to confirm fitness and appropriateness for listing
5. Neoadjuvant locoregional therapy could be employed for bridging with local discretion provided it was in alignment with national guidance
6. Transplantation with lymphadenectomy
7. Post-transplant monitoring

Radiological Evaluation and Surveillance

The diagnosis of intrahepatic cholangiocarcinoma is made by a combination of radiological appearances and tissue diagnosis.

MRI with Gadolinium is recommended as the standard cross-sectional imaging. The staging would include a dual phase CT of chest, abdomen and pelvis and a PET CT. If a patient, once been listed for transplant and waits more than 3 months from previous cross-sectional imaging, we recommended further re-assessment at that time point with a contrast MRI, a dual phase CT and a PET CT. We feel that the evaluation needs to be extensive to exclude patients with nascent extrahepatic disease and adverse biology to maximise the outcomes from service evaluation.

The post-transplant surveillance recommended by us include assessment of tumour markers at 3 monthly intervals for the first 2 years and cross-sectional imaging in the form of dual phase CT of chest, abdomen and pelvis at 6 monthly intervals for the first 2 years. After 2 years the cross-sectional imaging is recommended on an annual basis until the end of 5 years and the tumour markers are recommended at 6 monthly intervals, again until the end of 5 years.



Fitness Assessment
Fitness evaluation as per local practice and national guidelines for transplant assessment.

Removal from waiting list

Patients will be removed from the waiting list if

- An exclusion criteria from the pilot is met including
- Overall deterioration in patient's condition makes transplantation unsafe.
- Rapid radiological disease progression within liver [slow progression may be acceptable for remaining on the list].
- Evidence of macrovascular involvement
- Extra-hepatic disease.
- The need for multi-organ transplant

Cohort Size: 30 patients including patients with perihilar CCa undergoing liver transplantation. The number of patients registered on the liver transplant list will be monitored on a regular basis and reported to LAG.

Outcome measures:

1. Waiting list drop off
2. 1,2,5 year overall survival
3. 1,2,5 year disease free survival
4. Recurrence rate and pattern of recurrence

Evaluation monitoring

An independent Oversight Committee will be responsible for the running of the evaluation. This committee will consist of both clinicians and lay members.

The Oversight Committee will provide reports to the Liver Advisory Core Group and subsequent Liver Advisory Group meetings.

Termination of service development evaluation

The evaluation will be terminated if there is

- Evidence of poor outcome following liver transplantation.
- Evidence of poor recruitment to the service development evaluation.

The recruitment and data will be analysed yearly. If the recruitment is poor, it would be advisable for LAG core group to consider expanding of the inclusion criteria to 2-5 cm tumours, based on good prognostic factors on biopsy. The total number to be recruited would be 30 over three years including patients with perihilar CCa.

1. As the numbers are small, it was felt that trigger points should be based on events rather than percentage occurrence.
2. Adverse events of special interest include – vascular thrombosis within 3 months, recurrent cancer within 6 months, cancer related mortality within 12 months, re-transplantation for any reason.
3. These events should be reported and monitored by a CCa Advisory group that will overlook similar events for the perihilar CCa evaluation.
4. A moratorium will only be advised if the events were felt to be repetitive with a clear pattern behind the failures.

Dissemination of details of planned service development evaluation

1. Publication of protocol in a peer reviewed journal
2. NHSBT events
3. Dissemination through educational events, links with BTS, BASL, BSG, BLTG, GBIHPBA

Appendix E – Adult patients with Sickle Cell Hepatopathy

Sickle Cell Hepatopathy

Introduction

Sickle Cell Disease (SCD) is the most common genetic haematological disorder in the world and is estimated to affect 112 per 100,000 live births globally. Whilst the majority of these people live in Sub-Saharan Africa or India, in the USA, 1 in every 365 babies born to African-American parents has SCD and in the UK approximately 270 babies are born each year with the disease. Although the majority of children born in the lowest income countries die before the age of 5, over 95% of those living in the USA or UK with SCD live to adulthood with the life-expectancy of adults in the USA estimated at 58 and in a single center in the UK at 67 years of age.

Along with the increasing life-expectancy has come a change in the pattern of causes of death in patients with SCD. Advances in management and prevention of acute complications has led to a decline in deaths associated with these events, which are more prevalent in children and young adults. In contrast, deaths associated with chronic end-organ damage are on the rise, including chronic heart, liver, lung and kidney disease and managing these chronic complications has become the challenge that needs to be met by those caring for patients with SCD in high-resource settings. Solid organ transplantation is therefore an important component of the treatment options available for patients with SCD and end organ damage, as it is for patients with other causes of chronic organ dysfunction.

Sickle cell hepatopathy

Sickle cell hepatopathy (SCH) is an umbrella term encompassing a range of hepatic pathology arising from a wide variety of insults to the liver in patients with sickle cell disease. It occurs predominantly in patients with homozygous sickle cell anemia HbSS, and to a lesser extent in patients with other genotypes (including HbSC). Acute and chronic liver syndromes have been described. Liver disease may be caused primarily by the sickling process with subsequent vaso-occlusion or may be caused by the multiple transfusions that some patients require during their lifetime with the accompanying risks of acute and chronic viral hepatitis and iron overload. A significant proportion of patients have been found to have cirrhosis on autopsy. The direct manifestations of sickle cell disease in the liver are predominantly related to vascular occlusion from sickling with resultant acute ischemia, sequestration, and cholestasis. A further potential consequence of chronic hemolysis is the development of pigment stones which may lead to cholecystitis and biliary obstruction. The clinical spectrum of SCH ranges from mild liver function test abnormalities in asymptomatic patients, to dramatic clinical crises with marked hyperbilirubinemia and (acute on chronic) liver failure, to decompensated chronic liver disease.

Liver disease co-existent with sickle cell disease

A distinct clinical phenotype exists within the spectrum of liver disease in patients with SCD. This is of a patient with controlled SCD who has co-existent liver disease not thought to be caused by the sickling process or multiple transfusions (viral infection/ iron overload); for example, auto-immune liver disease. The incidence of patients within this distinct sub-group is difficult to ascertain, not least because clinical studies have often not specifically differentiated the phenotype from SCH. Moreover, when liver histology from patients with SCD is examined, there is often evidence for multifactorial injury. Examination of the explanted liver following transplantation in a patient with auto-immune liver disease and well-controlled SCD in our experience identifies significant sickling in the sinusoids in addition to an inflammatory infiltrate secondary to the auto-immune process (unpublished data). It may therefore be that this group of patients is still best considered under the umbrella term sickle cell hepatopathy.

Experience of Liver Transplantation in adult and paediatric patients with end stage liver disease in the context of Sickle Cell disease continues to accrue. Liver Transplant can now be recommended as the treatment of choice for highly selected patients following stringent multi-disciplinary assessment and review.

Sickle Hepatopathy is an accepted indication for transplant in paediatric patients, as a variant syndrome. Adult patients meeting the following indication and exclusion criteria should be registered on the variant syndrome pathway:

Indications:

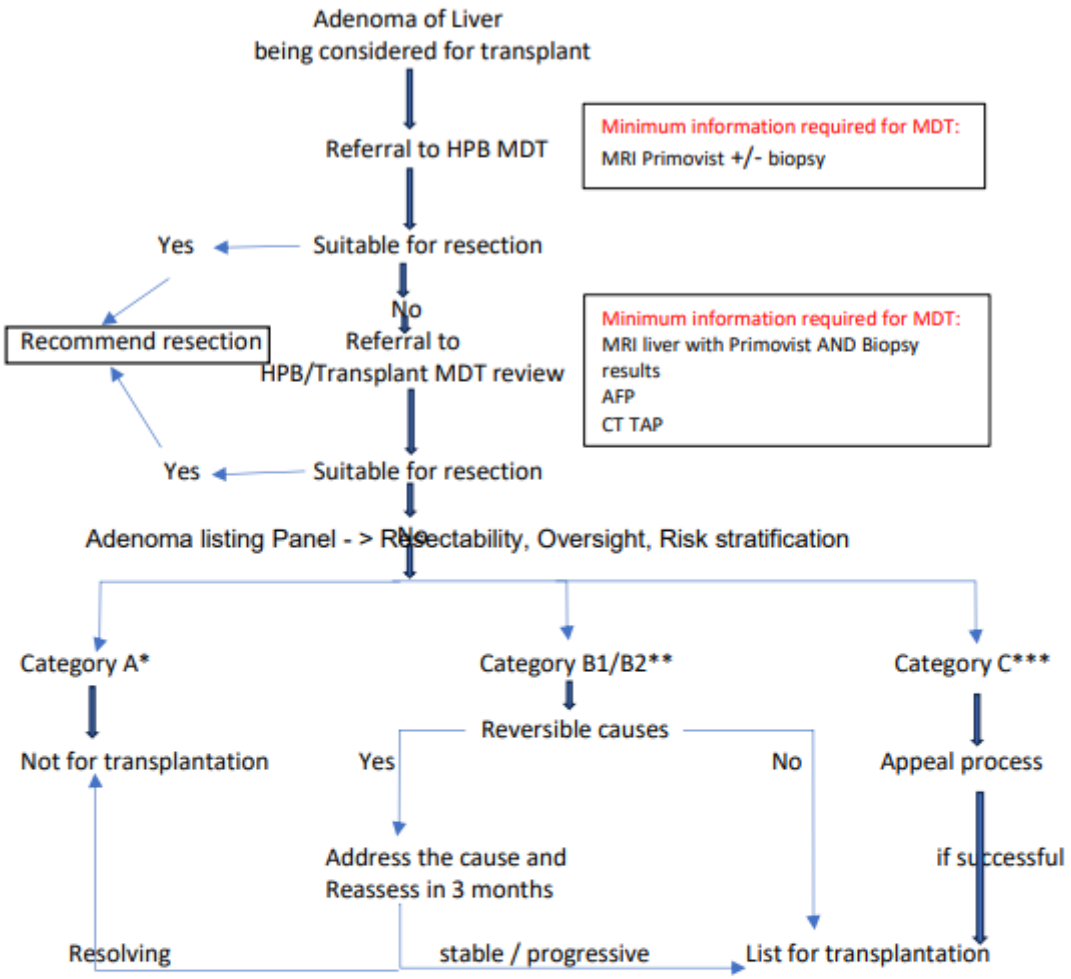
- Decompensated Chronic Liver Disease
- Age less than 50 years
- Full multi-disciplinary assessment to exclude significant non-hepatic sickle related end organ damage; particularly sickle related heart and lung disease, and cerebral vasculopathy
- Agreed haematological protocol for management of SCD pre-, peri- and post- LT (most often: maintenance of HbS fraction , 30%)

Exclusion criteria:

- Age greater than 50 years
- Acute liver disease/ Acute on Chronic Liver Failure
- Significant non-liver end organ damage as a consequence of SCD
- Failure to comply with exchange transfusion programme.

Appendix F – Algorithm for adenoma patients

Algorithm summarising the selection process of patients# with liver adenomas for liver transplantation:



***Category A:** Conventional HNF1a inactivated and inflammatory HCA with no concurrent beta-catenin activation.

****Category B:**
Category B1) Beta-catenin activated adenoma including exon 3 deletions or other high-risk mutations such as T41A, D32-S37
Category B2) Beta-catenin activated adenomas (+/- low risk mutations such as exon 3 S45 variant, exon 7/8 variants) AND any additional risk factors such as increasing size, male sex, changing to further high-risk characteristics, presence of background glycogen storage disorders, and vascular disorders (Abernathy syndrome).

*****Category C:** Patients that still need to go through an appeal process (including those in Category A) when the clinical team is considering them for LT (see document for some examples).