Pros, Cons and alternatives to MELD score in liver allocation

Criteria for assessing allocation policies

- Clear aim
  - Need, benefit, utility
- Patient based
  - Not centre based
- Transparent
- Legally compliant
  - Age, sex, ethnicity, non-discrimination
- Objective
- Evidence-based
  - Where possible

What are the possible aims of allocation?

- Waiting time
  - Liver offered to the person waiting longest
- Needs based
  - Liver offered to the sickest patient first (shortest mean survival estimate without a transplant)
- Utility based
  - Liver offered to maximise life years of graft (longest mean survival estimate with a transplant)
- Transplant benefit
  - Liver offered to patient predicted to gain most benefit (greatest difference in mean survival with and without a transplant)

Futility

- Is there a need to exclude futility?
- In UK, transplant candidates must have
  - >50% probability of being alive a 5 years
  - Quality of life acceptable to the patient
- Note that these variables are
  - Clinically sensible
  - arbitrary

Offering or allocation scheme?

- Lai et al (2012) review of OPTN 2005-10
- High quality grafts
  - Age 18-50y, >170cm, non-black, death from trauma, not CDC high risk, HCV neg
- 33389 candidates
  - 20% died/removed
  - 64% transplanted
- No of offers for all candidates: 5 (2-10)
- Of those who died
  - 84% received 1 or more offer
  - 57% received high quality offers

Why do so many offers get declined?

- Matching
  - Major: such as blood group
  - Minor: size, quality
- Risk
  - Patient
  - Doctor
  - Donor
  - Organ – risk of organ includes recipient factor
  - Unit
- Experience
- Fear from outcome monitoring

Other factors

- Donor risk
  - Deceased donor (DBD or DCD)
  - DRI is simplistic
    - Graft
    - Host
- Logistical issues
  - Cold ischemic time
  - Single or multi-organ transplants
- Patient risk
  - Age, co-morbidity, etc
- Patient choice
  - Risk perception

Needs a robust IT system that is flexible and accessible

The US approach

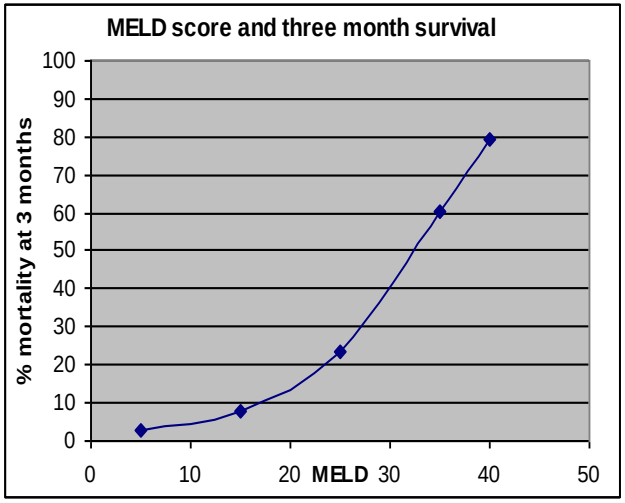
- Aim to reduce deaths on waiting list
- Use of MELD model to predict death
- Organs allocated to highest MELD score with some local sharing schemes
- Adjustment for HCC where outcome is not reflected by MELD
- Appeals panel with variable patterns

Outcomes of MELD scheme

- Deaths on waiting list fell
- Time to transplant falls
- No change in outcome
- Longer ITU stay and hospital costs
- Survival benefits of transplant when MELD >16

(see Wiesner 2003, Kim 2007, Freeman 2008, Brown 2005)

- MELD does not predict survival after transplant
- Variations of MELD such as
  - MELD sodium (Kim 2008)
  - MELD spike (Massie 2015)
  - MELD-lactate (Cardoso 2014)
  - MELD-albumin (Myers 2013)
  - iMELD (Biselli 2010)



- Paediatric patients have their own score

Concerns

- MELD was designed to predict short-term outcome of patients undergoing porto-caval shunt
- Appropriate to apply to another cohort?
- Validity in longer term
- Not time dependent
- Variations in appeals panels
- Parameters used are subject to
  - Gender differences
  - Inter-Laboratory variation
  - Gaming
- Less reliable for some groups
  - Hyponatremia
  - ascites
- No priority for those with non-life-threatening disease but indications such as
  - Intractable encephalopathy
  - Intractable pruritus

Inter-laboratory variation

UK NEQAS

Parameter	**Variation**	**P value**
INR	$F_{5.261}$ 1.39	0.21
Sodium	$F_{5.1676}$ 330.06	<0.0001
Bilirubin	$F_{5.1613}$ 158.4	<0.0001
Creatinine	$F_{5.1681}$ 82.8	<0.001

Does MELD apply in other countries

- Assess influence of MELD score at registration on risk of death on transplant list for UK patients
- Determine suitability of MELD as a predictor of mortality for UK patients
- If appropriate, develop and validate a UK specific mortality score

Methods

- Adult 1103 elective patients registered for a first liver transplant (excluding cancer patients) between 1 April 2003 to 31 March 2006 from all 7 liver transplant centres in the UK
- Cox regression analysis
- Analysis considered time on active transplant list
  - deaths and removals due to ‘condition deteriorated’ treated as outcome events
  - patients transplanted or removed for reasons other than ‘condition deteriorated’ were censored
  - patients remaining on list censored at time of analysis
- Patient-specific factors included in the model were:
  - age at registration, blood group, BMI, ethnicity, gender, height, weight, year of registration, primary disease

UK model for end stage liver disease - UKELD

Parameter estimates

Component variable	Parameter estimates	95% Confidence Interval
ln(INR)	1.079	0.394, 1.764
ln(creatinine)	0.297	-0.203, 0.798
ln(bilirubin)	0.626	0.433, 0.820
ln(sodium)	-16.313	-20.321, -12.305

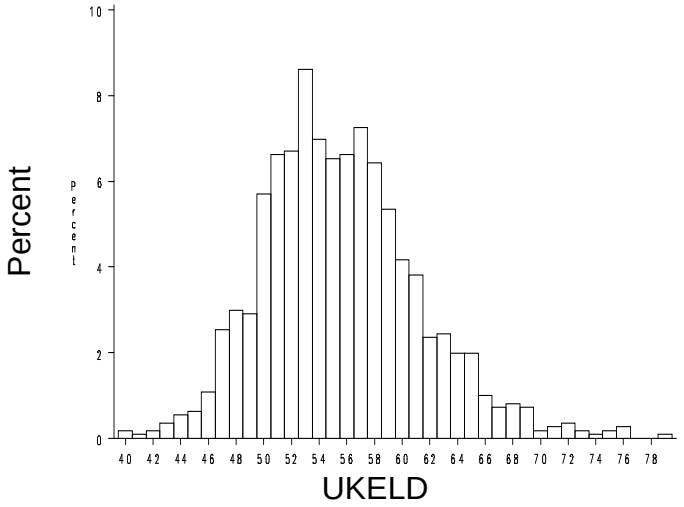
$$UKELD = \left[(5.395 \times \ln(INR)) + (1.485 \times \ln(creatinine)) + (3.130 \times \ln(bilirubin)) - (81.565 \times \ln(sodium))\right] + 435$$

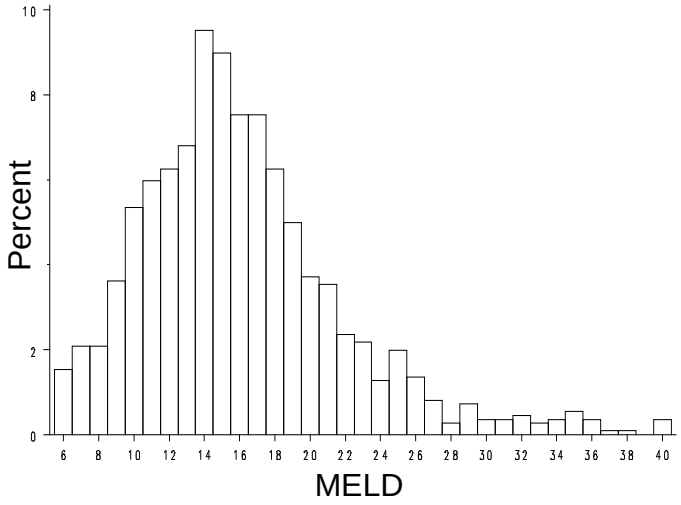
Distribution of UKELD and MELD

Summary statistics

- UKELD:
  median = 55, range = 40, 79

- MELD:
  median = 15, range = 6, 40





Weighting of MELD components

MELD parameter estimates for UK data

Component variable	UKELD weighting	MELD weighting
ln(creatinine).	0.297	1.40
ln(bilirubin)	0.297	0.55
ln(INR)	1.079	1.62

- MELD calculation gives greater weight to creatinine
- MELD weighting appropriate for bilirubin and INR

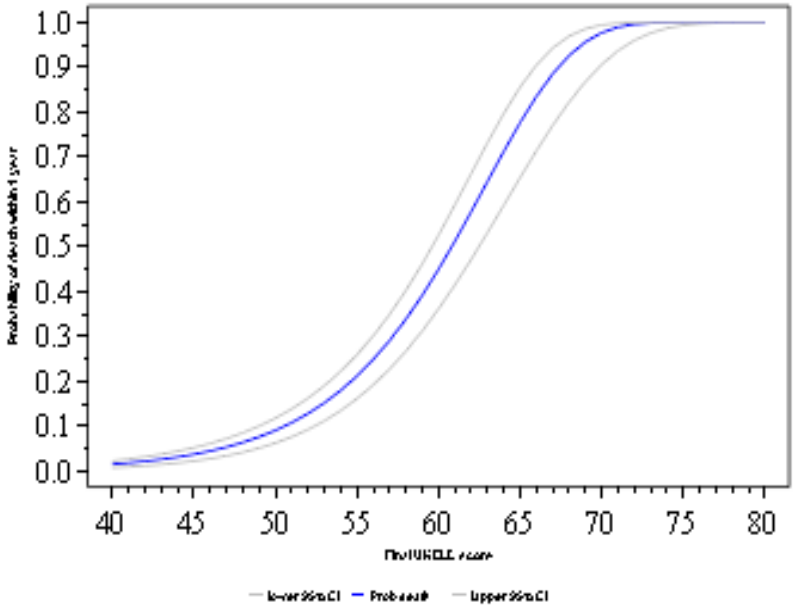
Comparison of UKELD and MELD

Score	-2 log likelihood statistic	Hazard ratio (95% CI)	p-value
UKELD	1677.6	1.22 (1.18, 1.26)	<0.0001
MELD	1754.8	1.13 (1.10, 1.16)	<0.0001

- UKELD model has the lowest –2 log likelihood statistic
- A one point increase in UKELD increases chance of death by around a fifth

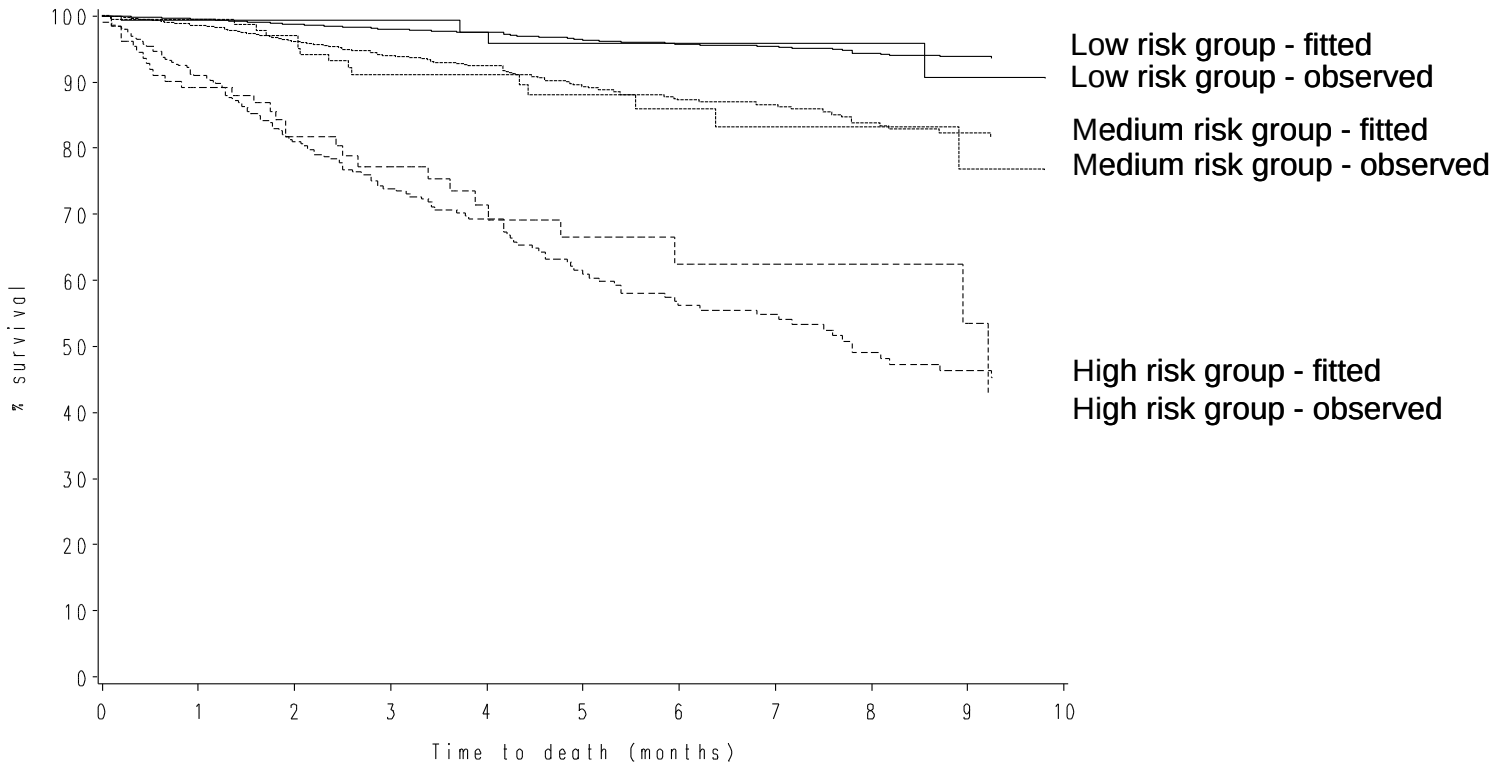
Probability of death on the transplant list

- 1 year patient survival = 88% (95% CI 87%-90%)
- Registration criteria where mortality on list within 1 year >10%
- Probability of death: 1-survivor function at 1 year



- UKELD = 49 has p(death within 1 year)=0.09 (95% CI 0.06, 0.12)

Validation - Risk score method



Model based fitted survivor functions track observed survivor functions reasonably well for each risk groups

why we use UKELD in UK

but do not advocate its use elsewhere

- UKELD score at registration a highly significant predictor of mortality on transplant list for UK patients
- UKELD a better predictor of mortality on transplant list than MELD for UK patients
- Validation confirmed UKELD an appropriate predictor of mortality on transplant list for UK patients
- Registration criteria based on a minimum UKELD score of 49

Should other countries develop their own equivalent of MELD?

Comparison of 6 score systems in Bologna 487 patients awaiting LT (Biselli 2010)

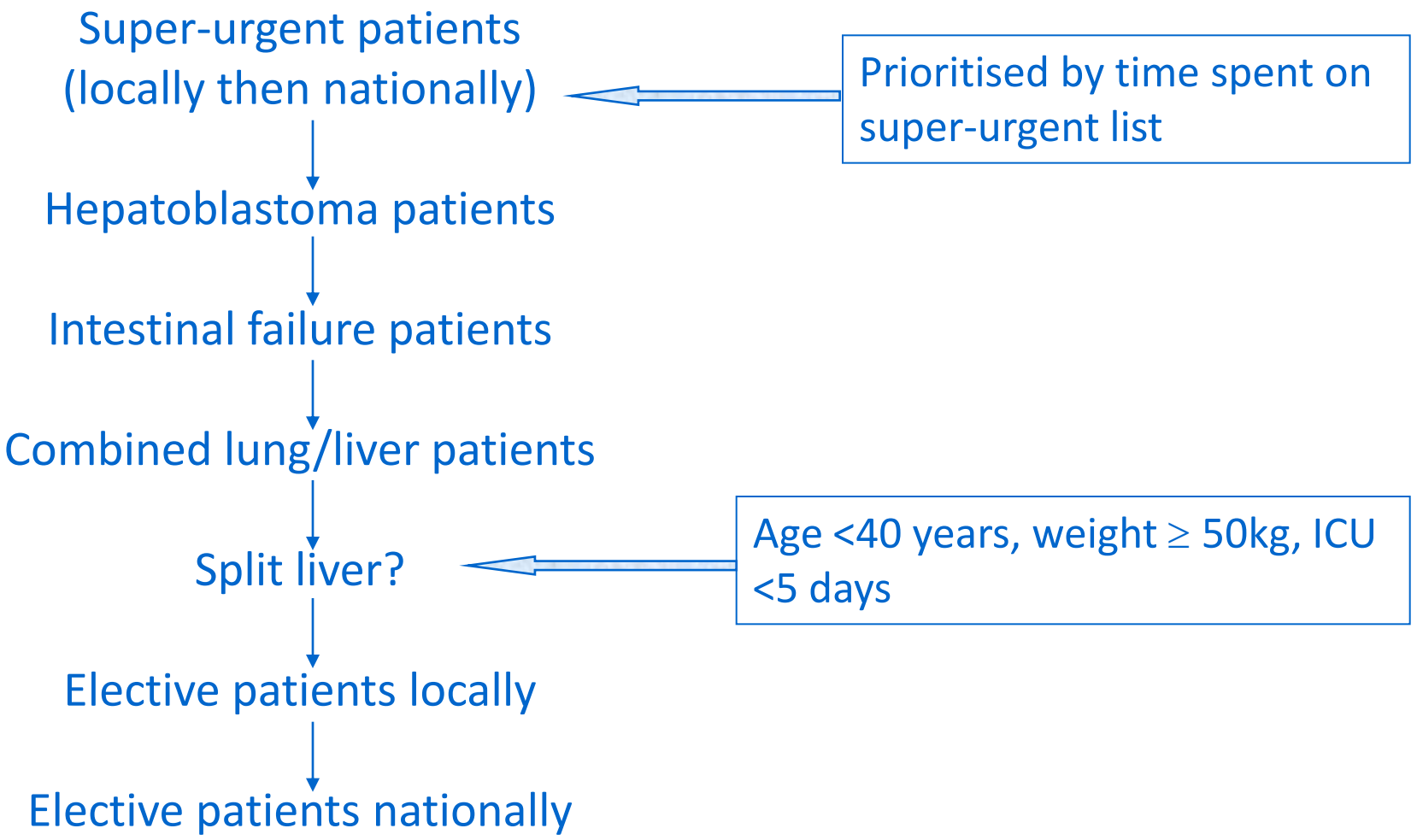
Score	AUC	p
MELD	0.759	-
mCTP	0.769	0.738
MELD-Na	0.798	0.03
iMELD	0.806	0.097
UKELD	0.781	0.489
uMELD	0.757	0.842

Zonal or National?

- Zonal
  - Lack of transparency
  - Possibility of inequity (perceived and real)
  - Allows surgeons to match donor and recipient
  - Allowance for resource
  - Zones need to be revised to match donation/list
- National
  - Clear and objective
  - Limitations:
    - Requires a national retrieval service
    - gaming,
    - validity of models,
    - balance competing groups (such as liver (end-stage versus QoL) or lung (Cystic versus IPF)

Current liver allocation scheme

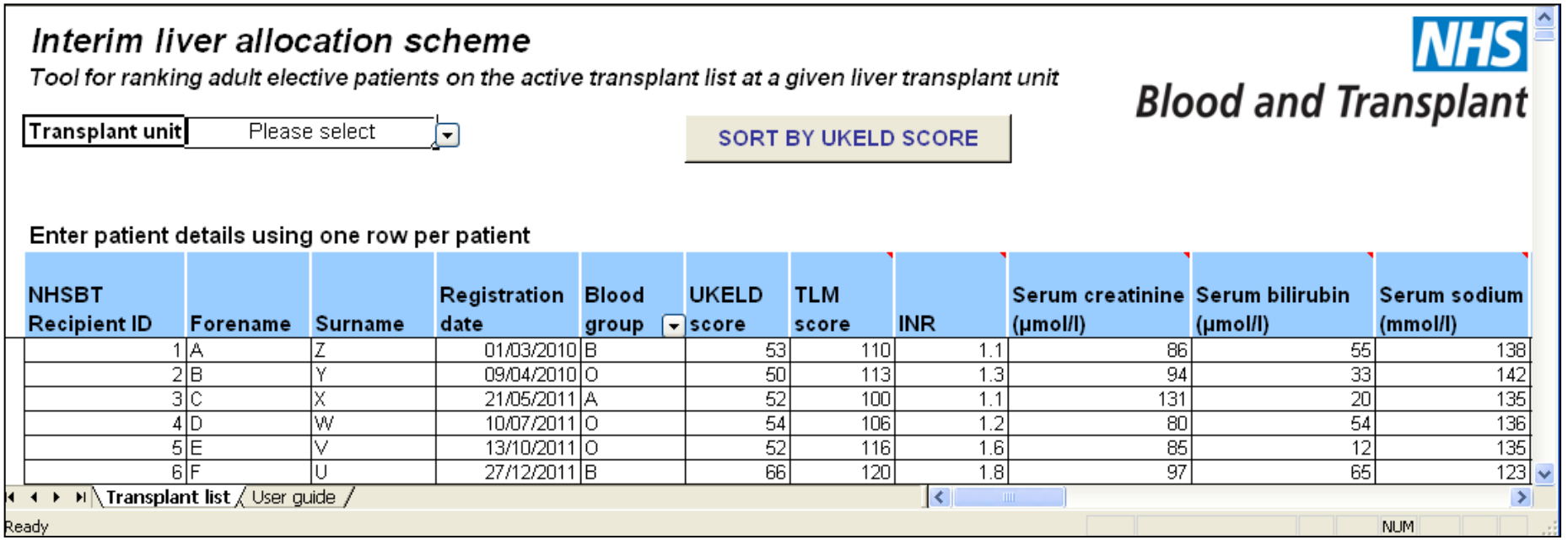
Priority order for all adult liver donors after brain death
(≥ 16 yrs, weight >35kg)



Allocation within centres

- Work on a national liver transplant allocation scheme (LTAS) ongoing
- Interim allocation scheme needed to improve transparency
- Patients on transplant list ranked by UKELD score with highest score at top of list
    - Adult elective patients only
    - Within each centre
    - Liver from DBD available
    - Started 1 April 2013
- Centres may select a patient who is not the highest ranked
- A reason why each higher ranked patient was not transplanted needs to be documented and retained by the centre.

Tool for ranking by UKELD



Interim liver allocation scheme

Tool for ranking adult elective patients on the active transplant list at a given liver transplant unit

NHS Blood and Transplant

Transplant unit: Please select

SORT BY UKELD SCORE

Enter patient details using one row per patient

NHSBT Recipient ID	Forename	Surname	Registration date	Blood group	UKELD score	TLM score	INR	Serum creatinine (µmol/l)	Serum bilirubin (µmol/l)	Serum sodium (mmol/l)
1	A	Z	01/03/2010	B	53	110	1.1	86	55	138
2	B	Y	09/04/2010	O	50	113	1.3	94	33	142
3	C	X	21/05/2011	A	52	100	1.1	131	20	135
4	D	W	10/07/2011	O	54	106	1.2	80	54	136
5	E	V	13/10/2011	O	52	116	1.6	85	12	135
6	F	U	27/12/2011	B	66	120	1.8	97	65	123

Transplant list / User guide

Ready NUM

Recording reasons for over-ruling UKELD ranking

REASON FOR OVER-RULING UKELD RANKING FORM

For donor after brain death (DBD) grafts performed at the centre, this form should be completed for every blood group identical and permitted categories of blood group compatible recipients who were ranked higher than the recipient transplanted. One form must be completed per recipient.

Transplant centre	
Donor ID	
Recipient ID	
Date of offer	
Recipient UKELD rank for this offer	
Reason graft was not offered to this particular recipient (use codes below)	
If code 13, 24 or 98, please specify	

Reason Codes

Donor factors

10 - History of malignancy
11 - History of infection
12 - Virology
13 - Other donor factors (please specify)

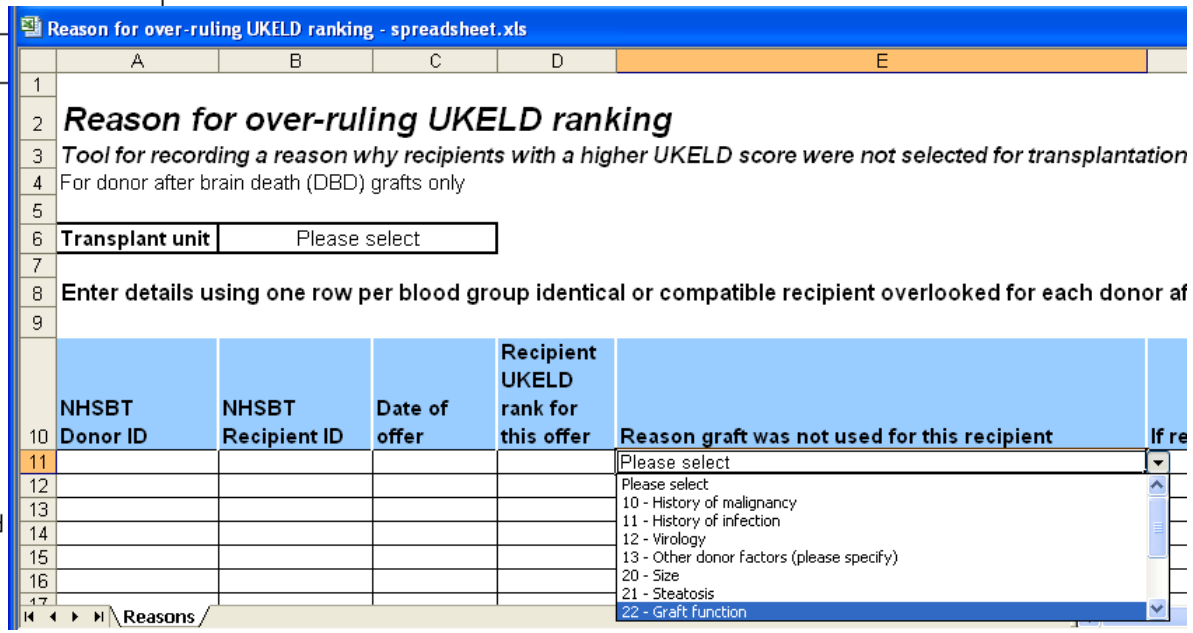
Graft related factors

20 - Size
21 - Steatosis
22 - Graft function
23 - Cold ischaemia + distant or complex recipient
24 - Other graft related factors (please specify)

30 - UKELD score is not a true reflection of this recipient's need

40 - HCC or other variant syndrome patient chosen

98 - Other reason (please specify)



Why we are considering changing method of deceased liver allocation

- Problems with existing, zonal scheme
  - Significant difference between centres in risk of death on transplant list and waiting time to transplant despite similar patient selection criteria
  - Not transparent so difficult to demonstrate that the allocation scheme in one centre is similar or comparable to that in another
  - Has difficulty in demonstrating equity of access to **all** potential recipients

- Following principles
  - Equity of access
  - Transparency of the allocation process
  - Outcomes at least as good as if not better than the centre based system

Development of new scheme

- Use past data to simulate proposed allocation schemes based on
  - Need
  - Benefit
  - utility
- Requirement to carry out real-time simulations so real-time patient data at the point a donor organ becomes available were required
- Collected ‘monthly’ data over a six month period from 1 August 2010 to 31 January 2011
  - All adult patients active on the elective transplant list for a liver only transplant at 1 August 2010
  - All new adult elective registrations
  - Bilirubin, INR, creatinine, sodium, patient weight, location and renal support
- Compare schemes in terms of:
  - characteristics of patients who would get transplanted
  - patient survival times compared to those under current arrangements

Modelling of outcomes

	%death/ Removal	Patient years	Predicted 1 yr survival%
Current	93 (7%)	4581	99.2
Need	48 (4%)	5187	99.5
Utility	95 (7%)	4779	100
Benefit	48 (4%)	5262	100

Median actual and predicted waiting time

Indication	Current	Need	Utility	Benefit
Cancer	204	753	57	747
HCV	218	64	863	87
ALD	218	190	259	118
Prev Tp	548	71	>461	119

Other issues

- How do we ensure all those who need a transplant have access
- How to balance length of life with quality of life *such as HE, pruritus, polycystic etc*
- How do we ensure flexibility to deal with progress and innovation
- Will national offering prolong offering time and increase cold ischemic time

Conclusions

- Allocation schemes are really offering schemes
- Essential to define aims of allocation scheme and review whether aims are met
- Allocation schemes must be flexible

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