

U.S. changes in Kidney Allocation

- Match kidneys with longest survival to patients with longest survival
 - No parallel matching for kidneys with lower survival potential
- Decrease discard of kidneys with lower survival potential
 - Increased sharing ...different from Eurotransplant
- Increase transplantation for highly sensitized patients
 - Some kidneys with long projected survival allocated to high risk patients (sensitized with long dialysis exposure)
- Backdated patients to dialysis start date
 - Improved access for ethnic minorities/low SES patients
 - Transplanting patients with long dialysis exposure – where survival benefit of transplantation compared to treatment with dialysis is less certain



Kidney Allocation in the UK: Did the Last System Work? What will the next one look like?

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CUTTING EDGE OF
TRANSPLANTATION

AST | AMERICAN SOCIETY OF
TRANSPLANTATION

RESOLVING THE ORGAN SHORTAGE



PRACTICE |



POLICY |



POLITICS

FEBRUARY 25-27, 2016 • PHOENIX, ARIZONA

Conflict of Interest Disclosure

- I have no relevant financial relationships to disclose.
- I will not discuss off label drug use
- I chair the Kidney Advisory Group of NHSBT
= Kidney committee of UNOS

UK & USA: two nations divided by a common language ... and an oval ball



You pass forwards
to score a touch down



We pass backwards to go
forwards to score a touchdown

UK Renal Replacement

Oversight:
NHS BT



\$ UK National Health Service
pays for all costs for life

UK population
60 million



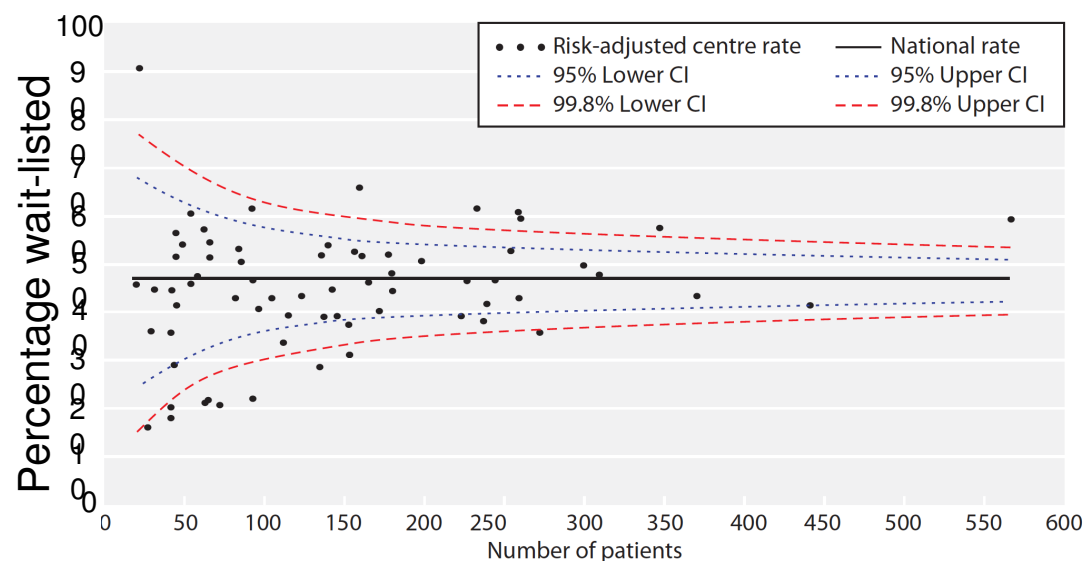
71 Local
Dialysis Centers



23 Regional
Transplant Centers

Access to the waiting list

- 52% of patients undergoing renal replacement therapy have a transplant
- Of those on dialysis 48% are listed for transplant



UK Renal Registry 2014

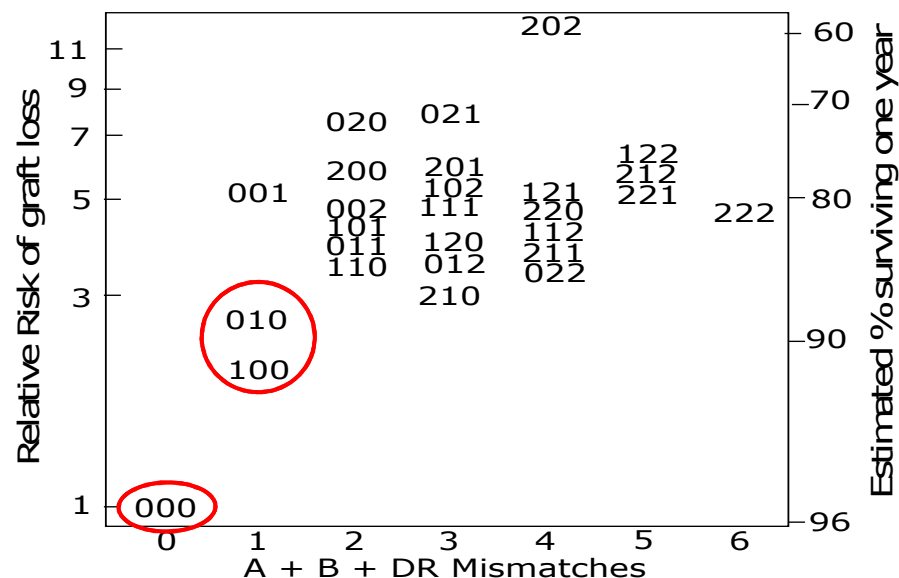
UK kidney allocation: Outline

- How we did we get here?
- Oversight in the UK
- Where are we going next?



1989 scheme: Beneficial matching

- Beneficial HLA match:
 - 000, 100, 010 mm
- One kidney shared
 - Preference for child / local patient
- One kidney kept locally



Gilks et al. Transplantation 1987;43:669

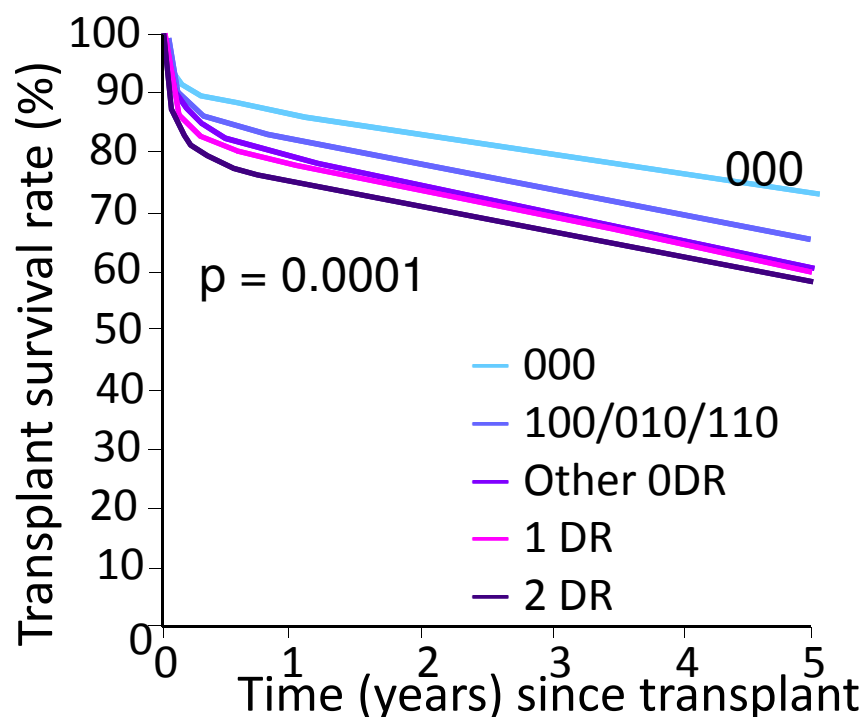
Analysis of 2282 kidney Tx in UK, 1979-84

Why not share both kidneys?

- Poorer outcomes of shared kidneys
 - 1.2 RR of graft failure
- Balance of exchange
 - North of England donate more kidneys
 - South of England list more recipients



1998 scheme: Favorable matching

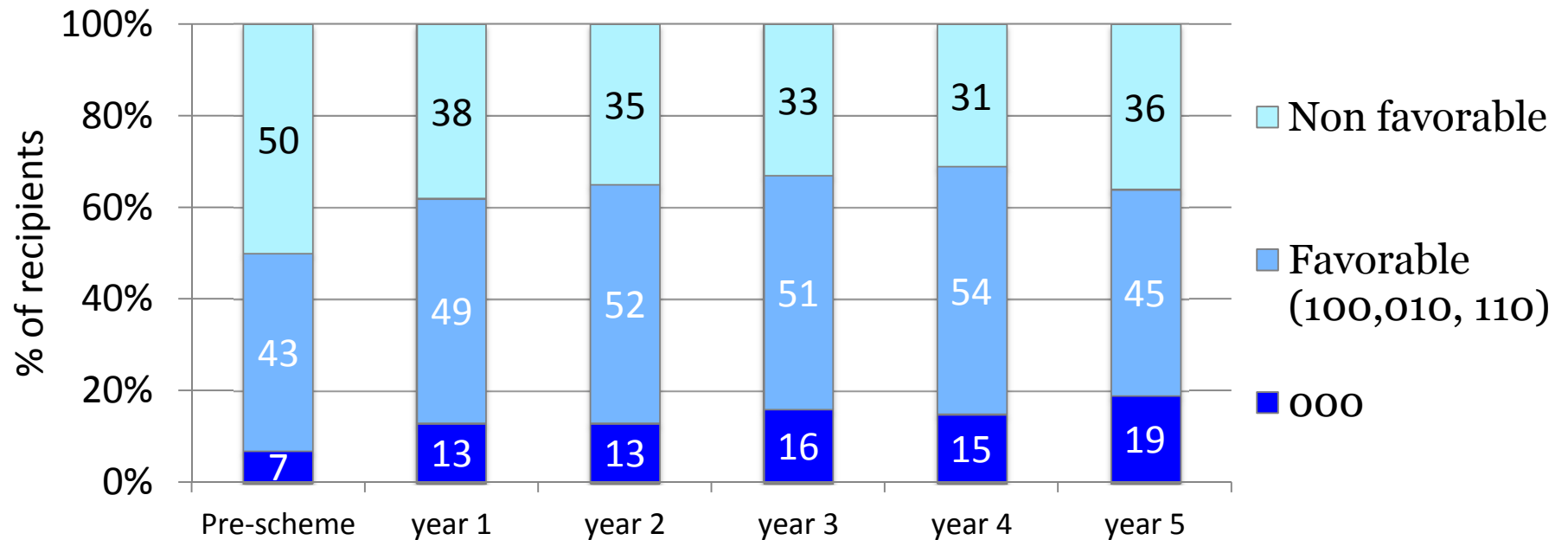


- Favorable mismatch 100, 010, 110
- Both kidneys offered for 000 or favorable
 - One kidney for non-favorable
- Priority
 - Highly sensitised
 - Children
 - Local vs. national patient

Analysis of 6338 Tx in UK, 1986-93

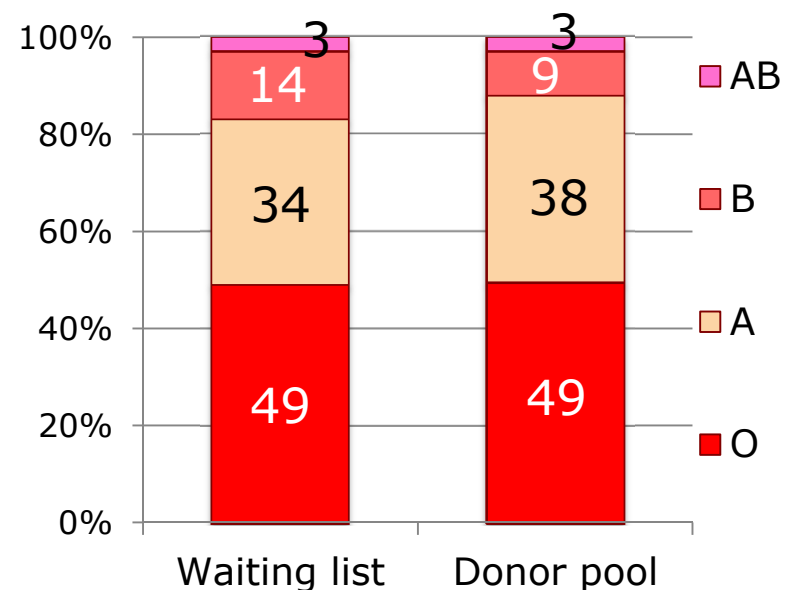
Morris et al. Lancet 1999;354:1147

Effect of favorable offering: better matching

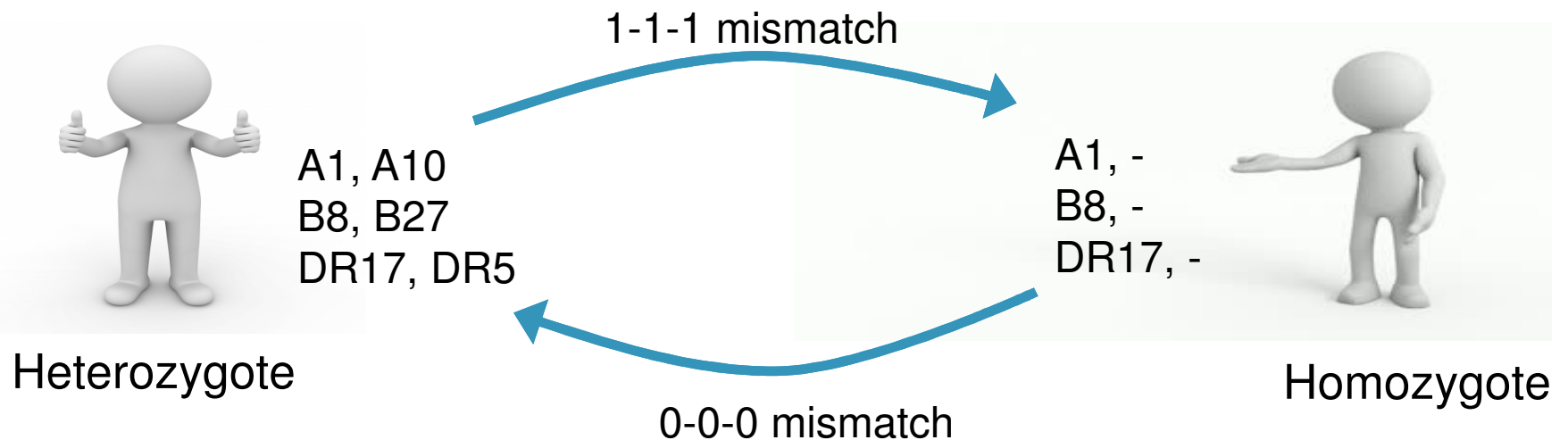


Problems with favorable matching

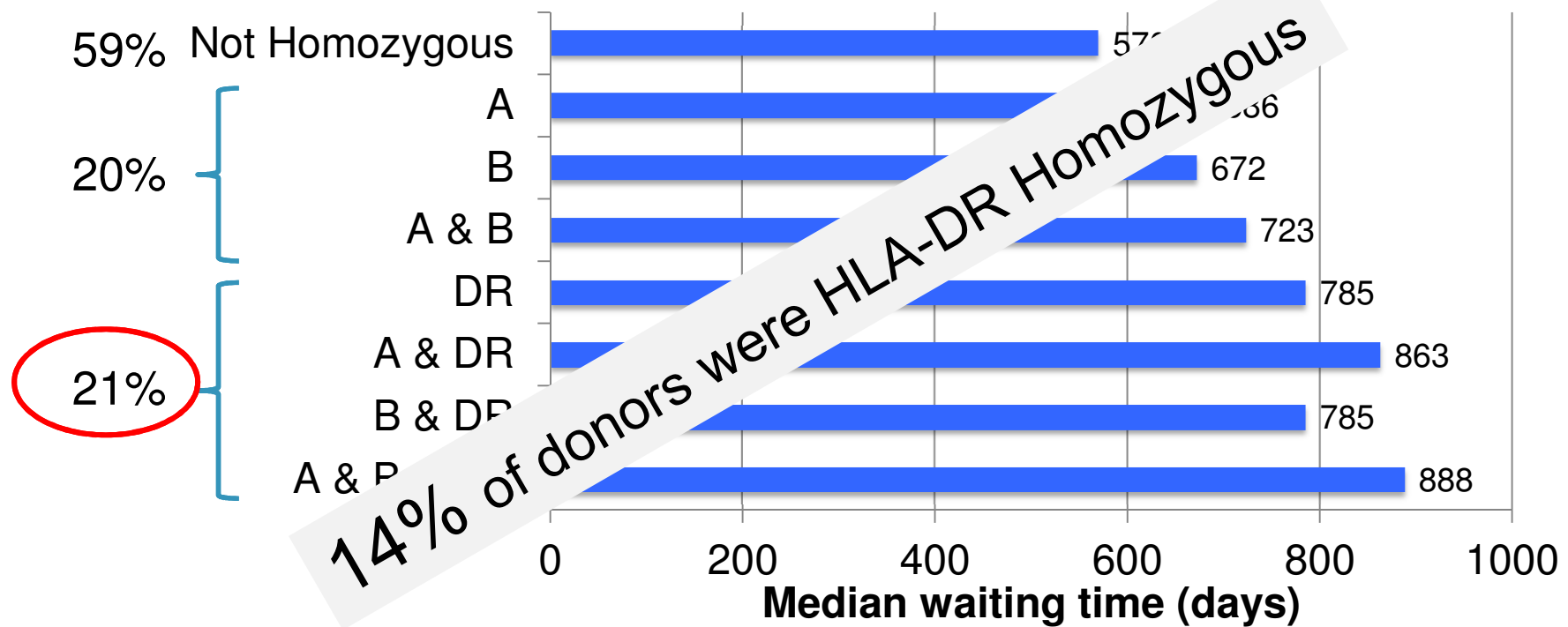
- Blood group B waited longer
 - And so ethnic minorities waited longer
- Bias against HLA DR homozygotes



Minimising HLA-DR mismatches penalises HLA-DR homozygotes



Homozygotes waited longer



2006 scheme aims

- Remove concept of ownership
 - Share both kidneys nationally
- Re-evaluate role of HLA
 - Match younger patients better than older
- Address existing inequalities
 - Long waiting patients
 - Ethnicity / Blood group
 - homozygosity
- Reduce cold ischaemic times



Default rare HLA types to related common type

- Rare HLA types are difficult to transplant
- Rare HLA types defaulted to more common ones based on
 - serological cross reaction
 - Sequence information
- *Consequence*
 - Improved access to first transplant
 - May result in sensitisation and longer wait for subsequent Tx

Rare specificity	Related specificity	% of donor pool
A36, A80	A1	18
A43	A10	4
B53	B5	5
B42, B73, B81	B7	15
B59	B8	13
B82, B83	B12	18
B46	B15	7
B67	B22	2
B47	B27	5
B70, B78	B35	7
B41, B48	B40	7
DR101, DR10	DR1	10
DR9	DR4	20
DR11, DR12	DR5	8

Johnson et al. Transplantation 2010; 89: 387

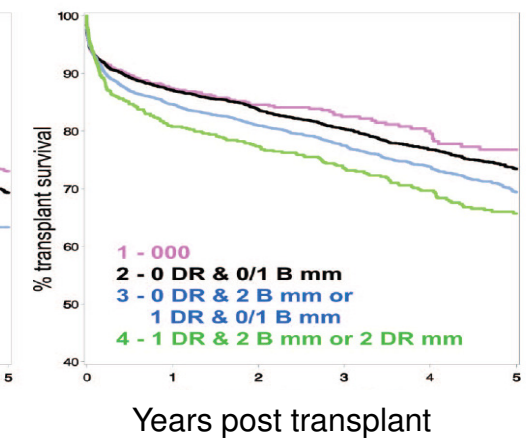
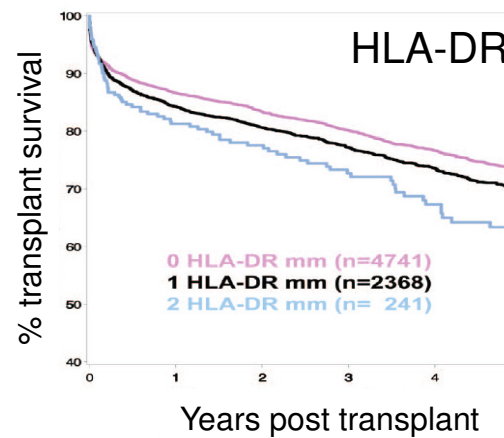
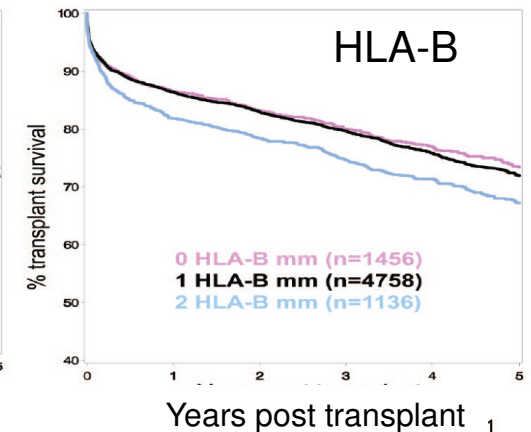
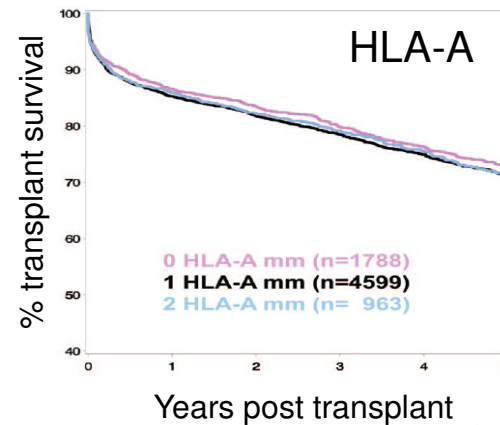
2006 scheme

- Points based scheme
 - Waiting time: 1 point for each day on list
 - HLA mismatch level & recipient age: maximum 3500

HLA mismatch and transplant survival

4 levels of mismatch

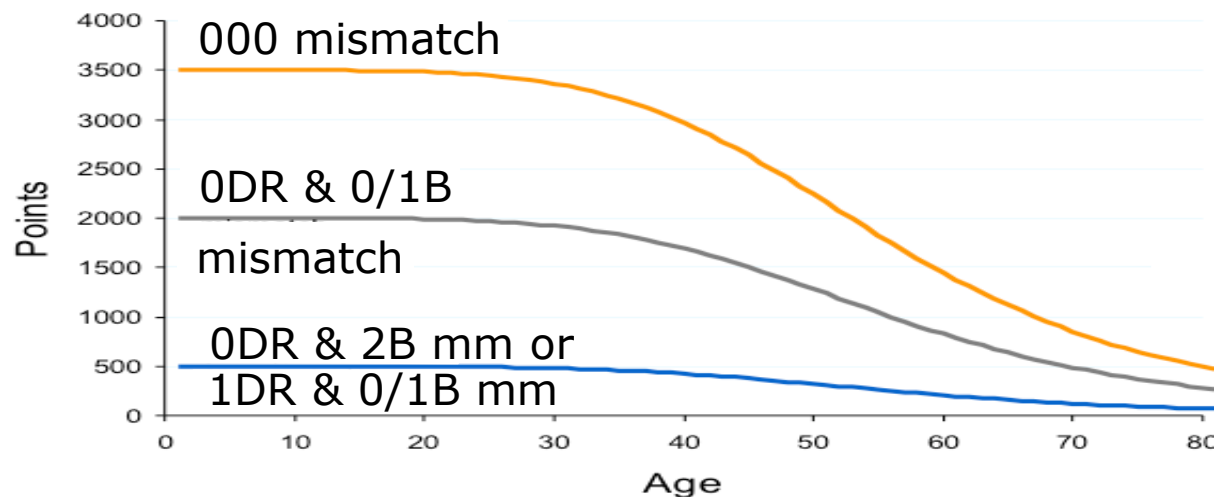
- 000 mismatch
- 0DR & 0/1 B mm
- 0DR & 2B mm
or 1 DR & 0/1 B mm
- Others



Johnson et al. Transplantation 2010; 89: 379

HLA mismatch / age relation

- Part of a points based allocation
- Age & HLA mismatch
 - More points for better matched kidney in young patient

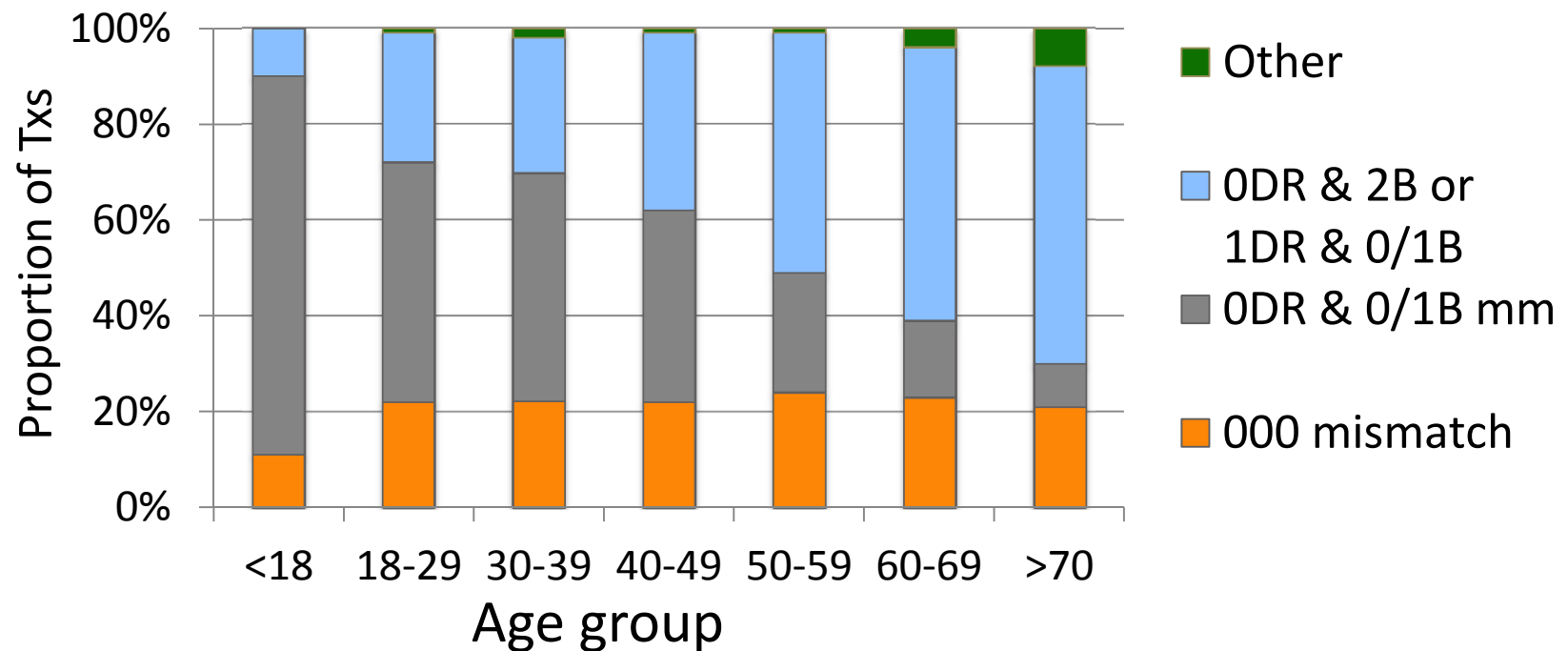


Johnson et al. Transplantation 2010; 89: 379

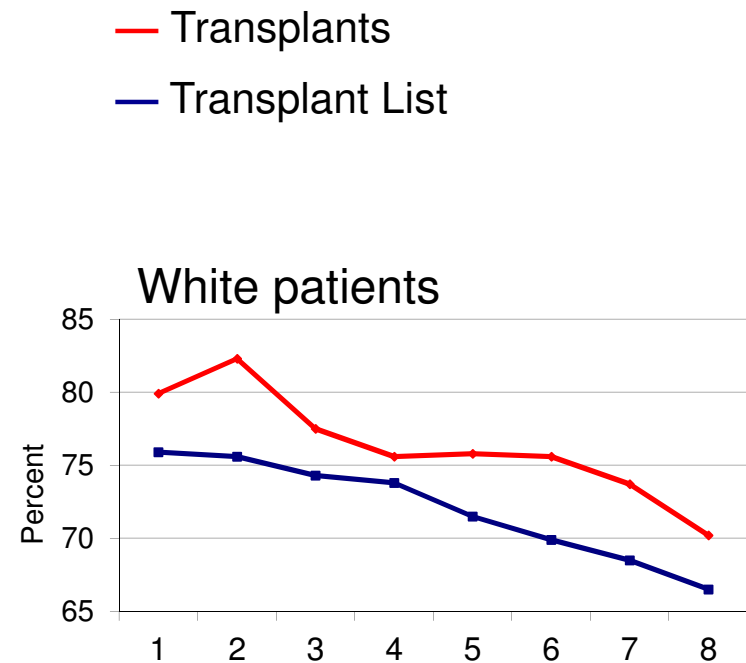
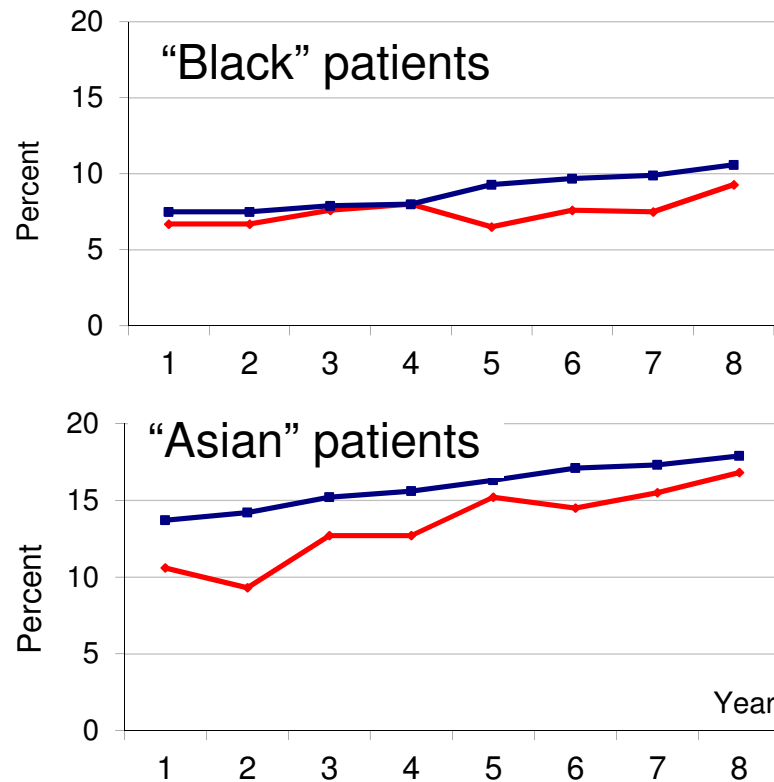
2006 scheme

- Other elements of scheme
 - Donor recipient age difference: $-0.5 \times (\text{don} - \text{recip age})^2$
 - Location of donor (minimise ischaemic time):
 - 900 if same centre (23 centres, 3m population)
 - 750 if same region (3 regions, 20m population)
 - HLA B homozygous: 100
 - HLA DR homozygous: 500

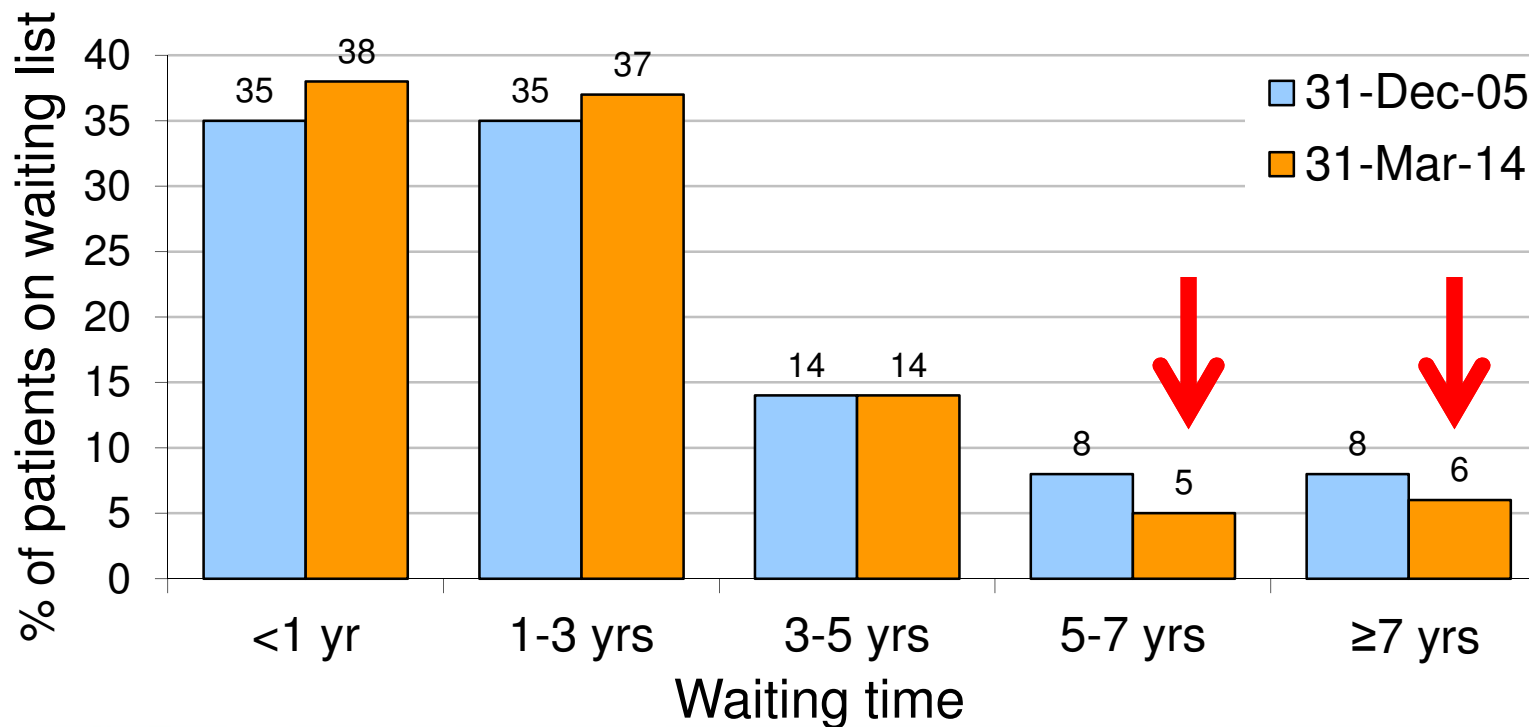
Effect of current scheme on HLA matching by age group



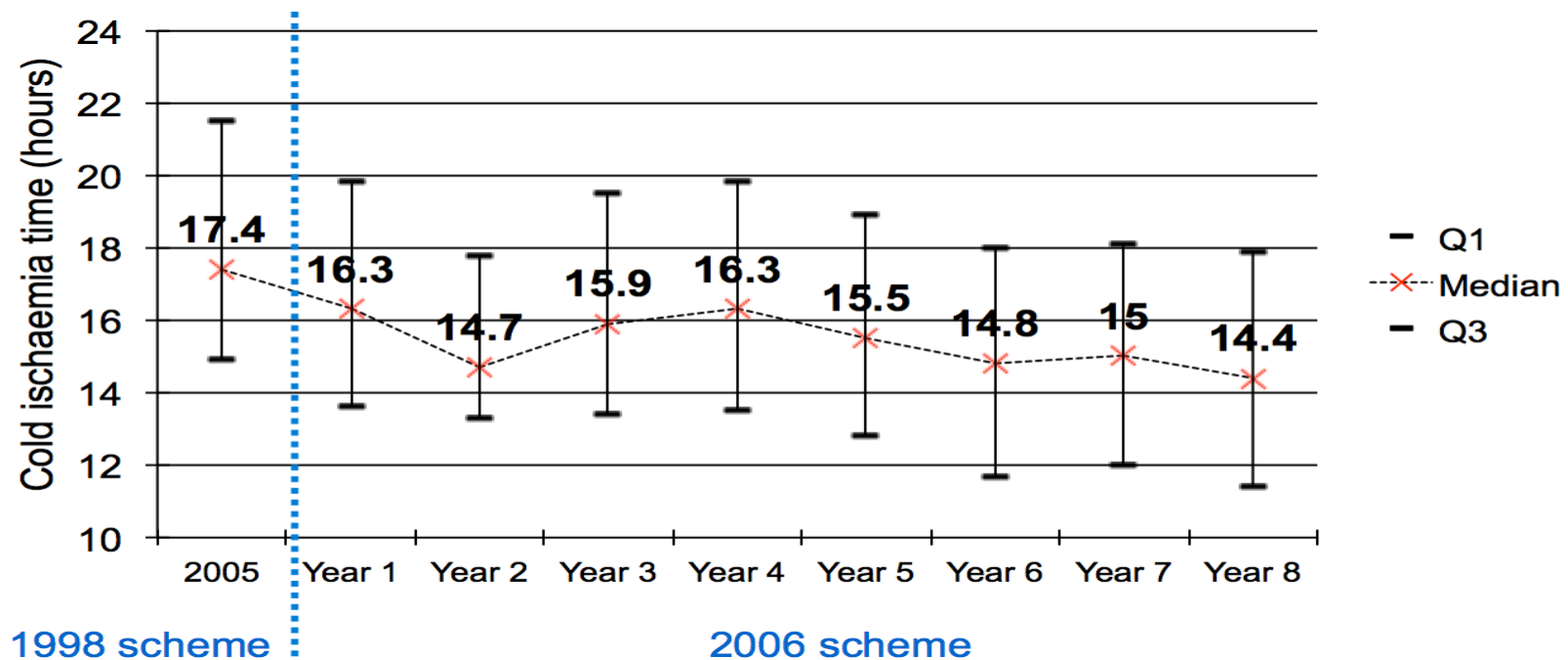
Transplants for ethnic minorities



Reduction in proportion of long waiting patients

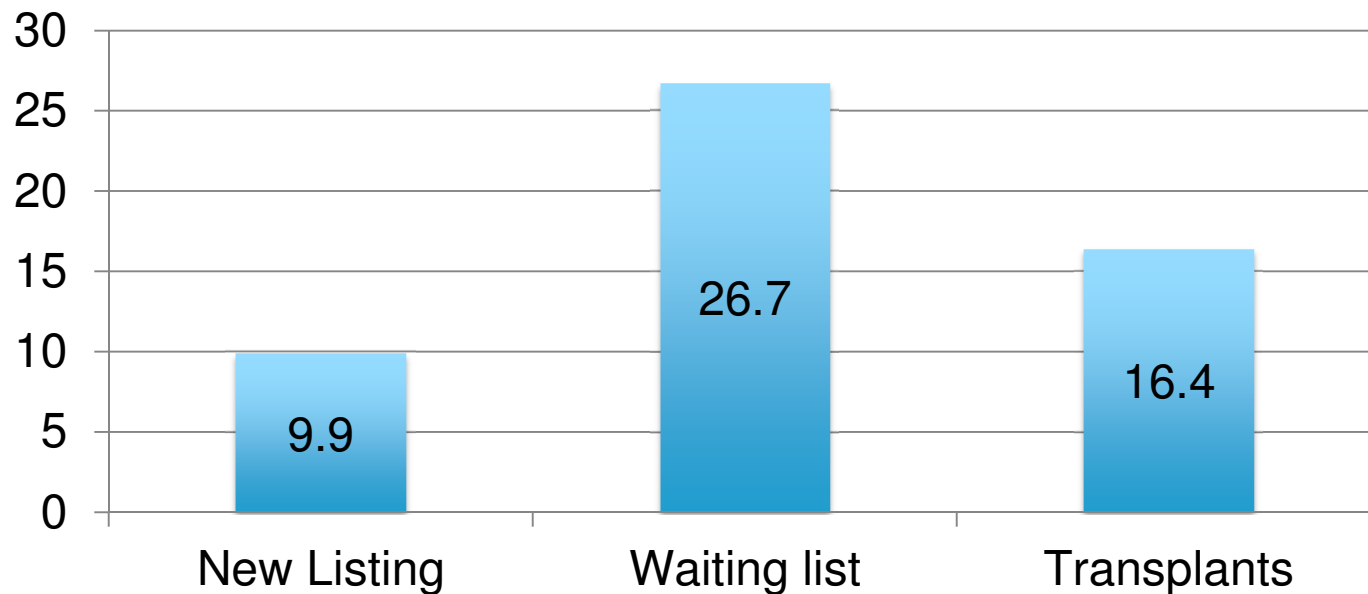


Cold ischaemic times since 2006



Problems with current scheme

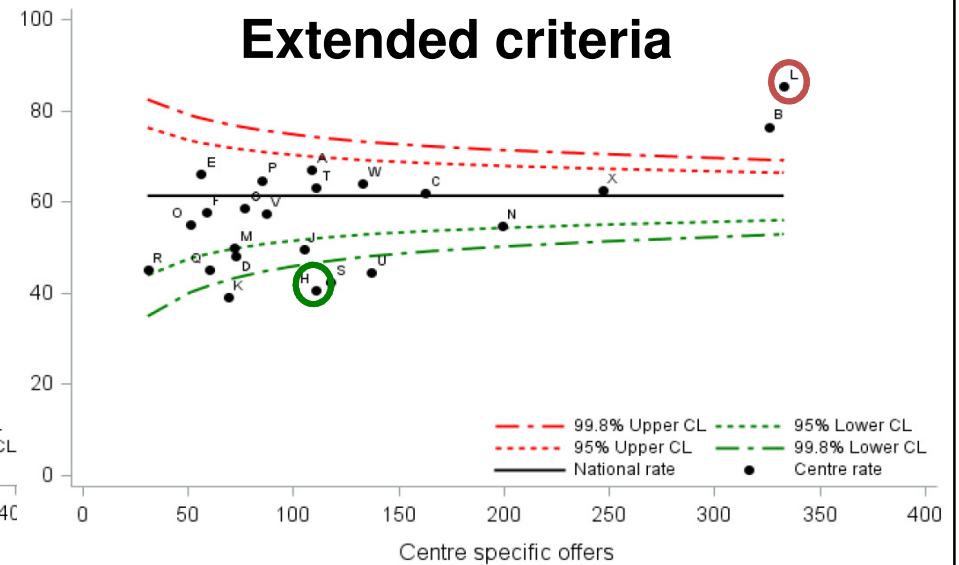
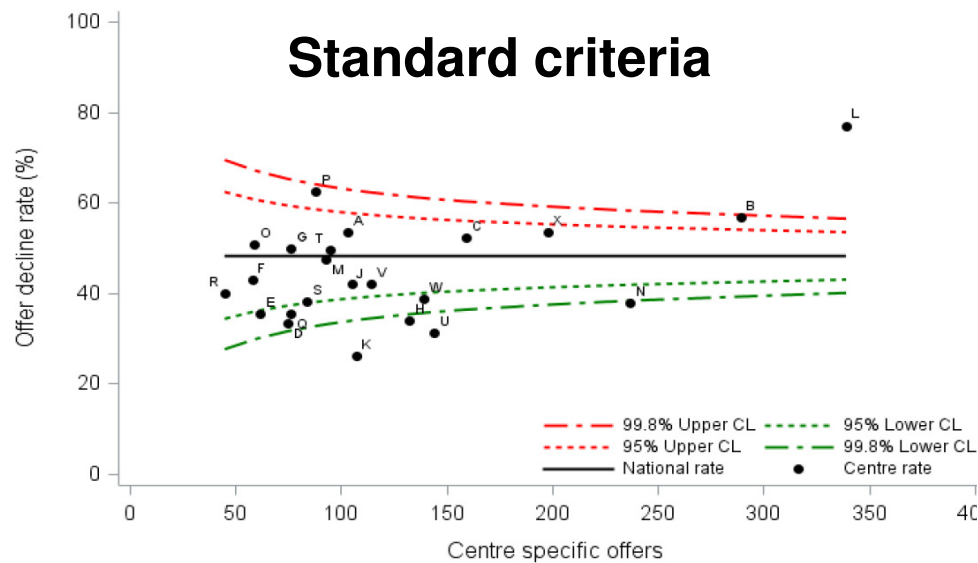
1. Excess of highly sensitised (cPRA* >85%) patients



*cPRA is termed calculated reaction frequency in UK, based on reactivity to 10000 UK donors

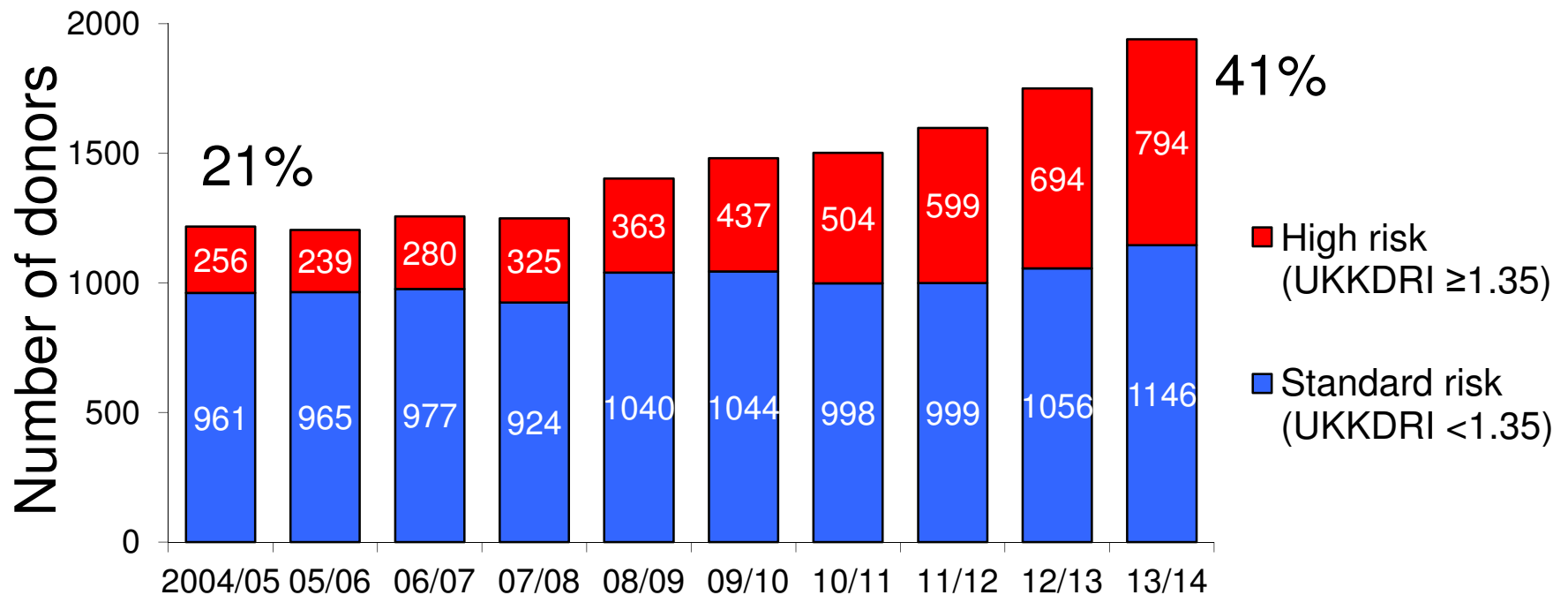
Problems with current scheme

2: Donor & Recipient factors not accounted for



NHSBT Annual Report on Kidney Transplantation 2015.
http://www.odt.nhs.uk/pdf/organ_specific_report_kidney_2015.pdf

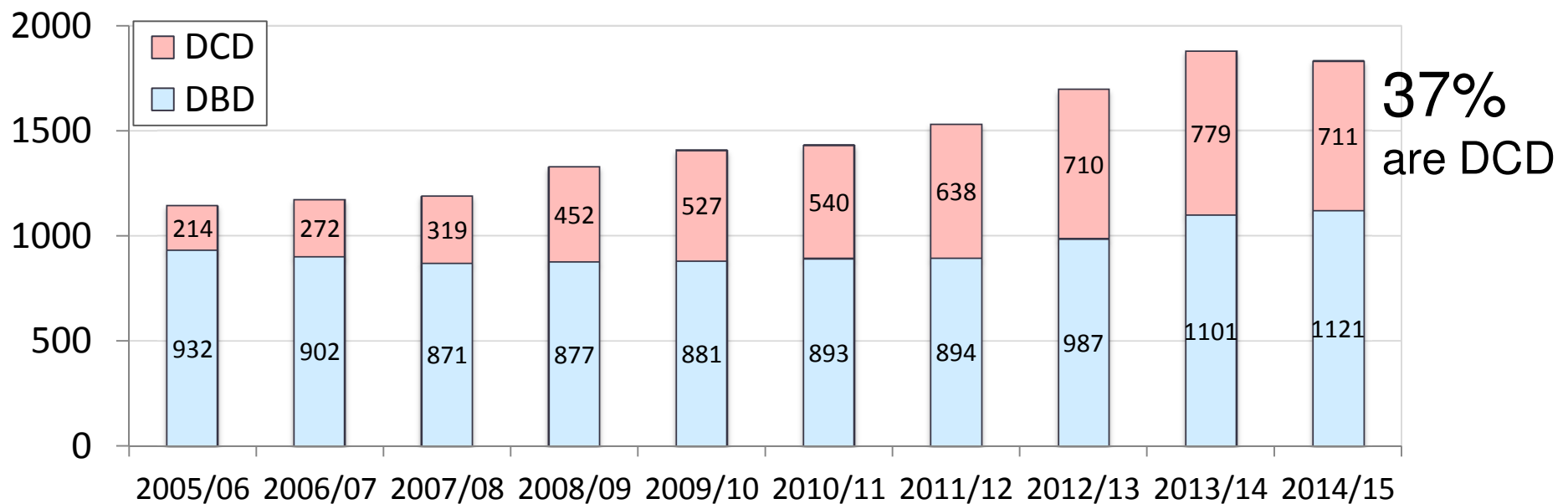
Proportion of “poorer quality” kidneys increasing



UKKDRI: Transplantation 2012; 93: 314. NHSBT data 1 Apr 2004 – 31 Apr 2014, courtesy Rachel Johnson

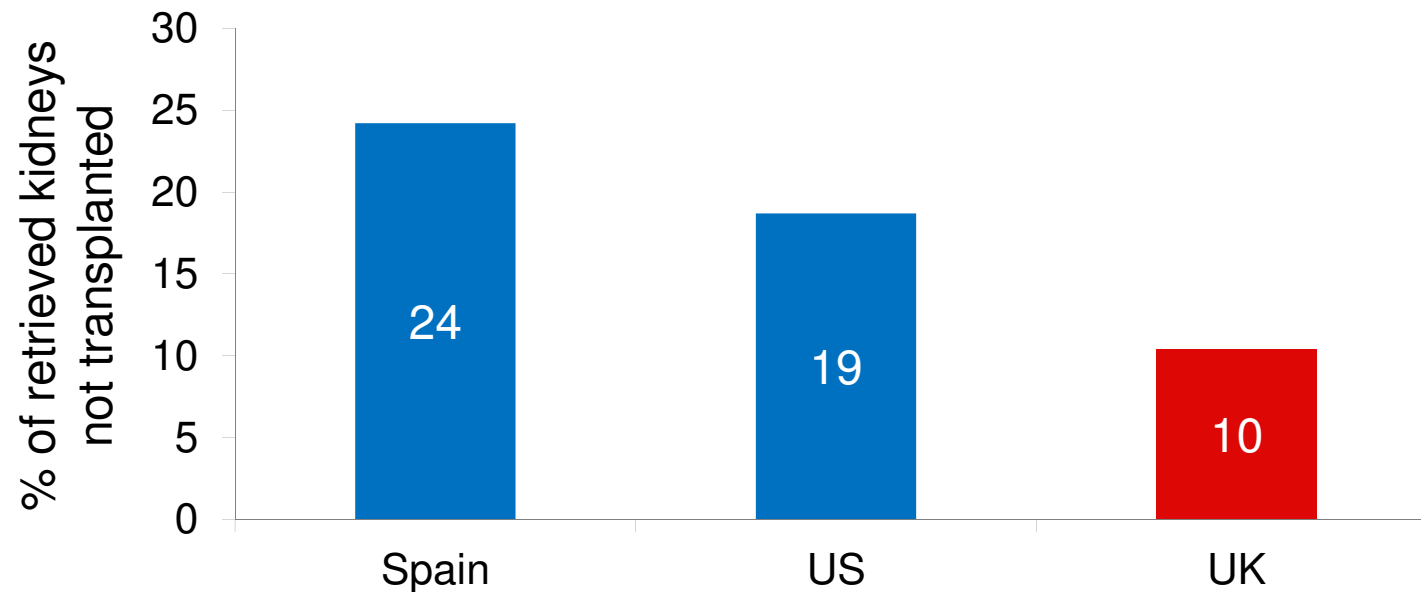
Problems with current scheme:

3: It doesn't integrate DCD kidney offering



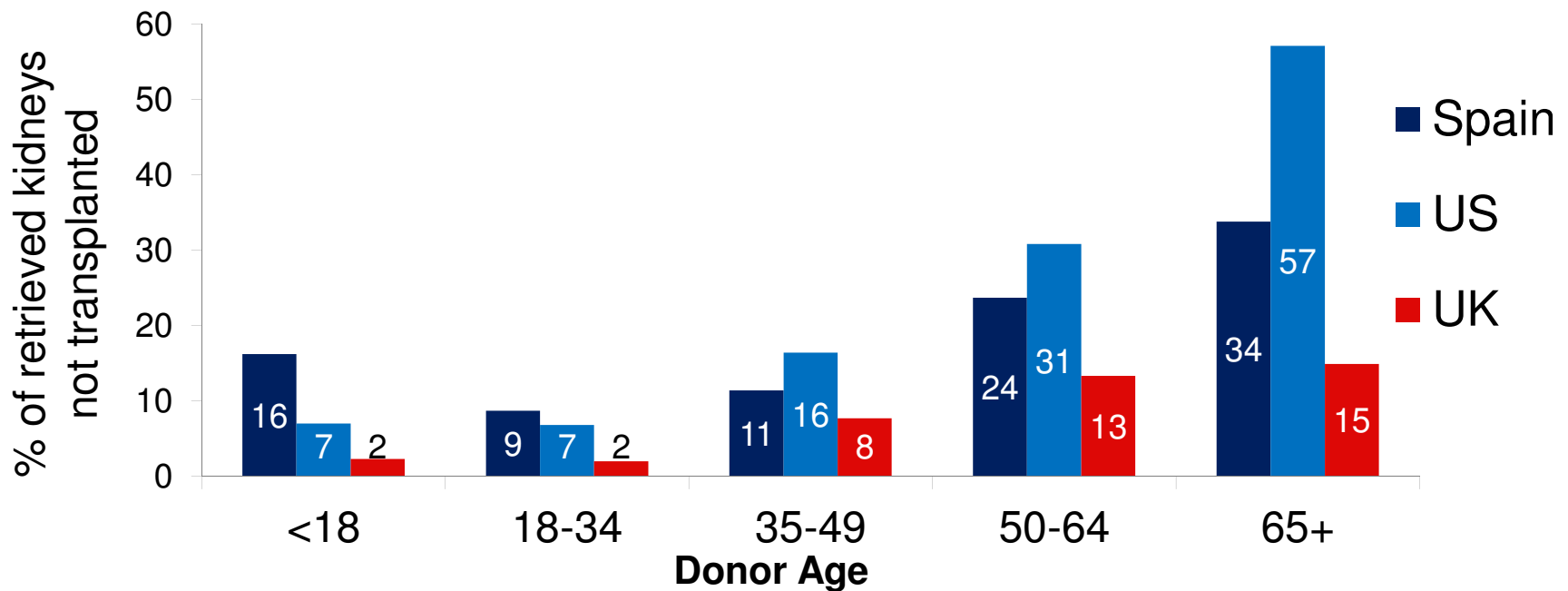
Deceased Kidney Donors in the UK 2005/6 to 2014/15 http://www.odt.nhs.uk/pdf/organ_specific_report_kidney_2015.pdf

Discard rates for kidneys from deceased donors, 2014



Source: ONT – Spain data, OPTN - US data, NHSBT - UK data

Discard rates for kidneys from deceased donors, 2014, by donor age

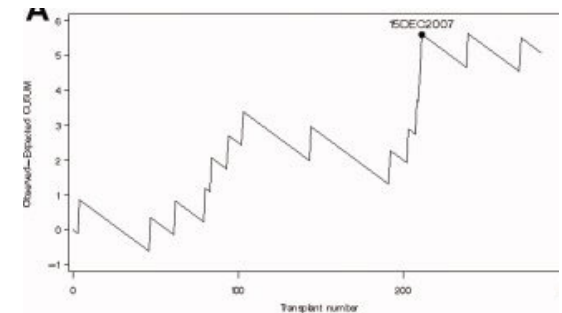


Source: ONT – Spain data, OPTN – US data, NHSBT - UK data

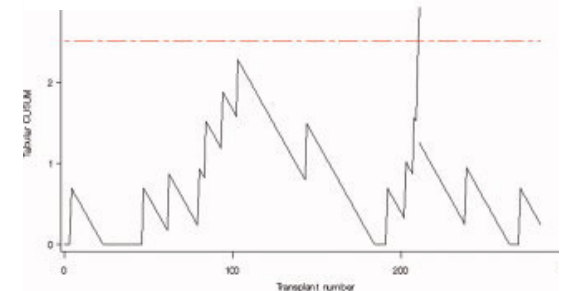
Oversight: CUSUM monitoring

- 3 month reports
- Triggers for graft loss & death
 - Baseline is that center's own past performance
- Letter from NHSBT to explain trigger
 - Response reviewed by
 - NHSBT medical director
 - Kidney committee chair
 - NHS Commissioner

O-E chart



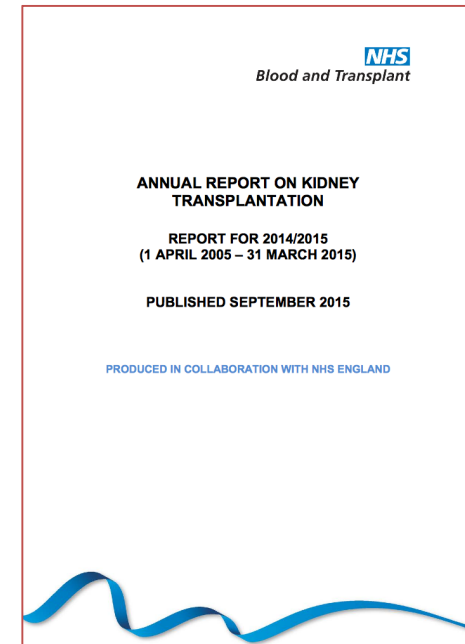
Tabular CUSUM



Liver Transplantation 2010;16:1119

Oversight: Publication of center specific data

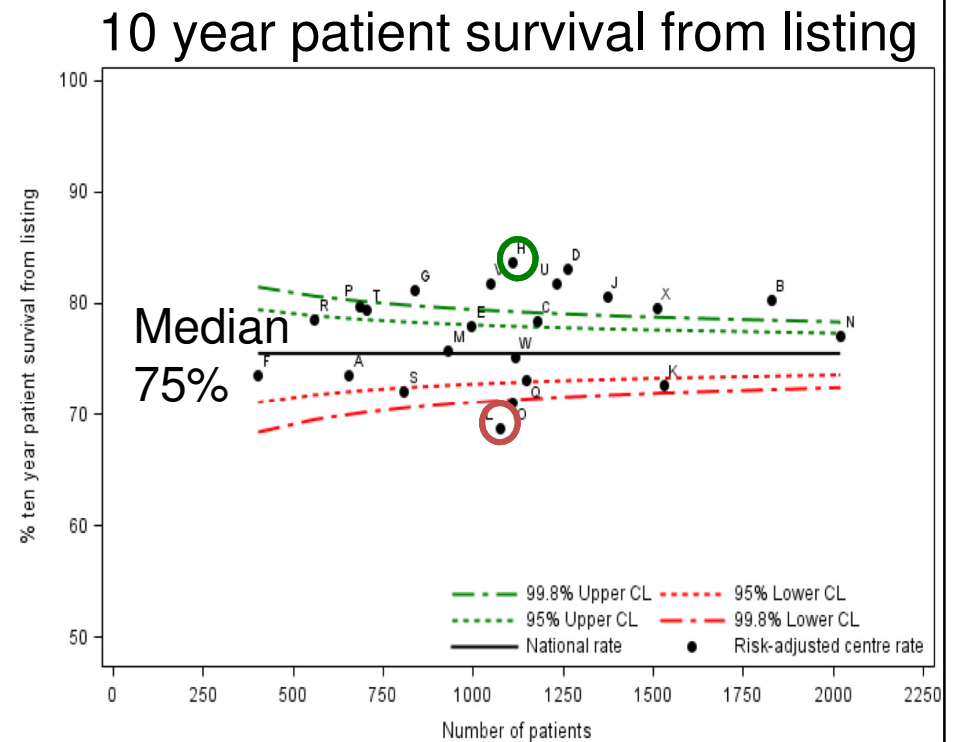
- Waiting list
 - Demographics
 - Waiting time
 - Pre-emptive listing rate
- Transplants
 - Demographics (DRI; DCD/DBD; LD)
 - Cold ischaemic time
 - Graft and patient survival



<http://www.odt.nhs.uk/uk-transplant-registry/organ-specific-reports/>

Survival from listing

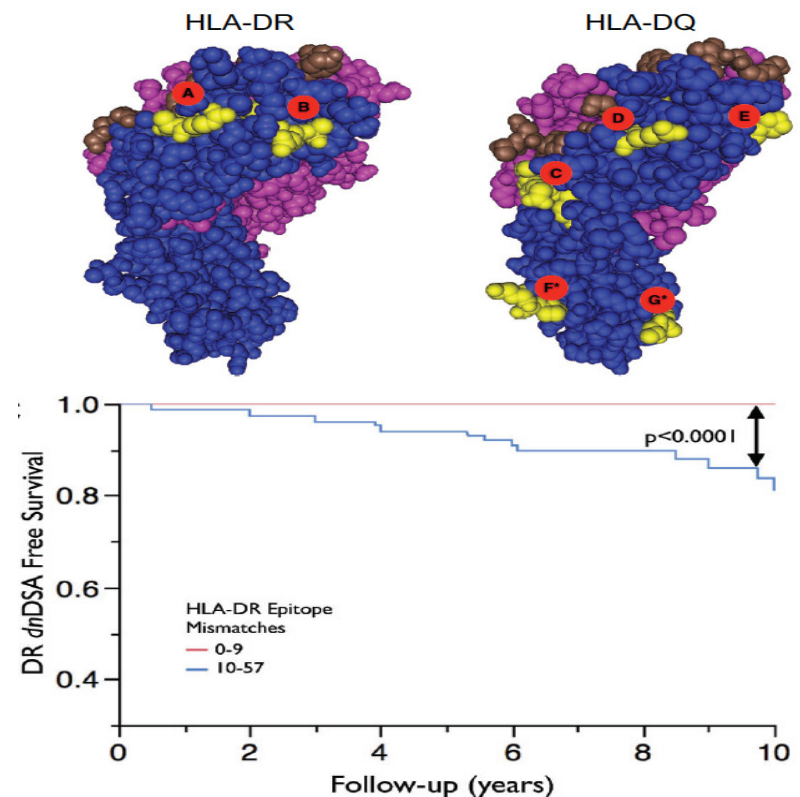
- 5 year patient survival
 - From listing: 87% (84 – 92%)
 - From transplant: 89% (81 – 95%)





The future: beyond HLA matching

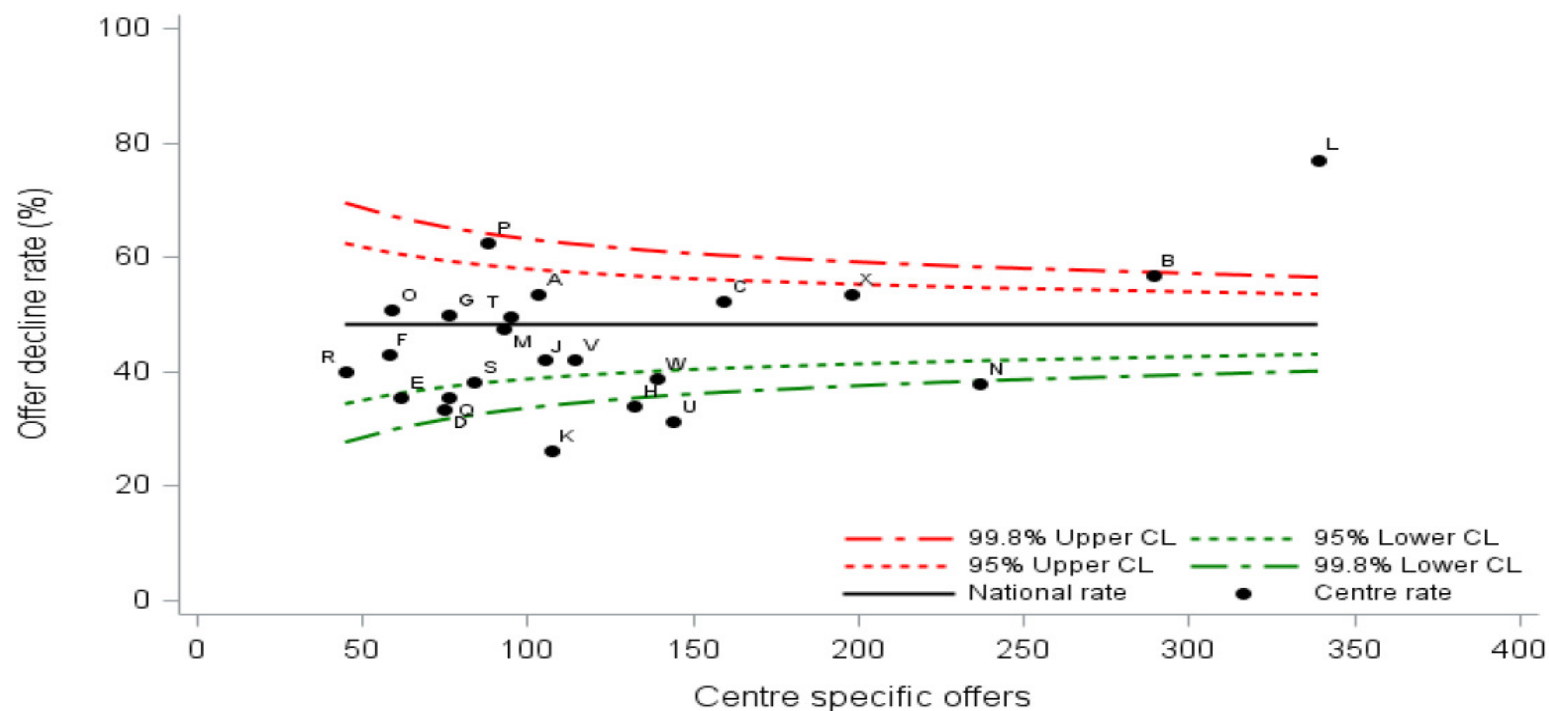
- Reduce sensitisation by improved matching
- HLA epitope
 - Not whole antigen
- Electrostatic charge minimisation



AJT 2013; 13: 3114
Hum Immunol 2011;72:1049

Future: Reduce offer decline rate

Each offer should be the best offer for that patient



ATTOM study

- **A**ccess to renal **T**ransplantation and **T**ransplant **O**utcome **M**easures study
- **S**ample (n=6862):
 - All incident dialysis patients in the UK in a year
 - All new kidney & Kidney/pancreas transplants
 - Plus matched controls

ATTOM Analyses

- Quality of life and quality of health
 - Including in depth interviews with subset
- Clinical data on co-morbidity
 - e.g. cardiac status
- Survival
- Health economics
- Analysis of unit differences in protocols and practice

The future: smarter offering

Recipient factors

- Age
 - Child vs. old adult
- Life expectancy
 - On dialysis
 - Post transplant
- Waiting time
 - From dialysis start
- Sensitization
- Quality of life

Donor factors

- DBD and DCD
- Ischaemic time
- Tissue matching
 - HLA / Epitope / electrostatic
- Donor kidney quality
 - e.g. KDPI
- Donor disease risk
- Others, e.g. cost effectiveness

Summary

UK allocation schemes have been developed using evidence-based modeling.

- evolved from simply matching for HLA
- Take some recipient & donor factors into account
- evolved from offering one kidney for a beneficial match, to both kidneys going into the national pool
- All schemes have losers and winners.
 - regular review and adjustment has been necessary to ensure fairness.
- The next scheme will further personalize offering.