Anti-A and Anti-B Titrations Pilot EQA Scheme

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Anti-A and Anti-B Titrations

Are used in clinical decision making

In ABO incompatible solid organ transplantation

In ABO mismatched stem cell transplantation

In ABO HDN

So it is important to get an accurate result

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Why do we need EQA for anti-A and anti-B titrations?

- To look at reliability and accuracy of tests that are used in clinical decision making
- To reinforce published guidance, where it exists
- To develop standard laboratory methodology to support developing clinical practice
- To work with clinicians using the results of antibody titrations
  - Relate titrations to outcomes
  - Understand need for therapeutic interventions based on titrations

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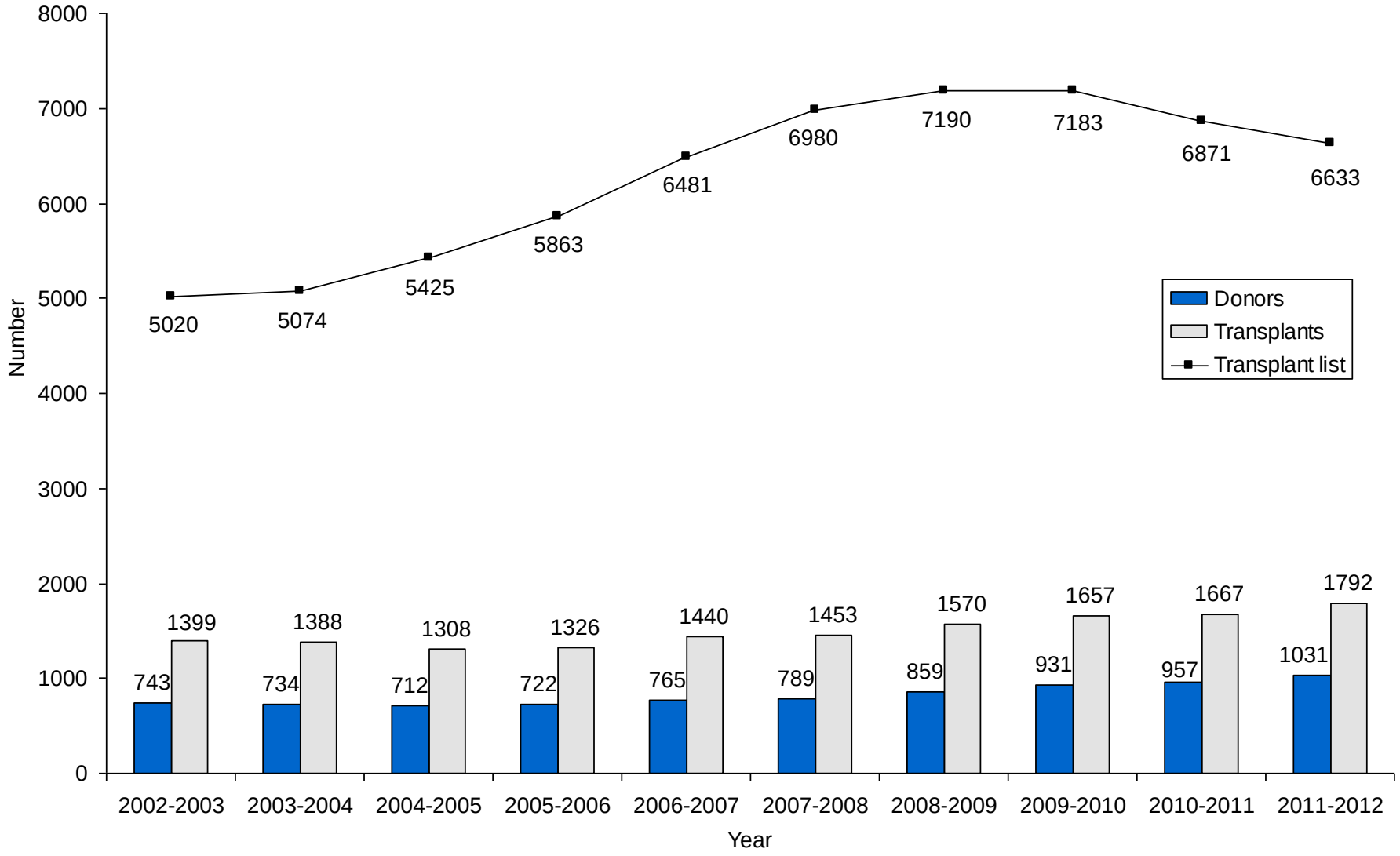
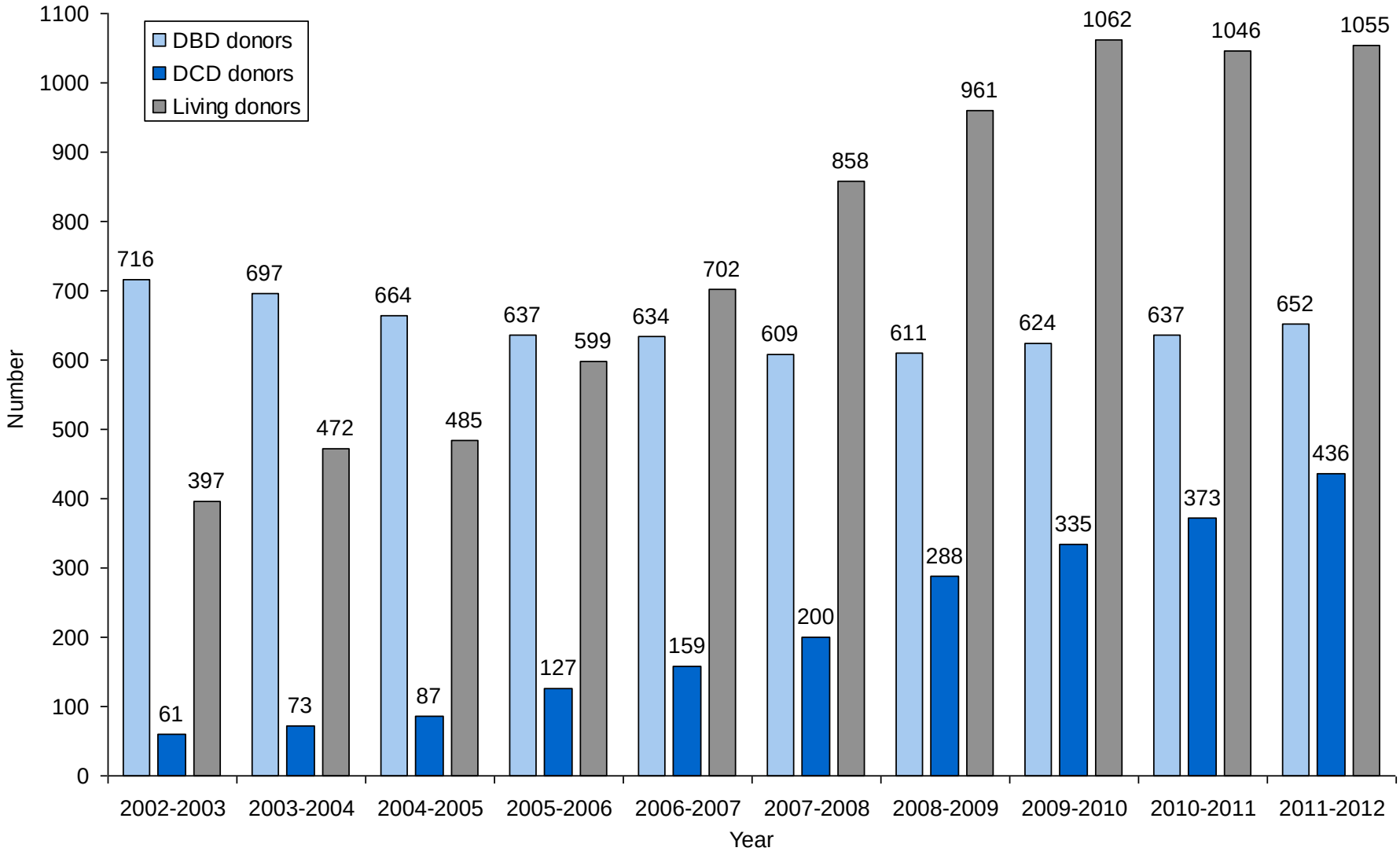
Deceased donor kidney programme in the UK, 1 April 2002 - 31 March 2012
Number of donors, transplants and patients on the active transplant list at 31 March



Source: Transplant activity in the UK, 2011-2012, NHS Blood and Transplant

Number of deceased and living donors in the UK, 1 April 2002 - 31 March 2012



Source: Transplant activity in the UK, 2011-2012, NHS Blood and Transplant

Anti-A and anti-B titrations

Are used at critical stages of the preparation for transplant

1. If titres to the donor RBCs are too high, can't go on ABOi transplant list **(e.g. >256)**
2. The recipient is given rituximab (anti-CD20) to suppress antibodies at d-30 and at time of transplant **(e.g. <32)**
3. The recipient has alternate daily plasma exchange/immunoabsorption from d-10 to d+2 and titres are monitored **(e.g.<4)**

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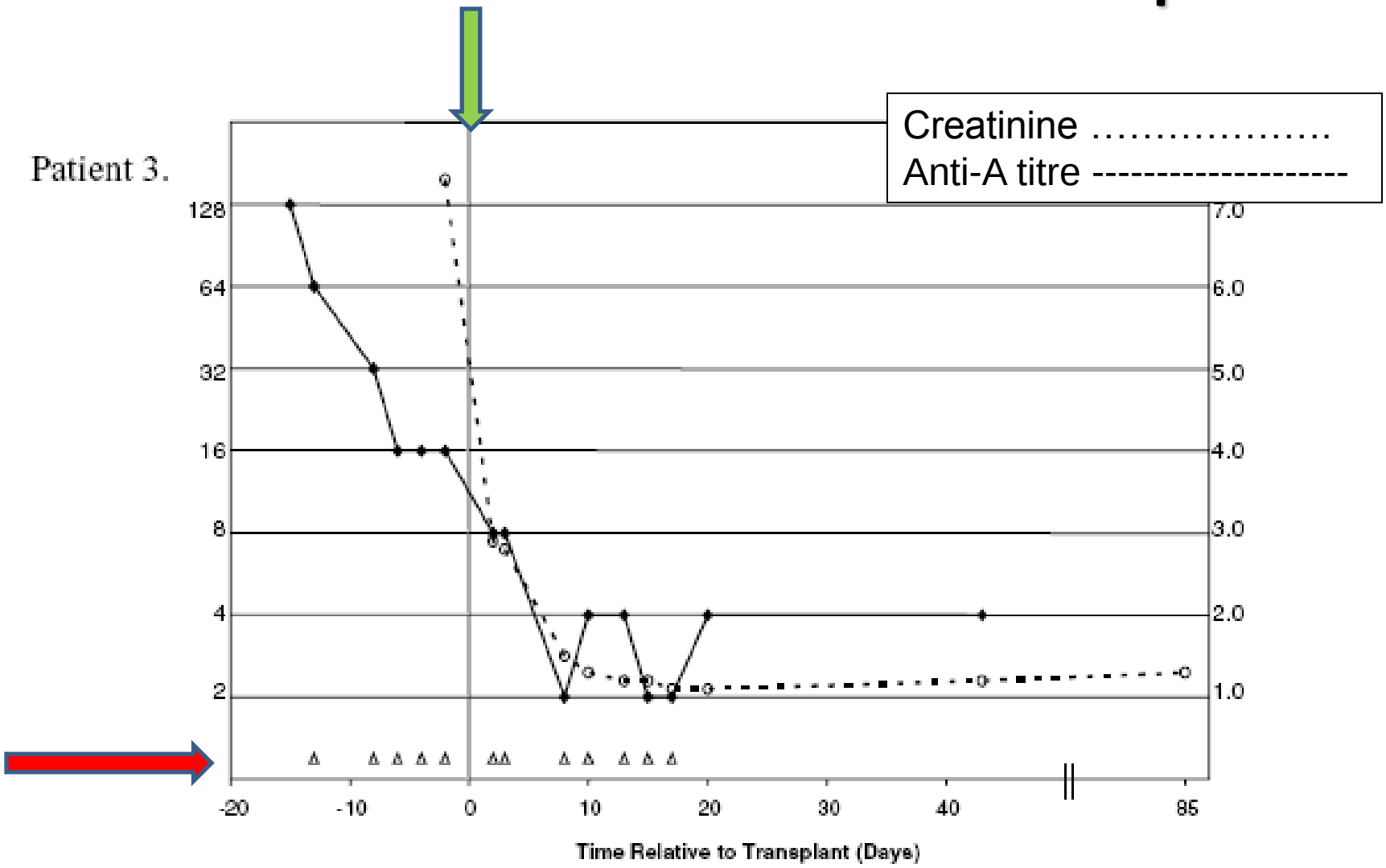
Serial anti-A titres in ABOi renal transplant



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UK NEQAS exploratory pilot

May 2009

Questions to be addressed;

- Was there a need for EQA?
- Was there variability in practice?

Recruited 52 participants from 15 countries via BTLP and H&I schemes; 26 UK, 26 non-UK

Reasons for titrating anti-A and anti-B

- **20 ABOi renal transplant**
- 13 BMT / HSCT
- 11 ABO HDN
- 5 Others

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Material

- Group O donor plasma (filtered FFP)
- Titrate anti-A and anti-B
  - Routine method
  - A_1 rr and B rr red cells provided
- On line questionnaire for methodology and protocols

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Anti-A and anti-B titrations

- No standard method

- Measurement of IgG, IgM or both?
  - IAT measures all of the antibody
  - DRT measures IgM but may pick up some IgG
  - Can treat plasma (DTT) to remove IgM before titrating by IAT

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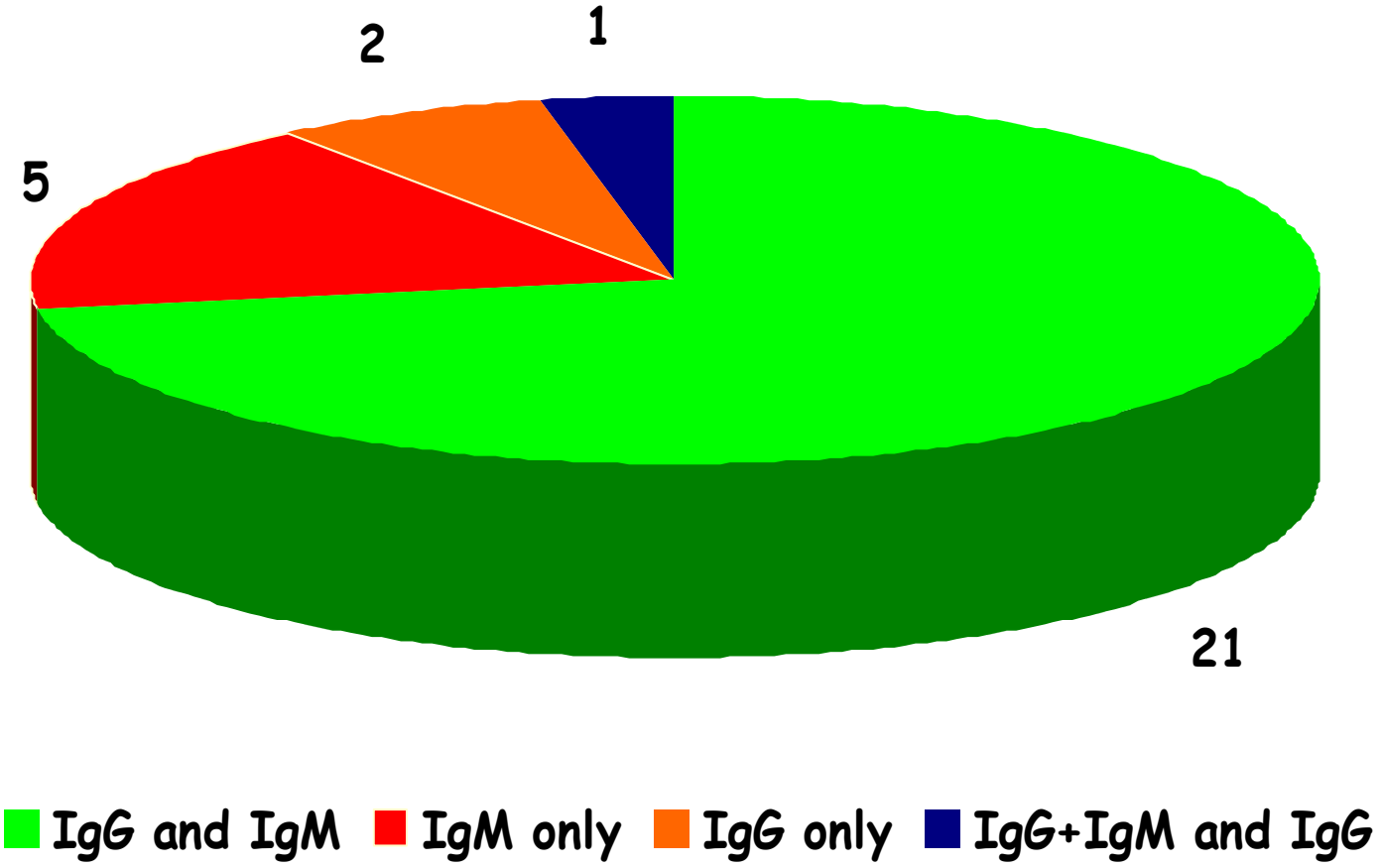
Reporting titration results to the clinicians



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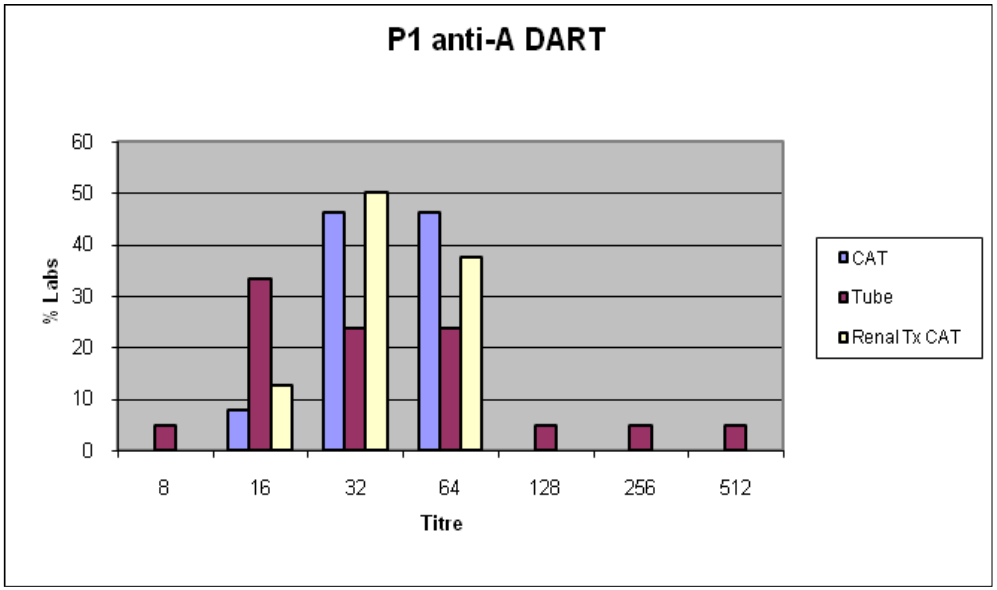
Results show considerable variation



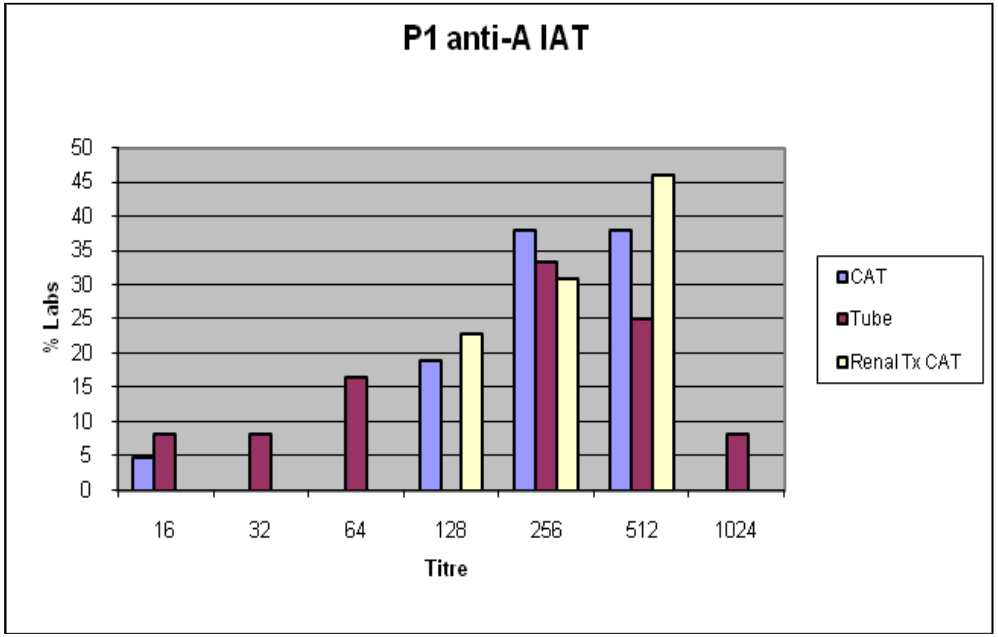
Overall median: **32**

CAT : median 32,

range 16-64

Tube: median 32,

range 8-512



Overall median: **256**

CAT: median 256,

range 16-512

Tube: median 256,

range 16-1024

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EQA Pre-Pilot for anti-A and anti-B titrations

- Preliminary results presented at **ISBT** and **BSHI**
- **UK NEQAS Scientific Advisory Group**
- Labs undertaking titrations for ABOi renal transplantation only
- Standard technique developed with **SAG** and **NHSBT**
  - based on DiaMed
  - IAT and DRT versions
  - Reporting all reaction grades throughout titre

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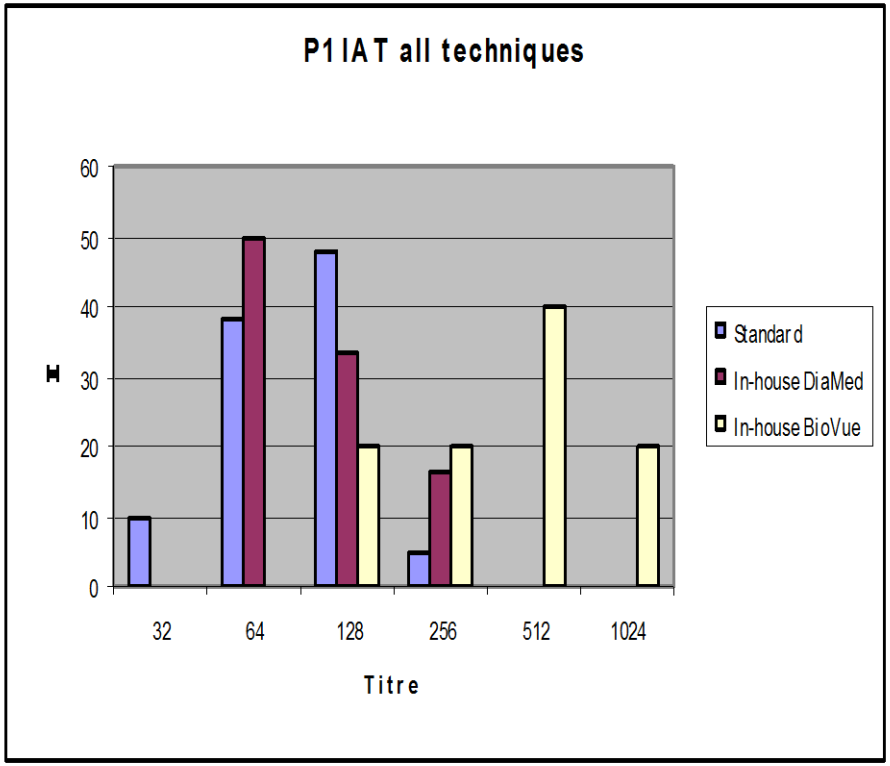
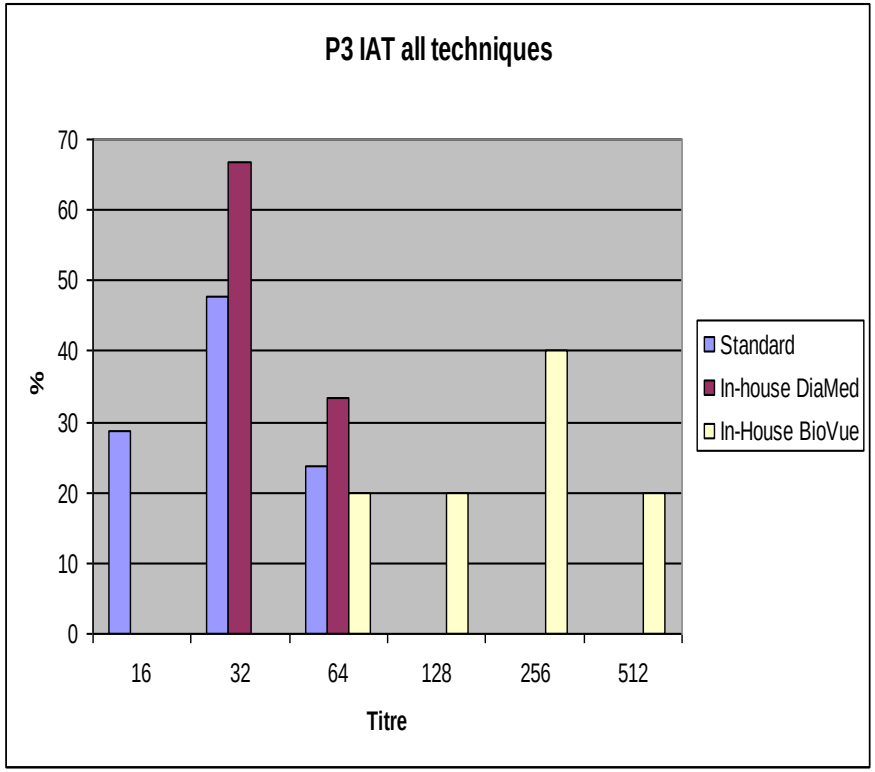
IAT results for P1 and P3





Results in normal distribution

BioVue higher method median than DiaMed

Standard method no better

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Reproducibility; P1 and P4

Number recording one tube difference between P1 & P4 (same pool)				
Technique	**1 tube difference**	**DiaMed**	**BioVue**	**Tube**
Standard DRT (n=18)	**4 (22%)**	**4/18**		
In-house DRT (n=24)	**7 (29%)**	**3/10**	**0/4**	**4/10**
Standard IAT (n=21)	**8 (38%)**	**8/21**		
In-house IAT (n=12)	**2 (17%)**	**2/6**	**0/5**	**0/1**
Treated plasma (n=6)	**4 (67%)**	**1/2**	**1/1**	**2/3**

Treated plasma - poor reproducibility

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Progress with EQA

- One exploratory pilot May ’09
- Three pre-pilot exercises in December ‘10, March and August ’11
- Pilot EQA Scheme 2012; 4 exercises/year, open to all UK and overseas labs (69 registered)

…….Similar results

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But we can't explain the variability

Other things to consider

- Method of preparing the dilutions
- RBC:plasma ratios
- Diluent ?
- Cards – IgG or polyspecific?
- End point detection - weak or 1+?
- Anything else??

Will knowledge of variability and inter-laboratory comparison improve the quality of the testing?

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Next steps

- How do titres correlate with clinical outcomes for ABOi renal transplant?
- Are patients:
  - at risk of hyperacute rejection?
  - over plasmapheresed?
  - denied access ABOi donor programs?
- How to proceed with EQA?
- Can more accurate methods be developed?

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UK Transplant

Stated aim to increase transplantation by 50%

Patients with high titre antibodies are a particularly difficult group

- Anti-A and/or anti-B in ABOi renal transplant
- HLA- antibodies in renal transplant

Strategy group to improve outcomes

Have accepted need to standardise methodology for antibody measurements

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ABOUT-K Study

- Based in Birmingham
- Looking at outcomes of ABOi renal transplants compared to
  - Antibody reduction methods
  - Titrations (IgG and IgM) performed by standard methodology
- Proposal that the UKT Registry should include this data for future analysis

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NHSBT Appropriate Use of Blood Group

Subgroup looking at support of renal patients

- Red cell support in chronic kidney disease
- Blood product/component replacement before, during and after renal transplant
  - FFP or albumin as replacement during antibody reduction by plasma exchange?
  - What effect does the choice of replacement fluid have on bleeding, transfusion reactions, infection as well as graft rejection

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Working Together

- UK NEQAS SAG (chair: Fiona Regan)
- NHSBT
  - AUBG Renal SubGroup
  - RCI and H&I laboratories
- UK Transplant
  - High titre antibodies strategy group
  - Renal transplant registry
- Transplant physicians, surgeons and nurses

OUR PARTICIPATING LABORATORIES!

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AboutK Study

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