Have we learned from our mistakes in pancreas transplantation?

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UNIVERSITY OF CAMBRIDGE

Learning from mistakes

The Pancreas Forum

- A forum for learning from the mistakes of others
  - And their good practice
- Annual meeting, now in its 14th year

National Pancreas Transplant Forum 2018

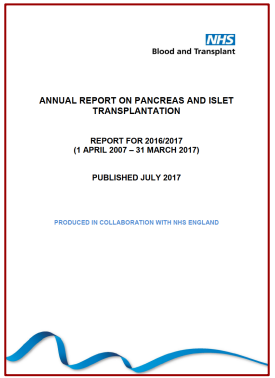
Venue: Radisson Blu Hotel, Cardiff CF10 3PL
Date: 2nd February 2018

PROGRAMME

9:00	Welcome
9:15	NHSBT Annual Pancreas and Islet Transplant Report 2016/17 *Claire Counter*
9:45	National Data on the impact of pancreas quality and retrieval logistics on the transplant outcome *Claire Counter*
10:00	Pancreas Discard Rate in UK – Are we all saying the same thing? *Sarina Comatsaru (Edinburgh)*
10:30	Discussion
10:45- 11:00	Coffee/Tea Break
11:00	Trends in pancreas transplantation – USA *Raja Kandaswamy (USA)*
11:40	Trends in pancreas transplantation – UK *Angelis Andreakis (Cardiff)*
12:00	Discussion
12:30	Lunch
13:30	Pancreas Transplantation in Type 2 DM *Sanjay Sinha (Oxford)* *Raja Kandaswamy (USA)*
14:15	Update on Immunotherapy Trials on Type 1 DM *Colin Dayan (Cardiff)*
14:45	Discussion
15:00-15:15	Coffee/Tea Break
15:15-16:15	Case presentations Cambridge, Edinburgh, Guys, Hammersmith, Manchester, Newcastle, Oxford, Cardiff

Annual Report on Pancreas transplantation

- Benchmarking centres against their peers
- Providing data for patients



NHS
Blood and Transplant

ANNUAL REPORT ON PANCREAS AND ISLET TRANSPLANTATION

REPORT FOR 2016/2017
(1 APRIL 2007 – 31 MARCH 2017)

PUBLISHED JULY 2017

PRODUCED IN COLLABORATION WITH NHS ENGLAND

Acknowledgements

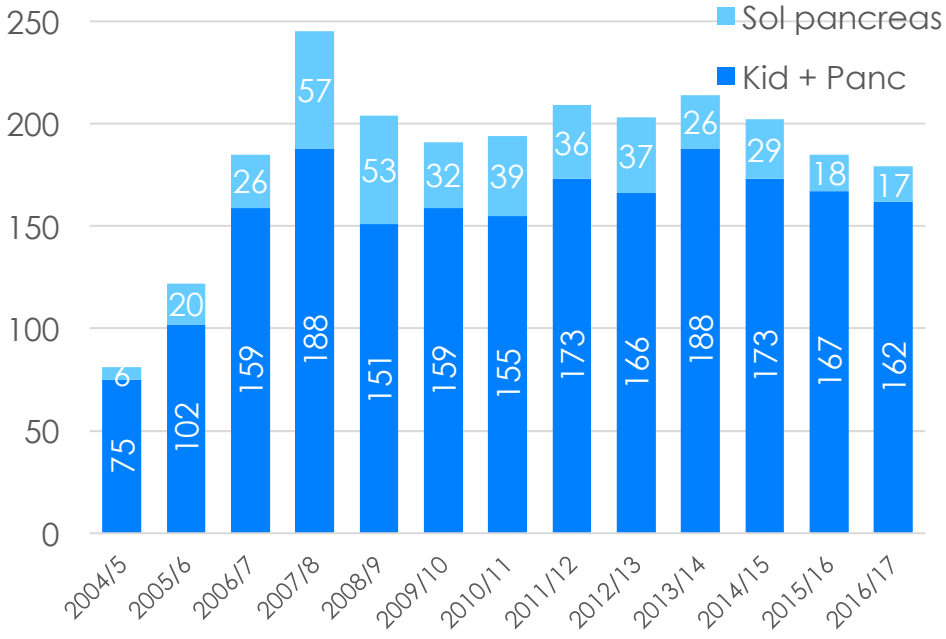
- Claire Counter

Mistakes?

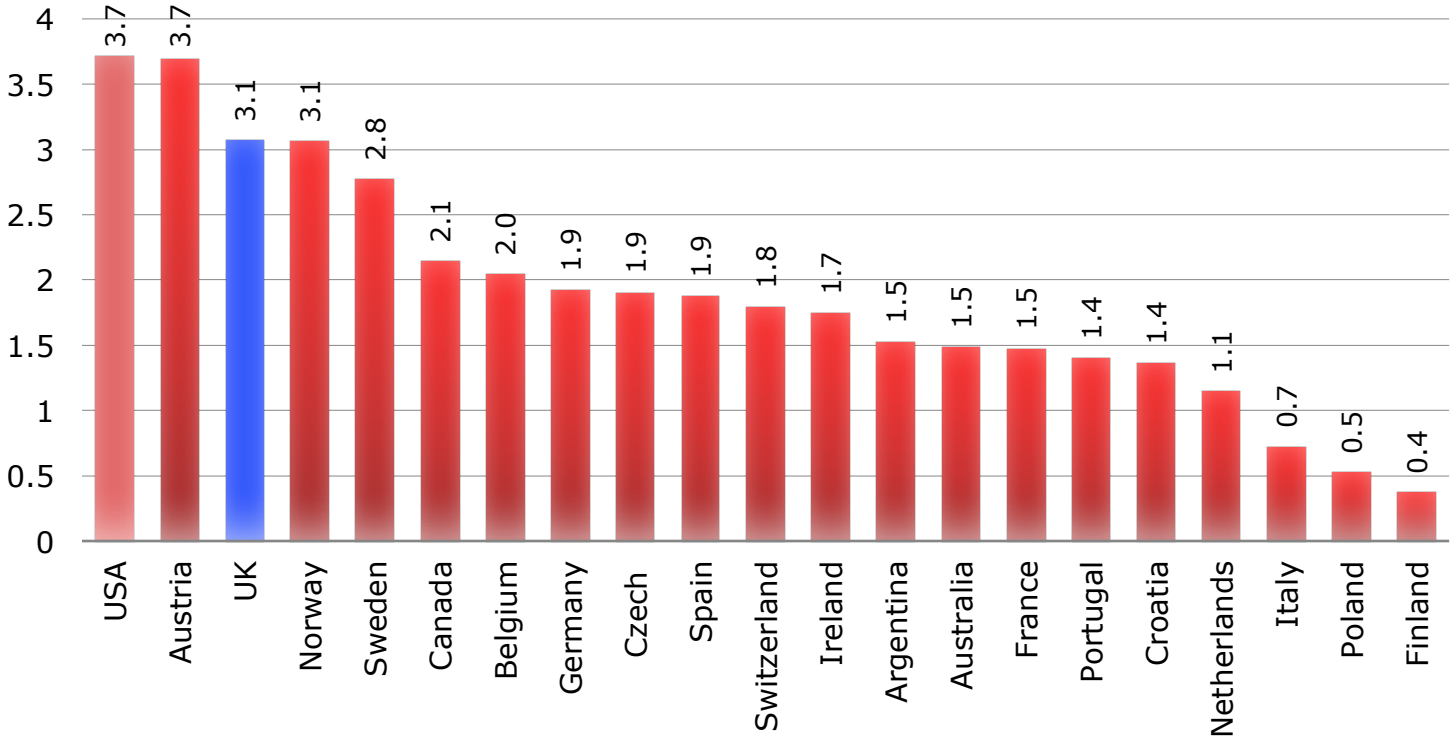
- Questions
  - What did we get right (if anything)?
  - What are our mistakes?
  - Did we learn from them?
- Considerations
  - Programme organisation
  - Indications
  - Patient Assessment
  - Implantation techniques
  - Immunosuppression

Development of pancreas transplantation in the UK

- National funding
  - Scotland 2002
  - England 2004
  - Wales 2006
  - Islets 2008
- Note:
  - Eurotransplant activity was 157 transplants in 2015



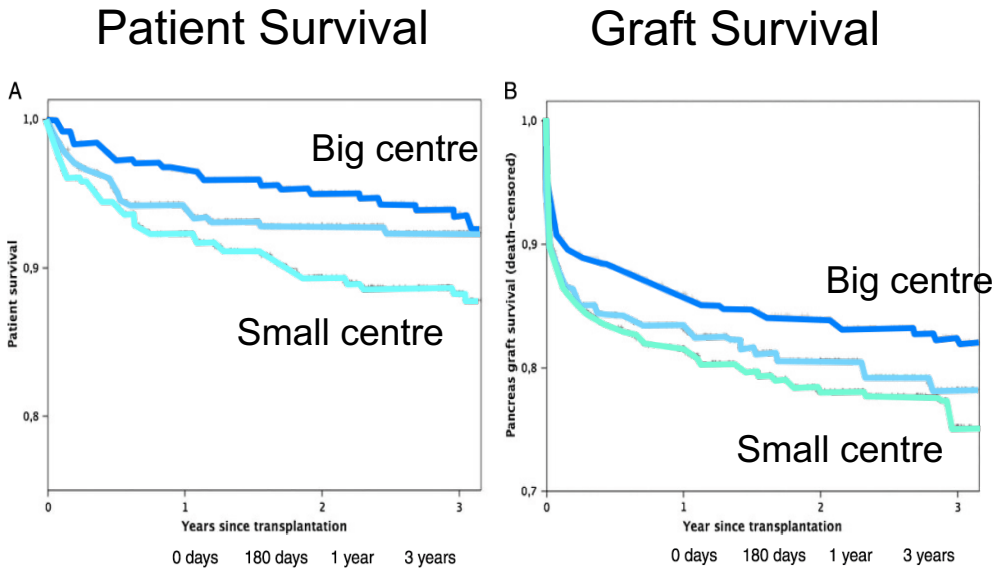
Pancreas transplantation in UK vs elsewhere



Global Observatory on Donation and Transplantation 2010 data https://reports.ont.es/caapmp.aspx

Centre volume affects SPK outcomes

- Pancreas transplants in EuroTransplant 2008-2013
- Centre volume
  - Big: ≥13 per year
  - Medium: 5-12 per year
  - Little: <5 per year



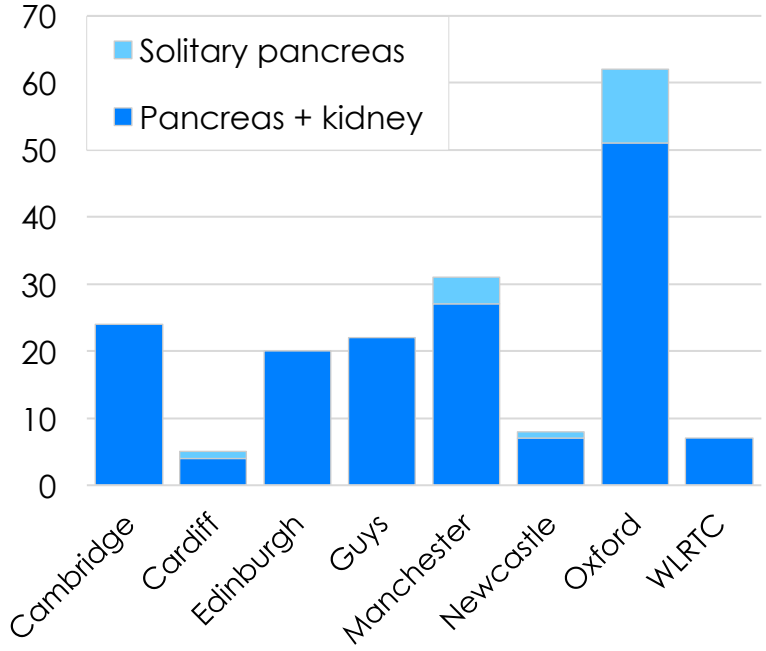
Kopp et al. Transplantation 2017;101:1247

Organisation of pancreas transplantation in the UK

- 8 centres
- Centrally funded
- NHSBT oversight

Centre activity in UK

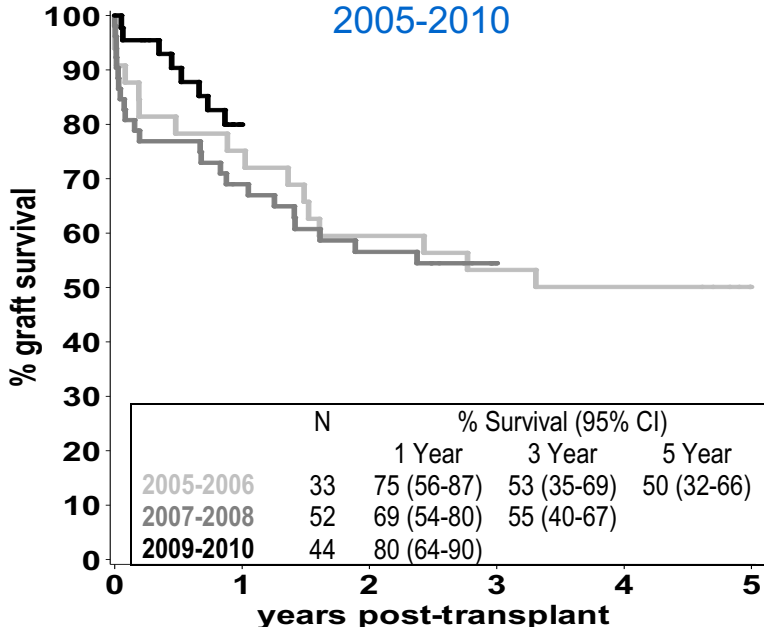
- Range 5 to 62
- 5/8 centres in “Big” category



NHSBT Centre specific data, 2016/17

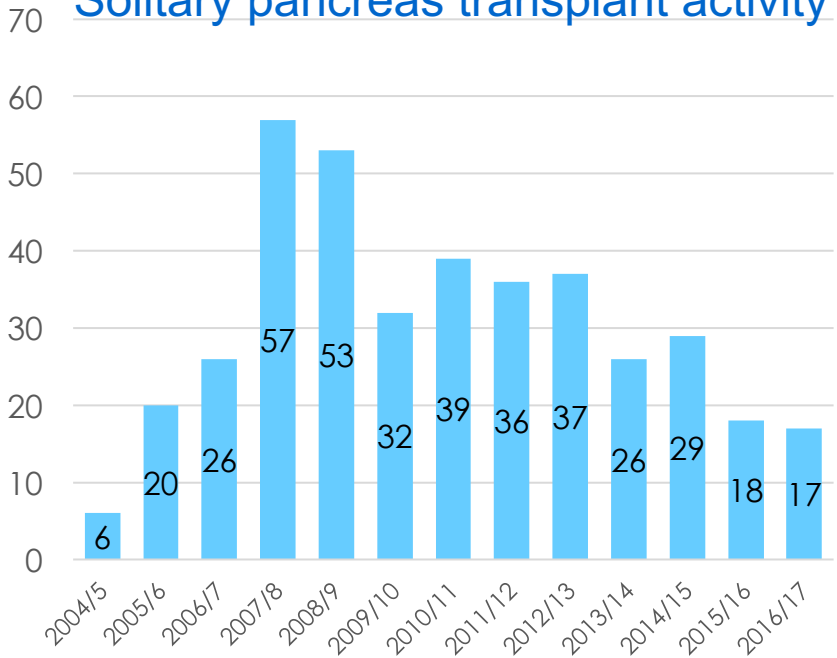
What did we learn:
Solitary pancreas transplantation

Pancreas graft survival
2005-2010



	N	% Survival (95% CI)		
		1 Year	3 Year	5 Year
2005-2006	33	75 (56-87)	53 (35-69)	50 (32-66)
2007-2008	52	69 (54-80)	55 (40-67)	
2009-2010	44	80 (64-90)		

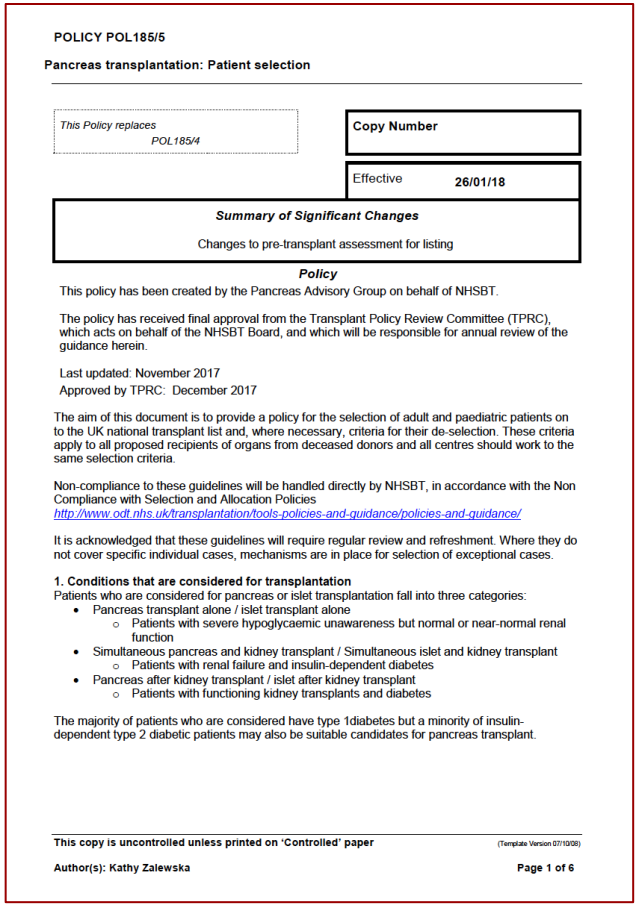
Solitary pancreas transplant activity



Data from Sue Madden & Lisa Mumford

Indications for transplant

- Type 1
- Insulin dependent type 2
  - BMI <30
- SPK: Renal failure
- PTA: Hypoglycaemic unawareness



POLICY POL185/5

Pancreas transplantation: Patient selection

This Policy replaces POL185/4

Copy Number

Effective **26/01/18**

Summary of Significant Changes

Changes to pre-transplant assessment for listing

Policy

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

The policy has received final approval from the Transplant Policy Review Committee (TPRC), which acts on behalf of the NHSBT Board, and which will be responsible for annual review of the guidance herein.

Last updated: November 2017
Approved by TPRC: December 2017

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 and all centres should work to the same selection criteria.

Non-compliance to these guidelines will be handled directly by NHSBT, in accordance with the Non Compliance with Selection and Allocation Policies
http://www.odt.nhs.uk/transplantation/tools-policies-and-guidance/policies-and-guidance/

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.

1. Conditions that are considered for transplantation

Patients who are considered for pancreas or islet transplantation fall into three categories:

- Pancreas transplant alone / islet transplant alone
  - Patients with severe hypoglycaemic unawareness but normal or near-normal renal function
- Simultaneous pancreas and kidney transplant / Simultaneous islet and kidney transplant
  - Patients with renal failure and insulin-dependent diabetes
- Pancreas after kidney transplant / islet after kidney transplant
  - Patients with functioning kidney transplants and diabetes

The majority of patients who are considered have type 1diabetes but a minority of insulin-dependent type 2 diabetic patients may also be suitable candidates for pancreas transplant.

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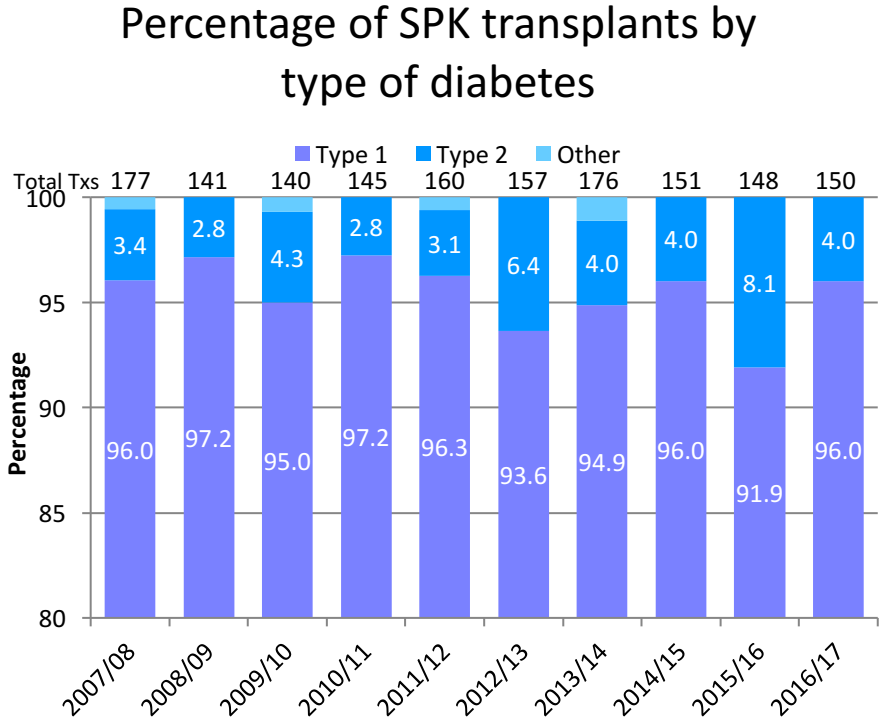
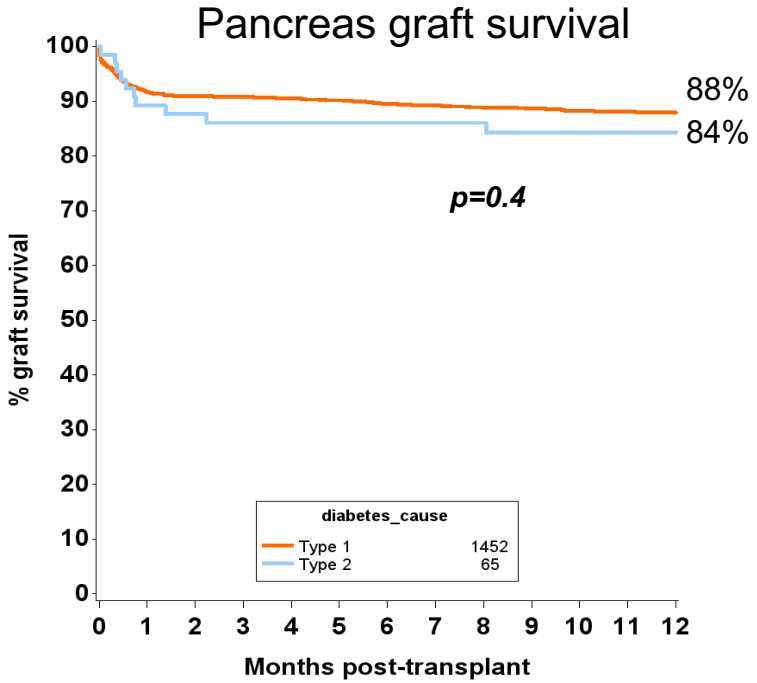
Author(s): Kathy Zalewska **Page 1 of 6**

https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/6525/pol185-pancreas-transplantation-patient-selection.pdf

Indications for transplant: No significant difference between type 1 and type 2

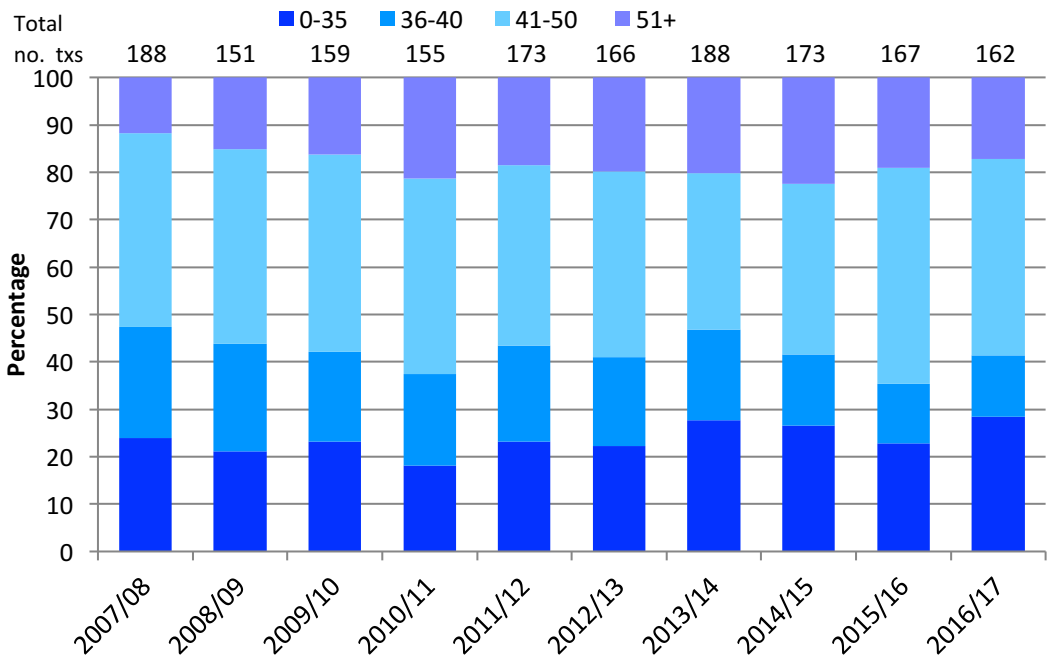




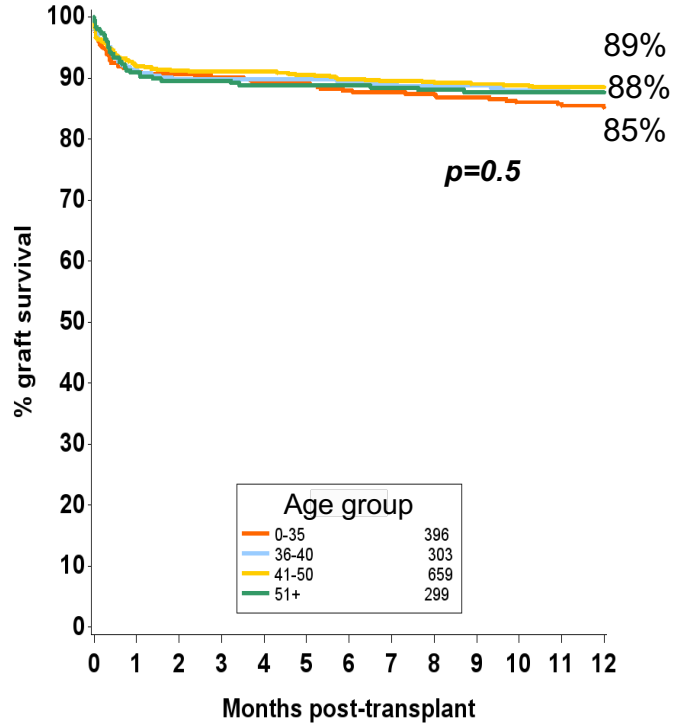
Type 2: Insulin dependent & BMI<30kg/m^2

Survival by age

Percentage of SPK transplants by age of patient

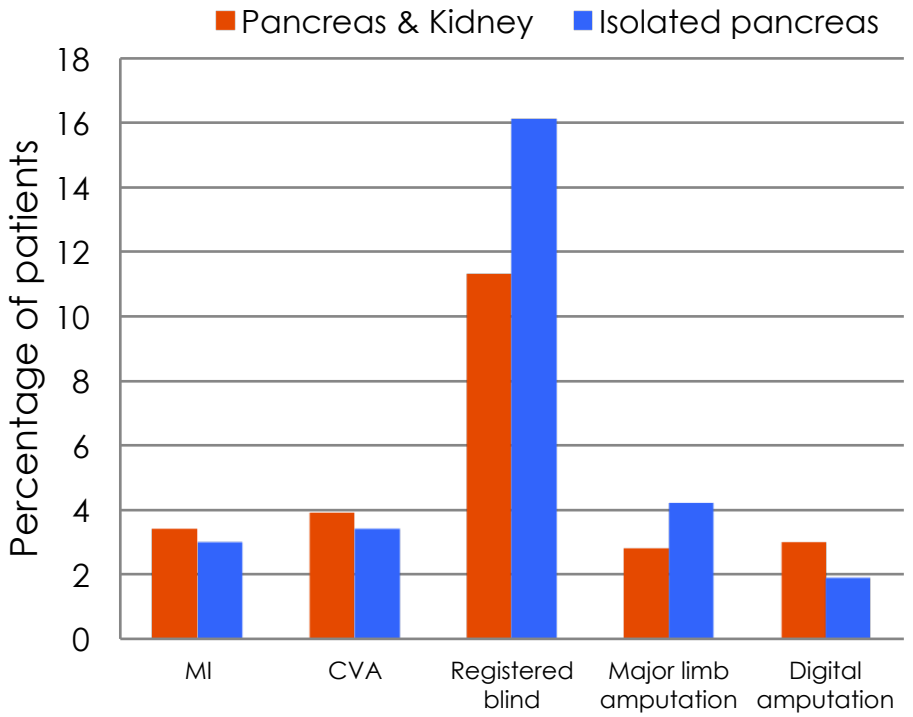


One year graft survival following SPK transplant, 1 April 2007 to 31 March 2017



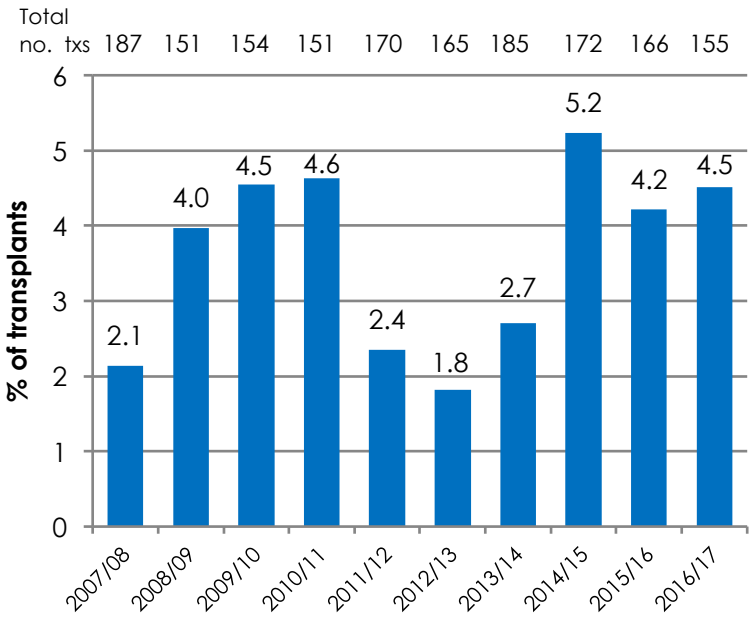
Patient assessment

- Diabetic comorbidity
  - Cardiovascular disease
    - Previous MI
  - Peripheral vascular disease
    - Previous amputations
  - Cerebrovascular disease
    - Previous TIAs/CVAs
- Renal failure
  - Dialysis burden

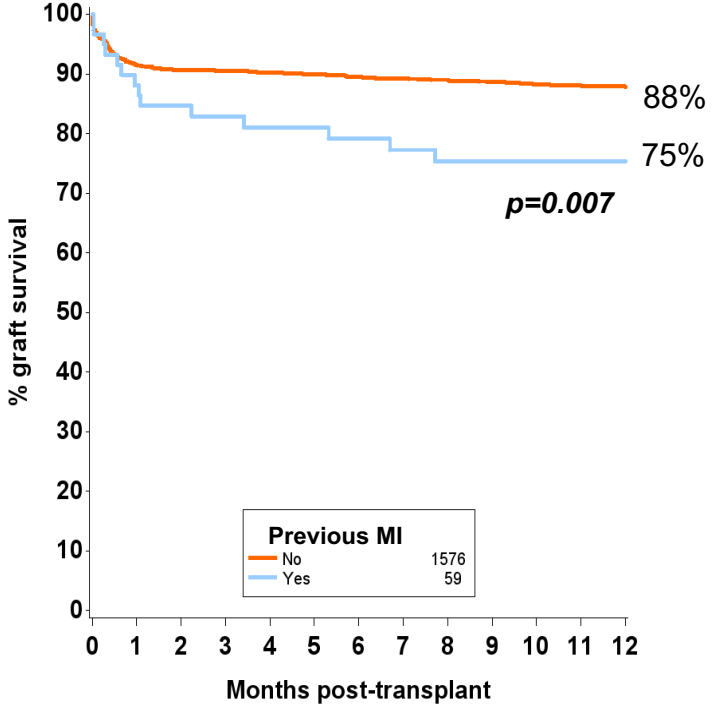


Pre-transplant MI is associated with poorer graft survival

Percentage of SPK transplants where patient had an MI pre-transplant

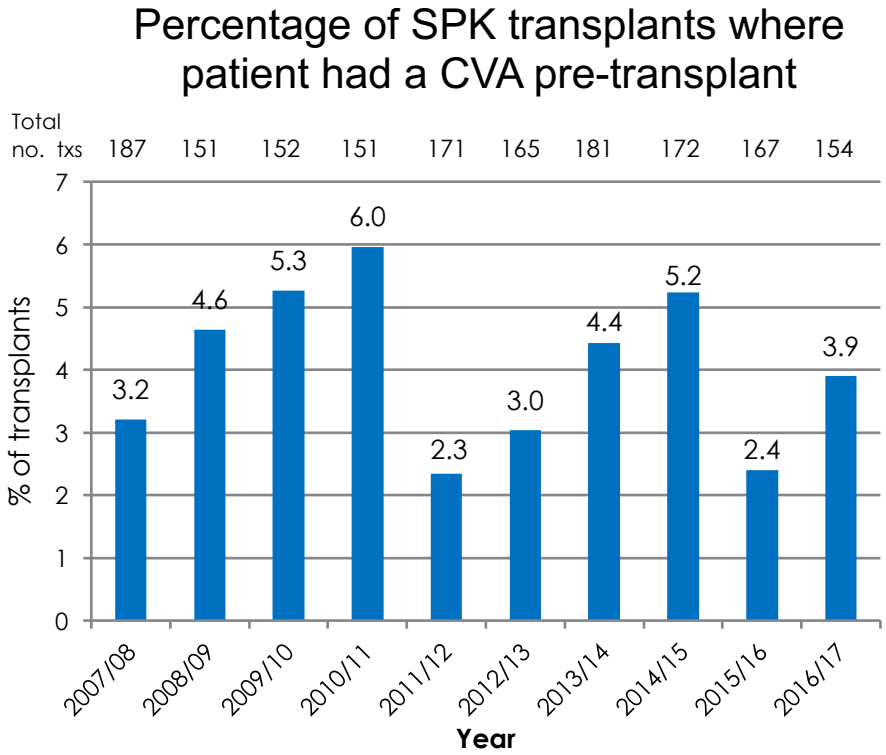


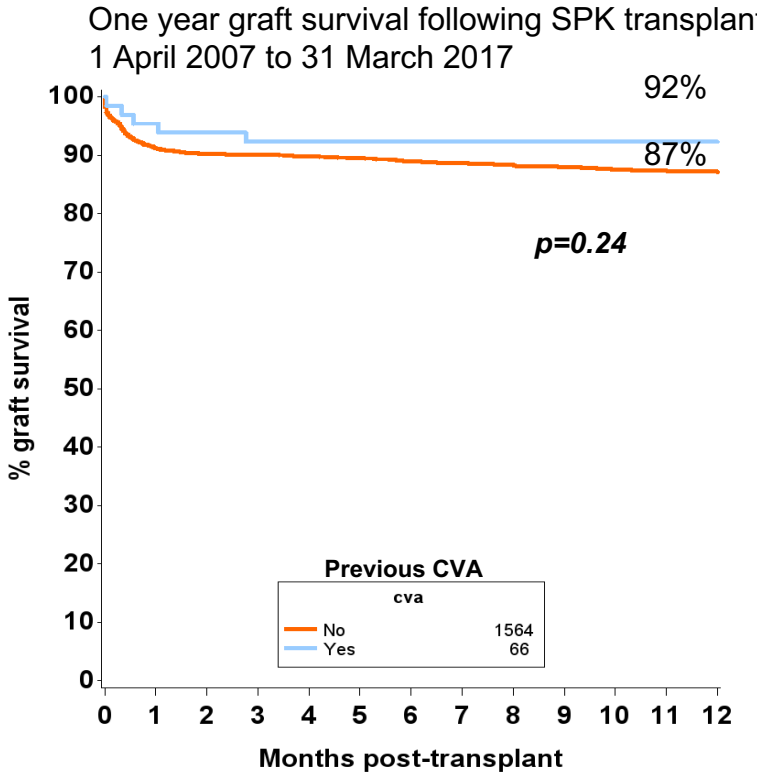
One year graft survival following SPK transplant , 1 April 2007 to 31 March 2017,



Still significant factor for one year graft survival after adjusting for donor age, BMI, donor type and waiting time: p=0.012

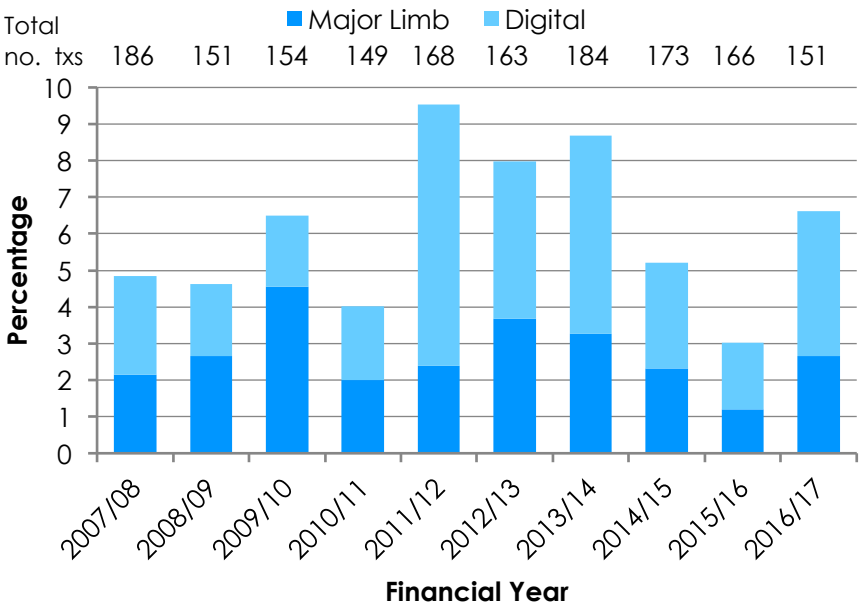
Pre-transplant CVA is not associated with poorer graft survival

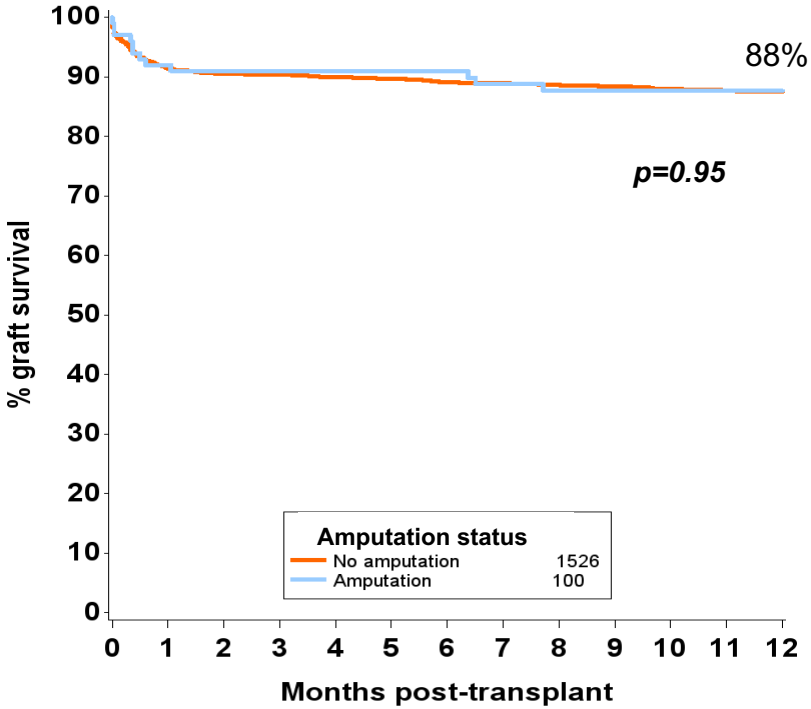




Previous amputation does not affect graft survival

Percentage of SPK transplants where patient had an amputation pre-transplant





Patient survival

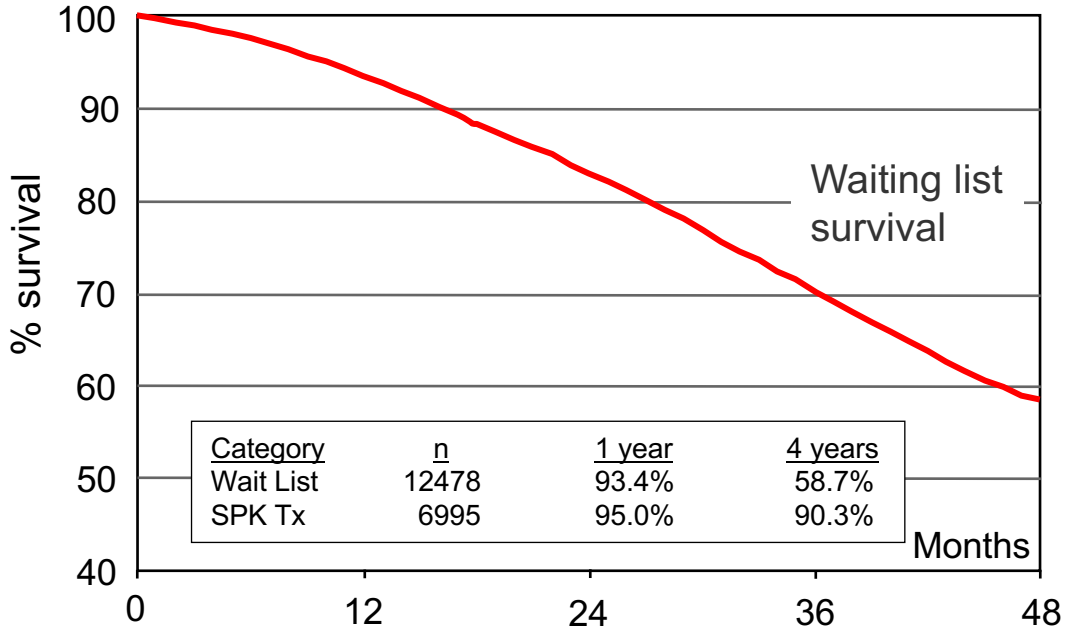
- One year patient survival is not affected by
  - Previous MI (p=0.29)
  - Previous CVA (p=0.16)
  - Smoker (p=0.27)
  - Limb amputation (p=0.25)

Assessment summary

- Solitary pancreas recipients have a 50% 5 year graft survival
- The outcomes are the same for patients with type 1 and insulin-dependent type 2 diabetes
- There is no clear difference in graft survival by recipient age
- A history of MI is associated with poorer graft survival
- Previous CVA or limb / digital amputation do not influence graft survival
  - But there may be selection bias involved here

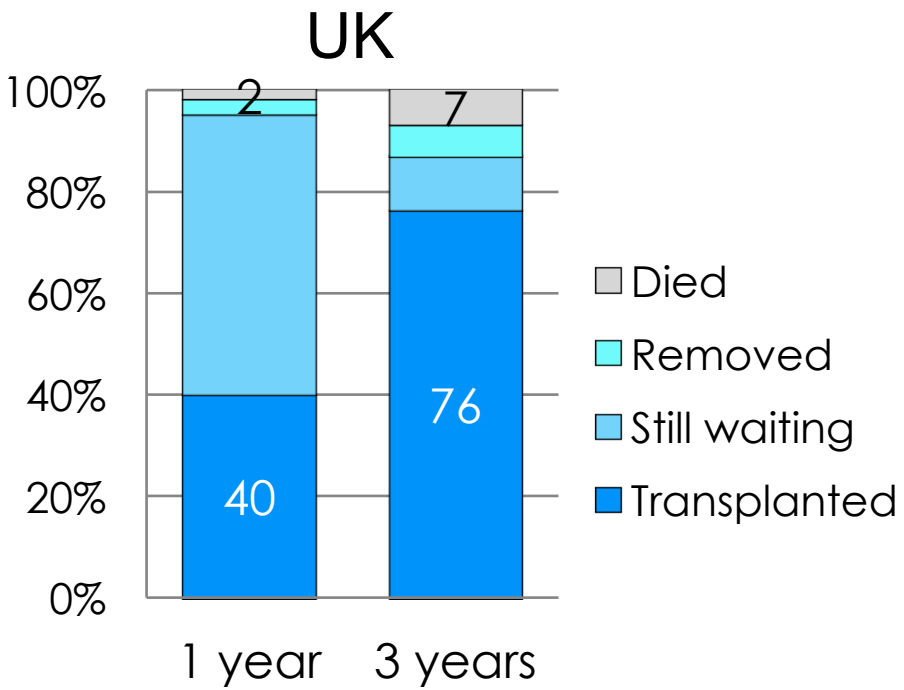
Waiting for a transplant

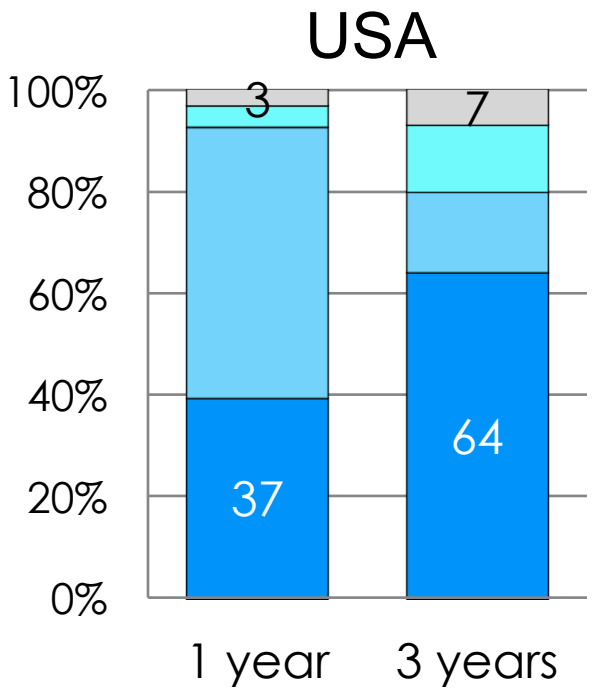
- Have we got this right compared to USA?



Am J Trans 2004

Outcome following listing for a simultaneous pancreas & kidney in 2013 pancreas in the UK





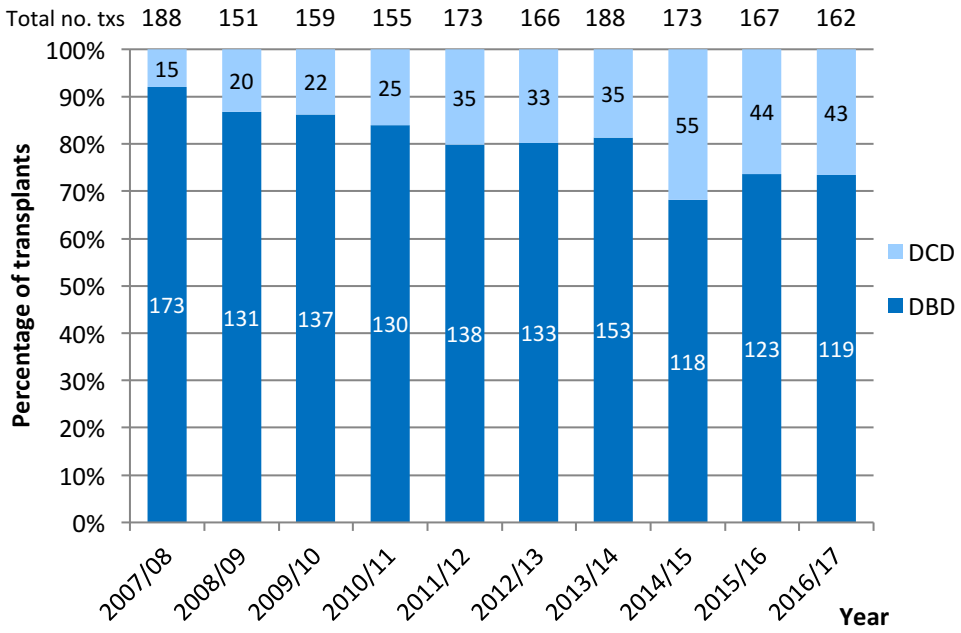
7% die waiting

UK figures are 4/13 to 3/14

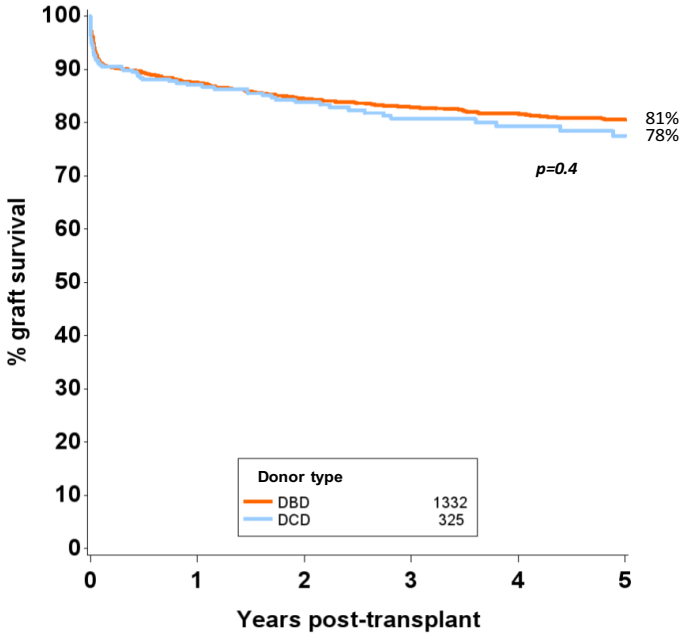
DONOR TYPES

The donors: DCD pancreases are as good as DBD pancreases

SPK transplants in the UK by donor type



5 year graft survival by donor type

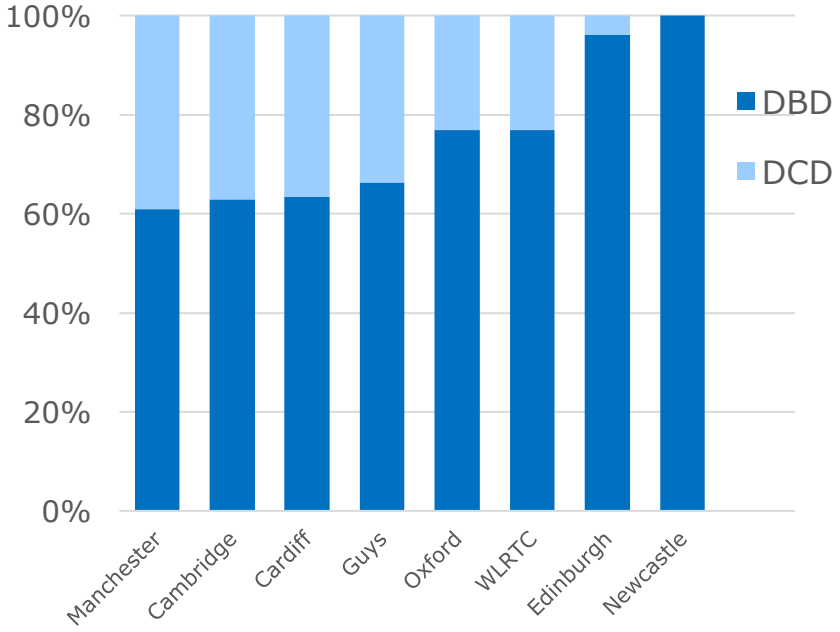


SPK transplants, 1st April 2007-31st March 2017

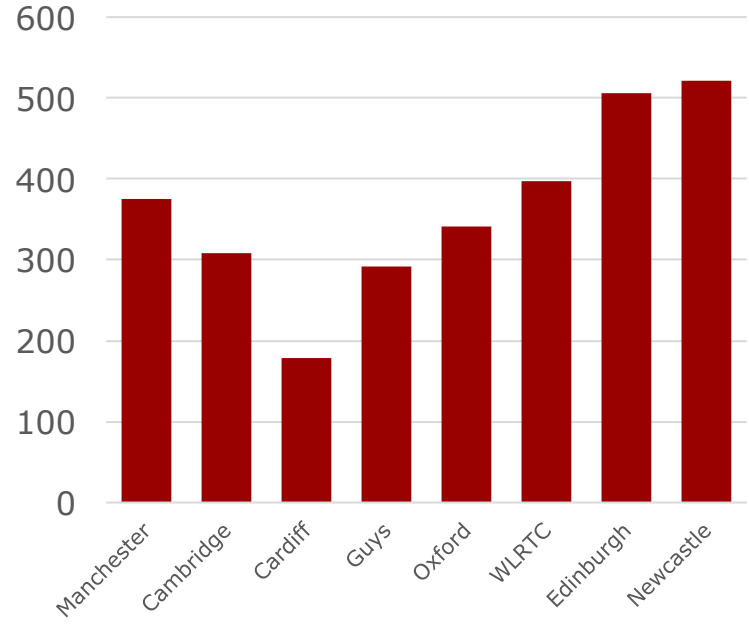
DCD pancreas use varies from 0 to 39%

in spite of there being no difference in outcomes

Proportion of DBD and DCD pancreases used by centres,1/4/14 to 31/3/17



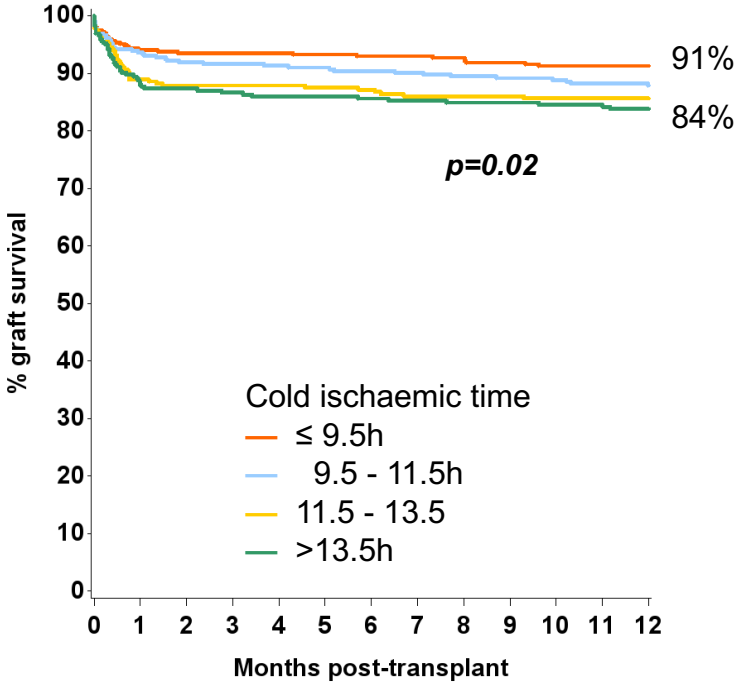
Median waiting time to transplant 2011/14



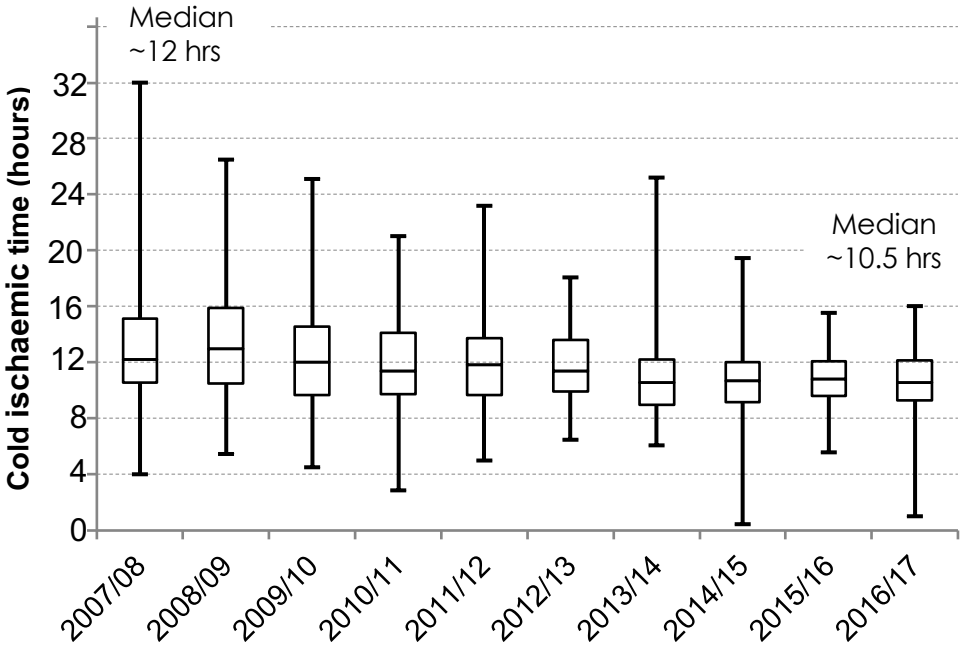
Data from NHSBT annual reports

Cold ischaemia affects graft survival: DBD donors

One year graft survival following DBD SPK transplant 1 April 2007 to 31 March 2017

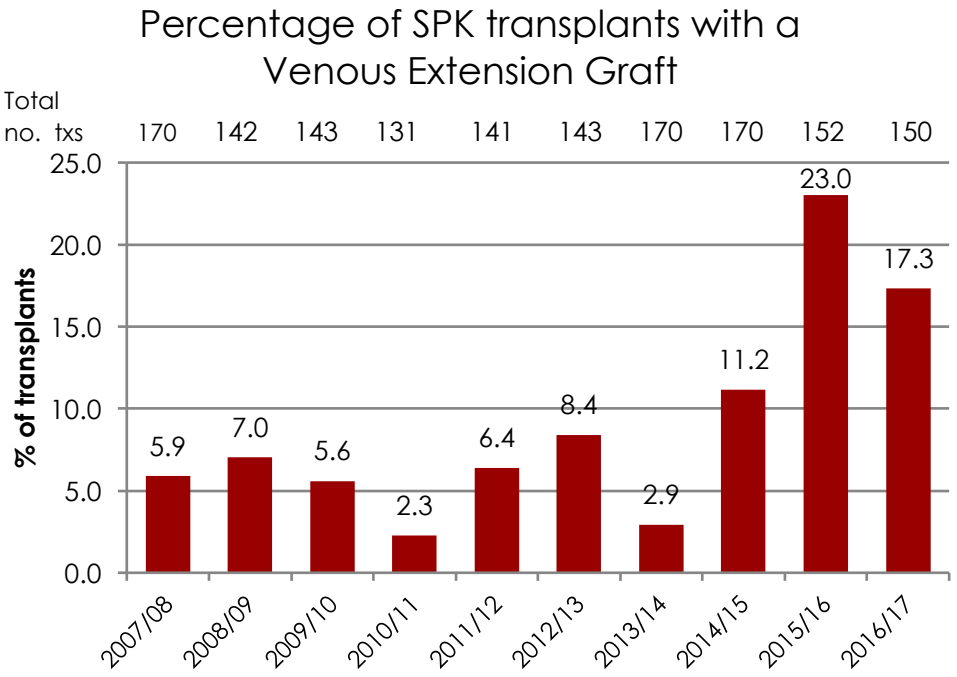


Median cold ischaemia time for SPK transplants from DBD donors

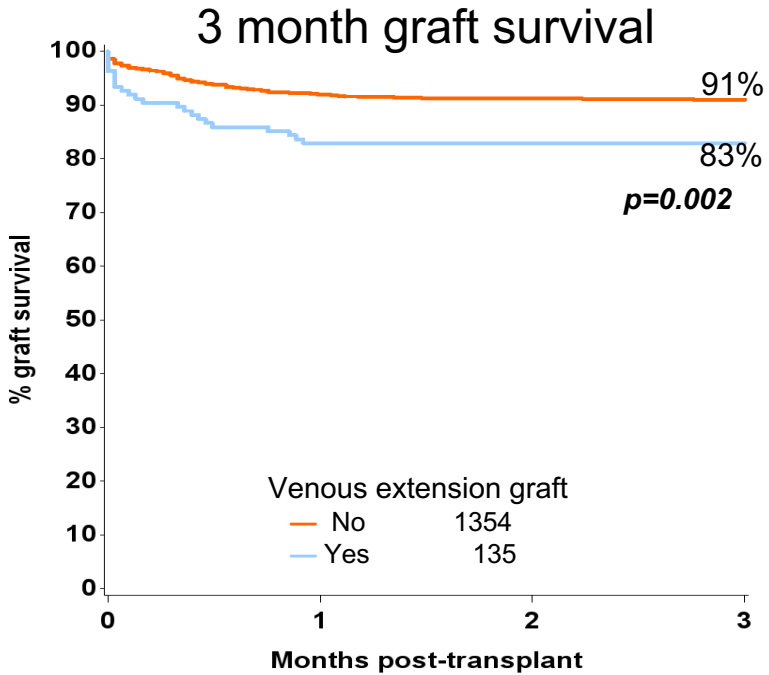


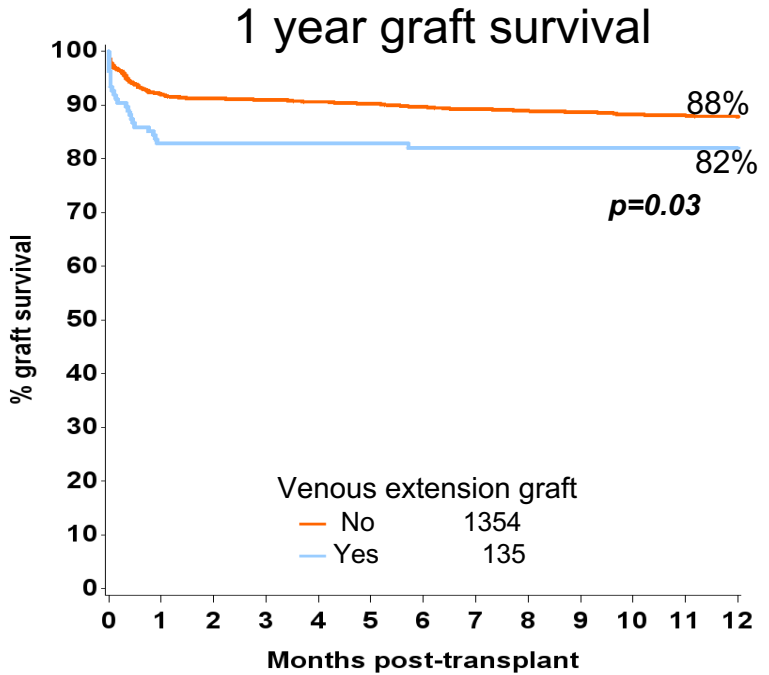
The plumbing

Portal vein extension graft on the donor pancreas



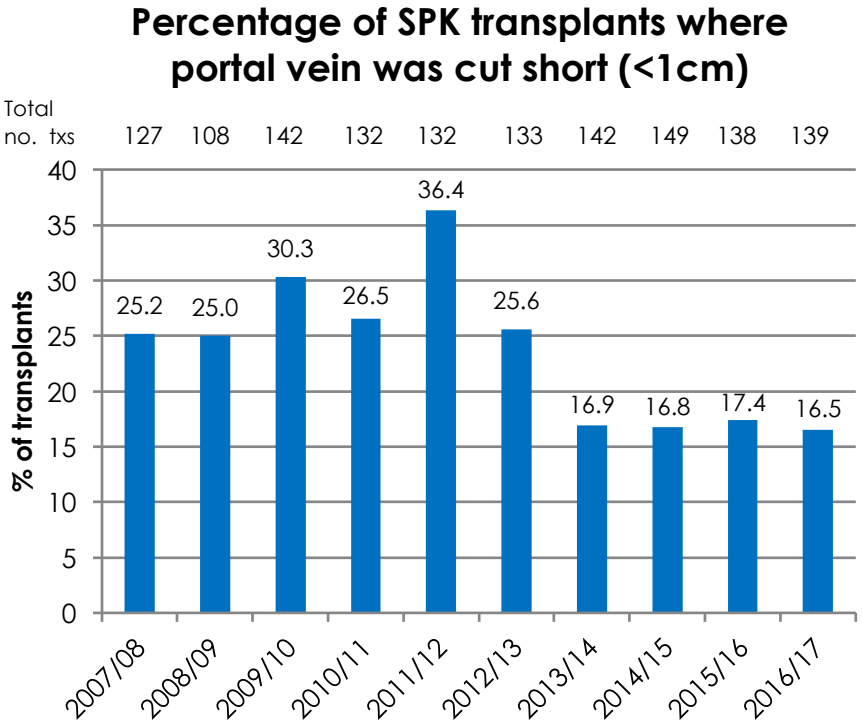
Venous extensions are associated with poorer graft outcomes

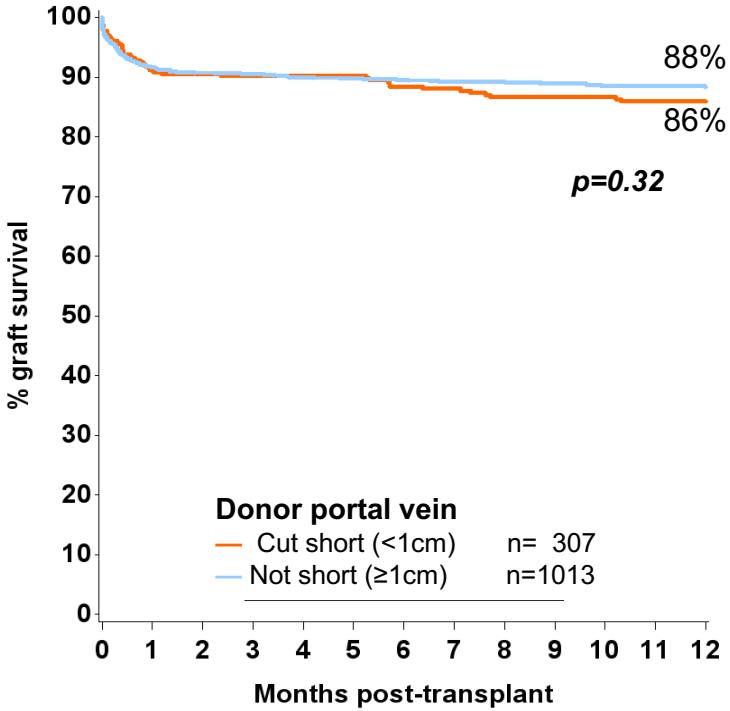




Still significant factor for one year graft survival after adjusting for donor age, BMI, donor type and waiting time: p=0.03

Is there a penalty for using a pancreas with a short portal vein?

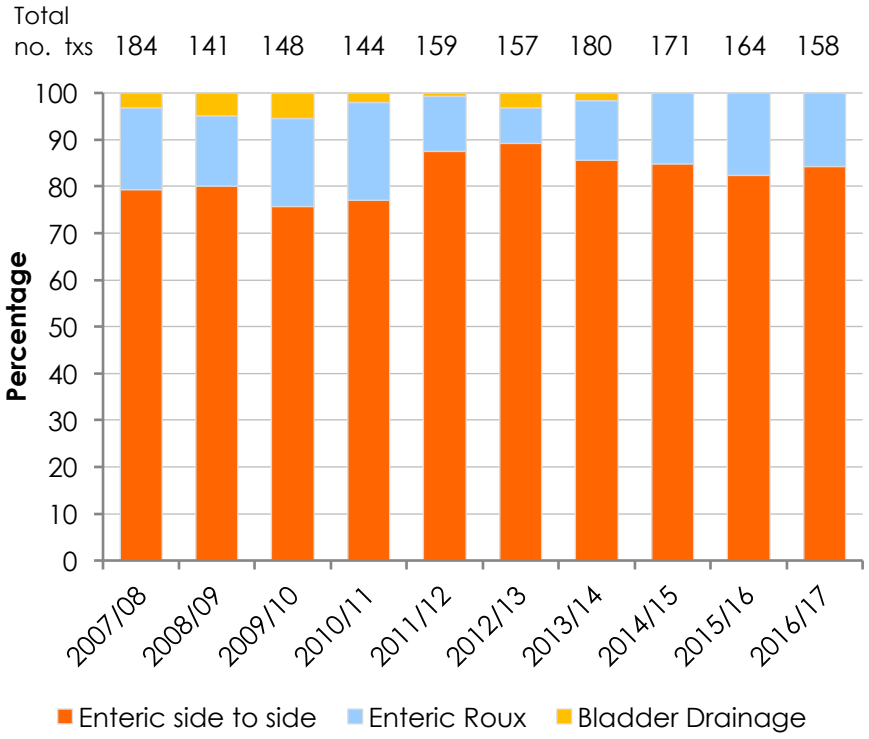


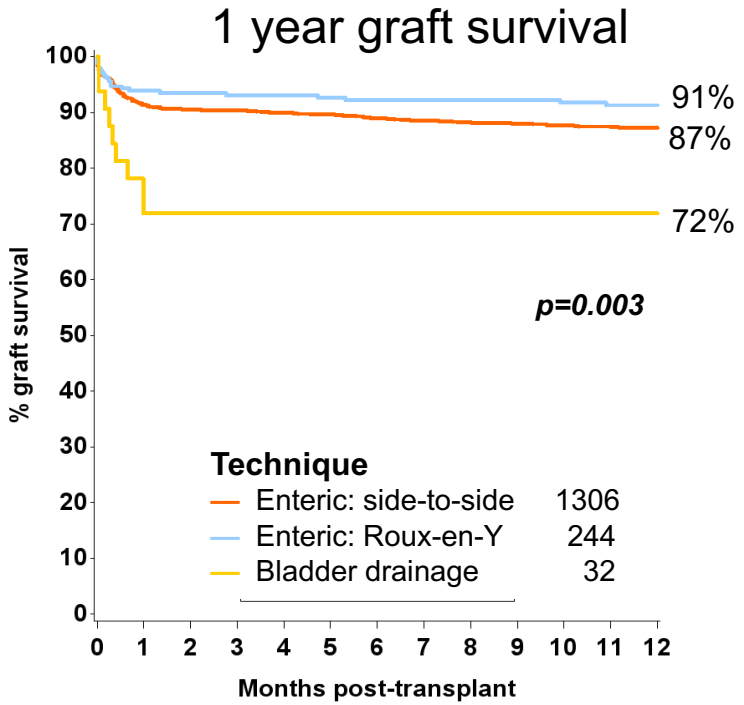


Duct management

- Enteric drainage
  - Duodeno-enterostomy
    - Side-to-side anastomosis
    - Roux-en-Y
  - Duodeno-duodenostomy
- Bladder drainage

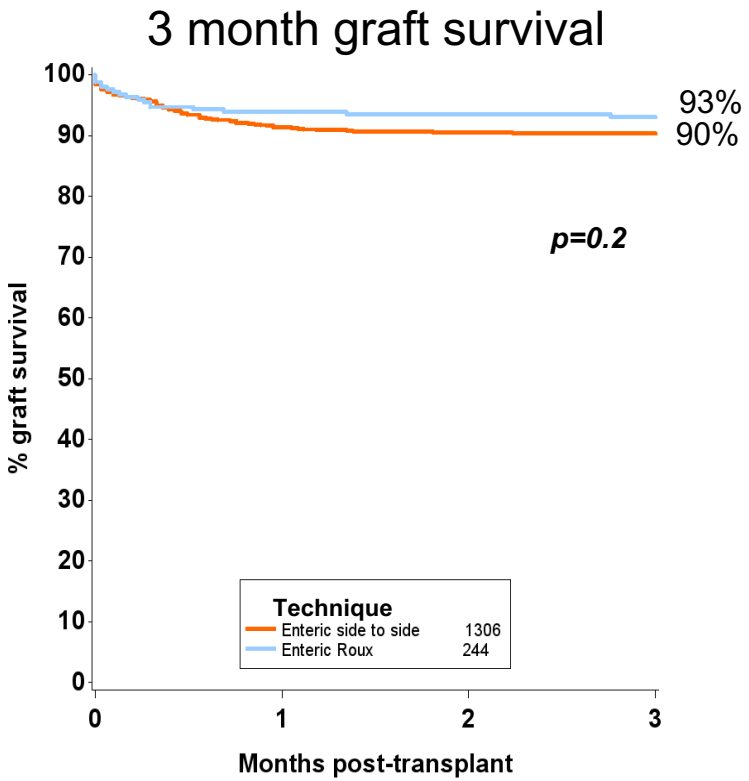
Duct management technique

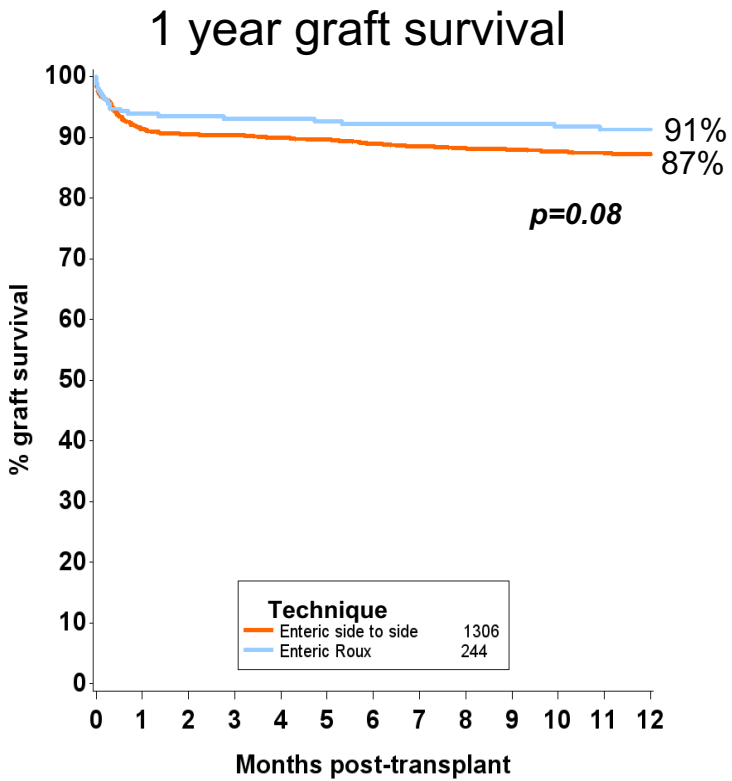




Still significant factor for one year graft survival after adjusting for donor age, BMI, donor type and waiting time: p=0.01

Roux or side-to-side enteric anastomosis?

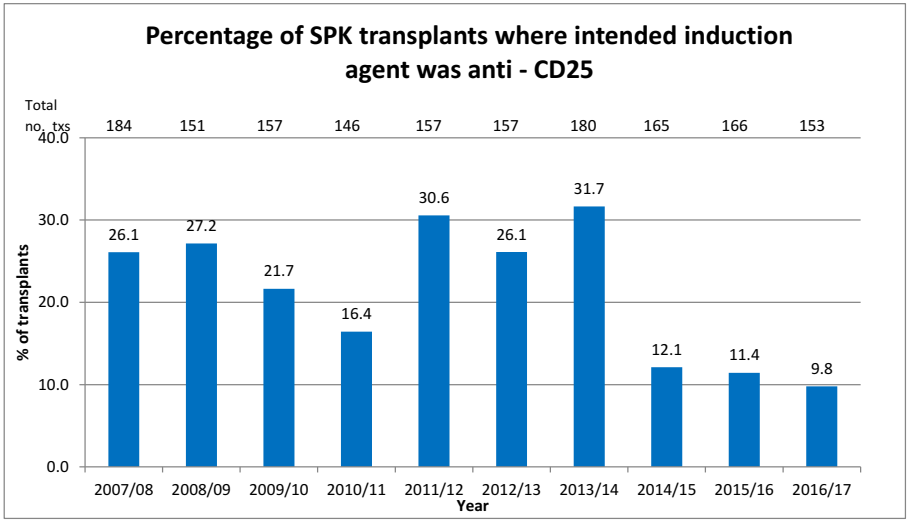




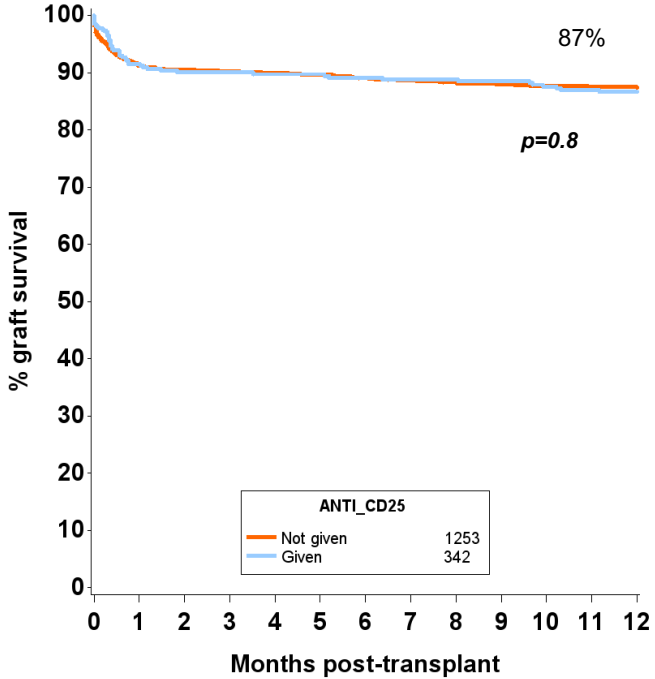
Immunosuppression

Note: The next slides include off-label use of immunosuppression

CD25 monoclonals do not affect graft survival

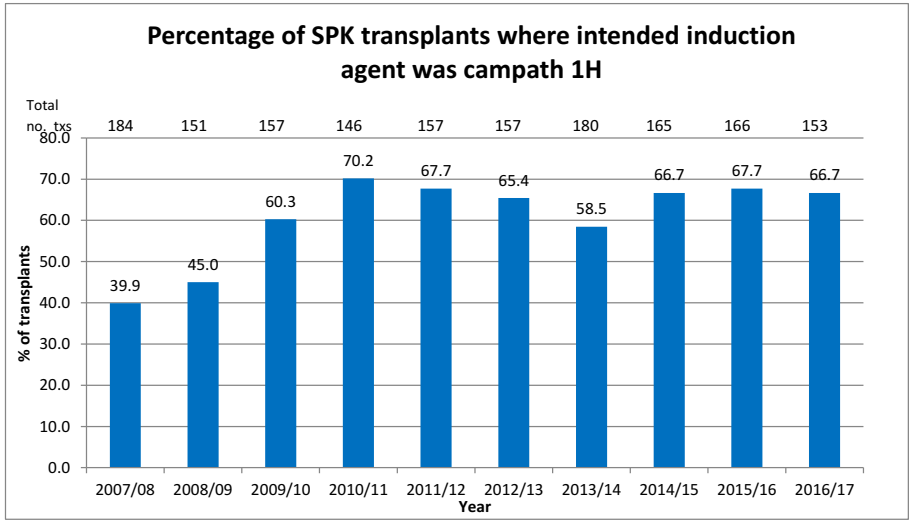


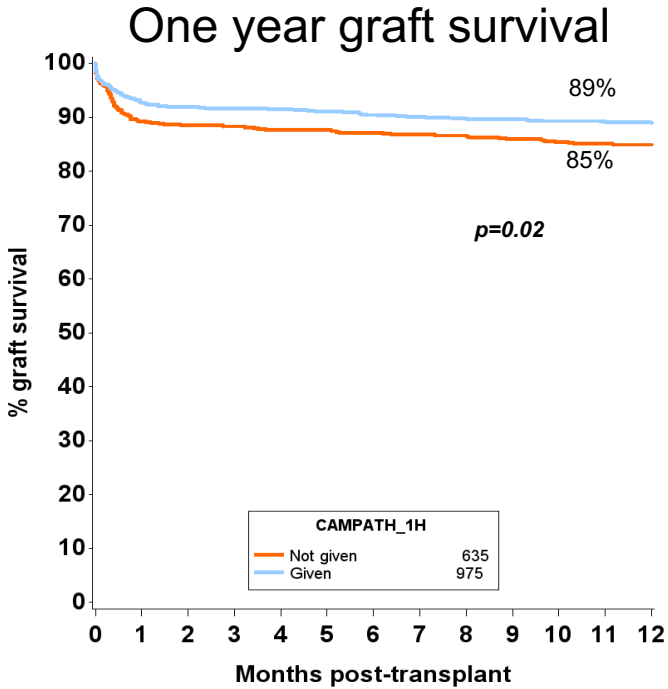
One year graft survival



SPK transplants in the UK between 1 April 2007 and 31 March 2017

Campath 1H (alemtuzumab) does improve 1year graft survival

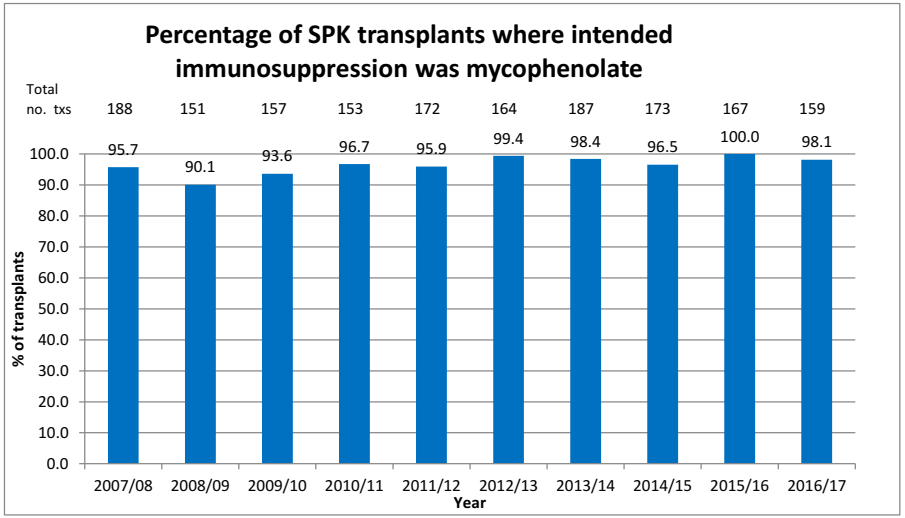




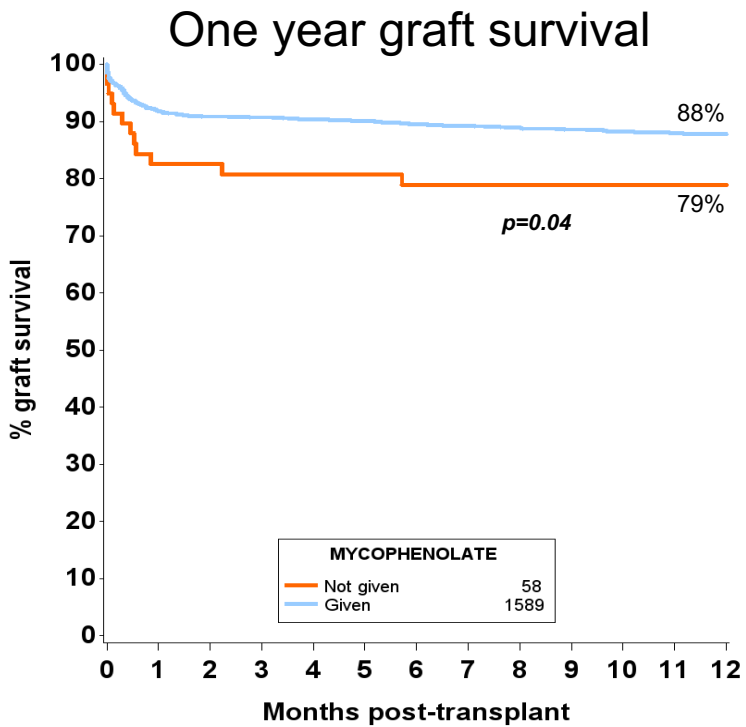
SPK transplants in the UK between 1 April 2007 and 31 March 2017

Still significant factor for one year graft survival after adjusting for donor age, BMI, donor type and waiting time – p=0.004. Increased significance after adjusting for these factors appears to be due to interaction between donor factors and Campath 1H.

Mycophenolate

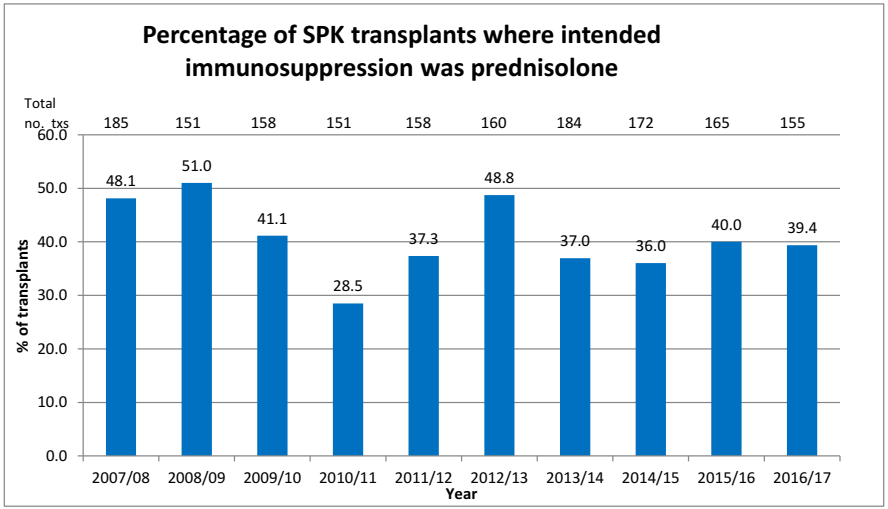


SPK transplants in the UK between 1 April 2007 and 31 March 2017

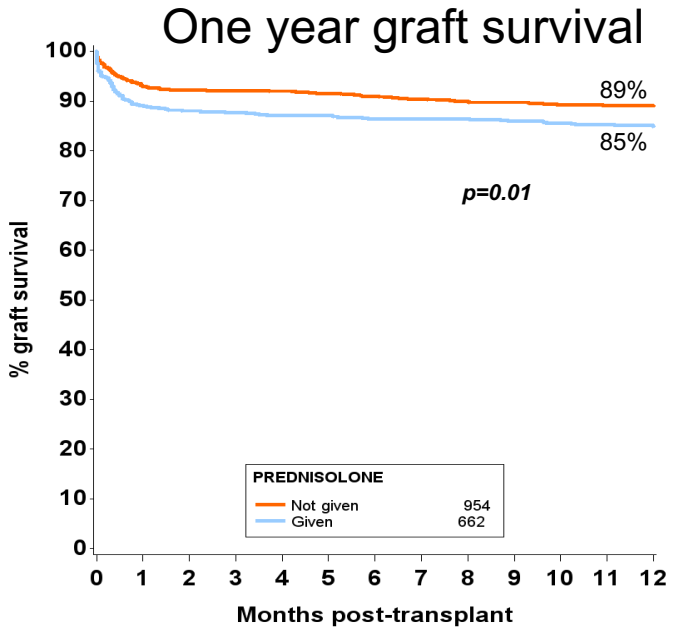


Not significant factor for one year graft survival after adjusting for donor age, BMI, donor type and waiting time – p=0.06

Prednisolone

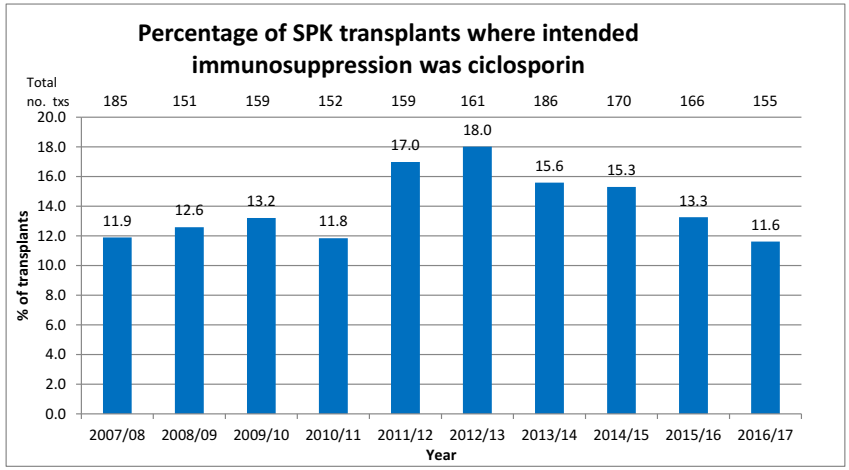


SPK transplants in the UK
between 1 April 2007 and 31 March 2017



Still significant factor for one year graft survival after adjusting for donor age, BMI, donor type and waiting time – p=0.003 Increased significance after adjusting for these factors appears to be due to interaction between donor factors and prednisolone.

Ciclosporin



SPK transplants in the UK
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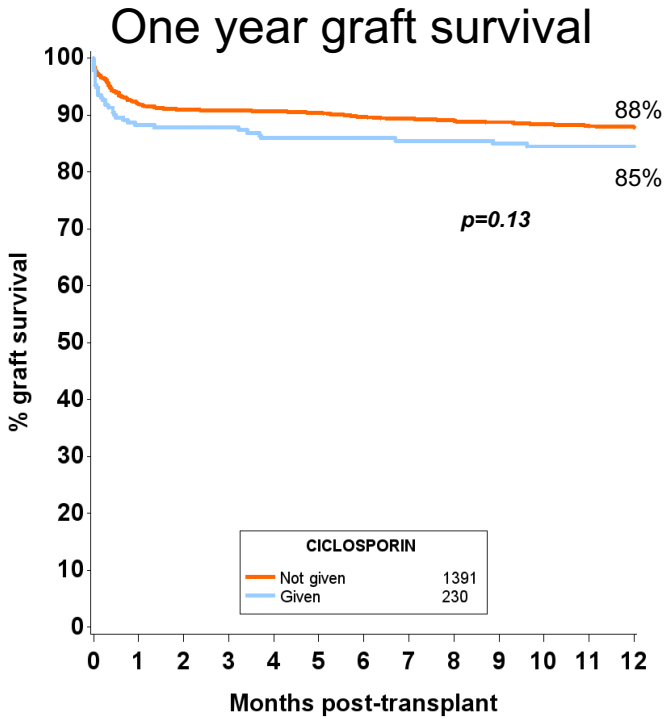
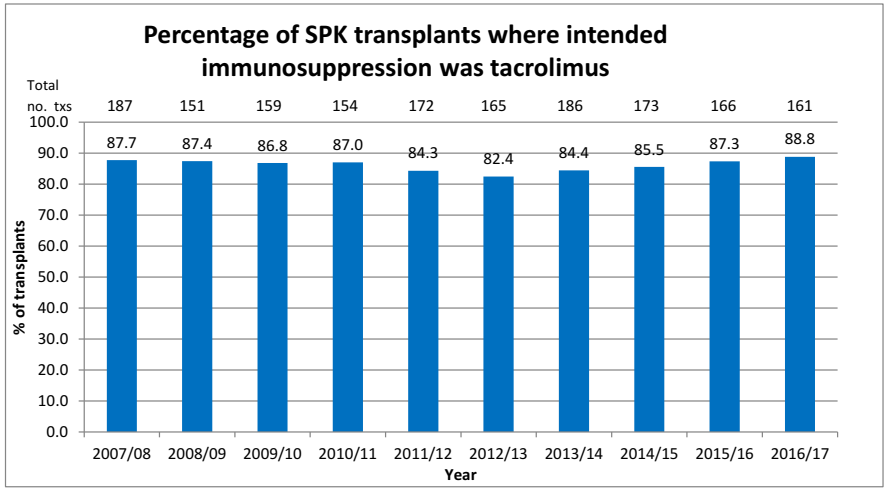
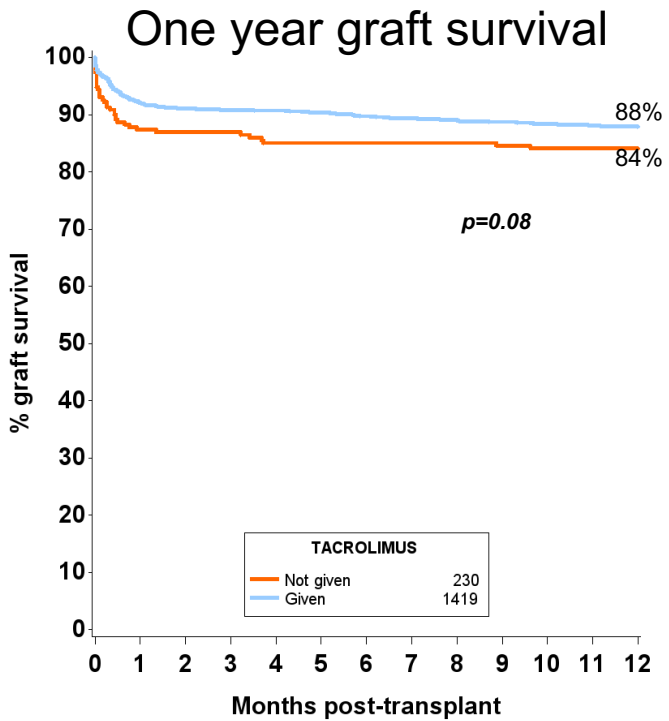


Tacrolimus

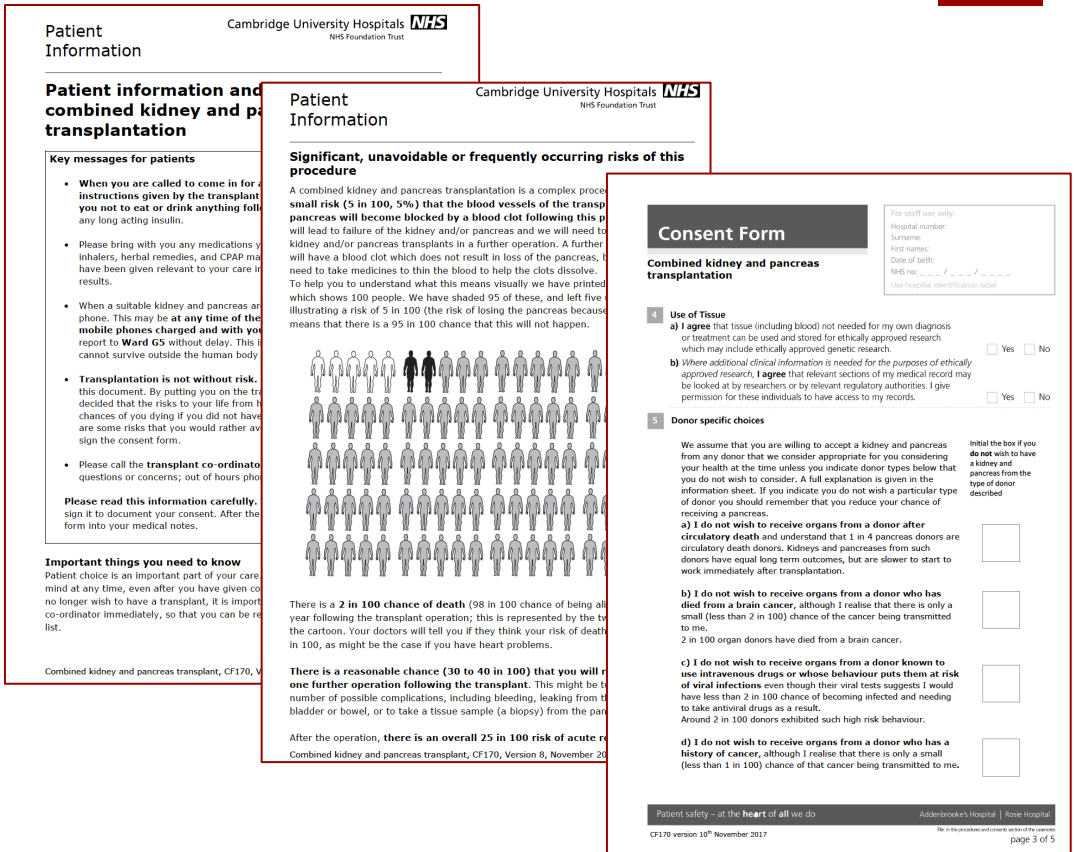




SPK transplants in the UK between 1 April 2007 and 31 March 2017

Cambridge practice – learning from mistakes or anecdote based medicine?

- Consent
  - Reoperation is common: 30%
  - Nerve damage
    - Spinal ischaemia 1%
  - Its miserable
    - But its great 3 months later



Patient Information

Cambridge University Hospitals NHS
NHS Foundation Trust

Patient information and
combined kidney and pa
transplantation

Key messages for patients

- **When you are called to come in for**
  instructions given by the transplant
  you not to eat or drink anything foll
  any long acting insulin.
- Please bring with you any medications y
  inhalers, herbal remedies, and CPAP ma
  have been given relevant to your care in
  results.
- When a suitable kidney and pancreas ar
  phone. This may be **at any time of the**
  mobile phones charged and with yo
  report to **Ward G5** without delay. This i
  cannot survive outside the human body
- **Transplantation is not without risk.**
  this document. By putting you on the tra
  decided that the risks to your life from h
  chances of you dying if you did not have
  are some risks that you would rather av
  sign the consent form.
- Please call the **transplant co-ordinato**
  questions or concerns; out of hours pho

Please read this information carefully.
sign it to document your consent. After the
form into your medical notes.

Important things you need to know
Patient choice is an important part of your care
mind at any time, even after you have given co
no longer wish to have a transplant, it is import
co-ordinator immediately, so that you can be re
list.

Combined kidney and pancreas transplant, CF170, V

Patient Information

Cambridge University Hospitals NHS
NHS Foundation Trust

Significant, unavoidable or frequently occurring risks of this procedure

A combined kidney and pancreas transplantation is a complex proce
small risk (5 in 100, 5%) that the blood vessels of the transp
pancreas will become blocked by a blood clot following this p
will lead to failure of the kidney and/or pancreas and we will need to
kidney and/or pancreas transplants in a further operation. A further
will have a blood clot which does not result in loss of the pancreas, h
need to take medicines to thin the blood to help the clots dissolve.
To help you to understand what this means visually we have printed
which shows 100 people. We have shaded 95 of these, and left five
illustrating a risk of 5 in 100 (the risk of losing the pancreas because
means that there is a 95 in 100 chance that this will not happen.

There is a **2 in 100 chance of death** (98 in 100 chance of being ali
year following the transplant operation; this is represented by the tw
the cartoon. Your doctors will tell you if they think your risk of death
in 100, as might be the case if you have heart problems.

There is a reasonable chance (30 to 40 in 100) that you will r
one further operation following the transplant. This might be t
number of possible complications, including bleeding, leaking from t
bladder or bowel, or to take a tissue sample (a biopsy) from the par

After the operation, **there is an overall 25 in 100 risk of acute re**

Combined kidney and pancreas transplant, CF170, Version 8, November 20

Consent Form

Combined kidney and pancreas transplantation

For staff use only:
Hospital number:
Surname:
First names:
Date of birth:
NHS no: _ _ _ / _ _ _ / _ _ _ _
Use hospital identification label

4 **Use of Tissue**

a) I agree that tissue (including blood) not needed for my own diagnosis or treatment can be used and stored for ethically approved research which may include ethically approved genetic research. ☐ Yes ☐ No

b) *Where additional clinical information is needed for the purposes of ethically approved research*, **I agree** that relevant sections of my medical record may be looked at by researchers or by relevant regulatory authorities. I give permission for these individuals to have access to my records. ☐ Yes ☐ No

5 **Donor specific choices**

We assume that you are willing to accept a kidney and pancreas from any donor that we consider appropriate for you considering your health at the time unless you indicate donor types below that you do not wish to consider. A full explanation is given in the information sheet. If you indicate you do not wish a particular type of donor you should remember that you reduce your chance of receiving a pancreas.

Initial the box if you **do not** wish to have a kidney and pancreas from the type of donor described

a) I do not wish to receive organs from a donor after circulatory death and understand that 1 in 4 pancreas donors are circulatory death donors. Kidneys and pancreases from such donors have equal long term outcomes, but are slower to start to work immediately after transplantation. ☐

b) I do not wish to receive organs from a donor who has died from a brain cancer, although I realise that there is only a small (less than 2 in 100) chance of the cancer being transmitted to me.
2 in 100 organ donors have died from a brain cancer. ☐

c) I do not wish to receive organs from a donor known to use intravenous drugs or whose behaviour puts them at risk of viral infections even though their viral tests suggests I would have less than 2 in 100 chance of becoming infected and needing to take antiviral drugs as a result.
Around 2 in 100 donors exhibited such high risk behaviour. ☐

d) I do not wish to receive organs from a donor who has a history of cancer, although I realise that there is only a small (less than 1 in 100) chance of that cancer being transmitted to me. ☐

Patient safety – at the **heart** of **all** we do — Addenbrooke's Hospital | Rosie Hospital

CF170 version 10th November 2017

File in the procedures and consents section of the casenotes

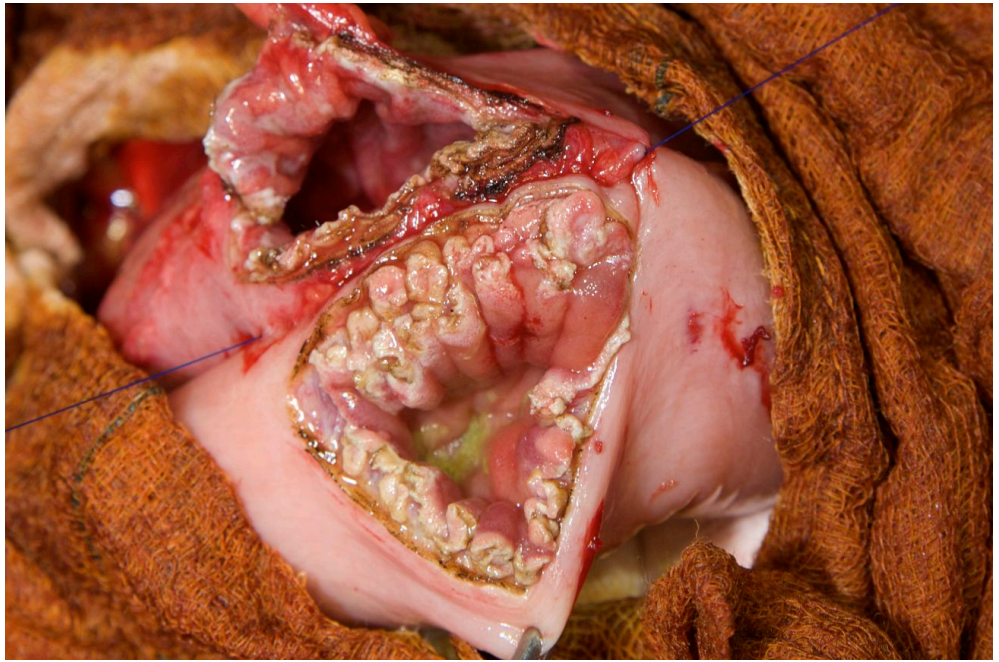
page 3 of 5

Cambridge practice – learning from mistakes or anecdote based medicine?

- Gastroparesis
  - Jejunostomy placed at surgery
  - Avoids PN

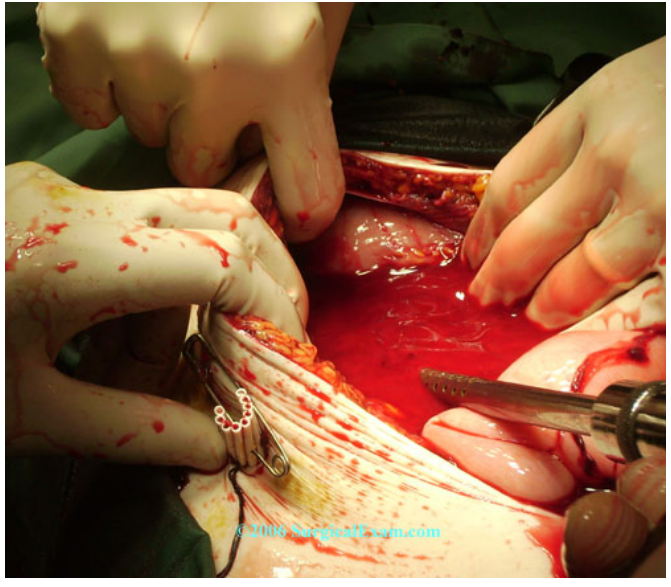
Cambridge practice – learning from mistakes or anecdote based medicine?

- Avoid betadine flush of donor duodenum
  - UW preserves epithelium better



Cambridge practice – learning from mistakes or anecdote based medicine?

- Reperfuse the vein first
  - Its easier to control the bleeding



Cambridge practice – learning from mistakes or anecdote based medicine?

- Appendicectomy
  - It sits on top of the pancreas
- Cholecystectomy
  - if stones:
  - 2 cases of early acute cholecystitis

Cambridge practice – learning from mistakes or anecdote based medicine?

- Air mattress
  - Heel ulcers common

Summary

- The following do not affect graft survival
  - Type 1 vs type 2 DM
  - Recipient age
  - Prior CVA
  - Prior amputation
  - CNI choice

- The following cause significantly worse graft survival
  - Prior MI
  - Increased cold ischaemia
  - Portal vein extension grafts
  - Bladder drainage
  - Steroid immunosuppression
  - Non-use of Campath and MMF