

What happens to patients returning to dialysis after transplant failure? Data from the UK Renal Registry



Dr Lynsey Webb¹, Dr Anna Casula¹, Dr Charlie Tomson², Dr David Ansell¹, Prof Chris Maggs^{1,3} and Prof Yoav Ben-Shlomo⁴



Background (1)

- 22,300 prevalent UK kidney transplant patients
- Transplant failure rate 2.9% per year
- Previous studies mostly from North America
- Recent work has suggest increased mortality following graft failure
- Analyses limited by choice of control group



Background (2)

Reference	Country	Number of cases	Mortality risk	Control group
Fernandez-Fresnedo G. et al Trans Proc (2008)	Spain	74	RR 2.05 (95% CI 1.26-3.35)	194 incident cohort patients
Gill J.S et al KI (2007)	USA	5,461	17.9/100 pat yrs (95%CI 15.7-20.3)	89,202 wait-listed patients 47,433 functioning transplants
Kaplan B. et al AJT (2002)	USA		Annual adjusted death rate 9.42%	78,564 transplant recipients
Knoll G. et al AJT (2005)	Canada	607	Adjusted HR 3.39 (95% CI 2.75-4.16)	4,136 functioning transplants
Rao P.S. et al NDT (2005)	Canada	675	Adjusted HR 0.9 (95% CI 0.75-1.09)	26,632 incident RRT patients
Rao P.S. et al AJKD (2007)	USA	10,748	HR1.78 (95%CI 1.71-1.86)	175,436 patients wait-listed



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Methods (1)

- UKRR data
- **Cases:** Patients starting dialysis after 1st transplant failure 01/01/2000 - 30/09/2008
- **Controls:** Patients starting RRT on dialysis 01/01/2000 - 30/09/2008, and wait-listed for transplantation within 2 years
- Followed to death, or loss to follow up, or 31/12/2008
- Censored if transplanted
- Exclusions: <18 yrs, missing primary renal diagnosis



Methods (2)

- Kaplan-Meier survival
- Hazard ratios calculated using Cox regression, adjusted for:
 - Age (linear)
 - Sex
 - Diabetes
 - Age x diabetes interaction
 - Ethnicity (missing kept in as “missing”)
 - Dialysis modality

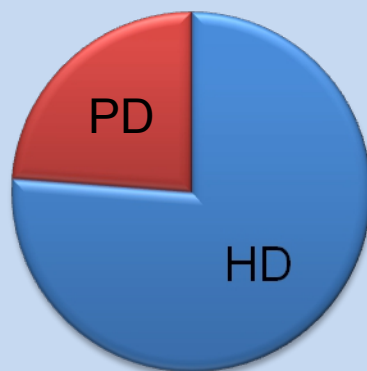
Results (1):

• Cases

3,417 patients

Mean age: 47.9 yrs

Modality:

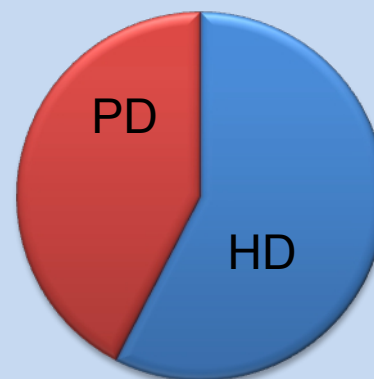


• Controls

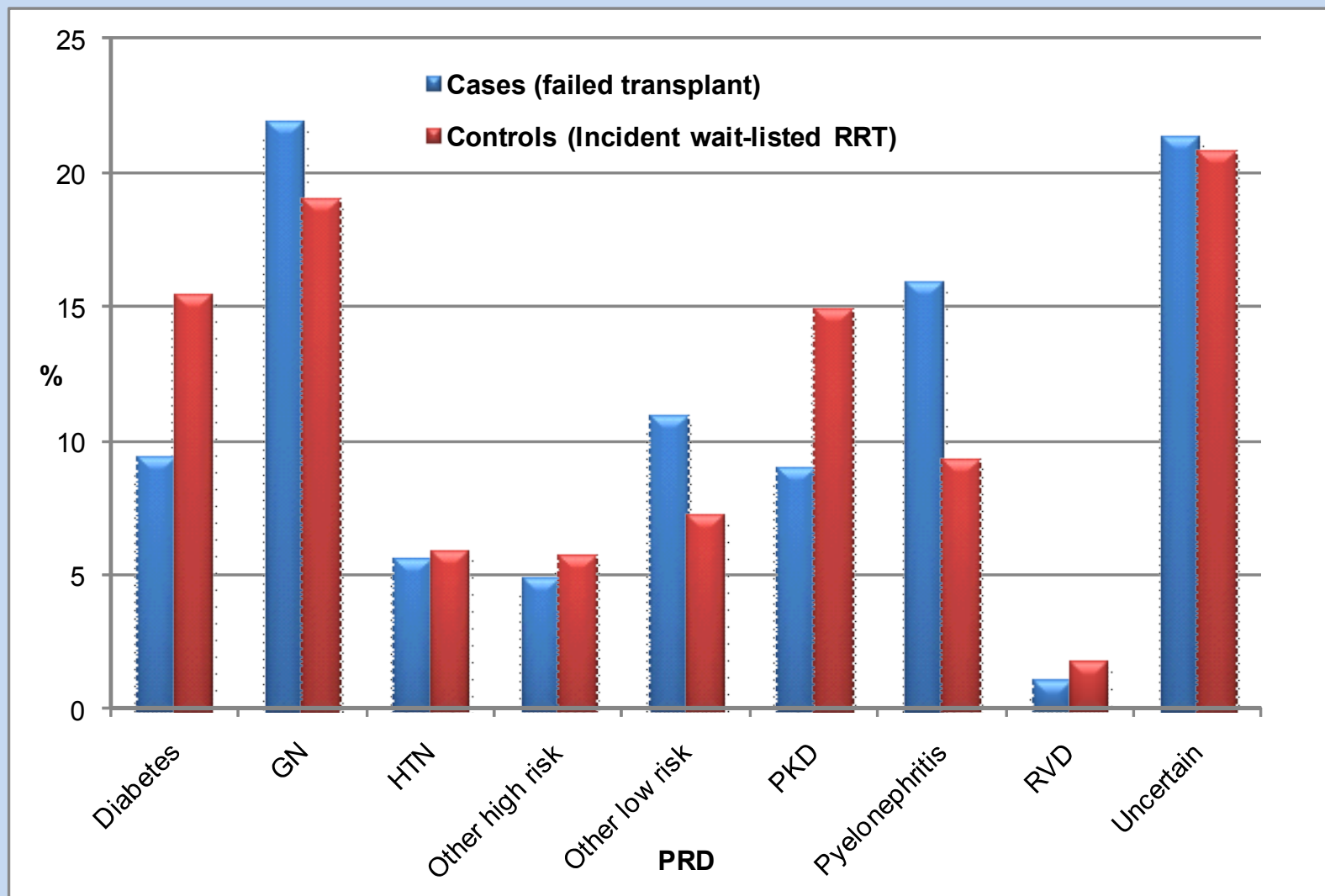
11,280 patients

Mean age: 47.4 yrs

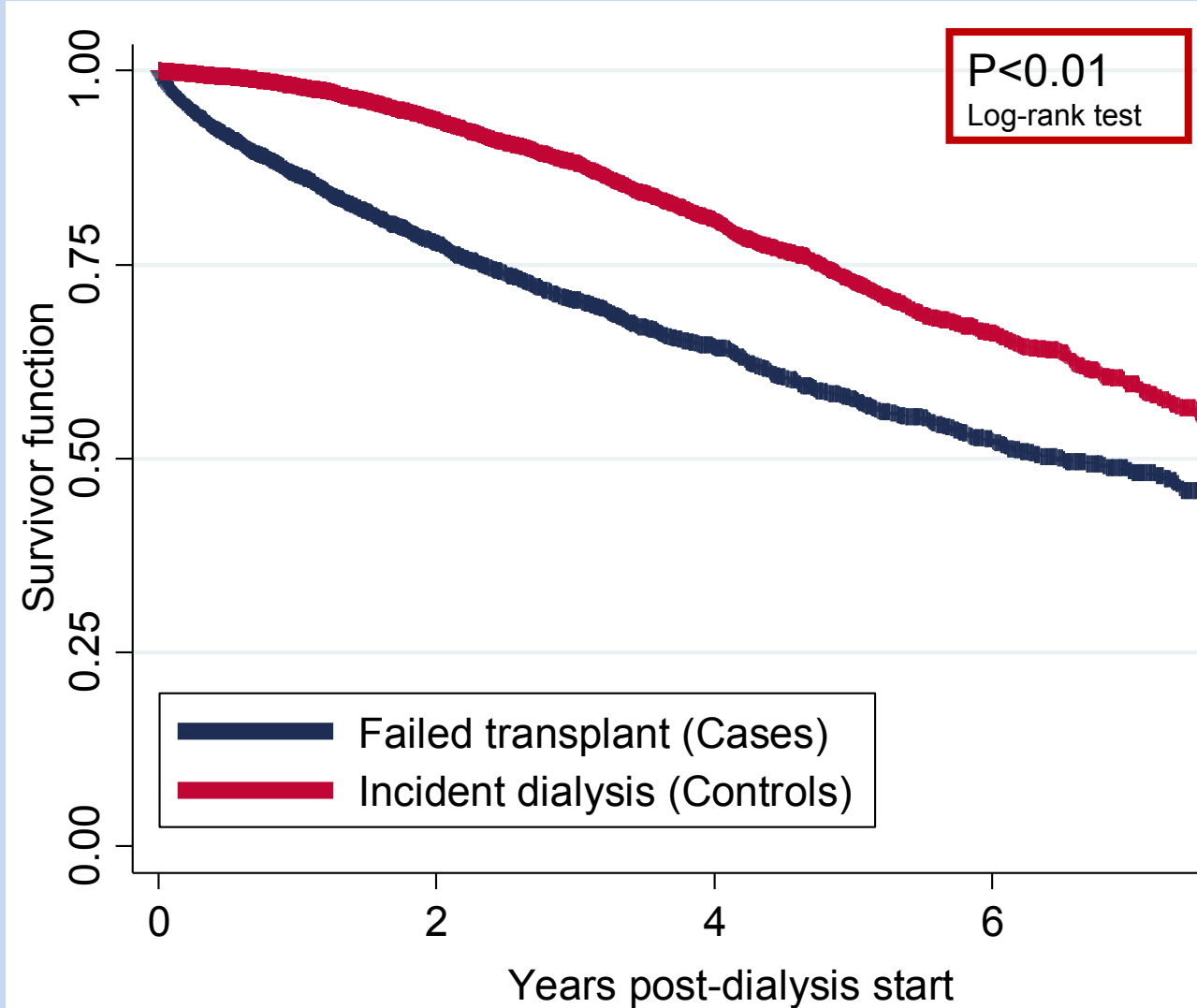
Modality:



Results (2): PRD



Results (3): KM survival (unadjusted)



Results (4): Risk of death in cases vs. controls



	Unadjusted HR					
HR 0-90 days	5.1					
HR 90-365 days	4.1					
HR 1-2 years	3.2					
HR 2-3 years	2.0					
HR 3-5 years	1.1					
HR 5+ years	0.9					

P <0.01

Results (5): Risk of death in cases vs. controls



	Unadjusted HR	+ age				
HR 0-90 days	5.1	5.3				
HR 90-365 days	4.1	4.2				
HR 1-2 years	3.2	3.4				
HR 2-3 years	2.0	2.3				
HR 3-5 years	1.1	1.4				
HR 5+ years	0.9	1.1				

P <0.01

Results (6): Risk of death in cases vs. controls



	Unadjusted HR	+ age	+ sex			
HR 0-90 days	5.1	5.3	5.3			
HR 90-365 days	4.1	4.2	4.3			
HR 1-2 years	3.2	3.4	3.4			
HR 2-3 years	2.0	2.3	2.3			
HR 3-5 years	1.1	1.4	1.4			
HR 5+ years	0.9	1.1	1.1			

P <0.01

Results (7): Risk of death in cases vs. controls



	Unadjusted HR	+ age	+ sex	+ DM + DM*age		
HR 0-90 days	5.1	5.3	5.3	5.4		
HR 90-365 days	4.1	4.2	4.3	4.3		
HR 1-2 years	3.2	3.4	3.4	3.7		
HR 2-3 years	2.0	2.3	2.3	2.6		
HR 3-5 years	1.1	1.4	1.4	1.5		
HR 5+ years	0.9	1.1	1.1	1.2		

P <0.01

Results (8): Risk of death in cases vs. controls



	Unadjusted HR	+ age	+ sex	+ DM + DM*age	+ ethnicity	
HR 0-90 days	5.1	5.3	5.3	5.4	5.4	
HR 90-365 days	4.1	4.2	4.3	4.3	4.5	
HR 1-2 years	3.2	3.4	3.4	3.7	3.7	
HR 2-3 years	2.0	2.3	2.3	2.6	2.6	
HR 3-5 years	1.1	1.4	1.4	1.5	1.5	
HR 5+ years	0.9	1.1	1.1	1.2	1.2	

P <0.01

Results (9): Risk of death in cases vs. controls



	Unadjusted HR	+ age	+ sex	+ DM + DM*age	+ ethnicity	+ HD or PD
HR 0-90 days	5.1	5.3	5.3	5.4	5.4	4.2
HR 90-365 days	4.1	4.2	4.3	4.3	4.5	4.1
HR 1-2 years	3.2	3.4	3.4	3.7	3.7	3.5
HR 2-3 years	2.0	2.3	2.3	2.6	2.6	2.6
HR 3-5 years	1.1	1.4	1.4	1.5	1.5	1.5
HR 5+ years	0.9	1.1	1.1	1.2	1.2	1.3

P <0.01

Results (10): Sub group

- 504 Pre-emptive transplants
- Controls – incident wait-listed dialysis patients

	0-90 days	90-365 days	1-2 years	2-3 years	3-5 years
Unadjusted HR	3.0	3.2	2.7	0.96	0.8
Adjusted HR	3.7	4.2	3.5	1.5	1.4
• All failed transplants					
Adjusted HR	4.2	4.1	3.5	2.6	1.5



Limitations

- Identifying best control group
 - Controls not exposed to long term immunosuppression
 - Cases longer cumulative time on RRT
 - Impact of comorbidity
- Data capture issues
 - UKRR coverage only 100% since 2008
 - Patients with graft failure, dialysed for a short time before death ? Not captured
- Missing data

Conclusions

- Significant increase in mortality risk in the 1st year following transplant failure
 - **4.1 x more likely to die** between 90-365 days if returning to dialysis after graft failure rather than starting dialysis as initial RRT
 - **4.2 x more likely to die** between 90-365 days if starting dialysis after failure of pre-emptive transplant
- Increased risk of death continues to 5 years post-graft failure

Future work (1)

Potentially modifiable variables

- Sudden vs. predictable graft loss
- Duration of immunosuppression
- Transplant nephrectomy
- Dialysis modality
- Attainment of RA/KDOQI targets
- Nutritional status
- Listing for retransplantation
- Frequency of outpatient clinics
- Structure/staffing of clinic
- Vascular access at dialysis start
- Contact with renal services/admissions



Future work (2)

- HES linkage: analysis of morbidity and transplant nephrectomy rates
- Case control study examining patient and centre level factors associated with survival after graft failure
- European registry collaboration (planned 2011):
 - increase statistical power
 - geographical variation
 - allow analysis of cause-specific death



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 - UKRR transplant sub-group
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 - NHS Blood and Transplant



Transplant CKD management

Parameter	Stage 5T (eGFR <15)	Dialysis Patients
Hb mean	11.0 ± 1.8	11.7
Hb % < 10 g/dl	32 **	14
Hb % < 11 g/dl	51 **	30
Ferritin median ng/ml	202 **	393
Ferritin % < 100 ng/ml	28 **	6
% Systolic BP > 130 mmHg	74 **	53
% Diastolic BP > 80 mmHg	68 **	62
% Chol > 200 mg/dl	34 **	17

**Chi-square P <0.001

Six-monthly hazard of death, by time on RRT and age band for 1997-2007 incident patients (after 90 days)

