Outcomes in paediatric kidney transplantation

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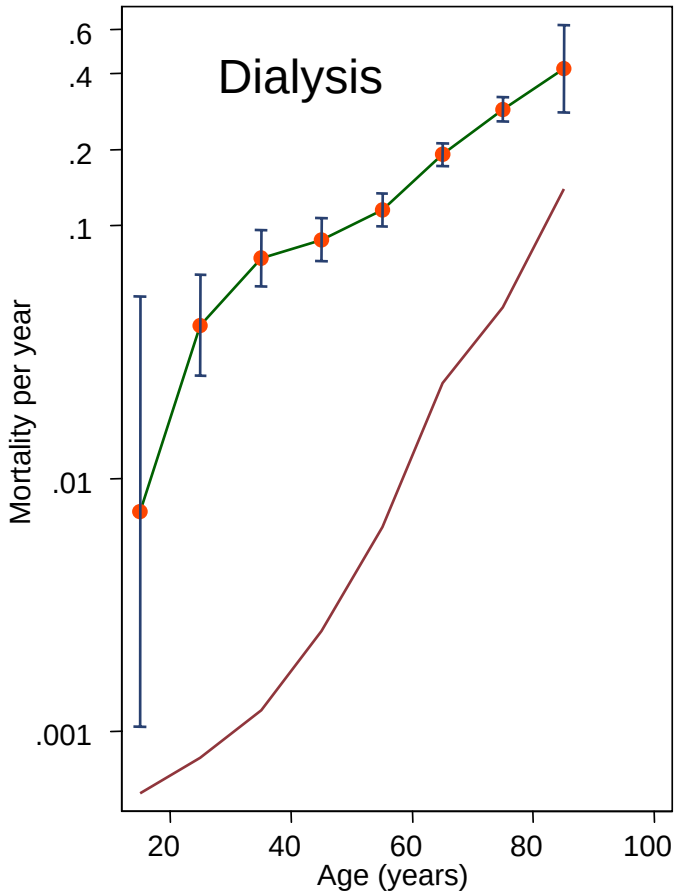
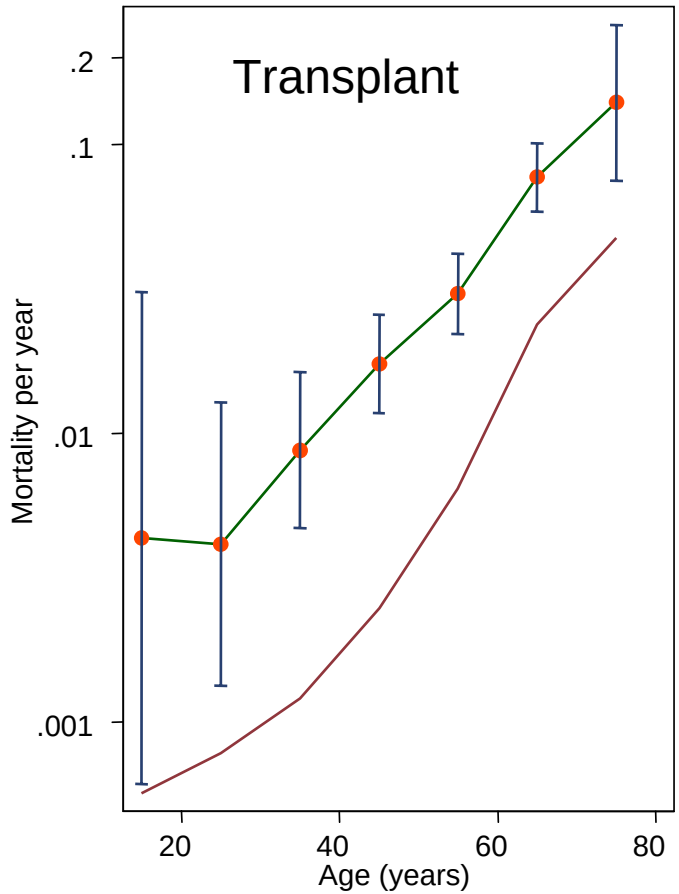
ANZDATA Registry

Introduction

- Over the past 25 years there has been substantial improvement in the outcomes among adult recipients, particularly in transplantation
  - Primarily due to reduced rates of graft loss in the short term
  - Longer term rates of graft loss have not changed
  - Rates of rejection continue to fall
- Challenges remain

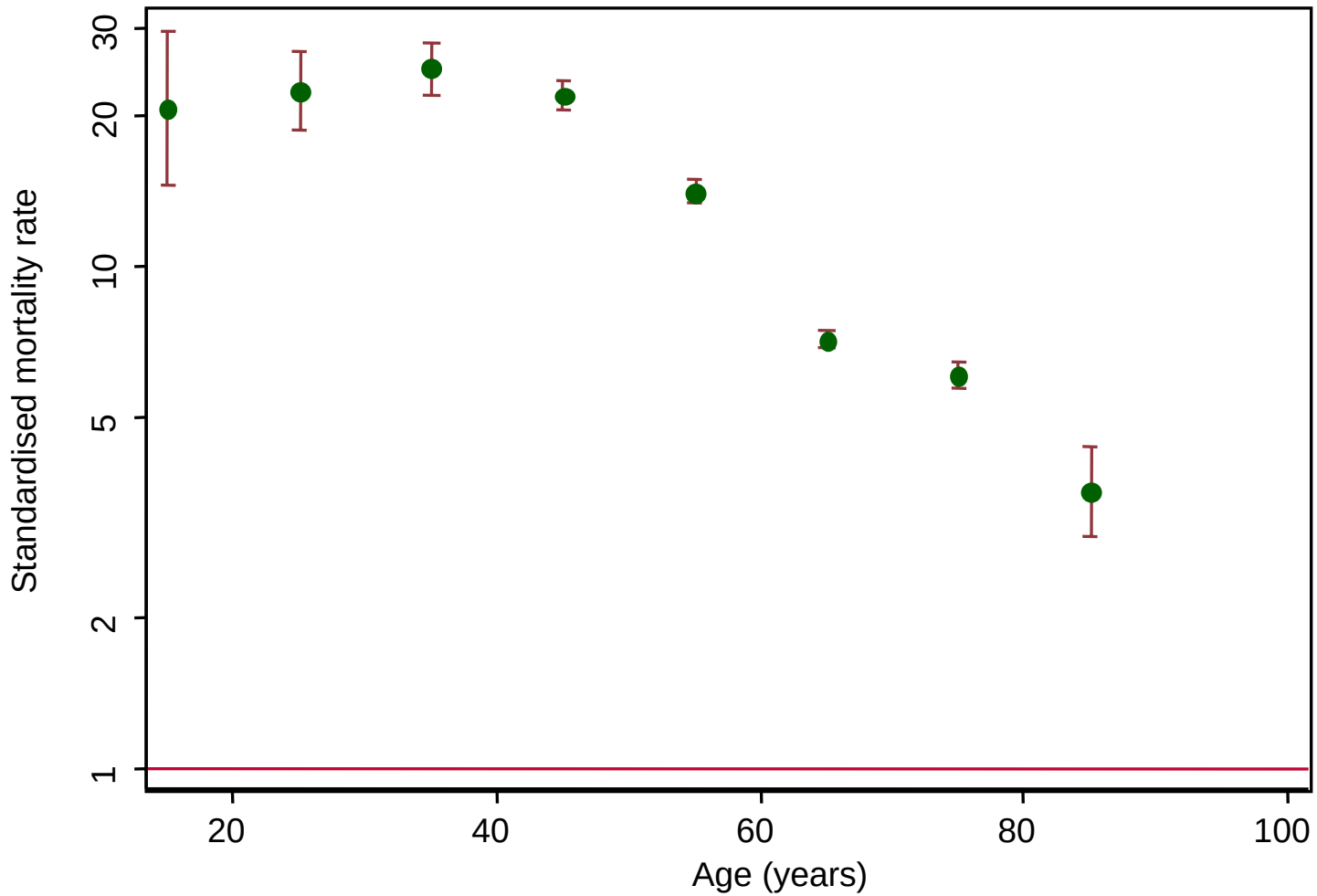
The challenge





Age specific mortality of prevalent RRT patients, Australia only, ANZDATA and ABS data for year 2002

The challenge



Standardised mortality rate ratios for prevalent RRT patients in Australia vs Australia population, 1997-2002

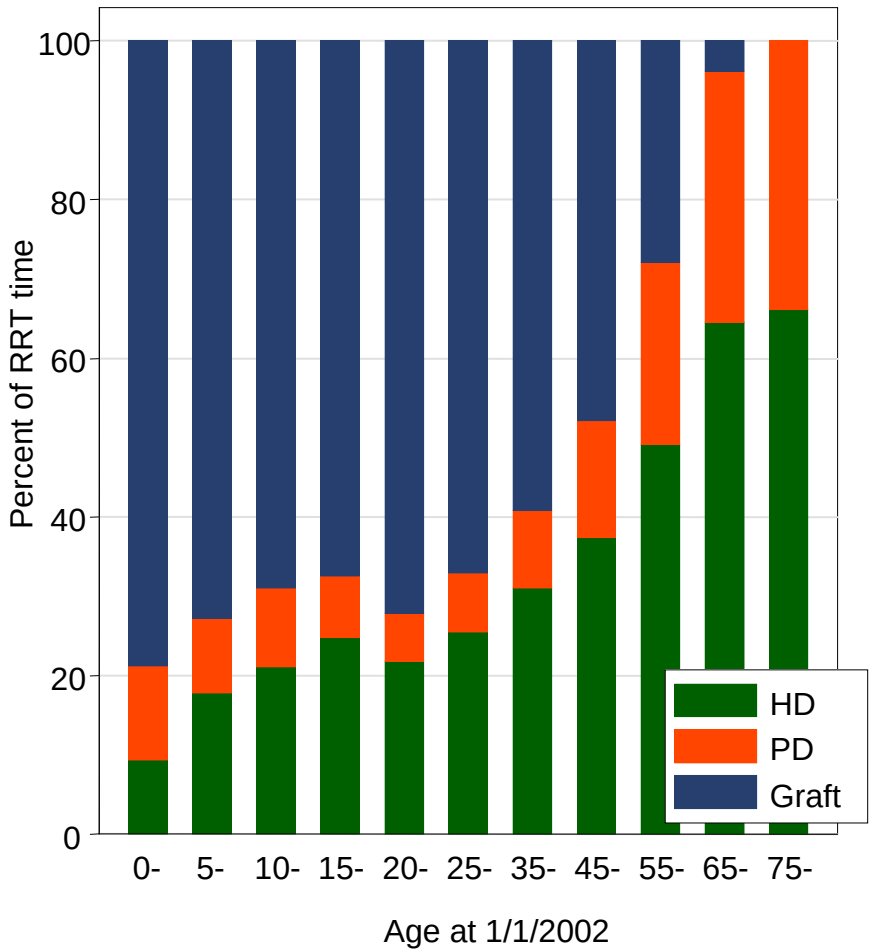
The challenge in kids

Year of start	0-4	5-9	10-14	15-19
1963-72	116 [37 to 358]*	236 [98 to 566]	111 [64 to 198]	52 [36 to 75]
1973-82	63 [26 to 151]	122 [75 to 199]	71 [49 to 104]	20 [14 to 28]
1983-92	30 [16 to 57]	30 [13 to 73]	37 [23 to 59]	19 [13 to 27]
1993-02	32 [17 to 59]	94 [39 to 226]	35 [16 to 78]	30 [18 to 49]

Age specific mortality rate ratios for 10 year survival of children beginning renal replacement therapy in Australia, 1963-2002, relative to the age-specific Australian population rates. *McDonald & Craig, NEJM, June 24, 2004*

Why focus on transplantation?

- Transplantation is the mainstay of paediatric RRT
  - More so than older age groups
- However, there are substantial differences in
  - Donor source
  - Balance of likely outcomes (death vs graft failure)
  - Treatment environment
  - Immunosuppressive treatment
- What about outcomes?



Person time by prevalent age and modality for 2002, Australia & NZ

Introduction

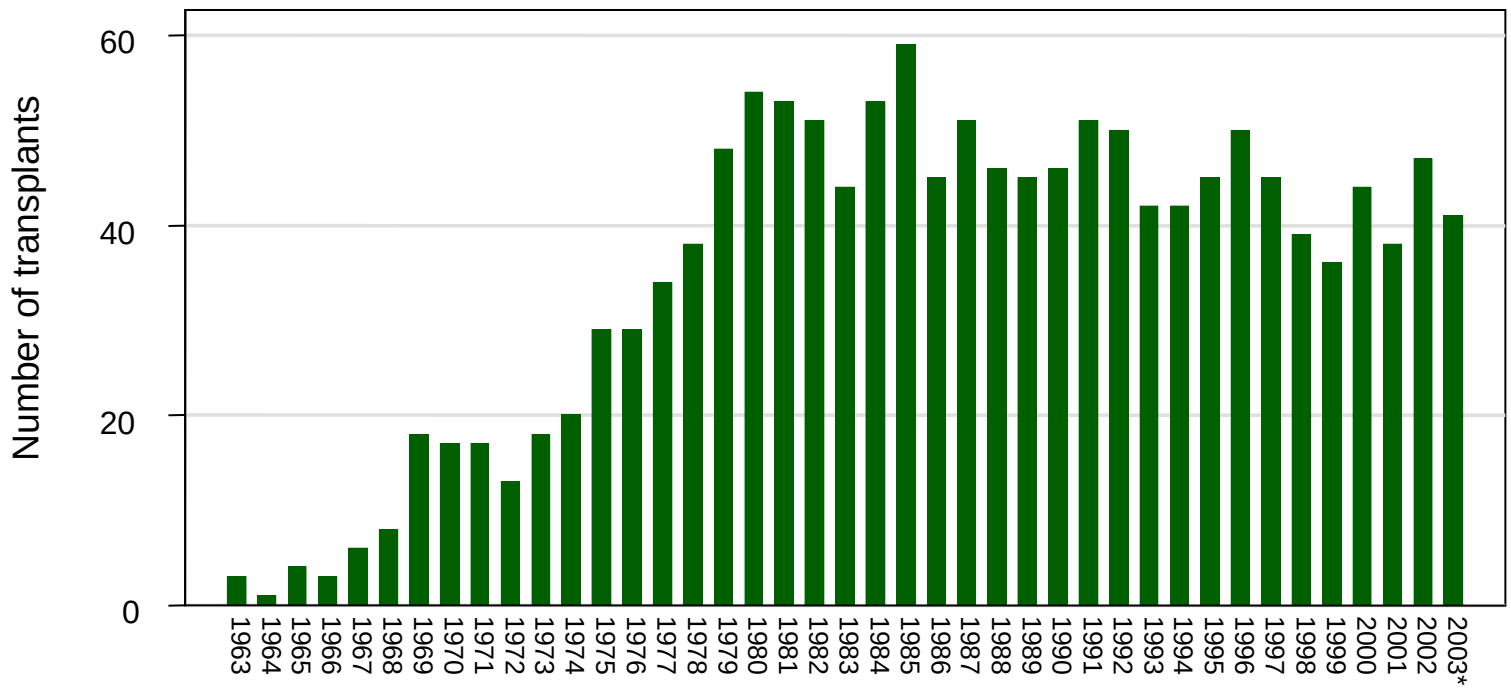
- Similarly to adults, the mortality of transplants recipients is substantially lower than comparably aged children receiving dialysis treatment.
  - Mortality 1/4 compared to those receiving dialysis therapy in recent analysis (McDonald & Craig, NEJM, 2004)

Methods

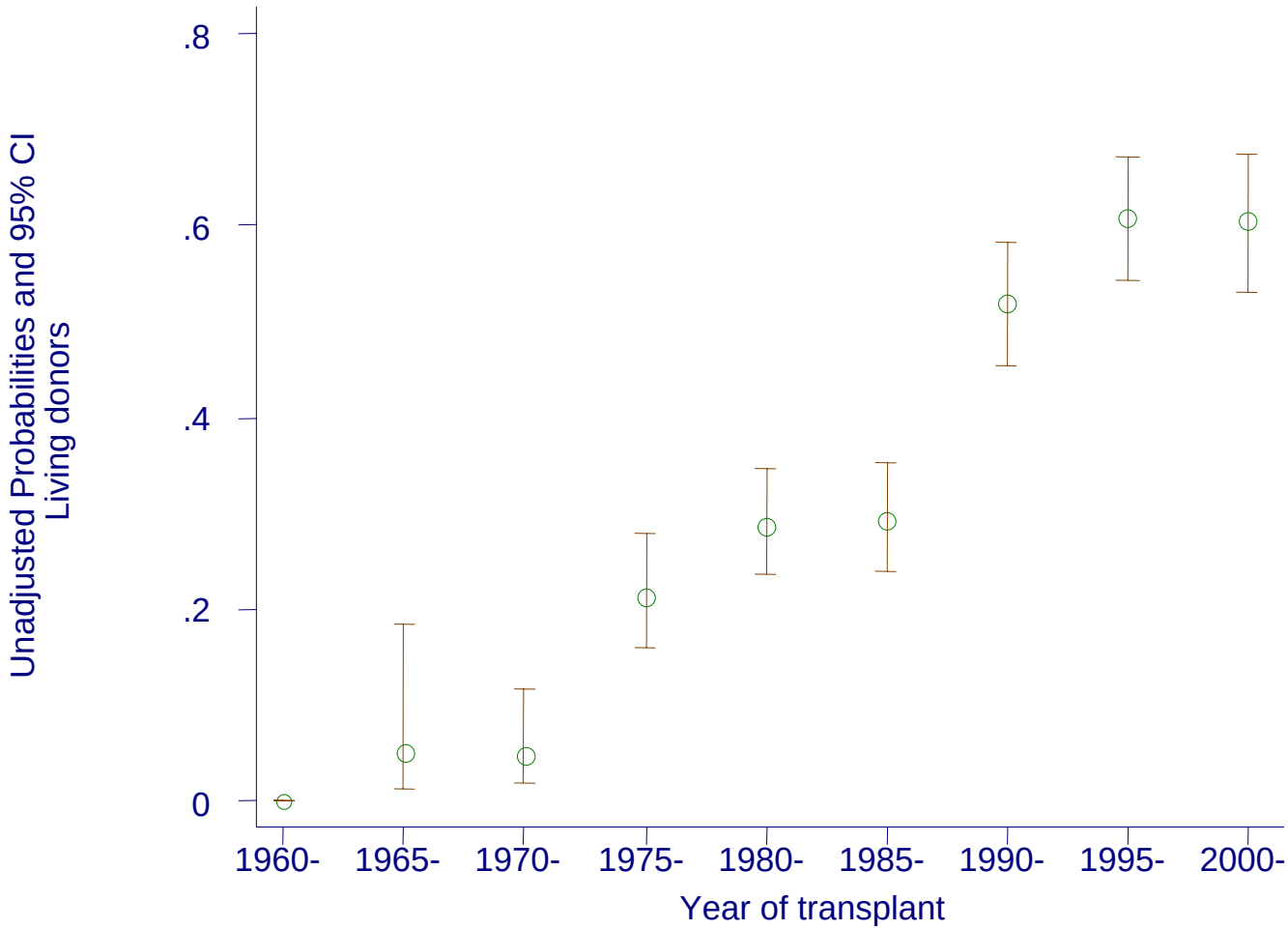
- Examination of
  - Recent practice changes
  - 2 outcomes with a focus on paediatric recipients (<20 years of age at time of transplantation)
    - Long term graft failure
    - Rejection

Results

- 1423 grafts to recipients <20 years of age
  - 1235 first grafts
  - 543 (38%) from living donors

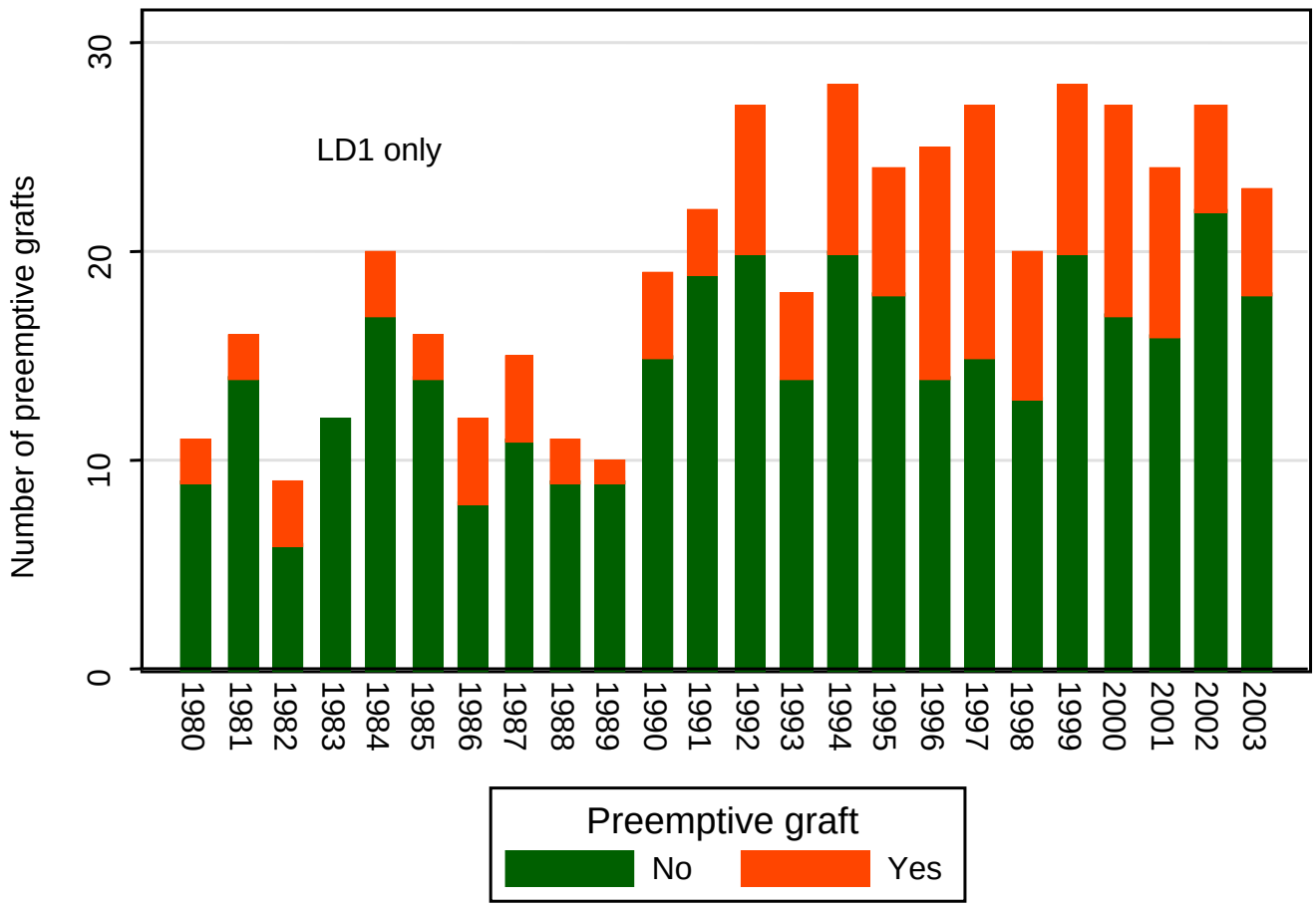


Proportion LD's



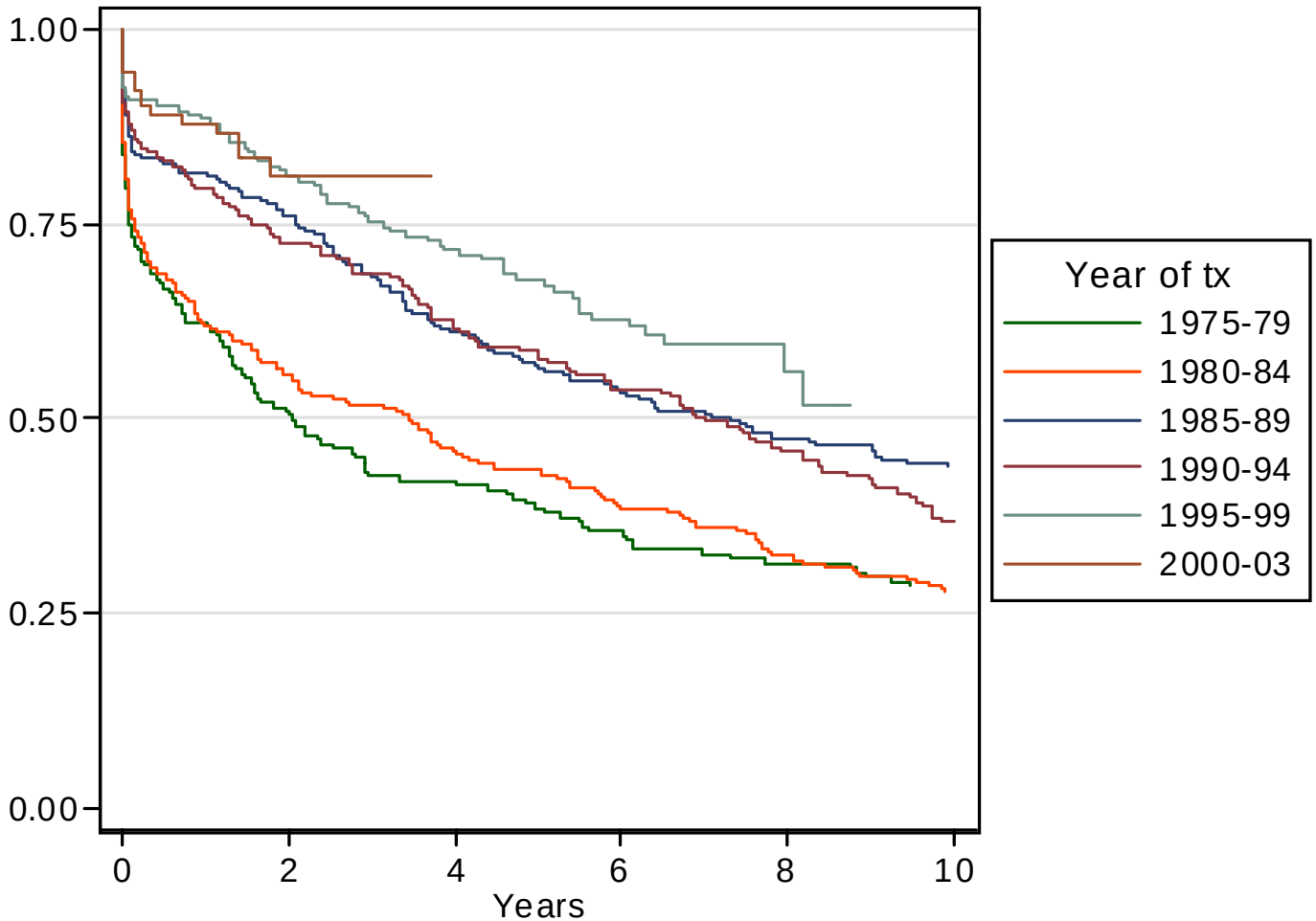
Proportion of grafts per year from living donors, Australia & New Zealand

Preemptive grafts



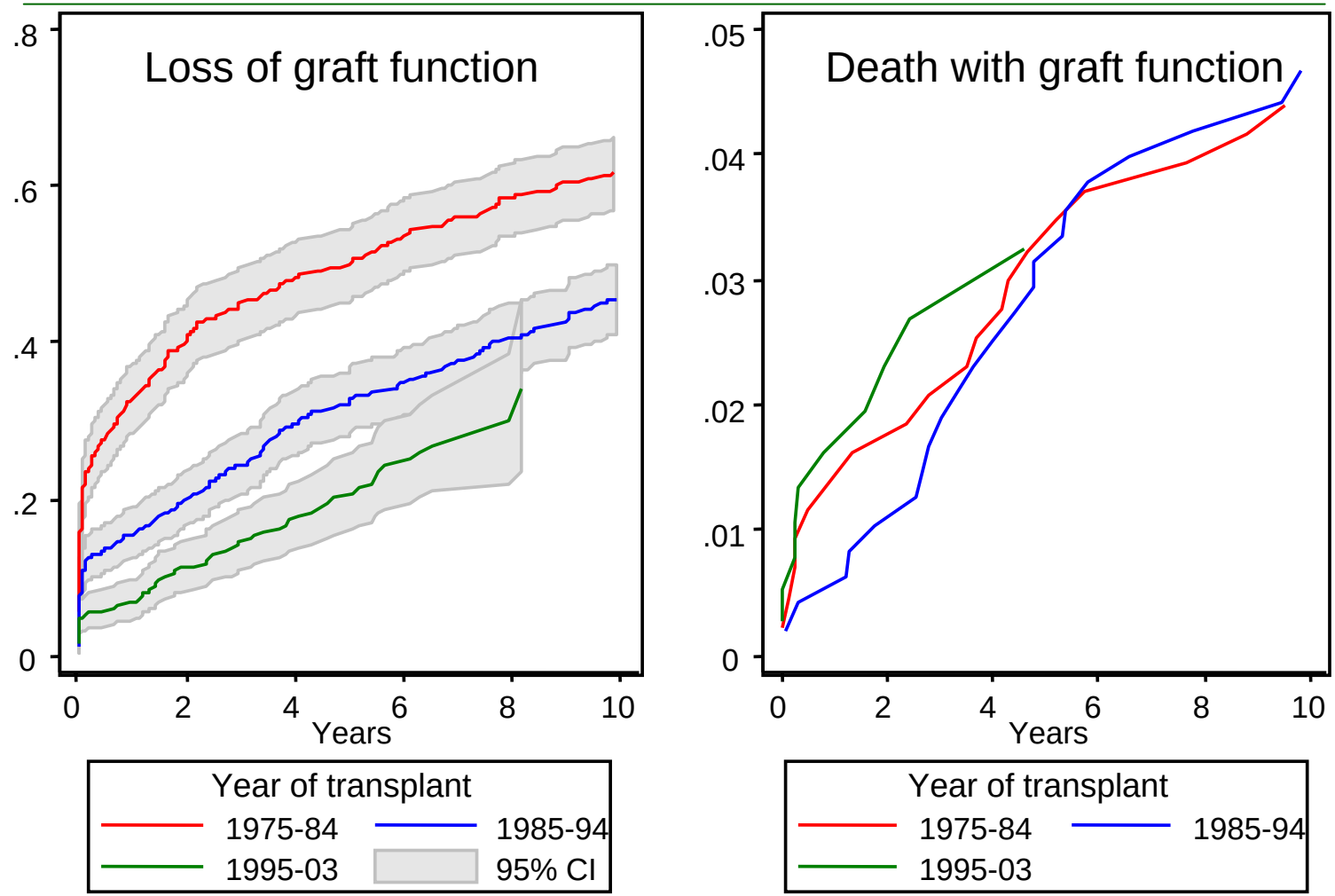
Number of pre-emptive grafts per year, Australia & New Zealand, LD1 only. P<0.01 for proportion of pre-emptives 1980-89 vs 1990-2003.

Graft survival over time



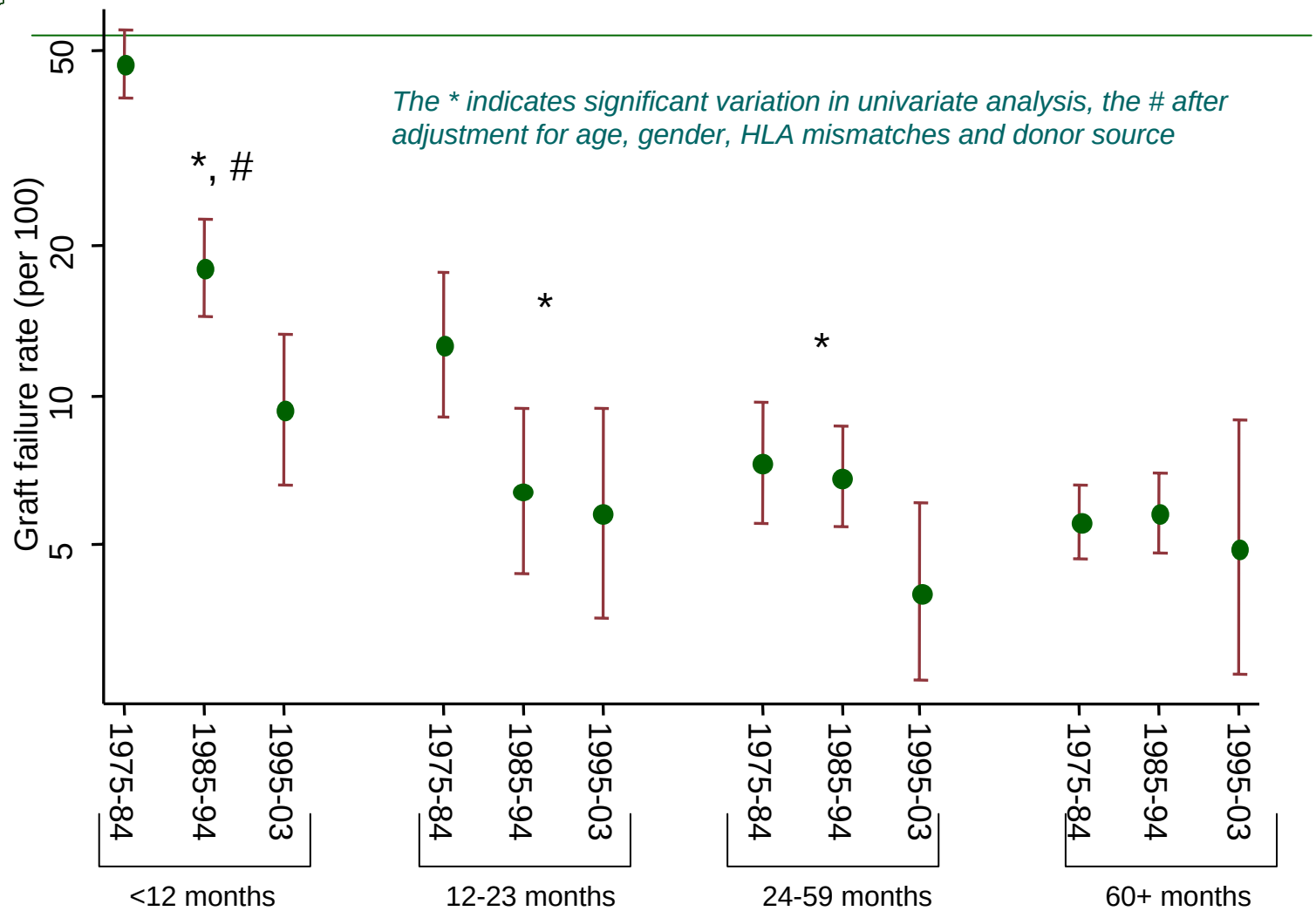
Kaplan-Meier curves, all grafts in Australia & New Zealand, recipients <20 years, adjusted for live vs. deceased donor

Competing risks



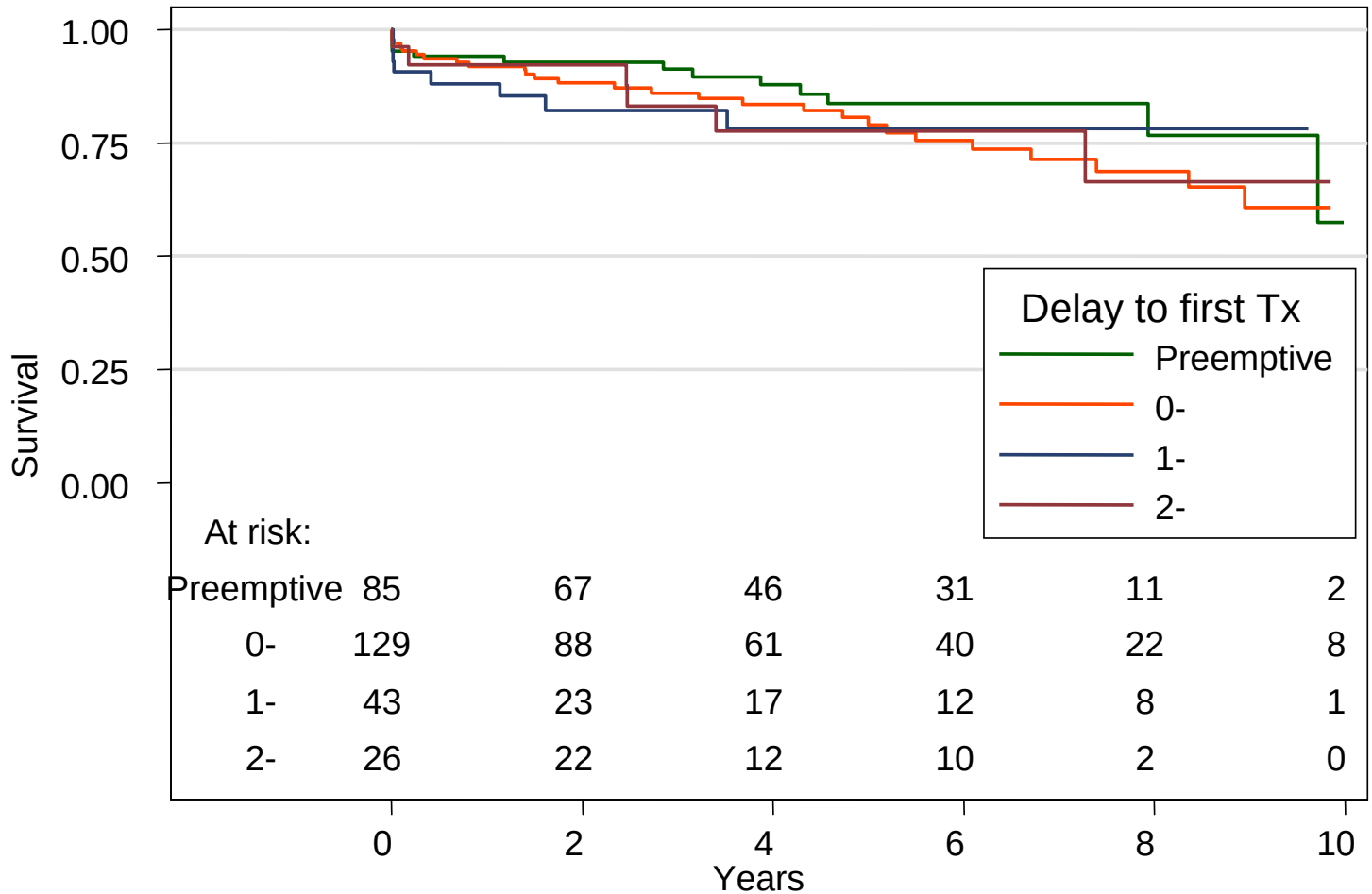
Cumulative incidence of graft failure, all grafts <20 years at Tx, adjusted for competing risks, by year of transplant. No significant differences among groups for death with graft function

Longer term outcomes



Graft failure rate by followup period, all grafts <20 years at transplant, Australia & NZ.

Time to transplantation

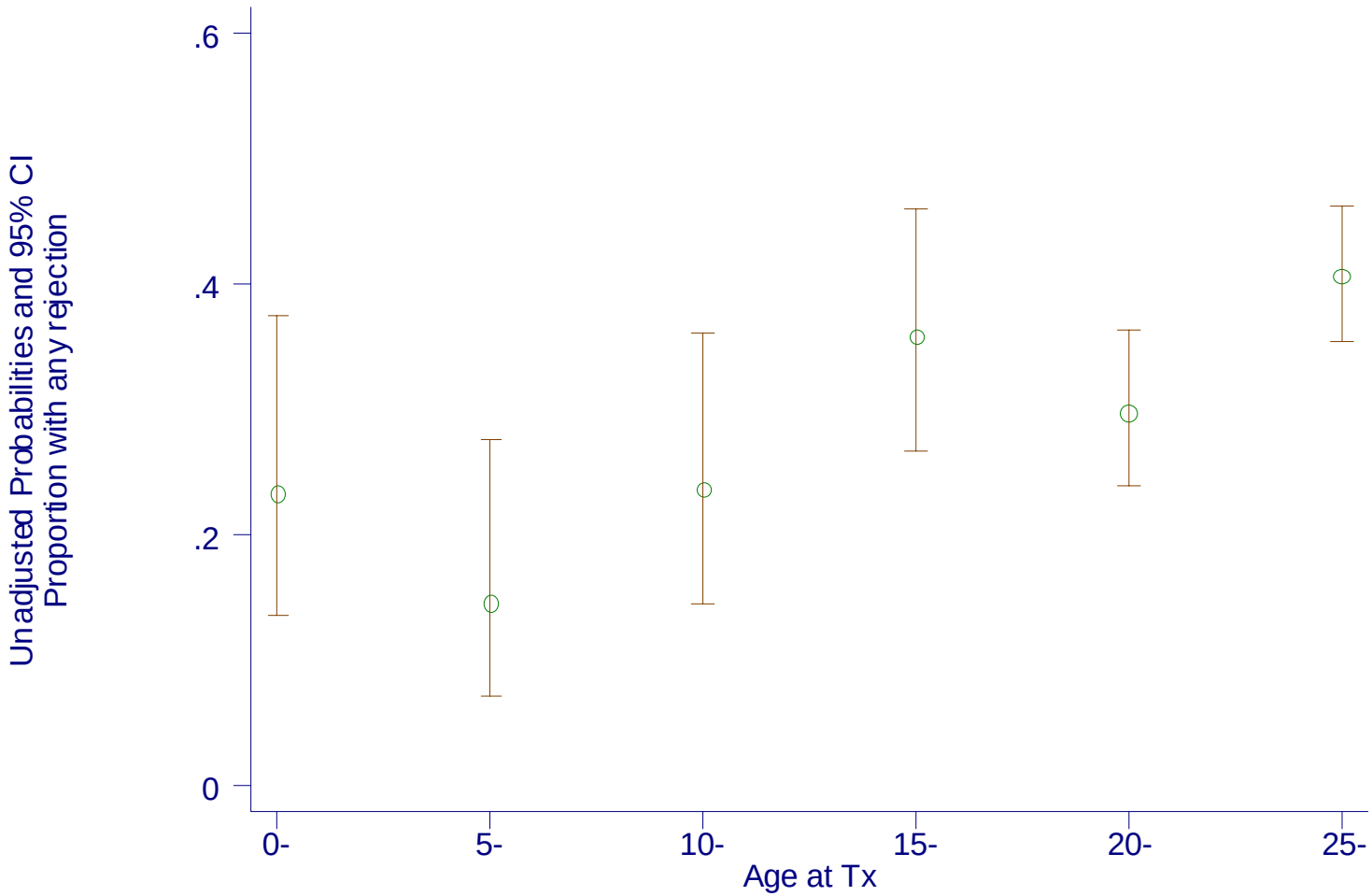


Graft survival of grafts performed >=1993 in Australia & New Zealand, by delay to first transplant, LD1 only to 30 Sep 2003.

Acute Rejection

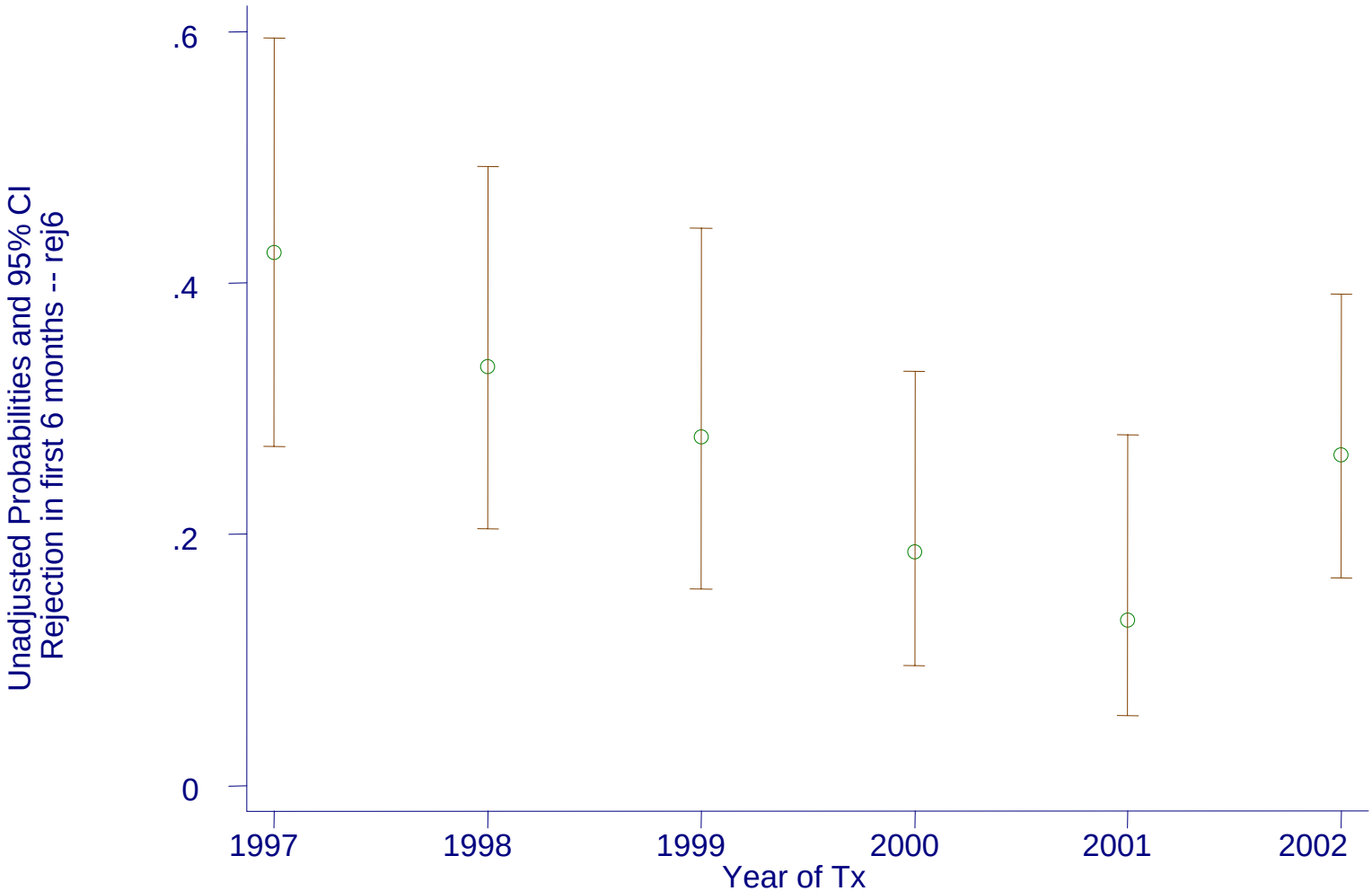
- Reports of renal allograft rejection within 6 months of operation date have been collected by ANZDATA since 1997
  - Since extended to all episodes of rejection
- This analysis includes data from grafts performed between 1 April 97 and 30 March 03, with follow-up to 30 Sep 03
- Relationship examined of age with:
  - occurrence of *any* rejection (< 6 months)

The effect of age



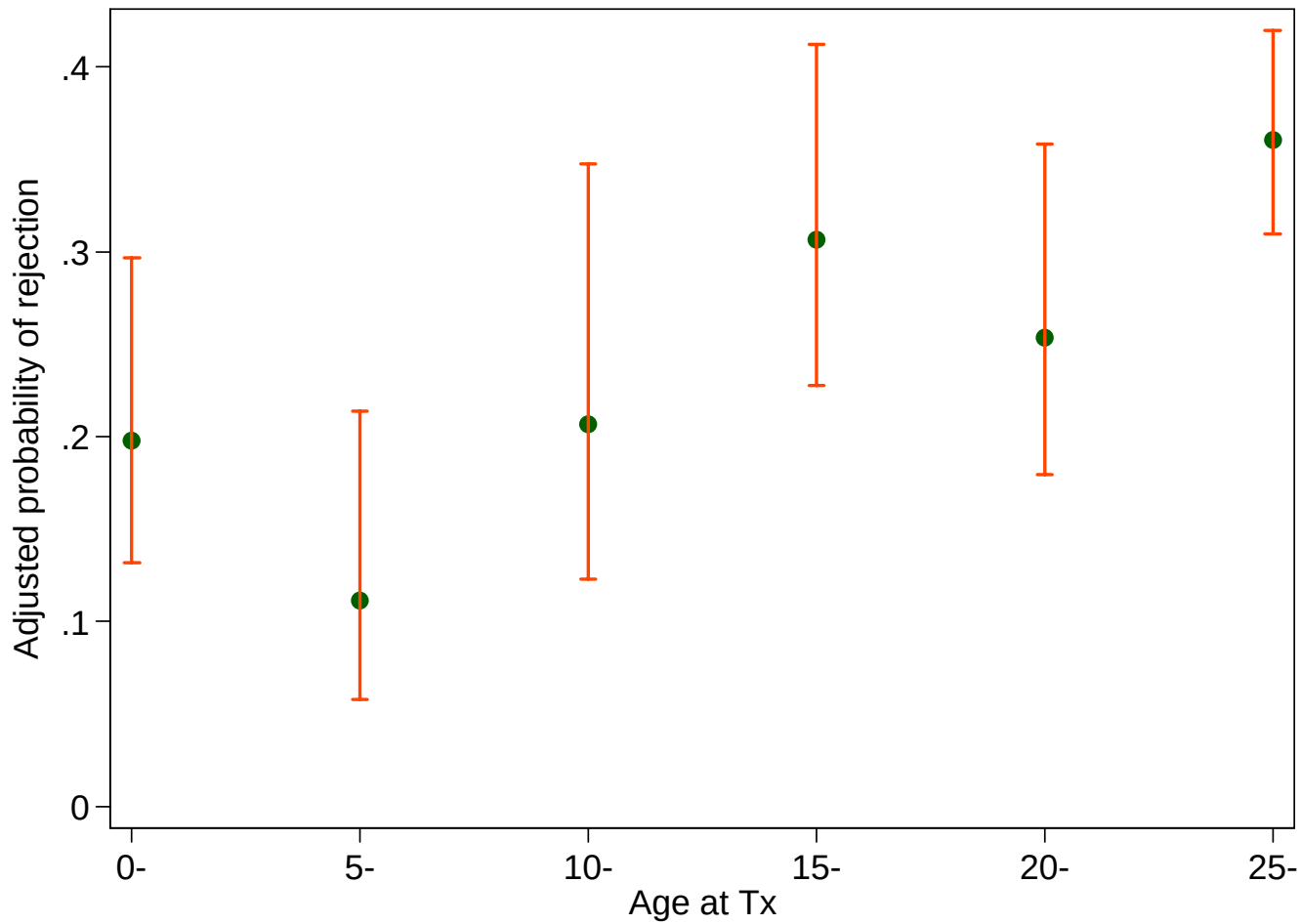
Proportion of grafts to recipients <30 years with any rejection within 6 months

Potential confounders



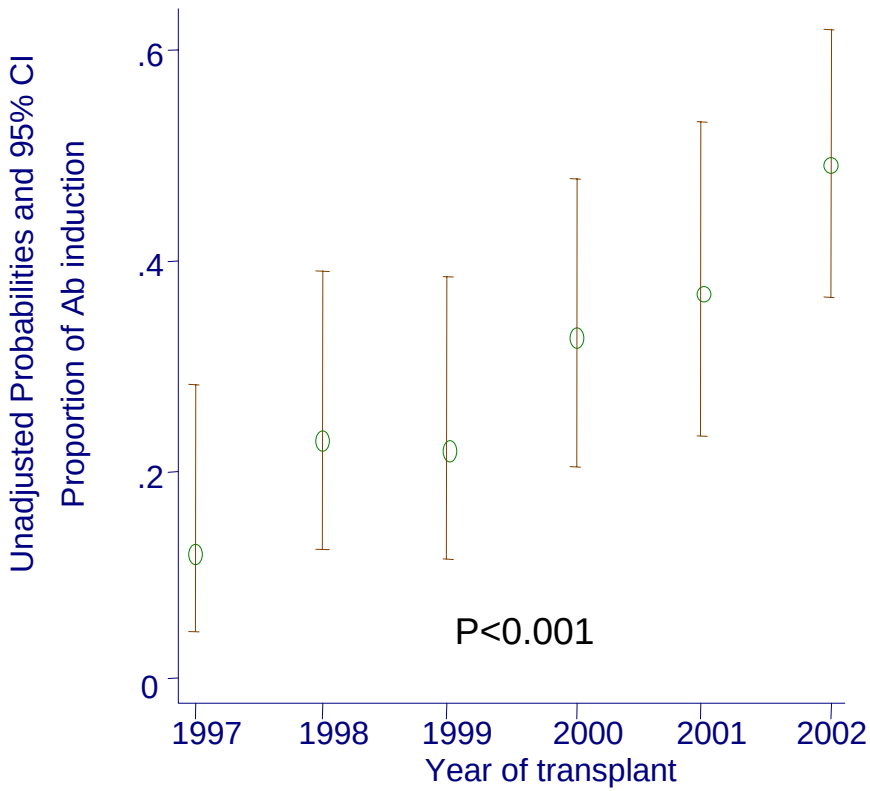
Occurrence of any rejection in the first 6 months post transplant, by year of Tx, age<20 years at time of Tx

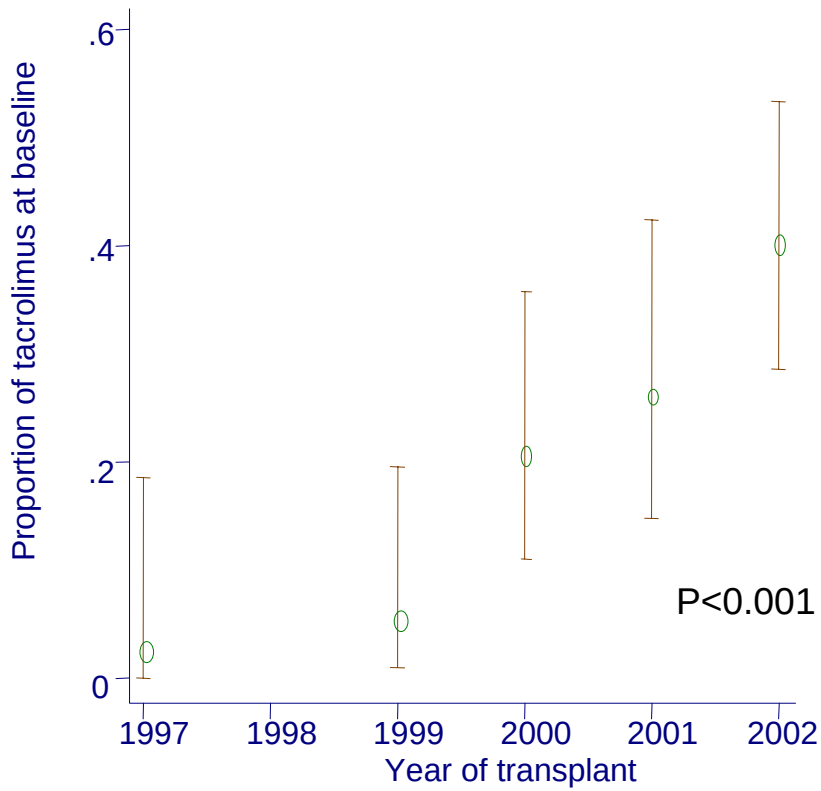
Age after adjustment for patient factors



Probability of any rejection in the first 6 months after adjustment for graft source, maximum PRA, HLA mismatches, year of transplant, gender

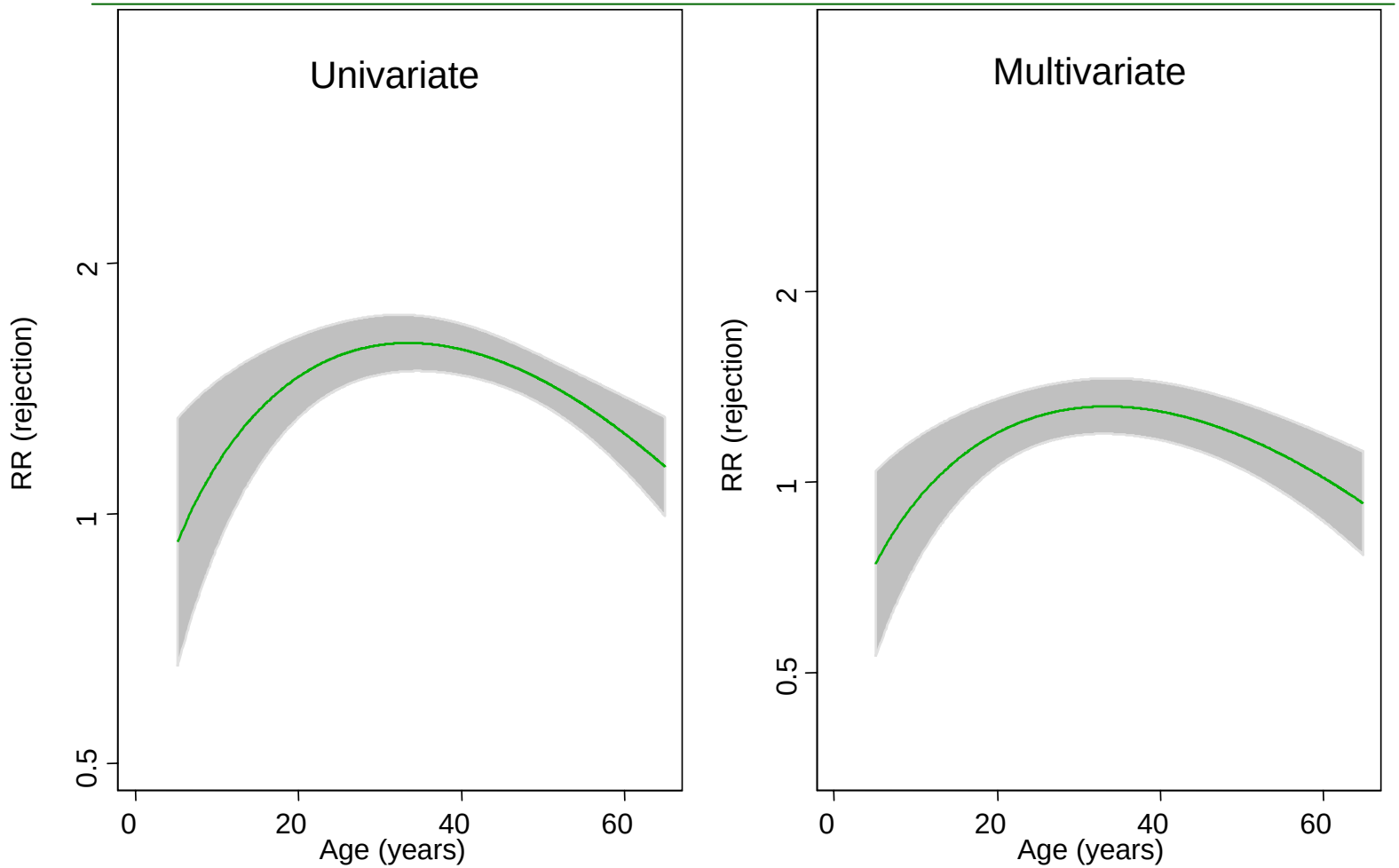
Confounding by treatment factors





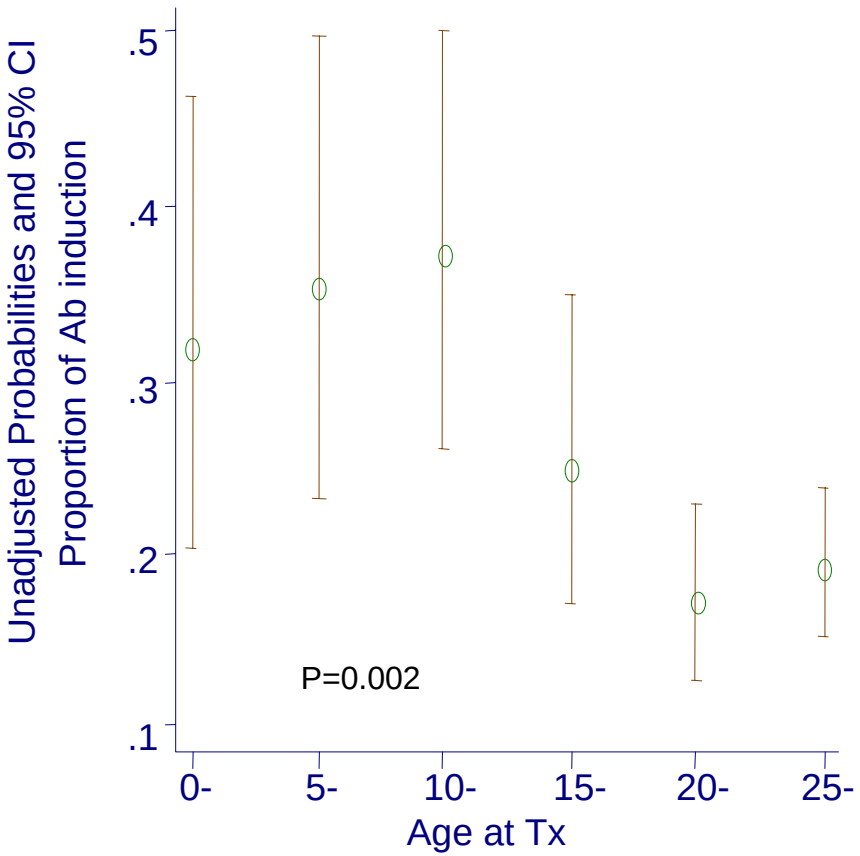
Proportion of transplant recipients <20 years of age receiving either antibody induction therapy or tacrolimus at baseline, by year of surgery

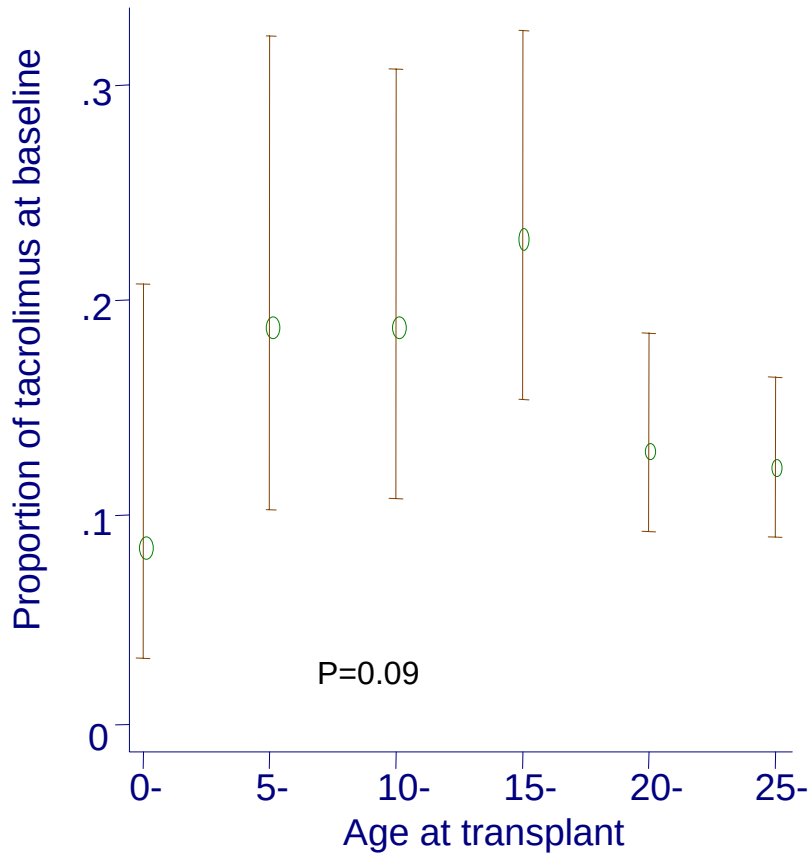
Age continuously



Fractional polynomial models: probability of any rejection in the first 6 months after adjustment for graft source, maximum PRA, HLA mismatches, year of transplant, gender.

Confounding by treatment factors 2

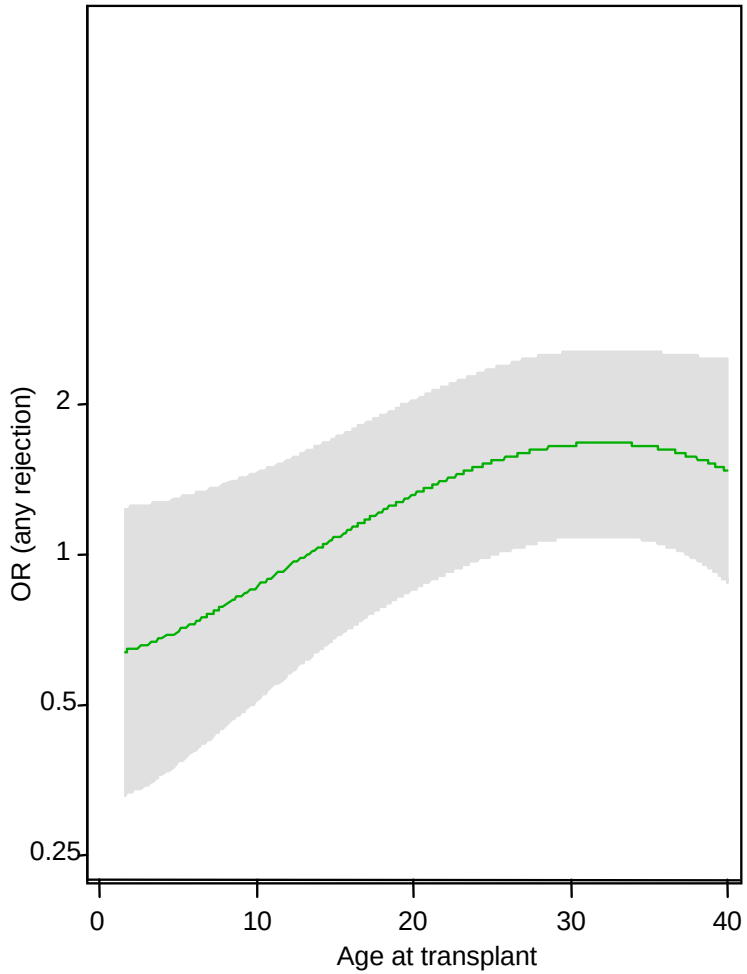




Proportion of transplant recipients <20 years of age receiving either antibody induction therapy or tacrolimus at baseline, by age at time of surgery

Adjustment for confounders

- After adjustment for use of antibody induction and tacrolimus (in addition to the other patient factors), there remains a significant increase in likelihood of rejection with age
  - Appears to peak in the early 30's



Conclusions

- Recent changes in paediatric transplantation include increasing use of LD and preemptive transplantation
- After accounting for these factors, paediatric longer term outcomes show a similar pattern to those observed among adults
  - greater improvement in short term outcomes
  - little improvement over time in longer term outcomes
- Rejection rates appear to rise progressively with age to around 30-35 years

Acknowledgements

- Thank you to all nephrologists, renal nurses and data collection staff in renal units around Australia & New Zealand.