

Long term outcome after renal transplantation

Influence of donor & recipient risk factors and the choice of immunosuppression

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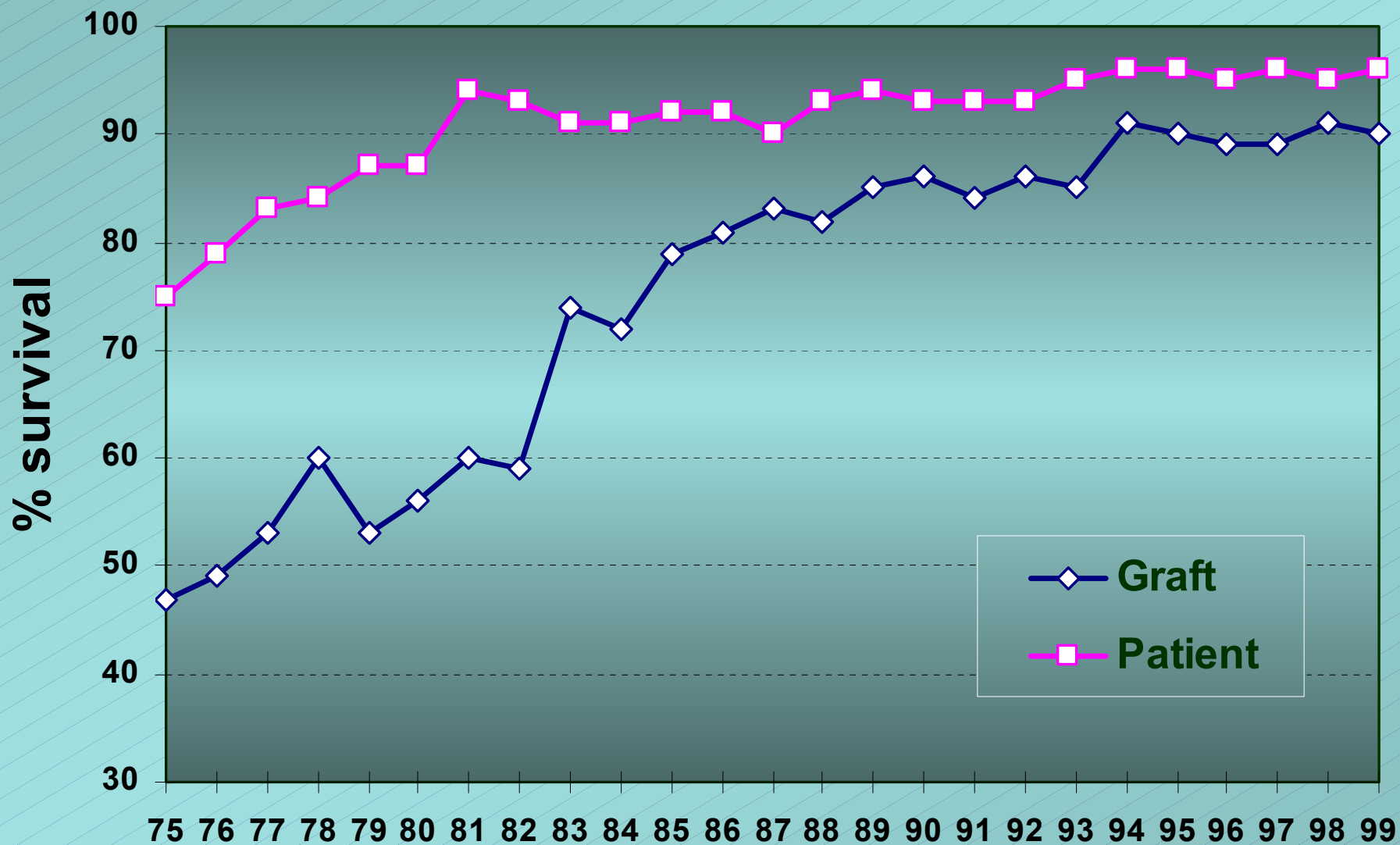
Source of data – *ANZDATA & ANZOD*

- Australia & New Zealand Dialysis & Transplant (ANZDATA) Registry
 - A voluntary registry documenting the outcome of all dialysis & transplant patients in Aus & NZ since 1965
 - 100% reporting and follow-up of ~24,000 patients
- Australia & New Zealand Organ Donor (ANZOD) Registry
 - Has acquired donor information since 1988
- Registries co-located

Long term outcome in renal transplantation

- The short term (1yr) outcome has improved substantially in recent times
- The long term outcome beyond 5 yrs has been little studied
- This study aims to assess the influence of various factors on long term graft (& patient outcome)
- All data is from ANZDATA and ANZOD Registries.

Australia CD1. One year survival 1975-99



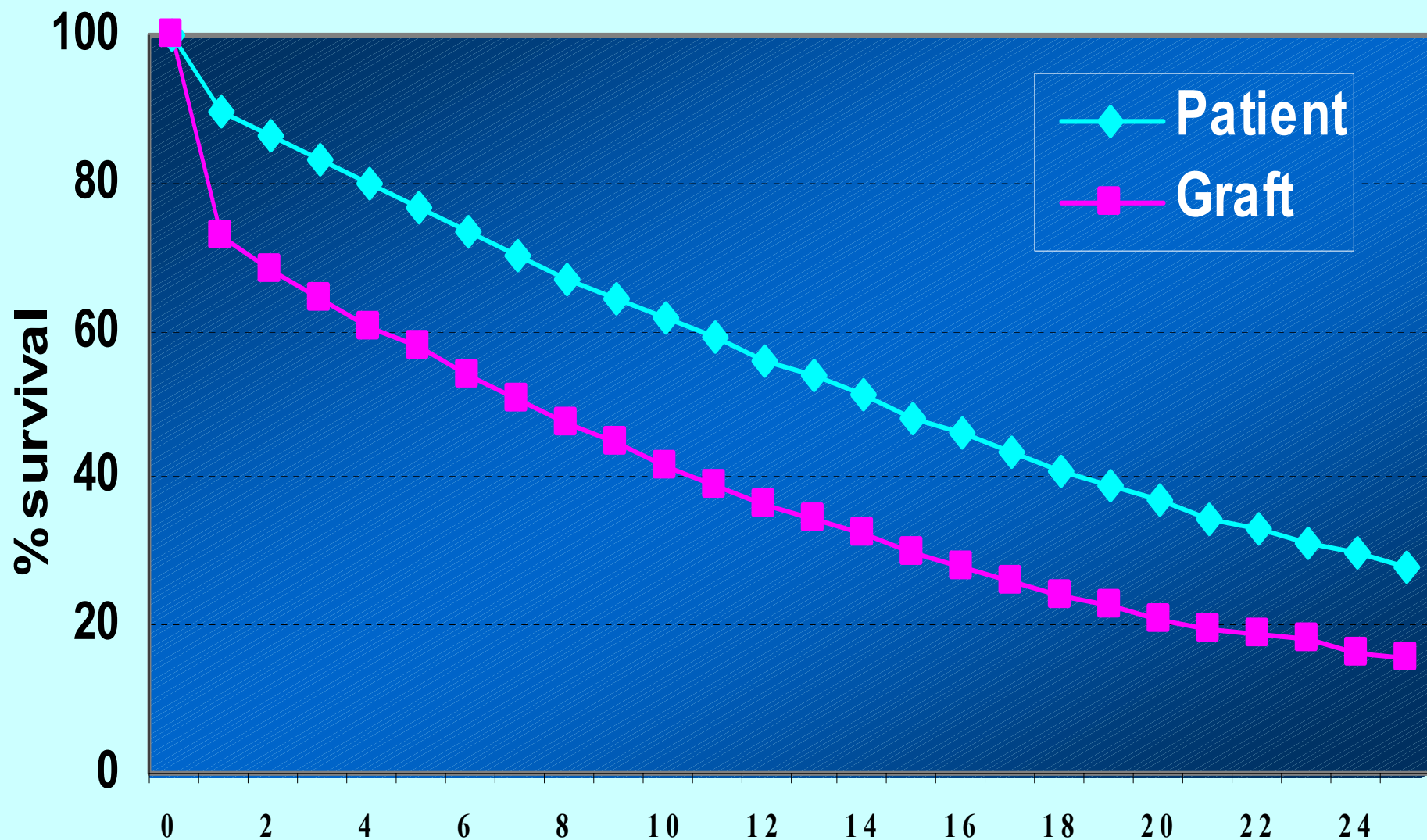
Predictive patient & donor characteristics significantly affecting 1yr survival on multivariate analysis (0n 1993-8 cohort) – Briganti et al

- Donor age $p=0.000$
- HLA mismatches $p=0.000$
- Vascular disease $p=0.002$
- Time on dialysis $p=0.004$
- Year of transplant $p=0.008$
- Allograft source $p=0.044$

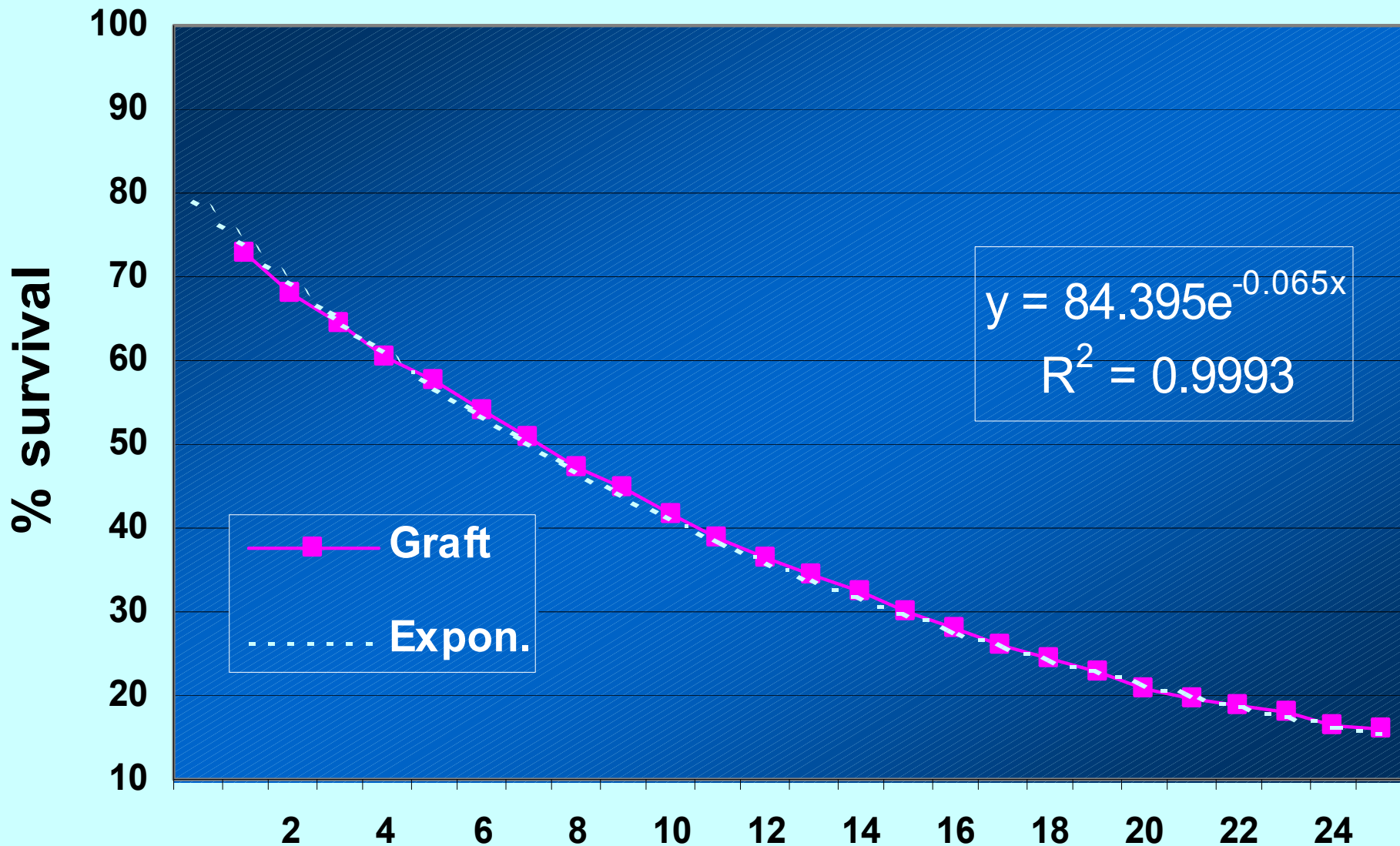
Long term outcome in renal transplantation

- The short term (1yr) outcome has improved substantially in recent times
- The long term outcome in CD1 & LD1 recipients beyond 5 yrs has been little studied
- This study aims to assess the influence of various factors on long term graft (& patient outcome)

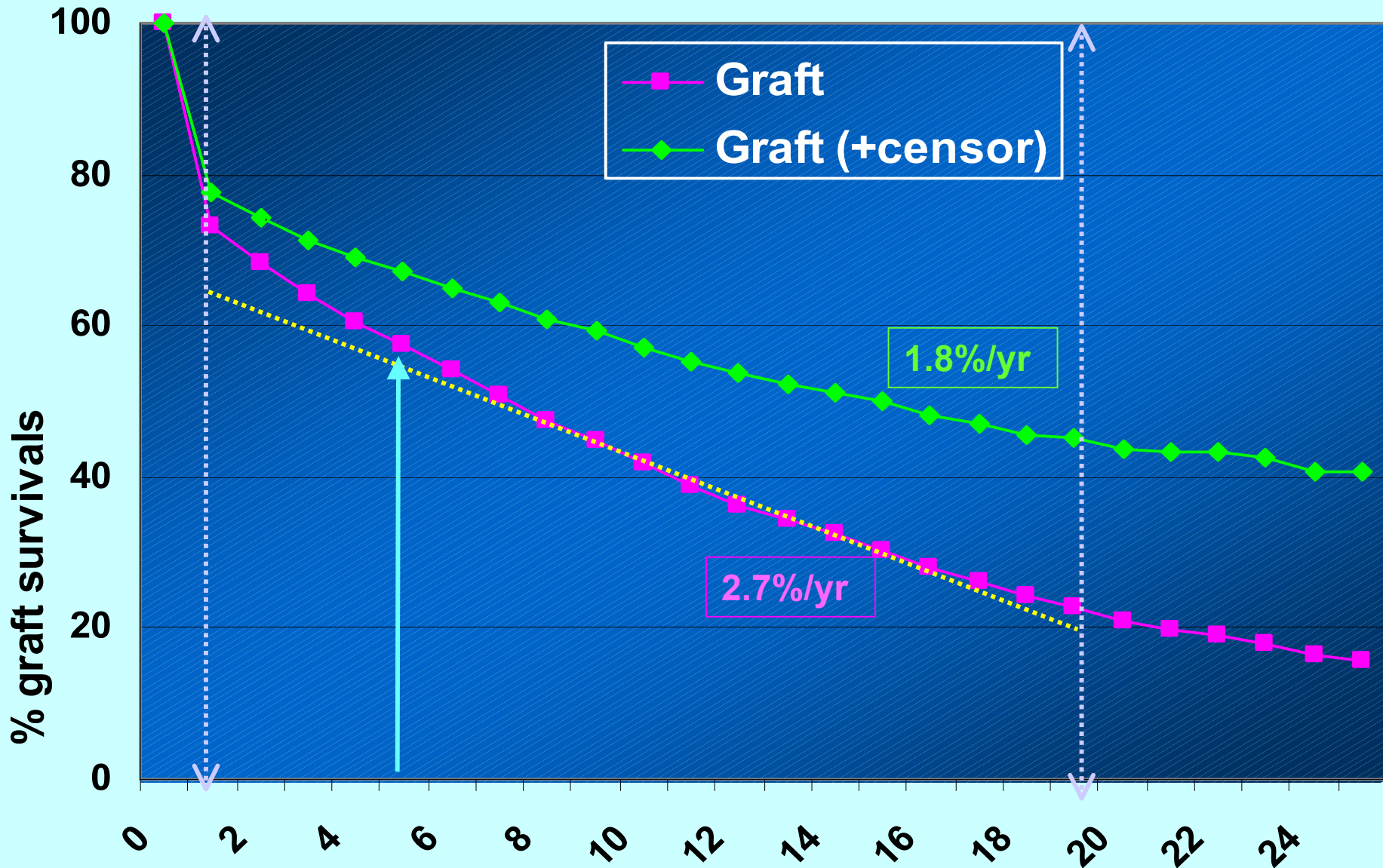
Australia primary patient & graft (CD & LD) survival 1970-94. $n = 7623$ grafts



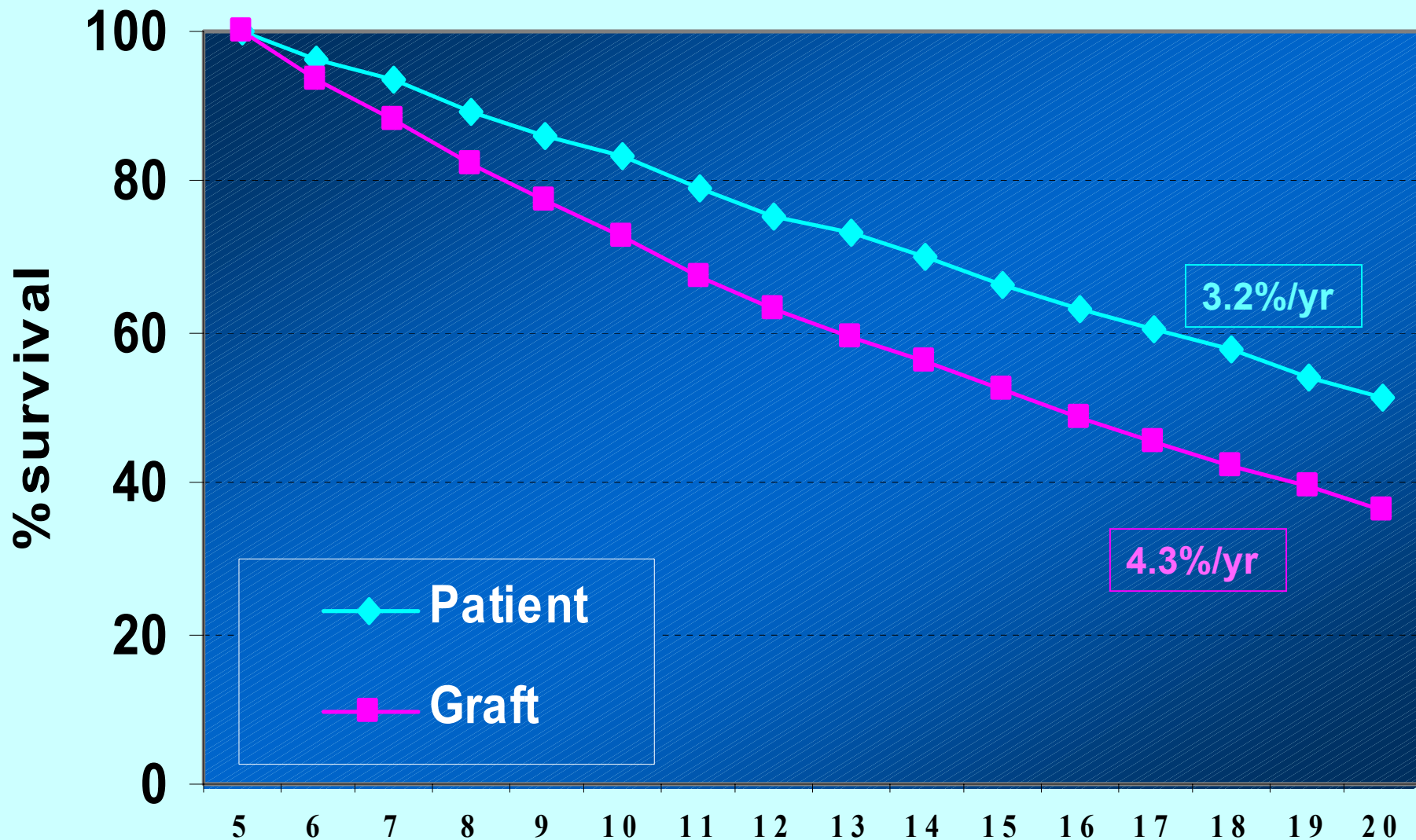
Australia primary graft (CD & LD) survival 1970-94. $n = 7623$ grafts. The decay is exponential.



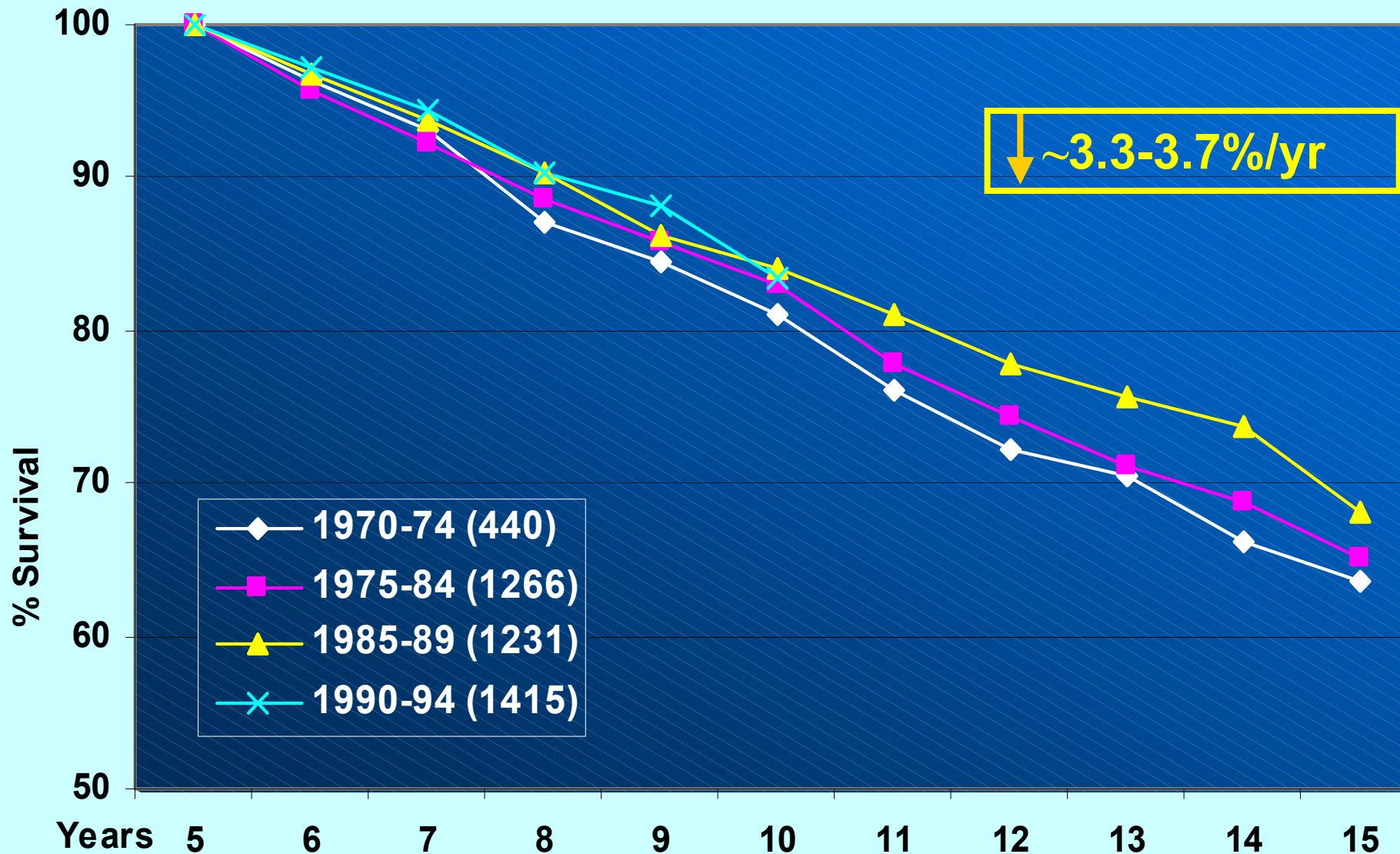
Australia primary graft survival 1970-94. $n = 7623$ grafts



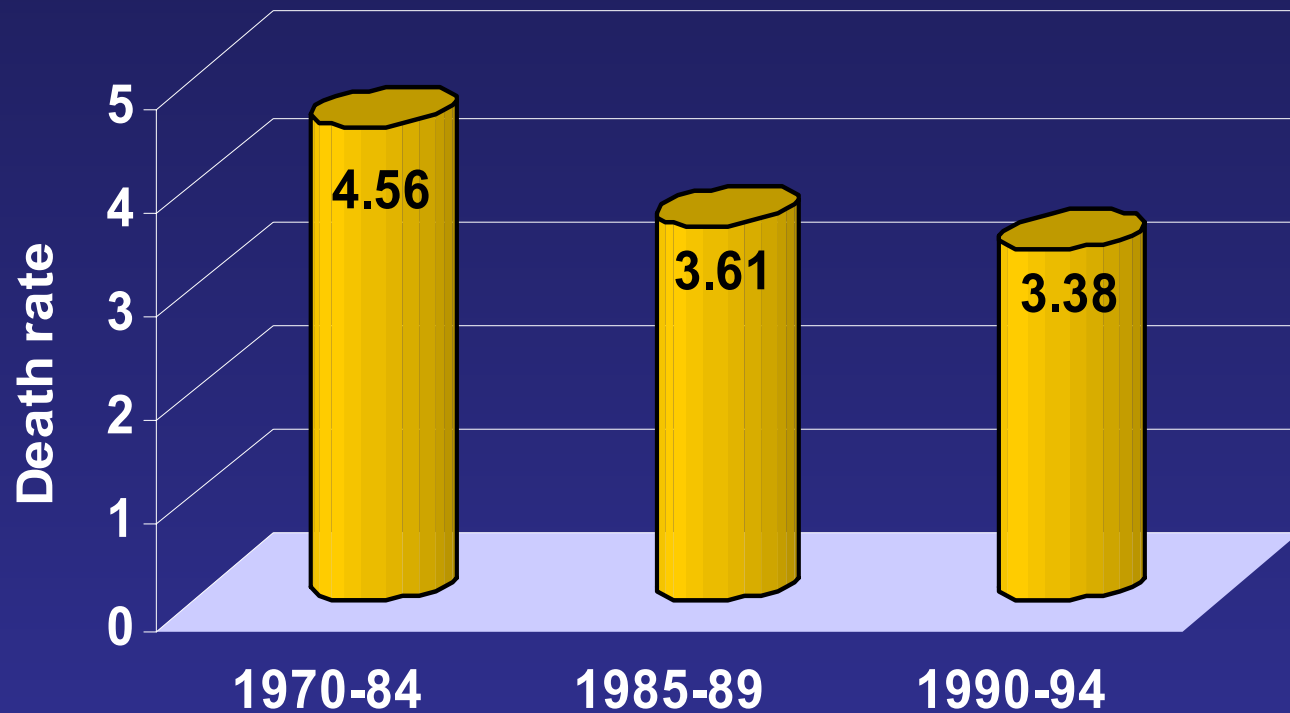
5 Yr+ survival for primary grafts (n= 4353) *Australia (1970-94)*



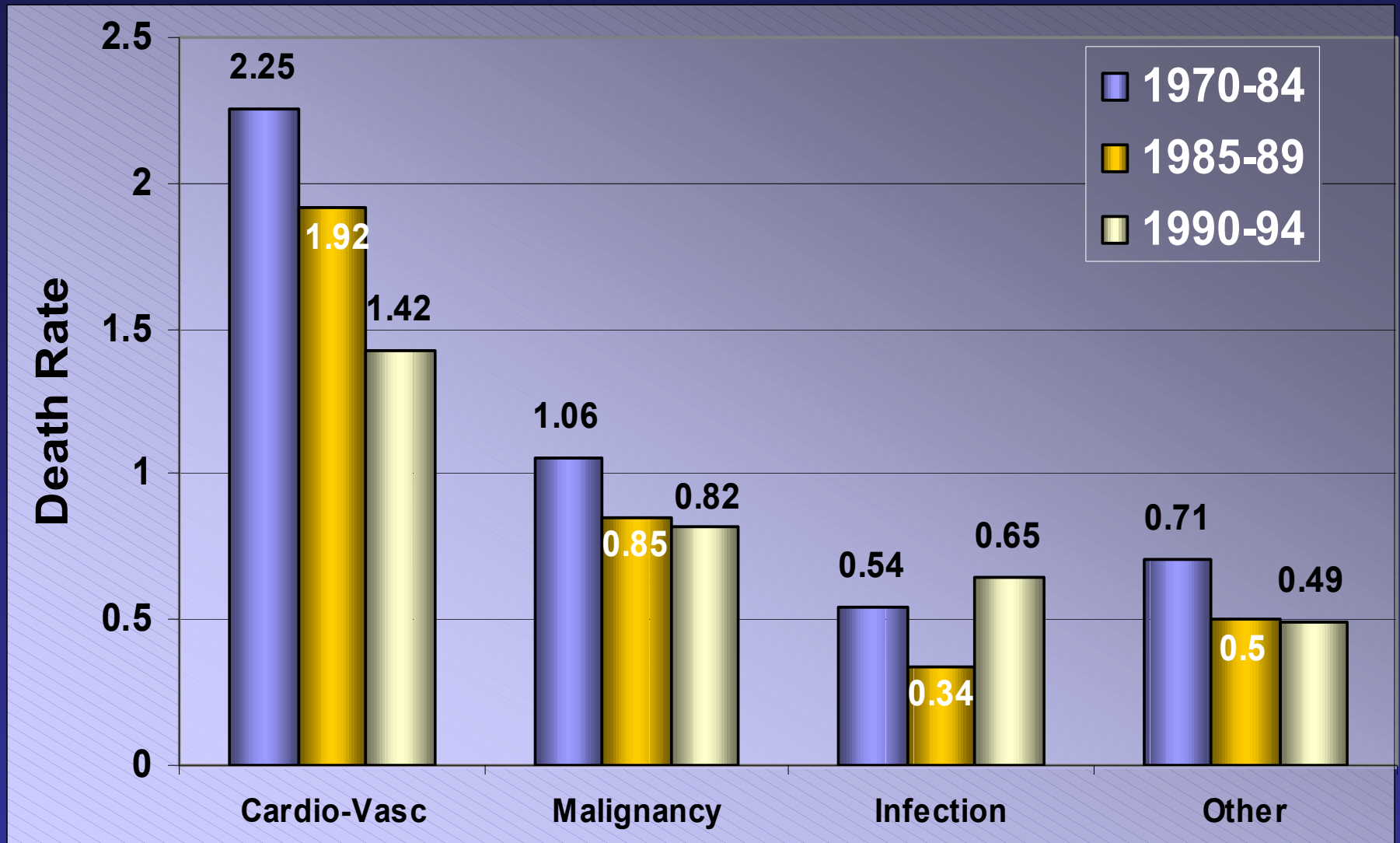
Patient survival after 5 yrs (*Aus CD1 & LD1*) by selected time periods – the death rate has declined



The death rate/100 patient years for primary renal grafts beyond 5 yrs is reducing in recent years

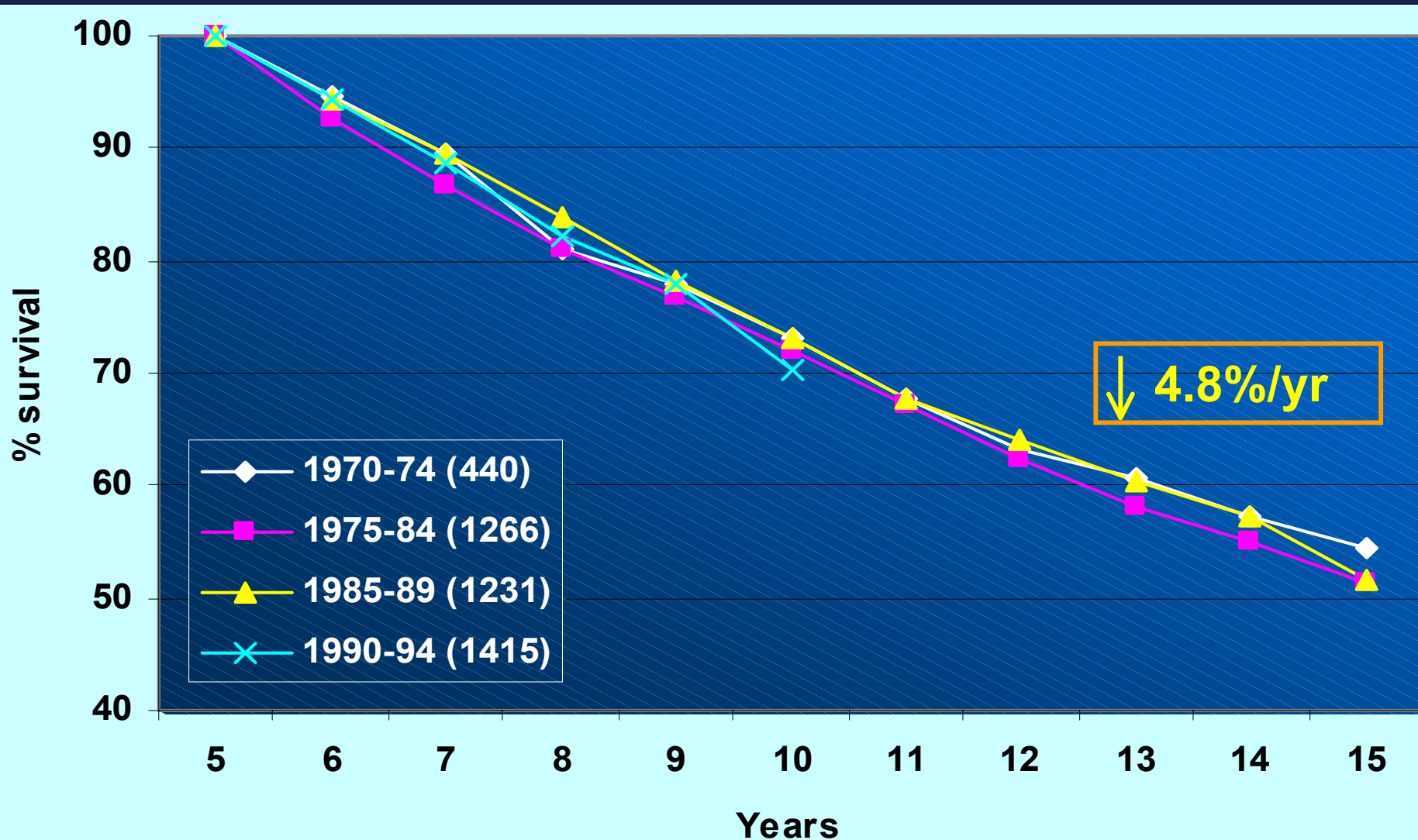


Death rate/100 patient years >5yrs post graft Australia CD1 & LD1 by period



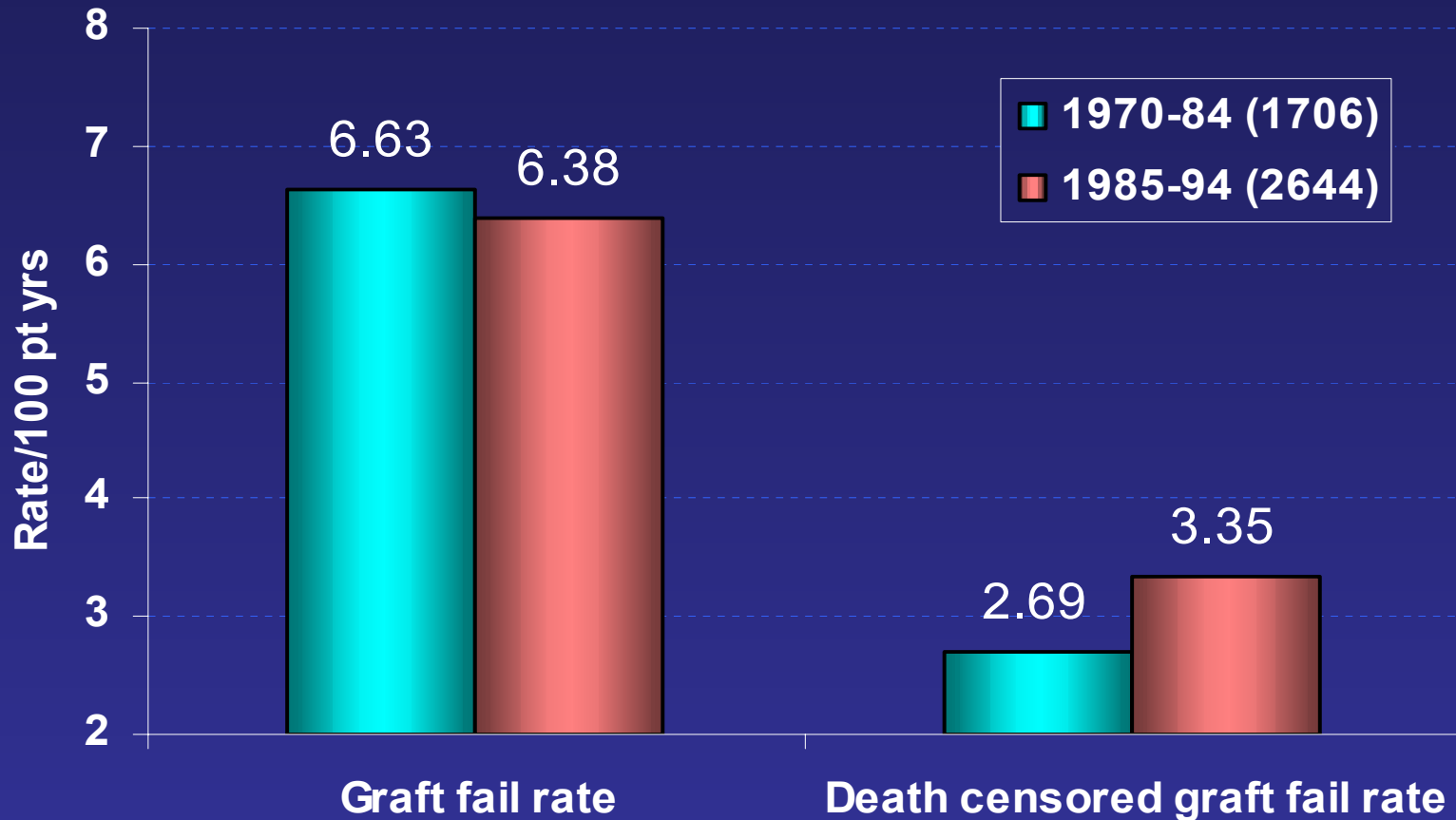
Graft survival beyond 5 yrs (*Aus CD1 & LD1*).

The decline is the same in each selected time period



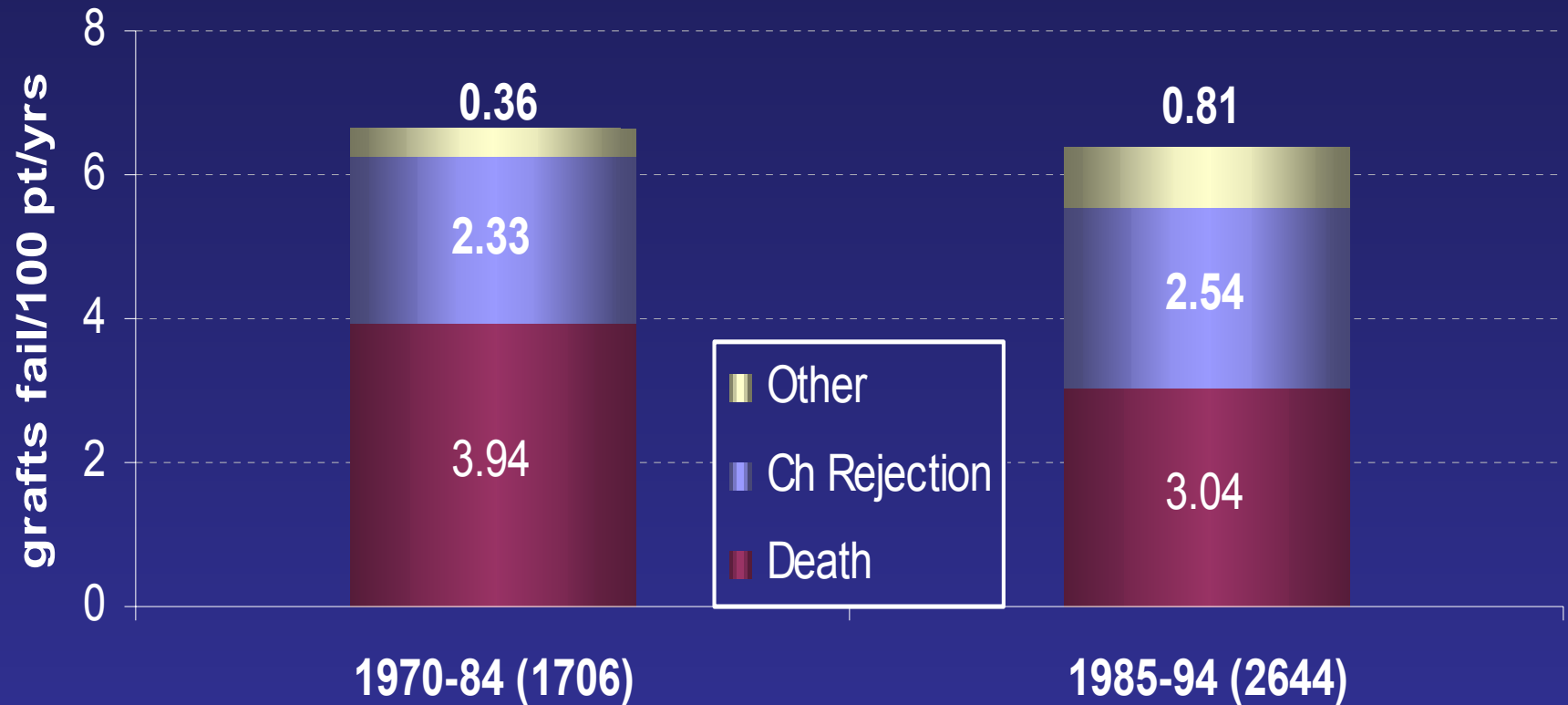
Death censored graft fail rate/100 graft/yr > 5yrs post has increased 33% since 1984

CD1& LD1 Australia



Cause of graft failure rate

The loss from 'chronic rejection' is increased in recent times



Predictive characteristics favoring primary graft survival beyond 5yrs

Significant factors on univariate analysis

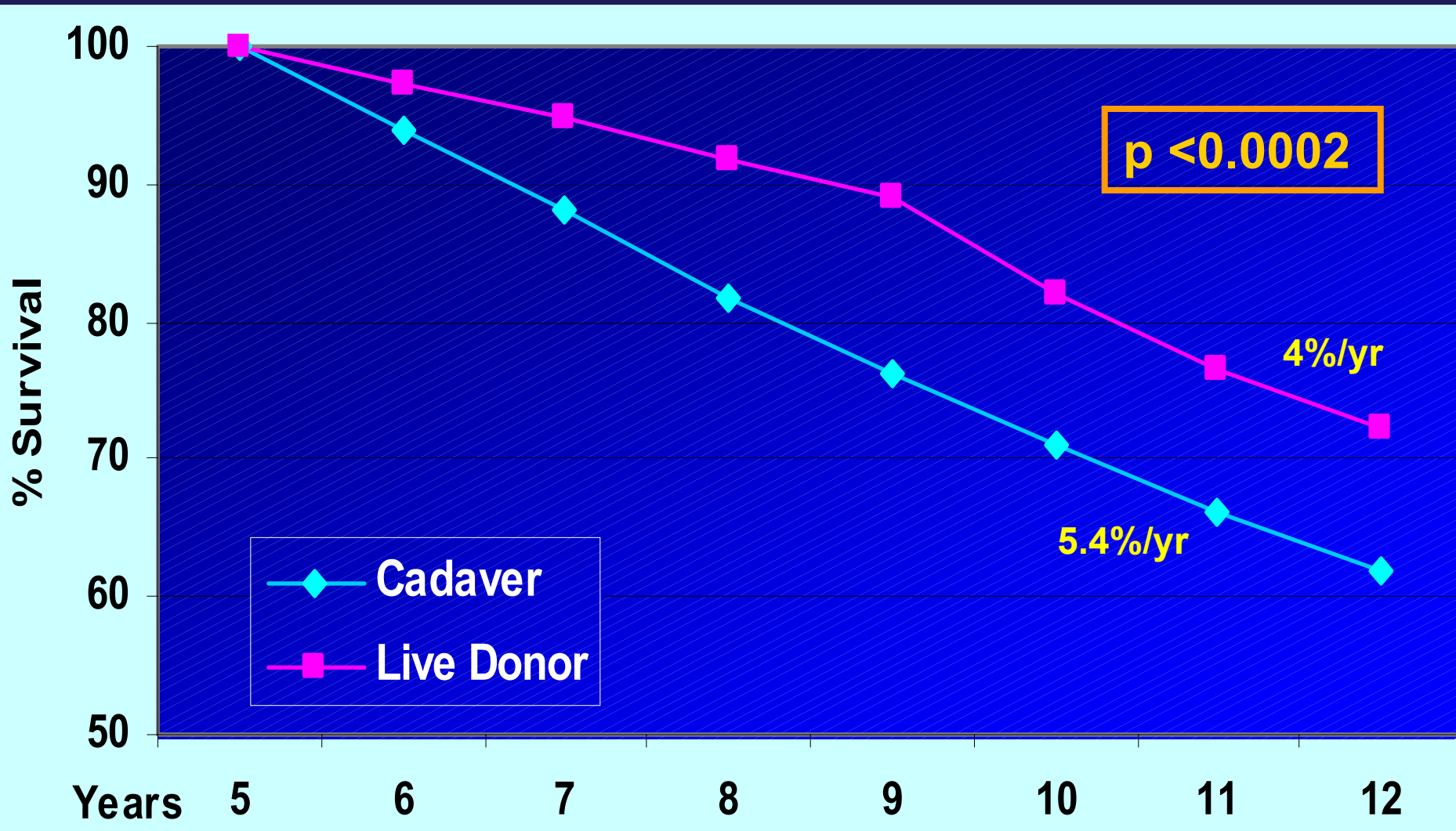
- Donor source LD $p=0.0002$
- Donor age <50yr $p=0.0002$
- Donor not 'marginal' $p=0.002$
- Donor death trauma $p=0.02$
- Recipient never smoked $p=0.0001$
- Not on CsA at 2 & 5yrs. $P=0.0004$

Predictive characteristics favoring primary graft survival beyond 5yrs

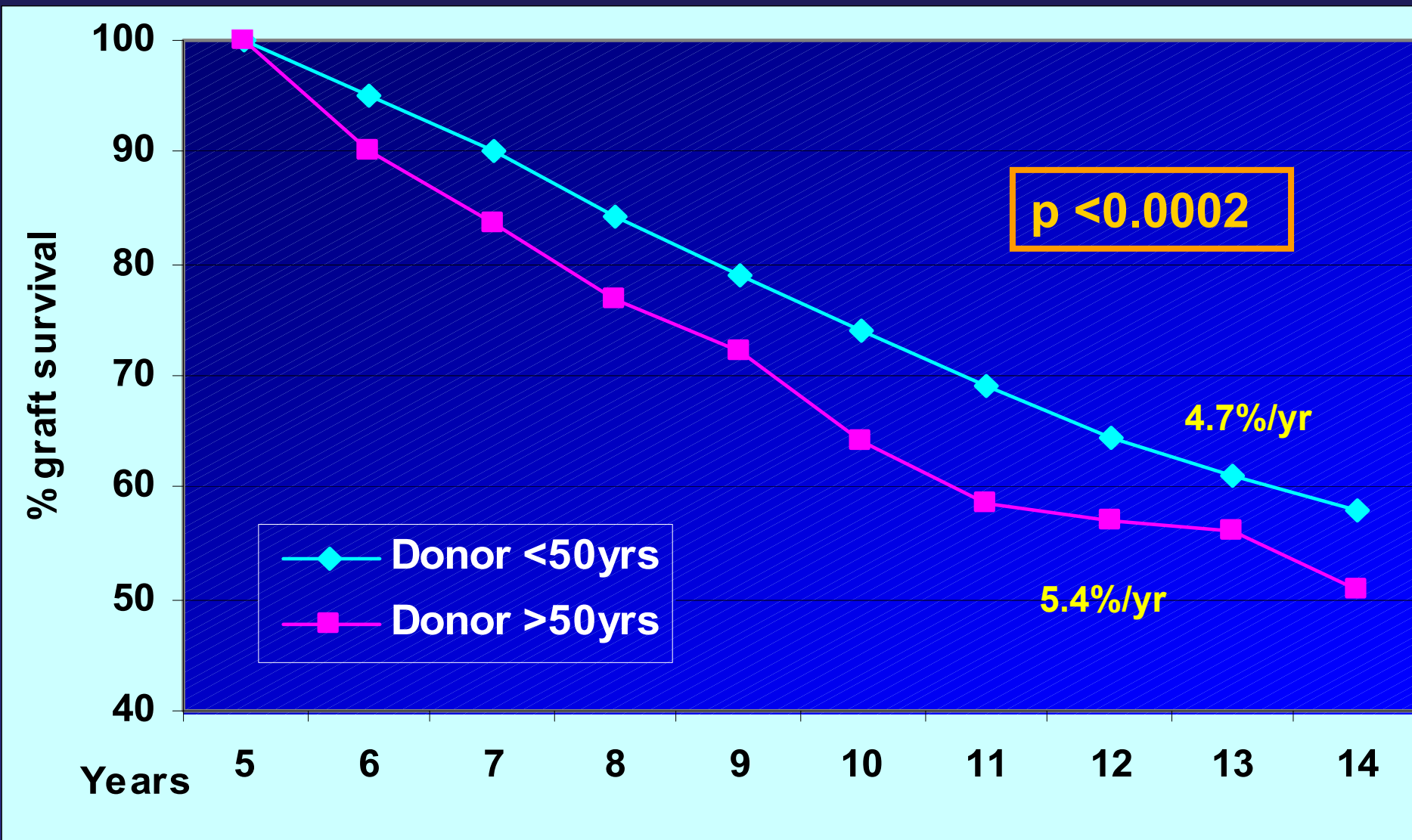
Non –significant factors on univariate analysis

- Donor hypertensive
- Donor oliguric
- Donor terminal creatinine $>120\mu\text{mol/l}$
- Donor smoked
- CsA dose $>5\text{mg/kg/d}$
- Primary renal disease
- Use of Ab for rejection in 1st 6m
- Delayed graft function $>7\text{d}$

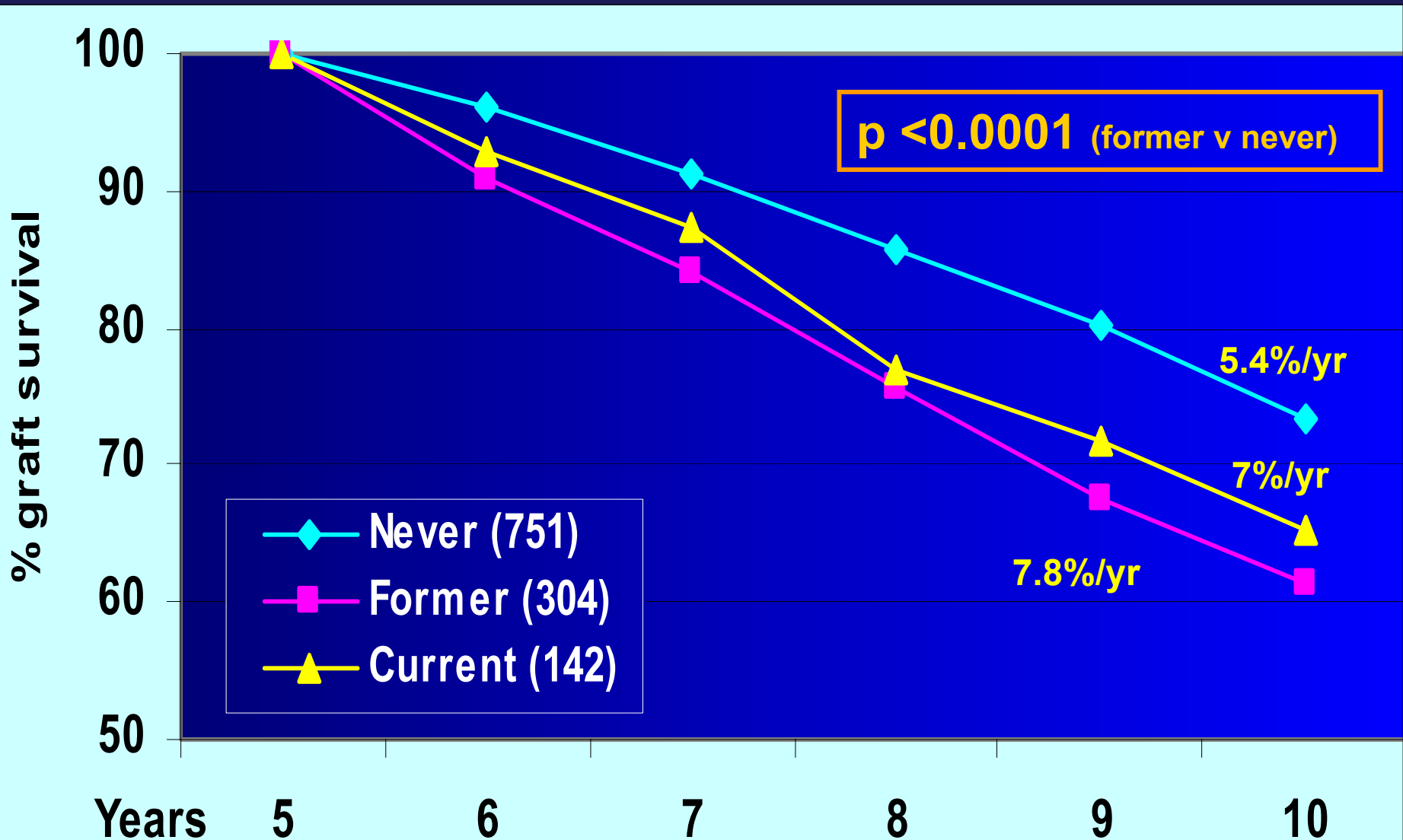
Effect of donor source on graft outcome >5yrs (Aus CD1 1985-94 – 2646 grafts)



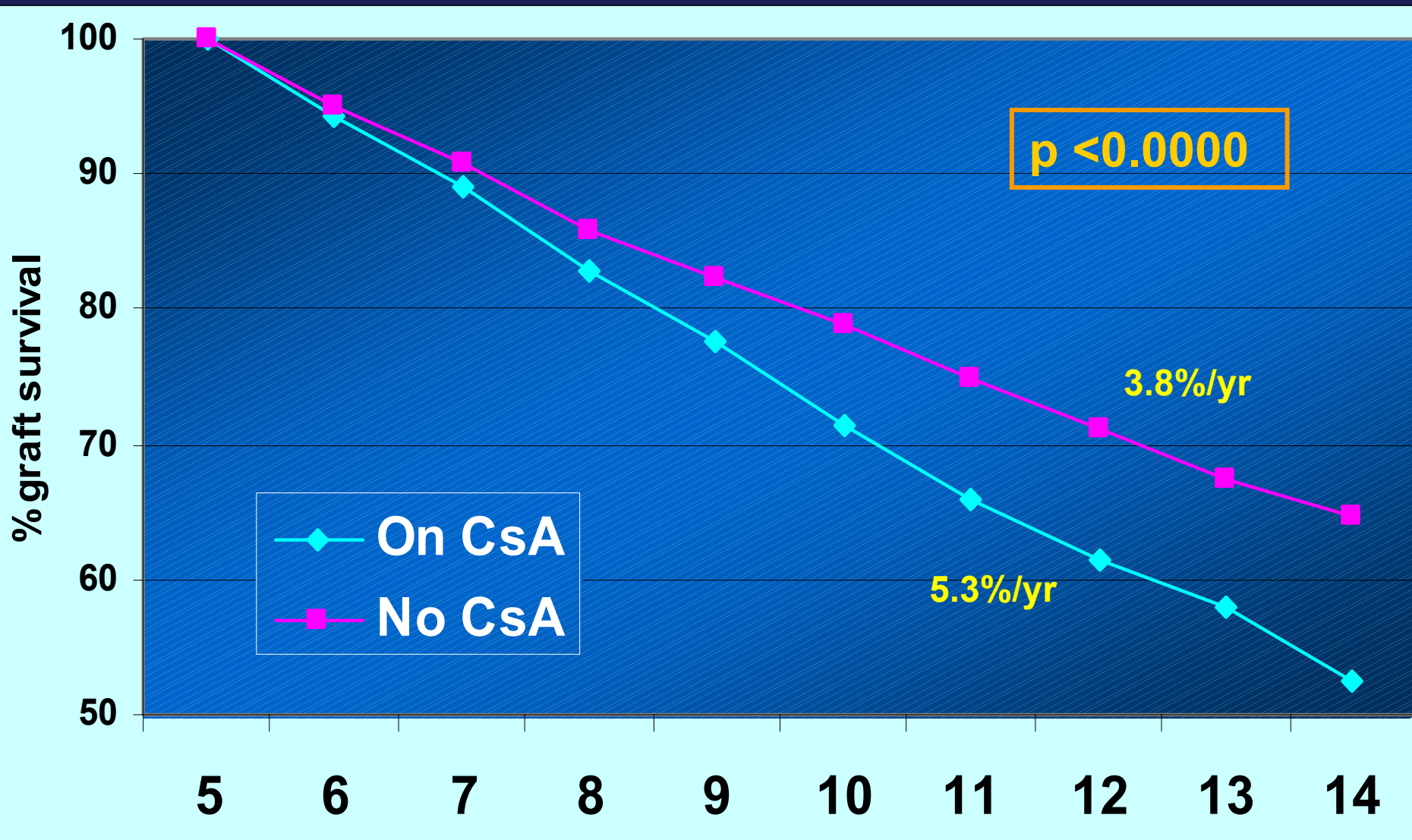
Effect of donor age on graft outcome >5yrs (Aus CD1 1985-94 – 2646 grafts)



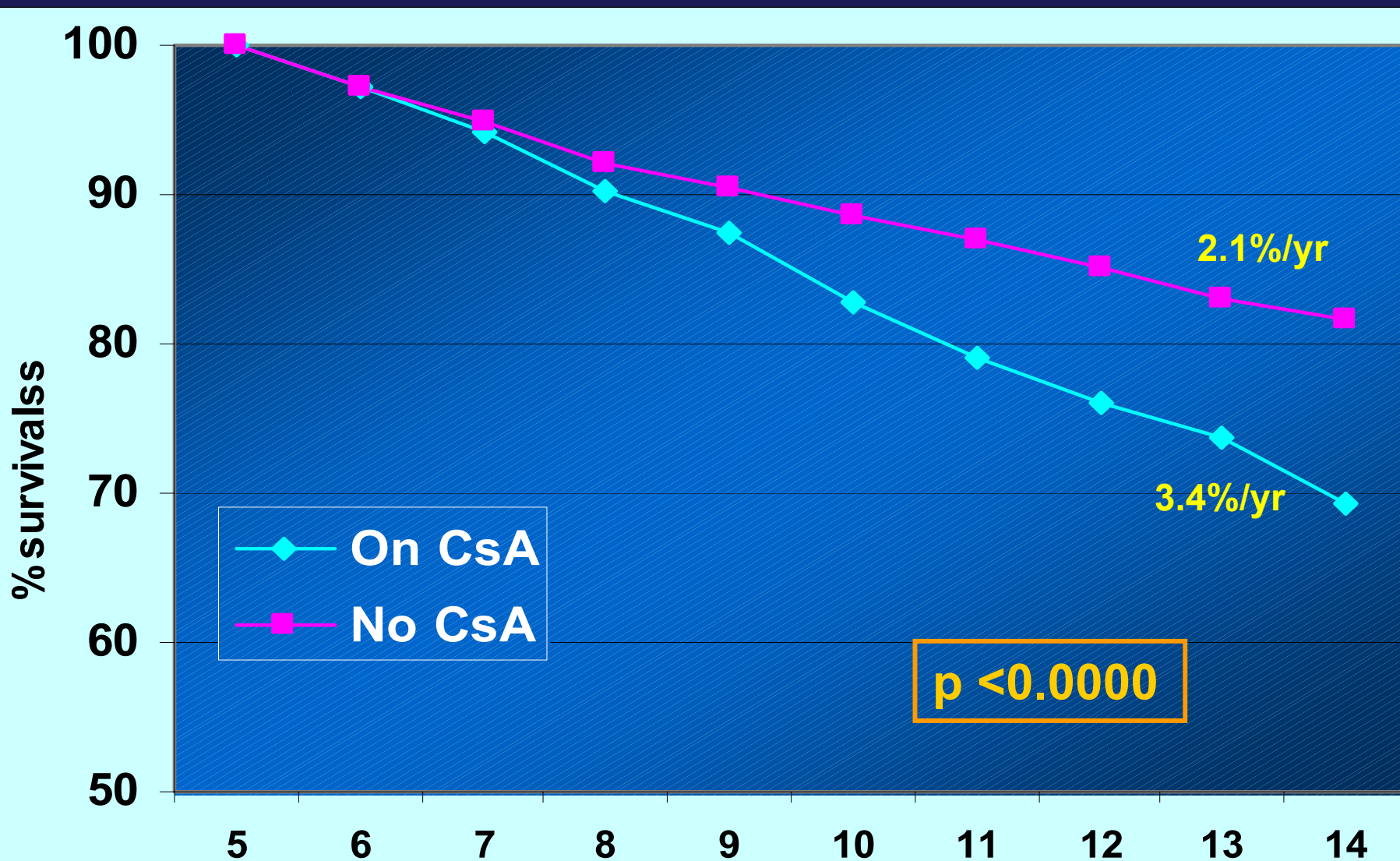
Effect of recipient smoking on graft outcome >5yrs (Aus CD1 1985-94 – 2646 grafts)



Graft survival on CsA is reduced >5yrs (Aus CD1 & LD1 n=4009)



Graft survival (death censored) 5yrs + CsA & no CsA (Aus CD1 & LD1)



Predictive characteristics favoring primary graft survival beyond 5yrs

Significant factors on univariate analysis

- Donor source LD* p=0.0002
- Donor age <50yr* p=0.0002
- Donor not 'marginal' p=0.002
- Recipient never smoked* p=0.0001
- Donor death trauma p=0.02
- Not on CsA at 2 & 5yrs* p=0.0004

* *Retained significance on multivariate analysis*

Multivariate analysis of factors affecting death censored primary graft outcome >5yrs

Significant factors

	HR	(CI)
• On CsA	1.9	(1.4-2.6)
• Recipient smoking	1.86	(1.3-2.6)
• Recipient <20yrs	1.55	(1.1-2.1)
• Donor Age >50yrs	1.51	(1.2-2.0)
• Recipient >50yrs	0.61	(0.5-0.8)
• Live donor	0.67	(0.4-1.00)

Multivariate analysis of factors affecting death censored primary graft outcome >5yrs

Non -Significant factors

- Mismatch on HLA
- Marginal donor status
- Vascular disease at entry
- Year of transplant
- Cause of donor death

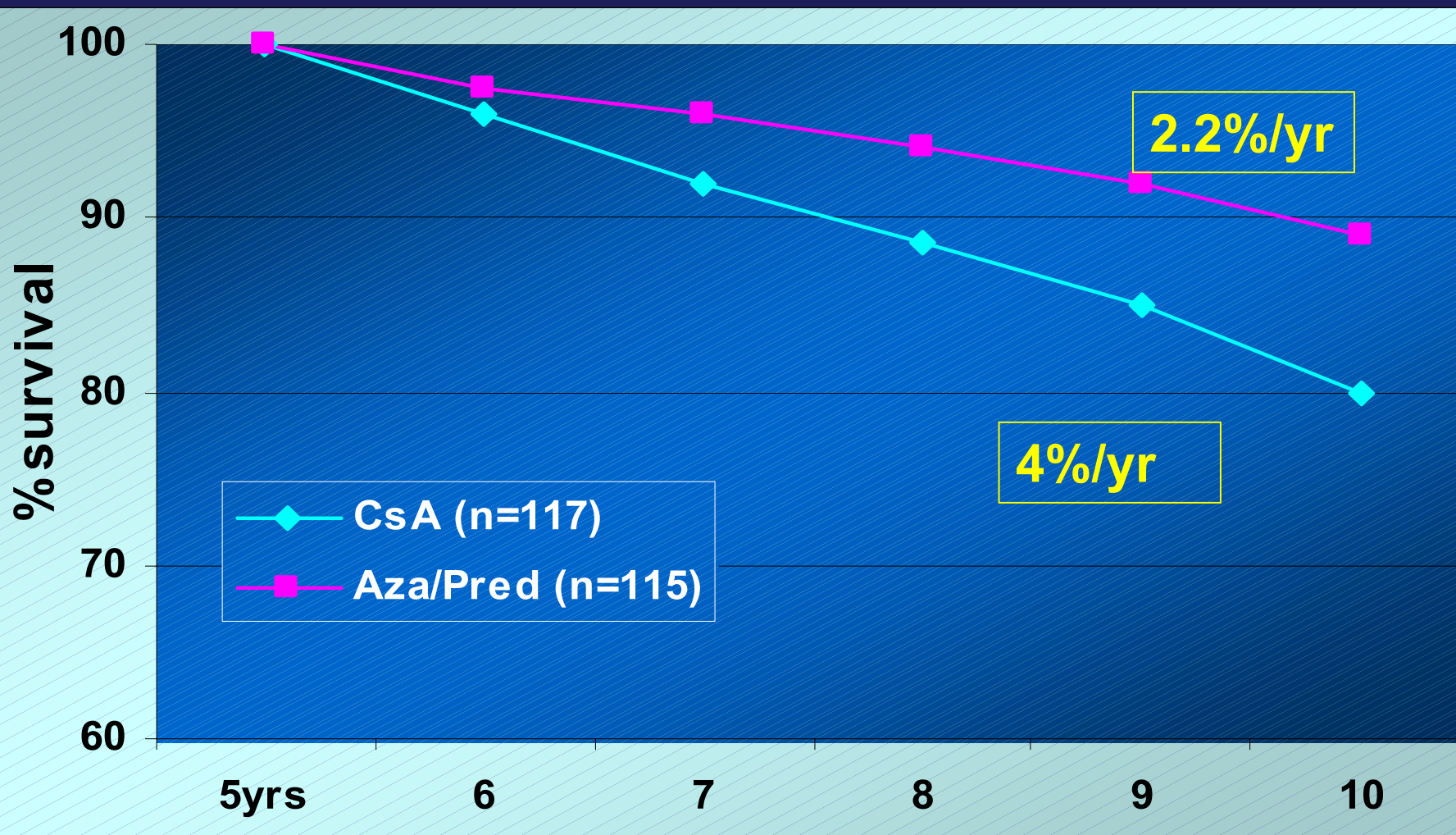
The effect of CsA on long term graft (*death censored*) outcome

- *Is statistically and clinically significant* : -
 - 10% difference over ten yrs
 - Most evident in those with S Cr <140umol/L at 1 yr
- *Not accounted for by*
 - donor source or quality
 - vascular disease pre entry
- *The patients on CsA had*
 - worse matching (-)
 - more recipients >50yrs (+)
 - more marginal donors (-)
 - more smokers (-)

(all marginally significant)

European Multicenter trial (*Transpl Proc* 25:527, 1993)

Data redrawn with 5yr survival adjusted to 100%. (ITT)



Conclusions on graft loss beyond 5 years

- *Grafts fail after 5 years through*
 1. Death. The death rate is currently decreasing & now accounts for 48% of losses
 2. Graft failure. The rate of loss is increasing due to an increase in 'chronic rejection' & 'other' causes
- *Increased* risk of late graft loss (death censored) with
 - Continuing exposure to CsA, donor age >50yrs, recipient age <20yrs, recipient smoking
- *Decreased* risk of late graft loss (death censored) with
 - Recipients >50yrs, live donors