

Deceased Donor Kidney Allocation

John Gill MD, MS
Associate Professor, UBC
President Canadian Organ Replacement Register
jgill@providencehealth.bc.ca

Expanded Criteria Donors

Background

- Deceased donor characteristics determine outcome
 - Age,
 - History of hypertension
 - Kidney function

Background

- Some ESRD patients
 - Will derive a survival advantage from transplantation versus dialysis, but their life expectancy is limited
 - Tolerate dialysis poorly and have a high likelihood of never being transplanted if waiting times are long
 - These patients do not require decades of transplant function and could be transplanted with organs with lower projected survival
 - Survival will be improved if they receive a transplant quickly with an organ that provides adequate function compared to waiting for an ideal organ

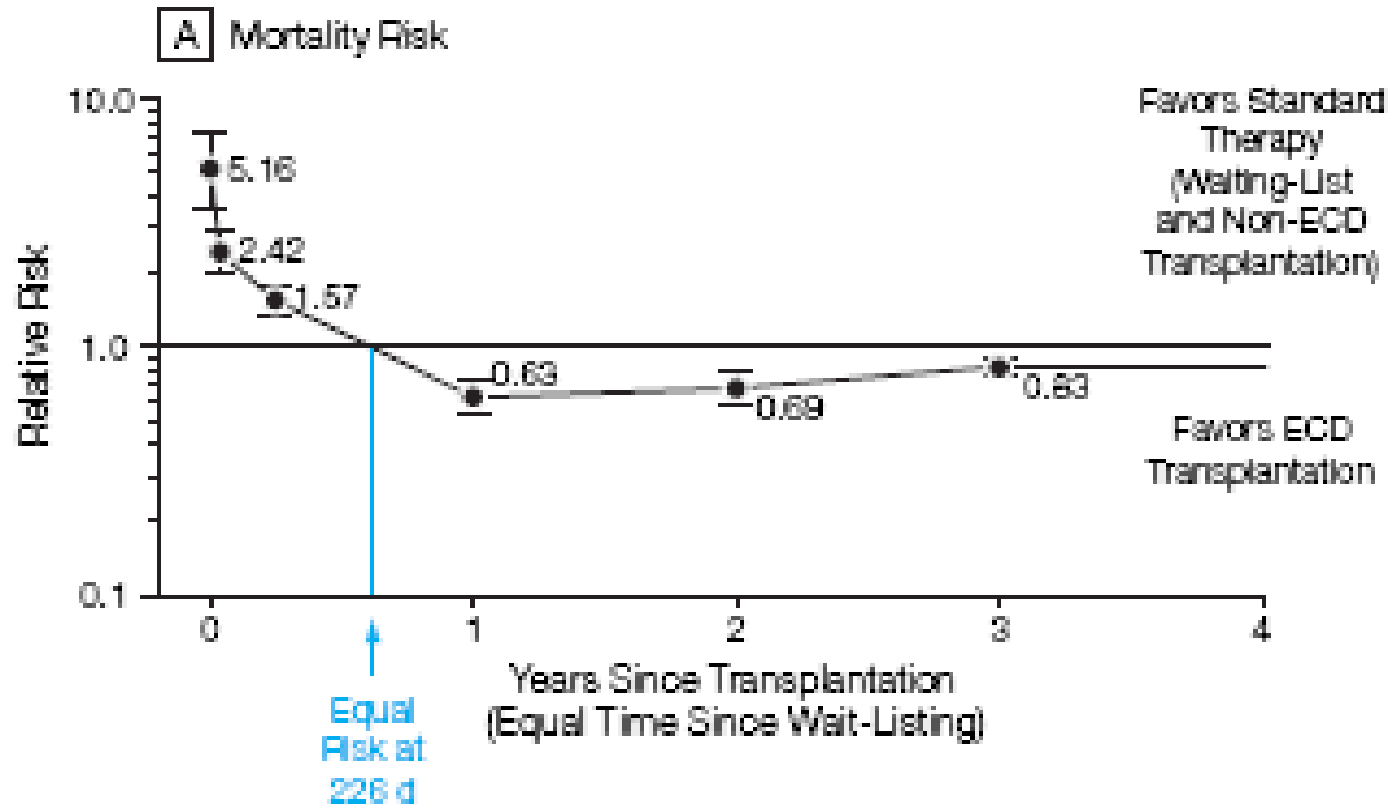
Expanded Criteria Donors

- Donor age 60 and above
- Donor age 50-59 and 2 of the following 3:
 - Serum creatinine > 132
 - History of hypertension
 - CVA as mechanism of death

ECD outcomes are inferior to SCD

- Compared to SCD recipients:
- Patient survival is
 - 5% lower at 1 year
 - 8-12% lower at 3-5 years for ECD kidney recipients
- Adjusted graft survival in ECD kidneys is
 - 8% lower at 1 year
 - 5-20% lower at 3-5 years after transplantation

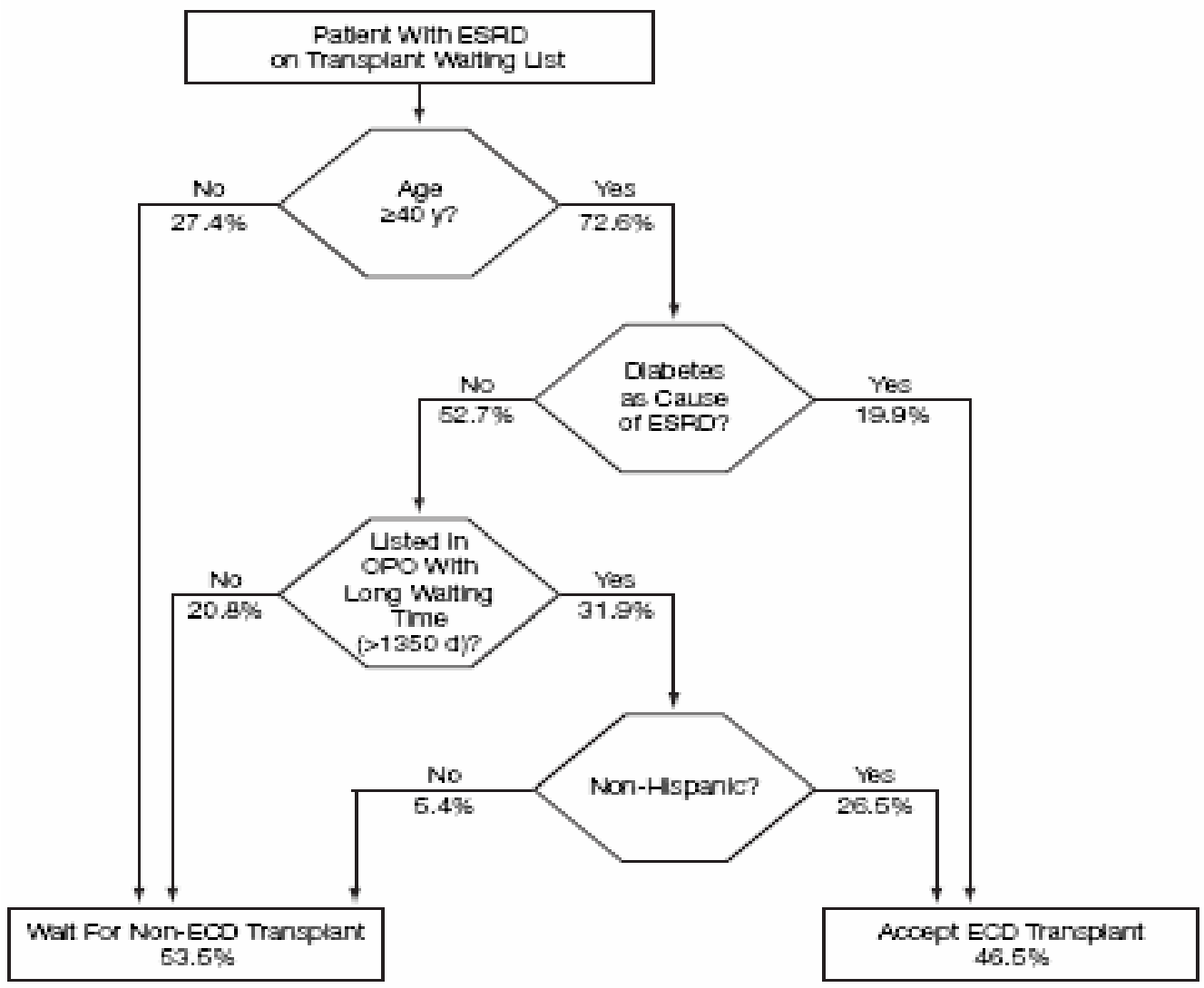
Should patients wait longer for a standard kidney opt for an ECD?



Merion et al JAMA December, 2005

Who should not be considered for ECD?

- < 40 years
- Among those over 40 years
 - Non-diabetics with waiting time < two years



Expanded Criteria Donors Procedure

- Wait-listed patients educated about ECD
- Given the choice to be considered for an ECD
- If patients chose ECD, still eligible for non-ECD kidney

For ECD to work waiting times must be short

- For patients to derive a benefit from ECD they must receive transplants with a shorter waiting time (< 2years ideally)
- How many patients we list thus depends on anticipated number (supply) of ECD kidneys

Donor kidneys over the age of 60 years in Canada and BC

Canada

- 1995: 45/475=9.5%
- 1996: 43/461=9.3%
- 1997: 62/480=12.9%
- 1998: 67/469=14.3%
- 1999: 71/435=16.3%
- 2000: 69/497=13.9%
- 2001: 67/476= 14.1%
- 2002: 62/470= 13.2%
- 2003: 91/511=17.8%
- 2004: 94/489=19.2%
- 2005: 95/459= 20.7%

British Columbia

- 1995: 5/74 =6.3%
- 1996: 2/76 =2.6%
- 1997: 0/65 =0.0%
- 1998: 6/42 =14.3%
- 1999: 4/55 =7.3%
- 2000: 0/55 =0.0%
- 2001: 2/50 =4.0%
- 2002: 1/37 = 6.2%
- 2003: 5/52 = 8.8%
- 2004: 4/46 =8.7%
- 2005: 5/36= 13.9%

Who should be offered ECD in BC?

- Maximum of 10 kidney/year
- Want waiting time to be 2 years or less
- Should have about 20-25 patients listed for ECD
- We have set the age cut-off for recipients as 60 years with anticipated waiting time of > 2 years

Age Matching

Many transplant programs were informally age matching in Canada

- Canadian Survey

Do you attempt to age match?

- 1/12 “yes” 20% age difference or less between donor/recipient
- 4/12 “loosely” old for old, young for young
- 4/12 no age matching
- 1/12 old for old used for ECD kidneys only

Background

- Canadian Council for Donation and Transplantation (CCDT) National Forum
 - “Kidney allocation in Canada”
 - Oct 25-7, 2006
 - Included all kidney transplant programs and OPOs in Canada
 - Patient representation
 - Kidney Foundation of Canada

Rank Order

Allocation of Standard Criteria Deceased Donor Kidneys

- **Overriding priority:** Medical urgency
- **High priority (listed in alphabetical order):**
 - Age: pediatric recipient
 - Age: young donor to pediatric recipient
 - Combined transplant: kidney/pancreas transplantation
 - Matching: zero ABDR mismatch
 - Sensitization: sensitized patient with PRA $\geq 80\%$
- **Medium priority (listed in alphabetical order):**
 - Age: young donor to young adult recipient
 - Sensitization: sensitized patient with PRA 50 – 79%
 - Wait-time
- **Low priority:** Matching: lesser degree of human leukocyte antigen matching below zero ABDR mismatch
- **No priority:** Pre-emptive transplantation

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“We recommend that young adults be given priority in a local/regional allocation scheme in order to facilitate their access to young standard criteria donor kidneys”

- Intent was to **facilitate access** to younger kidneys by younger recipients; not necessarily to reduce wait-times for younger recipients
- **No specific age cut-offs were defined!**

Considerations

- Clear evidence that increasing donor and recipient age are associated with an increased risk of graft failure and death
- Older donor kidneys are equally poor for young and old recipients
- Donor recipient age matching would improve survival in young recipients, but could adversely affect survival in old recipients by reducing availability of younger donor kidneys to this group

Our Goal: “Define Young”

- **Young recipient**
 - Recipient age cut-off below which patient life expectancy is > than expected duration of graft survival
- **Young donor (operational definition)**
 - Donor age cut-off below which young recipients have improved graft/patient survival
 - There has to be enough “young donor kidneys” to transplant “young recipients” ...if age cut off is too low, will not have enough kidneys for young recipients
 - Donor age cut-off above which there is the least adverse effect on graft/patient survival in older recipients
 - If age cut off is too high.....would deny OLDER RECIPIENTS opportunity for a YOUNGER KIDNEY

Data Set

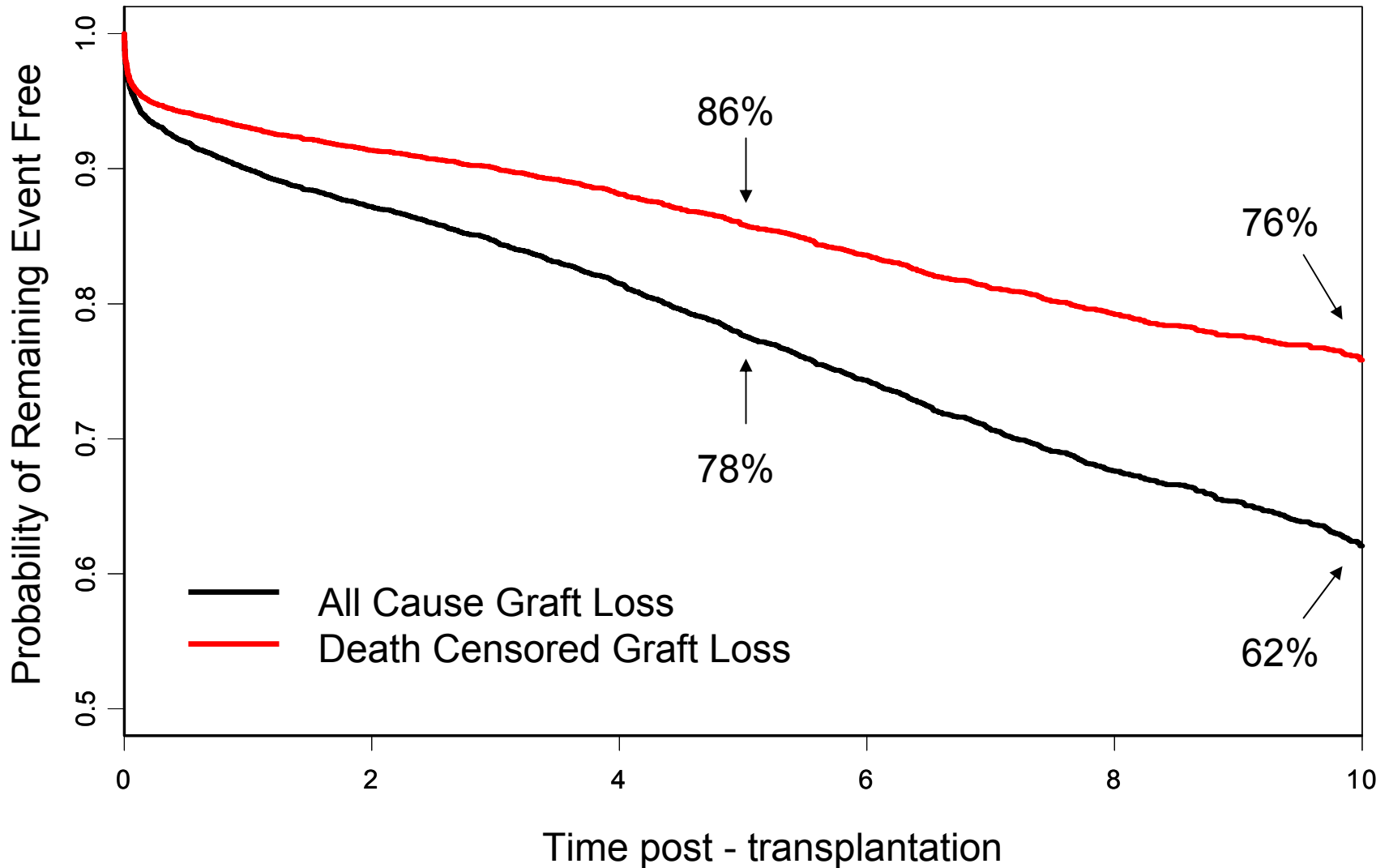
- Canadian Organ Replacement Register
- First kidney only deceased donor transplants 1995-2005
- End of follow-up: Nov. 2007
- Total N = 6,219 Working N = 6,191
- CORR –not validated for outcomes
 - Graft failure dates
 - Dialysis and repeat transplantation dates captured
 - Death dates are not validated

Summary Statistics n =6,191

| | |
|-------------------------------|-------------------|
| Age median (q1,q3) | 49 (38,58) |
| Male (%) | 63.6 |
| Race (%) | |
| White | 73.5 |
| Black | 4.0 |
| Asian | 7.1 |
| Aboriginal | 3.4 |
| Indian Sub-continent | 4.1 |
| Other | 7.9 |
| Cause of ESRD (%) | |
| GN | 40.2 |
| DM | 16.1 |
| Other | 43.8 |

| | |
|---|-----------------------|
| HLA Match(%) | |
| 0 | 15.9 |
| 1 | 23.9 |
| 2 | 24.0 |
| 3 | 16.9 |
| 4 | 8.0 |
| 5 | 2.3 |
| 6 | 0.5 |
| No data | 8.6 |
| PRA (%) | |
| 0 | 38.3 |
| 1-9 | 20.8 |
| 10 -29 | 8.3 |
| 30-49 | 7.3 |
| 50-79 | 3.1 |
| 80+ | 3.3 |
| No data | 18.8 |
| Years on Dialysis median (q1,q3) | 2.5 (1.3, 4.1) |

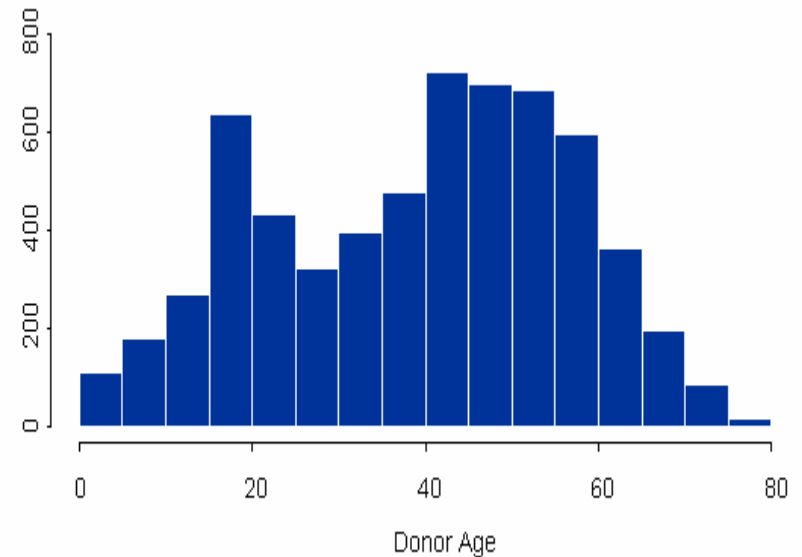
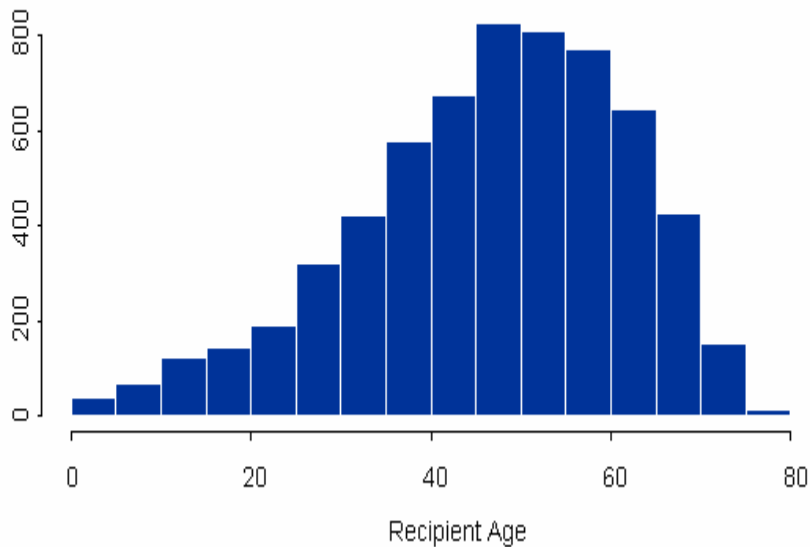
Graft Survival Unadjusted



Recipient and Donor Age Distribution

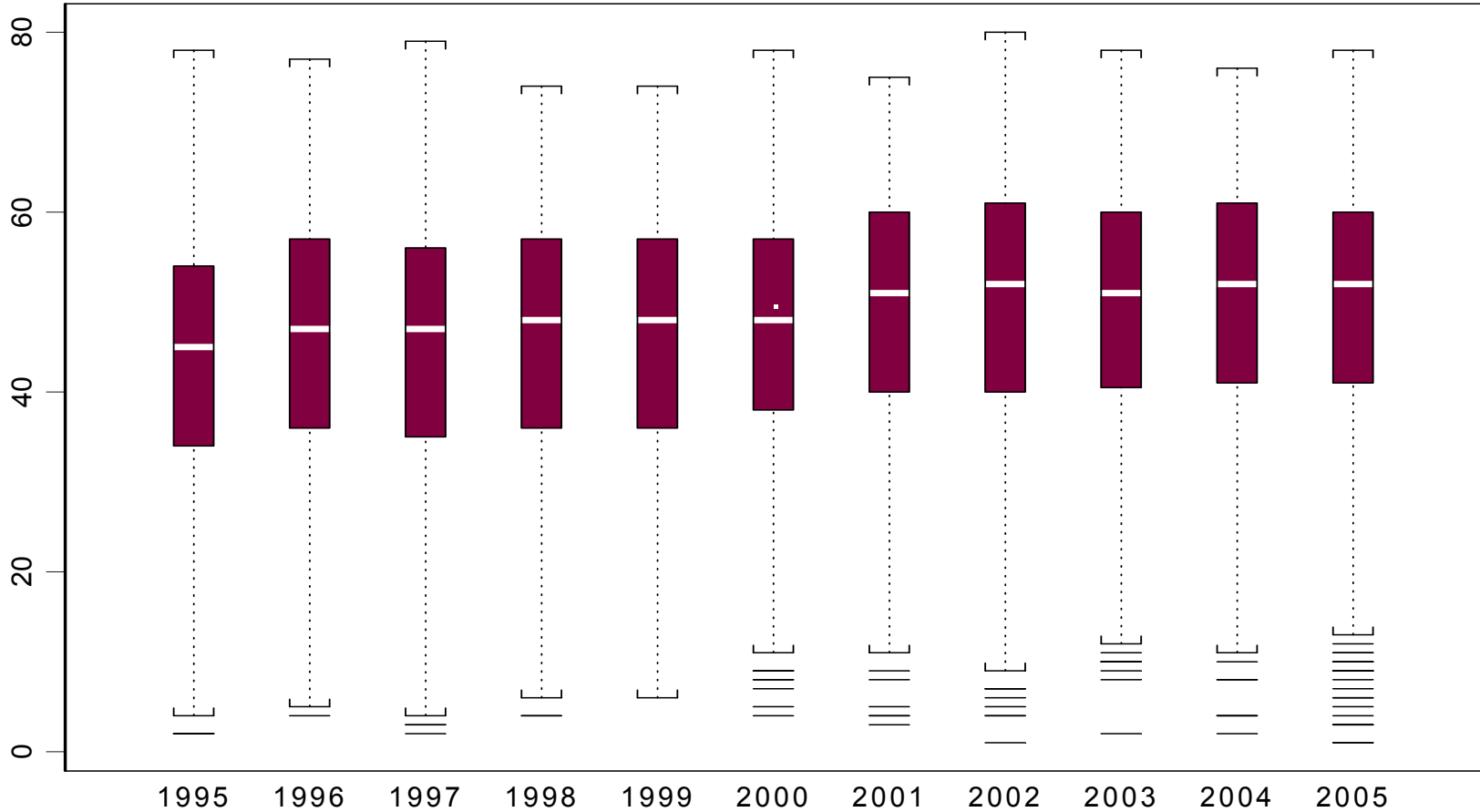
- 47.1 ± 15.0 years
- Median 49 (38,58)

- 39.8 ± 17.3 years
- Median 42 (24,53)



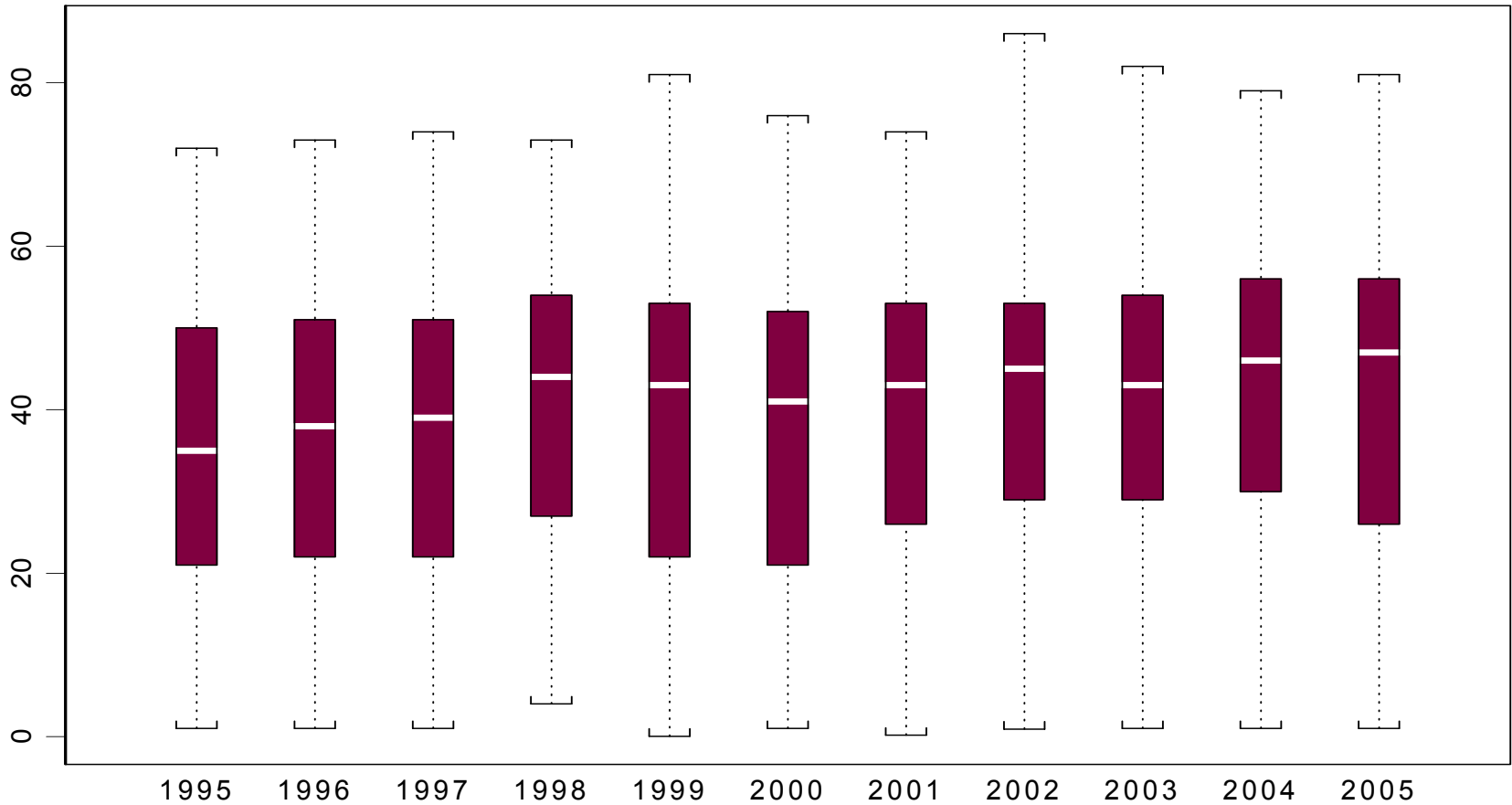
Recipient age

Increased from 43.9 (14.7) years in 1995 to 48.9(16.2) years in 2005 ($p < 0.0001$)

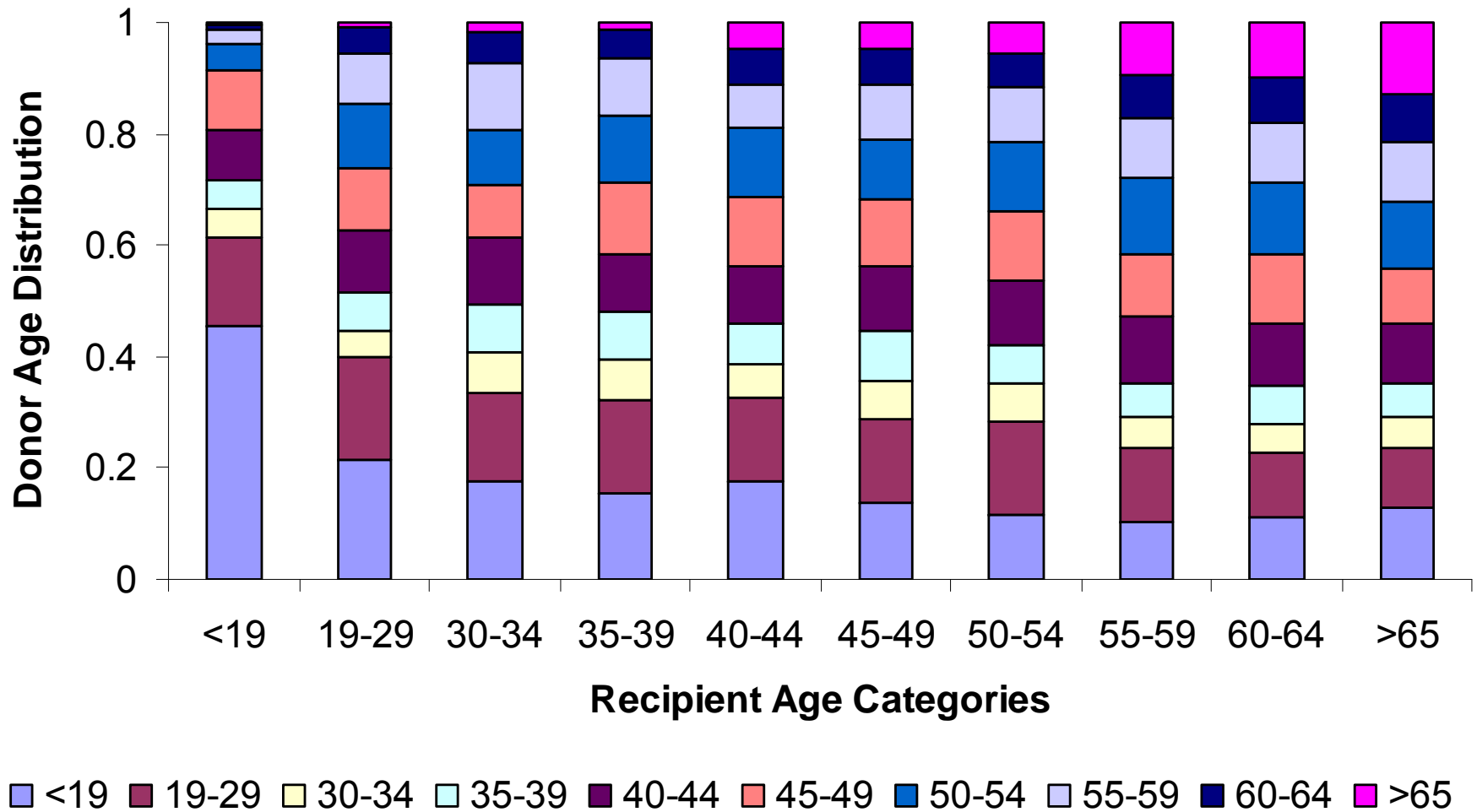


Donor age

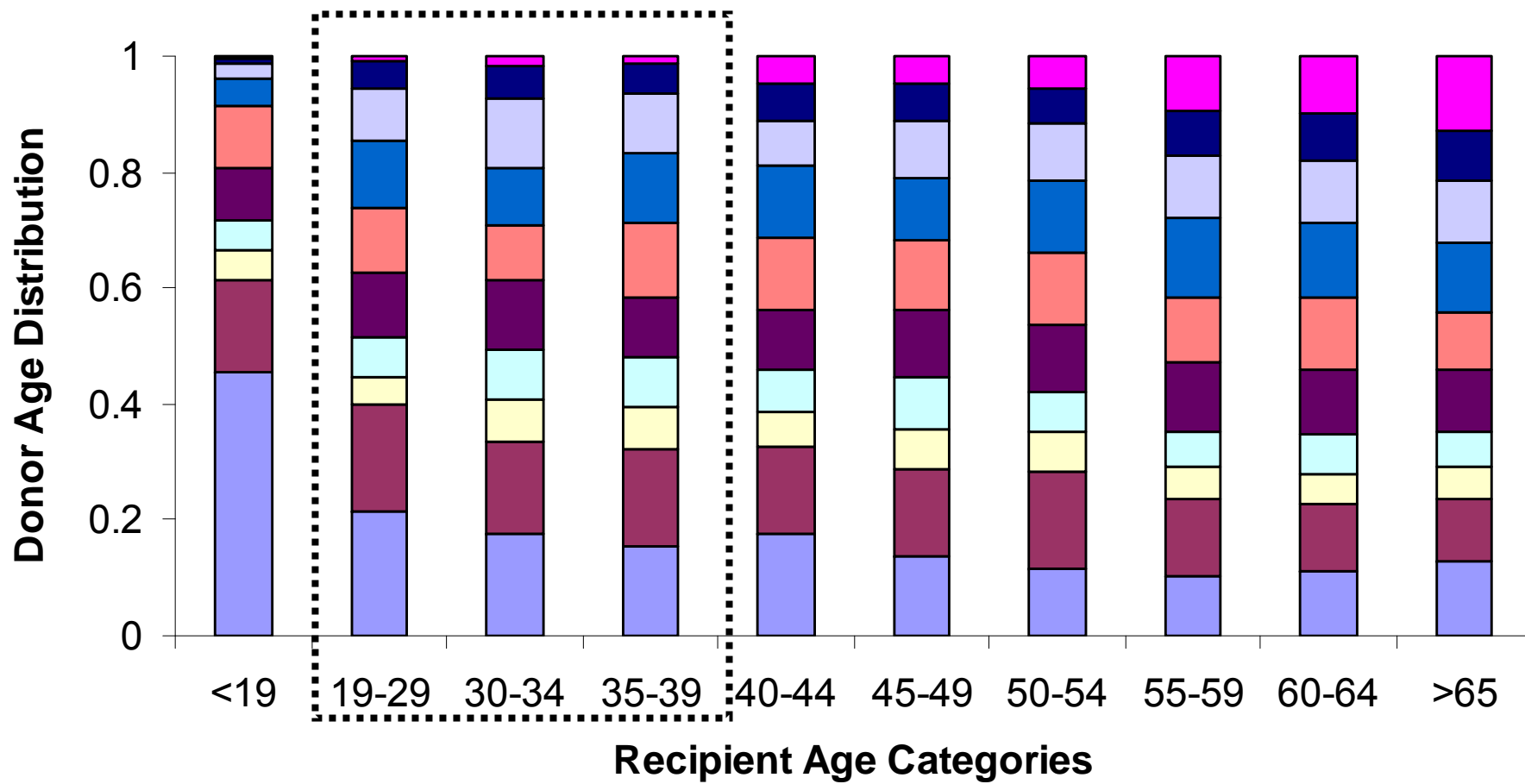
Increased from 35.7 (17.0) years in 1995 to 42.8 (17.9) years in 2005 ($p < 0.0001$)



Donor age distribution in recipients 1995-2005

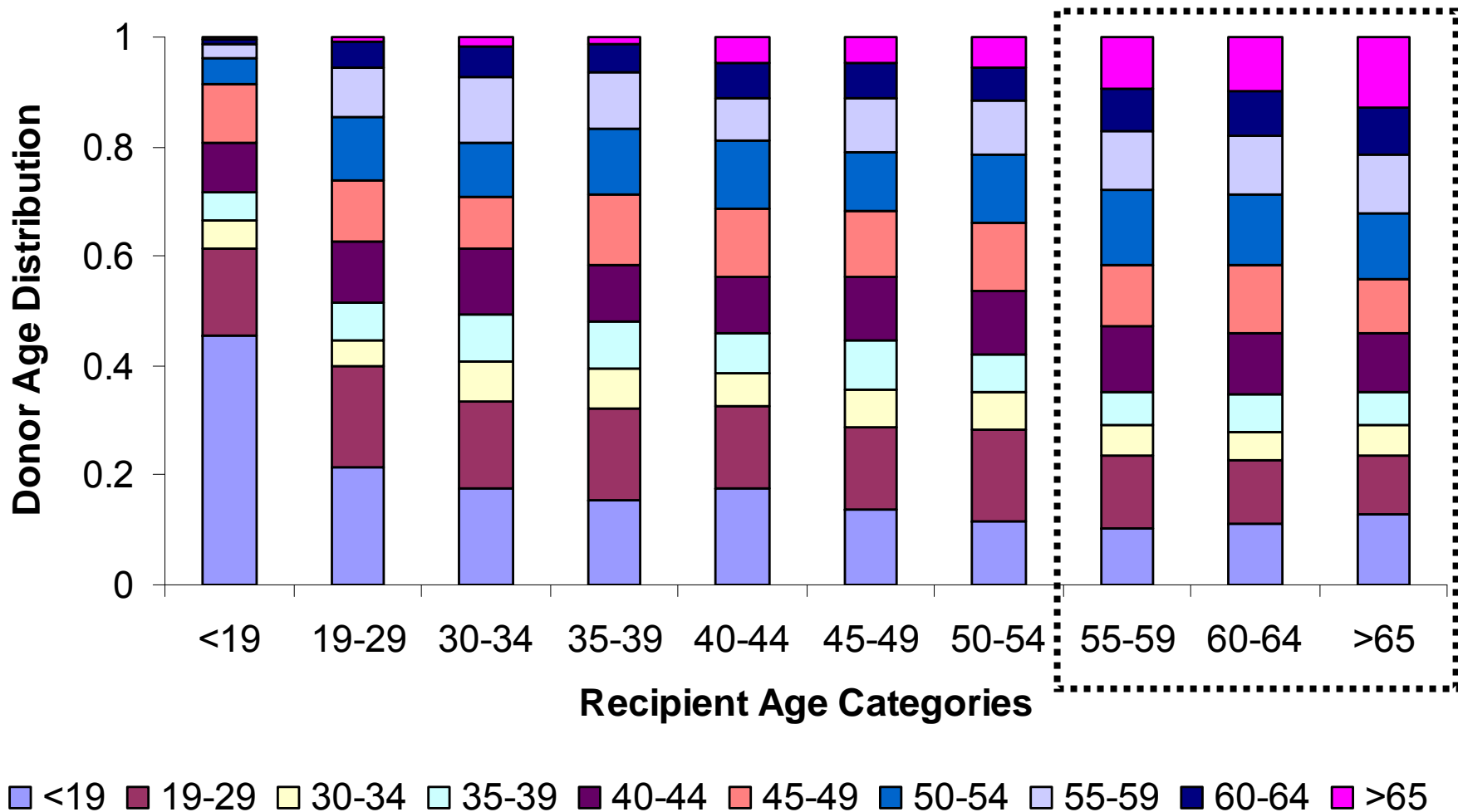


Among Recipients 19-39 years 28% had donors >50 years



<19 **19-29** **30-34** **35-39** **40-44** **45-49** **50-54** **55-59** **60-64** **>65**

Among Recipients >55 years 35% had donors <40 yrs



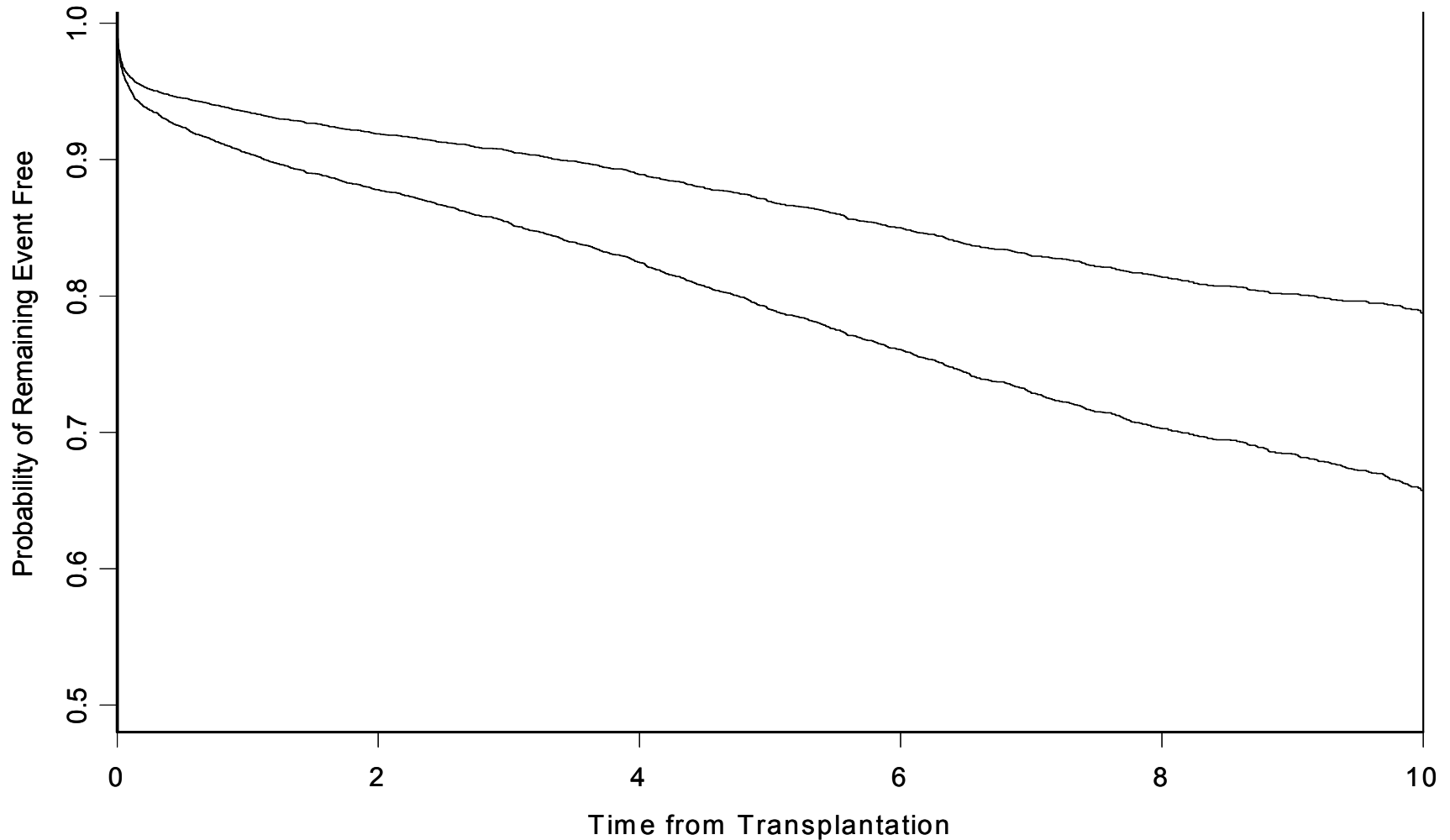
Cox multivariate regression models

- Outcomes
 - patient survival
 - death censored graft survival
- Plotted adjusted hazards from these models over a 10 year time horizon

All Cause Graft Loss Cox Multivariate Model (also adjusted for province)

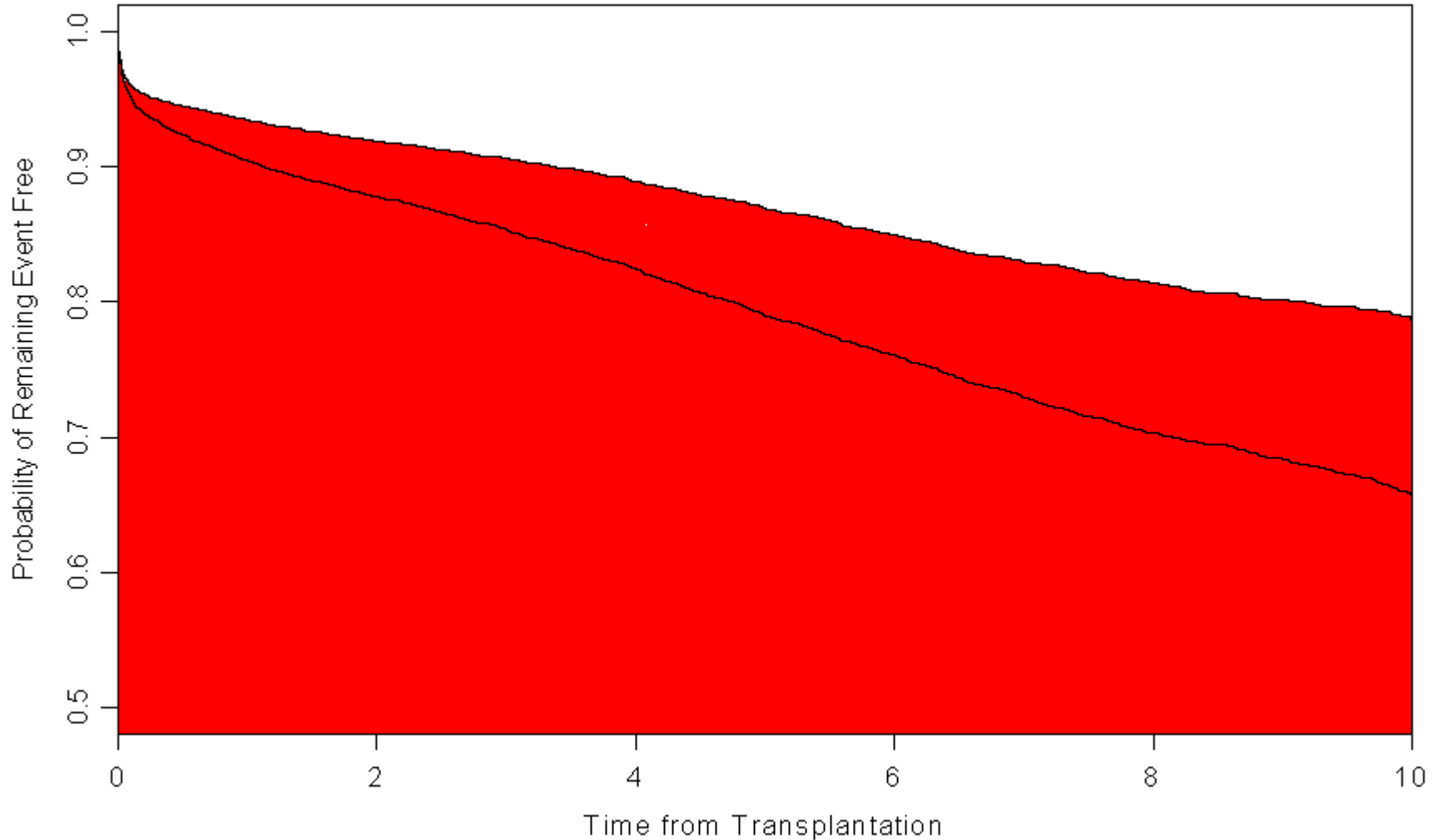
| | HR (95% CI) | P-Value |
|----------------------------|--------------------------|-------------------|
| Male | 0.92 (0.83,1.01) | 0.08 |
| GN | 1.00 | |
| DIAB | 1.50 (1.32, 1.71) | <0.0001 |
| OTHER | 1.05 (0.94, 1.16) | 0.38 |
| White | 1.00 | |
| Asian | 0.78 (0.64, 0.95) | 0.01 |
| Black | 0.83 (0.64, 1.07) | 0.71 |
| Indian Subcontinent | 0.68 (0.52, 0.88) | 0.0038 |
| Aboriginal | 1.07 (0.84, 1.37) | 0.17 |
| PRA>30 | 1.18 (1.01, 1.38) | 0.04 |
| HLA match: | | |
| 5-6 | 1.00 | |
| 3-4 | 0.79 (0.59, 1.07) | 0.13 |
| 1-2 | 0.81 (0.61, 1.08) | 0.81 |
| 0 | 0.90 (0.66, 1.23) | 0.90 |
| 1995-8 | 1.00 | |
| 1999-2002 | 0.68 (0.61, 0.76) | <0.0001 |
| 2003-5 | 0.59 (0.51, 0.70) | <0.0001 |
| Preemptive | 1.00 | |
| 0-1 y | 1.07 (0.78, 1.47) | 0.67 |
| 1.1-2.9 | 0.99 (0.74, 1.32) | 0.95 |
| 3.0-3.9 | 0.92 (0.67, 1.27) | 0.62 |
| 4.0 + | 0.99 (0.73, 1.35) | 0.94 |

Patient and death censored graft survival



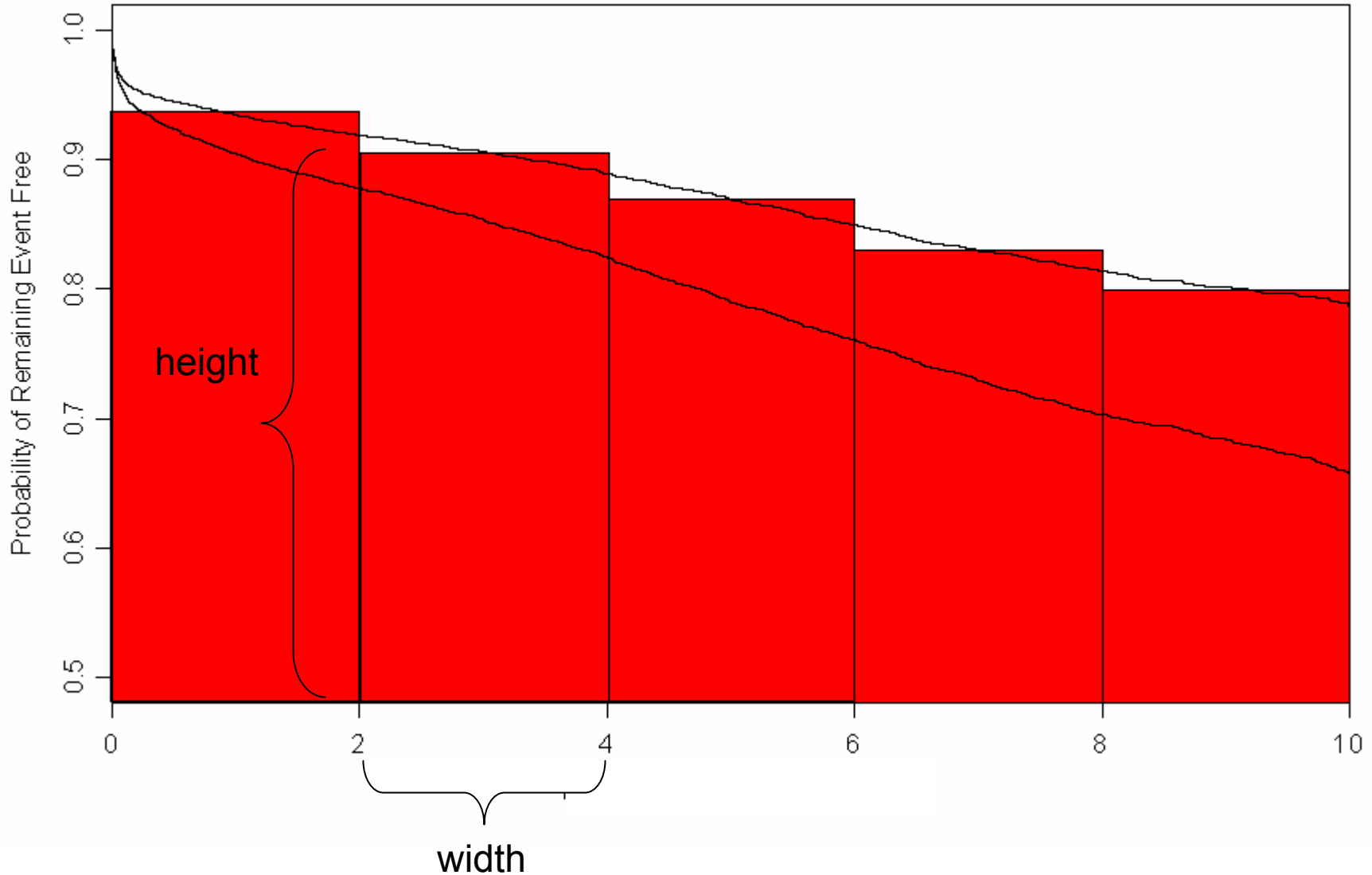
Cox multivariate model adjusting for differences in Gender, Race, Cause of ESRD, Time on dialysis prior to transplantation, HLA, PRA, Province of transplant, year of transplant

Area under top curve is Months of Patient Survival (max 120 months)

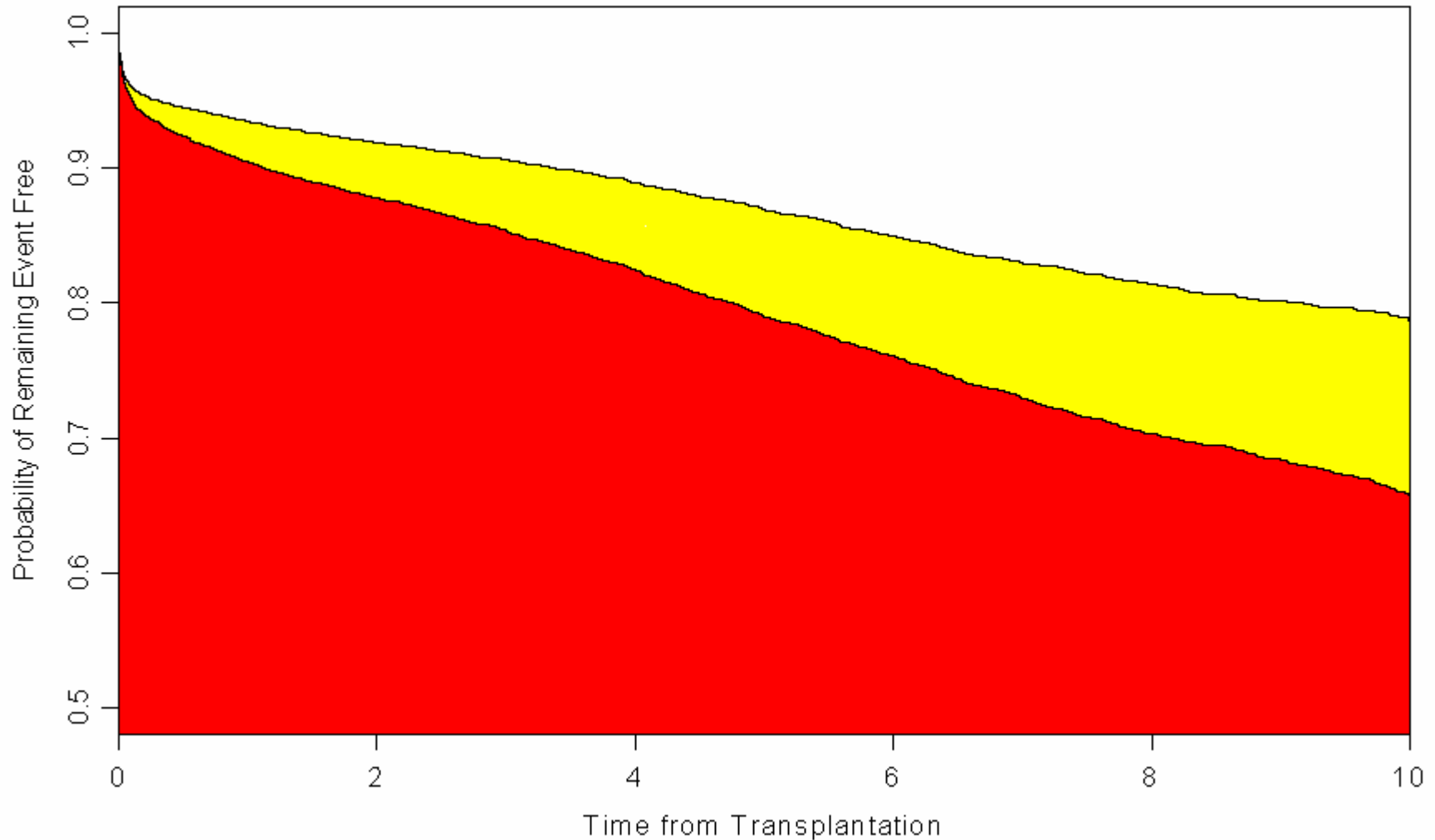


Estimate Area using Rectangles

Area = $\Sigma(\text{width} \times \text{height})$



Difference between area under patient survival curve and graft survival curve (death censored)
= Time on Dialysis After Transplant Failure



Our Goal: “Define Young”

- **Young recipient**

- Recipient age cut-off below which patient life expectancy is $>$ than expected duration of graft survival

Is David Young?



Identifying “young recipient” age cut-off Example

Using donor age cut point of <35 or ≥ 35 years

| Recipient Age | Survival if transplanted with Donor Age 19-34 (months) | | | Survival if transplanted with Donor Age 35-59 (months) | | | Benefit of this age group receiving donor kidney < 35 (Diff 2-1) |
|---------------|--|-------------------------------|--|--|-------------------------------|--|--|
| | Patient Survival | Death Censored Graft Survival | Patient Survival Minus Graft Survival (Diff 1) | Patient Survival | Death Censored Graft Survival | Patient Survival Minus Graft Survival (Diff 2) | |
| 19-39 | 118.94 | 106.95 | 11.99 | 118.00 | 99.44 | 18.56 | 6.57 |
| 40-49 | 116.39 | 117.05 | -0.66 | 111.77 | 104.73 | 7.04 | 7.04 |
| 50-54 | 119.58 | 119.49 | 0.09 | 112.15 | 110.93 | 1.22 | 1.13 |
| 55+ | 99.63 | 118.68 | -19.05 | 98.96 | 106.80 | -7.84 | -- |

Our Goal: “Define Young Recipient”

- “Young recipient”
 - Recipient age cut-off below which patient life expectancy is $>$ than expected duration of graft survival
 - All patients < 55 outlive their grafts and thus would benefit from receiving kidney from a young donor (using various donor age cut-points)
 - **Thus UNDER 55 years = YOUNG RECIPIENT**
- “Old recipient” - Patients ≥ 55 :
 - Are likely to die with a functioning graft and thus will not benefit from a young donor kidney
 - We do not significantly shorten the life expectancy of patients ≥ 55 by not transplanting them with younger donor kidneys
 - We could reasonably exclude patients ≥ 55 years from receiving young donor kidneys

Our Goal: “Define Young Donor”

- **Young donor (operational definition)**
 - Donor age cut-off below which young recipients have improved graft/patient survival
 - Donor age cut-off above which there is the least adverse effect on graft/patient survival in older recipients
- Should our young donor cut-off be 35 or 40 yrs?

Utility perspective:

No real difference if “young donor” defined as
< 35 or < 40 yrs

| | Patient Survival with donor <35 or <40 yrs (months) | Graft Survival with donor < 35 or <40 yrs (months) |
|------------------------|--|---|
| 19-39 yr recipients | 118.94 vs 118.82 | 106.98 vs 105.35 |
| 40-49 yr recipients | 111.77 vs 111.5 | 104.73 vs 104.16 |
| 50-54 yr recipients | 112.15 vs 111.42 | 110.93 vs 110.58 |

Equity

What is the Young Donor Age Cut-Off?

- Depends on
 - the number of “young recipients” (<55 years) who would be prioritized to receive “young donor kidneys”
 - the number of deceased donor kidneys at different age cut-offs (i.e. < 35yrs or < 40yrs)

Donor and Recipient Age Over Time

| | ERA 1 (1995-1998) | | ERA 2 (1999-2002) | | ERA 3 (2003-2005) | |
|----------------|----------------------|------------------------|----------------------|------------------------|----------------------|----------------------|
| Age | Donor | Recipient | Donor | Recipient | Donor | Recipient |
| 19-35 | 903 (42%) | 405 (19%) | 748 (35%) | 309 (14%) | 477 (31%) | 171 (11%) |
| <40 | 1,095 (50%) | 647 (30%) | 907 (42%) | 487 (23%) | 578 (37%) | 288 (18%) |
| <45 | 1,328 (61%) | 900 (41%) | 1,183 (55%) | 727 (34%) | 763 (49%) | 445 (29%) |
| <50 | 1,563 (72%) | 1,287 (59%) | 1,438 (67%) | 1,083 (51%) | 943 (61%) | 688 (44%) |
| <55 | 1,766 (81%) | 1,574 (72%) | 1,653 (77%) | 1,383 (65%) | 1,097 (70%) | 911 (59%) |
| <60 | 1,959 (90%) | 1,800 (83%) | 1,869 (87%) | 1,677 (79%) | 1,278 (82%) | 1,160 (75%) |
| >=60 | 214 (10%) | 373 (17%) | 268 (13%) | 460 (21%) | 280 (18%) | 398 (25%) |
| Total | N= 2,173 | | N=2,137 | | N=1,558 | |

N = Number of deceased donor organs transplanted

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Donor age cut-off < 35 or < 40 years?

- Choosing cut-off <35 will help minimize the potential negative impact on recipients ≥ 55 years
 - Also patients ≥ 55 can be prioritized for ECD kidneys

Projected Impact of Changes
2003-5, N =105 kidneys from donors 19-34
were transplanted to recipients aged 55+

| | Donor Age | | |
|---------------|-----------|-------|-----|
| | 19-34 | 35-59 | 60+ |
| Recipient Age | | | |
| 19-54 | 201 | 447 | 106 |
| 55+ | 105 | 373 | 174 |

Change in allocation should be offset by redistribution of ECD (60+) kidneys

| | Donor Age | | |
|---------------|-----------|-------|-----|
| | 19-34 | 35-59 | 60+ |
| Recipient Age | | | |
| 19-54 | 201 | 447 | 106 |
| 55+ | 105 | 373 | 174 |

Summary

Recommendations, Implementation,

- Wait-listed patients in Canada < 55 yrs should be prioritized to receive deceased donor kidneys from donors < 19-35 years
- Recommendation approved for implementation by all kidney transplant programs in Canada in 2008
- CST Kidney working group will track impact through CORR and reassess this recommendations in 3 years

CST Kidney Work Group and CORR will monitor
the impact of these changes

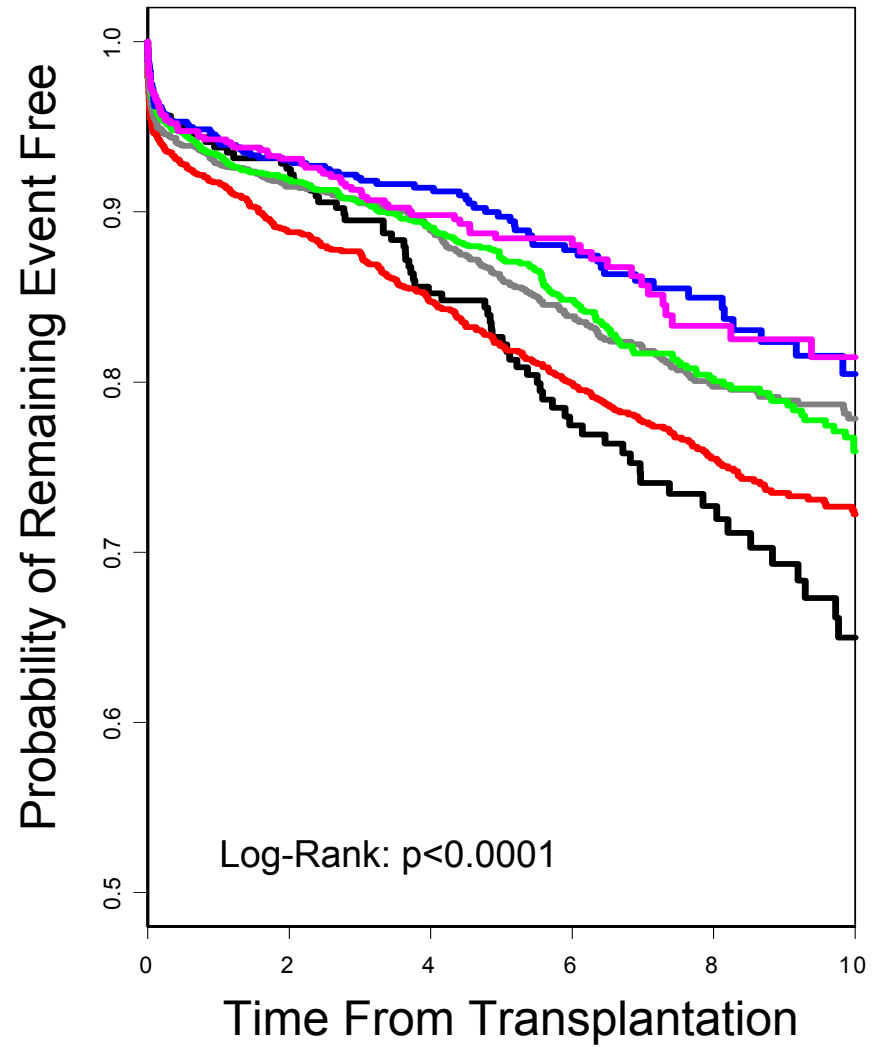
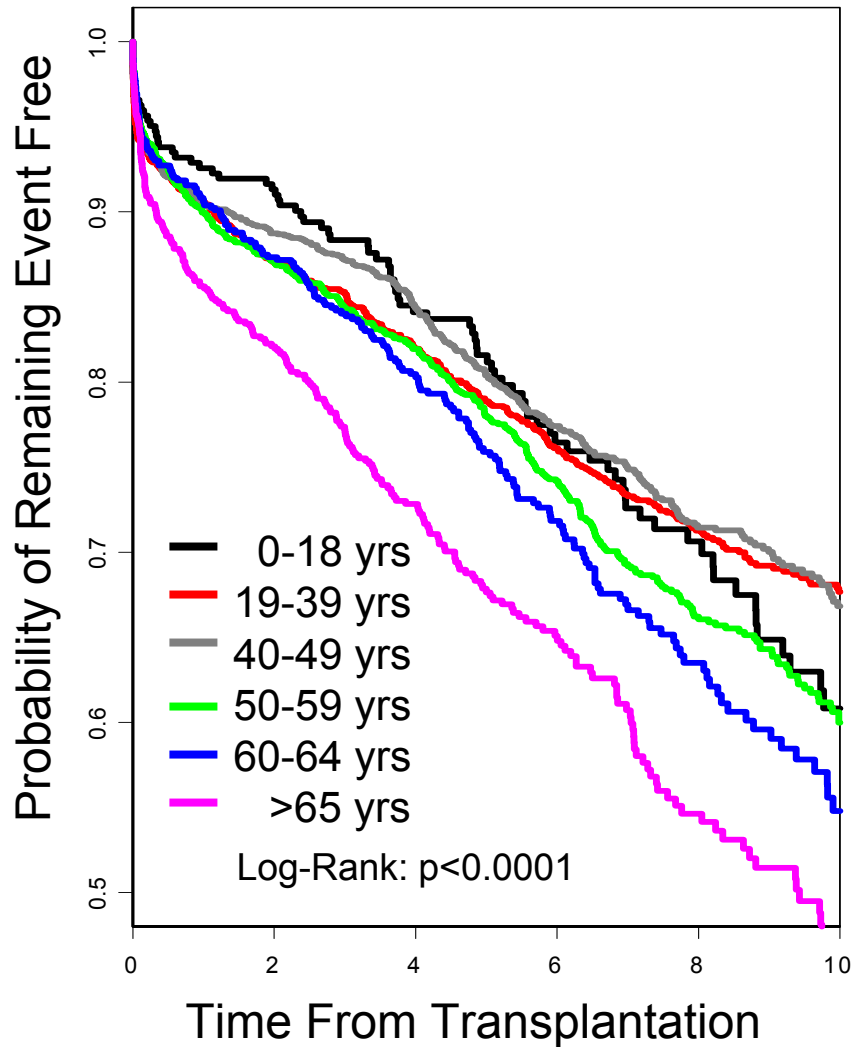
- Assess impact in 3 years
- Practice patterns
- Change in waiting time

Thank you!

Recipient Age and Graft Survival

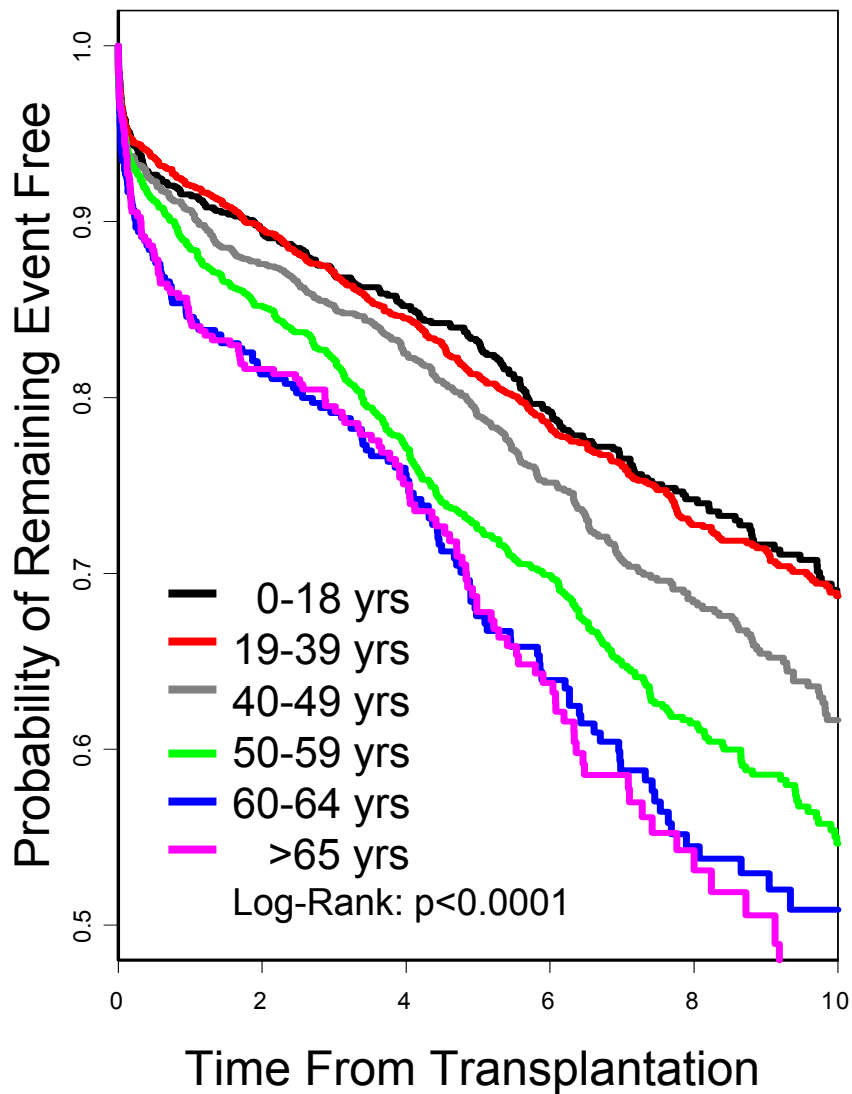
All Cause

Death Censored

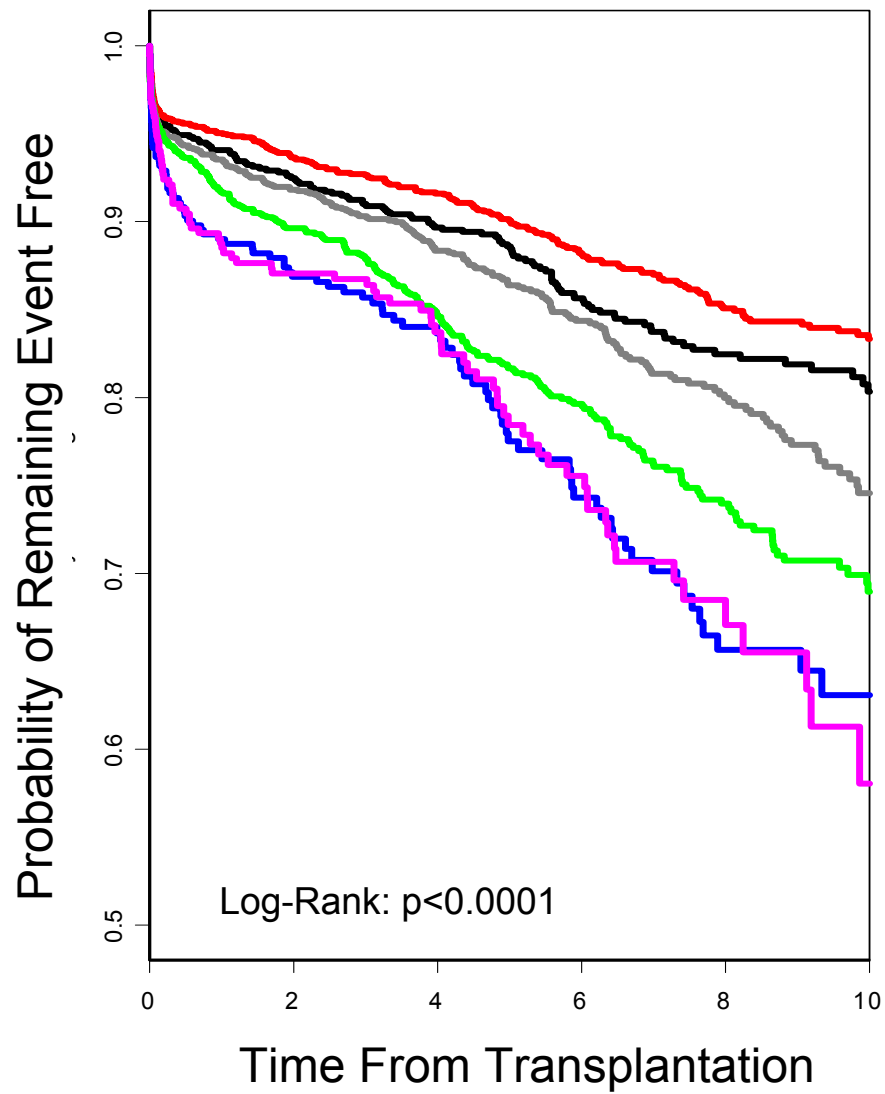


Donor Age and Graft Survival

All Cause



Death Censored



Our Goal: “Define Young”