



Simposio SIBO - XXII Congresso Nazionale S.I.T.R.A.C – 22 febbraio 2017, Firenze



# donor and transplantation

# The Influence of Donor

# Gender and Age

# in Cornea Transplantation

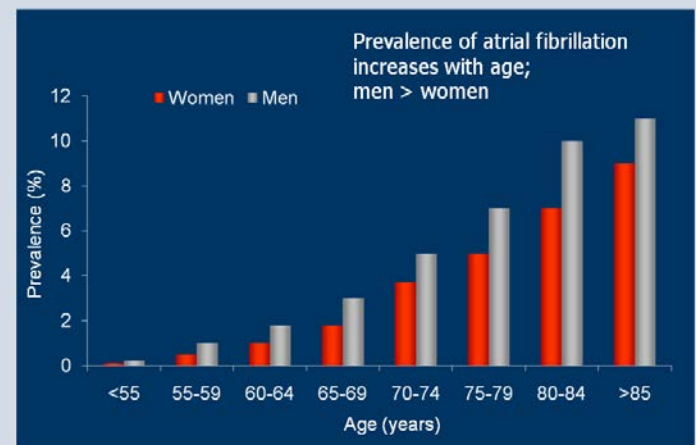
Federico Genzano Besso

Banca delle Cornee Piemonte e Valle d'Aosta

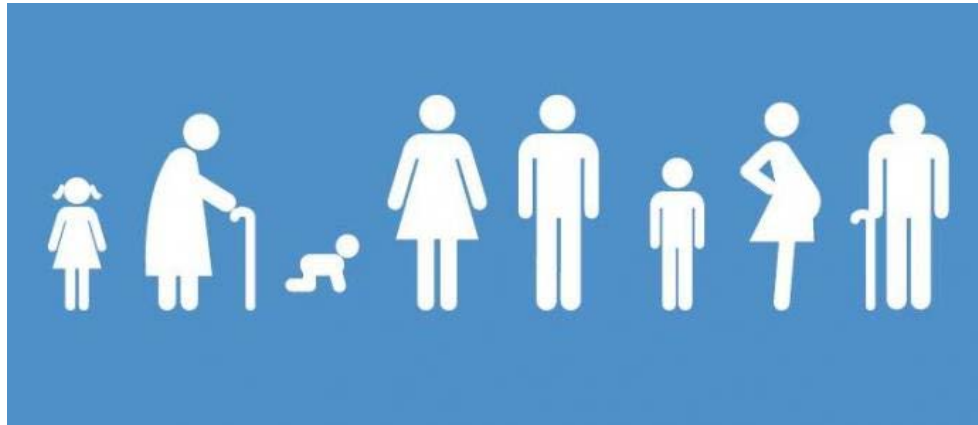
- Donor Age
- Donor Gender



Prevalence of AFib: Age and Gender



- **Donor Age**
- Donor Gendre





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## Factors Influencing the Suitability of Organ-Cultured Corneas for Transplantation

*W. John Armitage and David L. Easty*

### Suitability of Organ-Cultured Corneas for PKP

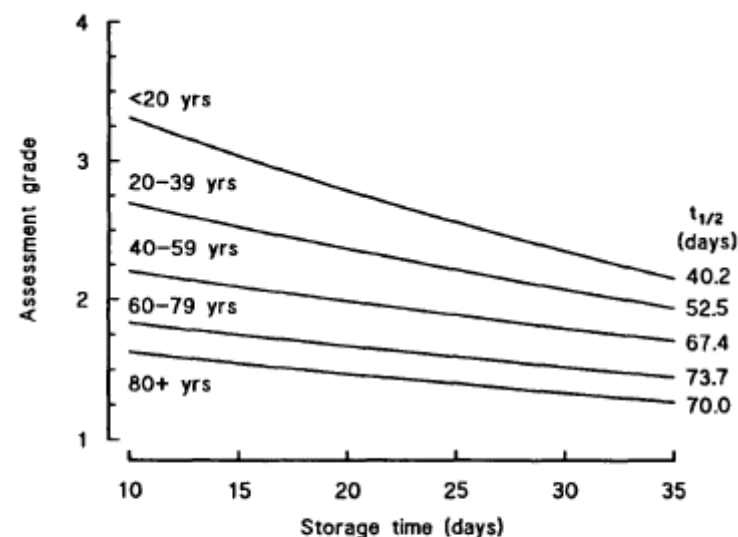
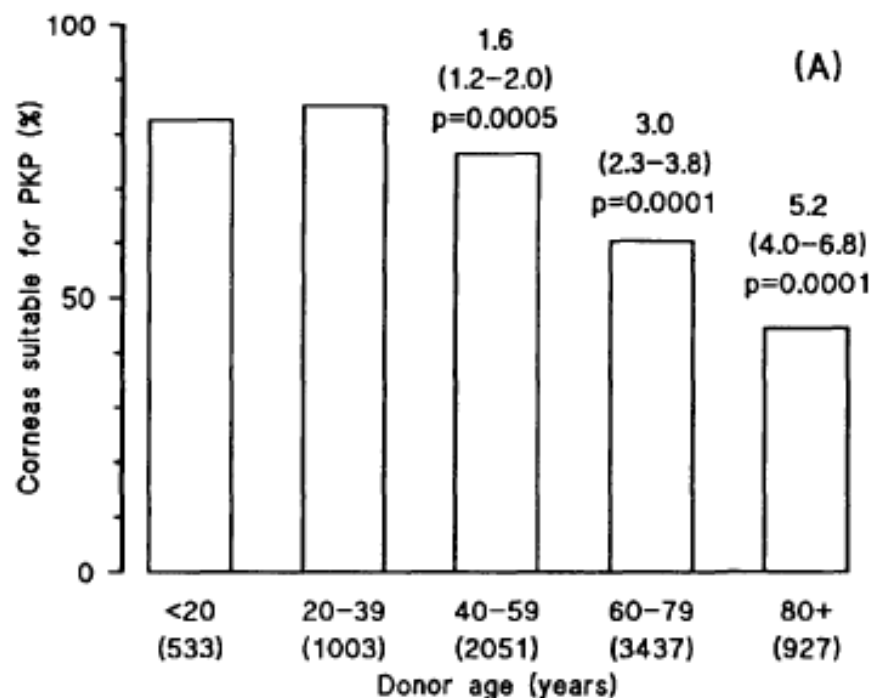


FIGURE 7. Decline in endothelial assessment grade with storage time stratified by donor age. Exponential curves of the type  $A_t = A_0 e^{-kt}$  ( $A_0$  = initial assessment grade;  $A_t$  = assessment grade at time  $t$ ;  $k$  = time constant; and  $t$  = time in days) were fitted to the data for each age group and are shown with the half-times ( $t_{1/2}$ ) for the decay.



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imum age limit for eye donors. On the other hand, the Corneal Transplant Follow-up Study in the United Kingdom,<sup>3</sup> which followed the progress of 2311 grafts (92% organ cultured), did not find a significant effect of donor age on graft survival at 1 year using proportional hazards regression, which simultaneously controlled for recipient and other factors. Indeed, graft survival was independent of all donor and storage factors. We have demonstrated, albeit in a limited study,



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# Donor Age and Factors Related to Endothelial Cell Loss 10 Years after Penetrating Keratoplasty

## *Specular Microscopy Ancillary Study*

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*Writing Committee for the Cornea Donor Study Research Group\**

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Table 2. Ten Year Endothelial Cell Density (ECD) in Eyes with Successful Transplant

Donor Age	N	Baseline ECD*	5-Year ECD	10-Year ECD	% Change from	N (%) with 10-Year ECD<500 cells/mm <sup>2</sup>	10-Year ECD P-value
		cells/mm <sup>2</sup>	cells/mm <sup>2</sup>	cells/mm <sup>2</sup>	Baseline to 10 Years <sup>†</sup> cells/mm <sup>2</sup>		
Median (Interquartile Range)							
Overall	176	2695 (2498, 2890)	786 (616, 1343)	611 (502, 769)	−76% (−82%, −70%)	42 (24%)	
Donor Age (years):							
12 to 65 years	125	2726 (2542, 2924)	870 (666, 1462)	628 (522, 850)	−76% (−80%, −68%)	25 (20%)	0.03
66 to 75 years	51	2617 (2426, 2747)	683 (560, 1142)	550 (483, 694)	−79% (−82%, −72%)	17 (33%)	
12 to 33 years	26	2950 (2731, 3082)	1309 (1021, 1624)	886 (584, 1126)	−67% (−79%, −60%)	1 (4%)	<0.001
34 to 52 years	42	2695 (2587, 2849)	792 (589, 1401)	654 (577, 764)	−75% (−78%, −72%)	5 (12%)	
53 to 71 years	90	2615 (2462, 2805)	748 (606, 1194)	581 (472, 698)	−78% (−82%, −72%)	30 (33%)	
72 to 75 years	18	2666 (2398, 2776)	719 (565, 1356)	563 (480, 706)	−78% (−82%, −71%)	6 (33%)	

P-values are from analysis of covariance models for the 2 and 4 level donor age groups. Both models were adjusted for baseline ECD. Models were fitted with van der Waerden scores of the ECD values at baseline and 10 years. While adjusting for baseline ECD, the p-value for the association between ECD at 10 years and continuous donor age was < 0.001.

\*Includes baseline ECD from eye bank for 53 eyes and from reading center for 123 eyes.

†Percent change from baseline to 10-year ECD = ECD at 10 years minus ECD at baseline divided by ECD at baseline and multiplied by 100%. A negative number indicates loss of cells.





Table 3. Endothelial Cell Density (ECD) at 10 Years by Baseline Recipient/Donor Factors Included in the Final Multivariate Model

Baseline Factors	No.	Baseline ECD, Median	10-Year ECD, Median	% Change in ECD,* Median	Multivariate P Value for 10-Year ECD <sup>†</sup>
Overall	176	2695	611	-76	
Recipient factors					
Age (yrs)					0.07 <sup>‡</sup>
40-<50	10	2794	700	-73	
50-<60	41	2690	595	-76	
60-<70	55	2673	618	-76	
70-86	70	2709	607	-78	
Diagnosis and lens status <sup>§</sup>					0.001 <sup>  </sup>
Fuchs: pre/post phakic	52	2696	640	-76	
Fuchs: pre phakic/post PA	64	2700	598	-78	
Fuchs: pre/post PA	29	2668	603	-77	
PACE: post PA	27	2636	760	-72	
Operative factors					
Donor tissue size (mm)					0.02 <sup>‡</sup>
7.00-7.75	39	2673	593	-78	
8.00	24	2676	523	-79	
8.25-9.00	113	2718	632	-76	
Donor factors					
Age (yrs)					<0.001 <sup>‡</sup>
12-<34	26	2950	886	-67	
34-<53	42	2695	654	-75	
53-<72	90	2615	581	-78	
72-75	18	2666	563	-78	





vival. *Invest Ophthalmol Vis Sci*. 2014;55:784-791. 10.1167/jov.13-13386

## The Suitability of Penetrating Keratoplasty Recipient Factors

W. John Armitage,<sup>1,2</sup> Mark J. Graham (for the NHSBT Ocular Transplant Study 12)

### Donor Factors and PK Outcome



### Graft Survival at 5 Years

The Kaplan-Meier survival estimate for first PK at 5 years was 73% (95% CI 72%–75%) across all indications (Fig. 1). The Cox model of factors influencing 5-year survival is shown in Table 6. The only donor factor to have an effect on graft survival was **donor sex**. Transplantation of corneas from male donors increased the risk of failure compared with female donors ( $P = 0.008$ ). None of the other donor factors (see note, Table 6) influenced graft survival. Indication had a major influence on graft survival (Fig. 2). Five-year survival for transplants for

FIGURE 1. Kaplan-Meier survival plot across all indications. Survival estimate at 5 years: 73% (95% CI 72%–75%). Numbers of grafts at risk: initially, 3014; 1 year, 2601; 2 years, 1864; 5 years, 424.



# Conclusions

Relative risk

## Donor Age



- Donor Age
- **Donor Gendre**







Transplantation. 2006 Oct 27;82(8):1037-41.

## **Matching of the minor histocompatibility antigen HLA-A1/H-Y may improve prognosis in corneal transplantation.**

Böhringer D<sup>1</sup>, Spierings E, Enczmann J, Böhringer S, Sundmacher R, Goulmy E, Reinhard T.

### **⊕ Author information**

#### **Abstract**

**BACKGROUND:** Minor histocompatibility (H) antigens are peptides of allelic intracellular proteins that play an important role in human leukocyte antigen (HLA) matched transplantations. In an animal model of keratoplasty, minor H antigens have even been reported to exceed the immunogenicity of major H antigens (MHC). This investigation is to assess any benefit of matching the broadly expressed gender (H-Y) and HA-3 antigens in HLA-A1 donor positive human keratoplasty.

**METHODS:** A total of 229 HLA-A1 donor positive keratoplasties were analyzed. A Cox proportional hazards model and Kaplan-Meier analysis were applied to estimate the effect of H-Y or HA-3 mismatches on rejection-free graft survival.

**RESULTS:** Eighty-one cases were mismatched for H-Y (male donor to female recipient). A mean follow up of two years showed graft survival as high as 88% in the H-Y compatible group compared to only 77% in the H-Y mismatched group ( $P = 0.02$ ). Eight out of 62 cases were mismatched for HA-3. No statistically significant influence of HA-3 matching on rejection-free graft survival was observed (85% vs. 73%,  $P=0.52$ ).

**CONCLUSION:** HLA-A1/H-Y matching and matching for other broadly expressed minor H antigens may further improve prognosis in keratoplasty.





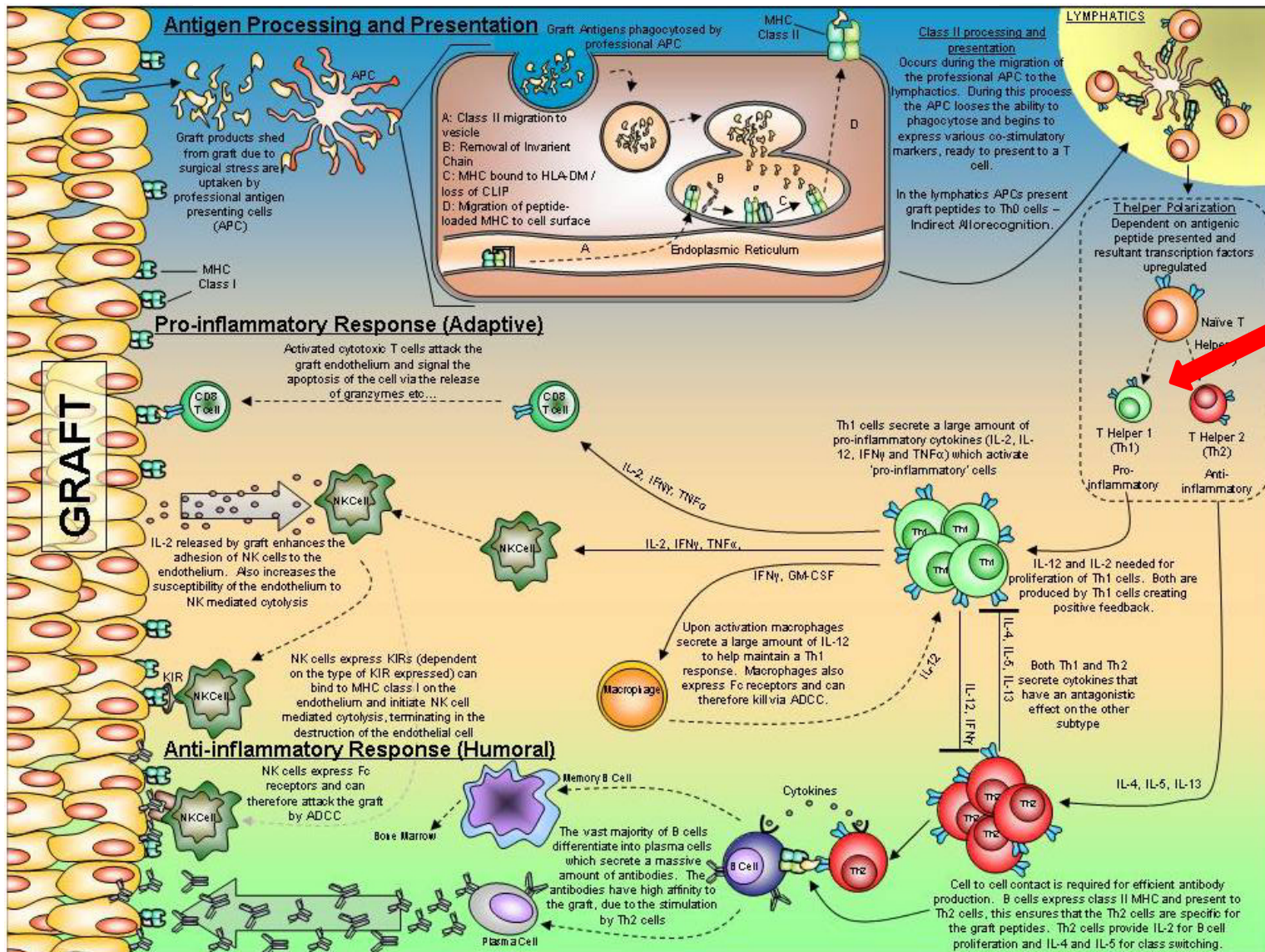
# The Influence of Donor and Recipient Gender Incompatibility on Corneal Transplant Rejection and Failure

C. L. Hopkinson<sup>1,†</sup>, V. Romano<sup>2,†</sup>, R. A. Kaye<sup>2</sup>,  
B. Steger<sup>2</sup>, R. M. K. Stewart<sup>2,3</sup>, M. Tsagakataki<sup>2</sup>,  
M. N. A. Jones<sup>1</sup>, D. F. P. Larkin<sup>4</sup> and  
S. B. Kaye<sup>2,3,\*</sup> on behalf of the National Health  
Service Blood Transplant Ocular Tissue  
Advisory Group and Contributing  
Ophthalmologists (OTAG Study 20)

tors. Of 18 171 patients, 4314 had undergone a trans-  
plant for FED, 4783 for KC, 3669 for PBK, 1903 for  
infection and 3502 for other disorders. H-Y mis-



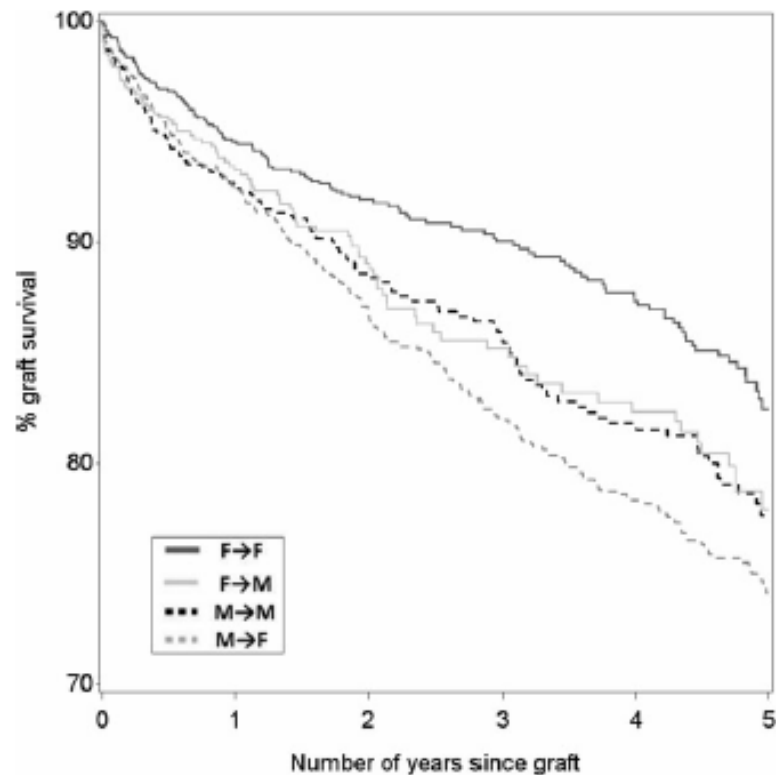
gen (mHA) H-Y-directed cytotoxicity (2). Scott et al subsequently reported that H-Y epitopes derived from intracellular proteins can be detected by CD4<sup>+</sup> T cells and presented on the cell surface via the major histocompatibility complex (MHC) (3). mHAs recognized by donor T





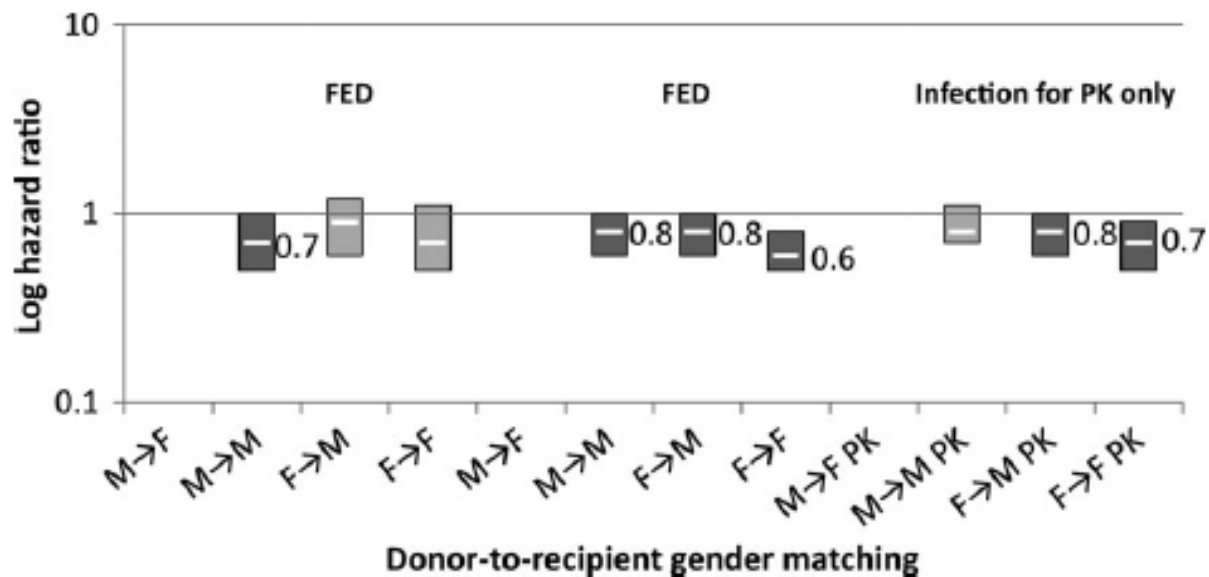


## Gender Matching and Corneal Transplant Failure



Donor to Recipient				
Level	F→F	F→M	M→M	M→F
N	1079	626	877	1464
Failed	128	88	132	267
Estimate	82	78	78	74
95% CI	79-85	73-82	74-81	71-77
p-Value	0.0001			

Figure 1: Kaplan-Meier estimate of graft survival for patients with Fuchs endothelial dystrophy (FED) according to gender match or mismatch. The effect of donor-to-recipient matching and mismatching on graft survival following corneal transplantation (penetrating keratoplasty and endothelial keratoplasty) for patients with FED. F, female; M, male.

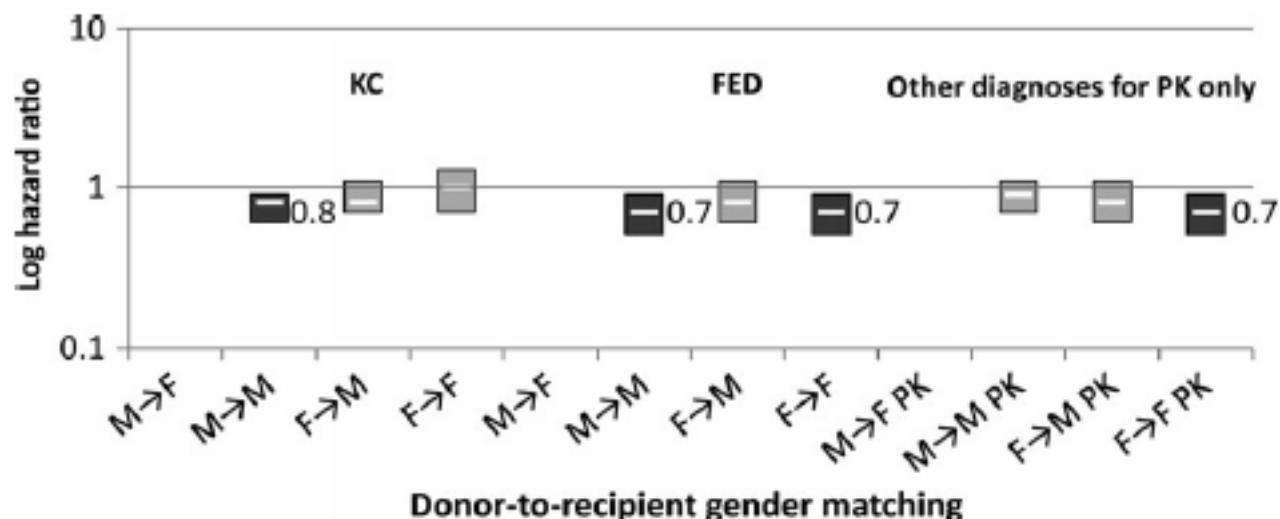


**Failure**

**Relative risk**

**Rejection**

**Relative risk**





# Conclusions

## Relative risk

This study demonstrates, overall, that gender matching was significantly associated with reduced graft failure and rejection in patients with KC and FED. For patients with





# Conclusions

Relative risk

## What to do tomorrow?







# Conclusions

## Relative risk





# Conclusions

Relative risk

## We'll do our homework

