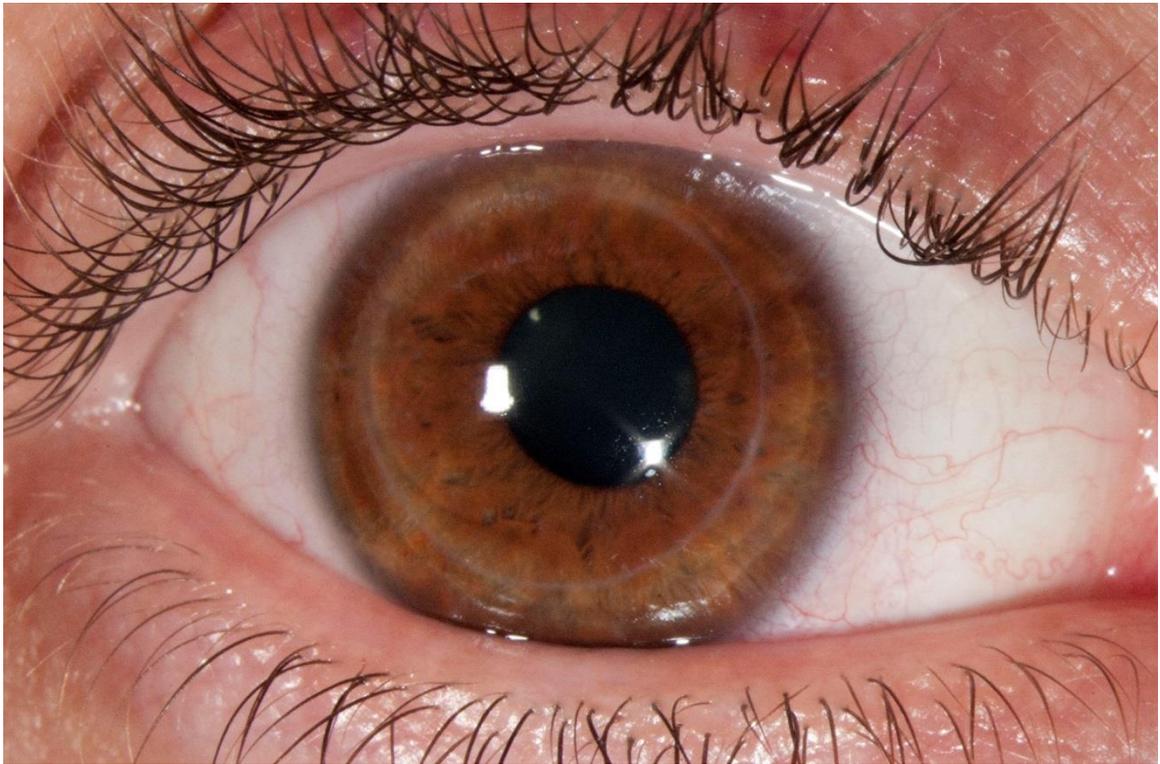


# THE AUSTRALIAN CORNEAL GRAFT REGISTRY



## 2018 REPORT

This report was published with assistance provided by The Australian Government Organ and Tissue Authority (DonateLife)

Please note: throughout this report some pages are intentionally left blank so that corresponding figures and tables will appear opposite one another when viewed in two-page side-by-side format.

To ensure that this PDF document displays correctly, please select “show cover page in two-page view” when using Adobe Acrobat programs to view this file.

**Cover photo by Angela Chappell**

# **THE AUSTRALIAN CORNEAL GRAFT REGISTRY**

## **2018 REPORT**

KA Williams, MC Keane, NE Coffey, VJ Jones, RAD Mills and DJ Coster

Department of Ophthalmology, Flinders University

South Australian Health and Medical Research Institute

# Acknowledgments

We appreciate the co-operation of the following eye banks:

Eye Bank of South Australia

Lions New South Wales Eye Bank

Lions Eye Bank of Western Australia

Lions Eye Donation Service, Victoria

Queensland Eye Bank

This report was published with assistance provided by The Australian Government Organ and Tissue Authority (DonateLife)

We acknowledge the assistance of the Australian Institute of Health and Welfare in keeping our records up-to-date via data linkage with the National Death Index

The Australian Corneal Graft Registry operates under the guidelines and approval of the Southern Adelaide Clinical Human Research Ethics Committee

Contact Details:

**The Australian Corneal Graft Registry**

Department of Ophthalmology, Flinders University

Flinders Medical Centre

Bedford Park SA 5042

Australia

Telephone: +61 8 8204 5321

Fax: +61 8 8277 0899

Email: [keryn.williams@flinders.edu.au](mailto:keryn.williams@flinders.edu.au)

# Introduction

The Australian Corneal Graft Registry (ACGR) opened in May 1985 and has now been operating for 33 years. Over the years, we have collected information on more than 33,000 corneal grafts.

At registration, we seek information on the donor, eye bank practices, the recipient, the surgeon, the graft type and the operative procedure. Follow-up then occurs at approximately yearly intervals for an indefinite period, and ceases upon graft failure, or the death or loss-to-follow-up of the patient. At each round of follow-up, we request information on the survival of the graft, the visual outcomes, and any relevant post-operative events and treatments.

The data are entered into an Access database and checked for consistency. Descriptive, univariate and multivariate analyses are subsequently performed using SPSS and Stata software, and the report is eventually collated. As has been the case in the past, a pdf of the final report is placed in a permanent, open-access institutional repository, so that it can be accessed freely. This report can be accessed at: <http://hdl.handle.net/2328/37917>.

We have analysed all grafts performed up to 30-04-2017 and registered with the Australian Corneal Graft Registry up to a census date of 31-07-2017. Penetrating keratoplasties (PKs), traditional lamellar keratoplasties (TLKs), deep anterior lamellar keratoplasties (DALKs), and the various forms of endothelial cell keratoplasty (DSEKs/DSAEKs and DMEKs) have been examined separately.

We thank our many contributors for their tireless efforts on our behalf. We hope this report is useful and relevant to your clinical practice.

# How to read our Kaplan-Meier Plots of Graft Survival

1. The vertical axis shows the probability of graft survival. "Perfect" survival (no failures) equates to a probability of 1.0. It may help to think of this as 100% survival.
2. The horizontal axis shows time elapsed from the date of graft. This is shown as years post-graft, although the analysis is performed on daily graft survival.
3. The p-values shown have been calculated by log-rank analysis and reflect a comparison of the behaviour of the curves as a whole (taking all available data into consideration), rather than at any one time-point.
4. The numbers of recipients being followed at given times after graft are shown below the curves in the "Number at risk" table. At time zero, all followed patients in the given cohort are at risk. At the furthestmost point on the right hand side of any curve, the patient(s) who have been followed for the longest time are at risk.

We suggest that you interpret the survival curves with this in mind. A sudden "dip" in survival at the far right of a given curve may merely mean, for example, that one of only two grafts that have been followed for this length of time has failed. When the survival curve drops to zero, this means that all grafts that have reached this length of follow-up have failed. It does not mean that all grafts in this stratum have failed, or will fail.

For example, a single graft may have been followed for 2 years, at which point it failed, while 20 grafts may have been followed for 1 year and 364 days and are all surviving at last follow-up. No other grafts have been followed for as long as the one that has failed, so the survival curve will drop to zero at this point. However, had the graft failed at 1 year and 364 days, the curve would not meet the horizontal axis, as there would be 20 other surviving grafts followed for the same amount of time.

# List of Contributors (1985 – 2017)

Aboud, JD  
Aboud, ND  
Achnad, J  
Adams, A  
Adamski, M  
Adler, P  
Agnello, R  
Albietz, JM  
Alexander, R  
Al-Horani, G  
Allan, B  
Ambler, J  
Anderson, IL  
Anderson, J  
Anderson, L  
Anderson, PF  
Andersons, V  
Ang, A  
Anzelmi, V  
Apel, AJG  
Apel, JVT  
Apiro, P  
Aralar, A  
Armstrong, RJ  
Arnold, JJ  
Asimakis, P  
Asten, G  
Astri, M  
Athanasidou, C  
Athanasiov, P  
Atkins, TJ  
Atkinson, GA  
Austin, CW  
Azar, D

Bahemia, AM  
Baig, SH  
Bailey, CP  
Bailey, MJ  
Baker, CH  
Balachandran, C  
Ball, M  
Bambery, SJ  
Barila, A  
Barker, NH  
Barnes, BJ  
Barnes, CJ  
Barnett, WJ  
Barrett, G  
Bassili, S  
Beaumont, P  
Beckingsale, P  
Beltz, I  
Beltz, J  
Benecke, P  
Benjamin, FA  
Bennett, C  
Benson, CJ  
Billson, FA  
Binetter, RG

Black, D  
Blane, JP  
Bolliger, PA  
Bonnellamb, T  
Booth, F  
Booth-Mason, S  
Boreham, C  
Borger, JP  
Bors, FH  
Bosky, T  
Both, R  
Bougher, GJ  
Boyce, J  
Bradshaw, H  
Brennan, MH  
Brian, G  
Briner, AM  
Brooks, AMV  
Brown, CJ  
Brunckhorst, A  
Buckley, CA  
Bui, C  
Burgess, FCL  
Burt, PF  
Burvill, MJ  
Buttery, RG  
Byrne, JB

Cains, SE  
Cairns, JD  
Calthorpe, M  
Cameron, R  
Campanella, G  
Campbell, DV  
Campbell, WG  
Candy, D  
Cano, DD  
Carey, TM  
Carroll, LA  
Cassidy, D  
Chadha, VB  
Chai, KC  
Chaing, M  
Challinor, CJ  
Chan, C  
Chan, DGW  
Chan, E  
Chan, I  
Chan, U  
Chandra, J  
Chang, A  
Chapman, PJ  
Charalambous, T  
Charawanamuttu, A  
Charley, N  
Chau, P  
Chehade, MA  
Chelvanayagam, D  
Cheok, FPG  
Cher, I

Cherny, M  
Chester, GH  
Chi, J  
Chin, D  
Chiu, DWK  
Ch'ng, AC  
Chow, S  
Chowdhury, V  
Chua, B  
Chua, SK  
Clark, B  
Cleary, G  
Clemens, I  
Cockie, P  
Cohen, PRA  
Cohn, GS  
Collie, DM  
Conaghan, T  
Confos, N  
Connell, B  
Conrad, D  
Constable, IJ  
Constantine, M  
Conway, RM  
Cooper, PS  
Cooper, RL  
Coote, BD  
Coote, MA  
Corbett, D  
Cornwell, R  
Coroneo, M  
Cosgrove, JM  
Coster, DJ  
Cottee, LB  
Craddock, N  
Cranstoun, PD  
Crawford, BA  
Crawford, GJ  
Crayford, BB  
Crock, GW  
Crompton, JL  
Cronin, B  
Cunningham, F  
Cutler, B  
Czigler, B

Da Rin, D  
Dal-Pra, ML  
Dalton, JA  
Dang, V  
Daniel, M  
Daniell, MD  
Danks, J  
Davey, JC  
Davies, GA  
Davies, IC  
Davies, J  
Davies, M  
Davies, P  
Davies, RP

Davis, GJ  
Davis, H  
Davis, JL  
De Vincentis, F  
De Wet, M  
Del Poppo, S  
Delahunty, D  
Delaney, MR  
Della, N  
Den, BD  
Denman, DP  
Dethlefs, RF  
Devereaux, J  
Diab, D  
Diamond, J  
Dickson, D  
Dinihan, IJ  
D'Mellow, G  
Dobinson, JS  
Don, B  
Donaldson, C  
Donaldson, M  
Donovan, B  
Dostal, F  
Douglas, I  
Downes, C  
Downie, NA  
Doyle, S  
D'Souza, B  
du Temple, DJ  
Duggan, JM  
Duke, PS  
Duncan, M  
Dunlop, AA  
Dunlop, C  
Dunlop, IS  
Durkin, DT  
Dyer, JA  
Dyson, C

Economos, AS  
Elder, JR  
Ellis, MF  
English, FP  
English, KP  
English, M  
Ennos, A  
Eshun-Wilson, T  
Evans, L

Farinelli, AC  
Farpour, B  
Farrah, J  
Favilla, I  
Favilla, ML  
Ferdinands, M  
Ferguson, M  
Fernando, G  
Field, AJ  
Finkelstein, E

Finnigan, S	Gupta, A	Howes, F	La Nauze, JH
Fitzsimons, SR	Gupta, N	Howsam, GN	Lai Kwon, N
Flaherty, MP	Gutteridge, I	Hughes, PH	Lam, CM
Flanders, M		Hunter, GT	Lam, GC
Fleming, PR	Hagen, E	Hunyor, A	Lamb, AM
Fong, LP	Hall, AJH	Hurley, IWJ	Landers, J
Foo, KPY	Hall, DR	Hutchinson, B	Landers, JAG
Forster, TDC	Hall, J	Huynh, T	Lane, MJ
Foster, AJ	Hall, P		Langford-Smith, J
Fraenkel, G	Hall, R	Ikladios, A	Lansdell, BJ
Frame, I	Halley, RM	Ingham, PN	Larkin, PW
Francis, D	Ham, BK	Ioannides, A	Latimer, A
Francis, IC	Ham, KB	Irvine, S	Latimer, PA
Franks, SS	Hammerton, ME	Isbell, G	Laureamo, J
Frauenfelder, G	Hand, C		Law, W
Frumar, KD	Handley, DE	Jacobi, L	Lawless, MA
Fullarton, F	Hann, J	Jamieson, IW	Lawson, DJ
	Hansen, C	Jaross, N	Le Feuvre, RJ
Galbraith, JEK	Hardy-Smith, P	Jefferies, P	Le May, M
Galbraith, JK	Harkness, MM	Jester, MP	Leber, GL
Game, J	Harris, A	Johnson, GW	Leckie, TD
Gardner, R	Harrisberg, BP	Jones, SA	Lee, A
Gaston, G	Harrison, JD	Jordan, AS	Lee, GA
Gaulke, S	Harrison, MR		Lee, JH
Gehling, NJ	Hart, DRL	Kalliris, A	Lee, V
Genge, J	Hatfield, E	Kappagoda, MB	Leikin, S
Gianarakis, N	Hauptman, O	Karagiannis, A	Lenton, LM
Gibbons, N	Haybittel, M	Karunaratne, DMS	Leow, Z
Giblin, ME	Hayes, PA	Karunaratne, N	Leppard, SD
Gibson, AG	Haymet, BT	Kaufman, DV	Leunig, GA
Gibson, AJG	Heery, SE	Kearney, RJ	Leunig, I
Gibson, BHL	Hefferan, W	Kearns, M	Leverett, M
Giles, M	Heine, DI	Keldoulis, T	Lewis, NL
Gillanders, W	Heiner, P	Kelly, AJ	Liew, S
Gillies, MC	Heiner, PC	Kelly, GJ	Lillicrap, GR
Gillies, WE	Heinze, JB	Kenna, J	Lim Joon, TH
Gin, M	Henderson, RG	Kennedy, IH	Lim, ASM
Glasson, WJ	Henderson, T	Kennedy, JE	Lim, P
Glastonbury, J	Hennessy, MP	Kent, DG	Lim, R
Glastonbury, JG	Henry, JG	Kent, R	Lindsay, R
Gnanaharan, P	Heron, H	Kerdraon, Y	Lister, J
Goddard, SJ	Heyworth, PLO	Kevin, JBR	Littlewood, KR
Godfrey, S	Hill, GO	Khalil, J	Liu, HA
Goggin, M	Hill, J	Khannah, G	Liubinas, J
Golchin, B	Hills, T	Khong, C	Livingstone, EA
Goldberg, I	Hing, SJ	Khurana, K	Lloyd, D
Gole, G	Hipwell, GC	Kim, P	Loane, ME
Golik, F	Hirst, LW	King, AC	Lockerbie, SE
Goodrich, M	Ho, RHT	Kingston, D	Lockie, P
Gorji, Z	Hobbs, I	Kingston, RA	Loh, R
Gormley, P	Hodson, T	Kirkwood, RA	Loibl, KJ
Graham, SL	Hogan, P	Kitchen, D	Lones, RI
Grant, P	Holden, HR	Knight, J	Loughnan, MS
Greaves, A	Hollenbach, E	Knights, A	Louw, Z
Greer, DV	Hollows, FC	Knox-Cartwright, N	Low, C
Gregor, DJ	Homewood, PA	Koh, LK	Lowe, DR
Gregory, EM	Hoole, GA	Kokak, G	
Grice, MJ	Horak, A	Kokkinakis, J	Maccheron, LK
Griffith, R	Hornbrook, JW	Koniuszko, GA	Macfarlane, S
Griffits, RKS	Hornsburgh, BJ	Kosmin, A	MacIntyre, R
Groeneveld, E	Hornsby, C	Kumar, NL	Macken, PL
Grover, VK	House, PH	Kwong, RNK	Mackey, DA
Gullifer, KP	Howe, E		Maclean, H

List of Contributors

MacRobert, I	Mitchell, L	Ohlrich, S	Reader, S
Madhok, P	Moloney, G	Okera, K	Readshaw, C
Mahendrarajah, T	Montgomery, PR	Okera, S	Readshaw, GG
Maher, M	Moo, G	O'Leary, BJP	Rees, I
Mahmood, MI	Moon, ME	O'Neill, JC	Reich, JA
Majzoub, U	Moore, CE	Ong, K	Reich, P
Malatt, AE	Moore, DC	Ong, T	Renehan, MJ
Males, J	Moore, F	Ooi, L	Renton, R
Maloney, P	Moore, GGD		Retsas, CW
Maloof, A	Moore, MC	Painter, GT	Rice, N
Manku, MS	Moran, DJ	Pakos, J	Richardi, J
Manning, LM	Morgan, MW	Panchapakesan, J	Richards, JC
Mantford, J	Morgan, WH	Parker, RW	Richardson, P
Mantzioros, N	Moriarty, AP	Patel, A	Riddington, LJ
Maragoudakis, G	Morlet, GC	Patel, D	Rigg, RW
Markwick, KC	Morlet, K	Patel, M	Rigney, M
Marshall, J	Morlet, N	Pater, JB	Robaei, D
Martin, FJ	Morrisey, CD	Patrick, RK	Roberts, J
Martin, PA	Morton, MR	Paul, RA	Roberts, TV
Martins, A	Moshegov, CN	Pavy, IG	Robertson, B
Marton, S	Mountford, J	Peachey, G	Robertson, IF
Materne, M	Mulholland	Pearce, B	Robinson, DI
Matus, M	Mulligan, NB	Pellew, JH	Robinson, LP
McAlister, JC	Mulligan, S	Perks, KC	Robinson, R
McAllan, A	Munchenberg, P	Perriam, DJ	Robson, M
McAuliffe, DJ	Munt, PC	Perrin, RL	Rodan, BA
McCartney, PJ	Murchland, JB	Perry, K	Roden, D
McClellan, KA	Murphy, C	Peters, J	Rodwell, S
McCluskey, PJ	Murrell, I	Petsoglou, C	Roebuck, M
McCombe, MF		Phakey, V	Rogers, CM
McDermott, ND	Nagle, FJ	Phillips, D	Rogers, JA
McDonald, MA	Nallari, L	Phillips, AJ	Rose, LVT
McDonald, RA	Nanda, U	Phillips, T	Rose, MJA
McGeorge, PA	Nardi, W	Philp, B	Rose, P
McGhee, CNJ	Narita, A	Phipps, S	Rosen, B
McGovern, RA	Nathan, F	Pieris, A	Rosen, PA
McGovern, ST	Newland, H	Pigott, LJ	Rosenberg, AM
McGree, MD	Newman, J	Pilgrim, B	Ross, CA
McGuinness, EF	Newman, M	Pittar, MR	Ross, R
McGuinness, R	Ng, P	Pittar, YA	Ross, SM
McGuinness, T	Nguyen, D	Playfair, TJ	Rosser, I
McKay, AL	Nicholls, SG	Plowman, L	Roussel, T
McKay, DL	Nicoll, AM	Pluschke, ME	Roydhouse, JD
McKay, R	Nixon, GK	Pluschke, WEW	Ruddell, TJ
McKee, H	Noble, JA	Poon, ACS	Rumbach, OW
McKinnies, C	Noble, M	Porter, GT	Runciman, JC
McKnight, DG	North, IM	Porter, RG	Russel, P
McLennan, M	Novakovic, P	Porter, WT	Russell, LJ
McMonnies, C		Pradhan, JS	Russell, M
McNeil, G	O'Hagan, S	Pyle, JD	
Meades, KV	O'Neill, D	Pyne, RJ	Saareste, AG
Meagher, PJ	O'Sullivan, M		Sack, M
Medownick, M	O'Brien, DP	Quatermass, ME	Sahetopy, L
Mele, EM	O'Callaghan, GJ	Qureshi, SH	Samarawickrama, C
Mihahidis, M	Ochsenbein, M		Samuel, MV
Miller, G	O'Connor, C	Radley, A	Saunders, BG
Millett, P	O'Connor, DM	Rait, JL	Saunders, S
Mills, RAD	O'Connor, PA	Ramani, V	Saw, V
Mills, W	O'Day, J	Ramsay, RJ	Scales, WTH
Milverton, EJ	O'Donnell, BA	Rathod, CB	Scargill, N
Minogue, FJ	Offerman, DM	Ratnalingham, V	Scargill, SW
Minogue, MJ	O'Hagan, S	Rawson, LR	Schiller, GM
Misra, A	Ohlrich, JG	Rawstron, J	Schilt, D

Scobie, MA	Stewart, ADH	Turnball, M	Whitehouse, CA
Scott, B	Stewart, PA	Tye, AA	Whitehouse, GM
Seawright, A	Strachan, G		Whitford, JD
Sebban, IA	Stubbs, GM	Unger, H	Whitford, RF
Serdiuk, A	Stuckey, GC		Whiting, M
Shanahan, LF	Sullivan, F	Vajpayee, RB	Whitney, JR
Sharma, AK	Sullivan, FP	Van Tricht, V	Wicks, LA
Sharma, D	Sullivan, LJ	Van Zyl, LM	Wicks, NS
Sharota, DT	Sultan, M	Vandeleur (Jnr), KW	Wiffen, SJ
Sheppard, CL	Sumich, PM	Vandeleur (Snr), KW	Willcocks, N
Siebert, S	Sutton, G	Velez, S	Williams, NB
Sigmont, R	Sutton, JEH	Vercoe, G	Williams, RD
Silva, M	Svoboda, E	Verma, N	Williams, W
Simon, A		Vernon, AC	Willoughby, JG
Simpson, MB	Talbot, AWR	Versace, P	Wilson, BG
Sindhu, KAS	Talbot, W	Vicary, D	Wilson, L
Singh, H	Tamblyn, DM	Violi, C	Wilson, RG
Singh, IC	Tandon, A	Vojlay, R	Wilson, T
Singh, P	Tang, KC	Von, ZYL	Win Law, W
Singh, R	Tangas, C	Vote, B	Windle, PL
Skalicky, SE	Tappin, M	Vu, P	Wingate, RJB
Slack, A	Taranto, B		Wise, GM
Slade, JH	Taylor, A	Waite, S	Wittles, N
Slade, M	Taylor, C	Waldie, MS	Wolfe, RJB
Slade, MP	Taylor, GAM	Walker, A	Wong-See, JJ-S
Smiles, JJ	Taylor, HR	Walker, FA	Woo, HY
Smith, G	Taylor, L	Walker, G	Wood, RFJ
Smith, J	Taylor, RF	Walker, N	Woods, SW
Smith, JEH	Tchen, T	Walker, TD	Workman, DMS
Smith, RL	Teske, SAH	Walland, MJ	Worner, CM
Snibson, GR	Tester, MP	Walsh, EM	Worsnop, DP
Soicher, E	Theron, A	Walsh, MA	Worthley, DA
Solanki, H	Thomas, CS	Warburton, C	Wright, H
Somerville, G	Thomas, K	Ward, WJ	Wunsh, MR
Soong, VW	Thomas, R	Wards, G	
Southgate, D	Thompson, C	Watson, SL	Yates, WHB
Spiro, HP	Thomson, CW	Watt, B	Yellachich, D
Spokes, D	Thomson, GGB	Watts, G	Yip, J
Spring, TF	Thyer, HW	Watts, WH	You, CS
Springhall, G	Tibbs, GJ	Waugh, ML	Young, SH
Squires, M	Tint, NL	Webb, A	Yow, CS
Stanley, M	Todd, B	Weber, A	Yuen, J
Starling, D	Tole, D	Wechsler, AW	
Starling, DB	Tolmie, N	Weir, P	Zabell, KW
Stasiuk, RM	Ton, Y	Welch, RT	Zamora-Alejo, K
Steer, N	Toohey, MG	Wenas, HJ	
Steiner, HE	Townsend, CL	Wenck, B	Medical
Steiner, M	Townsend, R	Weng, Ng	Superintendents of
Steiner, MD	Tregenza, P	West, R	various hospitals
Stephensen, D	Treloar, D	West, T	
Stern, H	Treplin, MCW	Westlake, W	(n=924)
Stern, W	Tridgell, DE	Westmore, RN	
Stevens, P	Tsang, B	Whaites, MA	

# Contents

<b>1</b>	<b>Overview of the Australian Corneal Graft Registry .....</b>	<b>1</b>
1.1	The database.....	1
1.1.1	Changing practice: annual increase in corneal graft registrations .....	4
1.1.2	Changing practice: the introduction of partial-thickness keratoplasties .....	5
1.1.3	Comparison of desired outcome for different types of keratoplasty .....	6
1.2	Overall survival probability.....	9
<b>2</b>	<b>Penetrating Keratoplasty .....</b>	<b>12</b>
2.1	Donor and Eye Banking Factors .....	12
2.1.1	Penetrating graft survival: influence of Australian eye bank .....	15
2.1.2	Penetrating graft survival: influence of death-to-enucleation times .....	16
2.1.3	Penetrating graft survival: influence of type of corneal storage media .....	18
2.1.4	Penetrating graft survival: influence of storage time – hypothermic medium.....	19
2.1.5	Penetrating graft survival: influence of donor sex.....	20
2.1.6	Penetrating graft survival: influence of donor age (years) .....	22
2.1.7	Penetrating graft survival: influence of cause of donor death .....	26
2.1.8	Penetrating graft survival: influence of multi-organ donor status .....	28
2.1.9	Penetrating graft survival: influence of donor central corneal endothelial cell density .....	29
2.2	Recipient Factors.....	30
2.2.1	Penetrating graft survival: influence of indication for graft .....	36
2.2.2	Penetrating graft survival: subcategory analyses .....	38
2.2.3	Penetrating graft survival: influence of Australian State where graft was performed.....	44
2.2.4	Penetrating graft survival: influence of interstate transportation .....	45
2.2.5	Penetrating graft survival: influence of recipient age (years).....	46
2.2.6	Penetrating graft survival: influence of donor/recipient sex match/mismatch .....	48
2.2.7	Penetrating graft survival: influence of pre- and post-graft lens status .....	49
2.2.8	Penetrating graft survival: influence of pre-graft corneal neovascularisation.....	50
2.2.9	Penetrating graft survival: influence of inflammation and/or steroid use at time of graft.....	51
2.2.10	Penetrating graft survival: influence raised intraocular pressure .....	52
2.2.11	Penetrating graft survival: influence of previous contralateral graft .....	53
2.2.12	Penetrating graft survival: influence of history of previous intraocular surgery in ipsilateral eye .....	54
2.3	Graft Era .....	55
2.3.1	Penetrating graft survival: influence of graft era .....	56
2.4	Surgery and Surgeon Factors .....	58
2.4.1	Penetrating graft survival: influence of graft size .....	61
2.4.2	Penetrating graft survival: influence of the Centre effect.....	62
2.4.3	Penetrating graft survival: influence of surgeon volume grouped by level of follow-up.....	64
2.5	Operative Procedures at the Time of Graft .....	65
2.5.1	Penetrating graft survival: influence of anterior vitrectomy at time of graft .....	66
2.5.2	Penetrating graft survival: influence of peripheral iridectomy at time of graft .....	67
2.6	Post-graft Events .....	69
2.6.1	Penetrating graft survival: influence of post-graft neovascularisation.....	72
2.6.2	Penetrating graft survival: influence of post-graft herpetic infection .....	73

2.6.3	Penetrating graft survival: influence of post-graft microbial keratitis .....	74
2.6.4	Penetrating graft survival: influence of post-graft synechiae .....	75
2.6.5	Penetrating graft survival: influence of post-graft uveitis .....	76
2.6.6	Penetrating graft survival: influence of post-graft raised IOP .....	77
2.6.7	Penetrating graft survival: influence of graft rejection episodes .....	78
2.6.8	Penetrating graft survival: influence of time to final removal of sutures .....	79
2.7	Multivariate Analysis .....	80
2.7.1	Significant differences in the PK multivariate model .....	84
2.8	Reasons for Graft Failure .....	88
2.9	Post-graft Changes in Best Corrected Visual Acuity .....	90
2.9.1	All indications for graft.....	90
2.9.2	Individual indications for graft.....	93
<b>3</b>	<b>Descemet's Stripping Endothelial Keratoplasty .....</b>	<b>100</b>
3.1	Donor and Eye Banking Factors.....	100
3.1.1	DS(A)EK survival: influence of Australian eye bank.....	103
3.1.2	DS(A)EK survival: influence of enucleation to storage time .....	104
3.1.3	DS(A)EK survival: influence of corneal storage media.....	105
3.1.4	DS(A)EK survival: influence of donor age (years).....	106
3.1.5	DS(A)EK survival: influence of pre-cut donor tissue .....	108
3.1.6	DS(A)EK survival: influence of donor central corneal endothelial cell density.....	109
3.2	Recipient Factors.....	110
3.2.1	DS(A)EK survival: influence of indication for graft.....	113
3.2.2	DS(A)EK survival: subcategory analyses.....	114
3.2.3	DS(A)EK survival: influence of Australian State where graft was performed .....	116
3.2.4	DSAEK survival: influence of interstate transportation .....	117
3.2.5	DS(A)EK survival: influence of recipient age (years) .....	118
3.2.6	DS(A)EK survival: influence of recipient sex.....	119
3.2.7	DS(A)EK survival: influence of donor/recipient sex match/mismatch .....	120
3.2.8	DS(A)EK survival: influence of pre- and post-graft lens status.....	121
3.2.9	DS(A)EK survival: influence of pre-graft corneal neovascularisation .....	122
3.2.10	DS(A)EK survival: influence of inflammation and/or steroid use at time of graft .....	123
3.2.11	DS(A)EK survival: influence of history of raised intraocular pressure (IOP).....	124
3.2.12	DS(A)EK survival: influence of previous contralateral graft.....	125
3.2.13	DS(A)EK survival: influence of history of previous intraocular surgery in ipsilateral eye.....	126
3.3	Graft Era .....	127
3.3.1	DS(A)EK survival: influence of era of graft.....	128
3.4	Surgery and Surgeon Factors.....	129
3.4.1	DS(A)EK survival: influence of graft size.....	132
3.4.2	DS(A)EK survival: influence of size of incision.....	133
3.4.3	DS(A)EK survival: influence of use of forceps.....	134
3.4.4	DS(A)EK survival: influence of use of viscoelastic .....	135
3.4.5	DS(A)EK survival: influence of the Centre effect.....	136
3.4.6	DS(A)EK survival: influence of surgeon volume grouped by level of follow-up .....	138
3.5	Operative Procedures at the Time of Graft.....	139
3.6	Post-graft Events .....	140
3.6.1	DS(A)EK survival: influence of post-graft corneal neovascularisation.....	143
3.6.2	DS(A)EK survival: influence of post-graft microbial keratitis .....	144

3.6.3	DS(A)EK survival: influence of post-graft raised IOP .....	145
3.6.4	DS(A)EK survival: influence of graft rejection episodes .....	146
3.7	Multivariate Analysis .....	148
3.7.1	Significant differences in the DS(A)EK multivariate model .....	152
3.8	Reasons for Graft Failure .....	154
3.9	Post-graft Changes in Best Corrected Visual Acuity .....	155
3.9.1	All indications for graft .....	155
3.9.2	Individual indications for graft .....	158
<b>4</b>	<b>Descemet's Membrane Endothelial Keratoplasty .....</b>	<b>161</b>
4.1	Donor and Eye Banking Factors .....	161
4.1.1	DMEK survival: influence of Australian eye bank .....	164
4.1.2	DMEK survival: influence of donor sex .....	165
4.1.3	DMEK survival: influence of donor age (years) .....	166
4.1.4	DMEK survival: influence of preparation of donor tissue (pre-cut) by eye bank .....	167
4.2	Recipient Factors .....	168
4.2.1	DMEK survival: influence of the number of previous ipsilateral grafts .....	172
4.2.2	DMEK survival: influence of Australian State where graft was performed .....	173
4.2.3	DMEK survival: influence of recipient age (years) .....	174
4.2.4	DMEK survival: influence of recipient sex .....	175
4.2.5	DMEK survival: influence of donor/recipient sex match/mismatch .....	176
4.3	Graft Era .....	177
4.3.1	DMEK survival: influence of era of graft .....	178
4.4	Surgery and Surgeon Factors .....	179
4.4.1	DMEK survival: influence of graft size .....	181
4.4.2	DMEK survival: influence of the Centre effect .....	182
4.4.3	DMEK survival: influence of surgeon volume grouped by level of follow-up .....	184
4.5	Operative Procedures at the Time of Graft .....	185
4.5.1	DMEK survival: influence of peripheral iridectomy at time of graft .....	186
4.6	Post-graft Events .....	187
4.7	Multivariate Analysis .....	189
4.7.1	Significant differences in the DMEK multivariate model .....	192
4.8	Reasons for Graft Failure .....	193
4.9	Post-graft Changes in Best Corrected Visual Acuity .....	194
4.9.1	All indications for graft .....	194
4.9.2	Individual indications for graft .....	197
<b>5</b>	<b>Deep Anterior Lamellar Keratoplasty .....</b>	<b>199</b>
5.1	Donor and Eye Banking Factors .....	199
5.1.1	DALK survival: influence of storage time to graft – organ culture medium .....	202
5.2	Recipient Factors .....	204
5.2.1	DALK survival: influence of indication for graft .....	206
5.2.2	DALK survival: influence of recipient age .....	208
5.2.3	DALK survival: influence of change in lens status .....	210
5.2.4	DALK survival: influence of pre-graft corneal neovascularisation .....	211
5.2.5	DALK survival: influence of pre-graft inflammation and/or steroid use .....	212
5.3	Graft Era .....	213
5.3.1	DALK survival: influence of era of graft .....	214

5.4	Surgery and Surgeon Factors.....	215
5.4.1	DALK survival: influence of graft type .....	217
5.4.2	DALK survival: influence of the Centre effect.....	218
5.5	Operative procedures at the time of graft .....	220
5.6	Post-graft Events .....	220
5.6.1	DALK survival: influence of post-graft corneal neovascularisation.....	222
5.7	Multivariate Analysis .....	223
5.7.1	Significant differences in the DALK multivariate model.....	226
5.8	Reasons for Graft Failure .....	227
5.9	Post-graft Changes in Best Corrected Visual Acuity .....	228
5.9.1	All indications for graft.....	228
5.9.2	Individual indications for graft.....	231
<b>6</b>	<b>Traditional Lamellar Keratoplasty .....</b>	<b>233</b>
6.1	Donor and Eye Banking Factors.....	233
6.1.1	Traditional lamellar graft survival: influence of Australian eye bank.....	236
6.1.2	Traditional lamellar graft survival: influence of modern corneal storage media.....	237
6.2	Recipient Factors.....	238
6.2.1	Traditional lamellar graft survival: influence of indication for graft.....	242
6.2.2	Traditional lamellar graft survival: influence of Australian State where graft was performed.....	244
6.2.3	Traditional lamellar graft survival: influence of interstate transportation.....	245
6.2.4	Traditional lamellar graft survival: influence of recipient age (years).....	246
6.2.5	Traditional lamellar graft survival: influence of change in lens status.....	248
6.2.6	Traditional lamellar graft survival: influence of pre-graft corneal neovascularisation .....	249
6.2.7	Traditional lamellar graft survival: influence of inflammation and/or steroid use at time of graft.....	250
6.2.8	Traditional lamellar graft survival: influence of history of raised intraocular pressure (IOP) .....	251
6.2.9	Traditional lamellar graft survival: influence of number of previous grafts in the contralateral eye..	252
6.3	Graft Era .....	253
6.3.1	Traditional lamellar graft survival: influence of era of graft.....	254
6.4	Surgery and Surgeon Factors.....	255
6.4.1	Traditional lamellar graft survival: influence of graft size.....	257
6.4.2	Traditional lamellar graft survival: influence of the Centre effect.....	258
6.5	Operative procedures at the time of graft .....	260
6.6	Post-graft Events .....	260
6.6.1	Traditional lamellar graft survival: influence of post-graft microbial keratitis.....	263
6.6.2	Traditional lamellar graft survival: influence of raised IOP post-graft .....	264
6.6.3	Traditional lamellar graft survival: influence of any rejection episode/s.....	265
6.7	Multivariate Analysis .....	266
6.7.1	Significant differences in the TLK multivariate model.....	269
6.8	Reasons for Graft Failure .....	270
6.9	Post-graft Changes in Best Corrected Visual Acuity .....	271
6.9.1	All indications for graft.....	271
6.9.2	Individual indications for graft.....	274
<b>7</b>	<b>Post-graft factors affecting visual acuity .....</b>	<b>275</b>
<b>8</b>	<b>Comparisons Across Graft Types.....</b>	<b>277</b>
8.1	Keratoconus.....	277
8.1.1	Survival of grafts for keratoconus: influence of graft type.....	278

8.2	Pseudophakic Bullous Keratopathy.....	280
8.2.1	Survival of grafts for pseudophakic bullous keratopathy: influence of graft type .....	281
8.3	Fuchs' Endothelial Dystrophy .....	284
8.3.1	Survival of grafts for Fuchs' endothelial dystrophy: influence of graft type .....	285
<b>9</b>	<b>Summary .....</b>	<b>288</b>
9.1	Donor and Eye Banking Factors .....	288
9.2	Recipient Factors.....	288
9.3	Graft Era .....	289
9.4	Surgery and Surgeon Factors .....	289
9.5	Post-graft Events .....	290
9.6	Comparisons Across Graft Types.....	290
<b>10</b>	<b>Methods and Definitions.....</b>	<b>291</b>
10.1	Registration and Follow-up.....	291
10.2	Definition of Variables.....	291
10.3	Graft Failure, Rejection and Complications.....	292
10.4	Statistical Analyses.....	293
10.5	References .....	294

# Abbreviations/Acronyms

ACGR = Australian Corneal Graft Registry

NA = Not Applicable

Abbreviations or acronyms used to refer to types of graft:

PK = Penetrating keratoplasty

DALK = Deep anterior lamellar keratoplasty

DS(A)EK = Descemet's stripping endothelial keratoplasty, Descemet's stripping automated endothelial keratoplasty and unspecified endothelial grafts

DMEK = Descemet's membrane endothelial keratoplasty

TLK = Traditional lamellar keratoplasty

Limbal = Limbal stem cell transplant

Misc. = Miscellaneous corneal transplant, not otherwise categorised

Acronyms used to refer to visual acuity:

VA = Visual acuity

CF = Count fingers

HM = Hand movements

LP = Light perception

NLP = No light perception

Acronyms used in statistical reporting:

p = probability

df = degrees of freedom

SE = standard error

CI = confidence interval

tvc = time-varying coefficient

# 1 Overview of the Australian Corneal Graft Registry

## 1.1 The database

At the time of census (31-07-2017), 33,920 grafts had been registered, of which 26,297 (77.5%) had been followed at least once. Table 1.1 shows the number of each type of graft that had been registered, had follow-up information provided and remained “active” (the graft had not failed and the recipient is not known to have died, or been lost to follow-up by the surgeon). Table 1.2 shows the status of these grafts, in more detail.

**Table 1.1 Registered, followed and active grafts, 1985 onwards**

	Registered	Followed*	Active
<b>PK</b>	24,827 (73.2%)	20,336 (77.3%)	5,567 (50.3%)
<b>DALK</b>	1,531 (4.5%)	921 (3.5%)	1,054 (9.5%)
<b>DS(A)EK</b>	4,736 (14.0%)	3,263 (12.4%)	3,189 (28.8%)
<b>DMEK</b>	1,250 (3.7%)	600 (2.3%)	932 (8.4%)
<b>TLK</b>	1,495 (4.4%)	1,114 (4.2%)	317 (2.9%)
<b>Limbal</b>	81 (0.2%)	63 (0.2%)	12 (0.1%)
<b>Total</b>	<b>33,920 (100.0%)</b>	<b>26,297 (100.0%)</b>	<b>11,071 (100.0%)</b>

Note: PK = penetrating keratoplasty. DALK = deep anterior lamellar keratoplasty. DS(A)EK = Descemet's stripping endothelial keratoplasty, Decemet's stripping automated endothelial keratoplasty, ultra-thin Decemet's stripping automated endothelial keratoplasty, or unspecified endothelial grafts. DMEK = Decemet's membrane endothelial keratoplasty. TLK = traditional lamellar keratoplasty, including peripheral and scleral patch grafts.

\*Excluding grafts where the recipient is known to have died but no further information has been provided.

**Table 1.2 Synopsis of the database, including registered, followed, surviving and active grafts**

	<b>PK</b>	<b>DALK</b>	<b>DS(A)EK</b>	<b>DMEK</b>	<b>TLK</b>	<b>Limbal</b>	<b>Total</b>
<b>Registered</b>	<b>24827 (100%)</b>	<b>1531 (100%)</b>	<b>4736 (100%)</b>	<b>1250 (100%)</b>	<b>1495 (100%)</b>	<b>81 (100%)</b>	<b>33920 (100%)</b>
<b>Followed*</b>	<b>20336 (82%)</b>	<b>921 (60%)</b>	<b>3263 (69%)</b>	<b>600 (48%)</b>	<b>1114 (75%)</b>	<b>63 (78%)</b>	<b>26297 (78%)</b>
Failed	5686 (23%)	113 (7%)	791 (17%)	251 (20%)	296 (20%)	30 (37%)	7167 (21%)
<i>Recipient still alive</i>	3784 (15%)	112 (7%)	744 (16%)	248 (20%)	201 (13%)	25 (31%)	5114 (15%)
<i>Recipient subsequently died</i>	1902 (8%)	1 (<1%)	47 (<1%)	3 (<1%)	95 (6%)	5 (6%)	2053 (6%)
Recipient died with surviving graft	4005 (16%)	14 (<1%)	140 (3%)	6 (<1%)	212 (14%)	9 (11%)	4386 (13%)
Lost post follow-up	6648 (27%)	234 (15%)	448 (9%)	37 (3%)	423 (28%)	18 (22%)	7808 (23%)
Followed, surviving and active	3997 (16%)	560 (37%)	1884 (40%)	306 (24%)	183 (12%)	6 (7%)	6936 (20%)
<b>Number of grafts not followed</b>	<b>4491 (18%)</b>	<b>610 (40%)</b>	<b>1473 (31%)</b>	<b>650 (52%)</b>	<b>381 (25%)</b>	<b>18 (22%)</b>	<b>7623 (22%)</b>
Recipient died pre follow-up	1033 (4%)	7 (<1%)	63 (1%)	9 (<1%)	106 (7%)	3 (4%)	1221 (4%)
Lost prior to follow-up	1888 (8%)	109 (7%)	105 (2%)	15 (1%)	141 (9%)	9 (11%)	2267 (7%)
Not yet followed but active	1570 (6%)	494 (32%)	1305 (28%)	626 (50%)	134 (9%)	6 (7%)	4135 (12%)
<b>Graft surviving when last seen</b>	<b>19141 (77%)</b>	<b>1418 (93%)</b>	<b>3945 (83%)</b>	<b>999 (80%)</b>	<b>1199 (80%)</b>	<b>51 (63%)</b>	<b>26753 (79%)</b>
Graft lost when surviving	8536 (34%)	343 (22%)	553 (12%)	52 (4%)	564 (38%)	27 (33%)	10075 (30%)
<i>Lost prior to follow-up</i>	1888 (8%)	109 (7%)	105 (2%)	15 (1%)	141 (9%)	9 (11%)	2267 (7%)
<i>Lost post follow-up</i>	6648 (27%)	234 (15%)	448 (9%)	37 (3%)	423 (28%)	18 (22%)	7808 (23%)
Recipient died with surviving graft	5038 (20%)	21 (1%)	203 (4%)	15 (1%)	318 (21%)	12 (15%)	5607 (17%)
<i>Recipient died pre follow-up</i>	1033 (4%)	7 (<1%)	63 (1%)	9 (<1%)	106 (7%)	3 (4%)	1221 (4%)
<i>Recipient died post follow-up</i>	4005 (16%)	14 (<1%)	140 (3%)	6 (<1%)	212 (14%)	9 (11%)	4386 (13%)
<b>Currently active grafts</b>	<b>5567 (22%)</b>	<b>1054 (69%)</b>	<b>3189 (67%)</b>	<b>932 (75%)</b>	<b>317 (21%)</b>	<b>12 (15%)</b>	<b>11071 (33%)</b>
Not yet followed but active	1570 (6%)	494 (32%)	1305 (28%)	626 (50%)	134 (9%)	6 (7%)	4135 (12%)
Followed, surviving and active	3997 (16%)	560 (37%)	1884 (40%)	306 (24%)	183 (12%)	6 (7%)	6936 (20%)

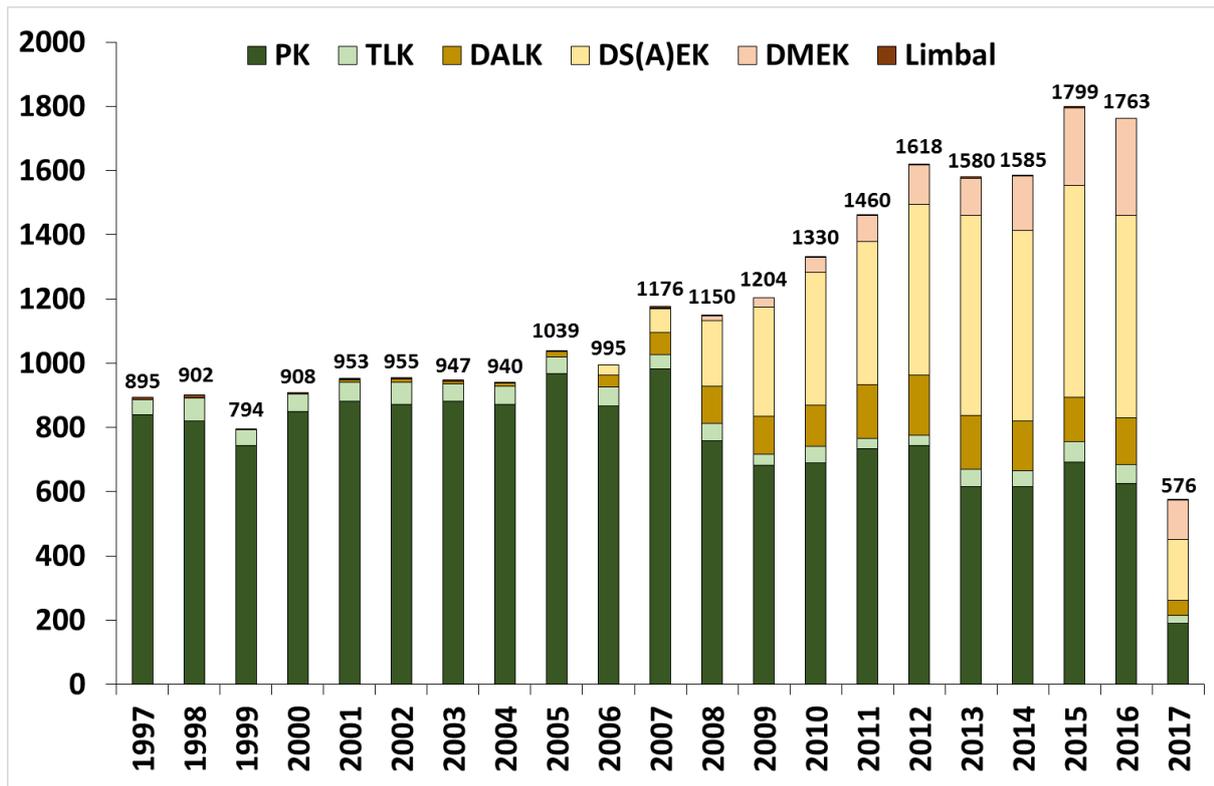
\*Excludes grafts where the recipient is known to have died but no further information has been provided regarding the survival of the graft.



### 1.1.1 Changing practice: annual increase in corneal graft registrations

The number of grafts registered with the Australian Corneal Graft Registry each year remained stable during the ten years to 2006, with an average of 933 grafts being registered annually. An increase was seen from this point, which coincided with the introduction of the newer endothelial transplantation techniques - DSEK and DSAEK, closely followed by DMEK. The number of grafts being registered continued to increase steadily from 2009 to 2012. There has been a further increase during the last two full years for which data is available, as shown in Figure 1.1.1.

**Figure 1.1.1 Number of grafts registered with the ACGR per year, 1997 onwards**

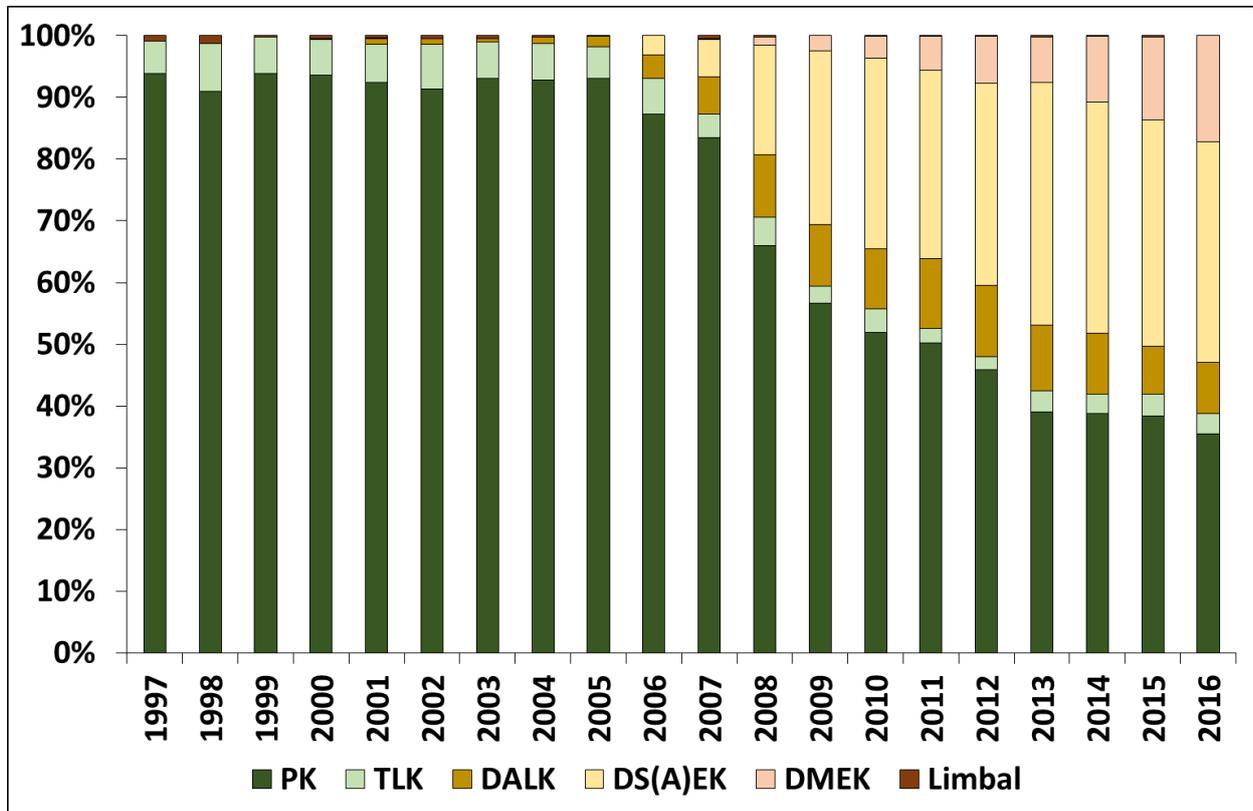


Note: Data relating to all registrations of grafts performed up to and including 30<sup>th</sup> April 2017, for which forms had been received by the ACGR prior to 1<sup>st</sup> August 2017, were included. Some grafts performed prior to this date may still be registered in the future.

### 1.1.2 Changing practice: the introduction of partial-thickness keratoplasties

Figure 1.1.2 shows registrations stratified by graft type over the last 20 years, for which data were available for the full year. Data from 2017 were excluded due to the low number of grafts registered at the census date.

Figure 1.1.2 Graft type by year of registration, 1997 onwards



The introduction of new types of partial-thickness corneal grafts has led to a marked shift away from full-thickness penetrating keratoplasty, so that ten years after their introduction, endothelial grafts (DS(A)EK and DMEK) account for more than half of all registered grafts.

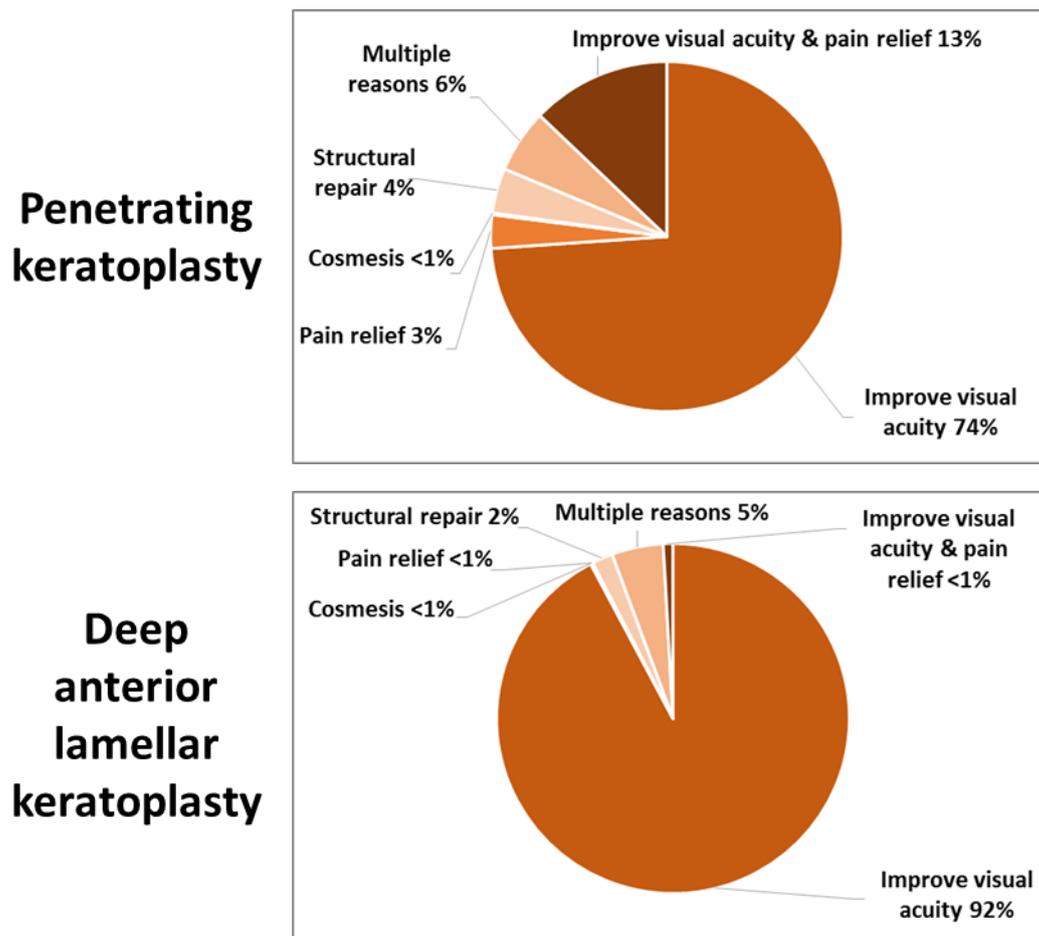
After a gradual increase from 2000 to 2008, the proportion of deep anterior lamellar keratoplasties (DALKs) remained stable for several years but has reduced recently, so that they account for under one-tenth of registered grafts.

### 1.1.3 Comparison of desired outcome for different types of keratoplasty

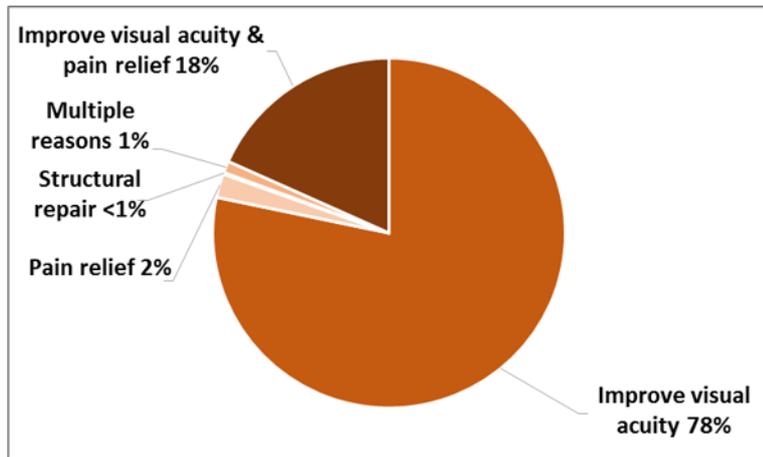
Surgeons indicated whether a graft was performed for: “improved visual acuity”, “pain relief”, “cosmesis”, “tectonic/structural repair”, or a combination of these reasons. Data were provided for 29,338 grafts (86%). Reason for graft was less likely to have been specified for TLK (80%), PK (84%) and limbal grafts (84%), compared with DALK (95%), DS(A)EK (96%), or DMEK (96%). Improved visual acuity was a desired outcome in 91% of these grafts, pain relief in 17%, structural repair in 9%, and cosmesis in 2%.

Desired outcome varied depending on graft type. The desired outcome most often selected for PK, DALK, DS(A)EK, and DMEK, was improvement in visual acuity. This was an aim in 92%, 98%, 98% and 99% of grafts being performed in each group (either as an individual aim or in conjunction with other desired outcomes), respectively. Traditional lamellar keratoplasty was most often performed to provide structural repair (71%). Figure 1.1.3 shows the desired outcomes indicated by surgeons, for each type of graft.

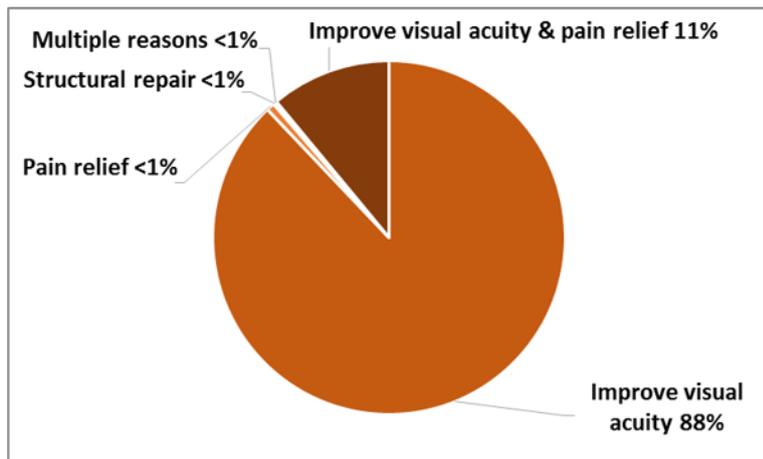
Figure 1.1.3 Reason for graft stratified by graft type



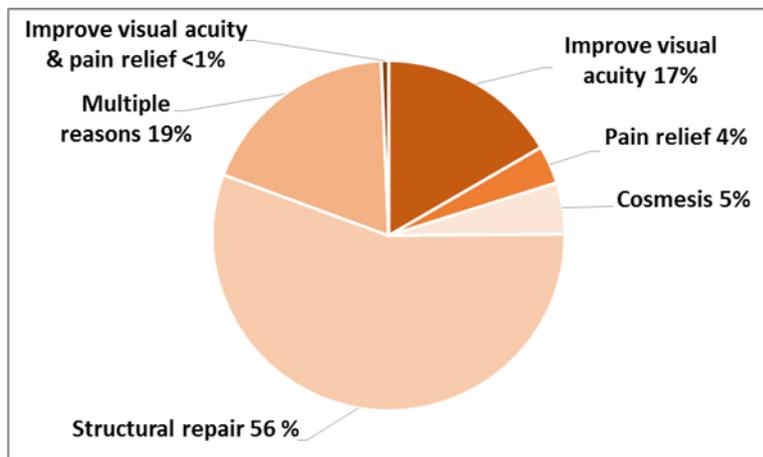
**Descemet's stripping (automated) endothelial keratoplasty**



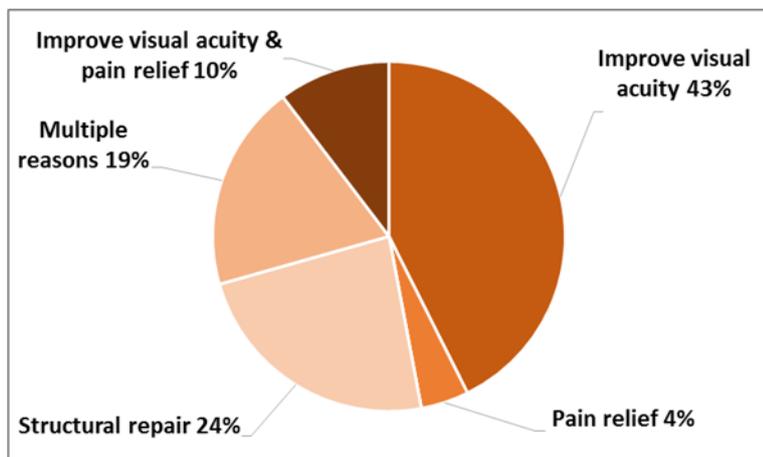
**Descemet's membrane endothelial keratoplasty**



**Traditional lamellar keratoplasty**



**Limbal graft**





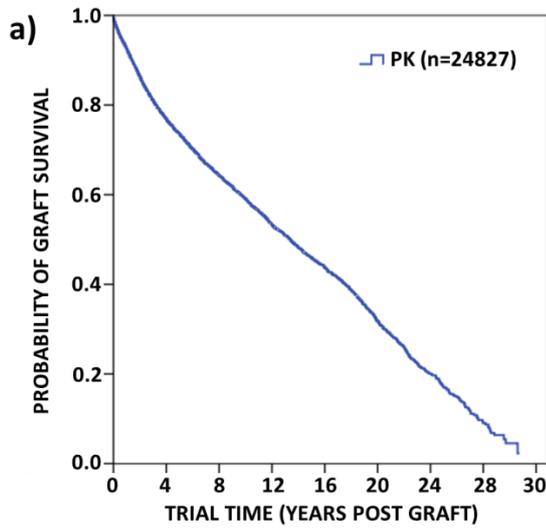
## 1.2 Overall survival probability

Figure 1.2.1 shows the survival curves for each type of graft. Grafts for which follow-up has not yet been provided are modelled as surviving at 1 day. The initial number at risk (including these modelled grafts) are given in the graph for each graft type. The number of grafts at risk, and the survival probability, are provided at various time points for each graft type. These time points vary depending on the maximum length of follow-up available for each graft type, and cease when fewer than 15 grafts had been followed.

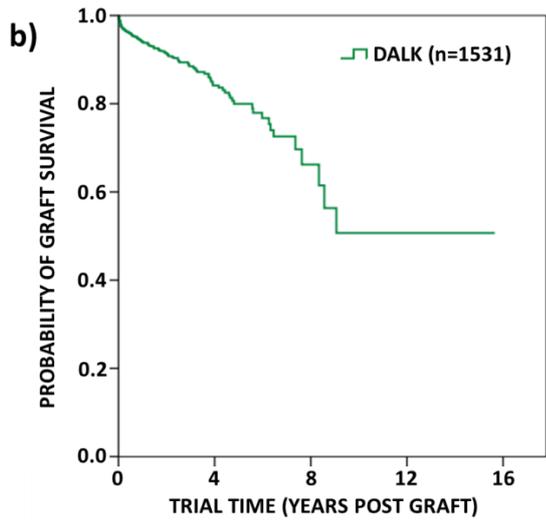
Primary graft failure was reported in 181 penetrating keratoplasty (0.8%), 15 traditional lamellar keratoplasties (1.2%), 14 deep anterior lamellar keratoplasties (1.5%), 221 Descemet's stripping (automated) endothelial keratoplasties (6.6%), 158 Descemet's membrane endothelial keratoplasties (25.9%), and 1 limbal graft (1.5%). Primary graft failure was reported for eight pairs of cornea (i.e. both corneas from the same donor).

When conducting survival analysis, comparisons across groups containing very small numbers, or very small proportions of the study population, are not considered reliable or informative. With this in mind, we have only analysed comparisons amongst categories for which data on more than 20 followed grafts were available for DALK, DS(A)EK, DMEK and TLK, and data on more than 50 followed grafts were available for PK (20 in subcategory analyses).

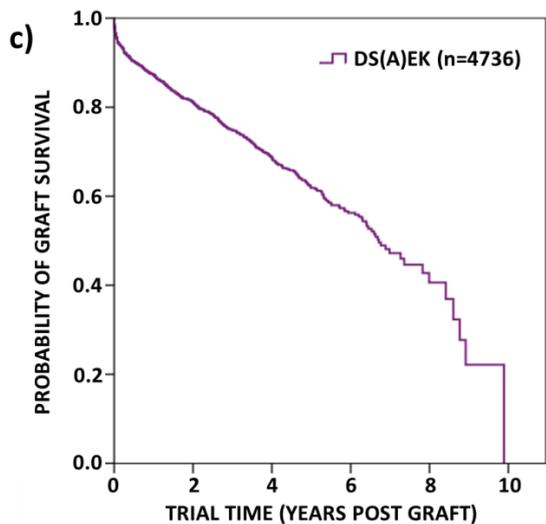
Figure 1.2.1 Survival of corneal grafts for a) penetrating keratoplasty, b) deep anterior lamellar keratoplasty, c) Descemet's stripping (automated) endothelial keratoplasty, d) Descemet's membrane endothelial keratoplasty, e) traditional lamellar keratoplasty, and f) limbal stem cell transplantation



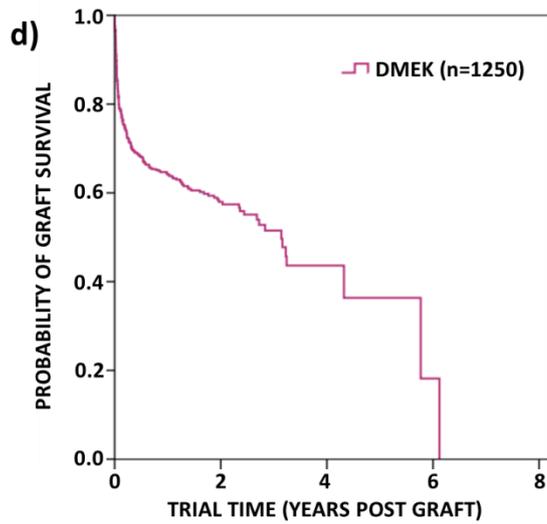
Years since graft	1	4	8	12	16	20	24	28
Number at risk	16877	7776	3454	1736	868	424	153	28
Survival probability	0.93	0.77	0.64	0.53	0.44	0.32	0.20	0.09



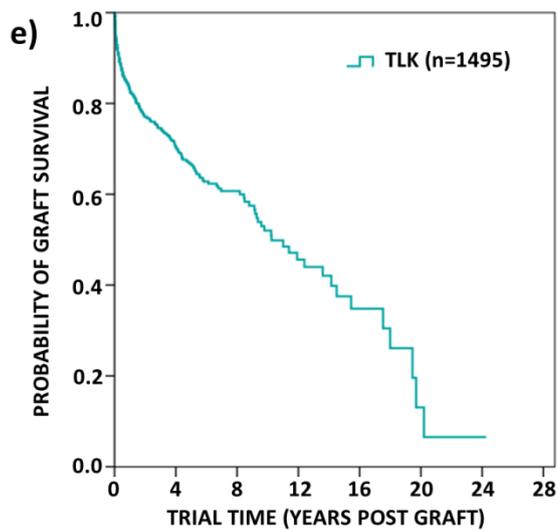
Years since graft	1	2	4	6	8
Number at risk	769	484	175	65	16
Survival probability	0.94	0.92	0.84	0.77	0.66



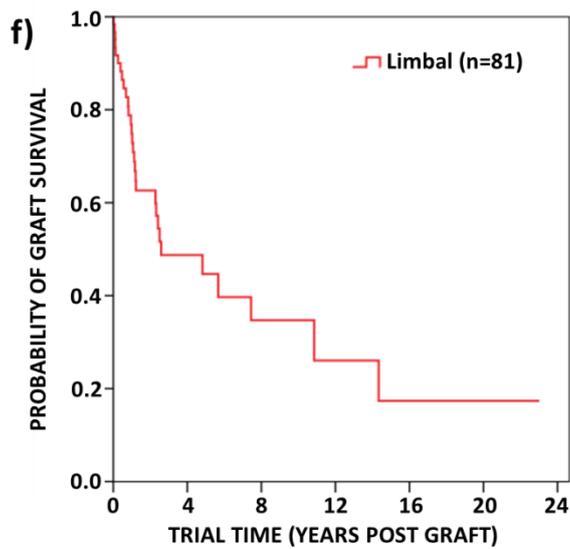
Years since graft	1	2	4	6	8
Number at risk	2306	1547	519	147	18
Survival probability	0.87	0.81	0.69	0.56	0.41



Years since graft	1	2	3
Number at risk	276	114	32
Survival probability	0.64	0.58	0.52



Years since graft	1	4	8	12
Number at risk	687	252	89	29
Survival probability	0.83	0.71	0.61	0.46



Years since graft	1	2	3
Number at risk	38	25	16
Survival probability	0.75	0.63	0.49

## 2 Penetrating Keratoplasty

This chapter presents the results of analyses conducted on data relating to the 24,827 penetrating keratoplasties registered with the ACGR. Kaplan-Meier survival analyses were conducted using IBM SPSS for Windows (Version 22.0), to compare the graft survival across groups for a range of variables relating to the corneal donor, graft recipient, surgical procedure, surgeon, and follow-up care.

### 2.1 Donor and Eye Banking Factors

Table 2.1 shows the number of grafts within each of the variable sub-groups, for the donor and eye banking factors found to be **significant** in univariate analyses. The sum for each variable equals the total number of grafts (24,827 registered and 20,336 with follow-up provided) and the percentages, summed vertically for each variable, total 100.

**Table 2.1 Donor and eye banking factors, significant in univariate analyses**

<b>Penetrating Corneal Graft Donor and Eye Banking Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Eye bank</b>		
Eye bank M	8667 (35%)	6750 (33%)
Eye bank K	4795 (19%)	3988 (20%)
Eye bank V	4407 (18%)	3576 (18%)
Eye bank J	2436 (10%)	1762 (9%)
Eye bank N	2812 (11%)	2604 (13%)
Not advised	1710 (7%)	1656 (8%)
<b>Death-to-enucleation time</b>		
Up to 3 hours	4872 (20%)	4317 (21%)
4 to 6 hours	5831 (23%)	4907 (24%)
7 to 9 hours	5390 (22%)	4423 (22%)
10 to 12 hours	4380 (18%)	3563 (18%)
13 to 15 hours	1762 (7%)	1323 (7%)
16 to 18 hours	1117 (4%)	752 (4%)
More than 18 hours	1145 (5%)	766 (4%)
Not advised	330 (1%)	285 (1%)
<b>Storage medium</b>		
Optisol	12535 (50%)	9832 (48%)
Organ culture	2825 (11%)	1844 (9%)
Moist pot	335 (1%)	316 (2%)
Superseded hypothermic	8974 (36%)	8202 (40%)
Other	6 (<1%)	6 (<1%)
Not advised	152 (<1%)	136 (<1%)

	Registered (%)	Followed (%)
<b>Storage-to-graft time – hypothermic</b>		
Within 5 days	13974 (56%)	11978 (59%)
6 or 7 days	2615 (11%)	2036 (10%)
More than a week	607 (2%)	481 (2%)
Not advised	4313 (17%)	3539 (17%)
Not applicable	3318 (13%)	2302 (11%)
<b>Sex of donor</b>		
Female	8884 (36%)	7291 (26%)
Male	15317 (62%)	12484 (61%)
Not advised	626 (3%)	561 (3%)
<b>Age group</b>		
Under 20 years	948 (4%)	775 (4%)
20 to 29 years	1260 (5%)	999 (5%)
30 to 39 years	1258 (5%)	1006 (5%)
40 to 49 years	2548 (10%)	2085 (10%)
50 to 59 years	4286 (17%)	3452 (17%)
60 to 69 years	6167 (25%)	5015 (25%)
70 to 79 years	5979 (24%)	5007 (25%)
80 years and older	2078 (8%)	1727 (8%)
Not advised	303 (1%)	270 (1%)
<b>Cause of death</b>		
Cardiac event	7410 (30%)	6123 (30%)
Malignancy	5838 (24%)	4685 (23%)
Trauma	2749 (11%)	2170 (11%)
Respiratory event	2302 (9%)	1935 (10%)
Intracranial/cerebral haemorrhage	4234 (17%)	3441 (17%)
Other specified	1179 (5%)	990 (5%)
Live donor	31 (<1%)	25 (<1%)
Not advised*	1084 (4%)	967 (5%)
<b>Multi-organ donor status</b>		
No	22684 (91%)	18654 (92%)
Yes	2143 (9%)	1682 (8%)
<b>Central corneal endothelial cell density</b>		
<2500 cells/mm <sup>2</sup>	452 (2%)	322 (2%)
2500 to 2749 cells/mm <sup>2</sup>	807 (3%)	554 (3%)
2750 to 2999 cells/mm <sup>2</sup>	1041 (4%)	736 (4%)
3000 to 3249 cells/mm <sup>2</sup>	1450 (6%)	956 (5%)
3250 to 3499 cells/mm <sup>2</sup>	771 (3%)	518 (3%)
≥ 3500 cells/mm <sup>2</sup>	510 (2%)	351 (2%)
Not advised	19796 (80%)	16899 (83%)
<b>Total</b>	<b>24827 (100%)</b>	<b>20336 (100%)</b>

\*ACGR advised that cause of death was not yet determined but there were no medical contraindications and the eye had been cleared for release, by the Medical Director, in accordance with EBAANZ guidelines.

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Likelihood of follow-up was significantly more likely ( $p < 0.05$ ) in some groups than others. Higher rates of follow-up were received for grafts where donor tissue was stored in hypothermic solution for five days or less. Rates were lower for grafts performed using donor tissue that had been stored in organ culture, for donor tissue from multi organ donors, and those that had died from trauma. Significant differences in follow-up were also found across groups for eye bank, death-to-enucleation times and donor age.

Table 2.2 shows the number of grafts within each of the variable sub-groups, for the donor and eye banking factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (24,827 registered and 20,336 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The result of the Kaplan-Meier survival analysis is also provided for each variable.

**Table 2.2 Donor and eye banking factors, not significant in univariate analyses**

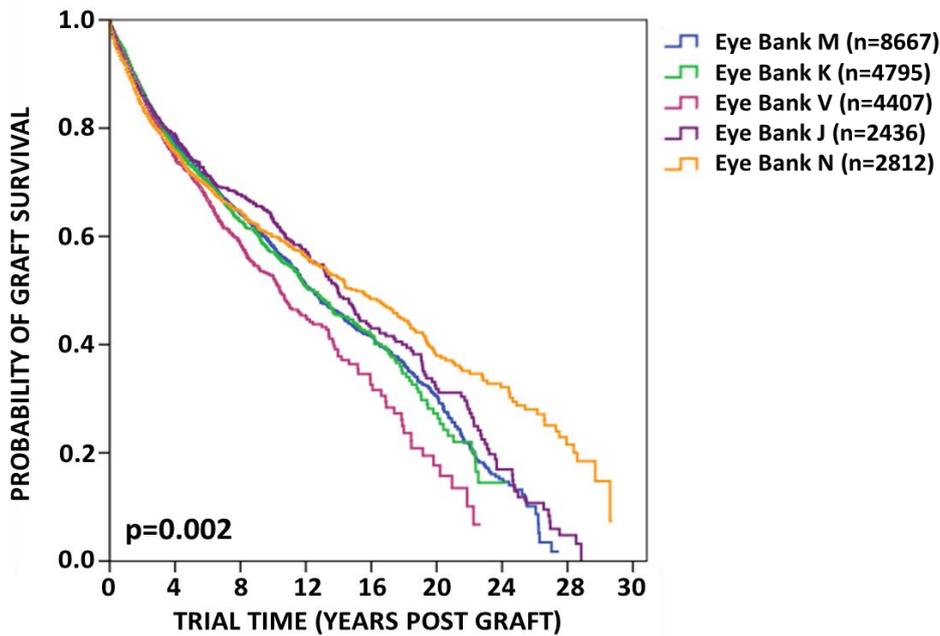
<b>Penetrating Corneal Graft Donor and Eye Banking Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Enucleation-to-storage time</b>		
Up to 3 hours	14764 (59%)	12307 (61%)
4 to 6 hours	2331 (9%)	1817 (9%)
7 to 12 hours	1135 (5%)	908 (5%)
13 hours or more	963 (4%)	769 (4%)
Not advised	5634 (23%)	4535 (22%)
<b>Chi<sup>2</sup>=4.00, df=3, p=0.262</b>		
<b>Storage to graft time - Organ culture</b>		
Up to 2 weeks	608 (2%)	399 (2%)
2 to 3 weeks	968 (4%)	600 (3%)
More than 3 weeks	288 (1%)	187 (<1%)
Not advised	961 (4%)	658 (3%)
Not applicable	22002 (89%)	18492 (91%)
<b>Chi<sup>2</sup>=2.34, df=2, p=0.311</b>		
	<b>24827 (100%)</b>	<b>20336 (100%)</b>

**Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable.**

**2.1.1 Penetrating graft survival: influence of Australian eye bank**

Donor corneas are retrieved, processed, stored and distributed by five eye banks around Australia. Figure 2.1.1 shows the comparison of graft survival for corneas provided by each of these eye banks. A significant difference was found across eye banks (Log Rank Statistic=16.94; df=4; p=0.002), with grafts performed in State V having poorer survival than those performed in State M (p=0.001) and State J (p<0.001). Data on this variable were not provided in 7% of cases, primarily registered with the ACRG in the 1980s. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=41.87; df=5; p<0.001). This variable was not retained in the multivariate analysis (see section 2.7) suggesting that this is **not** an independent factor significantly affecting graft survival.

**Figure 2.1.1 Australian eye bank**



**Number at risk (years post-graft)**

	1	4	8	12	16	20	24
<b>Eye Bank M</b>	5597	2578	1116	534	294	142	32
<b>Eye Bank K</b>	3434	1503	614	269	110	30	3
<b>Eye Bank V</b>	2860	1042	338	113	33	10	NA
<b>Eye Bank J</b>	1434	740	363	207	96	48	18
<b>Eye Bank N</b>	2160	1115	529	299	164	94	49

Note: NA = not applicable, as no grafts followed at this time point

**Probability of graft survival (years post-graft)**

	1	4	8	12	16	20	24
<b>Eye Bank M</b>	0.93	0.78	0.64	0.51	0.42	0.31	0.15
<b>Eye Bank K</b>	0.94	0.76	0.63	0.51	0.42	0.27	NA
<b>Eye Bank V</b>	0.93	0.75	0.59	0.45	0.33	NA	NA
<b>Eye Bank J</b>	0.92	0.79	0.68	0.57	0.43	0.32	NA
<b>Eye Bank N</b>	0.91	0.76	0.65	0.56	0.48	0.38	0.32

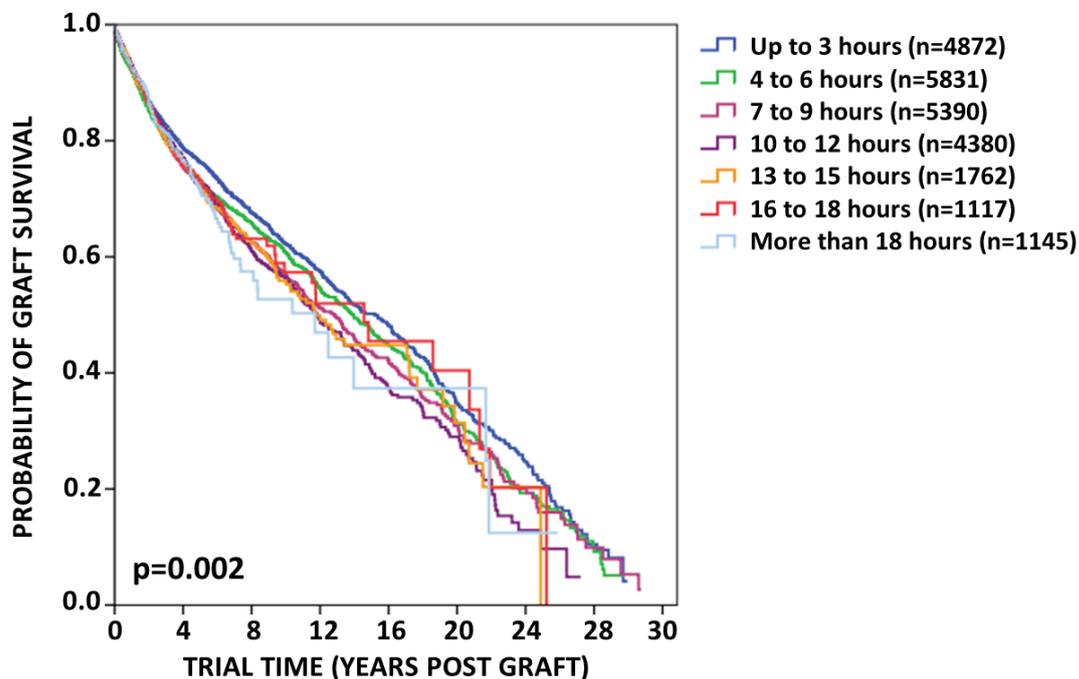
Note: NA = not applicable, as fewer than 20 grafts followed at this time point

### 2.1.2 Penetrating graft survival: influence of death-to-enucleation times

Donor corneas are retrieved as soon as possible following donor death. Retrieval is recommended within the first 18 hours and 95% of donor eyes were enucleated within this time-frame. Times are rounded to the nearest hour and the median time from donor death to enucleation was 7 hours (range 0-43 hours).

Figure 2.1.2 shows a comparison of graft survival depending on time from donor death to enucleation, stratified into three-hourly groups. A significant difference was found across time groups (Log Rank Statistic=20.58; df=6; p=0.002). Data on this variable were not provided in 1% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=21.60; df=7; p=0.003). Grafts performed using donor tissue collected within 3 hours of death showed better outcomes than those for which the tissue was collected 4 to 6 hours or 7 to 9 hours after death (both p<0.001). When this group (up to 3 hours) was excluded from the analysis, the difference across the remaining 6 groups was not significant (p=0.767). This variable was not retained in the final model (see section 2.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 2.1.2 Time from donor death to enucleation



**Number at risk (at years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>Up to 3 hours</b>	3610	1851	941	534	288	147	60
<b>4 to 6 hours</b>	4028	1950	882	449	242	120	45
<b>7 to 9 hours</b>	3664	1667	749	368	168	74	30
<b>10 to 12 hours</b>	2981	1336	536	234	100	50	10
<b>13 to 15 hours</b>	1107	458	165	67	26	11	1
<b>16 to 18 hours</b>	619	193	64	27	13	7	2
<b>More than 18 hours</b>	630	182	40	12	5	3	1

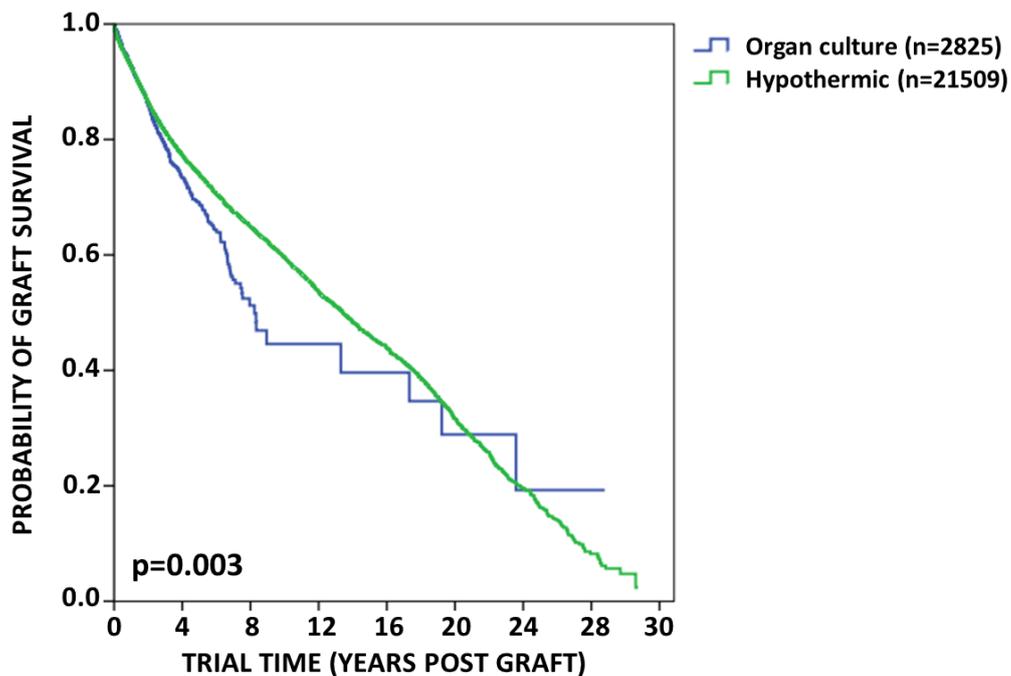
**Probability of graft survival (at years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>Up to 3 hours</b>	0.93	0.79	0.68	0.58	0.48	0.35	0.25
<b>4 to 6 hours</b>	0.92	0.76	0.66	0.55	0.45	0.31	0.19
<b>7 to 9 hours</b>	0.93	0.76	0.62	0.51	0.42	0.31	0.20
<b>10 to 12 hours</b>	0.93	0.77	0.61	0.49	0.37	0.29	NA
<b>13 to 15 hours</b>	0.92	0.76	0.62	0.50	0.45	NA	NA
<b>16 to 18 hours</b>	0.92	0.75	0.63	0.52	NA	NA	NA
<b>More than 18 hours</b>	0.93	0.77	0.58	NA	NA	NA	NA

### 2.1.3 Penetrating graft survival: influence of type of corneal storage media

In Australia, two storage methods are currently commonly used to preserve donor corneas prior to transplantation. In hypothermic storage, donor tissue is preserved and refrigerated below 4 degrees Celsius until required. The current storage media utilised for hypothermic preservation is Optisol GS, however a number of media have been used previously (e.g. K-Sol, Dextran, M-K medium). The alternative storage method, Organ Culture, involves warm storage, and was introduced to Australia in recent years. Data were not analysed for 335 grafts where the donor eye was stored in a moist pot, the cornea was preserved using another alternative specified method (n=6), or the eye bank did not specify which medium was used (n=152). Figure 2.1.3 shows the comparison of graft survival for corneas stored using hypothermic techniques compared to organ culture medium. A significant difference in outcomes was found between media (Log Rank Statistic=9.10; df=1; p=0.003). This variable was not retained in the final model (see section 2.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 2.1.3 Corneal storage media (modern media only)



#### Number at risk (at years post-graft)

	1	4	8	12	16	20	24	28
Organ culture	1574	394	42	11	NA	NA	NA	NA
Hypothermic	14937	7188	3298	1649	814	392	136	22

#### Probability of graft survival (at years post-graft)

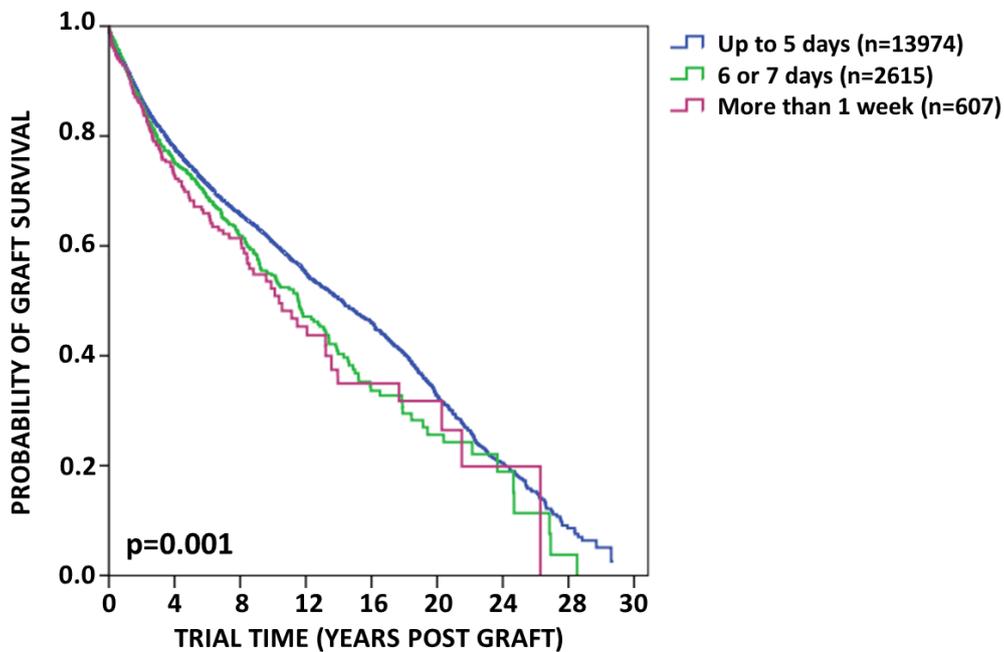
	1	4	8	12	16	20	24	28
Organ culture	0.93	0.73	0.51	0.45	NA	NA	NA	NA
Hypothermic	0.93	0.77	0.65	0.54	0.44	0.32	0.20	0.08

**2.1.4 Penetrating graft survival: influence of storage time – hypothermic medium**

Corneas stored in hypothermic medium are most often used within 5 days of storage and are rarely stored for longer than 7 days. Figure 2.1.4 shows the comparison of graft survival across storage time for those corneas stored in hypothermic medium. A significant difference was found across groups (Log Rank Statistic=14.01; df=2; p=0.001). Data on this variable were not provided in 30% of cases (13% of tissue was stored using a different technique, and the other 17% had no data provided). Two further categories were thus created called “not applicable” and “not advised”. A significant difference was still found across groups when these categories were included (Log Rank Statistic=19.49; df=4; p=0.001).

Grafts using donor tissue stored for up to 5 days exhibited better survival than those stored for 6 to 7 days (p=0.001) or more than a week (p=0.013). The difference in survival between the two groups of tissue stored for more than 5 days was not significant (p=0.359). This variable was not retained in the final model (see section 2.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

**Figure 2.1.4 Time from storage to graft, Optisol medium storage**



**Number at risk (at years post-graft)**

	1	4	8	12	16	20	24
<b>Within 5 days</b>	9941	4855	2305	1213	629	301	107
<b>6 to 7 days</b>	1681	709	289	114	41	19	6
<b>More than 1 week</b>	399	164	69	29	11	6	1

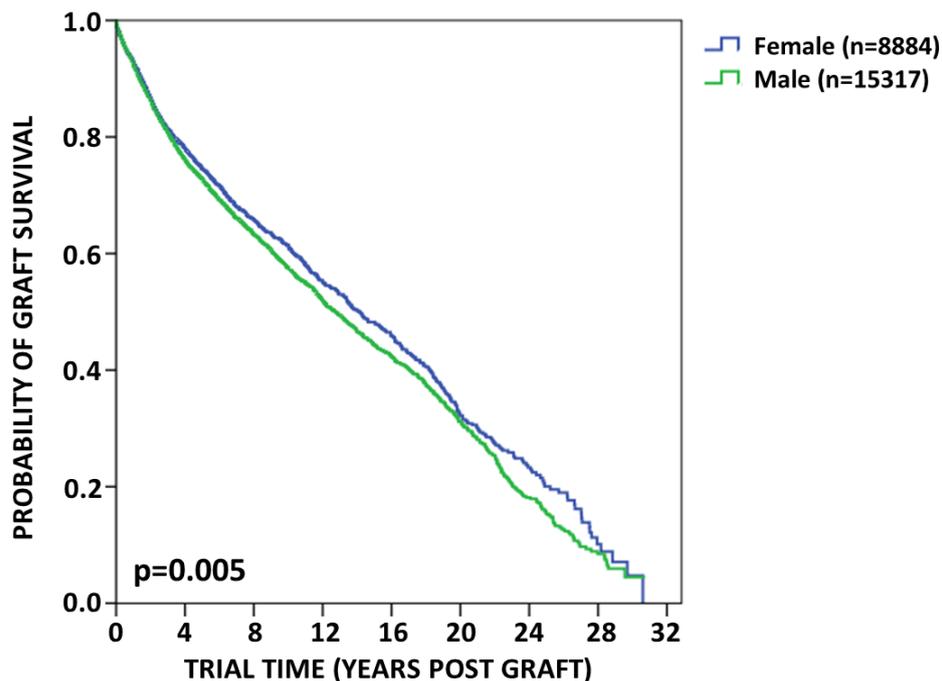
**Probability of graft survival (at years post-graft)**

	1	4	8	12	16	20	24
<b>Within 5 days</b>	0.93	0.78	0.66	0.55	0.46	0.33	0.21
<b>6 to 7 days</b>	0.93	0.75	0.62	0.47	0.34	NA	NA
<b>More than 1 week</b>	0.93	0.73	0.61	0.45	NA	NA	NA

### 2.1.5 Penetrating graft survival: influence of donor sex

Almost two-thirds of corneal donors were male. Figure 2.1.5 shows the comparison of graft survival depending on donor sex. A significant difference was found between groups (Log Rank Statistic=7.88; df=1; p=0.005). Data on this variable were not provided in 3% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=9.12; df=2; p=0.010). This variable was not included in the multivariate model (see section 2.7), as it is collinear with the variable analysing donor/recipient sex match/mismatch (see section 2.2.2), which **was** included.

Figure 2.1.5 Donor sex



#### Number at risk (at years post-graft)

	1	4	8	12	16	20	24
Female	6037	2768	1154	623	321	148	58
Male	10395	4777	2123	1032	495	248	89

#### Probability of graft survival (at years post-graft)

	1	4	8	12	16	20	24
Female	0.93	0.78	0.65	0.55	0.46	0.32	0.23
Male	0.92	0.76	0.63	0.52	0.42	0.31	0.18



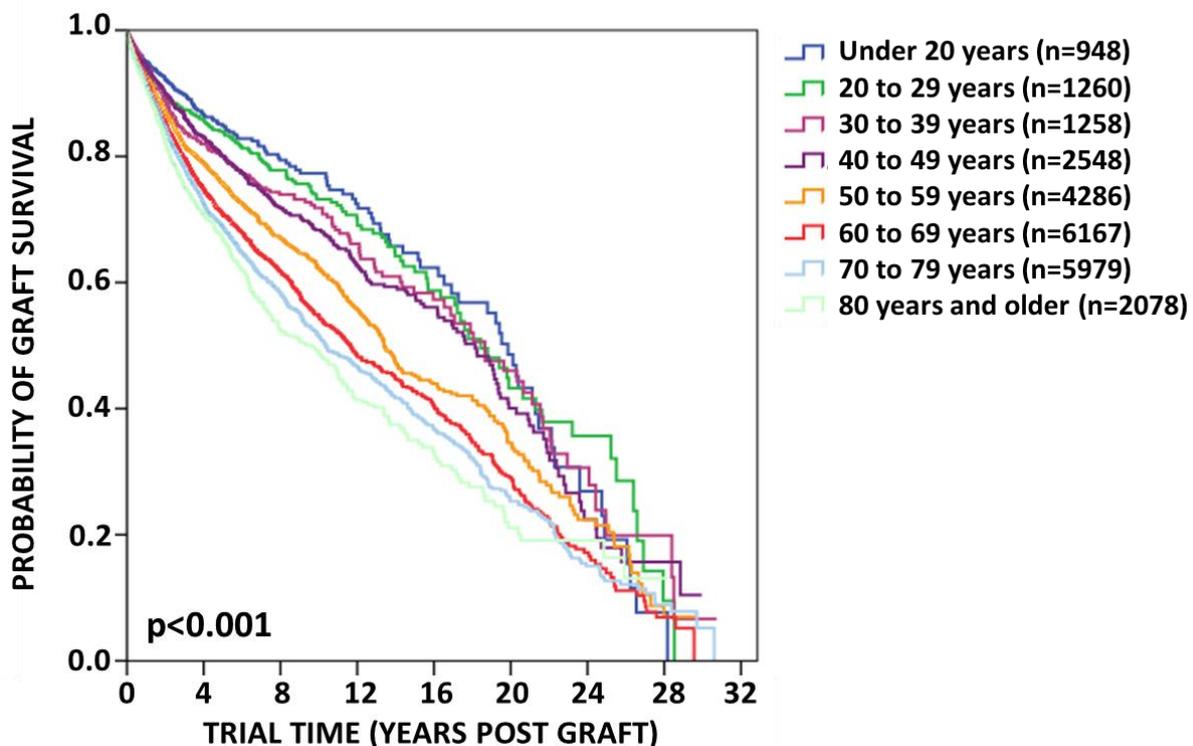
### 2.1.6 Penetrating graft survival: influence of donor age (years)

Figure 2.1.6 shows the comparison of graft survival depending on donor age, stratified by 10 year age groups. Donors aged under 10 years or over 90 years are rare, and so these data were combined with the adjacent age groups. A significant difference was found across groups (Log Rank Statistic=256.53; df=7;  $p<0.001$ ).

Grafts performed using tissue from donors aged under 20 years, 20 to 29 years, 30 to 39 years and 40 to 49 years, had significantly better survival than those performed using tissue from donors aged 50 to 59 years, 60 to 69 years, 70 to 79 years and 80 years and older (all comparisons  $p<0.001$ ). The differences in survival between grafts performed with tissue from donors aged 50 to 59 years and each of the three older age groups were also significantly different (all  $p<0.001$ ), as was the comparison between grafts performed with tissue from donors aged 60 to 69 years and those aged 80 years or older ( $p<0.001$ ). In all cases the younger donor tissue was associated with better survival. Donor age groups under 50 years were thus categorised together for multivariate analysis.

Data on this variable were not provided in 1% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=251.63; df=5;  $p<0.001$ ). This variable was retained in multivariate analysis (see section 2.7) suggesting that this is an independent factor significantly affecting graft survival.

Figure 2.1.6 Donor age



**Number at risk (at years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>Under 20 years</b>	677	350	170	96	48	29	7
<b>20 to 29 years</b>	845	439	228	126	57	27	14
<b>30 to 39 years</b>	866	411	199	111	53	29	12
<b>40 to 49 years</b>	1771	855	380	203	107	48	16
<b>50 to 59 years</b>	2897	1394	619	310	145	76	27
<b>60 to 69 years</b>	4163	1831	780	361	183	94	31
<b>70 to 79 years</b>	4048	1788	784	374	190	88	34
<b>80 years and older</b>	1387	584	219	109	58	22	9

**Probability of graft survival (at years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>Under 20 years</b>	0.95	0.87	0.79	0.73	0.62	0.49	NA
<b>20 to 29 years</b>	0.94	0.86	0.78	0.70	0.59	0.43	NA
<b>30 to 39 years</b>	0.94	0.82	0.76	0.66	0.57	0.46	NA
<b>40 to 49 years</b>	0.94	0.83	0.72	0.63	0.56	0.40	NA
<b>50 to 59 years</b>	0.93	0.79	0.67	0.56	0.44	0.35	0.22
<b>60 to 69 years</b>	0.92	0.75	0.62	0.48	0.40	0.59	0.17
<b>70 to 79 years</b>	0.92	0.73	0.58	0.47	0.37	0.25	0.15
<b>80 years and older</b>	0.91	0.71	0.52	0.41	0.33	0.21	NA

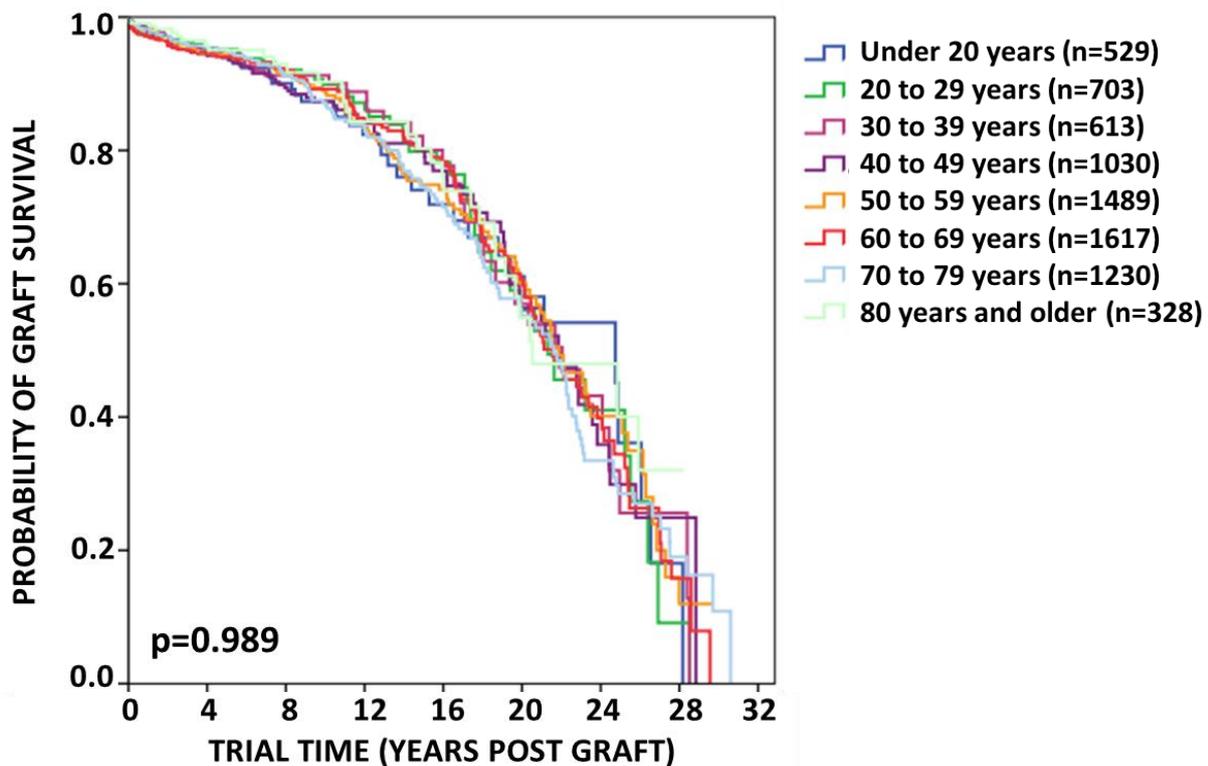
Donor age group is significantly correlated with central corneal endothelial cell count (ECC) (see section 2.1.9). Donors over the age of 60 had higher rates of ECC under 2500 cells/mm<sup>2</sup> than those in the younger age groups (Chi<sup>2</sup>=126.78, df=7, p<0.001). Data on ECC were unavailable for 80% of grafts and thus this variable was excluded from multivariate analysis. It is possible that the retention of donor age group in the multivariate model reflects the influence of ECC on graft survival.

### 2.1.6.1 Penetrating graft survival: influence of donor age (years) on grafts performed for keratoconus

Figure 2.1.7 shows the comparison of graft survival depending on donor age, stratified by 10 year age groups, for grafts performed for keratoconus. Donors aged under 10 years or over 90 years are rare, and so these data were combined with the adjacent age groups. No significant difference was found across groups (Log Rank Statistic=1.30; df=7;  $p=0.989$ ).

This finding is in contrast to that found for the entire cohort, suggesting that, despite this variable's retention in the final multivariate model, other unknown factors may be confounding this result.

Figure 2.1.7 Donor age, grafts performed for keratoconus



**Number at risk (at years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>Under 20 years</b>	389	206	106	61	32	20	6
<b>20 to 29 years</b>	488	260	146	87	46	19	8
<b>30 to 39 years</b>	424	211	105	61	33	18	10
<b>40 to 49 years</b>	751	382	194	118	69	31	12
<b>50 to 59 years</b>	1088	560	281	172	101	58	21
<b>60 to 69 years</b>	1195	575	293	184	115	67	24
<b>70 to 79 years</b>	938	502	287	181	111	64	27
<b>80 years and older</b>	254	131	74	55	35	17	7

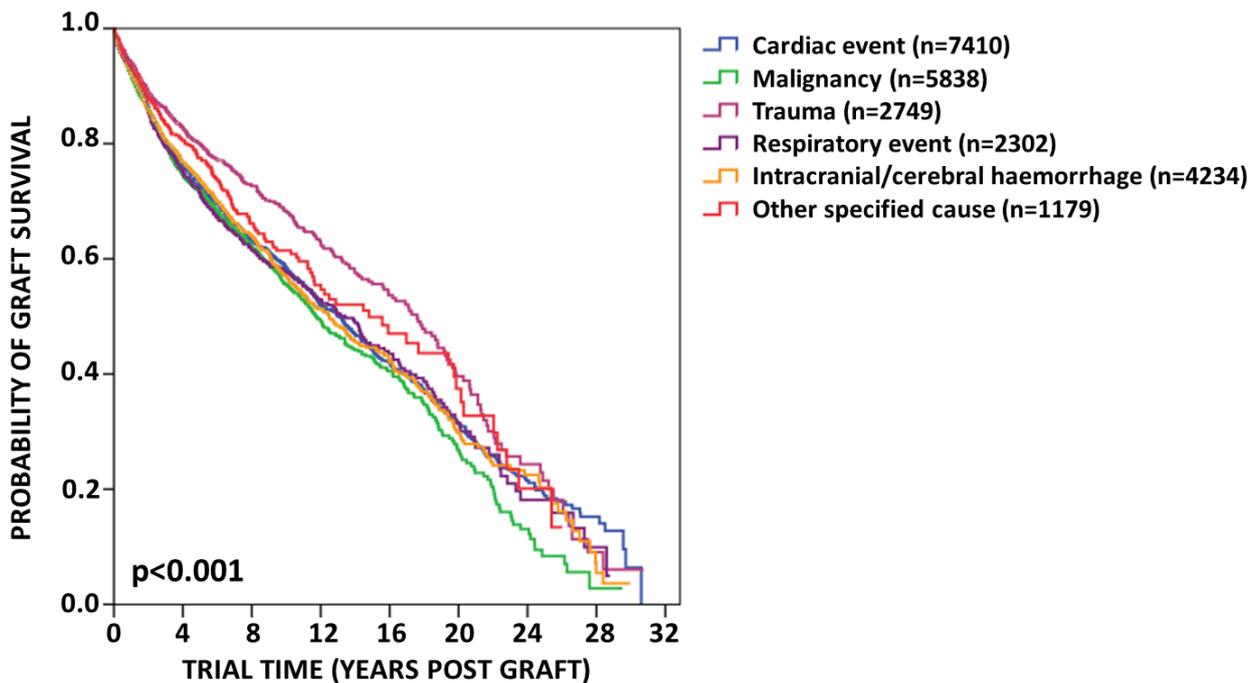
**Probability of graft survival (at years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>Under 20 years</b>	0.98	0.95	0.90	0.82	0.72	0.61	NA
<b>20 to 29 years</b>	0.97	0.95	0.91	0.87	0.78	NA	NA
<b>30 to 39 years</b>	0.98	0.95	0.91	0.89	0.78	NA	NA
<b>40 to 49 years</b>	0.98	0.94	0.89	0.84	0.77	0.56	NA
<b>50 to 59 years</b>	0.98	0.95	0.92	0.83	0.74	0.60	0.40
<b>60 to 69 years</b>	0.97	0.95	0.92	0.84	0.78	0.61	0.40
<b>70 to 79 years</b>	0.98	0.96	0.91	0.83	0.72	0.55	0.33
<b>80 years and older</b>	0.99	0.96	0.93	0.84	0.76	NA	NA

### 2.1.7 Penetrating graft survival: influence of cause of donor death

Few causes of death exclude a person from becoming a corneal donor. Figure 2.1.8 shows the comparison of graft survival depending on cause of donor death. 31 grafts were performed using donor tissue from live donors. These were excluded from the analysis. A significant difference was found across groups (Log Rank Statistic=55.24; df=5;  $p<0.001$ ). Cause of death was unknown to the ACGR for 4% of grafts. A further category was thus created called “unknown”. A significant difference was still found across groups when this category was included (Log Rank Statistic=55.19; df=6;  $p<0.001$ ). Grafts where the donor had died from trauma had significantly better survival than those where the donor had died from any of the other four major causes of death (all  $p<0.001$ ). Grafts where the donor had died from an “other specified cause” also had superior survival to those where the donor had died from malignancy ( $p=0.002$ ). This variable was not retained in the multivariate analysis (see section 2.7) suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 2.1.8 Cause of donor death



**Number at risk (at years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>Cardiac event</b>	5081	2433	1127	576	295	144	54
<b>Malignancy</b>	3898	1622	646	275	127	51	17
<b>Trauma</b>	1860	926	438	235	106	55	18
<b>Respiratory event</b>	1594	682	304	157	88	42	10
<b>Intracranial/cerebral haemorrhage</b>	2866	1339	576	280	140	65	25
<b>Other specified cause</b>	838	393	153	69	30	18	6

**Probability of graft survival (at years post-graft)**

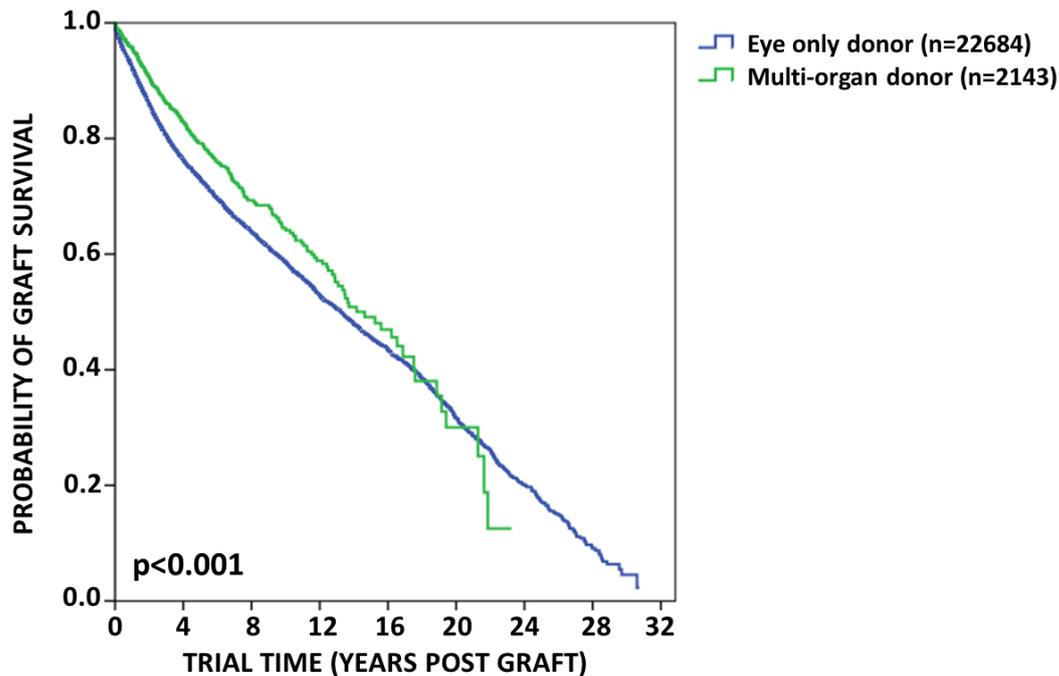
	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>Cardiac event</b>	0.93	0.76	0.63	0.52	0.42	0.31	0.22
<b>Malignancy</b>	0.92	0.75	0.62	0.49	0.41	0.27	NA
<b>Trauma</b>	0.94	0.83	0.73	0.63	0.54	0.40	NA
<b>Respiratory event</b>	0.93	0.75	0.62	0.53	0.44	0.32	NA
<b>Intracranial/cerebral haemorrhage</b>	0.92	0.77	0.64	0.53	0.42	0.30	0.23
<b>Other specified cause</b>	0.93	0.81	0.66	0.56	0.47	NA	NA

“Other specified causes” included donors who died from diseases of the liver, kidney, pancreas, gastro-intestinal tract, encephalopathy, sepsis, and rare diseases. It also included 271 cases, where the donor was listed as dying from brain damage or brain death. In 46% of these cases, the donor was a multi-organ donor (compared to 9% of the overall cohort). It is possible that a large proportion of this latter group had undergone some form of trauma.

### 2.1.8 Penetrating graft survival: influence of multi-organ donor status

Figure 2.1.9 shows the comparison of graft survival depending on whether the donor cornea was obtained from a multi-organ donor. A significant difference was found between groups (Log Rank Statistic=22.54; df=1;  $p<0.001$ ). This variable was not retained in the multivariate analysis (see section 2.7) suggesting that this is **not** an independent factor significantly affecting graft survival.

**Figure 2.1.9 Multi-organ donor status**



#### Number at risk (at years post-graft)

	1	4	8	12	16	20	24	28
Eye only donor	15387	7115	3214	1629	831	414	153	28
Multi organ donor	1490	661	240	107	37	10	NA	NA

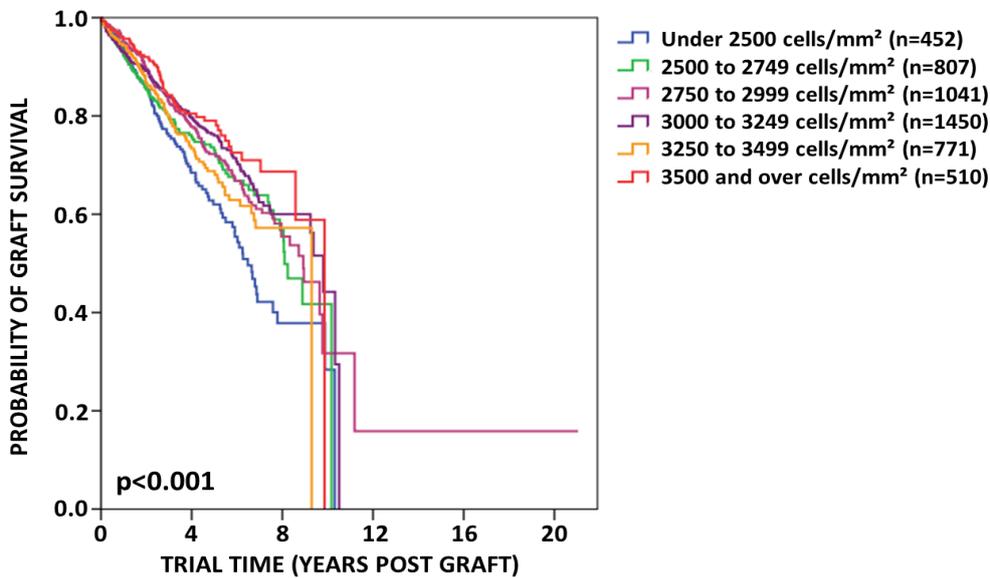
#### Probability of graft survival (at years post-graft)

	1	4	8	12	16	20	24	28
Eye only donor	0.92	0.76	0.64	0.53	0.44	0.32	0.20	0.09
Multi organ donor	0.96	0.83	0.69	0.59	0.47	NA	NA	NA

**2.1.9 Penetrating graft survival: influence of donor central corneal endothelial cell density**

Information on donor central corneal endothelial cell count (ECC) has been requested by the Registry in recent years. ECC was reported for one-fifth (20%) of registered penetrating grafts. Reported ECC ranged from 1388 to 4951 cells/mm<sup>2</sup>. Comparison of graft survival across donor ECC groups is shown in Figure 2.1.10. A significant difference was found across groups (Log Rank Statistic=24.77; df=3; p<0.001). Survival of grafts with less than 2500 cells/mm<sup>2</sup> had significantly poorer survival than those with 2750 to 2999 cells/mm<sup>2</sup>, 3000 to 3249 cells/mm<sup>2</sup>, or 3500 and over cells/mm<sup>2</sup> (all p<0.001). This variable was not included in the multivariate analysis (see section 2.7), due to the very high levels (80%) of missing data. Endothelial cell count differed significantly across donor age groups, (Chi<sup>2</sup>=126.78, df=7, p<0.001), with older donors (over 60) more likely to have cell counts below 2500 cells/mm<sup>2</sup>.

**Figure 2.1.10 Endothelial cell density**



**Number at risk (at years post-graft)**

	1	2	4	6	8
Less than 2500 cells/mm <sup>2</sup>	286	219	109	50	15
2500 – 2749 cells/mm <sup>2</sup>	477	351	166	85	27
2750 – 2999 cells/mm <sup>2</sup>	654	493	255	119	42
3000 – 3249 cells/mm <sup>2</sup>	835	655	337	161	52
3250 – 3499 cells/mm <sup>2</sup>	447	316	145	55	12
3500 or more cells/mm <sup>2</sup>	314	234	123	53	14

**Probability of graft survival (at years post-graft)**

	1	2	4	6	8
Less than 2500 cells/mm <sup>2</sup>	0.94	0.86	0.68	0.55	NA
2500 – 2749 cells/mm <sup>2</sup>	0.92	0.85	0.76	0.67	0.57
2750 – 2999 cells/mm <sup>2</sup>	0.95	0.90	0.78	0.67	0.56
3000 – 3249 cells/mm <sup>2</sup>	0.93	0.89	0.80	0.71	0.60
3250 – 3499 cells/mm <sup>2</sup>	0.94	0.87	0.73	0.63	NA
3500 or more cells/mm <sup>2</sup>	0.96	0.92	0.81	0.73	NA

## 2.2 Recipient Factors

Table 2.3 shows the number of grafts reported for each indication for graft, and also shows further sub-group breakdowns for each indication group. This breakdown is shown for all 24827 registered grafts as well as for the 20336 followed grafts. The total for each of the indication groups is the sum of the sub-categories shown below.

**Table 2.3 Indication for graft**

<b>Penetrating Corneal Graft Indication for Graft</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Keratoconus*</b>	<b>7621 (31%)</b>	<b>6262 (31%)</b>
Uncomplicated	7185 (29%)	5928 (29%)
With hydrops	477 (2%)	362 (2%)
<b>Failed previous graft</b>	<b>6294 (25%)</b>	<b>4996 (25%)</b>
<b>Bullous keratopathy</b>	<b>4628 (19%)</b>	<b>3932 (19%)</b>
Pseudophakic	3626 (15%)	3076 (15%)
Aphakic	673 (3%)	570 (3%)
Phakic	329 (1%)	286 (1%)
<b>Corneal dystrophy**</b>	<b>2378 (10%)</b>	<b>2048 (10%)</b>
Fuchs' (endothelial)	2067 (8%)	1794 (9%)
Granular (epithelial/stromal)	138 (<1%)	113 (<1%)
Macular (stromal)	56 (<1%)	41 (<1%)
Lattice (epithelial/stromal)	54 (<1%)	45 (<1%)
Posterior polymorphous (endothelial)	27 (<1%)	25 (<1%)
Schnyder (stromal)	21 (<1%)	19 (<1%)
Reis-Bücklers (epithelial/stromal)	13 (<1%)	9 (<1%)
Meesmann (epithelial)	2 (<1%)	2 (<1%)
<b>Herpetic eye disease</b>	<b>1109 (4%)</b>	<b>918 (5%)</b>
Inactive HSV, no perforation	680 (3%)	585 (3%)
Herpes zoster, no perforation	97 (<1%)	79 (<1%)
Active HSV, no perforation	82 (<1%)	67 (<1%)
HSV, or HZO, with perforation	250 (1%)	187 (<1%)
<b>Corneal scars and opacities</b>	<b>515 (2%)</b>	<b>407 (2%)</b>
With cataract	74 (<1%)	63 (<1%)
From trachoma	43 (<1%)	34 (<1%)
Other	398 (2%)	310 (2%)
<b>Corneal ulcers/perforation</b>	<b>505 (2%)</b>	<b>379 (2%)</b>
Perforated	415 (2%)	303 (1%)
No perforation	90 (<1%)	76 (<1%)

	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Trauma</b>	<b>641 (3%)</b>	<b>507 (2%)</b>
Burns	78 (<1%)	69 (<1%)
Beta radiation	11 (<1%)	11 (<1%)
With perforation	6 (<1%)	4 (<1%)
Unspecified	546 (2%)	423 (2%)
<b>Non-herpetic infections</b>	<b>445 (1%)</b>	<b>316 (2%)</b>
Microbial keratitis/abscess	169 (<1%)	118 (<1%)
Mycotic/fungal ulcer	86 (<1%)	66 (<1%)
Pseudomonas infection	58 (<1%)	34 (<1%)
Acanthamoeba keratitis	36 (<1%)	30 (<1%)
Viral keratitis	13 (<1%)	11 (<1%)
Endophthalmitis	12 (<1%)	10 (<1%)
Unspecified	71 (<1%)	46 (<1%)
<b>Corneal degenerations</b>	<b>223 (&lt;1%)</b>	<b>169 (&lt;1%)</b>
<b>Other***</b>	<b>518 (2%)</b>	<b>434 (2%)</b>
<b>Total</b>	<b>24827 (100%)</b>	<b>20336 (100%)</b>

\*In April 2015, *Gomes et al* [see reference 1], published a paper in *Cornea*, outlining a process to develop global consensus regarding the diagnosis and treatment of keratoconus and other ectatic diseases. The *Gomes et al* (2015) paper states that “Keratoconus and keratoglobus are different clinical entities”. The data published in previous ACGR reports included keratoglobus with keratoconus. This report separates keratoglobus cases from keratoconus, and classifies them under “Other”.

\*\*In February 2015 Weiss et al [see reference 2] published a paper in *Cornea*, updating the International Classification of Corneal Dystrophies “incorporating new clinical, histopathologic, and genetic information”. This classification system has been used for the 2018 ACGR Report.

\*\*\*Other included: Interstitial keratitis (156), ICE syndrome (58), Peters’ anomaly (39), unknown (35), descemetocoele (20), lipid keratopathy (17), pterygium (16), band keratopathy (15), keratoglobus (15), congenital glaucoma (12), aniridia (9), autograft (8), corneal neovascularisation (8), congenital cataract (7), epithelial defects (7), blood staining (6), glaucoma (6), congenital corneal opacity (5), cystinosis (5), irregular astigmatism (5), mucopolysaccharidosis (5), superative keratitis (5), squamous cell carcinoma (4), congenital rubella (4), corneal staphyloma (4), dermoid (3), congenital corneal calcification (3), scleral necrosis (3), amyloidosis (2), congenital microphthalmia (2), congenital syphilis (2), epithelial downgrowth (2), ichthyosis (2), pemphigoid (2), porphyria (2), retinal detachment (2), Stevens-Johnson syndrome (2), aphakia (1), astigmatism (1), childhood fever (1), Crouzon’s syndrome (1), heterochromic cyclitis (1), hypopyon (1), keratoconjunctivitis (1), melanoma (1), monoclonal gammopathy (1), myopia (1), neuroparalytic keratitis (1), ocular surface dysplasia (1), osteogenesis imperfecta (1), phthisis (1), rosacea (1), Silver-Russell syndrome (1), synechia (1), vitamin A deficiency (1), wound dehiscence following IOL insertion (1).

Chi<sup>2</sup> analysis indicated that follow-up was significantly more likely to have been received at least once for grafts performed for bullous keratopathy or corneal dystrophy, compared to other indications for graft ( $p < 0.001$ ).

Table 2.4 summarises the number of grafts within each of the variable sub-groups, for the recipient factors examined in this report that were found to be significant predictors of graft survival in univariate analyses. The sum for each variable equals the total number of grafts (24,827 registered and 20,336 followed) and the percentages, which should be summed vertically for each variable, total 100. The data are presented in the following sections.

**Table 2.4 Summary table of recipient factors, significant in univariate analyses**

<b>Penetrating Corneal Graft Recipient Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Australian State where graft was performed</b>		
State M	8857 (36%)	6940 (34%)
State K	5388 (22%)	4574 (22%)
State V	4711 (19%)	3944 (19%)
State J	2851 (11%)	2053 (10%)
State N	2422 (10%)	2275 (11%)
State C	572 (2%)	536 (3%)
Other	26 (<1%)	14 (<1%)
<b>Interstate transportation</b>		
No	21812 (88%)	17600 (87%)
Yes	1295 (5%)	1080 (5%)
Not advised/not applicable	1720 (7%)	1656 (8%)
<b>Recipient age group</b>		
<20 years	1130 (5%)	937 (5%)
20 to 29 years	3293 (13%)	2671 (13%)
30 to 39 years	2862 (12%)	2375 (12%)
40 to 49 years	2679 (11%)	2179 (11%)
50 to 59 years	2701 (11%)	2222 (11%)
60 to 69 years	3645 (15%)	3012 (15%)
70 to 79 years	4993 (20%)	4125 (20%)
≥ 80 years	3516 (14%)	2808 (14%)
Not advised	8 (<1%)	7 (<1%)
<b>Donor/recipient sex match</b>		
Female/female	4269 (17%)	3552 (17%)
Female/male	4615 (19%)	3739 (18%)
Male/female	7222 (29%)	5970 (29%)
Male/male	8095 (33%)	6514 (32%)
Not advised	626 (3%)	561 (3%)
<b>Change in lens status</b>		
Phakic/phakic	12220 (49%)	9959 (49%)
Phakic/pseudophakic	2422 (10%)	2076 (10%)
Other combination	10185 (41%)	8301 (41%)
<b>Pre-graft neovascularisation</b>		
None	16795 (68%)	13929 (69%)
One quadrant	2121 (9%)	1611 (8%)
Two quadrants	2652 (11%)	2100 (10%)
Three quadrants	1196 (5%)	995 (5%)
Four quadrants	2063 (8%)	1701 (8%)

	Registered (%)	Followed (%)
<b>Pre-graft inflammation and/or steroid use</b>		
No	17568 (71%)	14480 (71%)
Yes	6984 (28%)	5652 (28%)
Not advised	275 (1%)	204 (1%)
<b>Presence of raised intraocular pressure</b>		
IOP never known to be raised	20934 (84%)	17135 (84%)
IOP raised in past and/or at graft	3893 (16%)	3201 (16%)
<b>Prior contralateral corneal graft/s</b>		
None	19557 (79%)	16036 (79%)
One	4290 (17%)	3526 (17%)
Two or more	980 (4%)	774 (4%)
<b>Total</b>	<b>24827 (100%)</b>	<b>20336 (100%)</b>

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables for which a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Follow-up was significantly more likely ( $p < 0.05$ ) to have been received for grafts performed in female recipients, recipients with no history of inflammation and/or steroid use, grafts that had a no history of previous ipsilateral grafts, grafts that underwent a triple procedure (went from phakic to pseudophakic) and grafts performed with donor tissue that had been transported interstate. Follow-up was significantly lower for grafts performed in recipients from State M and State J, in recipients with mild pre-graft neovascularisation, and in recipients aged 80 or older. Forty-three percent of recipients known by the ACGR to have died prior to any follow-up having been received, were aged 80 or older at the time of graft, which may account for this lower level of follow-up.

Two-hundred and sixteen penetrating keratoplasties had been converted from a planned lamellar procedure: 195 DALK, seven DS(A)EK, three peripheral patch, two mushroom tuck-in, one DMEK, and eight unspecified. Thirty-seven had a concurrent graft (limbal or lamellar patch). Thirty-six eyes undergoing penetrating keratoplasty had a history of corneal cross-linking.

Table 2.5 shows the number of grafts within each of the variable sub-groups, for the recipient factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (24,827 registered and 20,336 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The result of the Kaplan-Meier survival analysis is also provided for each variable.

**Table 2.5 Recipient factors, not significant in univariate analyses**

<b>Penetrating Corneal Graft Recipient Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Recipient sex</b>		
Male	11798 (48%)	9800 (48%)
Female	13029 (52%)	10536 (52%)
<b>Chi<sup>2</sup>=0.17, df=1, p=0.677</b>		
<b>Eye grafted</b>		
Left	12345 (50%)	10120 (50%)
Right	12471 (50%)	10208 (50%)
Not advised	11 (<1%)	8 (<1%)
<b>Chi<sup>2</sup>=1.14, df=1, p=0.286</b>		
<b>Total</b>	<b>24827 (100%)</b>	<b>20336 (100%)</b>

Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised.



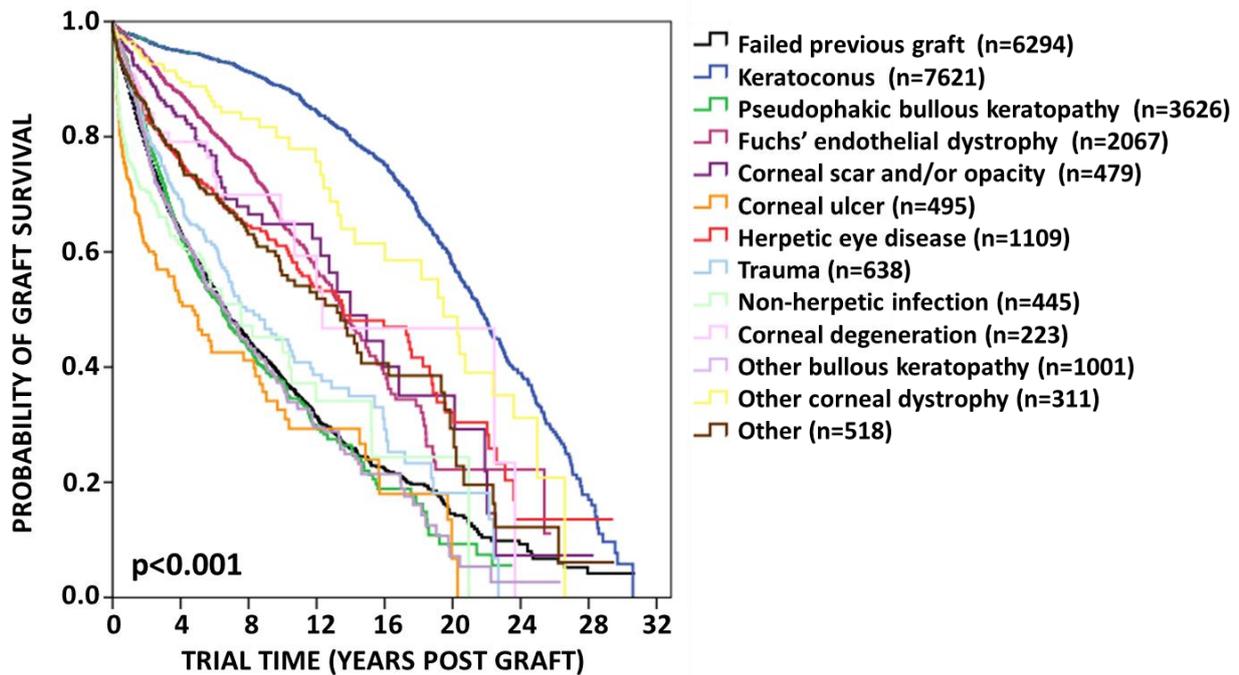
### 2.2.1 Penetrating graft survival: influence of indication for graft

Figure 2.2.1 shows the comparison of graft survival depending on indication for graft. All repeat grafts were analysed together, regardless of original pathology. A significant difference was found across groups (Log Rank Statistic=2478.70; df=12;  $p<0.001$ ).

Grafts performed for keratoconus had better survival than those performed for any other indication, except corneal dystrophies other than Fuchs' endothelial dystrophy. Grafts performed for Fuchs' endothelial dystrophy, other corneal dystrophy, or herpetic eye disease had better survival than those for failed previous graft, pseudophakic bullous keratopathy, corneal ulcer, trauma, non-herpetic infection, or other bullous keratopathy. Grafts performed for corneal scar and/or opacity had better survival than those for failed previous graft, pseudophakic bullous keratopathy, corneal ulcer, non-herpetic infection, and other bullous keratopathy. In addition to the indications mentioned above, grafts performed for corneal ulcer had poorer survival than those for failed previous graft, pseudophakic bullous keratopathy, trauma, corneal degeneration, other bullous keratopathy and other (all  $p\leq 0.001$ ).

This variable was retained in multivariate analysis (see section 2.7) suggesting that this is an independent factor significantly affecting graft survival.

Figure 2.2.1 Indication for graft



**Number at risk (years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>Failed previous graft</b>	4018	1651	596	251	102	44	16
<b>Keratoconus</b>	5597	2873	1519	944	559	302	117
<b>Pseudo bullous keratopathy</b>	2385	840	259	74	21	6	NA
<b>Fuchs' endothelial dystrophy</b>	1620	965	472	165	47	10	4
<b>Corneal scar/opacity</b>	304	133	48	25	9	6	1
<b>Ulcer/perforation</b>	211	75	30	16	6	1	NA
<b>Herpetic eye disease</b>	752	339	148	81	42	18	4
<b>Trauma</b>	408	179	73	35	15	6	NA
<b>Non-herpetic infection</b>	199	80	25	11	2	1	NA
<b>Corneal degeneration</b>	143	44	18	8	3	2	NA
<b>Other bullous keratopathy</b>	668	272	103	46	21	4	1
<b>Other dystrophy</b>	220	134	67	33	21	15	7
<b>Other</b>	352	187	96	47	20	9	3

**Probability of graft survival (years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>Failed previous graft</b>	0.88	0.63	0.45	0.31	0.22	0.15	NA
<b>Keratoconus</b>	0.98	0.95	0.91	0.84	0.75	0.58	0.39
<b>Pseudo bullous keratopathy</b>	0.91	0.63	0.43	0.30	0.19	NA	NA
<b>Fuchs' endothelial dystrophy</b>	0.97	0.88	0.75	0.57	0.39	NA	NA
<b>Corneal scar/opacity</b>	0.95	0.84	0.67	0.62	NA	NA	NA
<b>Ulcer/perforation</b>	0.72	0.51	0.41	NA	NA	NA	NA
<b>Herpetic eye disease</b>	0.91	0.76	0.65	0.54	0.47	NA	NA
<b>Trauma</b>	0.89	0.69	0.50	0.39	NA	NA	NA
<b>Non-herpetic infection</b>	0.76	0.61	0.47	NA	NA	NA	NA
<b>Corneal degeneration</b>	0.92	0.79	NA	NA	NA	NA	NA
<b>Other bullous keratopathy</b>	0.91	0.63	0.44	0.30	0.21	NA	NA
<b>Other dystrophy</b>	0.97	0.90	0.83	0.76	0.61	NA	NA
<b>Other</b>	0.90	0.75	0.63	0.53	0.41	NA	NA

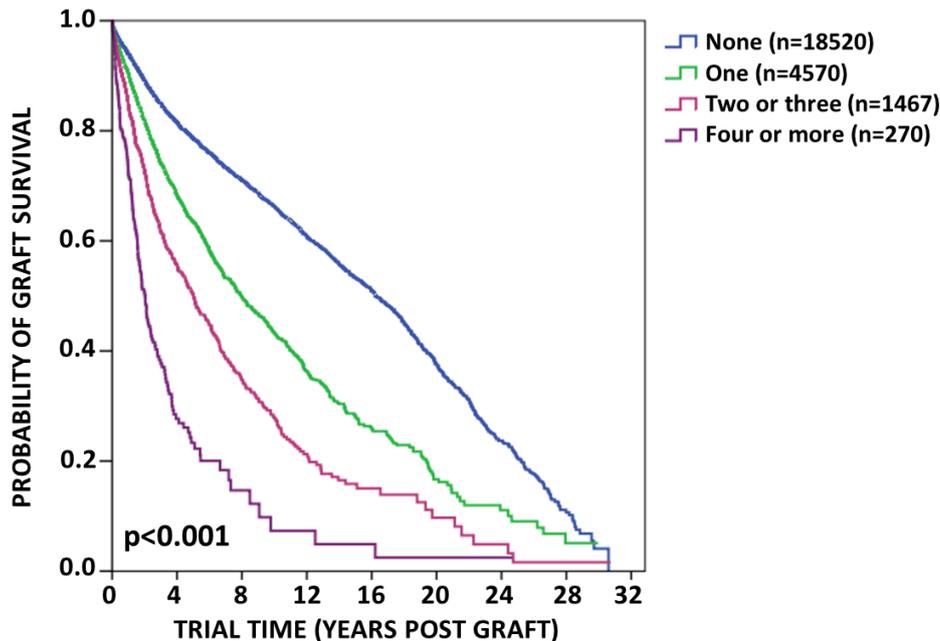
## 2.2.2 Penetrating graft survival: subcategory analyses

The analyses on pages 38 to 42 are of subcategories in individual indication for graft cohorts. The nature of the variables means that large percentages of the cohort do not have relevant data. These subgroup-analyses were therefore not included in multivariate analyses. The overarching variable “indication for graft” was included.

### 2.2.2.1 Penetrating graft survival: influence of the number of previous ipsilateral grafts

Survival was compared across groups based on the number of previous grafts in the same eye (range 1 to 12). Previous grafts may not have been penetrating keratoplasties. The ACGR has only specifically requested this information since 2016, consequently this is unknown in the majority (98%) of cases. Survival, shown in Figure 2.2.2, decreased (Log Rank Statistic=222.26, df=2,  $p<0.001$ ) as the number of grafts increased. Survival of first grafts is included in the Kaplan-Meier plot for visual reference but these data were excluded from the log rank calculation.

Figure 2.2.2 Number of previous ipsilateral grafts



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
One	2995	1264	482	205	85	36	12
Two or three	925	358	109	44	16	3	1
Four or more	144	35	7	3	2	1	1

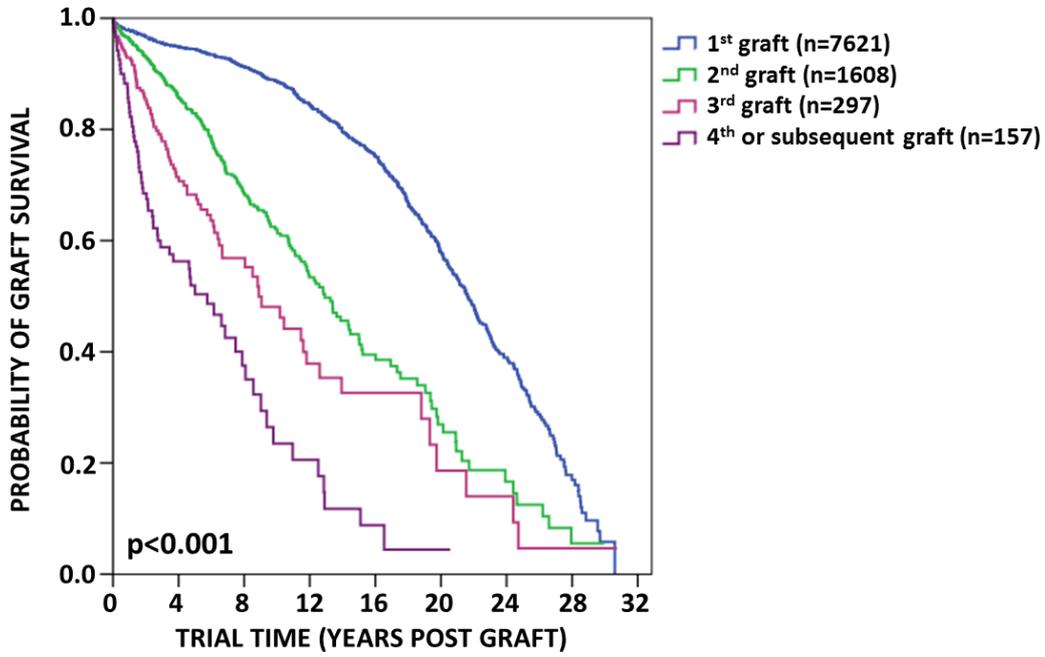
#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20
One	0.90	0.68	0.50	0.36	0.26	0.17
Two or three	0.85	0.56	0.35	0.21	NA	NA
Four or more	0.73	0.28	NA	NA	NA	NA

**2.2.2.2 Penetrating graft survival: keratoconus**

Figure 2.2.3 shows the comparison of graft survival for first versus repeat grafts for keratoconus. A significant difference was found across groups (Log Rank Statistic=644.55; df=3; p<0.001).

**Figure 2.2.3 First versus subsequent grafts for keratoconus**



**Number at risk (years post-graft)**

	1	4	8	12	16	20	24
<b>1<sup>st</sup> graft</b>	5597	2873	1519	944	559	302	117
<b>2<sup>nd</sup> graft</b>	1108	525	219	93	42	19	8
<b>3<sup>rd</sup> graft</b>	217	94	35	16	8	4	3
<b>4<sup>th</sup> or subsequent graft</b>	97	43	15	7	3	1	NA

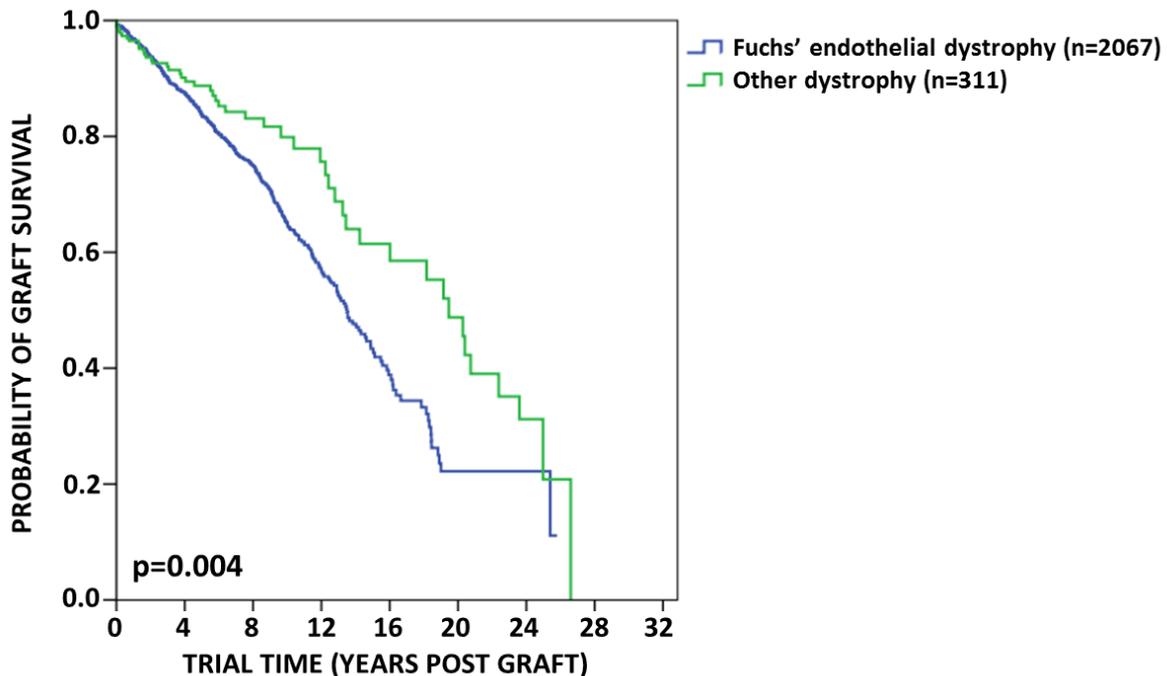
**Probability of graft survival (years post-graft)**

	1	4	8	12	16	20	24
<b>1<sup>st</sup> graft</b>	0.98	0.95	0.91	0.84	0.75	0.58	0.39
<b>2<sup>nd</sup> graft</b>	0.96	0.86	0.68	0.53	0.40	NA	NA
<b>3<sup>rd</sup> graft</b>	0.93	0.71	0.57	NA	NA	NA	NA
<b>4<sup>th</sup> or subsequent graft</b>	0.84	0.56	NA	NA	NA	NA	NA

### 2.2.2.3 Penetrating graft survival: influence of type of corneal dystrophy

Figure 2.2.4 shows the comparison of survival for grafts for Fuchs' endothelial dystrophy versus other corneal dystrophies. A significant difference was found across groups (Log Rank Statistic=8.52; df=1; p=0.004).

Figure 2.2.4 Type of corneal dystrophy



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
<b>Fuchs' endothelial dystrophy</b>	1620	965	472	165	47	10	4
<b>Other dystrophy</b>	220	134	67	33	21	15	7

#### Probability of graft survival (years post-graft)

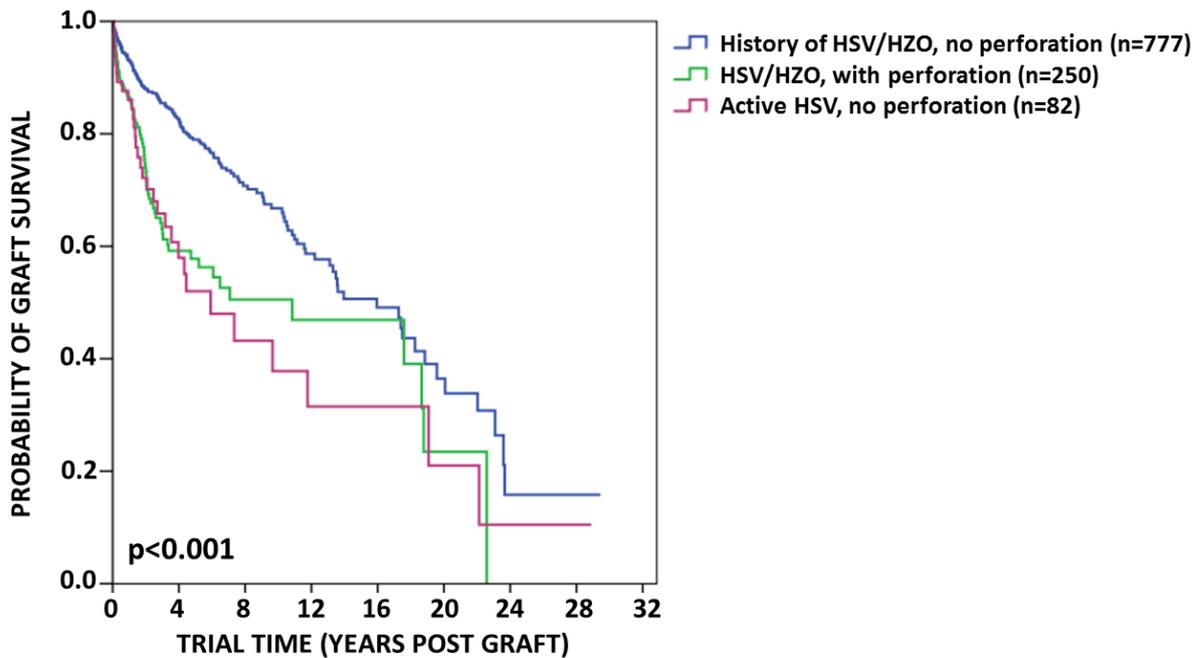
	1	4	8	12	16
<b>Fuchs' endothelial dystrophy</b>	0.97	0.88	0.75	0.57	0.39
<b>Other dystrophy</b>	0.97	0.90	0.83	0.76	0.61

The 311 'other' corneal dystrophies comprised: granular dystrophy (138), lattice dystrophy (54), macular dystrophy (56), posterior polymorphous dystrophy (27), Schnyder crystalline dystrophy (21), Reis-Bücklers dystrophy (13), and Meesmann dystrophy (2).

**2.2.2.4 Penetrating graft survival: influence of HSV eye disease at time of graft**

Figure 2.2.5 shows the survival of grafts performed for herpetic eye infection. The graph shows survival of grafts with a history of HSV or HZO but no perforation, to those with active HSV infection at the time of graft, with and without perforation. A significant difference was found across groups (Log Rank Statistic=33.26, df=2, p<0.001). Grafts without active HSV, and without perforation, exhibit better graft survival.

**Figure 2.2.5 Presence of active Herpes Simplex Virus (HSV) and perforation**



**Number at risk (years post-graft)**

	1	4	8	12	16	20	24
History of HSV/HZO, no perforation	560	268	119	63	32	14	3
HSV/HZO, with perforation	139	50	20	13	7	2	NA
Active HSV, no perforation	53	21	9	5	3	2	1

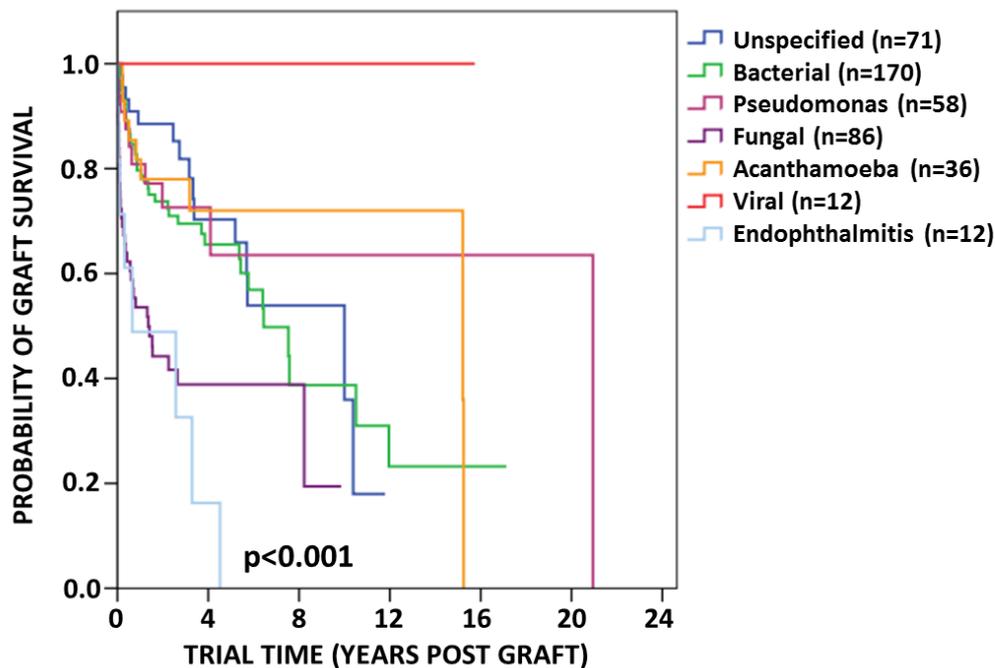
**Probability of graft survival (years post-graft)**

	1	4	8	12	16
History of HSV/HZO, no perforation	0.93	0.83	0.71	0.59	0.49
HSV/HZO, with perforation	0.86	0.59	0.51	NA	NA
Active HSV, no perforation	0.86	0.58	NA	NA	NA

### 2.2.2.5 Penetrating graft survival: influence of non-herpetic infections

Figure 2.2.6 shows the comparison of survival of penetrating keratoplasty for subcategories of non-herpetic infection. Grafts performed for viral infections and endophthalmitis are shown in the survival curve but were excluded from the statistical comparison due to low numbers. A significant difference was found between the remaining groups (Log Rank Statistic=31.67; df=4;  $p<0.001$ ).

Figure 2.2.6 Type of non-herpetic infection



#### Number at risk (years post-graft)

	1	2	3	4	5	6	8	10	12
Unspecified keratitis	36	31	22	18	16	9	3	3	NA
Bacterial keratitis	76	54	46	31	26	18	6	5	3
Pseudomonas keratitis	22	16	12	8	7	5	5	2	2
Fungal keratitis	30	18	12	7	6	4	2	NA	NA
Acanthamoeba keratitis	22	15	13	11	10	8	5	4	3

#### Probability of graft survival (years post-graft)

	1	2	3	4	5
Unspecified keratitis	0.89	0.89	0.82	NA	NA
Bacterial keratitis	0.80	0.74	0.70	0.66	0.66
Pseudomonas keratitis	0.81	NA	NA	NA	NA
Fungal keratitis	0.54	NA	NA	NA	NA
Acanthamoeba keratitis	0.82	NA	NA	NA	NA

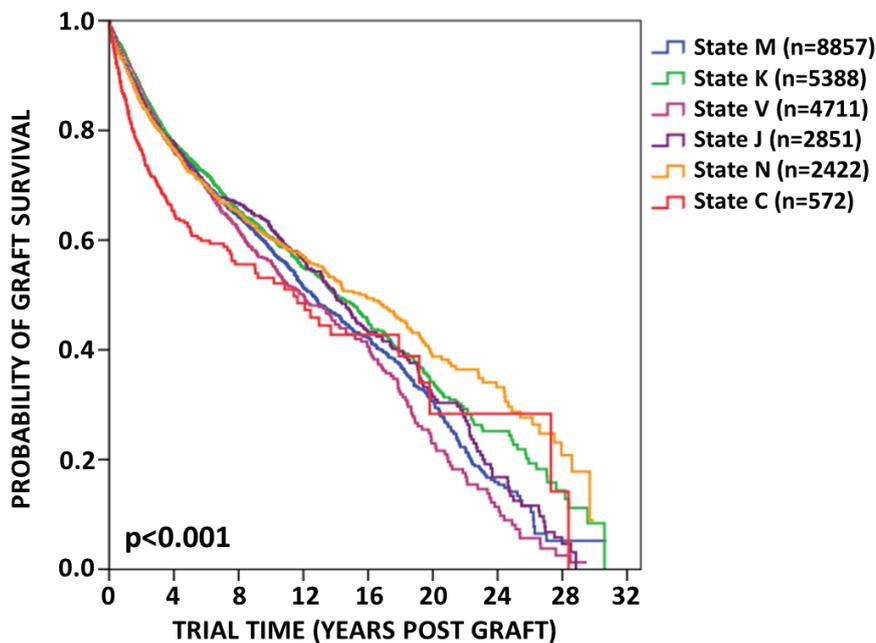
This concludes the subgroup-analyses. Analyses from page 44 onwards are again performed on the full cohort.



### 2.2.3 Penetrating graft survival: influence of Australian State where graft was performed

Figure 2.2.7 shows the comparison of graft survival depending on the Australian State in which the transplantation occurred. A significant difference was found across groups (Log Rank Statistic=36.94; df=5;  $p<0.001$ ), with all other States exhibiting better survival than State C (all  $p<0.001$ ), and State M exhibiting better survival than State V ( $p=0.001$ ). This variable was not retained in the multivariate analysis (see section 2.7) suggesting that this is **not** an independent factor significantly affecting graft survival.

**Figure 2.2.7 Australian State where graft was performed**



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
<b>State M</b>	5747	2652	1161	565	313	149	36
<b>State K</b>	3960	1874	854	439	203	102	40
<b>State V</b>	3154	1220	488	201	88	35	14
<b>State J</b>	1694	868	412	232	110	55	21
<b>State N</b>	1891	980	458	261	139	78	38
<b>State C</b>	423	179	80	38	15	5	4

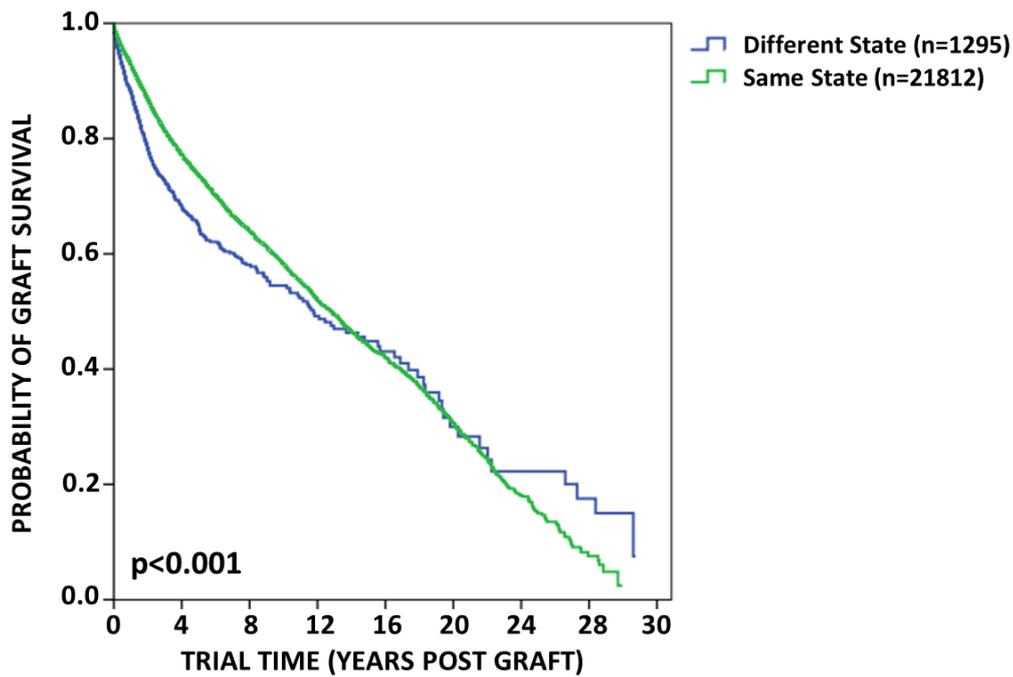
#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
<b>State M</b>	0.92	0.77	0.64	0.51	0.42	0.31	0.16
<b>State K</b>	0.94	0.78	0.65	0.55	0.45	0.34	0.25
<b>State V</b>	0.93	0.76	0.62	0.50	0.41	0.23	NA
<b>State J</b>	0.92	0.78	0.67	0.56	0.43	0.32	0.17
<b>State N</b>	0.92	0.77	0.65	0.57	0.49	0.39	0.33
<b>State C</b>	0.86	0.65	0.56	0.49	NA	NA	NA

**2.2.4 Penetrating graft survival: influence of interstate transportation**

In some cases corneas are transported interstate via air freight. Figure 2.2.8 shows the comparison of graft survival for grafts where the surgery was performed in the same State as the donor cornea was sourced, compared to those where the donor cornea was from interstate. A significant difference was found between groups (Log Rank Statistic=18.24; df=1; p<0.001). Those grafts where the donor cornea had been transported interstate had poorer survival. Data on this variable were not provided in 7% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=42.66; df=2; p<0.001). This variable was retained in the multivariate analysis (see section 2.7), despite indication for graft also being included, suggesting that this is an independent factor significantly affecting graft survival.

**Figure 2.2.8 Interstate transportation**



**Number at risk (at years post-graft)**

	1	4	8	12	16	20	24
Different State	876	404	183	93	48	19	11
Same State	14607	6574	2778	1329	649	305	91

**Probability of graft survival (at years post-graft)**

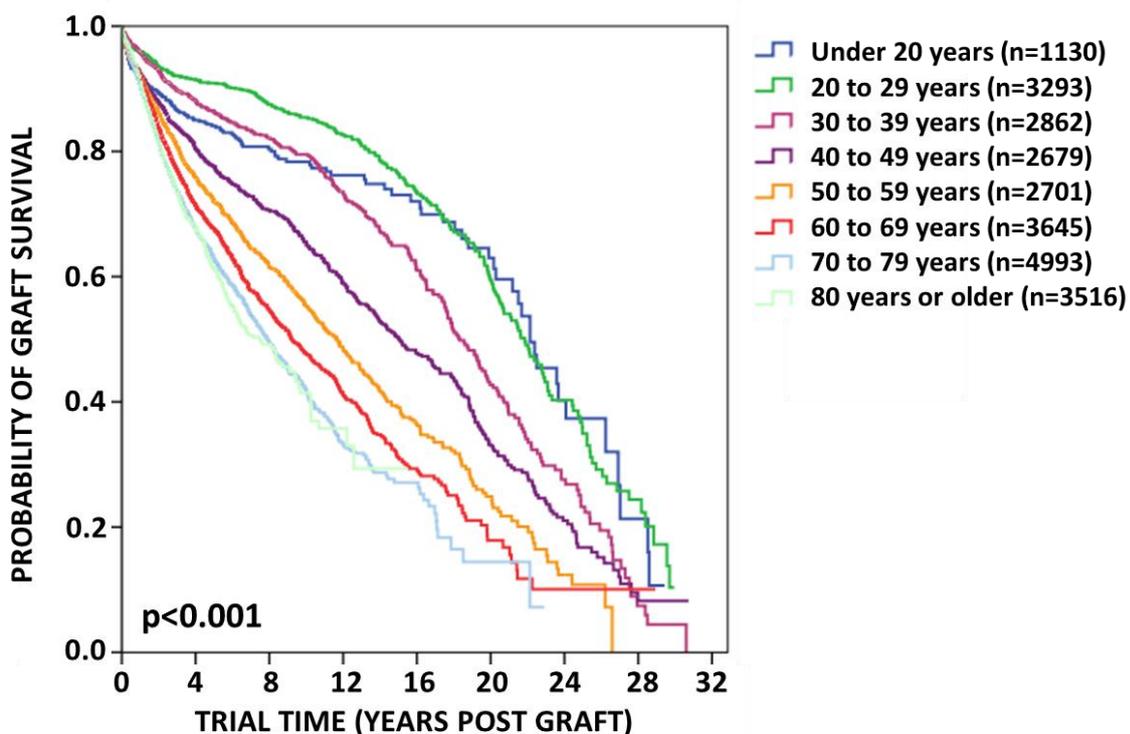
	1	4	8	12	16	20	24
Different State	0.88	0.68	0.58	0.49	0.43	NA	NA
Same State	0.93	0.77	0.64	0.52	0.42	0.31	0.18

### 2.2.5 Penetrating graft survival: influence of recipient age (years)

Figure 2.2.9 shows the comparison of graft survival depending on the age of the corneal transplant recipient. Data for the “0-9 years” group was combined with the “10 to 19 years” group, and all recipients aged 80 years and older were grouped together for analysis, due to the low number of recipients in these groups. Data were not available for 8 recipients. A significant difference was found across groups (Log Rank Statistic=1047.20; df=7;  $p<0.001$ ). All comparisons between age groups were significantly different at the  $p<0.001$  level, except for recipients aged 70 to 79 years versus 80 years or older ( $p=0.671$ ). In almost every case, the younger recipient group showed superior survival to the older group. The one exception was for recipients under 20 years, compared to those aged 20 to 29 years, where the latter group had superior survival.

The variable of recipient age was not retained in the multivariate analysis (see section 2.7) suggesting that this is **not** an independent factor significantly affecting graft survival. Recipient age is strongly associated with indication for graft (see section 2.2.1), with the majority of grafts for keratoconus performed in younger recipients, and the majority of grafts for bullous keratopathy and failed previous grafts, performed in older recipients. Indication for graft has long been shown by the ACGR to be a major explanatory factor for likelihood of graft survival, and was retained in the multivariate model.

Figure 2.2.9 Recipient age



**Number at risk (years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>0 to 19 years</b>	777	404	207	123	70	39	14
<b>20 to 29 years</b>	2297	1088	571	355	218	127	48
<b>30 to 39 years</b>	2070	1007	519	318	181	96	36
<b>40 to 49 years</b>	1869	1003	544	336	185	96	39
<b>50 to 59 years</b>	1910	996	477	234	106	42	12
<b>60 to 69 years</b>	2577	1268	549	227	76	21	3
<b>70 to 79 years</b>	3315	1434	478	128	32	3	NA
<b>80+ years</b>	2064	576	110	15	NA	NA	NA

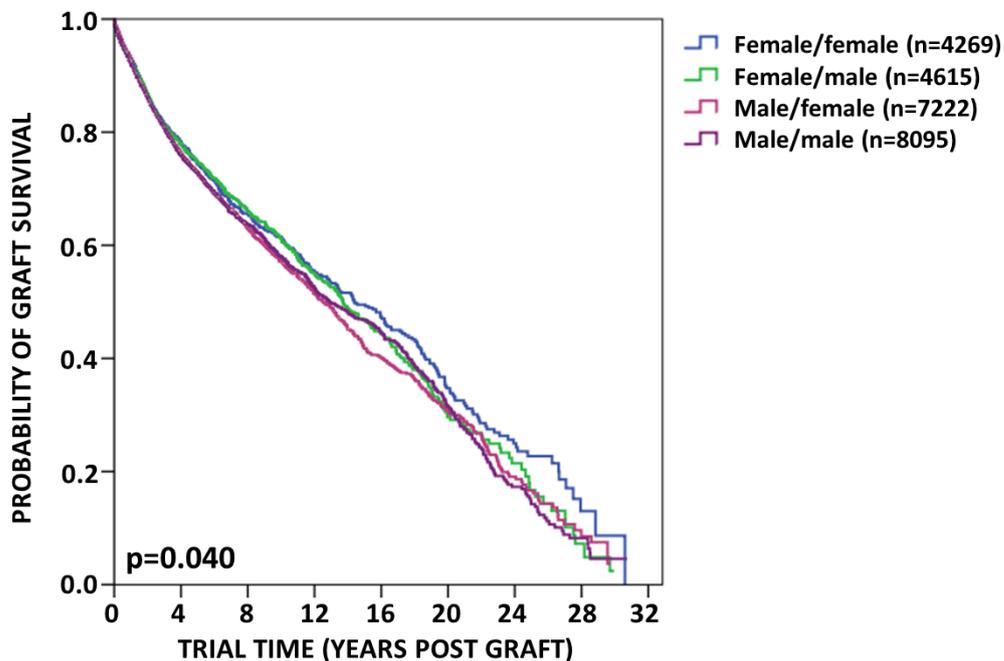
**Probability of graft survival (years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>0 to 19 years</b>	0.92	0.85	0.80	0.76	0.72	0.63	NA
<b>20 to 29 years</b>	0.96	0.91	0.88	0.83	0.74	0.59	0.40
<b>30 to 39 years</b>	0.96	0.88	0.82	0.74	0.61	0.43	0.28
<b>40 to 49 years</b>	0.92	0.81	0.71	0.59	0.48	0.33	0.21
<b>50 to 59 years</b>	0.92	0.76	0.62	0.48	0.37	0.25	NA
<b>60 to 69 years</b>	0.92	0.71	0.55	0.41	0.29	0.18	NA
<b>70 to 79 years</b>	0.90	0.68	0.50	0.34	0.27	NA	NA
<b>80+ years</b>	0.91	0.68	0.49	NA	NA	NA	NA

## 2.2.6 Penetrating graft survival: influence of donor/recipient sex match/mismatch

Comparison of graft survival between the four combinations of male and female donors and recipients is shown in Figure 2.2.10. A significant difference was found between groups (Log Rank Statistic=8.34; df=3; p=0.040). Data on this variable were not provided in 3% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=9.58; df=4; p=0.048). None of the group comparisons were significant in univariate analyses following Bonferroni correction, however the variable of donor/recipient sex match/mismatch was retained in the multivariate analysis (see section 2.7) suggesting that this is an independent factor significantly affecting graft survival. Poorer survival was observed for the male/male combination, compared to female/female (p<0.001).

Figure 2.2.10 Recipient sex



### Number at risk (years post-graft)

	1	4	8	12	16	20	24
Female/female	2944	1415	618	314	170	84	36
Female/male	3093	1353	580	309	151	64	22
Male/female	4996	2385	1080	520	233	119	45
Male/male	5398	2392	1043	512	262	129	43

### Probability of graft survival (years post-graft)

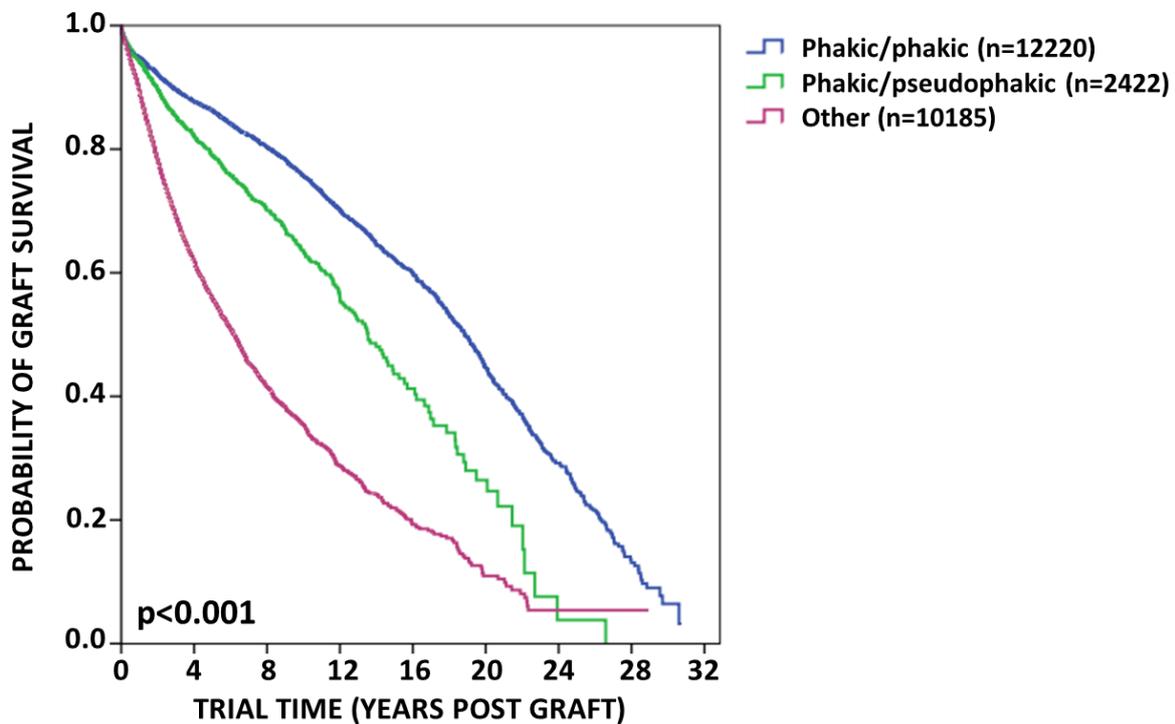
	1	4	8	12	16	20	24
Female/female	0.93	0.78	0.66	0.55	0.47	0.35	0.25
Female/male	0.93	0.78	0.66	0.55	0.45	0.30	0.22
Male/female	0.93	0.76	0.63	0.51	0.40	0.31	0.19
Male/male	0.92	0.76	0.64	0.53	0.45	0.32	0.17

**2.2.7 Penetrating graft survival: influence of pre- and post-graft lens status**

Figure 2.2.11 shows the comparison of graft survival stratified by the change of lens status from pre- to post-graft. “Phakic/phakic” means the eye was phakic both before and after the graft. “Phakic/pseudophakic” means the eye was phakic before the graft and pseudophakic afterwards, having undergone a triple procedure. “Other” means the eye was phakic, pseudophakic or aphakic before the graft and aphakic afterwards, or the eye was aphakic or pseudophakic before the graft and pseudophakic afterwards.

A significant difference was found across groups (Log Rank Statistic=1817.39; df=2; p<0.001), with all three group comparisons significant at the p<0.001 level. This variable was retained in the multivariate analysis (see section 2.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 2.2.11 Change in lens status from pre- to post-graft**



**Number at risk (years post-graft)**

	1	4	8	12	16	20	24
Phakic/phakic	8619	4408	2282	1321	732	383	148
Phakic/pseudophakic	1778	947	416	153	48	15	1
Other	6480	2419	756	262	88	26	4

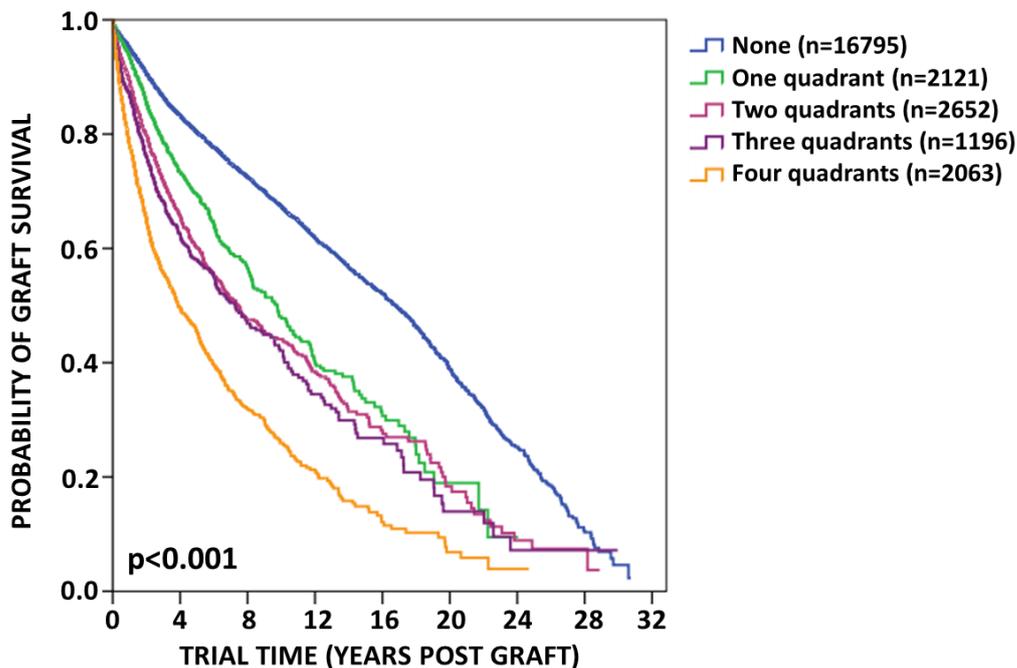
**Probability of graft survival (years post-graft)**

	1	4	8	12	16	20	24
Phakic/phakic	0.95	0.88	0.80	0.70	0.60	0.45	0.29
Phakic/pseudophakic	0.94	0.82	0.70	0.56	0.41	NA	NA
Other	0.89	0.62	0.42	0.29	0.19	0.11	NA

## 2.2.8 Penetrating graft survival: influence of pre-graft corneal neovascularisation

Figure 2.2.12 shows the comparison of graft survival between those recipients with various degrees of corneal neovascularisation pre-graft and those without (Log Rank Statistic=1464.79; df=4;  $p<0.001$ ). All group comparisons were significant at the  $p<0.001$  level except between survival for grafts with two or three quadrants of vascularisation ( $p=0.104$ ). These two groups were combined for multivariate analyses. This variable was retained in the multivariate analysis (see section 2.7), suggesting that this is an independent factor significantly affecting graft survival. Grafts performed in neovascularised eyes showed diminished graft survival.

**Figure 2.2.12 Pre-graft corneal neovascularisation**



### Number at risk (years post-graft)

	1	4	8	12	16	20	24
None	11963	5800	2748	1401	735	379	141
One quadrant	1369	579	212	92	39	6	1
Two quadrants	1649	708	237	128	47	21	2
Three quadrants	770	304	125	58	26	10	3
Four quadrants	1126	387	132	57	21	8	NA

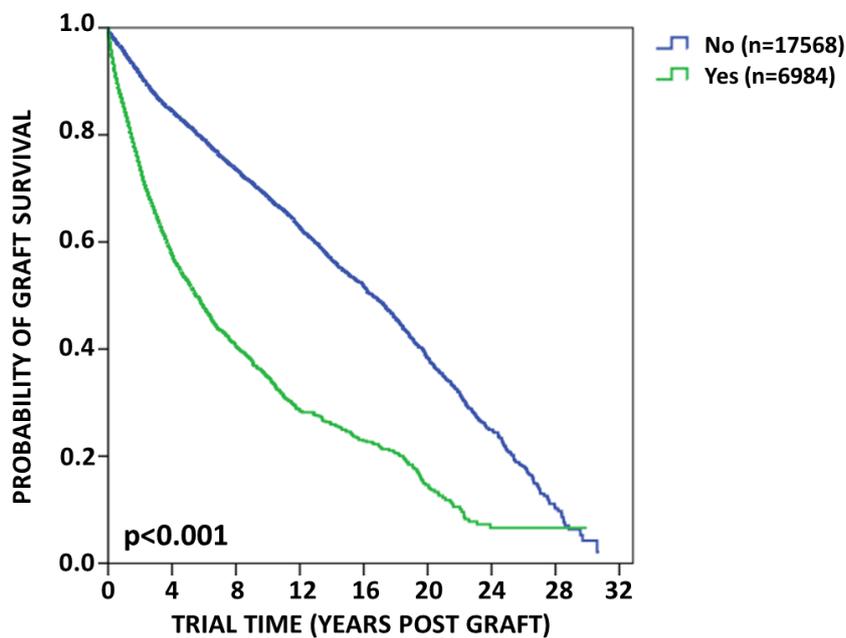
### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
None	0.95	0.83	0.73	0.62	0.52	0.39	0.25
One quadrant	0.93	0.73	0.57	0.44	0.31	NA	NA
Two quadrants	0.89	0.66	0.48	0.39	0.28	0.18	NA
Three quadrants	0.87	0.63	0.47	0.35	0.27	NA	NA
Four quadrants	0.78	0.50	0.32	0.21	0.12	NA	NA

**2.2.9 Penetrating graft survival: influence of inflammation and/or steroid use at time of graft**

Figure 2.2.13 shows the comparison of graft survival between grafts performed in an eye with current inflammation and/or steroid use within the past two weeks, compared to those with neither of these factors (Log Rank Statistic=1583.42; df=1; p<0.001). Data on this variable were not provided in 1% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=1583.10; df=2; p<0.001). This variable was retained in the multivariate analysis (see section 2.7), suggesting that this is an independent factor significantly affecting graft survival. Current inflammation and/or recent use of steroids was associated with poorer graft survival.

**Figure 2.2.13 Inflammation and/or steroid use at time of graft**



**Number at risk (years post-graft)**

	1	4	8	12	16	20	24
No inflammation/steroid use	12470	6077	2876	1487	747	374	142
Inflammation/steroid use	4249	1637	554	235	115	47	10

**Probability of graft survival (years post-graft)**

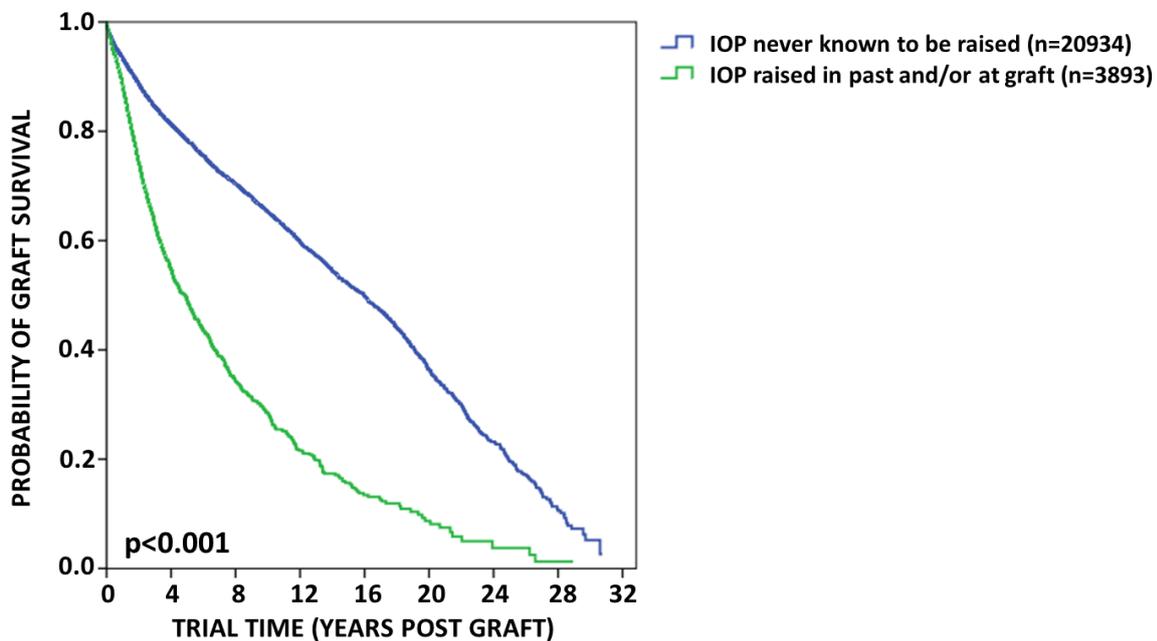
	1	4	8	12	16	20	24
No inflammation/steroid use	0.96	0.85	0.74	0.63	0.52	0.38	0.25
Inflammation/steroid use	0.85	0.58	0.41	0.28	0.23	0.15	NA

### 2.2.10 Penetrating graft survival: influence of the combination of history of raised intraocular pressure (IOP) and raised IOP at time of graft

Figure 2.2.14 shows the comparison of graft survival across groups based on whether the recipient had a history of raised IOP and/or raised IOP at the time of graft, in the eye being grafted (Log Rank Statistic=1178.55; df=1;  $p<0.001$ ). This variable was retained in the multivariate analysis (see section 2.7), suggesting that this is an independent factor significantly affecting graft survival.

“IOP never known to be raised” means there is no known history of raised IOP in the grafted eye and IOP was not raised at the time of graft. “IOP raised in past and/or at time of graft” means the eye either had a history of raised IOP, the IOP was raised at the time of graft, or both.

Figure 2.2.14 Raised intraocular pressure, in history and/or at time of graft



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
IOP never raised	14332	6822	3135	1614	827	410	150
IOP raised	2545	954	319	122	41	15	3

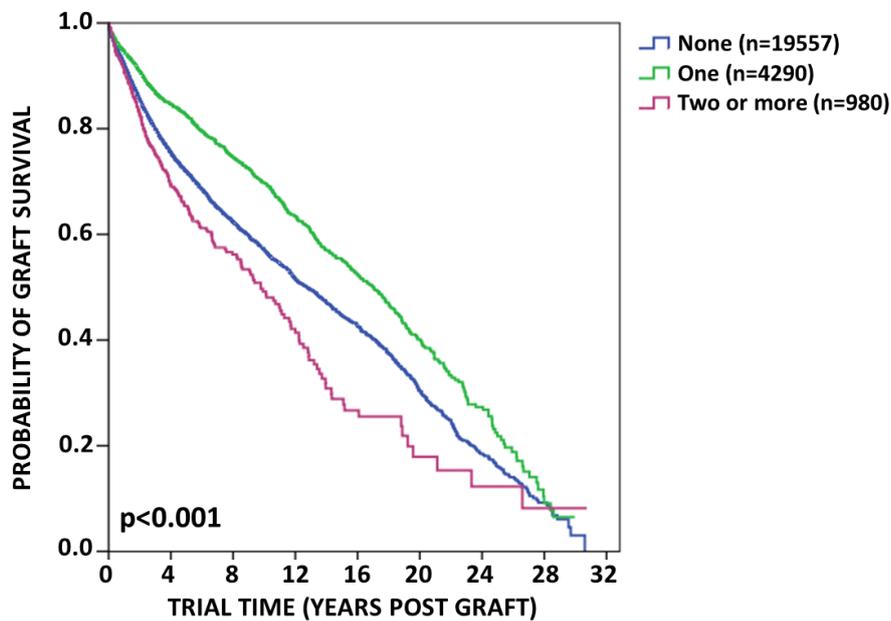
#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
IOP never raised	0.93	0.81	0.70	0.60	0.50	0.36	0.23
IOP raised	0.88	0.55	0.34	0.22	0.14	NA	NA

**2.2.11 Penetrating graft survival: influence of previous contralateral graft**

Figure 2.2.15 shows the comparison of graft survival between grafts where the recipient had undergone a single previous contralateral graft, multiple previous contralateral grafts, and no previous contralateral grafts. Recipients in each category may have undergone any number of previous ipsilateral grafts (see section 2.2.2.1 for analysis of the effect of number of previous ipsilateral grafts). A significant difference was found across groups (Log Rank Statistic=131.08; df=2; p<0.001), with those having two or more prior contralateral grafts exhibiting poorer survival than those with none or one, and those with one exhibiting significantly better survival than those with none (all p<0.001). This variable was retained in the multivariate analysis (see section 2.7) suggesting that this is an independent factor significantly affecting graft survival.

**Figure 2.2.15 Previous contralateral graft**



**Number at risk (years post-graft)**

	1	4	8	12	16	20	24
<b>None</b>	13193	5938	2558	1259	607	290	96
<b>One</b>	3030	1554	771	418	238	125	53
<b>Two or more</b>	654	284	124	59	23	9	2

**Probability of graft survival (years post-graft)**

	1	4	8	12	16	20	24
<b>None</b>	0.92	0.76	0.62	0.52	0.43	0.30	0.18
<b>One</b>	0.95	0.85	0.75	0.63	0.53	0.40	0.27
<b>Two or more</b>	0.91	0.69	0.56	0.41	0.27	NA	NA

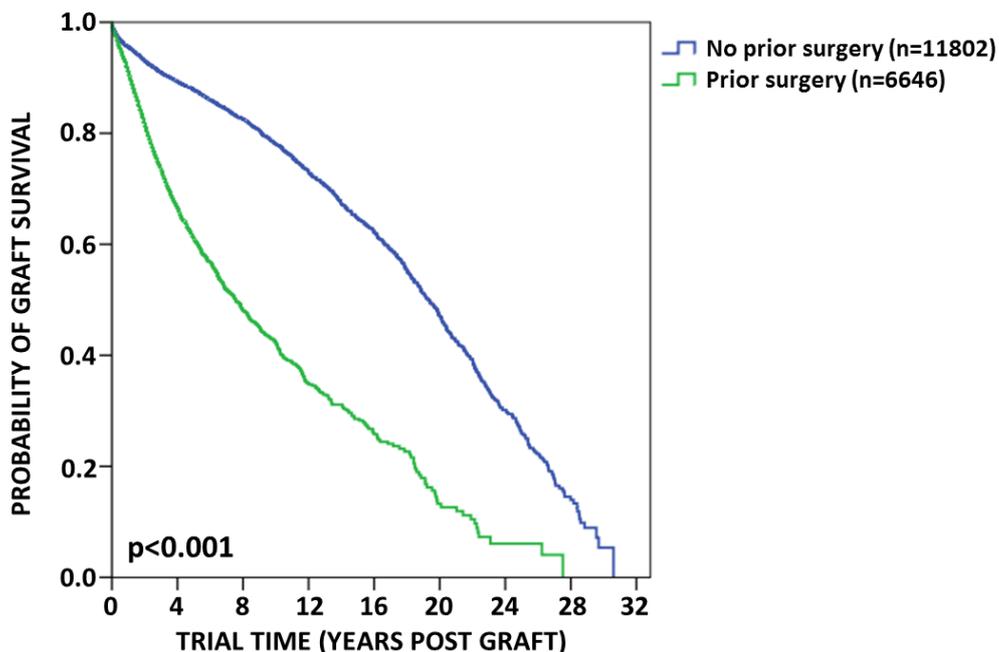
The majority (97%) of grafts performed for ulcer/perforation, herpetic infection, trauma and non-herpetic infection, which all have poor rates of survival, are only performed in one eye. These make up 13% of the grafts with no contralateral graft compared with <2% of those with a previous contralateral graft. Conversely, conditions with better survival, such as keratoconus or Fuchs’ endothelial dystrophy, are often bilateral and thus make up larger proportions of the group with previous contralateral grafts (37% vs 46%).

The analysis on page 54 is conducted using data only from **first grafts** (no previous ipsilateral grafts). This subgroup-analysis was not included in multivariate analyses, as it is collinear with indication for graft and change in lens status.

### 2.2.12 Penetrating graft survival: influence of history of previous intraocular surgery in ipsilateral eye

Figure 2.2.16 shows the comparison of graft survival between first grafts performed in an eye that had undergone previous intraocular surgery, compared with first grafts performed in an eye that had not (Log Rank Statistic=1202.46; df=1;  $p<0.001$ ). While surgeons were not asked to specify what type of previous surgery recipients had undergone, in the majority of cases (6166/6646, 93%) the lens status of the eye pre-graft (pseudophakic or aphakic) indicated that they had undergone cataract extraction, with or without IOL insertion. Surgeons were unable to say if previous surgery had occurred in 87 first grafts and these were excluded from the analysis.

Figure 2.2.16 History of previous intraocular surgery in the ipsilateral eye



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
No prior surgery	8498	4430	2261	1272	681	357	132
Prior surgery	4321	1676	589	207	80	22	4

#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
No prior surgery	0.96	0.89	0.83	0.73	0.62	0.47	0.30
Prior surgery	0.91	0.67	0.48	0.35	0.26	0.13	NA

## 2.3 Graft Era

Table 2.6 shows the number of grafts registered and followed, in blocks of five years. 2015 to 2017 includes all grafts performed during these years, for which data had been entered into the ACGR by the census date. The percentages, which should be summed vertically, total 100.

**Table 2.6 Graft era**

<b>Penetrating Corneal Graft Graft Era</b>		
<b>Year of graft</b>	<b>Registered (%)</b>	<b>Followed (%)</b>
1985 to 1989	2288 (9%)	2245 (11%)
1990 to 1994	5018 (20%)	4539 (22%)
1995 to 1999	4000 (16%)	3355 (17%)
2000 to 2004	4357 (18%)	3610 (18%)
2005 to 2009	4258 (17%)	3420 (17%)
2010 to 2014	3398 (14%)	2732 (13%)
2015 to 2017	1508 (6%)	435 (2%)
<b>Total</b>	<b>24827 (100 %)</b>	<b>20336 (100 %)</b>

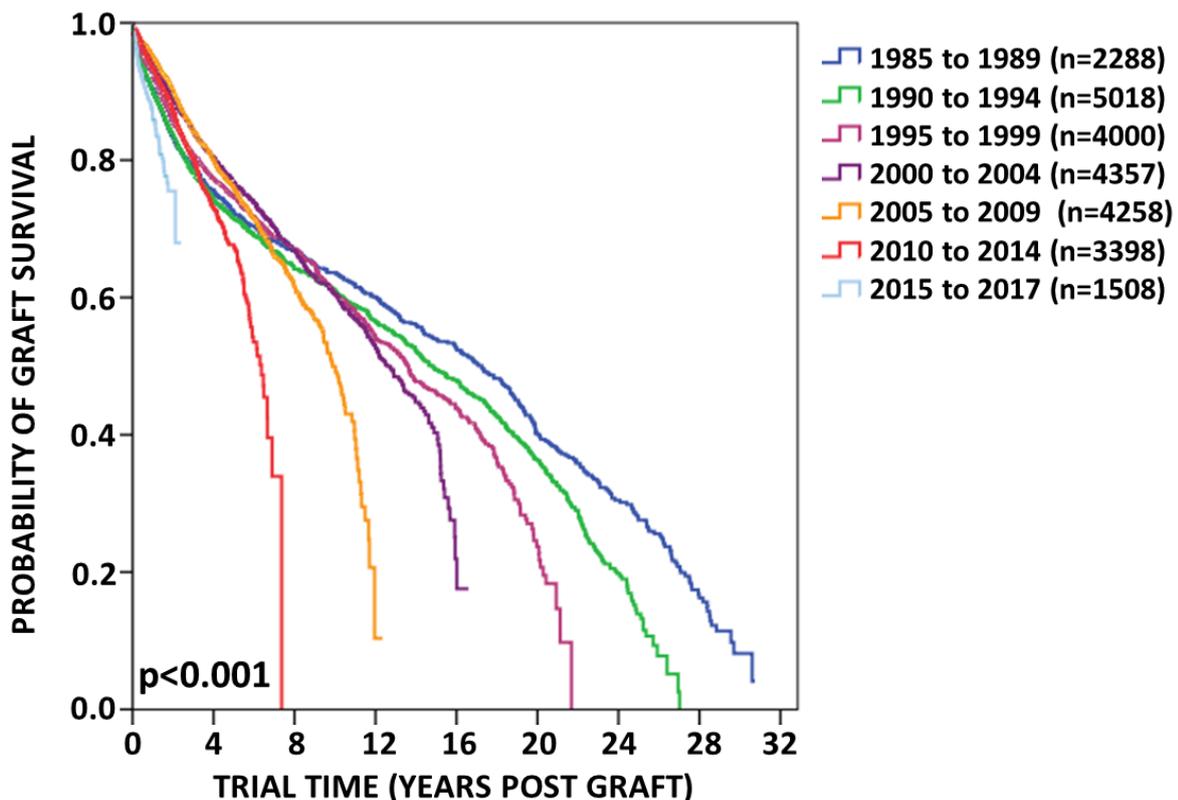
Comparisons amongst the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Follow-up was significantly lower ( $p < 0.001$ ) for grafts performed since 2015.

### 2.3.1 Penetrating graft survival: influence of graft era

Figure 2.3.1 shows the comparison of graft survival between year of graft, stratified into five-year groups (Log Rank Statistic=58.94; df=6;  $p<0.001$ ). Grafts performed from 2015 to 2017 had significantly worse survival than those performed in the four preceding eras (all  $p<0.001$ ), and from 1985 to 1989 ( $p=0.002$ ). Those performed from 2010 to 2014 had significantly worse survival than those performed in the three preceding eras (all  $p<0.001$ ). Grafts performed from 2005 to 2009 had significantly worse survival than those from 2000 to 2004 ( $p=0.001$ ). There were no significant differences between grafts performed in any of the eras between 1985 and 2004. This variable was retained in the multivariate analysis (see section 2.7) suggesting that this is an independent factor significantly affecting graft survival.

Consideration was given to the effect of follow-up lag time on this analysis. Up-to-date information on failed grafts is more likely to be known than for surviving grafts. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. A “lag time” operates at the furthest end of each curve in a Kaplan Meier plot. This effect is most pronounced in the early years following graft registration, when requests have not yet been made for follow-up information, and tends to reduce predictably over time. It can be seen, in the analysis below, that the survival curves tend to drop off suddenly, illustrating this skewing of the data. The variable is treated as “time variant” in multivariate analyses.

Figure 2.3.1 Graft era



**Number at risk (years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>1985 to 1989</b>	1805	1018	604	424	245	159	98
<b>1990 to 1994</b>	3561	1833	992	589	385	238	55
<b>1995 to 1999</b>	2707	1341	702	398	232	27	NA
<b>2000 to 2004</b>	3113	1424	725	324	6	NA	NA
<b>2005 to 2009</b>	3036	1570	431	1	NA	NA	NA
<b>2010 to 2014</b>	2362	589	NA	NA	NA	NA	NA
<b>2015 to 2017</b>	293	NA	NA	NA	NA	NA	NA

**Probability of graft survival (years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>1985 to 1989</b>	0.90	0.76	0.67	0.60	0.53	0.40	0.31
<b>1990 to 1994</b>	0.90	0.74	0.64	0.57	0.48	0.36	0.20
<b>1995 to 1999</b>	0.93	0.77	0.67	0.54	0.44	0.24	NA
<b>2000 to 2004</b>	0.94	0.80	0.67	0.53	NA	NA	NA
<b>2005 to 2009</b>	0.95	0.80	0.62	NA	NA	NA	NA
<b>2010 to 2014</b>	0.94	0.73	NA	NA	NA	NA	NA
<b>2015 to 2017</b>	0.86	NA	NA	NA	NA	NA	NA

## 2.4 Surgery and Surgeon Factors

Table 2.7 shows the number of grafts within each of the variable sub-groups, for the surgery and surgeon factors found to be **significant** in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (24,827 registered and 20,336 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 2.7 Surgery and surgeon factors, significant in univariate analyses**

<b>Penetrating Corneal Graft Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Size of graft (diameter)</b>		
Less than 7.75 mm	3229 (13%)	2764 (14%)
7.75 mm to <8.25 mm	11228 (45%)	9381 (46%)
8.25 mm to <8.75 mm	6930 (28%)	5520 (27%)
8.75 mm or more	1951 (8%)	1519 (7%)
Not advised	1489 (6%)	1152 (6%)
<b>The Centre effect</b>		
Fewer than 500 registered PK	12489 (50%)	9903 (49%)
Surgeon Q	1792 (7%)	1713 (8%)
Surgeon W	1245 (5%)	1210 (6%)
Surgeon E	1216 (5%)	968 (5%)
Surgeon R	1171 (5%)	1112 (5%)
Surgeon T	897 (4%)	474 (2%)
Surgeon Y	886 (4%)	422 (2%)
Surgeon U	847 (3%)	766 (4%)
Surgeon O	685 (3%)	634 (3%)
Surgeon P	661 (3%)	601 (3%)
Surgeon A	635 (3%)	501 (2%)
Surgeon S	634 (3%)	563 (3%)
Surgeon D	578 (2%)	575 (3%)
Surgeon F	569 (2%)	404 (2%)
Surgeon G	522 (2%)	490 (2%)
<b>Surgeon volume</b>		
Fewer than 500 registered PK	12489 (50%)	9903 (49%)
500+ registered PK, <82% follow-up	4203 (17%)	2769 (14%)
500+ registered PK, ≥82% follow-up	8135 (33%)	7664 (38%)
<b>Total</b>	<b>24827 (100 %)</b>	<b>20336 (100 %)</b>

82% was selected as the cut-off point for the follow-up categories as this (81.7%) was the average percentage of follow-up for all penetrating grafts.

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

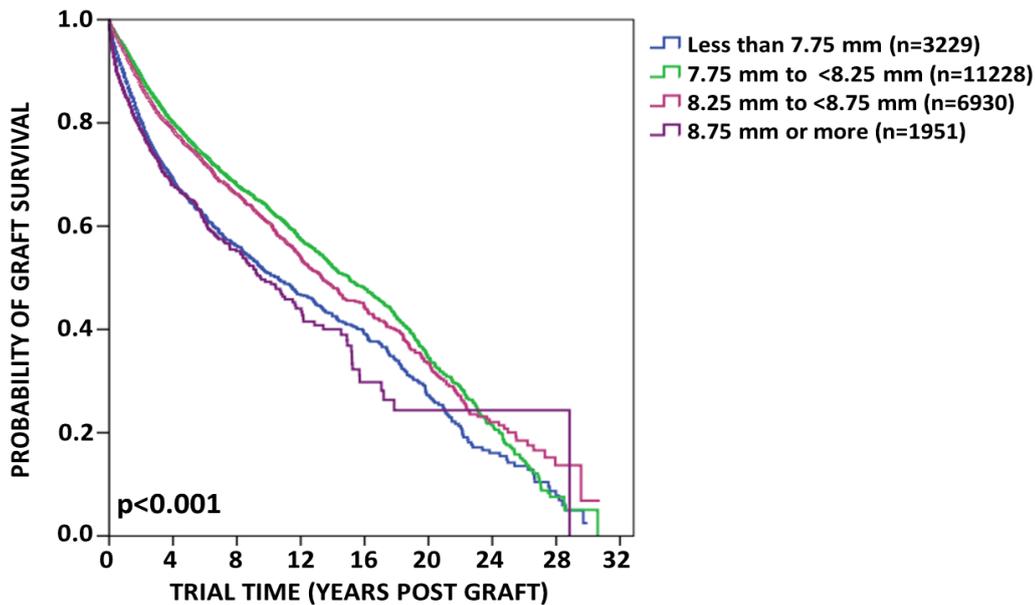
Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Follow-up was significantly lower ( $p < 0.05$ ) for larger grafts. There were significant differences in follow-up levels between individual surgeons. Due to the nature of the variable, follow-up was, significantly higher for grafts performed by surgeons with 500+ grafts and  $\geq 82\%$  follow-up.



**2.4.1 Penetrating graft survival: influence of graft size**

Figure 2.4.1 shows a comparison of graft survival depending on the size of the graft, based on the donor button diameter, as reported by surgeons. A significant difference was found across groups (Log Rank Statistic=198.82; df=3; p<0.001), with grafts under 7.75 mm, or 8.75 mm or more, both exhibiting poorer survival than those within these measurements (all p<0.001). Data on this variable were not provided in 6% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=217.81; df=4; p<0.001). This variable was retained in the final model, suggesting that this is an independent factor significantly affecting graft survival.

**Figure 2.4.1 Graft size**



**Number at risk (years post-graft)**

	1	4	8	12	16	20	24
<b>Less than 7.75 mm</b>	2144	1027	496	291	168	80	30
<b>7.75 mm to &lt; 8.25 mm</b>	8013	3739	1686	869	444	212	73
<b>8.25 mm to &lt; 8.75 mm</b>	4617	2120	950	436	203	114	42
<b>8.75 mm or more</b>	1149	483	171	70	23	3	1

**Probability of graft survival (years post-graft)**

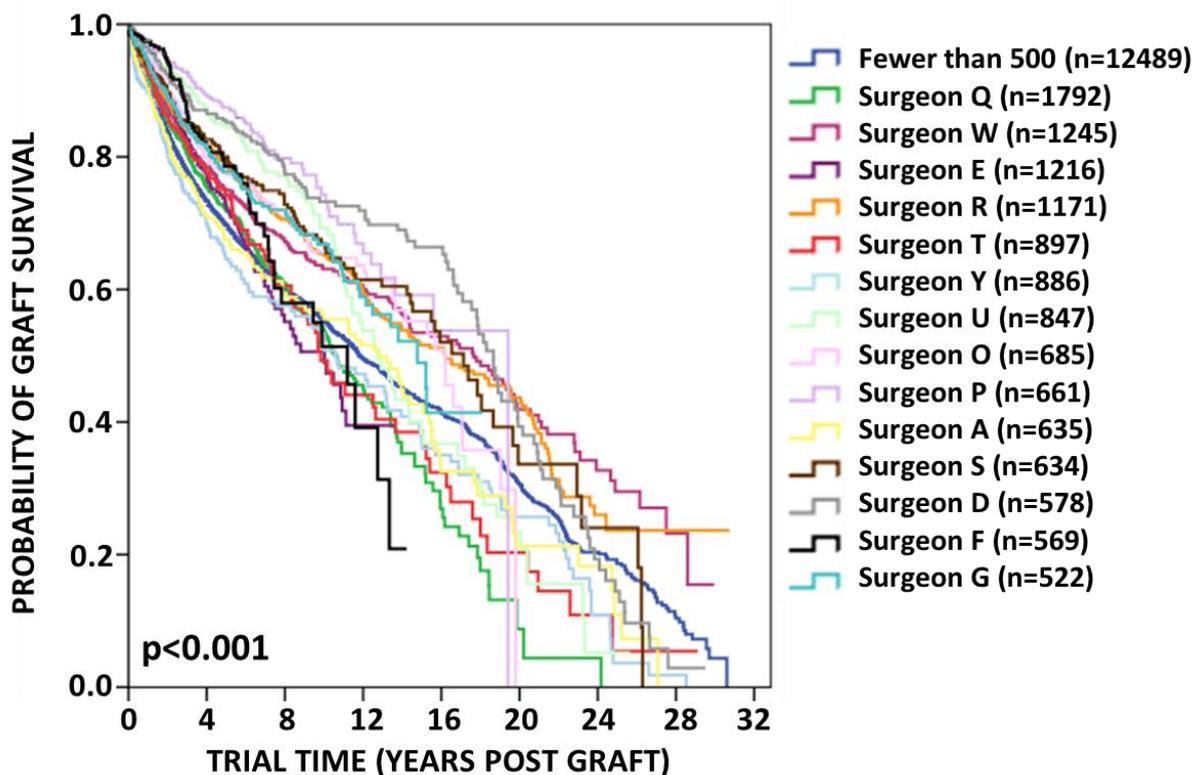
	1	4	8	12	16	20	24
<b>Less than 7.75 mm</b>	0.89	0.69	0.56	0.47	0.39	0.27	0.16
<b>7.75 mm to &lt; 8.25 mm</b>	0.94	0.80	0.68	0.57	0.48	0.35	0.22
<b>8.25 mm to &lt; 8.75 mm</b>	0.94	0.79	0.66	0.54	0.44	0.34	0.22
<b>8.75 mm or more</b>	0.86	0.68	0.55	0.44	0.30	NA	NA

The size of penetrating grafts has changed significantly across eras. They have increased in size during each five-year cohort. Just 6% of grafts performed since 2010 were less than 7.75 mm in diameter, compared with 21% pre-2000. At the other end of the spectrum, 17% of grafts performed since 2010 were 8.75 mm or more, compared with 5% pre-2000. 47% of grafts 8.75 mm or more were repeat grafts.

## 2.4.2 Penetrating graft survival: influence of the Centre effect

Figure 2.4.2 shows the comparison of graft survival for 14 individual surgeons for whom there were 500 or more penetrating keratoplasties registered with the ACGR, and all other grafts (performed by 448 identified individual surgeons, Australia-wide) combined (Log Rank Statistic=217.76; df=14;  $p < 0.001$ ). This analysis indicates that there is a significant Centre effect. This variable was not included in the multivariate analysis as it is collinear with the surgeon volume and follow-up variable shown in Figure 2.4.3.

Figure 2.4.2 The Centre effect



Note: To preserve anonymity, surgeons have been identified using random letters of the alphabet. These identifying letters do not correspond with those used in chapters reporting on other types of graft, i.e. Surgeon W in this chapter is not the same surgeon identified as Surgeon W in the chapter on Descemet stripping (automated) endothelial keratoplasty.

**Number at risk (years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>&lt;500 PK registered</b>	8083	3597	1497	771	414	206	80
<b>Surgeon Q</b>	1295	525	231	87	20	3	1
<b>Surgeon W</b>	997	553	279	166	93	53	22
<b>Surgeon E</b>	815	220	54	4	NA	NA	NA
<b>Surgeon R</b>	956	590	357	206	123	70	18
<b>Surgeon T</b>	399	185	56	24	15	8	3
<b>Surgeon Y</b>	319	145	76	52	36	23	6
<b>Surgeon U</b>	666	304	110	42	20	9	1
<b>Surgeon O</b>	580	260	118	56	19	NA	NA
<b>Surgeon P</b>	555	289	115	45	7	NA	NA
<b>Surgeon A</b>	404	166	99	61	21	11	6
<b>Surgeon S</b>	498	279	137	67	32	11	4
<b>Surgeon D</b>	506	292	179	101	61	30	12
<b>Surgeon F</b>	360	101	25	6	NA	NA	NA
<b>Surgeon G</b>	444	269	121	48	7	NA	NA

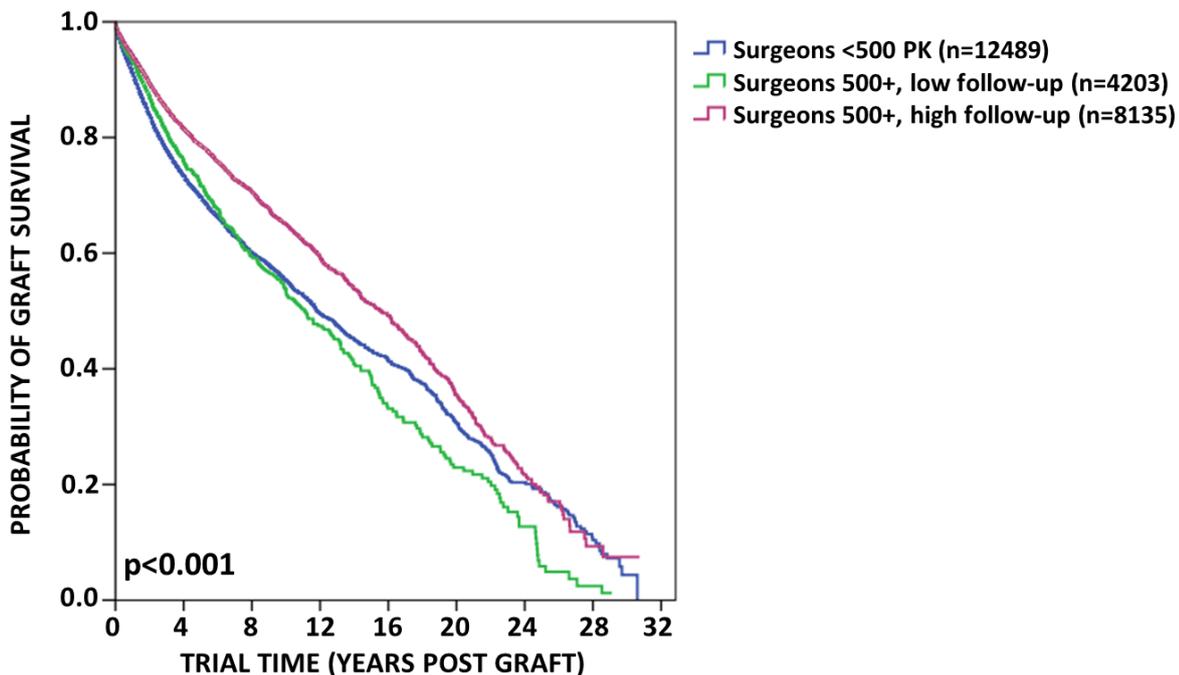
**Probability of graft survival (years post-graft)**

	<b>1</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>16</b>	<b>20</b>	<b>24</b>
<b>&lt;500 PK registered</b>	0.91	0.73	0.60	0.50	0.42	0.31	0.20
<b>Surgeon Q</b>	0.92	0.76	0.61	0.45	0.27	NA	NA
<b>Surgeon W</b>	0.93	0.79	0.67	0.60	0.53	0.42	0.33
<b>Surgeon E</b>	0.95	0.77	0.55	NA	NA	NA	NA
<b>Surgeon R</b>	0.94	0.82	0.71	0.60	0.51	0.44	NA
<b>Surgeon T</b>	0.93	0.78	0.61	0.44	NA	NA	NA
<b>Surgeon Y</b>	0.90	0.70	0.58	0.47	0.35	0.26	NA
<b>Surgeon U</b>	0.96	0.87	0.77	0.54	0.37	NA	NA
<b>Surgeon O</b>	0.95	0.80	0.71	0.64	NA	NA	NA
<b>Surgeon P</b>	0.98	0.89	0.80	0.67	NA	NA	NA
<b>Surgeon A</b>	0.91	0.71	0.59	0.52	0.33	NA	NA
<b>Surgeon S</b>	0.94	0.83	0.73	0.61	0.52	NA	NA
<b>Surgeon D</b>	0.97	0.87	0.78	0.72	0.66	0.39	NA
<b>Surgeon F</b>	0.97	0.82	0.58	NA	NA	NA	NA
<b>Surgeon G</b>	0.94	0.81	0.72	0.59	NA	NA	NA

### 2.4.3 Penetrating graft survival: influence of surgeon volume (500+ registered PK grafts) grouped by level of follow-up

Figure 2.4.3 shows the comparison of graft survival between grafts performed by surgeons with 500+ registered penetrating keratoplasties with average or better ( $\geq 82\%$ ) follow-up, to those with lower than average follow-up ( $< 82\%$ ), and to surgeons with fewer than 500 registered penetrating keratoplasties (Log Rank Statistic=127.76;  $df=2$ ;  $p<0.001$ ). Survival of grafts performed by high volume surgeons with average or better follow-up was significantly better than that of either of the other two groups (both  $p<0.001$ ). This variable was retained in the multivariate analysis (see section 2.7) suggesting that this is an independent factor significantly affecting graft survival.

Figure 2.4.3 Surgeon volume and level of follow-up



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
<500 registered PK	8083	3597	1497	771	414	206	80
500+ PK, low follow-up	2297	817	310	147	72	42	15
500+ PK, high follow-up	6497	3362	1647	818	382	176	58

#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
<500 registered PK	0.91	0.73	0.60	0.50	0.42	0.31	0.20
500+ PK, low follow-up	0.93	0.76	0.59	0.47	0.33	0.23	NA
500+ PK, high follow-up	0.94	0.82	0.71	0.59	0.49	0.36	0.22

## 2.5 Operative Procedures at the Time of Graft

Table 2.8 shows the number of grafts for which specified operative procedures were performed at the time of graft. The sum of these numbers for each variable equals the total number of grafts (24,827 registered and 20,336 followed) and the percentages, which should be summed vertically for each variable, total 100. While only anterior vitrectomy at time of graft was found to be significant at the  $p < 0.05$  level, peripheral iridectomy at time of graft met the  $p < 0.08$  level, for inclusion in multivariate analyses.

**Table 2.8 Operating procedures at the time of graft, significant in univariate analyses**

<b>Penetrating Corneal Graft Operative Procedures</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Anterior vitrectomy at time of graft</b>		
No	22791 (92%)	18620 (92%)
Yes	2036 (8%)	1716 (8%)
<b>Peripheral iridectomy at time of graft*</b>		
No	23328 (94%)	19315 (95%)
Yes	1499 (6%)	1021 (5%)
<b>Total</b>	<b>24827 (100 %)</b>	<b>20336 (100 %)</b>

\* Note: significant at  $p < 0.08$  for inclusion in multivariate analyses but not at  $p < 0.05$ .

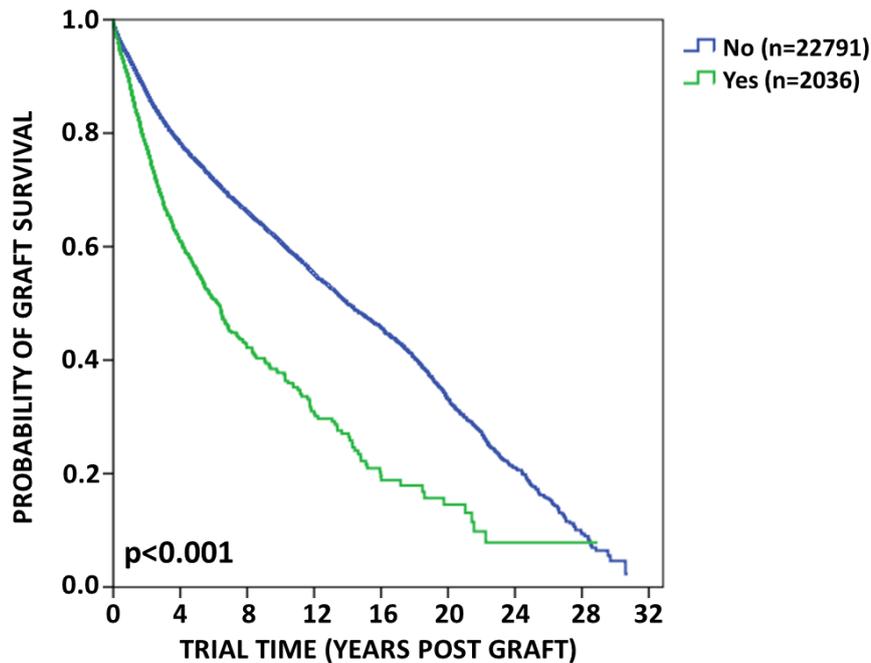
Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Follow-up was significantly higher for grafts that had undergone anterior vitrectomy at the time of graft ( $p = 0.007$ ), and significantly lower for those that had undergone peripheral iridectomy at time of graft ( $p < 0.001$ ).

### 2.5.1 Penetrating graft survival: influence of anterior vitrectomy at time of graft

Figure 2.5.1 shows the comparison of survival for grafts where an anterior vitrectomy was performed at the time of graft, to those where one was not. A significant difference was found across groups (Log Rank Statistic=255.42; df=1;  $p<0.001$ ). This variable was not retained in the final model, suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 2.5.1 Anterior vitrectomy at time of graft



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
No anterior vitrectomy	15596	7297	3284	1666	840	411	151
Anterior vitrectomy	1281	471	170	70	28	13	2

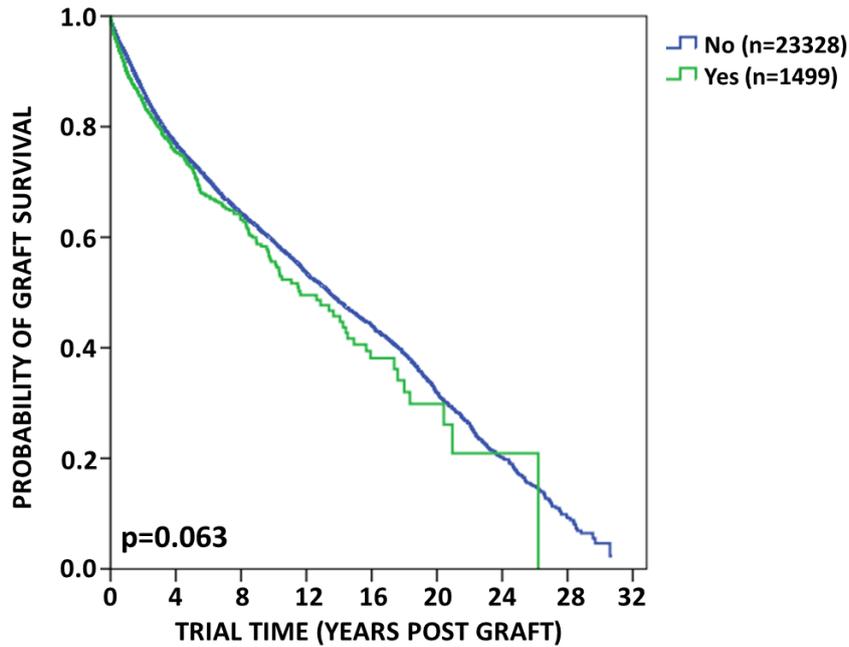
#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
No anterior vitrectomy	0.93	0.78	0.66	0.55	0.46	0.33	0.21
Anterior vitrectomy	0.89	0.61	0.42	0.31	0.20	NA	NA

**2.5.2 Penetrating graft survival: influence of peripheral iridectomy at time of graft**

Figure 2.5.2 shows survival for grafts where a peripheral iridectomy was performed at the time of graft, and those where one was not. No significant difference was found between groups (Log Rank Statistic=3.47; df=1; p=0.063), however this variable met the p<0.08 criteria for inclusion in the multivariate analyses. It was not retained in the final model (see section 2.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

**Figure 2.5.2 Peripheral iridectomy at time of graft**



**Number at risk (years post-graft)**

	1	4	8	12	16	20	24
<b>No peripheral iridectomy</b>	16034	7338	3271	1672	827	415	152
<b>Peripheral iridectomy</b>	843	439	183	64	29	9	1

**Probability of graft survival (years post-graft)**

	1	4	8	12	16	20	24
<b>No peripheral iridectomy</b>	0.93	0.77	0.64	0.54	0.44	0.32	0.20
<b>Peripheral iridectomy</b>	0.90	0.76	0.63	0.50	0.38	NA	NA



## 2.6 Post-graft Events

Table 2.9 shows the occurrence of post-graft events, and Table 2.10 shows post-graft surgical procedures, as reported by follow-up practitioners, found to be **significant** in univariate analyses. Please note: post-graft data may be incomplete when follow-up is based on a registration for a replacement graft.

**Table 2.9 Post-graft events, significant in univariate analyses**

<b>Penetrating Corneal Graft Post-graft Events</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Post-graft neovascularisation</b>		
No	23307 (94%)	18816 (93%)
Yes	1520 (6%)	1520 (7%)
<b>Post-graft herpetic infection</b>		
No	24399 (98%)	19908 (98%)
Yes	428 (2%)	428 (2%)
<b>Post-graft microbial keratitis</b>		
No	24251 (98%)	19760 (97%)
Yes	576 (2%)	576 (3%)
<b>Post-graft synechiae</b>		
No	24438 (98%)	19947 (98%)
Yes	389 (2%)	389 (2%)
<b>Post-graft uveitis</b>		
No	24544 (99%)	20053 (99%)
Yes	283 (1%)	283 (1%)
<b>Post-graft rise in IOP</b>		
No	20964 (84%)	16473 (81%)
Yes	3863 (16%)	3863 (19%)
<b>At least one rejection episode</b>		
No	20718 (83%)	16227 (80%)
Yes	4109 (17%)	4109 (20%)
<b>Time to removal of all sutures</b>		
Less than 6-months	590 (2%)	590 (3%)
6-months to <12 months	2155 (9%)	2155 (11%)
12 months to <24 months	5940 (24%)	5940 (29%)
24 months or more	2566 (10%)	2566 (13%)
Not yet removed/not advised*	13576 (55%)	9085 (45%)
<b>Total</b>	<b>24827 (100 %)</b>	<b>20336 (100 %)</b>

\* Some failed grafts had ROS dates provided which were after the date of failure and thus not included in analysis.

**Table 2.10: Post-graft surgical procedures**

3,092 penetrating keratoplasties were reported to have undergone a re-grafting procedure (separate to subsequent concurrent graft/s) at the date last seen. Of these, 2,168 had not had additional post-graft operative procedures reported, while 924 had.

<b>Penetrating Corneal Graft Post-graft Surgical Procedures Excluding Re-graft</b>	
	<b>Number</b>
Cataract removal and IOL insertion	1606
Cataract removal without IOL insertion	63
IOL insertion (cataract removed prior to graft)	149
IOL repositioned/removed/exchange	128
Insertion of piggyback lens	52
Implantable contact lens	20
Relaxing incision	1039
YAG laser	973
Suture adjustment	803
Wound repair/re-sutured	496
PRK laser	285
Compression sutures	391
LASIK	177
Wedge resection	147
Keratotomy	49
Keratotomy	25
Trabeculectomy	343
Cyclodiode	206
Tube insertion (Molteno: 135, Barveldt:31, unspecified: 2)	168
Vitrectomy	204
Tarsorrhaphy	126
Enucleation	62
Evisceration	28
Retinal detachment surgery	66
Conjunctival flap	83
Iridectomy	23
Iridotomy	17
Ptosis repair	37
Membrane peel	25
Bleb needling/revision	28
Intravitreal injection/s	97
Synecholysis	26
Concurrent subsequent graft (29 lamellar patch, 15 limbal/conjunctival)	44
Other*	561
<b>Total post-graft surgical procedures (number of grafts)</b>	<b>10149 (4713)</b>

Note: in calculating total number, cataract removal and IOL insertion are counted as two surgical procedures, even if done together. Where the same surgery was reported on multiple follow-ups for the same eye, it was only counted once. Surgeries listed in "other" are as reported to the ACGR by surgeons.

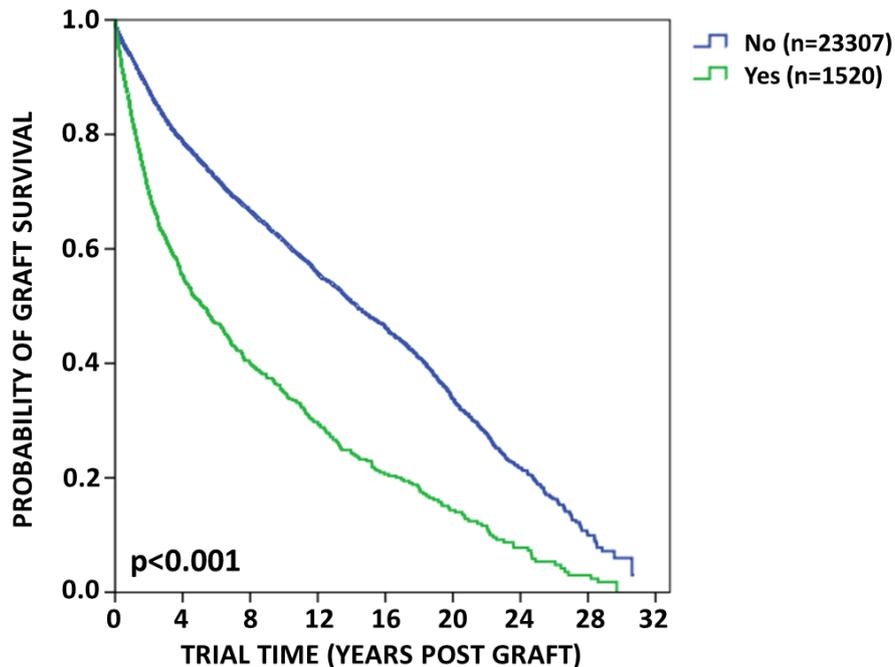
Penetrating Keratoplasty

\*Other included: Molteno tube revision/reposition (19); cryotherapy (16); ectropion repair (14); entropion repair (14); lid procedures (14); corneal scraping (13); punctal plugs (13); pterygium removal (13); scar removal (13); selective laser trabeculoplasty (12); cyst removal (11); amniotic membrane transplant (10); laser treatment not further specified (10); squint surgery (10); anterior chamber tap (9); biopsy (9); interface revision (9); punctal cautery (9); pupilloplasty (9); reformation of anterior chamber (9); strabismus surgery (9); band keratopathy removal (8); BCC removal (8); dacryocystorhinostomy (8); photocoagulation (8); corneal gluing (7); iris repair (7); refractive keratoplasty (7); removal of lens matter (7); scleral buckle (7); silicone oil insertion (7); Argon laser trabeculoplasty (6); blepharoplasty (6); epithelial debridement (6); foreign body removal (6); keratoprosthesis (6); anterior chamber washout (5); Botulinum toxin injection (5); filament removal (5); lensectomy (5); Molteno tube removal (5); plaque removal (5); scar removal (5); trabeculectomy revision (5); unspecified drainage device inserted (5); unspecified glaucoma surgery (5); capsulotomy (4); chalazion removal (4); corneal collagen cross-linking (4); corneal debridement (5); iridoplasty (4); lashes epilated (4); lysis (4); paracentesis (4); punctal occlusion repair (4); limbal lesion removal (4); silicone oil removal (4); vitreous aspiration (4); drainage of choroidal haemorrhage (3); IOL re-sutured (3); iris removal (3); Keraring insertion (3); macular hole repair (3); retinal photocoagulation (3); Baerveldt tube removal (2); Beta-radiation (2); canthoplasty (2); Endolaser (2); hyphaema evacuation (2); unspecified glaucoma drainage device inserted (2); Healon inserted in anterior chamber (2); Holmm laser sclerectomy (2); prolapsed iris repositioned (2); punctal snip (2); pupillary membrane removal (2); retained Descemet membrane removal (2); retinal laser surgery (2); retinoplexy (2); scleral buckle removal (2); superior conjunctival resection (2); trabeculectomy revision (2); trichiasis (2); unspecified gas insertion (2); vitreoretinal surgery (2); vitreous haemorrhage removal (2); anterior segment clearance (1); aspiration of anterior chamber (1); Argon laser of blood vessels at graft/host junction (1); Barrier laser (1); orbital compression (1); branch artery occlusion repair (1); canalicular repair (1); capsulectomy (1); cathoplasty (1); Cionni ring insertion (1); clearance of iris from the graft (1); conjunctival injection (1); conjunctival keratin removal (1); conjunctival resection (1); corneal cautery (1); division of angle adhesions & pupil membrane (1); epithelial plugs removed (1); exenteration (1); express drainage (1); eye muscle surgery (1); filter surgery (1); gas/fluid exchange (1); intracameral antibiotics (1); intracorneal injection for epithelium downgrowth (1); iris clip repositioned (1); iris implant inserted (1); irrigation of hyphaema (1); Jones tube inserted (1); lacrimal duct reconstruction (1); lacrimal plugs (1); laser treatment for diabetic retinopathy (1); lateral canthoplasty (1); needling of posterior capsule (1); occlusion of puncta (1); opened cloudy capsule (1); punctate diathermy (1); pupil block (1); pupil membrane removal (1); pupillary cerclage (1); reattachment of Descemet membrane (1); removal of blood from vitreous cavity (1); removal of Descemet folds (1); removal of epithelial dystrophy (1); removal of epithelium (1); removal of exposed scleral bullae (1); removal of fibrous bleb (1); removal of fibrous tissue (1); removal of iris from graft/host junction (1); removal of pannus (1); removal of SCC (1); repair of iridotomy (1); repeat refiltering surgery (1); reposition of Keraring segment (1); retrobulbar alcohol (1); revision of astigmatic keratotomy cuts (1); revision of vitrectomy (1); Scheie's operation (1); scleral flap (1); silicone oil exchange (1); sphincterotomy (1); submandibular gland transplant (1); subretinal tissue plasminogen activator (1); suture of conjunctival fold (1); syringed tear ducts (1); insertion of 'T' lens (1); tarsal snip (1); TBL inserted (1); temporal pinguecula removal (1); trabeculectomy removed (1); trabeculectomy repositioned (1); triescence (1); tube revision (1); tube shunt (1); unspecified secondary implant (1); viscocanalostomy (1); vitreolysis by laser (1); vitreous band dissection (1).

### 2.6.1 Penetrating graft survival: influence of post-graft neovascularisation

Figure 2.6.1 shows the influence of post-graft neovascularisation on graft survival. A significant difference was found across groups (Log Rank Statistic=491.58; df=1;  $p<0.001$ ). This variable was retained in the final model, suggesting that this is an independent factor significantly affecting graft survival.

**Figure 2.6.1 Post-graft neovascularisation**



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
No neovascularisation	15670	7237	3228	1608	798	385	136
Neovascularisation	1207	539	226	128	70	39	17

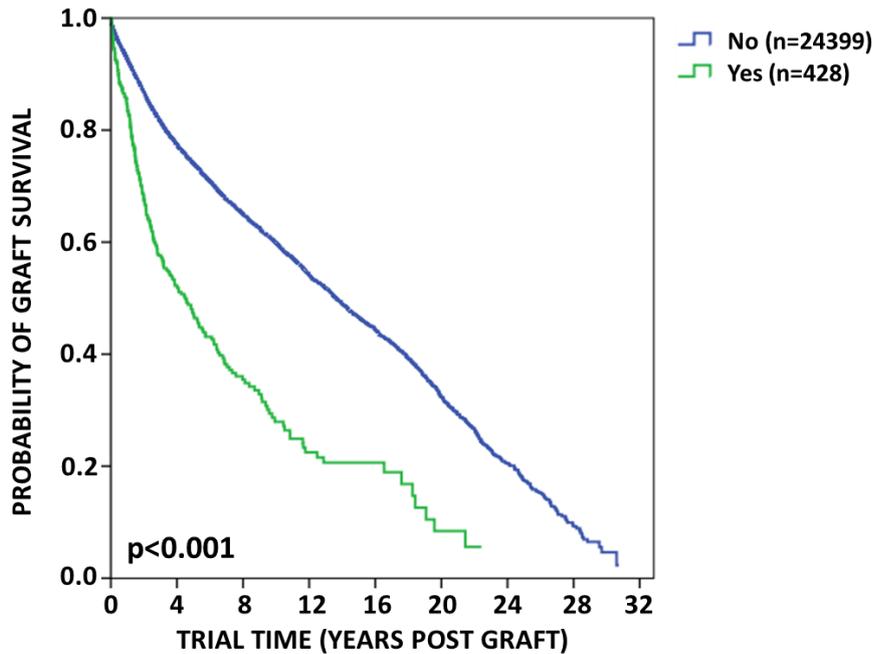
#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
No neovascularisation	0.93	0.79	0.67	0.56	0.46	0.34	0.22
Neovascularisation	0.83	0.55	0.40	0.30	0.21	0.14	NA

### 2.6.2 Penetrating graft survival: influence of post-graft herpetic infection

Figure 2.6.2 shows the influence of herpetic infection in a graft. A significant difference was found across groups (Log Rank Statistic=199.70; df=1; p<0.001). This variable was retained in the final model, suggesting that this is an independent factor significantly affecting graft survival.

Figure 2.6.2 Post-graft herpetic infection



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
No herpetic infection	16537	7634	3394	1710	855	420	153
Herpetic infection	340	142	60	26	13	4	NA

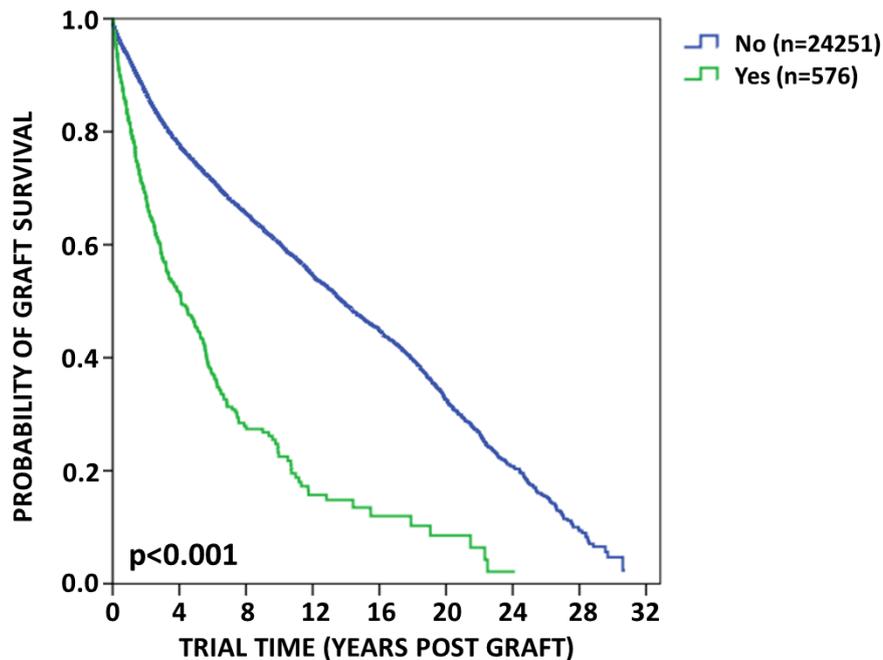
#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
No herpetic infection	0.93	0.77	0.65	0.54	0.44	0.32	0.21
Herpetic infection	0.84	0.52	0.36	0.23	NA	NA	NA

### 2.6.3 Penetrating graft survival: influence of post-graft microbial keratitis

Figure 2.6.3 shows the survival for grafts in which microbial keratitis occurred post-graft, including those where a stitch abscess occurred. A significant difference was found between groups (Log Rank Statistic=351.81; df=1;  $p<0.001$ ). This variable was retained in the multivariate analysis (see section 2.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 2.6.3 Post-graft microbial keratitis**



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
<b>No microbial keratitis</b>	16423	7590	3402	1716	861	419	152
<b>Microbial keratitis</b>	454	186	52	20	7	5	1

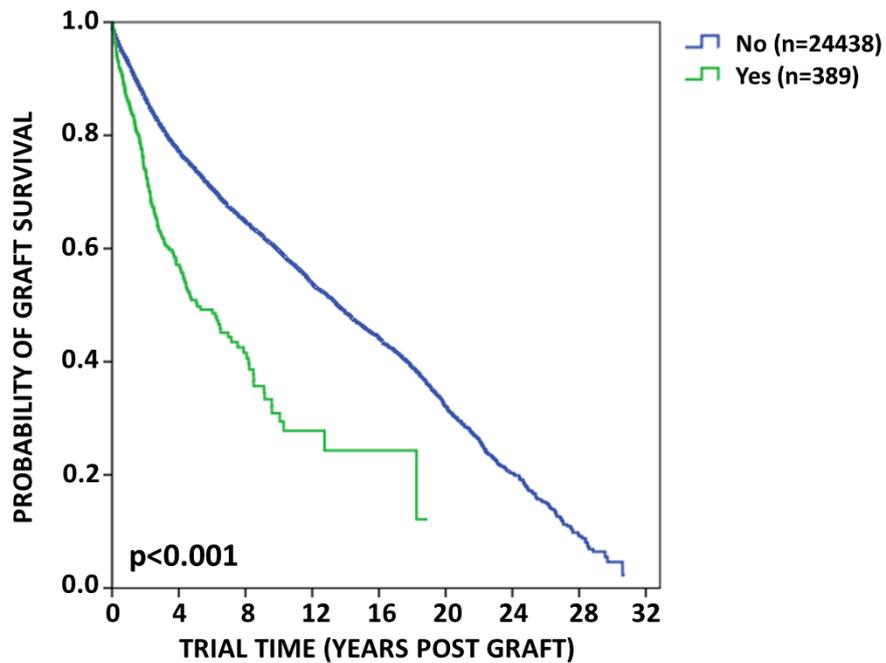
#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
<b>No microbial keratitis</b>	0.93	0.78	0.67	0.55	0.45	0.33	0.21
<b>Microbial keratitis</b>	0.82	0.52	0.28	0.16	NA	NA	NA

### 2.6.4 Penetrating graft survival: influence of post-graft synechia

Figure 2.6.4 shows the survival for grafts where the eye developed at least one synechia post-graft, compared to those where it did not. A significant difference was found between groups (Log Rank Statistic=108.61; df=1; p<0.001). This variable was not retained in the multivariate analysis (see section 2.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

**Figure 2.6.4 Post-graft synechia**



**Number at risk (years post-graft)**

	1	4	8	12	16	20	24
<b>No synechia</b>	16566	7648	3411	1724	866	424	153
<b>Synechia</b>	311	128	43	12	2	NA	NA

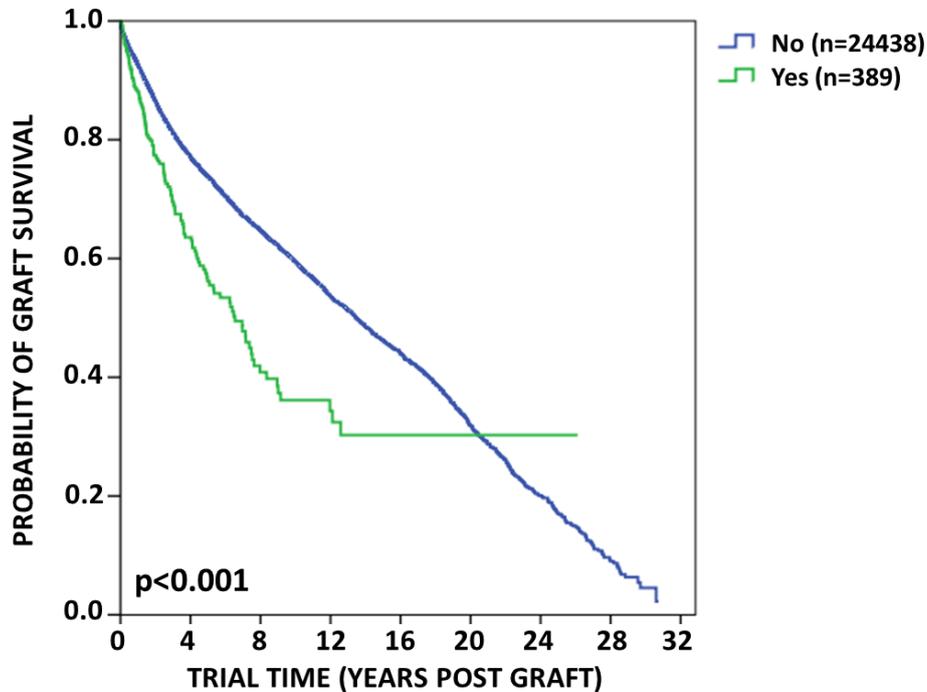
**Probability of graft survival (years post-graft)**

	1	4	8	12	16	20	24
<b>No synechia</b>	0.93	0.77	0.65	0.54	0.44	0.32	0.20
<b>Synechia</b>	0.86	0.57	0.42	NA	NA	NA	NA

## 2.6.5 Penetrating graft survival: influence of post-graft uveitis

Figure 2.6.5 shows the comparison of survival of grafts in eyes which developed uveitis compared with those that did not. A significant difference was found across groups (Log Rank Statistic=35.67; df=1;  $p<0.001$ ). This variable was not retained in the final model, suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 2.6.5 Post-graft uveitis



### Number at risk (years post-graft)

	1	4	8	12	16	20	24
No uveitis	16638	7668	3415	1718	863	421	152
Uveitis	239	108	39	18	5	3	1

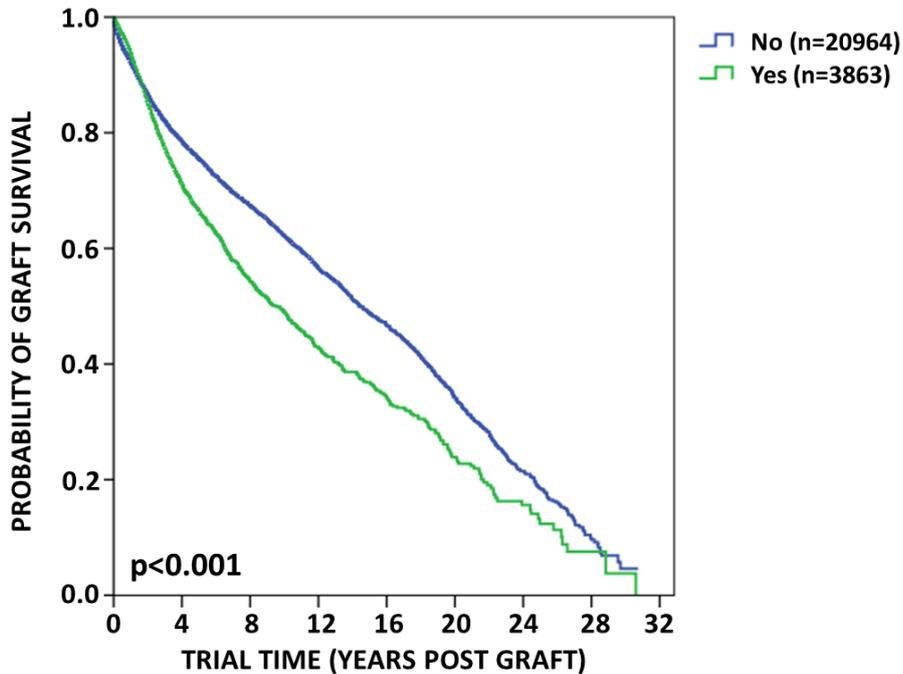
### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
No uveitis	0.93	0.77	0.65	0.54	0.44	0.32	0.20
Uveitis	0.88	0.64	0.41	NA	NA	NA	NA

### 2.6.6 Penetrating graft survival: influence of post-graft raised IOP

Figure 2.6.6 shows the comparison of graft survival for grafts where the eye was reported to have developed raised intraocular pressure post-graft to those where IOP was not reported as raised. A significant difference was found between groups (Log Rank Statistic=103.35; df=1; p<0.001). This variable was retained in the multivariate analysis (see section 2.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 2.6.6 Post-graft raised intraocular pressure



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
<b>No raised IOP</b>	13466	6040	2716	1396	716	360	130
<b>Raised IOP</b>	3411	1736	738	340	152	64	23

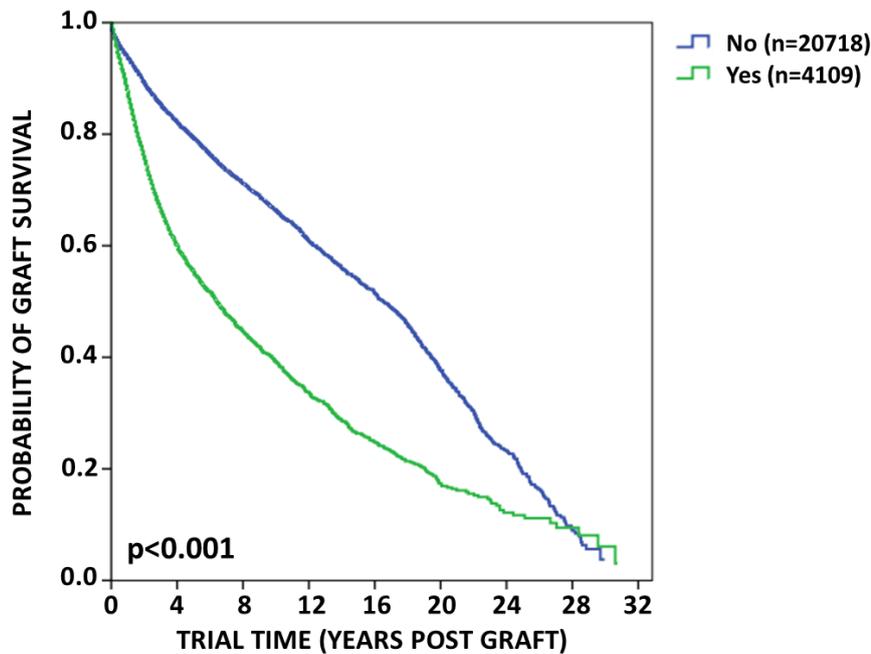
#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
<b>No raised IOP</b>	0.92	0.79	0.67	0.57	0.47	0.34	0.22
<b>Raised IOP</b>	0.94	0.71	0.54	0.43	0.34	0.24	0.16

### 2.6.7 Penetrating graft survival: influence of graft rejection episodes

Figure 2.6.7 shows the survival for grafts where the eye underwent at least one episode of post-graft immunological rejection, compared to those that did not. A significant difference was found between groups (Log Rank Statistic=885.30; df=1;  $p<0.001$ ). This variable was retained in the multivariate analysis (see section 2.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 2.6.7 Rejection episode(s)**



#### Number at risk (years post-graft)

	1	4	8	12	16	20	24
<b>No Rejection</b>	13382	6051	2627	1326	688	347	125
<b>Any rejection</b>	3495	1725	827	410	180	77	28

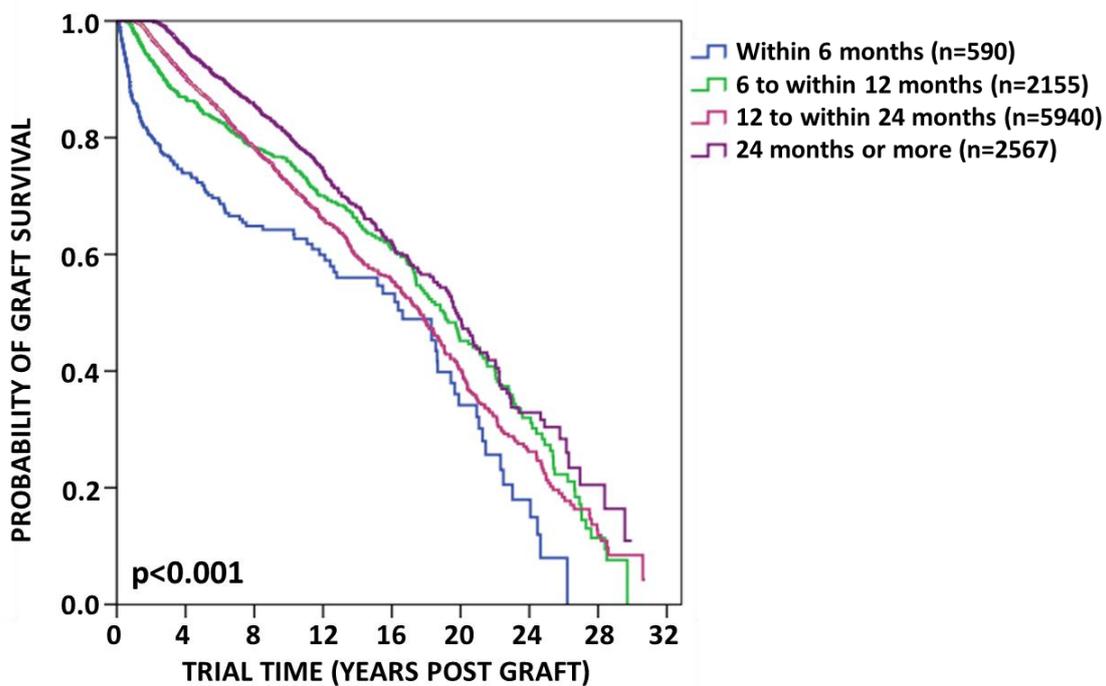
#### Probability of graft survival (years post-graft)

	1	4	8	12	16	20	24
<b>No Rejection</b>	0.94	0.82	0.71	0.61	0.52	0.38	0.23
<b>Any rejection</b>	0.88	0.60	0.45	0.34	0.25	0.17	0.12

**2.6.8 Penetrating graft survival: influence of time to final removal of sutures**

Figure 2.6.8 shows the comparison of graft survival depending on the time from graft to final suture removal. A significant difference was found amongst groups (Log Rank Statistic=154.01; df=3; p<0.001). Grafts where the sutures had been removed within 6 months had poorer survival than all other groups (all p<0.001). Additionally, grafts where the sutures were not removed until at least 24 months post-graft had significantly better survival than those where they were removed at between 6 months and 24 months (both p<0.001). Consideration should be given to the fact that grafts in each group must, by definition, have survived to the point of suture removal, meaning that all grafts in the 24 months or more group must have survived for 2 years, and so on. This information was only available for 11251 (55%) of followed grafts and therefore this variable was not included in the multivariate analysis.

**Figure 2.6.8 Time to final removal of sutures**



**Number at risk (years post-graft)**

	1	4	8	12	16	20	24
<b>Less than 6 months</b>	385	199	108	61	37	18	6
<b>6 months to &lt;12 months</b>	1896	895	449	273	151	84	39
<b>1 year to &lt;2 years</b>	5940	2822	1223	607	296	147	57
<b>2 years or more</b>	2567	1822	866	411	201	92	33

**Probability of graft survival (years post-graft)**

	1	4	8	12	16	20	24
<b>Less than 6 months</b>	0.86	0.74	0.65	0.60	0.53	NA	NA
<b>6 months to &lt;12 months</b>	0.98	0.87	0.78	0.70	0.61	0.45	0.32
<b>1 year to &lt;2 years</b>	1.00	0.91	0.78	0.66	0.56	0.40	0.26
<b>2 years or more</b>	1.00	0.95	0.86	0.75	0.62	0.49	0.33

## 2.7 Multivariate Analysis

A multivariate model was used to investigate the combined effect of variables on penetrating graft survival, adjusted for all other variables in the model. This analysis was performed using STATA version 15.

In the preceding univariate analyses, each registered penetrating graft, together with its archival follow-up records, was treated as a separate and independent entity. Some recipients had multiple penetrating grafts performed during the census period (registered by 31/7/2017), with some having repeat grafts in a single eye, some grafts in both eyes and some a combination of both. To control for potential inter-graft and/or inter-eye dependence in the multivariate analyses, the multivariate model was adjusted to allow for clustering by individual patient [see references 7 & 8].

Variables to be included in the Cox Proportional Hazards regression model were identified based on the results of the univariate Kaplan-Meier analyses, with a cut-off significance level of  $p < 0.08$  used to select variables for inclusion. Some variables which were found to be significant in the univariate analyses were omitted due to co-linearity, or because of large amounts of missing data ( $>25\%$ ). Each variable was initially analysed individually to determine if it remained significant once clustered by individual patient. Where the variable was no longer found to be significant ( $p > 0.08$ ), it was excluded from the multivariate analysis.

The best model was found by a backward elimination process, removing variables not appearing to be predictors of graft failure. The model excluded variables with a p-value of  $p \geq 0.05$  (or global p-value of  $p \geq 0.05$  for variables with more than two categories) in a stepwise manner, beginning with the least significant variable. The Kaplan-Meier plots, and additional appropriate STATA analyses, were used to assess whether each included variable met the assumption of proportional hazards. Where variables were found to be time-variant, they were treated as such in the multivariate model.

Table 2.11 shows each of the variables analysed in the univariate analyses, stratified by whether they were included in the initial multivariate model and whether they remained in the final model. Some variables that were found to be significant in the univariate analyses were excluded from the multivariate model as they were found to be co-linear with (i.e. were highly correlated and produced the same effect on the outcome as) another variable in the model.

Table 2.11 Multivariate model

<b>Penetrating Corneal Graft Multivariate Model</b>
<b>Not significant in univariate analysis</b>
Time from enucleation to storage
Storage time in organ culture
Recipient sex
Eye grafted
<b>Significant in univariate analysis but excluded from multivariate model due to co-linearity or missing data</b>
The Centre effect (co-linear with surgeon experience and level of follow-up)
Donor sex (co-linear with donor/recipient sex match/mismatch)
Number of previous ipsilateral grafts (co-linear with indication for graft)
Corneal endothelial cell density (missing data)
Time to removal of sutures (missing data)
<b>Significant in univariate analysis but not retained in multivariate model</b>
Peripheral iridectomy at time of graft (p>0.08 after clustering by patient)
Eye Bank
Cause of donor death
Storage medium: hypothermic vs organ culture
Time from death to enucleation
Storage time in Optisol
Multi-organ donor
Recipient State
Recipient age group
Anterior vitrectomy at time of graft
Post-graft uveitis
Post-graft synechia
<b>Significant in univariate analysis AND retained in multivariate model</b>
Donor age group
Indication for graft
Interstate transportation of donor cornea
Donor/recipient sex match/mismatch
Change in lens status pre- to post-graft
Pre-graft neovascularisation
Pre-graft inflammation and/or steroid use
History of raised intraocular pressure
Number of previous contralateral grafts
Graft era
Graft size
Surgeon experience and level of follow-up
Post-graft neovascularisation
Post-graft herpetic infection
Post-graft microbial keratitis
Raised intraocular pressure post-graft
Post-graft rejection episode(s)

Table 2.12 tabulates the parameter estimates resulting from the fit of the best clustered Cox model. The table shows the variable, the hazard ratio, the standard error of the regression coefficient, the corresponding probability value and the 95% confidence interval for the hazard ratio. The first level of each categorical variable was taken as the referent. The hazard ratios for a given variable are adjusted for all other variables in the model. This model included data from 24,827 penetrating keratoplasties, performed in 18,727 recipients. Where no valid response had been provided for one of the included variables, these cases were classified as “not advised”. This model includes variables with a p-value of  $p < 0.05$ , with variables eliminated in a stepwise manner, beginning with the least significant variable. For categorical variables, a global test was applied to calculate the overall p-value and Bonferroni adjusted post-hoc tests were conducted to determine between which groups the significant differences were observed. The overall model was highly significant: ( $\text{Chi}^2=4610.75$ ,  $\text{df}=56$ ,  $p < 0.0001$ ).

**Table 2.12 Clustered multivariate model**

<b>Penetrating Corneal Graft Clustered Multivariate Model</b>						
	<b>n</b>	<b>Hazard Ratio</b>	<b>Standard error</b>	<b>p-value</b>	<b>Global p-value</b>	<b>95% confidence interval</b>
<b>Indication for graft</b>						
Failed previous graft	6292	2.81	0.17	<0.001	<0.001	2.49 - 3.16
Keratoconus	7621	1.00				
Pseudophakic bullous keratopathy	3626	2.79	0.18	<0.001		
Fuchs' endothelial dystrophy	2067	1.89	0.13	<0.001		
Corneal scar and/or opacity	478	1.81	0.23	<0.001		
Corneal ulcer	495	4.43	0.47	<0.001		
Herpetic eye disease	1109	1.79	0.15	<0.001		
Trauma	638	2.71	0.25	<0.001		
Non-herpetic infection	444	3.60	0.45	<0.001		
Corneal degeneration	223	2.22	0.40	<0.001		
Other bullous keratopathy	1002	3.06	0.23	<0.001		
Other corneal dystrophy	311	1.52	0.23	0.005		
Other not yet specified	521	2.33	0.25	<0.001		
<b>Donor age group</b>						
Under 50 years	6014	0.79	0.03	<0.001	<0.001	0.73 - 0.86
50 to 59 years	4286	0.92	0.04	0.074		
60 to 69 years	6167	1.00				
70 to 79 years	5979	1.01	0.04	0.741		
80 years or older	2078	1.12	0.06	0.027		
Not advised	303	0.92	0.13	0.560		
<b>Donor/recipient sex match/mismatch</b>						
Female/female	4269	0.85	0.04	<0.001	0.007	0.78 - 0.93
Female/male	4615	0.96	0.04	0.279		
Male/female	7222	0.93	0.03	0.060		
Male/male	8095	1.00				
Not advised	626	0.90	0.09	0.298		
<b>Interstate transportation of donor cornea (tvc)</b>						
No	21812	1.00			<0.001	
Yes	1295	1.18	0.07	0.009		
Not advised	1720	0.78	0.06	<0.001		
<b>Pre-graft raised intraocular pressure</b>						
None	20934	1.00			<0.001	
In past and/or at graft	3893	1.41	0.05	<0.001		

	n	Hazard Ratio	Standard error	p-value	Global p-value	95% confidence interval
<b>Inflammation and/or steroid use at graft (tvc)</b>						
No	17568	1.00			<0.001	
Yes	6984	1.48	0.06	<0.001		1.36 - 2.61
Not advised	275	2.23	0.36	<0.001		1.63 - 3.06
<b>Size of graft</b>						
<7.75mm	3229	1.22	0.05	<0.001		1.12 - 1.32
7.75mm to <8.25mm	11228	1.00			<0.001	
8.25mm to <8.75mm	6930	1.01	0.03	0.875		0.94 - 1.08
8.75mm or more	1951	1.23	0.07	<0.001		1.10 - 1.38
Not advised	1489	1.18	0.07	0.007		1.05 - 1.34
<b>Pre-graft corneal neovascularisation</b>						
None	16795	1.00			<0.001	
One quadrant	2121	0.94	0.05	0.202		0.85 - 1.04
Two or three quadrants	3848	1.14	0.04	0.001		1.06 - 1.23
Four quadrants	2063	1.61	0.08	<0.001		1.46 - 1.77
<b>Number of previous contralateral grafts</b>						
None	19557	1.00			0.001	
One	4290	0.87	0.04	<0.001		0.80 - 0.94
Two or more	980	0.91	0.07	0.224		0.78 - 1.06
<b>Lens status pre- and post-graft</b>						
Phakic/phakic	12220	1.00			<0.001	
Phakic/pseudophakic	2422	1.05	0.06	0.433		0.94 - 1.17
Other	10185	1.55	0.07	<0.001		1.42 - 1.70
<b>Era in which graft was performed (tvc)</b>						
1985 to 1989	2288	1.27	0.07	<0.001		1.14 - 1.40
1990 to 1994	5018	1.00			<0.001	
1995 to 1999	4000	0.81	0.04	<0.001		0.74 - 0.89
2000 to 2004	4357	0.67	0.04	<0.001		0.61 - 0.75
2005 to 2009	4258	0.63	0.04	<0.001		0.56 - 0.70
2010 to 2014	3398	0.62	0.04	<0.001		0.55 - 0.70
2015 to 2017	1508	1.15	0.15	0.260		0.90 - 1.48
<b>Surgeon volume and level of follow-up (tvc)</b>						
<500 PK registered	12489	1.00			<0.001	
500+ PK registered, <82% followed	4203	1.11	0.05	0.020		1.02 - 1.22
500+ PK registered, 82%+ followed	8135	0.72	0.03	<0.001		0.66 - 0.77
<b>Post-graft corneal neovascularisation</b>						
No	23307	1.00				
Yes	1520	1.44	0.06	<0.001		1.32 - 1.56
<b>Post-graft herpetic infection</b>						
No	24399	1.00				
Yes	428	1.41	0.11	<0.001		1.21 - 1.64
<b>Post-graft microbial keratitis</b>						
No	24251	1.00				
Yes	576	1.59	0.10	<0.001		1.40 - 1.80
<b>Post-graft significant rise in IOP (tvc)</b>						
No	20964	1.00				
Yes	3863	0.73	0.03	<0.001		0.67 - 0.80
<b>Post-graft rejection episode(s) (tvc)</b>						
No	20718	1.00				
Yes	4109	2.32	0.09	<0.001		2.15 - 2.50

tvc= time varying coefficient.

## **2.7.1 Significant differences in the penetrating keratoplasty multivariate model for categories with more than two groups following Bonferroni correction for multiple comparisons**

### **2.7.1.1 Indication for graft**

Grafts performed for keratoconus had significantly better survival than those performed for any other indication for graft, except other corneal dystrophy (all  $p < 0.001$ ).

Grafts performed for Fuchs' endothelial dystrophy, other corneal dystrophy, or herpetic infection, had significantly better survival than those performed for failed previous graft/s, pseudophakic bullous keratopathy, corneal ulcer, trauma, non-herpetic infection, and other bullous keratopathy (all comparisons  $p < 0.001$ , except other corneal dystrophy vs. trauma,  $p = 0.001$ ).

Grafts performed for corneal scar and/or opacity had better survival than those for failed previous graft/s, pseudophakic bullous keratopathy, corneal ulcer, non-herpetic infection, and other bullous keratopathy (all  $p < 0.001$ ).

In addition to those indications for graft mentioned above, grafts performed for corneal ulcer had poorer survival than grafts performed for failed previous graft/s, pseudophakic bullous keratopathy, trauma, "other" indications for graft (all  $p < 0.001$ ), corneal degeneration and other bullous keratopathy (both  $p = 0.001$ ).

### **2.7.1.2 Donor age group**

Significantly better survival was shown for the under 50 years group, compared to each of the other age groups (all comparisons  $p < 0.001$ ).

Significantly better survival was shown for the 50 to 59 years group, compared to the 80 years and older group ( $p = 0.001$ ).

### **2.7.1.3 Donor/recipient sex match/mismatch**

Grafts performed in a female recipient using a donor cornea also from a female (F/F) exhibited significantly better survival than those performed in a male recipient using a male donor cornea (M/M,  $p < 0.001$ ), or in a male recipient using a female donor (F/M,  $p = 0.019$ ).

### **2.7.1.4 Interstate transportation of donor cornea**

Grafts performed with corneas that had been transported interstate had significantly poorer survival than those where they had not ( $p = 0.009$ ).

Grafts where it was not known whether the donor cornea had been transported interstate had significantly poorer survival than both other groups (both  $p < 0.001$ ).

### **2.7.1.5 Change in lens status pre- to post-graft**

Eyes that were phakic before and after graft, as well as those that underwent a triple procedure at graft (phakic/pseudophakic) exhibited significantly better survival than those with any other combination ( $p < 0.001$  in both cases).

### **2.7.1.6 Pre-graft corneal neovascularisation**

The survival of grafts performed in eyes with four quadrants of pre-graft corneal neovascularisation had significantly poorer survival than those with fewer quadrants or no neovascularisation (all  $p < 0.001$ ).

Grafts performed in eyes with two or three quadrants of pre-graft corneal neovascularisation had significantly poorer survival than those with none ( $p = 0.001$ ), or one quadrant ( $p < 0.001$ ).

### **2.7.1.7 Pre-graft inflammation and/or steroid use**

Grafts performed in eyes with pre-graft inflammation and/or steroid use within the prior two weeks had significantly poorer survival than those without ( $p < 0.001$ ).

Grafts performed in eyes where the presence of pre-graft inflammation and/or steroid use within the prior two weeks was not known to the surgeon, had significantly poorer survival than both those without ( $p < 0.001$ ) and those with ( $p = 0.004$ ) this pre-graft factor recorded.

### **2.7.1.8 Number of previous contralateral grafts**

Grafts performed in recipients who had a history of a single previous graft performed in their contralateral eye exhibited significantly better survival than those with no prior contralateral graft ( $p < 0.001$ ).

### **2.7.1.9 Graft era**

Grafts survival was significantly better in each subsequent era, up to 2000 to 2004. Grafts performed from 1990 to 1994 had better survival than those performed from 1985 to 1989 ( $p < 0.001$ ). Grafts performed from 1995 to 1999 had better survival than those performed from 1990 to 1994 ( $p < 0.001$ ). Grafts performed from 2000 to 2004 had better survival than those performed from 1995 to 1999 ( $p < 0.001$ ).

There were no significant differences in graft survival for grafts performed between 2000 to 2004, 2005 to 2009, and 2010 to 2014 (all  $p > 0.100$ ). Each of these groups had significantly better survival than the grafts performed in each era prior to the year 2000 (all  $p < 0.001$ ), and to grafts performed in the most recent era of 2015 to 2017 ( $p < 0.001$ ). The poor performance of grafts in this most recent era is likely due to the lag time effect discussed in section 2.3.1.

### **2.7.1.10 Graft size**

Survival of grafts that were 7.75 mm but less than 8.25 mm was significantly better than those that were under 7.75 mm, or over 8.25 mm (both  $p < 0.001$ ). They also had significantly better survival than grafts where the size was not reported to the ACGR ( $p = 0.007$ ).

Survival of grafts that were 8.25 mm but less than 8.75 mm was significantly better than those that were under 7.75 mm ( $p < 0.001$ ), or over 8.25 mm ( $p = 0.001$ ).

### **2.7.1.11 Volume of PK registered by surgeon and level of follow-up received**

Grafts performed by surgeons with 500 or more PK registered with the ACGR, and above average ( $> 82\%$ ) levels of follow-up had significantly better survival than those performed by surgeons with 500 or more PK registered with the ACGR, and below average ( $\leq 82\%$ ) levels of follow-up, and surgeons with fewer than 500 PK registered (both  $p < 0.001$ ).



## 2.8 Reasons for Graft Failure

Of the 20,336 followed grafts, 5,687 (28%) were known to have failed by the census date. This equates to 23% of the 24,827 registered grafts. Surgeons were asked to indicate the reason for graft failure. This information was also gathered from repeat registration forms, where the reason for failure of the previous graft was given.

Table 2.13 shows the reasons for failure given. Please note that for some of the reasons for failure given, the sub-categories do not add up to the total number of cases.

**Table 2.13 Reasons for failure**

<b>Penetrating Corneal Graft Reasons for Graft Failure</b>		
	<b>Sub-total</b>	<b>Total</b>
<b>Rejection</b>		<b>1594 (28%)</b>
Unspecified/endothelial cell failure	1329	
With glaucoma	67	
With non-herpetic infection	56	
With herpetic infection	31	
With vascularisation	28	
With scarring	19	
With other	64	
<b>Endothelial cell failure</b>		<b>1117 (20%)</b>
Pseudophakic	792	
Phakic	107	
Aphakic	218	
<b>Non-herpetic infection</b>		<b>451 (8%)</b>
Microbial/bacterial keratitis	213	
Endophthalmitis	72	
Fungal keratitis	55	
Other specified	29	
Unspecified	82	
<b>Glaucoma</b>		<b>293 (5%)</b>
With endothelial cell failure	33	
With other*	52	
<b>Corneal ulcer</b>		<b>191 (3%)</b>
Perforated	121	
<b>Primary graft failure</b>		<b>174 (3%)</b>
<b>Trauma</b>		<b>147 (3%)</b>
Rupture	47	
Penetrating eye injury	13	
Blunt force trauma	10	
Other specified	7	
Unspecified	70	

<b>Herpetic infection</b>	<b>138 (2%)</b>
<b>Astigmatism</b>	<b>102 (2%)</b>
<b>Scarring/opacity</b>	<b>105 (2%)</b>
<b>Other specified**</b>	<b>439 (8%)</b>
<b>Unspecified</b>	<b>936 (16%)</b>
<b>Total</b>	<b>5687 (100%)</b>

\* Other included: corneal neovascularisation (7), epithelial defect (7), uveitis (5), anterior chamber haemorrhage (3), band keratopathy (3), epithelial downgrowth (3), unspecified infection (3), central retinal vein occlusion (2), Descemet's membrane detachment (2), perforation (2), synechiae (2), blepharitis (1), cataract (1), calcification (1), corneal nebula (1), ICE syndrome (1), IOL complication (1), Peters' anomaly (1) phthisical eye (1), retinal detachment (1), retrocorneal membrane (1), scleral necrosis (1), trichiasis (1), wound leak (1).

\*\* Other included: limbal cell/epithelial failure (67), neovascularisation (52), recurrent keratoconus (42), corneal melt (38), unspecified ectasia (32), phthisis (27), recurrent dystrophy (20), wound dehiscence (20), band keratopathy (14), descemetocoele (12), retinal detachment (11), retrocorneal membrane (10), choroidal haemorrhage (8), carcinoma (5), hypotony (6), ICE syndrome (6), epithelial downgrowth (6), calcification (5), uveitis (5), dry eye (4), expulsive haemorrhage (4), rubeosis iridis (4), anterior segment ischaemia (2), fibrous ingrowth (2), keratoglobus (2), protein deposits (2), Stevens-Johnson syndrome (2), surgical complications (2), synechia (2), unspecified inflammation (2), aniridic keratopathy (1), anterior chamber haemorrhage (1), anterior segment dysgenesis (1), Descemet's detachment (1), erythroderma (1), hypopyon (1), keratomalacia (1), lipid keratopathy (1), meibomianitis (1), melanoma (1), necrosis (1), neurotrophic keratopathy (1), pemphigoid (1), Peter's anomaly (1), pterygium (1), pupillary membrane (1), recurrent erosions (1), retinal occlusion (1), Sjogren's syndrome (1), spontaneous graft detachment (1), striate keratopathy (1), stromal failure (1), stromal folds (1), vitreous disorder (1), vitreous haemorrhage (1).

Primary graft non-functions are defined as grafts that never thin and clear in the post-operative period. For penetrating grafts, the time from graft to failure is as reported by the surgeon. It was usually 1-2 days but seldom more than 7 days.

Of the 174 grafts reported by surgeons to have been primary graft failures, the majority (139) had no further information provided, while for a further five the surgeon stated that the donor tissue was of poor quality. Additional specific reasons given were: epithelial defect in donor (4), expulsive haemorrhage (3), oedema (3), wound dehiscence (3), corneal perforation (2), suture related complications (2), Acanthamoeba infection (1), allergic conjunctivitis (1), donor tissue damaged during transportation (1), donor tissue damaged during dissection (1), endophthalmitis (1), enucleation due to fungal keratitis (1), flat anterior chamber (1), herpetic infection (1), limbal stem cell failure (1), opacity (1), trauma (1), undersized graft (1), unspecified infection (1).

## 2.9 Post-graft Changes in Best Corrected Visual Acuity

### 2.9.1 All indications for graft

Post-graft best corrected visual acuity (BCVA) is an important outcome for corneal graft recipients. A desire for improved visual acuity was specified as a reason for graft in 19,253 (78%) of registered penetrating keratoplasties. In 62% of cases (15,430), this was the sole desired outcome indicated. It is likely that this was also at least part of the reason for graft in some of the further 3,952 (16%) grafts for which no reason was specified.

Follow-ups occur at varying times post-graft, depending on when a surgeon sees a recipient. Where post-graft best corrected visual acuity (without pinhole) information was provided, we categorised this according to the length of time since graft. The first two categories were:

- BCVA provided at between 6 and 12 months post-graft, and
- BCVA provided at between 12 and 18 months post-graft.

Subsequent groups were at yearly intervals. For each year point, any measurements provided within 6 months of that date, rounded to the nearest day, were included (e.g. for 2-year follow-up, any BCVA given at between 730 and 913 days post-graft was included).

We analysed post-graft visual acuity in several ways. Where more than 20 grafts had BCVA measurements provided, we examined:

1. The percentage of *surviving* grafts achieving different levels of Snellen visual acuity (6/6 or better, 6/7.5 to 6/12, 6/15 to 6/24, 6/36 to 6/60, count fingers (CF) or hand movements (HM), and light perception (LP) or no light perception (NLP)) at yearly time-points post-graft. Grafts that had been reported to have failed at the time of last follow-up, but had prior follow-ups with BCVA measurements provided when the graft was surviving, had these prior data included in these analyses.
2. The *average* Snellen visual acuity achieved at yearly intervals post-graft, again by *surviving* grafts.
3. The final BCVA reported at the time of failure.

Table 2.14 and Figure 2.9.1 show the reported post-graft best corrected visual acuity for all failed grafts at the time of last follow-up, separated by indication for graft. Visual acuity at time of failure was reported for 4256 (75%) of 5686 failed PK. As might be expected, the majority of failed grafts had accompanying poor visual acuity.

Table 2.14 Post-graft best corrected visual acuity

<b>Penetrating Corneal Graft: Visual Acuity in Failed Grafts (as reported at final follow-up)</b>						
	6/4 to 6/6	6/7.5 to 6/12	6/15 to 6/24	6/36 to 6/60	CF or HM	LP or NLP
Failed previous graft	2 (<1%)	36 (2%)	79 (5%)	219 (14%)	992 (63%)	259 (16%)
Keratoconus	2 (<1%)	39 (7%)	84 (15%)	158 (27%)	277 (48%)	19 (3%)
Pseudo bullous keratopathy	0 (0%)	9 (1%)	31 (4%)	96 (13%)	487 (64%)	136 (18%)
Fuchs' endothelial dystrophy	1 (<1%)	10 (3%)	30 (9%)	68 (21%)	195 (59%)	25 (8%)
Corneal scars and opacities	0 (0%)	0 (0%)	2 (4%)	11 (19%)	36 (63%)	8 (14%)
Corneal ulcers	0 (0%)	2 (2%)	3 (3%)	9 (8%)	72 (61%)	32 (27%)
Herpetic eye disease	0 (0%)	3 (2%)	5 (3%)	21 (11%)	119 (64%)	39 (21%)
Trauma	0 (0%)	4 (3%)	3 (2%)	16 (10%)	103 (66%)	29 (19%)
Non-herpetic infection	1 (1%)	2 (3%)	1 (1%)	5 (6%)	42 (54%)	27 (35%)
Corneal degeneration	0 (0%)	1 (4%)	2 (8%)	5 (19%)	14 (54%)	4 (15%)
Other bullous keratopathy	0 (0%)	1 (<1%)	10 (4%)	30 (12%)	164 (67%)	40 (16%)
Other dystrophies	0 (0%)	2 (5%)	5 (13%)	10 (25%)	22 (55%)	1 (3%)
Other specified	0 (0%)	1 (1%)	4 (4%)	14 (15%)	52 (54%)	25 (26%)
<b>Total</b>	<b>6 (&lt;1%)</b>	<b>110 (3%)</b>	<b>259 (6%)</b>	<b>662 (16%)</b>	<b>2575 (61%)</b>	<b>644 (15%)</b>

CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

Figure 2.9.1 Best corrected visual acuity at time of last follow-up for failed penetrating keratoplasties

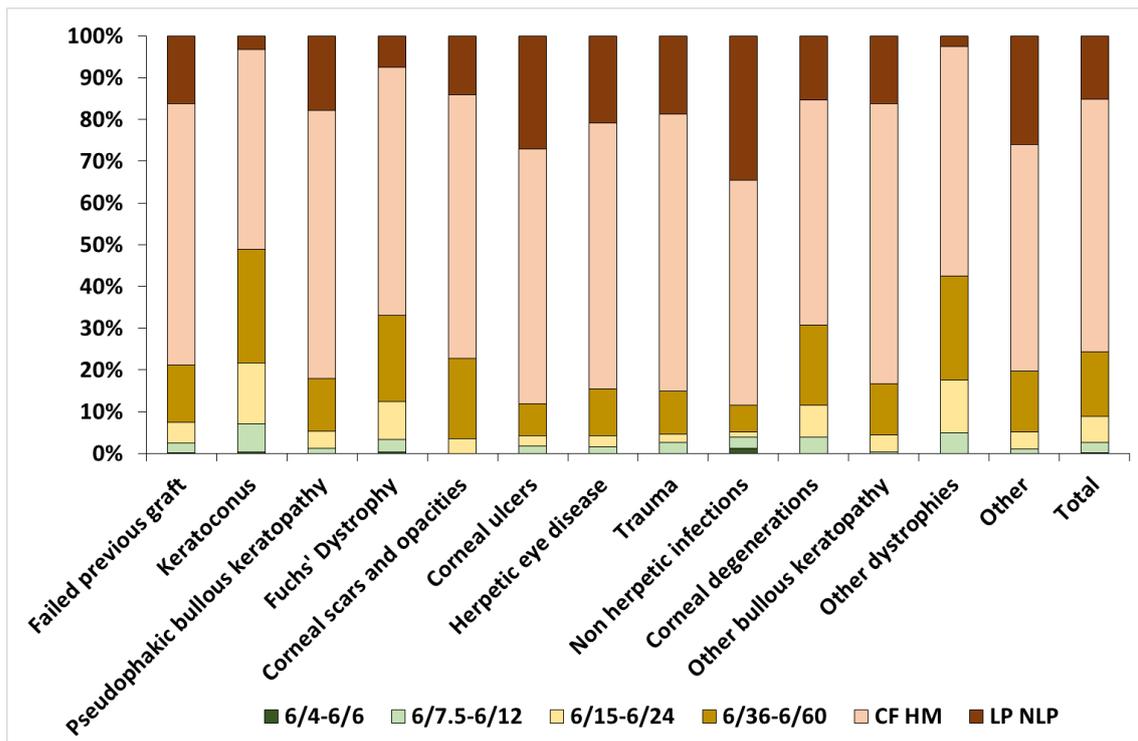
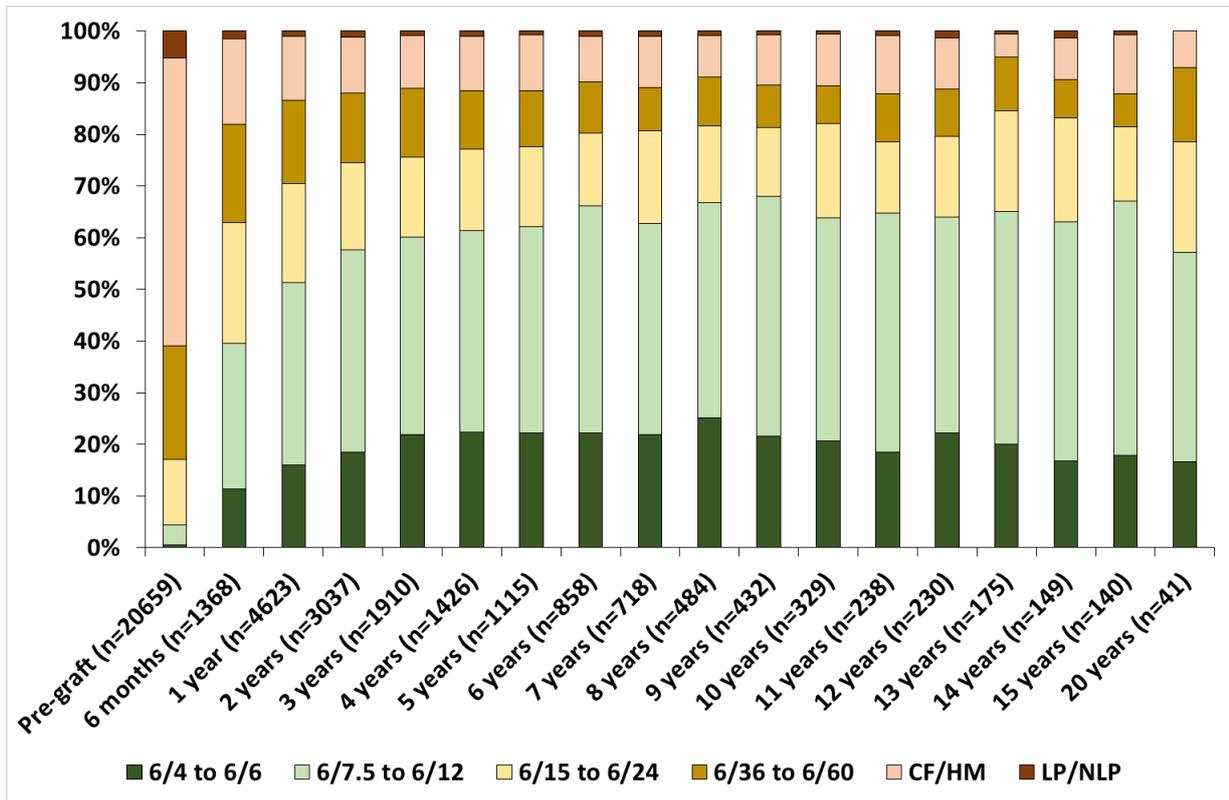


Figure 2.9.2 shows the best corrected visual acuity (without pinhole) in the grafted eye, as reported to the ACGR, and categorised into six levels of vision, for all penetrating grafts. Prior to graft more than 60% of eyes had vision of CF or worse, with another 20% having 6/36 to 6/60. By 2-years post-graft, approximately three-quarters of eyes with surviving grafts had vision of 6/24 or better, with approximately 60% having functional vision of 6/12 or better. This remained the case for surviving grafts followed for up to 20 years.

**Figure 2.9.2 Best corrected visual acuity for penetrating keratoplasties, surviving at time of measurement**



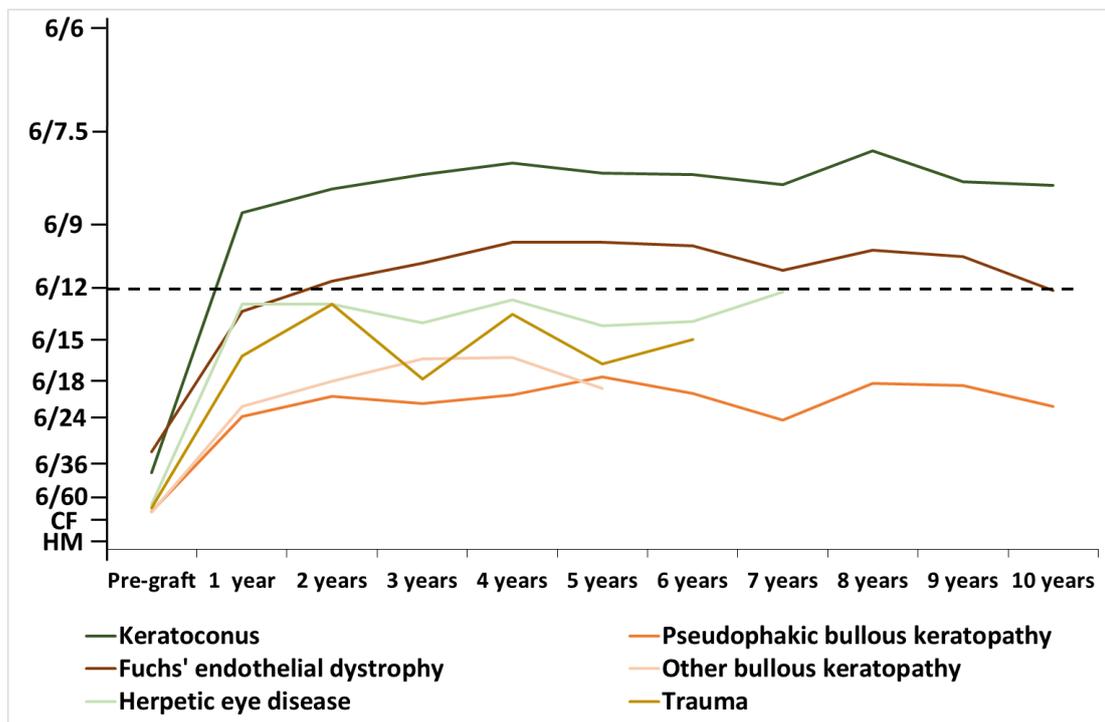
CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

### 2.9.2 Individual indications for graft

The following analyses show the post-graft best corrected (without pinhole) visual acuity obtained for surviving grafts performed for specific indications. Data are reported for each of: keratoconus, Fuchs' endothelial dystrophy, pseudophakic bullous keratopathy, herpetic eye disease, trauma, and other bullous keratopathy. Figure 2.9.3 shows the average BCVA reported for various indications for graft pre-graft, and at yearly time points (six-month timeframe cohorts), up to 10 years. The dashed line shows the point where vision reaches 6/12, sometimes referred to as "functional" vision.

On average, the best visual outcomes were seen for eyes grafted for keratoconus, followed by Fuchs' endothelial dystrophy. It can also be seen that these grafts had better pre-graft visual acuity levels than grafts for other indications. Grafts performed for these indications had mean post-graft vision of 6/12 or better by 12-months post-graft. On average, levels of vision obtained post-graft for bullous keratopathy (whether pseudophakic or otherwise), and trauma did not reach 6/12 or better. Eyes grafted for herpetic eye disease with surviving grafts had average visual acuity just under 6/12 up to 7-years post-graft.

**Figure 2.9.3 Average level of best corrected visual acuity reported at yearly time points for surviving penetrating keratoplasty performed for common indications for graft**



CF=count fingers at 1 metre, HM=hand movements

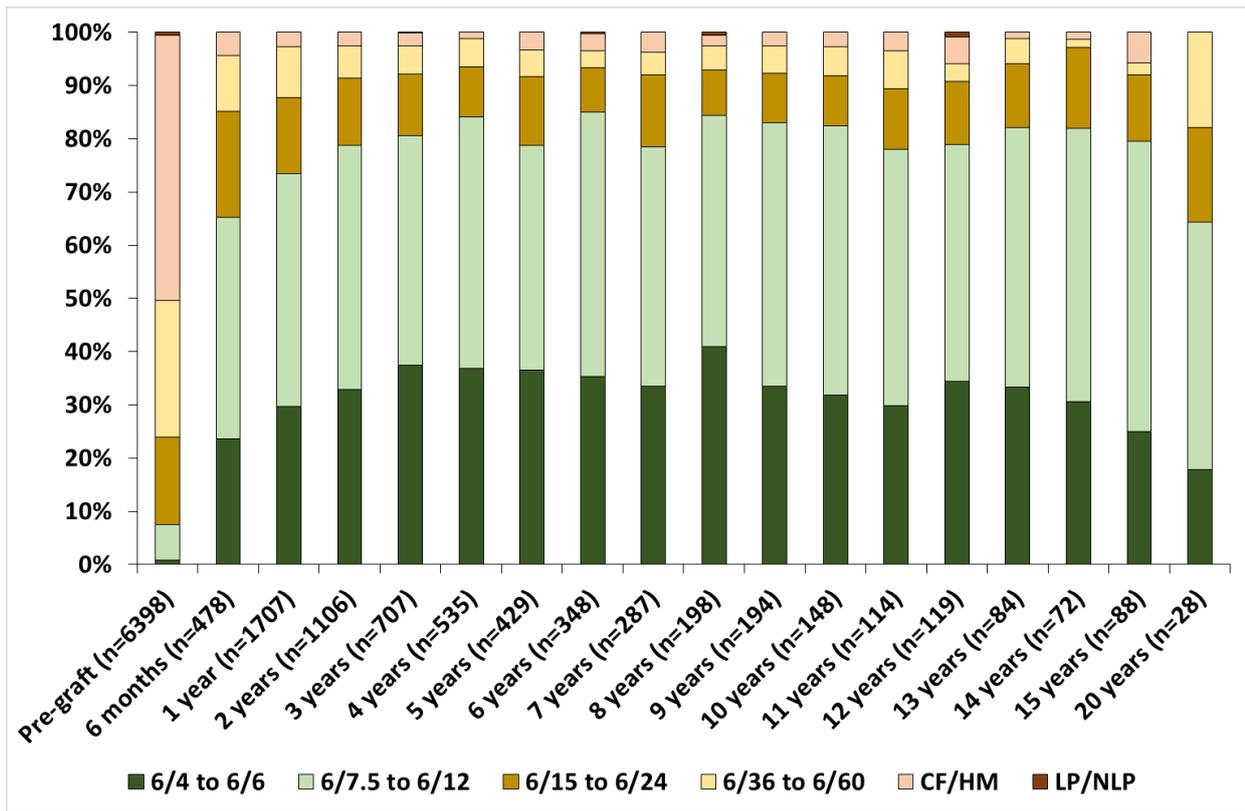
### Number of surviving grafts with visual acuity provided

	Pre	1	2	3	4	5	6	7	8	9	10
<b>Keratoconus</b>	6398	1707	1106	707	535	429	348	287	198	194	148
<b>Pseudo bullous keratopathy</b>	2976	664	372	232	155	118	100	66	47	31	25
<b>Other bullous keratopathy</b>	777	186	94	60	43	40	19	17	15	9	8
<b>Fuchs' endothelial dystrophy</b>	1792	412	309	206	152	136	128	116	75	66	53
<b>Herpetic eye disease</b>	808	208	128	88	58	47	26	35	19	12	12
<b>Trauma</b>	529	97	73	47	37	28	21	11	8	8	4

Penetrating Keratoplasty

Figure 2.9.4 shows levels of best corrected visual acuity reported to the ACGR at yearly intervals for **surviving** penetrating grafts performed for keratoconus. Post-graft vision of 6/12 or better was reported in three-quarters of surviving penetrating grafts performed for keratoconus that had BCVA measurements reported between 12 and 18-months post-graft. This percentage remained consistent up until 15-years post-graft.

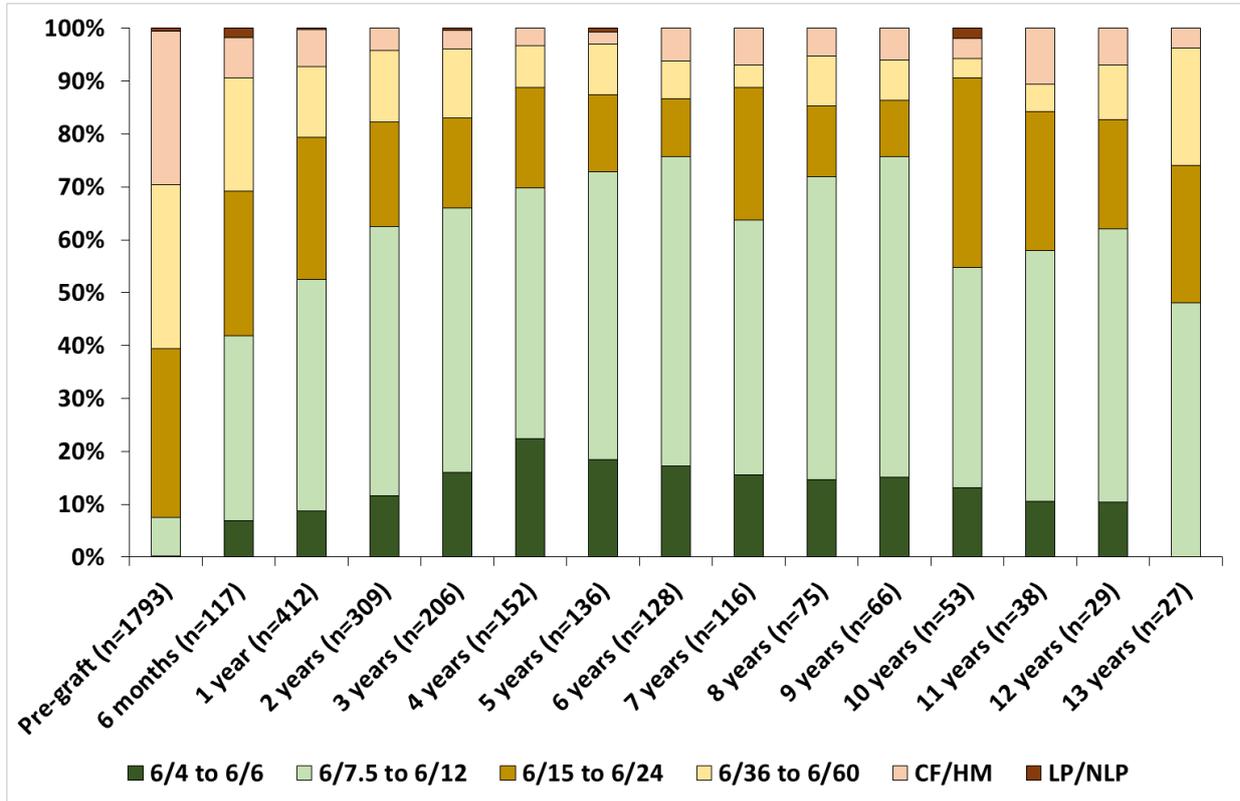
**Figure 2.9.4 Keratoconus: level of best corrected visual acuity reported at yearly time points for surviving grafts**



CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

Figure 2.9.5 shows levels of best corrected visual acuity reported to the ACGR at yearly intervals for **surviving** penetrating grafts performed for Fuchs' endothelial dystrophy. Post-graft vision of 6/12 or better was reported in more than half of surviving penetrating grafts performed for Fuchs' endothelial dystrophy that had BCVA measurements reported between 12 and 18-months post-graft. This percentage continued to increase up to approximately 70% by 5-years, and remained above 50% up to 13-years post-graft.

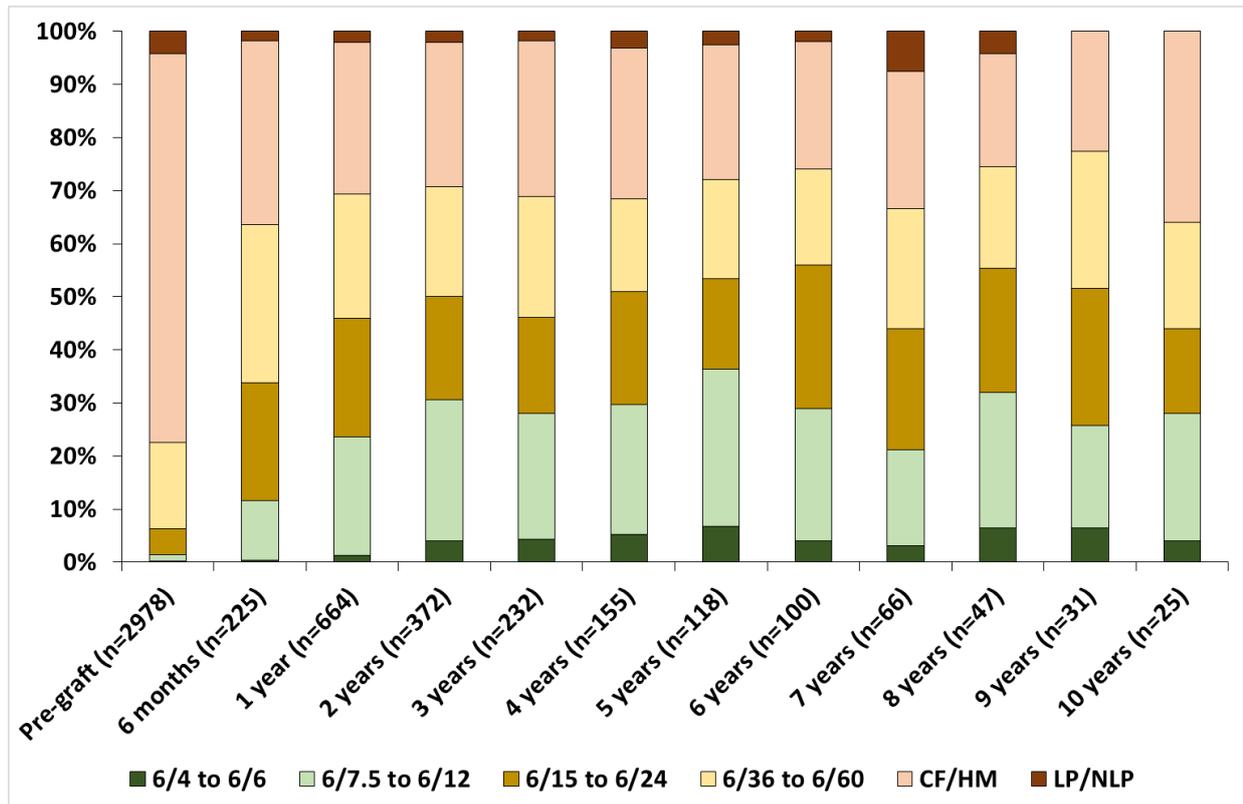
**Figure 2.9.5 Fuchs' endothelial dystrophy: level of best corrected visual acuity reported at yearly time points for surviving grafts**



CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

Figure 2.9.6 shows levels of best corrected visual acuity reported to the ACGR at yearly intervals for **surviving** penetrating grafts performed for pseudophakic bullous keratopathy. Post-graft vision of 6/12 or better was reported in only around one-quarter of surviving penetrating grafts performed for pseudophakic bullous keratopathy that had BCVA measurements reported between 12 and 18-months post-graft. This percentage remained similar over the 10-years immediately post-graft.

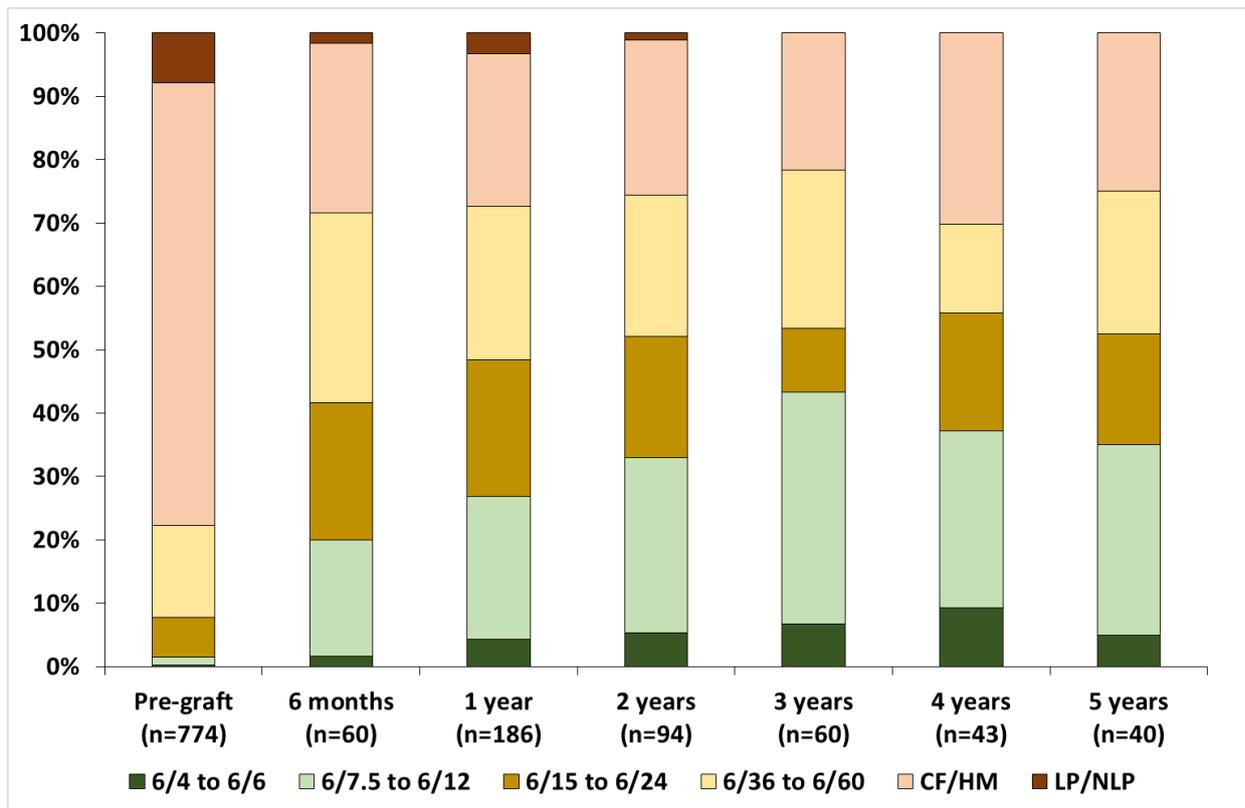
**Figure 2.9.6 Pseudophakic bullous keratopathy: level of best corrected visual acuity reported at yearly time points for surviving grafts**



CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

Figure 2.9.7 shows levels of best corrected visual acuity reported to the ACGR at yearly intervals for **surviving** penetrating grafts performed for non-pseudophakic (aphakic or phakic pre-graft) bullous keratopathy. Post-graft visual acuity was similar to that reported for penetrating keratoplasties performed for pseudophakic bullous keratopathy, with post-graft vision of 6/12 or better reported in approximately one-quarter of surviving penetrating grafts performed for non-pseudophakic bullous keratopathy that had BCVA measurements reported between 12 and 18-months post-graft. This percentage increased slightly, peaking at above 40% at 3-years post-graft.

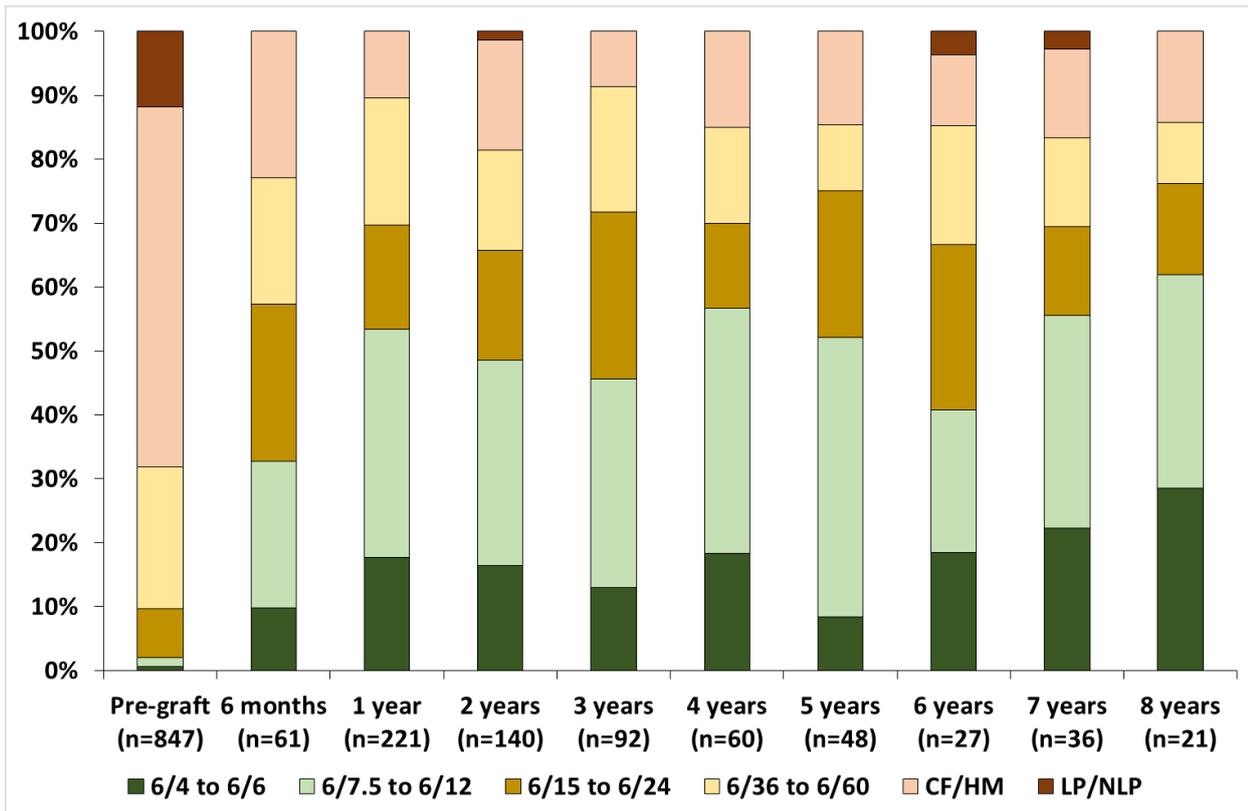
**Figure 2.9.7 Non-pseudophakic bullous keratopathy: level of best corrected visual acuity reported at yearly time points for surviving grafts**



CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

Figure 2.9.8 shows levels of best corrected visual acuity reported to the ACGR at yearly intervals for **surviving** penetrating grafts performed for herpetic eye disease. Post-graft vision of 6/12 or better was reported in more than half of surviving penetrating grafts performed for herpetic eye disease that had BCVA measurements reported between 12 and 18-months post-graft. This percentage varied slightly over the following years, but remained within the 40 to 60 percent range up to 8-years post-graft.

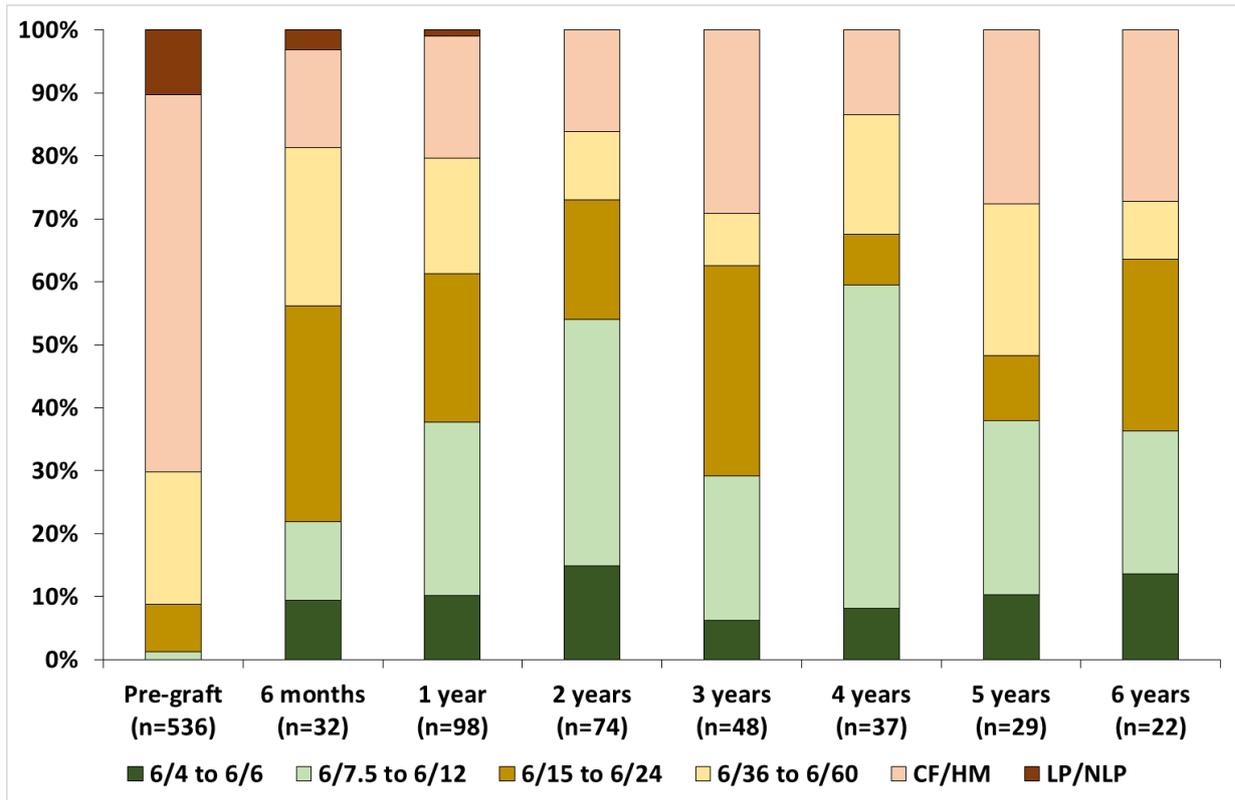
**Figure 2.9.8 Herpetic eye disease: level of best corrected visual acuity reported at yearly time points for surviving grafts**



CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

Figure 2.9.9 shows levels of best corrected visual acuity reported to the ACGR at yearly intervals for **surviving** penetrating grafts performed for trauma. Post-graft vision of 6/12 or better was reported in just under 40% of surviving penetrating grafts performed for trauma that had BCVA measurements reported between 12 and 18-months post-graft. This percentage varied markedly over the following years, from as low as 30% at 3-years post-graft, up to over 60% at 4-years, but returned to the 40% mark at 5 and 6-years post-graft.

**Figure 2.9.9 Trauma: level of best corrected visual acuity reported at yearly time points for surviving grafts**



CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

## 3 Descemet's Stripping Endothelial Keratoplasty

This chapter presents the results of analyses conducted on data relating to the 4,736 Descemet's stripping endothelial keratoplasties registered with the ACGR. The preparation of donor material may have been automated (DSAEK) or manual (DSEK). In some cases, this was unspecified by the contributing surgeon. All grafts in these three groups were analysed together and are referred to throughout this report as DS(A)EKs. Kaplan-Meier survival analyses were conducted using IBM SPSS for Windows (Version 22.0), to compare the graft survival across groups for a range of variables relating to the corneal donor, graft recipient, surgical procedure, surgeon, and follow-up care.

### 3.1 Donor and Eye Banking Factors

Table 3.1 shows the number of grafts within each of the variable sub-groups, for the donor factors found to be **significant** in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (4,736 registered and 3,263 followed) and the percentages, which should be summed vertically for each variable, total 100.

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Likelihood of follow-up was significantly more likely ( $p < 0.05$ ) in some groups than others. Higher rates of follow-up were received for grafts where it had been stored in hypothermic solution. Rates were lower for grafts performed using donor tissue that had been pre-cut by the eye bank and grafts where the specific type of procedure was known. Significant differences in follow-up were also found across groups for eye bank, death-to-enucleation times and enucleation-to-storage times.

Table 3.2 shows the number of grafts within each of the variable sub-groups, for the donor and eye banking factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (4,736 registered and 3,263 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The result of the Kaplan-Meier survival analysis is also provided for each variable.

Table 3.1 Donor and eye banking factors, significant in univariate analyses

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft Donor and Eye Banking Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Eye bank</b>		
Eye bank M	1683 (36%)	1145 (35%)
Eye bank K	925 (20%)	576 (18%)
Eye bank V	1195 (25%)	937 (29%)
Eye bank J	515 (11%)	303 (9%)
Eye bank N	418 (9%)	302 (9%)
<b>Enucleation-to-storage time*</b>		
≤ 3 hours	2460 (52%)	1622 (50%)
4 to 6 hours	535 (11%)	410 (13%)
7 to 12 hours	287 (6%)	214 (7%)
> 12 hours	402 (8%)	280 (9%)
Not advised	1052 (22%)	737 (23%)
<b>Storage medium</b>		
Hypothermic	2273 (48%)	1803 (55%)
Organ culture	2460 (52%)	1457 (45%)
Moist pot	2 (<1%)	2 (<1%)
Not advised	1 (<1%)	1 (<1%)
<b>Age group</b>		
<40 years	385 (8%)	263 (8%)
40 to 69 years	2891 (61%)	1981 (61%)
70 years and older	1460 (31%)	1019 (31%)
<b>Pre-cut by eye bank</b>		
No	3622 (77%)	2883 (88%)
Yes	1114 (24%)	380 (12%)
<b>Central corneal endothelial cell density</b>		
<2500 cells/mm <sup>2</sup>	271 (6%)	169 (5%)
2500 to 3249 cells/mm <sup>2</sup>	2240 (47%)	1430 (44%)
≥ 3250 cells/mm <sup>2</sup>	694 (15%)	445 (14%)
Not advised	1531 (32%)	1219 (37%)
<b>Total</b>	<b>4736 (100%)</b>	<b>3263 (100%)</b>

\* Note: significant at p<0.08 for inclusion in multivariate analyses but not at p<0.05.

Table 3.2 Donor and eye banking factors, not significant in univariate analyses

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft Donor and Eye Banking Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Death-to-enucleation time</b>		
≤ 6 hours	1108 (23%)	815 (25%)
7 to 12 hours	1727 (36%)	1285 (39%)
13 to 18 hours	1271 (27%)	814 (25%)
> 18 hours	621 (13%)	341 (10%)
Not advised	9 (<1%)	8 (<1%)
<b>Chi<sup>2</sup>=1.19, df=3, p=0.755</b>		
<b>Storage to graft time - Organ culture</b>		
Up to 2 weeks	543 (11%)	302 (9%)
2 to 3 weeks	942 (20%)	538 (17%)
More than 3 weeks	281 (6%)	173 (5%)
Not advised	694 (15%)	444 (14%)
Not applicable	2276 (48%)	1806 (55%)
<b>Chi<sup>2</sup>=4.42, df=2, p=0.110</b>		
<b>Storage to graft time - Hypothermic</b>		
Within 5 days	1329 (28%)	1069 (33%)
6 or 7 days	512 (11%)	385 (12%)
More than a week	74 (2%)	56 (2%)
Not advised	358 (8%)	293 (9%)
Not applicable	2463 (52%)	1460 (45%)
<b>Chi<sup>2</sup>=3.02, df=2, p=0.221</b>		
<b>Donor sex</b>		
Male	2921 (62%)	2049 (63%)
Female	1815 (38%)	1214 (37%)
<b>Chi<sup>2</sup>=0.23, df=1, p=0.629</b>		
<b>Cause of death</b>		
Cardiac event	1096 (23%)	748 (23%)
Malignancy	1742 (37%)	1216 (37%)
Trauma	408 (9%)	263 (8%)
Respiratory event	383 (8%)	283 (9%)
Intracranial bleed/cerebral haemorrhage	807 (17%)	538 (16%)
Other specified	257 (5%)	185 (6%)
Live donor	1 (<1%)	1 (<1%)
Not advised*	42 (<1%)	29 (<1%)
<b>Chi<sup>2</sup>=3.58, df=5, p=0.611</b>		
<b>Multi-organ donor status</b>		
No	4057 (86%)	2802 (86%)
Yes	679 (14%)	461 (14%)
<b>Chi<sup>2</sup>=0.37, df=1, p=0.545</b>		
<b>Total</b>	<b>4736 (100%)</b>	<b>3263 (100%)</b>

Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable.

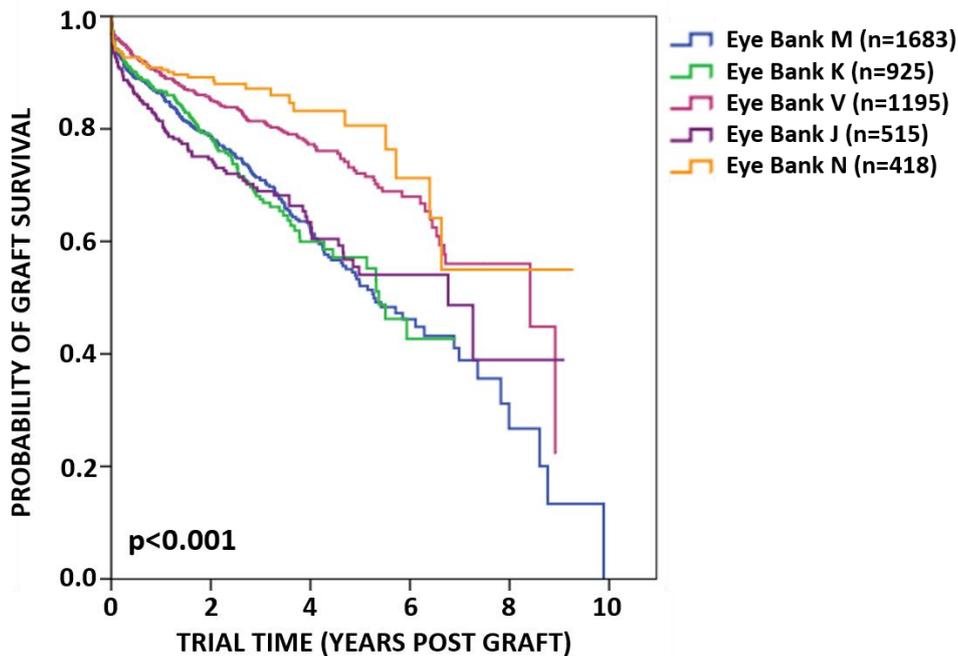
\*ACGR advised that cause of death was not yet determined but there were no medical contraindications and the eye had been cleared for release, by the Medical Director, in accordance with EBAANZ guidelines.

Descemet's Stripping (Automated) Endothelial Keratoplasty

### 3.1.1 DS(A)EK survival: influence of Australian eye bank

Donor corneas are retrieved, processed, stored and distributed by five eye banks around Australia. Figure 3.1.1 shows the comparison of graft survival for corneas provided by each of these eye banks. A significant difference was found across eye banks (Log Rank Statistic=53.50; df=4;  $p < 0.001$ ), with State V and State N having significantly better survival than all other states (all  $p < 0.001$ ). This variable was not retained in the final model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.1.1 Australian eye bank



#### Number at risk (years post-graft)

	1	2	4	6	8
Eye Bank M	791	521	141	38	6
Eye Bank K	410	247	54	10	NA
Eye Bank V	667	475	206	69	9
Eye Bank J	208	148	64	17	2
Eye Bank N	230	157	54	13	1

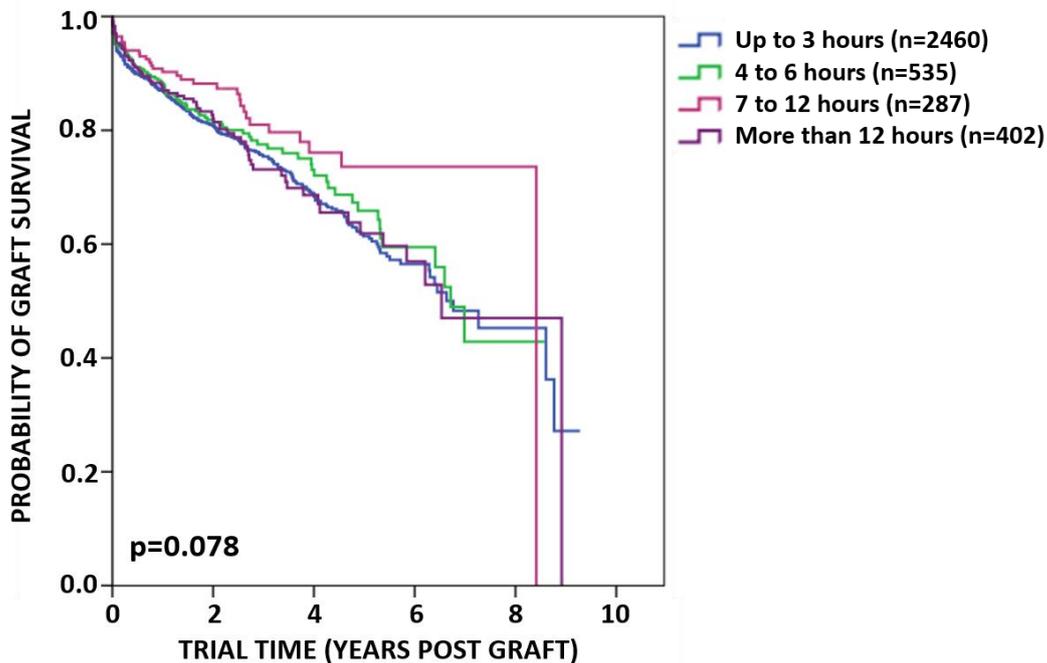
#### Probability of graft survival (years post-graft)

	1	2	4	6
Eye Bank M	0.86	0.79	0.62	0.46
Eye Bank K	0.87	0.78	0.60	NA
Eye Bank V	0.90	0.85	0.77	0.68
Eye Bank J	0.81	0.75	0.34	NA
Eye Bank N	0.91	0.89	0.83	NA

### 3.1.2 DS(A)EK survival: influence of enucleation to storage time

Figure 3.1.2 shows the comparison of graft survival across time to storage groups. Data were not provided for 1052 grafts and these were excluded from the analysis. The difference across groups was not statistically significant, (Log Rank Statistic=6.821; df=1;  $p=0.078$ ) and no individual comparisons between groups were significant following Bonferroni correction (all  $p>0.01$ ). This variable met the  $p<0.08$  criteria for potential inclusion in the multivariate analyses, however following further analyses in which the data were clustered by patient (see references 7 & 8), this was no longer the case ( $p=0.083$ ). This variable was therefore excluded from multivariate analyses and is **not** an independent factor significantly affecting graft survival.

Figure 3.1.2 Time from enucleation to storage of donor cornea



#### Number at risk (years post-graft)

	1	2	4	6	8
Up to 3 hours	1156	766	253	67	7
4 to 6 hours	292	194	72	24	2
7 to 12 hours	156	105	40	8	4
More than 12 hours	195	132	50	18	2

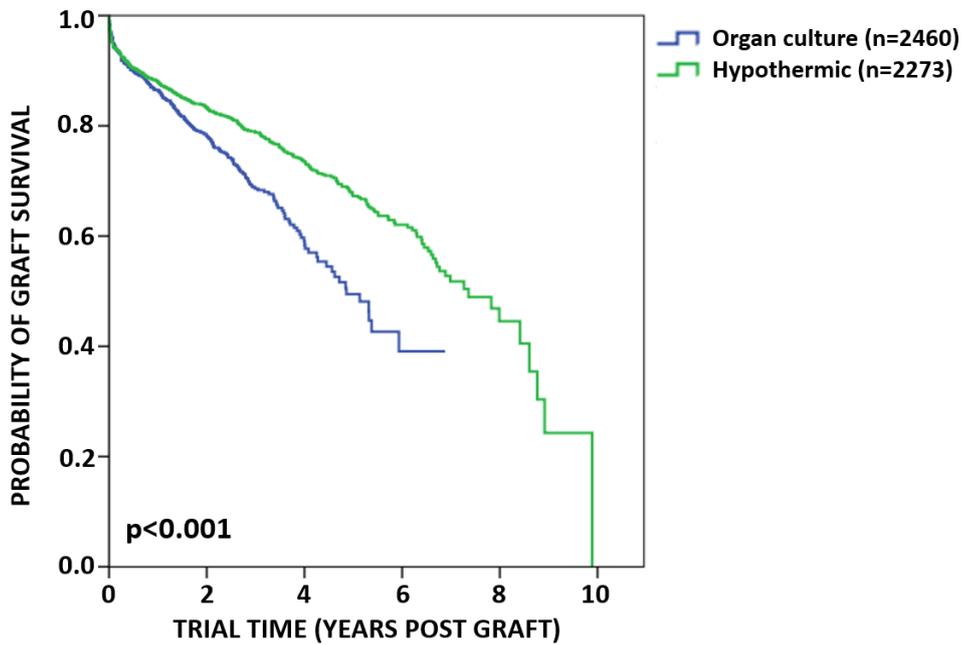
#### Probability of graft survival (years post-graft)

	1	2	4	6
Up to 3 hours	0.87	0.81	0.69	0.57
4 to 6 hours	0.88	0.81	0.73	0.60
7 to 12 hours	0.90	0.88	0.76	NA
More than 12 hours	0.87	0.82	0.69	NA

### 3.1.3 DS(A)EK survival: influence of corneal storage media

In Australia, two storage media are commonly used to preserve donor corneas prior to transplantation. Data were not analysed for 2 grafts where the donor eye was stored in a moist pot and 1 graft where the storage method was not specified. Figure 3.1.3 shows the comparison of graft survival for corneas stored in hypothermic medium compared to organ culture medium. A significant difference was found across groups (Log Rank Statistic=23.82; df=1; p<0.001). Following further analyses in which the data were clustered by patient [see references 7 & 8], this variable was no longer found to be significant (p=0.237). This variable was therefore excluded from multivariate analyses and is **not** an independent factor significantly affecting graft survival.

Figure 3.1.3 Corneal storage media



#### Number at risk (years post-graft)

	1	2	4	6	8
Organ culture	1008	601	90	9	NA
Hypothermic	1297	945	427	138	18

#### Probability of graft survival (years post-graft)

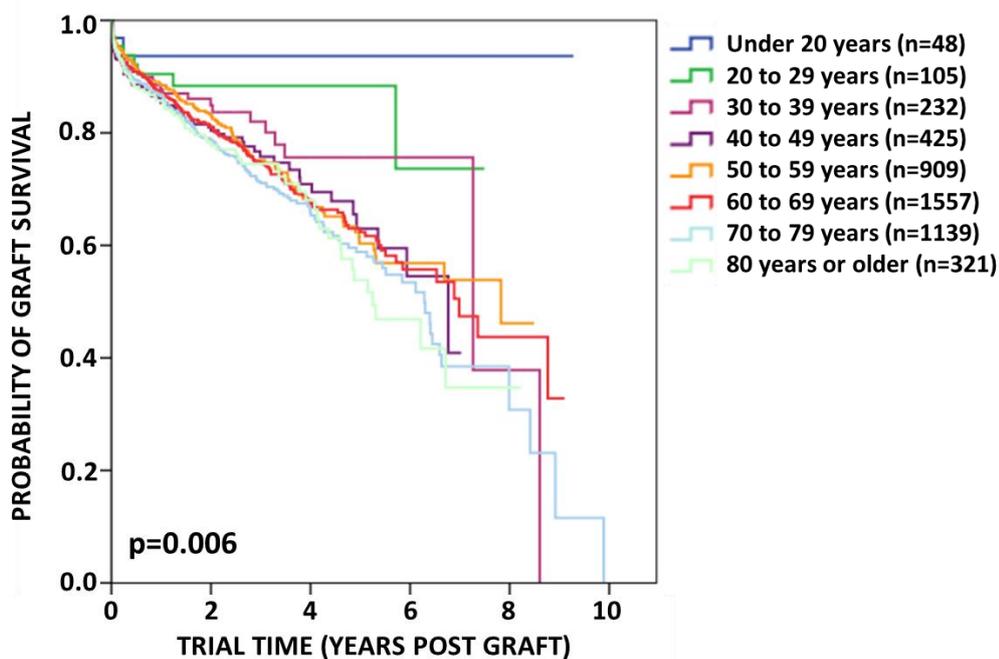
	1	2	4	6
Organ culture	0.87	0.78	0.59	NA
Hypothermic	0.88	0.83	0.74	0.62

### 3.1.4 DS(A)EK survival: influence of donor age (years)

Figure 3.1.4 shows the comparison of graft survival depending on donor age. Donors aged under 10 years or over 90 years are rare, and so these data were combined with the adjacent age groups. A significant difference was found across groups (Log Rank Statistic=19.90; df=7; p=0.006).

Further analyses, comparing age groups to those next in the sequence showed no significant differences between grafts performed with tissue from the three donor groups aged under 40 years (p=0.113), those aged 40 to 69 (p=0.826), and those aged 70 and over (p=0.885). The difference in survival across these three groups was significant (Log Rank Statistic=16.76; df=2; p<0.001), with survival for grafts performed with tissue from donors aged under 40 years significantly better than those aged 40 to 69 years (p=0.003) and 70 years or older (p<0.001). Donor age groups were thus categorised into these three groups for multivariate analysis. This variable was retained in the final model (see section 3.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 3.1.4 Donor age



**Number at risk (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>
<b>Under 20 years</b>	25	18	6	3	1
<b>20 to 29 years</b>	48	35	11	4	NA
<b>30 to 39 years</b>	116	72	29	6	1
<b>40 to 49 years</b>	203	141	51	11	NA
<b>50 to 59 years</b>	440	288	90	32	4
<b>60 to 69 years</b>	759	498	167	43	7
<b>70 to 79 years</b>	548	372	121	35	4
<b>80 years or older</b>	167	123	44	13	1

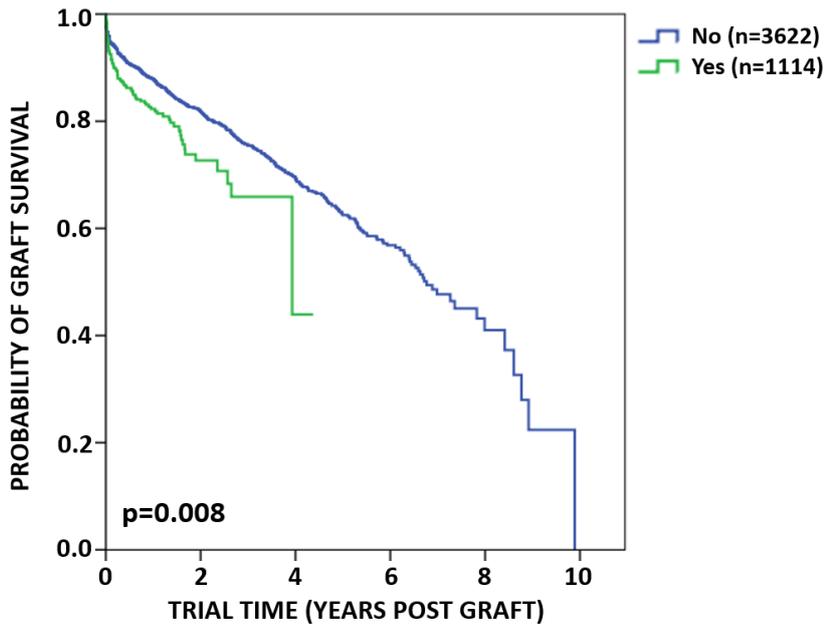
**Probability of graft survival (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>
<b>Under 20 years</b>	0.94	NA	NA	NA
<b>20 to 29 years</b>	0.91	0.88	NA	NA
<b>30 to 39 years</b>	0.88	0.85	0.76	NA
<b>40 to 49 years</b>	0.85	0.80	0.71	NA
<b>50 to 59 years</b>	0.89	0.83	0.68	0.57
<b>60 to 69 years</b>	0.87	0.81	0.68	0.56
<b>70 to 79 years</b>	0.87	0.79	0.66	0.53
<b>80 years or older</b>	0.86	0.78	0.68	NA

### 3.1.5 DS(A)EK survival: influence of pre-cut donor tissue

Donor tissue for endothelial grafts is increasingly pre-cut by eye banks. Figure 3.1.5 shows the comparison of graft survival between those DS(A)EK grafts that were pre-cut by the eye bank and those that were cut by the surgeon. A significant difference was found across groups (Log Rank Statistic=6.96; df=1; p=0.008). This variable was not retained in the final model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.1.5 Pre-cut donor tissue



#### Number at risk (years post-graft)

	1	2	4	6	8
Not pre-cut	2107	1494	517	147	18
Pre-cut	199	53	2	NA	NA

#### Probability of graft survival (years post-graft)

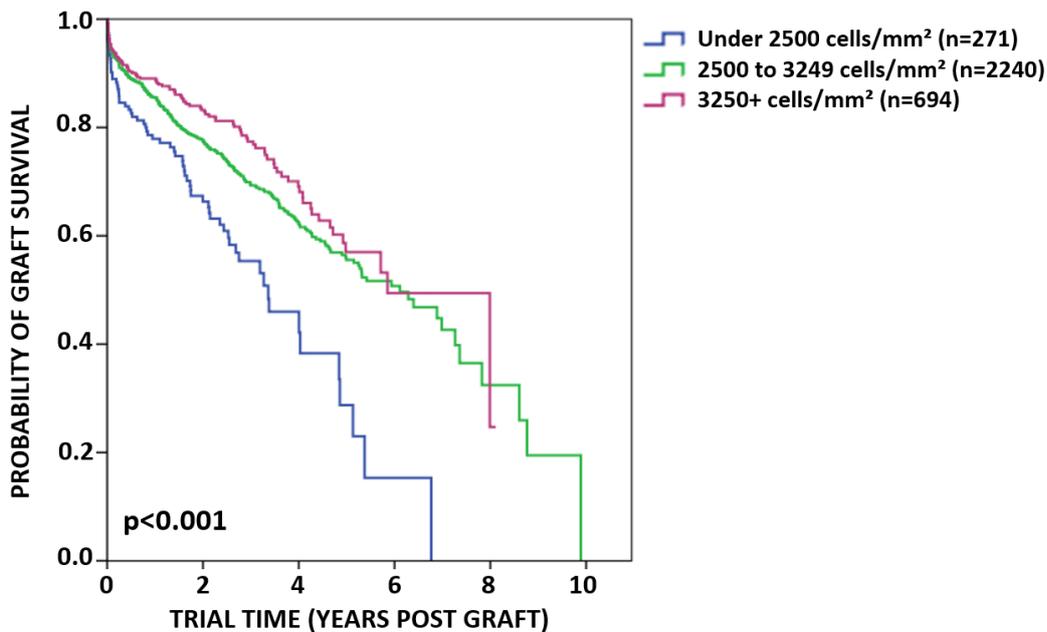
	1	2	4	6
Not pre-cut	0.88	0.82	0.69	0.57
Pre-cut	0.82	0.73	NA	NA

**3.1.6 DS(A)EK survival: influence of donor central corneal endothelial cell density**

Endothelial cell count (ECC) was reported for 68% of DSAEKs. Reported ECC ranged from 1700 to 4597 cells/mm<sup>2</sup>. Comparison of graft survival across donor ECC groups is shown in Figure 3.1.6. Preliminary analyses examined survival based on groupings of 250 cells/mm<sup>2</sup> increments. Based on the results, three ECC groups were created for the final comparison. A significant difference was found across groups (Log Rank Statistic=28.58; df=2; p<0.001) with grafts performed using donor tissue with cell counts under 2500 cells/mm<sup>2</sup> having significantly poorer survival than the other groups (both p<0.001).

Data on this variable were not provided in 32% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=87.02; df=3; p<0.001). ECC was thus categorised into these four groups for multivariate analysis. This variable was retained in the final model (see section 3.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 3.1.6 Endothelial cell density**



**Number at risk (years post-graft)**

	1	2	4	6	8
<b>Under 2500 cells/mm<sup>2</sup></b>	109	63	12	2	NA
<b>2500 to 3249 cells/mm<sup>2</sup></b>	986	647	188	50	7
<b>3250 or more cells/mm<sup>2</sup></b>	325	213	69	13	1

**Probability of graft survival (years post-graft)**

	1	2	4	6
<b>Under 2500 cells/mm<sup>2</sup></b>	0.78	0.66	NA	NA
<b>2500 to 3249 cells/mm<sup>2</sup></b>	0.86	0.78	0.62	0.51
<b>3250 or more cells/mm<sup>2</sup></b>	0.89	0.83	0.69	NA

## 3.2 Recipient Factors

Table 3.3 shows the number of grafts within each of the variable sub-groups, for the recipient factors examined in this report that were found to be **significant** predictors of graft survival in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (4,736 registered and 3,263 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 3.3 Recipient factors, significant in univariate analyses**

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft</b>		
<b>Recipient factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Indication for graft</b>		
Failed previous graft	993 (21%)	640 (20%)
Pseudophakic bullous keratopathy	1283 (27%)	865 (27%)
Fuchs' endothelial dystrophy	2282 (48%)	1603 (49%)
Other bullous keratopathy	136 (3%)	84 (3%)
Trauma	70 (1%)	49 (2%)
Other*	32 (<1%)	22 (<1%)
<b>Australian State where graft was performed</b>		
State M	1666 (35%)	1138 (35%)
State K	849 (18%)	523 (16%)
State V	1121 (24%)	873 (27%)
State J	627 (13%)	388 (12%)
State N	393 (8%)	278 (9%)
State C	80 (2%)	63 (2%)
<b>Interstate transportation</b>		
No	4533 (96%)	3109 (95%)
Yes	203 (4%)	154 (5%)
<b>Recipient age group</b>		
Under 50 years	238 (5%)	152 (5%)
50 to 59 years	480 (10%)	334 (10%)
60 to 69 years	1204 (25%)	867 (27%)
70 to 79 years	1477 (31%)	1007 (31%)
80 years or older	1337 (28%)	903 (28%)
<b>Recipient sex</b>		
Female	2700 (57%)	1858 (57%)
Male	2036 (43%)	1405 (43%)
<b>Donor/recipient sex match</b>		
Female/female	1016 (21%)	680 (21%)
Female/male	799 (17%)	534 (16%)
Male/female	1684 (36%)	1178 (36%)
Male/male	1237 (26%)	871 (27%)
<b>Change in lens status</b>		
Phakic/phakic	182 (4%)	124 (4%)
Phakic/pseudophakic	1137 (24%)	810 (25%)
Other combination	3417 (72%)	2329 (71%)

	Registered (%)	Followed (%)
<b>Pre-graft neovascularisation</b>		
No	4231 (89%)	2952 (90%)
Yes	505 (11%)	311 (10%)
<b>Pre-graft inflammation and/or steroid use</b>		
No	3464 (73%)	2362 (72%)
Yes	1203 (25%)	863 (26%)
Not advised	69 (1%)	38 (1%)
<b>History of raised intraocular pressure</b>		
IOP never known to be raised	3851 (81%)	2674 (82%)
IOP raised in past and/or at graft	885 (19%)	589 (18%)
<b>Prior contralateral corneal graft/s</b>		
None	3610 (76%)	2489 (76%)
One	933 (20%)	653 (20%)
Two or more	193 (4%)	121 (4%)
<b>Total</b>	<b>4736 (100%)</b>	<b>3263 (100%)</b>

\*Other included: ICE syndrome (14), posterior polymorphous dystrophy (3), herpetic infection (3), non-herpetic infection (2), complications from retinal detachment (1), congenital corneal dystrophy (1), congenital glaucoma (1), Descemet's membrane detachment (1), Descemet's membrane tear (1), granular dystrophy (1), primary endotheliopathy (1), Riegers' anomaly (1), toxic anterior segment syndrome (1), and unspecified corneal dystrophy (1).

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Likelihood of follow-up was significantly more likely ( $p < 0.05$ ) in some groups than others. Grafts in eyes where pre-graft inflammation and/or steroid use was reported, and in grafts where donor tissue had been transported interstate, were more likely to have been followed. Significant differences in follow-up were also found across groups for graft State, pre-graft corneal neovascularisation, and recipient age groups.

Table 3.4 shows the number of grafts within each of the variable sub-groups, for the recipient factor found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (4,736 registered and 3,263 with follow-up provided) and the percentages, summed vertically, total 100. The result of the Kaplan-Meier survival analysis is also provided.

**Table 3.4 Recipient factors, not significant in univariate analyses**

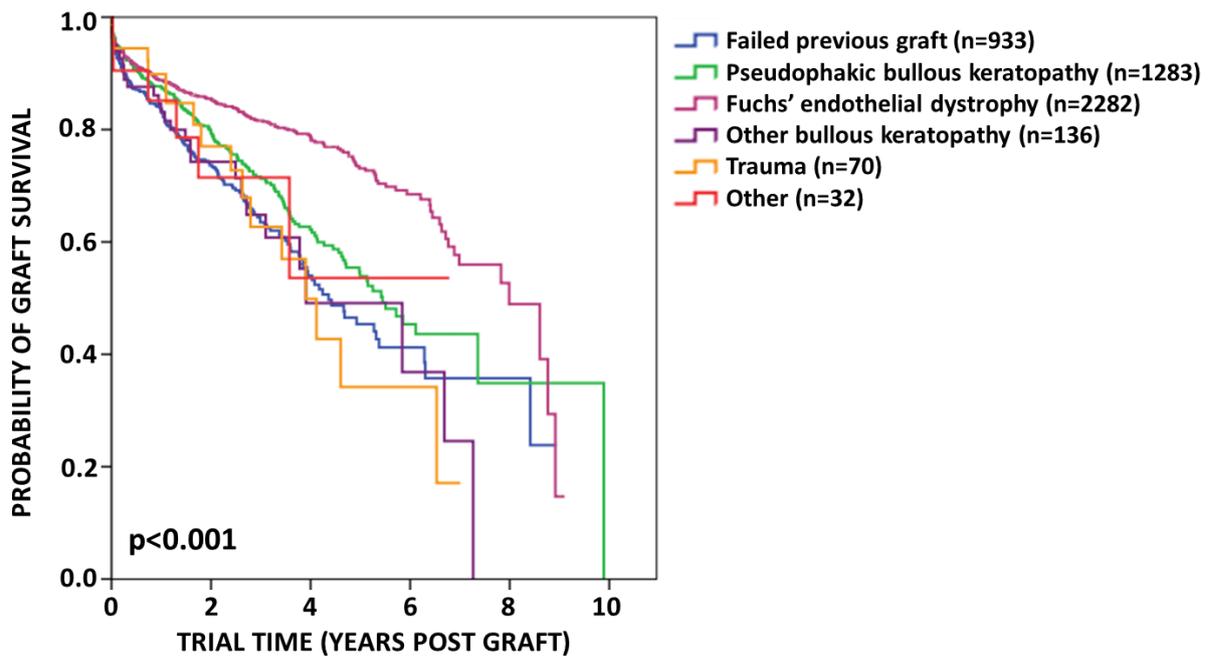
<b>Descemet's Stripping (Automated) Endothelial Corneal Graft</b>		
<b>Recipient Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Eye grafted</b>		
Left	2305 (49%)	1575 (48%)
Right	2431 (51%)	1688 (52%)
<b>Chi<sup>2</sup>=0.00, df=1, p=0.988</b>		
<b>Total</b>	<b>4736 (100%)</b>	<b>3263 (100%)</b>

Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable.

### 3.2.1 DS(A)EK survival: influence of indication for graft

Figure 3.2.1 shows the comparison of graft survival depending on indication for graft. All repeat grafts were analysed together, regardless of original pathology. A significant difference was found across groups (Log Rank Statistic=76.52; df=5; p<0.001), with grafts performed for Fuchs’ endothelial dystrophy having significantly better survival than those performed for the other four specified indications for graft groups (all p<0.003). This variable was retained in multivariate analysis (see section 3.7) suggesting that this is an independent factor significantly affecting graft survival.

Figure 3.2.1 Indication for graft



#### Number at risk (years post-graft)

	1	2	4	6	8
Failed previous graft	437	274	70	19	4
Pseudophakic bullous keratopathy	584	371	118	29	2
Fuchs’ endothelial dystrophy	1180	839	314	93	12
Other bullous keratopathy	55	35	8	3	NA
Trauma	35	19	7	2	NA
Other indication*	15	9	2	1	NA

\*See list on page 111

#### Probability of graft survival (years post-graft)

	1	2	4	6
Failed previous graft	0.84	0.74	0.54	NA
Pseudophakic bullous keratopathy	0.88	0.79	0.62	0.45
Fuchs’s endothelial dystrophy	0.89	0.85	0.79	0.69
Other bullous keratopathy	0.83	0.74	NA	NA
Trauma	0.90	NA	NA	NA
Other indication	NA	NA	NA	NA

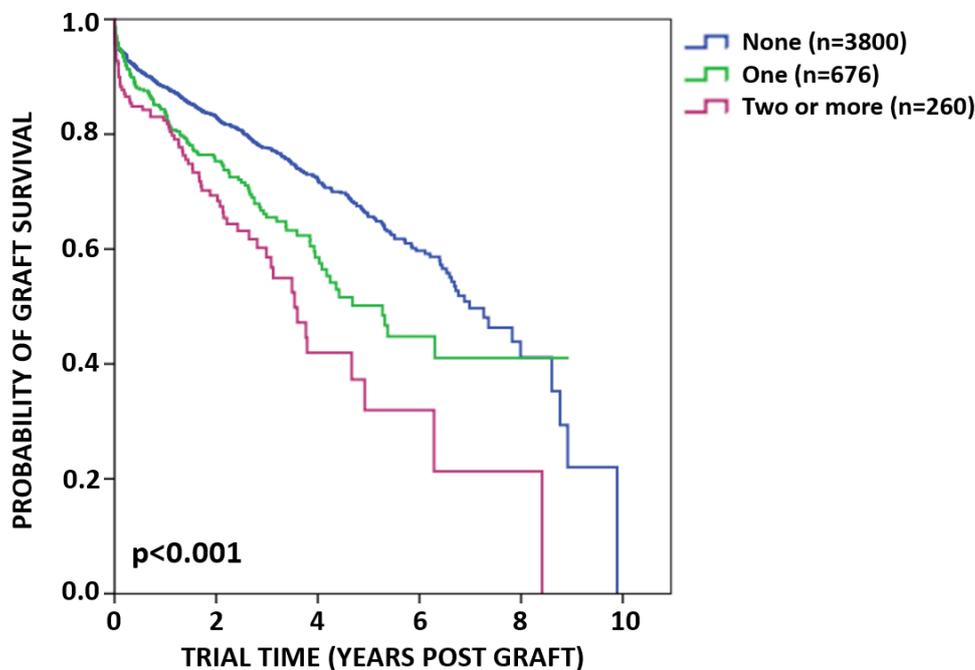
### 3.2.2 DS(A)EK survival: subcategory analyses

The analyses on pages 114 and 115 are of subcategories in an individual indication for graft cohort. The nature of the variables mean that a large percentage of the cohort do not have relevant data. These subgroup-analyses are therefore not included in multivariate analyses. The overarching variable “indication for graft” was included.

#### 3.2.2.1 DS(A)EK survival: influence of the number of previous ipsilateral grafts

Survival was compared across groups based on the number of previous grafts in the same eye (range 1 to 6), as shown in Figure 3.2.2. This difference was significant (Log Rank Statistic=5.60, df=1, p=0.018). Previous grafts may not have been Descemet’s stripping (automated) endothelial keratoplasties. Survival of first grafts is included in the Kaplan-Meier plot for visual reference but these data were excluded from the log rank calculation.

Figure 3.2.2 Number of previous ipsilateral grafts



#### Number at risk (years post-graft)

	1	2	4	6	8
One	311	202	59	16	3
Two or more	127	73	11	3	1

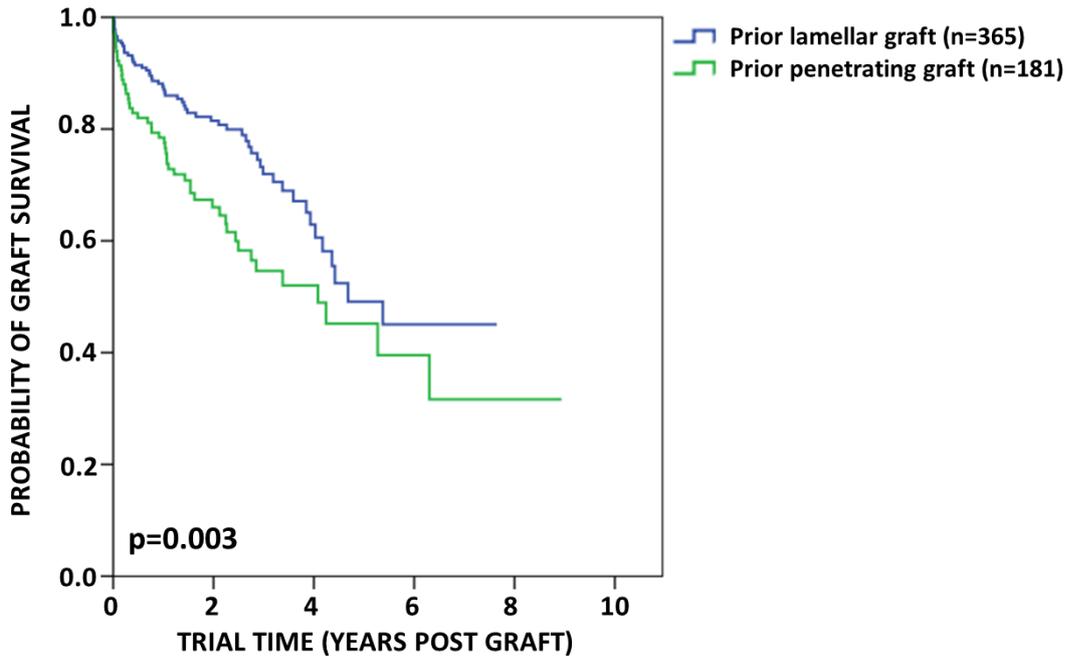
#### Probability of graft survival (years post-graft)

	1	2	4	6
One	0.84	0.75	0.59	NA
Two or more	0.82	0.69	NA	NA

**3.2.2.2 DS(A)EK survival: influence of previous penetrating keratoplasty**

Survival was compared across groups of second grafts (one prior ipsilateral graft) based on whether the previous graft in the same eye was a penetrating keratoplasty. The type of previous graft was not known to the ACGR for 130 grafts and these were excluded from the analysis. A significant difference in survival was found (Log Rank Statistic=8.92, df=1, p=0.003). Three grafts had a previous surviving concurrent graft, while the rest were repeat grafts.

**Figure 3.2.3 Prior penetrating keratoplasty in eye**



**Number at risk (years post-graft)**

	1	2	3	4	5	6
<b>Prior lamellar</b>	167	111	56	29	15	6
<b>Prior PK</b>	84	48	28	18	9	5

**Probability of graft survival (years post-graft)**

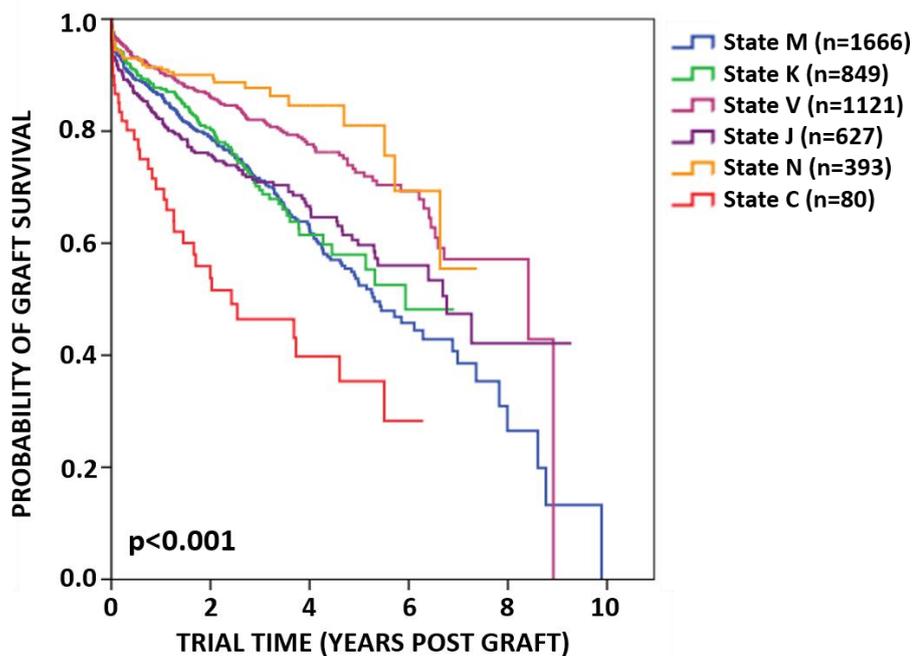
	1	2	3	4
<b>Prior lamellar</b>	0.88	0.82	0.72	0.63
<b>Prior PK</b>	0.79	0.66	0.55	NA

This concludes the subgroup-analyses. Analyses from page 116 onwards are again performed on the full cohort.

### 3.2.3 DS(A)EK survival: influence of Australian State where graft was performed

Figure 3.2.4 shows the comparison of graft survival depending on the Australian State in which the transplantation occurred. A significant difference was found across groups (Log Rank Statistic=78.76; df=5;  $p<0.001$ ), with survival of grafts performed in State C worse than those performed in any other State, and survival of grafts performed in State V or State N significantly better than those performed in State M, State K or State J (all  $p<0.001$ ). This variable was retained in the multivariate analysis (see section 3.7) suggesting that this is an independent factor significantly affecting graft survival.

**Figure 3.2.4 Australian State where graft was performed**



#### Number at risk (years post-graft)

	1	2	4	6	8
State M	788	522	143	38	6
State K	375	222	45	10	NA
State V	619	431	176	60	8
State J	276	206	102	27	4
State N	211	141	43	10	NA
State C	37	25	10	2	NA

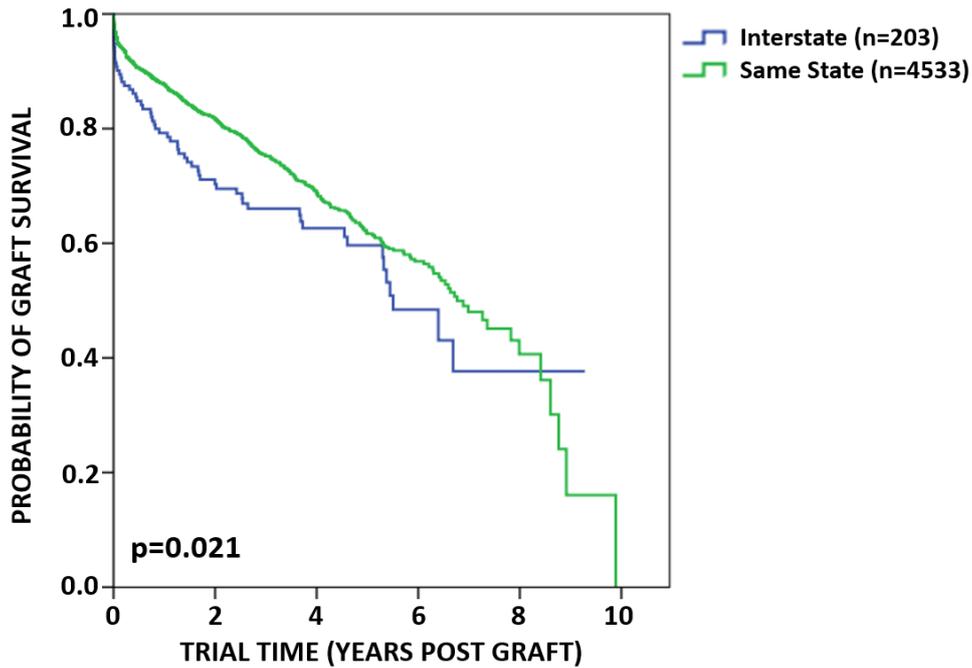
#### Probability of graft survival (years post-graft)

	1	2	4	6
State M	0.87	0.79	0.63	0.46
State K	0.88	0.80	0.62	NA
State V	0.90	0.86	0.78	0.69
State J	0.82	0.76	0.67	0.56
State N	0.91	0.90	0.85	NA
State C	0.70	0.54	NA	NA

### 3.2.4 DSAEK survival: influence of interstate transportation

In some cases corneas are transported interstate via air freight. Figure 3.2.5 shows the comparison of graft survival for grafts where the surgery was performed in the same State as the donor cornea was sourced, compared to those where the donor cornea was from interstate. A significant difference was found between groups (Log Rank Statistic=5.29; df=1; p=0.021). This variable was not retained in the final model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.2.5 Interstate transportation



#### Number at risk (years post-graft)

	1	2	4	6	8
Different State	111	89	51	12	2
Same State	2195	1458	468	135	16

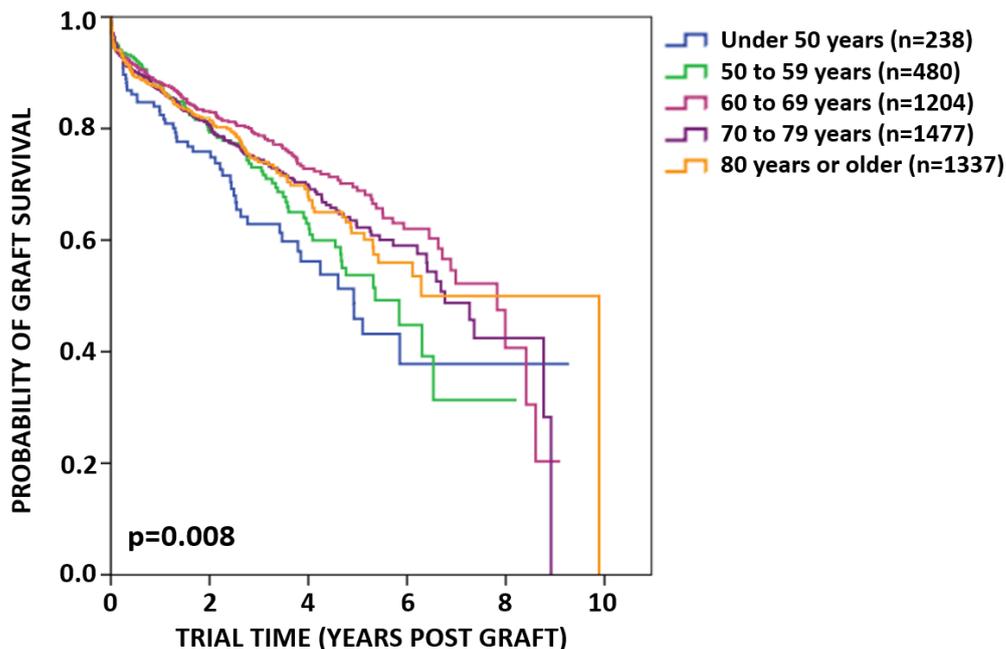
#### Probability of graft survival (years post-graft)

	1	2	4	6
Different State	0.79	0.70	0.63	NA
Same State	0.88	0.82	0.69	0.57

### 3.2.5 DS(A)EK survival: influence of recipient age (years)

Figure 3.2.6 shows the comparison of graft survival depending on the age of the corneal transplant recipient. Data for recipients aged under 40, and those aged over 90, were combined with the next category, due to small numbers in these groups. A significant difference was found across groups (Log Rank Statistic=13.69; df=4; p=0.008), with recipients under 50 years of age having significantly poorer survival than those aged 60 to 69 years (p=0.001). This variable was not retained in the final model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.2.6 Recipient age



#### Number at risk (years post-graft)

	1	2	4	6	8
Under 50 years	108	74	29	7	2
50 to 59 years	257	172	63	10	1
60 to 69 years	643	471	161	58	6
70 to 79 years	719	474	165	48	8
80 years or older	579	356	101	24	1

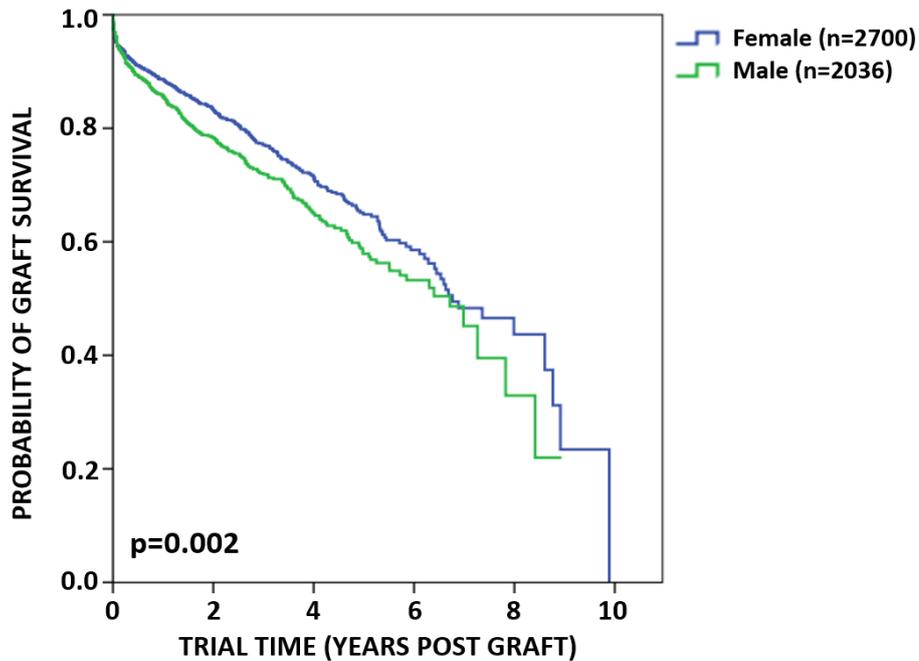
#### Probability of graft survival (years post-graft)

	1	2	4	6
Under 50 years	0.82	0.76	0.56	NA
50 to 59 years	0.88	0.79	0.63	NA
60 to 69 years	0.88	0.83	0.73	0.62
70 to 79 years	0.87	0.81	0.70	0.59
80 years or older	0.87	0.81	0.68	0.56

### 3.2.6 DS(A)EK survival: influence of recipient sex

Comparison of graft survival between male and female transplant recipients is shown in Figure 3.2.7. A significant difference was found between groups (Log Rank Statistic=9.74; df=1; p=0.002). This variable was retained in the final model, suggesting that this is an independent factor significantly affecting graft survival.

Figure 3.2.7 Recipient sex



#### Number at risk (years post-graft)

	1	2	4	6	8
<b>Female</b>	1316	903	319	89	14
<b>Male</b>	990	644	200	58	4

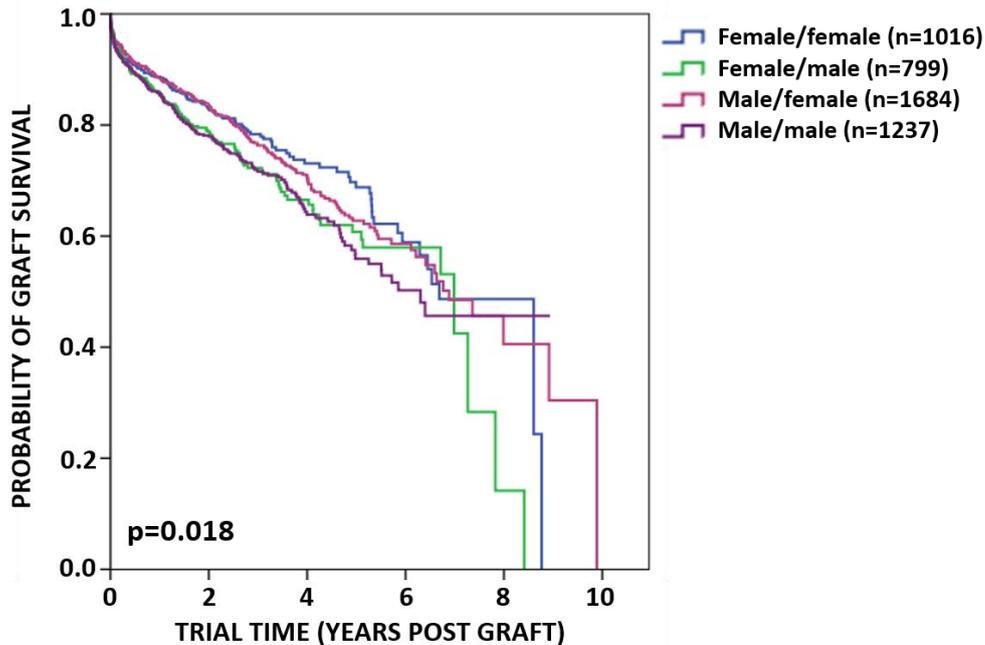
#### Probability of graft survival (years post-graft)

	1	2	4	6
<b>Female</b>	0.89	0.83	0.72	0.59
<b>Male</b>	0.86	0.78	0.65	0.53

### 3.2.7 DS(A)EK survival: influence of donor/recipient sex match/mismatch

Comparison of graft survival across groups based on donor/recipient sex combinations is shown in Figure 3.2.8. A significant difference was found across groups (Log Rank Statistic=10.07; df=3; p=0.018), however none of the individual comparisons were significantly different following Bonferroni correction (all p>0.008). This variable was not retained in the final model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.2.8 Donor/recipient sex match/mismatch



#### Number at risk (years post-graft)

	1	2	4	6	8
Female/female	477	306	111	31	6
Female/male	380	247	79	23	1
Male/female	839	597	208	58	8
Male/male	610	397	121	35	3

#### Probability of graft survival (years post-graft)

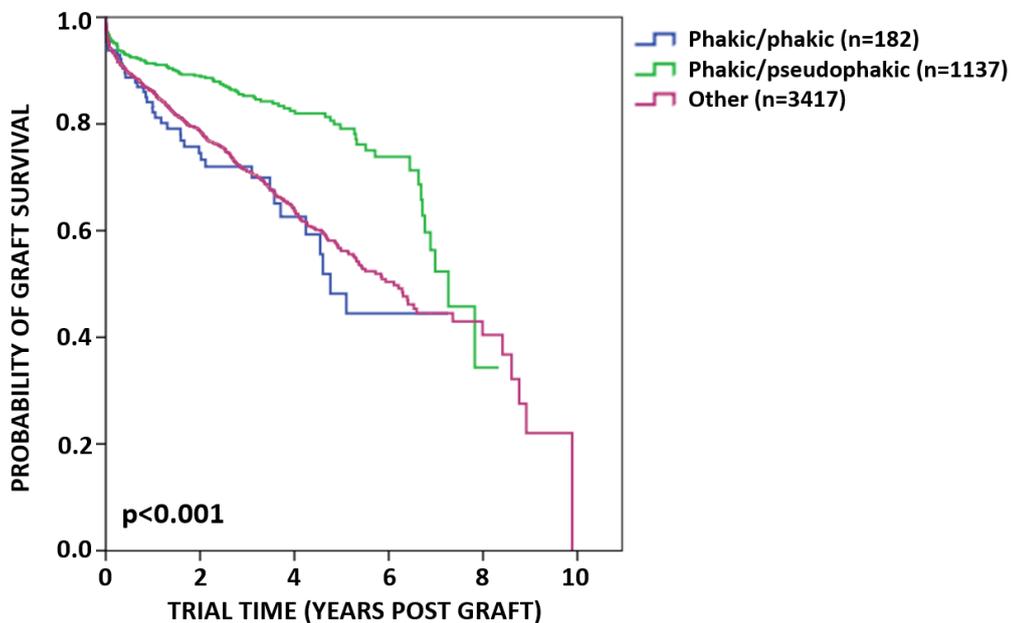
	1	2	4	6
Female/female	0.89	0.83	0.73	0.59
Female/male	0.85	0.79	0.67	0.58
Male/female	0.89	0.83	0.71	0.59
Male/male	0.86	0.78	0.64	0.50

### 3.2.8 DS(A)EK survival: influence of pre- and post-graft lens status

Figure 3.2.9 shows the comparison of graft survival stratified by the change of lens status from pre- to post-graft. “Phakic/phakic” means the eye was phakic both before and after the graft. “Phakic/pseudophakic” means the eye was phakic before the graft and pseudophakic afterwards, having undergone a triple procedure. “Other” means the eye was phakic, pseudophakic or aphakic before the graft and aphakic afterwards, or the eye was aphakic or pseudophakic before the graft and pseudophakic afterwards.

A significant difference was found across groups (Log Rank Statistic=51.11; df=2;  $p<0.001$ ), with grafts performed in eyes that underwent a triple procedure having significantly better survival than those in either of the other two groups (both  $p<0.001$ ). This variable was retained in the multivariate analysis (see section 3.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 3.2.9 Change in lens status from pre- to post-graft**



**Number at risk (years post-graft)**

	1	2	4	6	8
Phakic/phakic	84	60	21	7	NA
Phakic/pseudophakic	619	438	169	49	2
Other	1603	1049	329	91	16

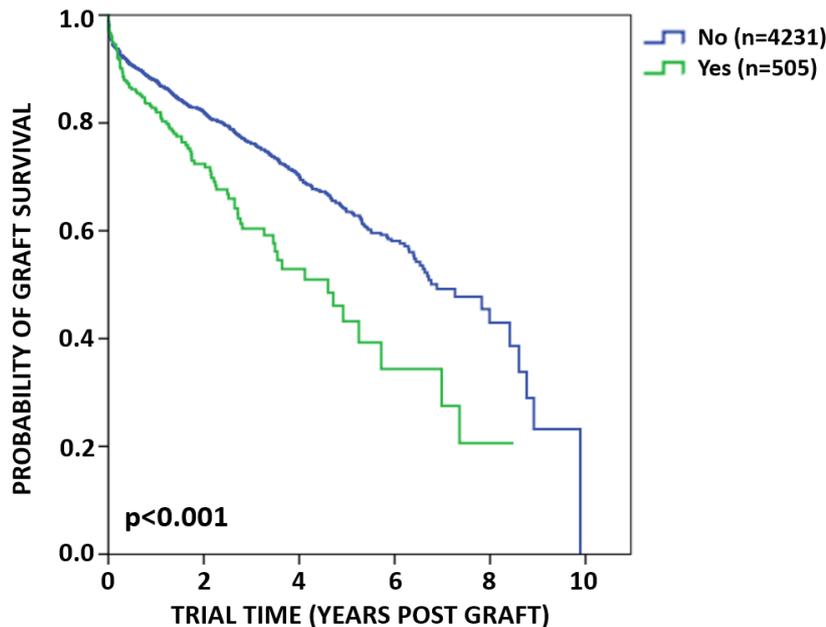
**Probability of graft survival (years post-graft)**

	1	2	4	6
Phakic/phakic	0.82	0.75	0.63	NA
Phakic/pseudophakic	0.91	0.89	0.82	0.74
Other	0.86	0.79	0.64	0.50

### 3.2.9 DS(A)EK survival: influence of pre-graft corneal neovascularisation

Figure 3.2.10 shows the comparison of graft survival between those recipients with corneal neovascularisation pre-graft and those without (Log Rank Statistic=24.11; df=1;  $p<0.001$ ). Recipients with pre-graft neovascularisation had poorer graft survival than those with avascular corneas. This variable was not retained in the final model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.2.10 Pre-graft corneal neovascularisation



#### Number at risk (years post-graft)

	1	2	4	6	8
No neovascularisation	2106	1432	490	141	16
Neovascularisation	200	115	29	6	2

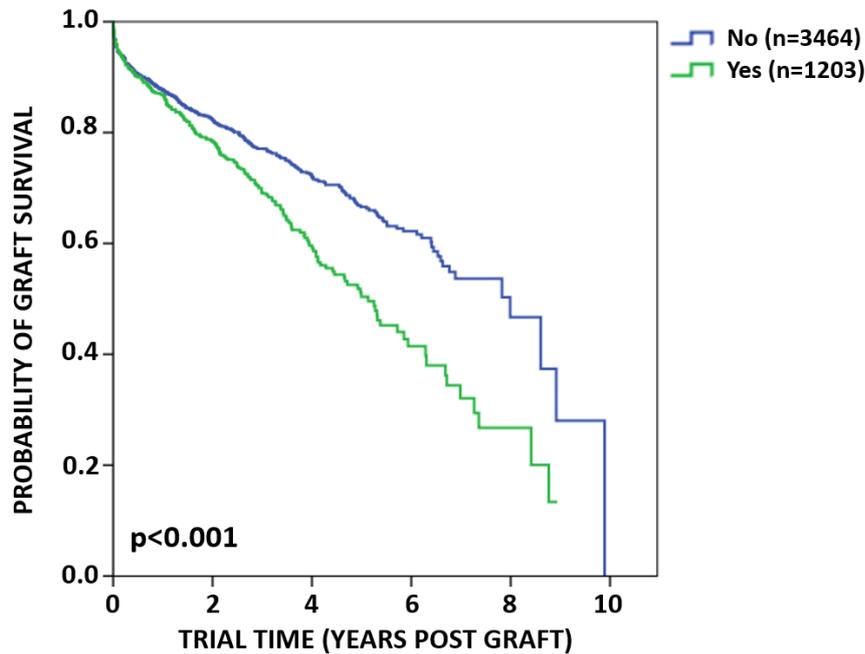
#### Probability of graft survival (years post-graft)

	1	2	4	6
No neovascularisation	0.88	0.82	0.70	0.58
Neovascularisation	0.82	0.72	0.53	NA

### 3.2.10 DS(A)EK survival: influence of inflammation and/or steroid use at time of graft

Figure 3.2.11 shows the comparison of graft survival between grafts performed in an eye with current inflammation and/or steroid use within the past two weeks, compared to those with neither of these factors. This information was not known for 69 grafts and these were excluded from the analysis. The difference was significant (Log Rank Statistic=23.41; df=1;  $p<0.001$ ). Following further analyses where the data were clustered by patient [see references 7 & 8], this variable was no longer found to be significant ( $p=0.134$ ). This variable was therefore excluded from multivariate analyses and is **not** an independent factor significantly affecting graft survival.

Figure 3.2.11 Inflammation and/or steroid use at time of graft



#### Number at risk (years post-graft)

	1	2	4	6	8
No inflammation/steroid use	1667	1129	392	117	12
Inflammation/steroid use	617	402	121	30	6

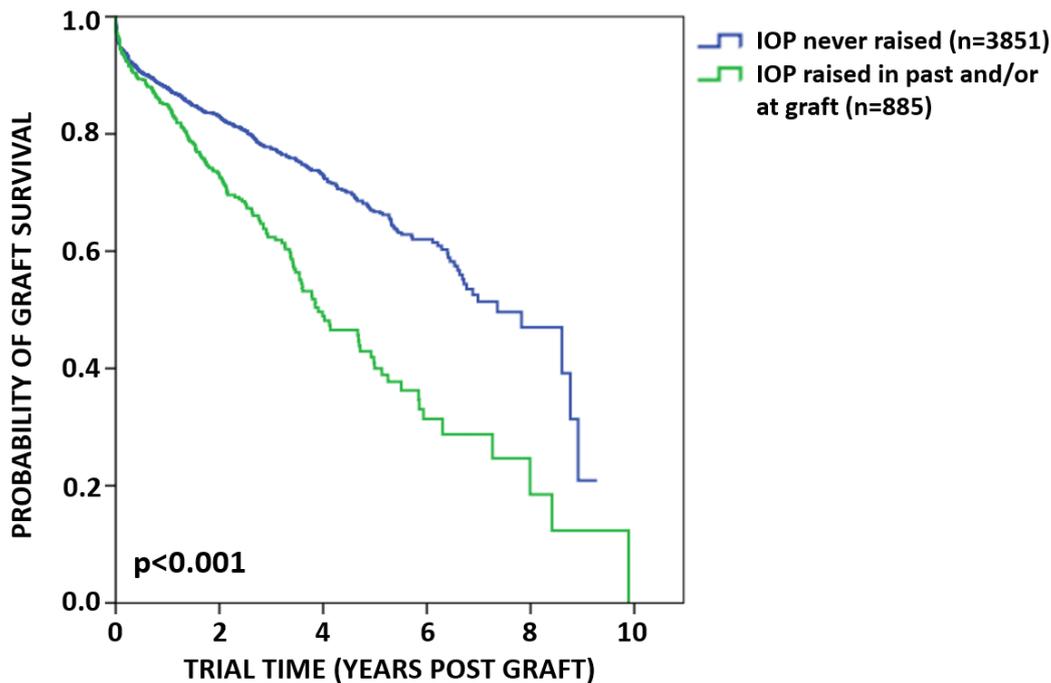
#### Probability of graft survival (years post-graft)

	1	2	4	6
No inflammation/steroid use	0.88	0.82	0.72	0.62
Inflammation/steroid use	0.87	0.78	0.60	0.41

### 3.2.11 DS(A)EK survival: influence of history of raised intraocular pressure (IOP)

Figure 3.2.12 shows the comparison of graft survival between groups based on whether the recipient had a history of raised intraocular pressure (Log Rank Statistic=53.83; df=1;  $p<0.001$ ). This was irrespective of whether IOP was raised at the time of graft. This variable was retained in the final model (see section 3.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 3.2.12 History of raised intraocular pressure**



#### Number at risk (years post-graft)

	1	2	4	6	8
No raised IOP	1898	1304	454	130	15
Raised IOP	408	243	65	17	3

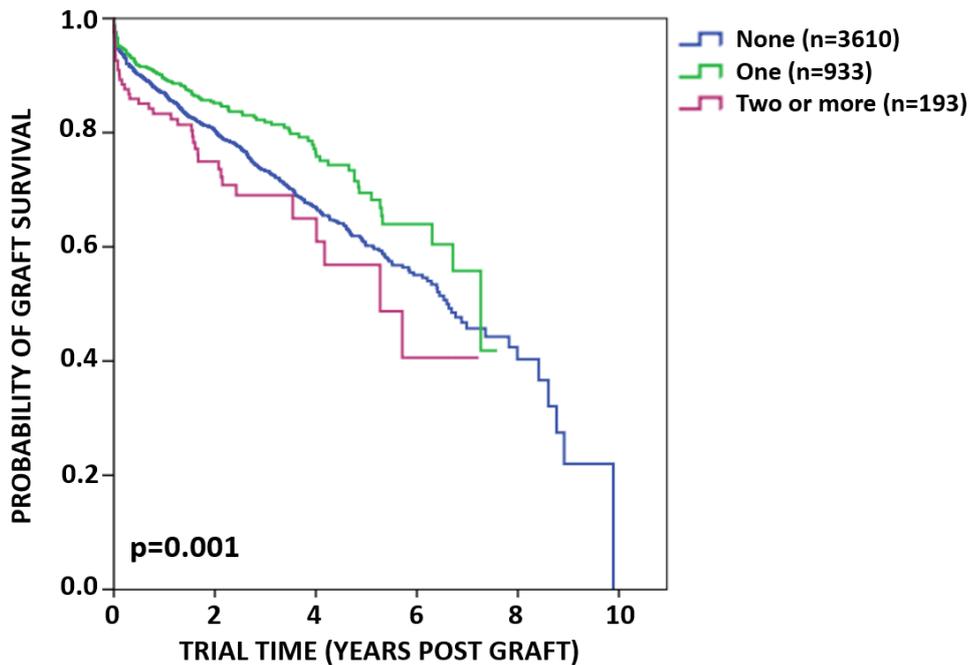
#### Probability of graft survival (years post-graft)

	1	2	4	6
No raised IOP	0.88	0.83	0.73	0.62
Raised IOP	0.85	0.73	0.49	NA

**3.2.12 DS(A)EK survival: influence of previous contralateral graft**

Figure 3.2.13 shows the comparison of graft survival between grafts where the recipient had undergone a previous contralateral graft and those where they had not. A significant difference was found across groups (Log Rank Statistic=15.10; df=2; p=0.001), with grafts performed in recipients who had undergone one prior corneal graft in the contralateral eye having better survival than those who had undergone none or more than one (both p=0.001). This variable was not retained in the final model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

**Figure 3.2.13 Previous contralateral graft/s**



**Number at risk (years post-graft)**

	1	2	4	6	8
None	1746	1170	394	118	18
One	470	319	109	25	NA
Two or more	90	58	16	NA	NA

**Probability of graft survival (years post-graft)**

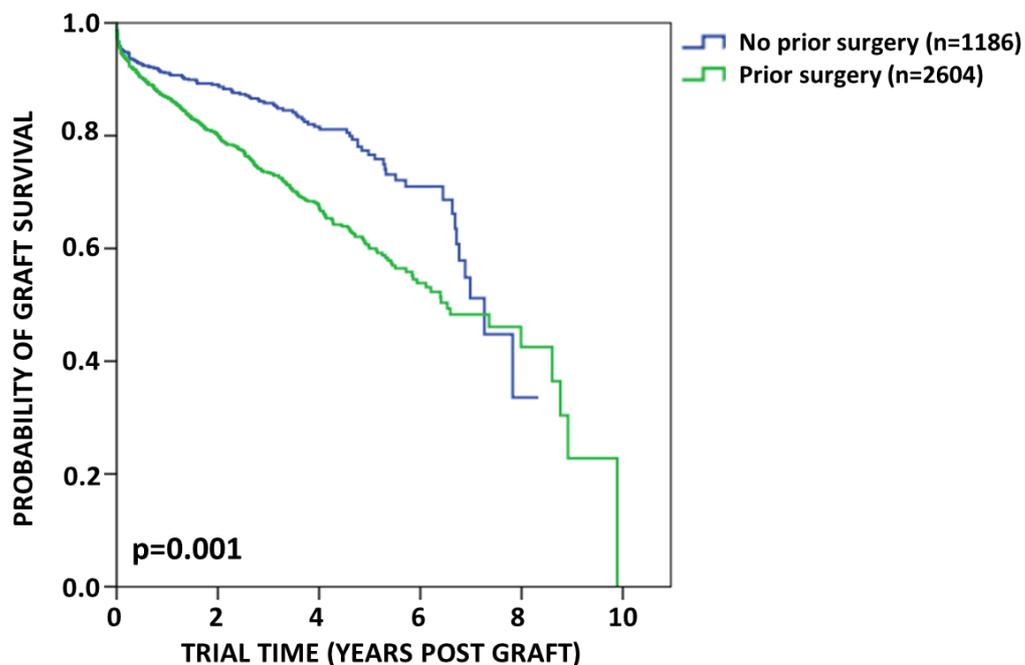
	1	2	4	6
None	0.87	0.80	0.67	0.55
One	0.90	0.85	0.77	0.64
Two or more	0.83	0.75	NA	NA

The analysis on page 126 is conducted using data only from **first grafts** (no previous ipsilateral grafts). This subgroup-analysis was not included in multivariate analyses, as it is collinear with indication for graft and change in lens status.

### 3.2.13 DS(A)EK survival: influence of history of previous intraocular surgery in ipsilateral eye

Figure 3.2.14 shows the comparison of graft survival between first grafts performed in an eye that had undergone previous intraocular surgery, compared with first grafts performed in an eye that had not (Log Rank Statistic=29.46; df=1;  $p<0.001$ ). While surgeons were not asked to specify what type of previous surgery recipients had undergone, in the majority of cases (2559/3790, 68%) the lens status of the eye pre-graft (pseudophakic or aphakic) indicated that they had undergone cataract extraction, with or without IOL insertion. Surgeons were unable to say if previous surgery had occurred in 10 first grafts and these were excluded from the analysis.

Figure 3.2.14 History of previous intraocular surgery in the ipsilateral eye



#### Number at risk (years post-graft)

	1	2	5	6	8
No prior surgery	626	456	176	52	2
Prior surgery	1238	813	272	76	12

#### Probability of graft survival (years post-graft)

	1	2	4	6
No prior surgery	0.91	0.89	0.82	0.71
Prior surgery	0.87	0.80	0.67	0.54

### 3.3 Graft Era

Table 3.5 shows the number of grafts registered and followed, in blocks of two years. The percentages, which should be summed vertically, total 100.

**Table 3.5 Graft era**

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft Graft Era</b>		
<b>Year of graft</b>	<b>Registered (%)</b>	<b>Followed (%)</b>
Pre 2006	2 (<1%)	2 (<1%)
2006/2007	103 (2%)	91 (3%)
2008/2009	545 (12%)	509 (16%)
2010/2011	858 (18%)	748 (23%)
2012/2013	1154 (24%)	966 (30%)
2014/2015	1253 (26%)	910 (28%)
2016/2017	821 (17%)	37 (1%)
<b>Total</b>	<b>4736 (100%)</b>	<b>3263 (100%)</b>

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses and found to be significant ( $p < 0.001$ ). Level of follow-up reduces as time since graft reduces, with 94% of grafts performed in 2008/09 followed, 87% of grafts performed in 2010/11, and 84% of grafts performed in 2012/13, compared with 73% of grafts performed in 2014/15 and just 5% of grafts performed in 2016/17.

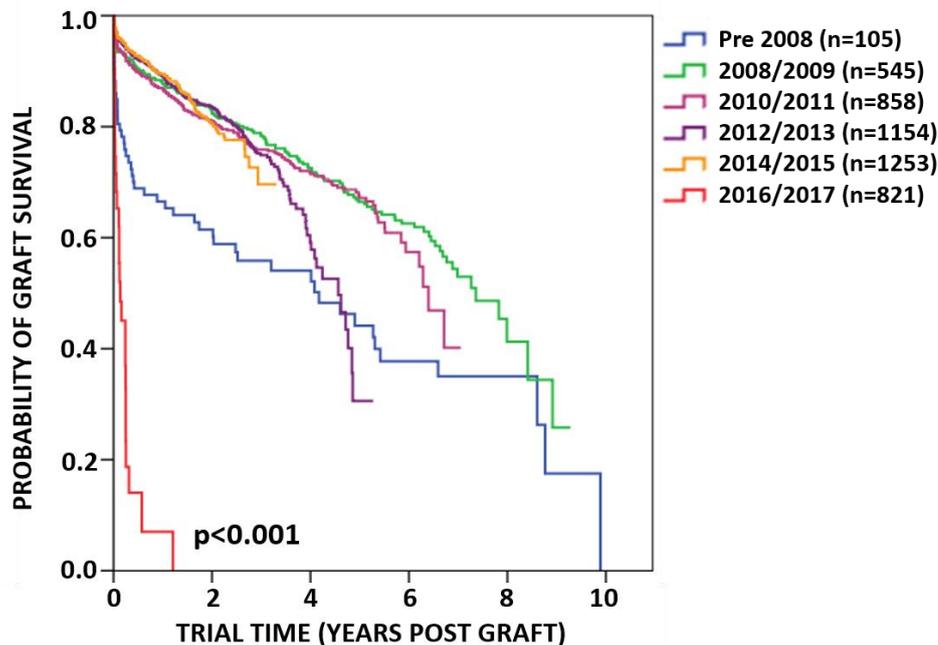
Consideration was given to the effect of follow-up lag time on this analysis. Up-to-date information on failed grafts is more likely to be known than for surviving grafts. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. A "lag time" operates at the furthest end of each curve in a Kaplan Meier plot. This effect is most pronounced in the early years following graft registration, when requests have not yet been made for follow-up information, and tends to reduce predictably over time. In consequence, the variable is treated as "time variant" in multivariate analyses.

Of the grafts performed in 2016/2017 just six of the grafts with follow-up were surviving at the time of follow-up. This equates to 16% of followed grafts, and <1% of registered grafts from this cohort. The remaining 31 grafts were early failures, the majority of which were recorded as failed when a replacement graft was registered.

### 3.3.1 DS(A)EK survival: influence of era of graft

Figure 3.3.1 shows the comparison of graft survival between eras of graft, stratified into two-year groups. The two grafts performed pre-2006 were combined with the 2006/2007 group for this analysis. The difference across groups was significant (Log Rank Statistic=57.38; df=5;  $p<0.001$ ), with grafts performed in 2016/2017 having significantly worse survival than those performed in any other era (all  $p<0.001$ , see comment regarding “lag time” on page 127), and grafts performed prior to 2008 having significantly worse survival than those performed in 2008/2009, 2010/2011 or 2014/2015 (all  $p<0.001$ ). This variable was retained in the final model (see section 3.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 3.3.1 Graft era



#### Number at risk (years post-graft)

	1	2	4	6	8
<b>Pre 2008</b>	55	47	28	15	9
<b>2008/2009</b>	390	311	194	104	9
<b>2010/2011</b>	557	445	252	28	NA
<b>2012/2013</b>	726	534	45	NA	NA
<b>2014/2015</b>	577	210	NA	NA	NA
<b>2016/2017</b>	1	NA	NA	NA	NA

#### Probability of graft survival (years post-graft)

	1	2	4	6
<b>Pre 2008</b>	0.67	0.62	0.54	NA
<b>2008/2009</b>	0.88	0.83	0.73	0.63
<b>2010/2011</b>	0.87	0.81	0.72	0.57
<b>2012/2013</b>	0.89	0.83	0.59	NA
<b>2014/2015</b>	0.90	0.80	NA	NA
<b>2016/2017</b>	NA	NA	NA	NA

### 3.4 Surgery and Surgeon Factors

Table 3.6 shows the number of grafts within each of the variable sub-groups, for the surgery and surgeon factors examined in this report, which were found to be **significant** in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (4,736 registered and 3,263 followed) and the percentages, which should be summed vertically for each variable, total 100.

69% was selected as the cut-off point for the follow-up categories as this (68.9%) was the average percentage of follow-up for all DS(A)EK, regardless of surgeon experience.

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Likelihood of follow-up was significantly more likely ( $p < 0.05$ ) in some groups than others. Lower rates of follow-up had been received for grafts performed using forceps. Significant differences in follow-up were also found across groups for graft and incision size, with larger grafts more likely to have follow-up. There were significant differences in follow-up levels between individual surgeons. Due to the nature of the variable, follow-up was, logically, significantly higher ( $p < 0.001$ ) for grafts performed by surgeons with 100+ followed grafts and  $\geq 69\%$  follow-up.

Table 3.6 Surgery and surgeon factors, significant in univariate analyses

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Size of graft (diameter)</b>		
Less than 8.25 mm	1361 (29%)	857 (26%)
8.25 mm or more	2974 (63%)	2114 (65%)
Not advised	401 (8%)	292 (9%)
<b>Size of incision</b>		
Up to 4.0 mm	481 (10%)	274 (8%)
4.1 mm to 4.5 mm	353 (7%)	195 (6%)
4.6 mm to 5.0 mm	818 (17%)	521 (16%)
5.1 mm or more	912 (19%)	684 (21%)
Not advised	2172 (46%)	1589 (49%)
<b>Use of forceps</b>		
No	1362 (29%)	520 (16%)
Yes	626 (13%)	355 (11%)
Not advised	2748 (58%)	2388 (73%)
<b>Use of viscoelastic</b>		
No	1543 (33%)	589 (18%)
Yes	230 (5%)	97 (3%)
Not advised	2963 (63%)	2577 (79%)
<b>The Centre effect</b>		
Fewer than 100 registered DS(A)EK	1663 (35%)	1051 (32%)
Surgeon H	507 (11%)	386 (12%)
Surgeon J	380 (8%)	291 (9%)
Surgeon K	239 (5%)	229 (7%)
Surgeon L	220 (5%)	176 (5%)
Surgeon Z	201 (4%)	147 (5%)
Surgeon X	166 (4%)	129 (4%)
Surgeon C	158 (3%)	136 (4%)
Surgeon V	150 (3%)	119 (4%)
Surgeon B	140 (3%)	104 (3%)
Surgeon N	135 (3%)	92 (3%)
Surgeon M	128 (3%)	115 (4%)
Surgeon Q	115 (2%)	22 (<1%)
Surgeon W	114 (2%)	70 (2%)
Surgeon E	111 (2%)	42 (1%)
Surgeon R	104 (2%)	74 (2%)
Surgeon T	105 (2%)	46 (1%)
Surgeon Y	100 (2%)	34 (1%)
<b>Surgeon volume</b>		
Fewer than 100 registered DS(A)EK	1663 (35%)	1051 (32%)
100+ registered DS(A)EK, <69% follow-up	1886 (40%)	1520 (47%)
100+ registered DS(A)EK, ≥69% follow-up	1187 (25%)	692 (21%)
<b>Total</b>	<b>4736 (100%)</b>	<b>3263 (100%)</b>

Table 3.7 shows the number of grafts within each of the variable sub-groups, for the donor and eye banking factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (4,736 registered and 3,263 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The result of the Kaplan-Meier survival analysis is also provided for each variable.

**Table 3.7 Surgery and surgeon factors, not significant in univariate analyses**

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Type of graft</b>		
DSEK	2571 (54%)	2044 (63%)
DSAEK	1936 (41%)	1080 (33%)
UT-DSAEK*	75 (2%)	19 (<1%)
Not advised	154 (3%)	120 (4%)
<b>Chi<sup>2</sup>=1.55, df=2, p=0.460</b>		
<b>Use of glide</b>		
No	320 (7%)	173 (5%)
Yes	2590 (55%)	1459 (45%)
Not advised	1826 (39%)	1631 (50%)
<b>Chi<sup>2</sup>=2.28, df=1, p=0.131</b>		
<b>Use of anterior chamber maintainer</b>		
No	1157 (24%)	459 (14%)
Yes	616 (13%)	227 (7%)
Not advised	2963 (63%)	2577 (79%)
<b>Chi<sup>2</sup>=0.66, df=1, p=0.418</b>		
<b>Donor lenticule folded</b>		
No	1751 (37%)	673 (21%)
Yes	55 (1%)	35 (1%)
Not advised	2930 (32%)	2555 (78%)
<b>Chi<sup>2</sup>=0.16, df=1, p=0.687</b>		
<b>Total</b>	<b>4736 (100%)</b>	<b>3263 (100%)</b>

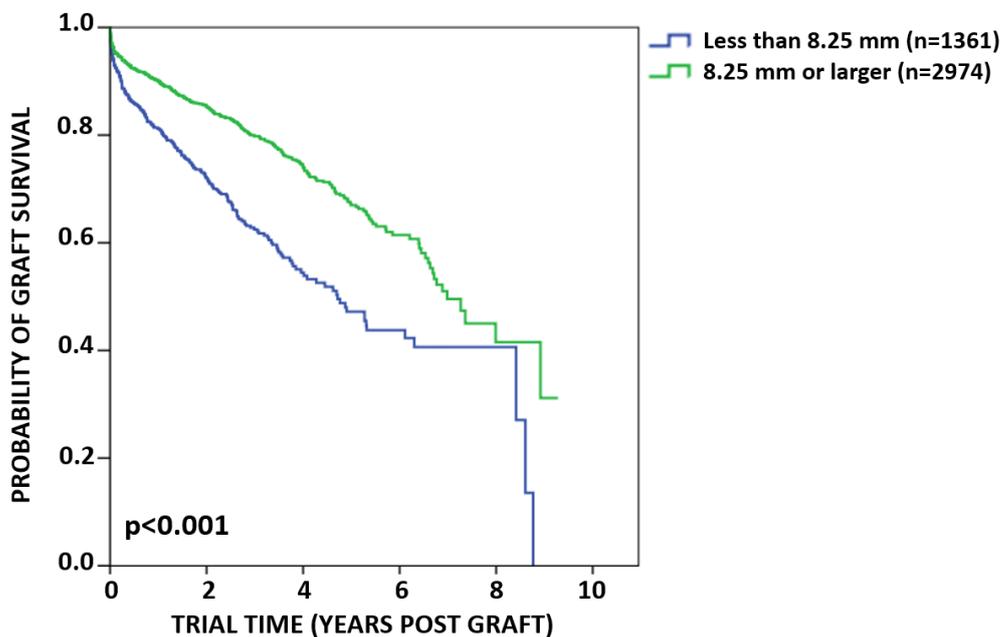
Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised.

\*UT-DSEK = Ultra-thin Descemet's Stripping Endothelial Keratoplasty

### 3.4.1 DS(A)EK survival: influence of graft size

Figure 3.4.1 shows a comparison of graft survival depending on the size of the graft, based on the donor button diameter, as reported by surgeons. This information was not reported for 401 grafts. A significant difference was found across groups (Log Rank Statistic=69.98; df=1;  $p<0.001$ ). Data on this variable were not provided in 8% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=68.80; df=2;  $p<0.001$ ). Graft size was thus categorised into these four groups for multivariate analysis. This variable was retained in the final model (see section 3.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 3.4.1 Graft size



#### Number at risk (years post-graft)

	1	2	4	6	8
Less than 8.25 mm	566	338	90	32	5
8.25 mm or more	1530	1052	350	100	11

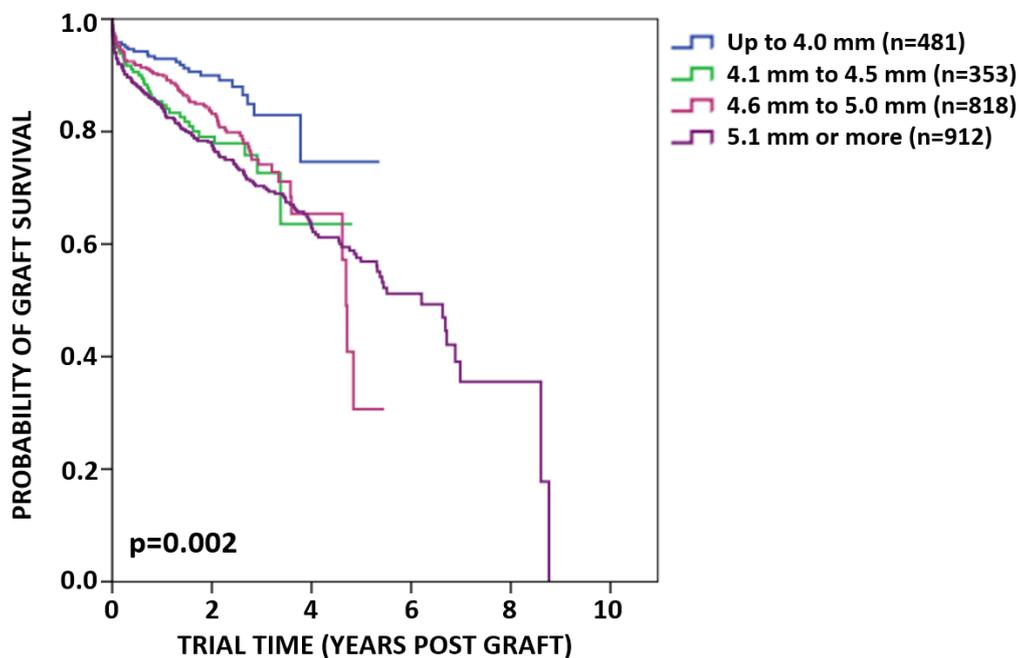
#### Probability of graft survival (years post-graft)

	1	2	4	6
Less than 8.25 mm	0.81	0.72	0.55	0.44
8.25 mm or more	0.90	0.85	0.74	0.61

### 3.4.2 DS(A)EK survival: influence of size of incision

Figure 3.4.2 shows a comparison of graft survival depending on the size of the incision made to insert the donor lenticule, as reported by surgeons. This information was not reported for 2172 grafts. A significant difference was found across groups (Log Rank Statistic=15.18; df=3; p=0.002), with grafts with an incision size up to 4.0 mm having significantly better survival than those with an incision size of 4.1 mm to 5.0 mm (p=0.006) and 5.1 mm or more (p<0.001). Data on this variable were not provided in 46% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=19.64; df=4; p=0.001). Incision size was thus categorised into these four groups for multivariate analysis. This variable was retained in the final model (see section 3.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 3.4.2 Size of incision



#### Number at risk (years post-graft)

	1	2	3	4	5	6
Up to 4.0 mm	190	113	34	6	2	NA
4.1 mm to 4.5 mm	130	70	20	2	NA	NA
4.6 mm to 5.0 mm	380	227	83	14	2	NA
5.1 mm or more	481	351	226	139	84	29

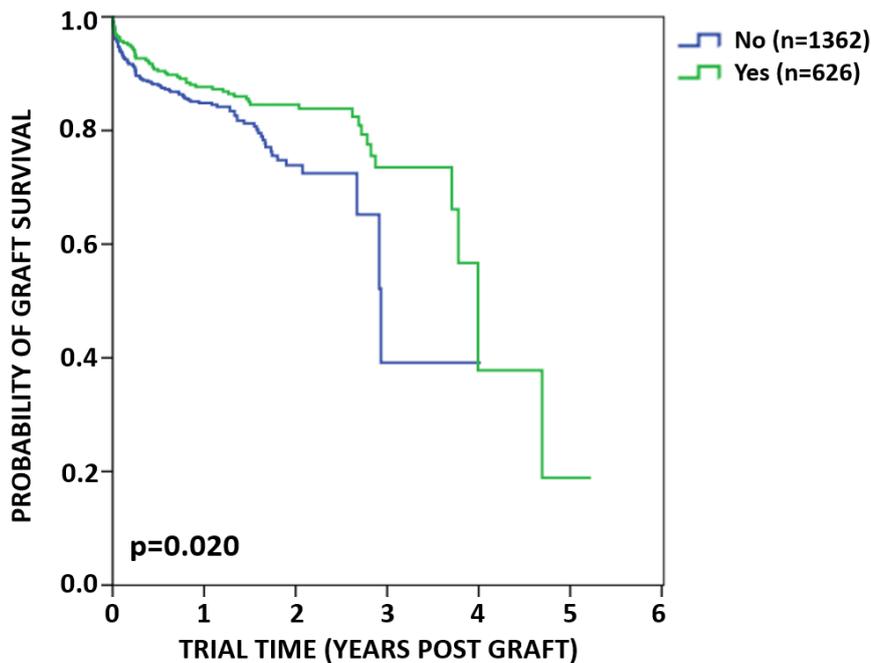
#### Probability of graft survival (years post-graft)

	1	2	3	4	5	6
Up to 4.0 mm	0.93	0.90	0.83	NA	NA	NA
4.1 mm to 4.5 mm	0.85	0.79	0.73	NA	NA	NA
4.6 mm to 5.0 mm	0.90	0.83	0.74	NA	NA	NA
5.1 mm or more	0.84	0.78	0.70	0.63	0.57	0.51

### 3.4.3 DS(A)EK survival: influence of use of forceps

Figure 3.4.3 shows a comparison of graft survival depending on whether forceps were used to perform the graft, as reported by surgeons. This information was not reported for 2748 grafts. A significant difference was found across groups (Log Rank Statistic=5.41; df=1; p=0.020). This variable was not included in the multivariate analyses due to the high percentage (58%) of missing data.

**Figure 3.4.3 Use of forceps**



#### Number at risk (years post-graft)

	1	2	3	4	5
<b>No forceps</b>	288	66	3	1	NA
<b>Forceps</b>	228	123	30	2	1

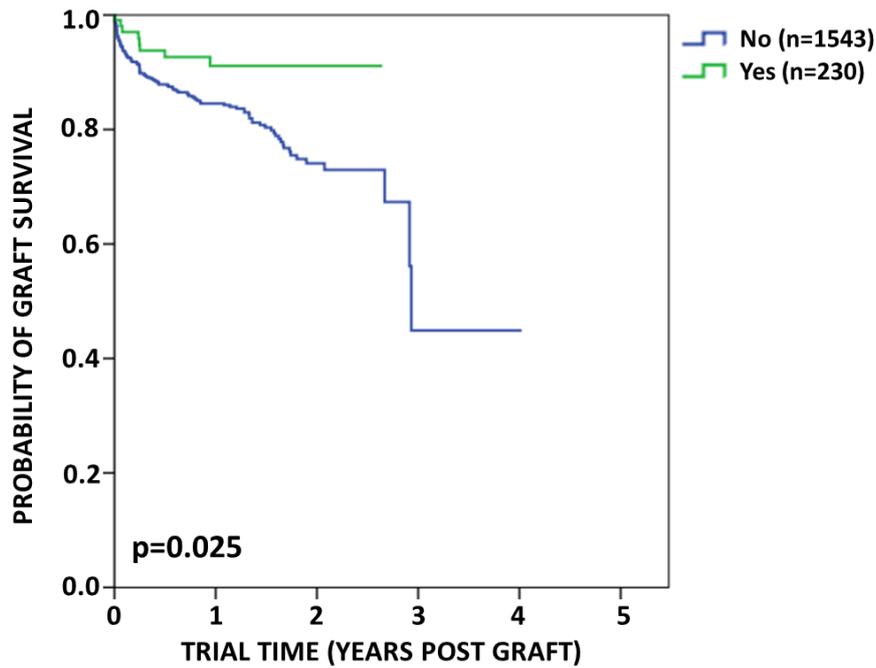
#### Probability of graft survival (years post-graft)

	1	2	3
<b>No forceps</b>	0.85	0.74	NA
<b>Forceps</b>	0.88	0.85	0.74

### 3.4.4 DS(A)EK survival: influence of use of viscoelastic

Figure 3.4.4 shows a comparison of graft survival depending on the use of viscoelastic, as reported by surgeons. This information was not reported for 2963 grafts. A significant difference was found across groups (Log Rank Statistic=5.00; df=1; p=0.025). This variable was not included in the multivariate analyses due to the high percentage (63%) of missing data.

**Figure 3.4.4 Use of viscoelastic**



#### Number at risk (years post-graft)

	1	2	3	4
No viscoelastic	325	81	4	1
Viscoelastic	55	8	NA	NA

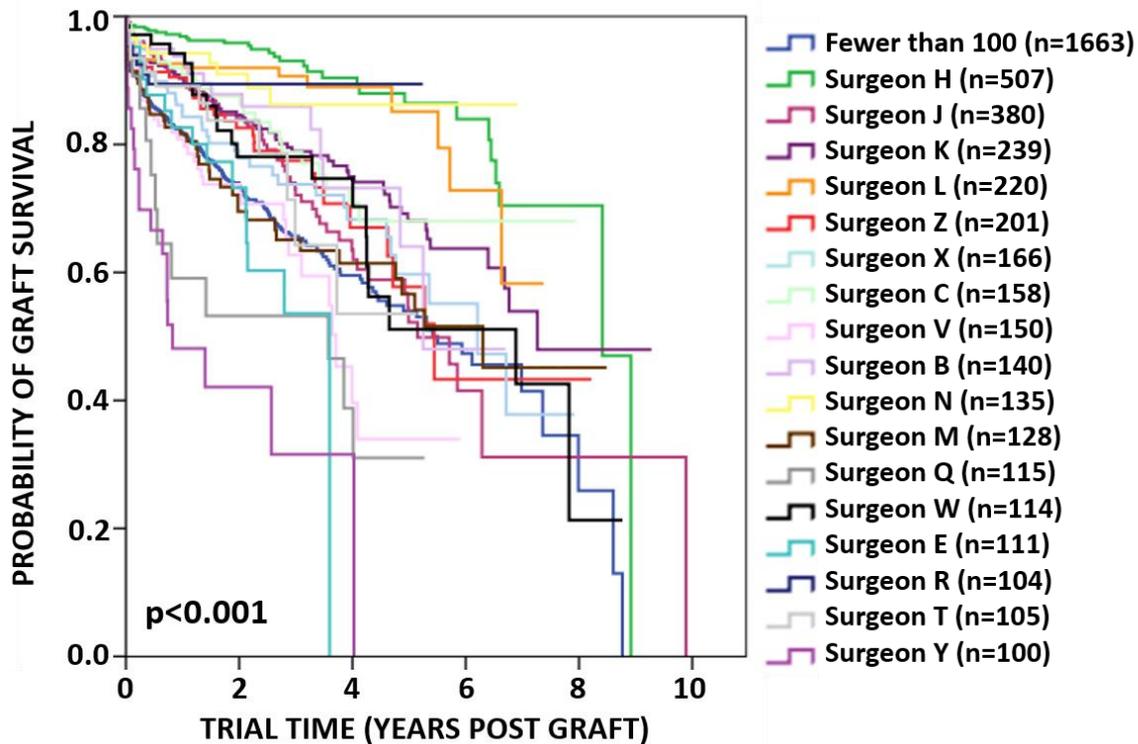
#### Probability of graft survival (years post-graft)

	1	2
No viscoelastic	0.85	0.74
Viscoelastic	0.91	NA

### 3.4.5 DS(A)EK survival: influence of the Centre effect

Figure 3.4.5 shows the comparison of graft survival for individual surgeons which there were 100 or more DS(A)EKs registered, and all other grafts (performed by 101 surgeons) combined (Log Rank Statistic=194.30; df=17;  $p<0.001$ ). This analysis indicates that there is a significant Centre effect. This variable was not included in the multivariate analysis as it was collinear with the surgeon volume and follow-up variable shown in Figure 3.4.6.

Figure 3.4.5 The Centre effect



Note: To preserve anonymity, surgeons have been identified using random letters of the alphabet. These identifying letters do not correspond with those used in chapters reporting on other types of graft, i.e. Surgeon W in this chapter is not necessarily the same surgeon identified as Surgeon W in the chapter on penetrating keratoplasty.

**Number at risk (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>
<b>&lt;100 DS(A)EK registered</b>	698	405	107	28	3
<b>Surgeon H</b>	306	213	75	34	7
<b>Surgeon J</b>	195	144	42	9	1
<b>Surgeon K</b>	194	160	89	27	4
<b>Surgeon L</b>	141	107	41	10	NA
<b>Surgeon Z</b>	113	79	18	2	1
<b>Surgeon X</b>	90	64	36	8	NA
<b>Surgeon C</b>	88	69	29	6	NA
<b>Surgeon V</b>	73	50	7	NA	NA
<b>Surgeon B</b>	71	47	10	3	NA
<b>Surgeon N</b>	69	44	3	2	NA
<b>Surgeon M</b>	74	53	29	16	1
<b>Surgeon Q</b>	10	9	5	NA	NA
<b>Surgeon W</b>	61	38	17	6	1
<b>Surgeon E</b>	32	17	NA	NA	NA
<b>Surgeon R</b>	42	23	6	NA	NA
<b>Surgeon T</b>	38	21	3	NA	NA
<b>Surgeon Y</b>	11	4	1	NA	NA

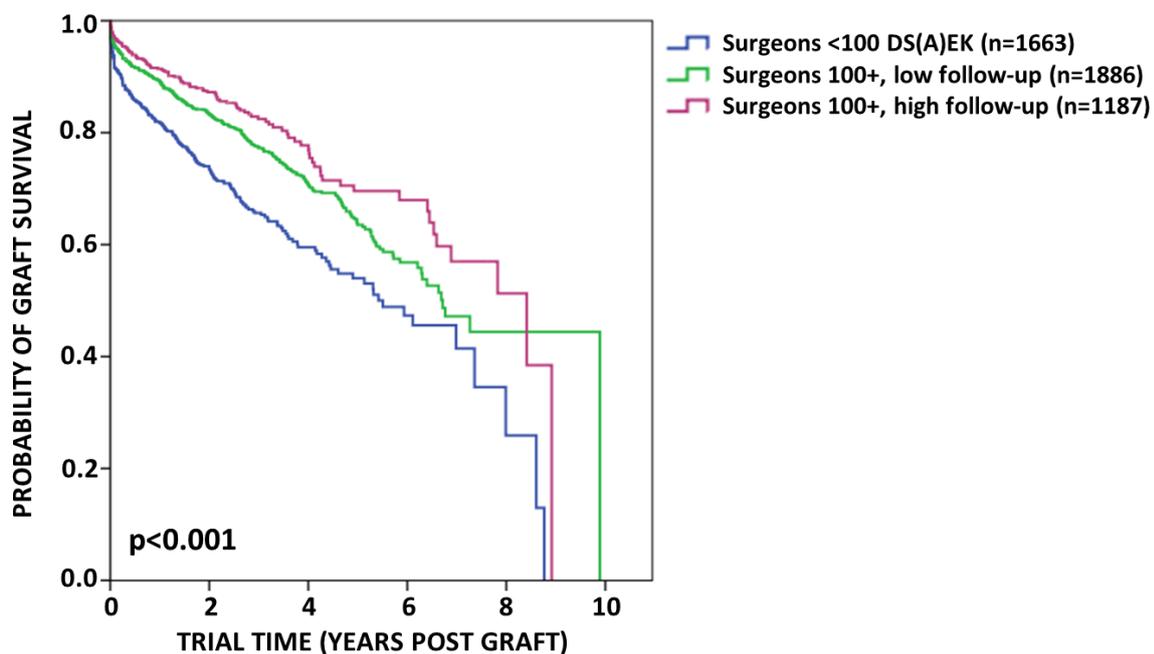
**Probability of graft survival (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>
<b>&lt;100 DS(A)EK registered</b>	0.82	0.74	0.60	0.47
<b>Surgeon H</b>	0.97	0.96	0.90	0.84
<b>Surgeon J</b>	0.90	0.84	0.64	NA
<b>Surgeon K</b>	0.90	0.85	0.75	0.64
<b>Surgeon L</b>	0.93	0.92	0.89	NA
<b>Surgeon Z</b>	0.91	0.83	NA	NA
<b>Surgeon X</b>	0.84	0.78	0.68	NA
<b>Surgeon C</b>	0.91	0.88	0.71	NA
<b>Surgeon V</b>	0.81	0.74	NA	NA
<b>Surgeon B</b>	0.94	0.88	NA	NA
<b>Surgeon N</b>	0.94	0.91	NA	NA
<b>Surgeon M</b>	0.82	0.70	0.61	NA
<b>Surgeon Q</b>	NA	NA	NA	NA
<b>Surgeon W</b>	0.94	0.78	NA	NA
<b>Surgeon E</b>	0.83	NA	NA	NA
<b>Surgeon R</b>	0.89	0.89	NA	NA
<b>Surgeon T</b>	0.89	0.84	NA	NA
<b>Surgeon Y</b>	NA	NA	NA	NA

### 3.4.6 DS(A)EK survival: influence of surgeon volume (25+ followed DS(A)EKs) grouped by level of follow-up

Figure 3.4.6 shows the comparison of graft survival between grafts performed by surgeons with 100+ DS(A)EKs with average or better ( $\geq 69\%$ ) follow-up, to those with lower than average follow-up ( $< 69\%$ ), and to low volume ( $< 100$ ) surgeons. This comparison was significant (Log Rank Statistic=61.06;  $df=2$ ;  $p<0.001$ ), with grafts performed by surgeons with 100+ DS(A)EKs with average or better ( $\geq 69\%$ ) follow-up having significantly better survival than the other two groups (both  $p<0.001$ ). This variable was retained in the multivariate analysis (see section 3.7) suggesting that this is an independent factor significantly affecting graft survival.

**Figure 3.4.6 Surgeon volume and level of follow-up**



#### Number at risk (years post-graft)

	1	2	4	6	8
<100 registered DS(A)EK	698	405	107	28	3
100+ DS(A)EK, low follow-up	1081	796	308	77	7
100+ DS(A)EK, high follow-up	527	346	104	41	8

#### Probability of graft survival (years post-graft)

	1	2	4	6
<100 registered DS(A)EK	0.82	0.74	0.60	0.47
100+ DS(A)EK, low follow-up	0.89	0.83	0.71	0.57
100+ DS(A)EK, high follow-up	0.91	0.87	0.78	0.68

### 3.5 Operative Procedures at the Time of Graft

Table 3.8 shows the number of grafts for which certain operative procedures were performed at the time of graft. The sum of these numbers for each variable equals the total number of grafts (4,736 registered and 3,263 followed) and the percentages, which should be summed vertically for each variable, total 100. Neither of these factors were found to be significant in univariate analyses. The result of the Kaplan-Meier survival analysis is also provided for each variable.

**Table 3.8 Operative procedures at graft, not significant in univariate analyses**

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Peripheral iridectomy at time of graft</b>		
No	4420 (93%)	3061 (94%)
Yes	316 (7%)	202 (6%)
<b>Chi<sup>2</sup>=0.34, df=1, p=0.854</b>		
<b>Anterior vitrectomy at time of graft</b>		
No	4653 (98%)	3211 (98%)
Yes	83 (2%)	52 (2%)
<b>Chi<sup>2</sup>=0.00, df=1, p=0.982</b>		
<b>Total</b>	<b>4736 (100%)</b>	<b>3263 (100%)</b>

### 3.6 Post-graft Events

Table 3.9 shows the occurrence of post-graft events, which were found to be **significant** in univariate analyses. Only 15 grafts had post-graft herpetic infection reported, 12 had post-graft synechia, and 11 had post-graft uveitis, and so the impact of these factors was not further analysed.

**Table 3.9 Post-graft events, significant in univariate analyses**

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft</b>		
<b>Post-graft Events</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Post-graft neovascularisation</b>		
No	4668 (99%)	3195 (98%)
Yes	68 (1%)	68 (2%)
<b>Post-graft microbial keratitis</b>		
No	4713 (99%)	3240 (99%)
Yes	23 (1%)	23 (1%)
<b>Post-graft rise in IOP</b>		
No	4248 (90%)	2775 (85%)
Yes	488 (10%)	488 (15%)
<b>At least one rejection episode</b>		
No	4474 (94%)	3001 (92%)
Yes	262 (6%)	262 (8%)
<b>Total</b>	<b>4736 (100 %)</b>	<b>3263 (100 %)</b>

Table 3.10 shows the time at which suture removal was reported to have occurred post-graft, categorised in five time-frame groups. This was **non-significant** in univariate analysis and the result of the Kaplan-Meier survival analysis is also provided. The sum of these numbers for each variable equals the total number of grafts (4,736 registered and 3,263 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 3.10 Post-graft events, not significant in univariate analyses**

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft Post-graft Events</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Time to removal of sutures</b>		
Within 1 month post-graft	73 (2%)	73 (2%)
Between 1 and 2 months post-graft	247 (5%)	247 (8%)
Between 2 and 3 months post-graft	117 (2%)	117 (4%)
Between 3 and 6-months post-graft	145 (3%)	145 (4%)
Over 6-months post-graft	122 (3%)	122 (4%)
Not yet removed/not advised	4032 (85%)	2559 (78%)
<b>Chi<sup>2</sup>=5.37, df=4, p=0.252</b>		
<b>Total</b>	<b>4736 (100%)</b>	<b>3263 (100%)</b>

Table 3.11 shows post-graft surgical procedures, as reported by follow-up practitioners. Please note: post-graft data may be incomplete when follow-up is based on a registration for a replacement graft.

**Table 3.11 Post-graft surgical procedures**

643 DS(A)EK were reported to have undergone a re-grafting procedure (separate to subsequent concurrent graft/s) at the date last seen. Of these 561 had not had additional post-graft operative procedures reported, while 49 had.

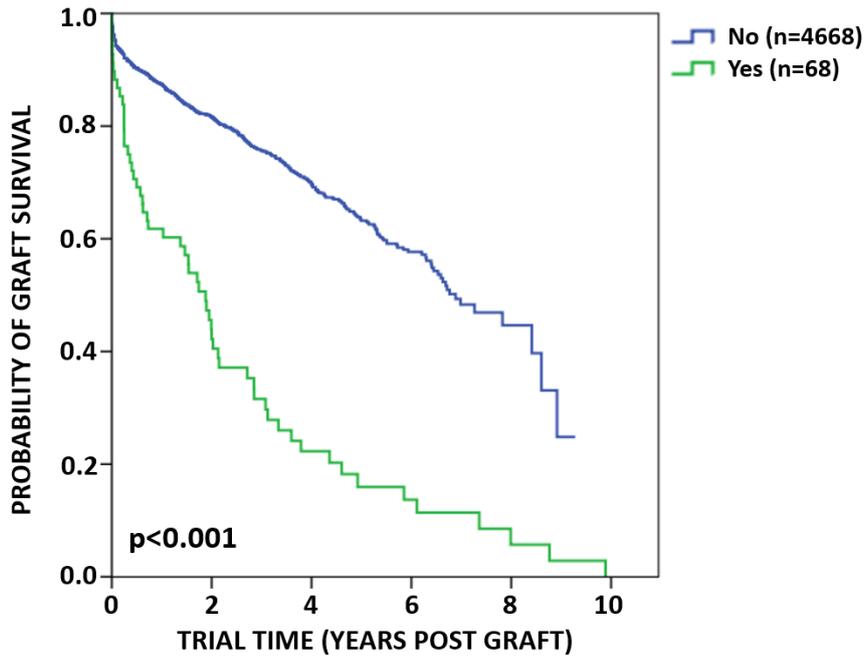
<b>Descemet's Stripping (Automated) Endothelial Corneal Graft Post-graft Surgical Procedures</b>	
	<b>Number</b>
Rebubbled	253
YAG laser	158
Cataract removal/IOL insertion (50 both, 2 cataract only, 8 IOL only)	60
IOL exchange/removal/reposition	19
PRK laser	10
Trabeculectomy	22
Intravitreal injection/s	22
Graft revision/wound repair	8
Cyclodiode	8
Tube insertion (Baerveldt: 8, 2 Molteno: 2, unspecified:4)	14
Vitrectomy	19
Graft repositioned	5
Bleb needling/revision	5
Insertion of piggyback lens	5
Other*	100
<b>Total number of surgical procedures (number of grafts)</b>	<b>708 (587)</b>

\* Other included: Iridotomy (4), membrane peel (4), removal of air bubble (4), concurrent subsequent lamellar patch graft (3), eyelid repair (3), keratectomy (3), ptosis repair (3), removal of remnant lens material (3), selective laser trabeculoplasty (3), anterior chamber tap (2), anterior stromal puncture (2), capsulotomy (2), ectropion repair (2), endolaser (2), epithelial debridement (2), evisceration (2), filter surgery (2), keratotomy (2), LASIK (2), macular hole repair (2), needling of trabeculectomy (2), punctal plug (2), pupilloplasty (2), removal of folds in Descemet's membrane (2), air-bubble adjustment (1), anterior chamber washout (1), amniotic membrane transplant (1), concurrent subsequent limbal graft (1), conjunctival resection (1), corneal diathermy (1), corneal scraping (1), cryotherapy (1), electrolysis (1), floater surgery (1), gas insertion (1), glaucoma tube repositioning (1), glaucoma tube revision and extension (1), gold weight insertion (1), Hughes flap (1), intraocular contact lens inserted (1), iridectomy (1), iridoplasty (1), iris prolapse repositioning (1), Molteno tube repositioning (1), pars plana tube insertion (1), pupilotomy (1), reformation of anterior chamber (1), relaxing incision (1), removal of band keratopathy (1), removal of basal cell carcinoma (1), removal of conjunctival melanoma (1), removal of epithelial cyst (1), removal of iris prosthesis (1), removal of upper tarsal concretions (1), retinal detachment repair (1), retinal laser surgery (1), retinoplexy (1), revision of Descemet's endothelial keratoplasty (1), scleral buckle removal (1), silicone oil inserted (1), silicone tube insertion (1), surgery for angle closure (1), suture adjustment (1), tarsorrhaphy (1), trabecular bypass stent (1), triescence (1), vitreous tap (1).

### 3.6.1 DS(A)EK survival: influence of post-graft corneal neovascularisation

Figure 3.6.1 shows the comparison of graft survival for grafts where the eye was reported to have had corneal neovascularisation post-graft to those that did not. A significant difference was found between groups (Log Rank Statistic=100.79; df=1; p<0.001). This variable was retained in the multivariate analysis (see section 3.7) suggesting that this is an independent factor significantly affecting graft survival.

Figure 3.6.1 Post-graft corneal neovascularisation



**Number at risk (years post-graft)**

	1	2	4	6	8
No neovascularisation	2265	1522	508	141	16
Neovascularisation	41	25	11	6	2

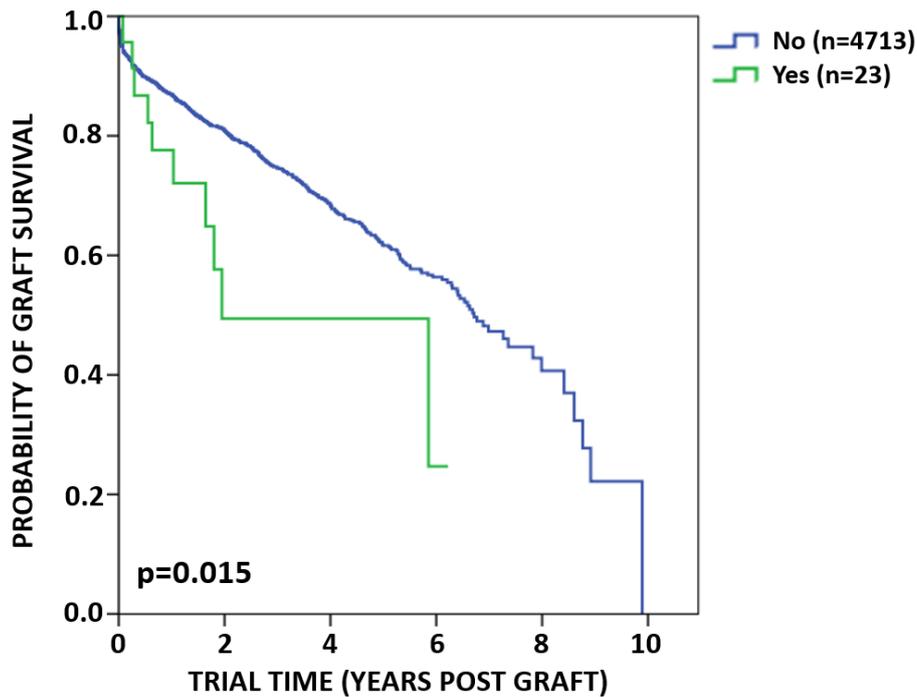
**Probability of graft survival (years post-graft)**

	1	2	4	6
No neovascularisation	0.88	0.82	0.70	0.58
Neovascularisation	0.62	0.42	NA	NA

### 3.6.2 DS(A)EK survival: influence of post-graft microbial keratitis

Figure 3.6.2 shows the comparison of graft survival for grafts where the eye was reported to have had microbial keratitis post-graft to those that did not. A significant difference was found between groups (Log Rank Statistic=5.89; df=1; p=0.015). This variable was not retained in the multivariate analysis (see section 3.7) suggesting that this is **not** an independent factor significantly affecting graft survival.

**Figure 3.6.2 Post-graft microbial keratitis**



#### Number at risk (years post-graft)

	1	2	4	6	8
<b>No microbial keratitis</b>	2292	1541	516	146	18
<b>Microbial keratitis</b>	14	6	3	1	NA

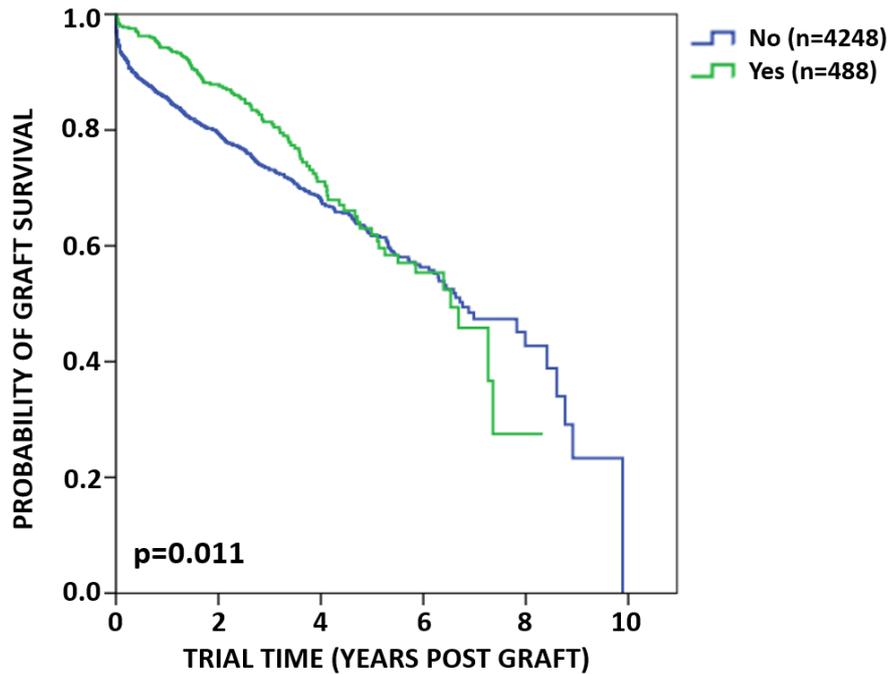
#### Probability of graft survival (years post-graft)

	1	2	4	6
<b>No microbial keratitis</b>	0.87	0.81	0.69	0.57
<b>Microbial keratitis</b>	NA	NA	NA	NA

### 3.6.3 DS(A)EK survival: influence of post-graft raised IOP

Figure 3.6.3 shows the comparison of graft survival for grafts where the eye was reported to have had raised intraocular pressure post-graft to those where the IOP remained in the normal range. A significant difference was found between groups (Log Rank Statistic=6.40; df=1; p=0.0011). This variable was retained in the multivariate analysis (see section 3.7) suggesting that this is an independent factor significantly affecting graft survival.

Figure 3.6.3 Post-graft raised intraocular pressure



#### Number at risk (years post-graft)

	1	2	4	6	8
No raised IOP	1898	1250	422	116	17
Raised IOP	408	297	97	31	1

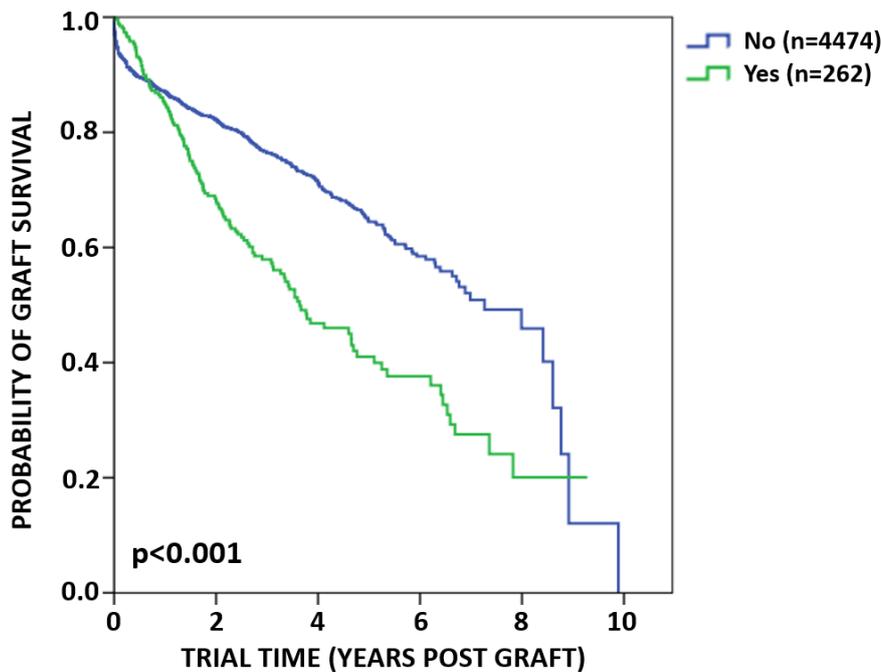
#### Probability of graft survival (years post-graft)

	1	2	4	6
No raised IOP	0.86	0.80	0.69	0.57
Raised IOP	0.94	0.88	0.71	0.55

### 3.6.4 DS(A)EK survival: influence of graft rejection episodes

Figure 3.6.4 shows the survival for grafts where the eye underwent at least one incidence of post-graft immunological rejection, compared to those that did not have any rejection episodes. A significant difference was found between groups (Log Rank Statistic=44.57; df=1;  $p<0.001$ ). This variable was retained in the multivariate analysis (see section 3.7) suggesting that this is an independent factor significantly affecting graft survival.

**Figure 3.6.4 Rejection episode(s)**



#### Number at risk (years post-graft)

	1	2	4	6	8
No Rejection	2094	1399	460	121	13
Any rejection	212	148	59	26	5

#### Probability of graft survival (years post-graft)

	1	2	4	6
No Rejection	0.88	0.83	0.72	0.59
Any rejection	0.85	0.68	0.47	0.38



### 3.7 Multivariate Analysis

A multivariate model was used to investigate the combined effect of variables on penetrating graft survival, adjusted for all other variables in the model. This analysis was performed using STATA version 11.

In the preceding univariate analyses, each registered DS(A)EK, together with its archival follow-up records, was treated as a separate and independent entity. Some recipients had multiple DS(A)EK performed during the census period (up to 31/7/2017), with some having repeat grafts in a single eye, some grafts in both eyes and some a combination of both. To control for potential inter-graft and/or inter-eye dependence in the multivariate analyses, the multivariate model was adjusted to allow for clustering by individual patient [see references 7 & 8].

Variables to be included in the Cox Proportional Hazards regression model were identified based on the results of the univariate Kaplan-Meier analyses, with a cut-off significance level of  $p < 0.08$  used to select variables for inclusion. Some variables that were found to be significant in the univariate analyses were omitted due to co-linearity, or because of large amounts of missing data ( $>50\%$ ). Where data were missing for 1% to 50% of cases, additional groups for each if these categorical variables were created, called “not advised”. Each variable was initially analysed individually to determine if it remained significant once clustered by individual patient. Where the variable was no longer found to be significant ( $p > 0.08$ ), it was excluded from the multivariate analysis.

The best model was found by a backward elimination process, removing variables not appearing to be predictors of graft failure. The model excluded variables with a p-value of  $p \geq 0.05$  (or global p-value of  $p \geq 0.05$  for variables with more than two categories) in a stepwise manner, beginning with the least significant variable. For categorical variables with more than two groups, Bonferroni adjustment was applied to determine if significant differences were present between groups. The Kaplan-Meier plots, and additional appropriate STATA analyses, were used to assess whether each included variable met the assumption of proportional hazards. Where variables were found to be time-variant, they were treated as such in the multivariate model.

Table 3.12 shows each of the variables analysed in the univariate analyses, stratified by whether they were included in the initial multivariate model and whether they remained in the final model.

Table 3.12 Multivariate model

### Descemet's Stripping (Automated) Endothelial Corneal Graft Multivariate Model

#### Not significant in univariate analysis

Donor sex  
Cause of donor death  
Multi-organ donor  
Time from death to enucleation  
Storage time in Optisol  
Storage time in organ culture  
Eye grafted  
Graft type  
Peripheral iridectomy at time of graft  
Anterior vitrectomy at time of graft  
Use of glide during surgery  
Use of anterior chamber maintainer during surgery  
Donor lenticule folded  
Descemet's membrane stripped by surgeon

#### Significant in univariate analysis but excluded from multivariate model due to collinearity or missing data

The centre effect (collinear with surgeon experience and level of follow-up)  
Use of forceps at time of graft (missing data)  
Use of viscoelastic at time of graft (missing data)

#### Significant in univariate analysis but not retained in multivariate model

Time from enucleation to storage ( $p > 0.08$  after clustering by patient)  
Storage medium ( $p > 0.08$  after clustering by patient)  
Pre-graft inflammation and/or steroid use ( $p > 0.08$  after clustering by patient)  
Donor/recipient sex match/mismatch  
Eye bank  
Cornea pre-cut by eye bank  
Pre-graft neovascularisation  
Recipient age group  
Previous contralateral graft(s)  
Interstate transportation  
Post-graft microbial keratitis

#### Significant in univariate analysis AND retained in multivariate model

Donor age group  
Endothelial cell density  
Indication for graft  
Australian State where graft was performed  
Recipient sex  
Raised intraocular pressure prior to and/or at graft  
Graft year  
Graft size  
Incision size  
Surgeon experience and level of follow-up  
Change in lens status pre- to post-graft  
Post-graft neovascularisation  
Raised intraocular pressure post-graft  
Post-graft rejection episode(s)

Table 3.13 tabulates the parameter estimates resulting from the fit of the best clustered Cox model. The table shows the variable, the hazard ratio, the standard error of the regression coefficient, the corresponding probability value and the 95% confidence interval for the hazard ratio. The group of each categorical variable with the highest number of cases was taken as the referent. The hazard ratios for a given variable are adjusted for all other variables in the model. This model included data from the 4,736 Descemet's stripping (automated) endothelial keratoplasties, performed in 3,755 recipients. Where no valid response had been provided for one of the included variables, these cases were classified as "not advised".

This model includes variables with a p-value of  $p < 0.05$ , with variables eliminated in a stepwise manner, beginning with the least significant variable. For categorical variables, a global test was applied to calculate the overall p-value. Bonferroni adjustment was applied for within-group comparisons. The overall model was highly significant: ( $\text{Chi}^2=608.46$ ,  $p < 0.0001$ ).

**Table 3.13 Clustered multivariate model**

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft Alternative Clustered Multivariate Model</b>						
	<b>n</b>	<b>Hazard Ratio</b>	<b>Standard error</b>	<b>p-value</b>	<b>Global p-value</b>	<b>95% confidence interval</b>
<b>Donor age group</b>						
Under 40	385	0.65	0.11	0.014	0.003	0.47 - 0.92
40 to 69	2891	1.00				1.00 - 1.35
70 or older	1460	1.16	0.09	0.048		1.00 - 1.35
<b>Central endothelial cell count</b>						
Under 2500 cells/mm <sup>2</sup>	271	4.70	0.22	<0.001	<0.001	1.31 - 2.20
2500 to 3249 cells/mm <sup>2</sup>	2240	1.00				0.67 - 1.06
3250 cells/mm <sup>2</sup> or more	694	0.84	0.10	0.127		0.50 - 1.10
Not advised	1531	0.74	0.15	0.137		0.50 - 1.10
<b>Indication for graft</b>						
Failed previous graft	933	1.35	0.14	0.004	0.004	1.10 - 1.65
Pseudophakic bullous keratopathy	1283	1.11	0.11	0.293		0.91 - 1.36
Fuchs' endothelial dystrophy	2282	1.00				1.24 - 2.82
Other bullous keratopathy	136	1.87	0.39	0.003		1.02 - 2.39
Trauma	70	1.56	0.34	0.042		0.68 - 3.99
Other specified indication	32	1.65	0.74	0.269		0.68 - 3.99
<b>Australian State where graft was performed (tvc)</b>						
State M	1666	1.00			<0.001	
State K	849	0.85	0.12	0.234		0.64 - 1.11
State V	1121	1.37	0.30	0.146		0.89 - 2.11
State J	627	1.52	0.21	0.002		1.16 - 1.98
State N	393	1.08	0.29	0.788		0.64 - 1.82
State C	80	2.32	0.45	<0.001		1.58 - 3.39
<b>Recipient sex</b>						
Female	2700	1.00			0.002	
Male	2036	1.25	0.09	0.002		1.08 - 1.44
<b>Raised intraocular pressure in past and/or at graft</b>						
No	3851	1.00			<0.001	
Yes	885	1.40	0.13	<0.001		1.17 - 1.67

	n	Hazard Ratio	Standard error	p-value	Global p-value	95% confidence interval
<b>Graft year (tvc)</b>						
Pre 2008	105	3.57	0.76	<0.001		2.34 - 5.43
2008/2009	545	1.84	0.29	<0.001		1.35 - 2.52
2010/2011	858	1.37	0.19	0.022		1.05 - 1.80
2012/2013	1154	1.15	0.13	0.225		0.92 - 1.43
2014/2015	1253	1.00			<0.001	
2016/2017	821	3.46	0.87	<0.001		2.11 - 5.68
<b>Size of graft</b>						
<8.25 mm	1361	1.63	0.13	<0.001		1.39 - 1.92
8.25 mm or larger	2974	1.00			<0.001	
Not advised	401	1.24	0.16	0.106		0.96 - 1.60
<b>Size of incision</b>						
Up to 4.0 mm	481	0.61	0.12	0.010		0.42 - 1.10
4.1 mm to 4.5 mm	353	0.87	0.15	0.428		0.62 - 1.23
4.6 mm to 5.0 mm	818	0.83	0.11	0.165		0.64 - 1.08
5.1 mm or larger	912	1.25	0.12	0.019		1.04 - 1.50
Not advised	2172	1.00			0.001	
<b>Experience of surgeon and percentage of follow-up (tvc)</b>						
< 100 DS(A)EK registered	1663	1.71	0.20	<0.001		1.35 - 2.15
100+ DS(A)EK registered, <69% followed	545	1.97	0.28	<0.001		1.49 - 2.61
100+ DS(A)EK registered, 69%+ followed	2528	1.00			<0.001	
<b>Change in lens status pre- to post-graft</b>						
Phakic post-graft	182	0.91	0.15	0.569		0.65 - 1.27
Phakic pre-graft, pseudophakic after	1137	0.69	0.08	0.001		0.55 - 0.86
Other*	3417	1.00			0.005	
<b>Post-graft corneal neovascularisation</b>						
No	4668	1.00				
Yes	68	2.14	0.32	<0.001		1.60 - 2.88
<b>Post-graft rise in intraocular pressure (tvc)</b>						
No	4248	1.00				
Yes	488	0.39	0.06	<0.001		0.29 - 0.54
<b>Post-graft rejection episode(s)</b>						
No	4474	1.00				
Yes	262	1.92	0.18	<0.001		1.59 - 2.31

tvc = time variant coefficient

\*Other includes: phakic/aphakic, aphakic/aphakic, aphakic/pseudophakic, pseudophakic/aphakic, and pseudophakic/pseudophakic

### **3.7.1 Significant differences in the Descemet's stripping (automated) endothelial keratoplasty multivariate model for categories with more than two groups following Bonferroni correction for multiple comparisons**

#### **3.7.1.1 Indication for graft**

Grafts performed for Fuchs' endothelial dystrophy had significantly better survival than those performed for other (non-pseudophakic) bullous keratopathy ( $p=0.003$ ), or failed previous graft ( $p=0.004$ ).

Grafts performed for pseudophakic bullous keratopathy had significantly better survival than those performed for other (non-pseudophakic) bullous keratopathy ( $p=0.015$ ).

#### **3.7.1.2 Donor age group**

Significantly better survival was shown for the under 40 years age category compared to the 40 to 69 years category ( $p=0.014$ ) and the 70 years and older category ( $p=0.001$ ).

#### **3.7.1.3 Central endothelial cell count**

Grafts where the central endothelial cell count was less than 2500 cells/mm<sup>2</sup>, exhibited significantly poorer survival than those with cell counts between 2500 and 3249 cells/mm<sup>2</sup>, or 3250 cells/mm<sup>2</sup> or more (both  $p<0.001$ ).

#### **3.7.1.4 Australian State where graft was performed**

Grafts performed in State C had significantly poorer survival than those performed in State M or State K (both  $p<0.001$ ), or in State N ( $p=0.005$ ).

Grafts performed in State J had significantly poorer survival than those performed in State M ( $p=0.002$ ) or State K ( $p<0.001$ ).

#### **3.7.1.5 Change in lens status pre- to post-graft**

Eyes that underwent a triple procedure at graft (phakic/pseudophakic) exhibited significantly better survival than those with any combination other than phakic/phakic ( $p=0.001$ ).

### **3.7.1.6 Graft era**

Grafts performed prior to 2008 had significantly poorer survival than those performed in 2008/2009, 2010/2011, 2012/2013 or 2014/2015 (all  $p < 0.001$ ).

Grafts performed in 2008/2009 had significantly poorer survival than those performed in 2012/2013 ( $p = 0.001$ ) or 2014/2015 ( $p < 0.001$ ).

Grafts performed in 2016/2017 had significantly poorer survival than those performed in 2008/2009, 2010/2011, 2012/2013 and 2014/2015 (all  $p < 0.001$ ).

### **3.7.1.7 Graft size**

Grafts that were smaller than 8.25mm had significantly poorer survival than those that were 8.25mm or larger ( $p < 0.001$ ).

### **3.7.1.8 Incision size**

Grafts where the incision size was greater than 5.0mm had significantly poorer survival than those where the incision size was 4.0mm or smaller ( $p < 0.001$ ), and those where the incision size was 4.6mm to 5.0mm in size ( $p = 0.002$ ).

Grafts where the incision size was not provided to the ACGR had significantly poorer survival than those where the incision size was 4.0mm or smaller ( $p = 0.010$ ),

### **3.7.1.9 Volume of DS(A)EK registered by surgeon and level of follow-up received**

Grafts performed by surgeons with 100 or more DS(A)EK registered with the ACGR, and above average ( $>69\%$ ) levels of follow-up had significantly better survival than those performed by surgeons with 100 or more DS(A)EK registered with the ACGR, and below average ( $\leq 69\%$ ) levels of follow-up, and surgeons with fewer than 100 DS(A)EK registered (both  $p < 0.001$ ).

### 3.8 Reasons for Graft Failure

Of the 3,263 followed grafts, 791 (24%) were known to have failed by the census date. This equates to 17% of the 4,736 registered grafts. Surgeons were asked to indicate the reason for graft failure. This information was also gathered from repeat registration forms, where the reason for failure of the previous graft was given. Table 3.14 shows the reasons for failure given.

**Table 3.14 Reasons for graft failure**

<b>Descemet's Stripping (Automated) Endothelial Corneal Graft Reasons for Graft Failure</b>	
Endothelial cell failure	252 (32%)
Primary graft failure	221 (28%)
Rejection	106 (13%)
Infection: Non herpetic (20), HSV (3)	23 (3%)
Scarring	18 (2%)
Glaucoma	15 (2%)
Other specified*	46 (6%)
Unspecified	110 (14%)
<b>Total</b>	<b>791 (100%)</b>

\* Other included: Descemet's folds/wrinkles (8), Graft detachment (7), ICE syndrome (6), trauma (6), astigmatism (4), corneal ulcer (4), band keratopathy (2), contraction of graft (1), epithelial defect (1), floppy iris syndrome (1), fibrosis (1), hyphaema (1), iris adhesion (1), limbal stem cell failure (1), pupillary block (1), suprachoroidal haemorrhage (1).

Primary graft non-functions are defined as grafts that never thin and clear in the post-operative period. For lamellar procedures, primary graft failure is recorded as reported by surgeons. Additional information is collected to ascertain whether this occurred within 28 days of the graft. Where surgeons indicate that the failure was due to surgical complications, this is also recorded.

Of the 221 grafts reported by surgeons to have been primary graft failures, the majority (155) had no further information provided. Specific reasons given were: failure to adhere/graft detachment (28), surgical trauma/complication (11), endothelial failure (7), folds in Descemet's membrane (6), oedema (4), endophthalmitis (2), rejection (2), scar/opacity (2), endothelial defect (1), epithelial defect (1), fungal infection in donor tissue (1), and presence of Fuchs' endothelial dystrophy in the donor tissue (1).

## 3.9 Post-graft Changes in Best Corrected Visual Acuity

### 3.9.1 All indications for graft

Post-graft best corrected visual acuity (BCVA) is an important outcome for corneal graft recipients. A desire for improved visual acuity was specified as a reason for graft in 4,423 (93%) of registered Descemet's stripping (automated) endothelial keratoplasties. In 75% of cases (3,571), this was the sole desired outcome indicated. It is likely that this was also at least part of the reason for graft in some of the further 201 (4%) grafts for which no reason was specified.

Follow-ups occur at varying times post-graft, depending on when a surgeon sees a recipient. Where post-graft best corrected visual acuity (without pinhole) information was provided, we categorised this according to the length of time since graft. The first two categories were:

- BCVA provided at between 6 and 12 months post-graft, and
- BCVA provided at between 12 and 18 months post-graft.

Subsequent groups were at yearly intervals. For each year point, any measurements provided within 6-months of that date, rounded to the nearest day, were included (e.g. for 2-year follow-up, any BCVA given at between 730 and 913 days post-graft was included).

We analysed post-graft visual acuity in several ways. Where more than 20 grafts had BCVA measurements provided, we examined:

1. The percentage of *surviving* grafts achieving different levels of Snellen visual acuity (6/6 or better, 6/7.5 to 6/12, 6/15 to 6/24, 6/36 to 6/60, count fingers (CF) or hand movements (HM), and light perception (LP) or no light perception (NLP)) at yearly time-points post-graft. Grafts that had been reported to have failed at the time of last follow-up, but had prior follow-ups with BCVA measurements provided when the graft was surviving, had these prior data included in these analyses.
2. The *average* Snellen visual acuity achieved at yearly intervals post-graft, again by *surviving* grafts.
3. The final BCVA reported at the time of failure.

Table 3.15 and Figure 3.9.1 show the reported post-graft best corrected visual acuity for all failed grafts at the time of last follow-up, separated by indication for graft. Visual acuity at time of failure was reported for 694 (88%) of 791 failed DS(A)EK. As might be expected, the majority of failed grafts had accompanying poor visual acuity.

**Table 3.15 Post-graft best corrected visual acuity**

	6/4 to 6/6	6/7.5 to 6/12	6/15 to 6/24	6/36 to 6/60	CF or HM	LP or NLP
<b>Failed previous graft</b>	1 (<1%)	5 (3%)	6 (3%)	42 (23%)	114 (63%)	14 (8%)
<b>Pseudo bullous keratopathy</b>	0 (0%)	4 (2%)	15 (8%)	36 (18%)	134 (67%)	11 (6%)
<b>Fuchs' endothelial dystrophy</b>	0 (0%)	17 (6%)	52 (19%)	66 (25%)	129 (48%)	3 (1%)
<b>Other bullous keratopathy</b>	0 (0%)	1 (4%)	2 (9%)	3 (13%)	14 (61%)	3 (13%)
<b>Trauma</b>	0 (0%)	0 (0%)	2 (12%)	2 (12%)	12 (71%)	1 (6%)
<b>Other specified</b>	0 (0%)	0 (0%)	0 (0%)	1 (20%)	3 (60%)	1 (20%)
<b>Total</b>	<b>1 (&lt;1%)</b>	<b>27 (4%)</b>	<b>77 (11%)</b>	<b>150 (22%)</b>	<b>406 (59%)</b>	<b>33 (5%)</b>

CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

**Figure 3.9.1 Best corrected visual acuity at time of last follow-up for failed Descemet's stripping (automated) endothelial keratoplasties**

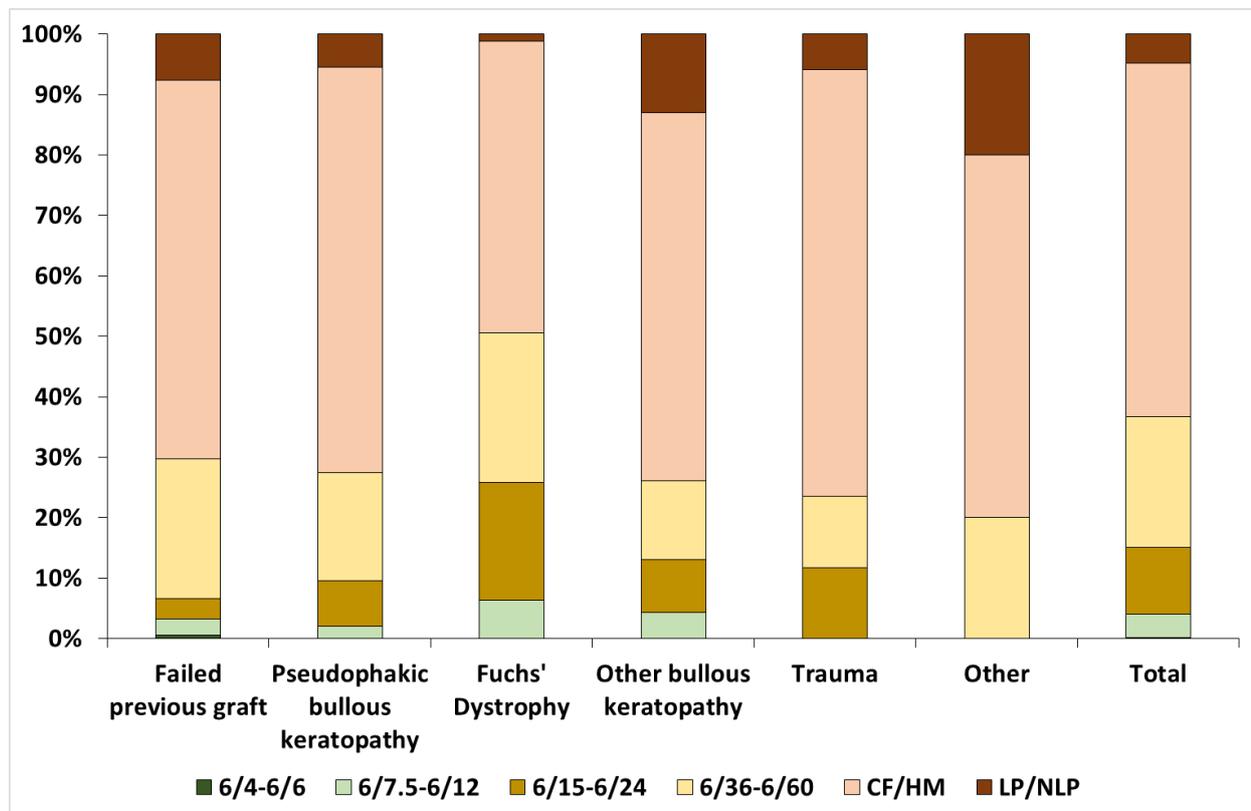
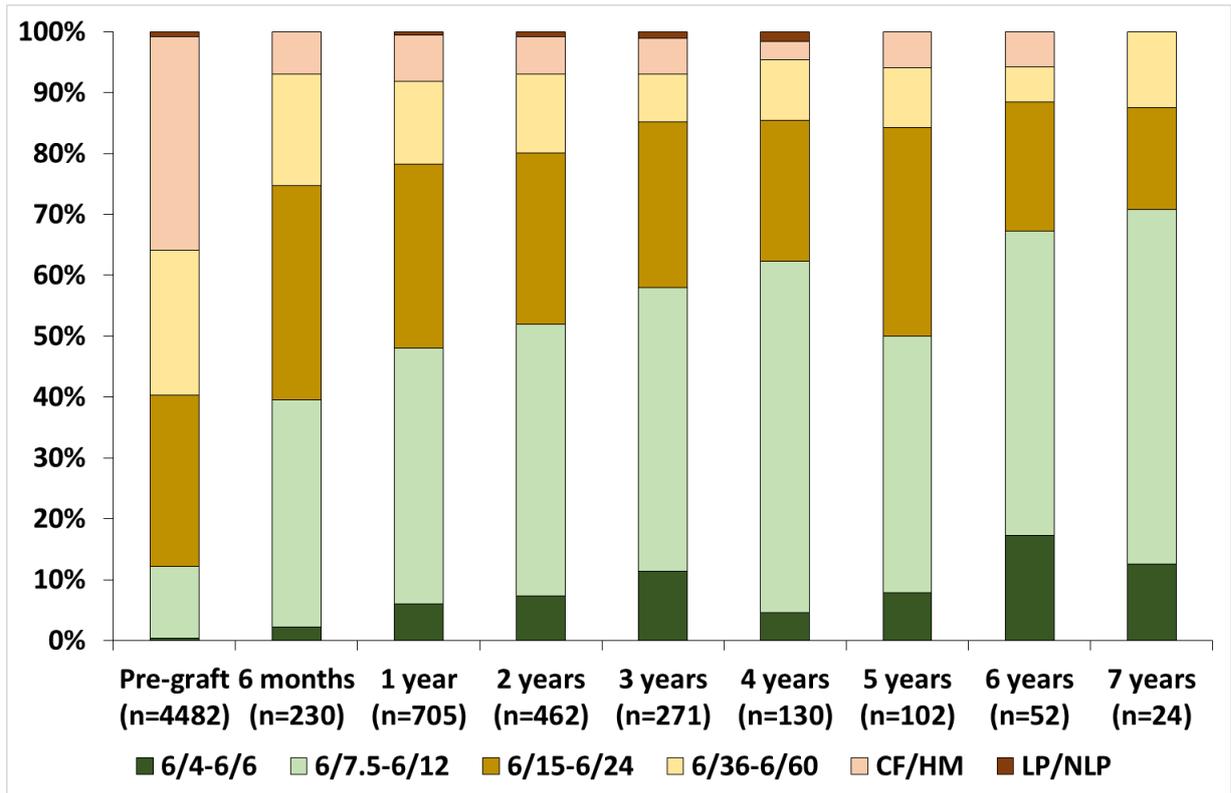


Figure 3.9.2 shows the best corrected visual acuity in the grafted eye, as reported to the ACGR, and categorised into six levels of vision, for all **surviving** Descemet's stripping (automated) endothelial keratoplasties. Prior to graft over one-third of eyes (36%) had vision of CF or worse, with almost another quarter (24%) having 6/36 to 6/60. By 2-years post-graft, approximately 80% of eyes with **surviving** grafts had vision of 6/24 or better, with more than half having functional vision of 6/12 or better. This remained the case for **surviving** grafts followed for up to 7-years post-graft.

**Figure 3.9.2 Best corrected visual acuity for Descemet's stripping (automated) endothelial keratoplasties, surviving at time of measurement**



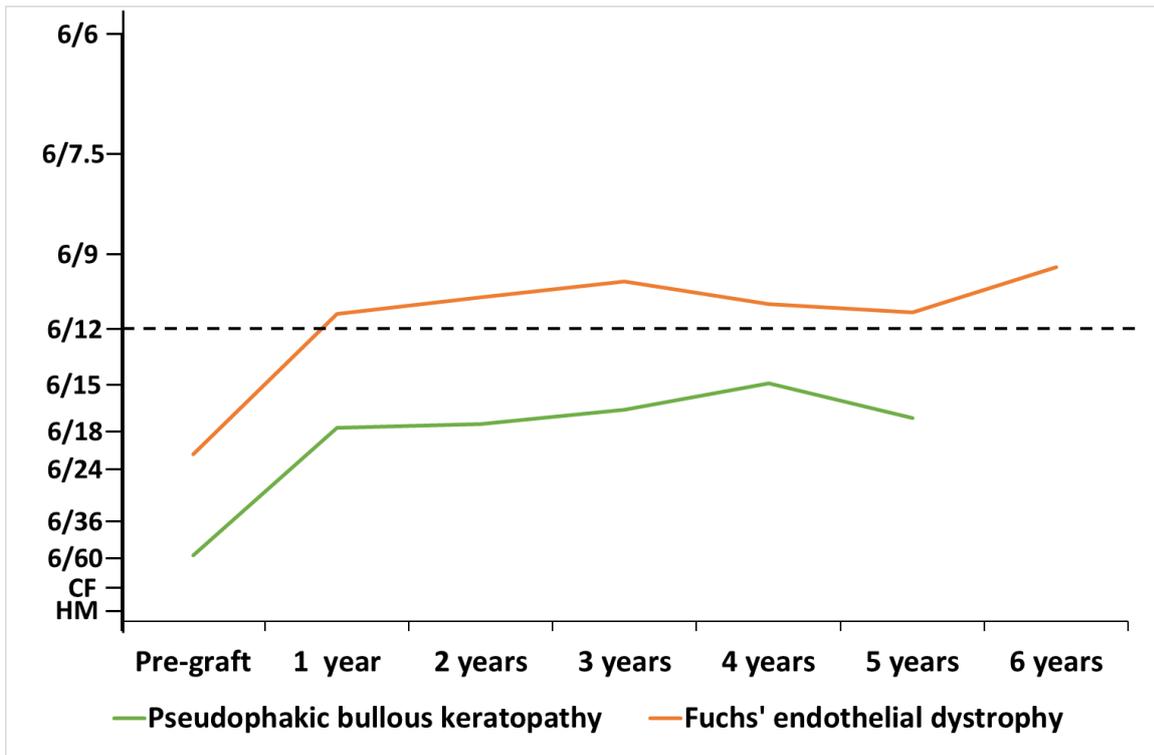
CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

### 3.9.2 Individual indications for graft

The following analyses show the post-graft best corrected visual acuity obtained for surviving grafts performed for specific indications. Data are reported for each of: Fuchs' endothelial dystrophy, and pseudophakic bullous keratopathy. Figure 3.9.3 shows the average BCVA reported for various indications for graft - pre-graft, at 6-months post-graft and at yearly time points (6-month timeframe cohorts), up to 7-years post-graft. The dashed line shows the point where vision reaches 6/12, sometimes referred to as "functional" vision.

On average, the best visual outcomes were seen for eyes grafted for Fuchs' endothelial dystrophy. It can also be seen that these grafts had better pre-graft visual acuity levels than grafts for pseudophakic bullous keratopathy. Grafts performed for Fuchs' endothelial dystrophy had mean post-graft vision of 6/12 or better by 12-months post-graft. On average, levels of vision obtained post-graft for pseudophakic bullous keratopathy did not reach 6/12 or better up to 5-years post-graft.

**Figure 3.9.3 Average level of best corrected visual acuity reported at yearly time points for surviving grafts performed for common indications for graft**



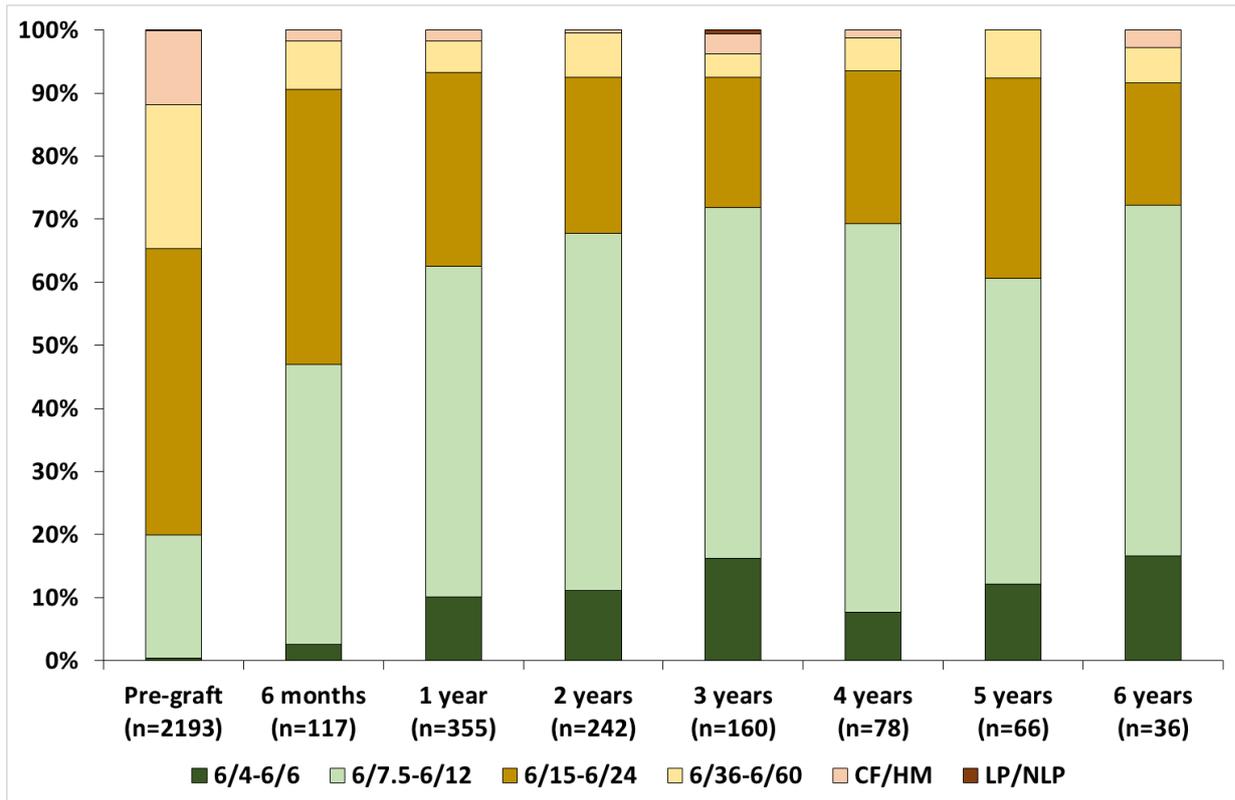
CF=count fingers at 1 metre, HM=hand movements

#### Number of surviving grafts with visual acuity provided

	Pre-graft	1	2	3	4	5	6
Pseudophakic bullous keratopathy	1209	167	115	57	27	24	11
Fuchs' endothelial dystrophy	2193	355	242	160	78	66	36

Figure 3.9.4 shows levels of best corrected visual acuity reported to the ACGR, at yearly intervals for **surviving** Descemet’s stripping (automated) endothelial keratoplasties for Fuchs’ endothelial dystrophy. Post-graft vision of 6/12 or better was reported in almost two-thirds (63%) of **surviving** Descemet’s stripping (automated) endothelial keratoplasties performed for Fuchs’ endothelial dystrophy that had BCVA measurements reported between 12 and 18-months post-graft. This percentage remained above 60% up to 6-years post-graft. More than 90% of grafts achieved vision of 6/24 or better over this period of follow-up.

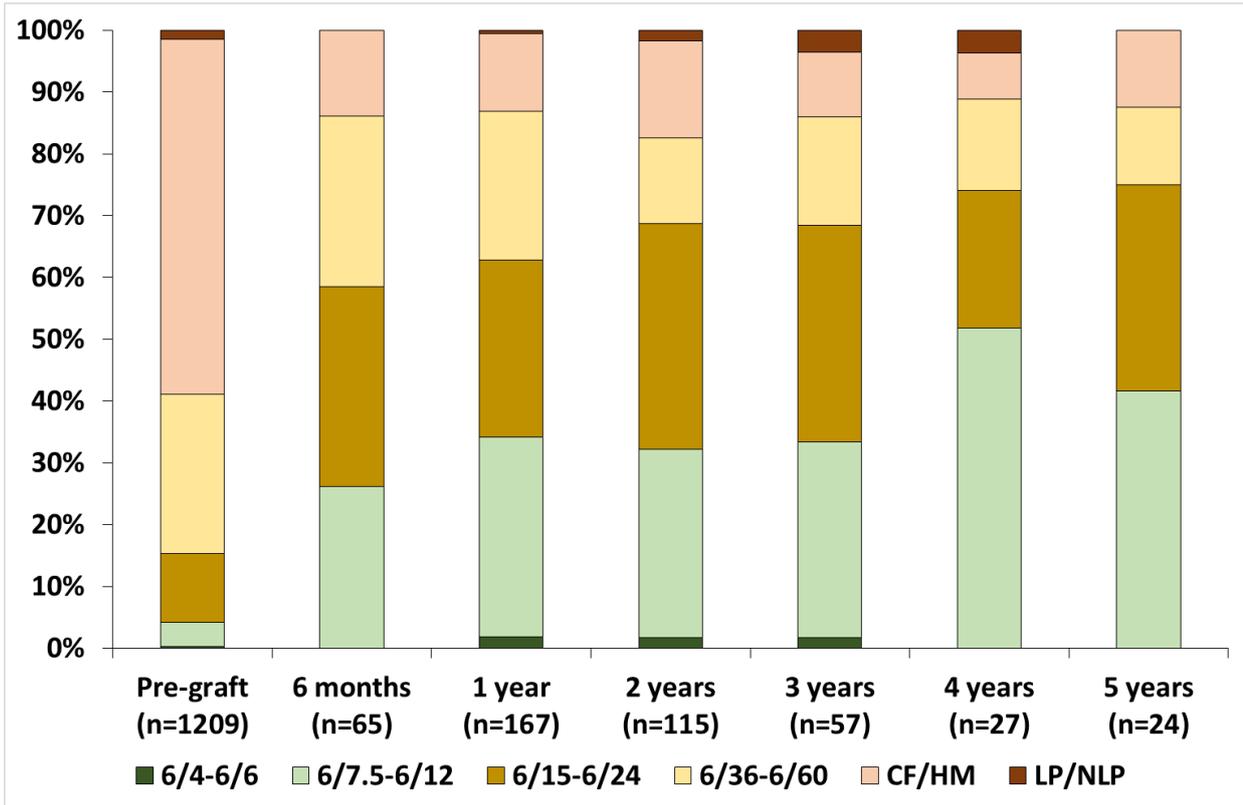
**Figure 3.9.4 Fuchs' endothelial dystrophy: level of best corrected visual acuity reported at yearly time points for surviving grafts**



CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

Figure 3.9.5 shows levels of best corrected visual acuity reported to the ACGR, at yearly intervals for **surviving** Descemet’s stripping (automated) endothelial keratoplasties for pseudophakic bullous keratopathy. Post-graft vision of 6/12 or better was reported in one-third (63%) of **surviving** Descemet’s stripping (automated) endothelial keratoplasties performed for pseudophakic bullous keratopathy that had BCVA measurements reported between 12 and 18-months post-graft. This percentage peaked 4-years post-graft, at 52%. Approximately 70% of grafts achieved vision of 6/24 or better over 5-years post-graft.

**Figure 3.9.5 Pseudophakic bullous keratopathy: level of best corrected visual acuity reported at yearly time points for surviving grafts**



CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

## 4 Descemet's Membrane Endothelial Keratoplasty

This chapter presents the results of analyses conducted on data relating to the 1,250 Descemet's membrane endothelial keratoplasties (DMEK) registered with the ACGR since 6<sup>th</sup> December 2007. Kaplan-Meier survival analyses were conducted using IBM SPSS for Windows (Version 22.0), to compare the graft survival across groups for a range of variables relating to the corneal donor, graft recipient, surgical procedure, surgeon, and follow-up care.

### 4.1 Donor and Eye Banking Factors

Table 4.1 shows the number of grafts within each of the variable sub-groups, for the donor factors found to be **significant** in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (1,250 registered and 600 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 4.1 Donor and eye banking factors, significant in univariate analyses**

<b>Descemet's Membrane Endothelial Corneal Graft Donor and Eye Banking Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Eye bank</b>		
Eye bank M	457 (37%)	158 (26%)
Eye bank K	64 (5%)	9 (2%)
Eye bank V	602 (48%)	361 (60%)
Eye bank J	122 (10%)	72 (12%)
Eye bank N	5 (<1%)	0 (0%)
<b>Donor sex*</b>		
Female	464 (37%)	237 (40%)
Male	786 (63%)	363 (61%)
<b>Age group</b>		
<50 years	132 (11%)	65 (11%)
50 to 59 years	239 (19%)	119 (20%)
60 to 69 years	442 (35%)	202 (34%)
70 to 79 years	345 (28%)	163 (27%)
80 years and older	92 (7%)	51 (9%)
<b>Prepared by eye bank (pre-cut)</b>		
No	1128 (90%)	568 (95%)
Yes	122 (10%)	32 (5%)
<b>Total</b>	<b>1250 (100%)</b>	<b>600 (100%)</b>

\* Note: significant at  $p < 0.08$  for inclusion in multivariate analyses but not at  $p < 0.05$ .

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Likelihood of follow-up was significantly less likely ( $p < 0.05$ ) in some groups than others. Lower rates of follow-up were received for grafts where donor tissue had been pre-cut by the eye bank. Significant differences in follow-up were also found across groups for eye bank, possibly relating to how recently the technique had started being used in certain States.

Table 4.2 shows the number of grafts within each of the variable sub-groups, for the donor and eye banking factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (1,250 registered and 600 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The result of the Kaplan-Meier survival analysis is also provided for each variable. There were insufficient data for comparisons to be made between those grafts where the donor tissue had been transported interstate and those where it had not.

**Table 4.2 Donor and eye banking factors, not significant in univariate analyses**

<b>Descemet's Membrane Endothelial Corneal Graft Donor and Eye Banking Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Death-to-enucleation time</b>		
≤ 6 hours	174 (14%)	69 (12%)
7 to 12 hours	435 (35%)	205 (34%)
13 to 18 hours	462 (37%)	252 (42%)
> 18 hours	177 (14%)	74 (12%)
Not advised	2 (%)	0 (0%)
<b>Chi<sup>2</sup>=0.82, df=3, p=0.845</b>		
<b>Enucleation-to-storage time</b>		
≤ 3 hours	595 (48%)	304 (51%)
4 to 6 hours	245 (20%)	143 (24%)
7 to 12 hours	96 (8%)	56 (9%)
> 12 hours	77 (6%)	25 (4%)
Not advised	237 (19%)	72 (12%)
<b>Chi<sup>2</sup>=3.74, df=3, p=0.290</b>		
<b>Storage medium</b>		
Optisol	747 (60%)	443 (74%)
Organ culture	503 (40%)	157 (26%)
<b>Chi<sup>2</sup>=0.33, df=1, p=0.568</b>		

	Registered (%)	Followed (%)
<b>Storage to graft time - Organ culture</b>		
Up to 2 weeks	111 (9%)	29 (5%)
2 to 3 weeks	179 (14%)	66 (11%)
More than 3 weeks	56 (4%)	21 (4%)
Not advised	157 (13%)	41 (7%)
Not applicable	747 (60%)	443 (74%)
<b>Chi<sup>2</sup>=5.00, df=2, p=0.082</b>		
<b>Storage to graft time - Hypothermic</b>		
Within 5 days	449 (36%)	287 (48%)
6 or 7 days	191 (15%)	111 (19%)
More than a week	27 (2%)	14 (2%)
Not advised	80 (6%)	31 (5%)
Not applicable	503 (40%)	157 (26%)
<b>Chi<sup>2</sup>=0.68, df=2, p=0.713</b>		
<b>Cause of donor death</b>		
Cardiac event	274 (22%)	127 (21%)
Malignancy	566 (45%)	301 (50%)
Trauma	82 (7%)	28 (5%)
Respiratory event	85 (7%)	38 (6%)
Intracranial bleed/cerebral haemorrhage	190 (15%)	80 (13%)
Other specified	45 (4%)	24 (4%)
Live donor	1 (<1%)	0 (0%)
Not advised*	7 (<1%)	2 (<1%)
<b>Chi<sup>2</sup>=1.28, df=5, p=0.937</b>		
<b>Multi-organ donor status</b>		
No	1139 (91%)	553 (92%)
Yes	111 (9%)	47 (8%)
<b>Chi<sup>2</sup>=1.73, df=1, p=0.189</b>		
<b>Central corneal endothelial cell density</b>		
<2500 cells/mm <sup>2</sup>	20 (2%)	10 (2%)
2500 to 2749 cells/mm <sup>2</sup>	57 (5%)	15 (3%)
2750 to 2999 cells/mm <sup>2</sup>	132 (11%)	48 (8%)
3000 to 3249 cells/mm <sup>2</sup>	226 (18%)	76 (13%)
3250 to 3499 cells/mm <sup>2</sup>	132 (11%)	54 (9%)
≥ 3500 cells/mm <sup>2</sup>	72 (6%)	35 (6%)
Not advised	611 (49%)	362 (60%)
<b>Chi<sup>2</sup>=9.07, df=5, p=0.106</b>		
<b>Total</b>	<b>1250 (100%)</b>	<b>600 (100%)</b>

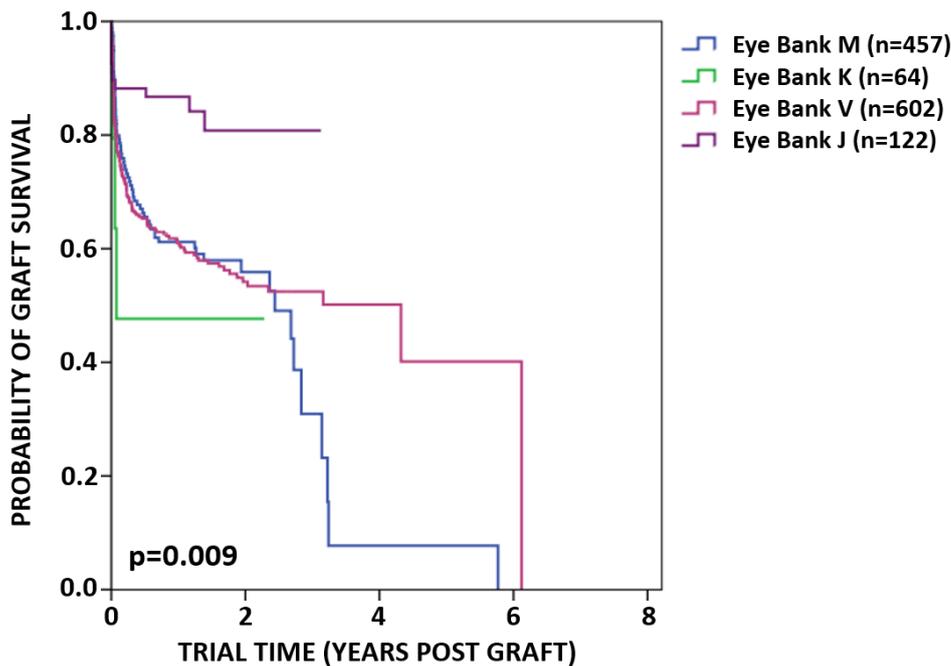
Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable.

\*ACGR advised that cause of death was not yet determined but there were no medical contraindications and the eye had been cleared for release, by the Medical Director, in accordance with EBAANZ guidelines.

#### 4.1.1 DMEK survival: influence of Australian eye bank

Donor corneas are retrieved, processed, stored and distributed by five eye banks around Australia. Figure 4.1.1 shows the comparison of graft survival for corneas provided by each of these eye banks. One eye bank had only supplied 5 corneas for use in DMEK procedures and these were excluded from the analysis. A significant difference was found across eye banks (Log Rank Statistic=11.57; df=3; p=0.009), with Eye Bank J having significantly better survival than Eye Bank V (p=0.001). This variable was not included in the multivariate analysis (see section 4.7) as it is collinear with the individual surgeon variable shown in Figure 4.4.2.

**Figure 4.1.1 Australian eye bank**



#### Number at risk (years post-graft)

	1	2	3	4	5
Eye Bank M	71	23	4	1	1
Eye Bank K	3	1	NA	NA	NA
Eye Bank V	149	74	27	6	2
Eye Bank J	53	16	1	NA	NA

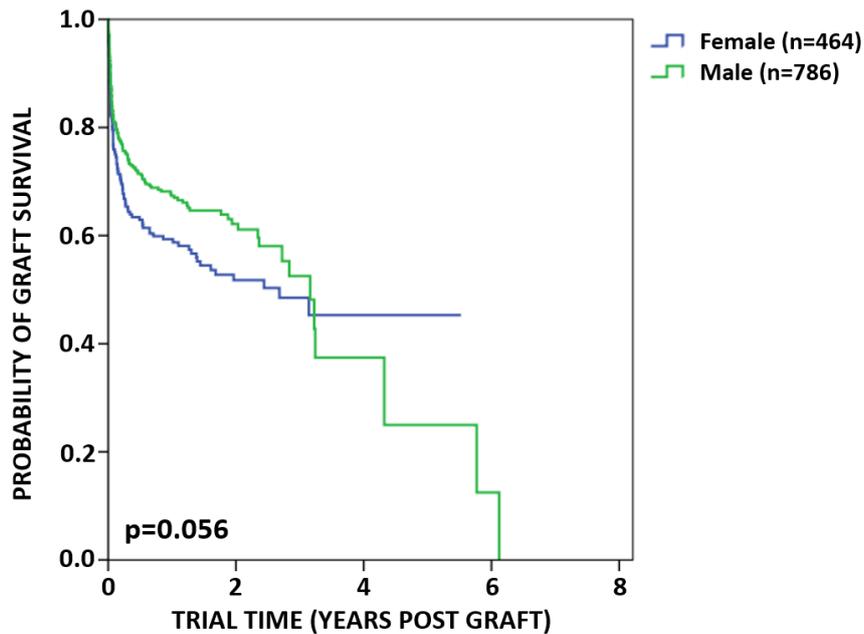
#### Probability of graft survival (years post-graft)

	1	2	3
Eye Bank M	0.61	0.56	NA
Eye Bank K	NA	NA	NA
Eye Bank V	0.61	0.54	0.52
Eye Bank J	0.87	NA	NA

### 4.1.2 DMEK survival: influence of donor sex

Almost two-thirds of corneal donors were male. Figure 4.1.2 shows the comparison of graft survival depending on donor sex. While a significant difference was not found between groups at the  $p < 0.05$  level, the result met the  $p < 0.08$  criteria for inclusion in the multivariate analysis (Log Rank Statistic=3.64;  $df=1$ ;  $p=0.056$ ). This variable was not included in the multivariate analysis (see section 4.7), as it is collinear with the variable analysing donor/recipient sex match/mismatch (see section 4.2.5), which was included.

Figure 4.1.2 Donor sex



#### Number at risk (years post-graft)

	1	2	3	4	5
<b>Female</b>	100	49	16	4	1
<b>Male</b>	176	65	16	3	2

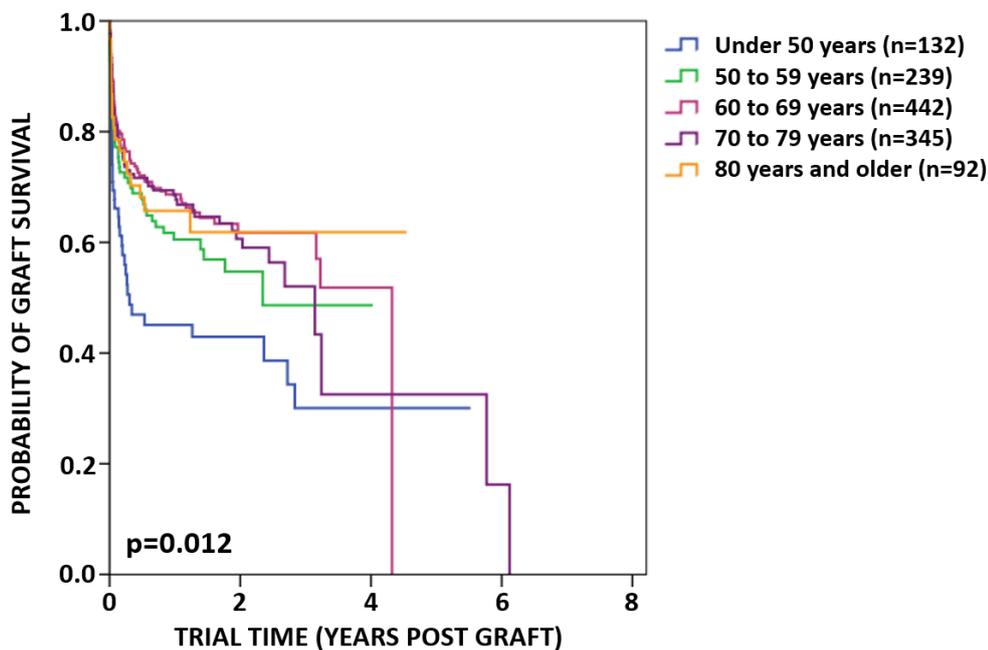
#### Probability of graft survival (years post-graft)

	1	2
<b>Female</b>	0.59	0.52
<b>Male</b>	0.67	0.62

### 4.1.3 DMEK survival: influence of donor age (years)

Figure 4.1.3 shows the comparison of graft survival depending on donor age, stratified by 10 year age groups. Due to low numbers, all donors aged under 50 years were categorised together, as well as all donors aged 80 years and over. A significant difference was found across groups (Log Rank Statistic=12.89; df=4; p=0.012), with survival for grafts performed with tissue from donors aged under 50 years significantly poorer than those aged 60 to 69 years (p=0.001) and 70 to 79 years (p=0.004). This variable was retained in the final multivariate model (see section 4.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 4.1.3 Donor age



#### Number at risk (years post-graft)

	1	2	3	4	5
Under 50 years	23	11	6	1	1
50 to 59 years	51	16	4	1	NA
60 to 69 years	102	37	13	1	NA
70 to 79 years	81	41	7	3	2
80 years or older	19	9	2	1	NA

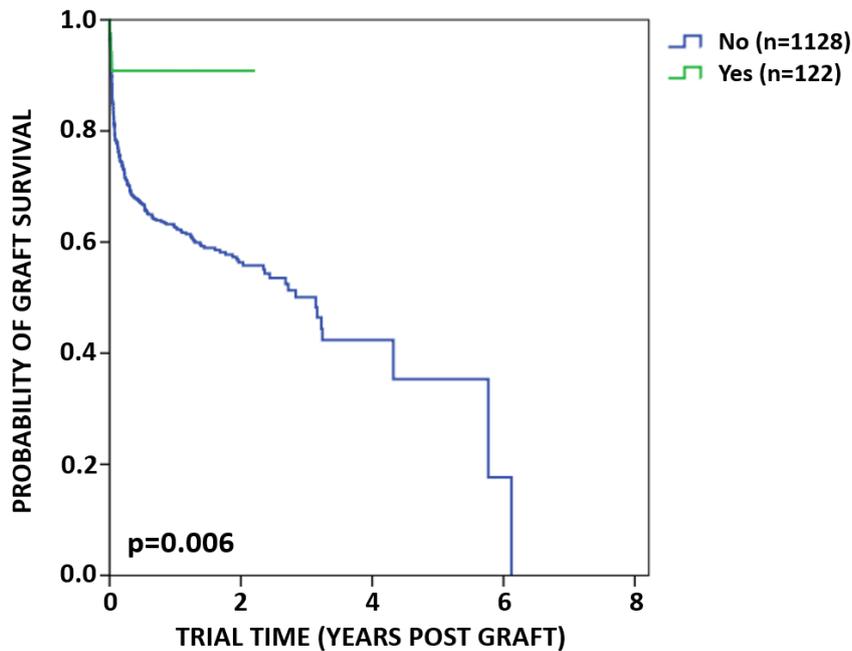
#### Probability of graft survival (years post-graft)

	1	2
Under 50 years	0.45	NA
50 to 59 years	0.61	NA
60 to 69 years	0.69	0.62
70 to 79 years	0.69	0.61
80 years or older	NA	NA

**4.1.4 DMEK survival: influence of preparatrion of donor tissue (pre-cut) by eye bank**

Donor tissue for endothelial grafts is increasingly prepared (pre-cut) by eye banks. Figure 4.1.4 shows the comparison of graft survival between those DMEK grafts that were pre-cut by the eye bank and those that were wholly cut by surgeons. A significant difference was found across groups (Log Rank Statistic=7.44; df=1; p=0.006). This variable was retained in the final multivariate model (see section 4.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 4.1.4 Preparation of donor tissue (pre-cut) by eye bank**



**Number at risk (years post-graft)**

	6 months	1	2	3	4	5
Not prepared	325	254	111	32	7	3
Prepared (pre-cut)	27	22	3	NA	NA	NA

**Probability of graft survival (years post-graft)**

	6 months	1	2	3
Not prepared	0.67	0.63	0.56	0.50
Prepared (pre-cut)	0.91	0.91	NA	NA

## 4.2 Recipient Factors

Table 3.3 shows the number of grafts within each of the variable sub-groups, for the recipient factors examined in this report that were found to be **significant** predictors of graft survival in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (1,250 registered and 600 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 4.3 Recipient factors, significant in univariate analyses**

<b>Descemet's Membrane Endothelial Corneal Graft</b>		
<b>Recipient factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Prior ipsilateral corneal graft/s</b>		
None	935 (75%)	416 (69%)
One	223 (18%)	131 (22%)
Two or more	92 (7%)	53 (9%)
<b>Australian State where graft was performed</b>		
State M	451 (36%)	152 (25%)
State K	54 (4%)	7 (<1%)
State V	601 (48%)	360 (60%)
State J	132 (11%)	80 (13%)
State N	5 (<1%)	0 (0%)
Other	7 (<1%)	1 (<1%)
<b>Recipient age group</b>		
Under 50 years	66 (5%)	38 (6%)
50 to 59 years	140 (11%)	62 (10%)
60 to 69 years	356 (28%)	180 (30%)
70 to 79 years	436 (35%)	205 (34%)
80 years or older	252 (20%)	115 (19%)
<b>Recipient sex</b>		
Female	709 (57%)	335 (56%)
Male	541 (43%)	265 (44%)
<b>Donor/recipient sex match</b>		
Female/female	246 (20%)	122 (20%)
Female/male	218 (17%)	115 (19%)
Male/female	463 (37%)	213 (36%)
Male/male	323 (26%)	150 (25%)
	<b>1250 (100%)</b>	<b>600 (100%)</b>

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Significant differences ( $p < 0.05$ ) in follow-up were found across groups for graft State, and number of previous ipsilateral grafts.

Table 4.4 shows the number of grafts within each of the variable sub-groups, for the recipient factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (1,250 registered and 600 with follow-up provided) and the percentages, summed vertically, total 100. The result of the Kaplan-Meier survival analysis is also provided.

**Table 4.4 Recipient factors, not significant in univariate analyses**

<b>Descemet's Membrane Endothelial Corneal Graft Recipient Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Indication for graft</b>		
Failed previous graft	315 (25%)	184 (31%)
Pseudophakic bullous keratopathy	214 (17%)	89 (15%)
Fuchs' endothelial dystrophy	680 (54%)	309 (52%)
Other*	41 (3%)	18 (3%)
<b>Chi<sup>2</sup>=0.24, df=3, p=0.971</b>		
<b>Eye grafted</b>		
Left	628 (50%)	307 (51%)
Right	621 (50%)	293 (49%)
Not advised	1 (<1%)	0 (0%)
<b>Chi<sup>2</sup>=0.07, df=1, p=0.786</b>		
<b>Pre-graft inflammation and/or steroid use</b>		
No	792 (63%)	391 (65%)
Yes	444 (36%)	206 (34%)
Not advised	14 (1%)	3 (<1%)
<b>Chi<sup>2</sup>=0.25, df=1, p=0.614</b>		
<b>History of raised intraocular pressure</b>		
IOP never known to be raised	1081 (86%)	528 (88%)
IOP raised in past and/or at graft	169 (14%)	72 (12%)
<b>Chi<sup>2</sup>=0.21, df=1, p=0.649</b>		
<b>Pre-graft neovascularisation</b>		
No	1080 (86%)	537 (90%)
Yes	170 (14%)	63 (11%)
<b>Chi<sup>2</sup>=1.82, df=1, p=0.178</b>		
<b>Prior contralateral corneal graft/s</b>		
None	855 (68%)	408 (68%)
One	306 (24%)	141 (24%)
Two or more	89 (7%)	51 (9%)
<b>Chi<sup>2</sup>=1.15, df=2, p=0.564</b>		
<b>Change in lens status</b>		
Phakic/phakic	64 (5%)	36 (6%)
Phakic/pseudophakic	275 (22%)	137 (23%)
Other combination	911 (73%)	427 (71%)
<b>Chi<sup>2</sup>=2.07, df=2, p=0.356</b>		
<b>Total</b>	<b>1250 (100%)</b>	<b>600 (100%)</b>

Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable.

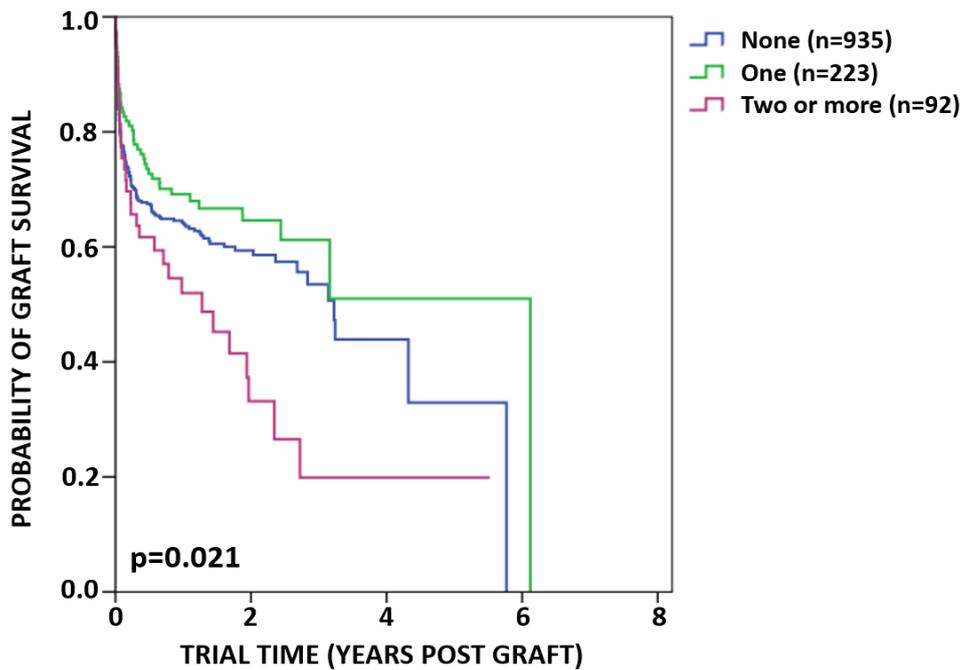
Descemet's Membrane Endothelial Keratoplasty

\*Other included: trauma (15), ICE syndrome (6), aphakic bullous keratopathy (3), corneal oedema (3), bullous keratopathy (2), congenital corneal dystrophy (2), surgical complications (2), congenital Descemet's membrane rupture (1), endophthalmitis (1), posterior polymorphous dystrophy (1), Fuchs' heterochromatic iridocyclitis (1), pseudoexfoliation syndrome (1), Rieger's anomaly (1), retrocorneal membrane (1), and unspecified endothelial dystrophy (1).

#### 4.2.1 DMEK survival: influence of the number of previous ipsilateral grafts

Survival was compared across groups based on the number of previous grafts in the same eye (range 1 to 7), as shown in Figure 4.2.1. Previous grafts may not have been Descemet's membrane endothelial keratoplasties. The difference across groups was significant (Log Rank Statistic=7.77, df=2, p=0.021), with eyes that had undergone one prior graft having superior survival to those having undergone two or more (p=0.004). This variable was not retained in the multivariate analysis suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.2.1 Number of previous ipsilateral grafts



#### Number at risk (years post-graft)

	1	2	3	4	5
None	192	80	20	4	1
One	64	26	9	2	1
Two or more	20	8	3	1	1

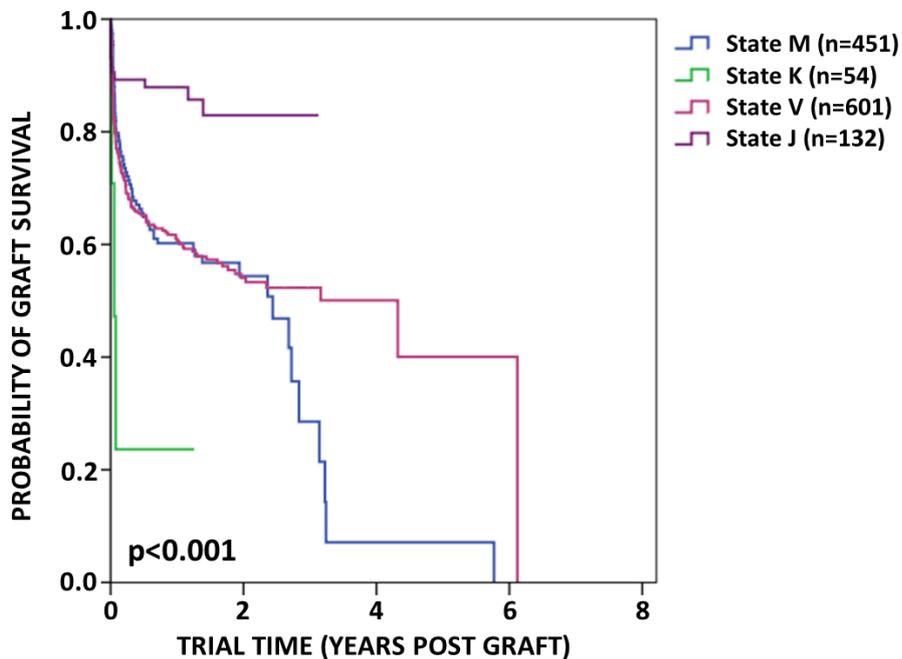
#### Probability of graft survival (years post-graft)

	1	2	3
None	0.64	0.59	0.54
One	0.69	0.65	NA
Two or more	0.52	NA	NA

**4.2.2 DMEK survival: influence of Australian State where graft was performed**

Figure 4.2.2 shows the comparison of graft survival depending on the Australian State in which the transplantation occurred. Twelve grafts that were not performed in the four included States were excluded from the analysis due to low numbers in these groups. A significant difference was found across groups (Log Rank Statistic=20.33; df=3; p<0.001), with State J having significantly better survival than State M (p=0.001) and State V (p<0.001). State M had significantly better survival than State K (p<0.001). However, the poor survival of grafts from State K is likely due to the lack of follow-up provided for these grafts, with just a single graft from this State having had follow-up provided by the surgeon (the other 6 followed grafts were known to have failed due to having regrafts registered with the ACGR). This variable was retained in the multivariate analysis suggesting that this is an independent factor significantly affecting graft survival.

**Figure 4.2.2 Australian State where graft was performed**



**Number at risk (years post-graft)**

	1	2	3	4	5
<b>State M</b>	66	19	4	1	1
<b>State K</b>	1	NA	NA	NA	NA
<b>State V</b>	149	74	27	6	2
<b>State J</b>	60	21	1	NA	NA

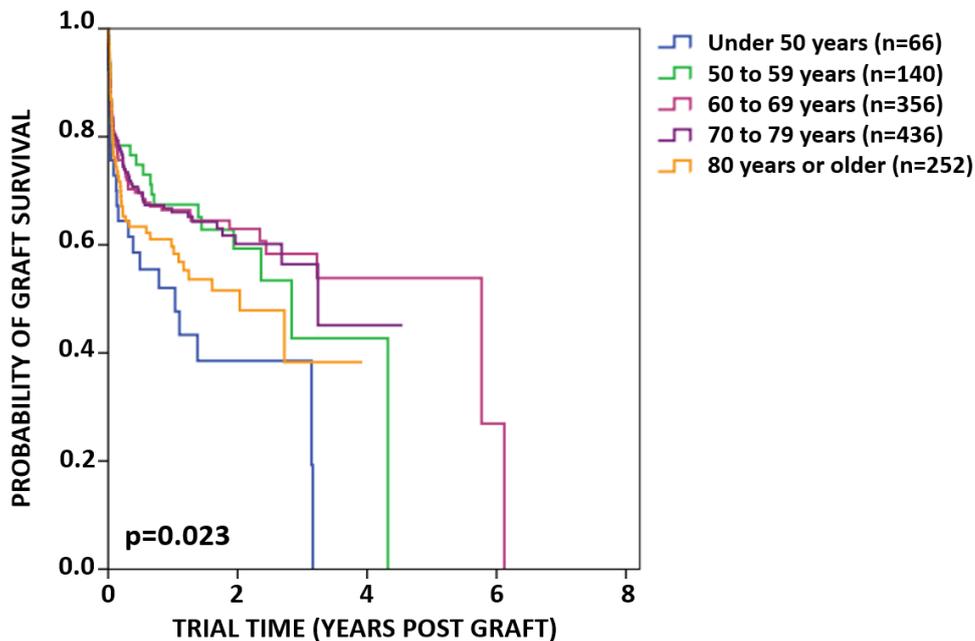
**Probability of graft survival (years post-graft)**

	1	2	3
<b>State M</b>	0.60	NA	NA
<b>State K</b>	NA	NA	NA
<b>State V</b>	0.61	0.54	0.52
<b>State J</b>	0.88	0.83	NA

### 4.2.3 DMEK survival: influence of recipient age (years)

Figure 4.2.3 shows the comparison of graft survival depending on the age of the corneal transplant recipient. Data for recipients aged under 50 were combined due to small numbers in these groups. A significant difference was found across groups (Log Rank Statistic=11.29; df=4; p=0.023). Significantly poorer survival was observed for grafts performed in recipients under 50 years old, compared to those aged 60 to 69 years (p=0.003), or 70 to 79 years (p=0.004). This variable was retained in the final multivariate model (see section 4.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 4.2.3 Recipient age**



#### Number at risk (years post-graft)

	1	2	3	4	5
Under 50 years	12	8	2	NA	NA
50 to 59 years	34	16	4	1	NA
60 to 69 years	90	36	14	5	3
70 to 79 years	96	37	9	1	NA
80 years or older	44	17	3	NA	NA

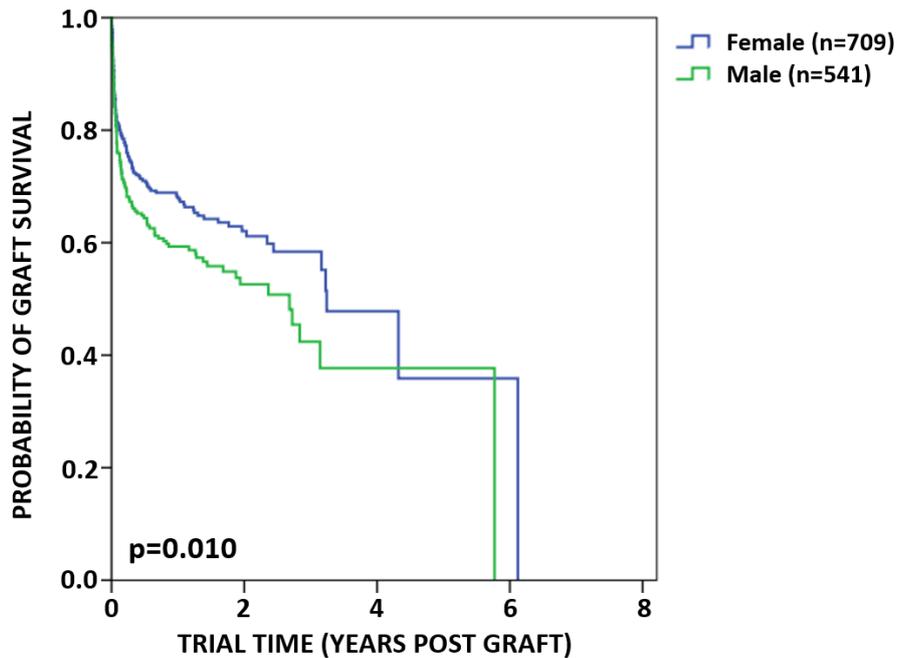
#### Probability of graft survival (years post-graft)

	1	2
Under 50 years	NA	NA
50 to 59 years	0.68	NA
60 to 69 years	0.66	0.63
70 to 79 years	0.66	0.60
80 years or older	0.60	NA

### 4.2.4 DMEK survival: influence of recipient sex

Comparison of graft survival between male and female transplant recipients is shown in Figure 4.2.4. A significant difference was found between groups (Log Rank Statistic=6.71; df=1; p=0.010). This variable was not included in the multivariate analysis (see section 4.7), as it is collinear with the variable analysing donor/recipient sex match/mismatch (see section 4.2.5), which was included.

Figure 4.2.4 Recipient sex



#### Number at risk (years post-graft)

	1	2	3	4	5
<b>Female</b>	169	70	22	4	2
<b>Male</b>	107	44	10	3	1

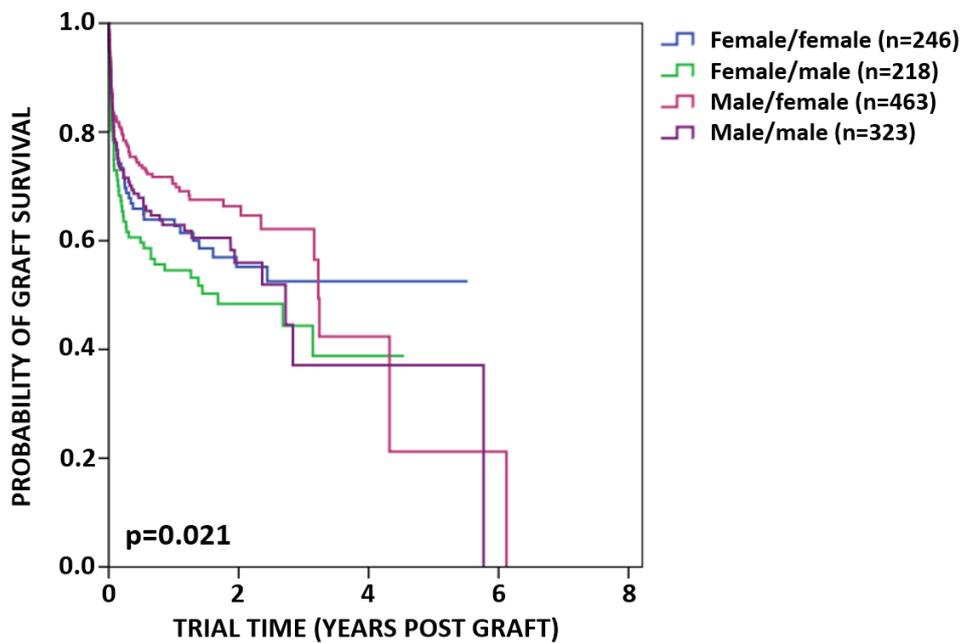
#### Probability of graft survival (years post-graft)

	1	2	3
<b>Female</b>	0.68	0.62	0.58
<b>Male</b>	0.59	0.53	NA

#### 4.2.5 DMEK survival: influence of donor/recipient sex match/mismatch

Further analysis examined whether there was any effect of a cornea being transplanted into a recipient of a different sex to the donor. Comparison of graft survival across groups based on donor/recipient sex combinations is shown in Figure 4.2.5. A significant difference was found across groups (Log Rank Statistic=9.78; df=3; p=0.021). Grafts performed in females using male donor tissue had significantly better survival than those performed in males using female donor tissue (p=0.002). This variable was not retained in the final multivariate model, suggesting that this is **not** an independent factor significantly affecting graft survival.

**Figure 4.2.5 Donor/recipient sex match/mismatch**



##### Number at risk (years post-graft)

	1	2	3	4	5
Female/female	55	28	8	2	1
Female/male	45	21	8	2	NA
Male/female	114	42	14	2	1
Male/male	62	23	2	1	1

##### Probability of graft survival (years post-graft)

	1	2
Female/female	0.64	0.55
Female/male	0.55	0.48
Male/female	0.71	0.66
Male/male	0.63	0.56

### 4.3 Graft Era

Table 4.5 shows the number of grafts registered and followed, in blocks of two years. The first two DMEK registered were performed in December of 2007 and these have been combined with the 2008/2009 group. The percentages, which should be summed vertically, total 100.

**Table 4.5 Graft era**

<b>Descemet’s Membrane Endothelial Corneal Graft Graft Era</b>		
<b>Year of graft</b>	<b>Registered (%)</b>	<b>Followed (%)</b>
2007/2008/2009	45 (4%)	28 (5%)
2010/2011	127 (10%)	99 (17%)
2012/2013	239 (19%)	158 (26%)
2014/2015	412 (33%)	258 (43%)
2016/2017	427 (34%)	57 (10%)
<b>Total</b>	<b>1250 (100%)</b>	<b>600 (100%)</b>

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses and found to be significant (p<0.001). Level of follow-up reduces as time since graft reduces, with 78% of grafts performed in 2010/11 followed, 66% of grafts performed in 2012/13, and 63% of grafts performed in 2014/15, compared with just 10% of grafts performed in 2016/17.

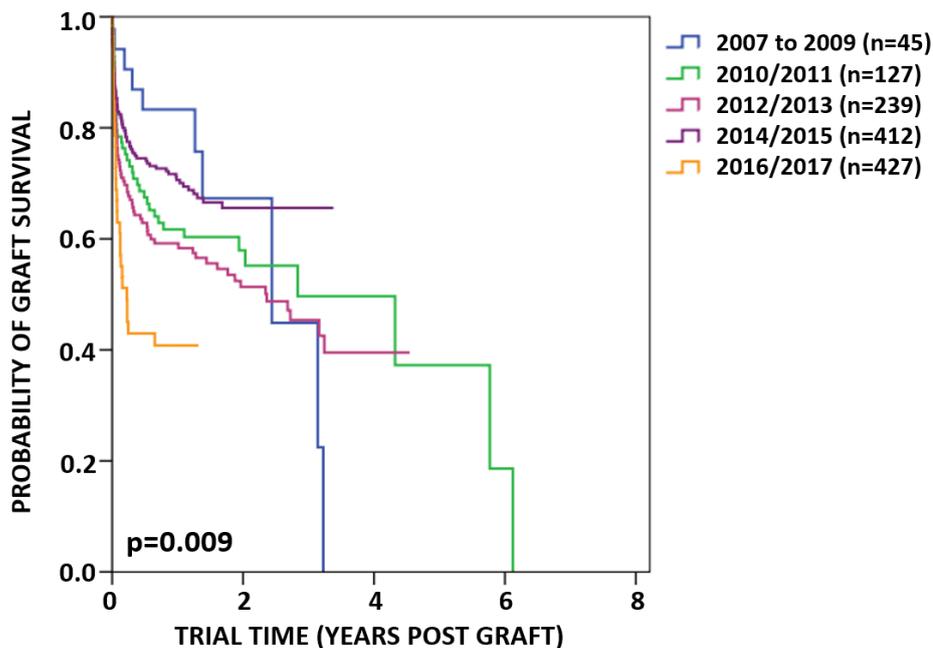
Consideration was given to the effect of follow-up lag time on this analysis. Up-to-date information on failed grafts is more likely to be known than for surviving grafts. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. A “lag time” operates at the furthest end of each curve in a Kaplan Meier plot. This effect is most pronounced in the early years following graft registration, when requests have not yet been made for follow-up information, and tends to reduce predictably over time.

Of the grafts performed in 2016/2017 just twenty-one of the grafts with follow-up were surviving at the time of follow-up. This equates to 37% of followed grafts, and 5% of registered grafts from this cohort. The remaining 36 grafts were early failures, the majority of which were recorded as failed when a replacement graft was registered.

### 4.3.1 DMEK survival: influence of era of graft

Figure 4.3.1 shows the comparison of graft survival between years of graft, stratified into two-year groups, with the two grafts performed in 2007 combined with those from 2008/2009. The difference across groups was significant (Log Rank Statistic=13.42; df=4;  $p=0.009$ ), with grafts performed in 2016/2017 having significantly poorer survival than those performed in 2007/2008/2009 and 2014/2015 (both  $p=0.001$ ). This finding is thus likely due to the lag time discussed on the previous page. This variable was retained in the final multivariate model (see section 4.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 4.3.1 Graft era



#### Number at risk (years post-graft)

	1	2	3	4	5
<b>2007/2008/2009</b>	15	3	1	NA	NA
<b>2010/2011</b>	50	21	7	4	3
<b>2012/2013</b>	68	46	20	3	NA
<b>2014/2015</b>	129	44	3	NA	NA
<b>2016/2017</b>	14	NA	NA	NA	NA

#### Probability of graft survival (years post-graft)

	1	2	3
<b>2007/2008/2009</b>	NA	NA	NA
<b>2010/2011</b>	0.62	0.58	NA
<b>2012/2013</b>	0.59	0.51	0.45
<b>2014/2015</b>	0.71	0.66	NA
<b>2016/2017</b>	NA	NA	NA

## 4.4 Surgery and Surgeon Factors

Table 4.6 shows the number of grafts within each of the variable sub-groups, for the surgery and surgeon factors examined in this report, which were found to be **significant** in univariate analyses. Only four grafts were reported to have been done using forceps, three using viscoelastic, and two using an anterior chamber maintainer. Thus, the impact of these factors was not further analysed. The sum of these numbers for each variable equals the total number of grafts (1,250 registered and 600 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 4.6 Surgery and surgeon factors, significant in univariate analyses**

<b>Descemet's Membrane Endothelial Corneal Graft Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Size of graft (diameter)</b>		
Less than 8.5 mm	683 (55%)	388 (65%)
8.5 mm to <8.75 mm	160 (13%)	70 (12%)
8.75 mm or more	340 (27%)	99 (17%)
Not advised	67 (5%)	43 (7%)
<b>The Centre effect</b>		
Fewer than 25 registered DMEK	94 (8%)	32 (5%)
Surgeon F	367 (29%)	271 (45%)
Surgeon D	364 (29%)	115 (19%)
Surgeon S	131 (10%)	80 (13%)
Surgeon A	56 (4%)	10 (2%)
Surgeon P	56 (4%)	20 (3%)
Surgeon O	35 (3%)	11 (2%)
Surgeon U	30 (2%)	4 (<1%)
Surgeon Y	30 (2%)	18 (3%)
Surgeon T	31 (2%)	13 (2%)
Surgeon R	28 (2%)	18 (3%)
Surgeon E	28 (2%)	8 (1%)
<b>Surgeon volume</b>		
Fewer than 25 registered DMEK	94 (8%)	32 (5%)
25+ registered DMEK, < 48% follow-up	600 (48%)	181 (30%)
25+ registered DMEK, ≥ 48% follow-up	556 (44%)	387 (65%)
<b>Total</b>	<b>1250 (100%)</b>	<b>600 (100%)</b>

48% was selected as the cut-off point for the follow-up categories as this (48.0%) was the average percentage of follow-up for all DMEK, regardless of surgeon experience.

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Likelihood of follow-up was significantly more likely ( $p < 0.05$ ) in some groups than others. Significant differences in follow-up were also found across groups for graft size, with grafts in the range of 8mm to 8.25mm most likely to have follow-up. There were significant differences in follow-up levels between individual surgeons. Due to the nature of the variable, follow-up was, logically, significantly higher ( $p < 0.001$ ) for grafts performed by surgeons with 25+ followed grafts and  $\geq 48\%$  follow-up.

Table 4.7 shows the number of grafts within each of the variable sub-groups, for the donor and eye banking factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (1,250 registered and 600 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The result of the Kaplan-Meier survival analysis is also provided for each variable.

**Table 4.7 Surgery and surgeon factors, not significant in univariate analyses**

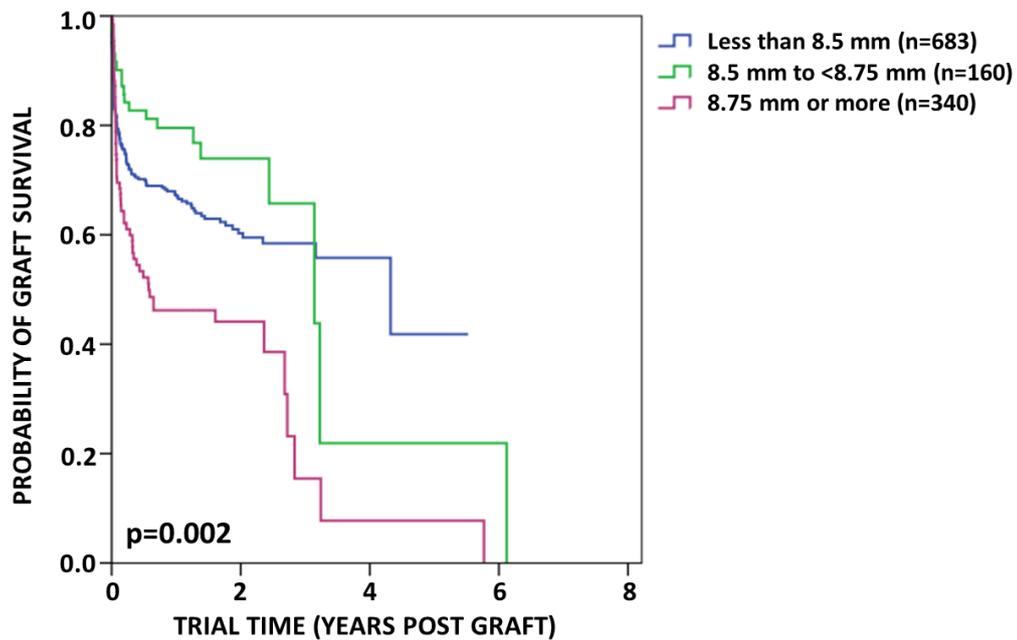
<b>Descemet's Membrane Endothelial Corneal Graft Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Size of incision</b>		
Up to 2.4 mm	185 (15%)	79 (13%)
2.5 mm to 2.7 mm	229 (18%)	129 (22%)
2.8 mm to 3.9 mm	102 (8%)	49 (8%)
4.0 mm or more	216 (17%)	81 (14%)
Not advised	518 (41%)	262 (44%)
<b>Chi<sup>2</sup>=2.99, df=3, p=0.393</b>		
<b>Use of glide</b>		
No	719 (58%)	245 (41%)
Yes	36 (3%)	17 (3%)
Not advised	495 (40%)	338 (56%)
<b>Chi<sup>2</sup>=0.60, df=1, p=0.439</b>		
<b>Donor lenticule folded</b>		
No	718 (57%)	246 (41%)
Yes	44 (4%)	22 (4%)
Not advised	488 (39%)	332 (55%)
<b>Chi<sup>2</sup>=1.87, df=1, p=0.172</b>		
<b>Total</b>	<b>1250 (100%)</b>	<b>600 (100%)</b>

Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised.

### 4.4.1 DMEK survival: influence of graft size

Figure 4.4.1 shows a comparison of graft survival depending on the size of the graft, based on the donor button diameter, as reported by surgeons. This information was not reported for 67 grafts. A significant difference was found across groups (Log Rank Statistic=12.39; df=2; p=0.002), with grafts of 8.75mm or more having significantly worse survival than those that were less than 8.5mm (p=0.008) or 8.5mm to <8.75mm (p<0.001). Data on this variable were not provided in 5% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=14.47; df=3; p=0.002). Graft size was thus categorised into these four groups for multivariate analysis. This variable was not retained in the final multivariate model, suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.4.1 Graft size



#### Number at risk (years post-graft)

	1	2	3	4	5
Less than 8.5 mm	189	82	25	5	1
8.5 mm to < 8.75 mm	39	15	3	1	1
8.75 mm or more	34	11	2	1	1

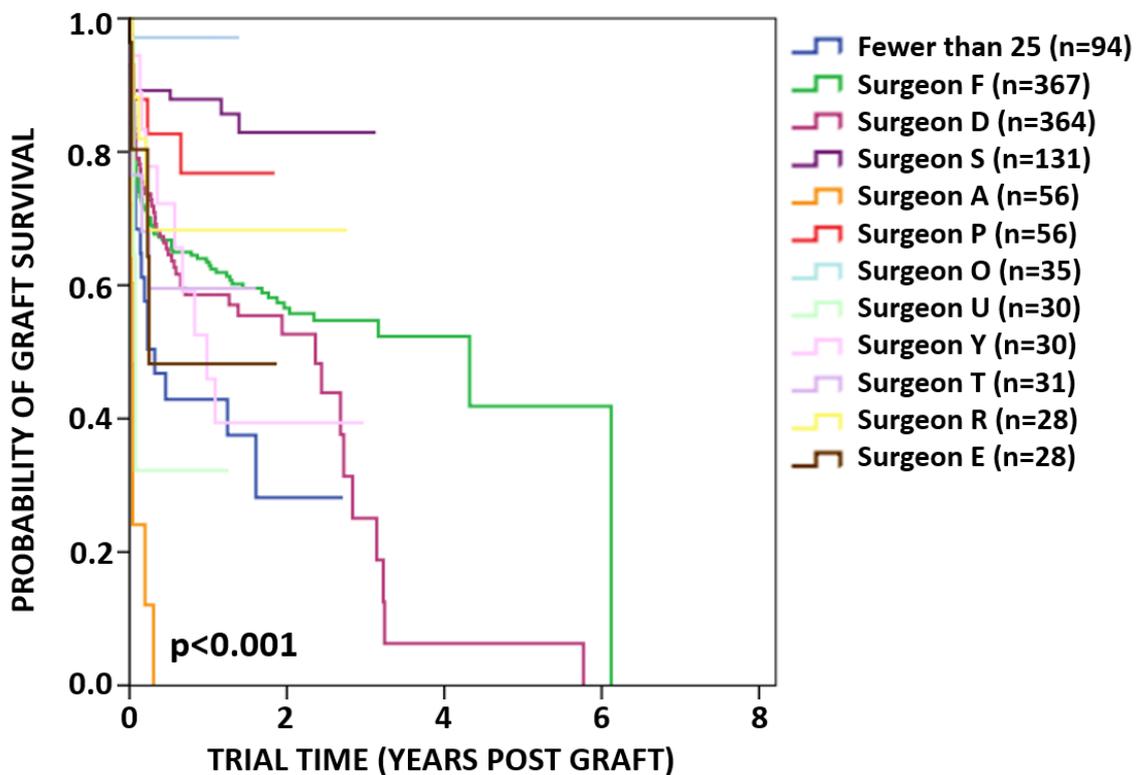
#### Probability of graft survival (years post-graft)

	1	2	3
Less than 8.5 mm	0.67	0.60	0.58
8.5 mm to < 8.75 mm	0.80	NA	NA
8.75 mm or more	0.46	NA	NA

#### 4.4.2 DMEK survival: influence of the Centre effect

Figure 4.4.2 shows the comparison of graft survival for individual surgeons (shown in ascending order of number of grafts registered) for which there were 25 or more DMEKs registered, and all other grafts (performed by 33 surgeons) combined (Log Rank Statistic=54.87; df=11;  $p<0.001$ ). This analysis indicates that there is a significant Centre effect. This variable was not included in the multivariate analysis (see section 4.7), as it is collinear with the variable analysing surgeon volume and level of follow-up (see section 4.4.3), and Australian State where the graft was performed (see section 4.2.2), which were included.

Figure 4.4.2 The Centre effect



Note: To preserve anonymity, surgeons have been identified using random letters of the alphabet. These identifying letters do not correspond with those used in chapters reporting on other types of graft, i.e. Surgeon A in this chapter is not necessarily the same surgeon identified as Surgeon A in the chapter on penetrating keratoplasty.

**Number at risk (years post-graft)**

	1	2	3	4	5
<b>&lt;25 DMEK registered</b>	10	2	NA	NA	NA
<b>Surgeon F</b>	121	70	27	6	2
<b>Surgeon D</b>	50	16	4	1	1
<b>Surgeon S</b>	60	21	NA	NA	NA
<b>Surgeon A</b>	NA	NA	NA	NA	NA
<b>Surgeon P</b>	4	NA	NA	NA	NA
<b>Surgeon O</b>	8	NA	NA	NA	NA
<b>Surgeon U</b>	1	NA	NA	NA	NA
<b>Surgeon Y</b>	7	3	NA	NA	NA
<b>Surgeon T</b>	4	NA	NA	NA	NA
<b>Surgeon R</b>	9	2	NA	NA	NA
<b>Surgeon E</b>	2	NA	NA	NA	NA

**Probability of graft survival (years post-graft)**

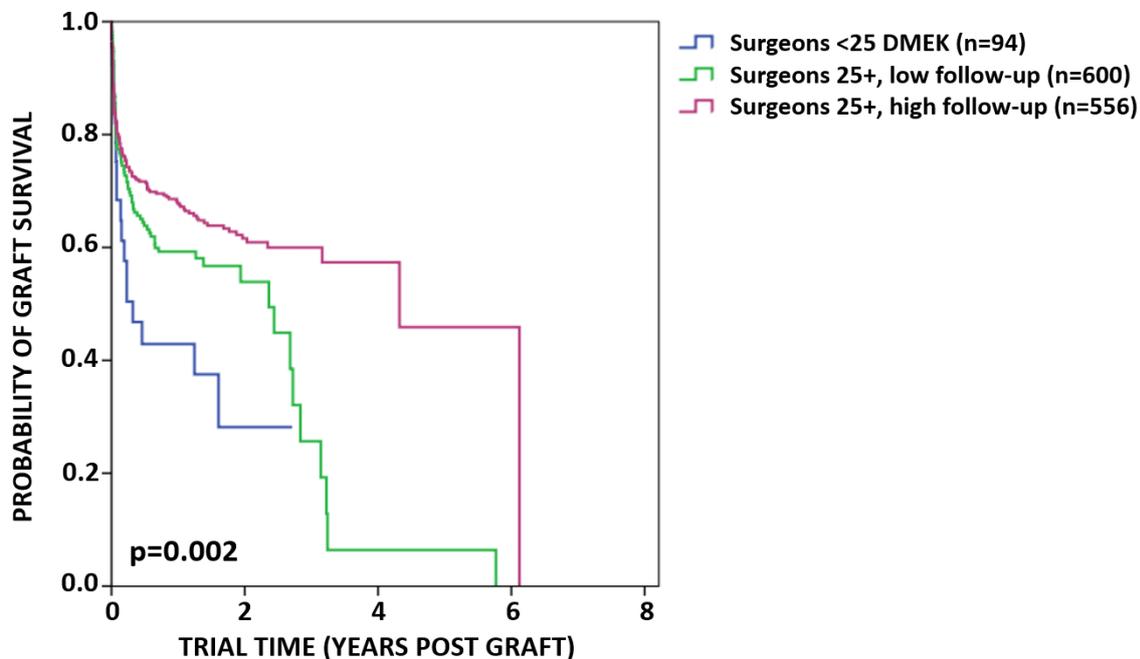
	1	2	3
<b>&lt;25 DMEK registered</b>	NA	NA	NA
<b>Surgeon F</b>	0.64	0.57	0.55
<b>Surgeon D</b>	0.59	NA	NA
<b>Surgeon S</b>	0.88	0.83	NA
<b>Surgeon A</b>	NA	NA	NA
<b>Surgeon P</b>	NA	NA	NA
<b>Surgeon O</b>	NA	NA	NA
<b>Surgeon U</b>	NA	NA	NA
<b>Surgeon Y</b>	NA	NA	NA
<b>Surgeon T</b>	NA	NA	NA
<b>Surgeon R</b>	NA	NA	NA
<b>Surgeon E</b>	NA	NA	NA

Note: For the majority of surgeons, there is very limited data for follow-up to one year. This is primarily due to the grafts being performed very recently and follow-up not yet being requested. As such, the curves in the Kaplan-Meier survival graph appear to have severe early drops in survival for these surgeons (e.g. Surgeon A, Surgeon U). This is due to the majority of grafts with follow-up for these surgeons, being those that have failed and been regrafted.

#### 4.4.3 DMEK survival: influence of surgeon volume (25+ followed DS(A)EKs) grouped by level of follow-up

Figure 4.4.3 shows the comparison of graft survival between grafts performed by surgeons with 25+ DMEKs with average or better ( $\geq 48\%$ ) follow-up, to those with lower than average follow-up ( $< 48\%$ ), and to low volume ( $< 25$ ) surgeons (Log Rank Statistic=12.40; df=2;  $p=0.002$ ). Grafts performed by surgeons with fewer than 25 DMEK registered with the ACGR had significantly poorer survival than surgeons with 25+ registered and either low levels of follow-up ( $p=0.014$ ), or high levels of follow-up ( $p=0.004$ ). Following further analyses where the data were clustered by patient [see references 7 & 8], this variable was no longer found to be significant ( $p=0.202$ ). This variable was therefore excluded from multivariate analyses and was **not** an independent factor significantly affecting graft survival.

Figure 4.4.3 Surgeon volume and level of follow-up



#### Number at risk (years post-graft)

	1	2	3	4	5
<25 registered DMEK	10	2	NA	NA	NA
25+ DMEK, low follow-up	69	16	4	1	1
25+ DMEK, high follow-up	197	96	28	6	2

#### Probability of graft survival (years post-graft)

	1	2	3
<25 registered DMEK	NA	NA	NA
25+ DMEK, low follow-up	0.59	NA	NA
25+ DMEK, high follow-up	0.68	0.62	0.60

## 4.5 Operative Procedures at the Time of Graft

Table 4.8 shows the number of grafts for which certain operative procedures were performed at the time of graft. The sum of these numbers for each variable equals the total number of grafts (1,250 registered and 600 followed) and the percentages, which should be summed vertically for each variable, total 100. Only 10 grafts had an anterior vitrectomy at the time of graft. Thus, this factor was not further analysed.

**Table 4.8 Operative procedures at graft, significant in univariate analyses**

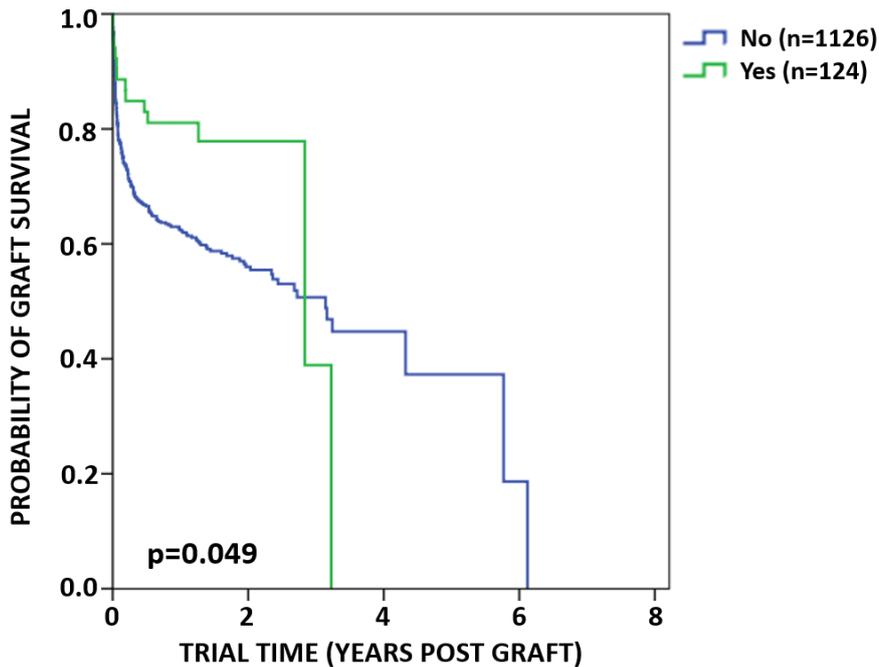
<b>Descemet's Membrane Endothelial Corneal Graft Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Peripheral iridectomy at time of graft</b>		
No	1126 (90%)	543 (90%)
Yes	124 (10%)	57 (10%)
<b>Total</b>	<b>1250 (100%)</b>	<b>600 (100%)</b>

Chi<sup>2</sup> analysis revealed no significant difference in rates of follow-up across sub-groups.

### 4.5.1 DMEK survival: influence of peripheral iridectomy at time of graft

Figure 4.5.1 shows a comparison of graft survival depending on whether a peripheral iridectomy was also performed at the time of the graft. A significant difference was found across groups (Log Rank Statistic=3.86; df=1; p=0.049). This variable was not retained in the final multivariate model, suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.5.1 Peripheral iridectomy at time of graft



#### Number at risk (years post-graft)

	1	2	3	4	5
No peripheral iridectomy	243	107	31	7	3
Peripheral iridectomy	33	7	1	NA	NA

#### Probability of graft survival (years post-graft)

	1	2	3
No peripheral iridectomy	0.63	0.56	0.51
Peripheral iridectomy	0.81	NA	NA

## 4.6 Post-graft Events

Table 4.9 shows the occurrence of post-graft events, neither of which were found to be significant in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (1,250 registered and 600 followed) and the percentages, which should be summed vertically for each variable, total 100. The result of the Kaplan-Meier survival analysis is also provided for each variable.

Only 18 grafts had post-graft corneal neovascularisation, two had post-graft herpetic infection, three had post-graft microbial keratitis, three had post-graft synechia, and three had post-graft uveitis reported. Thus, these factors was not further analysed. All of the grafts with a date of suture removal reported (n=23) were surviving and thus no further analyses was possible for this variable.

**Table 4.9 Post-graft events, not significant in univariate analyses**

<b>Descemet's Membrane Endothelial Corneal Graft</b>		
<b>Post-graft Events</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Post-graft rise in IOP</b>		
No	1203 (96%)	553 (92%)
Yes	47 (4%)	47 (8%)
<b>Chi<sup>2</sup>=0.31, df=1, p=0.580</b>		
<b>At least one rejection episode</b>		
No	1228 (98%)	578 (96%)
Yes	22 (2%)	22 (4%)
<b>Chi<sup>2</sup>=0.49, df=1, p=0.483</b>		
<b>Total</b>	<b>1250 (100 %)</b>	<b>600 (100 %)</b>

Table 4.10 shows post-graft surgical procedures, as reported by follow-up practitioners. Please note: post-graft data may be incomplete when follow-up is based on a registration for a replacement graft.

#### Table 4.10 Post-graft surgical procedures

243 DMEK were reported to have undergone a re-grafting procedure at the date last seen. Of these 219 had not had additional post-graft operative procedures reported, while 24 had.

<b>Descemet's Membrane Endothelial Corneal Graft Post-graft Surgical Procedures</b>	
	<b>Number</b>
Rebubbled	138
YAG laser	28
Cataract removal/IOL insertion (10 both, 2 IOL only)	12
Vitrectomy	11
IOL exchange/removal/reposition	9
Trabeculectomy	6
Membrane peel	4
Intravitreal injection/s	3
Insertion of piggyback lens	2
Baerveldt tube insertion	2
Paracentesis	2
Other*	18
<b>Total number of surgical procedures (number of grafts)</b>	<b>235 (184)</b>

\* Other included: air removed to reverse pupil block (1), blepharoplasty (1), collagen cross linking (1), corneal scraping (1), cyclodiode (1), drainage device inserted (1), entropion repair (1), graft repositioned (1), intraocular contact lens inserted (1), iridectomy (1), iridoplasty (1), macular hole repair (1), ptosis repair (1), removal of air bubble (1), removal of scar (1), retinal detachment surgery (1), suturing of IOL (1), synechiolysis (1).

## 4.7 Multivariate Analysis

A multivariate model was used to investigate the combined effect of variables on penetrating graft survival, adjusted for all other variables in the model. This analysis was performed using STATA version 11.

In the preceding univariate analyses, each registered DMEK, together with its archival follow-up records, was treated as a separate and independent entity. Some recipients had multiple DMEK performed during the census period (up to 31/7/2017), with some having repeat grafts in a single eye, some grafts in both eyes and some a combination of both. To control for potential inter-graft and/or inter-eye dependence in the multivariate analyses, the multivariate model was adjusted to allow for clustering by individual patient [see references 7 & 8].

Variables to be included in the Cox Proportional Hazards regression model were identified based on the results of the univariate Kaplan-Meier analyses, with a cut-off significance level of  $p < 0.08$  used to select variables for inclusion. Some variables that were found to be significant in the univariate analyses were omitted due to co-linearity. Where data were missing for 1% to 50% of cases, additional groups for each of these categorical variables were created, called "not advised". Each variable was initially analysed individually to determine if it remained significant once clustered by individual patient. Where the variable was no longer found to be significant ( $p > 0.08$ ), it was excluded from the multivariate analysis.

The best model was found by a backward elimination process, removing variables not appearing to be predictors of graft failure. The model excluded variables with a p-value of  $p \geq 0.05$  (or global p-value of  $p \geq 0.05$  for variables with more than two categories) in a stepwise manner, beginning with the least significant variable. For categorical variable with more than two groups, Bonferroni adjustment was applied to determine if significant differences were present between groups. The Kaplan-Meier plots, and additional appropriate STATA analyses, were used to assess whether each included variable met the assumption of proportional hazards. Where variables were found to be time-variant, they were treated as such in the multivariate model.

Table 4.11 shows each of the variables analysed in the univariate analyses, stratified by whether they were included in the initial multivariate model and whether they remained in the final model.

**Table 4.11 Multivariate model**

### **Descemet's Membrane Endothelial Corneal Graft Multivariate Model**

**Not significant in univariate analysis**

Storage medium  
 Time from death to enucleation  
 Time from enucleation to storage  
 Storage time in Optisol  
 Storage time in organ culture  
 Cause of donor death  
 Multi-organ donor  
 Endothelial cell density  
 Indication for graft  
 Eye grafted  
 Change in lens status pre- to post-graft  
 Raised intraocular pressure prior to and/or at graft  
 Pre-graft inflammation and/or steroid use  
 Pre-graft neovascularisation  
 Previous contralateral graft(s)  
 Incision size  
 Use of glide during surgery  
 Donor lenticule folded  
 Descemet's membrane stripped by surgeon  
 Raised intraocular pressure post-graft  
 Post-graft rejection episode(s)

**Significant in univariate analysis but excluded from multivariate model due to collinearity**

Donor sex (with donor/recipient sex match/mismatch)  
 Recipient sex (with donor/recipient sex match/mismatch)  
 Eye bank (with Australian State where graft was performed)  
 The Centre effect (with surgeon experience and level of follow-up)

**Significant in univariate analysis but not retained in multivariate model**

Surgeon experience and level of follow-up  
 Peripheral iridectomy at time of graft  
 Graft size  
 Previous ipsilateral graft/s  
 Donor/recipient sex match/mismatch

**Significant in univariate analysis AND retained in multivariate model**

Donor age group  
 Cornea pre-cut by eye bank  
 Recipient age group  
 Graft year  
 Australian State where graft was performed

Table 4.12 tabulates the parameter estimates resulting from the fit of the best clustered Cox model. The table shows the variable, the hazard ratio, the standard error of the regression coefficient, the corresponding probability value and the 95% confidence interval for the hazard ratio. The group of each categorical variable with the highest number of cases was taken as the referent. The hazard ratios for a given variable are adjusted for all other variables in the model. This model included data from the 1,238 Descemet's membrane endothelial keratoplasties, performed in 903 recipients, with appropriate data available for each included variable (12 cases that were not performed in one of the four included States were excluded from the analysis).

This model includes variables with a p-value of  $p < 0.05$ , with variables eliminated in a stepwise manner, beginning with the least significant variable. For categorical variables, a global test was applied to calculate the overall p-value. The overall model was highly significant: ( $\text{Chi}^2 = 139.31$ ,  $p < 0.0001$ ).

**Table 4.12 Clustered multivariate model**

<b>Descemet's Membrane Endothelial Corneal Graft Clustered Multivariate Model</b>						
	<b>n</b>	<b>Hazard Ratio</b>	<b>Standard error</b>	<b>p-value</b>	<b>Global p-value</b>	<b>95% confidence interval</b>
<b>Donor age group</b>						
0 to 49 years	131	1.92	0.40	0.002		1.28 - 2.88
50 to 59 years	236	1.28	0.25	0.201		0.88 - 1.86
60 to 69 years	439	1.00			0.008	
70 to 79 years	340	0.96	0.17	0.831		0.69 - 1.35
80 years or older	92	1.04	0.28	0.881		0.62 - 1.75
<b>Cornea pre-cut by eye bank</b>						
No	1123	1.00				
Yes	115	0.14	0.07	<0.001		0.05 - 0.39
<b>Recipient age group</b>						
0 to 49 years	66	2.19	0.47	<0.001		1.43 - 3.34
50 to 59 years	137	0.86	0.18	0.470		0.58 - 1.29
60 to 69 years	353	0.96	0.17	0.817		0.68 - 1.36
70 to 79 years	432	1.00			<0.001	
80 years or older	250	1.29	0.23	0.161		0.90 - 1.83
<b>Graft year</b>						
Pre 2010	45	0.24	0.09	<0.001		0.11 - 0.49
2010/2011	127	0.37	0.10	<0.001		0.22 - 0.63
2012/2013	239	0.45	0.11	0.001		0.28 - 0.71
2014/2015	411	0.36	0.08	<0.001		0.23 - 0.54
2016/2017	416	1.00			<0.001	
<b>Australian State where graft was performed</b>						
State M	451	0.80	0.16	0.260		0.55 - 1.18
State K	54	7.02	2.40	<0.001		3.59 - 13.73
State V	601	1.00			<0.001	
State J	132	0.69	0.20	0.196		0.39 - 1.21

#### **4.7.1 Significant differences in the Descemet's membrane endothelial keratoplasty multivariate model for categories with more than two groups following Bonferroni correction for multiple comparisons**

##### **4.7.1.1 Donor age group**

Significantly poorer survival was found for the under 50 years age category, compared to the 60 to 69 years ( $p=0.002$ ), and 70 to 79 years ( $p=0.001$ ) categories.

##### **4.7.1.2 Australian State where graft was performed**

Grafts performed in State K had significantly poorer survival than those performed in State M, State V or State J (all  $p<0.001$ ). The poor performance of grafts in this category is likely due to the lack of follow-up provided for these grafts, with just a single graft from this State having had follow-up provided by the surgeon (the other 6 followed grafts were known to have failed due to having regrafts registered with the ACGR).

##### **4.7.1.3 Recipient age group**

Significantly poorer survival was found for the under 50 years age category, compared to the 50 to 59 years, 60 to 69 years, and 70 to 79 years age groups (all  $p<0.001$ ).

##### **4.7.1.4 Graft era**

Graft survival was significantly poorer for the most recent grafts, performed in 2016 and 2017, compared to all other years (all  $p<0.001$ , except 2012/2013 where  $p=0.001$ ). The poor performance of grafts in this category is likely due to the lag time effect discussed in section 2.3.1.

## 4.8 Reasons for Graft Failure

Of the 921 followed grafts, 251 (27%) were known to have failed by the census date. This equates to 20% of the 1,250 registered grafts. Surgeons were asked to indicate the reason for graft failure. This information was also gathered from repeat registration forms, where the reason for failure of the previous graft was given. Table 4.13 shows the reasons for failure given.

**Table 4.13 Reasons for graft failure**

<b>Descemet’s Membrane Endothelial Corneal Graft Reasons for Graft Failure</b>	
Primary graft failure	160 (64%)
Endothelial cell failure	46 (18%)
Rejection	9 (4%)
Scarring	5 (2%)
Other specified*	14 (6%)
Unspecified	17 (7%)
<b>Total</b>	<b>251 (100%)</b>

\* Other included: Infection (3), folds (2), persistent graft detachment (2), trauma (2), astigmatism (1), glaucoma (1), keratoconus (1), retained Descemet’s membrane (1), wound dehiscence (1).

Primary graft non-functions are defined as grafts that never clear in the post-operative period. For lamellar procedures, primary graft failure is recorded as reported by surgeons. Additional information is collected to ascertain whether this occurred as “early failure, within 28 days of the graft. Where surgeons indicate that the failure was due to surgical complications, this is also recorded.

Of the 160 grafts reported by surgeons to have been primary graft failures, the majority (89) had no further information provided. Specific reasons given were: failure to adhere/graft detachment (39), surgical trauma/complication (12), endothelial failure (7), folds in Descemet’s membrane (4), upside down insertion (4), oedema (2), haemorrhage (1), rejection (1), and ulcer (1).

## 4.9 Post-graft Changes in Best Corrected Visual Acuity

### 4.9.1 All indications for graft

Post-graft best corrected visual acuity (BCVA) is an important outcome for corneal graft recipients. A desire for improved visual acuity was specified as a reason for graft in 1,194 (96%) of registered Descemet's membrane endothelial keratoplasties. In 85% of cases (1,060), this was the sole desired outcome indicated. It is likely that this was also at least part of the reason for graft in some of the further 45 (4%) grafts where no reason was specified.

Follow-ups occur at varying times post-graft, depending on when a surgeon sees a recipient. Where post-graft best corrected visual acuity (without pinhole) information was provided, we categorised this according to the length of time since graft. The first two categories were:

- BCVA provided at between 6 and 12 months post-graft, and
- BCVA provided at between 12 and 18 months post-graft.

Subsequent groups were at yearly intervals. For each year point, any measurements provided within 6-months of that date, rounded to the nearest day, were included (e.g. for 2-year follow-up, any BCVA given at between 730 and 913 days post-graft was included).

We analysed post-graft best corrected visual acuity in several ways. Where more than 20 grafts had BCVA measurements provided, we examined:

1. The percentage of *surviving* grafts achieving different levels of Snellen visual acuity (6/6 or better, 6/7.5 to 6/12, 6/15 to 6/24, 6/36 to 6/60, count fingers (CF) or hand movements (HM), and light perception (LP) or no light perception (NLP)) at yearly time-points post-graft. Grafts that had been reported to have failed at the time of last follow-up, but had prior follow-ups with BCVA measurements provided when the graft was surviving, had these prior data included in these analyses.
2. The *average* Snellen visual acuity achieved at yearly intervals post-graft, again by *surviving* grafts.
3. The final BCVA reported at the time of failure.

Table 4.14 and Figure 4.9.1 show the reported post-graft best corrected visual acuity for all failed grafts at the time of last follow-up, separated by indication for graft. Visual acuity at time of failure was reported for 223 (89%) of 251 failed DMEK. As might be expected, the majority of failed grafts had accompanying poor visual acuity.

**Table 4.14 Post-graft best corrected visual acuity**

<b>Descemet's Membrane Endothelial Keratoplasty: Visual Acuity in Failed Grafts (as reported at final follow-up)</b>						
	6/4 to 6/6	6/7.5 to 6/12	6/15 to 6/24	6/36 to 6/60	CF or HM	LP or NLP
<b>Failed previous graft</b>	1 (1%)	6 (8%)	5 (7%)	14 (20%)	44 (62%)	1 (1%)
<b>Pseudo bullous keratopathy</b>	0 (0%)	1 (3%)	1 (3%)	3 (9%)	27 (84%)	0 (0%)
<b>Fuchs' endothelial dystrophy</b>	0 (0%)	3 (3%)	13 (12%)	17 (15%)	79 (70%)	1 (<1%)
<b>Other specified</b>	0 (0%)	0 (0%)	0 (0%)	1 (14%)	6 (86%)	0 (0%)
<b>Total</b>	<b>1 (&lt;1%)</b>	<b>10 (4%)</b>	<b>19 (9%)</b>	<b>35 (16%)</b>	<b>156 (70%)</b>	<b>2 (1%)</b>

CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

**Figure 4.9.1 Best corrected visual acuity at time of last follow-up for failed Descemet's membrane endothelial keratoplasties**

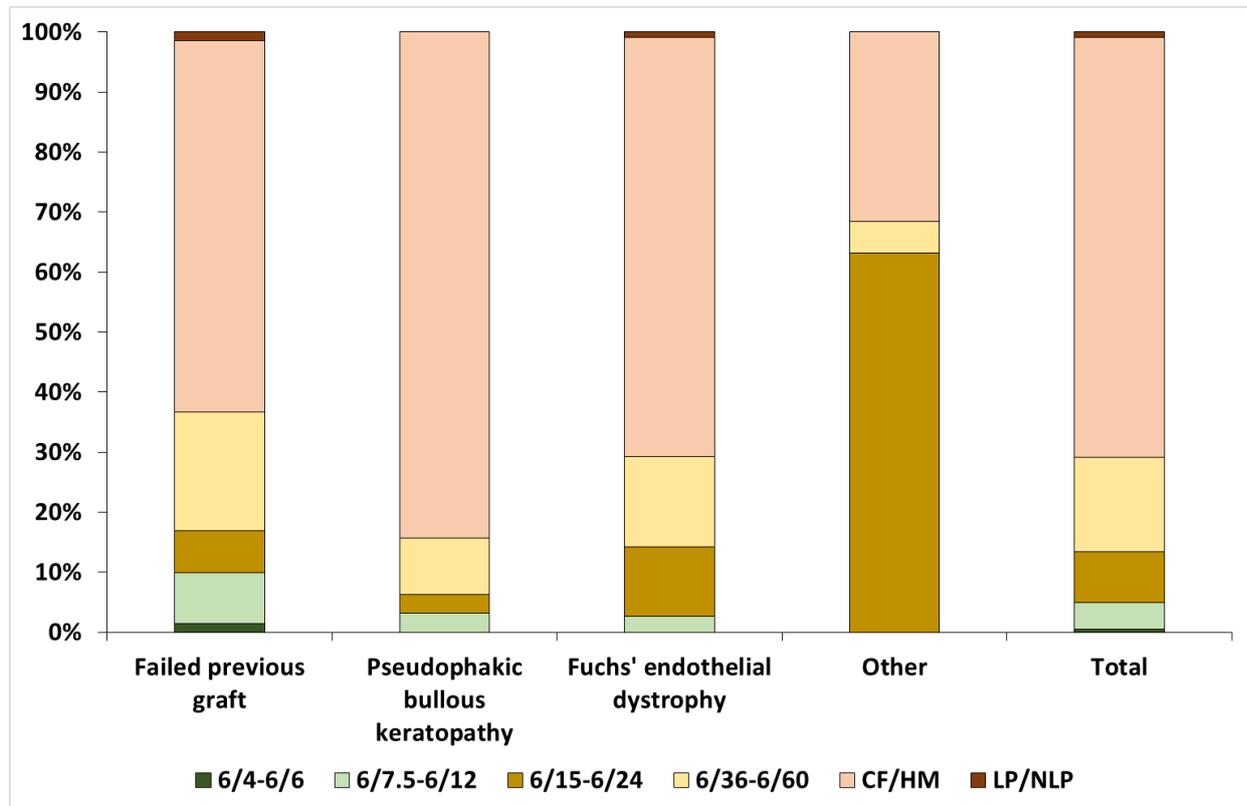
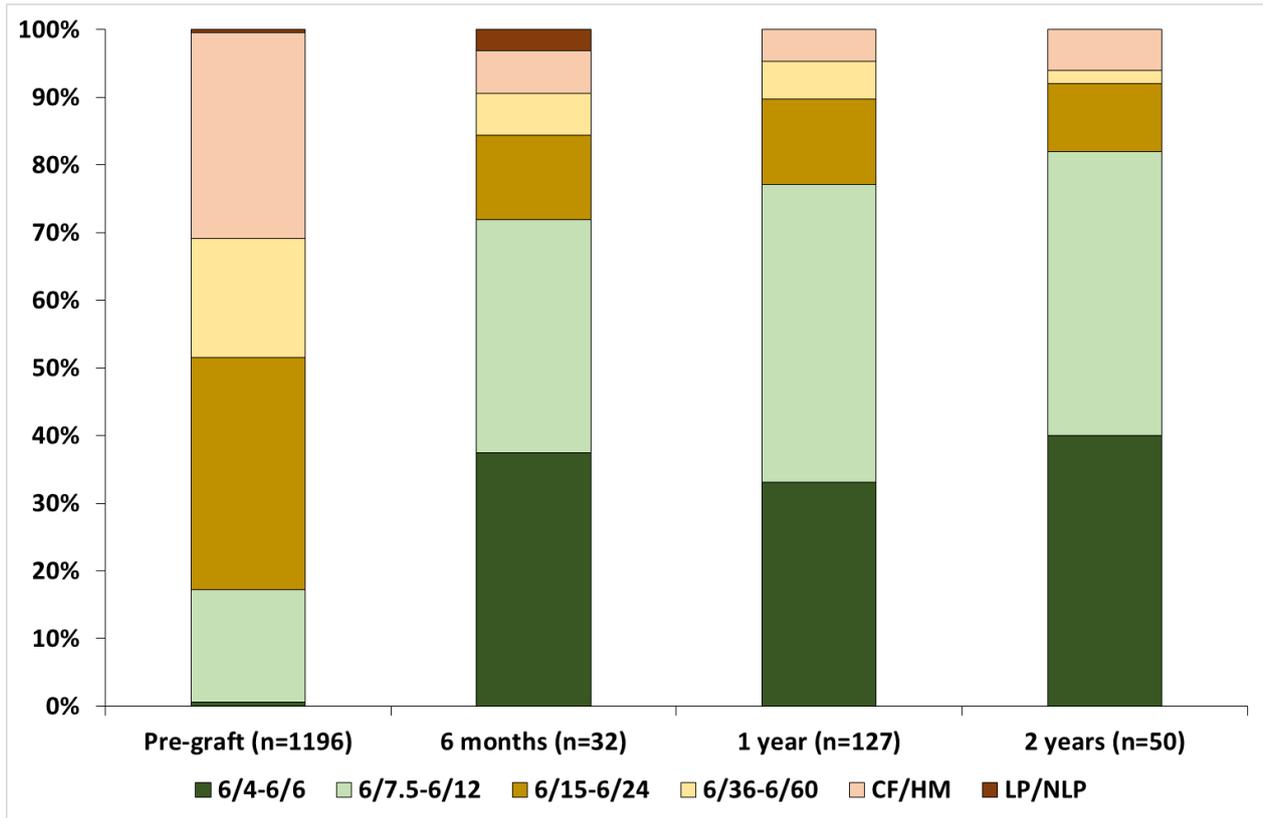


Figure 4.9.2 shows the best corrected visual acuity in the grafted eye, as reported to the ACGR, and categorised into six levels of vision, for all **surviving** Descemet’s membrane endothelial keratoplasties. Prior to graft almost one-third of eyes (31%) had vision of CF or worse, with almost another fifth (18%) having 6/36 to 6/60. By 2-years post-graft, over 90% of eyes with **surviving** grafts had vision of 6/24 or better, with more than 80 percent having functional vision of 6/12 or better.

**Figure 4.9.2 Best corrected visual acuity for Descemet's membrane endothelial keratoplasties, surviving at time of measurement**

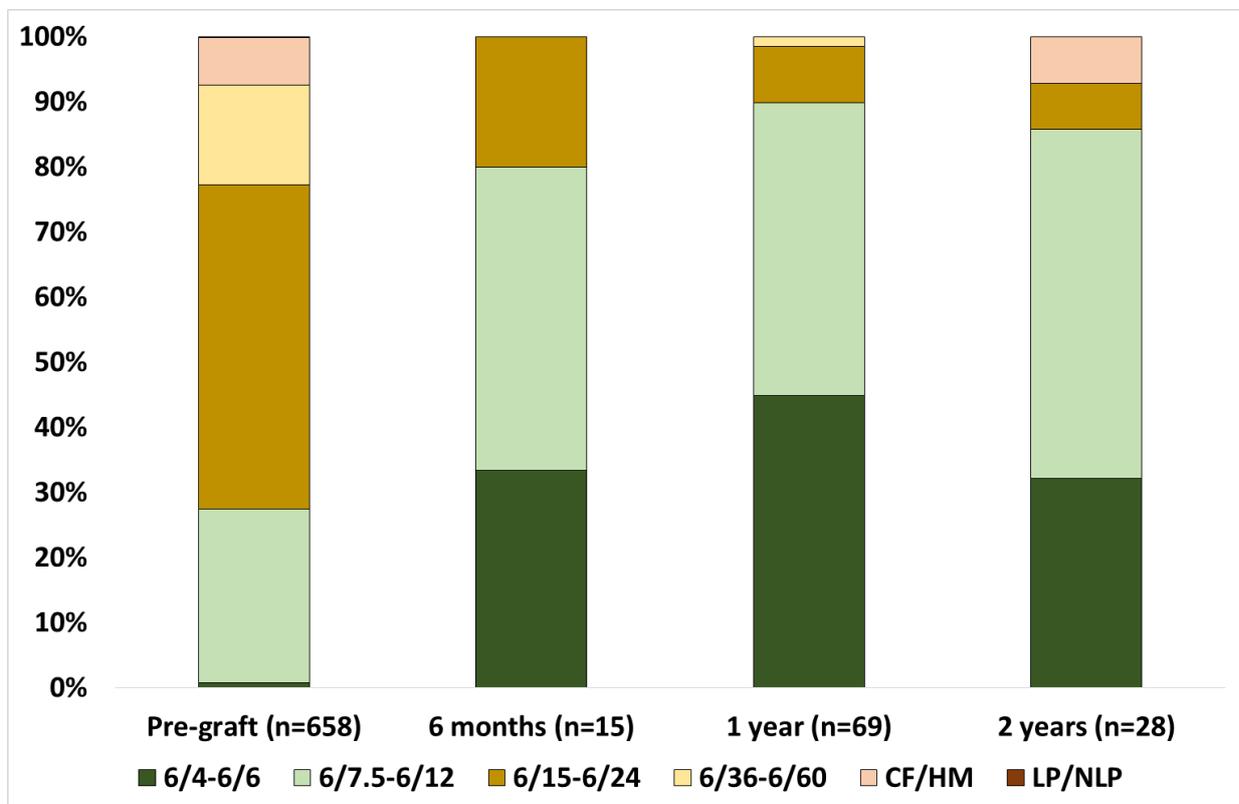


CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

### 4.9.2 Individual indications for graft

The only indication for graft with sufficient data to examine the visual outcomes individually was Fuchs' endothelial dystrophy. Figure 4.9.3 shows levels of best corrected visual acuity reported to the ACGR, at yearly intervals for **surviving** Descemet's membrane endothelial keratoplasties for Fuchs' endothelial dystrophy. Post-graft vision of 6/12 or better was reported in the vast majority (90%) of **surviving** Descemet's membrane endothelial keratoplasties performed for Fuchs' endothelial dystrophy that had BCVA measurements reported between 12 and 18-months post-graft. This percentage remained above 85% at 2-years post-graft.

**Figure 4.9.3 Fuchs' endothelial dystrophy: level of best corrected visual acuity reported at yearly time points for surviving grafts**





## 5 Deep Anterior Lamellar Keratoplasty

This chapter presents the results of analyses conducted on data relating to the 1,531 deep anterior lamellar keratoplasties (DALK) registered with the ACGR. Kaplan-Meier survival analyses were conducted using IBM SPSS for Windows (Version 22.0), to compare the graft survival across groups for a range of variables relating to the corneal donor, graft recipient, surgical procedure, surgeon, and follow-up care.

### 5.1 Donor and Eye Banking Factors

Table 5.1 shows the number of grafts within each of the variable sub-groups, for the donor factors examined in this report that we found to be **significant** in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (1,531 registered and 921 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 5.1 Donor and eye banking factors, significant in univariate analyses**

Deep Anterior Lamellar Corneal Graft Donor and Eye Banking Factors		
	Registered (%)	Followed (%)
<b>Storage-to-graft time - organ culture</b>		
Up to 2 weeks	140 (9%)	74 (8%)
2 to 3 weeks	220 (14%)	114 (12%)
More than 3 weeks	82 (5%)	43 (5%)
Not advised	276 (18%)	131 (14%)
Not applicable	813 (53%)	559 (61%)
<b>Total</b>	<b>1531 (100%)</b>	<b>921 (100%)</b>

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category were examined using Chi<sup>2</sup> analyses. Likelihood of follow-up was significantly less likely (p<0.001) for grafts using the Melles technique.

Table 5.2 shows the number of grafts within each of the variable sub-groups, for the donor and eye banking factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (1,351 registered and 921 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The result of the Kaplan-Meier survival analysis is also provided for each variable.

Table 5.2 Donor and eye banking factors, not significant in univariate analyses

<b>Deep Anterior Lamellar Corneal Graft Donor and Eye Banking Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Eye bank</b>		
Eye bank M	723 (47%)	335 (36%)
Eye bank K	272 (18%)	201 (22%)
Eye bank V	343 (22%)	264 (29%)
Eye bank J	79 (5%)	38 (4%)
Eye bank N	113 (7%)	82 (9%)
Not advised*	1 (<1%)	1 (<1%)
<b>Chi<sup>2</sup>=5.58, df=4, p=0.233</b>		
<b>Death-to-enucleation time</b>		
≤ 3 hours	151 (10%)	117 (19%)
4 to 6 hours	234 (15%)	140 (15%)
7 to 9 hours	261 (17%)	145 (16%)
10 to 12 hours	304 (20%)	194 (21%)
13 to 15 hours	204 (13%)	128 (14%)
16 to 18 hours	170 (11%)	89 (10%)
> 18 hours	202 (13%)	105 (11%)
Not advised	5 (<1%)	3 (<1%)
<b>Chi<sup>2</sup>=9.08, df=6, p=0.169</b>		
<b>Enucleation-to-storage time</b>		
≤ 3 hours	707 (46%)	411 (45%)
4 to 6 hours	157 (10%)	114 (12%)
7 to 12 hours	84 (5%)	58 (6%)
> 12 hours	122 (8%)	94 (10%)
Not advised	461 (30%)	244 (26%)
<b>Chi<sup>2</sup>=2.31, df=3, p=0.510</b>		
<b>Storage medium</b>		
Optisol	809 (53%)	559 (61%)
Organ culture	718 (47%)	362 (39%)
Moist pot	4 (<1%)	0 (0%)
<b>Chi<sup>2</sup>=0.07, df=1, p=0.792</b>		
<b>Storage-to-graft time - Optisol</b>		
Within 5 days	406 (27%)	288 (31%)
6 to 7 days	140 (9%)	97 (11%)
Longer than 1 week	78 (5%)	61 (7%)
Not advised	185 (12%)	113 (12%)
Not applicable	722 (47%)	362 (39%)
<b>Chi<sup>2</sup>=0.33, df=2, p=0.847</b>		

	Registered (%)	Followed (%)
<b>Deswelling time - organ culture</b>		
Less than 2 days	127 (8%)	25 (3%)
2 to 3 days	49 (3%)	9 (1%)
Longer than 3 days	46 (3%)	9 (1%)
Not advised	587 (38%)	448 (49%)
Not applicable	722 (47%)	362 (39%)
<b>Chi<sup>2</sup>=0.83, df=2, p=0.659</b>		
<b>Sex of donor</b>		
Female	658 (43%)	398 (43%)
Male	873 (57%)	523 (57%)
<b>Chi<sup>2</sup>=0.90, df=1, p=0.343</b>		
<b>Age group</b>		
Under 20 years	45 (3%)	27 (3%)
20 to 29 years	54 (4%)	34 (4%)
30 to 39 years	82 (5%)	48 (5%)
40 to 49 years	148 (10%)	76 (8%)
50 to 59 years	308 (20%)	171 (19%)
60 to 69 years	457 (30%)	277 (30%)
70 to 79 years	324 (21%)	208 (23%)
80 years or older	113 (7%)	80 (9%)
<b>Chi<sup>2</sup>=4.48, df=7, p=0.723</b>		
<b>Cause of death</b>		
Cardiac event	342 (22%)	220 (24%)
Malignancy	571 (37%)	341 (37%)
Trauma	129 (8%)	76 (8%)
Respiratory event	109 (7%)	69 (7%)
Intracranial/cerebral haemorrhage	278 (18%)	159 (17%)
Other specified	78 (5%)	42 (5%)
Not advised**	24 (2%)	14 (2%)
<b>Chi<sup>2</sup>=5.47, df=5, p=0.361</b>		
<b>Multi-organ donor status</b>		
No	1314 (86%)	794 (86%)
Yes	217 (14%)	127 (14%)
<b>Chi<sup>2</sup>=1.87, df=1, p=0.171</b>		
<b>Central corneal endothelial cell density</b>		
<2500 cells/mm <sup>2</sup>	122 (8%)	66 (7%)
2500 to 2749 cells/mm <sup>2</sup>	142 (9%)	81 (9%)
2750 to 2999 cells/mm <sup>2</sup>	195 (13%)	93 (10%)
3000 to 3249 cells/mm <sup>2</sup>	262 (17%)	141 (15%)
3250 to 3499 cells/mm <sup>2</sup>	195 (13%)	103 (11%)
≥ 3500 cells/mm <sup>2</sup>	118 (8%)	64 (7%)
Not advised	497 (32%)	457 (50%)
<b>Chi<sup>2</sup>=3.25, df=5, p=0.662</b>		
<b>Total</b>	<b>1531 (100%)</b>	<b>921 (100%)</b>

Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable, or categories with fewer than 20 grafts.

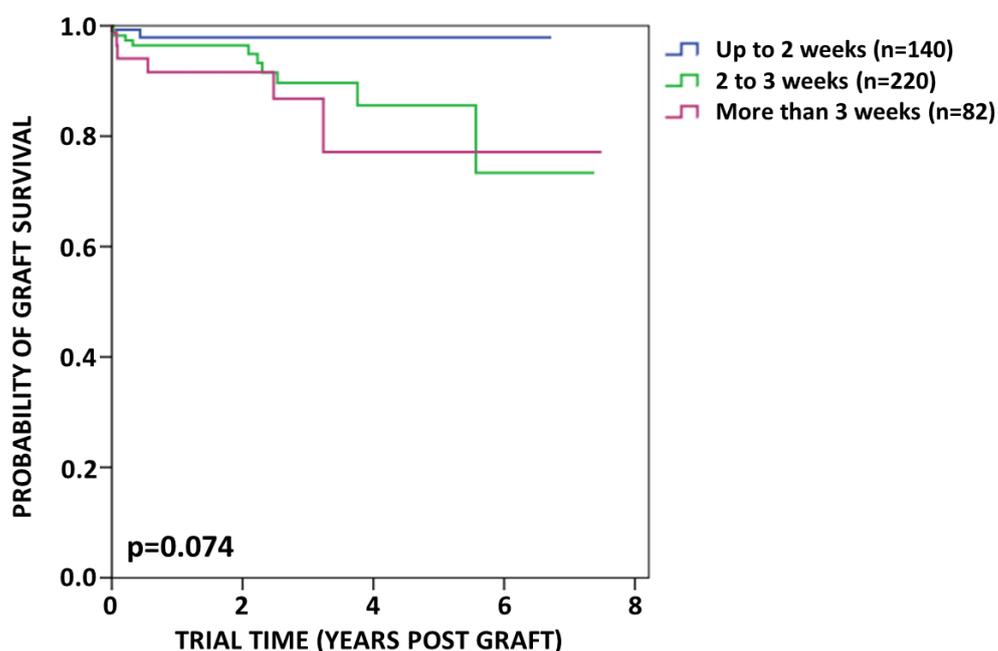
\* One autograft with no eye bank given

\*\* ACGR advised that cause of death was not yet determined but there were no medical contraindications and the eye had been cleared for release, by the Medical Director, in accordance with EBAANZ guidelines.

### 5.1.1 DALK survival: influence of storage time to graft – organ culture medium

Organ culture storage can allow preservation times of up to four weeks. Figure 5.1.1 shows the comparison of graft survival across storage time for those corneas stored in organ culture medium. Data were not provided for 276 grafts. These were excluded from the analysis. No significant difference was found across groups (Log Rank Statistic=5.22; df=2; p=0.074), and none of the subgroup analyses were significant after Bonferroni correction (all p>0.016). While the difference met the p<0.08 criteria for potential inclusion in multivariate analysis, the high proportion of the cohort that it was not relevant to (53%) and the additional rate of missing data (18%) meant that data were only available for 28% of DALK and it was thus excluded from multivariate analysis.

Figure 5.1.1 Time from storage to graft, organ culture medium storage



#### Number at risk (years post-graft)

	1	2	4	6
Less than 2 weeks	65	40	6	4
2 to 3 weeks	100	65	20	5
More than 3 weeks	35	22	2	1

#### Probability of graft survival (years post-graft)

	1	2	4
Less than 2 weeks	0.98	0.98	NA
2 to 3 weeks	0.96	0.96	0.86
More than 3 weeks	0.92	0.92	NA



## 5.2 Recipient Factors

Table 5.3 shows the number of grafts within each of the variable sub-groups, for the recipient factors examined in this report that were found to be **significant** predictors of graft survival in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (1,531 registered and 921 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 5.3 Recipient factors, significant in univariate analyses**

<b>Deep Anterior Lamellar Corneal Graft Recipient Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Indication for graft</b>		
Failed previous graft	66 (4%)	38 (4%)
Keratoconus	1161 (76%)	688 (75%)
Herpetic eye disease	63 (4%)	47 (5%)
Corneal degenerations	58 (4%)	32 (3%)
Corneal dystrophies	41 (3%)	22 (2%)
Non-herpetic infections	53 (3%)	37 (4%)
Corneal scars and opacities	36 (2%)	24 (3%)
Other*	53 (3%)	33 (4%)
<b>Recipient age group</b>		
<20 years	106 (7%)	62 (7%)
20 to 29 years	490 (32%)	293 (32%)
30 to 39 years	395 (26%)	240 (26%)
40 to 49 years	225 (15%)	130 (14%)
50 to 59 years	140 (9%)	87 (9%)
60 to 69 years	97 (6%)	61 (7%)
70 years or older	78 (5%)	48 (5%)
<b>Change in lens status pre- to post-graft</b>		
Phakic/Phakic	1442 (94%)	866 (94%)
Other	89 (6%)	55 (6%)
<b>Pre-graft neovascularisation</b>		
None	1363 (89%)	815 (88%)
One quadrant	64 (4%)	42 (5%)
Two quadrants	61 (4%)	38 (4%)
Three quadrants	22 (1%)	14 (2%)
Four quadrants	21 (1%)	12 (1%)
<b>Pre-graft inflammation and/or steroid use</b>		
No	1384 (90%)	823 (89%)
Yes	133 (9%)	91 (10%)
Not advised	14 (1%)	7 (1%)
<b>Total</b>	<b>1531 (100%)</b>	<b>921 (100%)</b>

\* Other included: trauma (18), corneal ulcer/perforation (8), keratoglobus (6), interstitial keratitis (5), congenital abnormality (4), descemetocoele (4), metabolic deposits (4), irregular astigmatism (1), limbal dermoid (1), Wegener's granulomatosis (1).

Comparisons between the percentages of grafts registered and followed in each category showed no significant differences across groups (all  $p > 0.05$ ).

Deep Anterior Lamellar Keratoplasty

Table 5.4 shows the number of grafts within each of the variable sub-groups, for the recipient factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (1,531 registered and 921 with follow-up provided) and the percentages, summed vertically, total 100. The result of the Kaplan-Meier survival analysis is also provided.

**Table 5.4 Recipient factors, not significant in univariate analyses**

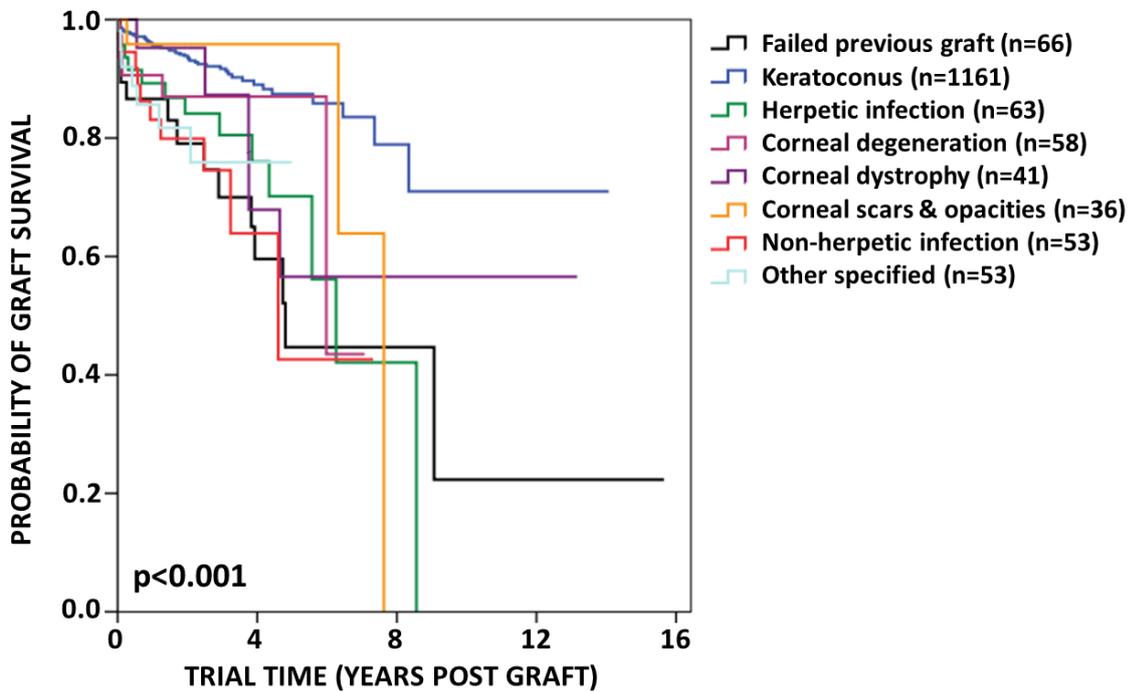
<b>Deep Anterior Lamellar Corneal Graft</b>		
<b>Recipient Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Australian State where graft was performed</b>		
State M	727 (47%)	340 (37%)
State K	268 (18%)	199 (22%)
State V	326 (21%)	249 (27%)
State J	91 (6%)	45 (5%)
State N	98 (6%)	73 (8%)
State C	18 (1%)	15 (2%)
Other	3 (<1%)	0 (0%)
<b>Chi<sup>2</sup>=5.96, df=4, p=0.202</b>		
<b>Interstate transportation</b>		
No	1482 (97%)	890 (97%)
Yes	45 (3%)	30 (3%)
Not advised	4 (<1%)	1 (<1%)
<b>Chi<sup>2</sup>=0.01, df=1, p=0.919</b>		
<b>Recipient sex</b>		
Female	582 (38%)	364 (40%)
Male	949 (62%)	557 (60%)
<b>Chi<sup>2</sup>=0.84, df=1, p=0.360</b>		
<b>Donor/recipient sex match/mismatch</b>		
Female/female	246 (16%)	143 (16%)
Female/male	412 (27%)	255 (28%)
Male/female	336 (22%)	221 (24%)
Male/male	537 (35%)	302 (33%)
<b>Chi<sup>2</sup>=2.23, df=3, p=0.527</b>		
<b>Eye in which graft was performed</b>		
Left	773 (50%)	475 (52%)
Right	758 (50%)	446 (48%)
<b>Chi<sup>2</sup>=0.52, df=1, p=0.473</b>		
<b>Prior existing contralateral graft</b>		
No	1277 (83%)	799 (87%)
Yes	254 (17%)	122 (13%)
<b>Chi<sup>2</sup>=0.14, df=1, p=0.710</b>		
<b>Total</b>	<b>1531 (100%)</b>	<b>921 (100%)</b>

Note: Kaplan-Meier analyses did not include categories with fewer than 20 grafts. Fifteen eyes undergoing deep anterior lamellar keratoplasty had a history of corneal cross-linking. This was an insufficient number for survival comparisons with those that had not.

### 5.2.1 DALK survival: influence of indication for graft

Figure 5.2.1 shows the comparison of graft survival depending on the indication for graft. A significant difference was found across groups (Log Rank Statistic=45.37; df=7;  $p<0.001$ ), with survival of grafts performed for keratoconus significantly better than those performed for failed previous grafts, herpetic infections or non-herpetic infections (all  $p<0.001$ ), and other specified indications ( $p=0.001$ ). This variable was not retained in the final multivariate model (see section 5.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 5.2.1 Indication for graft



**Number at risk (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>	<b>10</b>
<b>Failed previous graft</b>	27	19	11	5	3	1
<b>Keratoconus</b>	586	360	123	46	11	5
<b>Herpetic infection</b>	39	32	16	4	1	NA
<b>Corneal degeneration</b>	26	17	8	1	NA	NA
<b>Corneal dystrophy</b>	19	13	7	3	1	1
<b>Corneal scars &amp; opacities</b>	21	13	5	4	NA	NA
<b>Non-herpetic infection</b>	27	16	4	2	NA	NA
<b>Other indication</b>	24	14	1	NA	NA	NA

**Probability of graft survival (years post-graft)**

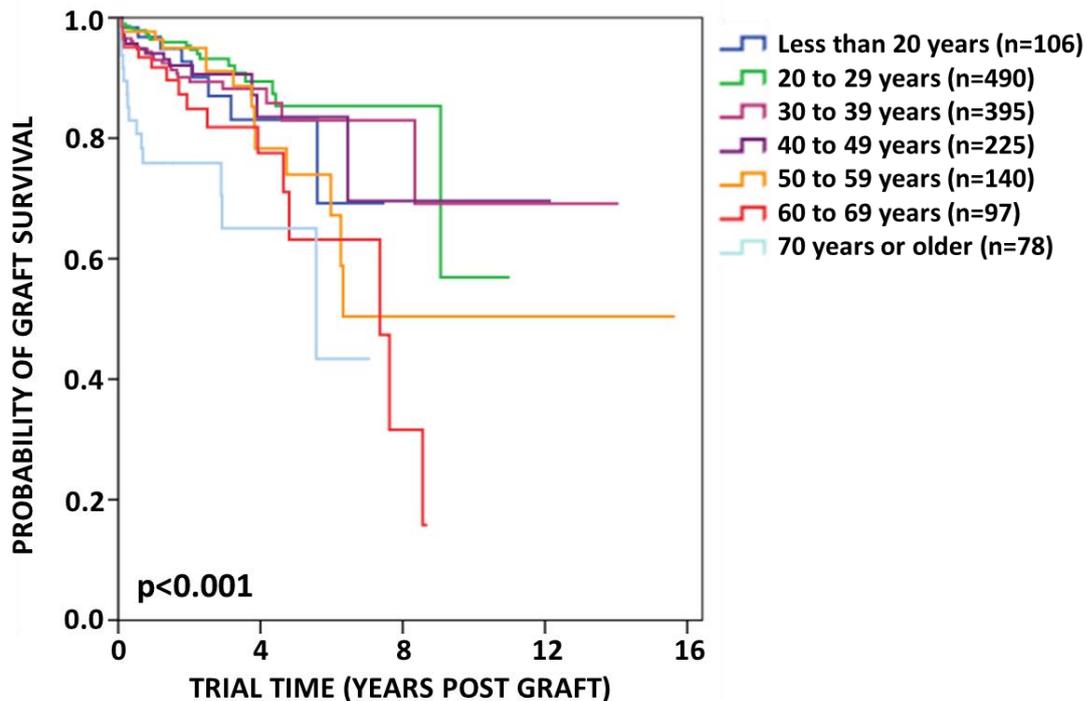
	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>
<b>Failed previous graft</b>	0.87	NA	NA	NA
<b>Keratoconus</b>	0.96	0.94	0.89	0.86
<b>Herpetic infection</b>	0.89	0.84	NA	NA
<b>Corneal degeneration</b>	0.91	NA	NA	NA
<b>Corneal dystrophy</b>	NA	NA	NA	NA
<b>Corneal scars &amp; opacities</b>	0.96	NA	NA	NA
<b>Non-herpetic infection</b>	0.83	NA	NA	NA
<b>Other indication</b>	0.86	NA	NA	NA

### 5.2.2 DALK survival: influence of recipient age

Figure 5.2.2 shows the comparison of graft survival depending on the age of the corneal transplant recipient. Data for recipients aged under 20, and 70 and over, were combined due to small numbers in these groups. A significant difference was found across groups (Log Rank Statistic=31.19; df=6;  $p<0.001$ ), with recipients aged 70 years or older having poorer survival than those aged 20 to 29 years, 30 to 39 years (both  $p<0.001$ ) or 40 to 49 years ( $p=0.002$ ), and recipients aged 60 to 69 years having poorer survival than those aged 20 to 29 years ( $p=0.002$ ).

Further analyses, showed no significant differences between the groups under 60 years (overall  $p=0.386$ , all individual comparisons  $p>0.05$ ). These groups were categorised together for multivariate analysis. This variable was retained in the final multivariate model (see section 5.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 5.2.2 Recipient age



**Number at risk (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>	<b>10</b>
<b>Less than 20 years</b>	53	36	16	5	NA	NA
<b>20 to 29 years</b>	248	150	53	20	3	2
<b>30 to 39 years</b>	202	122	39	14	7	3
<b>40 to 49 years</b>	225	110	67	21	9	3
<b>50 to 59 years</b>	75	58	21	10	1	1
<b>60 to 69 years</b>	54	34	17	5	2	NA
<b>70 years or older</b>	27	17	8	2	NA	NA

**Probability of graft survival (years post-graft)**

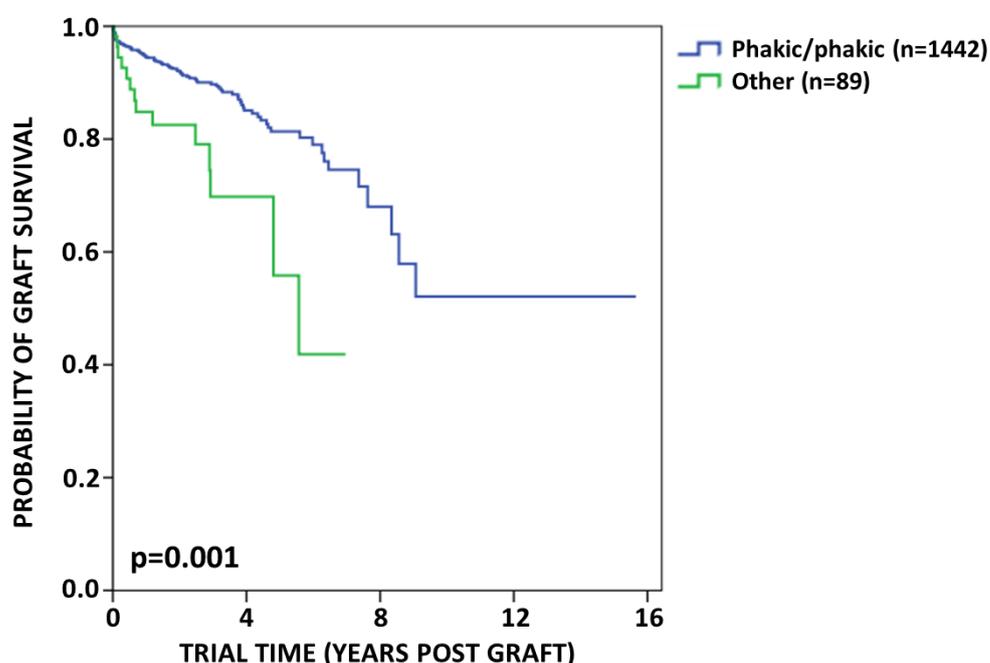
	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>
<b>Less than 20 years</b>	0.97	0.93	NA	NA
<b>20 to 29 years</b>	0.96	0.95	0.89	0.85
<b>30 to 39 years</b>	0.93	0.90	0.88	NA
<b>40 to 49 years</b>	0.94	0.92	0.84	NA
<b>50 to 59 years</b>	0.98	0.95	0.78	NA
<b>60 to 69 years</b>	0.92	0.85	NA	NA
<b>70 years or older</b>	0.76	NA	NA	NA

### 5.2.3 DALK survival: influence of change in lens status

Figure 5.2.3 shows the comparison of graft survival stratified by the change of lens status from pre- to post-graft. “Phakic/phakic” means the eye was phakic both before and after the graft. “Other” means the eye was phakic, pseudophakic or aphakic before the graft, and either aphakic or pseudophakic afterwards.

A significant difference was found across groups (Log Rank Statistic=11.78; df=1;  $p=0.001$ ). This variable was not retained in the final multivariate model (see section 5.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 5.2.3 Change in lens status from pre- to post-graft



#### Number at risk (years post-graft)

	1	2	4	6	8	10
Phakic/phakic	730	457	165	62	16	7
Other	39	27	10	3	NA	NA

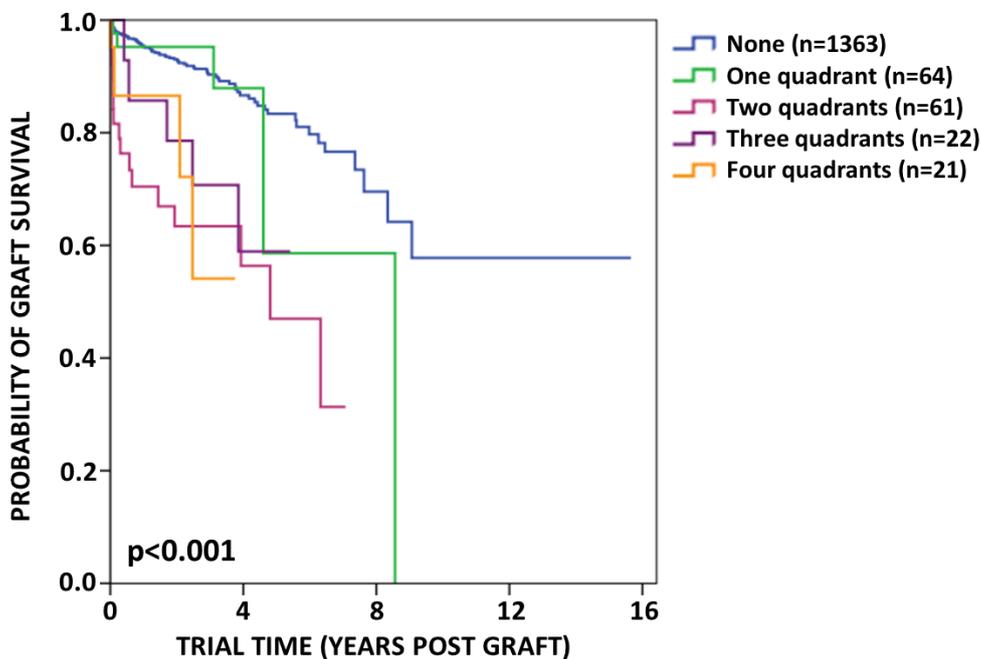
#### Probability of graft survival (years post-graft)

	1	2	4	6
Phakic/phakic	0.95	0.92	0.85	0.79
Other	0.85	0.83	NA	NA

### 5.2.4 DALK survival: influence of pre-graft corneal neovascularisation

Figure 5.2.4 shows the comparison of graft survival between those recipients with various levels of corneal neovascularisation pre-graft and those without (Log Rank Statistic=53.35; df=4; p<0.001), with those with avascular corneas having significantly better survival than those with 2 or 4 quadrants of neovascularisation (both p<0.001), and those with 1 quadrant having better outcomes than those with 4 (p=0.004). Recipients with avascular corneas pre-graft, or one quadrant of pre-graft neovascularisation, had better graft survival than those with greater levels of corneal neovascularisation (Log Rank Statistic=50.02; df=1; p<0.001). This variable was recategorised for the multivariate analysis, according to this finding. This variable was retained in the multivariate analysis (see section 5.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 5.2.4 Pre-graft corneal neovascularisation



#### Number at risk (years post-graft)

	1	2	4	6	8	10
None	691	424	154	59	15	7
One quadrant	36	24	8	2	1	NA
Two quadrants	22	18	8	4	NA	NA
Three quadrants	12	11	5	NA	NA	NA
Four quadrants	8	7	NA	NA	NA	NA

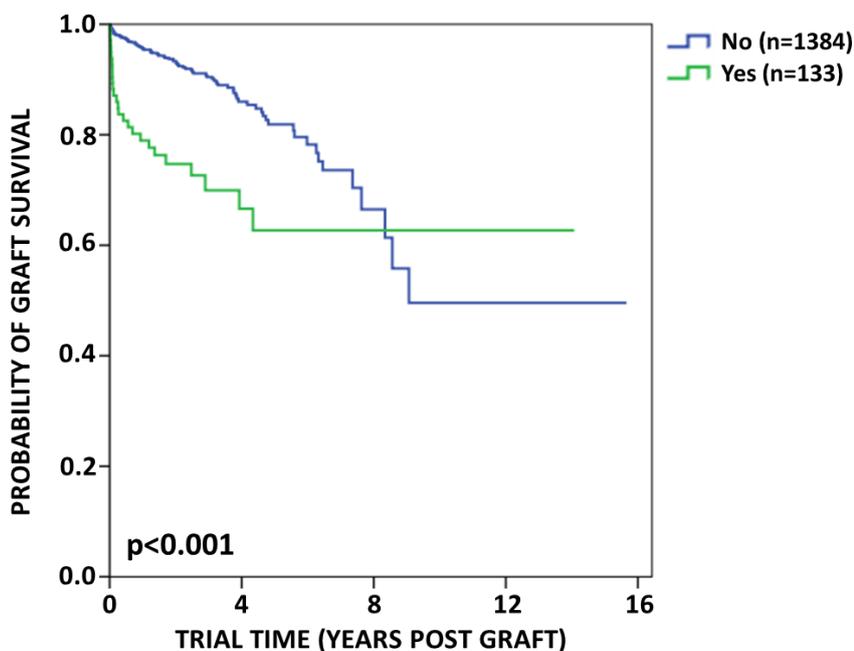
#### Probability of graft survival (years post-graft)

	1	2	4	6
None	0.95	0.93	0.87	0.80
One quadrant	0.95	0.95	NA	NA
Two quadrants	0.70	NA	NA	NA
Three quadrants	NA	NA	NA	NA
Four quadrants	NA	NA	NA	NA

### 5.2.5 DALK survival: influence of pre-graft inflammation and/or steroid use

Figure 5.2.5 shows the comparison of graft survival depending on whether the eye grafted had a history of inflammation and/or steroid use pre-graft. A significant difference was found across groups (Log Rank Statistic=27.26; df=1;  $p<0.001$ ). This variable was retained in the multivariate analysis (see section 5.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 5.2.5 Pre-graft inflammation and/or steroid use**



#### Number at risk (years post-graft)

	1	2	4	6	8	10
No inflammation/steroid use	698	432	154	58	14	6
Inflammation/steroid use	64	46	19	6	2	1

#### Probability of graft survival (years post-graft)

	1	2	4	6
No inflammation/steroid use	0.96	0.93	0.86	0.78
Inflammation/steroid use	0.79	0.75	NA	NA

### 5.3 Graft Era

Table 5.5 shows the number of grafts registered and followed, in blocks of two years. The percentages, which should be summed vertically, total 100.

**Table 5.5 Graft Era**

<b>Deep Anterior Lamellar Corneal Graft Graft Era</b>		
<b>Year of graft</b>	<b>Registered (%)</b>	<b>Followed (%)</b>
2000 to 2004	35 (2%)	31 (3%)
2005 to 2009	362 (24%)	275 (30%)
2010 to 2014	804 (53%)	542 (59%)
2015 to 2017	330 (22%)	73 (8%)
<b>Total</b>	<b>1531 (100%)</b>	<b>921 (100%)</b>

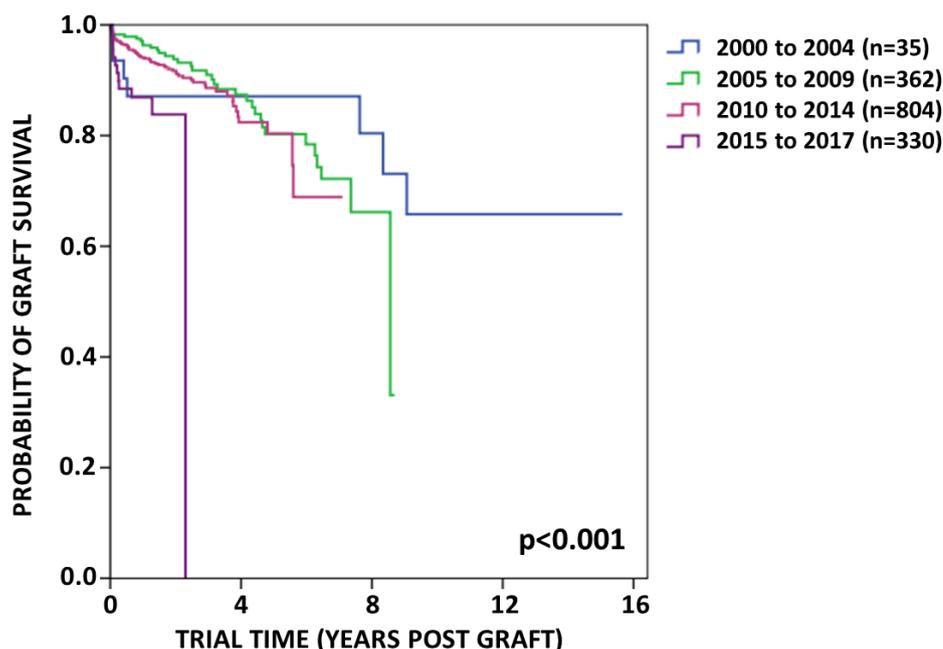
Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses and found to be significant (p<0.001). Follow-up was lower for grafts performed in more recent years.

Consideration was given to the effect of follow-up lag time on this analysis. Up-to-date information on failed grafts is more likely to be known than for surviving grafts. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft.

### 5.3.1 DALK survival: influence of era of graft

Figure 5.3.1 shows the influence of year of graft, stratified into five-year groups. The difference in survival was significant (Log Rank Statistic=12.75; df=3; p=0.005), with those performed in 2015 to 2017 exhibiting poorer survival than those performed from 2005 to 2009 (p<0.001) or 2010 to 2014 (p=0.003). This finding is likely due to the lag time discussed on the previous page. This variable was retained in the final multivariate model (see section 5.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 5.3.1 Graft era**



#### Number at risk (years post-graft)

	1	2	4	6	8	10
<b>2000 to 2004</b>	25	20	17	13	12	7
<b>2005 to 2009</b>	241	157	82	43	4	NA
<b>2010 to 2014</b>	457	305	76	9	NA	NA
<b>2015 to 2017</b>	46	2	NA	NA	NA	NA

#### Probability of graft survival (years post-graft)

	1	2	4	6
<b>2000 to 2004</b>	0.87	0.87	NA	NA
<b>2005 to 2009</b>	0.96	0.94	0.87	0.78
<b>2010 to 2014</b>	0.94	0.92	0.82	NA
<b>2015 to 2017</b>	0.87	NA	NA	NA

## 5.4 Surgery and Surgeon Factors

Table 5.6 shows the number of grafts within each of the variable sub-groups, for the surgery and surgeon factors examined in this report that were found to be **significant** predictors of graft survival in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (1,531 registered and 921 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 5.6 Surgery and surgeon factors, significant in univariate analyses**

<b>Deep Anterior Lamellar Corneal Graft Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Graft type</b>		
Big bubble	371 (24%)	244 (26%)
Melles	443 (29%)	156 (17%)
Not advised	717 (47%)	521 (57%)
<b>The Centre effect</b>		
Fewer than 30 registered DALK	463 (30%)	304 (33%)
Surgeon M	422 (28%)	109 (12%)
Surgeon N	101 (7%)	79 (9%)
Surgeon B	95 (6%)	87 (9%)
Surgeon V	76 (5%)	53 (6%)
Surgeon C	74 (5%)	52 (6%)
Surgeon X	64 (4%)	52 (6%)
Surgeon Z	56 (4%)	35 (4%)
Surgeon L	51 (3%)	43 (5%)
Surgeon K	47 (3%)	40 (4%)
Surgeon J	46 (2%)	40 (4%)
Surgeon H	36 (2%)	27 (3%)
<b>Total</b>	<b>1531 (100%)</b>	<b>921(100%)</b>

Comparisons between the percentages of grafts registered and followed in each category showed no significant differences.

Table 5.7 shows the number of grafts within each of the variable sub-groups, for the surgeon and surgery factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (1,531 registered and 921 with follow-up provided) and the percentages, summed vertically, total 100. The result of the Kaplan-Meier survival analyses are also provided.

**Table 5.7 Surgery and surgeon factors, not significant in univariate analyses**

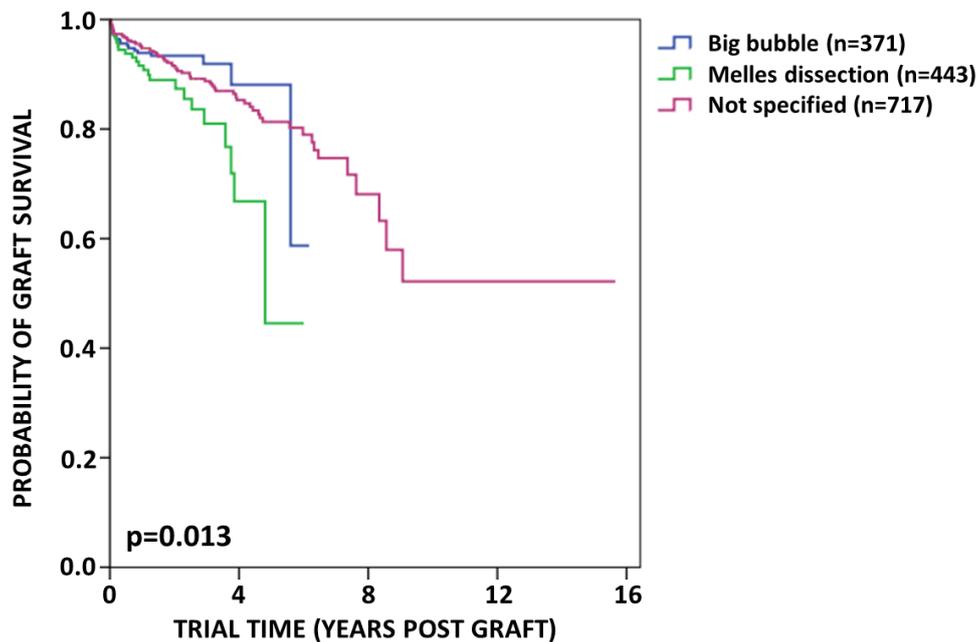
<b>Deep Anterior Lamellar Corneal Graft Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Graft size</b>		
Less than 8.0 mm	169 (11%)	109 (12%)
8.0 mm to <8.25 mm	286 (19%)	192 (21%)
8.25 mm to <8.5 mm	303 (20%)	224 (24%)
8.5 mm to <8.75mm	204 (13%)	112 (12%)
8.75 mm or more	463 (30%)	199 (22%)
Not advised	106 (7%)	85 (9%)
<b>Chi<sup>2</sup>=7.86, df=4, p=0.097</b>		
<b>Surgeon volume</b>		
Fewer than 30 registered DALK	463 (30%)	304 (33%)
30+ registered DALK	1068 (70%)	617 (67%)
<b>Chi<sup>2</sup>=0.235, df=1, p=0.628</b>		
<b>Total</b>	<b>1531 (100%)</b>	<b>921(100%)</b>

### 5.4.1 DALK survival: influence of graft type

Two different techniques are frequently employed by surgeons to perform DALK grafts. Surgeons have been asked to indicate whether they utilise the “Melles” manual dissection technique, or the “Big Bubble” technique introduced by Anwar and Teichman. This information is not always provided. The overall comparison of the three groups was significant (Log Rank Statistic=8.64; df=2; p=0.013) and is shown in Figure 5.4.1.

A significant difference was found in the outcomes from the two different techniques (Log Rank Statistic=6.15; df=1; p=0.013) and grafts where the technique used was not specified exhibited significantly better survival than “Melles” dissection (p=0.008). This variable was not retained in the final multivariate model (see section 5.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 5.4.1 Type of graft



#### Number at risk (years post-graft)

	1	2	4	6	8	10
<b>Big bubble</b>	207	129	17	1	NA	NA
<b>Melles dissection</b>	116	57	11	1	NA	NA
<b>Not specified</b>	446	298	147	63	16	7

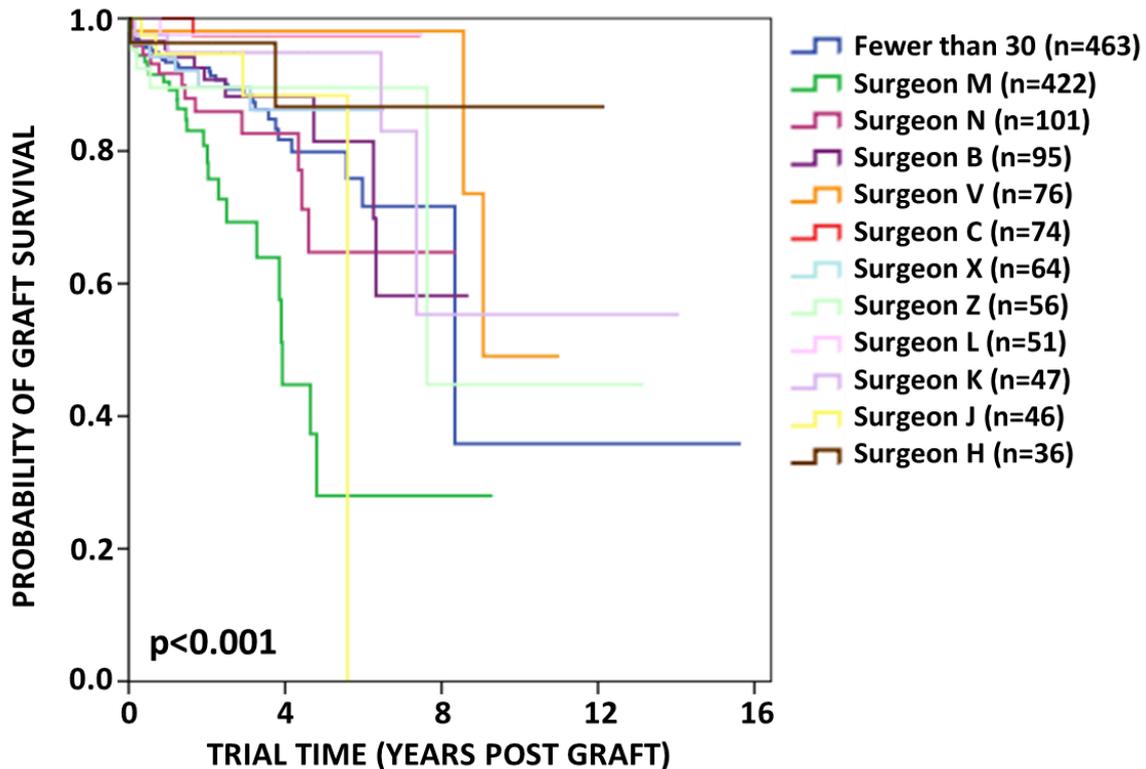
#### Probability of graft survival (years post-graft)

	1	2	4	6
<b>Big bubble</b>	0.94	0.93	NA	NA
<b>Melles dissection</b>	0.92	0.89	NA	NA
<b>Not specified</b>	0.95	0.92	0.85	0.79

### 5.4.2 DALK survival: influence of the Centre effect

Figure 5.4.2 shows the comparison of graft survival for individual surgeons (shown in random order) who had 30 or more deep anterior lamellar keratoplasties registered with the ACGR, and all other grafts (performed by 72 surgeons) combined (Log Rank Statistic=42.91; df=11;  $p<0.001$ ). This analysis indicates that there was a significant Centre effect. This variable was retained in the final multivariate model (see section 5.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 5.4.2 The Centre effect



Note: To preserve anonymity, surgeons have been identified using random letters of the alphabet. These identifying letters do not correspond with those used in chapters reporting on other types of graft, i.e. Surgeon X in this chapter is not the same surgeon identified as Surgeon X in the chapter on Descemet's stripping (automated) endothelial keratoplasty.

**Number at risk (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>	<b>10</b>
<b>&lt;30 DALK registered</b>	246	161	45	17	3	1
<b>Surgeon M</b>	78	32	7	2	1	NA
<b>Surgeon N</b>	62	38	16	4	1	NA
<b>Surgeon B</b>	76	50	19	8	2	NA
<b>Surgeon V</b>	51	37	15	7	4	2
<b>Surgeon C</b>	48	30	11	3	NA	NA
<b>Surgeon X</b>	46	35	18	2	NA	NA
<b>Surgeon Z</b>	31	18	5	3	1	1
<b>Surgeon L</b>	37	21	8	6	NA	NA
<b>Surgeon K</b>	36	27	16	9	1	1
<b>Surgeon J</b>	32	20	6	NA	NA	NA
<b>Surgeon H</b>	26	15	9	4	3	2

**Probability of graft survival (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>
<b>&lt;30 DALK registered</b>	0.93	0.93	0.82
<b>Surgeon M</b>	0.90	0.81	NA
<b>Surgeon N</b>	0.92	0.86	NA
<b>Surgeon B</b>	0.94	0.91	NA
<b>Surgeon V</b>	0.98	0.98	NA
<b>Surgeon C</b>	1.00	0.97	NA
<b>Surgeon X</b>	0.94	0.90	NA
<b>Surgeon Z</b>	0.90	NA	NA
<b>Surgeon L</b>	0.98	0.98	NA
<b>Surgeon K</b>	0.95	0.95	NA
<b>Surgeon J</b>	0.95	0.95	NA
<b>Surgeon H</b>	0.96	NA	NA

## 5.5 Operative procedures at the time of graft

Only one DALK had an anterior vitrectomy at the time of graft and four had a peripheral iridectomy. Thus, these factors were not further analysed.

## 5.6 Post-graft Events

Table 5.8 shows the occurrence of post-graft events, which were found to be **significant** in univariate analyses.

**Table 5.8 Post-graft events, significant in univariate analyses**

<b>Deep Anterior Lamellar Corneal Graft</b>		
<b>Post-graft Events</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Post-graft neovascularisation</b>		
No	1470 (96%)	860 (93%)
Yes	61 (4%)	61 (7%)
<b>Total</b>	<b>1531 (100 %)</b>	<b>921 (100 %)</b>

Table 5.9 shows the number of grafts within each of the variable sub-groups, for the post-graft events found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (1,531 registered and 921 with follow-up provided) and the percentages, summed vertically, total 100. The result of the Kaplan-Meier survival analysis is also provided. Only six DALK had post-graft herpetic infection, 15 had microbial keratitis, one had synechia, and four had uveitis reported. Thus, these factors were not further analysed. Please note: post-graft data may be incomplete when follow-up is based on a registration for a replacement graft.

**Table 5.9 Post-graft events, not significant in univariate analyses**

<b>Deep Anterior Lamellar Corneal Graft</b>		
<b>Post-graft Events</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Post-graft rise in IOP</b>		
No	1469 (96%)	859 (93%)
Yes	62 (4%)	62 (7%)
<b>Chi<sup>2</sup>=1.71, df=1, p=0.191</b>		
<b>At least one rejection episode</b>		
No	1476 (96%)	866 (94%)
Yes	55 (4%)	55 (6%)
<b>Chi<sup>2</sup>=0.07, df=1, p=0.792</b>		
<b>Time to removal of sutures</b>		
Within 6-months post-graft	24 (2%)	24 (3%)
Between 6 and 12 months post-graft	103 (7%)	103 (11%)
Between 1 and 2-years post-graft	194 (13%)	194 (21%)
More than 2-years post-graft	44 (3%)	44 (5%)
Not yet removed/not advised	1166 (76%)	556 (60%)
<b>Chi<sup>2</sup>=0.21, df=3, p=0.976</b>		
<b>Total</b>	<b>1531 (100 %)</b>	<b>921 (100 %)</b>

Table 5.10 shows post-graft surgical procedures, as reported by follow-up practitioners. Please note: post-graft data may be incomplete when follow-up is based on a registration for a replacement graft.

### Table 5.10 Post-graft surgical procedures

91 DALK were reported to have undergone a re-grafting procedure (separate to subsequent concurrent graft/s) at the date last seen. Of these 74 had not had additional post-graft operative procedures reported, while 17 had.

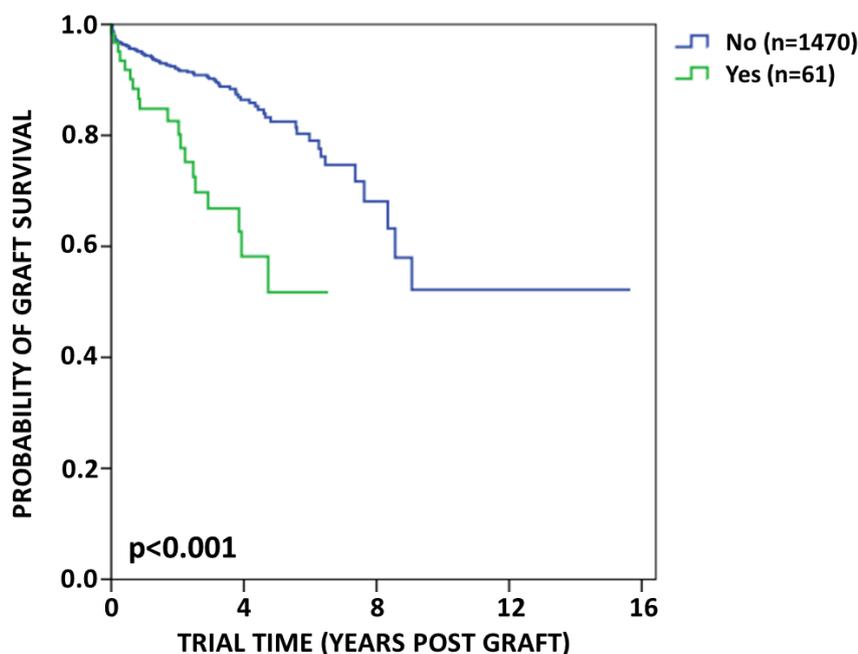
<b>Deep Anterior Lamellar Corneal Graft Post-Graft Surgical Procedures</b>	
Type of procedure	Number
Cataract removal/IOL insertion (87 both, 2 cataract only, 2 IOL only)	91
IOL exchange/reposition/piggyback lens	7
Wound repair/resutured	49
PRK laser	29
YAG laser	19
Suture adjustment	17
Keratectomy	9
Relaxing incision	9
Intravitreal injection(s)	9
LASIK	7
Tarsorrhaphy	7
Air bubble	6
Other*	44
<b>Total number of surgical procedures (number of grafts)</b>	<b>303 (277)</b>

\* Other included: additional concurrent graft (4), keratotomy (4), compression sutures (4), wedge resection (4), vitrectomy (4), retinal detachment surgery (3), corneal cross-linking (2), corneal laser regularisation (2), cryotherapy (2), removal of cyst (2), removal of folds/wrinkles in membrane (2), trabeculectomy (2), Baerveldt tube inserted (1), chalazion removal (1), corneal diathermy (1), creation of flaps for glaucoma (1), drainage of double anterior chamber (1), ectropion repair (1), entropion surgery (1), epithelial debridement (1), evisceration (1), fine needling (1), graft rotation (1), intraocular contact lens inserted (1), iridotomy (1), lash epilation (1), limbal renal lever (1), membrane peel (1), non-specified glaucoma drainage device inserted (1), paracentesis (1), periotomy (1), pterygium repair (1), ptosis surgery (1), removal of interface fluid (1), removal of foreign body (1), removal of Kerarings (1), removal of limbal lesion (1), removal of silicone oil (1), removal of superficial opacity (1), silicone oil insertion (1), strabismus surgery (1).

### 5.6.1 DALK survival: influence of post-graft corneal neovascularisation

Figure 5.6.1 shows the survival for grafts where post-graft corneal neovascularisation was reported, compared to those that did not have any post-graft corneal neovascularisation. A significant difference was found between groups (Log Rank Statistic=21.76; df=1;  $p<0.001$ ). This variable was retained in the final multivariate model, suggesting that this is an independent factor significantly affecting graft survival.

**Figure 5.6.1 Post-graft corneal neovascularisation**



#### Number at risk (years post-graft)

	1	2	4	6	8	10
No neovascularisation	722	450	163	63	16	7
Neovascularisation	47	34	12	2	NA	NA

#### Probability of graft survival (years post-graft)

	1	2	4	6
No neovascularisation	0.95	0.92	0.87	0.79
Neovascularisation	0.85	0.83	NA	NA

## 5.7 Multivariate Analysis

A multivariate model was used to investigate the combined effect of variables on penetrating graft survival, adjusted for all other variables in the model. This analysis was performed using STATA version 11.

In the preceding univariate analyses, each registered DALK, together with its archival follow-up records, was treated as a separate and independent entity. Some recipients had multiple DALK performed during the census period (up to 31/7/2017), with some having repeat grafts in a single eye, some grafts in both eyes and some a combination of both. To control for potential inter-graft and/or inter-eye dependence in the multivariate analyses, the multivariate model was adjusted to allow for clustering by individual patient [see references 7 & 8].

Variables to be included in the Cox Proportional Hazards regression model were identified based on the results of the univariate Kaplan-Meier analyses, with a cut-off significance level of  $p < 0.08$  used to select variables for inclusion. Some variables that were found to be significant in the univariate analyses were omitted due to co-linearity, or because of large amounts of missing data ( $>50\%$ ). Where data were missing for 1% to 50% of cases, additional groups for each if these categorical variables were created, called “not advised”. Each variable was initially analysed individually to determine if it remained significant once clustered by individual patient. Where the variable was no longer found to be significant ( $p > 0.08$ ), it was excluded from the multivariate analysis.

The best model was found by a backward elimination process, removing variables not appearing to be predictors of graft failure. The model excluded variables with a p-value of  $p \geq 0.05$  (or global p-value of  $p \geq 0.05$  for variables with more than two categories) in a stepwise manner, beginning with the least significant variable. For categorical variables with more than two groups, Bonferroni adjustment was applied to determine if significant differences were present between groups. The Kaplan-Meier plots, and additional appropriate STATA analyses, were used to assess whether each included variable met the assumption of proportional hazards. Where variables were found to be time-variant, they were treated as such in the multivariate model.

Table 5.11 shows each of the variables analysed in the univariate analyses, stratified by whether they were included in the initial multivariate model and whether they remained in the final model.

Table 5.11 Multivariate model

### Deep Anterior Lamellar Corneal Graft Multivariate Model

#### Not significant in univariate analysis

Donor sex  
 Donor age group  
 Cause of donor death  
 Multi-organ donor  
 Storage medium  
 Time from death to enucleation  
 Time from enucleation to storage  
 Storage time in Optisol  
 Endothelial cell density  
 Australian State where graft was performed  
 Interstate transportation  
 Recipient sex  
 Donor/recipient sex match/mismatch  
 Eye grafted  
 Graft size  
 Previous contralateral graft(s)  
 Surgeon experience and level of follow-up  
 Raised intraocular pressure post-graft  
 Post-graft rejection episode(s)  
 Time to removal of sutures

#### Significant in univariate analysis but excluded from the multivariate model due to missing data

Storage time in organ culture\*

#### Significant in univariate analysis but not retained in the multivariate model

Indication for graft  
 Change in lens status pre- to post-graft  
 Type of DALK

#### Significant in univariate analysis AND retained in the multivariate model

Recipient age group  
 Pre-graft neovascularisation  
 Pre-graft inflammation and/or steroid use  
 Graft era  
 The Centre effect  
 Post-graft corneal neovascularisation

\*p<0.08

Table 5.12 tabulates the parameter estimates resulting from the fit of the best clustered Cox model. The table shows the variable, the hazard ratio, the standard error of the regression coefficient, the corresponding probability value and the 95% confidence interval for the hazard ratio. The group of each categorical variable with the highest number of cases was taken as the referent. The hazard ratios for a given variable are adjusted for all other variables in the model. This model included data from the 1,517 deep anterior lamellar keratoplasties, performed in 1,382 recipients, for whom there were valid responses for each of the included variables (14 cases were excluded as their pre-graft inflammation and/or steroid use status was unknown).

This model includes variables with a p-value of  $p < 0.05$ , with variables eliminated in a stepwise manner, beginning with the least significant variable. For categorical variables, a global test was applied to calculate the overall p-value. The overall model was highly significant: ( $\text{Chi}^2 = 156.80$ ,  $p < 0.0001$ ).

**Table 5.12 Clustered multivariate model**

<b>Deep Anterior Lamellar Corneal Graft Clustered Multivariate Model</b>						
	<b>n</b>	<b>Hazard Ratio</b>	<b>Standard error</b>	<b>p-value</b>	<b>Global p-value</b>	<b>95% confidence interval</b>
<b>Recipient age group</b>						
Under 60 years	1343	1.00			0.016	
60 years to 69 years	97	1.16	0.31	0.590		0.68 - 1.95
70 years or older	77	2.60	0.86	0.004		1.36 - 4.99
<b>Pre-graft inflammation and/or steroid use (tvc)</b>						
No	1384	1.00				
Yes	133	3.24	1.11	0.001		1.65 - 6.35
<b>Pre-graft corneal neovascularisation</b>						
None or one quadrant	1413	1.00				
More than one quadrant	104	2.13	0.60	0.008		1.22 - 3.71
<b>Graft era</b>						
2000-2004	35	0.58	0.39	0.347		0.18 - 1.82
2005-2009	359	0.85	0.21	0.499		0.53 - 1.37
2010-2014	796	1.00			0.025	
2015-2017	327	2.37	0.77	0.008		1.25 - 4.48
<b>Individual surgeon</b>						
< 30 DALK registered	461	1.00				
Other surgeons (lowest HR highest HR)	1056	0.23 3.08	0.23 0.86	0.148 <0.001	<0.001	0.03 - 1.69 1.78 - 5.34
<b>Post-graft corneal neovascularisation</b>						
No	1457	1.00				
Yes	60	1.79	0.50	0.037		1.04 - 3.08

tvc= time varying coefficient

## **5.7.1 Significant differences in the deep anterior lamellar keratoplasty multivariate model for categories with more than two groups following Bonferroni correction for multiple comparisons**

### **5.7.1.1 Recipient age group**

Grafts performed in recipients aged 70 years or older had significantly poorer survival than those performed in recipients aged 60 to 69 ( $p=0.035$ ) or under 60 years or age ( $p=0.004$ ).

### **5.7.1.2 Graft era**

Grafts survival was significantly poorer for the most recent grafts, performed between 2015 and 2017, compared to all other eras ( $p=0.030$ ,  $p=0.005$ , and  $p=0.008$ , respectively). The poor performance of grafts in this category is likely due to the lag time effect discussed in section 2.3.1.

### **5.7.1.3 The Centre effect**

Individual results varied widely for surgeons with 30 or more DALK registered with the ACGR compared to the balance of the database (DALK performed by surgeons with fewer than 30 registered DALK). The hazard ratios ranged from 0.23 to 3.08.

## 5.8 Reasons for Graft Failure

Of the 921 followed grafts, 113 (12%) were known to have failed by the census date. This equates to 7% of the 1,531 registered grafts. Surgeons were asked to indicate the reason for graft failure. This information was also gathered from repeat registration forms, where the reason for failure of the previous graft was provided. Table 5.13 shows the reasons for failure specified.

**Table 5.13 Reasons for graft failure**

<b>Deep Anterior Lamellar Corneal Graft Reasons for Graft Failure</b>	
Scarring	14 (12%)
Primary graft failure	14 (12%)
Non herpetic infection	13 (12%)
Astigmatism	10 (9%)
Corneal ulcer	7 (6%)
Endothelial cell failure	6 (5%)
Trauma	5 (4%)
Other specified*	21 (19%)
Unspecified	23 (20%)
<b>Total</b>	<b>113 (100%)</b>

\*Other included: vascularisation (4), herpetic infection (3), lattice dystrophy (3), corneal melt (2), rejection (2), Descemet’s detachment (1), exposure keratopathy (1), granular dystrophy (1), inflammation (1), lipid keratopathy (1), recurrent Reis Buckler dystrophy (1), unspecified dystrophy (1).

Primary graft non-functions are defined as grafts that never thin and clear in the post-operative period. For lamellar procedures, primary graft failure is recorded as reported by surgeons. Additional information is collected to ascertain whether this occurred within 28 days of the graft. Where surgeons indicate that the failure was due to surgical complications, this is also recorded.

Of the 14 grafts reported by surgeons to have been primary graft failures, in nine cases no further information was provided. Specific reasons given in the remaining five were: Descemet’s detachment (1), Descemet’s rupture (1), fungal keratitis (1), oedema (1) and residual opacity (1).

## 5.9 Post-graft Changes in Best Corrected Visual Acuity

### 5.9.1 All indications for graft

Post-graft best corrected visual acuity (BCVA) is an important outcome for corneal graft recipients. A desire for improved visual acuity was specified as a reason for graft in 1,429 (93%) of registered deep anterior lamellar keratoplasties. In 92% of cases (1,411), this was the sole desired outcome indicated. It is likely that this was also at least part of the reason for graft in some of the further 70 (5%) grafts where no reason was specified.

Follow-ups occur at varying times post-graft, depending on when a surgeon sees a recipient. Where post-graft best corrected visual acuity (without pinhole) information was provided, we categorised this according to the length of time since graft. The first two categories were:

- BCVA provided at between 6 and 12 months post-graft, and
- BCVA provided at between 12 and 18 months post-graft.

Subsequent groups were at yearly intervals. For each year point, any measurements provided within 6-months of that date, rounded to the nearest day, were included (e.g. for 2-year follow-up, any BCVA given at between 730 and 913 days post-graft was included).

We analysed post-graft best corrected visual acuity in several ways. Where more than 20 grafts had VA measurements provided, we examined:

1. The percentage of *surviving* grafts achieving different levels of Snellen visual acuity (6/6 or better, 6/7.5 to 6/12, 6/15 to 6/24, 6/36 to 6/60, count fingers (CF) or hand movements (HM), and light perception (LP) or no light perception (NLP)) at yearly time-points post-graft. Grafts that had been reported to have failed at the time of last follow-up, but had prior follow-ups with BCVA measurements provided when the graft was surviving, had these prior data included in these analyses.
2. The *average* Snellen visual acuity achieved at yearly intervals post-graft, again by *surviving* grafts.
3. The final BCVA reported at the time of failure.

Table 5.14 and Figure 5.9.1 show the reported post-graft best corrected visual acuity for all failed grafts at the time of last follow-up, separated by indication for graft. Visual acuity at time of failure was reported for 90 (80%) of 113 failed DALK. As might be expected, the majority of failed grafts had accompanying poor visual acuity.

**Table 5.14 Post-graft best corrected visual acuity**

<b>Deep Anterior Lamellar Keratoplasty: Visual Acuity in Failed Grafts (as reported at final follow-up)</b>						
	<b>6/4 to 6/6</b>	<b>6/7.5 to 6/12</b>	<b>6/15 to 6/24</b>	<b>6/36 to 6/60</b>	<b>CF or HM</b>	<b>LP or NLP</b>
<b>Failed previous graft</b>	0 (0%)	0 (0%)	2 (15%)	5 (38%)	4 (31%)	2 (15%)
<b>Keratoconus</b>	0 (0%)	4 (8%)	7 (14%)	13 (25%)	24 (47%)	3 (6%)
<b>Herpetic eye disease</b>	0 (0%)	0 (0%)	0 (0%)	1 (8%)	11 (92%)	0 (0%)
<b>Corneal degeneration</b>	0 (0%)	0 (0%)	0 (0%)	2 (40%)	3 (60%)	0 (0%)
<b>Corneal dystrophy</b>	0 (0%)	0 (0%)	2 (50%)	1 (25%)	1 (25%)	0 (0%)
<b>Corneal scars &amp; opacity</b>	0 (0%)	0 (0%)	1 (50%)	0 (0%)	1 (50%)	0 (0%)
<b>Non-herpetic infection</b>	0 (0%)	0 (0%)	3 (33%)	1 (11%)	3 (33%)	2 (22%)
<b>Other specified</b>	0 (0%)	1 (25%)	0 (0%)	2 (50%)	1 (25%)	0 (0%)
<b>Total</b>	<b>0 (0%)</b>	<b>5 (5%)</b>	<b>15 (15%)</b>	<b>25 (25%)</b>	<b>48 (48%)</b>	<b>7 (7%)</b>

CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

**Figure 5.9.1 Best corrected visual acuity at time of last follow-up for failed deep anterior lamellar keratoplasties**

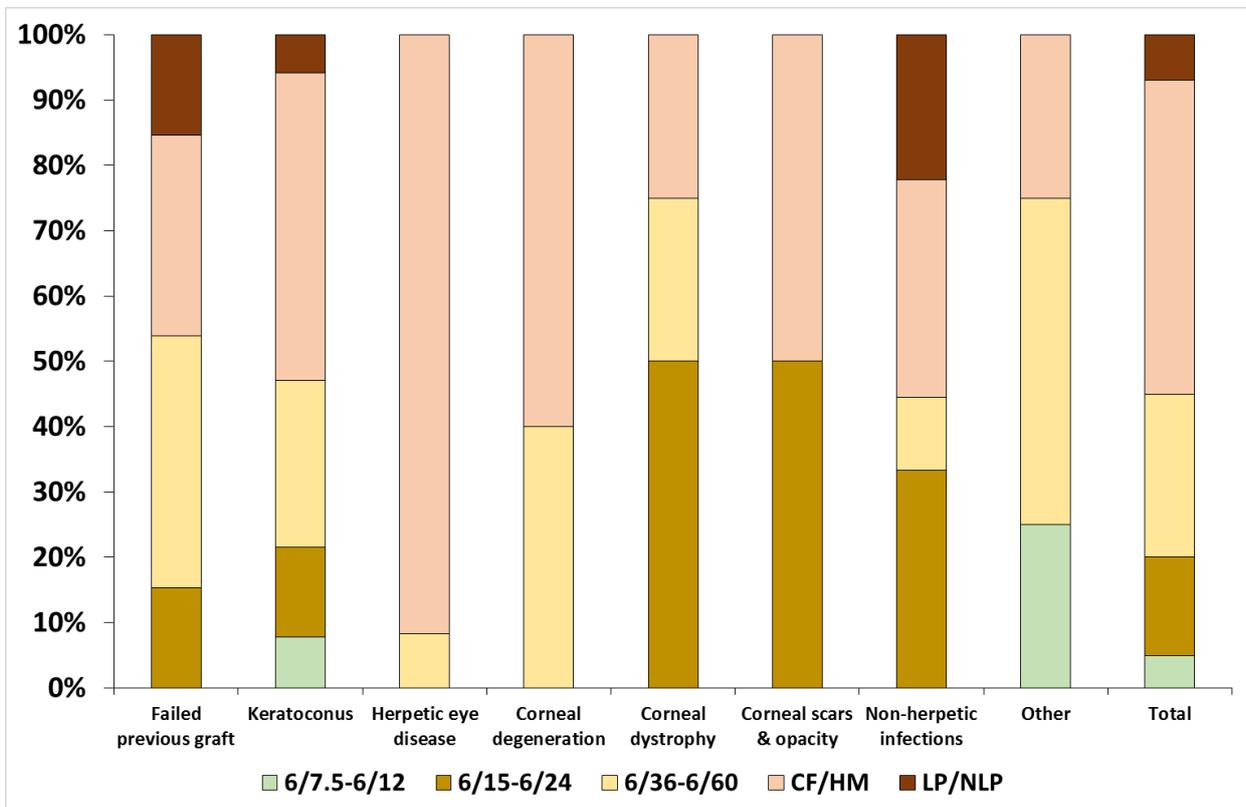
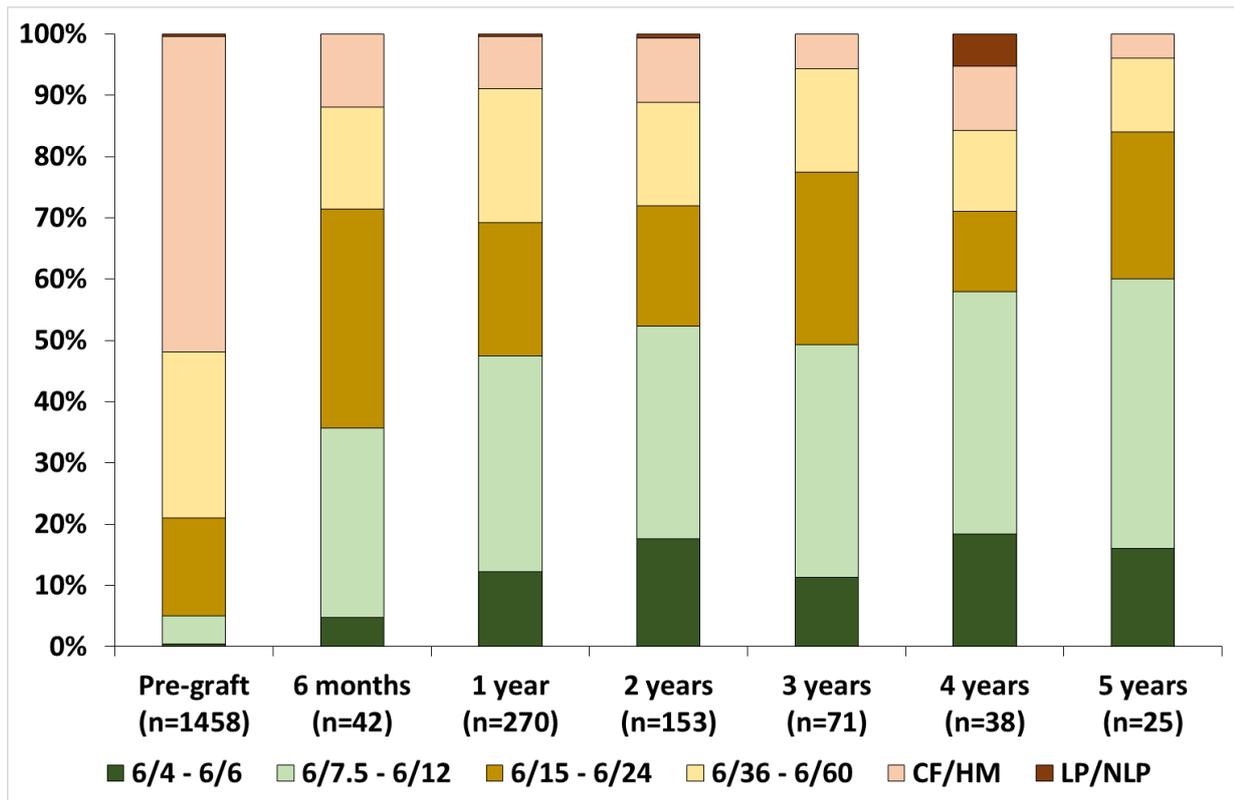


Figure 5.9.2 shows the best corrected visual acuity in the grafted eye, as reported to the ACGR, and categorised into six levels of vision, for all **surviving** deep anterior lamellar keratoplasties. Prior to graft over half of eyes (52%) had vision of CF or worse, with another quarter (27%) having 6/36 to 6/60. By 6-months post-graft, almost three-quarters (71%) of eyes with **surviving** grafts had vision of 6/24 or better, with almost half (47%) having functional vision of 6/12 or better by 12-months post-graft. Similar patterns could be seen for surviving grafts followed for up to 5-years post-graft.

**Figure 5.9.2 Best corrected visual acuity for deep anterior lamellar keratoplasties, surviving at time of measurement**

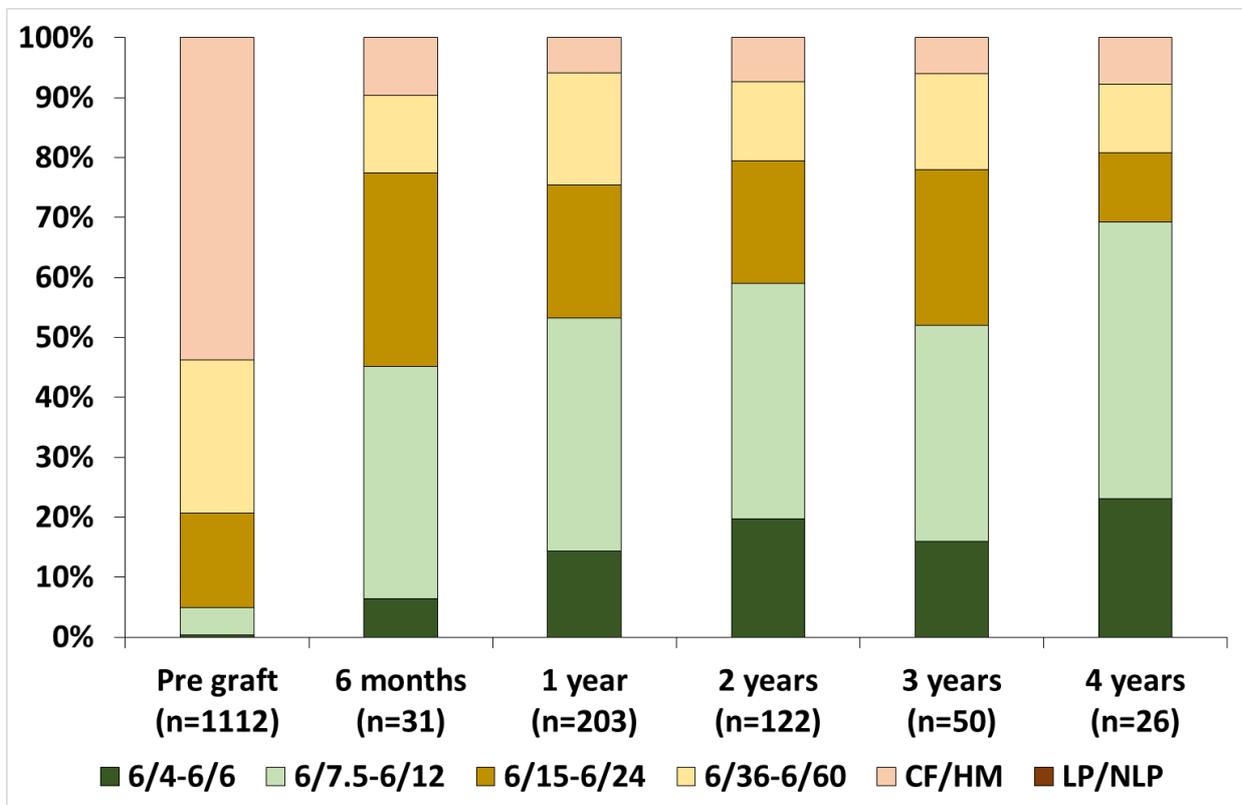


CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

### 5.9.2 Individual indications for graft

The only indication for graft with sufficient data to examine the visual outcomes individually was keratoconus. Figure 5.9.3 shows levels of best corrected visual acuity reported to the ACGR, at yearly intervals for **surviving** deep anterior lamellar keratoplasties for keratoconus. Approximately three-quarters of grafts had visual acuity of 6/24 or better by 6-months post-graft. This percentage remained consistent up to 4-years post-graft. Post-graft vision of 6/12 or better was reported in the just over half (53%) of **surviving** deep anterior lamellar keratoplasties for keratoconus that had BCVA measurements reported between 12 and 18-months post-graft. This percentage was also maintained up to 4-years post-graft.

**Figure 5.9.3 Keratoconus: level of best corrected visual acuity reported at yearly time points for surviving grafts**



CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception



## 6 Traditional Lamellar Keratoplasty

This chapter presents the results of analyses conducted on data relating to the 1,495 traditional lamellar keratoplasties (TLK) registered with the ACGR. These are all the lamellar grafts registered with the ACGR that are not deep anterior lamellar keratoplasties or endothelial keratoplasties. Kaplan-Meier survival analyses were conducted using IBM SPSS for Windows (Version 22.0), to compare the graft survival across groups for a range of variables relating to the corneal donor, graft recipient, surgical procedure, surgeon, and follow-up care.

### 6.1 Donor and Eye Banking Factors

Table 6.1 shows the number of grafts within each of the variable sub-groups, for the donor factors found to be **significant** in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (1,495 registered and 1,114 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 6.1 Donor and eye banking factors, significant in univariate analyses**

<b>Traditional Lamellar Corneal Grafts Donor and Eye Banking Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Eye bank</b>		
Eye bank M	824 (55%)	605 (54%)
Eye bank K	200 (13%)	146 (13%)
Eye bank V	160 (11%)	121 (11%)
Eye bank J	132 (9%)	82 (7%)
Eye bank N	129 (9%)	115 (10%)
Not advised	50 (3%)	45 (4%)
<b>Storage medium</b>		
Optisol	378 (25%)	266 (24%)
Organ culture	140 (9%)	75 (7%)
Moist pot	757 (51%)	588 (53%)
Superseded media	200 (13%)	167 (15%)
Not advised	20 (1%)	18 (2%)
<b>Total</b>	<b>1495 (100%)</b>	<b>1114 (100%)</b>

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category were examined using Chi<sup>2</sup> analyses. Likelihood of follow-up was significantly less likely ( $p < 0.001$ ) for grafts from Eye bank J and grafts stored in organ culture.

Table 6.2 shows the number of grafts within each of the variable sub-groups, for the donor and eye banking factors found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (1,495 registered and 1,114 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The result of the Kaplan-Meier survival analysis is also provided for each variable.

**Table 6.2 Donor and eye banking factors, not significant in univariate analysis**

<b>Traditional Lamellar Corneal Grafts Donor and Eye Banking Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Death-to-enucleation time</b>		
≤ 3 hours	178 (12%)	136 (12%)
4 to 6 hours	306 (20%)	236 (21%)
7 to 9 hours	338 (23%)	255 (23%)
10 to 12 hours	301 (20%)	234 (21%)
13 to 15 hours	163 (11%)	114 (10%)
16 to 18 hours	82 (5%)	55 (5%)
≥ 18 hours	84 (6%)	46 (4%)
Not advised	43 (3%)	38 (3%)
<b>Chi<sup>2</sup>=5.74, df=6, p=0.453</b>		
<b>Enucleation-to-storage time</b>		
≤ 3 hours	766 (51%)	571 (51%)
4 to 6 hours	149 (10%)	108 (10%)
7 to 12 hours	74 (5%)	60 (5%)
≥ 13 hours	56 (4%)	41 (4%)
Not advised	450 (30%)	334 (30%)
<b>Chi<sup>2</sup>=1.98, df=3, p=0.578</b>		
<b>Storage-to-graft time - hypothermic</b>		
Within 5 days	214 (14%)	169 (15%)
6 to 7 days	64 (4%)	47 (4%)
More than a week	157 (11%)	115 (10%)
Not advised	937 (63%)	694 (62%)
Not applicable	123 (8%)	89 (8%)
<b>Chi<sup>2</sup>=1.82, df=2, p=0.403</b>		
<b>Storage-to-graft time - organ culture</b>		
Within 2 weeks	36 (2%)	22 (2%)
2 to 3 weeks	40 (3%)	19 (2%)
More than 3 weeks	33 (2%)	17 (2%)
Not advised	31 (2%)	17 (2%)
Not applicable	1355 (91%)	1039 (93%)
<b>Chi<sup>2</sup>=3.97, df=2, p=0.138</b>		

	Registered (%)	Followed (%)
<b>Death-to-graft time - moist pot</b>		
Within 48 hours	86 (6%)	71 (6%)
2 to 7 days	136 (9%)	109 (10%)
8 to 14 days	107 (7%)	90 (8%)
More than 2 weeks	203 (14%)	149 (13%)
Not advised	225 (15%)	169 (15%)
Not applicable	738 (49%)	526 (47%)
<b>Chi<sup>2</sup>=3.12, df=3, p=0.373</b>		
<b>Sex of donor</b>		
Female	620 (41%)	459 (41%)
Male	828 (55%)	612 (55%)
Not Advised	47 (3%)	43 (3%)
<b>Chi<sup>2</sup>=0.21, df=1, p=0.650</b>		
<b>Age group</b>		
Under 50 years	159 (11%)	121 (11%)
50 to 59 years	181 (12%)	126 (11%)
60 to 69 years	381 (25%)	282 (25%)
70 to 79 years	478 (32%)	355 (32%)
80 years or older	262 (18%)	200 (18%)
Not advised	34 (2%)	30 (3%)
<b>Chi<sup>2</sup>=6.86, df=4, p=0.144</b>		
<b>Cause of death</b>		
Cardiac event	513 (34%)	384 (34%)
Malignancy	351 (23%)	266 (24%)
Trauma	86 (6%)	64 (6%)
Respiratory event	158 (11%)	121 (11%)
Intracranial/cerebral haemorrhage	237 (16%)	170 (15%)
Other specified	66 (4%)	49 (4%)
Not advised*	84 (6%)	60 (5%)
<b>Chi<sup>2</sup>=6.40, df=5, p=0.269</b>		
<b>Multi-organ donor status</b>		
No	1408 (94%)	1056 (95%)
Yes	87 (6%)	58 (5%)
<b>Chi<sup>2</sup>=0.02, df=1, p=0.876</b>		
<b>Central corneal endothelial cell density</b>		
<2500 cells/mm <sup>2</sup>	41 (3%)	25 (2%)
2500 to 2749 cells/mm <sup>2</sup>	46 (3%)	25 (2%)
2750 to 2999 cells/mm <sup>2</sup>	39 (3%)	18 (2%)
≥ 3000 cells/mm <sup>2</sup>	49 (3%)	31 (3%)
Not advised	1320 (88%)	1015 (91%)
<b>Chi<sup>2</sup>=4.49, df=3, p=0.213</b>		
<b>Total</b>	<b>1495 (100%)</b>	<b>1114 (100%)</b>

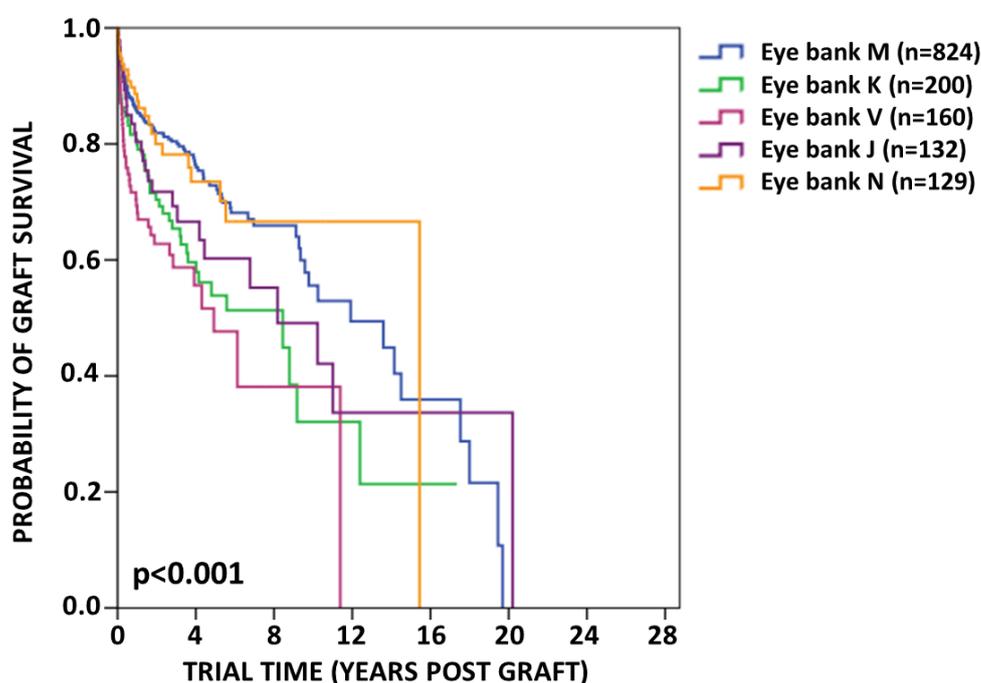
Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable.

\* ACGR advised that cause of death was not yet determined but there were no medical contraindications and the eye had been cleared for release, by the Medical Director, in accordance with EBAANZ guidelines.

### 6.1.1 Traditional lamellar graft survival: influence of Australian eye bank

Donor corneas are retrieved, processed, stored and distributed by five eye banks around Australia. Figure 6.1.1 shows the comparison of graft survival for corneas provided by each of these eye banks. Data were not available for 1 case. A significant difference was found across eye banks (Log Rank Statistic=30.20; df=4;  $p<0.001$ ), with grafts performed using tissue from Eye Bank M having better survival than those using tissue from Eye Bank K or Eye Bank V (both  $p<0.001$ ), and grafts performed using tissue from Eye Bank N having better survival than those using tissue from Eye Bank V ( $p=0.001$ ). This variable was not retained in the multivariate analysis (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.1.1 Australian eye bank



#### Number at risk (years post-graft)

	1	2	4	6	8	10	12
Eye bank M	385	268	138	74	48	22	13
Eye bank K	94	62	35	20	10	5	3
Eye bank V	58	40	16	6	3	1	NA
Eye bank J	52	33	22	15	9	7	4
Eye bank N	72	45	28	15	9	8	4

#### Probability of graft survival (years post-graft)

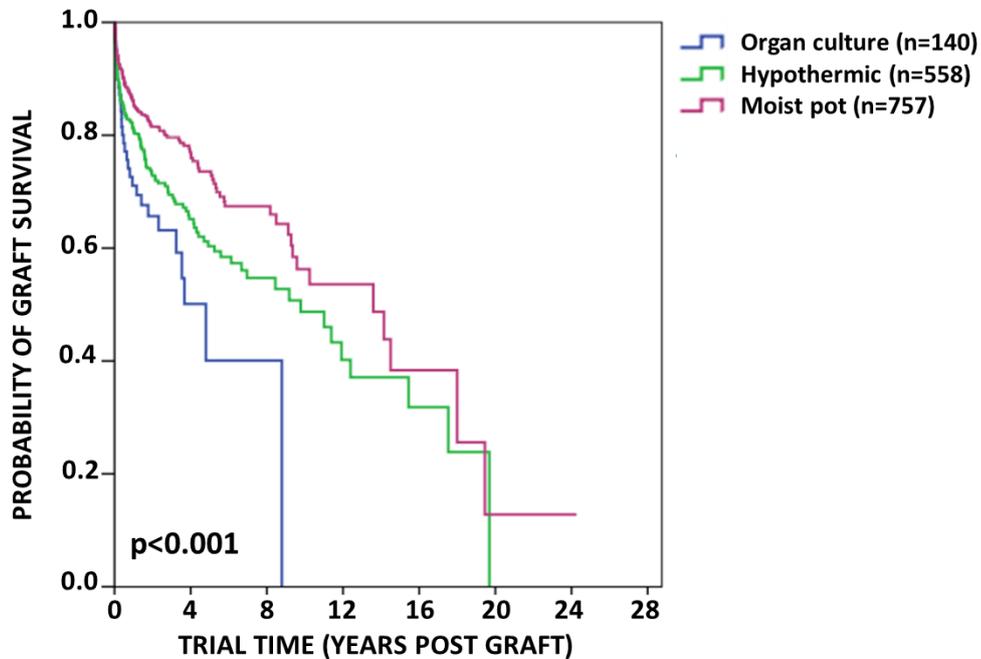
	1	2	4	6	8	10
Eye bank M	0.86	0.82	0.77	0.68	0.66	0.52
Eye bank K	0.79	0.70	0.60	0.51	NA	NA
Eye bank V	0.68	0.63	0.56	NA	NA	NA
Eye bank J	0.80	0.72	0.67	NA	NA	NA
Eye bank N	0.89	0.80	0.74	NA	NA	NA

### 6.1.2 Traditional lamellar graft survival: influence of modern corneal storage media

In Australia, two storage media are currently commonly used to preserve donor corneas prior to transplantation. Further details of these storage media can be found in Section 2.1.3 of this report. A third storage technique, in which the donor eye is stored in a moist pot, is also still used occasionally, particularly for donor tissue to be used in a traditional lamellar graft. Data were not analysed for 20 donor corneas for which the eye bank did not specify the medium used.

Figure 6.1.2 shows the comparison of graft survival for corneas stored in hypothermic medium compared to organ culture medium and moist pot. A significant difference was found between media (Log Rank Statistic=19.75; df=2; p<0.001), with those stored in moist pot having better survival than the other two groups (both p<0.001). This variable was not retained in the multivariate analysis (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.1.2 Modern corneal storage media



#### Number at risk (years post-graft)

	1	2	4	6	8	10	12
Organ culture	44	30	9	3	1	NA	NA
Hypothermic	256	167	92	53	33	22	13
Moist pot	366	253	140	75	50	23	14

#### Probability of graft survival (years post-graft)

	1	2	4	6	8	10
Organ culture	0.71	0.66	NA	NA	NA	NA
Hypothermic	0.81	0.73	0.65	0.59	0.55	0.49
Moist pot	0.86	0.82	0.77	0.67	0.67	0.56

## 6.2 Recipient Factors

Table 6.3 shows the number of grafts within each of the variable sub-groups, for the recipient factors examined in this report that were found to be **significant** predictors of graft survival in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (1,495 registered and 1,114 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 6.3 Recipient factors, significant in univariate analysis**

<b>Traditional Lamellar Corneal Grafts Recipient Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Indication for graft</b>		
Failed previous	221 (15%)	160 (14%)
Keratoconus	105 (7%)	71 (6%)
Corneal scars and opacities	29 (2%)	20 (2%)
Corneal ulcer/perforation	190 (13%)	130 (12%)
Herpetic eye disease	63 (4%)	50 (4%)
Trauma	70 (5%)	51 (5%)
Non herpetic infections	50 (3%)	41 (4%)
Corneal degenerations	73 (5%)	57 (5%)
Descemetocoele	31 (2%)	22 (2%)
Pterygium	234 (16%)	202 (18%)
Scleral necrosis	200 (13%)	149 (13%)
Limbal dermoid	72 (5%)	56 (5%)
Cancer	42 (3%)	30 (3%)
Glaucoma	29 (2%)	12 (1%)
Other*	86 (6%)	63 (6%)
<b>Australian State where graft was performed</b>		
State M	828 (55%)	609 (55%)
State K	188 (13%)	133 (12%)
State V	151 (10%)	115 (10%)
State J	155 (10%)	99 (9%)
State N	120 (8%)	106 (10%)
State C	52 (3%)	51 (5%)
Other	1 (<1%)	1 (<1%)
<b>Interstate transportation</b>		
Yes	84 (6%)	73 (7%)
No	1361 (91%)	996 (89%)
Not advised	50 (3%)	45 (4%)
<b>Recipient age group</b>		
Under 20 years	111 (7%)	88 (8%)
20 to 29 years	108 (7%)	82 (7%)
30 to 39 years	149 (10%)	123 (11%)
40 to 49 years	161 (11%)	123 (11%)
50 to 59 years	195 (13%)	151 (14%)
60 to 69 years	250 (17%)	185 (17%)
70 to 79 years	315 (21%)	229 (21%)
80 years or older	206 (14%)	133 (12%)

	Registered (%)	Followed (%)
<b>Change in lens status pre- to post-graft</b>		
Phakic/phakic	1150 (77%)	882 (79%)
Other	345 (23%)	232 (21%)
<b>Pre-graft neovascularisation</b>		
None	988 (66%)	712 (64%)
One quadrant	130 (9%)	95 (9%)
Two quadrants	171 (11%)	139 (12%)
Three quadrants	63 (4%)	55 (5%)
Four quadrants	143 (10%)	113 (10%)
<b>Pre-graft inflammation and/or steroid use</b>		
No	831 (56%)	617 (55%)
Yes	602 (40%)	452 (41%)
Not advised	62 (4%)	45(4%)
<b>History of raised intraocular pressure</b>		
No	1341 (90%)	1013 (91%)
Yes	154 (10%)	101 (9%)
<b>Prior existing contralateral graft/s</b>		
None	1366 (91%)	1018 (91%)
One	94 (6%)	73 (7%)
Two or more	35 (2%)	23 (2%)
<b>Total</b>	<b>1495 (100%)</b>	<b>1114 (100%)</b>

\*Other included: wound dehiscence (19), corneal dystrophy (15), pseudophakic bullous keratopathy (8), scleromalacia (7), interstitial keratitis (4), keratoglobus (4), lipid keratopathy (4), band keratopathy (3), not advised (3), amyloidosis (2), ectodermal dysplasia (2), scleral fistula (2), aniridic keratopathy (1), aphakia (1), atopic keratoconjunctivitis (1), autograft repair (1), congenital cataract (1), epithelial defect (1), Goldenhar's syndrome (1), limbal stem cell failure (1), ocular sarcoidosis (1), reticular pigmentary disorder (1), rosacea (1), Sjogren's syndrome (1), Stevens Johnson syndrome (1).

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Follow-up was significantly more likely ( $p < 0.05$ ) to have been received for grafts performed with tissue transported interstate, in recipients who remained phakic post-graft, those with no history of raised intraocular pressure, and those with pre-graft corneal neovascularisation. Significant differences in follow-up were also found across groups for recipient State, recipient age, and indication for graft.

Table 6.4 shows the number of grafts within each of the variable sub-groups, for the recipient factor found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (1,495 registered and 1,114 with follow-up provided) and the percentages, summed vertically, total 100. The result of the Kaplan-Meier survival analysis is also provided.

**Table 6.4 Recipient factors, not significant in univariate analysis**

<b>Traditional Lamellar Corneal Grafts Recipient Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Recipient sex</b>		
Female	596 (40%)	447 (40%)
Male	899 (60%)	667 (60%)
<b>Chi<sup>2</sup>=2.69, df=1, p=0.101</b>		
<b>Donor/recipient sex match/mismatch</b>		
Female/female	255 (17%)	190 (17%)
Female/male	365 (24%)	269 (24%)
Male/female	322 (22%)	241 (22%)
Male/male	506 (34%)	371 (33%)
Not advised	47 (3%)	43 (4%)
<b>Chi<sup>2</sup>=2.43, df=3, p=0.489</b>		
<b>Eye in which graft was performed</b>		
Left	771 (52%)	577 (52%)
Right	723 (48%)	536 (48%)
Not advised	1 (<1%)	1 (<1%)
<b>Chi<sup>2</sup>=0.13, df=1, p=0.715</b>		
<b>Total</b>	<b>1495 (100%)</b>	<b>1114 (100%)</b>

Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised.

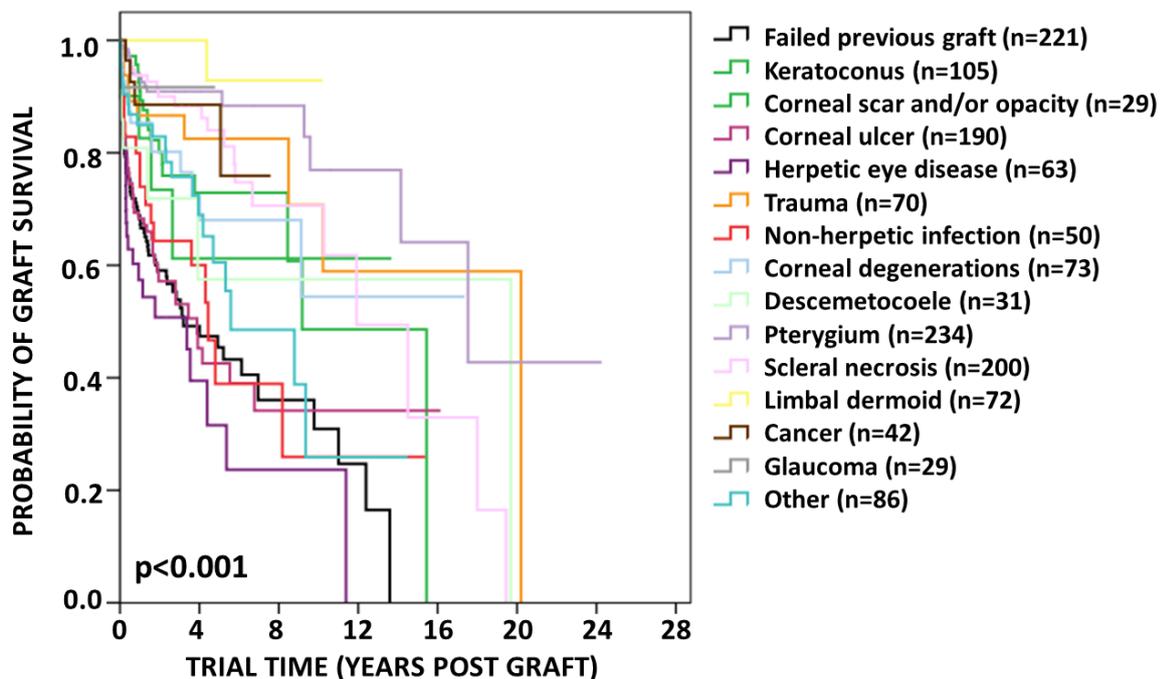


### 6.2.1 Traditional lamellar graft survival: influence of indication for graft

Figure 6.2.1 shows the comparison of graft survival depending on indication for graft. All repeat grafts were analysed together, regardless of original pathology. A significant difference was found across groups (Log Rank Statistic=159.57; df=14;  $p<0.001$ ). Grafts performed for herpetic eye disease had significantly poorer survival than those performed for keratoconus, trauma, corneal degenerations, pterygium, scleral necrosis, or limbal dermoid (all  $p<0.001$ ). Grafts performed for a failed previous graft, or corneal ulcer, had significantly poorer survival than those performed for keratoconus, trauma, pterygium, scleral necrosis, or limbal dermoid (all  $p<0.0005$ ). Grafts performed for non-herpetic infections had significantly poorer survival than those performed for pterygium, scleral necrosis, or limbal dermoid (all  $p<0.0005$ ).

There was no significant difference ( $p=0.443$ ) in the survival of grafts performed for any of the indications for graft for which fewer than 50 grafts had been registered (including those already classified as “other”) and so these groups were combined for the multivariate analysis. Survival of grafts performed in eyes with one previous graft (of any kind) and those performed in eyes with more than one previous graft (of any kind) was not significantly different ( $p=0.330$ ). Indication for graft was retained in multivariate analysis (see section 6.7) suggesting that this is an independent factor significantly affecting graft survival.

Figure 6.2.1 Indication for graft



**Number at risk (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>	<b>10</b>
<b>Failed previous graft</b>	90	58	27	16	8	5
<b>Keratoconus</b>	56	38	20	15	7	4
<b>Corneal scar/opacity</b>	11	7	4	2	2	2
<b>Ulcer/perforation</b>	63	34	17	11	5	1
<b>Herpetic eye disease</b>	19	14	5	3	3	2
<b>Trauma</b>	34	30	16	10	7	6
<b>Non-herpetic infection</b>	26	18	12	4	3	1
<b>Corneal degeneration</b>	41	25	17	8	5	4
<b>Descemetocoele</b>	13	8	4	3	2	2
<b>Pterygium</b>	127	85	47	32	24	12
<b>Scleral necrosis</b>	92	65	41	21	14	8
<b>Limbal dermoid</b>	44	29	15	7	3	1
<b>Cancer</b>	19	13	7	5	NA	NA
<b>Glaucoma</b>	8	6	1	NA	NA	NA
<b>Other</b>	44	38	19	7	6	2

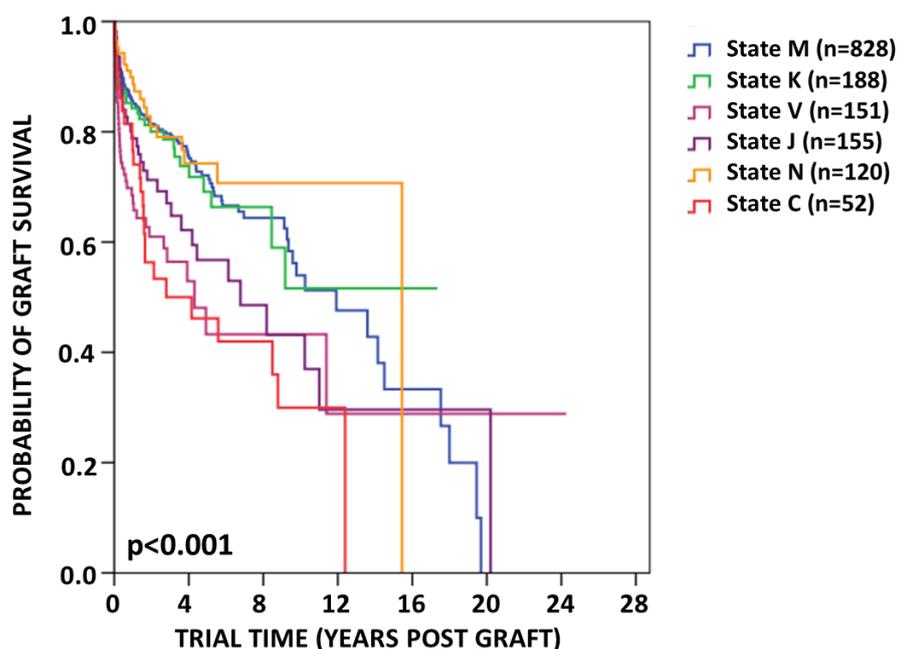
**Probability of graft survival (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>
<b>Failed previous graft</b>	0.68	0.59	0.49	NA	NA
<b>Keratoconus</b>	0.91	0.80	0.73	NA	NA
<b>Corneal scar/opacity</b>	NA	NA	NA	NA	NA
<b>Ulcer/perforation</b>	0.68	0.57	NA	NA	NA
<b>Herpetic eye disease</b>	NA	NA	NA	NA	NA
<b>Trauma</b>	0.87	0.87	NA	NA	NA
<b>Non-herpetic infection</b>	0.77	NA	NA	NA	NA
<b>Corneal degeneration</b>	0.85	0.80	NA	NA	NA
<b>Descemetocoele</b>	NA	NA	NA	NA	NA
<b>Pterygium</b>	0.93	0.91	0.91	0.88	0.88
<b>Scleral necrosis</b>	0.94	0.90	0.88	0.75	NA
<b>Limbal dermoid</b>	1.00	1.00	NA	NA	NA
<b>Cancer</b>	NA	NA	NA	NA	NA
<b>Glaucoma</b>	NA	NA	NA	NA	NA
<b>Other</b>	0.85	0.83	NA	NA	NA

## 6.2.2 Traditional lamellar graft survival: influence of Australian State where graft was performed

Figure 6.2.2 shows the comparison of graft survival depending on the Australian State in which the transplantation occurred. One graft was performed in the Northern Territory, and was excluded from the analysis. A significant difference was found across groups (Log Rank Statistic=33.08; df=5;  $p<0.001$ ), with grafts performed in State M and State N having better survival than those performed in State V and State C (all  $p<0.001$ ), and grafts performed in State K having better survival than those performed in state C ( $p=0.002$ ). This variable was not retained in the multivariate analysis (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.2.2 Australian State where graft was performed



### Number at risk (years post-graft)

	1	2	4	6	8	10	12
State M	386	268	137	72	47	21	12
State K	90	66	37	20	11	7	5
State V	50	33	13	7	5	3	2
State J	60	38	24	16	9	7	4
State N	70	44	29	16	10	8	4
State C	31	19	13	9	8	4	2

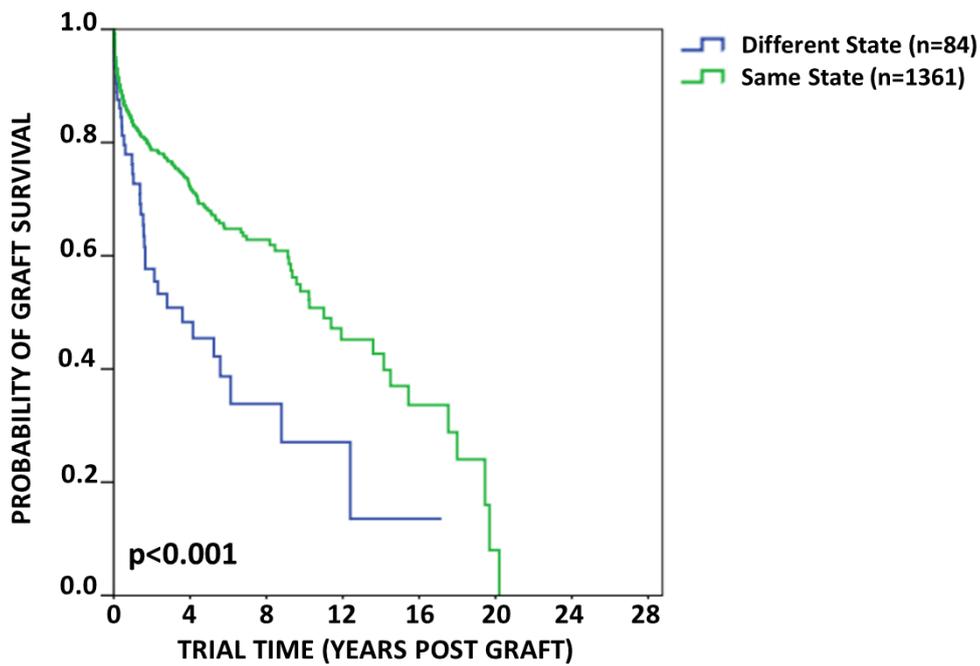
### Probability of graft survival (years post-graft)

	1	2	4	6	8	10
State M	0.85	0.81	0.76	0.66	0.64	0.54
State K	0.84	0.80	0.74	0.66	NA	NA
State V	0.67	0.61	NA	NA	NA	NA
State J	0.79	0.71	0.62	NA	NA	NA
State N	0.90	0.81	0.74	NA	NA	NA
State C	0.79	NA	NA	NA	NA	NA

### 6.2.3 Traditional lamellar graft survival: influence of interstate transportation

In the majority of transplants, donor corneas are sourced in the same State as the surgery occurs, however, in some cases corneas are transported interstate via air freight. Figure 6.2.3 shows the comparison of graft survival for grafts where the surgery was performed in the same State as the donor cornea was sourced, compared to those where the donor cornea was from interstate. The graft where donor State was not available was excluded from the analysis. A significant difference was found between groups (Log Rank Statistic=16.78; df=1; p<0.001). This variable was not retained in the multivariate analysis (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.2.3 Interstate transportation



**Number at risk (years post-graft)**

	1	2	4	6	8	10	12
Different State	43	27	17	8	6	4	2
Same State	619	421	222	122	73	39	22

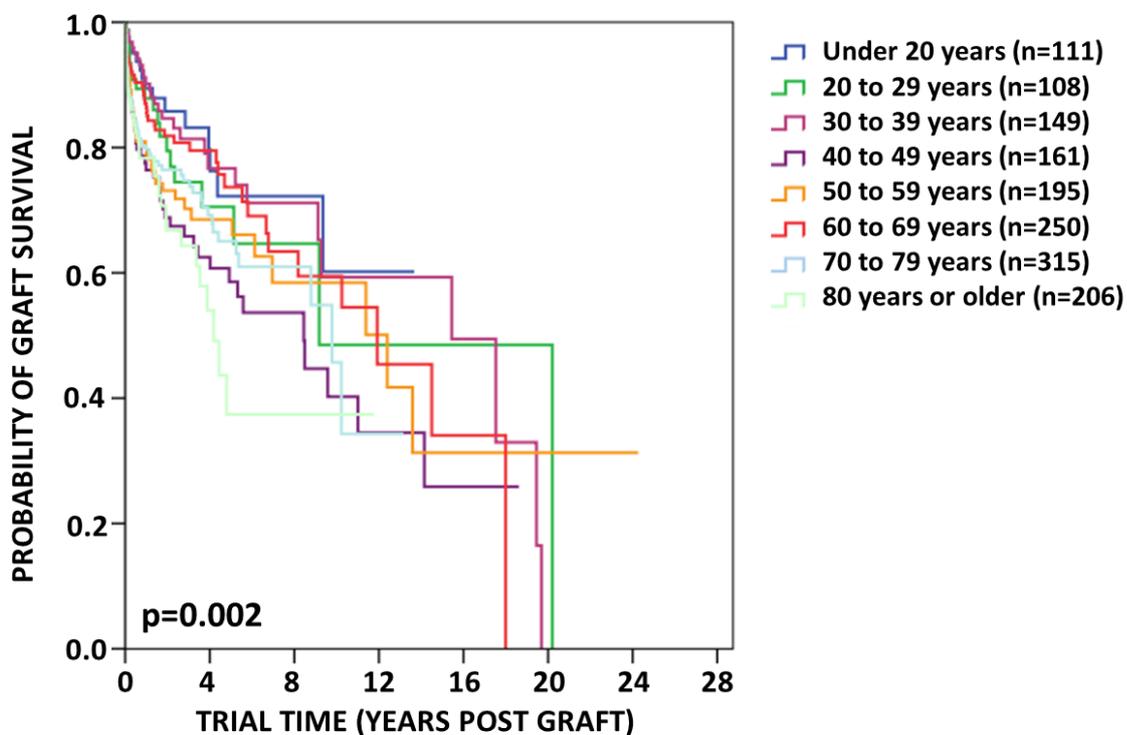
**Probability of graft survival (years post-graft)**

	1	2	4	6	8	10	12
Different State	0.74	0.58	NA	NA	NA	NA	NA
Same State	0.83	0.79	0.72	0.65	0.63	0.54	0.45

### 6.2.4 Traditional lamellar graft survival: influence of recipient age (years)

Figure 6.2.4 shows the comparison of graft survival depending on the age of the corneal transplant recipient. Data for grafts where the recipient was aged under 20 years, and those where they were aged over 80 years, were all analysed together due to the low numbers in these groups. A significant difference was found across groups (Log Rank Statistic=22.84; df=7;  $p=0.002$ ), with poorer survival for grafts performed in recipients aged 80 years or older compared to those aged under 20 years, 30 to 39 years and 60 to 69 years (all  $p<0.001$ ). This variable was not retained in the multivariate analysis (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.2.4 Recipient age



**Number at risk (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>	<b>10</b>	<b>12</b>
<b>Under 20 years</b>	62	40	23	12	7	4	1
<b>20 to 29 years</b>	56	33	15	9	7	3	3
<b>30 to 39 years</b>	88	63	32	23	15	10	8
<b>40 to 49 years</b>	69	51	35	18	15	8	5
<b>50 to 59 years</b>	85	61	34	21	13	8	6
<b>60 to 69 years</b>	128	82	46	29	16	12	5
<b>70 to 79 years</b>	138	105	53	24	12	4	1
<b>80 years or older</b>	61	33	14	4	4	1	NA

**Probability of graft survival (years post-graft)**

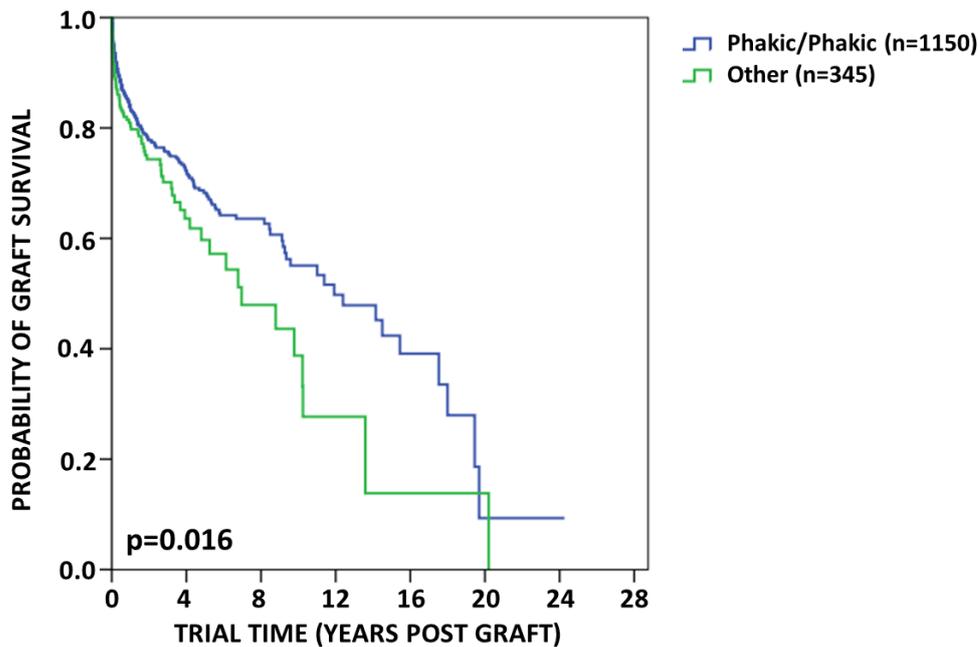
	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>
<b>Under 20 years</b>	0.90	0.86	0.80	NA
<b>20 to 29 years</b>	0.88	0.79	NA	NA
<b>30 to 39 years</b>	0.90	0.85	0.77	0.71
<b>40 to 49 years</b>	0.76	0.69	0.63	NA
<b>50 to 59 years</b>	0.79	0.73	0.69	0.66
<b>60 to 69 years</b>	0.86	0.82	0.80	0.69
<b>70 to 79 years</b>	0.80	0.76	0.69	0.61
<b>80 years or older</b>	0.78	0.67	NA	NA

### 6.2.5 Traditional lamellar graft survival: influence of change in lens status

Figure 6.2.5 shows the comparison of graft survival stratified by the change of lens status from pre- to post-graft. “Phakic/phakic” means the eye was phakic both before and after the graft. “Other” means the eye was phakic, pseudophakic or aphakic before the graft, and either aphakic or pseudophakic afterwards.

A significant difference was found across groups (Log Rank Statistic=5.79; df=1;  $p=0.016$ ). This variable was not retained in the multivariate analysis (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.2.5 Change in lens status



#### Number at risk (years post-graft)

	1	2	4	6	8	10	12
Phakic/phakic	548	375	212	120	76	43	26
Other	139	93	40	20	13	7	3

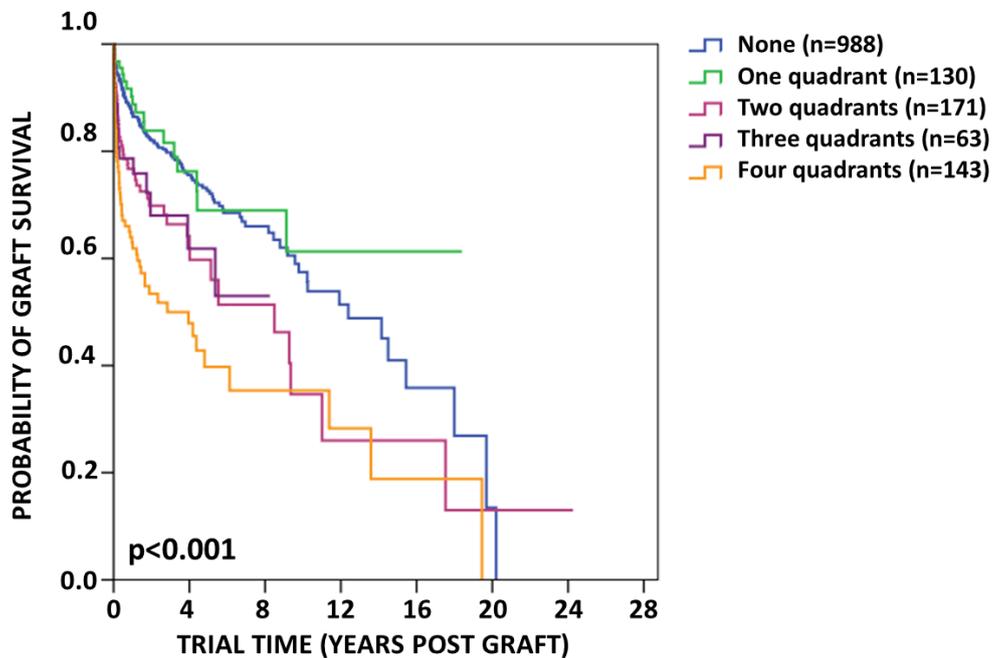
#### Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12
Phakic/phakic	0.84	0.78	0.72	0.64	0.64	0.55	0.50
Other	0.80	0.74	0.64	0.57	NA	NA	NA

### 6.2.6 Traditional lamellar graft survival: influence of pre-graft corneal neovascularisation

Figure 6.2.6 shows the comparison of graft survival between those recipients with corneal neovascularisation pre-graft and those without (Log Rank Statistic=56.36; df=4; p<0.001). Recipients with avascular corneas pre-graft, or one quadrant of pre-graft neovascularisation, had significantly better survival than those with two or four quadrants of neovascularisation (all p<0.005). Recipients with avascular corneas pre-graft, or one quadrant of pre-graft neovascularisation, did not have significantly different graft survival (p=0.440). Recipients with two or three quadrants of pre-graft neovascularisation, did not have significantly different graft survival (p=0.972). This variable was recategorised for the multivariate analysis, according to this finding. This variable was retained in the multivariate analysis (see section 6.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 6.2.6 Pre-graft corneal neovascularisation



#### Number at risk (years post-graft)

	1	2	4	6	8	10	12
None	460	325	168	99	58	34	20
One quadrant	61	32	24	15	10	7	3
Two quadrants	78	51	29	11	10	4	3
Three quadrants	29	15	9	5	4	NA	NA
Four quadrants	59	35	22	10	7	5	3

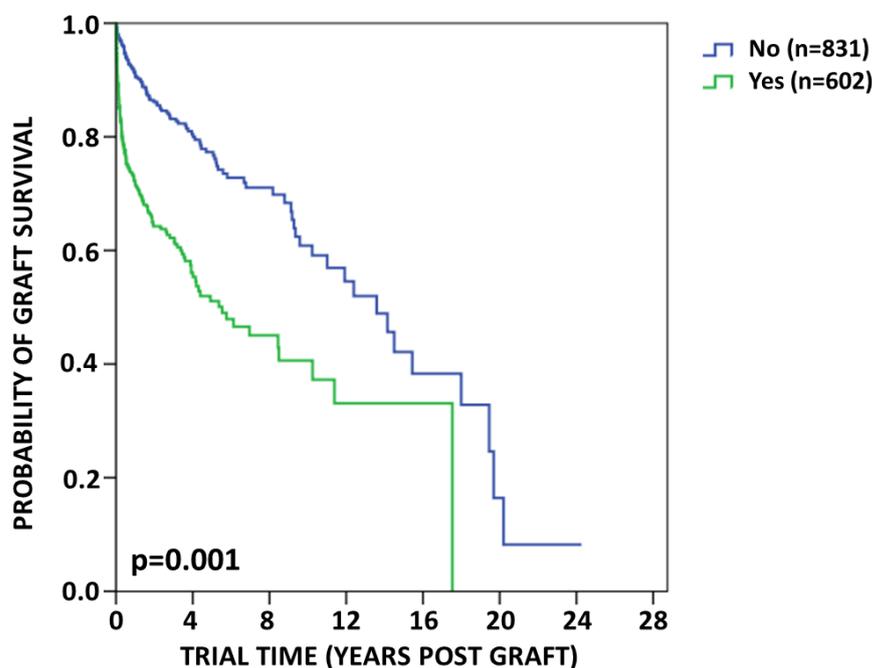
#### Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12
None	0.87	0.82	0.76	0.69	0.66	0.57	0.51
One quadrant	0.89	0.84	0.76	NA	NA	NA	NA
Two quadrants	0.77	0.70	0.64	NA	NA	NA	NA
Three quadrants	0.79	NA	NA	NA	NA	NA	NA
Four quadrants	0.62	0.53	0.48	NA	NA	NA	NA

### 6.2.7 Traditional lamellar graft survival: influence of inflammation and/or steroid use at time of graft

Figure 6.2.7 shows the comparison of graft survival between grafts performed in an eye with current inflammation and/or steroid use within the past two weeks, compared to those with neither of these factors (Log Rank Statistic=67.89; df=1;  $p<0.001$ ). Data on this variable were not provided in 4% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=68.26; df=2;  $p<0.001$ ). Inflammation and/or steroid use was thus categorised into these three groups for multivariate analysis. This variable was retained in the multivariate analysis (see section 6.7), suggesting that this is an independent factor significantly affecting graft survival.

**Figure 6.2.7 Inflammation and/or steroid use at time of graft**



#### Number at risk (years post-graft)

	1	2	4	6	8	10	12
No inflammation/steroid use	424	291	163	99	61	37	22
Inflammation/steroid use	234	155	78	37	26	12	6

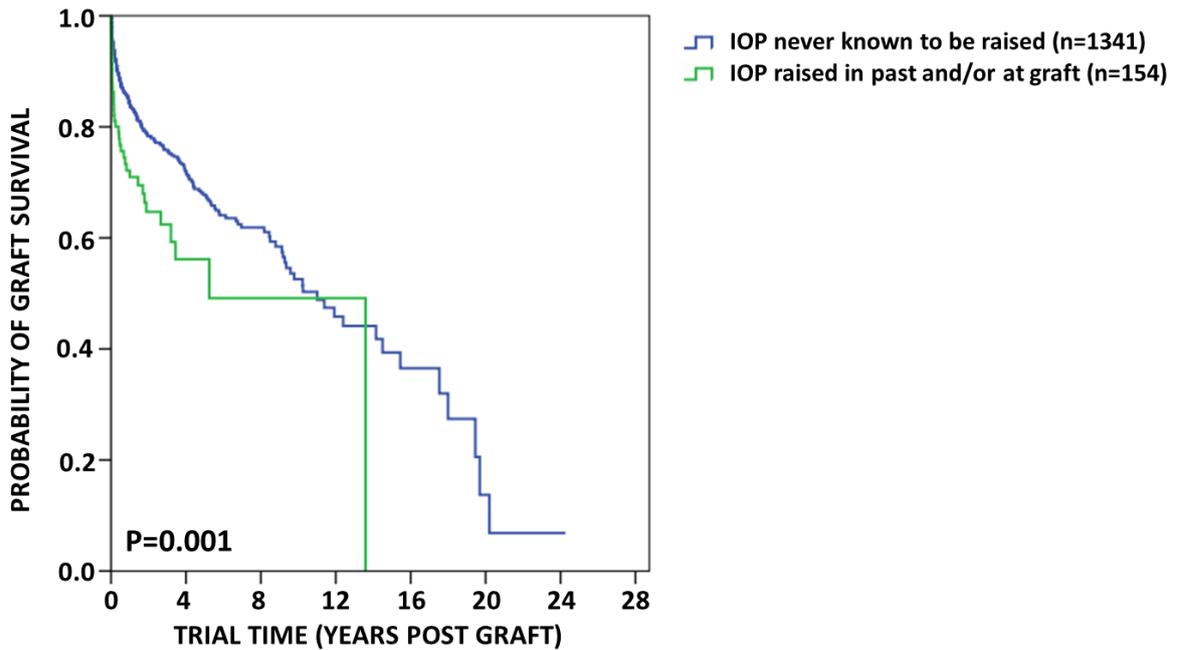
#### Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12
No inflammation/steroid use	0.91	0.86	0.81	0.73	0.71	0.61	0.55
Inflammation/steroid use	0.72	0.64	0.56	0.48	0.45	NA	NA

### 6.2.8 Traditional lamellar graft survival: influence of history of raised intraocular pressure (IOP)

Figure 6.2.8 shows the comparison of graft survival between grafts with a history of raised IOP and those without. A history of raised IOP, means IOP had been raised in the eye previously, regardless of whether it was raised at the time of the graft. A significant difference was found across groups (Log Rank Statistic=10.69; df=1; p=0.001). This variable was not retained in the multivariate analysis (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.2.8 History of raised intraocular pressure



**Number at risk (years post-graft)**

	1	2	4	6	8	10	12
No raised IOP	628	434	237	134	85	48	28
Raised IOP	59	34	15	6	4	2	1

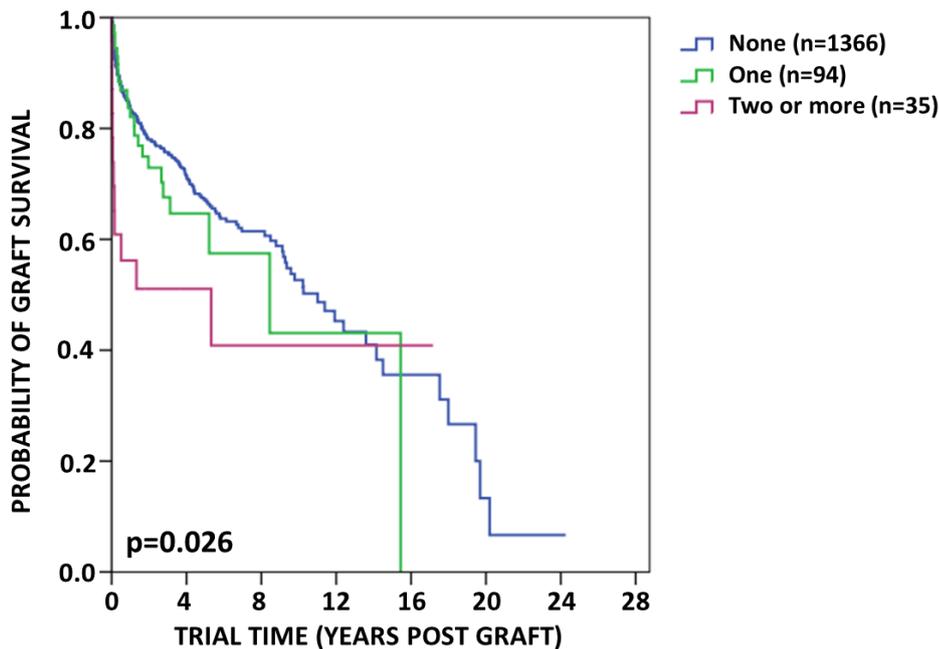
**Probability of graft survival (years post-graft)**

	1	2	4	6	8	10	12
No raised IOP	0.84	0.78	0.72	0.64	0.62	0.53	0.46
Raised IOP	0.71	0.65	NA	NA	NA	NA	NA

### 6.2.9 Traditional lamellar graft survival: influence of number of previous grafts in the contralateral eye

Figure 6.2.9 shows the comparison of graft survival between grafts where the recipient had undergone a single previous contralateral graft, multiple previous contralateral grafts, and no previous contralateral grafts. Recipients in each category may have undergone any number of previous ipsilateral grafts. A significant difference was found across groups (Log Rank Statistic=7.28; df=2; p=0.026), with grafts performed in recipients with two or more previous grafts in the contralateral eye having poorer survival (p=0.008). This variable was not retained in the multivariate analysis (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.2.9 Number of previous grafts in the contralateral eye



#### Number at risk (years post-graft)

	1	2	4	6	8	10	12
None	625	425	229	129	81	45	24
One	50	35	18	8	6	3	3
Two or more	12	8	5	3	2	2	2

#### Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12
None	0.84	0.78	0.72	0.64	0.62	0.53	0.45
One	0.82	0.73	NA	NA	NA	NA	NA
Two or more	NA						

## 6.3 Graft Era

Table 6.5 shows the number of grafts registered and followed, in blocks of five years. The percentages, which should be summed vertically, total 100.

**Table 6.5 Graft era**

<b>Traditional Lamellar Corneal Graft Graft Era</b>		
<b>Year of graft</b>	<b>Registered (%)</b>	<b>Followed (%)</b>
1985 to 1989	93 (6%)	76 (7%)
1990 to 1994	243 (16%)	209 (19%)
1995 to 1999	255 (17%)	205 (18%)
2000 to 2004	293 (20%)	217 (19%)
2005 to 2009	242 (16%)	186 (17%)
2010 to 2014	223 (15%)	166 (15%)
2015 to 2017	146 (10%)	55 (5%)
<b>Total</b>	<b>1495 (100%)</b>	<b>1114 (100%)</b>

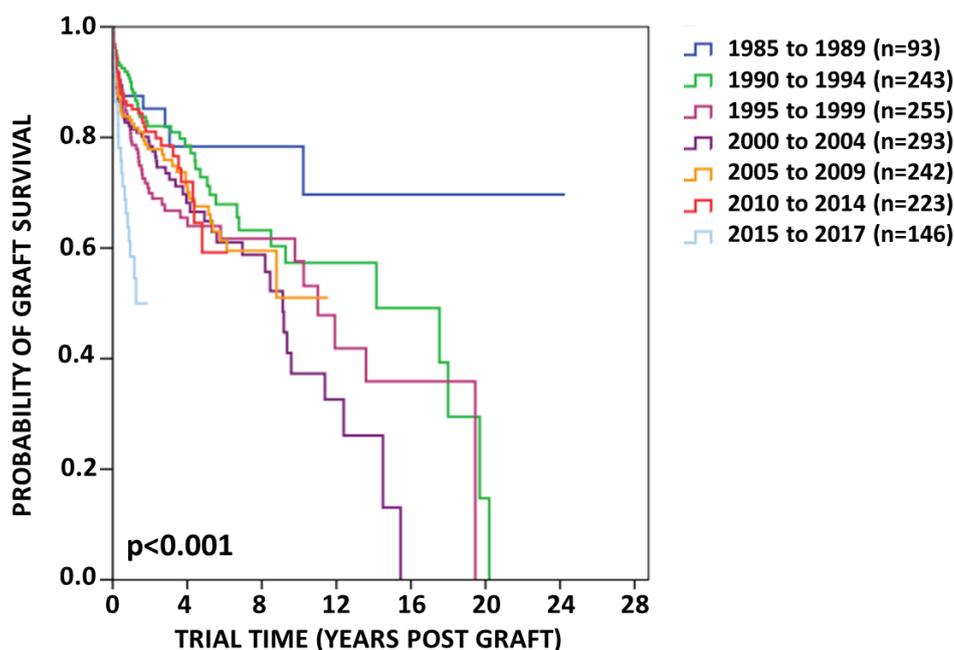
Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses and found to be significant ( $p < 0.001$ ). Follow-up was lower for grafts performed in more recent years.

Consideration was given to the effect of follow-up lag time on this analysis. Up-to-date information on failed grafts is more likely to be known than for surviving grafts. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft.

### 6.3.1 Traditional lamellar graft survival: influence of era of graft

Figure 6.3.1 shows the comparison of graft survival between year of graft, stratified into five-year groups (Log Rank Statistic=34.97; df=6;  $p<0.001$ ), with all prior eras having superior survival to 2015-2017 (all  $p<0.001$ ). This finding is likely due to the lag time discussed on the previous page. This variable was not retained in the multivariate analysis (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.3.1 Graft era



#### Number at risk (years post-graft)

	1	2	4	6	8	10	12
1985 to 1989	40	33	20	15	11	9	7
1990 to 1994	138	93	63	32	22	14	10
1995 to 1999	114	75	44	26	20	14	7
2000 to 2004	131	87	44	31	21	10	5
2005 to 2009	125	94	59	34	15	3	NA
2010 to 2014	120	86	22	2	NA	NA	NA
2015 to 2017	19	NA	NA	NA	NA	NA	NA

#### Probability of graft survival (years post-graft)

	1	2	4	6	8
1985 to 1989	0.88	0.85	0.78	NA	NA
1990 to 1994	0.89	0.82	0.79	0.68	0.63
1995 to 1999	0.79	0.70	0.66	0.62	0.62
2000 to 2004	0.82	0.78	0.68	0.61	0.59
2005 to 2009	0.83	0.78	0.71	0.61	NA
2010 to 2014	0.86	0.81	0.72	NA	NA
2015 to 2017	NA	NA	NA	NA	NA

## 6.4 Surgery and Surgeon Factors

Table 6.6 shows the number of grafts within each of the variable sub-groups, for the surgery and surgeon factors examined in this report that were found to be **significant** in univariate analyses.

**Table 6.6 Surgery and surgeon factors, significant in univariate analysis**

<b>Traditional Lamellar Corneal Grafts Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Size of graft (diameter)</b>		
6.0 mm or less	350 (23%)	266 (24%)
6.1 to 8.0 mm	427 (29%)	335 (30%)
More than 8.0 mm	281 (19%)	216 (19%)
Not advised	437 (29%)	297 (27%)
<b>The Centre effect</b>		
Fewer than 30 registered TLK	903 (60%)	656 (59%)
Surgeon A	133 (9%)	128 (11%)
Surgeon S	126 (8%)	71 (6%)
Surgeon D	93 (6%)	84 (8%)
Surgeon F	71 (5%)	65 (6%)
Surgeon G	48 (3%)	16 (1%)
Surgeon H	45 (3%)	35 (3%)
Surgeon J	42 (3%)	41 (4%)
Surgeon K	34 (2%)	18 (2%)
<b>Total</b>	<b>1495 (100%)</b>	<b>1114 (100%)</b>

Differences in rates of follow-up across sub-groups may affect survival calculations for these factors. This is because, while information on surviving grafts must be provided by a surgeon, the fact that a graft has failed may also be known when a registration is received for a replacement graft. Differences in survival across sub-groups for variables where a significant difference was found in rates of follow-up should thus be interpreted with this in mind.

Comparisons between the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi<sup>2</sup> analyses. Due to the nature of the variable, follow-up was, logically, significantly higher ( $p < 0.001$ ) for grafts performed by surgeons with 30+ registered grafts and  $\geq 75\%$  follow-up.

Table 6.7 shows the number of grafts within each of the variable sub-groups, for the surgery and surgeon factors found to be **non-significant** in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (1,495 registered and 1,114 followed) and the percentages, which should be summed vertically for each variable, total 100.

**Table 6.7 Surgery and surgeon factors, not significant in univariate analysis**

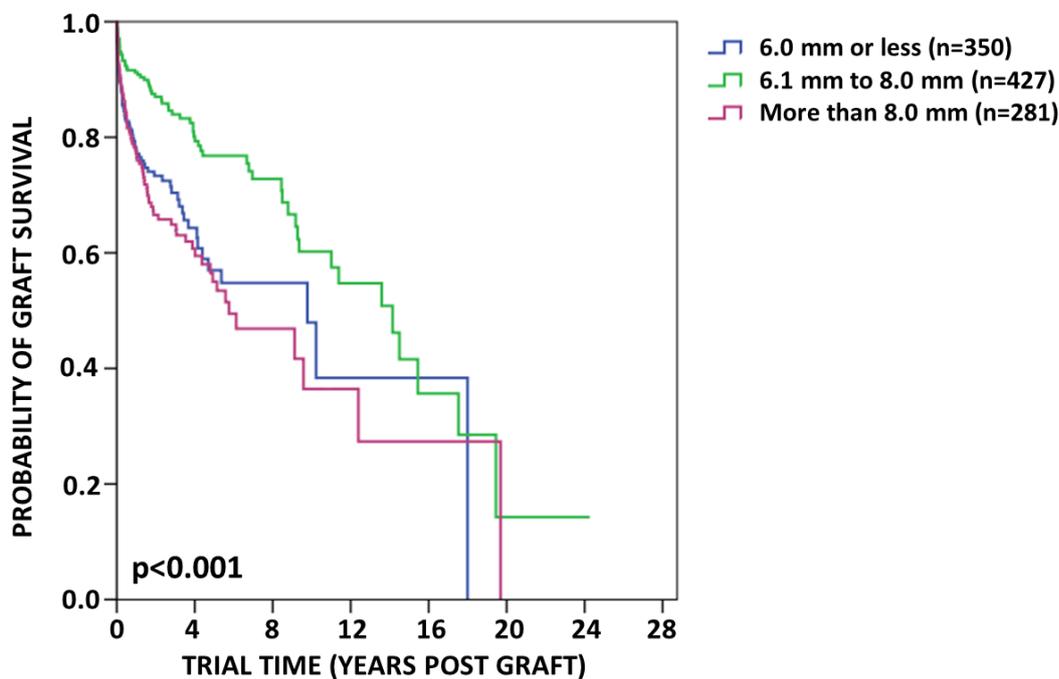
<b>Traditional Lamellar Corneal Grafts Surgery and Surgeon Factors</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Surgeon volume</b>		
Fewer than 30 registered TLK	903 (60%)	656 (59%)
30+ registered TLK, <75% follow-up	208 (14%)	105 (9%)
30+ registered TLK, ≥75% follow-up	384 (26%)	353 (32%)
<b>Chi<sup>2</sup>=0.50, df=2, p=0.780</b>		
<b>Total</b>	<b>1495 (100%)</b>	<b>1114 (100%)</b>

75% was selected as the cut-off point for the follow-up categories as this (74.5%) was the average percentage of follow-up for all penetrating grafts, regardless of surgeon experience.

### 6.4.1 Traditional lamellar graft survival: influence of graft size

Figure 6.4.1 shows a comparison of graft survival depending on the size of the graft, based on the donor button diameter, as reported by surgeons. A significant difference was found across groups (Log Rank Statistic=28.36; df=2; p<0.001), with survival of grafts sized 6.1mm to 8.0mm significantly better than both those smaller and larger (both p<0.001). Data on this variable were not provided in 29% of cases. A further category was thus created called “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=29.07; df=3; p<0.001). Graft size was thus categorised into these four groups for multivariate analysis. This variable was retained in the final model (see section 6.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 6.4.1 Graft size



#### Number at risk (years post-graft)

	1	2	4	6	8	10	12
<b>6.0 mm or less</b>	146	98	42	22	13	6	2
<b>6.1 mm to 8.0 mm</b>	231	161	100	66	42	25	17
<b>More than 8.0 mm</b>	134	88	48	23	11	7	4

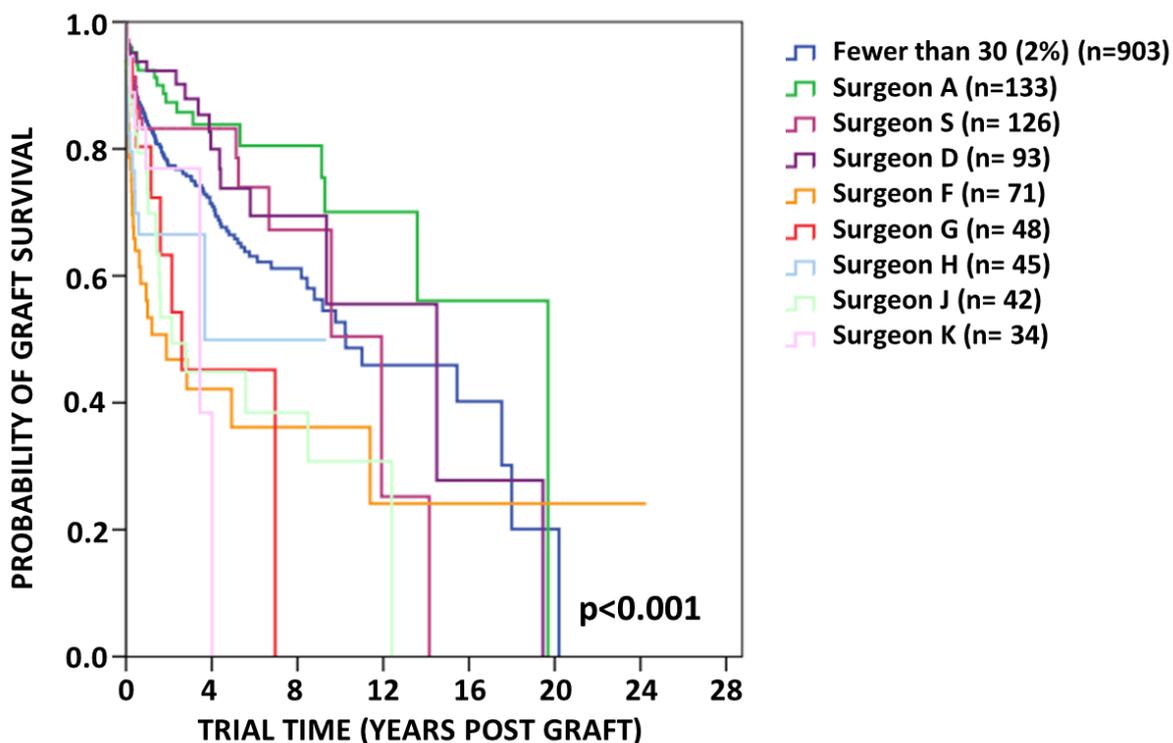
#### Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12
<b>6.0 mm or less</b>	0.78	0.73	0.64	0.55	NA	NA	NA
<b>6.1 mm to 8.0 mm</b>	0.91	0.87	0.80	0.77	0.73	0.60	NA
<b>More than 8.0 mm</b>	0.77	0.67	0.61	0.50	NA	NA	NA

### 6.4.2 Traditional lamellar graft survival: influence of the Centre effect

Figure 6.4.2 shows the comparison of graft survival for individual surgeons (shown in random order) for which 30 or more traditional lamellar keratoplasties had been registered with the ACGR, and all other TLK (performed by 177 surgeons) combined (Log Rank Statistic=55.55; df=8;  $p<0.001$ ). This variable was retained in the multivariate analysis (see section 6.7), suggesting that this is an independent factor significantly affecting graft survival.

Figure 6.4.2 The centre effect



Note: To preserve anonymity, surgeons have been identified using random letters of the alphabet. These identifying letters do not correspond with those used in chapters reporting on other types of graft, i.e. Surgeon A in this chapter is not the same surgeon identified as Surgeon A in the chapter on penetrating keratoplasty.

**Number at risk (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>	<b>10</b>	<b>12</b>
<b>&lt;30 TLK registered</b>	405	269	143	77	45	28	15
<b>Surgeon A</b>	87	63	35	24	17	11	7
<b>Surgeon S</b>	49	39	25	12	7	2	1
<b>Surgeon D</b>	63	48	29	14	10	4	2
<b>Surgeon F</b>	20	12	7	5	4	3	2
<b>Surgeon G</b>	10	7	3	1	NA	NA	NA
<b>Surgeon H</b>	18	11	1	1	1	NA	NA
<b>Surgeon J</b>	23	13	8	6	5	3	2
<b>Surgeon K</b>	12	6	1	NA	NA	NA	NA

**Probability of graft survival (years post-graft)**

	<b>1</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>8</b>	<b>10</b>
<b>&lt;30 TLK registered</b>	0.85	0.77	0.71	0.63	0.61	0.53
<b>Surgeon A</b>	0.92	0.87	0.84	0.81	NA	NA
<b>Surgeon S</b>	0.83	0.83	0.83	NA	NA	NA
<b>Surgeon D</b>	0.92	0.92	0.80	NA	NA	NA
<b>Surgeon F</b>	0.53	NA	NA	NA	NA	NA
<b>Surgeon G</b>	NA	NA	NA	NA	NA	NA
<b>Surgeon H</b>	NA	NA	NA	NA	NA	NA
<b>Surgeon J</b>	0.73	NA	NA	NA	NA	NA
<b>Surgeon K</b>	NA	NA	NA	NA	NA	NA

## 6.5 Operative procedures at the time of graft

Only seventeen TLKs had an anterior vitrectomy at the time of graft and ten had a peripheral iridectomy. Thus, these factors were not further analysed.

## 6.6 Post-graft Events

Table 6.8 shows the occurrence of post-graft events, which were found to be **significant** in univariate analyses.

**Table 6.8 Post-graft events, significant in univariate analysis**

<b>Traditional Lamellar Corneal Graft Post-graft Events</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Post-graft microbial keratitis</b>		
No	1460 (98%)	1079 (97%)
Yes	35 (2%)	35 (3%)
<b>Post-graft rise in intraocular pressure*</b>		
No	1424 (95%)	1043 (94%)
Yes	71 (5%)	71 (6%)
<b>At least one rejection episode</b>		
No	1462 (98%)	1081 (97%)
Yes	33 (2%)	33 (3%)
<b>Total</b>	<b>1495 (100 %)</b>	<b>1114 (100 %)</b>

\* Note: significant at  $p < 0.08$  for inclusion in multivariate analyses but not at  $p < 0.05$ .

Table 6.9 shows the number of grafts within each of the variable sub-groups, for the post-graft events found to be **non-significant** in univariate analyses. The sum for each variable equals the total number of grafts (1,495 registered and 1,114 with follow-up provided) and the percentages, summed vertically, total 100. The result of the Kaplan-Meier survival analysis is also provided. Only 18 TLK had post-graft herpetic infection, four had post-graft synechia, and eight had post-graft uveitis reported. Thus, the impact of these factors was not further analysed.

Table 6.9 Post-graft events, not significant in univariate analysis

<b>Traditional Lamellar Corneal Graft Post-graft Events</b>		
	<b>Registered (%)</b>	<b>Followed (%)</b>
<b>Post-graft neovascularisation</b>		
No	1389 (93%)	1009 (91%)
Yes	105 (7%)	105 (9%)
<b>Chi<sup>2</sup>=1.22, df=1, p=0.269</b>		
<b>Time to removal of sutures</b>		
Within 3 months post-graft	114 (8%)	114 (10%)
Between 3 and 6 months post-graft	113 (8%)	113 (10%)
Between 6 and 12 months post-graft	85 (6%)	85 (8%)
More than 12 months post-graft	117 (8%)	117 (11%)
Not yet removed/not advised	1056 (71%)	675 (61%)
<b>Chi<sup>2</sup>=2.63, df=3, p=0.453</b>		
<b>Total</b>	<b>1495 (100 %)</b>	<b>1114 (100 %)</b>

Table 6.10 shows post-graft surgical procedures, as reported by follow-up practitioners. Please note: post-graft data may be incomplete when follow-up is based on a registration for a replacement graft.

### Table 6.10 Post-graft surgical procedures

206 TLK were reported to have undergone a re-grafting procedure (separate to subsequent concurrent graft/s) at the date last seen. Of these 177 had not had additional post-graft operative procedures reported, while 29 had.

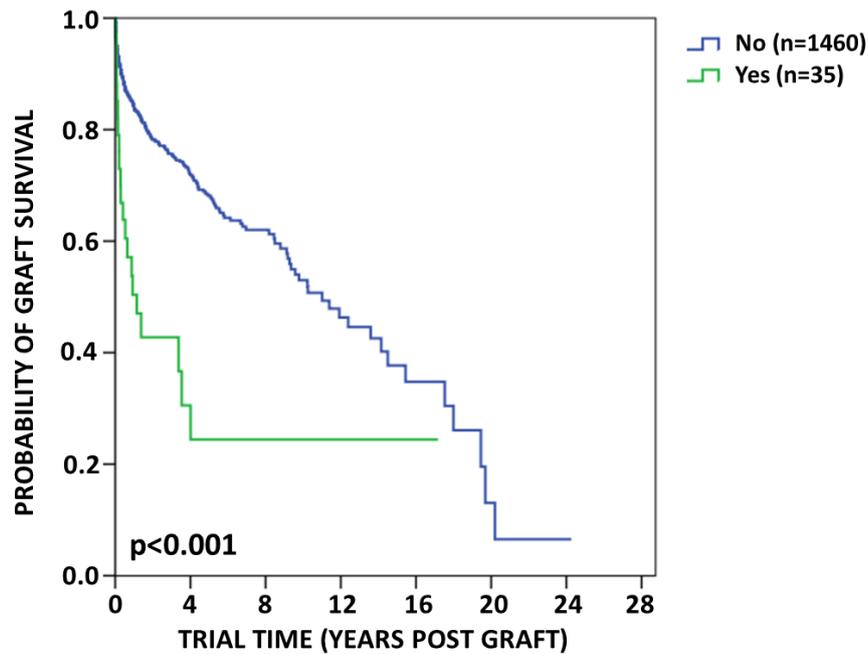
<b>Traditional Lamellar Corneal Grafts Post-graft Surgical Procedures</b>	
Type of procedure	Number
Cataract removal/IOL insertion (90 both, 2 cataract only, 7 IOL only)	99
Additional concurrent graft (5, TLK, 4 PK, 4 conjunctival, 1 DSEK)	14
YAG laser	13
Tarsorrhaphy	12
Gunderson flap	11
Enucleation	9
Wound repair/resutured	9
Relaxing incision	7
Suture adjustment	7
Pterygium removal	5
PRK laser	5
LASIK	4
Glaucoma tube insertion: 2 Baerveldt, 1 Molteno	3
Evisceration	3
Intravitreal injection	3
Vitrectomy	3
Wedge resection	3
Other*	40
<b>Total number of surgical procedures (number of grafts)</b>	<b>250 (203)</b>

\* Other included: amniotic membrane transplant (2), cryotherapy (2), IOL exchange (2), lash epilation (2), removal of calcified plaque (2), trabeculectomy (2), argon laser trabeculoplasty (1), collagen cross-linking (1), conjunctival resection (1), corneal gluing (1), corneal scraping (1), cyclodiode (1), debridement of corneal ulcer (1), de-bulking (1), entropion repair (1), epithelial debridement (1), evacuation of haematoma under lamellar graft (1), exenteration (1), iridectomy (1), iridoplasty (1), keratectomy (1), keratotomy (1), ptosis repair (1), punctal cautery (1), punctal occlusion surgery (1), removal of Gunderson flap (1), removal of limbal lesion (1), removal of bank keratopathy (1), removal of gold weight from eyelid (1), removal of conjunctival tumour (1), removal of cysts (1), removal of giant cell granuloma (1), removal of small cell carcinoma (1), scleral buckle (1).

**6.6.1 Traditional lamellar graft survival: influence of post-graft microbial keratitis**

Figure 6.6.1 shows the survival for grafts where the eye had microbial keratitis post-graft, compared to those where there was no such infection. A significant difference was found between groups (Log Rank Statistic=28.80; df=1; p<0.001). This variable was not retained in the multivariate analysis (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

**Figure 6.6.1 Post-graft microbial keratitis**



**Number at risk (years post-graft)**

	1	2	4	6	8	10	12
<b>No microbial keratitis</b>	673	460	247	137	88	49	28
<b>Microbial keratitis</b>	15	8	5	3	1	1	1

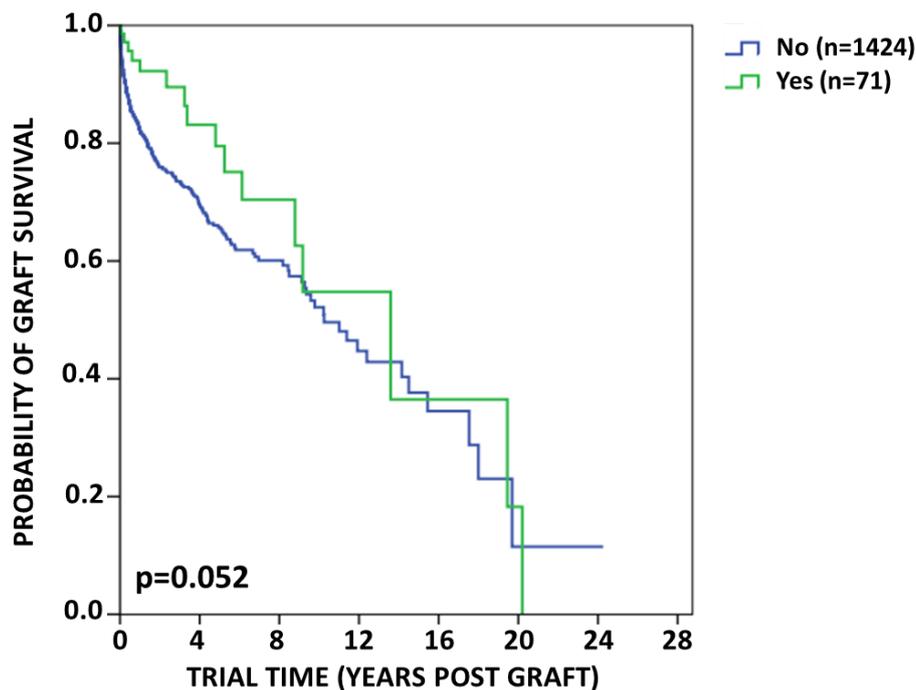
**Probability of graft survival (years post-graft)**

	1	2	4	6	8	10	12
<b>No microbial keratitis</b>	0.84	0.78	0.72	0.64	0.62	0.53	0.46
<b>Microbial keratitis</b>	NA						

### 6.6.2 Traditional lamellar graft survival: influence of raised IOP post-graft

Figure 6.6.2 shows the comparison of graft survival for grafts where the eye was reported to have had raised intraocular pressure post-graft to those where the IOP remained in the normal range. No significant difference was found between groups (Log Rank Statistic=3.79; df=1; p=0.052), however this variable met the p<0.08 criteria for inclusion in the multivariate analyses. It was not retained in the final model (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.6.2 Post-graft raised intraocular pressure



#### Number at risk (years post-graft)

	1	2	4	6	8	10	12
No raised IOP	636	431	227	124	79	43	24
Raised IOP	51	37	25	16	10	7	5

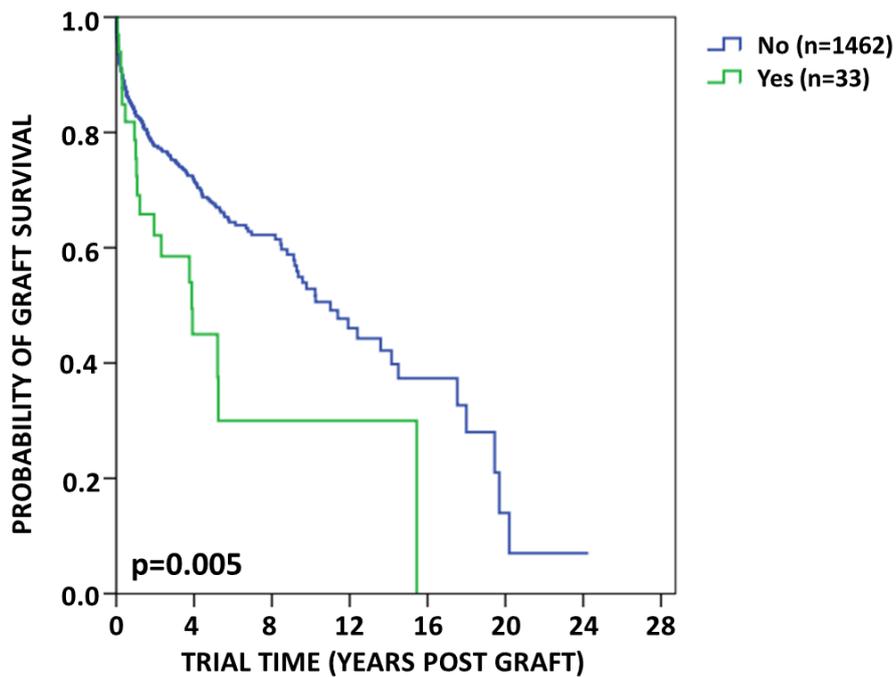
#### Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12
No raised IOP	0.82	0.76	0.70	0.62	0.60	0.52	0.45
Raised IOP	0.92	0.92	0.83	NA	NA	NA	NA

### 6.6.3 Traditional lamellar graft survival: influence of any rejection episode/s

Figure 6.6.3 shows the comparison of graft survival depending on whether the graft underwent at least one rejection episode. A significant difference was found between groups (Log Rank Statistic=7.91; df=1; p=0.005). This variable was not retained in the final model (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

**Figure 6.6.3 Any rejection**



**Number at risk (years post-graft)**

	1	2	4	6	8	10	12
<b>No rejection</b>	663	451	242	136	85	48	27
<b>Any rejection</b>	25	17	10	4	4	2	2

**Probability of graft survival (years post-graft)**

	1	2	4	6	8	10	12
<b>No rejection</b>	0.83	0.78	0.72	0.64	0.62	0.53	0.46
<b>Any rejection</b>	0.79	NA	NA	NA	NA	NA	NA

## 6.7 Multivariate Analysis

A multivariate model was used to investigate the combined effect of variables on penetrating graft survival, adjusted for all other variables in the model. This analysis was performed using STATA version 11.

In the preceding univariate analyses, each registered TLK, together with its archival follow-up records, was treated as a separate and independent entity. Some recipients had multiple TLK performed during the census period (up to 31/7/2017), with some having repeat grafts in a single eye, some grafts in both eyes and some a combination of both. To control for potential inter-graft and/or inter-eye dependence in the multivariate analyses, the multivariate model was adjusted to allow for clustering by individual patient [see references 7 & 8].

Variables to be included in the Cox Proportional Hazards regression model were identified based on the results of the univariate Kaplan-Meier analyses, with a cut-off significance level of  $p < 0.08$  used to select variables for inclusion. No variables were excluded due to collinearity or missing data. Each variable was initially analysed individually to determine if it remained significant once clustered by individual patient. Where the variable was no longer found to be significant ( $p > 0.08$ ), it was excluded from the multivariate analysis.

The best model was found by a backward elimination process, removing variables not appearing to be predictors of graft failure. The model excluded variables with a p-value of  $p \geq 0.05$  (or global p-value of  $p \geq 0.05$  for variables with more than two categories) in a stepwise manner, beginning with the least significant variable. For categorical variable with more than two groups, Bonferroni adjustment was applied to determine if significant differences were present between groups. The Kaplan-Meier plots, and additional appropriate STATA analyses, were used to assess whether each included variable met the assumption of proportional hazards. Where variables were found to be time-variant, they were treated as such in the multivariate model.

Table 6.11 shows each of the variables analysed in the univariate analyses, stratified by whether they were included in the initial multivariate model and whether they remained in the final model.

Table 6.11 Multivariate model

### Traditional Lamellar Corneal Graft Multivariate Model

#### Not significant in univariate analysis

Donor sex  
 Donor age group  
 Cause of donor death  
 Multi-organ donor  
 Time from death to enucleation  
 Time from enucleation to storage  
 Storage time in Optisol  
 Storage time in organ culture  
 Time from death to graft - moist pot storage  
 Endothelial cell density  
 Recipient sex  
 Donor/recipient sex match/mismatch  
 Eye grafted  
 Surgeon experience and level of follow-up  
 Post-graft corneal neovascularisation  
 Time to removal of sutures

#### Significant in univariate analysis but not retained in multivariate model

Eye Bank  
 Storage medium  
 Interstate transportation  
 Recipient State  
 Recipient age group  
 Change in lens status pre- to post-graft  
 History of raised intraocular pressure  
 Previous contralateral graft(s)  
 Graft era  
 Post-graft microbial keratitis  
 Raised intraocular pressure post-graft\*  
 Post-graft rejection episode(s)

#### Significant in univariate analysis AND retained in multivariate model

Indication for graft  
 Pre-graft inflammation and/or steroid use  
 Pre-graft corneal neovascularisation  
 Graft size  
 The Centre effect

\*p<0.08



## **6.7.1 Significant differences in the traditional lamellar keratoplasty multivariate model for categories with more than two groups following Bonferroni correction for multiple comparisons**

### **6.7.1.1 Indication for graft**

Grafts performed for pterygium had significantly better survival than those performed for herpetic eye disease, failed previous grafts, corneal ulcers, and non-herpetic infections (all  $p < 0.001$ ), and those performed for “other” specified indications ( $p = 0.003$ ).

Grafts performed for trauma had significantly better survival than those performed for herpetic eye disease ( $p < 0.001$ ), failed previous graft ( $p = 0.001$ ), corneal ulcer ( $p = 0.001$ ), and non-herpetic infections ( $p = 0.003$ ).

Grafts performed for scleral necrosis had significantly better survival than those performed for herpetic eye disease ( $p < 0.001$ ), failed previous graft ( $p < 0.001$ ), and corneal ulcers ( $p = 0.001$ ).

Grafts performed for limbal dermoid had significantly better survival than those performed for herpetic eye disease ( $p = 0.002$ ).

### **6.7.1.2 Pre-graft corneal neovascularisation**

Grafts performed in eyes with no, or one quadrant of, pre-graft corneal neovascularisation had significantly better survival than those with two or three quadrants ( $p = 0.002$ ), or four quadrants ( $p < 0.001$ ).

### **6.7.1.3 Graft size**

Grafts that were 6.1 mm up to 8.0 mm had significantly better survival than grafts that were 6.0 mm or smaller ( $p = 0.001$ ) and those that were 8.1 mm or larger ( $p < 0.001$ ).

### **6.7.1.4 Individual surgeon**

Individual results varied widely for surgeons with 30 or more TLK registered with the ACGR compared to the balance of the database (TLK performed by surgeons with fewer than 30 registered TLK). The hazard ratios ranged from 0.53 to 2.40.

## 6.8 Reasons for Graft Failure

Of the 1,114 followed grafts, 296 (27%) were known to have failed by the census date. This equates to 20% of the 1,495 registered grafts. Surgeons were asked to indicate the reason for graft failure. This information was also gathered from repeat registration forms, where the reason for failure of the previous graft was given. Table 6.13 shows the reasons for failure given.

**Table 6.13 Reasons for graft failure**

<b>Traditional Lamellar Corneal Grafts Reasons for Graft Failure</b>	
Corneal melt	37 (13%)
Corneal ulcer/perforation	37 (13%)
Non herpetic infection	31 (11%)
Primary graft failure	15 (5%)
Scarring	15 (5%)
Endothelial cell failure	13 (4%)
Herpetic infection	12 (4%)
Rejection	11 (4%)
Scleral necrosis	11 (4%)
Recurrent pterygium	10 (3%)
Astigmatism	10 (3%)
Other specified*	40 (14%)
Unspecified	54 (18%)
<b>Total</b>	<b>296 (100%)</b>

\*Other included: cancer recurrence (9), wound leak (7), vascularisation (5), epithelial defect (3), keratoconus (2), Stevens-Johnson syndrome (2), trauma (2), atopic keratoconjunctivitis (1), band keratopathy (1), cataract (1), corneal thinning (1), descemetocoele (1), glaucoma (1), keratoglobus (1), ocular pemphigoid (1), symblepharon (1), Wegener's granulomatosis (1).

Of the 15 grafts reported by surgeons to have been primary graft failures, eight had no further information provided. Specific reasons given were: corneal melt (3), persistent wound leakage (2), perforation (1) and surgical trauma (1).

## 6.9 Post-graft Changes in Best Corrected Visual Acuity

### 6.9.1 All indications for graft

Post-graft best corrected visual acuity (BCVA) is an important outcome for many corneal graft recipients. A desire for improved visual acuity was specified as a reason for graft in 322 (22%) of registered traditional lamellar keratoplasties. In 20% of cases (303), this was the sole desired outcome indicated. These percentages were much lower than for any other type of grafts, with traditional lamellar keratoplasties most often performed for structural repair (see section 1.1.3).

Follow-ups occur at varying times post-graft, depending on when a surgeon sees a recipient. Where post-graft best corrected visual acuity (without pinhole) information was provided, we categorised this according to the length of time since graft. The first two categories were:

- BCVA provided at between 6 and 12 months post-graft, and
- BCVA provided at between 12 and 18 months post-graft.

Subsequent groups were at yearly intervals. For each year point, any measurements provided within 6-months of that date, rounded to the nearest day, were included (e.g. for two year follow-up, any BCVA given at between 730 and 913 days post-graft was included).

We analysed post-graft best corrected visual acuity in several ways. Where more than 20 grafts had BCVA measurements provided, we examined:

1. The percentage of *surviving* grafts achieving different levels of Snellen visual acuity (6/6 or better, 6/7.5 to 6/12, 6/15 to 6/24, 6/36 to 6/60, count fingers (CF) or hand movements (HM), and light perception (LP) or no light perception (NLP)) at yearly time-points post-graft. Grafts that had been reported to have failed at the time of last follow-up, but had prior follow-ups with BCVA measurements provided when the graft was surviving, had these prior data included in these analyses.
2. The *average* Snellen visual acuity achieved at yearly intervals post-graft, again by *surviving* grafts.
3. The final BCVA reported at the time of failure.

Table 6.14 and Figure 6.9.1 show the reported post-graft best corrected visual acuity for all failed grafts at the time of last follow-up, separated by indication for graft. Visual acuity at time of failure was reported for 191 (65%) of 296 failed TLK. Where fewer than 10 grafts had visual acuity reported at time of failure for a particular indication, these data were included in the “other specified” group. As might be expected, the majority of failed grafts had accompanying poor visual acuity, though large proportions of the TLK performed for pterygium or scleral necrosis had good visual acuity despite having failed.

**Table 6.14 Post-graft best corrected visual acuity**

<b>Traditional Lamellar Corneal Graft: Visual Acuity in Failed Grafts (as reported at final follow-up)</b>						
	<b>6/4 to 6/6</b>	<b>6/7.5 to 6/12</b>	<b>6/15 to 6/24</b>	<b>6/36 to 6/60</b>	<b>CF or HM</b>	<b>LP or NLP</b>
<b>Failed previous graft</b>	0 (0%)	4 (8%)	2 (4%)	6 (12%)	24 (48%)	14 (28%)
<b>Keratoconus</b>	0 (0%)	0 (0%)	2 (17%)	1 (8%)	9 (75%)	0 (0%)
<b>Corneal ulcers</b>	1 (3%)	6 (18%)	0 (0%)	3 (9%)	13 (39%)	10 (30%)
<b>Herpetic eye disease</b>	0 (0%)	0 (0%)	1 (5%)	3 (16%)	12 (63%)	3 (16%)
<b>Non-herpetic infection</b>	0 (0%)	0 (0%)	2 (15%)	3 (23%)	5 (38%)	3 (23%)
<b>Pterygium</b>	4 (33%)	4 (33%)	0 (0%)	2 (17%)	2 (17%)	0 (0%)
<b>Scleral necrosis</b>	1 (9%)	3 (27%)	2 (18%)	1 (9%)	4 (36%)	0 (0%)
<b>Other specified</b>	1 (2%)	6 (15%)	1 (2%)	6 (15%)	23 (56%)	4 (10%)
<b>Total</b>	<b>7 (4%)</b>	<b>23 (12%)</b>	<b>10 (5%)</b>	<b>25 (13%)</b>	<b>92 (48%)</b>	<b>34 (18%)</b>

CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

**Figure 6.9.1 Best corrected visual acuity at time of last follow-up for failed traditional lamellar keratoplasties**

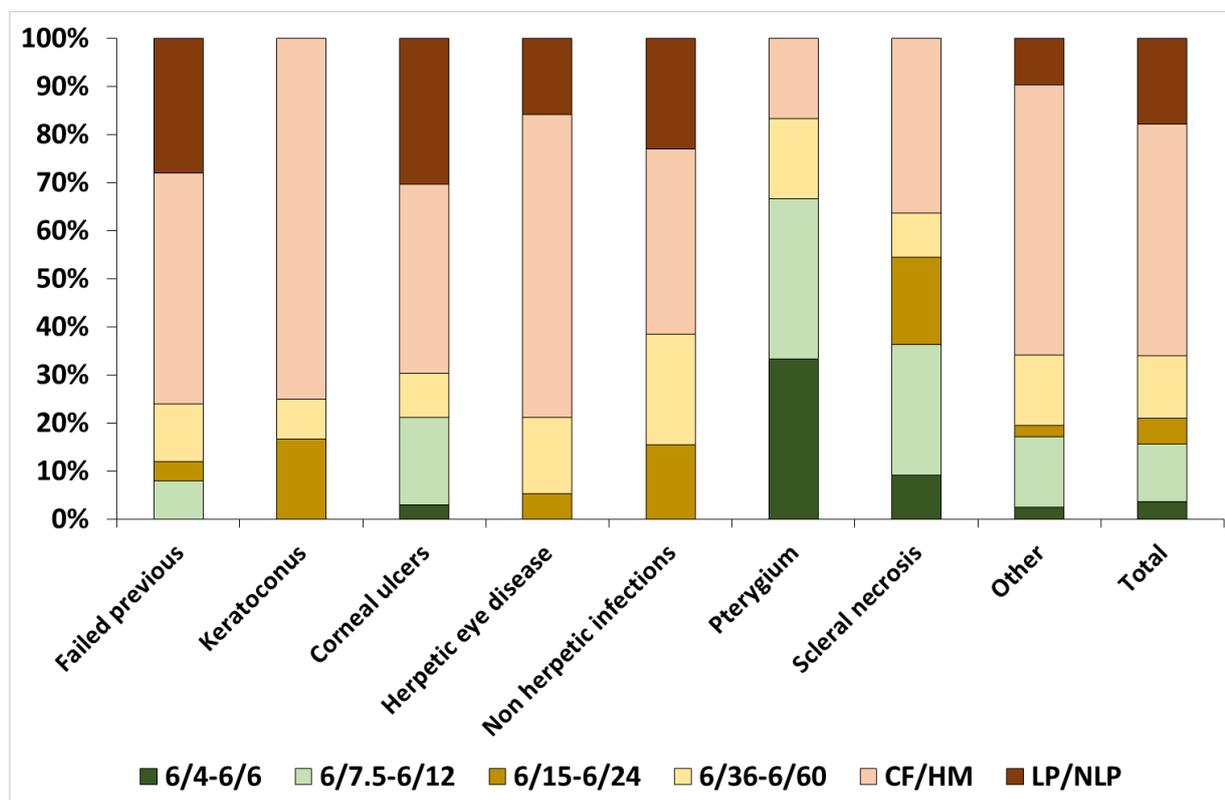
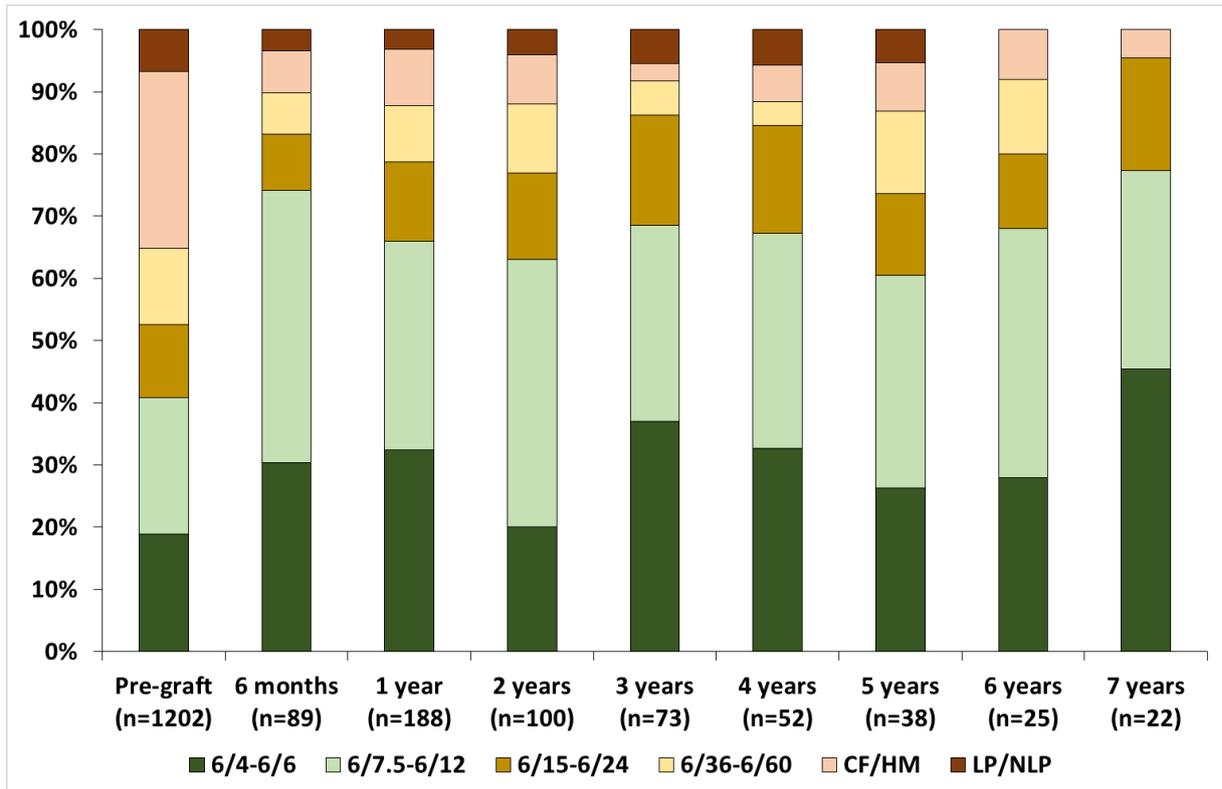


Figure 6.9.2 shows the best corrected visual acuity in the grafted eye, as reported to the ACGR, and categorised into six levels of vision, for all **surviving** traditional lamellar keratoplasties. Prior to graft over a third of eyes (35%) had vision of CF or worse. By 6-months post-graft, almost three-quarters (74%) of eyes with **surviving** grafts had functional vision of 6/12 or better. Only 10% of eyes had vision of CF or worse by 6-months post-graft. Similar patterns could be seen for **surviving** grafts followed for up to 7-years post-graft.

**Figure 6.9.2 Best corrected visual acuity for traditional lamellar keratoplasties, surviving at time of measurement**



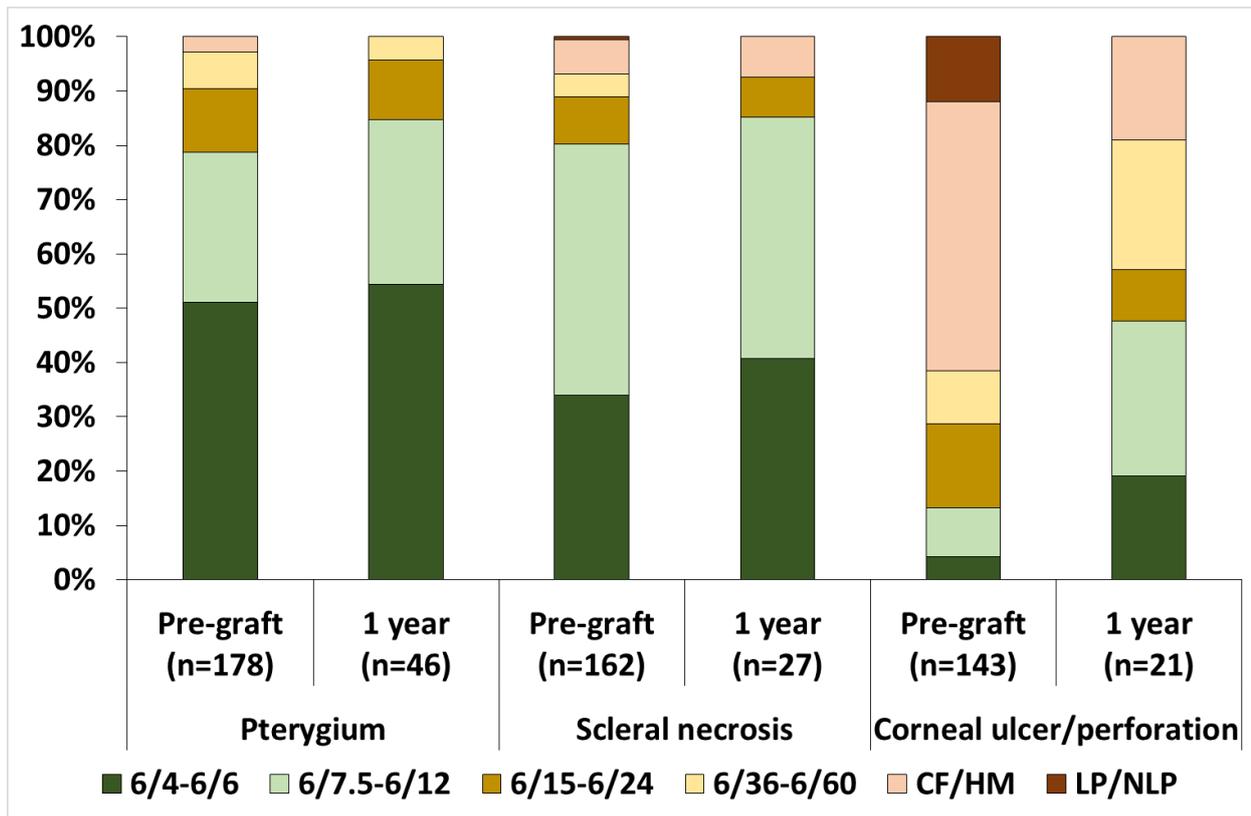
CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

### 6.9.2 Individual indications for graft

There were insufficient data to examine changes in best corrected visual acuity for the majority of indications for graft. Levels of visual acuity reported to the ACGR, pre-graft and at 1-year post-graft for **surviving** grafts performed for pterygium, scleral necrosis or corneal ulcers are shown in Figure 6.9.3.

There were very minimal changes in the visual acuity for grafts performed for pterygium or scleral necrosis, both of which had approximately 80% of grafts with visual acuity of 6/12 or better pre-graft, and rarely listed improvement in visual acuity as a reason for graft (14%). Just under half (48%) of the **surviving** grafts performed for corneal ulcers and/or perforations had achieved 6/12 vision by 1-year post-graft, an increase from just 13% pre-graft. Interestingly, less than 10% of TLK performed for this reason had indicated a desired improvement in visual acuity as a reason for graft.

**Figure 6.9.3 Level of best corrected visual acuity reported at 1-year post-graft for surviving grafts**



CF=count fingers at 1 metre, HM=hand movements, LP=light perception, NLP=no light perception

## 7 Post-graft factors affecting visual acuity

Surgeons reported additional factors affecting visual acuity in the grafted eye. These are shown in Table 7.1. Percentages given are of the number of followed grafts.

**Table 7.1 Factors affecting visual acuity in the grafted eye at last follow-up**

	PK	DS(A)EK	DMEK	DALK	TLK
<b>Glaucoma*</b>	2359 (12%)	481 (15%)	42 (7%)	29 (3%)	49 (4%)
<b>Macular degeneration</b>	1805 (9%)	197 (6%)	16 (3%)	4 (<1%)	37 (3%)
<b>Opacity/scar</b>	1168 (6%)	183 (6%)	31 (5%)	61 (7%)	77 (7%)
<b>Anisometropia</b>	1284 (6%)	6 (<1%)	0 (0%)	5 (<1%)	14 (1%)
<b>Cystoid macular oedema</b>	1085 (5%)	71 (2%)	16 (3%)	6 (<1%)	11 (1%)
<b>Cataract</b>	829 (4%)	6 (<1%)	1 (<1%)	49 (5%)	62 (6%)
<b>Myopia</b>	640 (3%)	8 (<1%)	0 (0%)	18 (2%)	17 (2%)
<b>Amblyopia</b>	546 (3%)	27 (<1%)	6 (1%)	21 (2%)	39 (4%)
<b>Retinal detachment</b>	354 (2%)	41 (1%)	3 (<1%)	5 (<1%)	7 (<1%)
<b>Diabetic retinopathy</b>	113 (<1%)	26 (<1%)	0 (0%)	3 (<1%)	4 (<1%)

\* Surgeons were asked to indicate if patients had glaucoma. While often related, this was a separate question to whether they had experienced raised intraocular pressure post-graft, which could occur for other reasons.

In addition, major astigmatism (defined as 5 dioptres or more) was reported in 3,469 (17%) penetrating keratoplasties, 56 (2%) Descemet's stripping (automated) endothelial keratoplasties, 5 (<1%) Descemet's membrane endothelial keratoplasties, 111 (12%) deep anterior lamellar keratoplasties, and 54 (5%) traditional lamellar keratoplasties.

In grafts performed for keratoconus, 1,371 penetrating keratoplasties (22%) were reported to have major astigmatism at last follow-up, compared to 97 deep anterior lamellar keratoplasties (14%). This difference was statistically significant,  $\chi^2=22.14$   $p<0.001$ .

The specific amount of astigmatism, in dioptres, was provided for 2,323 penetrating keratoplasties (968 in grafts performed for keratoconus) and 89 deep anterior lamellar keratoplasties (78 in grafts performed for keratoconus). The severity of major astigmatism in eyes grafted for keratoconus did not differ between penetrating keratoplasties and deep anterior lamellar keratoplasties ( $p=0.574$ ).

Surgeons reported whether graft recipients used visual aids (glasses and/or contact lens) to attain the best corrected visual acuity at the time of last follow-up.

Table 7.2 shows the proportion of followed grafts for each graft type for which the recipient wore glasses and a contact lens. It also shows the proportions of followed recipients for each graft type who had an IOL in place. Note: this group does not include those known to have an IOL inserted at time of graft but for which no follow-up information has been received. Percentages given are of the number of followed grafts.

**Table 7.2 Post-graft visual correction**

	<b>PK</b>	<b>DS(A)EK</b>	<b>DMEK</b>	<b>DALK</b>	<b>TLK</b>
<b>IOL</b>	10622 (52%)	3146 (96%)	566 (94%)	148 (16%)	299 (27%)
<b>Glasses</b>	8429 (41%)	1407 (43%)	238 (40%)	297 (32%)	317 (29%)
<b>Contact lens</b>	1223 (6%)	18 (<1%)	8 (1%)	60 (7%)	22 (2%)

In some cases, recipients were reported to use both glasses and contact lenses, or to use these in conjunction with an existing IOL. Table 7.3 shows the combinations of visual aids used following the different types of graft.

**Table 7.3 Post-graft visual correction combinations**

	<b>PK</b>	<b>DS(A)EK</b>	<b>DMEK</b>	<b>DALK</b>	<b>TLK</b>
<b>None</b>	5088 (25%)	85 (3%)	24 (4%)	477 (52%)	579 (52%)
<b>IOL only</b>	5883 (29%)	1758 (54%)	332 (55%)	97 (11%)	201 (18%)
<b>Glasses &amp; IOL</b>	4505 (22%)	1372 (42%)	226 (38%)	45 (5%)	96 (9%)
<b>Glasses only</b>	3637 (18%)	30 (<1%)	10 (2%)	242 (26%)	216 (19%)
<b>Contact lens only</b>	764 (4%)	1 (<1%)	0 (0%)	47 (5%)	16 (1%)
<b>Glasses &amp; contact lens</b>	225 (1%)	1 (<1%)	0 (0%)	7 (<1%)	4 (<1%)
<b>Contact lens &amp; IOL</b>	172 (<1%)	12 (<1%)	6 (<1%)	3 (<1%)	1 (<1%)
<b>All three</b>	62 (<1%)	4 (<1%)	2 (<1%)	3 (<1%)	1 (<1%)

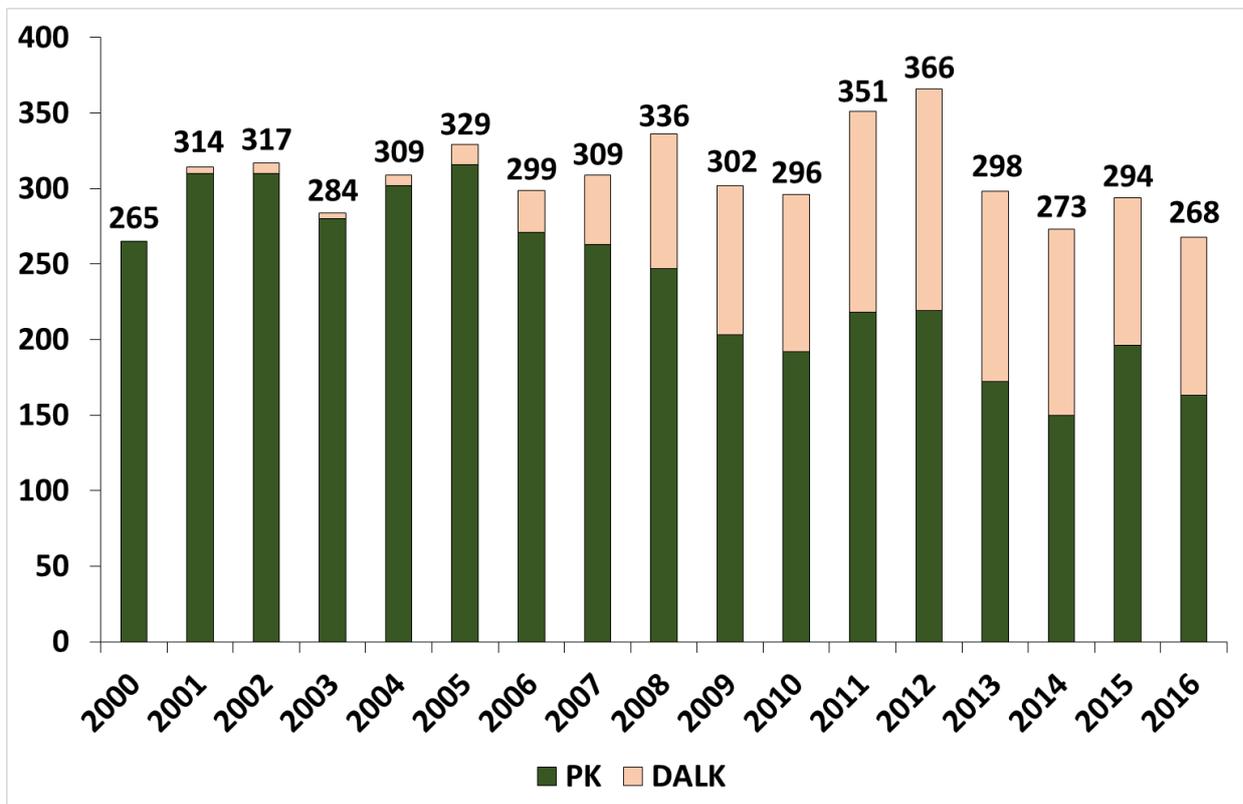
## 8 Comparisons Across Graft Types

This chapter presents the results of analyses which compare the outcomes of different types of grafts, performed for the same indications, across the same time period. Kaplan-Meier survival analyses were conducted using IBM SPSS for Windows (Version 22.0), to compare the graft survival across groups.

### 8.1 Keratoconus

Two types of graft are primarily performed for keratoconus: penetrating keratoplasty and deep anterior lamellar keratoplasty. The latter technique has increased in use for the treatment of keratoconus over recent years, as shown in Figure 8.1.1.

**Figure 8.1.1** Number of grafts performed each year, by type of graft performed, for keratoconus, 2000 to 2016

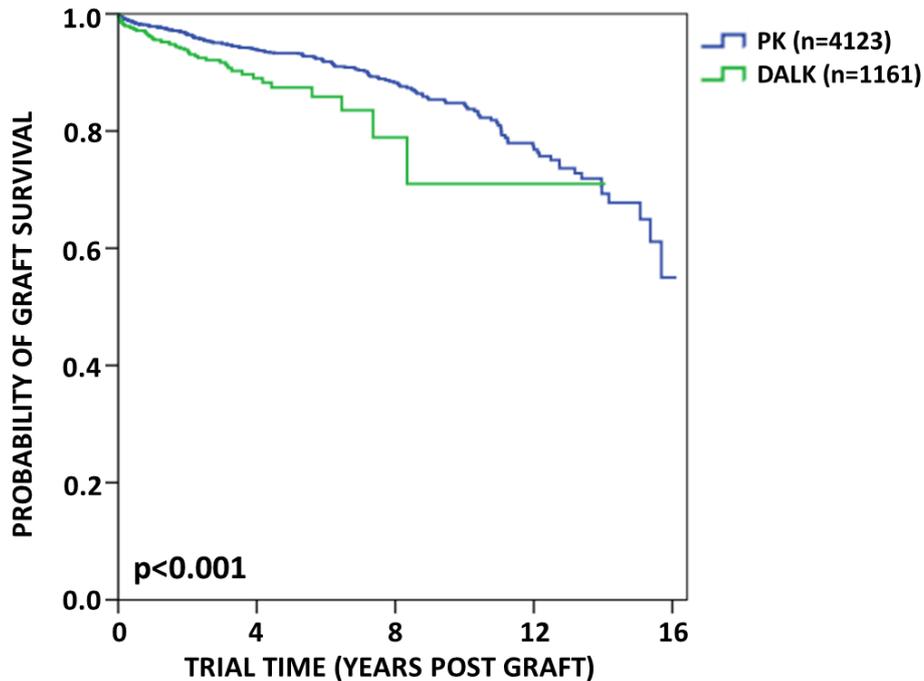


Note: the majority of grafts performed in 2017 had not been entered into the registry at the censor date and so these data are not shown. At 31<sup>st</sup> January 2018, 249 grafts for keratoconus, which had been performed in 2017, were registered with the ACGR. A further graft that had been performed for this indication in 2016, had also been registered.

### 8.1.1 Survival of grafts for keratoconus: influence of graft type

Figure 8.1.2 shows the comparison of survival between penetrating keratoplasties and deep anterior lamellar keratoplasties performed for keratoconus since the year 2000, up to the censor date.

Figure 8.1.2 Type of graft for keratoconus, 2000 onwards



#### Number at risk (years post-graft)

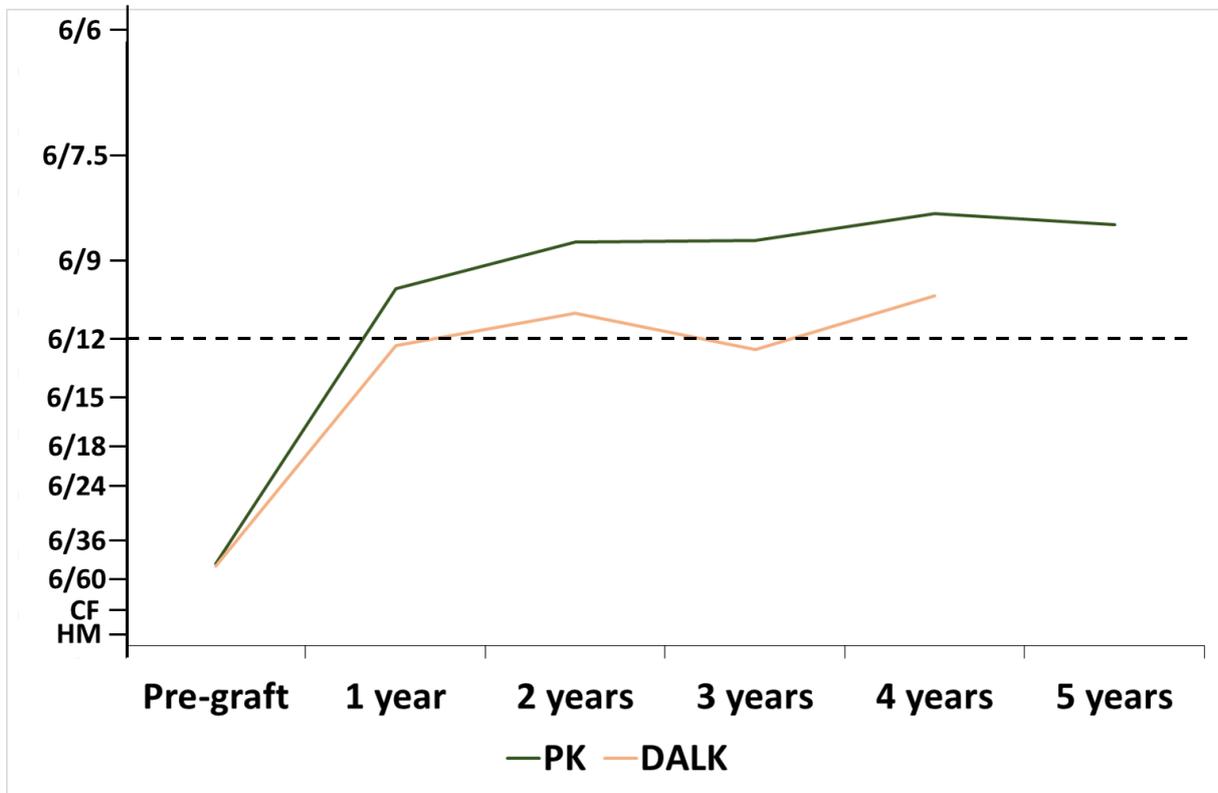
	1	2	4	6	8	10	12	14
PK	2815	2016	1126	691	405	349	141	49
DALK	586	360	123	46	11	5	2	1

#### Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12	14
PK	0.98	0.97	0.94	0.92	0.88	0.85	0.77	0.69
DALK	0.96	0.94	0.89	0.86	NA	NA	NA	NA

Figure 8.1.3 shows the mean visual acuity reported for grafts performed for keratoconus, since 2000, pre-graft and at various time-points post-graft. Pre-graft visual acuity is based on all registered grafts with this condition for which this information was provided. Post-graft visual acuity is for grafts that were **surviving** at these time points.

**Figure 8.1.3 Change in visual acuity in surviving grafts performed for keratoconus, since 2000, stratified by graft type, over time post-graft**



**Number of surviving grafts with visual acuity provided**

	Pre-graft	6-months	1 year	2 years	3 years	4 years
<b>PK</b>	3963	95	773	628	315	222
<b>DALK</b>	1112	31	203	122	50	26

There was no significant difference ( $p=0.376$ ) in the pre-graft visual acuity reported for eyes undergoing penetrating keratoplasty for keratoconus compared to those undergoing deep anterior lamellar keratoplasty since the year 2000.

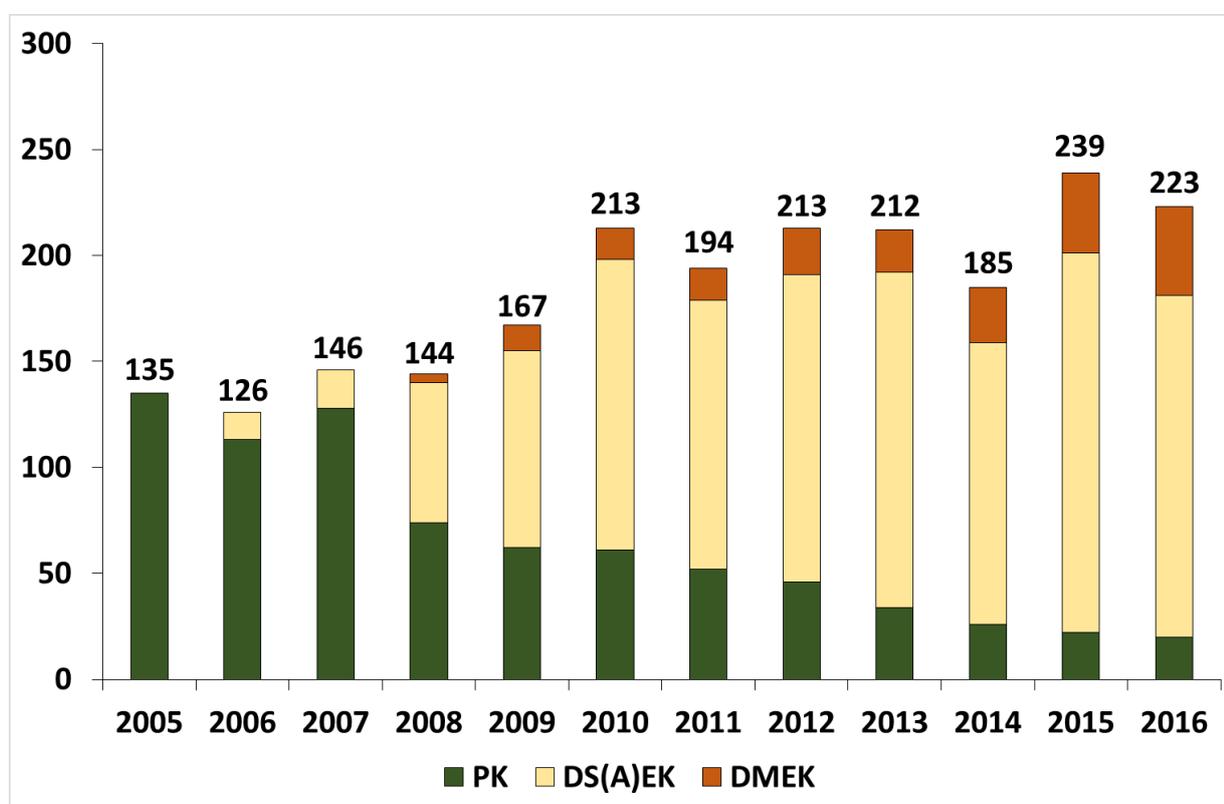
Visual acuity in **surviving** grafts was significantly improved ( $p<0.001$ ) at 1-year post-graft, and this difference remained significant up to 4-years post-graft ( $p<0.001$ ), for both penetrating keratoplasty and deep anterior lamellar keratoplasty. At 1-year post-graft the mean visual acuity reported for **surviving** penetrating keratoplasties had reached the 6/12 level. It increased to 6/9 by 2-years post-graft and remained above it up to 10-years post-graft. The average post-graft visual acuity also reached 6/12 level for **surviving** DALK at 1-year post-graft. It remained at this level until 4-years post-graft.

The difference in post-graft visual acuity in **surviving** PK versus DALK grafts was not significantly different at 6-months post-graft ( $p=0.305$ ), however it became significant at 12-months post-graft and remained so at 2 and 3-years post-graft (all  $p<0.001$ ). At 4-years post-graft, the difference was again non-significant ( $p=0.060$ ).

## 8.2 Pseudophakic Bullous Keratopathy

Two types of graft are primarily performed for pseudophakic bullous keratopathy, these being penetrating keratoplasty and Descemet's stripping (automated) endothelial keratoplasty. Descemet's membrane endothelial keratoplasties have also been performed for this indication, in smaller numbers. The DS(A)EK technique was introduced in Australia in 2006 and its use in treating pseudophakic bullous keratopathy has continuously increased since then, so that it is now the more common technique used to treat this condition. This has accompanied an increase in recent years, in the total number of transplants being performed for pseudophakic bullous keratopathy, as shown in Figure 8.2.1.

**Figure 8.2.1** Number of grafts performed each year, by type of graft performed, for pseudophakic bullous keratopathy, 2005 to 2016

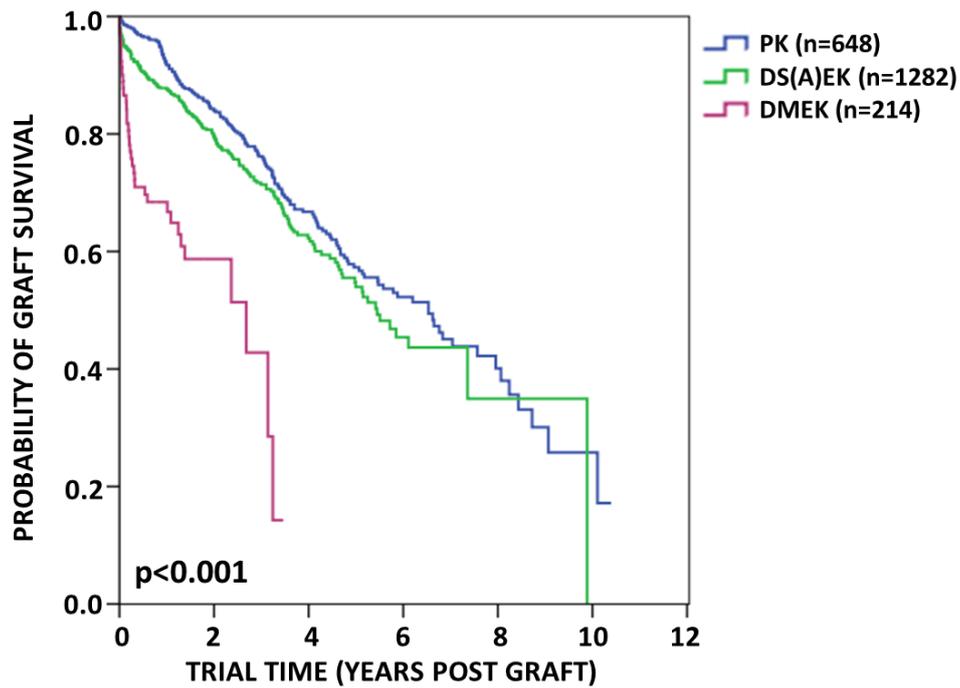


Note: the majority of grafts performed in 2017 had not been entered into the registry at the censor date and so these data are not shown. At 31<sup>st</sup> January 2018, 238 grafts for pseudophakic bullous keratopathy, which had been performed in 2017, were registered with the ACGR. A further seven grafts that had been performed for this indication in 2016 had also been registered, as had a further two grafts from 2006 and one from each of 2007 and 2009.

### 8.2.1 Survival of grafts for pseudophakic bullous keratopathy: influence of graft type

Figure 8.2.2 shows the comparison of survival between penetrating keratoplasties, Descemet’s membrane endothelial keratoplasties, and Descemet’s stripping (automated) endothelial keratoplasties, performed for pseudophakic bullous keratopathy since the introduction of the latter technique in 2006 up to the censor date. A significant difference was found between the three groups (Log Rank Statistic=54.83; df=2; p<0.001). PKs had significantly better survival than DS(A)EK (p=0.032) and DMEK (p<0.001), and DS(A)EK also had superior survival to DMEK (p<0.001).

**Figure 8.2.2 Type of graft for pseudophakic bullous keratopathy, 2006 onwards**



**Number at risk (years post-graft)**

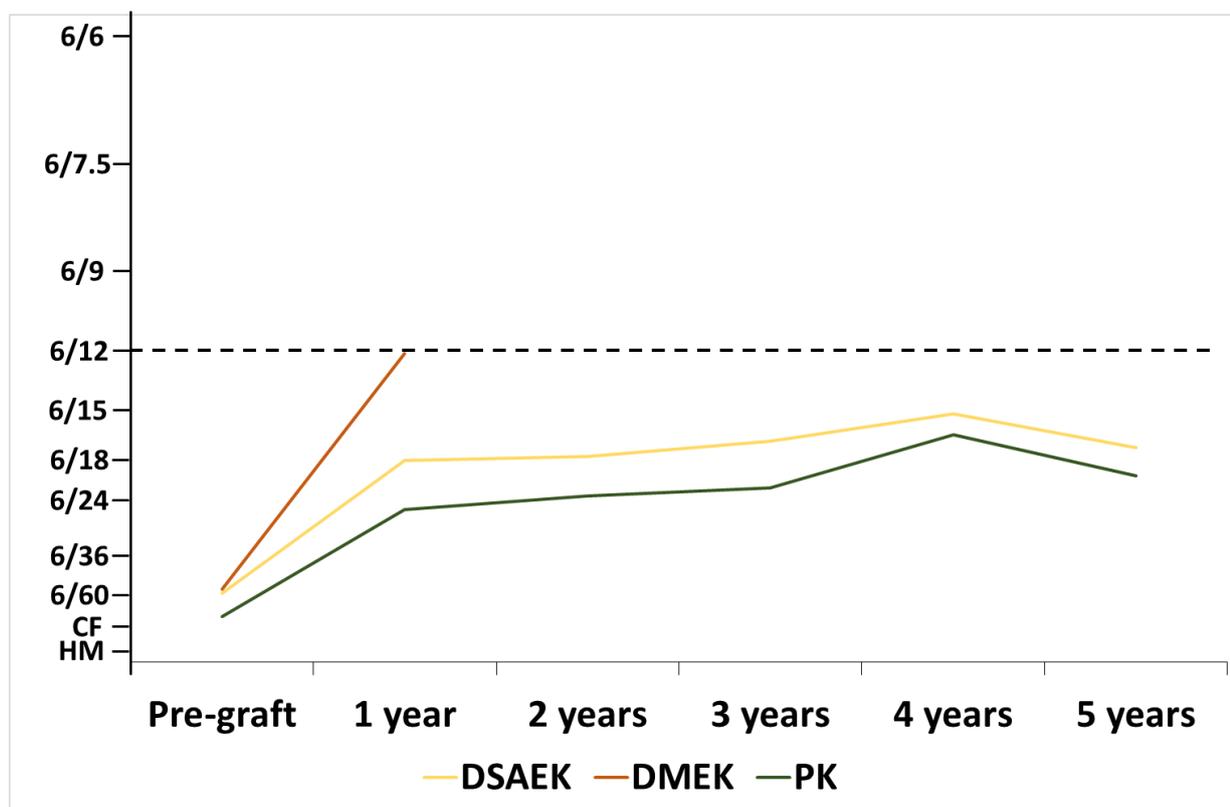
	1	2	4	6	8	10
<b>PK</b>	402	301	154	68	19	4
<b>DS(A)EK</b>	584	371	118	29	2	NA
<b>DMEK</b>	41	12	NA	NA	NA	NA

**Probability of graft survival (years post-graft)**

	1	2	4	6
<b>PK</b>	0.92	0.84	0.67	0.52
<b>DS(A)EK</b>	0.88	0.79	0.62	0.45
<b>DMEK</b>	0.68	NA	NA	NA

Figure 8.2.3 shows the mean visual acuity reported for grafts performed for pseudophakic bullous keratopathy, since 2006, pre-graft and at various time-points post-graft. Pre-graft visual acuity is based on all registered grafts with this condition for which this information was provided. Post-graft visual acuity is for grafts that were **surviving** at these time points.

**Figure 8.2.3 Change in visual acuity in surviving grafts performed for pseudophakic bullous keratopathy since 2006, stratified by graft type, over time post-graft**



#### Number of surviving grafts with visual acuity provided

	Pre-graft	1 year	2 years	3 years	4 years	5 years
PK	620	86	89	44	33	24
DS(A)EK	1208	167	115	57	27	24
DMEK	200	20	4	1	0	0

The pre-graft visual acuity reported for eyes undergoing penetrating keratoplasty for pseudophakic bullous keratopathy since the year 2006 was significantly worse than for those undergoing Descemet's stripping (automated) endothelial keratoplasty or Descemet's membrane endothelial keratoplasty (both  $p < 0.001$ ).

Visual acuity in **surviving** grafts was significantly improved ( $p < 0.001$ ) at 1-year post-graft, for all three types of graft, reaching 6/24 for PK, 6/18 for DS(A)EK and 6/12 for DMEK. This difference remained significant up to 4-years post-graft ( $p < 0.001$ ), for both PK and DS(A)EK. There were insufficient numbers of grafts with both pre- and post-graft vision after these points to make comparisons. The average post-graft visual acuity remained under 6/15 for **surviving** PK and reached it at 4-years post-graft for **surviving** DS(A)EK, before dropping back under at 5-years post-graft.

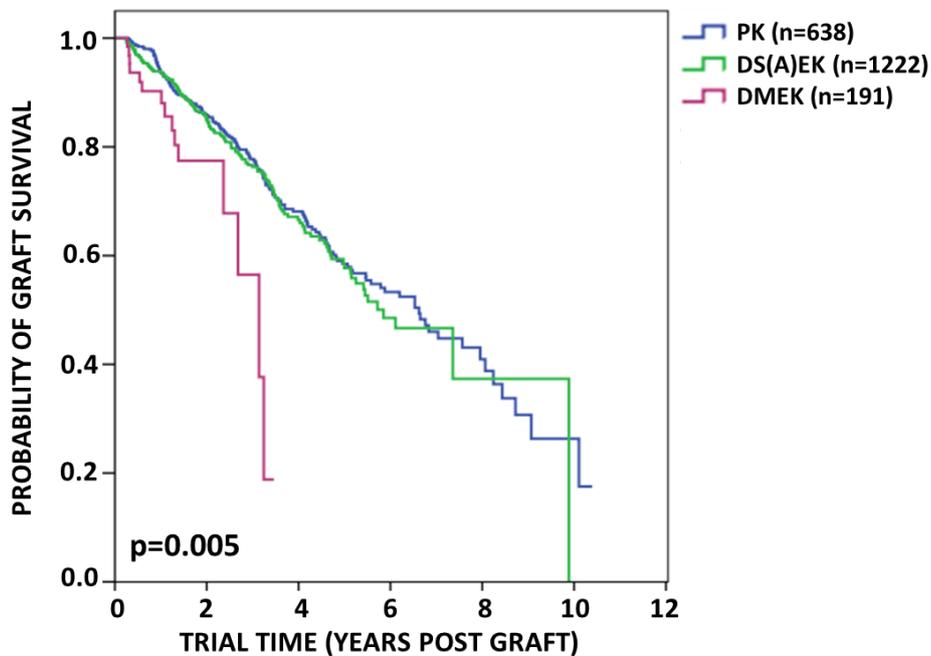
#### Comparisons Across Graft Types

**8.2.1.1 Survival of grafts for pseudophakic bullous keratopathy: influence of graft type and early failures**

A greater proportion of Descemet’s stripping (automated) endothelial keratoplasties, and Descemet’s membrane endothelial keratoplasties performed for pseudophakic bullous keratopathy than penetrating keratoplasties for the same indication, failed within three months (90 days) of graft (60/1282=4.7% and 23/214=10.7% vs. 10/648=1.5%).

Figure 8.2.4 shows the comparison of survival between penetrating keratoplasties, Descemet’s membrane endothelial keratoplasties, and Descemet’s stripping (automated) endothelial keratoplasties performed for pseudophakic bullous keratopathy since the introduction of the latter technique in 2006, excluding these early failures. A significant difference was still found between the three groups (Log Rank Statistic=10.63; df=2; p=0.005), however the difference between PK and DS(A)EK was no longer significant (Log Rank Statistic=0.33; df=1; p=0.565).

**Figure 8.2.4 Type of graft for pseudophakic bullous keratopathy, 2006 onwards, excluding early failures**



**Number at risk (years post-graft)**

	1	2	4	6	8	10
<b>PK</b>	402	301	154	68	19	4
<b>DS(A)EK</b>	584	371	118	29	2	NA
<b>DMEK</b>	41	12	NA	NA	NA	NA

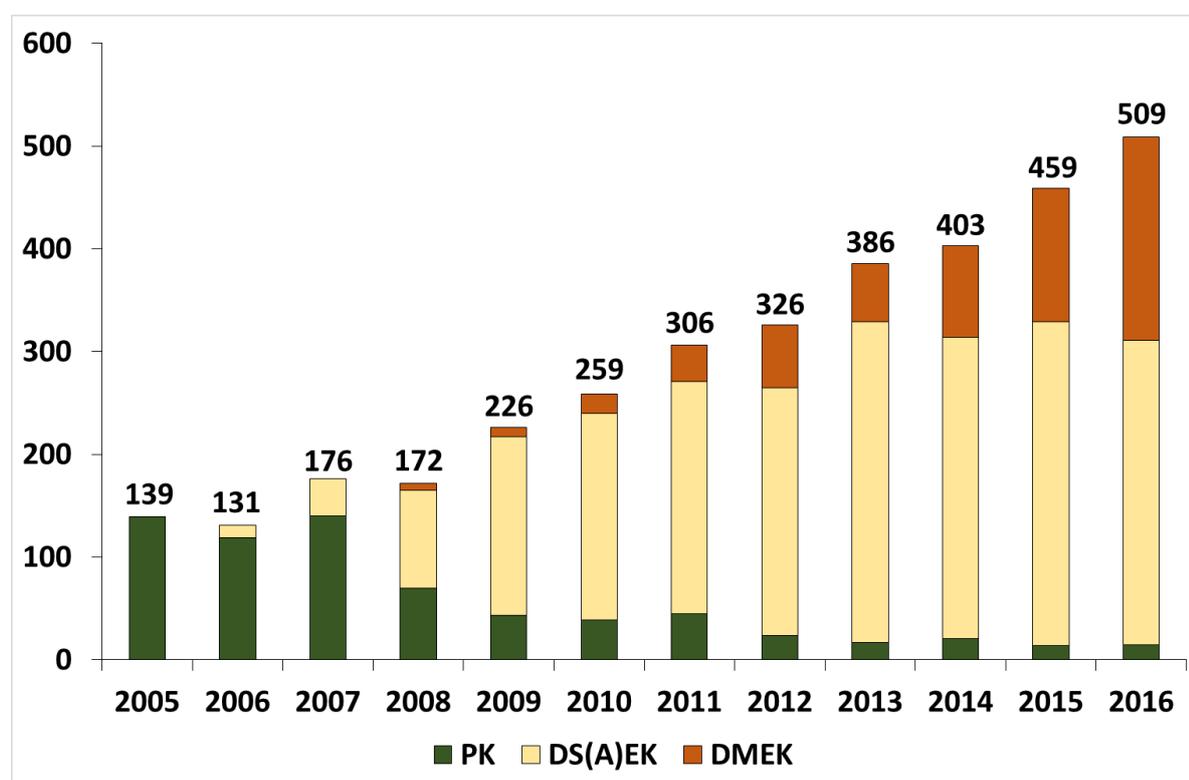
**Probability of graft survival (years post-graft)**

	1	2	4	6
<b>PK</b>	0.94	0.86	0.68	0.53
<b>DS(A)EK</b>	0.94	0.85	0.67	0.49
<b>DMEK</b>	0.90	NA	NA	NA

## 8.3 Fuchs' Endothelial Dystrophy

Two types of graft are primarily performed for Fuchs' endothelial dystrophy, these being Descemet's stripping (automated) endothelial keratoplasty and Descemet's membrane endothelial keratoplasties. Penetrating keratoplasty is now rarely performed for this indication. The DS(A)EK technique was introduced in Australia in 2006 and its use in treating Fuchs' endothelial dystrophy has increased since then, so that it is now the more common technique used to treat this condition. The use of DMEK has also continually increased over the past five years. This has accompanied a corresponding large increase in recent years (of approximately three times the overall numbers reported when the new techniques were first introduced), in the total number of transplants being performed for Fuchs' endothelial dystrophy. This continues on an upward trajectory to 2016, as shown in Figure 8.3.1.

**Figure 8.3.1 Number of grafts performed each year, by type of graft performed, for Fuchs' endothelial dystrophy, 2005 to 2016**

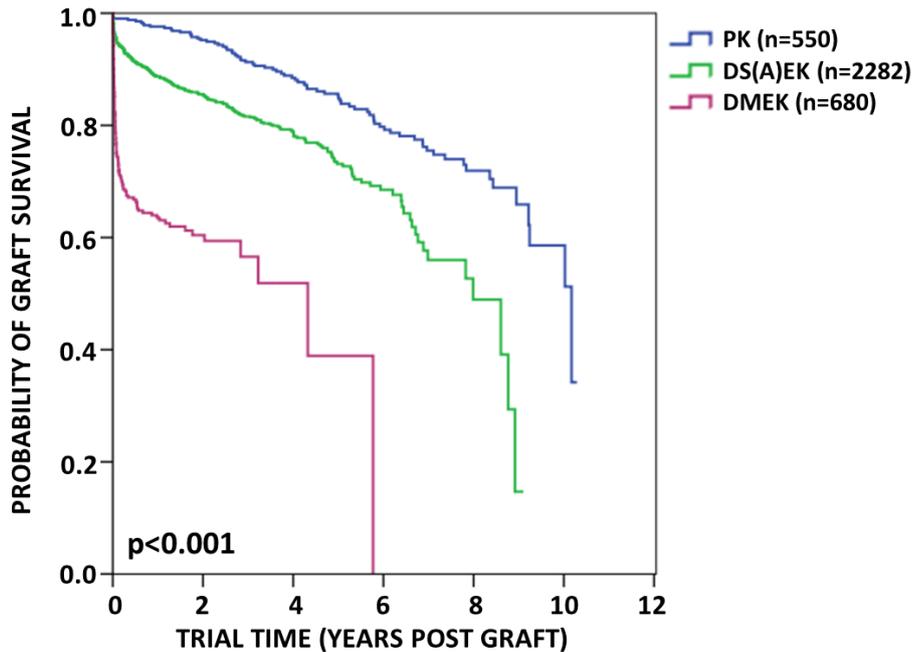


Note: the majority of grafts performed in 2017 had not been entered into the registry at the censor date and so these data are not shown. At 31<sup>st</sup> January 2018, 525 grafts for Fuchs' endothelial dystrophy, which had been performed in 2017, were registered with the ACGR. A single further graft that had been performed for this indication, had also been registered in each of 2006, 2008, 2009, 2010, and 2013.

### 8.3.1 Survival of grafts for Fuchs' endothelial dystrophy: influence of graft type

Figure 8.3.2 shows the comparison of survival between penetrating keratoplasties, Descemet's stripping (automated) endothelial keratoplasties, and Descemet's membrane endothelial keratoplasties performed for Fuchs' endothelial dystrophy since 2006 up to the censor date. A significant difference was found between the three groups (Log Rank Statistic=219.18; df=2; p<0.001). PKs had significantly better survival than DS(A)EK and DMEK (both p<0.001), and DS(A)EK also had superior survival to DMEK (p<0.001).

Figure 8.3.2 Type of graft for Fuchs' endothelial dystrophy, 2006 onwards



#### Number at risk (years post-graft)

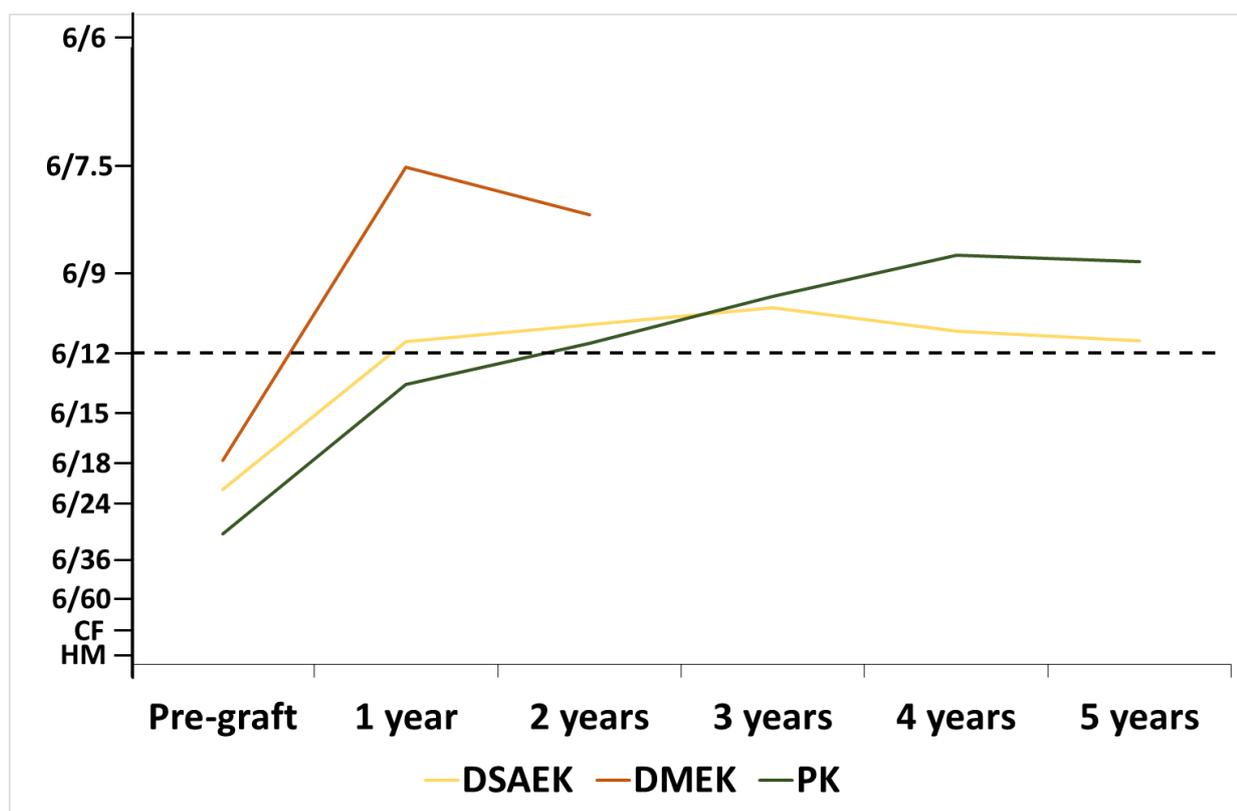
	1	2	4	6	8	10
PK	403	338	231	148	65	8
DS(A)EK	1179	839	314	93	12	NA
DMEK	144	65	4	NA	NA	NA

#### Probability of graft survival (years post-graft)

	1	2	4	6	8
PK	0.98	0.95	0.89	0.80	0.72
DS(A)EK	0.89	0.85	0.79	0.69	NA
DMEK	0.64	0.60	NA	NA	NA

Figure 8.3.3 shows the mean visual acuity reported for grafts performed for Fuchs' endothelial dystrophy, since 2006, pre-graft and at various time-points post-graft. Pre-graft visual acuity is based on all registered grafts with this condition for which this information was provided. Post-graft visual acuity is for grafts that were **surviving** at these time points.

**Figure 8.3.3 Change in visual acuity in surviving grafts performed for Fuchs' endothelial dystrophy, since 2006, stratified by graft type, over time post-graft**



#### Number of surviving grafts with visual acuity provided

	Pre-graft	1 year	2 years	3 years	4 years	5 years
PK	530	78	89	49	47	38
DS(A)EK	2193	355	242	160	78	66
DMEK	658	69	28	6	1	0

The pre-graft visual acuity reported for eyes undergoing penetrating keratoplasty for Fuchs' endothelial dystrophy since the year 2006 was significantly worse than for those undergoing Descemet's stripping (automated) endothelial keratoplasty or Descemet's membrane endothelial keratoplasty (both  $p < 0.001$ ). The pre-graft visual acuity reported for eyes undergoing DMEK was also significantly better than those undergoing DS(A)EK ( $p < 0.001$ ).

Visual acuity in **surviving** grafts was significantly improved ( $p < 0.001$ ) at 1-year post-graft, for all three types of graft. This difference remained significant up to 2-years post-graft for DMEK and up to 4-years post-graft for both PK and DS(A)EK (all  $p < 0.001$ ). There were insufficient numbers of grafts with both pre- and post-graft vision after these points to make comparisons. The average post-graft visual acuity in **surviving** grafts reached 6/12 for all three groups - by 1-year post-graft for DMEK and DS(A)EK, and 2-years post-graft for PK.

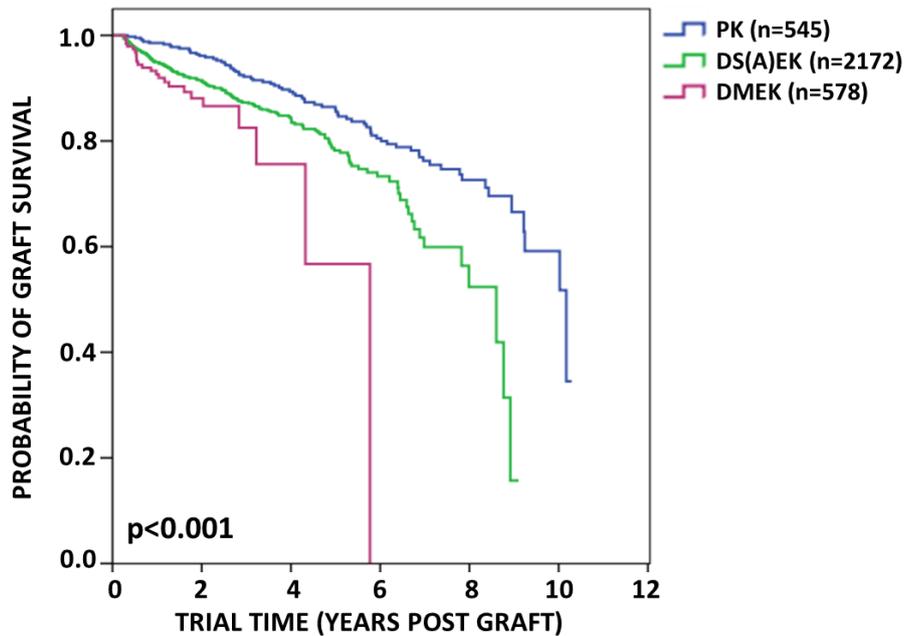
#### Comparisons Across Graft Types

**8.3.1.1 Survival of grafts for Fuchs' endothelial dystrophy: influence of graft type and early failures**

A greater proportion of Descemet's stripping (automated) endothelial keratoplasties, and Descemet's membrane endothelial keratoplasties performed for Fuchs' endothelial dystrophy than penetrating keratoplasties for the same indication, failed within three months (90 days) of graft (110/2282=4.8% and 102/680=15.0% vs. 5/550=0.9%).

Figure 8.3.3 shows the comparison of survival between penetrating keratoplasties, Descemet's membrane endothelial keratoplasties, and Descemet's stripping (automated) endothelial keratoplasties performed for Fuchs' endothelial dystrophy since the introduction of the latter technique in 2006, excluding these early failures. A significant difference was still found between the three groups (Log Rank Statistic=23.65; df=2; p<0.001). PKs still had significantly better survival than DS(A)EK and DMEK (both p<0.001), while the difference in survival between DS(A)EK and DMEK was no longer significant (p=0.039), once Bonferroni correction was applied.

**Figure 8.3.4 Type of graft for Fuchs' endothelial dystrophy, 2006 onwards, excluding early failures**



**Number at risk (years post-graft)**

	1	2	4	6	8	10
<b>PK</b>	403	338	231	148	65	8
<b>DS(A)EK</b>	1179	839	314	93	12	NA
<b>DMEK</b>	144	65	4	NA	NA	NA

**Probability of graft survival (years post-graft)**

	1	2	4	6	8
<b>PK</b>	0.99	0.96	0.89	0.81	0.73
<b>DS(A)EK</b>	0.95	0.91	0.84	0.73	NA
<b>DMEK</b>	0.93	0.88	NA	NA	NA

## 9 Summary

Up to 31<sup>st</sup> July 2017, 33,920 grafts were registered with the Australian Corneal Graft Registry. 26,297 (78%) of these had follow-up received by the census date. The introduction of partial-thickness lamellar keratoplasty techniques have resulted in a shift away from full-thickness penetrating keratoplasties.

### 9.1 Donor and Eye Banking Factors

No donor or eye banking factors were found to be significant independent risk factors for failure of deep anterior lamellar keratoplasty (DALK) or traditional lamellar keratoplasty (TLK).

Donor age group was retained in multivariate analysis relating to penetrating keratoplasty, Descemet's stripping (automated) endothelial keratoplasty (DS(A)EK) and Descemet's membrane endothelial keratoplasty (DMEK), with grafts performed using tissue from younger donors exhibiting better survival for PK and DS(A)EK, but poorer survival for DMEK.

For DS(A)EK, pre-graft central endothelial cell density was a significant independent risk factor with grafts performed using donor tissue with <2500 cells/mm<sup>2</sup> exhibiting poorer survival. Endothelial cell density was excluded from the multivariate model for PK due to a high proportion of missing data, but grafts with <2500 cells/mm<sup>2</sup> also exhibited poorer survival in the univariate analysis.

### 9.2 Recipient Factors

Indication for graft was found to be a significant independent risk factor for failure of PK, DS(A)EK, and TLK. There was a large amount of variation in survival across indications for PK. Superior survival was observed for grafts performed for keratoconus, while the poorest survival was observed for grafts performed for corneal ulcer. Grafts performed for Fuchs' endothelial dystrophy had the best survival for DS(A)EK. For TLK, grafts for pterygium, trauma and scleral necrosis had superior survival, while those for herpetic eye disease fared most poorly. Recipient age group was found to be a significant independent factor for DMEK and DALK survival. Grafts performed in recipients under 50 years of age had poor survival for DMEK. For DALK, grafts performed in recipients aged under 60 had superior survival to those performed in recipients aged 60 and over.

Interstate transportation of corneas for PK was shown to result in a higher risk of failure, while for DS(A)EK and DMEK the Australian State where the graft had been registered was a significant independent risk factor. For DS(A)EK, male recipients had poorer survival than female recipients, while for PK the donor and recipient sexes in combination were a significant risk factor, with female to female grafts exhibiting superior survival to donor lenticules from either sex grafted into male recipients. The presence of a single prior corneal graft in the contralateral eye was an independent significant factor associated with superior survival in PK.

The change in lens status from pre- to post-graft was a significant independent risk factor for both PK and DS(A)EK. In both cohorts, poorest survival occurred in eyes that were aphakic before and/or after the graft, or eyes that were pseudophakic both before and after graft. Pre-graft inflammation or steroid use was a significant independent risk factor for failure of PK, DALK and TLK. A history of raised intraocular pressure prior to, or at the time of, graft was a significant independent risk factor for failure of PK and DS(A)EK. Pre-graft corneal neovascularisation was a significant independent risk factor for failure of PK, DALK, and TLK, with grafts performed in eyes with greater than one quadrant of neovascularisation having poorer survival. For DMEK, a pre-cut donor lenticule was an independent significant factor associated with superior survival.

### 9.3 Graft Era

Graft era, stratified into 5-year groups, was a significant independent risk factor for survival of PK and DALK, with improved outcomes in more recent eras for PK. PK and DALK performed from 2015 to 2017 had poorer survival than those performed in any other era from 2000 onwards. Graft era, stratified into 2-year groups, was a significant independent risk factor for survival of DS(A)EK and DMEK. For both cohorts, grafts performed in 2016/2017 had poorer survival than earlier eras. The single exception for this was DS(A)EK performed prior to 2008, which also had poorer survival than all grafts performed in subsequent eras.

The effect of lag time on these analyses is acknowledged, the effect being most pronounced in the early years following graft registration. This is most likely to affect the data relating to grafts from the most recent cohorts, which have not yet had follow-up requested.

### 9.4 Surgery and Surgeon Factors

Graft size was a significant independent risk factor for PK, with grafts outside of the range of 7.75 mm to 8.75 mm, exhibiting significantly poorer survival. An optimal graft size window was also found for TLK with those between 6.1 mm and 8.0 mm having better survival than those that were either smaller or larger. For DS(A)EK, both graft size and incision size were found to be significant independent factors in graft survival, with grafts 8.25 mm or larger faring better, but those with an incision size of 5.0 mm or greater exhibiting poorer survival.

Surgeon experience and level of follow-up was shown to be a significant independent risk factor in the survival of PK and DS(A)EK. For both types of graft, surgeons with lower volumes of registered grafts, and those with high volumes of registered grafts but below average levels of follow-up, exhibited poorer survival. The Centre effect was a significant independent factor for DALK and TLK.

## 9.5 Post-graft Events

Significantly poorer graft survival was found in multivariate analyses for PK and DS(A)EK that had undergone at least one episode of post-graft rejection. Post-graft rejection occurred most frequently following penetrating keratoplasty and very few lamellar grafts underwent more than one post-graft rejection episode (see Table 9.1).

**Table 9.1 Number of post-graft rejection episodes stratified by graft type**

	None	One	Two	Three or more
<b>PK</b>	20717 (83%)	2991 (12%)	692 (3%)	427 (2%)
<b>DS(A)EK</b>	4473 (94%)	236 (5%)	20 (<1%)	7 (<1%)
<b>DMEK</b>	1228 (98%)	21 (2%)	1 (<1%)	0 (0%)
<b>DALK</b>	1476 (96%)	45 (3%)	8 (<1%)	2 (<1%)
<b>TLK</b>	1462 (98%)	29 (2%)	3 (<1%)	1 (<1%)

Higher risk of graft failure was also found for PK, DS(A)EK and DALK that had post-graft corneal neovascularisation. Lower risk was associated with raised intraocular pressure post-graft for both PK and DS(A)EK. Presence of post-graft microbial keratitis, and post-graft herpetic infection, were both significant independent factors affecting graft survival for PK.

## 9.6 Comparisons Across Graft Types

Primary graft failure was reported most often following DMEK and DS(A)EK (13% and 5% of registered grafts, respectively), and least often following PK, DALK and TLK (all <1% of registered grafts).

PK performed for keratoconus since 2000, exhibited significantly better survival than DALK performed for the same reason over the same period. There were no significant differences in the pre-graft best corrected visual acuity (BCVA) recorded for PK and DALK, however there were significant differences in post-graft BCVA over time. Average post-graft BCVA was greatly improved and reached 6/12 for both groups.

PK performed for pseudophakic bullous keratopathy (PBK) since 2006, exhibited significantly better survival than both DS(A)EK and DMEK performed for the same reason over the same period, and DS(A)EK exhibited significantly better survival than DMEK. Poorer survival was still observed for DMEK following removal of early failures from the analysis. Eyes undergoing PK for PBK had significantly worse pre-graft BCVA than those undergoing DS(A)EK or DMEK. Post-graft BCVA in surviving grafts improved for all graft types.

PK performed for Fuchs' endothelial dystrophy (FED) since 2006, exhibited significantly better survival than both DS(A)EK and DMEK performed for the same reason over the same period, and DS(A)EK exhibited significantly better survival than DMEK. Superior survival of PK was still observed following removal of early failures from the analysis. Eyes undergoing PK for FED had significantly worse pre-graft BCVA than those undergoing DS(A)EK, which had significantly worse BCVA than those undergoing DMEK. Post-graft BCVA improved and reached 6/12 for surviving grafts of all types.

Summary

## 10 Methods and Definitions

### 10.1 Registration and Follow-up

Grafts are registered by contributing surgeons as soon as possible after the graft. Follow-up information is requested by the ACGR at intervals of about 12 months. Follow-up is initially sought from the operating surgeon. Thereafter, it may be sought from either the operating surgeon or an alternative follow-up practitioner (ophthalmologist or optometrist), as advised by the operating surgeon. Information is provided by mail, with missing data routinely sought via follow-up letter or via phone.

Each graft is followed until graft failure or until the death or loss to follow-up of the patient. Data-linkage with the National Death Index is performed on a five-yearly basis, the most recent linkage being completed in 2014. The study period for the analyses in this report was May 1985 to July 2017 (32 years), except where otherwise stated.

### 10.2 Definition of Variables

All information regarding diagnoses, ocular history and treatment are provided to the Registry by the operating surgeons. Information on donor factors is provided by eye banks. Multiple processes are in place to cross-check data consistency.

A history of past inflammation is recorded if the individual is specifically reported to have had such an episode or if there is a history of the use of topical corticosteroids in that eye in the weeks immediately preceding the graft.

Vessel ingrowth into the cornea at the time of graft is scored on a scale of 0-4, with 0 representing no growth in any quadrant, 1 representing growth in 1 quadrant, 2 representing growth in 2 quadrants, 3 being vessel ingrowth in 3 quadrants and 4 being vessel ingrowth in 4 quadrants. No distinction is made between superficial or deep vessels, patent or ghost vessels, or single or multiple vessel leashes. After corneal transplantation, the presence of even one vessel leash extending into the graft is considered enough to classify that graft as vascularized.

The intraocular pressure (IOP) is generally considered to be raised if a reading of 25 mm of mercury or greater is made by applanation tonometry, but the decision is at the discretion of the ophthalmologist.

Original pathology, current indications for graft, post-operative complications and reasons for graft failure are provided by individual surgeons and are coded by Registry staff using the ICD.9.CM system (US Department of Health and Human Services). Original pathologies for repeat grafts are cross-checked with previous information provided to the Registry.

Information is collected on recipient bed size, incision size and donor button size, as relevant. For the purpose of examining the influence of graft size, the latter is used.

## 10.3 Graft Failure, Rejection and Complications

Primary graft non-functions are defined as grafts that never thin and clear in the post-operative period. For penetrating grafts, the time from graft to failure is as reported by the surgeon. It is usually 1-2 days but no more than 7 days. For lamellar procedures, primary graft failure can occur after a longer period of time and is analysed as reported by surgeons. Additional information is collected to ascertain whether this occurred within 28 days of the graft. Where surgeons indicate that the failure was due to surgical complications, this is also recorded.

Any existing graft that is replaced by another in the same eye, irrespective of graft clarity and for whatever reason, is classified as a failed graft. An example in this category would be a clear graft with an unacceptably high degree of irregular astigmatism, not improved by refractive surgery, which is then replaced. In all other cases, graft failure is defined as oedema and irremediable loss of clarity in a previously thin, clear graft. The day of failure is the first day the patient is seen with an oedematous, opaque graft that subsequently fails to thin and clear.

In some cases, partial-thickness grafts are performed in eyes that have undergone previous full-thickness grafts. The original penetrating grafts are still considered to have failed in these cases and are recorded as such. In a very small number of cases, recipients have multiple concurrent grafts in the same eye (e.g. a deep anterior lamellar graft and a Descemet's stripping (automated) endothelial keratoplasty). In these cases, both grafts are considered to be surviving, regardless of the order they were performed.

Rejection is defined as the development of a rejection line (epithelial or endothelial) or a unilateral anterior chamber reaction with corneal infiltrates and spreading corneal oedema in a previously thin, clear graft.

Any development with the potential to compromise graft outcome is considered to be a complication. Post-operative complications are collected in two ways. First, a number of specified complications (stitch abscess, microbial keratitis, neovascularization of the graft, synechiae, uveitis, rise in IOP, cataract, rejection episode, herpetic recurrence, early changes of bullous keratopathy), refractive and related errors (anisometropia,  $\geq 5$  dioptres astigmatism) and factors potentially affecting visual outcome but unrelated to the graft (cataract, amblyopia, retinal detachment, age related macular degeneration and diabetic retinopathy) are listed, requiring a yes/no answer. Second, contributors are asked to specify any other relevant complications, information or departures from their preferred treatment.

For surviving grafts, trial time was calculated as the time between the date of graft and the date on which the patient was last seen. For failed grafts, trial time was calculated as the time between the date of graft and the date of failure, specified on a daily basis. Although data were collected centrally within the Registry at least once yearly, individual patient data were collected at source according to a frequency determined by the ophthalmic surgeon.

## 10.4 Statistical Analyses

The Australian Corneal Graft Registry database is constructed in Microsoft Access and was designed by Ms Sandra Bobleter. This has subsequently been modified by Mrs Helene Holland, Ms Ngaere Hornsby, Ms Carmel McCarthy, Mrs Chris Bartlett, Mrs Marie Lowe, Dr Rachel Galettis, Ms Louise Smith and Dr Miriam Keane.

For this report, data were extracted from the Access database, via an automated import process, into SPSS version 22 (SPSS Inc.). Individual databases were also created for each type of graft analysed. Univariate Kaplan–Meier survival analyses [see reference 3] were performed in IBM SPSS for Windows (Version 22.0) with significance set at  $p < 0.05$  [Mantel–Cox log-rank<sup>2</sup> statistic – see references 4 & 5]. Bonferroni correction was applied for multiple comparisons [see reference 6]. Corresponding survival curves were generated in SPSS, for use in the report. The SPSS database was also saved as a STATA data file and multivariate Cox-proportional hazards regression analyses were performed using STATA version 11 [see references 7 & 8]. The report was prepared using Microsoft Office 2010.

## 10.5 References

1. Gomes JAP, Tan D, Rapuano CJ, Belin MW, Ambrosio Jr. R, Guell JL, Malecaze F, Nishida K, Sangwan VS, et al. Global consensus on keratoconus and ectatic diseases. *Cornea* 2015; 34; 359-369.
2. Weiss JS, Møller HU, Aldave AJ, Seitz B, Bredrup C, Kivelä T, Munier FL, Rapuano CJ, Nischall KK, et al. IC3D classification of corneal dystrophies - edition 2. *Cornea* 2015; 34; 117-159.
3. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association* 1958; 53; 475-81.
4. Peto R, Pike MC, Armitage P, Breslow NE, Cox DR, Howard SV, Mantel N, McPherson K, Peto J, and Smith PG. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. I Introduction and design. *British Journal of Cancer* 1976; 34:585-612.
5. Peto R, Pike MC, Armitage P, Breslow NE, Cox DR, Howard SV, Mantel N, McPherson K, Peto J, and Smith PG. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. II Analysis and examples. *British Journal of Cancer* 1977; 35:1-39.
6. McDonald, JH; 2014. Handbook of Biological Statistics (3rd ed.). Sparky House Publishing, Baltimore, Maryland.
7. Cleves MA, Gould WW, Gutierrez RG, AND Marchenko YV; 2010. An introduction to Survival Analysis using Stata (Third edition). Stata Press, College Station, Texas.
8. Williams RL. A note on robust variance estimation for cluster-correlated data. *Biometrics* 2000; 56:645.

# Australian Corneal Graft Registry Publications

## Journal articles

1. Williams KA, Sawyer M, Alfrich SJ, Joseph L, White MA, Coster DJ, Mahmood M. First report of the Australian Corneal Graft Registry. *Aust NZ J Ophthalmol* 1987; 15: 291-302.
2. Williams KA, Roder D, Esterman A, Muehlberg SM, Coster DJ. Factors predictive of corneal graft survival: report from the Australian Corneal Graft Registry. *Ophthalmology* 1992; 99: 403-414.
3. Williams KA, Muehlberg SM, Wing SJ, Coster DJ. The Australian Corneal Graft Registry, 1990-1992 report. *Aust NZ J Ophthalmol* 1993; 21 (suppl): 1-48.
4. Williams KA, Muehlberg SM, Lewis RF and Coster DJ, on behalf of all contributors to the Australian Corneal Graft Registry (ACGR). How successful is corneal transplantation? A report from the Australian Corneal Graft Register. *Eye* 1995; 9: 219-227.
5. Williams KA, Muehlberg SM, Lewis RF and Coster DJ on behalf of all contributors to the Australian Corneal Graft Registry. Influence of advanced recipient and donor age on the outcome of corneal transplantation. *Br J Ophthalmol* 1997; 81: 835-839.
6. Williams KA, Esterman AJ, Bartlett C, Holland H, Hornsby NB, Coster DJ on behalf of all contributors to the Australian Corneal Graft Registry. How effective is penetrating corneal transplantation? Factors influencing long-term outcome in multivariate analysis. *Transplantation* 2006; 81: 896-901.
7. Williams KA, Lowe M, Bartlett C, Kelly T-L, Coster DJ on behalf of all contributors. Risk factors for human corneal graft failure within the Australian Corneal Graft Registry. *Transplantation* 2008; 86: 1720-1724.
8. Williams KA, Kelly TL, Lowe MT, Coster DJ, on behalf of all contributors to the Australian Corneal Graft Registry. The influence of rejection episodes in recipients of bilateral corneal grafts. *Am J Transplant* 2010; 10: 921-30.
9. Lowe MT, Keane MC, Coster DJ, Williams KA. The outcome of corneal transplantation in infants, children, and adolescents. *Ophthalmology* 2011; 118: 492-7.
10. Kelly T-L, Williams KA, Coster DJ. Corneal transplantation for keratoconus: a registry study. *Arch Ophthalmol* 2011; 129: 691-7. (Reviewed by Faculty of 1000)
11. Kelly T-L, Coster DJ, Williams KA. Repeat penetrating keratoplasty in patients with keratoconus. *Ophthalmology* 2011; 118: 1538-42.
12. Keane MC, Lowe MT, Coster DJ, Pollock GA, Williams KA. The influence of Australian eye banking practices on corneal graft survival. *Med J Aust* 2013; 199: 275-279.
13. Coster DJ, Lowe MT, Keane MC, Williams KA for the Australian Corneal Graft Registry Contributors. A comparison of lamellar and penetrating keratoplasty outcomes. A registry study. *Ophthalmology* 2014; 121: 979-87.
14. Keane MC, Galettis RA, Mills RA, Coster DJ, & Williams KA, for Contributors to the Australian Corneal Graft Registry. A comparison of endothelial and penetrating keratoplasty outcomes following failed penetrating keratoplasty: a registry study. *British Journal of Ophthalmology* 2016; 100: 1569-75.
15. Keane MC, Mills RA, Coster DJ, Williams KA, for Contributors to the Australian Corneal Graft Registry. Is there evidence for a surgeon learning curve for endothelial keratoplasty in Australia? *Clinical & Experimental Ophthalmology* 2017; 45: 575-83.

## Letters to the Editor

1. Williams KA, Coster DJ. In response to Dr Cavanagh. Repeat penetrating keratoplasty for keratoconus. *Ophthalmology* 2012; 119: 1088-1089.
2. Williams KA, Coster DJ. Reply to Letter to the Editor. *Ophthalmology* 2012; 119: 882.
3. Coster DJ, Keane MC, Williams, KA. Reply to correspondence from Dr Kosker. *Ophthalmology* 2014 Oct;121(10):e59-60. doi: 10.1016/j.ophtha.2014.05.035. Epub 2014 Jul 8.
4. Coster DJ, Keane MC, Williams, KA. Reply to correspondence from Dr Baydoun, Dr Liarakos, Dr Dapena and Dr Melles. *Ophthalmology* 2014 Nov;121(11):e62-3. doi: 10.1016/j.ophtha.2014.06.008. Epub 2014 Oct 24.
5. Coster DJ, Keane MC, Williams, KA. Reply to correspondence from Drs Somner, Hardman-Lea, Bourne, Burr and Shah. *Ophthalmology* 2015 Jan;122(1):e10-1. doi: 10.1016/j.ophtha.2014.06.039.
6. Coster DJ, Keane MC, Williams, KA. Reply to correspondence from Drs Basu and Hoshing. *Ophthalmology* 2015 Jan;122(1):e8-9. doi: 10.1016/j.ophtha.2014.07.004.

## Registry reports to contributors

1. Williams KA, Sawyer MA, Joseph L, Alfrich S, White M, Coster DJ, Mahmood M. First report of the Australian Graft Registry, 1986 pp 1-26.
2. Williams KA, Sawyer MA, White MA, Coster DJ. Report from the Australian Corneal Graft Registry, 1988. Flinders Press, Adelaide pp1-54.
3. Williams KA, Sawyer MA, White MA, Muehlberg SM, Mahmood M, Coster DJ. Report from the Australian Corneal Graft Registry, 1989. Flinders Press, Adelaide pp 1-60.
4. Williams KA, Muehlberg SM, Lewis RF, Coster DJ. Report from the Australian Corneal Graft Registry, 1994. Mercury Press, Adelaide pp 1-96.
5. Williams KA, Muehlberg SM, Lewis RF, Coster DJ. Report from the Australian Corneal Graft Registry, 1997. Mercury Press, Adelaide pp1-132.
6. Williams KA, Muehlberg SM, Bartlett CM, Esterman A, Coster DJ. Report from the Australian Corneal Graft Registry, 1999. Snap Printing, Adelaide pp1-137.
7. Williams KA, Hornsby NB, Bartlett CM, Holland HK, Esterman A, Coster DJ. The Australian Corneal Graft Registry 2004 Report. Snap Printing, Adelaide 2004: pp 1-192.
8. Williams KA, Lowe MT, Bartlett CM, Kelly L, Coster DJ, eds. The Australian Corneal Graft Registry Report 2007. Flinders University Press, Adelaide 2008: pp 1-194.
9. Williams KA, Lowe MT, Keane MC, Jones VJ, Loh RS, Coster DJ, eds. The Australian Corneal Graft Registry 2012 Report. Department of Ophthalmology, Adelaide: 2012 pp 1-246. URL: <http://hdl.handle.net/2328/25859>
10. Williams KA, Keane MC, Galettis RA, Jones VJ, Mills RAD, Coster DJ, eds. The Australian Corneal Graft Registry 2015 Report. Department of Ophthalmology, Adelaide: 2015 pp 1-247. URL: <http://hdl.handle.net/2328/35402>
11. Williams KA, Keane MC, Coffey NE, Jones VJ, Mills RAD, Coster DJ, eds. The Australian Corneal Graft Registry 2015 Report. Department of Ophthalmology, Adelaide: 2018 pp 1-303. URL: <http://hdl.handle.net/2328/37917>

# **CURRENT REGISTRATION AND FOLLOW-UP FORMS USED BY THE AUSTRALIAN CORNEAL GRAFT REGISTRY**

Registry No.	<b>THE AUSTRALIAN CORNEAL GRAFT REGISTRY REGISTRATION FORM</b>	Date Rec'd
Registry use only		Registry use only

OPERATING SURGEON (surname and initial): \_\_\_\_\_

STATE: \_\_\_\_\_

CONSULTANT (if different): \_\_\_\_\_

SEND FOLLOW-UP REQUESTS TO: \_\_\_\_\_

**RECIPIENT IDENTIFICATION**

Patient's name: \_\_\_\_\_

SURNAME

FIRST NAME

Patient's record number (if applicable): \_\_\_\_\_

Please select applicable boxes

Patient's date of birth:        /        /

Patient's sex:

**Male****Female**

Date of graft:                /        /

Eye grafted:

**R****L****EYE BANK AND DONOR INFORMATION**

Collection Eye Bank State: \_\_\_\_\_

Eye Bank number: \_\_\_\_\_

Interim Eye Bank number (if applicable): \_\_\_\_\_

Donor age (in years): 

Donor sex:

 Male Female

Multiple organ donor:

 No YesBone donor 

Cause of donor death: \_\_\_\_\_

OFFICE USE ONLY

**TIMES AND DATES** (please fill in as many as are known using a 24 hour clock)**STORAGE METHOD** (please tick)

Donor death:

Time

:

Date

/

/

Optisol 

Enucleation of eye:

Time

:

Date

/

/

Organ culture 

Storage of cornea:

Time

:

Date

/

/

Moist pot 

De-swelling commenced:

Time

:

Date

/

/

Endothelial cell count (per mm<sup>2</sup>): \_\_\_\_\_

Pre-cut tissue:

 No Yes**RECIPIENT HISTORY****Past** history/original pathology/underlying diseases (in words): \_\_\_\_\_

Office use only

**Current** indications for graft/current pathology (in words): \_\_\_\_\_If this is a **repeat** graft, what was the **reason** for, and **date** of, failure of the **previous graft** (tick/specify):Primary graft failure  Detachment  Rejection  Endothelial failure 

Date of failure:

Other: \_\_\_\_\_

/ /

Immediately **prior** to the graft, the eye to be grafted was (please circle): Phakic Aphakic PseudophakicNumber of **previous** grafts (EXCLUDING THIS GRAFT) in the eye **grafted today** (PLEASE ENSURE EYE IS INDICATED ABOVE):Penetrating: Endothelial: DALK: Limbal: Other: **TOTAL:** Number of grafts in **contralateral** eye (if known):

Pre-graft **best corrected** visual acuity, without pinhole (please advise acuity in both eyes):

<b>R:</b>	<b>L:</b>
-----------	-----------

Please tick applicable boxes

**Does the patient have any of the following:**

- History of collagen cross-linking on grafted eye
- Current inflammation of eye/use of topical steroids in past 2 weeks
- Active HSV infection at time of graft
- History of raised intraocular pressure/glaucoma
- Raised intraocular pressure at time of graft
- History of **glaucoma** surgery in grafted eye
- History of **any intraocular** surgery in grafted eye (including previous grafts)

Yes	No	Unknown

Presence of vessels in the recipient cornea:

Please select applicable boxes

4 Quadrant	3 Quadrant	2 Quadrant	1 Quadrant	None
------------	------------	------------	------------	------

Desired outcomes (please select as many as apply):

Pain Relief	Improved Visual Acuity	Tectonic/ Structural Repair	Cosmesis
-------------	------------------------	-----------------------------	----------

**OPERATIVE DETAILS: Please tick relevant graft type and complete all applicable details**

**Penetrating**  Converted from lamellar  No  Yes  Planned type: \_\_\_\_\_  
 Donor button size:  mm Host bed size:  mm

**DALK** Big Bubble  Melles  Other (please specify): \_\_\_\_\_  
 Donor button size:  mm Host bed size:  mm

**Endothelial Keratoplasty** DSEK  DSAEK  UT-DSEK  DMEK   
 Other (please specify): \_\_\_\_\_

**Insertion technique** (please tick as many as apply)  
 Glide  Glide type: \_\_\_\_\_ IOL injector  AC maintainer   
 Viscoelastic  Forceps  Folded  Suture pull through   
 Other (please specify): \_\_\_\_\_

Descemet's Membrane stripped  No  Yes  By surgeon?  No  Yes  Suture/s to wound  No  Yes   
 Donor button size:  mm Incision size:  mm

**Limbal (scleral/stem-cell/conjunctival)**  Details: \_\_\_\_\_  
**Peripheral patch** To cornea  To sclera  To both   
**Other lamellar**  Details: \_\_\_\_\_  
 Donor button size:  mm Host bed size:  mm

**TIME OF DAY GRAFT PERFORMED:**  :  AM  PM

**ACCOMPANYING PROCEDURES** (please tick as many as apply)  
 Cataract removal  Trabeculectomy  Peripheral iridectomy  Vitrectomy   
 IOL inserted : Pseudophakic  Phakic  IOL exchanged  Type of IOL: \_\_\_\_\_  
 Glaucoma tube repositioned  Other (please specify): \_\_\_\_\_

Immediately **following** the graft, the grafted eye was (please circle): 

Phakic	Aphakic	Pseudophakic
--------	---------	--------------

FURTHER COMMENTS: \_\_\_\_\_

**CONSENT:** Please remember that you should gain consent from your patient for data to be forwarded to the ACGR

**PLEASE RETURN THIS FORM TO:** The Australian Corneal Graft Registry, Department of Ophthalmology, Flinders Medical Centre, BEDFORD PARK S.A. 5042 PHONE: (08) 8204 5321 FAX: (08) 8277 0899

Registry No.	<b>THE AUSTRALIAN CORNEAL GRAFT REGISTRY PENETRATING GRAFT FOLLOW-UP FORM</b>	Date Rec'd
Registry use only		Registry use only

SURGEON: \_\_\_\_\_ STATE: \_\_\_\_\_

### PATIENT IDENTIFICATION

Patient name: \_\_\_\_\_ UR Number: \_\_\_\_\_  
 Date of birth:     /     /     Eye: \_\_\_\_\_  
 Date of graft:     /     /     Follow-up previously provided up to:     /     /

### GRAFT STATUS

DATE PATIENT LAST SEEN **BY YOU**

GRAFT SURVIVING ON THIS DATE  Yes  No (please circle) If no, REGRAFTED?

IF NO, DATE GRAFT **FAILED**

REASONS FOR GRAFT FAILURE:	1.	Office use only
	2.	

### PATIENT STATUS (please tick if applicable and provide any further information known)

DECEASED (if known)  DATE OF DEATH (if known)

LOST TO FOLLOW-UP  DATE LOST

FOLLOW-UP ELSEWHERE  (please advise the name and address of the follow-up doctor below)

### POST OPERATIVE EVENTS

**ALL SUTURES REMOVED**  Yes  No If yes, date of **final** suture removal

WERE ANTI-VIRAL MEDICATIONS USED?  Yes  No

HAVE ANY OF THE FOLLOWING OCCURRED SINCE LAST REPORTED FOLLOW-UP (please tick all that apply):

NEOVASCULARIZATION OF GRAFT	<input type="checkbox"/>	RECURRENT HERPETIC DISEASE	<input type="checkbox"/>	OEDEMA	<input type="checkbox"/>
CATARACT DEVELOPED SINCE GRAFT	<input type="checkbox"/>	MICROBIAL KERATITIS/ABSCCESS	<input type="checkbox"/>	UVEITIS	<input type="checkbox"/>
INTERFACE/STROMAL HAZE OR OPACITY	<input type="checkbox"/>	SIGNIFICANT RISE IN IOP	<input type="checkbox"/>	→ STEROID INDUCED?	<input type="checkbox"/> Y <input type="checkbox"/> N

### REJECTION EPISODES SINCE PREVIOUS FOLLOW-UP

NUMBER  DATES

WERE THE EPISODES REVERSIBLE?  Yes  No  Yes  No  Yes  No  Yes  No

OTHER SIGNIFICANT EVENTS Office use only


**OPERATIVE PROCEDURES ON THE GRAFTED EYE**

**SINCE THE LAST RECORDED FOLLOW-UP** (since date of graft if this is the first follow-up)

HAVE ANY OPERATIVE PROCEDURES BEEN PERFORMED ON THE GRAFTED EYE? **PRIOR TO REGRAFT, IF APPLICABLE** (please tick as many as apply)

Yes	No
-----	----

CATARACT REMOVAL	<input type="checkbox"/>	PSEUDOPHAKIC IOL INSERTION	<input type="checkbox"/>	PHAKIC IOL INSERTION	<input type="checkbox"/>
IOL REMOVAL	<input type="checkbox"/>	IOL EXCHANGE	<input type="checkbox"/>	YAG LASER/CAPSULOTOMY	<input type="checkbox"/>
PIGGY-BACK IOL	<input type="checkbox"/>	TARSORRHAPHY	<input type="checkbox"/>	VITRECTOMY	<input type="checkbox"/>
				TRABECULECTOMY	<input type="checkbox"/>

OTHER (please specify): \_\_\_\_\_

HAS ANY REFRACTIVE SURGERY BEEN PERFORMED ON THE GRAFTED EYE?

Yes	No
-----	----

(please tick as many as apply)

SUTURE ADJUSTMENT	<input type="checkbox"/>	RELAXING INCISION	<input type="checkbox"/>	<b>EXCIMER LASER</b>	LASIK	<input type="checkbox"/>
COMPRESSION SUTURES	<input type="checkbox"/>	WEDGE RESECTION	<input type="checkbox"/>		LASEK	<input type="checkbox"/>
OTHER (please specify):	_____				PRK	<input type="checkbox"/>
					PTK	<input type="checkbox"/>

**POST GRAFT VISUAL OUTCOME**

IN THE GRAFTED EYE DOES THE PATIENT HAVE:

AN INTRAOCULAR LENS 

Yes	No
-----	----

 If yes, what type: \_\_\_\_\_

TO ACHIEVE BEST CORRECTED VISUAL ACUITY IN THE GRAFTED EYE (please circle):

ARE SPECTACLES WORN? 

Yes	No
-----	----

 ARE CONTACT LENSES WORN? 

Yes	No
-----	----

**SNELLEN ACUITY** (please provide BCVA with preferred correction but without pinhole)

EYE HAS NO VISUAL POTENTIAL (tick if applicable)	<input type="checkbox"/>	GRAFTED EYE	<input type="checkbox"/>	CONTRALATERAL EYE	<input type="checkbox"/>
SNELLEN ACUITY WITH PINHOLE:		GRAFTED EYE	<input type="checkbox"/>	CONTRALATERAL EYE	<input type="checkbox"/>

**FACTORS AFFECTING VISUAL ACUITY IN GRAFTED EYE** (please tick all that apply)

ANISOMETROPIA	<input type="checkbox"/>	MAJOR ASTIGMATISM (≥5D)	<input type="checkbox"/>	Dioptres: _____			
				K-Reading: _____			
CATARACT	<input type="checkbox"/>	CME	<input type="checkbox"/>	MYOPIA	<input type="checkbox"/>	RETINAL DETACHMENT	<input type="checkbox"/>
GLAUCOMA	<input type="checkbox"/>	ARMD	<input type="checkbox"/>	AMBLYOPIA	<input type="checkbox"/>	DIABETIC RETINOPATHY	<input type="checkbox"/>
OPACITY/SCAR	<input type="checkbox"/>	APHAKIA	<input type="checkbox"/>	OTHER (please specify):	_____		

IF GRAFTED FOR PAIN, HAS PAIN BEEN RELIEVED? 

Yes	No
-----	----

CENTRAL GRAFT PACHYMETRY  ENDOTHELIAL CELL COUNT (per mm<sup>2</sup>)

**OTHER COMMENTS**

\_\_\_\_\_  
 \_\_\_\_\_

**PLEASE RETURN THIS FORM TO:** The Australian Corneal Graft Registry, Department of Ophthalmology, Flinders Medical Centre, BEDFORD PARK S.A. 5042 PHONE: (08) 8204 5321 FAX: (08) 8277 0899

Registry No.	<b>THE AUSTRALIAN CORNEAL GRAFT REGISTRY LAMELLAR GRAFT FOLLOW-UP FORM</b>	Date Rec'd
Registry use only		Registry use only

SURGEON: \_\_\_\_\_ STATE: \_\_\_\_\_

### PATIENT IDENTIFICATION

Patient name: \_\_\_\_\_ UR Number: \_\_\_\_\_  
 Date of birth:     /     /     Eye: \_\_\_\_\_  
 Date of graft:     /     /     Follow-up previously provided up to:     /     /

### GRAFT STATUS

DATE PATIENT LAST SEEN **BY YOU**     /     /

GRAFT SURVIVING ON THIS DATE     Yes     No     (please circle)     If no, REGRAFTED?     

IF NO, DATE GRAFT **FAILED**     /     /

REASONS FOR  
GRAFT FAILURE:

1.

2.

Office use only

### PATIENT STATUS (please tick if applicable and provide any further information known)

DECEASED (if known)          DATE OF DEATH (if known)     /     /

LOST TO FOLLOW-UP          DATE LOST     /     /

FOLLOW-UP ELSEWHERE          (please advise the name and address of the follow-up doctor below)

### POST OPERATIVE EVENTS

ALL SUTURES REMOVED     Yes     No     N/A     If yes, date of final suture removal     /     /

WERE ANTI-VIRAL MEDICATIONS USED?     Yes     No

HAVE ANY OF THE FOLLOWING OCCURRED SINCE LAST REPORTED FOLLOW-UP (please tick all that apply):

NEOVASCULARIZATION OF GRAFT	<input type="checkbox"/>	RECURRENT HERPETIC DISEASE	<input type="checkbox"/>	OEDEMA	<input type="checkbox"/>
CATARACT DEVELOPED SINCE GRAFT	<input type="checkbox"/>	MICROBIAL KERATITIS/ABSCESS	<input type="checkbox"/>	UVEITIS	<input type="checkbox"/>
INTERFACE/STROMAL HAZE OR OPACITY	<input type="checkbox"/>	SIGNIFICANT RISE IN IOP	<input type="checkbox"/>	→ STEROID INDUCED?	<input type="checkbox"/> Y <input type="checkbox"/> N

### REJECTION EPISODES SINCE PREVIOUS FOLLOW-UP

NUMBER          DATES     /     /     /     /     /     /     /     /

WERE THE EPISODES REVERSIBLE?     Yes     No     Yes     No     Yes     No     Yes     No

OTHER SIGNIFICANT EVENTS

Office use only

**OPERATIVE PROCEDURES ON THE GRAFTED EYE**

**SINCE THE LAST RECORDED FOLLOW-UP** (since date of graft if this is the first follow-up)

HAVE ANY OPERATIVE PROCEDURES BEEN PERFORMED ON THE GRAFTED EYE? **PRIOR TO REGRAFT, IF APPLICABLE** (please tick as many as apply)

Yes	No
-----	----

CATARACT REMOVAL	<input type="checkbox"/>	PSEUDOPHAKIC IOL INSERTION	<input type="checkbox"/>	PHAKIC IOL INSERTION	<input type="checkbox"/>
IOL REMOVAL	<input type="checkbox"/>	IOL EXCHANGE	<input type="checkbox"/>	YAG LASER/CAPSULOTOMY	<input type="checkbox"/>
PIGGY-BACK IOL	<input type="checkbox"/>	TARSORRHAPHY	<input type="checkbox"/>	VITRECTOMY	<input type="checkbox"/>
				TRABECULECTOMY	<input type="checkbox"/>

OTHER (please specify): \_\_\_\_\_

HAS ANY REFRACTIVE SURGERY BEEN PERFORMED ON THE GRAFTED EYE?

Yes	No
-----	----

IF YES, PLEASE SPECIFY: \_\_\_\_\_

**FOR ENDOTHELIAL GRAFTS ONLY**

HAVE ANY OF THE FOLLOWING OCCURRED (please tick or circle all that apply):

PRIMARY NON-FUNCTIONING GRAFT (cornea never cleared)	<input type="checkbox"/>	FAILED WITHIN 28 DAYS	<input type="checkbox"/>	Yes	No
		INTERFACE OPACITY	<input type="checkbox"/>	DOUBLE ANTERIOR CHAMBER	<input type="checkbox"/>
COMPLETE GRAFT DETACHMENT	<input type="checkbox"/>	PARTIAL GRAFT DETACHMENT	<input type="checkbox"/>		
RE-BUBBLED	<input type="checkbox"/>	Yes	No	NO. OF REBUBBLES:	_____
				SUCCESSFUL RE-ATTACHMENT	<input type="checkbox"/>
				Yes	No

**POST GRAFT VISUAL OUTCOME**

IN THE GRAFTED EYE DOES THE PATIENT HAVE:

AN INTRAOCULAR LENS  Yes  No If yes, what type: \_\_\_\_\_

TO ACHIEVE BEST CORRECTED VISUAL ACUITY IN THE GRAFTED EYE (please circle):

ARE SPECTACLES WORN?  Yes  No ARE REMOVABLE CONTACT LENSES WORN?  Yes  No

**SNELLEN ACUITY** (please provide BCVA with preferred correction but without pinhole)

EYE HAS NO VISUAL POTENTIAL (tick if applicable)	<input type="checkbox"/>	GRAFTED EYE	<input type="checkbox"/>	CONTRALATERAL EYE	<input type="checkbox"/>
SNELLEN ACUITY WITH PINHOLE:		GRAFTED EYE	<input type="checkbox"/>	CONTRALATERAL EYE	<input type="checkbox"/>

**FACTORS AFFECTING VISUAL ACUITY IN GRAFTED EYE** (please tick all that apply)

ANISOMETROPIA	<input type="checkbox"/>	MAJOR ASTIGMATISM (≥5D)	<input type="checkbox"/>	Dioptres: _____	K-reading: _____
CATARACT	<input type="checkbox"/>	CME	<input type="checkbox"/>	MYOPIA	<input type="checkbox"/>
GLAUCOMA	<input type="checkbox"/>	ARM D	<input type="checkbox"/>	AMBLYOPIA	<input type="checkbox"/>
OPACITY/SCAR	<input type="checkbox"/>	APHAKIA	<input type="checkbox"/>	OTHER (please specify):	_____

IF GRAFTED FOR PAIN, HAS PAIN BEEN RELIEVED?

Yes	No
-----	----

CENTRAL GRAFT PACHYMETRY  ENDOTHELIAL CELL COUNT (per mm<sup>2</sup>)

**OTHER COMMENTS:** \_\_\_\_\_

**PLEASE RETURN THIS FORM TO:** The Australian Corneal Graft Registry, Department of Ophthalmology, Flinders Medical Centre, BEDFORD PARK S.A. 5042 PHONE: (08) 8204 5321 FAX: (08) 8277 0899