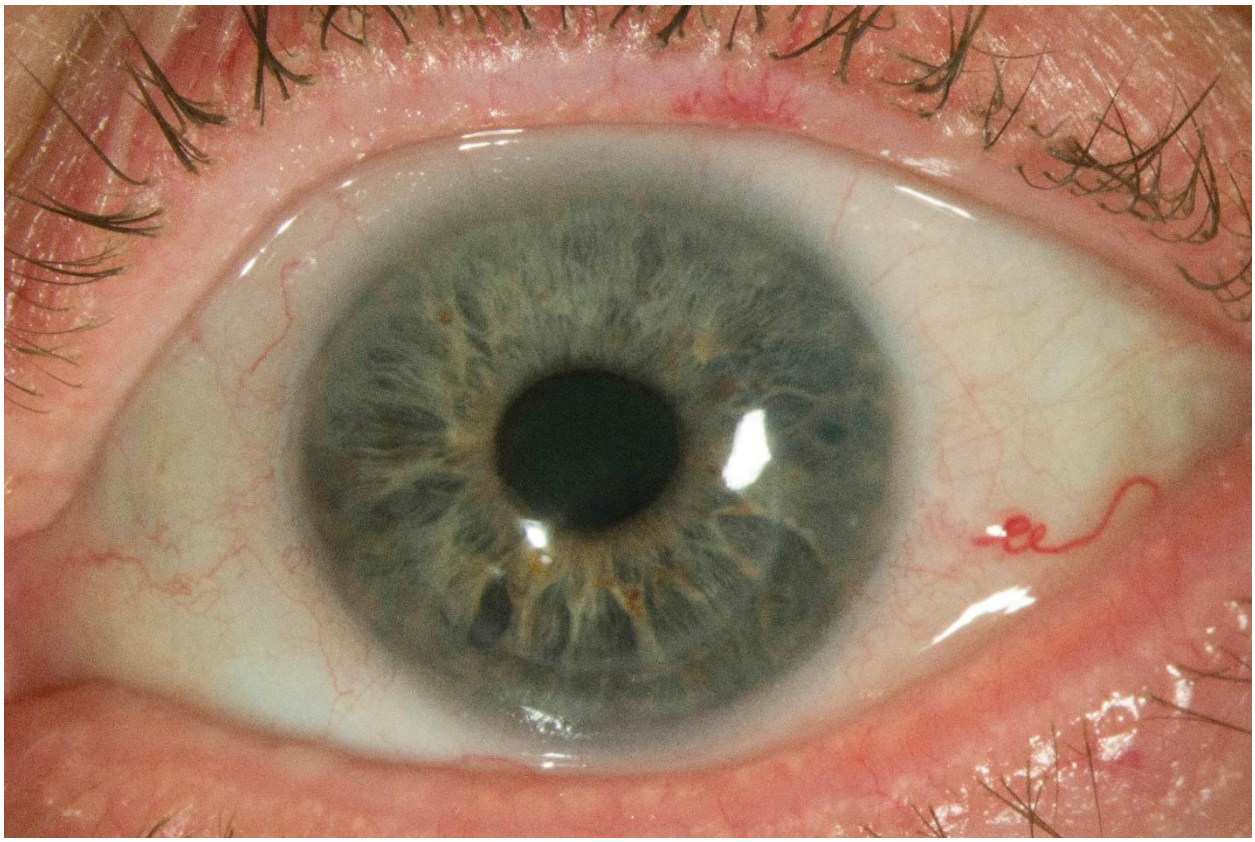
THE AUSTRALIAN CORNEAL GRAFT REGISTRY



2021/22 REPORT

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

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2021/22 REPORT

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South Australian Health and Medical Research Institute

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Acknowledgments

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Eye Bank of South Australia

Lions New South Wales Eye Bank

Lions Eye Bank of Western Australia

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Queensland Eye Bank

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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

The Australian Corneal Grafts Registry is a prescribed activity under the Commonwealth Government Qualified Priviledge Scheme

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Introduction

The Australian Corneal Graft Registry (ACGR) opened in May 1985 and has now been operating for 37 years. Over the years, we have collected information on more than 40,000 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 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: https://doi.org/10.25957/9vyp-0j93.

We have analysed all grafts performed up to 31-12-2020 and registered with the Australian Corneal Graft Registry up to a census date of 31-03-2021. 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.

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Wright, H
Wu, J
Wunsh, MR

Yates, WHB
Yellachich, D
Yeung, S
Yip, J
York, N
You, CS
Young, SH
Yow, CS
Yuen, J

Zabell, KW
Zacharia, Z
Zadeh, R
Zahn, R
Zamora-Alejo, K

Medical Superintendents of various hospitals

(n=1125)

Contents

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, ultra-thin 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:

BCVA = Best corrected 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 Methods and Definitions

1.1 Registration and Follow-up

Grafts are registered by contributing surgeons using a consistent paper form, as soon as possible after the graft. The database used in this report includes registrations for all grafts performed prior to 2021 that had been received by the ACGR up to, and including, 31st March 2021.

A formal written request for follow-up information is mailed out by the ACGR. The timing of this has varied over the history of the ACGR, though it occurrs at roughly yearly intervals. Follow-up is initially requested at least 9 months, and no more than 21 months, post-graft. Since 2018, the follow-up request has occurred each September, and incorporates all grafts performed prior to that year. If follow-up information is not received by the time of the next ACGR request mail-out a year later, it will be requested again.

While the request for follow-up from the ACGR occurs at a consistent time of year, the timing of the return of the forms will depend on when the graft recipient is seen by the surgeon. Surgeons indicate the date the patient was last seen by them on the form and this is used to determine when future follow-up requests will be made. A second request for follow-up will be forwarded at the next mail-out that is at least a year after this last seen date. Once follow-up has been received twice, the interval between requests is extended to every 2 years, and once it has been received five times, it is extended to every 3 years. However, where a recipient has bilateral grafts, follow-up is requested for both eyes when either is due, enabling future follow-up requests for a single recipient to become synchronised.

Follow-up is initially sought from the operating surgeon. Thereafter, it may be sought from either the operating surgeon or an alternative follow-up practioner (ophthalmologist or optometrist), as advised by the operating surgeon. Missing data are 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 recipient. Grafts are recorded as failed if the surgeon provides this information in response to a follow-up request, or if a subsequent repeat graft is registered with the ACGR. Information regarding the death of recipients may be obtained from surgeons or via data-linkage with the National Death Index, which is performed no more than once every 5 years, with the most recent linkage completed in 2014. Grafts are deemed “lost to follow-up” when the surgeon informs the ACGR that the patient is no longer seen by them, without providing details of an alternative follow-up practitioner. Additionally, they will be lost when at least three ACGR follow-up requests have not been returned and a time-period of at least 5 years has elapsed since follow-up was last received for the recipient. Grafts performed in recipients who are lost to follow-up may be reactivated in the database if a future graft, either ipsilateral or contralateral, is registered with the ACGR.

Consideration should be given to the effect of follow-up lag time on the analyses included in this report. 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 are less likely to have been made for follow-up information and tends to reduce predictably over time.

This lag-time effect is most obvious in analyses comparing survival of grafts performed over different time periods (graft era) where the survival curves tend to drop off suddenly, illustrating this skewing of the data. This will also affect results where the variable of interest may be related to graft era, where differences in rates of follow-up across sub-groups may affect survival calculations. Instances where registered grafts are missing information were more common in earlier cohorts, and data on some variables have only been collected for later cohorts. The impact of lag-time on survival calculations should be considered when comparing outcomes between different types of graft.

This report contains all follow-up data for grafts that had been received by the census date of 31st December 2020. The study period for the analyses is May 1985 to December 2020 (35 years), except where otherwise stated.

1.2 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.

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°C until required. The current storage media utilised for hypothermic preservation is Optisol GS, however a number of media have been used previously (CSM, K-Sol, Dextran, M-K medium). These older types of hypothermic storage media all went

out of use in the late 1990s or early 2000s. They are collectively referred to in this report as “superseded media” and are analysed together, where relevant. Optisol is analysed separately. The alternative storage method, organ culture, involves warm storage, and was re-introduced to Australia in 2007, having previously been used occasionally in the 1980s and 1990s. A third method of storage is occasionally used, known as moist pot storage, which sees the entire globe of the eye stored, with the intention of use within 24 hours. This form of storage has been, and continues to be, reported in small numbers each year.

1.3 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. 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, where one has replaced the anterior segment and the other the posterior segment (e.g. a deep anterior lamellar graft and a Descemet’s membrane endothelial keratoplasty). Concurrent grafts can also be in the form of peripheral patch grafts to cover glaucoma tubes (classified as traditional lamellar keratoplasty in this report) or limbal stem cell grafts. These additional grafts may be performed in eyes that already have prior penetrating or lamellar grafts but are for a separate purpose. In each of 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, ≥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 is calculated as the time between the date of graft and the date on which the patient was last seen. For failed grafts, trial time is calculated as the time between the date of graft and the date of failure, specified on a daily basis. Although data are collected centrally within the Registry at least once yearly, individual patient data are collected at source according to a frequency determined by the ophthalmic surgeon.

1.4 Statistical Analyses

1.4.1 The Australian Corneal Graft Registry database

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 SPPS version 25 (SPSS Inc.). Individual databases were also created for each type of graft analysed. Univariate Kaplan–Meier survival analyses [see reference 1] were performed in IBM SPSS for Windows (Version 25.0) with significance set at $p<0.05$ [Mantel–Cox log-rank^2 statistic – see references 2 & 3]. 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 16.1 [see references 4 & 5]. Holm-Bonferroni correction was applied for multiple comparisons [see references 6 & 7]. The report was prepared using Microsoft Office 2016.

1.4.2 Categorisation of variables for Kaplan-Meier analyses

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 2% of grafts were available for the graft type in question. Where categories with fewer grafts than this could be logically combined with another category, we have done so. In other cases, the data for these categories are excluded from the analyses. Corresponding probability of graft survival is only provided in the accompanying tables where at least 20 grafts in a category are followed.

For variables relating to the size of the graft and incision (for endothelial keratoplasties), the size of the graft was the donor button diameter, as reported by surgeons. Grafts were initially categorised in increments of 0.25 mm, 0.50 mm or 1.00 mm increases, depending on the numbers of grafts of various sizes registered. For these and other scale variables that have been categorised, e.g. age groups or graft year, further analyses determined whether adjacent groups differed significantly. Where no significant difference was found, these groups were combined for the final Kaplan-Meier analyses and subsequent multivariate regressions.

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

- 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.
- 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.
- 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.
- 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 furthermost 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.

1.4.4 Combining variables for multivariate analysis

Analysis of the impact of indication for graft and number of previous grafts in the ipsilateral eye are inherently linked, due to one of the main indications for graft groups being “failed previous graft”. Where both variables were found to be significant in univariate analysis, they were combined for analysis in the multivariate model.

Where significant differences in survival were found relating to the type of storage media used and the time a donor cornea was stored in a specific storage media, these variables were combined for analysis in the multivariate model.

In both cases, if the combined variable was retained in the resulting final model, it was then determined whether group differences were present relating to both original variables. If not, the model was rerun excluding the non-significant variable and including the original variable that was found to have a significant effect.

1.4.5 Excluding variables from multivariate analysis

Where data were missing for more than half of cases, the variable was excluded from multivariate analysis. The variables relating to surgeon caseload and level of follow-up and the centre effect are linked. Where both were found to be significant in univariate analysis, surgeon caseload and follow-up was used. The variables relating to eye bank, graft State and interstate transportation are linked. Where all three variables were found to be significant in the multivariate analyses, those relating to eye bank and interstate transportation were initially included in the multivariate modelling. If both variables were subsequently excluded from the model, graft State was inserted at that point, to check that it did not independently affect survival.

1.4.6 Procedure for multivariate analyses

For each type of graft examined, multivariate models were used to investigate the combined effect of variables on graft survival, adjusted for all other variables in the model. These analyses were performed using STATA version 16.

In the preceding univariate analyses, each registered graft, together with its archival follow-up records, was treated as a separate and independent entity. Some recipients had multiple grafts of the same type performed during the census period (registered by 31/3/2021), 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 4 & 5].

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. 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 meet the inclusion criteria ($p>0.08$), 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 variables with more than two categories, within group comparisons were evaluated using the Holm-Bonferroni correction method to determine significance. 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.

1.4.7 Qualified privilege

In December 2018 the Australian Corneal Graft Registry was declared as a quality assurance activity under the Commonwealth Government Qualified Privilege Scheme. Due to increased confidentiality requirements relating to this declaration, we cannot provide information that may lead to the identification of outcomes relating to individual eye banks or surgeons. For this reason, eye banks have been assigned a random letter of the alphabet and numbers of grafts at risk are not provided for these variables to reduce the chance of inadvertent identification. Additionally, the results of the univariate analyses of the centre effect are not provided and where this variable was included in the final multivariate model, individual surgeon results are not published.

1.4.8 Procedure for visual acuity analyses

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 three categories were:

- BCVA provided at between 3- and 6-months post-graft,
- BCVA provided at between 6- and 9-months post-graft, and
- BCVA provided at between 12- and 15-months post-graft.

Subsequent groups were at yearly intervals.

For each year-point, any measurements provided within 3 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 821-days post-graft was included). Median BCVA was included in analyses where 10 or more grafts in the relevant group had data available at the relevant time-point.

We analysed post-graft visual acuity for grafts that were **surviving** at each yearly time point. Note that a graft did not have to have visual acuity data provided for each time point to be included, but rather all grafts with data available at a single time point were included for that time point. For example, if a graft had BCVA provided at 3-months, 2-years, 4-years and 5-years post-graft, and it was reported to have failed at 5-years, the visual acuity data for this graft would be included at 3-months, 2-years, and 4-years, but not at 6-months, 1-year, 3-years or 5-years post-graft.

Methods and definitions

2 Overview of the Australian Corneal Graft Registry

2.1 The Database

At the time of census (31-03-2021), 40,0864 grafts had been registered, of which 31,460 (77.0%) 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
PK	26924 (65.9%)	22058 (70.1%)	5807 (42.9%)
DS(A)EK	6947 (17.0%)	5091 (16.2%)	4008 (29.6%)
DMEK	3215 (7.9%)	1756 (5.6%)	2296 (16.9%)
DALK	2018 (4.9%)	1241 (3.9%)	1075 (7.9%)
TLK	1670 (4.1%)	1248 (4.0%)	344 (2.5%)
Limbal	90 (0.2%)	66 (0.2%)	16 (0.1%)
Total	*40864 (100.0%)*	*31460 (100.0%)*	*13546 (100.0%)*

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

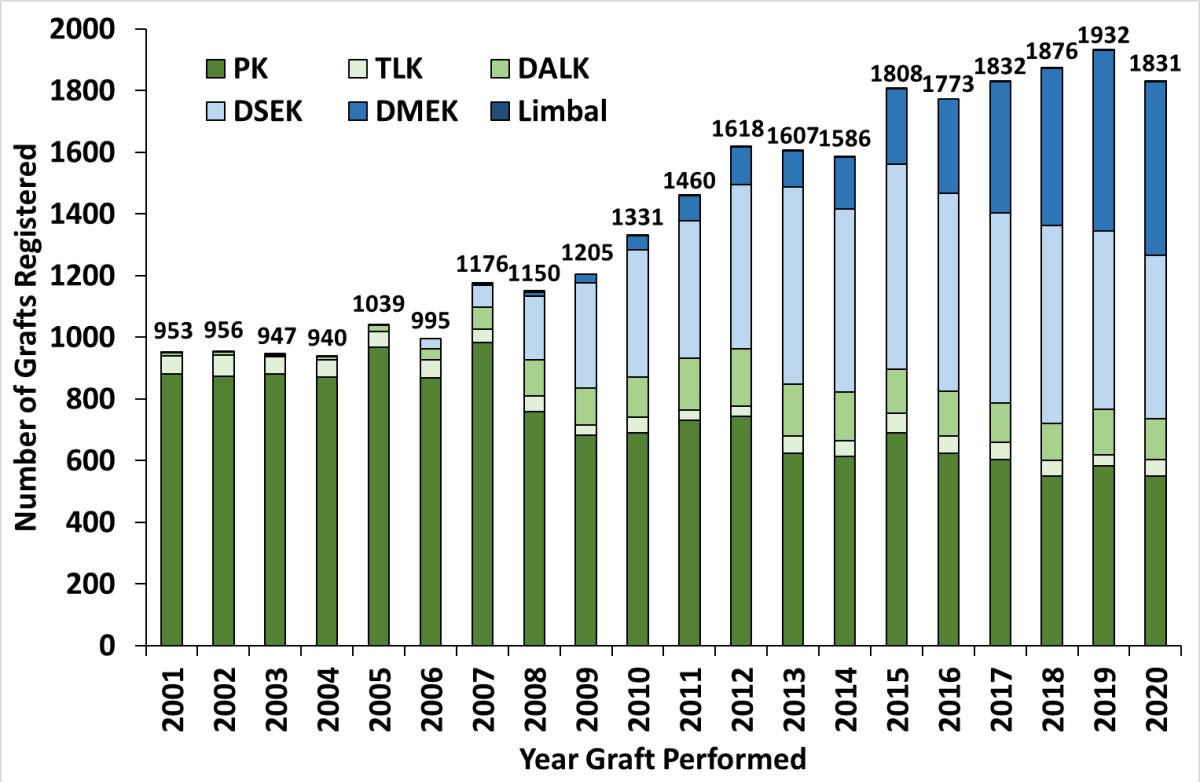
	PK	DS(A)EK	DMEK	DALK	TLK	Limbal	Total
Registered	**26924 (100%)**	**6947 (100%)**	**3215 (100%)**	**2018 (100%)**	**1670 (100%)**	**90 (100%)**	**40864 (100%)**
Followed*	**22058 (82%)**	**5091 (73%)**	**1756 (55%)**	**1241 (61%)**	**1248 (75%)**	**66 (73%)**	**31460 (77%)**
Failed	6722 (25%)	1442 (21%)	564 (18%)	161 (8%)	353 (21%)	31 (34%)	9273 (23%)
Recipient still alive	*4816 (18%)*	*1386 (20%)*	*559 (17%)*	*159 (8%)*	*257 (15%)*	*25 (28%)*	*7202 (18%)*
Recipient subsequently died	*1906 (7%)*	*56 (<1%)*	*5 (<1%)*	*2 (<1%)*	*96 (6%)*	*6 (7%)*	*2071 (5%)*
Recipient died with surviving graft	4139 (15%)	234 (3%)	18 (<1%)	17 (<1%)	224 (13%)	9 (10%)	4641 (11%)
Lost post follow-up	7224 (27%)	947 (14%)	207 (6%)	493 (24%)	485 (29%)	20 (22%)	9376 (23%)
Followed, surviving and active	3973 (15%)	2468 (36%)	967 (30%)	570 (28%)	186 (11%)	6 (7%)	8170 (20%)
Number of grafts not followed	**4866 (18%)**	**1856 (27%)**	**1459 (45%)**	**777 (39%)**	**422 (25%)**	**24 (27%)**	**9404 (23%)**
Recipient died pre follow-up	1038 (4%)	72 (1%)	12 (<1%)	7 (<1%)	107 (6%)	3 (3%)	1239 (3%)
Lost prior to follow-up	1994 (7%)	244 (4%)	118 (4%)	265 (13%)	157 (9%)	11 (12%)	2789 (7%)
Not yet followed but active	1834 (7%)	1540 (22%)	1329 (41%)	505 (25%)	158 (9%)	10 (11%)	5376 (13%)
Graft surviving when last seen	**14395 (53%)**	**1497 (22%)**	**355 (11%)**	**782 (39%)**	**973 (58%)**	**43 (48%)**	**18045 (44%)**
Graft lost when surviving	9218 (34%)	1191 (17%)	325 (10%)	758 (38%)	642 (38%)	31 (34%)	12165 (30%)
Lost prior to follow-up	*1994 (7%)*	*244 (4%)*	*118 (4%)*	*265 (13%)*	*157 (9%)*	*11 (12%)*	*2789 (7%)*
Lost post follow-up	*7224 (27%)*	*947 (14%)*	*207 (6%)*	*493 (24%)*	*485 (29%)*	*20 (22%)*	*9376 (23%)*
Recipient died with surviving graft	5177 (19%)	306 (4%)	30 (<1%)	24 (1%)	331 (20%)	12 (13%)	5880 (14%)
Recipient died pre follow-up	*1038 (4%)*	*72 (1%)*	*12 (<1%)*	*7 (<1%)*	*107 (6%)*	*3 (3%)*	*1239 (3%)*
Recipient died post follow-up	*4139 (15%)*	*234 (3%)*	*18 (<1%)*	*17 (<1%)*	*224 (13%)*	*9 (10%)*	*4641 (11%)*
Currently active grafts	**5807 (22%)**	**4008 (56%)**	**2296 (71%)**	**1075 (53%)**	**344 (21%)**	**16 (18%)**	**13546 (33%)**
Not yet followed but active	1834 (7%)	1540 (22%)	1329 (41%)	505 (25%)	158 (9%)	10 (11%)	5376 (13%)
Followed, surviving and active	3973 (15%)	2468 (36%)	967 (30%)	570 (28%)	186 (11%)	6 (7%)	8170 (20%)

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

2.1.1 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, at which point there was a plateau for a couple of years, followed by a further increase in 2015. The number registered has again remained fairly consistent from 2015 to 2020, as shown in Figure 1.1.1, though small increases were seen in the last few years prior to 2020.

Figure 1.1.1 Number of grafts registered with the ACGR per year, 2001 to 2020



Note: Data relating to all registrations of grafts performed up to and including 31st December 2020, for which forms had been received by the ACGR prior to 31st March 2021, were included. Some grafts performed prior to this date may still be registered in the future.

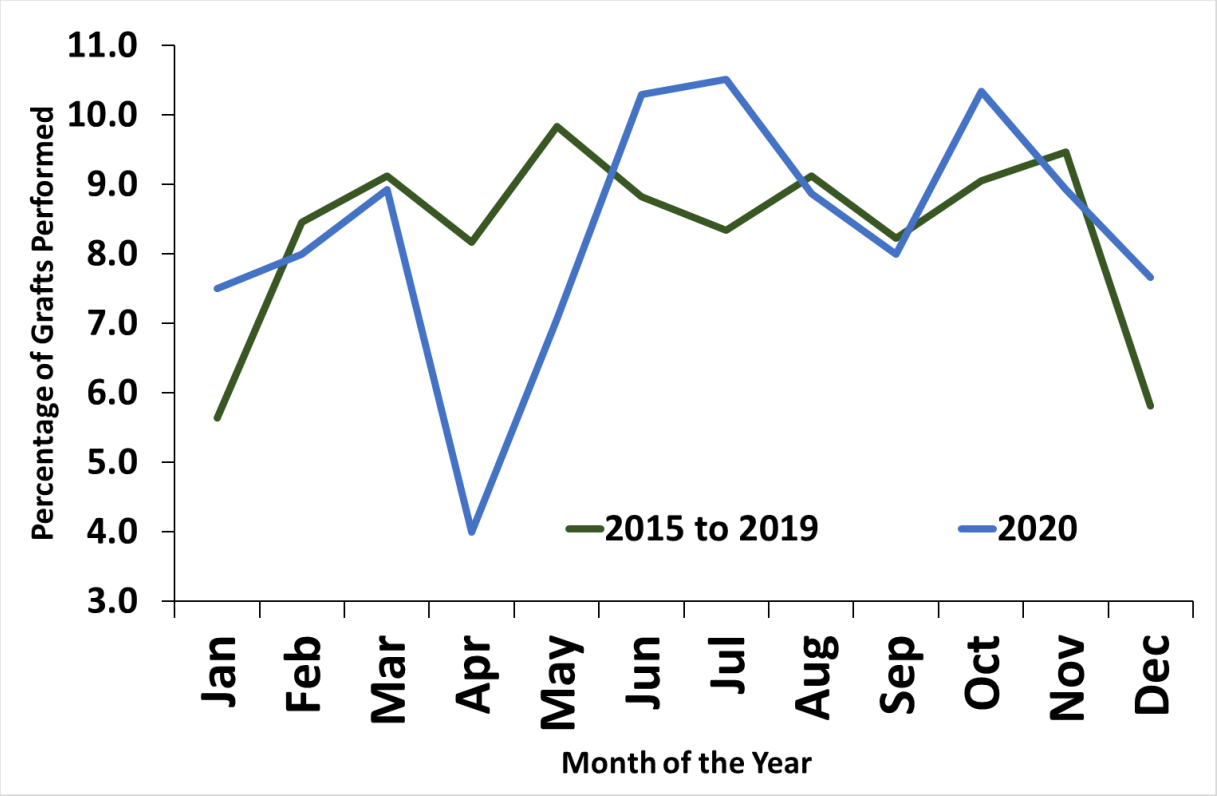
2.1.2 Changing practice: impact of the COVID-19 pandemic

In 2020, the world was first challenged by the coronavirus pandemic (COVID-19). Australia, as a nation, was able to implement measures that initially reduced the spread of the virus in the majority of the country. This involved a national lockdown in March and April 2020. Further, more localised, lockdowns were then implemented in specific States at later times, the most profound of which was in Victoria from July to October.

The impact of COVID-19 on the provision of corneal transplants in Australia was examined through comparison of monthly graft registrations during 2020 compared with the usual pattern of practice over the five years prior. As shown in Figure 1.1.1, the number of grafts registered in 2020 was similar to that registered annually in the five years prior.

Figure 1.1.2 shows the percentage of grafts registered nationally in each month of the year from 2015 to 2019 compared to in 2020. Prior to the pandemic, 8 to 10% of grafts were performed each month from February to November, with the traditional holiday period of December/January seeing a lower rate of registrations, at around 5-6%. The distribution of grafts in 2020 was much more varied. The national lockdown saw a corresponding dip in April, as only emergency sergeries could be performed, and then a subsequent surge in June and July, as surgeons strove to reduce the backlog. Rates could be viewed as dropping back to normal levels in August and September, though in reality this shows the reduction once again in Victorian surgeries as they entered their second major lockdown. A second increase to the higher levels can then be seen once these restrictions were eased in October.

Figure 1.1.2 Monthly pattern of corneal grafts being performed in Australia



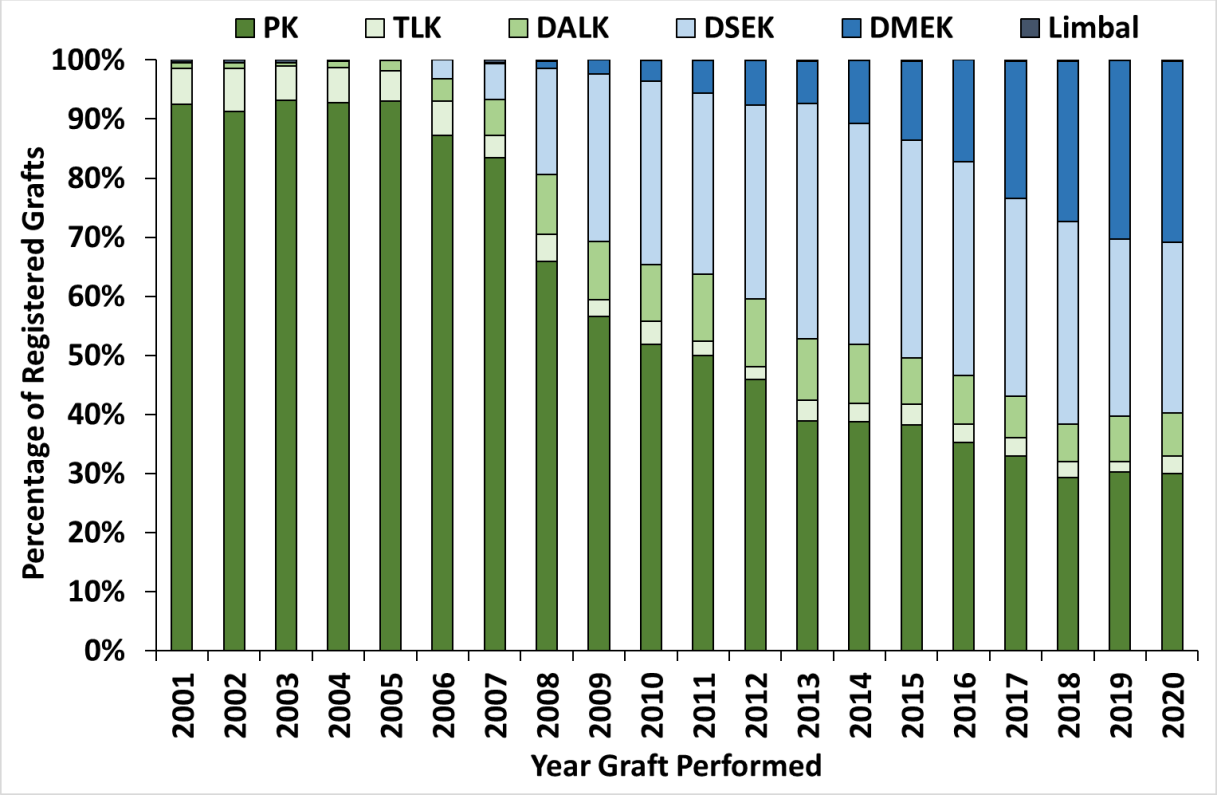
2.1.3 Changing practice: the introduction of partial-thickness keratoplasties

Figure 1.1.3 shows registrations stratified by graft type over the last 20 years. The introduction of new types of partial-thickness corneal grafts led to a marked shift away from full-thickness penetrating keratoplasty, which had dropped from more than 90% of registered grafts in the early 2000s, to just 50% by 2011.

The peak for DS(A)EK was in 2013, when they accounted for almost 40% of all registered grafts. By 2016, ten years after their introduction, endothelial grafts accounted for more than half of all registered grafts. While the uptake of DMEK was more gradual than DS(A)EK, this steadily increased from 2014 to 2019, and in 2019 the number of DMEK, DS(A)EK and PK was approximately equal, with each accounting for 30% of registered grafts. In 2020, DMEK had become the most frequently registered technique at 31%, while the proportion of DS(A)EK reduced slightly to 29%.

After a gradual increase from 2001 to 2008, the proportion of deep anterior lamellar keratoplasties (DALKs) remained stable for several years at approximately 10% of registered grafts. There has been a slight reduction since 2015, with the number registered dropping to about three-quarters of their 2012 peak, so that they now account for 7% of registered grafts.

Figure 1.1.3 Graft type by year of registration, 2001 onwards

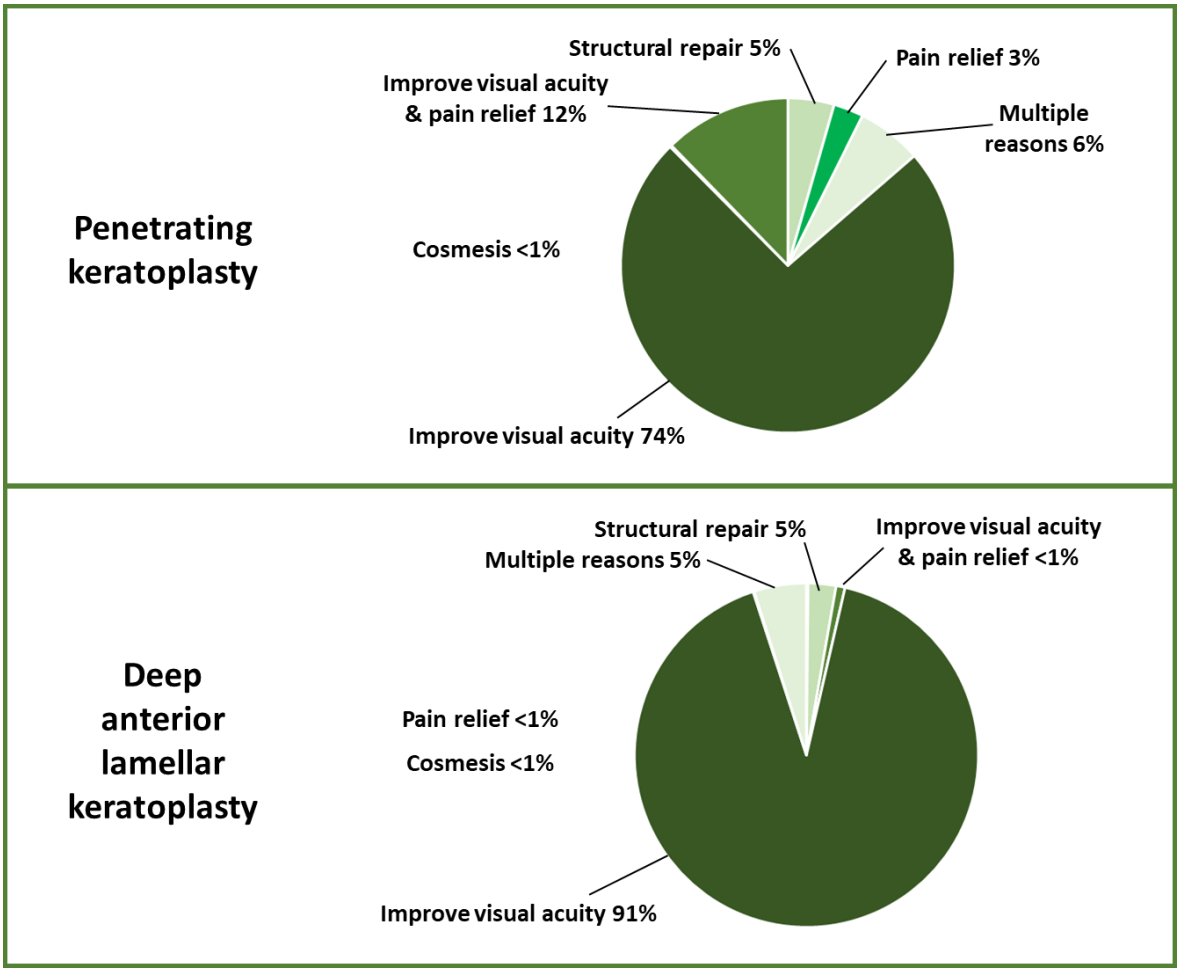


2.1.4 Comparison of desired outcome for different types of keratoplasty

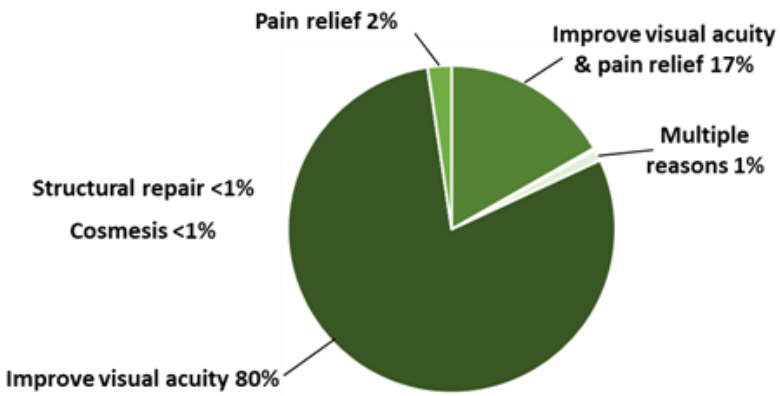
Surgeons indicated whether a graft was performed for: “improved visual acuity”, “pain relief”, “cosmesis”, “tectonic/structural repair”, or a combination of these reasons. Data were provided for 35,760 grafts (88%). Reason for graft was less likely to have been specified for TLK (81%), PK (85%) and limbal grafts (83%), compared with DALK (95%), DS(A)EK (95%), or DMEK (95%). Improved visual acuity was a desired outcome in 91% of these grafts, pain relief in 16%, 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%, 97%, 97% 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 (74%). Figure 1.1.4 shows the desired outcomes indicated by surgeons, for each type of graft.

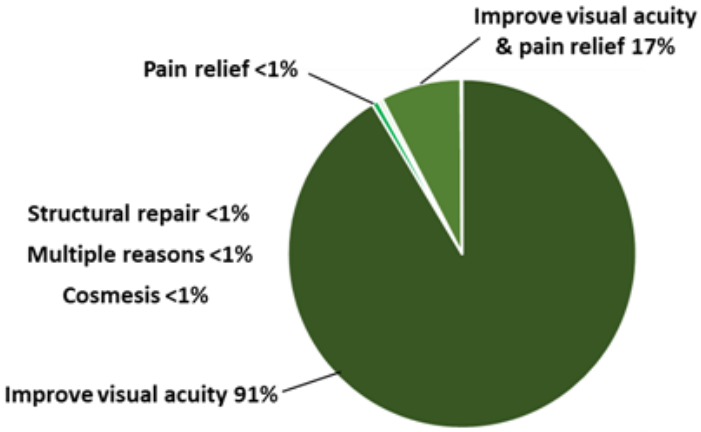
Figure 1.1.4 Reason for graft stratified by graft type



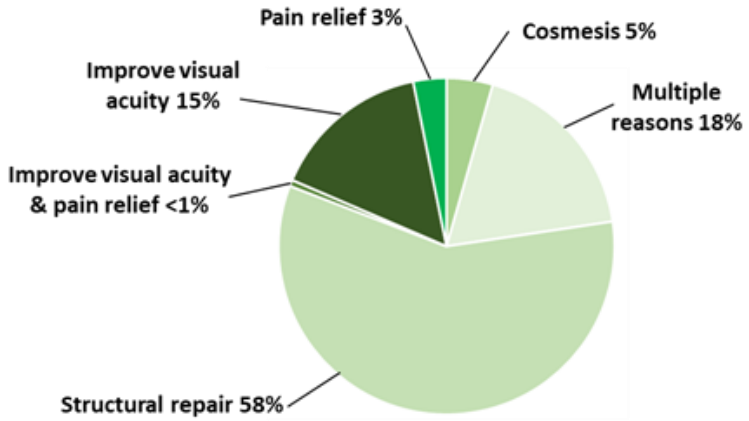
Descemet's stripping (automated) endothelial keratoplasty



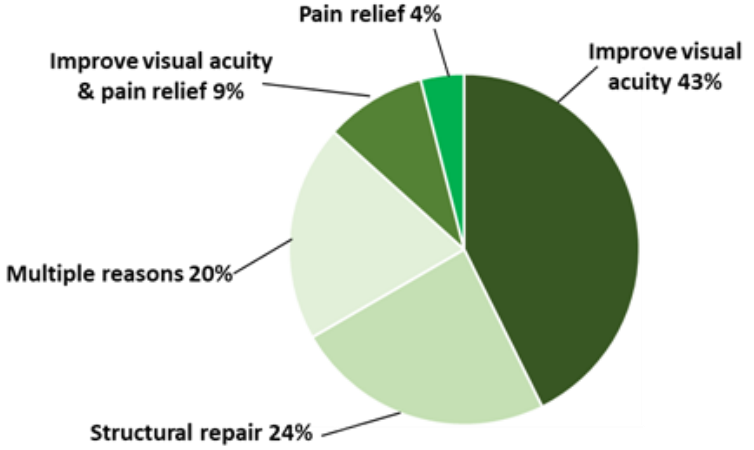
Descemet's membrane endothelial keratoplasty



Traditional lamellar keratoplasty



Limbal graft

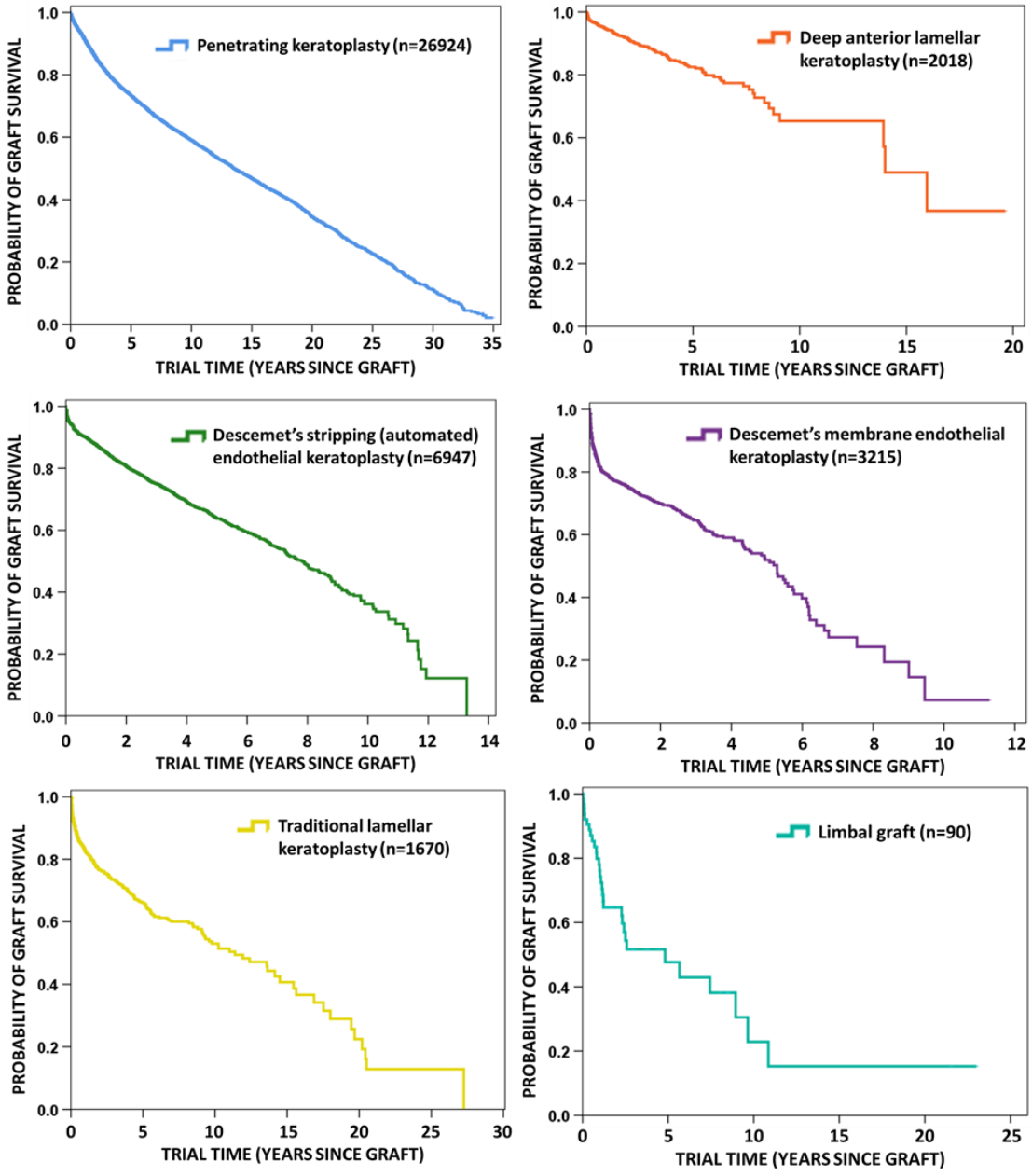


2.2 Overall survival probability

Primary graft failure was reported in 192 penetrating keratoplasty (0.7%), 18 traditional lamellar keratoplasties (1.1%), 20 deep anterior lamellar keratoplasties (1.0%), 352 Descemet's stripping (automated) endothelial keratoplasties (5.1%), 299 Descemet's membrane endothelial keratoplasties (9.3%), and 1 limbal graft (1.1%). Primary graft failure was reported for 25 pairs of cornea (i.e. both corneas from the same donor).

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 in the tables, at yearly time points, for each graft type, for as long as is relvant. The survival probabilities are not provided when fewer than 20 grafts had been followed.

Figure 1.2.1 Survival of entire cohort, for each graft type



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
PK	18393	13945	10954	8947	7392	6204	5186	4345	3718	3185
DALK	1048	693	465	322	221	143	97	53	31	20
DS(A)EK	3729	2710	1882	1310	929	597	378	223	119	56
DMEK	987	511	270	128	71	30	12	7	4	1
TLK	781	549	423	320	243	176	139	115	89	69
Limbal	41	28	17	14	12	9	9	8	4	3

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
PK	0.93	0.86	0.81	0.77	0.73	0.70	0.67	0.64	0.62	0.59
DALK	0.94	0.91	0.88	0.85	0.83	0.79	0.77	0.73	0.68	0.65
DS(A)EK	0.88	0.81	0.75	0.69	0.64	0.60	0.54	0.49	0.42	0.36
DMEK	0.76	0.70	0.65	0.59	0.52	0.40	NA	NA	NA	NA
TLK	0.83	0.77	0.74	0.70	0.66	0.62	0.60	0.60	0.58	0.53
Limbal	0.76	0.65	NA	NA	NA	NA	NA	NA	NA	NA

Number at risk (years post-graft)

	11	12	13	14	15	16	17	18	19	20
PK	2771	2393	2072	1755	1525	1309	1156	1005	887	739
DALK	13	9	8	6	4	3	3	2	1	NA
DS(A)EK	19	4	1	NA	NA	NA	NA	NA	NA	NA
DMEK	1	NA	NA	NA	NA	NA	NA	NA	NA	NA
TLK	53	42	36	27	22	18	14	11	9	7
Limbal	2	2	2	2	2	2	2	2	2	2

Probability of graft survival (years post-graft)

	11	12	13	14	15	16	17	18	19	20
PK	0.57	0.54	0.52	0.49	0.47	0.45	0.42	0.40	0.38	0.35
TLK	0.51	0.48	0.47	0.44	0.41	NA	NA	NA	NA	NA

Number at risk (years post-graft)

	21	22	23	24	25	26	27	28	29	30	31	32	33	34
PK	629	536	445	383	322	263	202	144	107	79	49	29	14	6
TLK	4	3	2	2	1	1	1	NA	NA	NA	NA	NA	NA	NA
Limbal	2	1	1	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Probability of graft survival (years post-graft)

	21	22	23	24	25	26	27	28	29	30	31	32
PK	0.32	0.30	0.27	0.25	0.23	0.20	0.18	0.15	0.13	0.11	0.09	0.07

3 Penetrating Keratoplasty

This chapter presents analyses of the 26,924 penetrating keratoplasties registered with the ACGR since the inception of the Registry in 1985. Kaplan-Meier survival analyses were conducted 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 and eye banking factors found to be **significant** in univariate analyses. The sum for each variable equals the total number of grafts (26,924 registered and 22,058 with follow-up provided) and the percentages, summed vertically for each variable, total 100.

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

Penetrating Keratoplasty

Donor and Eye Banking Factors

	Registered (%)	Followed (%)
Eye bank		
	9135 (34%)	7162 (32%)
Eye banks are not identified due to	5213 (19%)	4410 (20%)
confidentiality constraints. See	5174 (19%)	4190 (19%)
section 1.4.8 for further information.	3007 (11%)	2719 (12%)
	2686 (10%)	1921 (9%)
Not advised	1709 (6%)	1656 (8%)
Age of donor		
0 to 19 years	1021 (4%)	828 (4%)
20 to 29 years	1353 (5%)	1079 (5%)
30 to 49 years	4245 (16%)	3389 (15%)
50 to 59 years	4669 (17%)	3776 (17%)
60 to 69 years	6671 (25%)	5486 (25%)
70 to 79 years	6459 (24%)	5386 (24%)
80 years and older	2204 (8%)	1845 (8%)
Not advised	302 (1%)	269 (1%)
Sex of donor		
Female	9714 (36%)	7964 36%)
Male	16585 (62%)	13533 (61%)
Not advised	625 (2%)	561 (3%)
Cause of death		
Cardiovascular	7747 (29%)	6436 (29%)
Malignancy	6545 (24%)	5250 (24%)
Trauma	2979 (11%)	2335 (11%)
Respiratory	2523 (9%)	2106 (9%)
Intracranial/cerebral haemorrhage	4561 (17%)	3742 (17%)
Other specified	1434 (5%)	1181 (5%)
Not advised/live donor*	1135 (4%)	1008 (4%)

	Registered (%)	Followed (%)
Donor type		
Eye donor only	24281 (90%)	20082 (91%)
Solid organ and/or bone/tissue donor	2643 (10%)	1976 (9%)
Central corneal endothelial cell density		
Under 2500 cells/mm²	584 (2%)	442 (2%)
2500 to 2749 cells/mm²	1081 (4%)	748 (3%)
2750 to 2999 cells/mm²	1360 (5%)	948 (4%)
3000 to 3249 cells/mm²	1751 (7%)	1201 (5%)
3250 to 3499 cells/mm²	940 (3%)	657 (3%)
3500+ cells/mm²	613 (2%)	428 (2%)
Not advised	20595 (76%)	17634 (80%)
Storage media		
Optisol	13158 (49%)	10616 (48%)
Organ culture	4296 (16%)	2758 (13%)
Superseded media	8974 (33%)	8225 (37%)
Moist pot	333 (1%)	316 (1%)
Frozen	7 (<1%)	4 (<1%)
Not advised/autograft	156 (1%)	139 (1%)
Interstate transportation		
Same State	23818 (88%)	19240 (87%)
Different States	1397 (5%)	1162 (5%)
Not advised	1709 (6%)	1656 (8%)
Death-to-enucleation time		
Up to 3 hours	4987 (19%)	4416 (20%)
4 to 6 hours	6049 (22%)	5118 (23%)
7 to 9 hours	5660 (21%)	4692 (21%)
10 to 12 hours	4634 (17%)	3827 (17%)
13 to 15 hours	2026 (8%)	1549 (7%)
16 to 18 hours	1420 (5%)	1031 (5%)
More than 18 hours	1817 (7%)	1141 (5%)
Not advised	331 (1%)	284 (1%)
Enucleation-to-storage time		
Up to 1 hour	3310 (12%)	2924 (13%)
1 to 3 hours	12686 (47%)	10246 (46%)
4 to 6 hours	2705 (10%)	2110 (10%)
7 to 9 hours	753 (3%)	589 (3%)
10 to 12 hours	541 (2%)	455 (2%)
13 to 18 hours	864 (3%)	682 (3%)
More than 18 hours	1262 (5%)	1099 (5%)
Not advised	4803 (18%)	3953 (18%)
Storage-to-graft time - hypothermic		
Within 5 days	14253 (53%)	12374 (56%)
More than 5 days	3487 (13%)	2778 (13%)
Not advised	4392 (16%)	3689 (17%)
Not applicable	4792 (18%)	3271 (15%)
	26924 (100%)	**22058 (100%)**

*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.

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 (26,924 registered and 22,058 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

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

Penetrating Keratoplasty
Donor and Eye Banking Factors

	Registered (%)	Followed (%)
Storage-to-graft time – organ culture		
Up to 2 weeks	930 (3%)	643 (3%)
2 to 3 weeks	1651 (6%)	961 (4%)
More than 3 weeks	573 (2%)	301 (1%)
Not advised	1142 (4%)	853 (4%)
Not applicable	22628 (84%)	19300 (87%)
Chi²=2.01, df=2, p=0.367		
Deswelling-to-graft time – organ culture		
Within 2 days	798 (3%)	419 (2%)
2 to 3 days	613 (2%)	259 (1%)
More than 3 days	629 (2%)	267 (1%)
Not advised	2556 (9%)	1813 (8%)
Not applicable	22628 (84%)	19300 (87%)
Chi²=2.37, df=2, p=0.306		
	26924 (100%)	**22058 (100%)**

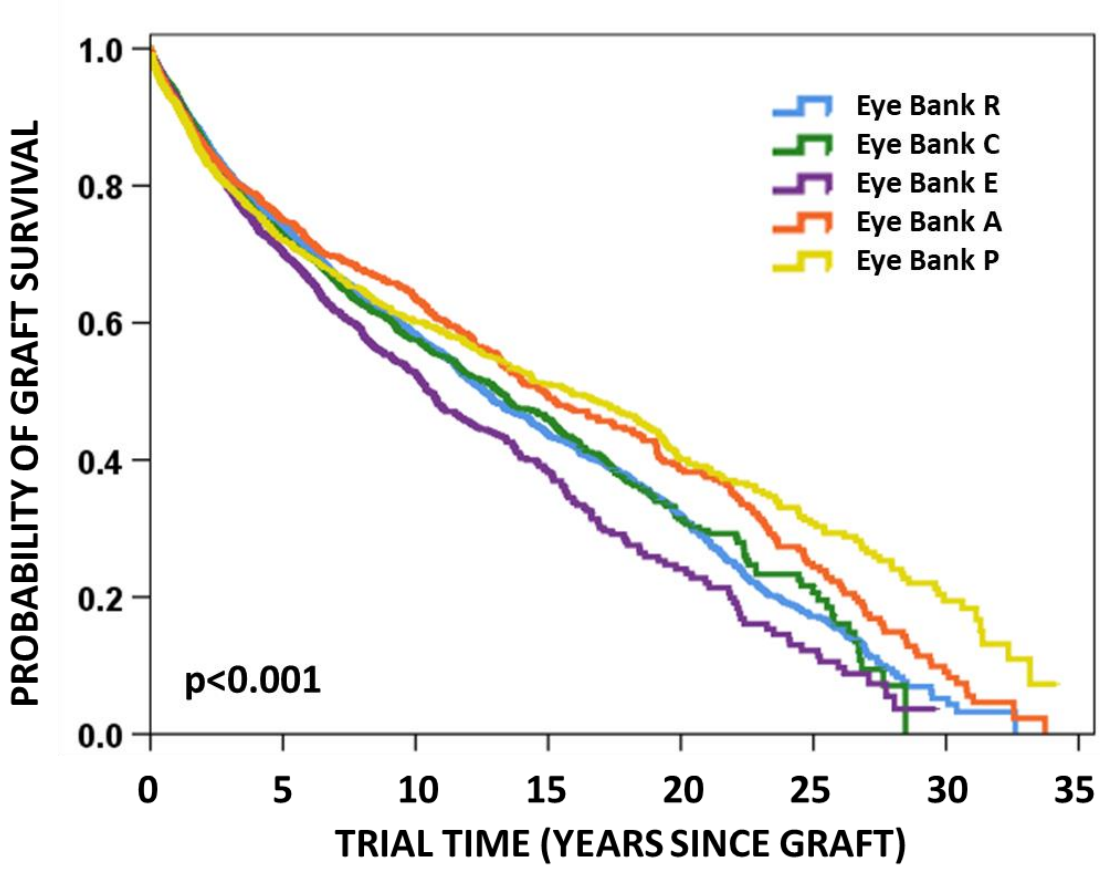
Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable.

Penetrating Keratoplasty

3.1.1 Penetrating keratoplasty 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=37.25; df=4; p<0.001), with grafts performed in State E having poorer survival than those performed in other States (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=85.06; df=5; p<0.001). However, this variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.1.1 Australian eye bank



Probability of graft survival (years post-graft)

	1	5	10	15	20
Eye Bank R	0.93	0.74	0.58	0.44	0.32
Eye Bank C	0.93	0.73	0.58	0.46	0.31
Eye Bank E	0.92	0.70	0.53	0.38	0.24
Eye Bank A	0.92	0.75	0.64	0.49	0.39
Eye Bank P	0.92	0.72	0.60	0.51	0.40

Note: Further information is not provided due to confidentiality constraints (see section 1.4.8).

3.1.2 Penetrating keratoplasty survival: influence of donor age (in years)

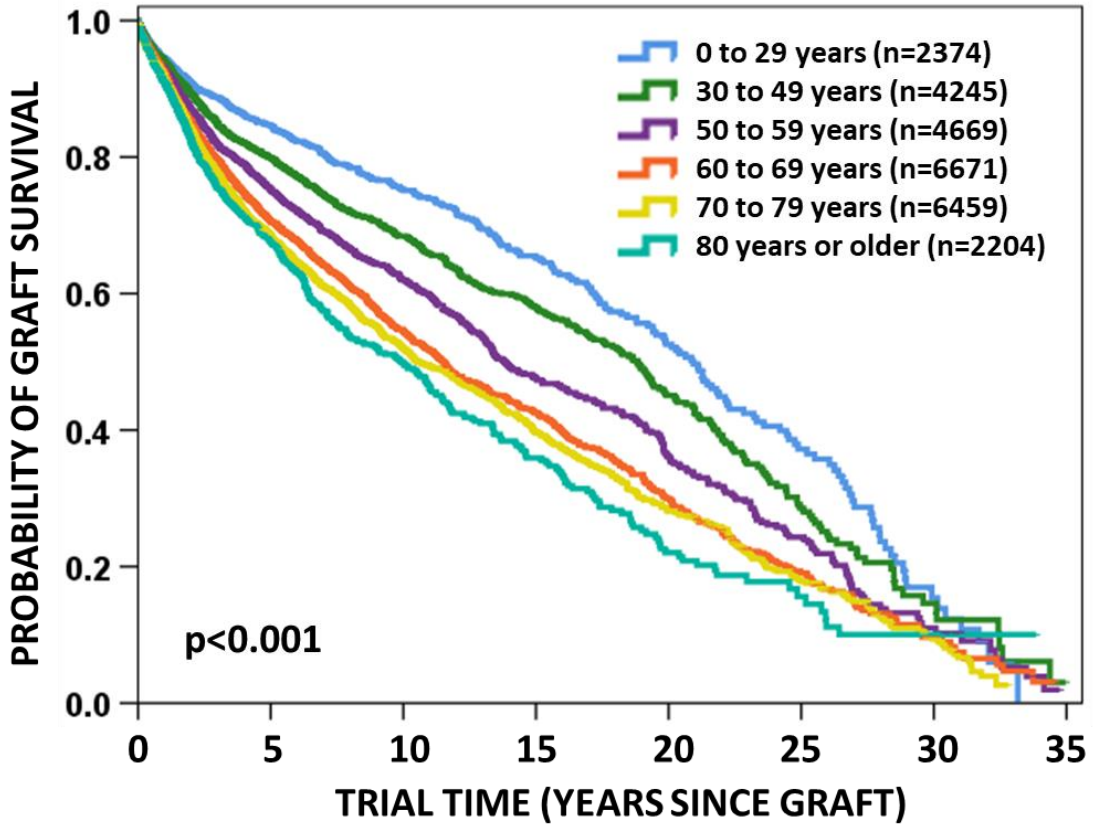
Figure 3.1.2 shows the comparison of graft survival depending on donor age. Donors were initially stratified by 10-year age groups. Donors aged under 10 years or over 90 years are rare, and so these data were combined with the adjacent age groups. A significant difference was found across groups (Log Rank Statistic=302.07; df=7; $p<0.001$).

Further analyses examined whether there were significant differences between adjacent age groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=301.13; df=5; $p<0.001$).

For each of the age group categories of 0 to 29 years, 30 to 49 years and 50 to 59 years, survival was significantly better when compared to each older donor age group (all $p<0.001$). Grafts performed using tissue from donors aged 60 to 69 years also had significantly better survival than those using tissue from donors aged 80 years and older ($p<0.001$). Data on this variable were not provided in 1% of cases and these were categorised as “not advised”. This group was excluded from further analysis. This variable was retained in the final multivariate model (see section 3.7).

Donor age group is significantly correlated with central corneal endothelial cell count (ECC) (see section 3.1.6). The proportion of donors with rates of ECC under 2500 cells/mm² increases with age ($Chi^2=187.71$, df=5, $p<0.001$). Data on ECC were unavailable for 76% of grafts and this variable was not included in the final multivariate model. It is possible that the retention of donor age group in the multivariate model reflects the influence of ECC on graft survival.

Figure 3.1.2 Donor age group



Number at risk (years post-graft)

	1	5	10	15	20	25	30
0 to 29 years	1639	759	398	198	125	53	10
30 to 49 years	2894	1223	554	286	139	52	12
50 to 59 years	3197	1345	604	283	133	63	14
60 to 69 years	4578	1744	669	295	148	60	15
70 to 79 years	4371	1648	679	328	148	72	22
80 years or older	1492	564	214	95	39	14	5

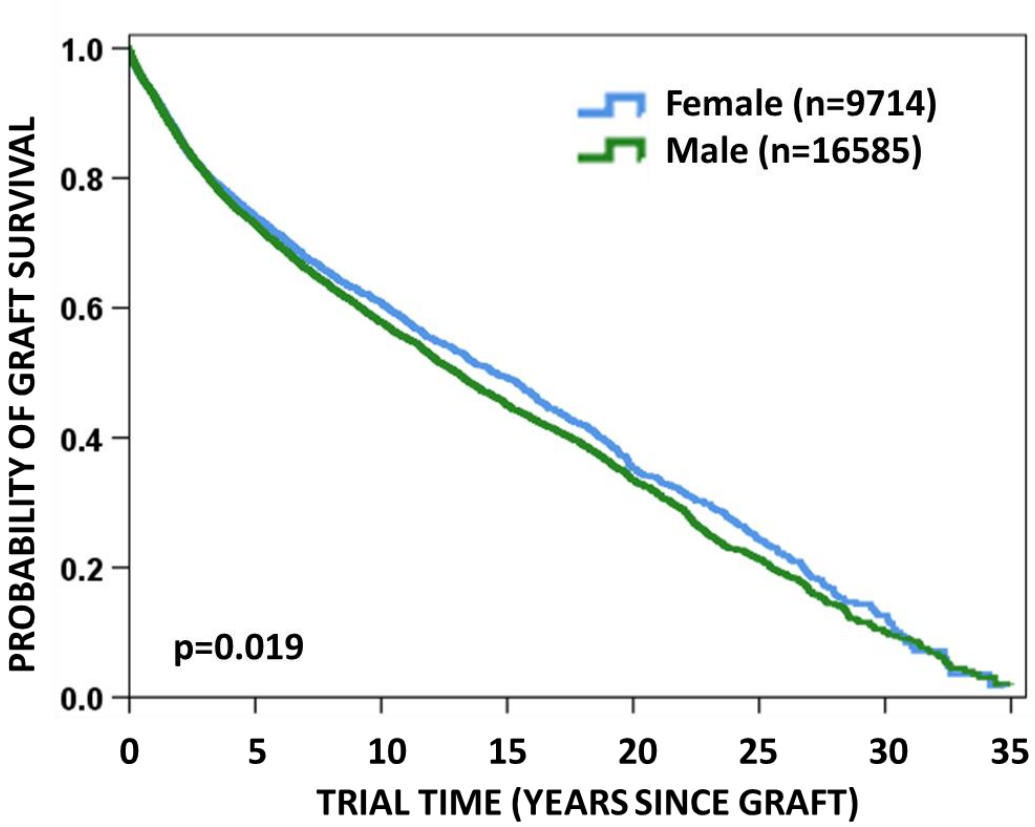
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
0 to 29 years	0.94	0.85	0.75	0.65	0.54	0.37	NA
30 to 49 years	0.94	0.80	0.68	0.58	0.45	0.29	NA
50 to 59 years	0.93	0.75	0.62	0.48	0.36	0.24	NA
60 to 69 years	0.92	0.71	0.55	0.43	0.30	0.19	NA
70 to 79 years	0.92	0.69	0.52	0.40	0.28	0.18	0.09
80 years or older	0.91	0.68	0.50	0.36	0.22	NA	NA

3.1.3 Penetrating keratoplasty survival: influence of donor sex

Almost two-thirds of corneal donors were male. Figure 3.1.3 shows the comparison of graft survival depending on donor sex. A significant difference was found between groups (Log Rank Statistic=5.48; df=1; p=0.019). Data on this variable were not provided in 2% 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=8.47; df=2; p=0.014). However, this variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.1.3 Donor sex



Number at risk (years post-graft)

	1	5	10	15	20	25	30
Female	6622	2621	1127	557	262	122	32
Male	11324	4567	1944	895	433	183	45

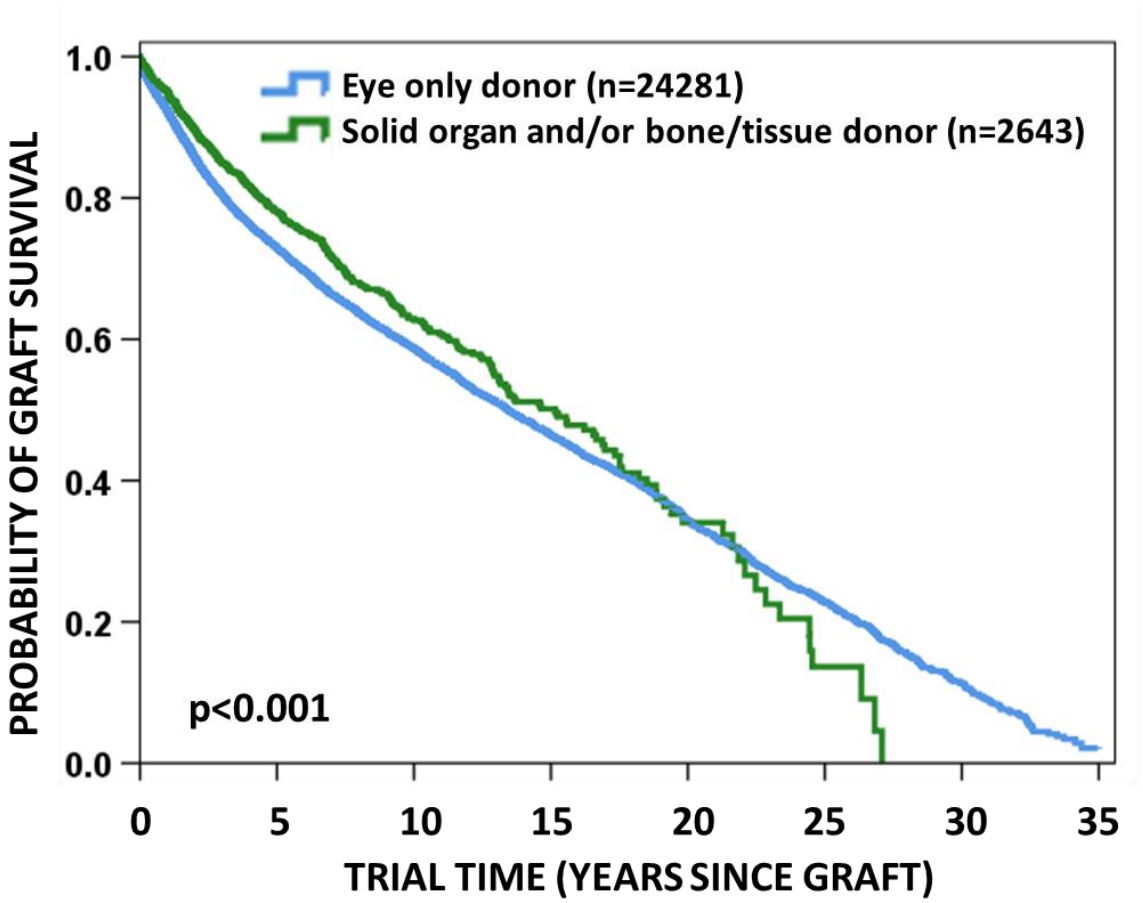
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
Female	0.93	0.74	0.61	0.49	0.35	0.24	0.13
Male	0.93	0.73	0.58	0.45	0.34	0.21	0.10

3.1.4 Penetrating keratoplasty survival: influence of donor type

Corneal donors may be eye only donors, or may also donate other bones, tissue, or solid organs. Figure 3.1.4 shows the comparison of graft survival depending on whether the donor cornea was obtained from an eye only donor. A significant difference was found between groups (Log Rank Statistic=14.39; df=1; p<0.001). However, this variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.1.4 Multi-organ donor status



Number at risk (at years post-graft)

	1	5	10	15	20	25	30
Eye only donor	16679	6757	2942	1431	712	317	79
Solid organ and/or bone/tissue donor	1714	635	243	94	27	5	NA

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

Probability of graft survival (at years post-graft)

	1	5	10	15	20	25	30
Eye only donor	0.92	0.73	0.59	0.47	0.34	0.23	0.11
Solid organ and/or bone/tissue donor	0.95	0.78	0.63	0.50	0.34	NA	NA

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

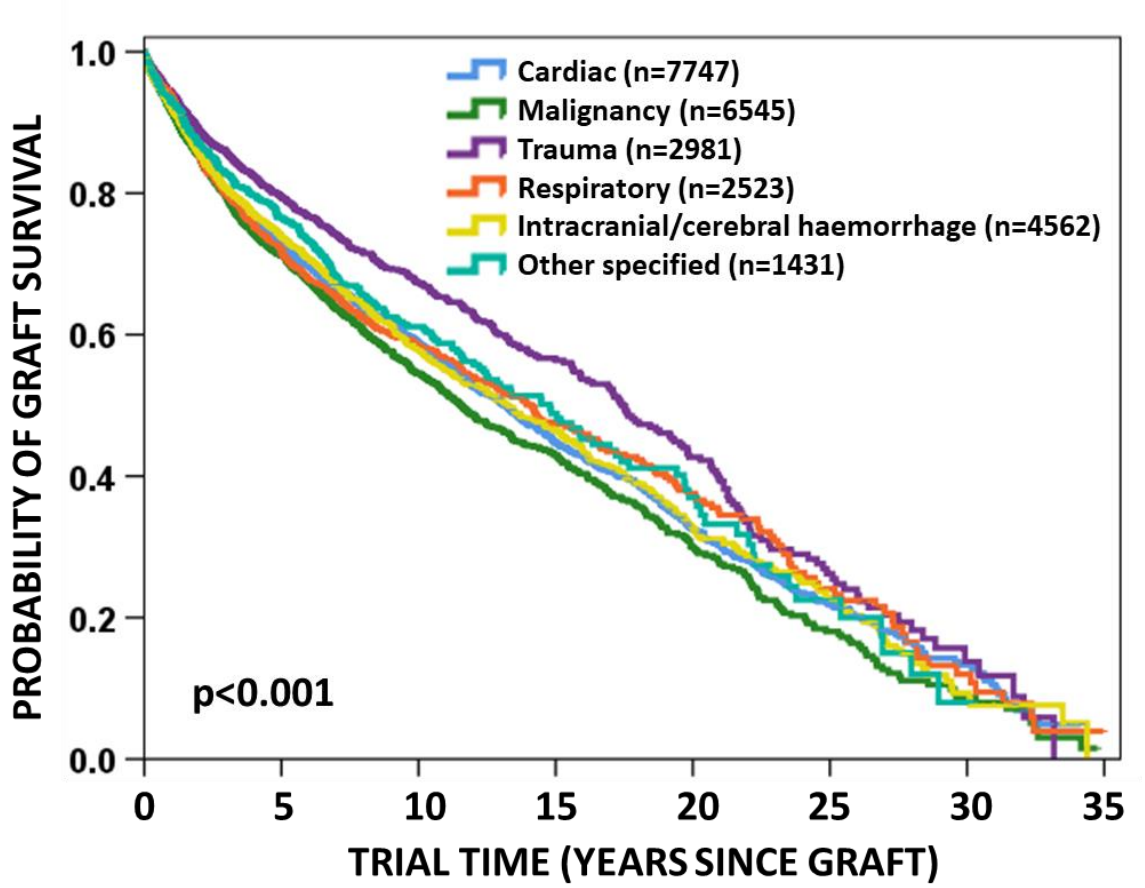
3.1.5 Penetrating keratoplasty survival: influence of cause of donor death

Figure 3.1.5 shows the comparison of graft survival depending on cause of donor death. A significant difference was found across groups (Log Rank Statistic=59.37; df=5; p<0.001). Cause of death was unknown to the ACGR for 4% of grafts and 37 grafts were performed using donor tissue from live donors. A further category was thus created called "Not advised/autograft". A significant difference was still found across groups when this category was included (Log Rank Statistic=61.85; 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). However, this variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

"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 346 cases, where the donor was listed as dying from cerebral hypoxia/ischaemia and/or brain death with no other specified cause. In 45% of these cases, the donor was a solid organ donor (compared to 9% of the overall cohort).

Figure 3.1.5 Cause of donor death



Number at risk (years post-graft)

	1	5	10	15	20	25	30
Cardiovascular	5371	2230	1019	477	224	98	25
Malignancy	4394	1611	576	245	104	45	13
Trauma	2002	860	402	188	94	37	7
Respiratory	1745	667	290	146	78	29	10
Intracranial/cerebral haemorrhage	3114	1266	526	272	128	53	11
Other specified	999	413	167	74	32	9	1

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
Cardiovascular	0.93	0.73	0.59	0.45	0.32	0.22	0.13
Malignancy	0.92	0.71	0.55	0.43	0.30	0.18	NA
Trauma	0.94	0.80	0.67	0.57	0.43	0.26	NA
Respiratory	0.93	072	0.59	0.47	0.38	0.24	NA
Intracranial/cerebral haemorrhage	0.92	0.74	0.58	0.46	0.34	0.22	NA
Other specified	0.93	0.77	0.61	0.49	0.37	NA	NA

3.1.6 Penetrating keratoplasty survival: influence of donor central corneal endothelial cell density

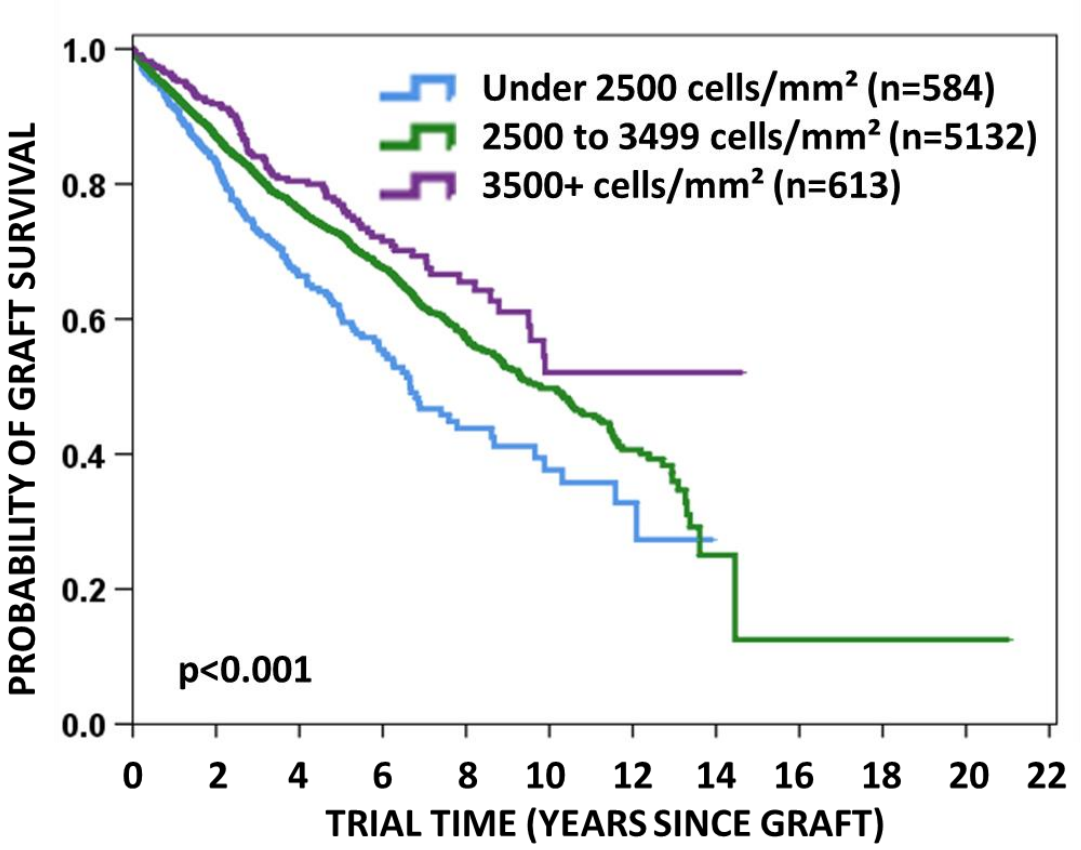
Information on donor central corneal endothelial cell count (ECC) has been requested by the Registry since 2006. ECC was reported for just under one-quarter (24%) of registered penetrating grafts. Reported ECC ranged from 1388 to 5100 cells/mm². Preliminary analyses examined survival based on groupings of 250 cells/mm² increments, with all grafts performed with donor tissue with an ECC below 2500 grouped together, and all grafts performed with donor tissue with an ECC of 3500 and above grouped together. A significant difference was found across groups (Log Rank Statistic=30.71; df=5; p<0.001).

Further analyses examined whether there were significant differences between adjacent ECC groups. There was no significant difference in survival of grafts performed using tissue from donors with ECC counts of 2500 to 2749 cells/mm², 2750 to 2999 cells/mm², 3000 to 3249 cells/mm² or 3250 to 3499 cells/mm² (p=0.257). Based on the results, three ECC groups were created for the final comparison, as shown in Figure 2.1.6, with the resulting analyses remaining significant (Log Rank Statistic=26.82; df=2; p<0.001).

Survival of grafts with fewer than 2500 cells/mm² was significantly poorer than those with 2500 to 3499 cells/mm², or 3500 or more cells/mm² (both p<0.001), and survival of grafts with 2500 to 3499 cells/mm² was significantly poorer than those with 3500 or more cells/mm² (p=0.014).

Due to the high level (76%) of missing data, this variable was not included in the multivariate analysis (see section 3.7). Endothelial cell count differed significantly across donor age groups (Chi²=187.71, df=5, p<0.001), with the proportion of donors with an ECC below 2500 cells/mm² increasing with age, and the proportion with an ECC rate of 3500 or more cells/mm² decreasing. See section 3.1.2 for further discussion on the impact of donor age.

Figure 3.1.6 Endothelial cell density



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14
Under 2500 cells/mm²	374	289	154	86	41	21	7	NA
2500 to 3499 cells/mm²	3098	2408	1355	794	406	187	71	4
3500+ cells/mm²	377	286	182	110	56	22	7	1

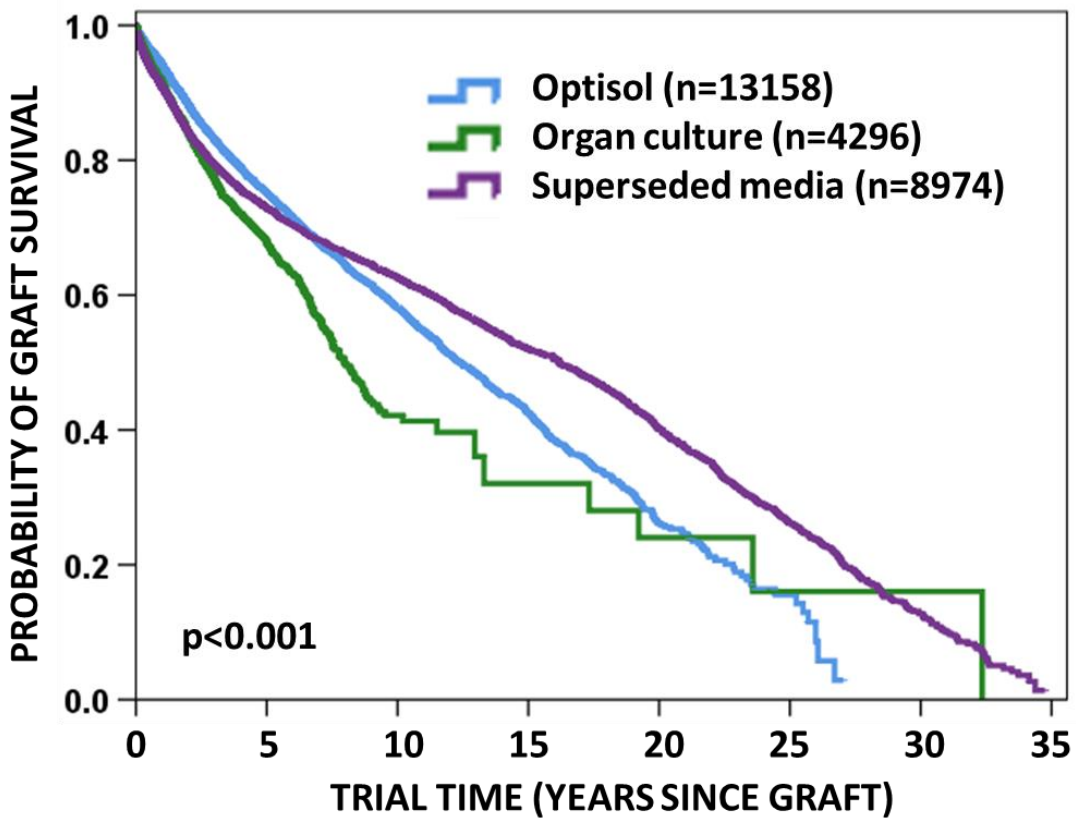
Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12
Under 2500 cells/mm²	0.91	0.83	0.66	0.55	0.44	0.38	NA
2500 to 3499 cells/mm²	0.93	0.87	0.76	0.68	0.57	0.50	0.41
3500+ cells/mm²	0.96	0.92	0.80	0.72	0.66	0.52	NA

3.1.7 Penetrating keratoplasty survival: influence of storage media

Figure 3.1.7 shows the comparison of graft survival for corneas stored using hypothermic techniques (split into Optisol and superseded media, see section 1.2 for further details) compared to organ culture medium. Data were not analysed for 333 grafts where the donor eye was stored in a moist pot, the cornea was preserved using another alternative specified method (n=7), or the eye bank did not specify which medium was used (n=156). A significant difference in outcomes was found between media (Log Rank Statistic=59.80; df=2; p<0.001). Survival of grafts stored in organ culture was significantly poorer than those stored in either Optisol or superseded hypothermic media (both p<0.001). However, this variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.1.7 Storage media



Number at risk (years post-graft)

	1	5	10	15	20	25	30
Optisol	9179	3652	1434	477	99	15	NA
Organ culture	2314	608	59	8	5	2	2
Superseded media	6534	2959	1589	978	601	282	69

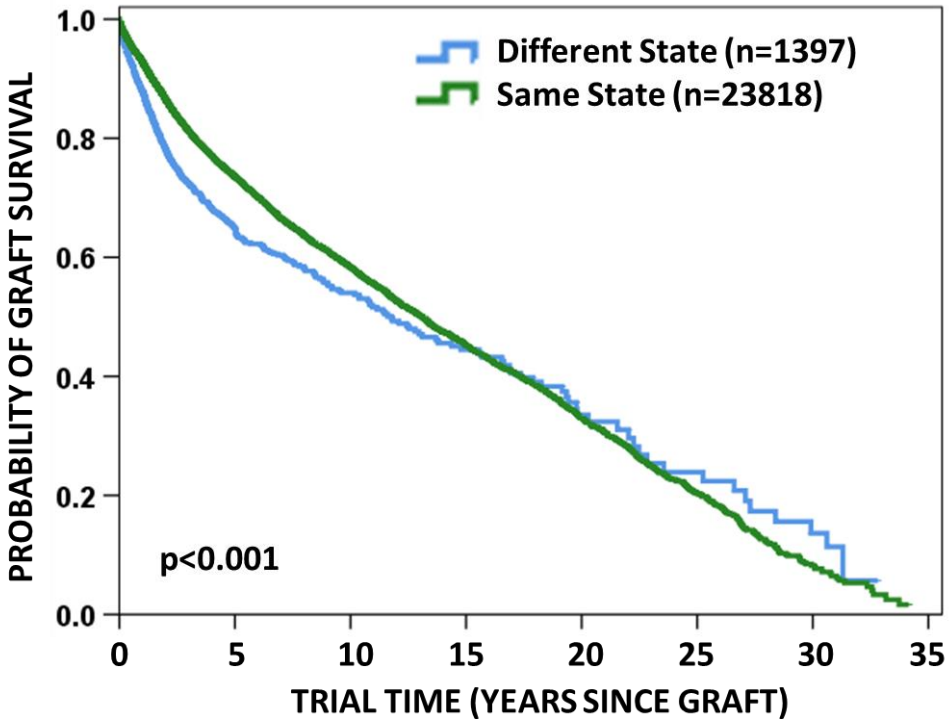
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
Optisol	.94	.75	.58	.43	.26	NA	NA
Organ culture	.92	.68	.42	NA	NA	NA	NA
Superseded media	.91	.73	.63	.52	.40	.26	.13

3.1.8 Penetrating keratoplasty survival: influence of interstate transportation

In the majority of transplants, donor corneas are sourced from the State in which the surgery occurs, however, in some cases corneas are transported interstate via air freight. Figure 3.1.8 shows the comparison of graft survival for grafts where the surgery was performed in the same State, compared to those where the donor cornea was from interstate. A significant difference was found between groups (Log Rank Statistic=18.32; df=1; p<0.001). Data for this variable were not available for the 6% of cases where the donor State was not advised (see section 3.1.1). 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=68.27; df=2; p<0.001). However, this variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.1.8 Interstate transportation



Number at risk (years post-graft)

	1	5	10	15	20	25	30
Different State	933	369	172	80	32	16	6
Same State	16060	6289	2589	1190	553	206	31

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
Different State	0.88	0.65	0.54	0.45	0.34	NA	NA
Same State	0.93	0.74	0.58	0.45	0.33	0.20	0.08

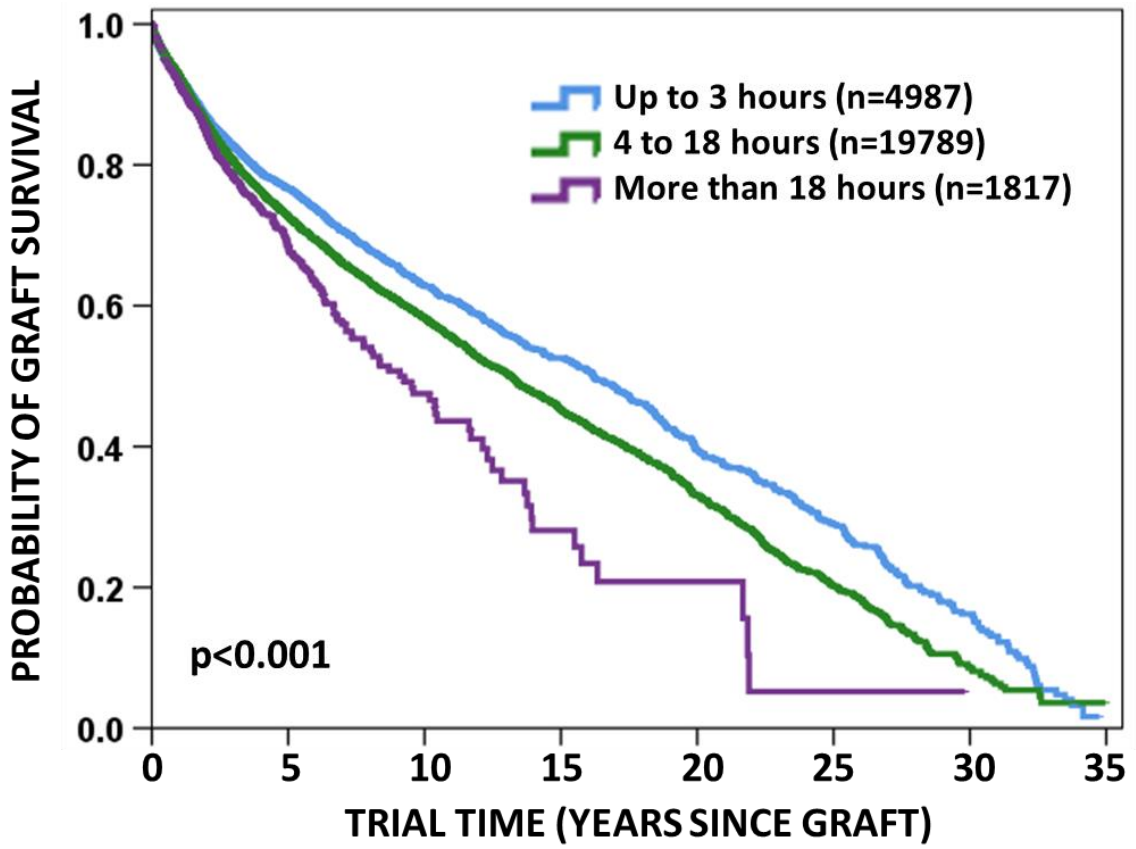
3.1.9 Penetrating keratoplasty survival: influence of death-to-enucleation time

Donor corneas are retrieved as soon as possible following donor death. Retrieval is recommended within the first 18 hours and 93% of donor eyes were enucleated within this time-frame. Times are rounded down to the nearest hour and the median time from donor death to enucleation was 8 hours (range 0-46 hours).

Figure 3.1.9 shows a comparison of graft survival depending on time from donor death to enucleation. Times were initially stratified into three-hourly groups. Very few enucleations occur within the hour following donor death and so these were combined with those performed between 1 to 3 hours. A significant difference was found across time groups (Log Rank Statistic=54.14; df=6; $p<0.001$). Further analyses examined whether there were significant differences between adjacent time groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=46.31; df=2; $p<0.001$).

Data on this variable were not provided in 1% of cases and these were categorised as “not advised”. This was not a sufficient proportion of the cohort to include this group in further analysis. Grafts performed using donor tissue collected within 3 hours since donor death had better survival than those for which the tissue was collected 4 to 18 hours, or more than 18 hours, after death (both $p<0.001$). Grafts performed using donor tissue collected 4 to 18 hours after death had better survival than those collected more than 18 hours after death ($p<0.001$). However, this variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.1.9 Time from donor death to enucleation



Number at risk (years post-graft)

	1	5	10	15	20	25	30
Up to 3 hours	3711	1705	847	480	256	133	43
4 to 18 hours	13512	5330	2217	996	462	178	33
More than 18 hours	932	233	54	13	5	1	NA

Probability of graft survival (years post-graft)

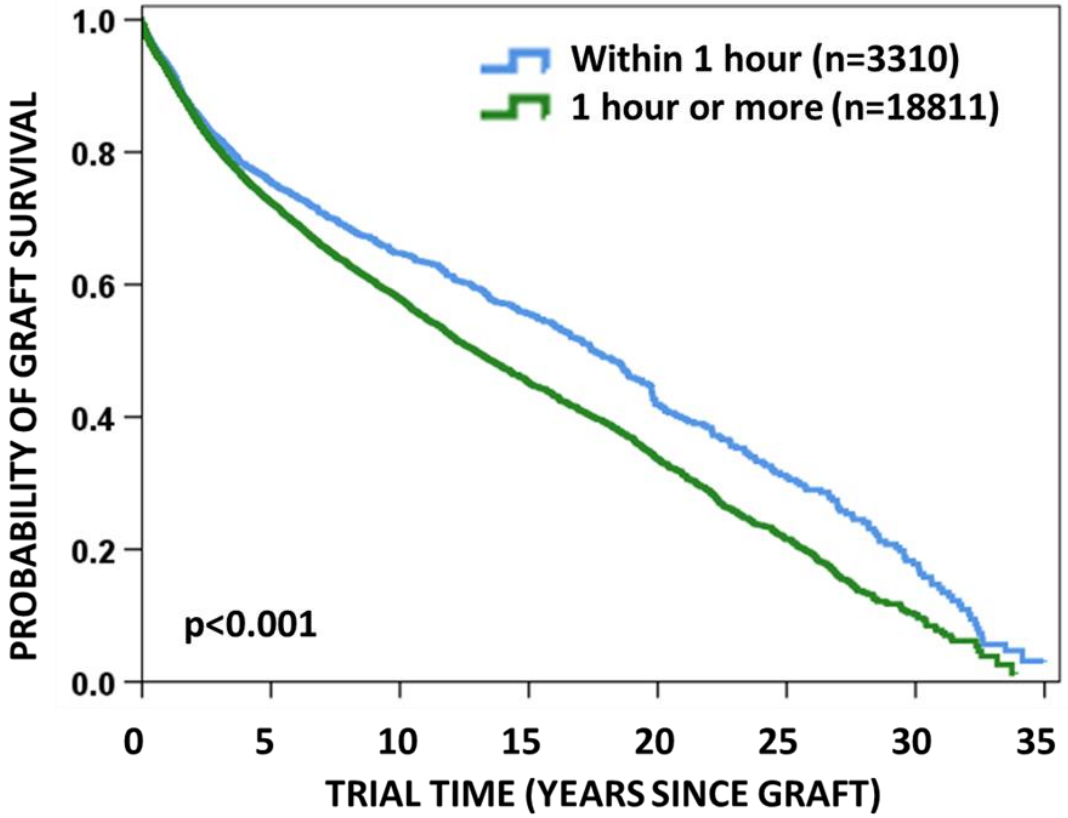
	1	5	10	15	20	25	30
Up to 3 hours	0.93	0.77	0.63	0.53	0.40	0.29	0.16
4 to 18 hours	0.93	0.73	0.58	0.45	0.33	0.20	0.09
More than 18 hours	0.92	0.68	0.48	NA	NA	NA	NA

3.1.10 Penetrating keratoplasty survival: influence of enucleation-to-storage time

Figure 3.1.10 shows a comparison of graft survival depending on time from enucleation of the donor cornea to initial storage in preservation media. Times were initially stratified into those that were stored immediately (within 1 hour of enucleation) and then in three-hourly groups. Due to low numbers in the categories 13 to 15 hours and 16 to 18 hours, these groups were combined. A significant difference was found across time groups (Log Rank Statistic=36.28; df=6; p<0.001). Further analyses examined whether there were significant differences between adjacent time groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=32.69; df=1; p<0.001).

Data on this variable were not provided in 18% of cases and these were categorised as "not advised". A significant difference was still found across groups when this category was included (Log Rank Statistic=33.77; df=1; p<0.001). However, this variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.1.10 Time from enucleation to storage



Number at risk (years post-graft)

	1	5	10	15	20	25	30
Within 1 hour	2496	1156	611	348	169	86	36
1 hour or more	12515	4806	2028	983	500	210	39

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
Within 1 hour	0.93	0.76	0.65	0.56	0.42	0.31	0.16
1 hour or more	0.92	0.72	0.58	0.45	0.34	0.22	0.10

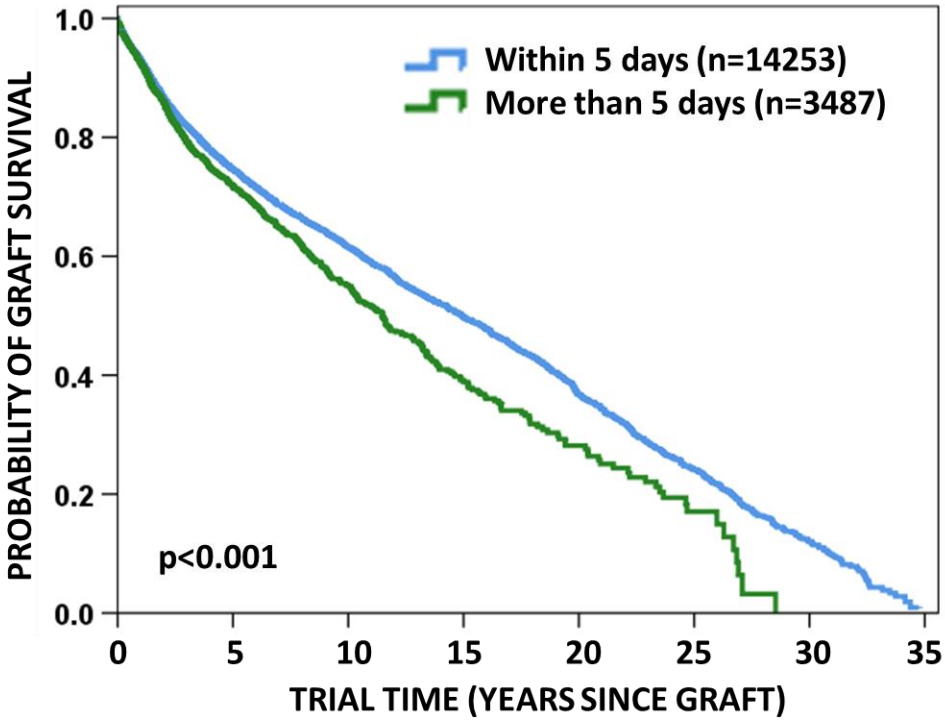
3.1.11 Penetrating keratoplasty survival: influence of storage-to-graft time in hypothermic media

Figure 3.1.11 shows a comparison of graft survival depending on time from initial storage of the donor cornea in hypothermic preservation media (Optisol or superseded media) to graft. Times were initially stratified into daily groups. A significant difference was found across time groups (Log Rank Statistic=32.38; df=7; p<0.001). Further analyses examined whether there were significant differences between adjacent time groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=23.27; df=1; p<0.001).

This variable was not applicable for the 4792 corneas not stored in hypothermic solution and the data for these grafts were excluded from the analysis. Data on this variable were not provided in 16% of cases and these were categorised as “not advised”. A significant difference was still found across groups when this category was included (Log Rank Statistic=24.23; df=1; p<0.001).

This variable was combined with the variable relating to type of storage media (see section 3.1.7) for the multivariate analysis (see section 3.7). However, this combined variable was not retained in the final model, suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.1.11 Time from storage to graft for hypothermic media



Number at risk (years post-graft)

	1	5	10	15	20	25	30
Within 5 days	10338	4429	2072	1073	532	230	59
More than 5 days	2303	841	346	123	48	13	NA

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
Within 5 days	0.93	0.75	0.62	0.50	0.37	0.24	0.12
More than 5 days	0.93	0.72	0.55	0.39	0.28	NA	NA

3.2 Recipient Factors

Table 3.3 shows the number of grafts reported for each indication for graft. It also shows further sub-group breakdowns for each indication group. This breakdown is shown for all 26,924 registered grafts as well as for the 22,058 followed grafts. The total for each of the indication groups is the sum of the sub-categories shown below.

Table 3.3 Indication for graft

Penetrating Keratoplasty
Indication for Graft

	Registered (%)	Followed (%)
Keratoconus*	**8135 (30%)**	**6716 (30%)**
Uncomplicated	7597 (28%)	6322 (29%)
With hydrops	538 (2%)	394 (2%)
Failed previous graft/s	**7328 (27%)**	**5765 (26%)**
Bullous keratopathy/endothelial failure	**4603 (17%)**	**3921 (18%)**
Pseudophakic	3641 (14%)	3093 (14%)
Aphakic	677 (3%)	580 (3%)
Phakic	285 (1%)	248 (1%)
Corneal dystrophy**	**2468 (9%)**	**2167 (10%)**
Fuchs' (endothelial)	2100 (8%)	1852 (8%)
Granular (epithelial/stromal)	76 (<1%)	60 (<1%)
Macular (stromal)	60 (<1%)	46 (<1%)
Lattice (epithelial/stromal)	58 (<1%)	51 (<1%)
Posterior polymorphous (endothelial)	35 (<1%)	32 (<1%)
Reis-Bücklers (epithelial/stromal)	14 (<1%)	11 (<1%)
Schnyder (stromal)	12 (<1%)	11 (<1%)
Congenital hereditary (endothelial)	9 (<1%)	7 (<1%)
Francois (Stromal)	2 (<1%)	2 (<1%)
Thiel-Behnke (Epithelial/stromal)	1 (<1%)	1 (<1%)
Congenital (stromal)	1 (<1%)	1 (<1%)
Gelatinous drop-like (epithelial)	1 (<1%)	1 (<1%)
Unspecified endothelial	84 (<1%)	79 (<1%)
Unspecified stromal	12 (<1%)	10 (<1%)
Unspecified epithelial	3 (<1%)	3 (<1%)
Herpetic eye disease	**1238 (5%)**	**1019 (5%)**
Inactive HSV, no perforation	724 (3%)	617 (3%)
Herpes zoster, no perforation	130 (<1%)	105 (<1%)
Active HSV, no perforation	86 (<1%)	72 (<1%)
HSV with perforation	298 (1%)	225 (1%)

	Registered (%)	Followed (%)
Trauma	**724 (3%)**	**568 (3%)**
Penetrating eye injury	257 (1%)	199 (1%)
Burns	101 (<1%)	85 (<1%)
Blunt injury	32 (<1%)	28 (<1%)
Surgical complications	29 (<1%)	20 (<1%)
Traumatic rupture	16 (<1%)	11 (<1%)
Foreign body	8 (<1%)	7 (<1%)
Unspecified	281 (1%)	218 (1%)
Non-herpetic infections	**614 (2%)**	**437 (2%)**
Microbial keratitis (excluding Pseudomonas)	204 (1%)	141 (1%)
Mycoticulcer/fungal keratitis	106 (<1%)	77 (<1%)
Pseudomonas keratitis	69 (<1%)	42 (<1%)
Trachoma	59 (<1%)	49 (<1%)
Acanthamoeba keratitis	46 (<1%)	35 (<1%)
Endophthalmitis	14 (<1%)	11 (<1%)
Viral keratitis (not HSV/HZO)	13 (<1%)	11 (<1%)
Unspecified keratitis	103 (<1%)	71 (<1%)
Corneal ulcers/perforation	**577 (2%)**	**438 (2%)**
Perforated	471 (2%)	349 (2%)
No perforation	106 (<1%)	89 (<1%)
Other* **	**1237 (5%)**	**1027 (5%)**
Total	***26924 (100%)***	***22058 (100%)***

*In April 2015, *Gomes et al* [see reference 8], 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". Data published in previous ACGR reports up to 2015 included keratoglobus with keratoconus. This report separates keratoglobus cases from keratoconus and classifies them under "Other".

**In February 2015 Weiss et al [see reference 9] 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 since the 2018 ACGR Report. In the subsequent survival analyses, Fuchs' endothelial dystrophies are analysed separately, with all other dystrophies included in the "Other" indications category.

***Other included: corneal scarring/opacity not further specified (334), interstitial keratitis (159), pellucid marginal degeneration (127), iridocorneal endothelial syndrome (91), Peters' anomaly (36), corneal scarring/opacity with cataract (34), unknown (34), band keratopathy 23), descemetocoele (20), keratoglobus (17), lipid keratopathy (17), pterygium (17), cataract not further specified (16), Axenfeld-Reiger syndrome (13), corneal ectasia (13), corneal melt (13), mucopolysaccharidosis (13), congenital glaucoma (12), aniridia (10), corneal leukoma of unspecified cause (9), Terrien's marginal degeneration (9), autograft (8), congenital rubella (8), corneal neovascularisation (8), epithelial defects (8), irregular astigmatism (8), Salzmann's nodular degeneration (8), beta radiation (7), congenital cataract (7), glaucoma (7), retinal detachment (7), blood staining (6), cystinosis (6), keratoconjunctivitis (6), malignancy (6), rosacea (6),

congenital corneal opacity (5), Descemet's membrane detachment (5), anterior segment dysgenesis (4), astigmatism (4), corneal membrane change (4), corneal staphyloma (4), dermoid (4), pemphigoid (4), suppurative keratitis (4), congenital corneal calcification (3), congenital syphilis (3), corneal scarring post radial keratotomy (3), ichthyosis (3), scleral necrosis (3), amyloidosis (2), brittle cornea syndrome (2), climatic droplet keratopathy (2), congenital microphthalmia (2), corneal pigmentation (2), corneal thinning (2), epithelial downgrowth (2), heterochromic cyclitis (2), lecithin cholesterol acyltransferase deficiency (2), monoclonal gammopathy (2), myopia (2), nystagmus with corneal opacity (2), porphyria (2), rheumatoid arthritis with scarring (2), Stevens-Johnson syndrome (2), unspecified keratopathy (2), anterior chamber clearage syndrome (1), buphthalmos (1), childhood fever (1), cholesterol metabolic disorder (1), cone dystrophy (1), corneal hydrops of unspecified cause (1), corneal instability (1), corneal thickening (1), Crouzon's syndrome (1), Descemet's membrane tear (1),dry eye syndrome with scarring (1), dyskeratosis (1),exudative macular degeneration (1), hypopyon (1), limbal stem cell failure with scarring (1), neuroparalytic keratitis (1), ocular surface dysplasia (1), osteogenesis imperfecta (1), phthisis (1), pseudoexfoliation syndrome (1), retinopathy of prematurity (1), Rothmund-Thomson syndrome (1), scleral melt (1), Silver-Russell syndrome (1), Sjogren's syndrome (1), synechia (1), vitamin A deficiency (1), Weill-Marchesani syndrome (1), wound dehiscence following IOL insertion (1).

Table 3.4 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 (26,924 registered and 22,058 followed) and the percentages, which should be summed vertically for each variable, total 100. The data are presented in the following sections.

Table 3.4 Summary table of recipient factors, significant in univariate analyses

Penetrating Keratoplasty

Recipient Factors

	Registered (%)	Followed (%)
Prior ipsilateral corneal graft/s		
None	19583 (73%)	16285 (74%)
One	5245 (19%)	4114 (19%)
Two	1323 (5%)	1043 (5%)
Three or more	773 (3%)	616 (3%)
Australian State where graft was performed		
States are not identified due to confidentiality constraints. See section 1.4.8 for further information.	9346 (35%)	7358 (33%)
	5772 (21%)	4972 (23%)
	5467 (20%)	4530 (21%)
	3093 (11%)	2227 (10%)
	2609 (10%)	2387 (11%)
	634 (2%)	583 (3%)
	3 (<1%)	1 (<1%)

	Registered (%)	Followed (%)
Recipient age group		
0 to 19 years	1165 (4%)	995 (5%)
20 to 29 years	3474 (13%)	2861 (13%)
30 to 39 years	3102 (12%)	2572 (12%)
40 to 49 years	2953 (11%)	2393 (11%)
50 to 59 years	3062 (11%)	2502 (11%)
60 to 69 years	4044 (15%)	3333 (15%)
70 to 79 years	5355 (20%)	4411 (20%)
80 years or older	3761 (17%)	2984 (14%)
Not advised	8 (<1%)	7 (<1%)
Pre-graft corneal neovascularisation		
None	17987 (67%)	14936 (68%)
One quadrant	2401 (9%)	1825 (8%)
Two quadrants	2895 (11%)	2313 (10%)
Three quadrants	1320 (5%)	1081 (5%)
Four quadrants	2321 (9%)	1903 (9%)
Pre-graft inflammation and/or steroid use		
No	18717 (70%)	15445 (70%)
Yes	7711 (29%)	6231 (28%)
Not advised	496 (2%)	382 (2%)
Presence of raised intraocular pressure		
IOP never known to be raised	22572 (84%)	18495 (84%)
IOP raised in past and/or at graft	4352 (16%)	3563 (16%)
Prior contralateral corneal graft/s		
None	21014 (78%)	17239 (78%)
One	4737 (18%)	3895 (18%)
Two or more	1173 (4%)	924 (4%)
Prior intraocular surgery in first grafts		
No	12533 (47%)	10446 (47%)
Yes	6941 (26%)	5764 (26%)
Not advised	109 (<1%)	75 (<1%)
Not applicable (repeat and/or prior concurrent)	7341 (27%)	5773 (26%)
Total	***26924 (100%)***	***22058 (100%)***

Three-hundred-and-seventy-one penetrating keratoplasties had been converted from a planned lamellar procedure: 328 DALK, nine DS(A)EK, five DMEK, three peripheral patch, three mushroom tuck-in, and 23 unspecified. Forty-Six had a previous known surviving concurrent graft (limbal or lamellar patch). One-hundred-and-two eyes undergoing penetrating keratoplasty had a history of corneal cross-linking.

Table 3.5 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 (26,924 registered and 22,058 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

Table 3.5 Recipient factors, not significant in univariate analyses

Penetrating Keratoplasty

Recipient Factors

	Registered (%)	Followed (%)
Recipient sex		
Male	14225 (53%)	11504 (52%)
Female	12699 (47%)	10554 (48%)
Chi²=0.02, df=1, p=0.887		
Donor/recipient sex match		
Female/female	4615 (17%)	3845 (17%)
Female/male	5099 (19%)	4119 (19%)
Male/female	7778 (29%)	6431 (29%)
Male/male	8807 (33%)	7102 (32%)
Not advised	625 (2%)	561 (3%)
Chi²=5.90, df=3, p=0.117		
Eye grafted		
Left	13387 (50%)	10954 (50%)
Right	13527 (50%)	11097 (50%)
Not advised	10 (<1%)	7 (<1%)
Chi²=1.04, df=1, p=0.307		
Total	**26924 (100%)**	**22058 (100%)**

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

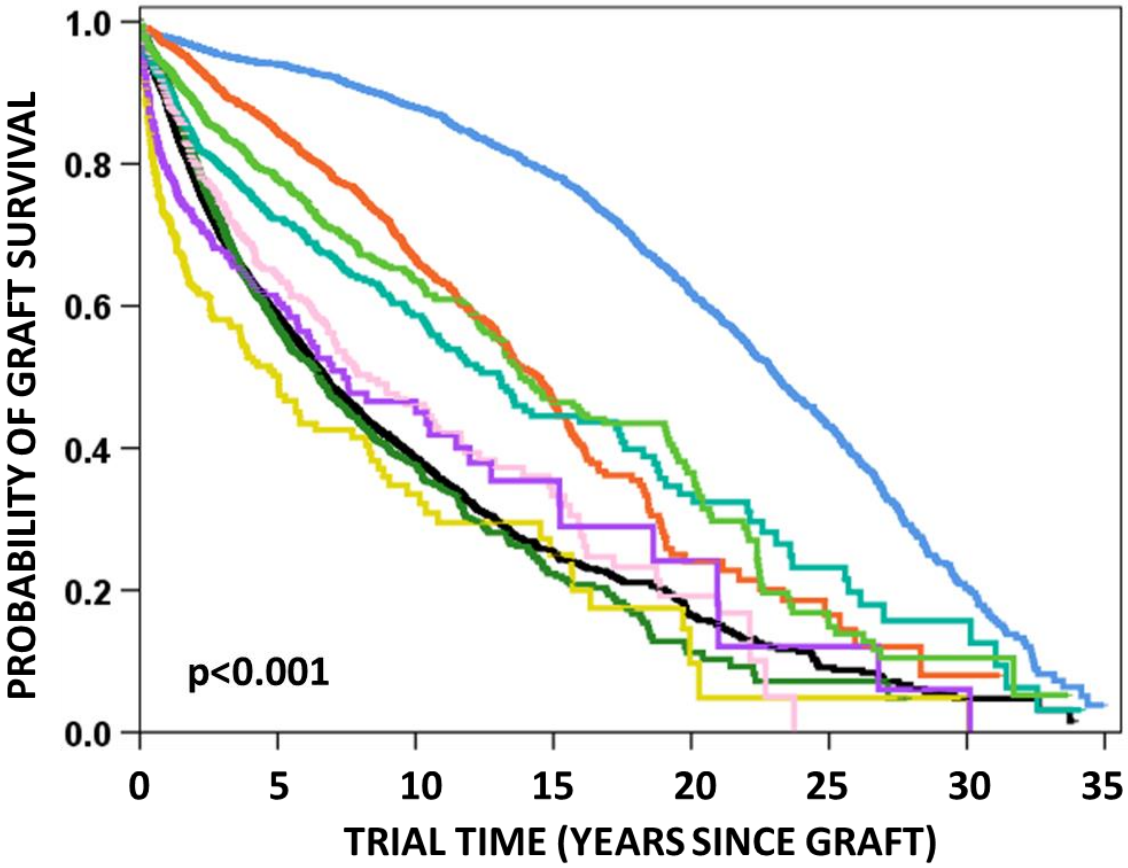
3.2.1 Penetrating keratoplasty survival: influence of indication for graft

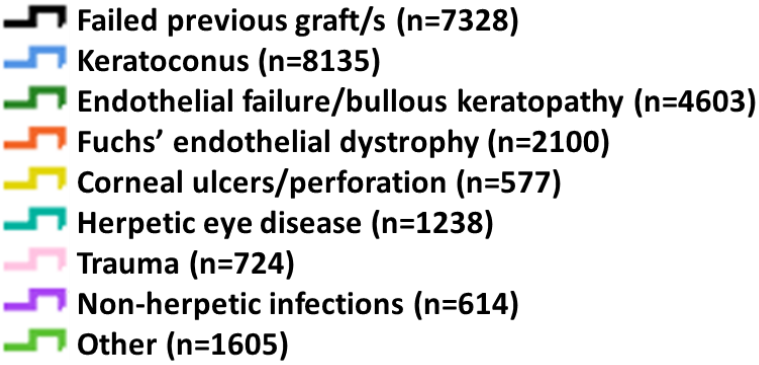
Figure 3.2.1 shows the comparison of graft survival depending on indication for graft. All repeat grafts were analysed together, regardless of original pathology. A significant difference was found across groups (Log Rank Statistic=2707.64; df=8; p<0.001).

Grafts performed for keratoconus had better survival than those performed for any other indication. Grafts performed for corneal ulcers/perforation had poorer survival than those performed for any other indication. Grafts performed for Fuchs' endothelial dystrophy had better survival than those performed for any other indication aside from keratoconus and "other" indications. Additionally, grafts performed for 'other' indications had better survival than those performed for failed previous grafts, bullous keratopathy/endothelial failure, trauma and non-herpetic infections. Grafts performed for herpetic keratitis had better survival than those performed for failed previous grafts, bullous keratopathy/endothelial failure, trauma and non-herpetic infections. All comparisons were significant at the p<0.001 level, except non-herpetic infection versus corneal ulcers/perforations (p=0.004).

This variable was combined with the variable relating to number of previous ipsilateral grafts (see section 3.2.2) for the multivariate analysis (see section 3.7). This combined variable was retained in the final model.

Figure 3.2.1 Indication for graft





Number at risk (years post-graft)

	1	5	10	15	20	25	30
Failed previous graft/s	4660	1632	547	195	80	24	5
Keratoconus	6034	2850	1556	955	531	253	64
Endothelial failure/bullous keratopathy	3047	853	235	64	14	5	NA
Fuchs' endothelial dystrophy	1679	917	396	118	25	8	1
Corneal ulcers/perforation	251	73	25	11	2	1	1
Herpetic eye disease	838	313	133	60	30	14	5
Trauma	466	172	58	24	8	NA	NA
Non-herpetic infections	296	102	30	11	4	2	1
Other	1122	480	205	87	45	15	2

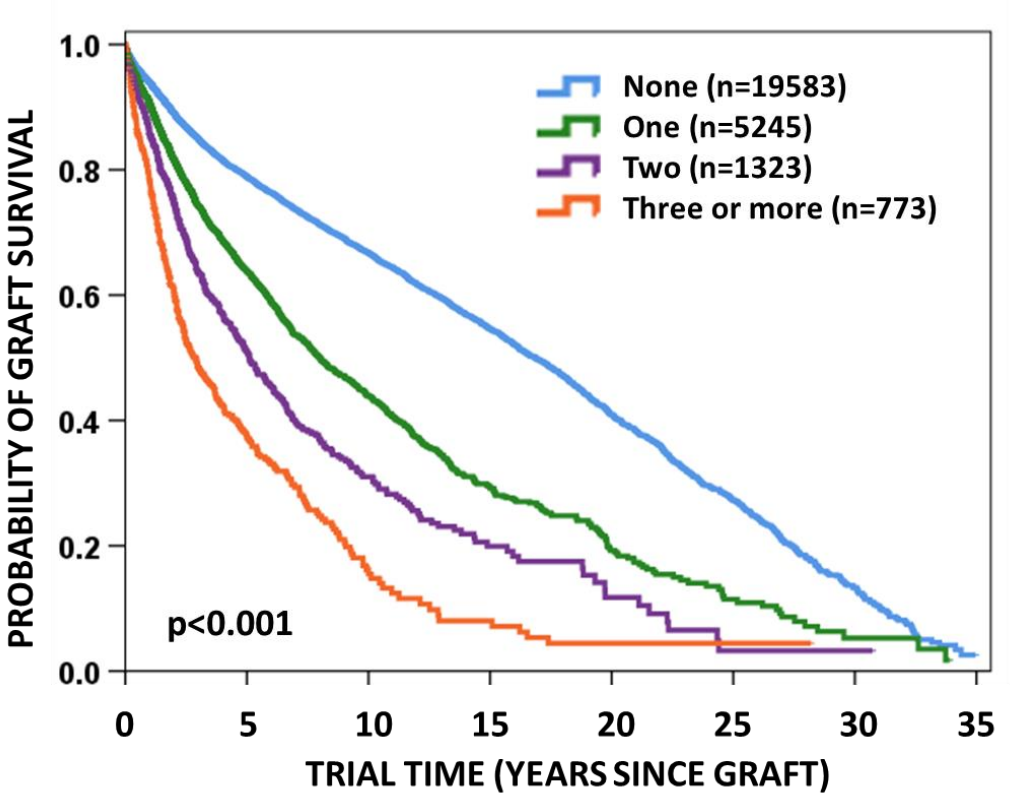
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
Failed previous graft/s	0.89	0.59	0.39	0.25	0.16	0.09	NA
Keratoconus	0.98	0.94	0.88	0.78	0.62	0.43	0.20
Endothelial failure/bullous keratopathy	0.91	0.57	0.38	0.22	NA	NA	NA
Fuchs' endothelial dystrophy	0.97	0.85	0.67	0.47	0.24	NA	NA
Corneal ulcer/perforation	0.73	0.50	0.34	NA	NA	NA	NA
Herpetic eye disease	0.91	0.72	0.59	0.45	0.34	NA	NA
Trauma	0.89	0.64	0.46	0.33	NA	NA	NA
Non-herpetic infections	0.79	0.61	0.47	NA	NA	NA	NA
Other	0.93	0.78	0.64	0.46	0.37	NA	NA

3.2.2 Penetrating keratoplasty 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 0 to 13). Previous grafts may not have been penetrating keratoplasties, and the type is unknown in the majority (85%) of cases. Survival, shown in Figure 3.2.2 decreased (Log Rank Statistic=1337.62, df=3, p<0.001) as the number of grafts increased. This variable was combined with the variable relating to overall indication for graft (see section 3.2.1) for the multivariate analysis (see section 3.7). This combined variable was retained in the final model.

Figure 3.2.2 Number of previous ipsilateral grafts



Number at risk (years post-graft)

	1	5	10	15	20	25	30
None	13727	5756	2637	1329	659	298	74
One	3395	1264	444	160	67	21	4
Two	823	253	80	27	9	2	1
Three or more	448	119	24	9	4	1	NA

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
None	0.94	0.79	0.67	0.55	0.41	0.27	0.13
One	0.91	0.64	0.44	0.29	0.19	0.12	NA
Two	0.86	0.51	0.31	0.20	NA	NA	NA
Three or more	0.78	0.38	0.16	NA	NA	NA	NA

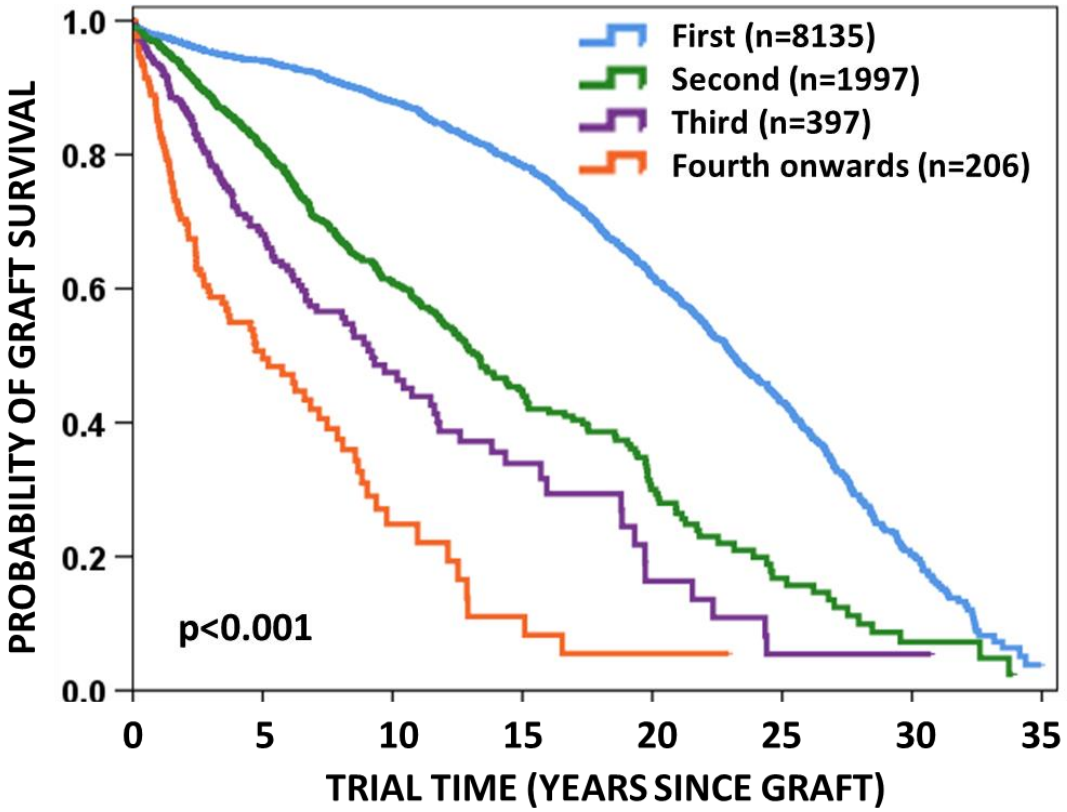
3.2.3 Penetrating keratoplasty survival: indication subcategory analyses

The analyses on pages 47 to 54 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.

3.2.3.1 Penetrating keratoplasty survival: influence of keratoconus factors

Figure 3.2.3 shows the comparison of graft survival for first versus repeat grafts for keratoconus. A significant difference was found across groups (Log Rank Statistic=829.34; df=3; p<0.001).

Figure 3.2.3 First versus subsequent grafts for keratoconus



Number at risk (years post-graft)

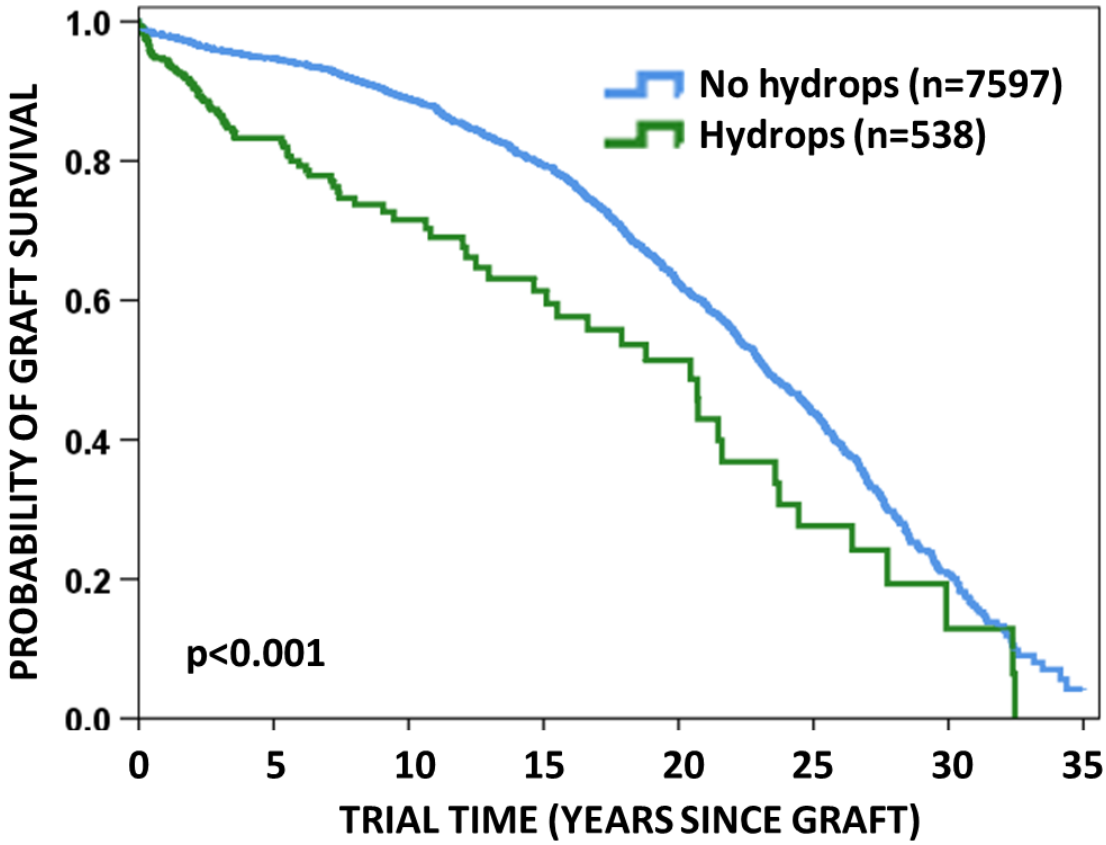
	1	5	10	15	20	25	30
First graft	6034	2850	1556	955	531	253	64
Second graft	1371	612	233	93	44	16	4
Third graft	268	104	40	13	6	2	1
Fourth graft onwards	131	44	11	4	2	NA	NA

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
First graft	0.98	0.94	0.88	0.78	0.62	0.43	0.20
Second graft	0.97	0.81	0.61	0.44	0.30	NA	NA
Third graft	0.93	0.68	0.48	NA	NA	NA	NA
Fourth graft onwards	0.84	0.50	NA	NA	NA	NA	NA

Figure 3.2.4 shows the comparison of graft survival for first grafts for keratoconus where the eye had corneal hydrops versus where it did not. A significant difference was found across groups (Log Rank Statistic=51.57; df=1; p<0.001).

Figure 3.2.4 Keratoconus without hydrops versus keratoconus with hydrops



Number at risk (years post-graft)

	1	5	10	15	20	25	30
No hydrops	5696	2718	1496	921	512	244	62
Hydrops	338	132	60	34	19	9	2

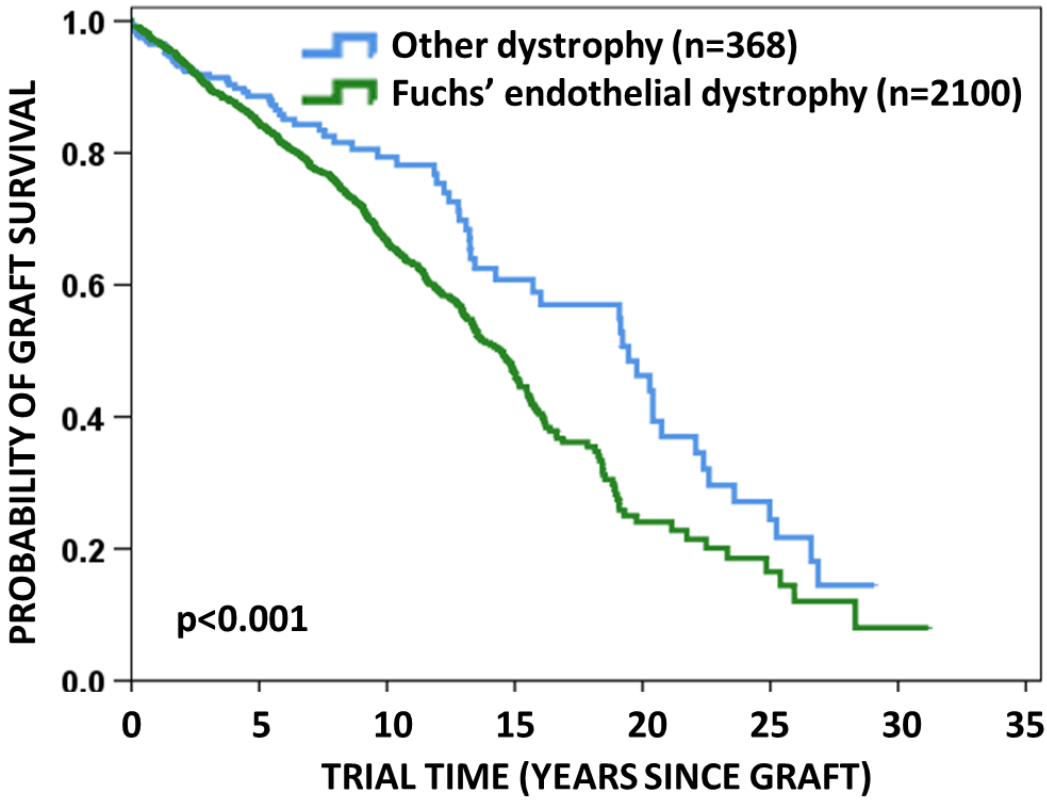
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
No hydrops	0.98	0.95	0.89	0.79	0.63	0.44	.21
Hydrops	0.95	0.83	0.72	0.61	NA	NA	NA

3.2.3.2 Penetrating keratoplasty survival: influence of type of corneal dystrophy

Figure 3.2.5 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=8.18; df=1; p=0.004).

Figure 3.2.5 Type of corneal dystrophy



Number at risk (years post-graft)

	1	5	10	15	20	25
Other dystrophy	278	140	66	33	21	9
Fuchs' endothelial dystrophy	1679	917	396	118	25	8

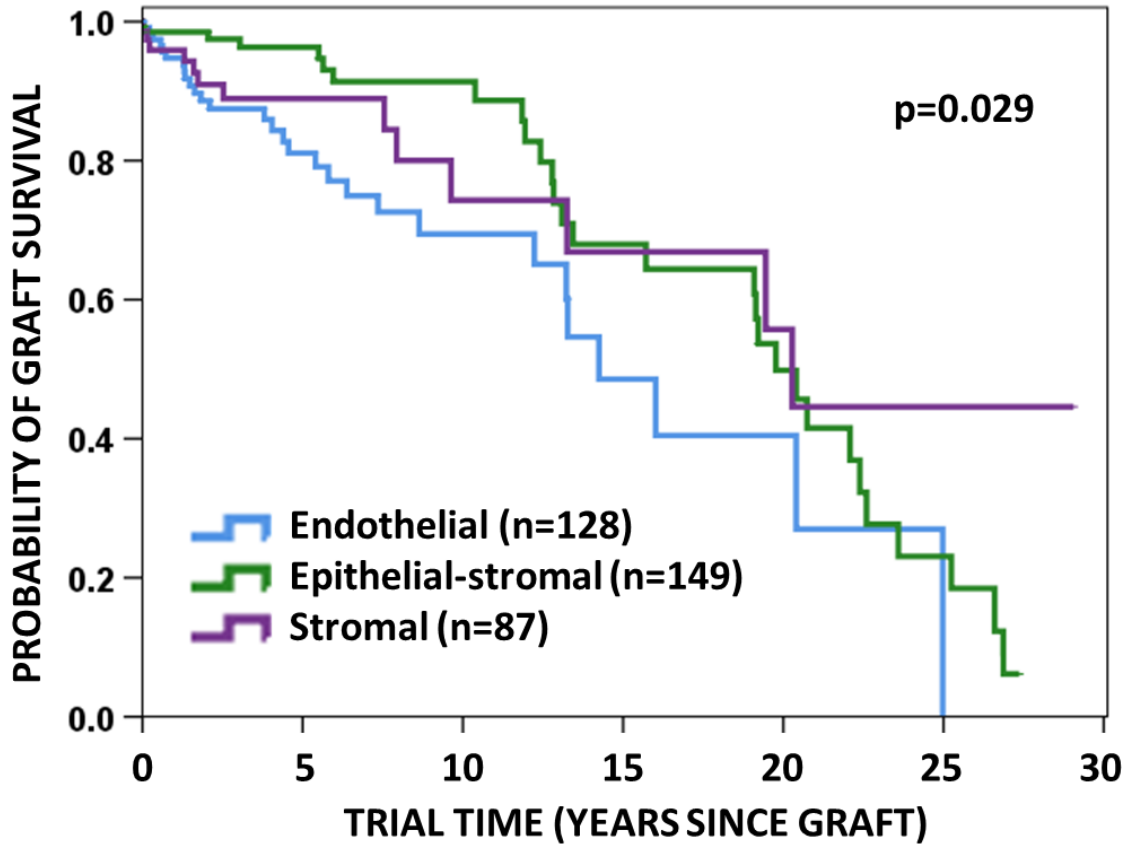
Probability of graft survival (years post-graft)

	1	5	10	15	20
Other dystrophy	0.97	0.89	0.79	0.61	0.46
Fuchs' endothelial dystrophy	0.97	0.85	0.67	0.47	0.24

The 368 'other' corneal dystrophies comprised: unspecified endothelial dystrophy (84), granular dystrophy (76), macular dystrophy (60), lattice dystrophy (58), posterior polymorphous dystrophy (35), Reis-Bücklers dystrophy (14), Schnyder crystalline dystrophy (12), unspecified stromal dystrophy (12), congenital hereditary endothelial dystrophy (9), unspecified epithelial dystrophy (3), central cloudy dystrophy of Francois (2), Thiel-Behnke epithelial stromal dystrophy (1), congenital stromal dystrophy (1), gelatinous drop-like epithelial dystrophy (1).

Figure 3.2.6 shows the comparison of survival for grafts for endothelial corneal dystrophies other than Fuchs' endothelial dystrophy, versus epithelial-stromal corneal dystrophies, versus stromal corneal dystrophies. A significant difference was found across groups (Log Rank Statistic=7.06; df=2; p=0.029). The four epithelial dystrophies registered were excluded from this analysis.

Figure 3.2.6 Type of corneal dystrophy



Number at risk (years post-graft)

	1	5	10	15	20
Endothelial dystrophy	100	45	19	6	3
Epithelial-stromal dystrophy	112	65	34	20	13
Stromal dystrophy	62	30	13	7	5

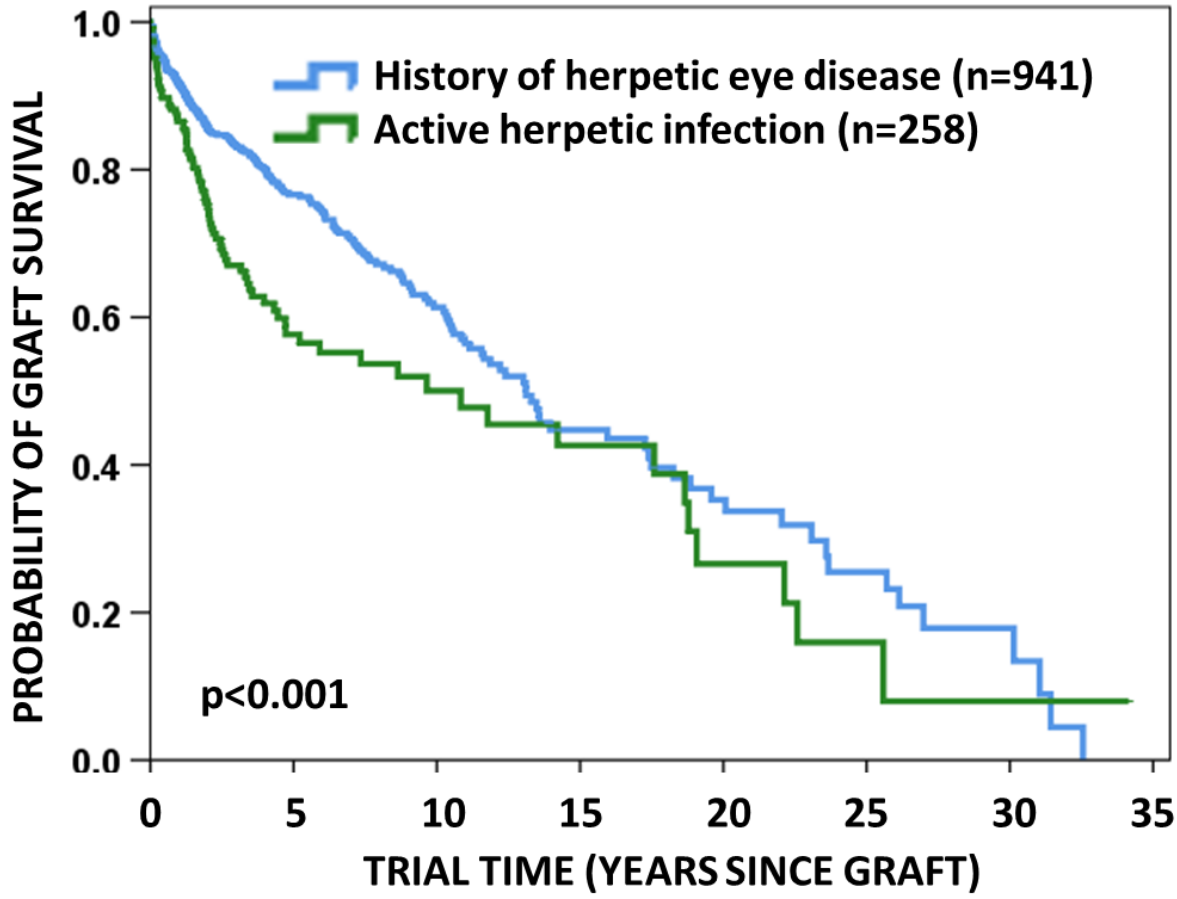
Probability of graft survival (years post-graft)

	1	5	10	15
Endothelial dystrophy	0.95	0.81	NA	NA
Epithelial-stromal dystrophy	0.99	0.96	0.91	0.68
Stromal dystrophy	0.96	0.89	NA	NA

3.2.3.3 Penetrating keratoplasty survival: influence of herpetic eye disease factors

Figure 3.2.7 shows the survival of grafts performed for herpetic eye infection. The graph shows survival of grafts with a history of herpetic eye disease compared to those with an active herpetic infection at the time of graft. It excludes the 39 cases where the Registry was unable to determine whether the herpetic infection was active. A significant difference was found across groups (Log Rank Statistic=12.49, df=1, p<0.001). Grafts without active HSV exhibit better graft survival.

Figure 3.2.7 Presence of active herpetic eye disease at time of graft



Number at risk (years post-graft)

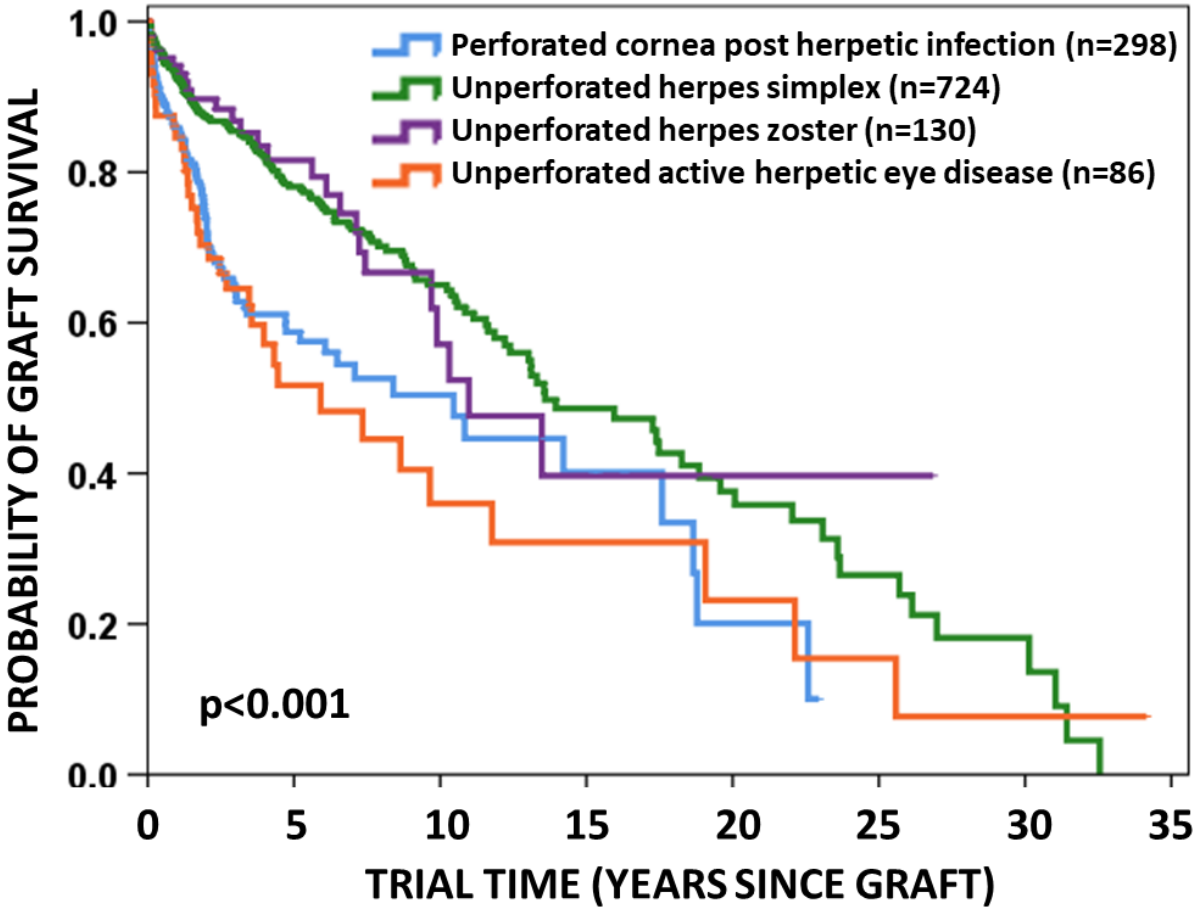
	1	5	10	15	20	25
History of herpetic eye disease	655	258	106	43	23	12
Active herpetic infection	160	50	25	15	6	2

Probability of graft survival (years post-graft)

	1	5	10	15	20
History of herpetic eye disease	0.92	0.77	0.61	0.45	0.35
Active herpetic infection	0.87	0.58	0.50	NA	NA

Figure 3.2.8 shows the survival of grafts performed for various types of herpetic eye infection where the cornea had not perforated, versus herpetic eye infections (whether active or historic) in which the cornea had perforated. The graph shows survival of grafts with a history of herpetic eye disease compared to those with an active herpetic infection at the time of graft. A significant difference was found across groups (Log Rank Statistic=33.66, df=3, p<0.001). Grafts performed in eyes with active HSV or in eyes with perforated herpetic infections exhibit poorer graft survival.

Figure 3.2.8 Perforation of herpetic eye disease



Number at risk (years post-graft)

	1	5	10	15	20	25
Perforated cornea post herpetic infection	167	48	19	9	3	NA
Unperforated herpes simplex	522	211	94	40	21	11
Unperforated herpes zoster	91	38	12	5	3	1
Unperforated active infection	58	16	8	6	3	2

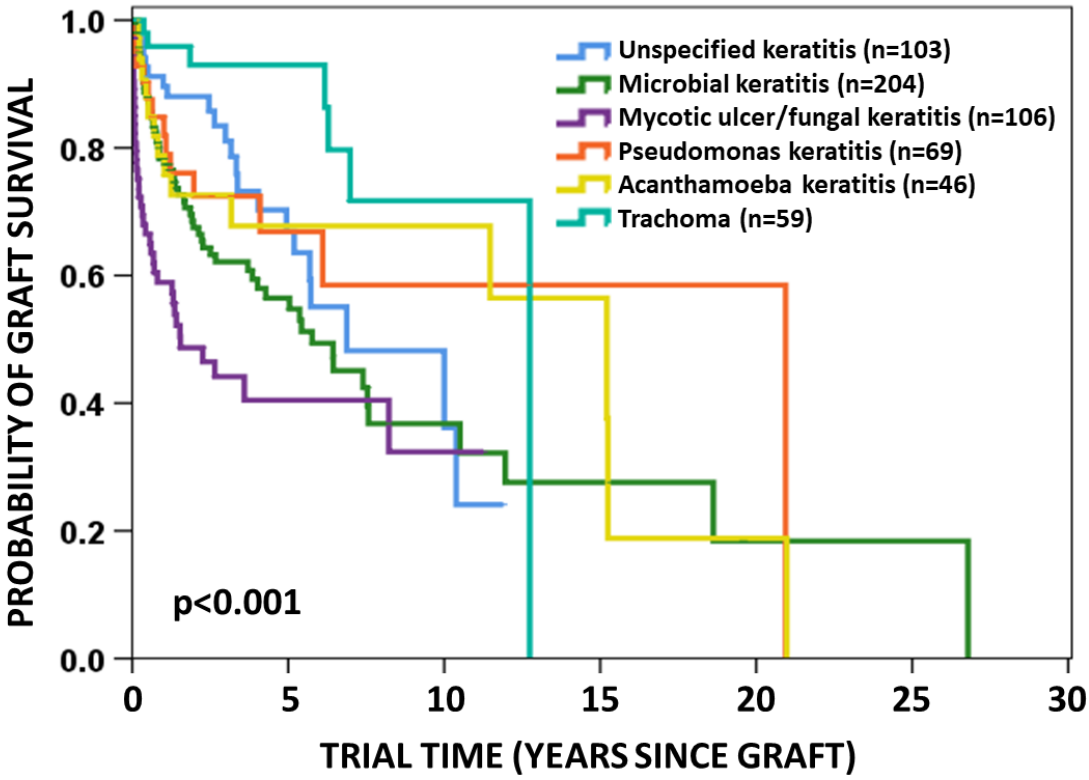
Probability of graft survival (years post-graft)

	1	5	10	15	20
Perforated cornea post herpetic infection	0.86	0.59	NA	NA	NA
Unperforated herpes simplex	0.93	0.78	0.65	0.49	0.38
Unperforated herpes zoster	0.94	0.82	NA	NA	NA
Unperforated active infection	0.85	NA	NA	NA	NA

3.2.3.4 Penetrating keratoplasty survival: influence of non-herpetic infections

Figure 3.2.9 shows the comparison of survival of penetrating keratoplasty for subcategories of non-herpetic infection. Grafts performed for non-herpetic viral infections and endophthalmitis were excluded from the statistical comparison due to low numbers. Pseudomonas was the only sub-category of microbial keratitis that had sufficient numbers to be analysed separately. A significant difference was found between the remaining groups (Log Rank Statistic=35.35; df=5; p<0.001).

Figure 3.2.9 Type of non-herpetic infection



Number at risk (years post-graft)

	1	2	3	4	5	6	7
Unspecified keratitis	57	44	34	25	20	12	7
Microbial keratitis	91	65	55	42	33	24	18
Mycotic ulcer/fungal keratitis	38	24	16	11	9	9	7
Pseudomonas keratitis	29	20	15	13	10	8	6
Acanthamoeba keratitis	26	17	15	13	11	9	8
Trachoma	41	31	26	19	16	14	7

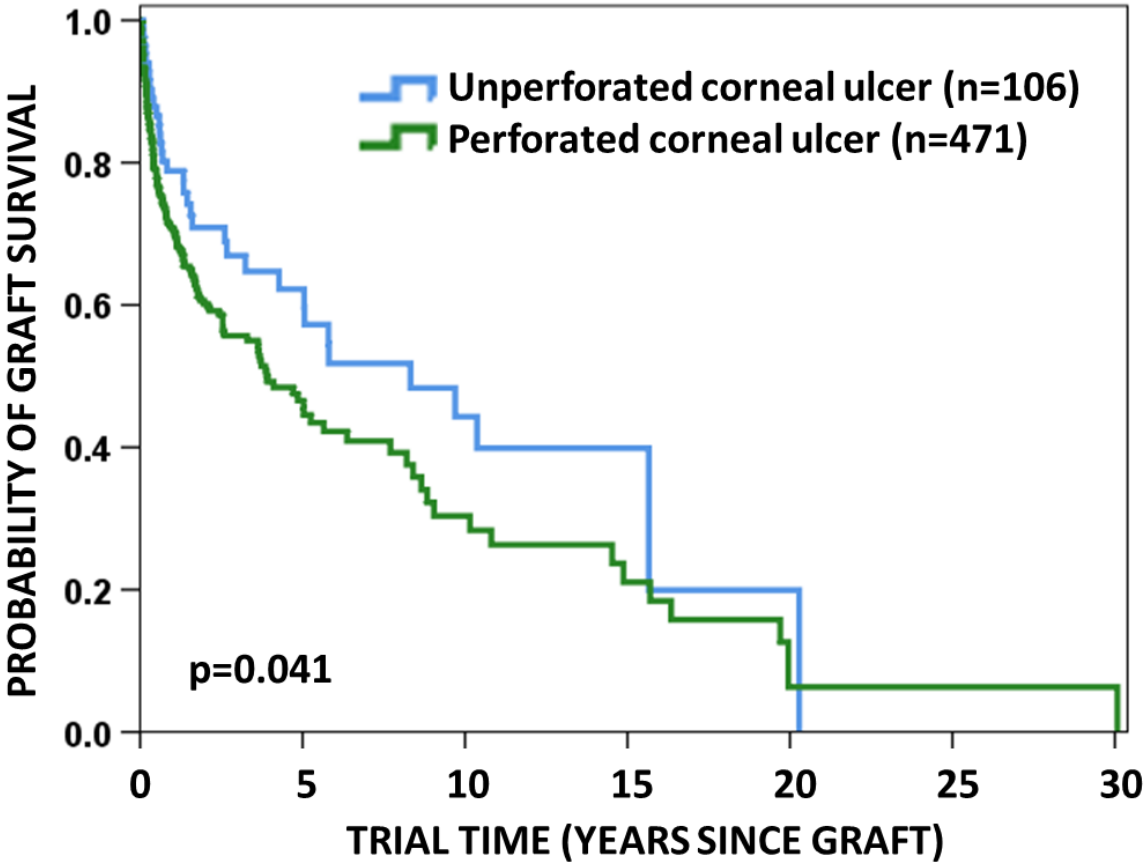
Probability of graft survival (years post-graft)

	1	2	3	4	5	6
Unspecified keratitis	0.90	0.88	0.81	0.73	0.67	NA
Bacterial keratitis	0.78	0.68	0.62	0.59	0.57	0.49
Fungal keratitis	0.59	0.49	NA	NA	NA	NA
Pseudomonas keratitis	0.85	0.72	NA	NA	NA	NA
Acanthamoeba keratitis	0.79	NA	NA	NA	NA	NA
Trachoma	0.96	0.93	0.93	NA	NA	NA

3.2.3.5 Penetrating keratoplasty survival: influence of perforation of ulcer

Figure 3.2.10 shows the comparison of survival of penetrating keratoplasty for perforated verses non-perforated ulcers. A significant difference was found between groups (Log Rank Statistic=4.18; df=1; p=0.041).

Figure 3.2.10 Type of non-herpetic infection



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9
Unperforated corneal ulcer	55	37	31	27	25	19	18	15	13
Perforated corneal ulcer	196	129	83	65	48	34	27	23	17

Probability of graft survival (years post-graft)

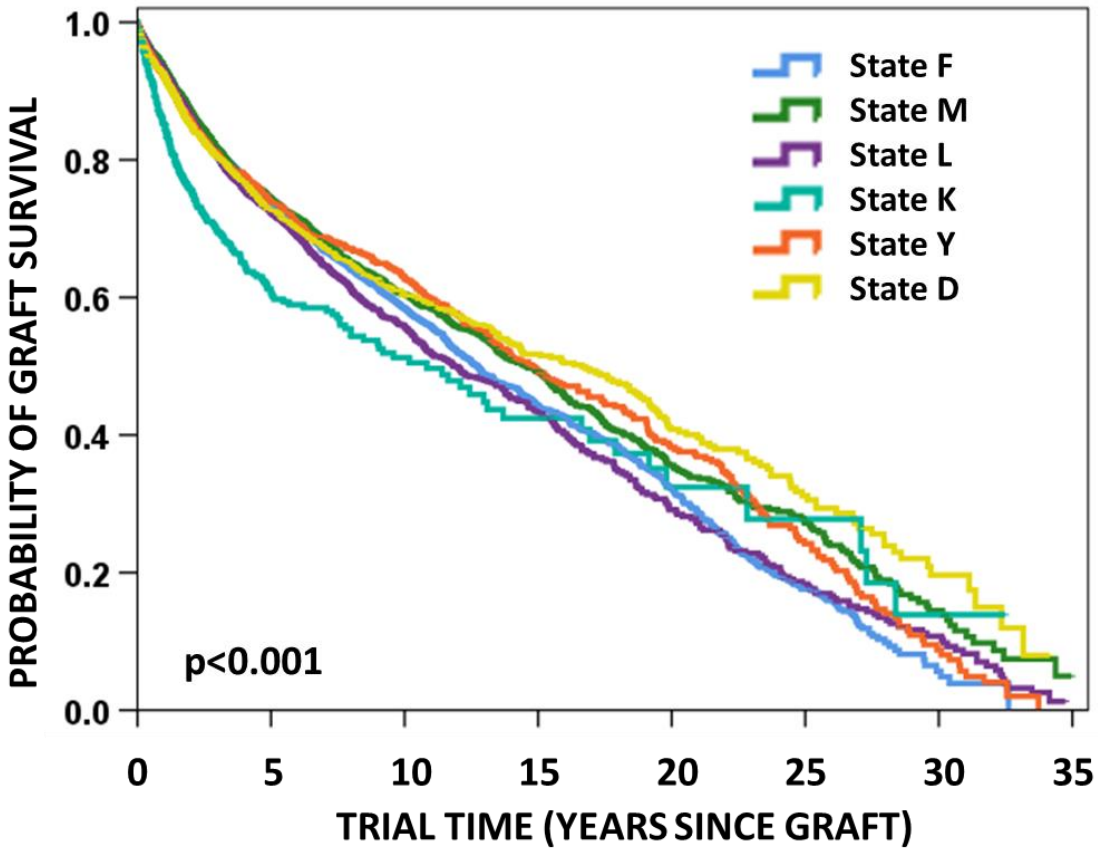
	1	2	3	4	5	6	7	8
Unperforated corneal ulcer	0.79	0.71	0.67	0.65	0.62	NA	NA	NA
Perforated corneal ulcer	0.71	0.60	0.56	0.49	0.47	0.42	0.41	0.39

This concludes the subgroup-analyses. Analyses from page 55 onwards are again performed on the full cohort.

3.2.4 Penetrating keratoplasty survival: influence of Australian State where graft was performed

Figure 3.2.11 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=45.16; df=5; p<0.001), with all other States exhibiting better survival than State K (all p<0.001), and State M and State D both exhibited better survival than State F and State L (all p<0.01). This variable was initially excluded from the multivariate analysis due to collinearity with other significant variables (see section 1.4.5 for explanation) but was subsequently included. However, this variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.2.11 Australian State where graft was performed



Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
State F	0.93	0.74	0.59	0.44	0.32	0.18	NA
State M	0.93	0.74	0.60	0.49	0.36	0.27	0.15
State L	0.93	0.73	0.56	0.43	0.29	0.18	0.11
State K	0.85	0.61	0.51	0.43	NA	NA	NA
State Y	0.92	0.74	0.63	0.49	0.38	0.24	NA
State D	0.92	0.73	0.60	0.52	0.41	0.31	NA

Note: Further information is not provided due to confidentiality constraints (see section 1.4.8).

3.2.5 Penetrating keratoplasty survival: influence of recipient age (years)

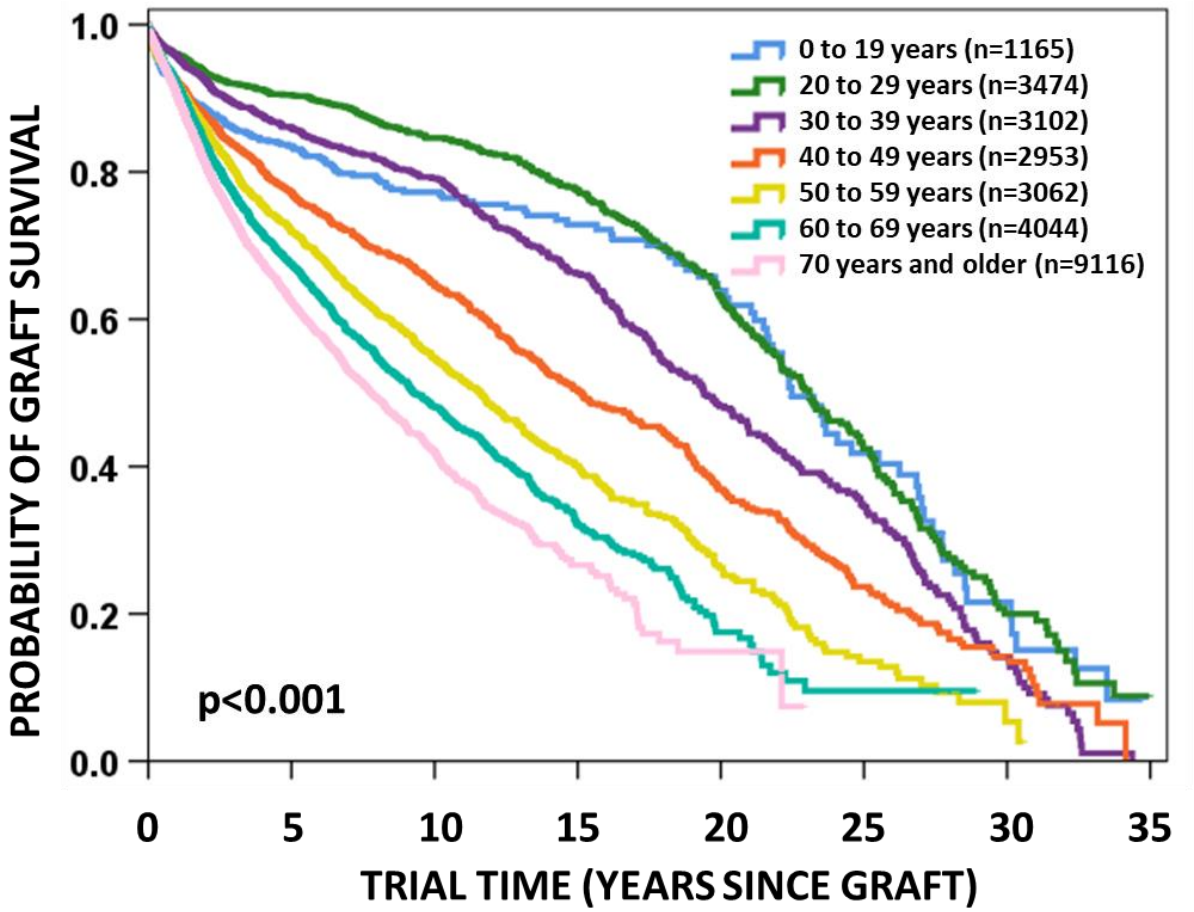
Figure 3.2.12 shows the comparison of graft survival depending on the age of the corneal transplant recipient. Recipients were initially stratified by 10-year age groups. Data for the “0-9 years” group was combined with the “10 to 19 years” group, and all recipients aged 80 years and older were grouped 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=1196.41; df=7; p<0.001).

Further analyses examined whether there were significant differences between adjacent age groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=1196.30; df=6; p<0.001).

All comparisons between age groups were significantly different at the p<0.001 level, except for recipients aged 0 to 19 years versus 30 to 39 years (p=0.608). 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. However, this variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Recipient age is strongly associated with indication for graft (see section 3.2.1), 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 risk factor for likelihood of graft survival or failure and was retained in the multivariate model.

Figure 3.2.12 Recipient age group



Number at risk (years post-graft)

	1	5	10	15	20	25	30
0 to 19 years	828	380	197	112	66	29	10
20 to 29 years	2481	1051	571	370	221	97	26
30 to 39 years	2241	1006	540	327	179	93	22
40 to 49 years	2065	1026	548	311	163	79	19
50 to 59 years	2159	1015	471	204	75	19	2
60 to 69 years	2868	1234	472	139	30	5	NA
70 years and older	5749	1680	386	63	5	NA	NA

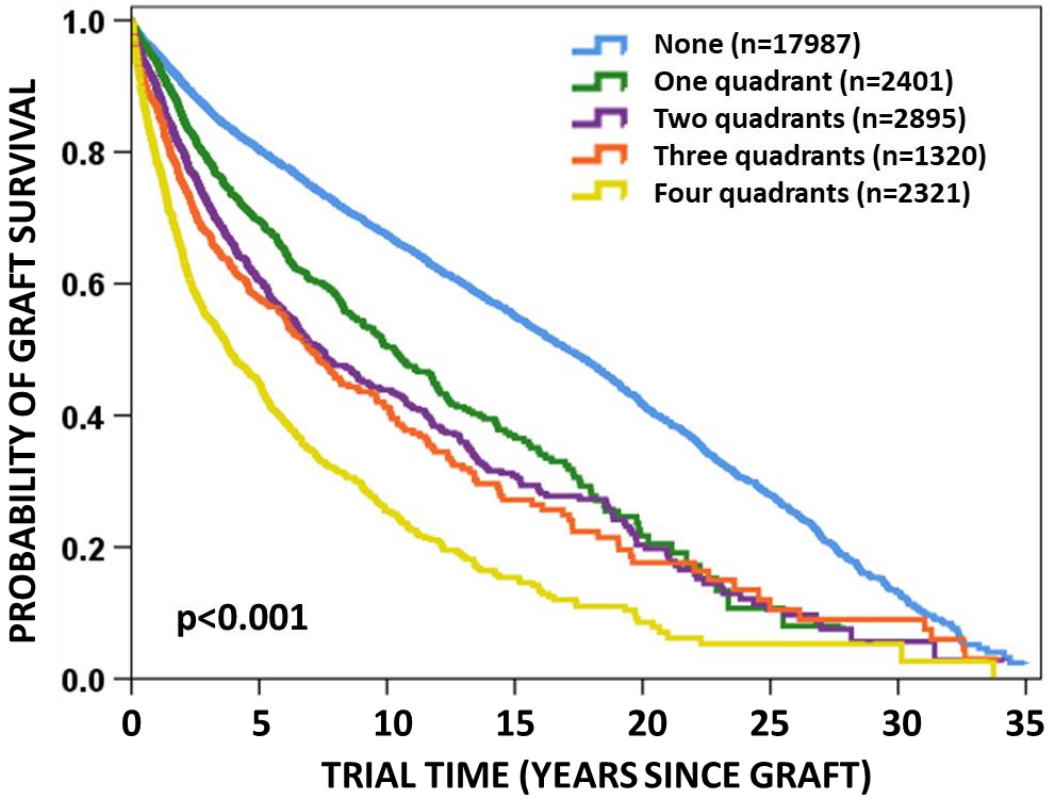
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
0 to 19 years	0.92	0.84	0.77	0.73	0.64	0.42	NA
20 to 29 years	0.96	0.91	0.85	0.78	0.63	0.42	0.20
30 to 39 years	0.96	0.86	0.79	0.66	0.48	0.35	0.14
40 to 49 years	0.92	0.77	0.65	0.50	0.37	0.24	NA
50 to 59 years	0.92	0.72	0.55	0.40	0.26	NA	NA
60 to 69 years	0.92	0.68	0.48	0.32	0.18	NA	NA
70 years and older	0.91	0.63	0.42	0.27	NA	NA	NA

3.2.6 Penetrating keratoplasty survival: influence of pre-graft corneal neovascularisation

Figure 3.2.13 shows the comparison of graft survival between those recipients with various degrees of corneal neovascularisation pre-graft and those without (Log Rank Statistic=1643.21; 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=0.049). Grafts performed in neovascularised eyes showed diminished graft survival. This variable was retained in the final multivariate model (see section 3.7).

Figure 3.2.13 Pre-graft corneal neovascularisation



Number at risk (years post-graft)

	1	5	10	15	20	25	30
None	12887	5574	2573	1280	650	293	69
One quadrant	1559	570	201	80	22	4	NA
Two quadrants	1833	620	210	84	35	13	2
Three quadrants	841	276	99	42	18	7	6
Four quadrants	1273	352	102	39	14	5	2

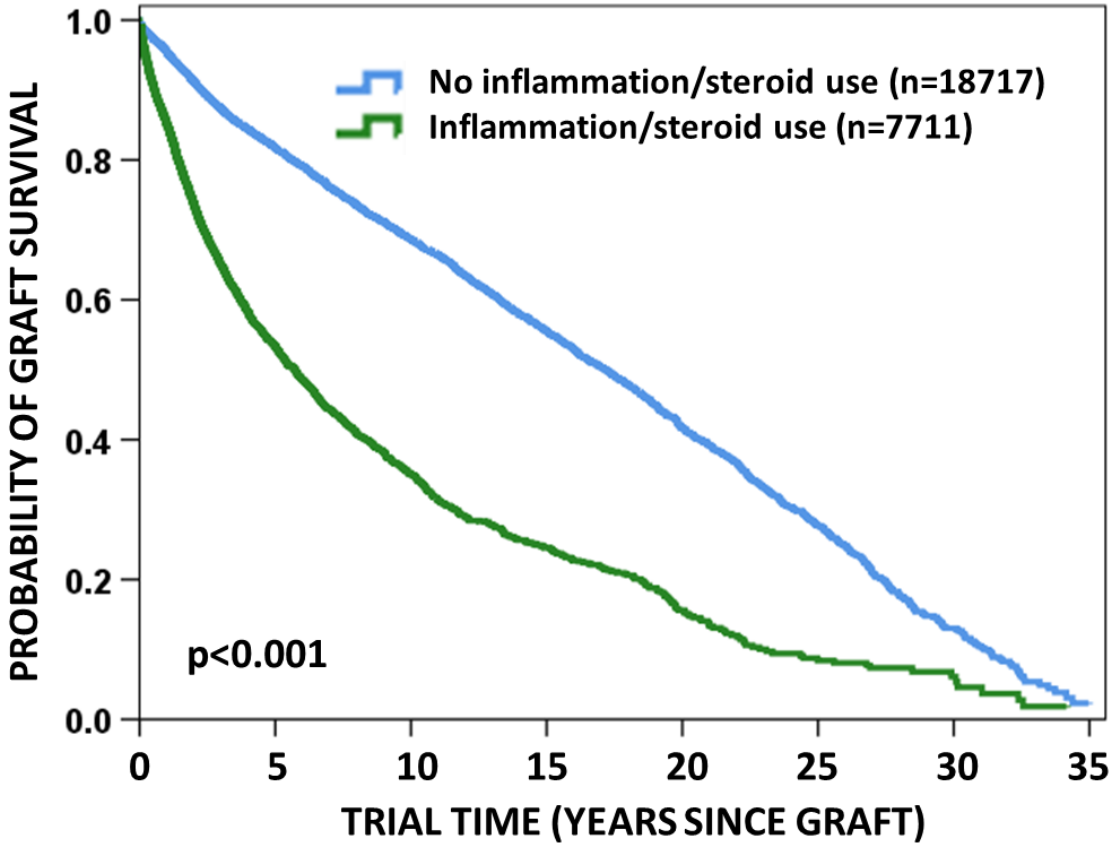
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
None	0.95	0.80	0.68	0.55	0.42	0.28	0.13
One quadrant	0.94	0.70	0.50	0.37	0.22	NA	NA
Two quadrants	0.90	0.61	0.44	0.31	0.20	NA	NA
Three quadrants	0.87	0.58	0.41	0.27	NA	NA	NA
Four quadrants	0.78	0.45	0.26	0.15	NA	NA	NA

3.2.7 Penetrating keratoplasty survival: influence of pre-graft inflammation and/or steroid use

Figure 3.2.14 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=1750.79; df=1; p<0.001). Data on this variable were not provided in 496 (<2%) cases. This was not a sufficient proportion of the cohort to include this group in further analysis and so these cases were excluded in the multivariate analysis. This variable was retained in the final multivariate model (see section 3.7).

Figure 3.2.14 Inflammation and/or steroid use at time of graft



Number at risk (years post-graft)

	1	5	10	15	20	25	30
No inflammation/steroid use	13360	5767	2687	1316	657	291	68
Inflammation/steroid use	4727	1526	456	188	73	25	8

Probability of graft survival (years post-graft)

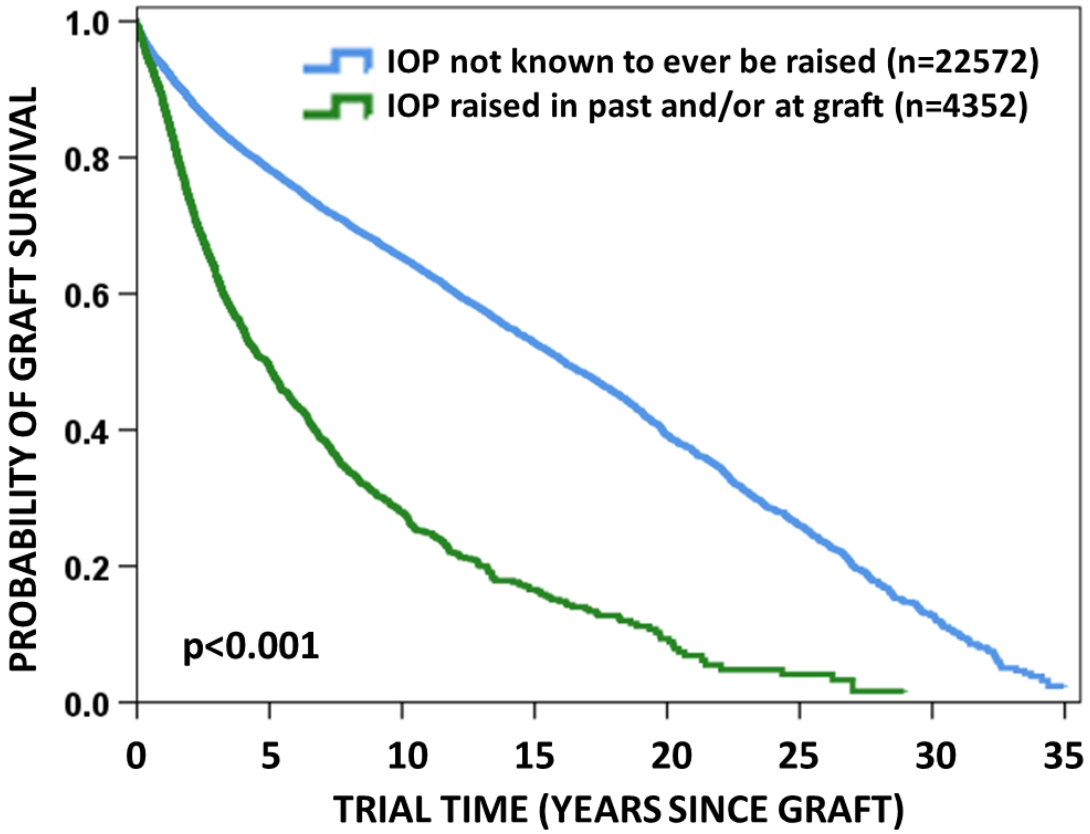
	1	5	10	15	20	25	30
No inflammation/steroid use	0.10	0.82	0.69	0.56	0.42	0.28	0.13
Inflammation/steroid use	0.85	0.53	0.35	0.25	0.16	0.08	NA

3.2.8 Penetrating keratoplasty survival: influence of history of raised intraocular pressure (IOP)

Figure 3.2.15 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=1374.54; df=1; p<0.001). This variable was retained in the final multivariate model (see section 3.7).

"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 3.2.15 History of raised intraocular pressure



Number at risk (years post-graft)

	1	5	10	15	20	25	30
IOP never raised	15569	6540	2939	1453	719	316	79
IOP raised	2824	852	246	72	20	6	NA

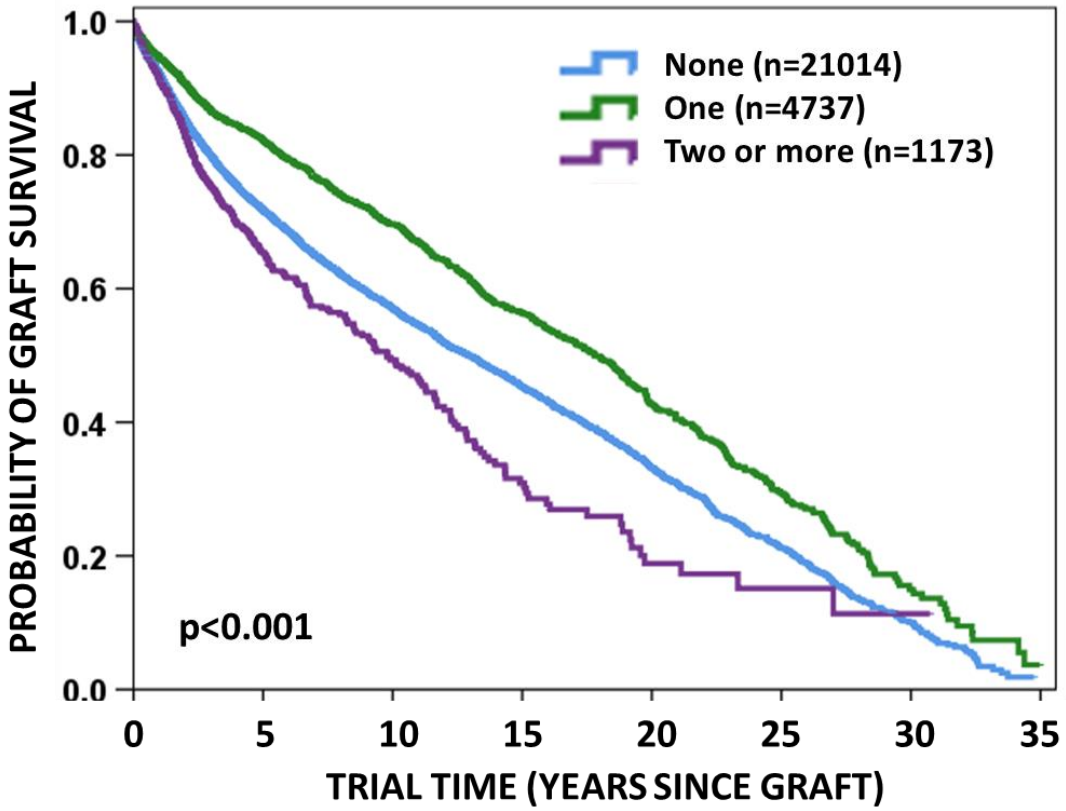
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
IOP never raised	0.93	0.78	0.65	0.53	0.39	0.26	0.13
IOP raised	0.88	0.49	0.28	0.17	0.09	NA	NA

3.2.9 Penetrating keratoplasty survival: influence of prior contralateral corneal graft/s

Figure 3.2.16 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 for analysis of the effect of number of previous ipsilateral grafts). A significant difference was found across groups (Log Rank Statistic=155.69; 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 final multivariate model (see section 3.7).

Figure 3.2.16 Number of prior contralateral corneal grafts



Number at risk (years post-graft)

	1	5	10	15	20	25	30
None	14250	5549	2300	1069	506	210	54
One	3361	1556	772	415	218	105	24
Two or more	782	287	113	41	15	7	1

Probability of graft survival (years post-graft)

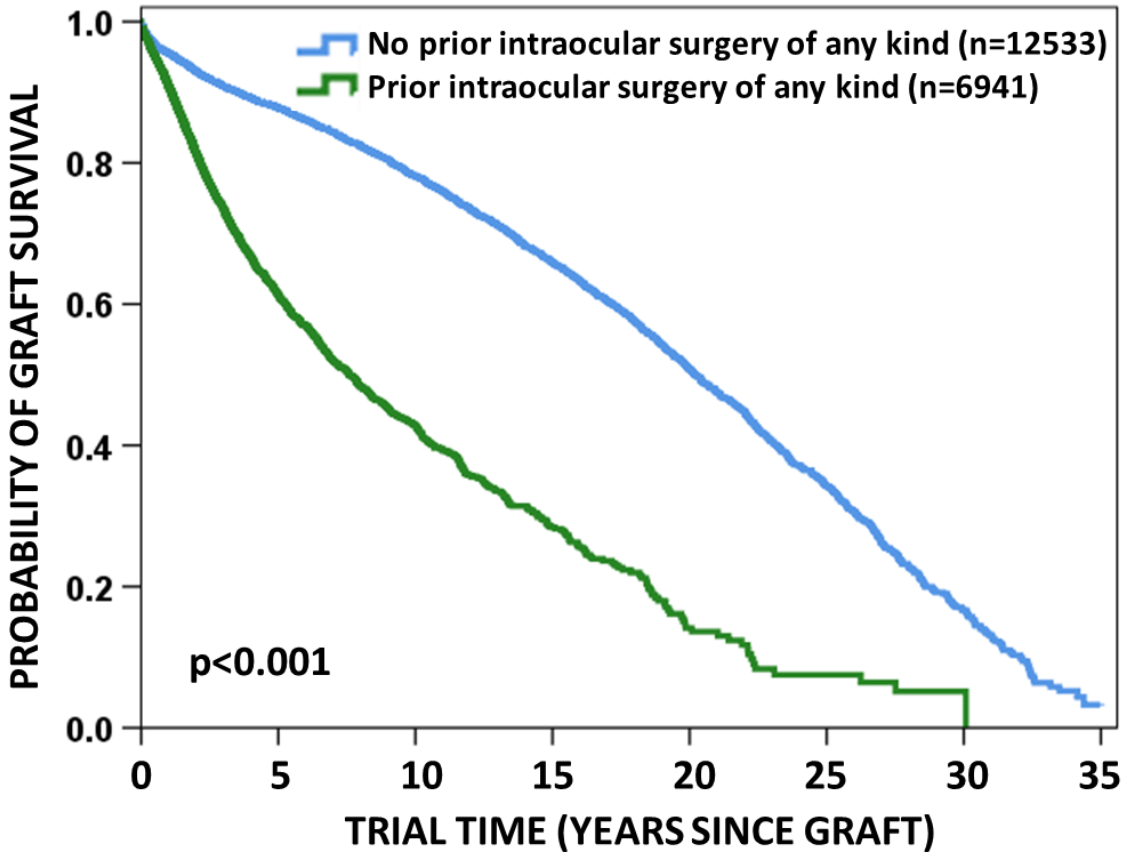
	1	5	10	15	20	25	30
None	0.92	0.72	0.57	0.45	0.33	0.21	0.10
One	0.95	0.82	0.70	0.56	0.43	0.29	0.15
Two or more	0.91	0.65	0.49	0.31	NA	NA	NA

3.2.10 Penetrating keratoplasty survival: influence of prior intraocular surgery

The analysis on page 62 is of a sub-cohort of penetrating grafts which had **not** undergone a previous corneal transplant. Sub-cohort variables are excluded from multivariate analysis.

Data were not available for 109 grafts and these are excluded from the analysis. Figure 3.2.17 shows the comparison of graft survival between grafts where the recipient had undergone prior intraocular surgery (excluding prior graft) compared to those that had not (Log Rank Statistic=1337.65; df=1; p<0.001).

Figure 3.2.17 prior intraocular surgery



Number at risk (years post-graft)

	1	5	10	15	20	25	30
No prior surgery	9114	4324	2211	1190	627	289	73
Prior surgery	4547	1415	417	132	28	8	1

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
No prior surgery	0.96	0.88	0.78	0.66	0.51	0.34	0.17
Prior surgery	0.91	0.61	0.43	0.28	0.14	NA	NA

3.3 Graft Era/Year

Table 3.6 shows the number of grafts registered and followed based on single years combined. Grafts were initially stratified by yearly groups with grafts performed in 1985 and 1986 grouped together, due to low numbers. A significant difference was found across year groups (Log Rank Statistic=342.68; df=34; p<0.001).

Further analyses examined whether there were significant differences between adjacent year groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=326.29; df=10; p<0.001). The percentages, which should be summed vertically, total 100.

Table 3.6 Graft era/year

Penetrating Keratoplasty
Graft Era/Year

Year of graft	Registered (%)	Followed (%)
1985 to 1992	5472 (20%)	5208 (24%)
1993 to 1995	2618 (10%)	2257 (10%)
1996	809 (3%)	668 (3%)
1997 to 2005	7730 (29%)	6492 (29%)
2006 to 2011	4711 (17%)	3924 (18%)
2012 to 2013	1368 (5%)	1147 (5%)
2014 to 2016	1929 (7%)	1564 (7%)
2017	603 (2%)	373 (2%)
2018	550 (2%)	293 (1%)
2019	584 (2%)	118 (1%)
2020	550 (2%)	14 (<1%)
Total	***26924 (100 %)***	***22058 (100 %)***

See section 1.1 for a discussion of the impact that lag time to follow-up may have on survival depending on graft year/era. Comparisons amongst the percentages of grafts registered and followed in each category showed some differences. These differences were examined using Chi^2 analyses. Follow-up became increasingly significantly (p<0.001) lower for grafts performed in more recent cohorts. Grafts performed between 1996 and 2013 did not differ significantly on rates of follow-up (p=0.617).

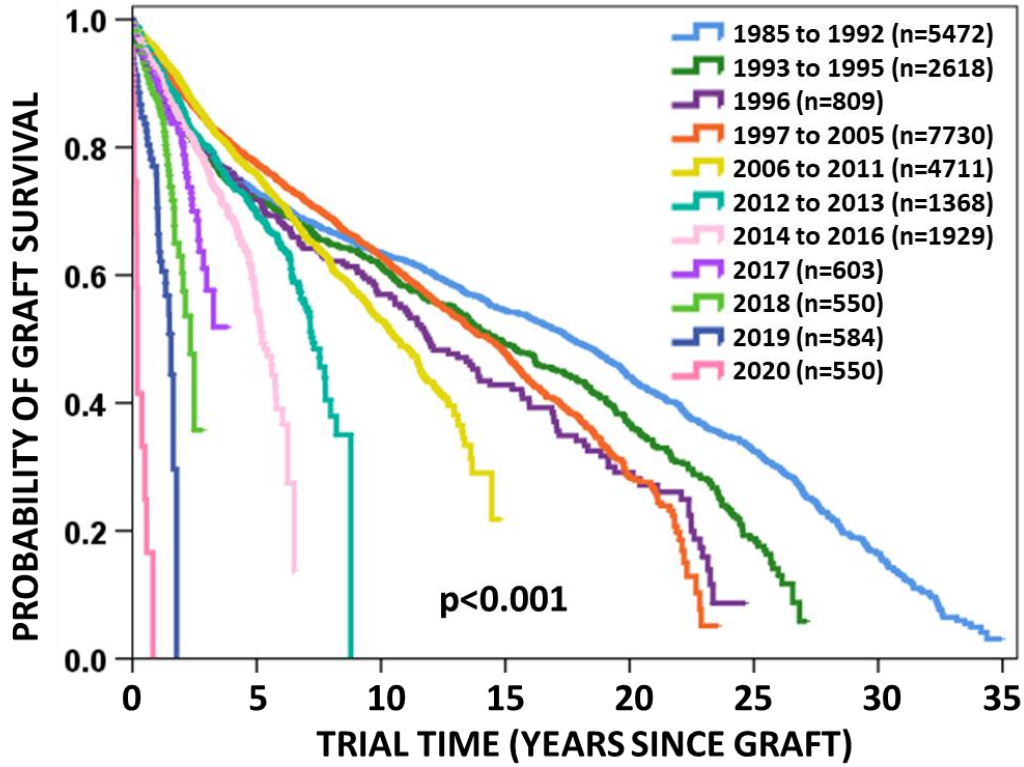
3.3.1 Penetrating keratoplasty survival: influence of era of graft

Figure 3.3.1 shows the comparison of graft survival between year of graft, stratified into the groups outlined above (Log Rank Statistic=326.29; df=10; p<0.001). From 1997 to 2005 through to 2020, survival was significantly poorer for each newer graft era compared to each of those which had come before (all p<0.001, except 2014 to 2016 versus 2017, p=0.002). Grafts performed from 2014 to 2016, or in 2018, 2019 or 2020 also had significantly poorer survival than those performed from 1985 to 1992, 1933 to 1995 or in 1996 (all p<0.001). Grafts performed in 2017 had poorer survival than those performed from 1985 to 1992 or 1993 to 1995 (both p=0.002), while grafts performed from 1985 to 1992 had better survival than those performed in 2012/2013 (p=0.002) but poorer survival than those performed from 1993 to 1995, or in 1996 (both p<0.001). This variable was retained in the final multivariate model (see section 3.7).

Penetrating Keratoplasty

Note: no grafts performed in 2020 had follow-up of one year by the census date and so this category is excluded from the number at risk and probability of graft survival tables.

Figure 3.3.1 Graft era



Number at risk (years post-graft)

	1	5	10	15	20	25	30
1985 to 1992	4163	1993	1098	681	453	286	79
1993 to 1995	1793	803	420	260	157	36	NA
1996	531	240	113	64	30	NA	NA
1997 to 2005	5542	2343	1185	520	99	NA	NA
2006 to 2011	3505	1610	369	NA	NA	NA	NA
2012 to 2013	1010	347	NA	NA	NA	NA	NA
2014 to 2016	1308	85	NA	NA	NA	NA	NA
2017	298	NA	NA	NA	NA	NA	NA
2018	189	NA	NA	NA	NA	NA	NA
2019	56	NA	NA	NA	NA	NA	NA

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
1985 to 1992	0.90	0.73	0.64	0.55	0.44	0.32	0.16
1993 to 1995	0.91	0.73	0.62	0.49	0.37	0.19	NA
1996	0.91	0.72	0.57	0.43	0.29	NA	NA
1997 to 2005	0.94	0.78	0.63	0.48	0.29	NA	NA
2006 to 2011	0.95	0.76	0.53	NA	NA	NA	NA
2012 to 2013	0.93	0.77	NA	NA	NA	NA	NA
2014 to 2016	0.92	0.55	NA	NA	NA	NA	NA
2017	0.90	NA	NA	NA	NA	NA	NA
2018	0.90	NA	NA	NA	NA	NA	NA
2019	0.73	NA	NA	NA	NA	NA	NA

3.4 Surgery and Surgeon Factors

Table 3.7 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 (26,924 registered and 22,058 followed) and the percentages, which should be summed vertically for each variable, total 100.

Table 3.7 Surgery and surgeon factors, significant in univariate analyses

Penetrating Keratoplasty Surgery and Surgeon Factors	Registered (%)	Followed (%)
Size of graft (diameter)		
Less than 7.75 mm	3310 (12%)	2846 (13%)
7.75 mm to 7.99 mm	1744 (6%)	1412 (6%)
8.00 mm to 8.24 mm	10112 (38%)	8555 (39%)
8.25 mm to 8.49 mm	4239 (16%)	3289 (15%)
8.50 mm to 8.74 mm	3580 (13%)	2862 (13%)
8.75 mm or more	2380 (9%)	1848 (8%)
Not advised	1559 (6%)	1246 (6%)
Change in lens status		
Phakic post-graft	13284 (49%)	10847 (49%)
Aphakic post-graft	1750 (6%)	1494 (7%)
Phakic/pseudophakic	2542 (9%)	2186 (10%)
Not phakic/pseudophakic	9348 (35%)	7531 (34%)
Surgeon caseload and level of follow-up		
Fewer than 539 (2%) registered PK	14162 (53%)	11233 (51%)
539+ registered PK, <82% follow-up	4496 (17%)	3052 (14%)
539+ registered PK, ≥82% follow-up	8266 (31%)	7773 (35%)
The centre effect		
Fewer than 539 (2%) registered PK	14162 (53%)	11233 (51%)
	1792 (7%)	1718 (8%)
	1473 (5%)	1170 (5%)
	1245 (5%)	1212 (5%)
	1170 (4%)	1114 (5%)
	909 (3%)	465 (2%)
Individual surgeons are not identified	897 (3%)	488 (2%)
due to confidentiality constraints.	858 (3%)	775 (4%)
See section 1.4.8 for further information.	704 (3%)	654 (3%)
	662 (2%)	619 (3%)
	640 (2%)	516 (2%)
	633 (2%)	576 (3%)
	624 (2%)	530 (2%)
	578 (2%)	575 (3%)
	577 (2%)	413 (2%)
Total	***26924 (100 %)***	***22058 (100 %)***

Note: 539 was selected as the cut-off point for high caseload surgeons as this was 2% of all registered penetrating keratoplasties. 82% was selected as the cut-off point for the follow-up categories as this was the average percentage of follow-up for all penetrating grafts.

3.4.1 Penetrating keratoplasty survival: influence of graft size

Figure 3.4.1 shows a comparison of graft survival depending on the size of the graft. Grafts were initially stratified in 0.25 mm incriments, with all grafts measuring under 7.75 mm analysed together, and all grafts measuring 8.75 mm and over analysed together. A significant difference was found across groups (Log Rank Statistic=223.85; df=5; p<0.001).

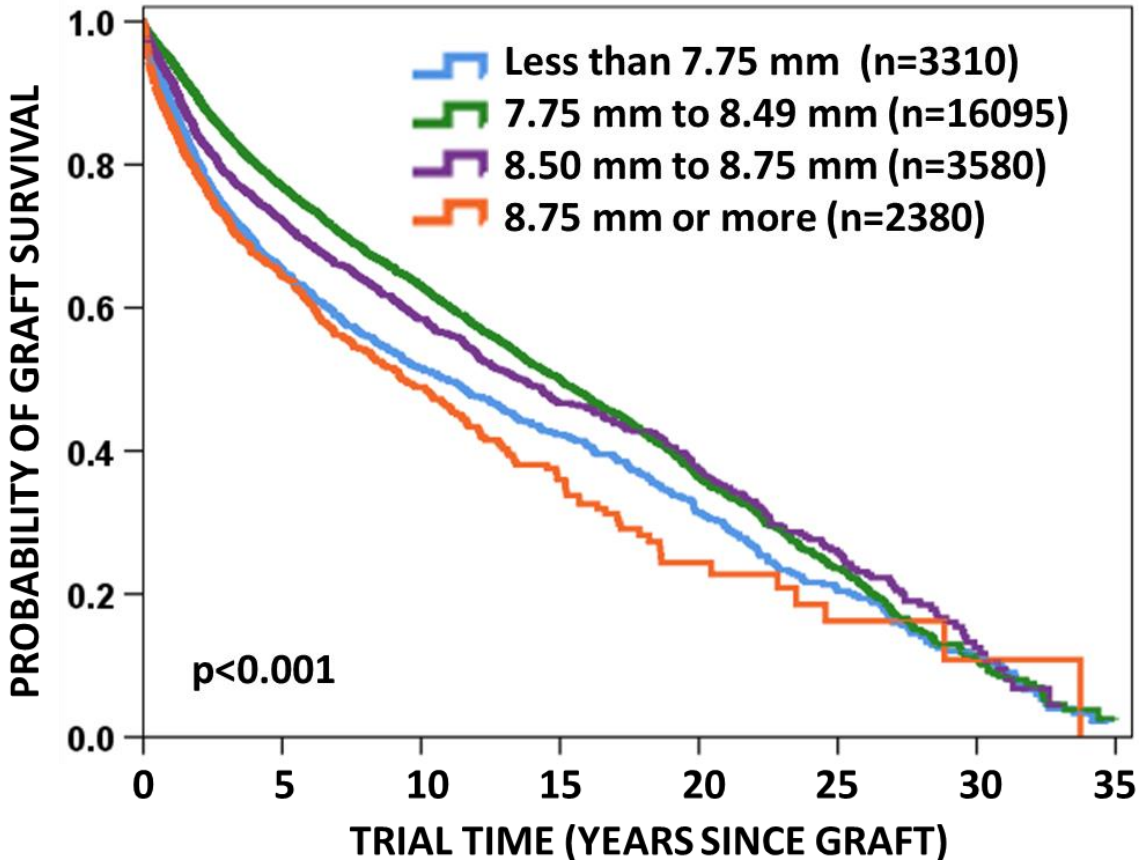
Further analyses examined whether there were significant differences between adjacent size groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=222.11; df=3; p<0.001).

Grafts measuring less than 7.75 mm, and those measuring 8.75 mm or more, had poorer survival than those which were 7.75 mm to 8.49 mm, or 8.50 mm to 8.74 mm (all p<0.001). Grafts that were 7.75 mm to 8.49 mm in size had better survival than those which were 8.50 mm to 8.74mm mm (p<0.001). Grafts that were under 7.75 mm in size had better survival than those that were 8.75mm or more (p=0.043).

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=240.74; df=4; p<0.001). This variable was retained in the final multivariate model (see section 3.7).

The size of penetrating grafts has changed significantly across eras. They have increased in size during each five-year cohort since 1985. Just 5% 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. 50% of grafts 8.75 mm or more were repeat grafts.

Figure 3.4.1 Graft size



Number at risk (years post-graft)

	1	5	10	15	20	25	30
Less than 7.75 mm	2211	916	434	248	131	65	25
7.75 mm to 8.49 mm	11354	4523	1964	906	412	171	36
8.50 mm to 8.74 mm	2371	1053	477	250	152	69	16
8.75 mm or more	1419	511	179	66	17	6	2

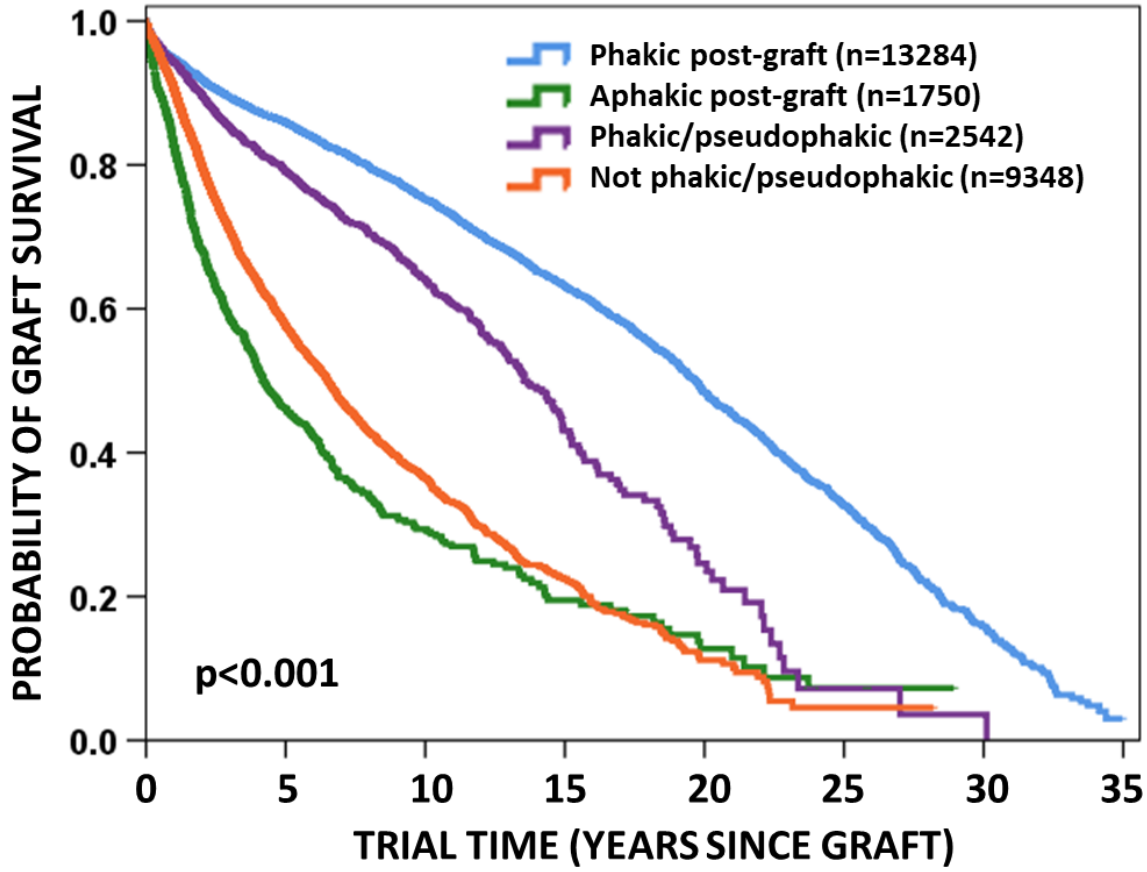
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
Less than 7.75 mm	0.88	0.65	0.52	0.42	0.31	0.20	0.12
7.75 mm to 8.49 mm	0.95	0.77	0.63	0.50	0.36	0.24	0.11
8.50 mm to 8.74 mm	0.92	0.72	0.58	0.47	0.37	0.56	NA
8.75 mm or more	0.86	0.64	0.49	0.36	NA	Na	NA

3.4.2 Penetrating keratoplasty survival: influence of change in lens status

Figure 3.4.2 shows the comparison of graft survival stratified by the change of lens status from pre- to post-graft. “Phakic post-graft” means the eye was phakic both before and after the graft. “Aphakic post-graft” means the eye was left aphakic post-graft, regardless of what its lens status was pre-graft. “Phakic/pseudophakic” means the eye was phakic before the graft and pseudophakic afterwards, having undergone a triple procedure. “Not phakic/pseudophakic” means the eye was pseudophakic or aphakic before the graft and pseudophakic afterwards. A significant difference was found across groups (Log Rank Statistic=2206.30; df=3; p<0.001), with all between group comparisons significant at the p<0.001 level. This variable was retained in the final multivariate model (see section 3.7).

Figure 3.4.2 Change in lens status from pre- to post-graft



Number at risk (years post-graft)

	1	5	10	15	20	25	30
Phakic post-graft	9449	4431	2287	1278	678	313	78
Aphakic post-graft	1072	290	87	31	12	3	NA
Phakic/pseudophakic	1884	882	340	90	22	2	1
Not phakic/pseudophakic	5988	1789	471	126	27	4	NA

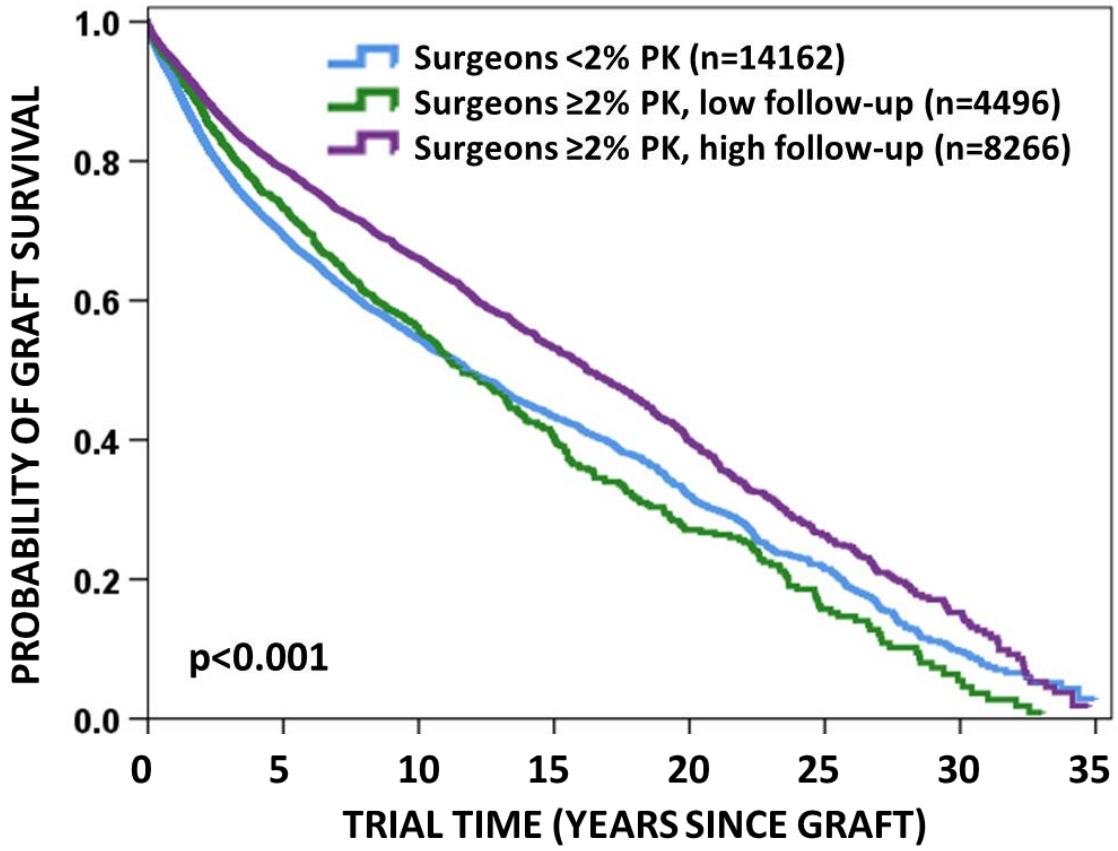
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
Phakic post-graft	0.95	0.86	0.75	0.63	0.48	0.33	0.16
Aphakic post-graft	0.83	0.46	0.30	0.20	NA	NA	NA
Phakic/pseudophakic	0.95	0.79	0.64	0.43	0.25	NA	NA
Not phakic/pseudophakic	0.91	0.58	0.36	0.26	0.11	NA	NA

3.4.3 Penetrating keratoplasty survival: influence of surgeon caseload grouped by level of follow-up

Figure 3.4.3 shows the comparison of graft survival between grafts performed by surgeons with 539+ (≥2%) registered penetrating keratoplasties with average or better (≥82%) follow-up, to those with lower than average follow-up (<82%), and to surgeons with fewer than 539 (<2%) registered penetrating keratoplasties (Log Rank Statistic=169.39; df=2; p<0.001). Survival of grafts performed by high caseload 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 final multivariate model (see section 3.7). volume

Figure 3.4.3 Surgeon caseload and level of follow-up



Number at risk (years post-graft)

	1	5	10	15	20	25	30
<2% registered PK	9206	3482	1361	652	333	151	36
≥2% PK, low follow-up	2558	815	351	164	81	31	6
≥2% PK, high follow-up	6629	3095	1473	709	325	140	37

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
<2% registered PK	0.91	0.69	0.55	0.43	0.32	0.22	0.10
≥2% PK, low follow-up	0.94	0.73	0.56	0.40	0.27	0.16	NA
≥2% PK, high follow-up	0.94	0.79	0.66	0.53	0.40	0.26	0.15

3.5 Operative procedures at the time of graft

Table 3.8 shows the number of grafts for which specified operative procedures were performed at the time of graft. This did not include cataract extraction, pseudophakic IOL insertion, or pseudophakic IOL extraction, as these were covered by the variable relating to change in lens (see section 3.4.2).

Table 3.8 Operative procedures at the time of graft

Penetrating Keratoplasty
Operative Procedures at Time of Graft

	Number
Vitrectomy	2122
Partial iridectomy	1581
Pseudophakic IOL exchanged	348
Synechiolysis	196
Tarsorrhaphy	188
Pupilloplasty	137
Trabeculectomy	68
Iris suture	43
Iridoplasty	42
Sphincterotomy	36
Intravitreal/intracameral/conjunctival injection/s*	31
Molteno tube trimmed/revised	31
Iris adhesion dissected	30
Glaucoma tube inserted (Molteno: 24, Baerveldt: 3, unspecified: 1)	28
Pterygium excision	27
Retrocorneal membrane removed	27
IOL repositioned	26
Conjunctival flap (Gunderson flap: 13, unspecified: 11)	24
Iris repair	24
Keratoprosthesis inserted	17
Retinal detachment repair - unspecified	17
Anterior chamber washout	16
Complete iridectomy	16
Glaucoma tube repositioned	16
Cautery	13
Concurrent graft (5 scleral patch, 8 limbal/conjunctival)	13
Gluing/tissue adhesive	12
Removal of residual lens material	12
Removal of silicone oil	12
Amniotic membrane transplant	11
Anterior chamber reconstruction/revision	11
Capsulectomy	11
Membrane peel	11
Piggyback IOL removed	10
IOL sutured to iris	10
Other**	314
Total operative procedures (number of grafts)	**5531 (4736)**

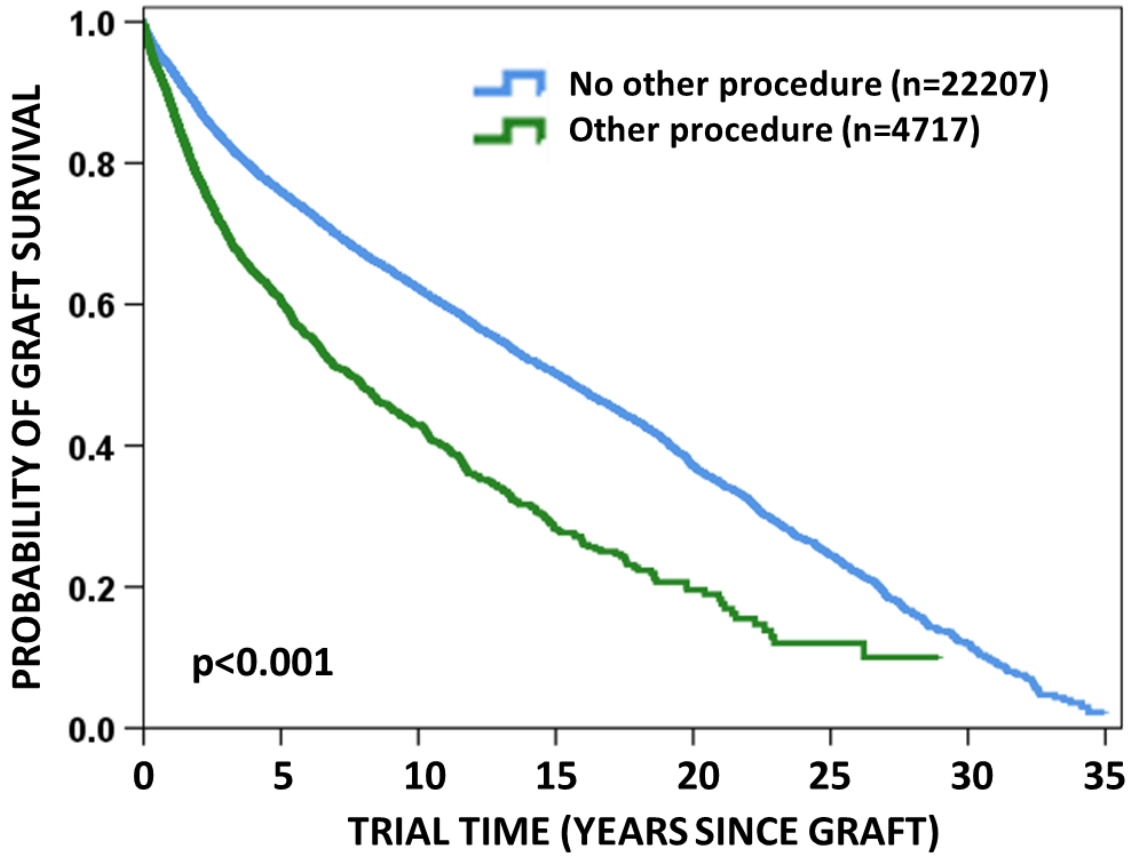
**Avastin (12), unspecified antibiotics (8), Dexamethasone (2), Voriconazole (2), 5FU (1), Amphotericin (1), Gentamicin (1), silicone oil (1), Triamcinolone (1), unspecified steroid (1), unspecified (1).

Other included: artificial iris inserted (9), iridotomy (9), pupil reconstruction (9), removal of cyclitic membranes (9), dissection of fibrous tissue adhesion (8), IOL sutured to sclera (8), cryotherapy (7), cyclodialysis (7), phakic IOL inserted (7), piggyback IOL inserted (7), removal of fibrous tissue (7), removal of pupillary membrane (7), iris repositioned (6), peritomy (6), phakic IOL removed (6), anterior chamber tap (5), biopsy (5), glaucoma tube trimmed/revised (5), IOL sutured (5), removal of gunderson flap (5), Gunderson flap repositioned/revised (4), healon (4), posterior sclerotomy (4), removal of foreign body (4), removal of hypopyon (4), removal of iris clip on IOL (4), removal of keratoprosthesis (4), suture pupil (4), capsulotomy (3), conjunctival resection (3), drainage of fluid (3), endolaser (3), keratectomy (3), pupil stretch (3), removal of conjunctival flap (3), removal of feet of IOL (3), removal of intracorneal ring segment (3), removal/dissection of unspecified corneal adhesions (3), repair of expulsive haemorrhage (3), sclerectomy (3), cardone implant (2), corioplasty (2), EDTA chelation (2), IOL polished (2), iris cerclage (2), iris resection (2), needling (2), punctal plugs (2), pupil suture (2), removal of AlphaCor (2), removal of band keratopathy (2), removal of dermoid (2), removal of fibrin (2), removal of iris cysts (2), removal of iris membrane (2), removal of membrane over IOL (2), removal of pus (2), repair of iridodialysis (2), scleral buckle (2), trabeculectomy revision (2), unspecified (2), unsuccessful psudophakic iol insertion (2), anterior chamber paracentisis (1), aphakic iol inserted (1), capsular phimosis (1), capsular tension ring inserted (1), cereoplasty (1), corneal debridement (1), corneal diathermy (1), Cypass (1), dissection of adherent leukoma (1), dissection of inflammatory membranes (1), division of posterior capsule (1), division of symblepharon (1), electrolysis (1), enlargement of anterior capsulotomy (1), evisceration (1), Frost suture (1), glaucoma tube flushed (1), IOL reduction (1), iridodialysis sutured (1), iris dilation (1), iris segment implanted (1), lateral rectus recession (1), lens capsule cleared (1), limbal incision (1), limbal lesion excision (1), Molteno tube cleared (1), Molteno tube sutured to iris (1), Molteno tube removed (1), phakic iol exchanged (1), posterior chamber repair (1), pseudoexfoliation (1), pupil dissection (1), pupillary incisions (1), removal of aniridia (1), removal of calcium (1), removal of cataract remnants (1), removal of conjunctival cyst (1), removal of corneal intraepithelial neoplasia (1), removal of IOL remnant (1), removal of macular segment (1), removal of nuclear fragment (1), removal of pannus (1), removal of protruding uveal tissue (1), removal of scar tissue (1), removal of surface neoplasia lesion (1), removal of sutures from cataract surgery (1), removal of vitreous from front of lens (1), repair choroidal detachment (1), repair of penetrating lacerations (1), repair of trauma (1), resuturing of iridectomy (1), resuturing of scleral tunnel (1), retinotomy (1), scar removal (1), scleral resection (1), scleral wound repair (1), silicon tube extension to sulcus (1), silicone oil exchange (1), Sommering's ring inserted (1), sutured aniridia (1), unspecified laser (1), unspecified posterior corneal excision (1), visumax laser (1), vitreous cut with vannas scissors (1), vitreous tap (1).

3.5.1 Penetrating keratoplasty survival: influence of other operative procedure/s at time of graft

Figure 3.5.1 shows the comparison of survival for grafts where other operative procedure/s were performed at the time of graft (excluding cataract extraction, pseudophakic IOL insertion, and pseudophakic IOL removal), to those where one was not. A significant difference was found across groups (Log Rank Statistic=405.51; df=1; p<0.001). This variable was retained in the final multivariatemodel (see section 3.7)

Figure 3.5.1 Other procedure/s at time of graft



Number at risk (years post-graft)

	1	5	10	15	20	25	30
No other procedure	15516	6351	2831	2019	705	313	79
Other procedure	2877	1041	354	112	34	9	NA

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
No other procedure	0.93	0.76	0.62	0.56	0.37	0.25	0.12
Other procedure	0.88	0.61	0.43	0.28	0.20	NA	NA

3.6 Post-graft Events

Table 3.9 shows post-graft surgical procedures, as reported by follow-up practitioners. 3,868 penetrating keratoplasties were reported to have failed and undergone a re-grafting procedure at the date last seen. Of these, 2045 had not had additional post-graft operative procedures reported.

Table 3.9 Post-surgical procedures

Penetrating Keratoplasty

Post-graft Surgical Procedures Excluding Re-graft

	Number
Cataract removal and IOL insertion	2087
Cataract removal without IOL insertion	48
IOL insertion (cataract removed prior to graft)	204
IOL repositioned/removed/exchange	198
Insertion of piggyback lens	72
Implantable contact lens	70
Relaxing incision	1088
YAG laser	1077
Trabeculectomy	1056
Suture adjustment	822
Wound repair/re-sutured	599
Vitrectomy	257
Compression sutures	411
PRK laser	339
Keratectomy	204
Tube insertion*	202
Intravitreal/intracameral/conjunctival injection/s**	201
LASIK	183
Keratotomy	176
Wedge resection	157
Tarsorrhaphy	149
Keratoplasty (refractive: 98, conducive: 4, unspecified:12)	114
Cyclodiode	103
Conjunctival flap (Gunderson: 48, unspecified: 44)	92
Retinal detachment surgery not otherwise specified	85
Enucleation	77
Concurrent graft (patch: 45, limbal/conjunctival: 12)	57

Evisceration	44
Cryotherapy	41
Ptosis repair	40
Mitomycin C	39
Bleb needling/revision	34
Corneal debridement/scraping	31
Iridectomy	27
Epiretinal membrane peel	25
Interface revision	25
Other***	722
Total post-graft surgical procedures (number of grafts)	**12521 (7591)**

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.

Note: see section 1.3 for an explanation of concurrent grafts.

*Molteno valve (138), Baerveldt tube (44), XEN stent (4), iStent (2), Jones tube (1), unspecified (13).

**Avastin (121), 5FU (13), silicone oil (12), Triamcinolone (8), unspecified antibiotics (8), Lucentis (7), Botulinum toxin (6), Eylea (6), Anti-VEGF (4), Bevacizumab (1), periocular steroid (1), SF6 (1), subretinal tissue plasmogen activator (1), Voriconazole (1), unspecified - conjunctival (1), unspecified - for epithelial downgrowth (1), unspecified - for neovascularisation (1), unspecified (8).

***Other included: Removal of corneal scar (22); corneal gluing (21); revision of Molteno valve (21); ectropion repair (19); iridotomy (19); photocoagulation (19); refractive surgery - unspecified (19); punctal cautery (17); amniotic membrane transplant (16); division of anterior synechiae (16); corneal collagen cross linking (15); punctal plug inserted (15); synechiolysis (15); entropion repair (14); removal of pterygium (14); blepharoplasty (12); revision of trabeculectomy (12); trabeculoplasty (12); anterior chamber reformation (11); anterior chamber tap (11); biopsy (11); glaucoma surgery - unspecified (11); pupilloplasty (11); removal of cyst (11); selective laser trabeculoplasty (10); squint repair (10); anterior chamber washout (9); laser - unspecified (9); removal of band keratopathy (9); removal of carcinoma (9); scleral buckle (9); strabismus surgery (9); dacryocystorhinostomy (7); lid surgery - unspecified (7); removal of foreign body (7); epilation of eyelashes (6); keratoprosthesis inserted (6); ocular surgery - unspecified (6); removal of chalazion (6); removal of silicone oil (6); canthoplasty (5); capsulotomy (5); iris repair (5); removal of Baerveldt tube (5); removal of filaments (5); removal of lid lesion (5); removal of limbal lesion (5); removal of Molteno valve (5); removal of natural lens for reason other than cataract (5); removal of residual lens material (5); trabeculectomy revision (5); cautery (4); drainage of choroidal haemorrhage (4); iridoplasty (4); Keraring inserted (4); laser to retinal tear (4); removal of retained Descemet membrane (4); revision of graft host junction (4); revision of unspecified glaucoma drainage device (4); Fassanella Servat procedure (3); insertion of punctal plugs (3); paracentesis (3); punctal snip (3); removal of hyphaema (3); removal of plaque (3); removal of pupillary membrane (3); repair iris prolapse (3); repair of vitreous haemorrhage (3); retrobulbar alcohol (3); revision of Baerveldt tube (3); suture manipulation (3); trichiasis treatment - unspecified (3); vitreous tap (3); air tampanade (2); alcohol delamination (2); beta irradiation (2); capsulectomy (2); conjunctival resection (2); drainage operation - unspecified (2); EDTA chelation (2);

healon to anterior chamber (2); Holmm sclerectomy (2); iris implant inserted (2); laser to suture (2); LASIK enhancement (2); macular hole surgery (2); removal of epithelial plugs (2); removal of iris cyst (2); removal of prolapsed iris (2); removal of scleral buckle (2); reposition iris (2); resection of conjunctiva (2); vitreolysis - laser (2); vitreoretinal surgery - unspecified (2); aborted trabeculectomy (1); artificial iris inserted (1); bubble to split Descemet's membrane (1); canalicular repair (1); clearance of iris from the graft (1); division of angle adhesions and pupil membrane (1); docryoceptothinostomy (1); elevation of IOL into anterior chamber (1); esotropia surgery (1); excimer laser debridement to area of vacuolation (1); exenteration (1); eye muscle surgery unspecified (1); fluid-gas exchange (1); gold weight insertion (1); goniosynechiolysis (1); grooved on slit-lamp (1); implantable contact lens replaced (1); implantable contact lens rotated (1); insertion of artificial iris (1); insertion of Morcher capsular tension ring (1); internal limiting membrane peel (1); iris clip repositioned (1); iris repositioned (1); lacrimal duct reconstruction (1); lysis - unspecified (1); ocular exploration (1); oil exchange (1); orbital decompression (1); pupil block (1); pupillary cerclage (1); reattachment of Descemet's membrane (1); removal of conjunctival keratin (1); removal of epithelial dystrophy from graft host junction (1); removal of exposed scleral bullae (1); removal of fibrosis (1); removal of implantable contact lens (1); removal of intraocular material (1); removal of iris from graft host junction (1); removal of ocular fluid (1); removal of pannus (1); removal of pinguecula (1); removal of retrocorneal membrane (1); removal of tarsorrhaphy (1); removal of trabeculectomy (1); removal of unspecified glaucoma drainage device (1); repair of iridotomy (1); repair of vitreous prolapse (1); repositioning of Keraring segment (1); retinectomy (1); revision of astigmatic keratotomy (1); revision of vitrectomy (1); Scheie's operation (1); scleral flap (1); secondary implant - unspecified (1); silicon bond encirclement (1); sphincterotomy (1); submandibular gland transplant (1); synechiotomy (1); syringing of tear ducts (1); tarsorrhaphy release (1); viscocanalostomy (1); vitreous band dissection (1).

Table 3.10 shows the occurrence of post-graft events, 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 3.10 Post-graft events, significant in univariate analyses

Penetrating Keratoplasty
Post-graft Events

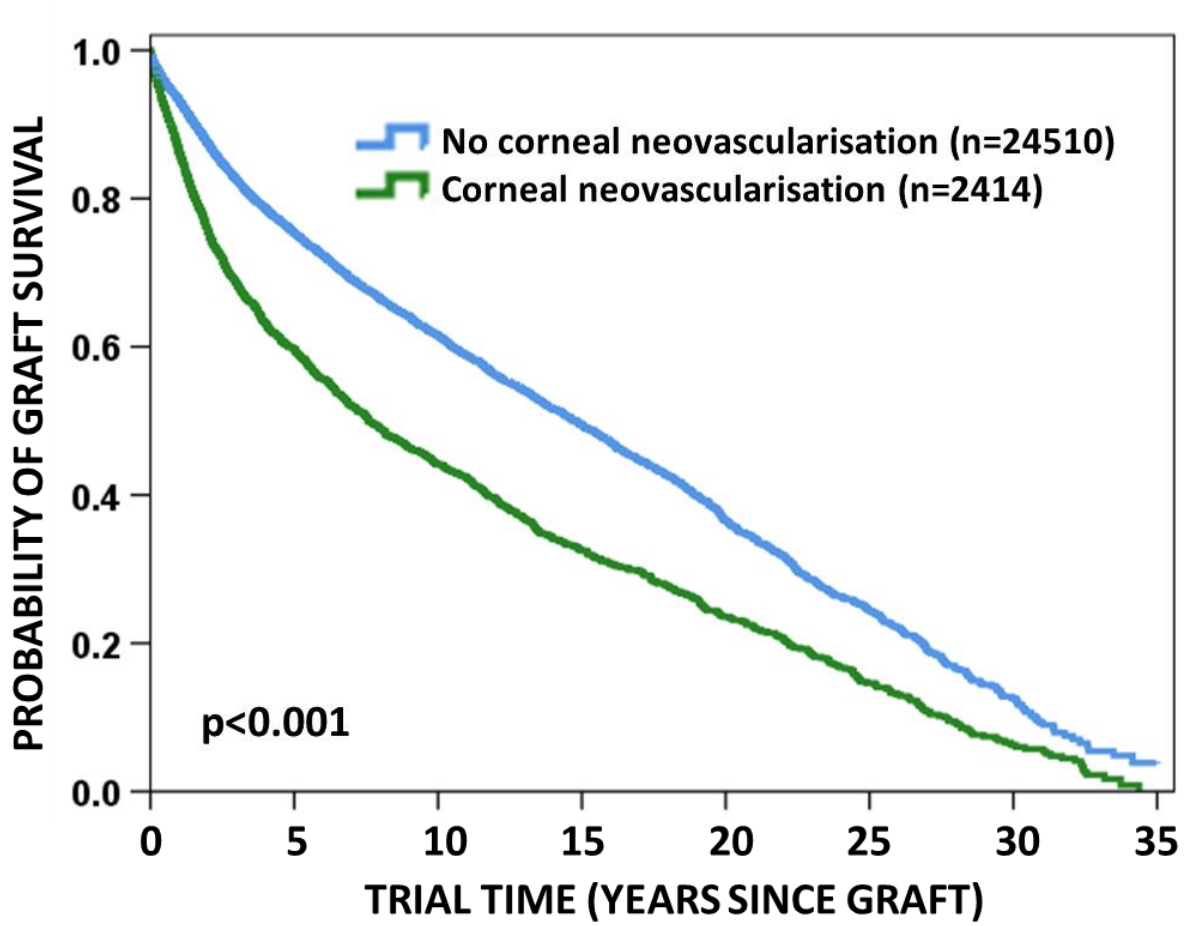
	Registered (%)	Followed (%)
Post-graft neovascularisation		
No	24510 (91%)	19644 (89%)
Yes	2414 (9%)	2414 (11%)
Post-graft herpetic infection		
No	26320 (97%)	21454 (98%)
Yes	604 (3%)	604 (2%)
Post-graft oedema		
No	21152 (93%)	20114 (91%)
Yes	1944 (7%)	1944 (9%)
Post-graft microbial keratitis		
No	25982 (97%)	21116 (96%)
Yes	942 (3%)	942 (4%)
Post-graft rise in intraocular pressure		
No	22693 (84%)	17827 (81%)
Yes	4231 (16%)	4231 (19%)
At least one rejection episode		
No	22387 (83%)	17521 (79%)
Yes	4537 (17%)	4537 (21%)
Time to removal of all sutures		
Within 6 months	605 (2%)	605 (3%)
7 months to 24 months	8582 (32%)	8582 (39%)
More than 2 years	2847 (11%)	2847 (13%)
Not yet removed/not advised*	14890 (55%)	10024 (45%)
Total	***26924 (100 %)***	***22058 (100 %)***

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

3.6.1 Penetrating keratoplasty survival: influence of post-graft neovascularisation

Figure 3.6.1 shows the influence of post-graft neovascularisation on graft survival. A significant difference was found across groups (Log Rank Statistic=284.57; df=1; p<0.001). This variable was retained in the final multivariate model (see section 3.7).

Figure 3.6.1 Post-graft neovascularisation



Number at risk (years post-graft)

	1	5	10	15	20	25	30
No neovascularisation	16371	6394	2681	1241	577	245	57
Neovascularisation	2022	1400	504	284	162	77	22

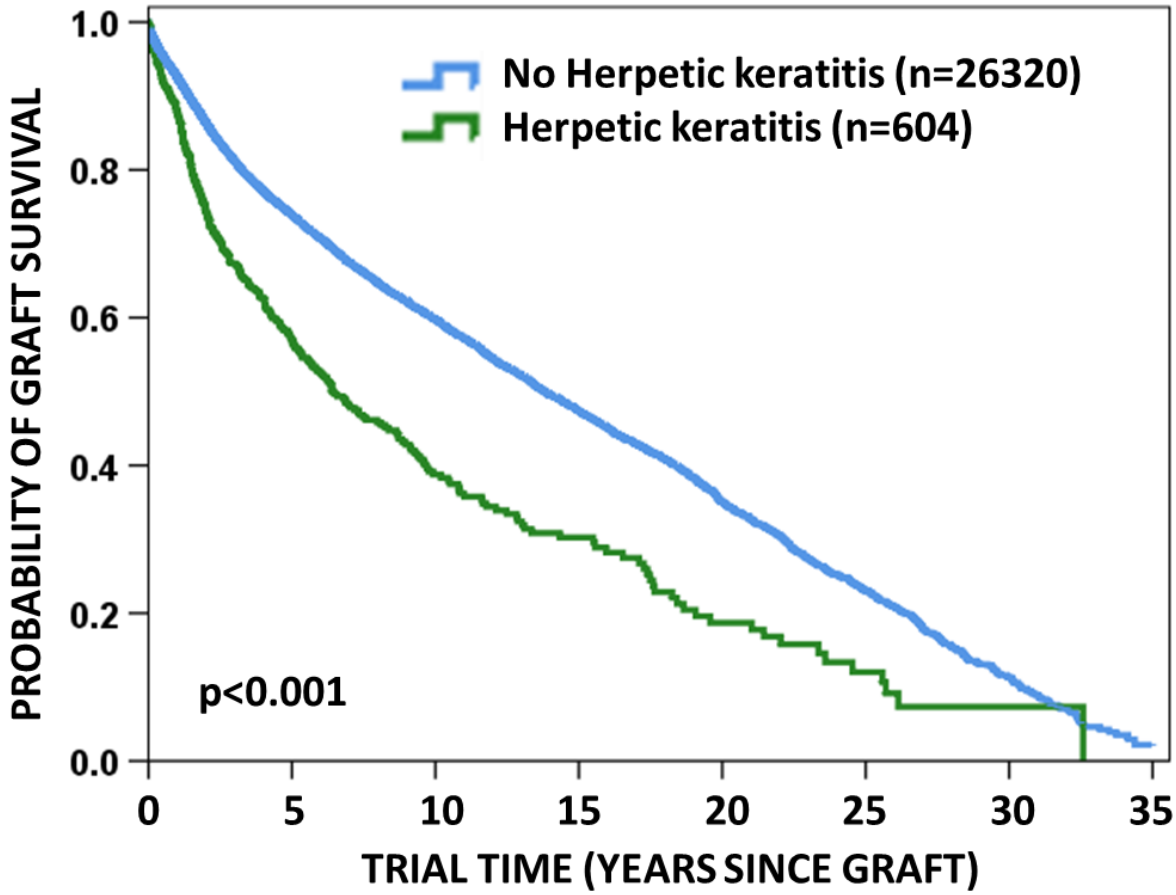
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
No neovascularisation	0.93	0.75	0.62	0.50	0.37	0.24	0.13
Neovascularisation	0.86	0.70	0.44	0.33	0.24	0.15	0.06

3.6.2 Penetrating keratoplasty survival: influence of post-graft herpetic infection

Figure 3.6.2 shows the influence of post-graft herpetic infection on graft survival. A significant difference was found across groups (Log Rank Statistic=102.67; df=1; p<0.001). This variable was not retained in the final multivariate model (see section 3.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 3.6.2 Post-graft herpetic infection



Number at risk (years post-graft)

	1	5	10	15	20	25	30
No herpetic infection	17881	7157	3093	1013	719	313	78
Herpetic infection	512	235	92	48	20	9	1

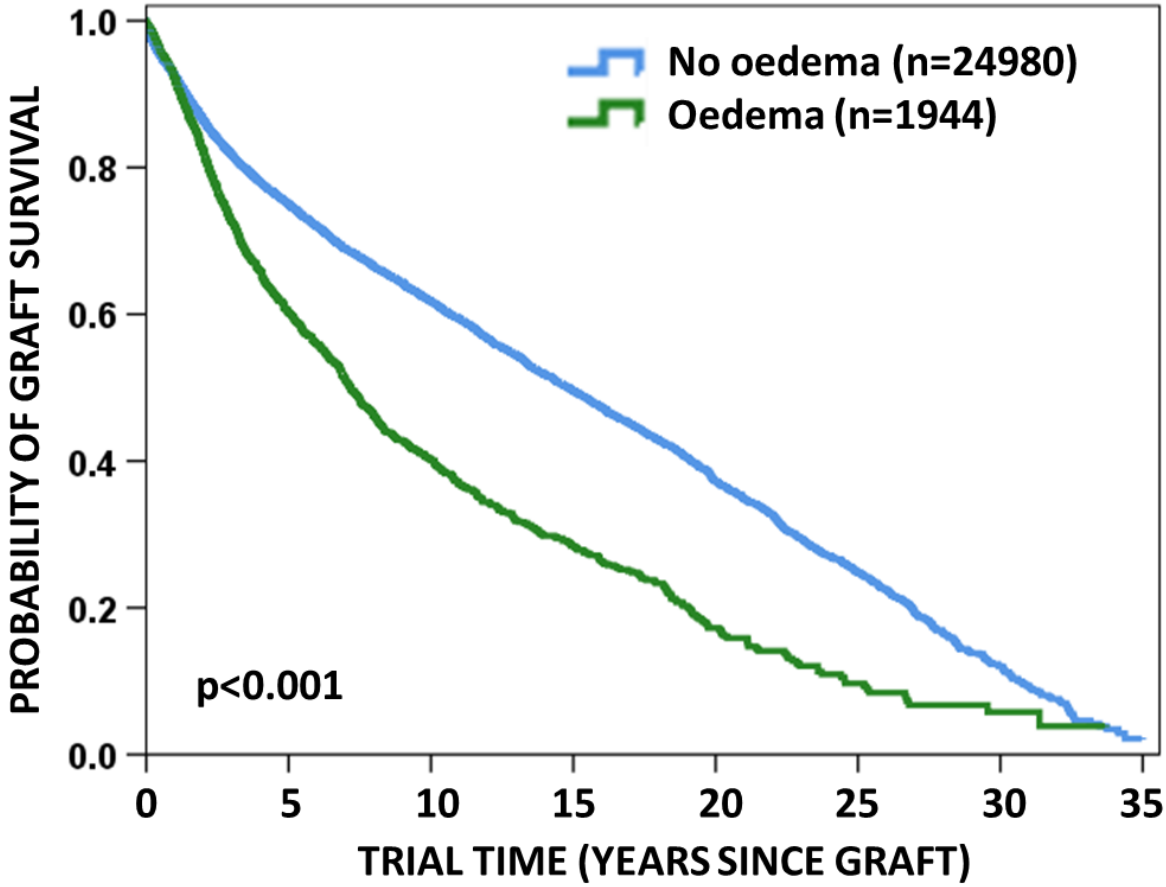
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
No herpetic infection	0.93	0.74	0.60	0.42	0.35	0.23	0.11
Herpetic infection	0.88	0.57	0.39	0.30	0.19	NA	NA

3.6.3 Penetrating keratoplasty survival: influence of post-graft corneal oedema

Figure 3.6.3 shows the influence of post-graft corneal oedema on graft survival. A significant difference was found across groups (Log Rank Statistic=251.90; df=1; p<0.001). This variable was retained in the final multivariate model (see section 3.7).

Figure 3.6.3 Post-graft corneal oedema



Number at risk (years post-graft)

	1	5	10	15	20	25	30
No oedema	16659	6598	2841	1363	673	299	75
Oedema	1734	794	344	162	66	23	4

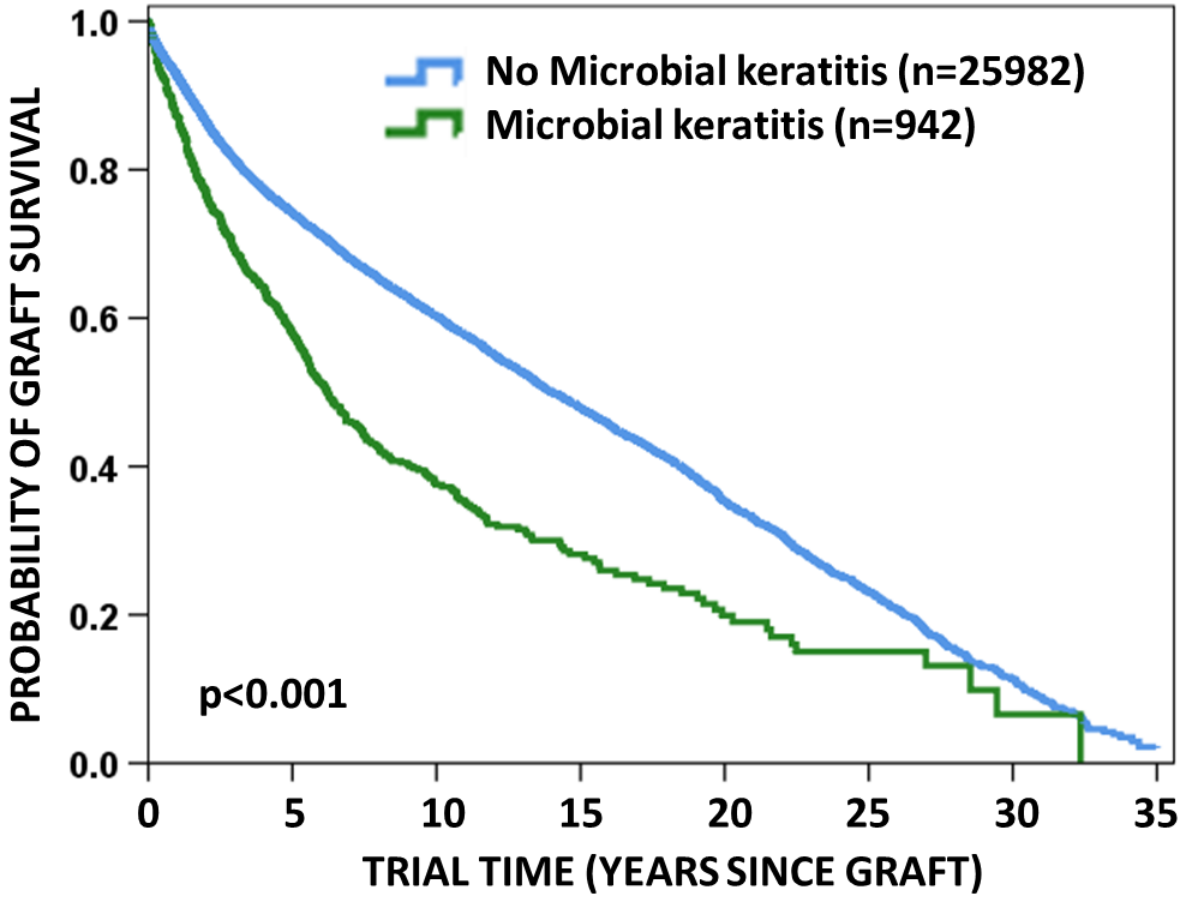
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
No oedema	0.93	0.75	0.62	0.50	0.37	0.25	0.12
Oedema	0.92	0.60	0.40	0.28	0.17	0.10	NA

3.6.4 Penetrating keratoplasty survival: influence of post-graft microbial keratitis

Figure 3.6.4 shows the influence of post-graft microbial keratitis on graft survival. A significant difference was found across groups (Log Rank Statistic=155.41; df=1; p<0.001). This variable was retained in the final multivariate model (see section 3.7).

Figure 3.6.4 Post-graft microbial keratitis



Number at risk (years post-graft)

	1	5	10	15	20	25	30
No microbial keratitis	17593	7037	3054	1471	715	313	77
Microbial keratitis	800	355	131	54	24	9	2

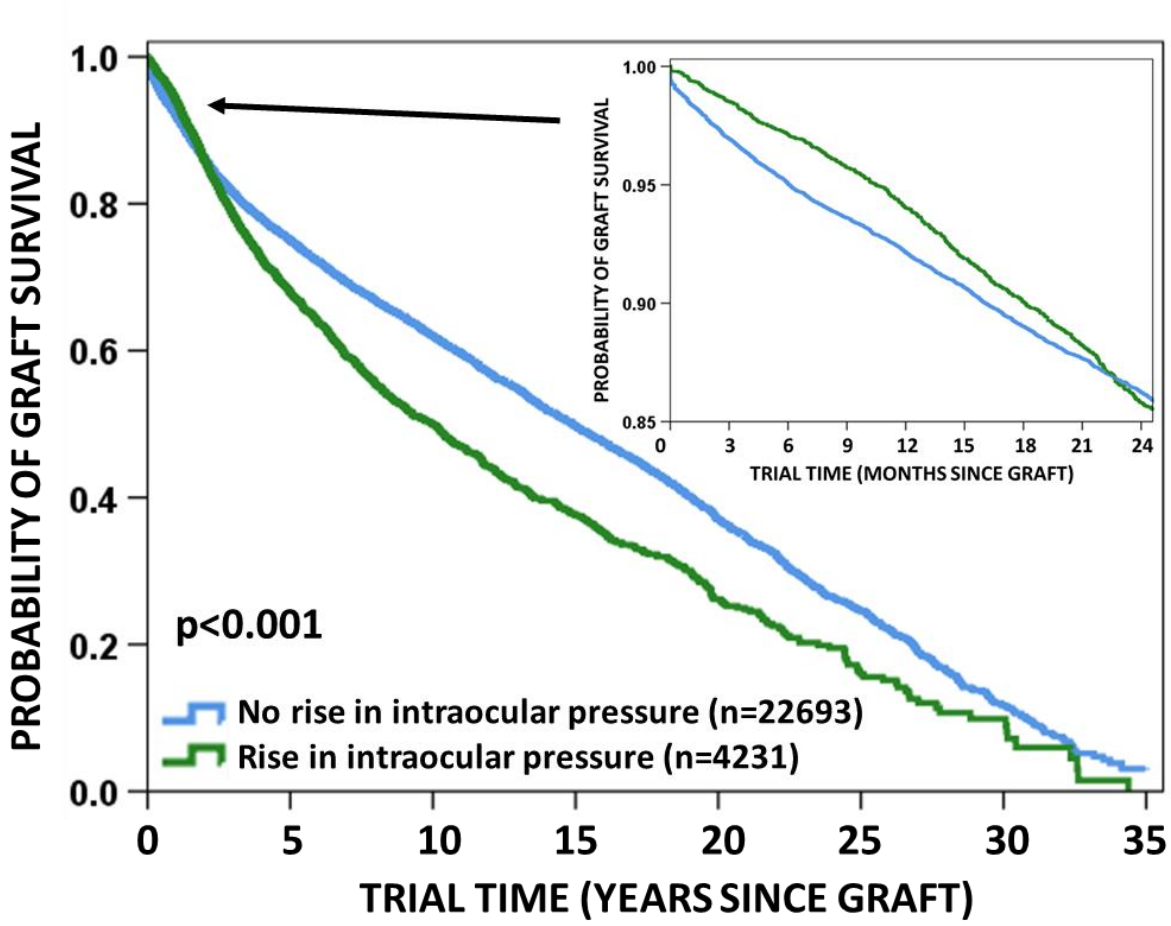
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
No microbial keratitis	0.93	0.74	0.60	0.48	0.35	0.23	0.11
Microbial keratitis	0.87	0.58	0.38	0.28	0.20	NA	NA

3.6.5 Penetrating keratoplasty survival: influence of post-graft rise in intraocular pressure (IOP)

Figure 3.6.5 shows the influence of post-graft rise in intraocular pressure on graft survival. A significant difference was found across groups (Log Rank Statistic=88.25; df=1; p<0.001). The inset magnification of the survival curve for approximately the first two years post-graft, shows that those grafts with a post-graft rise in IOP reported had superior survival over this time frame, before the survival curves crossed and those with raised IOP had poorer survival past this point. This variable was retained in the final multivariate model (see section 3.7).

Figure 3.6.5 Post-graft rise in intraocular pressure



Number at risk (years post-graft)

	6m	1	18m	2	5	10	15	20	25	30
No rise in IOP	16015	14636	12616	10897	5691	2502	1239	622	284	68
Rise in IOP	4017	3757	3409	3048	1701	683	286	117	38	11

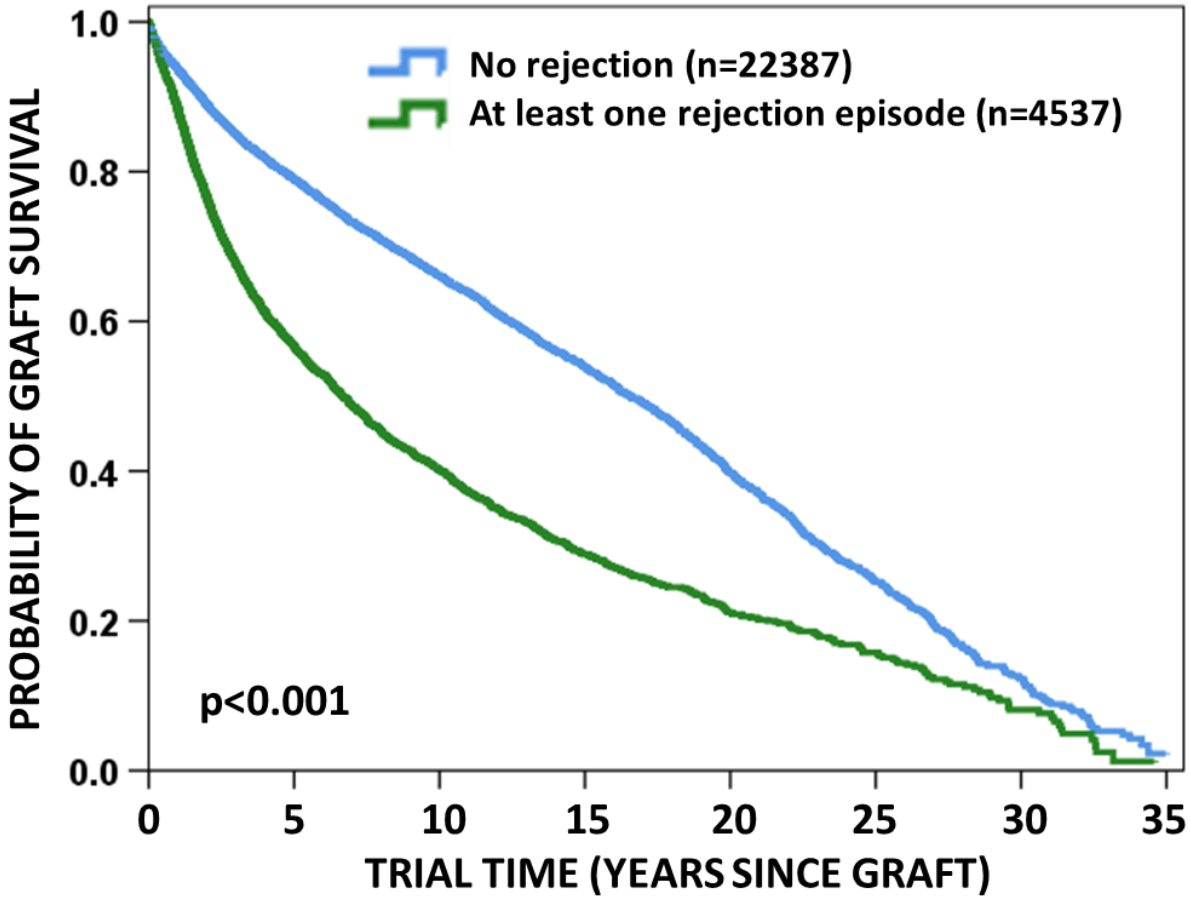
Probability of graft survival (years post-graft)

	6m	1	18m	2	5	10	15	20	25	30
No rise in IOP	0.95	0.92	0.89	0.86	0.75	0.62	0.50	0.37	0.25	0.12
Rise in IOP	0.97	0.94	0.90	0.86	0.68	0.50	0.38	0.26	0.16	NA

3.6.6 Penetrating keratoplasty survival: influence of any graft rejection

Figure 3.6.6 shows the influence of any episodes of graft rejection on graft survival. A significant difference was found across groups (Log Rank Statistic=813.83; df=1; p<0.001). This variable was retained in the final multivariate model (see section 3.7).

Figure 3.6.6 Any graft rejection



Number at risk (years post-graft)

	1	5	10	15	20	25	30
No rejection	14481	2690	2437	1174	582	251	61
Any rejection	3912	1702	748	351	157	71	18

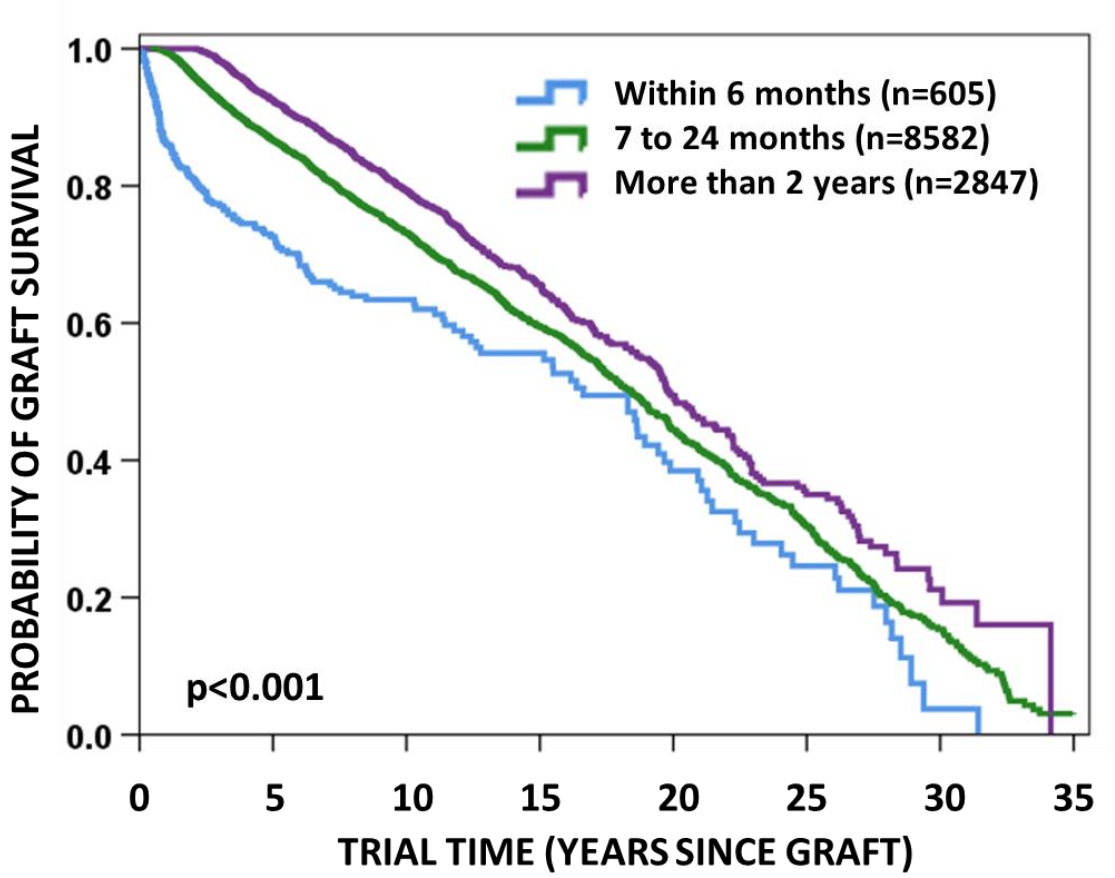
Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
No rejection	0.94	0.79	0.66	0.54	0.40	0.25	0.12
Any rejection	0.89	0.57	0.40	0.29	0.21	0.16	NA

3.6.7 Penetrating keratoplasty survival: influence of time to suture removal

Figure 3.6.7 shows the influence of time to suture removal on graft survival. Times were initially stratified into 6-month post-graft time frames, with all grafts where sutures were removed after more than two years categorised together. A significant difference was found across groups (Log Rank Statistic=131.32; df=4; p<0.001). Further analyses examined whether there were significant differences between adjacent time groups, and where no significant difference was found, these groups were categorised together. The difference across groups remained significant (Log Rank Statistic=130.86; df=2; p<0.001). All three between groups comparisons were significant (all p<0.001). Due to the high level (55%) of missing data, this variable was not included in the multivariate analysis (see section 3.7).

Figure 3.6.7 Time to suture removal



Number at risk (years post-graft)

	1	5	10	15	20	25	30
Within 6 months	401	180	94	58	29	14	1
7 to 24 months	8313	3416	1504	746	381	179	52
More than 24 months	2847	1730	754	325	138	64	11

Probability of graft survival (years post-graft)

	1	5	10	15	20	25	30
Within 6 months	0.86	0.73	0.63	0.56	0.39	NA	NA
7 to 24 months	0.99	0.87	0.73	0.60	0.45	0.30	0.15
More than 24 months	1.00	0.93	0.79	0.66	0.49	0.35	NA

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 (see section 1.4.6 for further information).

Table 3.11 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 collinear with (i.e. were highly correlated and produced the same effect on the outcome as) another variable in the model or the number of grafts with missing data (>50%) was too high.

Table 3.11 Multivariate model

Penetrating Keratoplasty
Multivariate Model

Not significant in univariate analysis
- Time from storage of donor tissue to graft – organ culture
- Time in deswelling media for tissue stored in organ culture media
- Recipient sex
- Eye grafted
- Donor/recipient sex match/mismatch

Significant in univariate analysis but excluded from multivariate model due to collinearity and/or missing data
- Australian State in which graft was performed (collinear with eye bank and interstate transportation)
- The centre effect (collinear with surgeon caseload and level of follow-up)
- Central endothelial cell count (missing data)
- Time to removal of sutures (missing data)

Significant in univariate analysis but not retained in multivariate model
- Cause of donor death
- Eye only donor
- Recipient age group
- Time from donor death to enucleation of donor tissue
- Time from enucleation to storage of donor tissue
- Eye bank
- Interstate transportation of donor cornea
- Time from storage of donor tissue to graft – hypothermic storage
- Storage medium
- Post-graft herpetic eye infection
- Donor sex

Significant in univariate analysis AND retained in multivariate model
- Donor age group
- Indication for graft (combined with number of previous ipsilateral grafts)
- Pre-graft corneal neovascularisation
- Number of pervious contralateral grafts
- Pre-graft inflammation and/or steroid use
- Raised intraocular pressure in past and/or at graft
- Graft size
- Change in lens status from pre- to post-graft
- Other operative procedure at graft
- Surgeon caseload and level of follow-up
- Graft era/year
- Any post-graft rejection
- Post-graft corneal neovascularisation
- Post-graft corneal oedema
- Post-graft microbial keratitis
- Post-graft rise in intraocular pressure

Table 3.12 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, except where it made logical sense to use a different group.

The hazard ratios for a given variable are adjusted for all other variables in the model. This model included data from 26,143 penetrating keratoplasties, performed in 19,540 recipients. Where no valid response had been provided for one of the included variables, these cases were classified as "not advised" and these categories were included where 2% of cases were included in this group. The overall model was highly significant: (Chi^2=5280.64, p<0.0001).

Table 3.12 Clustered multivariate model

	n	Hazard ratio	Standard Error	p-value	Global p-value	95% Confidence Interval
Donor age group						
0 to 29	2337	1.00			<0.0001	
30 to 49	4168	1.11	0.07	0.091		0.98 to 1.26
50 to 59	4584	1.25	0.08	<0.001		1.11 to 1.41
60 to 69	6553	1.39	0.08	<0.001		1.24 to 1.56
70 to 79	6340	1.43	0.08	<0.001		1.27 to 1.60
80 or older	2161	1.47	0.10	<0.001		1.29 to 1.68
Indication for graft						
One failed previous graft	5074	2.62	0.14	<0.001		2.35 to 2.92
Two failed previous grafts	1274	3.18	0.22	<0.001		2.77 to 3.65
Three or more failed previous grafts	738	3.95	0.34	<0.001		3.33 to 4.68
Keratoconus	7943	1.00			<0.0001	
Endothelial failure/bullous keratopathy	4444	2.96	0.18	<0.001		2.64 to 3.33
Fuchs' endothelial dystrophy	2060	1.83	0.12	<0.001		1.61 to 2.07
Corneal ulcers/perforation	567	4.30	0.41	<0.001		3.56 to 5.19
Herpetic eye disease	1202	2.08	0.15	<0.001		1.80 to 2.41
Trauma	702	2.79	0.24	<0.001		2.36 to 3.31
Non herpetic infection	603	3.19	0.34	<0.001		2.89 to 4.21
Other	1536	2.17	0.15	<0.001		1.90 to 2.48
Pre-graft corneal neovascularisation (tvc)						
None	17416	1.00			<0.0001	
1 quadrant	2365	0.97	0.05	0.506		0.88 to 1.07
2 quadrants	2815	1.20	0.05	<0.001		1.10 to 1.31
3 quadrants	1294	1.41	0.08	<0.001		1.25 to 1.58
4 quadrants	2253	1.83	0.09	<0.001		1.65 to 2.02
Pre-graft inflammation and/or steroid use (tvc)						
No	18508	1.00			<0.0001	
Yes	7635	1.60	0.06			1.48 to 1.73
Raised intraocular pressure in past or at graft						
No	21921	1.00			<0.0001	
Yes	4222	1.37	0.05			1.28 to 1.47
Previous contralateral grafts						
None	20390	1.00			<0.0001	
One	4618	0.80	0.03	<0.001		0.75 to 0.86
Two or more	1135	0.79	0.05	<0.001		0.69 to 0.90
Graft size						
Less than 7.75 mm	3190	1.23	0.05	<0.001		1.14 to 1.32
7.75 mm to 8.49 mm	15680	1.00			<0.0001	
8.50 mm to 8.74 mm	3490	1.09	0.04	0.026		1.01 to 1.17
8.75 mm or more	2333	1.24	0.06	<0.001		1.13 to 1.36
Not advised	1450	1.22	0.07	<0.001		1.09 to 1.35

Lens status pre and post-graft (tvc)						
Phakic post	12938	1.00			<0.0001	
Aphakic post	1679	1.62	0.03	<0.001		1.44 to 1.83
Triple procedure	2481	1.05	0.06	0.404		0.94 to 1.17
Pseudophakic post (not triple)	9045	1.37	0.07	<0.001		1.24 to 1.52
Other ocular procedure at time of graft						
No	24462	1.00			<0.0001	
Yes	1681	1.18	0.05			1.10 to 1.28
Surgeon caseload and level of follow-up						
Low caseload surgeons	13677	1.31	0.04	<0.001		1.23 to 1.39
High caseload, low follow-up	4310	1.46	0.06	<0.001		1.34 to 1.58
High caseload, high follow-up	8126	1.00			<0.0001	
Graft era/year (tvc)						
1985 to 1992	5165	1.64	0.09	<0.001		1.47 to 1.82
1993 to 1995	2500	1.50	0.08	<0.001		1.35 to 1.68
1996	775	1.36	0.11	<0.001		1.16 to 1.59
1997 to 2005	7615	1.10	0.05	0.021		1.01 to 1.19
2006 to 2011	4637	1.00			<0.0001	
2012 to 2013	1347	1.08	0.07	0.233		0.95 to 1.23
2014 to 2016	1911	1.23	0.08	0.001		1.09 to 1.39
2017	559	1.66	0.19	<0.001		1.32 to 2.08
2018	537	2.37	0.28	<0.001		1.87 to 2.99
2019	562	3.61	0.58	<0.001		2.63 to 4.96
2020	535	5.19	1.43	<0.001		3.03 to 8.89
Post-graft rejection (tvc)						
None	21729	1.00			<0.0001	
Any	4414	2.24	0.08			2.09 to 2.40
Post-graft corneal neovascularisation						
No	23782	1.00			<0.0001	
Yes	2361	1.29	0.04			1.21 to 1.38
Post-graft oedema						
No	24234	1.00			<0.0001	
Yes	1909	1.18	0.05			1.10 to 1.28
Post-graft microbial keratitis						
No	25226	1.00			0.0001	
Yes	917	1.22	0.06			1.10 to 1.35
Post-graft rise in intraocular pressure (tvc)						
No	22036	1.00			<0.0001	
Yes	4107	0.72	0.03			0.66 to 0.78

Note: tvc = time variant coefficient

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

3.7.1.1 Donor age group

Significantly better survival was shown for the under 30 years group, compared to each of the four age groups 50 years and over (all p<0.001).

Significantly better survival was shown for the 30 to 49 years group compared to each of the three age groups 60 years and over (all p<0.001).

Significantly better survival was shown for the 50 to 59 years group, compared to the 60 to 69 years group (p=0.008), 70 to 79 years group (p=0.001), and the 80 years and older group (p=0.002)

3.7.1.2 Indication for graft

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

Grafts performed for Fuchs' endothelial dystrophy had significantly better survival than those performed for failed previous graft/s (regardless of number of previous grafts), endothelial failure/bullous keratopathy, corneal ulcer, trauma, and non-herpetic infection (all p<0.001).

Grafts performed for herpetic eye disease or "other" indications for graft, had significantly better survival than those for multiple failed previous grafts (both two and three or more), endothelial failure/bullous keratopathy, corneal ulcer, and non-herpetic infection (all p<0.001). Grafts performed for herpetic eye disease also had significantly better survival than those performed for a single previous failed graft (p=0.001) or trauma (p=0.002).

In addition to those indications for graft mentioned above, grafts performed for corneal ulcer had significantly poorer survival than grafts performed for endothelial failure/bullous keratopathy, trauma, a single previous failed graft (all p<0.001), and two previous failed grafts (p=0.002); grafts performed for three or more previous failed grafts had significantly poorer survival than those performed for endothelial failure/bullous keratopathy (p<0.001) or trauma (p=0.001); and grafts performed for non-herpetic infection (p=0.001), or multiple failed previous grafts (both p<0.001) had poorer survival than those performed following a single previous failed graft.

3.7.1.3 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 either two or three quadrants of pre-graft corneal neovascularisation had significantly poorer survival than those with none, or one quadrant (all p<0.001).

Grafts performed in eyes with three quadrants of pre-graft corneal neovascularisation had significantly poorer survival than those with two quadrants (p=0.008).

3.7.1.4 Number of previous contralateral grafts

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

3.7.1.5 Graft size

Survival of grafts that were 7.75 mm to 8.49 mm was significantly better than those that were under 7.75 mm, or over 8.75 mm. They also had significantly better survival than grafts where the size was not reported to the ACGR (all p<0.001).

3.7.1.6 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 that were aphakic post graft or those that had undergone lens removal prior to graft and were pseudophakic post graft (all p<0.001).

Eyes that were aphakic post graft had significantly poorer survival than those that had undergone lens removal prior to graft and were pseudophakic post graft (p=0.001).

3.7.1.7 Number of PK registered by surgeon and level of follow-up received

Grafts performed by surgeons with 539 or more PK registered (>2% of the cohort) with the ACGR, and above average (>82%) levels of follow-up had significantly better survival than those performed by surgeons with 539 or more PK registered with the ACGR, and below average (≤82%) levels of follow-up, and surgeons with fewer than 539 PK registered (both p<0.001). Low caseload surgeons also had significantly better survival than high caseload surgeons with low follow-up (p=0.008).

3.7.1.8 Graft era/year

Grafts performed in 2019 and 2020 had significantly poorer survival than those performed in all prior eras/years, excluding 2018 (all p<0.001). Grafts performed in 2018 had significantly poorer survival than those performed in any era/year between 1993 and 2016 (all p<0.001). Grafts performed in 2017 had significantly poorer survival than those performed from 1997 to 2013 (all p≤0.001). The poor performance of grafts in these most recent years is likely due to the lag time effect discussed in section 2.3.

Grafts performed from 1993 to 1995 had poorer survival than those performed from 1997 to 2013, and grafts performed between 1985 to 1992 had significantly poorer survival than those performed from 1997 to 2016 (all p<0.001). Graft survival was also significantly poorer for grafts performed in 1996 compared to those performed between 2006 and 2011 (p<0.001).

Grafts survival was significantly better for grafts performed from 2006 to 2011 compared to those performed from 2014 to 2016 (p=0.001). Following Bonferroni correction, there were no other significant differences in graft survival for grafts performed between 1997 and 2016.

3.8 Reasons for Graft Failure

Of the 22,058 followed grafts, 6722 (30%) were known to have failed by the census date. This equates to 25% of the 26,924 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 3.13 shows the reasons for failure provided by the surgeon, with subcategory totals provided where specified.

Table 3.13 Reasons for graft failure

Penetrating Keratoplasty
Reasons for Graft Failure

		Number
Rejection		1774 (26%)
Unspecified/endothelial cell failure	1484	
With glaucoma/raised IOP	75	
With non-herpetic infection	56	
With herpetic infection	35	
With vascularisation	32	
With scarring	19	
With other	73	
Endothelial cell failure		1477 (22%)
Phakic	294	
Aphakic	131	
Pseudophakic	1052	
Non-herpetic infection		562 (8%)
Microbial/bacterial keratitis	270	
Endophthalmitis	86	
Fungal keratitis	72	
Acanthamoeba keratitis	7	
Viral keratitis	4	
Glaucoma/raised IOP		297 (4%)
With endothelial cell failure	34	
With other*	51	
Corneal ectasia/keratoconus/thinning/astigmatism		242 (3%)
Primary graft failure		192 (3%)
Corneal ulcer		185 (3%)
Perforated	125	
Trauma		180 (3%)
Rupture	62	
Penetrating eye injury	16	
Blunt force trauma	14	
Surgical trauma	4	
Burns	3	

		Number
Herpetic infection		165 (2%)
Corneal scarring/opacity		127 (2%)
Stem cell/epithelial failure		119 (2%)
Other specified*		330 (4%)
Unspecified		1072 (16%)
	Total	**6722 (100%)**

* Other included: corneal neovascularisation (7), uveitis (6), anterior chamber haemorrhage (3), band keratopathy (3), epithelial downgrowth (3), synechiae (3), unspecified infection (3), central retinal vein occlusion (2), Descemet's membrane detachment (2), epithelial defect (2), ICE syndrome (2), perforation (2), blepharitis (1), cataract (1), calcification (1), corneal nebula (1), IOL complication (1), Peters' anomaly (1) phthisical eye (1), pseudophakic touch (1), retinal detachment (1), retrocorneal membrane (1), scleral necrosis (1), trichiasis (1), wound leak (1).

** Other included: neovascularisation (57), corneal melt (51), phthisis (32), recurrent dystrophy (32), wound dehiscence (20), band keratopathy (14), descemetocoele (12), retinal detachment (12), choroidal haemorrhage (8), hypotony (6), ICE syndrome (6), Descemet's detachment (5), epithelial downgrowth (5), calcification (4), dry eye (4), expulsive haemorrhage (4), lipid keratopathy (4), rubeosis iridis (4), squamous cell carcinoma (4), anterior segment ischaemia (3), neurotrophic keratopathy (3), spontaneous graft detachment (3), uveitis (3), protein deposits (2), recurrent erosions (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 membrane folds (1), erythroderma (1), fibrous ingrowth (1), hypopyon (1), keratomalacia (1), meibomianitis (1), necrosis (1), nuclear sclerosis (1), pemphigoid (1), Peters anomaly (1), pterygium (1), pupillary membrane (1), retinal occlusion (1), Sjogren's syndrome (1), stromal failure (1), stromal folds (1), unspecified systemic illness (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 192 grafts reported by surgeons to have been primary graft failures, the majority (157) had no further information provided, while for a further nine the surgeon stated that the donor tissue was of poor quality.

Additional specific reasons given were: epithelial defect in donor (4), wound dehiscence (4), expulsive haemorrhage (5), oedema (3), corneal perforation (2), opacity (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), trauma (1), ulcer (1), undersized graft (1), unspecified infection (1), unspecified intraoperative complications at graft (1).

3.9 Post-graft Best Corrected Visual Acuity

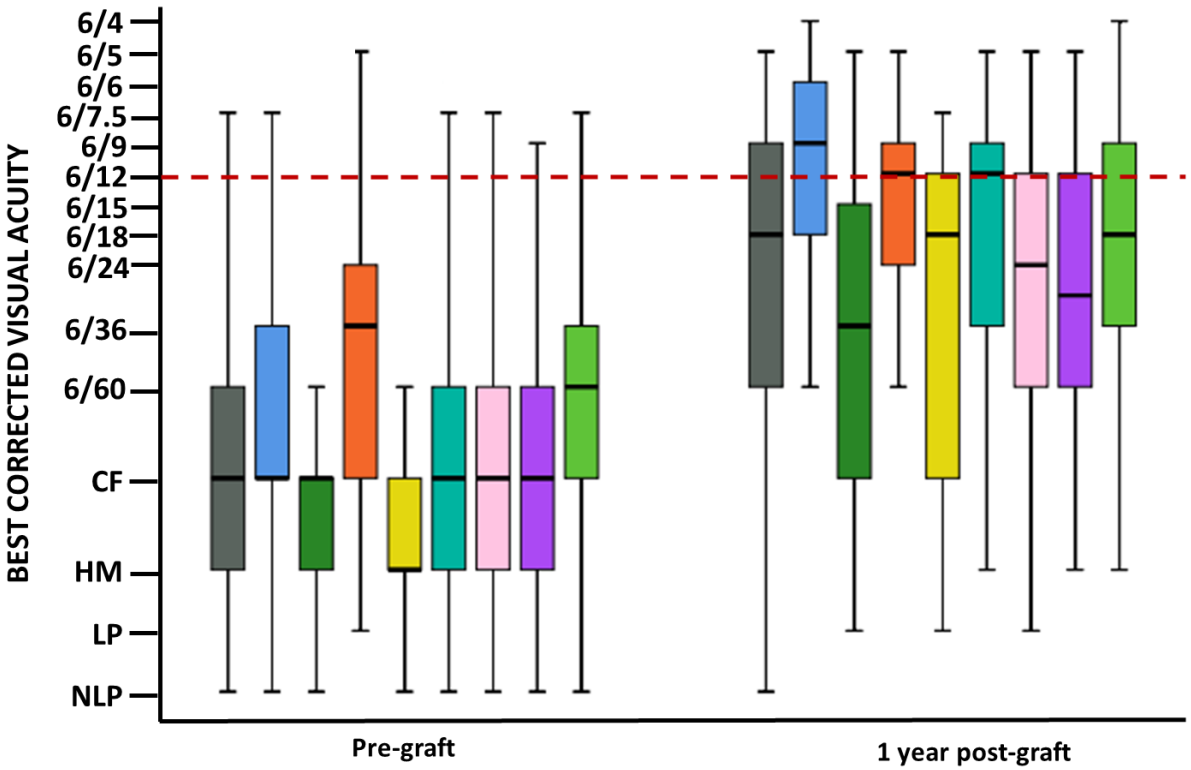
Post-graft best corrected visual acuity (BCVA) is an important outcome for corneal graft recipients. A desire for improved visual acuity was specified as a reason for graft in 20,995 (78%) of registered penetrating keratoplasties. In 63% of cases (16,860), this was the sole desired outcome indicated. All analyses are conducted on data for **surviving** grafts. See section 1.4.7 for further explanation of the methods used to analyse visual acuity data.

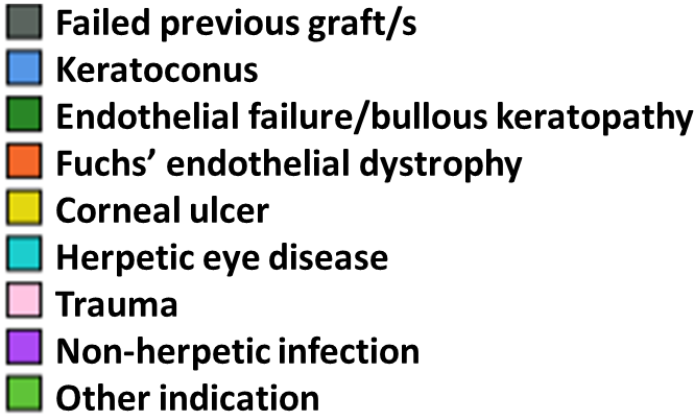
3.9.1 Penetrating keratoplasty: One-year post-graft visual acuity change by indications for graft

Figure 3.9.1 shows the pre-graft best corrected visual acuity, and the one-year post-graft best corrected visual acuity, reported for eyes undergoing penetrating keratoplasty for each of the indication for graft groups. The central line within each box-and-whisker plot shows the median BCVA reported for the group, the box represents the inter-quartile range, while the whisker shows the range. Please note that outliers were included in the calculation of the box and whisker plots but are not shown in the figures. The dashed line indicates a BCVA of 6/12, which represents functional vision.

Median pre-graft BCVA was worst for grafts for corneal ulcers (Hand Movement) and best for grafts for Fuchs' endothelial dystrophy (6/36). All other individual categories had median pre-graft BCVA of Count Fingers while other indications had 6/60. At one-year post-graft, there had been a significant improvement in BCVA for all indications for graft (all p<0.001), with grafts for Fuchs' endothelial dystrophy and herpetic eye disease achieving a median BCVA of 6/12, and those for keratoconus achieving 6/9.

Figure 3.9.1 Best corrected visual acuity pre-graft and one-year post-graft





Number of grafts with BCVA data available at each time point

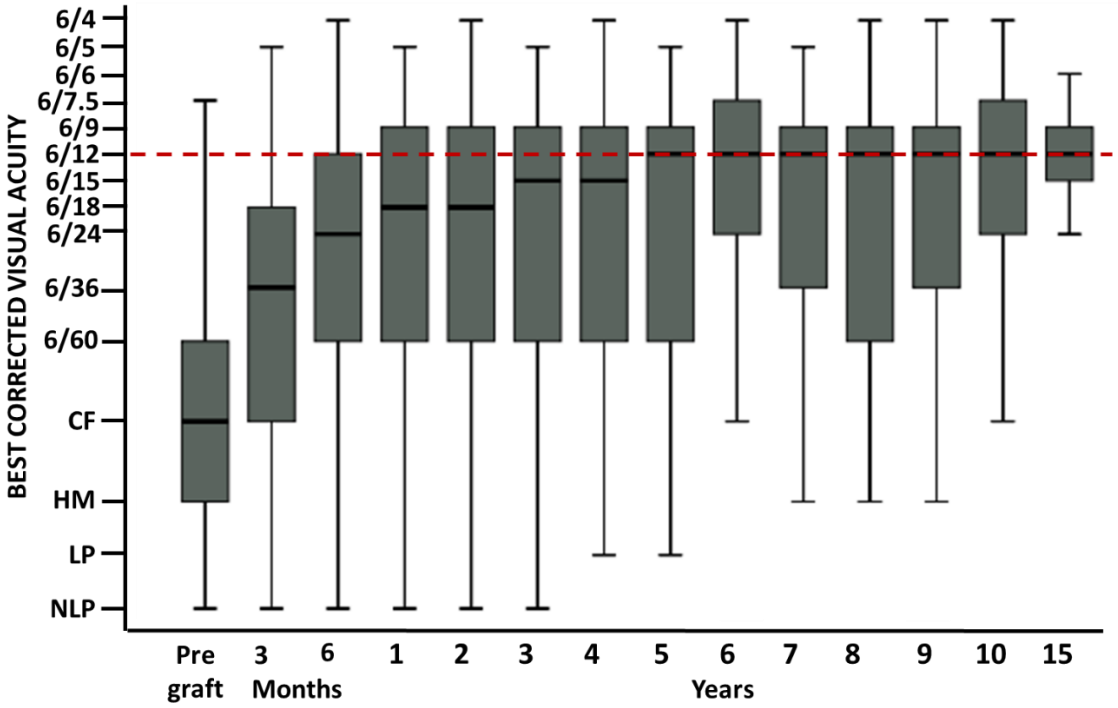
	Pre	3m	6m	1y	2y	3y	4y	5y
Failed previous graft/s	6247	215	277	542	427	254	199	149
Keratoconus	6845	343	481	1006	666	390	285	235
Endothelial failure/bullous keratopathy	3717	246	283	460	253	153	105	74
Fuchs' endothelial dystrophy	1819	60	114	211	167	117	78	62
Corneal ulcer	458	20	30	31	26	14	9	8
Herpetic eye disease	959	57	62	131	77	53	40	28
Trauma	614	28	29	63	52	34	24	15
Non-herpetic infections	498	14	27	42	23	19	15	11
Other	1278	71	100	185	113	64	55	36

	6y	7y	8y	9y	10y	15y	20y	25y	30y
Failed previous graft/s	117	102	56	55	49	13	4	1	0
Keratoconus	208	163	113	123	91	67	22	16	4
Endothelial failure/bullous keratopathy	57	45	39	22	17	6	1	0	0
Fuchs' endothelial dystrophy	73	59	43	30	31	12	1	0	0
Corneal ulcer	2	2	0	1	0	1	0	0	0
Herpetic eye disease	14	20	11	8	6	5	4	0	0
Trauma	15	8	6	4	3	0	0	0	0
Non-herpetic infections	6	7	6	1	0	0	0	0	0
Other	23	21	29	15	13	3	2	0	0

The figures on pages 96 to 104 look at the median BCVA achieved over time for individual indications for graft.

3.9.2 Penetrating keratoplasty: Changes in best corrected visual acuity over time by individual indications for graft

Figure 3.9.2. Best corrected visual acuity for surviving penetrating keratoplasties performed for failed previous graft/s, over time



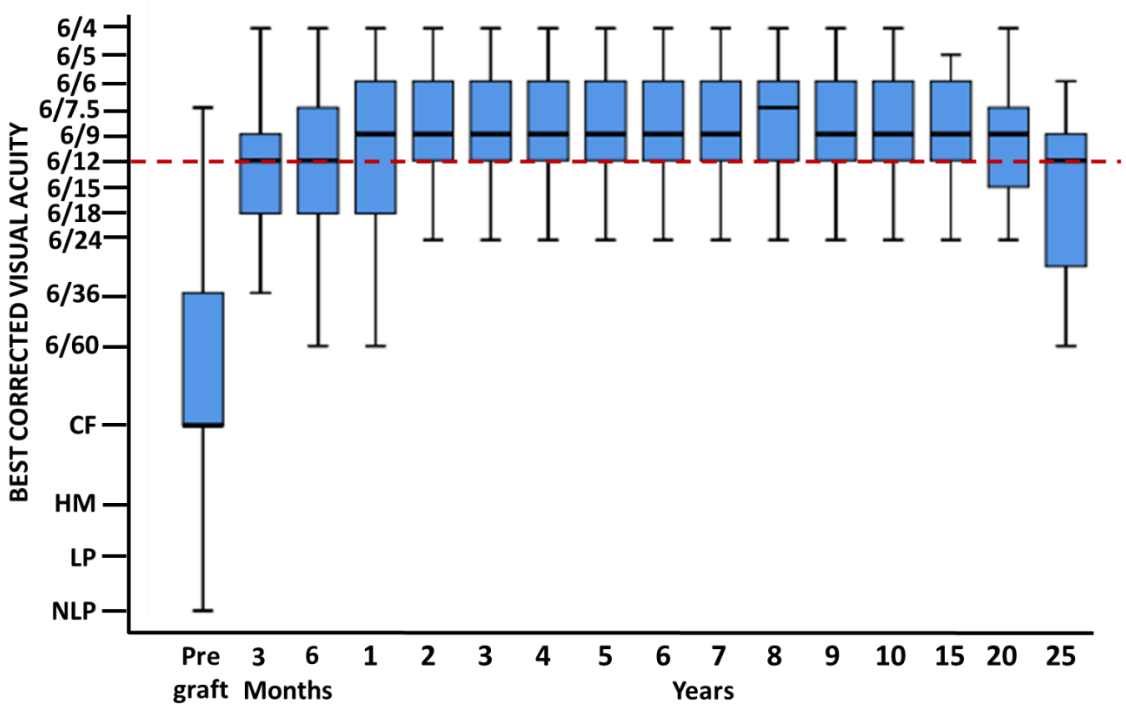
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y	15y
6247	215	277	542	427	254	199	149	117	102	56	55	49	13

The median BCVA obtained following penetrating keratoplasty for failed previous graft improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$) and continued to improve significantly at each individual time-point compared to the previous time-point up to 2-years post graft ($p=0.007$, $p=0.007$, $p=0.023$, respectively). There were no significant changes in median BCVA after 2-years post-graft. The difference compared to pre-graft BCVA remained significant to 15-years post-graft (all $p<0.001$).

Penetrating keratoplasties performed for failed previous graft/s, which survived for 5-years, achieved a median BCVA of 6/12. This remained the median BCVA up to 15 years post-graft for surviving grafts for failed previous graft/s.

Figure 3.9.3 Best corrected visual acuity for surviving penetrating keratoplasties performed for keratoconus, over time



Number of grafts with data at each time point

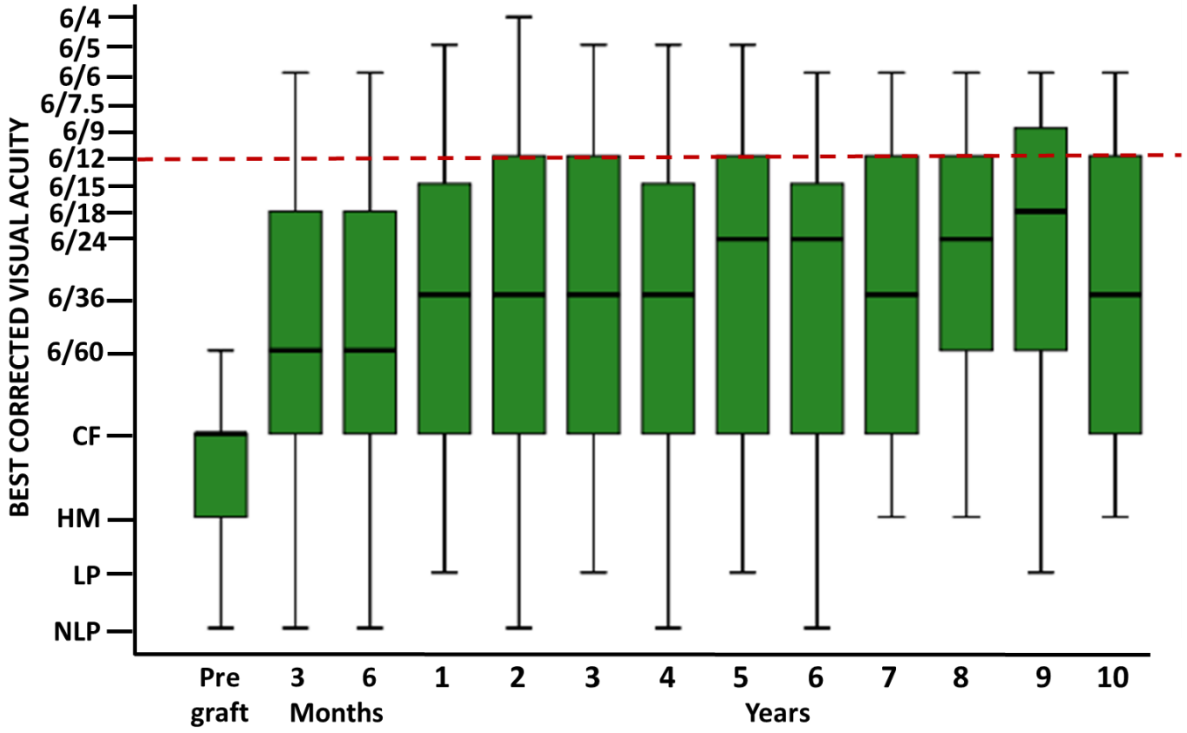
Pre	3m	6m	1y	2y	3y	4y	5y
6845	343	481	1006	666	390	285	235

6y	7y	8y	9y	10y	15y	20y	25y
208	163	113	123	91	67	22	16

The median BCVA obtained following penetrating keratoplasty for keratoconus improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$) and continued to improve significantly at each individual time-point compared to the previous time-point up to 2-years post graft ($p=0.043$, $p=0.027$, $p<0.001$, respectively). There was another significant improvement in median BCVA between 7-years and 8-years post-graft ($p=0.037$) but no other changes were significant compared to the previous time-point. The difference compared to pre-graft BCVA remained significant to 25-years post-graft (all $p<0.001$).

Penetrating keratoplasties performed for keratoconus, which survived for 3-months, achieved a median BCVA of 6/12. This improved to 6/9 at 1-year post graft. This remained the median BCVA up to 20 years post-graft for surviving grafts for keratoconus, and it remained at 6/12 at 25 years post graft.

Figure 3.9.4 Best corrected visual acuity for surviving penetrating keratoplasties performed for endothelial failure/bullous keratopathy, over time



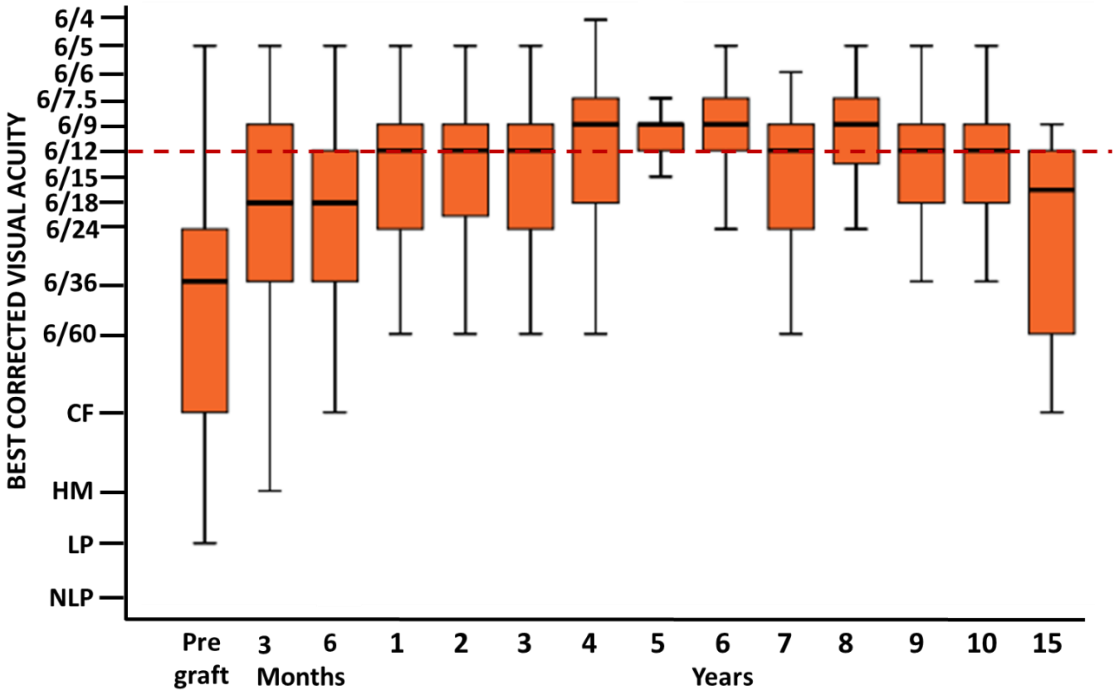
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y
3717	246	283	460	253	153	105	74	57	45	39	22	17

The median BCVA obtained following penetrating keratoplasty for endothelial failure/bullous keratopathy improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). This difference was maintained at 6-months but did not improve significantly again until 1-year post-graft ($p=0.003$). There were no significant changes in median BCVA after 1-year post-graft. The difference compared to pre-graft BCVA remained significant to 10-years post-graft (all $p<0.001$).

Penetrating keratoplasties performed for endothelial failure/bullous keratopathy, which survived for 5-years, achieved a median BCVA of 6/24. The median BCVA never reached the 6/12 level, varying between 6/36 and 6/24 up to 10-years post-graft for surviving grafts performed for endothelial failure/bullous keratopathy.

Figure 3.9.5 Best corrected visual acuity for surviving penetrating keratoplasties performed for Fuchs' endothelial dystrophy, over time



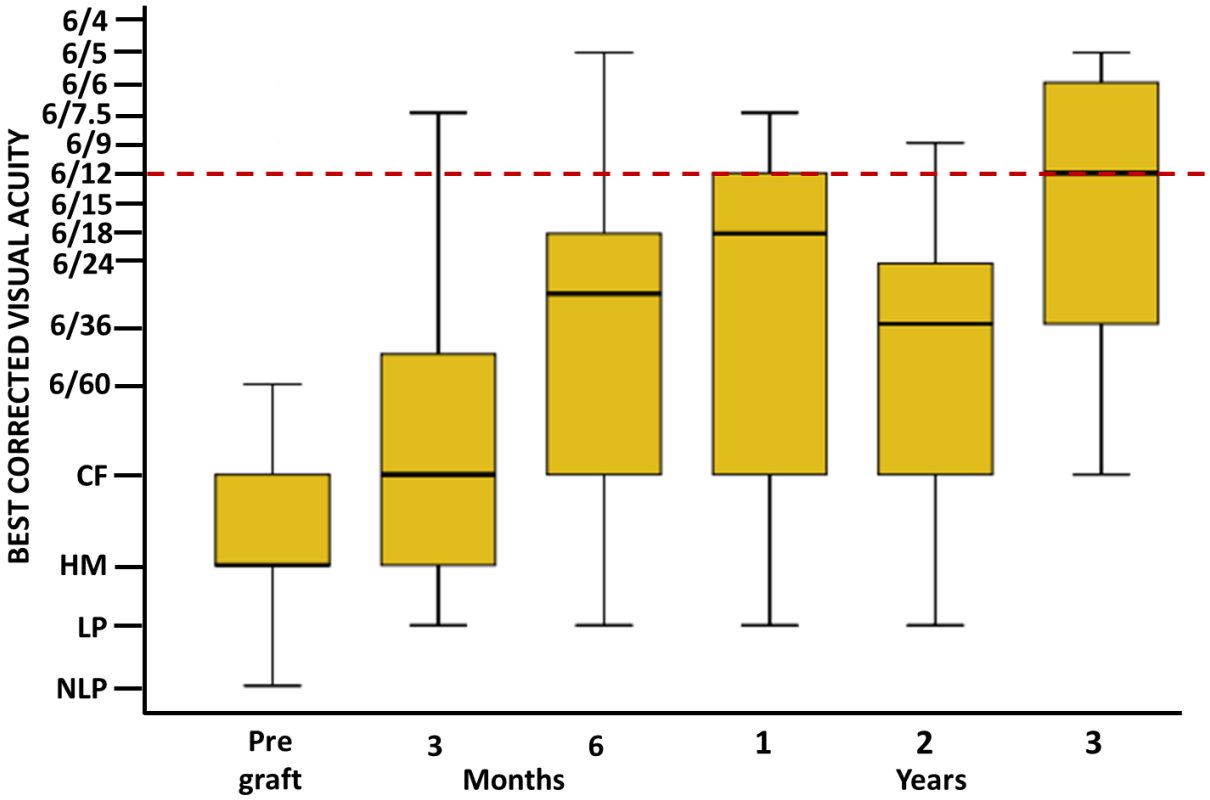
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y	15y
1819	60	114	211	167	117	78	62	73	59	43	30	31	12

The median BCVA obtained following penetrating keratoplasty for Fuchs' endothelial dystrophy improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). This difference was maintained at 6-months but did not improve significantly again until 1-year post-graft ($p=0.002$). There was a significant drop in median BCVA between 6-years and 7-years post-graft ($p=0.041$) but this significantly improved again between 7-years and 8-years post-graft ($p=0.048$). There was also a significant drop in median BCVA between 10-years and 15-years post-graft ($p=0.040$). No other changes were significant compared to the previous time-point. The difference compared to pre-graft BCVA remained significant to 15-years post-graft (all $p<0.001$, except 15-years $p=0.025$).

Penetrating keratoplasties performed for Fuchs' endothelial dystrophy, which survived for 1-year, achieved a median BCVA of 6/12. The median BCVA remained above the 6/12 level, varying between 6/9 and 6/12 up to 10-years post-graft for surviving grafts performed for Fuchs' endothelial dystrophy. At 15-years post-graft the median BCVA had dropped back below the 6/12 level to 6/18.

Figure 3.9.6 Best corrected visual acuity for surviving penetrating keratoplasties performed for corneal ulcer, over time



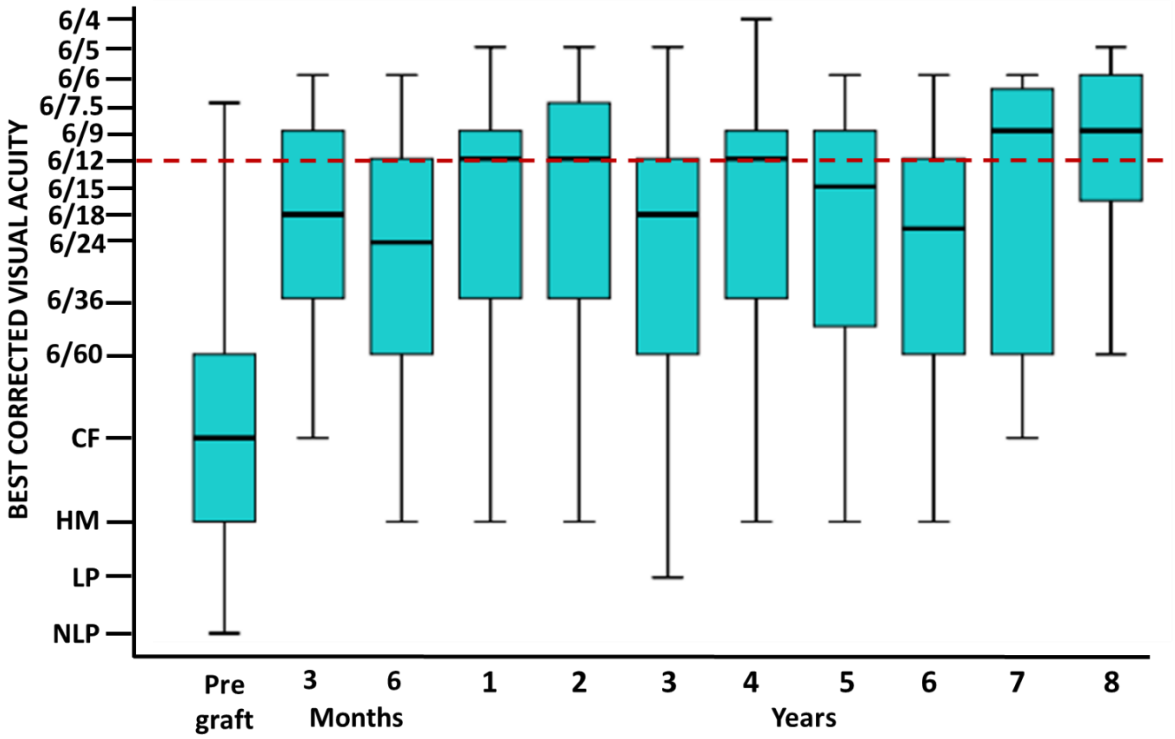
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y
458	20	30	31	26	14

The median BCVA obtained following penetrating keratoplasty for corneal ulcers improved significantly compared to pre-graft levels by 3-months post-graft (p=0.027). This difference improved again between 3-months and 6-months (p=0.026). From 6-months up to 3-years, the difference compared to pre-graft median BCVA was highly significant (all p<0.001). The median BCVA was significantly poorer at 2-years post graft compared to 1-year (p=0.033), but this improved significantly between 2-years and 3-years post-graft (p=0.004).

Penetrating keratoplasties performed for corneal ulcers, which survived for 3-years, achieved a median BCVA of 6/12. There were insufficient data for surviving grafts performed for corneal ulcers for longer than 3-years to perform further analyses.

Figure 3.9.7 Best corrected visual acuity for surviving penetrating keratoplasties performed for herpetic eye disease, over time



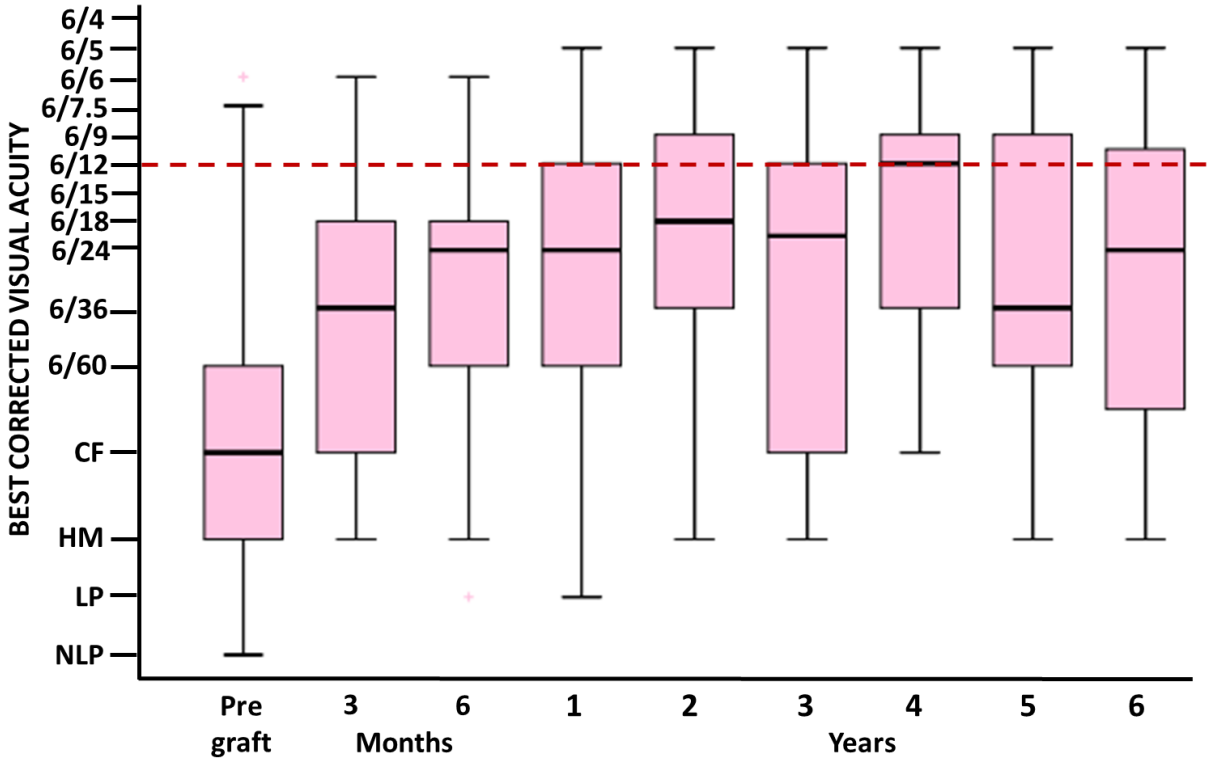
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y	6y	7y	8y
959	57	62	131	77	53	40	28	14	20	11

The median BCVA obtained following penetrating keratoplasty for herpetic eye disease improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). This difference was maintained at 6-months but did not improve significantly again until 1-year post-graft ($p=0.016$). There was a significant drop in median BCVA between 2-years and 3-years post-graft ($p=0.041$). No other changes were significant compared to the previous time-point. The difference compared to pre-graft BCVA remained significant to 8-years post-graft (all $p<0.001$).

Penetrating keratoplasties performed for herpetic eye disease, which survived for 1-year, achieved a median BCVA of 6/12. The median BCVA vacillated above and below the 6/12 level, varying between 6/9 and 6/18 up to 8-years post-graft for surviving grafts performed for herpetic eye disease. There were insufficient data for surviving grafts performed for herpetic eye disease for longer than 8-years to perform further analyses.

Figure 3.9.8 Best corrected visual acuity for surviving penetrating keratoplasties performed for trauma, over time



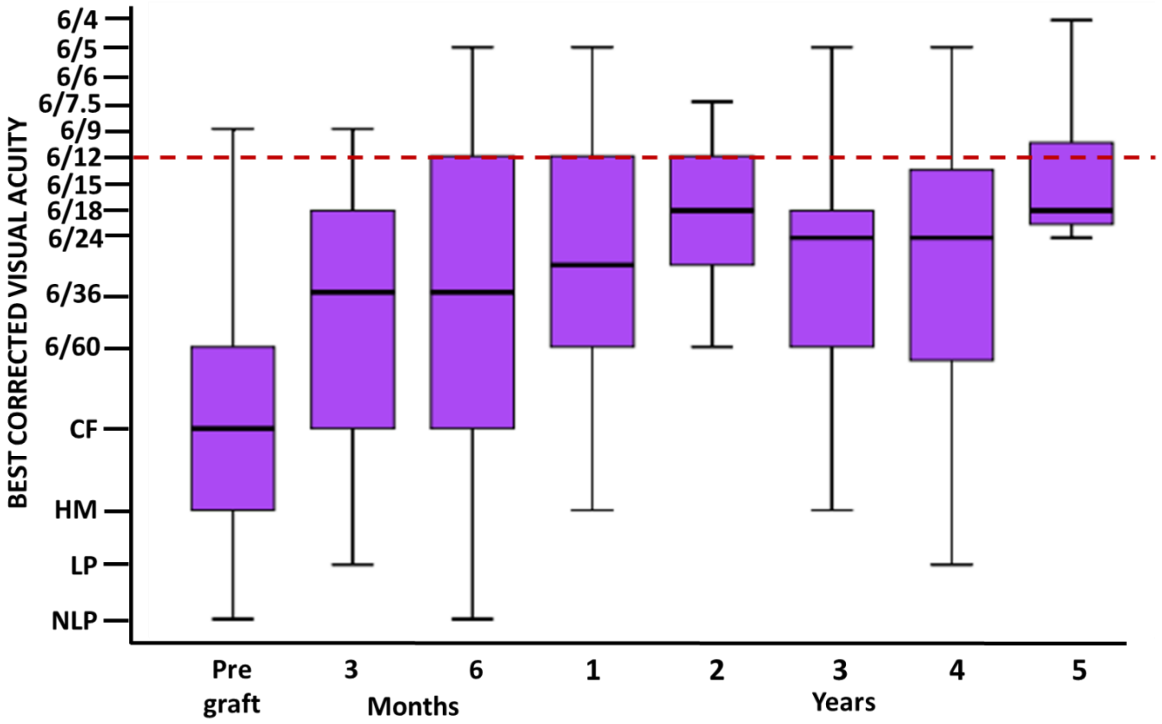
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y	6y
614	28	29	63	52	34	24	15	15

The median BCVA obtained following penetrating keratoplasty for trauma improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). The median BCVA did not differ significantly again between adjacent time-points, however the median BCVA at 4-years post-graft was significantly better than at 3-months and 6-months ($p=0.002$ and $p=0.047$, respectively). The difference compared to pre-graft BCVA remained significant to 6-years post-graft (all $p<0.001$).

Penetrating keratoplasties performed for trauma, which survived for 4-years, achieved a median BCVA of 6/12. The median BCVA varied between 6/12 and 6/36 up to 6-years post-graft for surviving grafts performed for trauma. There were insufficient data for surviving grafts performed for trauma for longer than 6-years to perform further analyses.

Figure 3.9.9 Best corrected visual acuity for surviving penetrating keratoplasties performed for non-herpetic infections, over time



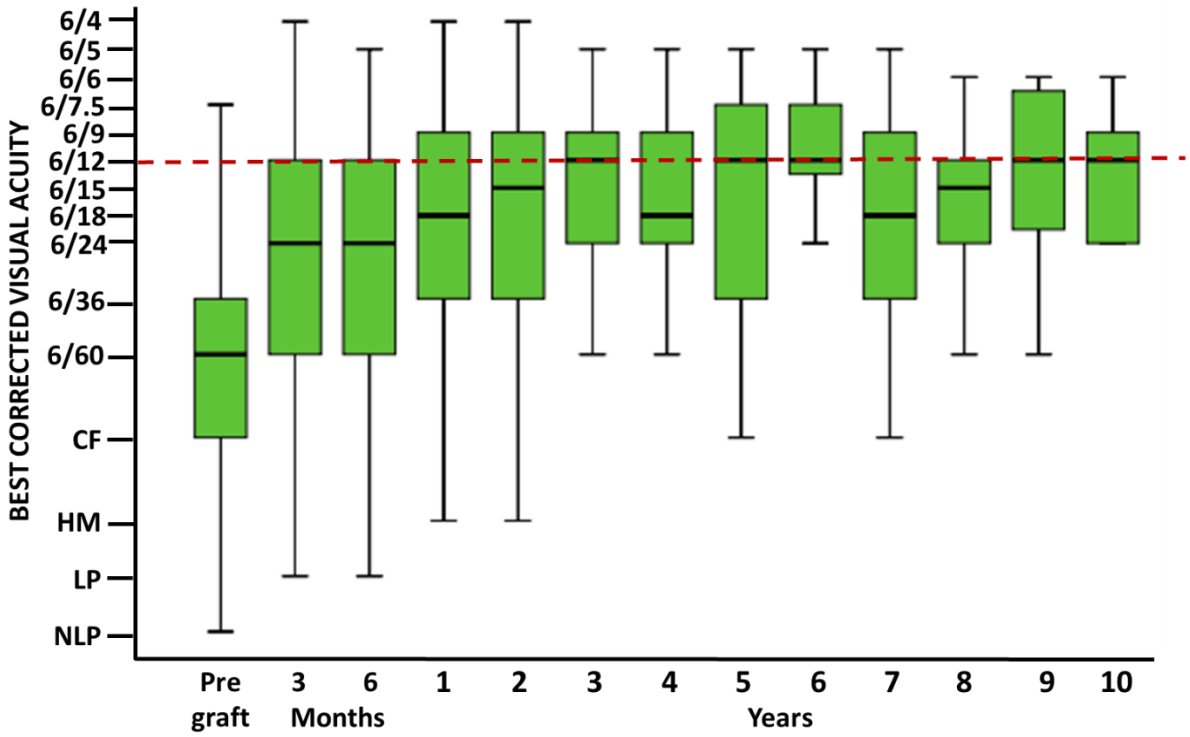
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y
498	14	27	42	23	19	15	11

The median BCVA obtained following penetrating keratoplasty for non-herpetic infections improved significantly compared to pre-graft levels by 3-months post-graft (p=0.001). The median BCVA did not differ significantly again between adjacent time-points. The difference compared to pre-graft BCVA remained significant to 5-years post-graft (all p<0.001).

Surviving penetrating keratoplasties performed for non-herpetic infections, did not achieve a median BCVA of 6/12 up to 5-years post-graft. The median BCVA varied between 6/18 and 6/36 up to 5-years post-graft for surviving grafts performed for non-herpetic infections. There were insufficient data for surviving grafts performed for non-herpetic infections for longer than 5-years to perform further analyses.

Figure 3.9.10 Best corrected visual acuity for surviving penetrating keratoplasties performed for other indications, over time



Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y
1278	71	100	185	113	64	55	36	23	21	29	15	13

The median BCVA obtained following penetrating keratoplasty for other indications for graft improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). This difference was maintained at 6-months but did not improve significantly again until 1-year post-graft ($p=0.031$ versus 3-months, $p=0.016$ versus 6-months). No other changes were significant compared to the previous time-point. The difference compared to pre-graft BCVA remained significant to 10-years post-graft (all $p<0.001$).

Penetrating keratoplasties performed for other indications for graft, which survived for 3-years, achieved a median BCVA of 6/12. The median BCVA varied between 6/12 and 6/18 up to 10-years post-graft for surviving grafts performed for other indications.

4 Descemet's Stripping Endothelial Keratoplasty

This chapter presents analyses of the 6,947 Descemet's stripping endothelial keratoplasties registered with the ACGR. The preparation of donor material may have been automated (DSAEK) or manual (DSEK). Some automated procedures are specified as having been performed with ultra-thin donor lenticules (UT-DSEK). In some cases, the type of surgery was unspecified by the contributing surgeon. In most instanced, grafts in these four groups were analysed together and are referred to as DS(A)EKs. Kaplan-Meier survival analyses were conducted 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 (6,947 registered and 5,091 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

Descemet's Stripping (Automated) Endothelial Keratoplasty

Donor and Eye Banking Factors

	Registered (%)	Followed (%)
Eye bank		
	2457 (35%)	1751 (34%)
Eye banks are not identified due to confidentiality constraints. See section 1.4.5 for further information.	1484 (21%)	1103 (22%)
	1624 (23%)	1330 (26%)
	777 (11%)	449 (9%)
	605 (9%)	458 (9%)
Age of donor		
0 to 29 years	232 (3%)	169 (3%)
30 to 39 years	320 (5%)	250 (5%)
40 to 49 years	665 (10%)	474 (9%)
50 to 59 years	1276 (18%)	942 (19%)
60 to 69 years	2201 (32%)	1649 (32%)
70 to 79 years	1759 (25%)	1264 (25%)
80 years and older	494 (7%)	343 (7%)
Central corneal endothelial cell density		
Less than 2500 cells/mm²	433 (6%)	314 (6%)
2500 to 2749 cells/mm²	1017 (15%)	687 (13%)
2750 to 2999 cells/mm²	1255 (18%)	838 (16%)
3000 to 3249 cells/mm²	1267 (18%)	921 (18%)
3250 to 3499 cells/mm²	682 (10%)	473 (9%)
3500 cells/mm² or more	316 (5%)	211 (4%)
Not advised	1977 (28%)	1647 (32%)

	Registered (%)	Followed (%)
Storage media		
Optisol	2712 (39%)	2317 (46%)
Organ culture	4233 (61%)	2772 (54%)
Moist pot	2 (<1%)	2 (<1%)
Interstate transportation		
Same State	6650 (4%)	214 (4%)
Different States	297 (96%)	4877 (96%)
Death-to-enucleation time		
Up to 3 hours	532 (8%)	402 (8%)
4 to 6 hours	934 (13%)	731 (14%)
7 to 9 hours	1148 (17%)	893 (13%)
10 to 12 hours	1104 (16%)	896 (13%)
13 to 15 hours	918 (13%)	677 (13%)
16 to 18 hours	989 (14%)	711 (14%)
More than 18 hours	1310 (19%)	772 (15%)
Not advised	12 (<1%)	9 (<1%)
Enucleation-to-storage time		
Within 1 hour	210 (3%)	102 (2%)
1 to 3 hours	3645 (52%)	2532 (50%)
4 to 6 hours	788 (11%)	610 (12%)
7 to 9 hours	238 (3%)	187 (4%)
10 to 12 hours	142 (2%)	113 (2%)
13 to 15 hours	204 (3%)	156 (3%)
16 to 18 hours	194 (3%)	133 (3%)
More than 18 hours	235 (3%)	169 (3%)
Not advised	1291 (19%)	1089 (21%)
Storage-to-graft time – Organ culture		
Up to 2 weeks	870 (13%)	589 (12%)
2 to 3 weeks	1793 (26%)	1076 (21%)
More than 3 weeks	551 (8%)	328 (6%)
Not advised	1019 (15%)	781 (15%)
Not applicable	2714 (39%)	2317 (46%)
Cornea pre-cut by eye bank		
No	4531 (65%)	3690 (72%)
Yes	2416 (35%)	1401 (28%)
Total	***6947 (100%)***	***5091 (100%)***

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 (6,947 registered and 5,091 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

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

Descemet's Stripping (Automated) Endothelial Keratoplasty

Donor and Eye Banking Factors

	Registered (%)	Followed (%)
Sex of donor		
Female	2720 (39%)	1987 (39%)
Male	4227 (61%)	3104 (61%)
Chi²=0.12, df=1, p=0.729		
Donor type		
Eye donor only	5757 (83%)	4249 (83%)
Solid organ and/or bone/tissue donor	1190 (17%)	842 (17%)
Chi²=0.70, df=1, p=0.402		
Cause of death		
Cardiovascular	1538 (22%)	1113 (22%)
Malignancy	2499 (36%)	1870 (37%)
Trauma	639 (9%)	453 (9%)
Respiratory	545 (8%)	404 (8%)
Intracranial/cerebral haemorrhage	1190 (17%)	872 (17%)
Other specified	472 (7%)	335 (7%)
Not advised/live donor*	64 (1%)	44 (<1%)
Chi²=2.08, df=5, p=0.838		
Storage-to-graft time - Optisol		
Within 5 days	1532 (22%)	1339 (26%)
More than 5 days	778 (11%)	624 (12%)
Not advised	402 (6%)	352 (7%)
Not applicable	4235 (61%)	2776 (55%)
Chi²=0.88, df=1, p=0.349		
Deswelling-to-graft time – Organ culture		
Within 2 days	793 (11%)	461 (9%)
>2 to 3 days	787 (11%)	368 (7%)
>3 to 4 days	479 (7%)	256 (5%)
More than 4 days	325 (5%)	179 (4%)
Not advised	1849 (27%)	1510 (30%)
Not applicable	2714 (39%)	2317 (46%)
Chi²=4.20, df=3, p=0.241		
Total	**6947 (100%)**	**5091 (100%)**

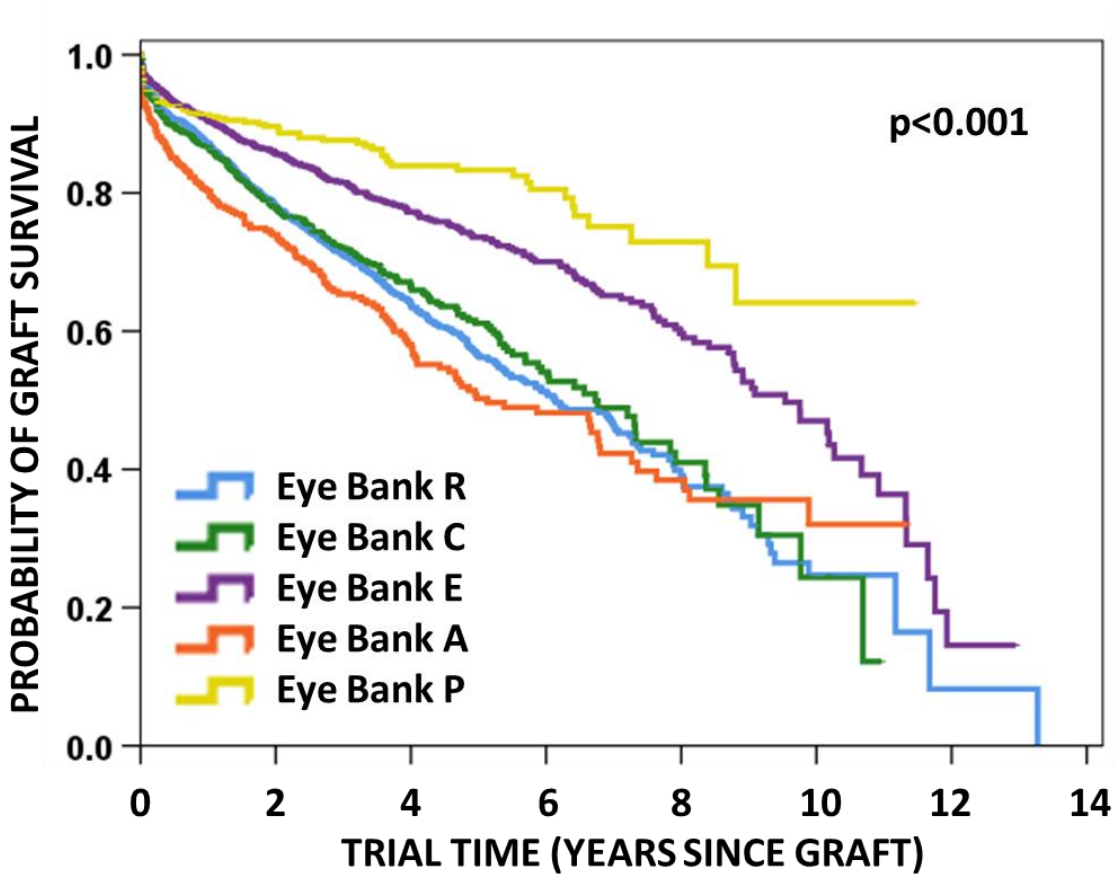
Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable, or groups with fewer than 2% of grafts.

*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 Descemet's stripping (automated) endothelial keratoplasty 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. A significant difference was found across eye banks (Log Rank Statistic=118.37; df=4; p<0.001). State P had significantly better survival than State R, State C, State A (all p<0.001), and State E (p=0.004). State E also had significantly better survival than State R, State C and State A (all p<0.001), and State A had poorer survival than State C (p=0.008) and State R (p=0.024). This variable was retained in the final multivariate model (see section 4.7).

Figure 4.1.1 Australian eye bank



Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Eye Bank R	0.87	0.78	0.71	0.64	0.56	0.51	0.47	0.39	0.33	NA
Eye Bank C	0.87	0.78	0.72	0.67	0.61	0.54	0.49	0.41	NA	NA
Eye Bank E	0.90	0.86	0.82	0.77	0.74	0.70	0.65	0.60	0.53	0.47
Eye Bank A	0.80	0.74	0.65	0.58	0.50	0.48	0.42	0.39	NA	NA
Eye Bank P	0.91	0.90	0.88	0.84	0.83	0.81	0.75	0.73	NA	NA

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

Note: Further information is not provided due to confidentiality constraints (see section 1.4.8).

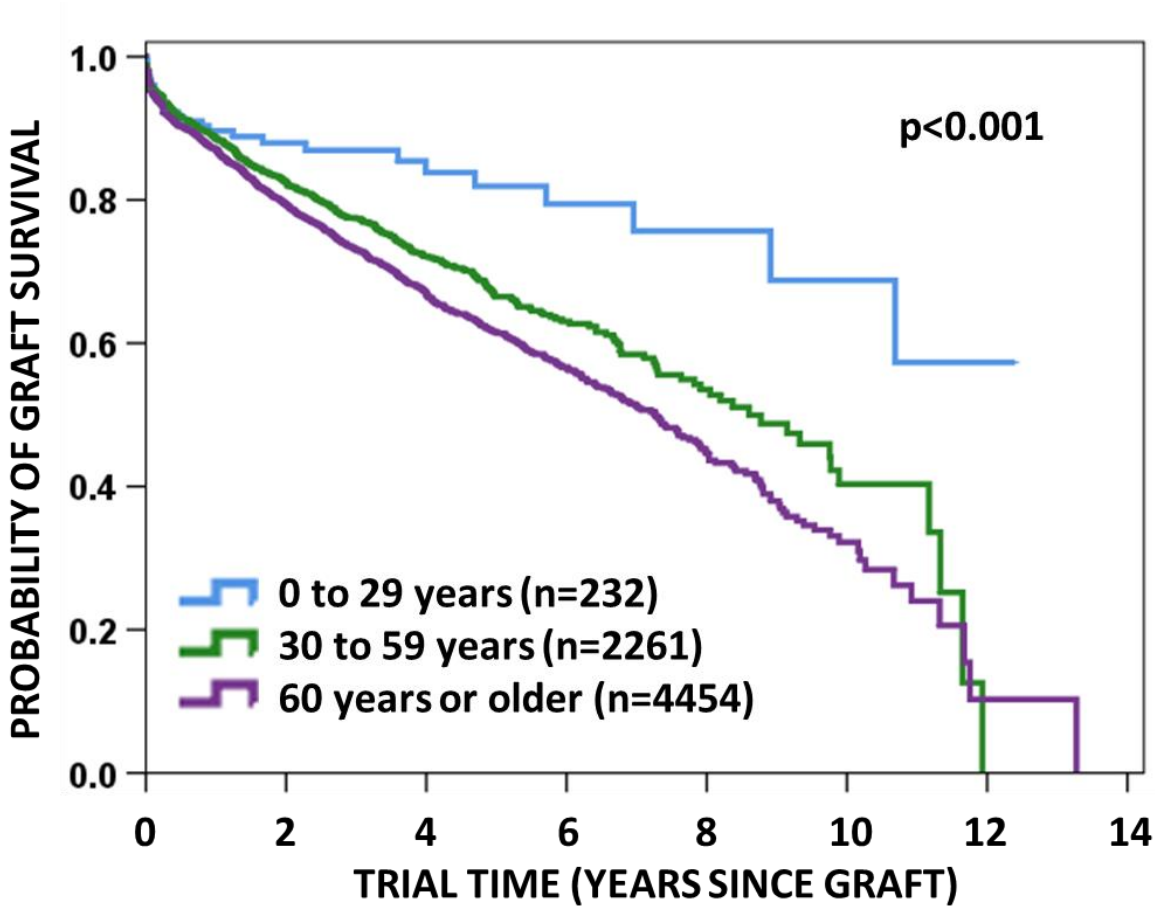
4.1.2 Descemet's stripping (automated) endothelial keratoplasty survival: influence of donor age (years)

Figure 4.1.2 shows the comparison of graft survival depending on donor age. Donors were initially stratified by 10-year age groups. Donors aged under 20 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=31.94; df=6; p<0.001).

Further analyses examined whether there were significant differences between adjacent age groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=28.94; df=2; p<0.001).

Both age group categories of 0 to 29 years and 30 to 59 had significantly better survival when compared to those using tissue from donors aged 60 years and older (both p<0.001). Grafts performed using donor tissue from donors aged 0 to 29 also had significantly better survival than those using tissue from donors aged 30 to 59 (p=0.002). However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 4.1.2 Donor age group



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
0 to 29 years	123	91	68	52	41	30	20	15	9	7	4
30 to 59 years	1255	930	647	452	311	190	118	70	38	16	6
60 years and older	2351	1689	1167	806	577	377	240	138	72	32	9

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
0 to 29 years	0.90	0.88	0.87	0.84	0.82	0.79	0.76	NA	NA	NA
30 to 59 years	0.89	0.82	0.77	0.72	0.67	0.63	0.59	0.54	0.49	NA
60 years and older	0.87	0.79	0.73	0.67	0.62	0.57	0.51	0.45	0.38	0.32

4.1.3 Descemet's stripping (automated) endothelial keratoplasty survival: influence of donor central corneal endothelial cell density

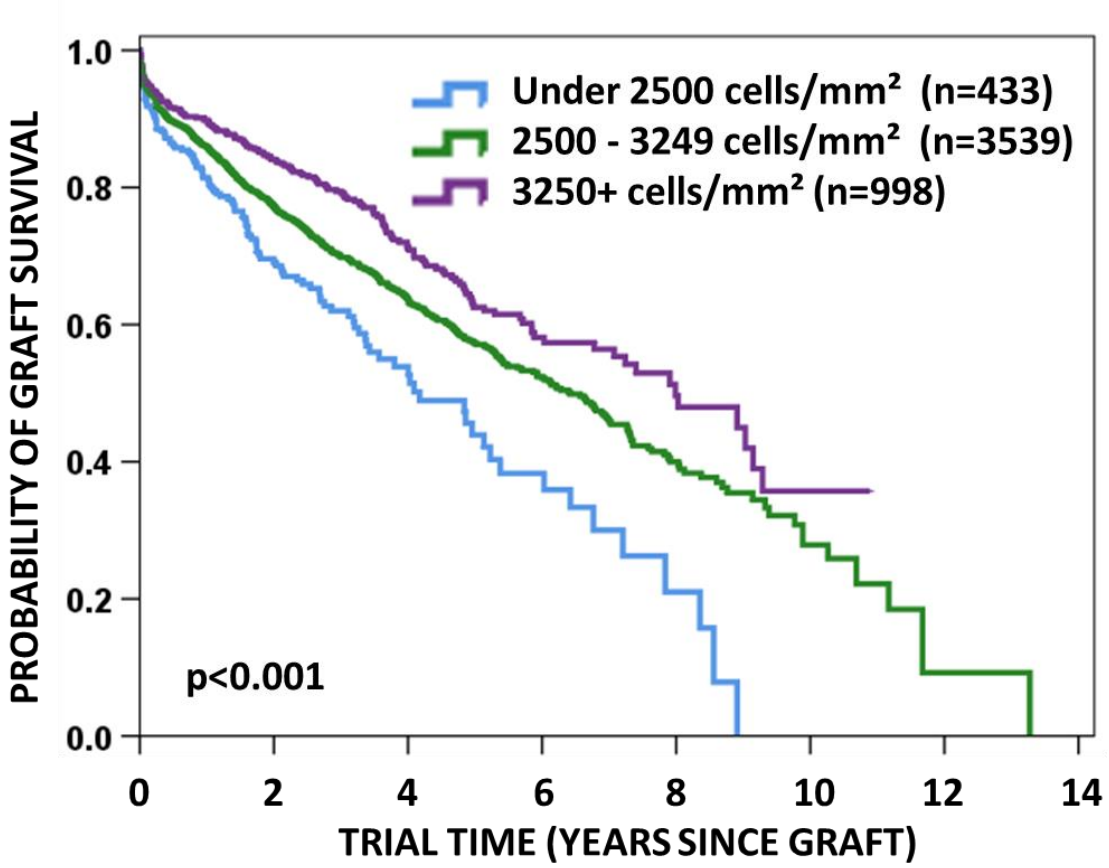
Endothelial cell count (ECC) was reported for 72% of registered DS(A)EKs. Reported ECC ranged from 1700 to 4597 cells/mm². Preliminary analyses examined survival based on groupings of 250 cells/mm² increments, with all grafts performed with donor tissue with an ECC below 2500 grouped together, and all grafts performed with donor tissue with an ECC of 3500 and above grouped together. A significant difference was found across groups (Log Rank Statistic=36.54; df=5; p<0.001).

Further analyses examined whether there were significant differences between adjacent ECC groups. There was no significant difference in survival of grafts performed using tissue from donors with ECC counts of 2500 to 2749 cells/mm², 2750 to 2999 cells/mm², or 3000 to 3249 cells/mm² (p=0.641). There was no significant difference in survival of grafts performed using tissue from donors with ECC counts of 3250 to 2=3499 cells/mm² or 3500 or more cells/mm² (p=0.363). Based on the results, three ECC groups were created for the final comparison, as shown in Figure 4.1.3, with the resulting analyses remaining significant (Log Rank Statistic=35.03; df=2; p<0.001).

Grafts performed using donor tissue with cell counts under 2500 cells/mm² had significantly poorer survival than the other groups (both p<0.001), and those with cell counts of 2500 to 3249 cells/mm² had significantly poorer survival than those with cell counts of 3250 cells/mm² and above (p<0.001).

Data on this variable were not provided in 28% 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=134.43; df=3; p<0.001). ECC was thus categorised into these four groups for multivariate analysis. This variable was retained in the final multivariate model (see section 4.7).

Figure 4.1.3 Endothelial cell density



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Under 2500 cells/mm²	212	137	81	45	26	16	9	4	NA	NA
2500-3249 cells/mm²	1771	1233	783	533	358	228	138	75	38	17
3250+ cells/mm²	533	384	282	189	130	76	54	30	15	4

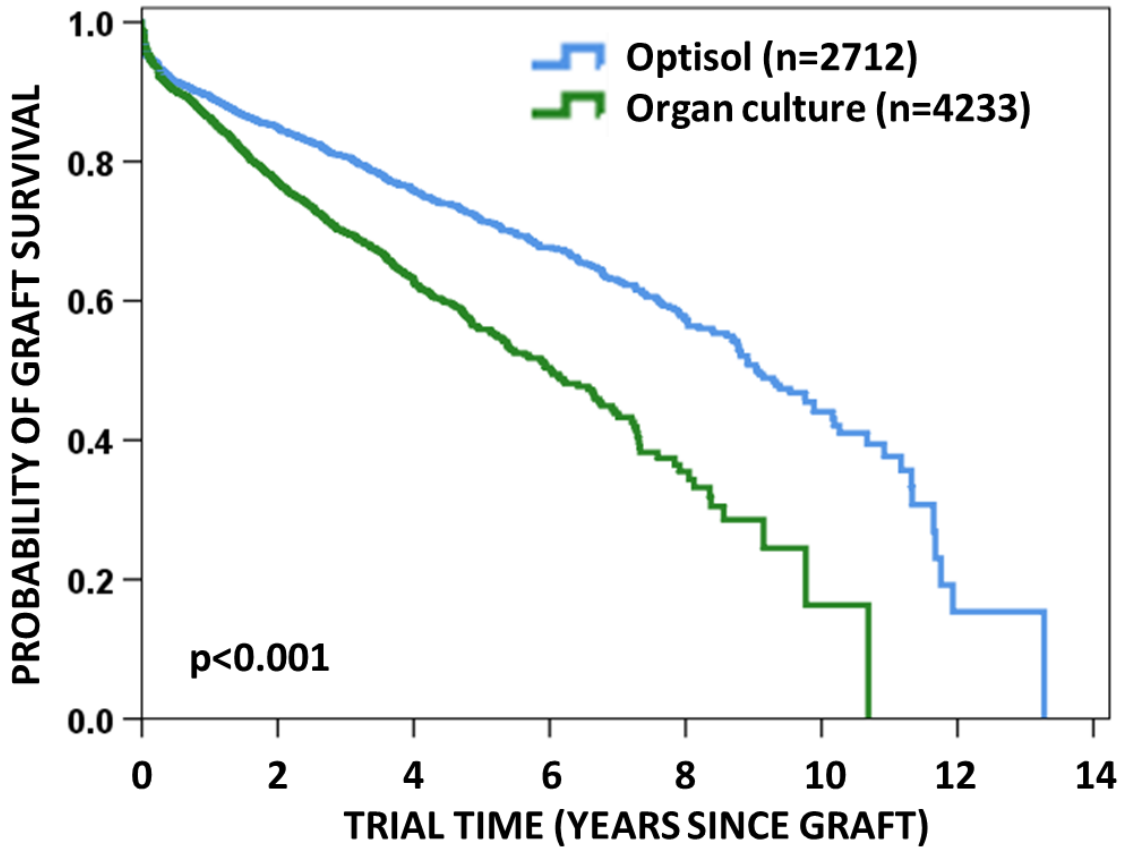
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9
Under 2500 cells/mm²	0.81	0.69	0.62	0.54	0.44	NA	NA	NA	NA
2500-3249 cells/mm²	0.86	0.77	0.70	0.64	0.57	0.52	0.46	0.40	0.36
3250+ cells/mm²	0.90	0.84	0.79	0.71	0.63	0.58	0.56	0.50	NA

4.1.4 Descemet's stripping (automated) endothelial keratoplasty survival: influence of storage media

Figure 4.1.4 shows the comparison of graft survival for corneas stored using Optisol compared to organ culture medium. Two donor corneas had been stored in a moist pot, and these were excluded from the analysis (see section 1.2 for further details about storage media). A significant difference in outcomes was found between media (Log Rank Statistic=80.90; df=1; p<0.001). However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 4.1.4 Storage media



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Optisol	1735	1362	1045	781	607	428	300	191	111	55	19
Organ culture	1994	1348	837	529	322	169	78	32	8	1	NA

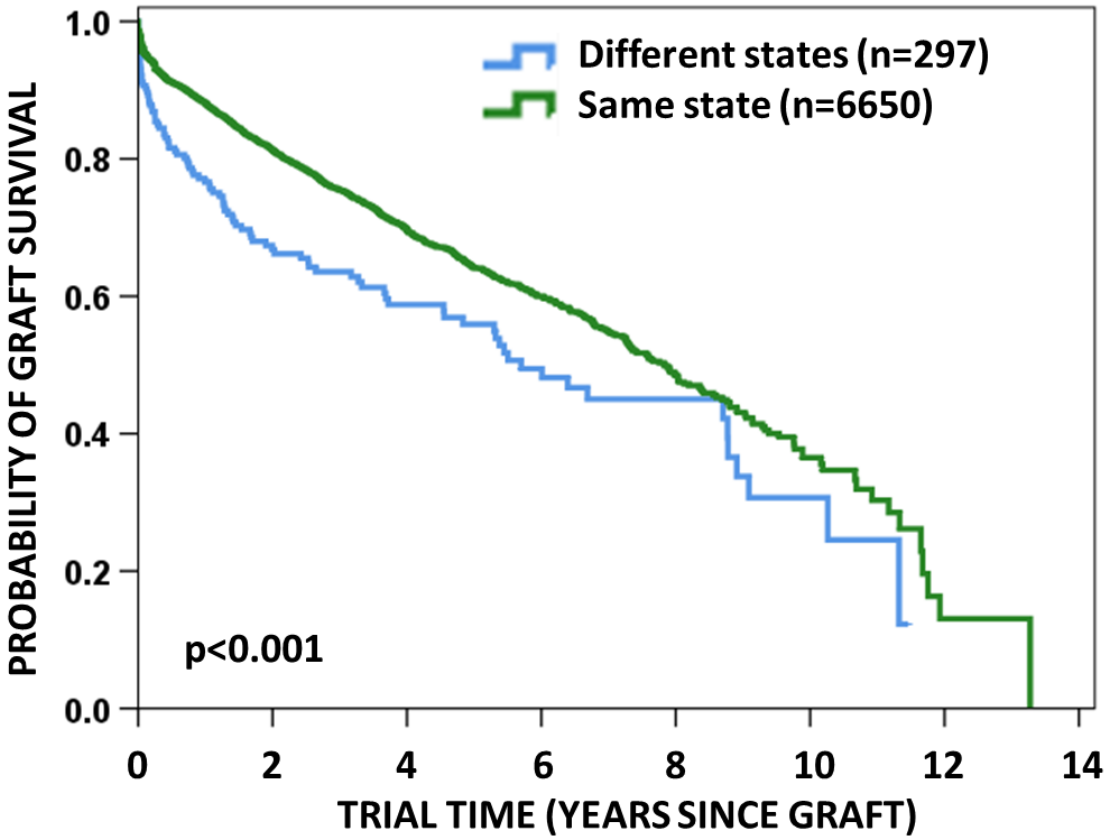
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Optisol	0.89	0.85	0.81	0.76	0.72	0.68	0.63	0.57	0.51	0.44
Organ culture	0.86	0.77	0.70	0.63	0.56	0.50	0.44	0.36	NA	NA

4.1.5 Descemet's stripping (automated) endothelial keratoplasty survival: influence of interstate transportation

In the majority of transplants, donor corneas are sourced from the State in which the surgery occurs, however, in some cases corneas are transported interstate via air freight. Figure 4.1.5 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=16.09; df=1; p<0.001). This variable was retained in the final multivariate model (see section 4.7).

Figure 4.1.5 Interstate transportation



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Different State	150	111	87	66	55	38	24	20	12	5	2
Same State	3579	2599	1795	1244	874	559	354	203	107	51	17

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Different State	0.77	0.67	0.64	0.59	0.56	0.50	0.45	0.45	NA	NA
Same State	0.88	0.81	0.76	0.70	0.64	0.60	0.55	0.49	0.43	0.37

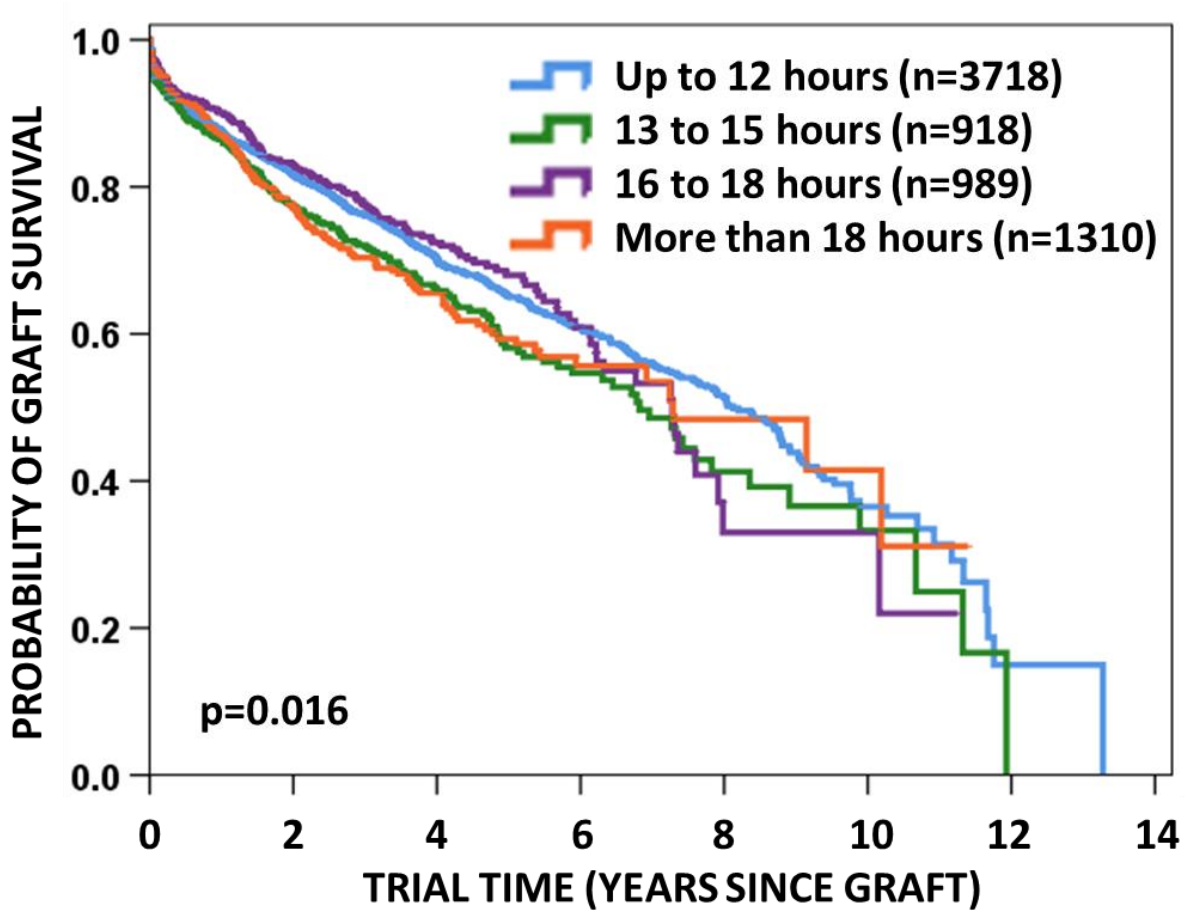
4.1.6 Descemet's stripping (automated) endothelial keratoplasty survival: influence of death-to-enucleation time

Donor corneas are retrieved as soon as possible following donor death. Retrieval is recommended within the first 18 hours and 81% of donor eyes were enucleated within this time-frame. Times are rounded down to the nearest hour and the median time from donor death to enucleation was 12 hours (range 0-46 hours).

Figure 4.1.6 shows a comparison of graft survival depending on time from donor death to enucleation. Times were initially stratified into three-hourly groups. Very few enucleations occur within the hour following donor death and so these were combined with those performed between 1 to 3 hours. Data on this variable were not provided in 12 cases and these were excluded from the analysis. A non-significant difference was found across time groups (Log Rank Statistic=12.13; df=6; $p<0.059$), however it met the $p<0.08$ level for inclusion in multivariate analyses.

Further analyses examined whether there were significant differences between adjacent time groups. Where no significant difference was found, these groups were combined, with the resulting analysis becoming significant (Log Rank Statistic=10.31; df=3; $p=0.016$). However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 4.1.6 Time from donor death to enucleation



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Up to 12 hours	2171	1636	1172	849	633	429	281	176	92	39	14
13 to 15 hours	474	337	235	156	99	65	43	23	13	9	3
16 to 18 hours	532	381	261	172	107	59	27	8	5	3	1
More than 18 hours	545	349	209	131	88	43	25	15	8	4	1

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Up to 12 hours	0.88	0.82	0.76	0.70	0.65	0.61	0.56	0.51	0.44	0.37
13 to 15 hours	0.87	0.77	0.72	0.66	0.58	0.55	0.49	0.41	NA	NA
16 to 18 hours	0.90	0.83	0.78	0.72	0.68	0.61	0.53	NA	NA	NA
More than 18 hours	0.87	0.77	0.70	0.66	0.59	0.56	0.54	NA	NA	NA

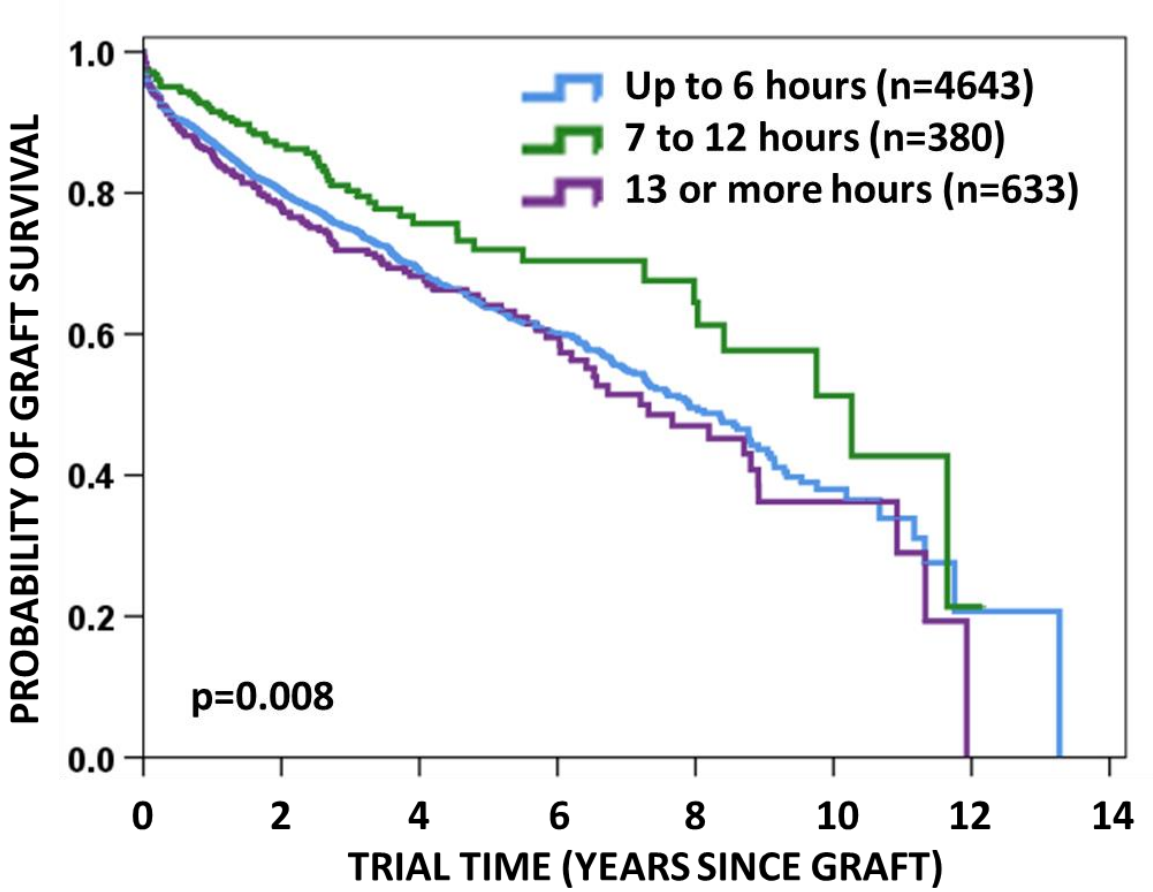
4.1.7 Descemet's stripping (automated) endothelial keratoplasty survival: influence of enucleation-to-storage time

Figure 4.1.7 shows a comparison of graft survival depending on time from enucleation of the donor cornea to initial storage in preservation media. Times were initially stratified into three-hourly groups. Due to low numbers in the categories above 18 hours, these groups were combined. A non-significant difference was found across time groups (Log Rank Statistic=14.04; df=7; $p<0.050$), however it met the $p<0.08$ level for inclusion in multivariate analyses.

Further analyses examined whether there were significant differences between adjacent time groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=11.06; df=2; $p=0.004$).

Data on this variable were not provided in 19% of cases and these were categorised as "not advised". A significant difference was still found across groups when this category was included (Log Rank Statistic=12.39; df=3; $p=0.006$). Grafts performed using donor tissue stored between 7 to 15 hours after enucleation had better survival than those for which the tissue was stored within 6 hours ($p=0.007$), or more than 15 hours ($p<0.001$), after enucleation. However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 4.1.7 Time from enucleation to storage



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Up to 6 hours	2346	1701	1196	832	592	379	230	131	70	30	12
7 to 12 hours	222	160	104	69	55	37	27	21	15	8	2
13 or more hours	324	233	164	111	83	55	39	28	15	8	4

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Up to 6 hours	0.87	0.80	0.75	0.69	0.64	0.60	0.5	0.50	0.44	0.38
7 to 12 hours	0.92	0.87	0.80	0.76	0.72	0.70	0.70	0.65	NA	NA
13 or more hours	0.86	0.78	0.72	0.68	0.64	0.60	0.51	0.47	NA	NA

4.1.8 Descemet's stripping (automated) endothelial keratoplasty survival: influence of storage-to-graft time in organ culture

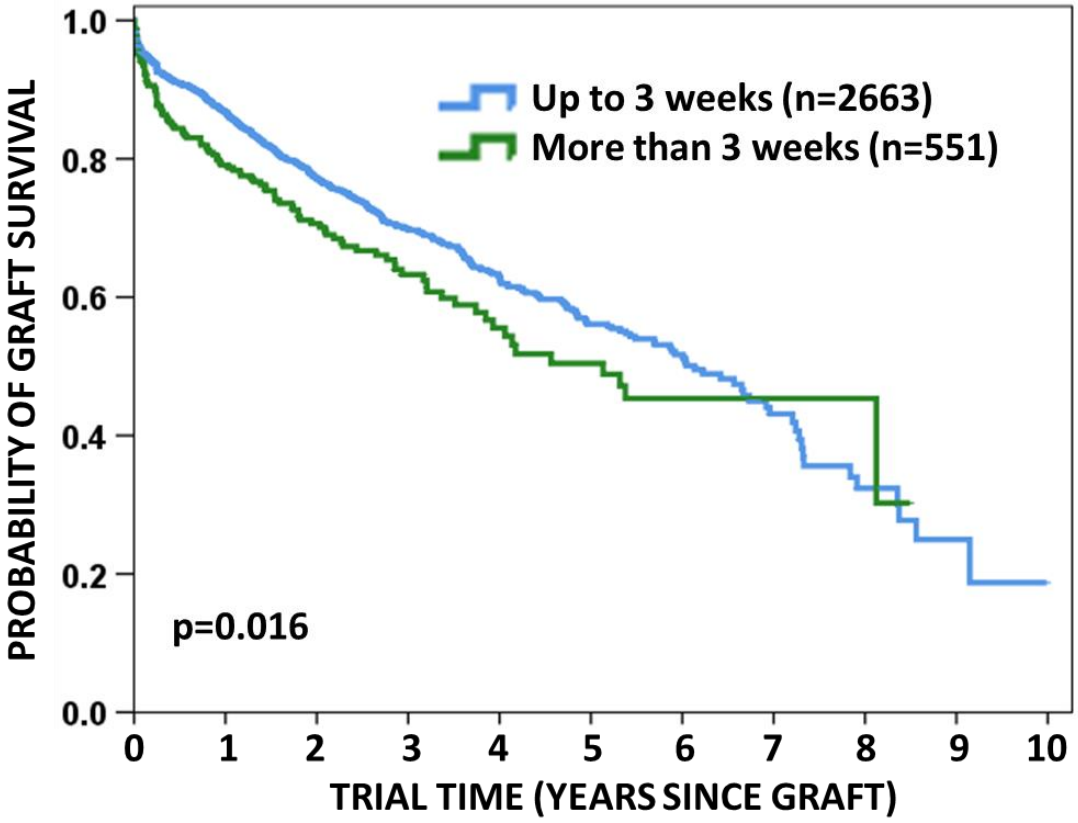
Figure 4.1.8 shows a comparison of graft survival depending on time from initial storage of the donor cornea in organ culture to graft. Times were initially stratified into weekly groups, with those within the first week combined with those 1 to 2 weeks post-storage, due to low numbers. A significant difference was found across time groups (Log Rank Statistic=7.17; df=2; p<0.001).

Further analyses examined whether there were significant differences between adjacent time groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=5.78; df=1; p=0.016).

This variable was not applicable for the 2714 corneas not stored in organ culture and the data for these grafts were excluded from the analysis. Data on this variable were not provided in 24% of grafts stored in organ culture (15% of all grafts) and these were categorised as "not advised". A significant difference was still found across groups when this category was included (Log Rank Statistic=8.77; df=2; p=0.012).

As this variable was not applicable to the 39% of grafts that were stored in Optisol, this variable was initially combined with the variable relating to storage media (see section 4.1.4) for the purpose of multivariate analysis. However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 4.1.8 Time from storage to graft for organ culture media



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8
Up to 3 weeks	1189	793	496	308	189	99	43	17
More than 3 weeks	213	137	80	47	34	17	8	4

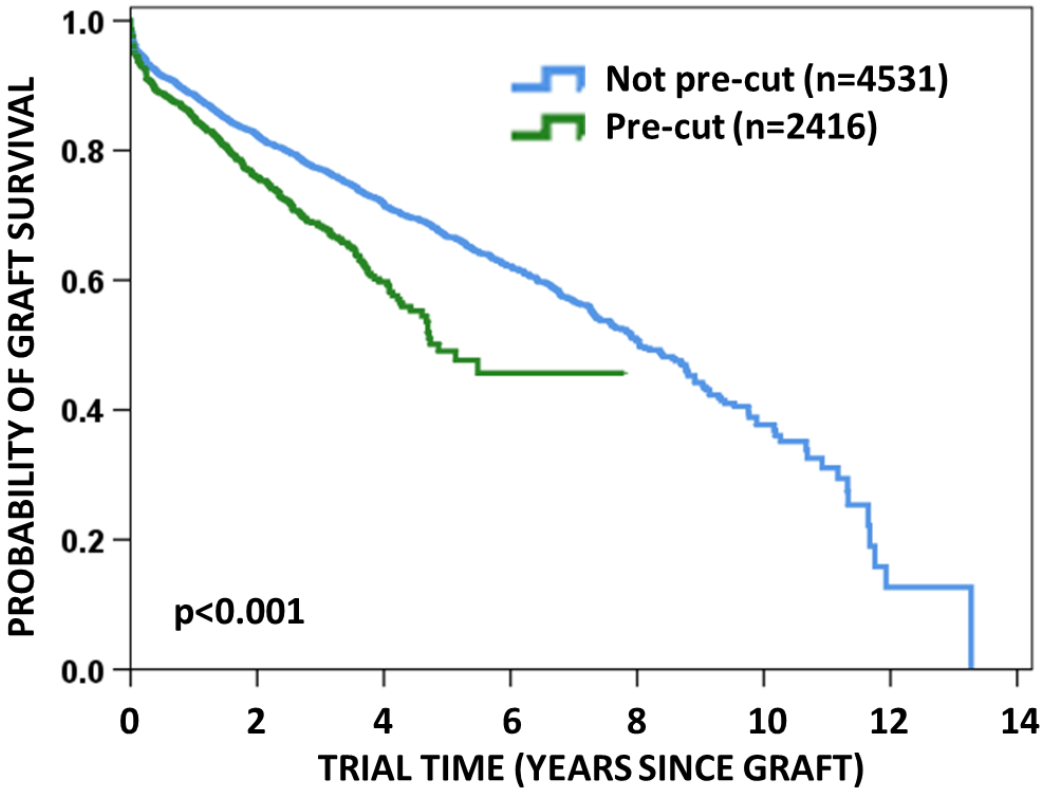
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7
Up to 3 weeks	0.87	0.77	0.70	0.63	0.56	0.52	0.43
More than 3 weeks	0.79	0.71	0.63	0.56	0.50	NA	NA

4.1.9 Descemet's stripping (automated) endothelial keratoplasty survival: influence of pre-cut of donor button by eye bank

It has become increasingly common for the donor button used in DS(A)EK to be pre-cut by eye banks prior to provision to surgeons. Figure 4.1.9 shows the comparison of survival of grafts performed with pre-cut tissue and those where the tissue was cut by the surgeon. A significant difference was found between groups (Log Rank Statistic=37.91; df=1; p<0.001). However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 4.1.9 Pre-cut of donor button by eye bank



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Not pre-cut	2764	2110	1586	1187	886	585	375	223	119	56	19
Pre-cut	965	600	296	123	43	12	3	NA	NA	NA	NA

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Not pre-cut	0.89	0.82	0.77	0.72	0.67	0.62	0.57	0.51	0.44	0.38
Pre-cut	0.85	0.76	0.68	0.60	0.49	NA	NA	NA	NA	NA

4.2 Recipient Factors

Table 4.3 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 (6,947 registered and 5,091 followed) and the percentages, which should be summed vertically for each variable, total 100

Table 4.3 Recipient factors, significant in univariate analyses

Descemet's Stripping (Automated) Endothelial Keratoplasty

Recipient factors

	Registered (%)	Followed (%)
Indication for graft		
Failed previous graft	1580 (23%)	1095 (22%)
Endothelial failure/bullous keratopathy	2052 (30%)	1459 (29%)
Fuchs' endothelial dystrophy	3159 (45%)	2423 (48%)
Other*	156 (2%)	114 (2%)
Previous ipsilateral grafts		
None	5356 (77%)	3989 (78%)
One	1115 (16%)	782 (15%)
Two or more	476 (7%)	320 (6%)
Australian State where graft was performed		
States are not identified due to confidentiality constraints. See section 1.4.8 for further information.	2438 (35%) 1347 (19%) 1558 (22%) 899 (13%) 561 (8%) 142 (2%) 2 (<1%)	1742 (83%) 1001 (20%) 1265 (25%) 549 (11%) 434 (9%) 100 (2%) 0 (0%)
Recipient age group		
0 to 49 years	366 (5%)	258 (5%)
50 to 59 years	687 (10%)	498 (10%)
60 to 69 years	1709 (25%)	1323 (26%)
70 to 79 years	2303 (33%)	1626 (32%)
80 to 89 years	1628 (23%)	1204 (24%)
90 years or older	254 (4%)	182 (4%)
Recipient sex		
Female	3846 (55%)	2847 (56%)
Male	3101 (45%)	2244 (44%)
Donor/recipient sex match		
Female/female	1484 (21%)	1087 (21%)
Female/male	1236 (18%)	900 (18%)
Male/female	2362 (34%)	1760 (35%)
Male/male	1865 (27%)	1344 (26%)

	Registered (%)	Followed (%)
Pre-graft corneal neovascularisation		
None	6098 (88%)	4536 (89%)
One quadrant	408 (6%)	257 (5%)
Two quadrants	259 (4%)	177 (3%)
Three or four quadrants	182 (3%)	121 (2%)
Pre-graft inflammation and/or steroid use		
No	5011 (72%)	3689 (72%)
Yes	1762 (25%)	1279 (25%)
Not advised	174 (3%)	123 (2%)
History of raised intraocular pressure		
IOP never known to be raised	5417 (78%)	4037 (79%)
IOP raised in past and/or at graft	1530 (22%)	1054 (21%)
Previous contralateral grafts		
None	5183 (75%)	3789 (74%)
One	1438 (21%)	1076 (21%)
Two or more	326 (5%)	226 (4%)
Prior intraocular surgery of any kind		
No	1599 (23%)	1216 (24%)
Yes	3734 (54%)	2757 (54%)
Not advised	23 (<1%)	16 (<1)
Not applicable (repeat and/or prior concurrent)	1591 (23%)	1102 (22%)
Total	***6947 (100%)***	***5091 (100%)***

*Other included: trauma (110), ICE syndrome (17), herpetic infection (5), non-herpetic infection (4), posterior polymorphous dystrophy (4), band keratopathy (2), congenital corneal dystrophy (2), Descemet's membrane detachment (2), aniridia (1), complications from retinal detachment (1), corneal melt (1), Descemet's membrane tear (1), granular dystrophy (1), Peter's anomaly (1), Riegers' anomaly (1), Stevens-Johnson syndrome (1), toxic anterior segment syndrome (1), and unspecified endothelial dystrophy (1).

Table 4.4 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 (6,947 registered and 5,091 with follow-up provided) and the percentages, summed vertically, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

Table 4.4 Recipient factors, not significant in univariate analyses

Descemet's Stripping (Automated) Endothelial Keratoplasty

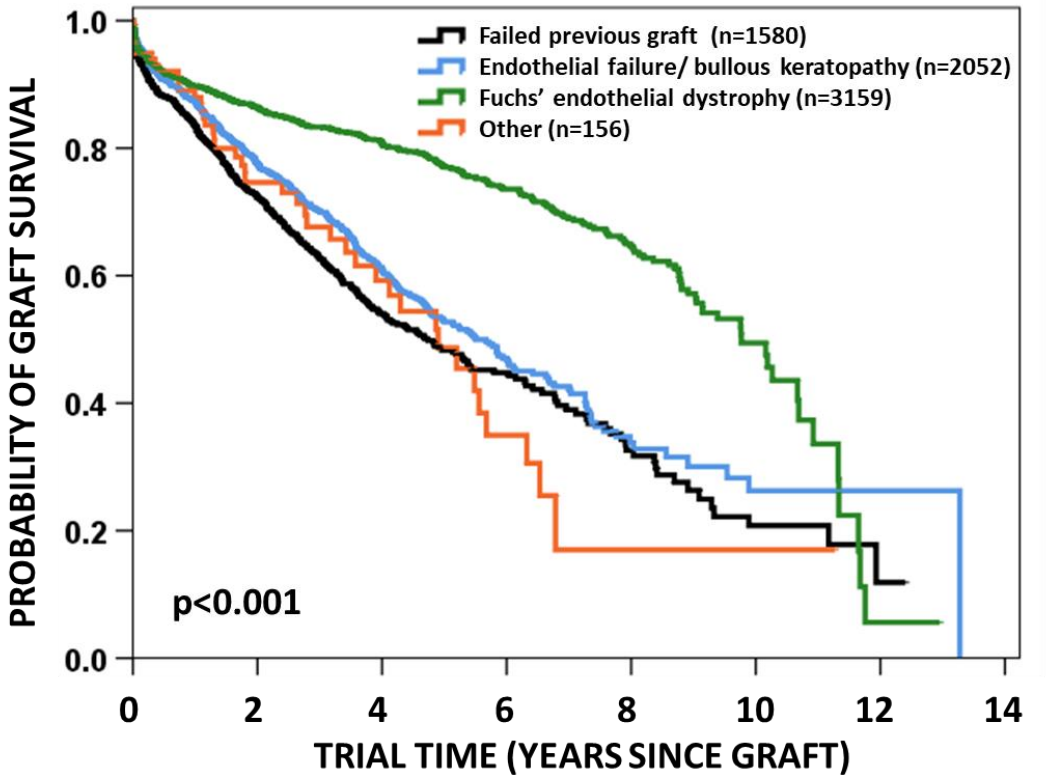
Recipient Factors

	Registered (%)	Followed (%)
Eye grafted		
Left	3396 (49%)	2458 (48%)
Right	3551 (51%)	2633 (52%)
Chi²=0.413, df=1, p=0.520		
Total	***6947 (100%)***	***5091 (100%)***

4.2.1 Descemet's stripping (automated) endothelial keratoplasty survival: influence of indication for graft

Figure 4.2.1 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=203.30; df=3; p<0.001), with grafts performed for Fuchs' endothelial dystrophy having significantly better survival than those performed for the other three specified indications for graft groups (all p<0.001). Repeat grafts for any indication also had significantly poorer survival than first grafts for endothelial failure/bullous keratopathy (p=0.004). This variable was retained in the final multivariate model (see section 4.7).

Figure 4.2.1 Indication for graft



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Failed previous graft	762	511	347	224	154	93	59	37	21	13	7
Endothelial failure/bullous keratopathy	1033	704	457	299	195	122	76	36	18	11	4
Fuchs' endothelial dystrophy	1852	1441	1042	761	563	373	241	149	79	31	7
Other	82	54	36	26	17	9	2	1	1	1	1

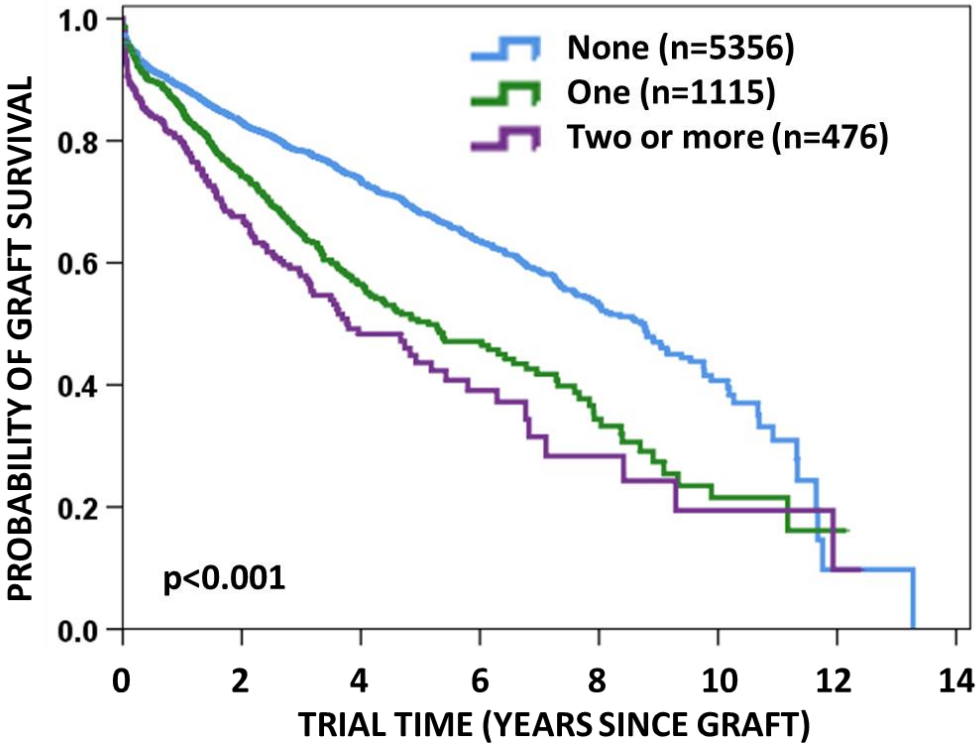
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Failed previous graft	0.84	0.72	0.63	0.54	0.48	0.45	0.39	0.33	0.26	NA
Endothelial failure/bullous keratopathy	0.87	0.78	0.70	0.61	0.53	0.47	0.43	0.34	NA	NA
Fuchs' endothelial dystrophy	0.90	0.86	0.83	0.81	0.77	0.74	0.69	0.65	0.57	0.49
Other	0.88	0.75	0.68	0.59	NA	NA	NA	NA	NA	NA

4.2.2 Descemet's stripping (automated) endothelial keratoplasty 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 0 to 7). Previous grafts may not have been Descemet's stripping (automated) endothelial keratoplasties, and in the majority of cases (51%) the type of at least one previous graft was unknown. Survival, shown in Figure 4.2.2 differed significantly across groups (Log Rank Statistic=105.85.62, df=2, p<0.001). Those with no prior grafts had significantly better survival than those with any number (both p<0.001), and those with multiple prior grafts had significantly poorer survival than those with one (p=0.012). This variable was initially combined with the variable relating to overall indication for graft (see section 4.2.1) for the multivariate analysis (see section 4.7). However, it did not make a significant contribution to the final multivariate model and so was removed (see section 1.4.4), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.2.2 Number of previous ipsilateral grafts



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
None	2961	2197	1533	1084	775	504	319	186	98	43	12
One	548	367	254	173	118	72	48	30	16	9	4
Two or more	220	146	95	53	36	21	11	7	5	4	3

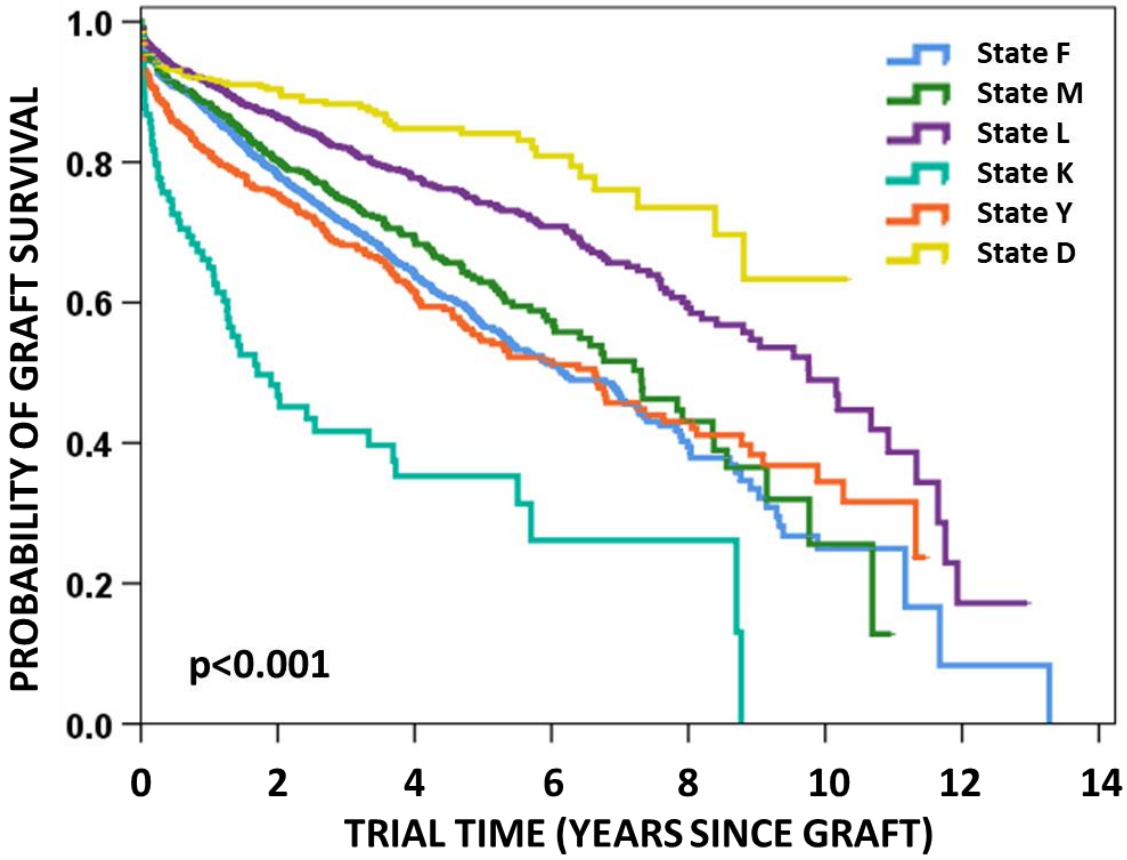
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
None	0.89	0.83	0.78	0.74	0.68	0.64	0.59	0.53	0.47	0.41
One	0.85	0.74	0.65	0.57	0.50	0.47	0.42	0.34	NA	NA
Two or more	0.80	0.68	0.58	0.48	0.44	0.39	NA	NA	NA	NA

4.2.3 Descemet's stripping (automated) endothelial keratoplasty survival: influence of Australian State where graft was performed

Figure 4.2.3 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=183.99; df=5; p<0.001), with survival of grafts performed in State K worse than those performed in any other State, and survival of grafts performed in State D or State L significantly better than those performed in State F, State M or State Y (all p<0.001). Additionally, State D had significantly better survival than State L (p=0.006), and State M had significantly better survival than State Y (p=0.008). This variable was excluded from the multivariate analysis (see section 4.7) as it was collinear with the variables relating to eye bank (see section 4.1.1) and interstate transportation (see section 4.1.5), both of which were retained in the final multivariate model.

Figure 4.2.3 Australian State where graft was performed



Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
State F	0.87	0.78	0.71	0.64	0.57	0.51	0.47	0.40	0.34	NA
State M	0.88	0.80	0.74	0.69	0.63	0.57	0.52	0.43	NA	NA
State L	0.91	0.86	0.82	0.78	0.74	0.71	0.66	0.59	0.55	0.49
State K	0.65	0.47	0.42	NA	NA	NA	NA	NA	NA	NA
State Y	0.81	0.75	0.68	0.62	0.55	0.52	0.46	0.43	0.38	NA
State D	0.92	0.90	0.88	0.85	0.84	0.81	0.76	0.74	NA	NA

Note: Further information is not provided due to confidentiality constraints (see section 1.4.8).

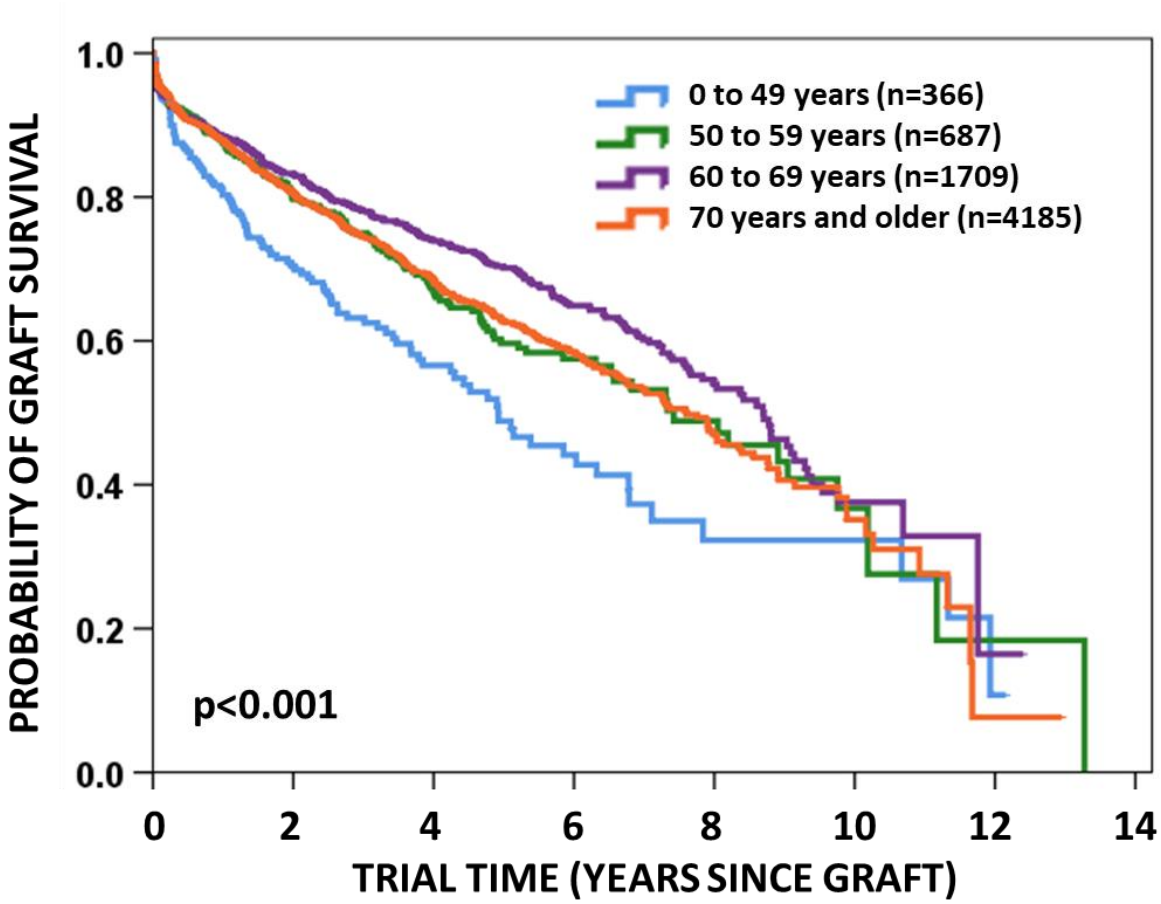
4.2.4 Descemet's stripping (automated) endothelial keratoplasty survival: influence of recipient age (years)

Figure 4.2.4 shows the comparison of graft survival depending on the age of the corneal transplant recipient. Recipients were initially stratified by 10-year age groups. Data for recipients aged under 50 years were combined, due to the small numbers in these groups. A significant difference was found across groups (Log Rank Statistic=29.58; df=5; p<0.001).

Further analyses examined whether there were significant differences between adjacent age groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=27.21; df=3; p<0.001).

Grafts in recipients under 50 years of age had significantly poorer survival than those aged 50 to 59 years (p=0.003) and those aged 60 to 69 years or 70 years and older (both p<0.001). Grafts in recipients aged 60 to 69 years also had significantly better survival than those aged either 50 to 59 years (p=0.037), or 70 years and older (p=0.005). However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.2.4 Recipient age group



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
0 to 49 years	181	131	93	68	47	32	17	12	9	6	5
50 to 59 years	385	290	215	149	100	64	43	30	18	7	3
60 to 69 years	1034	811	603	446	336	215	147	83	46	22	4
70 years and older	2129	1478	972	647	446	286	171	98	60	21	7

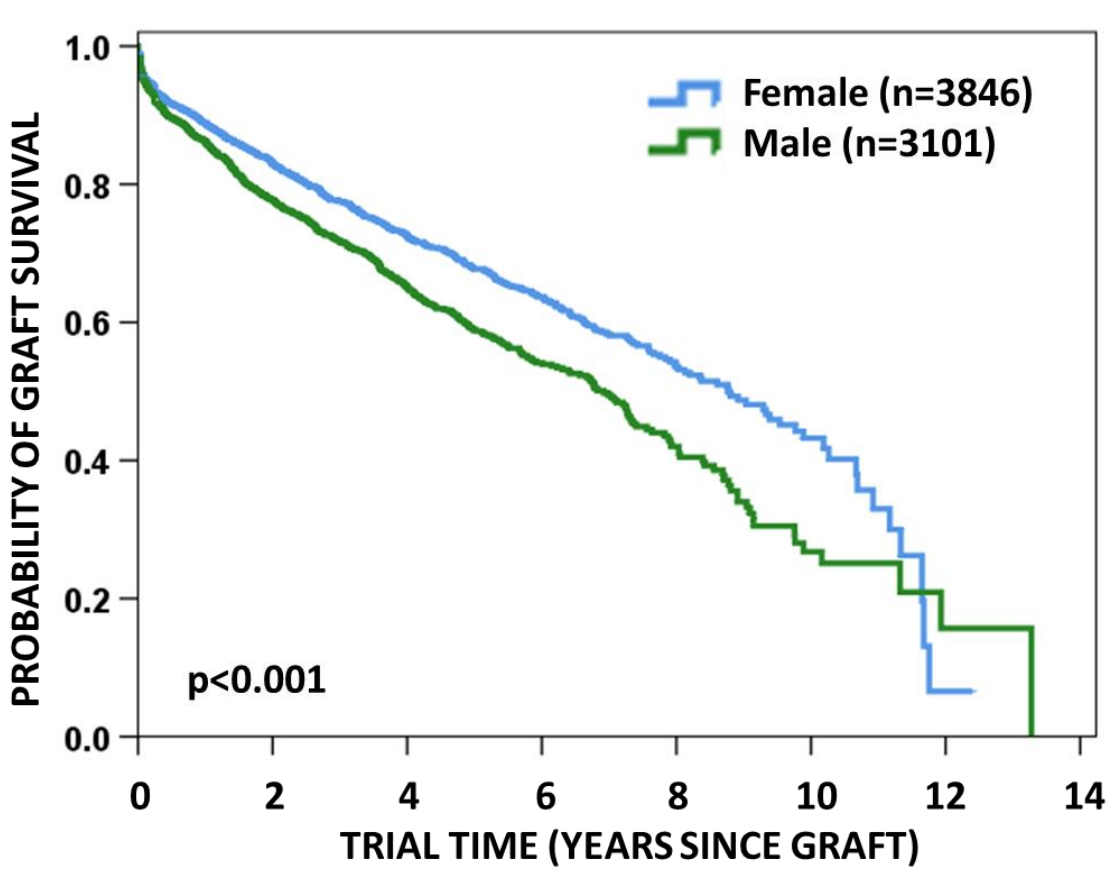
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
0 to 49 years	0.80	0.70	0.63	0.57	0.49	0.44	NA	NA	NA	NA
50 to 59 years	0.88	0.80	0.75	0.67	0.60	0.58	0.53	0.49	NA	NA
60 to 69 years	0.88	0.83	0.78	0.74	0.70	0.65	0.60	0.54	0.46	0.38
70 years and older	0.88	0.81	0.75	0.68	0.63	0.59	0.53	0.47	0.44	0.35

4.2.5 Descemet's stripping (automated) endothelial keratoplasty survival: influence of recipient sex

Comparison of graft survival between male and female transplant recipients is shown in Figure 4.2.5. A significant difference was found between groups (Log Rank Statistic=30.12; df=1; p<0.001), with grafts performed in females having better survival than those in males. This variable was retained in the final multivariate model (see section 4.7)

Figure 4.2.5 Recipient sex



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Female	2115	1552	1079	767	552	363	232	141	77	37	11
Male	1614	1158	803	543	377	234	146	82	42	19	8

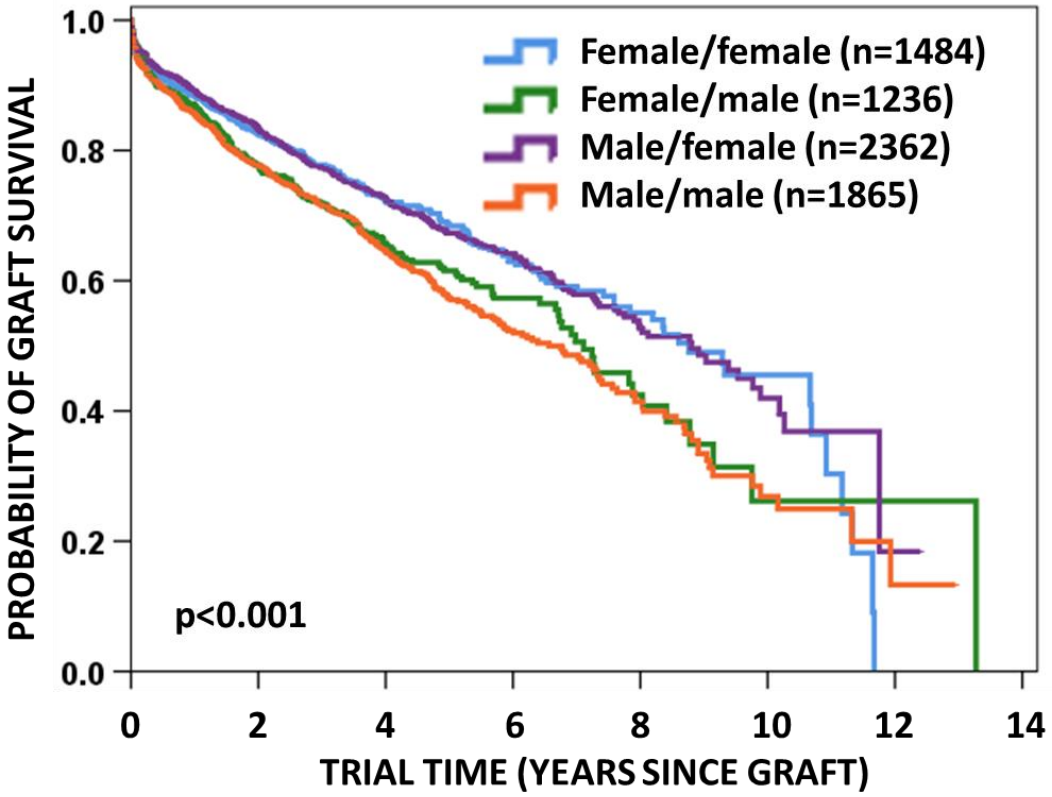
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Female	0.89	0.83	0.78	0.73	0.68	0.64	0.58	0.54	0.49	0.43
Male	0.86	0.78	0.72	0.65	0.59	0.54	0.49	0.42	0.34	NA

4.2.6 Descemet's stripping (automated) endothelial keratoplasty survival: influence of donor/recipient sex match/mismatch

Comparison of graft survival across groups based on donor/recipient sex combinations is shown in Figure 4.2.6. A significant difference was found across groups (Log Rank Statistic=30.86; df=3; p<0.001). Both combinations with a female recipient had significantly better survival than both combinations with a male recipient (all p<0.001, except F/F vs F/M, p=0.004). However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.2.6 Donor/recipient sex match/mismatch



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Female/female	811	581	399	280	209	131	87	53	29	14	5
Female/male	645	448	316	209	140	84	46	25	10	3	1
Male/female	1304	971	680	487	343	232	145	88	43	23	6
Male/male	969	710	487	334	237	150	100	57	32	16	7

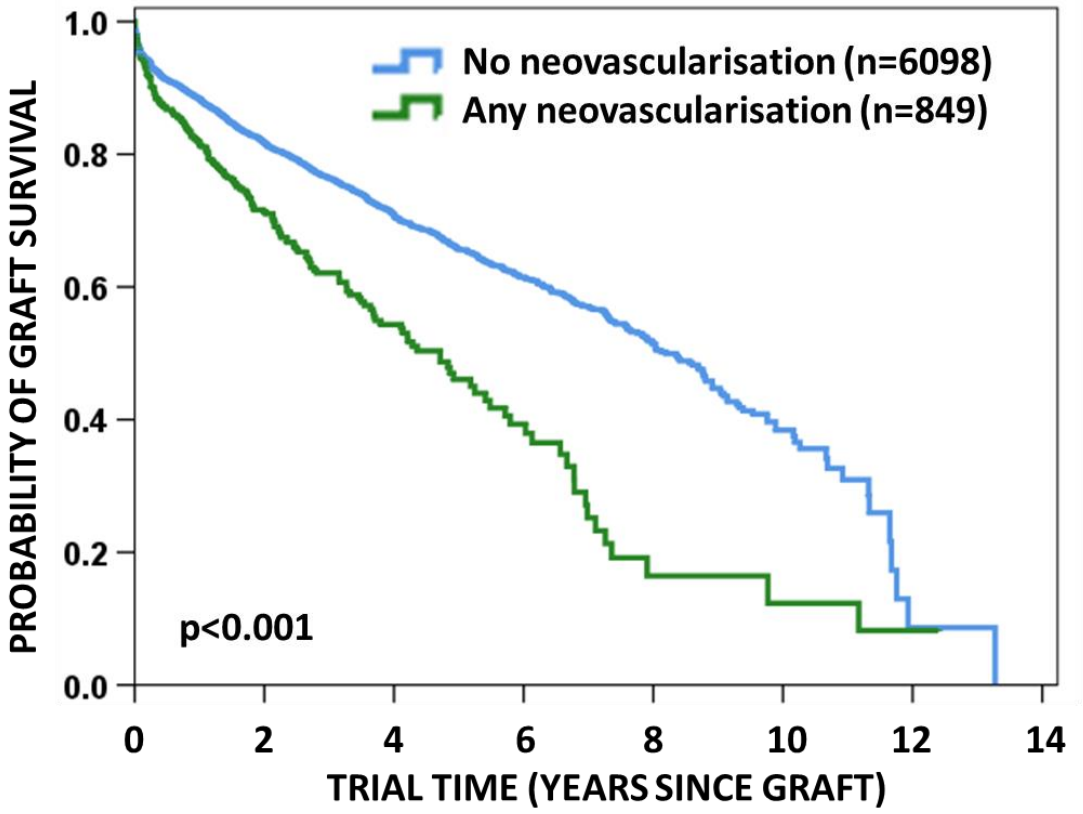
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Female/female	0.88	0.83	0.78	0.72	0.68	0.63	0.59	0.55	0.49	NA
Female/male	0.87	0.78	0.72	0.66	0.62	0.57	0.51	0.43	NA	NA
Male/female	0.89	0.83	0.77	0.73	0.67	0.64	0.58	0.53	0.49	0.42
Male/male	0.86	0.78	0.72	0.65	0.57	0.52	0.49	0.41	0.34	NA

4.2.7 Descemet's stripping (automated) endothelial keratoplasty survival: influence of pre-graft corneal neovascularisation

Figure 4.2.7 shows the comparison of graft survival between those recipients with corneal neovascularisation pre-graft and those without (Log Rank Statistic=61.65; df=1; p<0.001). Recipients with pre-graft neovascularisation had poorer graft survival than those with avascular corneas. However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.2.7 Pre-graft corneal neovascularisation



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
No neovascularisation	3370	2476	1744	1223	881	568	365	217	115	53	16
Any neovascularisation	359	234	138	87	48	29	13	6	4	3	3

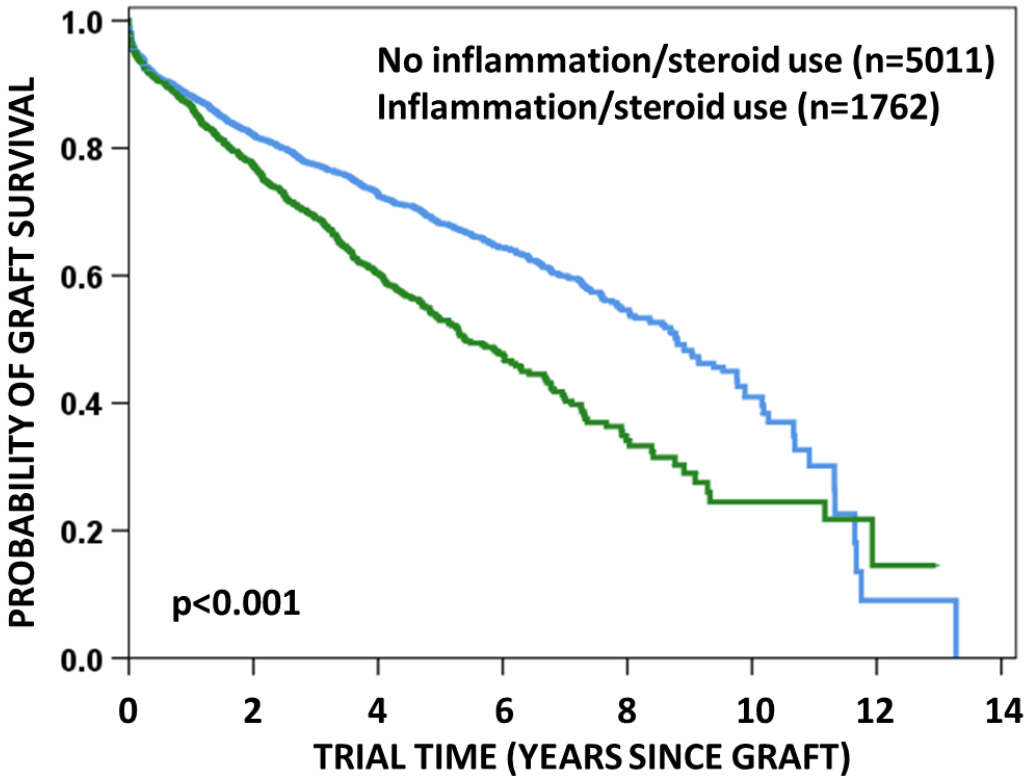
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No neovascularisation	0.88	0.82	0.76	0.71	0.66	0.62	0.57	0.51	0.45	0.38
Any neovascularisation	0.82	0.71	0.62	0.54	0.46	0.39	NA	NA	NA	NA

4.2.8 Descemet's stripping (automated) endothelial keratoplasty survival: influence of previous graft inflammation or recent steroid use

Figure 4.2.8 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 difference was significant (Log Rank Statistic=51.79; df=1; p<0.001). Data on this variable were not provided in 174 cases (3%) and so a further category called "Not advised" was created. The difference between groups remained significant (Log Rank Statistic=62.04; df=2; p<0.001) and so these groups were used for multivariate analysis. However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.2.8 Previous graft inflammation



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
No inflammation/steroid use	2703	2000	1406	988	711	462	292	177	97	41	10
Inflammation/steroid use	943	657	455	310	210	130	82	44	22	15	9

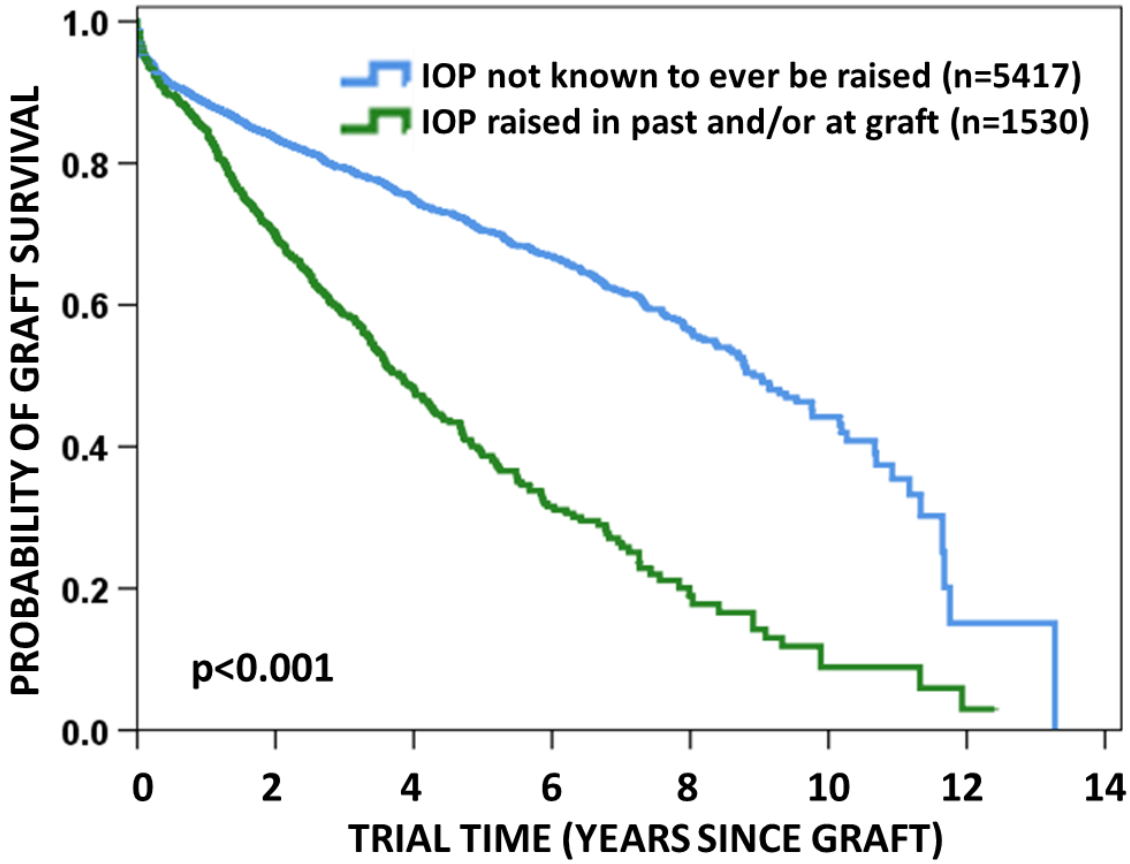
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No inflammation/steroid use	0.88	0.82	0.77	0.73	0.68	0.64	0.60	0.55	0.48	0.41
Inflammation/steroid use	0.87	0.77	0.69	0.61	0.53	0.48	0.41	0.34	0.29	NA

4.2.9 Descemet's stripping (automated) endothelial keratoplasty survival: influence of history of raised intraocular pressure (IOP)

Figure 4.2.9 shows the comparison of graft survival between groups based on whether the recipient had a history of raised intraocular pressure (Log Rank Statistic=218.88; 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 multivariate model (see section 4.7).

Figure 4.2.9 History of raised intraocular pressure (IOP)



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
IOP never raised	2971	2220	1574	1117	811	527	337	207	107	50	16
IOP raised	757	490	308	193	118	70	41	16	12	6	3

Probability of graft survival (years post-graft)

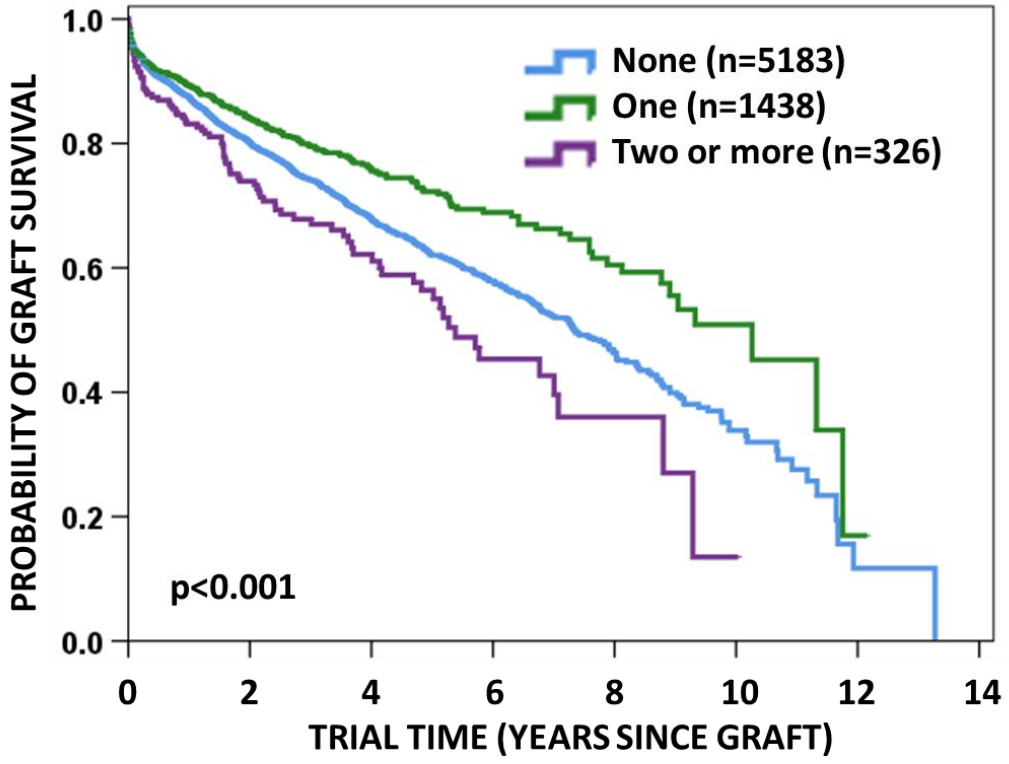
	1	2	3	4	5	6	7	8	9	10
IOP never raised	0.89	0.84	0.79	0.75	0.71	0.67	0.62	0.56	0.50	0.44
IOP raised	0.85	0.70	0.59	0.48	0.39	0.32	0.27	NA	NA	NA

4.2.10 Descemet's stripping (automated) endothelial keratoplasty survival: influence of prior contralateral corneal graft/s

Figure 4.2.10 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 4.2.2 for analysis of the effect of number of previous ipsilateral grafts). A significant difference was found across groups (Log Rank Statistic=29.87; df=2; p<0.001).

Grafts performed in recipients who had undergone one prior corneal graft in the contralateral eye had better survival than those who had undergone none or more than one (both p<0.001). Grafts performed in recipients who had undergone no prior corneal grafts in the contralateral eye also had significantly better survival than those performed in recipients who had undergone more than one prior contralateral graft (p=0.008). This variable was retained in the final multivariate model (see section 4.7).

Figure 4.2.10 Number of prior contralateral corneal grafts



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
None	2779	2020	1399	965	681	453	277	162	91	45	15
One	781	570	401	288	206	122	87	55	25	10	4
Two or more	169	120	82	57	40	22	14	6	3	1	NA

Probability of graft survival (years post-graft)

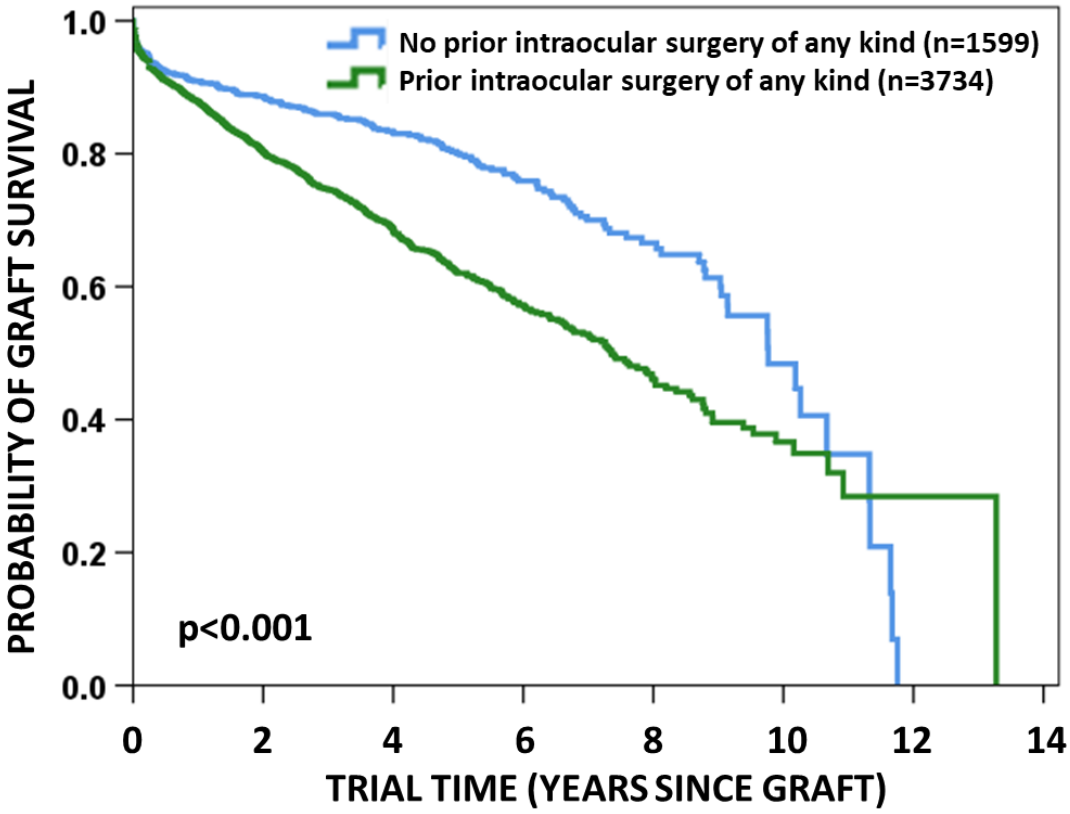
	1	2	3	4	5	6	7	8	9	10
None	0.88	0.80	0.74	0.68	0.62	0.58	0.52	0.46	0.40	0.34
One	0.89	0.84	0.80	0.76	0.72	0.69	0.66	0.61	0.56	NA
Two or more	0.83	0.74	0.68	0.62	0.56	0.45	NA	NA	NA	NA

4.2.11 Descemet's stripping (automated) endothelial keratoplasty survival: influence of prior intraocular surgery

The analysis on page 138 is of a sub-cohort of Descemet's stripping (automated) endothelial grafts which had **not** undergone a previous corneal transplant. Sub-cohort variables are excluded from multivariate analysis.

Data were not available for 23 grafts and these are excluded from the analysis. Figure 4.2.11 shows the comparison of graft survival between grafts where the recipient had undergone prior intraocular surgery (excluding prior graft) compared to those that had not (Log Rank Statistic=56.97; df=1; p<0.001). The nature of the variable means that a large percentage of the cohort (23%) are not included. While the type of prior surgery was not specified, in 98% of first grafts, the eye had undergone prior cataract extraction.

Figure 4.2.11 History of previous intraocular surgery in the ipsilateral eye



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
No prior surgery	952	768	580	431	317	212	131	79	46	17	5
Prior surgery	1995	1418	951	652	457	292	188	107	52	26	7

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No prior surgery	0.91	0.89	0.86	0.83	0.80	0.76	0.70	0.67	0.61	NA
Prior surgery	0.88	0.80	0.75	0.69	0.62	0.57	0.53	0.46	0.40	0.37

4.3 Graft Era/Year

Table 4.5 shows the number of grafts registered and followed based on single years combined. Grafts were initially stratified by yearly groups with all grafts performed prior to 2009 grouped together, due to low numbers. A significant difference was found across year groups (Log Rank Statistic=169.38; df=12; p<0.001).

Further analyses examined whether there were significant differences between adjacent year groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=161.92; df=4; p<0.001). The percentages, which should be summed vertically, total 100.

Table 4.5 Graft era/year

Descemet's Stripping (Automated) Endothelial Keratoplasty

Graft Era/Year

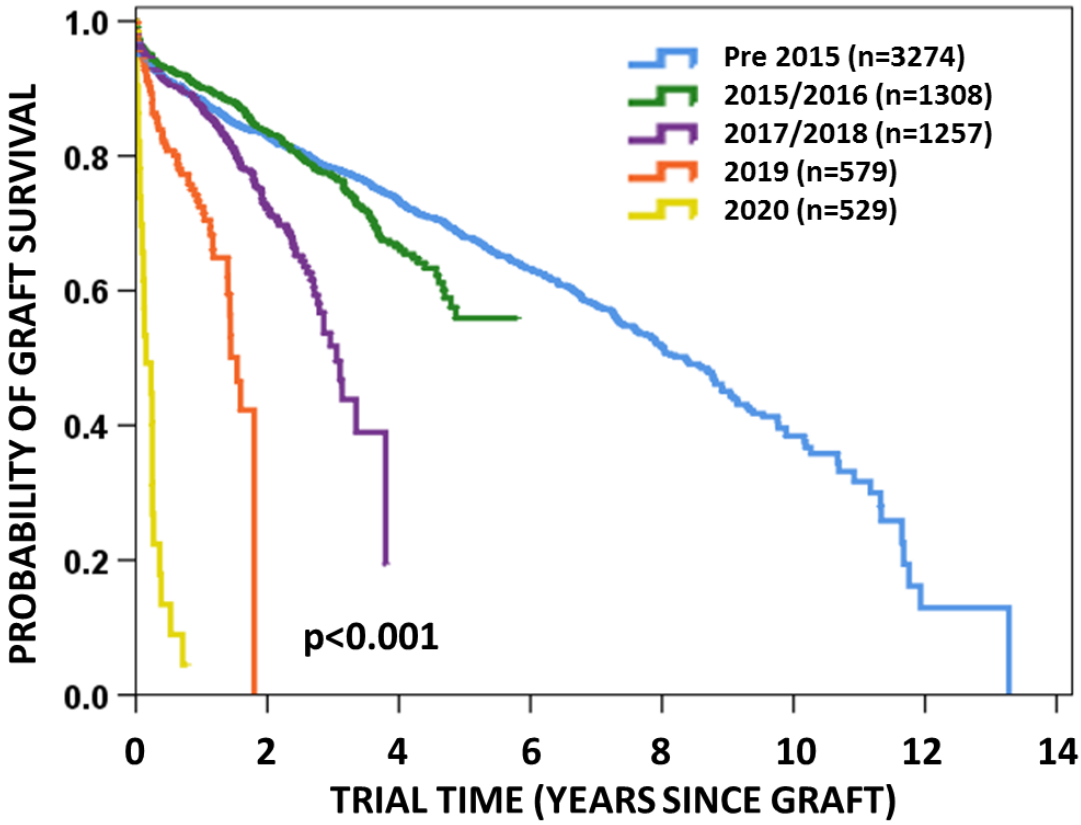
	Registered (%)	Followed (%)
Year of graft		
Pre 2015	3274 (47%)	2939 (58%)
2015/2016	1308 (19%)	1075 (21%)
2017/2018	1257 (18%)	853 (17%)
2019	579 (8%)	192 (4%)
2020	529 (8%)	32 (<1%)
Total	***6947 (100%)***	***5091 (100%)***

See section 1.1 for a discussion of the impact that lag time to follow-up may have on survival depending on graft year/era. Comparisons amongst the percentages of grafts registered and followed in each category showed some differences. Level of follow-up reduces as time since graft reduces, with 93% of grafts performed prior to 2015 followed, 85% of grafts performed in 2015/16, 67% of grafts performed in 2017/18, 43% of grafts performed in 2019 and just 9% of grafts performed in 2020. Of this last group, 78% were primary non-functioning grafts, failing within 3-months and recorded as such when a replacement graft was registered.

4.3.1 Descemet's stripping (automated) endothelial keratoplasty survival: influence of era of graft

Figure 4.3.1 shows the comparison of graft survival between eras of graft, stratified into the groups outlined in section 4.3 (Log Rank Statistic=161.92; df=4; p<0.001). Except for the comparison between grafts performed pre-2015 and those performed in 2015/2016 (p=0.108), all between group comparisons were significant (p<0.001), with survival better for each earlier era/year cohort. This variable was retained in the final multivariate model (see section 4.7).

Figure 4.3.1 Graft Era



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Pre 2015	2281	1871	1492	1183	900	597	378	223	119	56	19
2015/2016	825	622	365	127	29	NA	NA	NA	NA	NA	NA
2017/2018	547	217	25	NA	NA	NA	NA	NA	NA	NA	NA
2019	76	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Pre 2015	0.88	0.83	0.78	0.73	0.68	0.63	0.58	0.52	0.45	0.38
2015/2016	0.90	0.84	0.77	0.67	0.56	NA	NA	NA	NA	NA
2017/2018	0.87	0.72	0.52	NA	NA	NA	NA	NA	NA	NA
2019	0.72	NA	NA	NA	NA	NA	NA	NA	NA	NA

Note: no grafts performed in 2020 had follow-up of one year by the census date and so this category is excluded from the above tables.

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. The sum of these numbers for each variable equals the total number of grafts (6,947 registered and 5,091 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

Descemet's Stripping (Automated) Endothelial Keratoplasty

Surgery and Surgeon Factors

	Registered (%)	Followed (%)
Type of graft		
DSEK	2933 (42%)	2445 (48%)
DSAEK	3549 (51%)	2418 (48%)
UT-DSAEK	309 (4%)	101 (2%)
Unspecified*	156 (2%)	127 (3%)
Size of graft (diameter)		
Less than 8.00 mm	704 (10%)	438 (9%)
8.00 mm to 8.24 mm	1732 (25%)	1129 (22%)
8.25mm to 8.49 mm	641 (9%)	468 (9%)
8.50 mm to 8.74 mm	2242 (32%)	1815 (36%)
8.75mm or more	1121 (16%)	853 (17%)
Not advised	507 (7%)	388 (8%)
Size of incision		
Up to 4.00 mm	1083 (16%)	714 (14%)
4.01 mm to 5.00 mm	2145 (25%)	1433 (28%)
5.01 mm to 6.00 mm	883 (13%)	608 (12%)
6.01 mm or more	165 (2%)	141 (3%)
Not advised	2671 (38%)	2195 (43%)
Change in lens status		
Phakic/Pseudophakic	1589 (23%)	1211 (24%)
Other	5358 (77%)	3880 (76%)
Use of forceps		
No	2941 (42%)	1698 (33%)
Yes	1257 (18%)	915 (18%)
Not advised	2749 (40%)	2478 (49%)
Suture used to close wound		
No	1188 (17%)	884 (17%)
Yes	2891 (42%)	1606 (32%)
Not advised	2868 (41%)	2601 (51%)
Surgeon volume and level of follow-up		
Fewer than 139 (2%) registered DS(A)EK	2743 (40%)	1895 (37%)
139+ registered DS(A)EK, <74% follow-up	1533 (22%)	869 (17%)
139+ registered DS(A)EK, ≥74% follow-up	2671 (38%)	2327 (46%)

	Registered (%)	Followed (%)
The centre effect		
Fewer than 139 (2%) registered DS(A)EK	2743 (39%)	1895 (37%)
	713 (10%)	598 (12%)
	495 (7%)	408 (8%)
	320 (5%)	211 (4%)
	286 (4%)	260 (5%)
	268 (4%)	249 (5%)
	263 (4%)	184 (4%)
	255 (4%)	227 (4%)
Individual surgeons are not identified	182 (3%)	164 (3%)
due to confidentiality constraints.	181 (3%)	85 (2%)
See section 1.4.8 for further information.	165 (2%)	137 (3%)
	160 (2%)	39 (1%)
	157 (2%)	140 (3%)
	155 (2%)	101 (2%)
	155 (2%)	76 (2%)
	151 (2%)	94 (2%)
	150 (2%)	144 (3%)
	148 (2%)	79 (2%)
Total	***6947 (100%)***	***5091 (100%)***

*The majority of grafts in this group were registered prior to the ACGR routinely requesting specification of DS(A)EK type. Subsequent enquiries have been unable to ascertain their categorisation.

Note: 139 was selected as the cut-off point for high volume surgeons as this was 2% of all registered Descemet's stripping (automated) endothelial keratoplasties. 74% was selected as the cut-off point for the follow-up categories as this was the average percentage of follow-up for all Descemet's stripping (automated) endothelial keratoplasties.

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 (6,947 registered and 5,091 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

Table 4.7 Surgery and surgeon factors, not significant in univariate analyses

Descemet's Stripping (Automated) Endothelial Keratoplasty

Surgery and Surgeon Factors

	Registered (%)	Followed (%)
Use of glide		
No	658 (9%)	408 (8%)
Yes	4461 (64%)	3017 (59%)
Not advised	1828 (26%)	1666 (33%)
Chi²=0.12, df=1, p=0.729		
Use of anterior chamber maintainer		
No	2514 (36%)	1507 (30%)
Yes	1469 (21%)	904 (18%)
Not advised	3983 (57%)	2680 (53%)
Chi²=0.54, df=1, p=0.462		
Use of viscoelastic		
No	3380 (49%)	2023 (40%)
Yes	603 (9%)	388 (8%)
Not advised	2964 (43%)	2680 (53%)
Chi²=2.94, df=1, p=0.086		
Descemet's membrane stripped		
No	1066 (15%)	691 (14%)
Yes	2938 (42%)	1740 (34%)
Not advised	2943 (42%)	2660 (52%)
Chi²=2.61, df=1, p=0.106		
Total	***6947 (100%)***	***5091 (100%)***

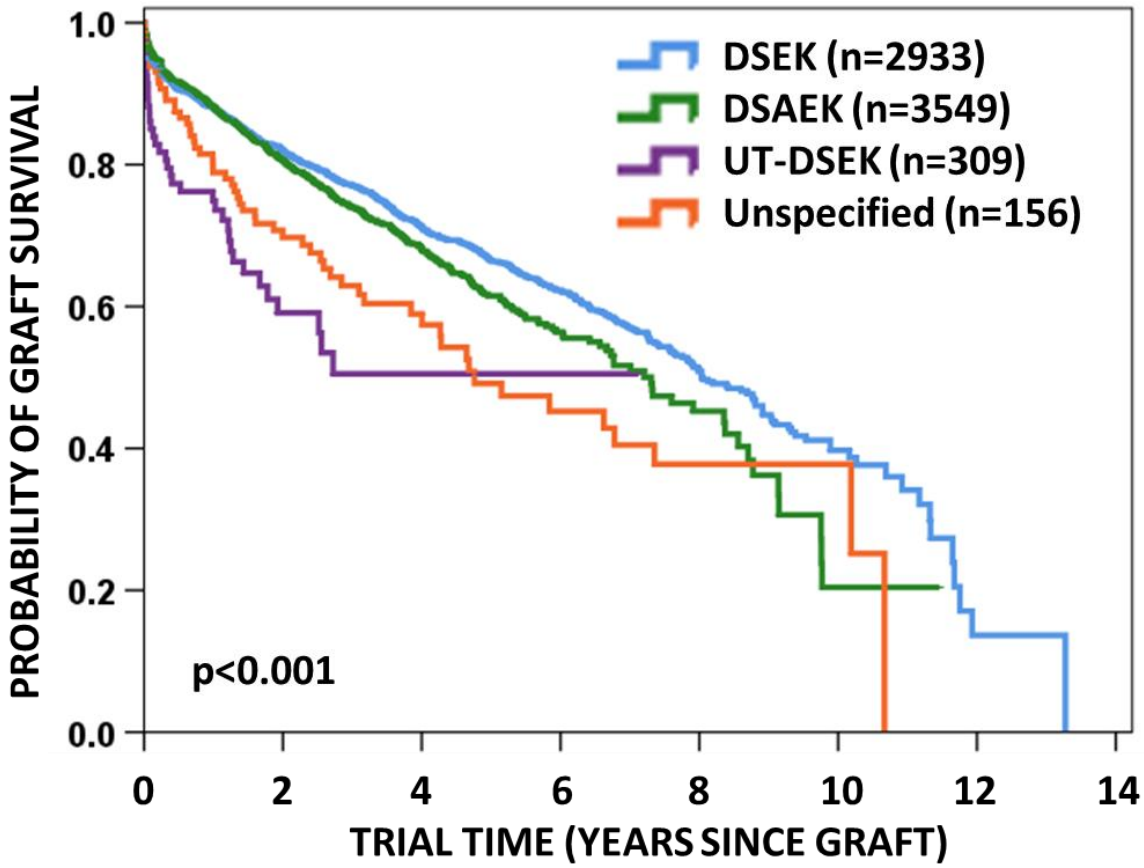
Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised.

There were insufficient data available to analyse the impact of the use of an IOL injector or Geuder injector in the insertion of the donor button. There were also insufficient data to analyse the impact of using the suture pull-through technique, folding of the donor button, or use of sulphur hexafluoride (SF6) gas.

4.4.1 Descemet's stripping (automated) endothelial keratoplasty survival: influence of type of graft

Figure 4.4.1 shows the comparison of graft survival across different variations of DSEK graft – manual, automated, ultra-thin and unspecified. A significant difference was found across groups (Log Rank Statistic=36.71; df=3; p<0.001). DSEK exhibited significantly better survival compared to all other groups (DSAEK p=0.003, UT-DSEK and unspecified both p<0.001) and DSAEK had significantly better survival than UT-DSEK (p<0.001) and unspecified (p=0.027). This variable was retained in the final multivariate model (see section 4.7).

Figure 4.4.1 Type of graft



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
DSEK	1856	1452	1116	848	650	440	292	178	98	49	17
DSAEK	1725	1158	699	411	245	135	68	35	15	3	2
UT-DSEK	57	30	16	10	5	2	1	NA	NA	NA	NA
Unspecified	91	70	51	40	28	20	17	10	6	4	NA

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
DSEK	0.88	0.82	0.77	0.71	0.67	0.62	0.57	0.51	0.45	0.40
DSAEK	0.88	0.81	0.74	0.68	0.62	0.56	0.52	0.45	NA	NA
UT-DSEK	0.75	0.59	NA	NA	NA	NA	NA	NA	NA	NA
Unspecified	0.79	0.70	0.63	0.59	0.49	0.45	NA	NA	NA	NA

4.4.2 Descemet's stripping (automated) endothelial keratoplasty survival: influence of graft size

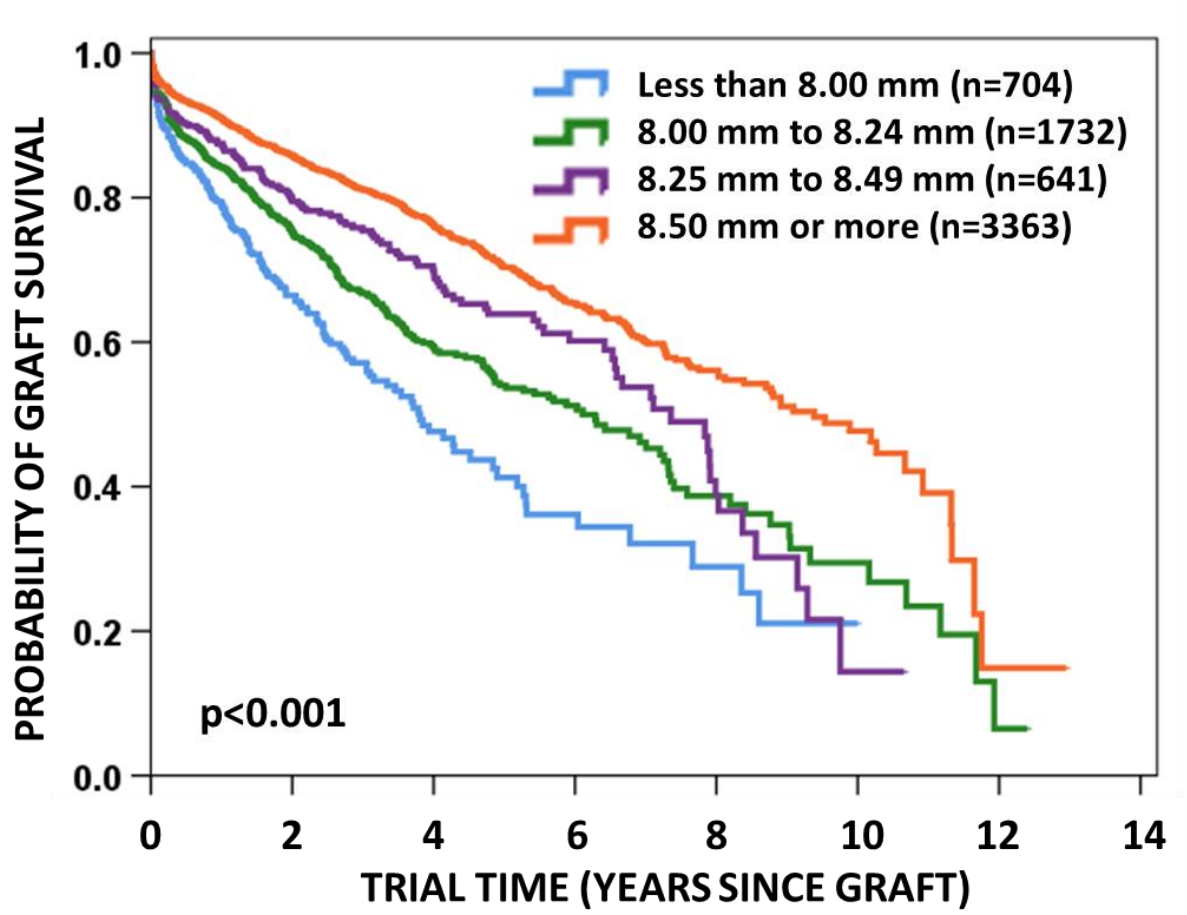
Figure 4.4.2 shows a comparison of graft survival depending on the size of the graft. Grafts were initially stratified in 0.25 mm incriments, with all grafts measuring under 8.00 mm analysed together, and all grafts measuring 8.75 mm and over analysed together. A significant difference was found across groups (Log Rank Statistic=150.01; df=4; p<0.001).

Further analyses examined whether there were significant differences between adjacent size groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=150.01; df=3; p<0.001).

Graft survival improved as graft size increased. Grafts measuring less than 8.00 mm had poorer survival than the three other groups (all p<0.001). Grafts that were 8.00 mm to 8.24 mm had poorer survival than those which were 8.25 mm to 8.49 mm (p=0.042) and those that were 8.50 mm or larger (p<0.001). Grafts that were 8.25 mm to 8.49 mm had poorer survival than those that were 8.50 mm and larger (p<0.001).

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=147.12; df=4; p<0.001). Graft size was thus categorised into these five groups for multivariate analysis. This variable was retained in the final multivariate model (see section 4.7).

Figure 4.4.2 Graft size



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Less than 8.00 mm	280	171	97	54	33	22	14	8	5	NA	NA
8.00 mm to 8.24 mm	806	527	337	210	144	85	54	32	21	14	6
8.25 mm to 8.49 mm	344	251	171	123	84	55	37	19	7	2	NA
8.50 mm or more	2014	1548	1121	804	579	366	221	129	76	38	12

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Less than 8.00 mm	0.79	0.67	0.57	0.48	0.41	0.36	NA	NA	NA	NA
8.00 mm to 8.24 mm	0.84	0.75	0.67	0.59	0.54	0.51	0.46	0.39	0.35	NA
8.25 mm to 8.49 mm	0.88	0.80	0.75	0.70	0.64	0.60	0.54	NA	NA	NA
8.50 mm or more	0.91	0.86	0.81	0.76	0.70	0.65	0.60	0.56	0.51	0.48

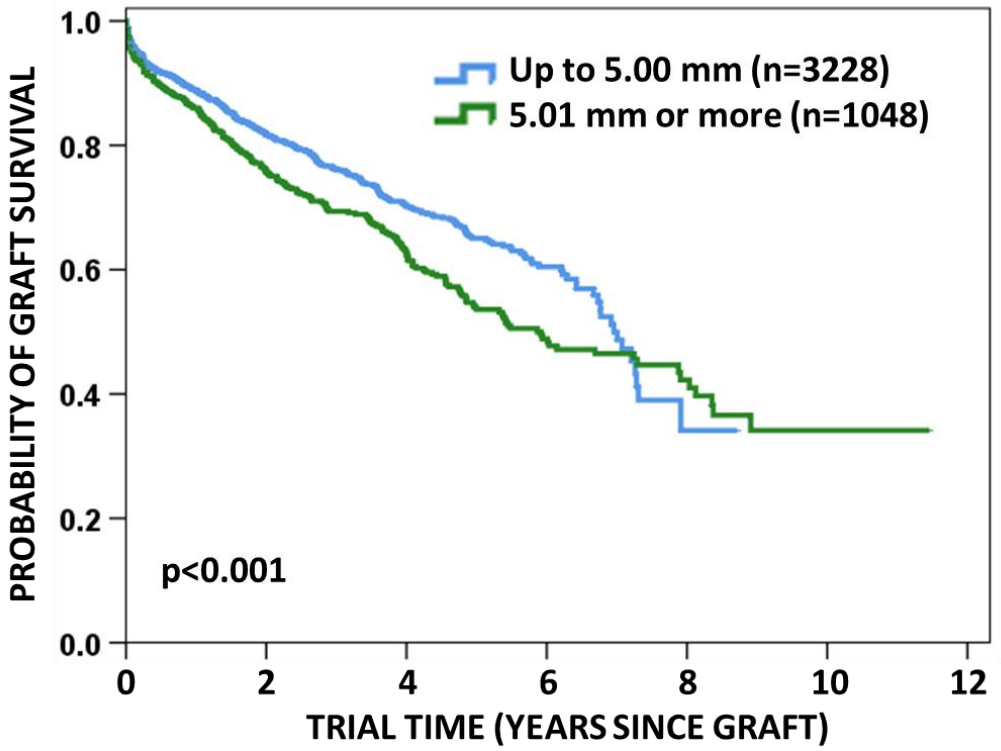
4.4.3 Descemet's stripping (automated) endothelial keratoplasty survival: influence of incision size

Figure 4.4.3 shows a comparison of graft survival depending on the size of the incision made to insert the donor lenticule, as reported by surgeons. Grafts were initially categorised in increments of 1.00 mm increases, with all grafts 4.00 mm and smaller, and all grafts over 6.00 mm, grouped together. A significant difference was found across groups (Log Rank Statistic=12.79; df=3; p=0.005).

Further analyses examined whether there were significant differences between adjacent size groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=10.88; df=1; p<0.001).

Data on this variable were not provided in 38% 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=15.32; df=2; p<0.001). Incision size was thus categorised into these three groups for multivariate analysis. This variable was retained in the final multivariate model (see section 4.7).

Figure 4.4.3 Size of incision



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9
Up to 5.00 mm	1543	1029	626	377	233	111	40	5	NA
5.01 mm or more	538	394	283	211	142	87	60	33	13

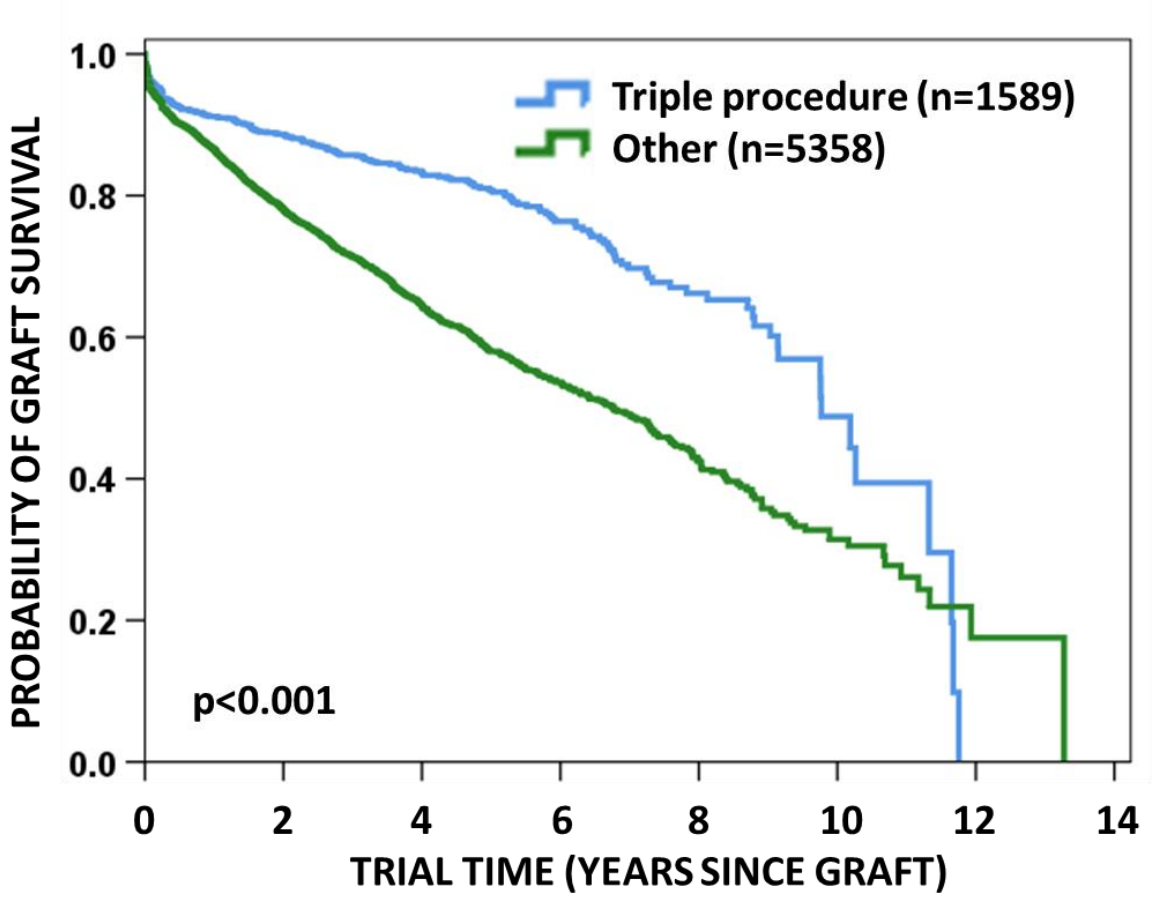
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8
Up to 5.00 mm	0.89	0.82	0.76	0.70	0.65	0.61	0.50	0.34
5.01 mm or more	0.86	0.76	0.69	0.63	0.54	0.49	0.47	0.42

4.4.4 Descemet's stripping (automated) endothelial keratoplasty survival: influence of change in lens status

Figure 4.4.3 shows the comparison of graft survival stratified by the change of lens status from pre- to post-graft. Grafts were initially categorised in four groups, however there was no significant difference in survival (p=0.919) for the grafts that had not undergone a triple procedure (cataract extraction, IOL insertion and graft) and so these were combined. A significant difference was found across groups (Log Rank Statistic=97.53; df=1; p<0.001). This variable was retained in the final multivariate model (see section 4.7).

Figure 4.4.4 Change in lens status



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Triple procedure	955	752	555	418	308	204	127	76	44	15	4
Other	2774	1958	1327	892	621	393	251	147	75	41	15

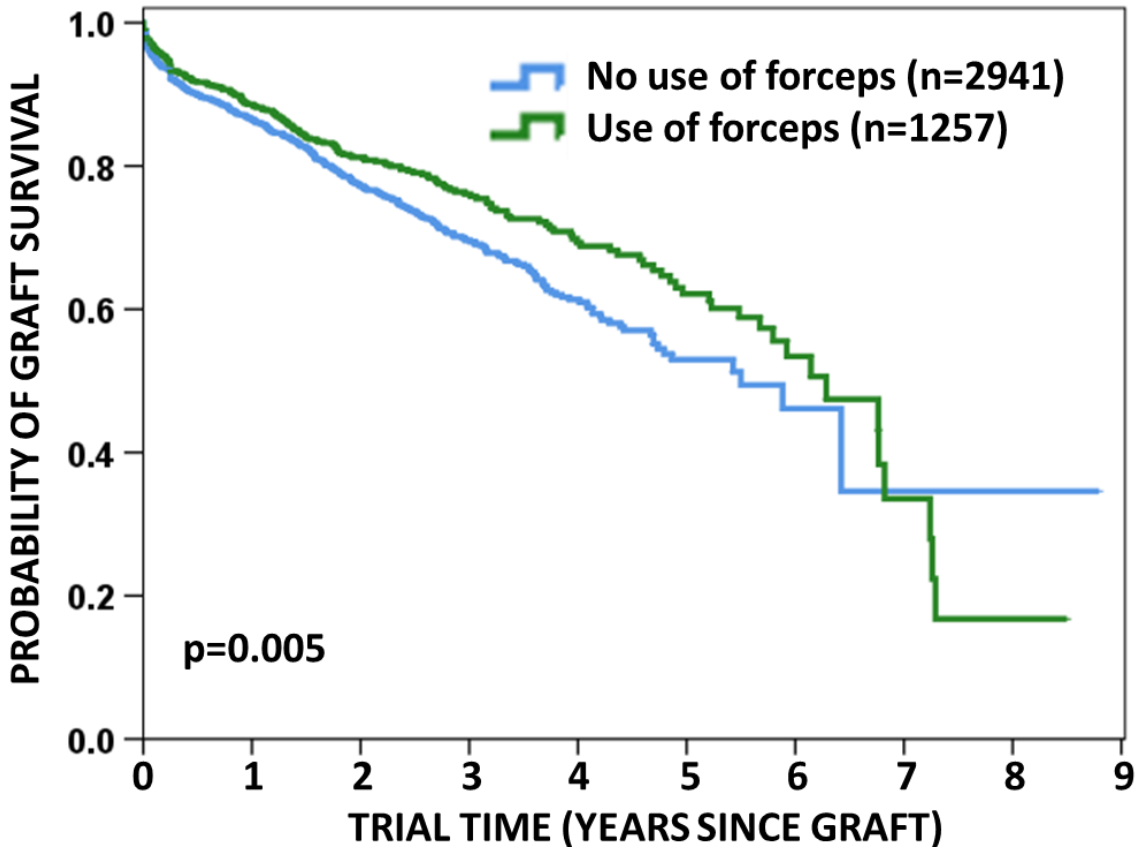
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Triple procedure	0.91	0.89	0.86	0.83	0.81	0.76	0.70	0.66	0.62	NA
Other	0.87	0.78	0.71	0.65	0.58	0.54	0.49	0.43	0.36	0.32

4.4.5 Descemet's stripping (automated) endothelial keratoplasty survival: influence of use of forceps

Figure 4.4.5 shows a comparison of graft survival depending on whether forceps were used to perform the graft, as reported by surgeons. A significant difference was found across groups (Log Rank Statistic=7.71; df=1; p=0.005). Data on this variable were not provided in 40% 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=27.67; df=2; p=0.001). Use of forceps was thus categorised into these three groups for multivariate analysis. However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.4.5 Use of forceps



Number at risk (years post-graft)

	1	2	3	4	5	6	7
No use of forceps	1191	724	381	164	58	12	3
Use of forceps	614	416	244	135	72	21	7

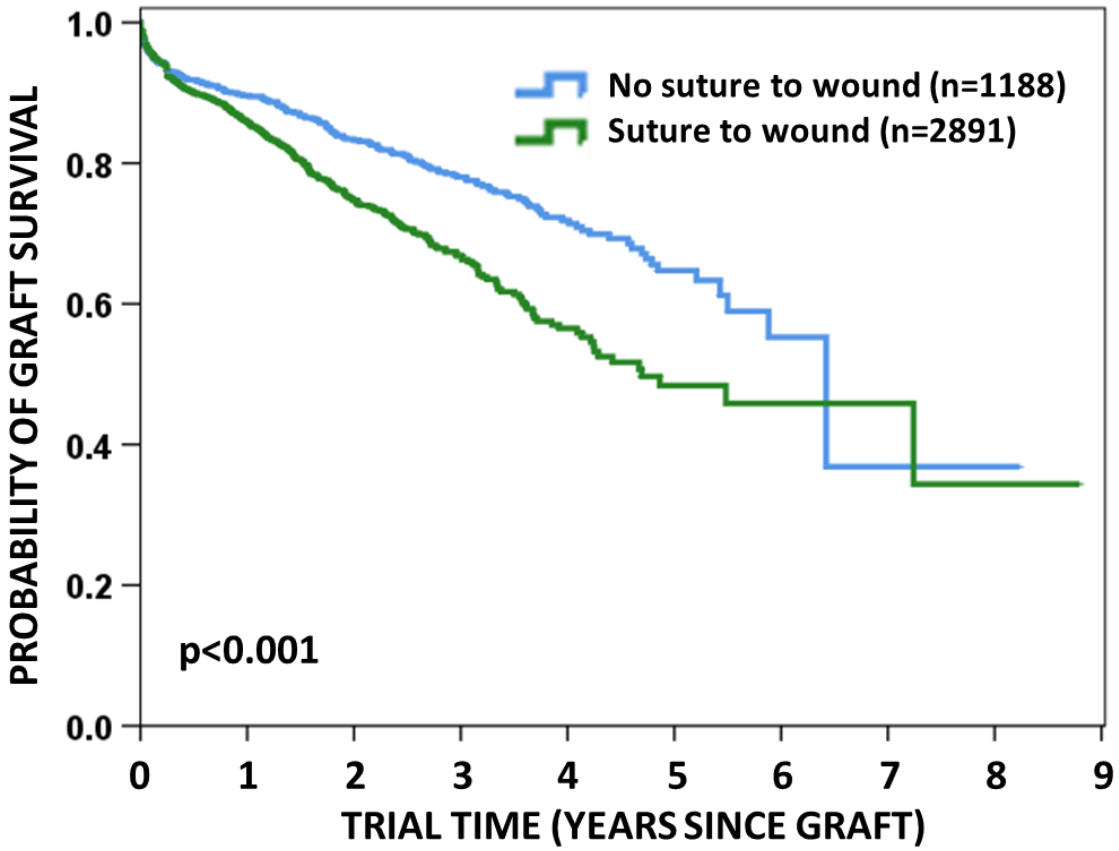
Probability of graft survival (years post-graft)

	1	2	3	4	5	6
No use of forceps	0.87	0.77	0.70	0.61	0.53	NA
Use of forceps	0.89	0.81	0.76	0.69	0.62	0.53

4.4.6 Descemet's stripping (automated) endothelial keratoplasty survival: influence of use of suture to close wound

Figure 4.4.6 shows a comparison of graft survival depending on whether a suture was used to close the wound. A significant difference was found across groups (Log Rank Statistic=25.74; df=1; p<0.001). Data on this variable were not provided in 41% 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=40.95; df=2; p<0.001). Presence of wound suture was thus categorised into these three groups for multivariate analysis. However, this variable was not retained in the final multivariate model (see section 4.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.4.6 Use of suture to close wound



Number at risk (years post-graft)

	1	2	3	4	5	6
No suture to wound	692	517	322	156	64	12
Suture to wound	1025	544	241	98	32	7

Probability of graft survival (years post-graft)

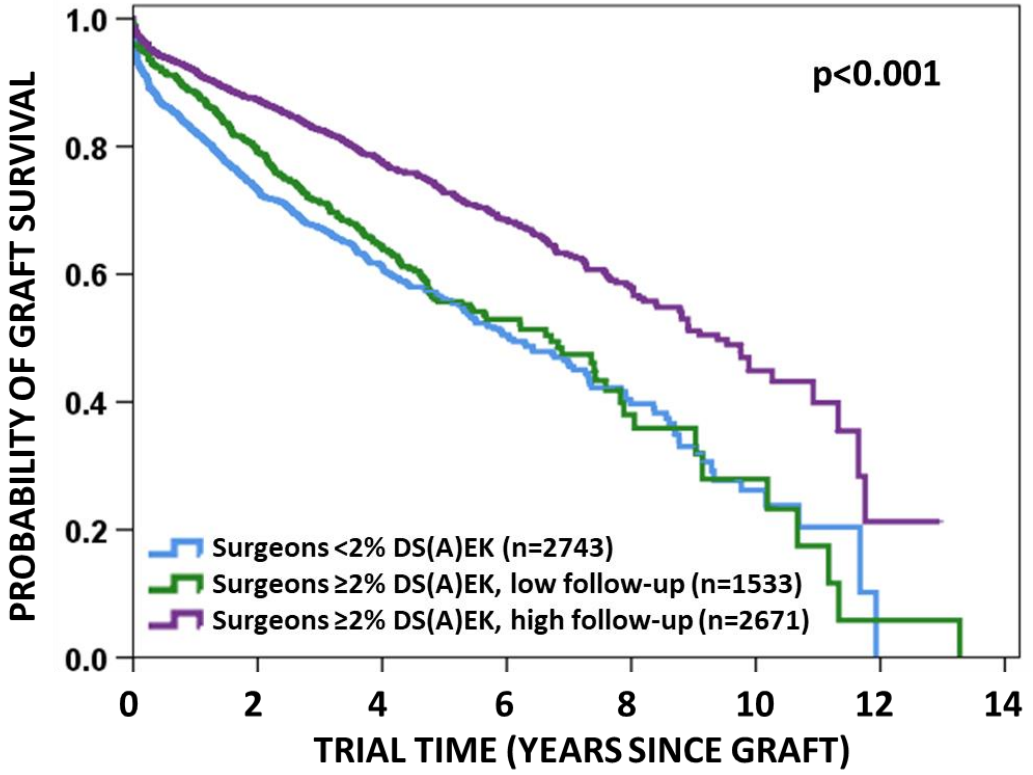
	1	2	3	4	5
No suture to wound	0.90	0.83	0.78	0.72	0.55
Suture to wound	0.86	0.75	0.67	0.57	0.48

4.4.7 Descemet's stripping (automated) endothelial keratoplasty survival: influence of surgeon caseload grouped by level of follow-up

Figure 4.4.7 shows the comparison of graft survival between grafts performed by surgeons with 139+ (≥2%) registered Descemet's stripping (automated) endothelial keratoplasties with average or better (≥74%) follow-up, to those with lower than average follow-up (<74%), and to surgeons with fewer than 139 (<2%) registered Descemet's stripping (automated) endothelial keratoplasties (Log Rank Statistic=133.72; df=2; p<0.001).

Survival of grafts performed by high caseload surgeons with average or better follow-up was significantly better than that of either of the other two groups (both p<0.001) and survival of grafts performed by high caseload surgeons with below average follow-up was also significantly better than that of low caseload surgeons (p=0.024). This variable was retained in the final multivariate model (see section 4.7).

Figure 4.4.7 Surgeon caseload and level of follow-up



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
<2% registered DS(A)EK	1299	869	572	373	250	151	94	62	30	13	5
≥2% DS(A)EK, low follow-up	669	467	315	211	129	72	45	18	9	6	3
≥2% DS(A)EK, high follow-up	1761	1374	995	726	550	374	239	143	80	37	11

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
<2% registered DS(A)EK	0.82	0.73	0.67	0.61	0.56	0.51	0.46	0.40	0.33	NA
≥2% DS(A)EK, low follow-up	0.88	0.79	0.71	0.64	0.56	0.53	0.47	NA	NA	NA
≥2% DS(A)EK, high follow-up	0.92	0.87	0.83	0.78	0.73	0.69	0.63	0.58	0.51	0.45

4.5 Operative procedures at the time of graft

Table 4.8 shows the number of grafts for which specified operative procedures were performed at the time of graft. This did not include cataract extraction, pseudophakic IOL insertion, or pseudophakic IOL extraction, as these were covered by the variable relating to change in lens (see section 4.4.4).

Table 4.8 Operative procedures at the time of graft

Descemet's Stripping (Automated) Endothelial Keratoplasty Operative Procedures at Time of Graft	
	Number
Peripheral iridectomy	550
Vitrectomy	121
Pseudophakic IOL exchanged	63
Synechiolysis	28
Glaucoma tube repositioned	22
Pupilloplasty	17
Intravitreal/intracameral/conjunctival injection/s*	16
IOL repositioned	13
Iridoplasty	12
Glaucoma tube trimmed (Molteno: 1, Baerveldt: 2, unspecified: 8)	11
Glaucoma tube inserted (Molteno: 4, Baerveldt: 3, unspecified: 2)	9
Keratoprosthesis inserted	6
Keratectomy	5
EDTA chelation	4
Piggyback IOL inserted	4
Removal of silicone oil	4
Removal of band keratopathy	4
Other**	60
Total operative procedures (number of grafts)	**949 (861)**

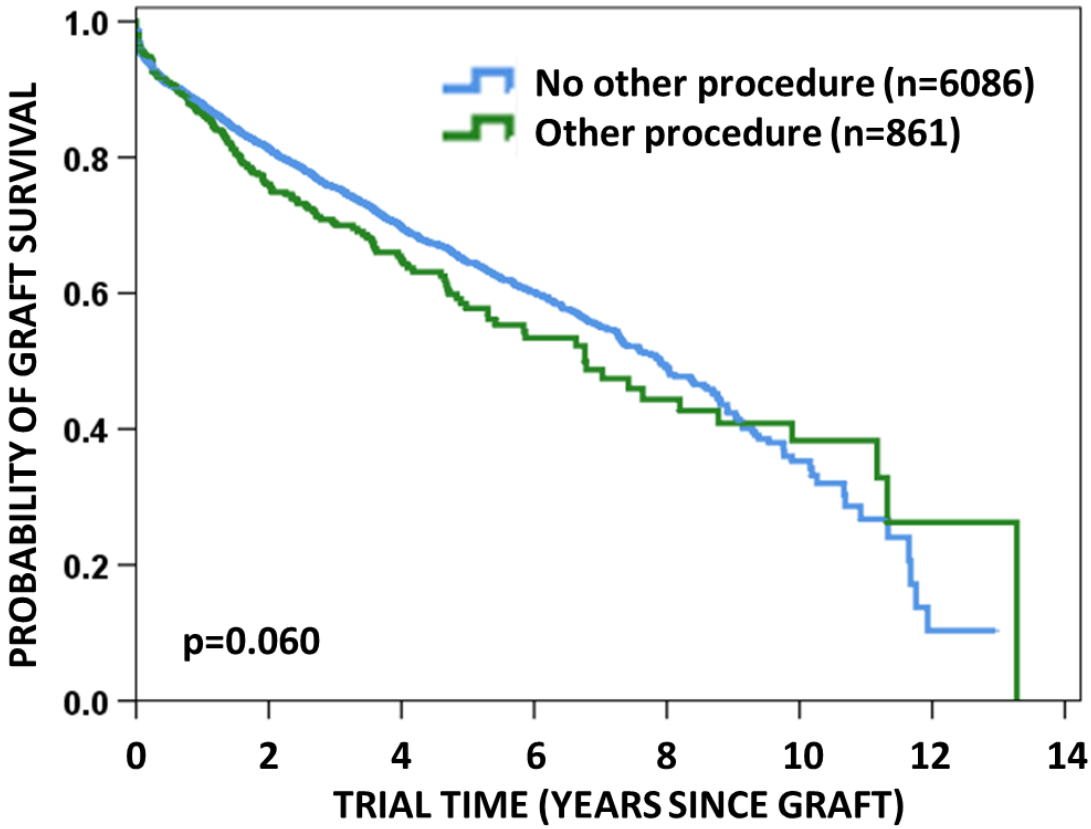
**5FU (6), Triamcinolone (4), Avastin (3), Voriconazole (1), viscoelastic (1), unspecified (1).

Other included: artificial iris segment inserted (3), iris suture (3), removal of retrocorneal membrane (3), trabeculectomy (3), wound repair (3), epitheliectomy (2), iris repair (2), removal of Morcher iris prosthesis (2), removal of phakic IOL (2), removal of residual lens material (2), scleral patch graft (2), tarsorrhaphy (2), anterior chamber tap (1), bleb inserted (1), capsular tension ring inserted (1), cyclodialysis (1), carcinoma resection (1), clip lens repositioned (1), ICE membrane stripped (1), IOL enclavation (1), iridotomy (1), iris clip inserted (1), iris repositioned (1), lateral canthotomy (1), limbal graft (1), minimally invasive glaucoma surgery (MIGS) (1), pterygium excision (1), pupil reconstruction (1), pupil stretch (1), molteno tube lengthened (1), removal of cyclitic membranes (1), removal of fibrous tissue (1), removal of foreign body (1), removal of endothelial tap (1), removal of iris clip on IOL (1), removal of PAUL glaucoma device (1), removal of vitreous strands (1), scleral tunnel inserted (1), suture pupil (1), unspecified membrane dissection (1), unsuccessful psudophakic iol exchange (1), vent incisions (1), wedge resection (1).

4.5.1 Descemet's stripping (automated) endothelial keratoplasty survival: influence of other operative procedure/s at time of graft

Figure 4.5.1 shows the comparison of survival for grafts where other operative procedure/s were performed at the time of graft (excluding cataract extraction, pseudophakic IOL insertion, and pseudophakic IOL removal), to those where one was not. A non-significant difference was found across groups (Log Rank Statistic=3.55; df=1; p=0.060), however this met the p<0.08 level of significance for inclusion in the multivariate analysis. This variable was not retained in the final multivariate model (see section 4.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 4.5.1 Other procedure/s at time of graft



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
No other procedure	3316	2445	1718	1195	850	543	341	196	97	42	12
Other procedure	413	265	164	115	79	54	37	27	22	14	7

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No other procedure	0.88	0.81	0.76	0.70	0.65	0.60	0.55	0.49	0.42	0.35
Other procedure	0.86	0.76	0.70	0.65	0.58	0.53	0.49	0.44	0.41	NA

4.6 Post-graft Events

Table 4.9 shows post-graft surgical procedures, as reported by follow-up practitioners. 1125 Descemet's stripping (automated) endothelial keratoplasties were reported to have undergone a re-grafting procedure at the date last seen. Of these, 902 had not had additional post-graft operative procedures reported.

Table 4.9 Post-graft surgical procedures

Descemet's Stripping (Automated) Endothelial Keratoplasty

Post-graft Surgical Procedures

	Number
Rebubbled	432
YAG laser	318
Trabeculectomy	107
Cataract removal and IOL insertion	67
IOL insertion (cataract removed prior to graft)	12
IOL repositioned/removed/exchange	45
Insertion of piggyback lens	13
Vitrectomy	49
Intravitreal/intracameral/conjunctival injection/s*	47
Tube insertion (Baerveldt: 20, Molteno: 4, XEN stent: 2, unspecified: 7)	33
Wound repair/re-sutured	21
Cyclodiode	18
PTK laser	14
PRK laser	12
Concurrent graft (patch: 9, limbal/conjunctival: 3)	11
Graft repositioned	11
Keratectomy	11
Ptosis repair	11
Bleb needling/revision	10
Ectropion repair	8
Iridotomy	7
Selective laser trabeculoplasty	7
Blepharoplasty	6
Pupiloplasty	6
Revision of glaucoma tube	6
Membrane peel	5
Removal of air bubble	5
Tarsorrhaphy	5
Other**	104
Total number of surgical procedures (number of grafts)	***1403 (1182)***

*Avastin (9), Lucentis (9), Eylea (7), Triamcinolone (7), Anti-VEGF (3), silicone oil (3), unspecified – for age related macular degeneration (2), Botulinum toxin (1), submacular tissue plasmogen activator (1), unspecified antibiotics (1), unspecified - for central retinal vein occlusion (1), unspecified - for cystoid macular oedema (1), unspecified (2).

** Other included: corneal scraping/debridement (4), implantable contact lens (4), removal of remnant lens material (4), retinal detachment repair (4), anterior chamber tap (3), anterior stromal puncture (3), endolaser (3), evisceration (3), eyelid repair (3), keratotomy (3), removal of lid lesion (3), unspecified glaucoma surgery (3), cataract removal without IOL insertion (2), cryotherapy (2), EDTA chelation (2); epiretinal membrane peel (2), insertion of Morcher implant (2), insertion of punctal plug (2), LASIK (2), macular hole repair (2), panretinal photocoagulation laser (2), reformation of anterior chamber (2), relaxing incision (2), removal of basal cell carcinoma (2), removal of folds in Descemet's membrane (2), removal of limbal tumour (2), retinopexy (2), air-bubble adjustment (1), anterior chamber washout (1), amniotic membrane transplant (1), conjunctival resection (1), corneal diathermy (1), Dacryocystorhinostomy (1), drainage of conjunctival cyst (1), electrolysis (1), enucleation (1), filter surgery (1), floater surgery (1), goniosynechiolysis (1); Gunderson flap (1), Hughes flap (1), insertion of gold weight (1), insertion of scleral buckle (1), iridectomy (1), iridoplasty (1), iris prolapse repositioning (1), lacrimal punctoplasty (1), lateral tarsal snip (1), punctal cautery (1), removal of band keratopathy (1), removal of epithelial cyst (1), removal of glaucoma drainage device (1), removal of iris prosthesis (1), removal of metallic foreign body (1), removal of pterygium (1), removal of pterygium scar (1), removal of scleral buckle (1), removal of upper tarsal concretions (1), revision of trabeculectomy (1), suture adjustment (1), temporal laser treatment (1), unspecified refractive surgery (1), vitreous tap (1).

Table 4.10 shows the occurrence of post-graft events, which were found to be **significant** in univariate analyses. Only 35 grafts had post-graft herpetic infection reported, 65 had microbial keratitis, and 30 had post-graft uveitis, and so the impact of these factors was not further analysed. 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 events, significant in univariate analyses

Descemet's Stripping (Automated) Endothelial Keratoplasty Post-graft Events	Registered (%)	Followed (%)
Post-graft neovascularisation		
No	6762 (97%)	4906 (96%)
Yes	185 (3%)	185 (4%)
Post-graft oedema		
No	6446 (93%)	4590 (90%)
Yes	501 (7%)	501 (10%)
Post-graft rise in intraocular pressure		
No	6087 (88%)	4231 (83%)
Yes	860 (12%)	860 (17%)
At least one rejection episode		
No	6530 (94%)	4674 (92%)
Yes	417 (6%)	417 (8%)
Total	***6947 (100 %)***	***5091 (100 %)***

Table 4.11 shows the occurrence of post-graft events, which were found to be **non-significant** in univariate analysis. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable. The sum of these numbers for each variable equals the total number of grafts (6,947 registered and 5,091 followed) and the percentages, which should be summed vertically for each variable, total 100.

Table 4.11 Post-graft events, not significant in univariate analyses

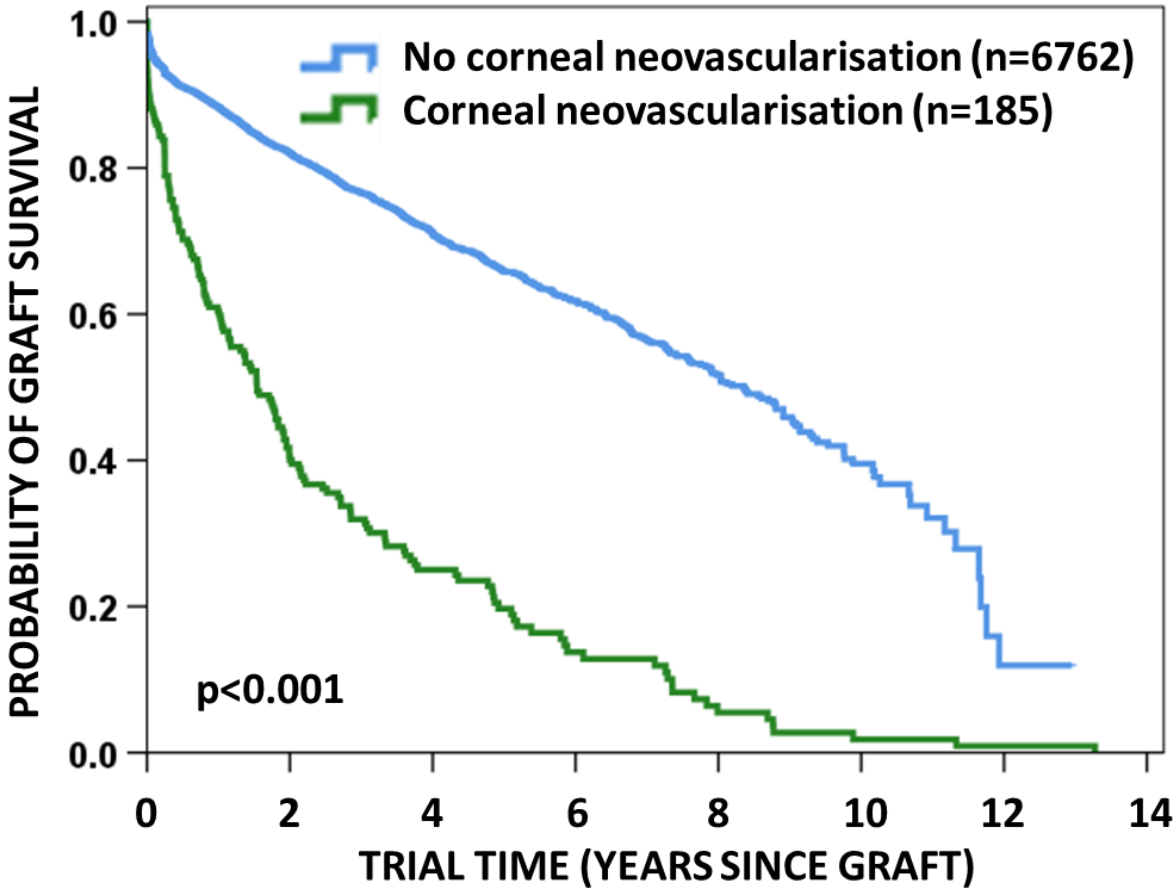
Descemet's Stripping (Automated) Endothelial Keratoplasty Post-graft Events	Registered (%)	Followed (%)
Time to removal of sutures		
Within 1 month	133 (2%)	133 (3%)
2 to 3 months	769 (11%)	769 (15%)
4 to 6 months	322 (5%)	322 (6%)
More than 6-months	241 (3%)	241 (5%)
Not yet removed/not advised*	5482 (79%)	3626 (71%)
Chi^2=0.96, df=3, p=0.810		
Post-graft interface opacity		
No	6668 (96%)	4812 (95%)
Yes	279 (4%)	279 (5%)
Chi^2=0.00, df=1, p=0.996		
Total	***6947 (100%)***	***5091 (100%)***

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

4.6.1 Descemet's stripping (automated) endothelial keratoplasty survival: influence of post-graft neovascularisation

Figure 4.6.1 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=329.82; df=1; p<0.001). This variable was retained in the final multivariate model (see section 4.7).

Figure 4.6.1 Post-graft corneal neovascularisation



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
No neovascularisation	3618	2638	1830	1274	904	582	364	217	116	54	17
Neovascularisation	111	72	52	36	25	15	14	6	3	2	2

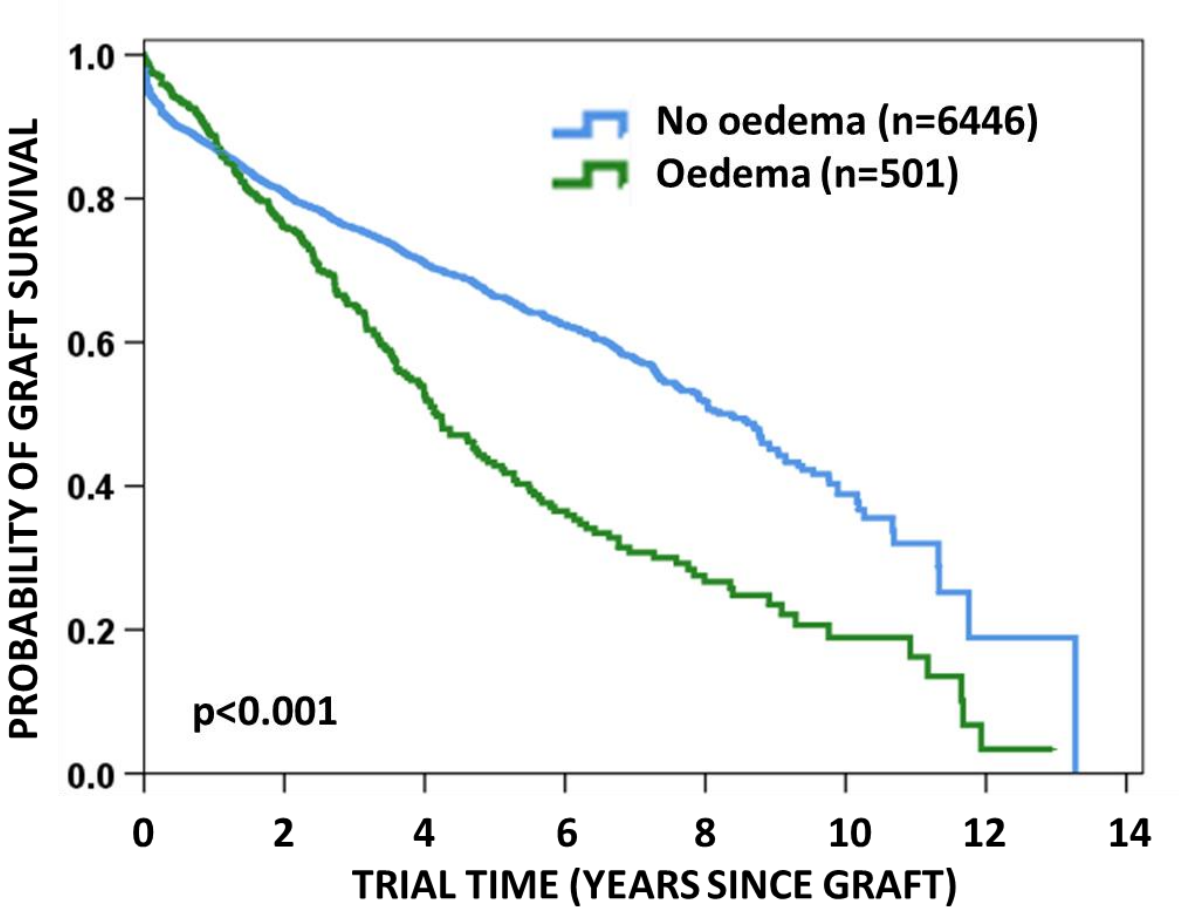
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No neovascularisation	0.89	0.82	0.77	0.71	0.66	0.62	0.57	0.52	0.46	0.40
Neovascularisation	0.60	0.40	0.32	0.25	0.20	NA	NA	NA	NA	NA

4.6.2 Descemet's stripping (automated) endothelial keratoplasty survival: influence of post-graft oedema

Figure 4.6.2 shows the comparison of graft survival for grafts where the eye was reported to have had corneal oedema post-graft to those that did not. A significant difference was found between groups (Log Rank Statistic=51.88; df=1; p<0.001). This variable was retained in the final multivariate model (see section 4.7).

Figure 4.6.2 Post-graft oedema



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
No oedema	3345	2423	1692	1181	843	536	334	192	102	46	13
Oedema	384	287	190	129	86	61	44	31	17	10	6

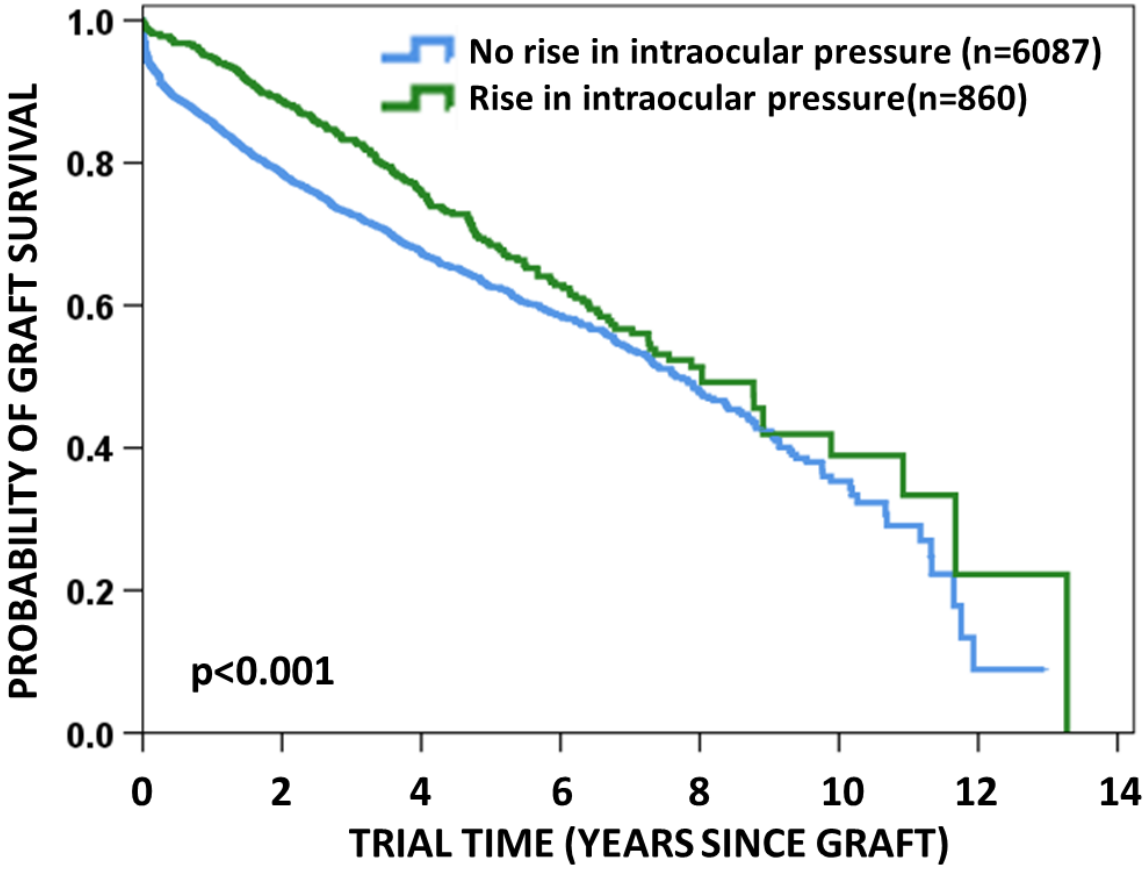
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No oedema	0.88	0.81	0.76	0.72	0.67	0.63	0.58	0.52	0.45	0.39
Oedema	0.89	0.76	0.65	0.53	0.43	0.37	0.31	0.27	NA	NA

4.6.3 Descemet's stripping (automated) endothelial keratoplasty survival: influence of post-graft rise in intraocular pressure

Figure 4.6.3 shows the comparison of graft survival for grafts where the eye was reported to have had a rise in intraocular pressure post-graft to those that did not. A significant difference was found between groups (Log Rank Statistic=20.58; df=1; p<0.001). This variable was retained in the final multivariate model (see section 4.7).

Figure 4.6.3 Post-graft rise in intraocular pressure



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
No rise in IOP	3002	2135	1453	1008	719	451	285	173	96	45	14
Rise in IOP	727	575	429	302	210	146	93	50	23	11	5

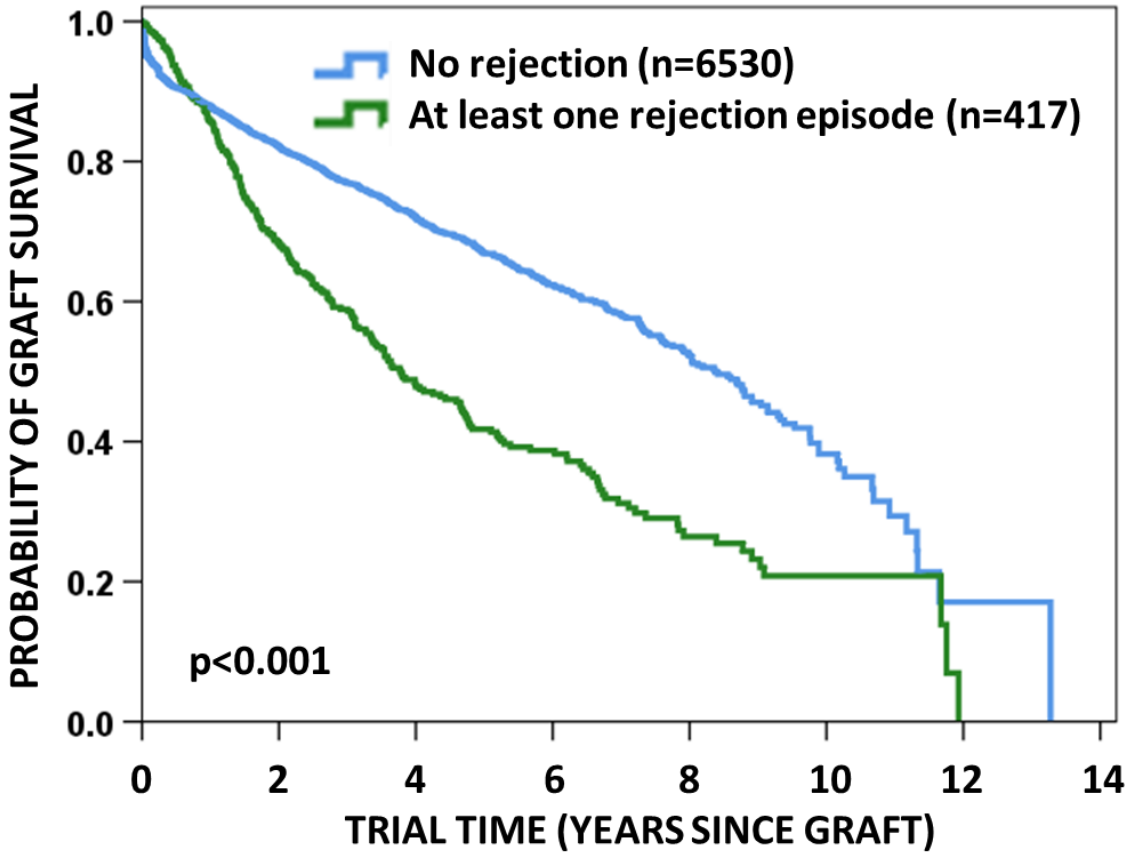
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No rise in IOP	0.86	0.79	0.73	0.68	0.63	0.59	0.54	0.48	0.43	0.36
Rise in IOP	0.95	0.89	0.83	0.76	0.68	0.63	0.57	0.51	0.42	NA

4.6.4 Descemet's stripping (automated) endothelial keratoplasty survival: influence of rejection episodes

Figure 4.6.4 shows the comparison of graft survival for grafts with no rejection episodes compared to those with one or more rejection episodes. A significant difference was found between groups (Log Rank Statistic=84.69; df=1; p<0.001). This variable was retained in the final multivariate model (see section 4.7).

Figure 3.6.4 Post-graft rejection episodes



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
No Rejection	3379	2452	1690	1170	824	520	331	193	99	44	13
Any Rejection	350	258	192	140	105	77	47	30	20	12	6

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No Rejection	0.88	0.82	0.77	0.72	0.67	0.62	0.58	0.52	0.46	0.38
Any Rejection	0.86	0.68	0.59	0.48	0.42	0.39	0.31	0.26	0.23	NA

4.7 Multivariate Analysis

A multivariate model was used to investigate the combined effect of variables on Descemet's stripping (automated) endothelial graft survival, adjusted for all other variables in the model (see section 1.4.6 for further information).

Table 4.12 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. Some variables that were found to be significant in the univariate analyses were excluded from the multivariate model as they were found to be collinear with (i.e. were highly correlated and produced the same effect on the outcome as) another variable in the model.

Table 4.12 Multivariate model

Descemet's Stripping (Automated) Endothelial Keratoplasty Multivariate Model

Not significant in univariate analysis

- Donor sex
- Eye only donor
- Cause of donor death
- Time from storage of donor tissue to graft – Optisol
- Time in deswelling media for tissue stored in organ culture media
- Eye grafted
- Use of glide during insertion
- Use of anterior chamber maintainer
- Use of viscoelastic
- Stripping of recipient Descemet's membrane by surgeon
- Time to removal of sutures
- Interface opacity post graft

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

- The centre effect (collinear with surgeon experience and level of follow-up)
- Australian State in which graft was performed (collinear with eye bank and interstate transportation of donor cornea)

Significant in univariate analysis but not retained in multivariate model

- Donor cornea pre-cut by eye bank
- Pre-graft corneal neovascularisation
- Other operative procedure at graft
- Use of forceps
- Time from donor death to enucleation of donor tissue
- Recipient age group
- Use of suture to close wound
- Pre-graft inflammation and/or steroid use
- Time from enucleation to storage of donor tissue
- Donor age group
- Number of previous ipsilateral grafts
- Donor/recipient sex match/mismatch
- Storage medium
- Time from storage of donor tissue to graft – organ culture

Significant in univariate analysis AND retained in multivariate model

- Eye bank
- Central endothelial cell count
- Interstate transportation of donor cornea
- Recipient sex
- Indication for graft
- Raised intraocular pressure in past and/or at graft
- Number of pervious contralateral grafts
- Graft size
- Incision size
- Change in lens status from pre- to post-graft
- Type of graft
- Surgeon caseload and level of follow-up
- Graft era/year
- Post-graft corneal neovascularisation
- Post-graft corneal oedema
- Post-graft rise in intraocular pressure
- Any post-graft rejection

Table 4.13 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 first level of each categorical variable was taken as the referent, except where it made logical sense to use a different group.

The hazard ratios for a given variable are adjusted for all other variables in the model. This model included data from 6,947 Descemet's stripping (automated) endothelial keratoplasties, performed in 5,291 recipients. Where no valid response had been provided for one of the included variables, these cases were classified as "not advised" and these categories were included where 2% of cases were in this group. The overall model was highly significant: (Chi^2=1321.55, p<0.0001).

Table 4.13 Clustered multivariate model

	n	Hazard ratio	Standard Error	p-value	Global p-value	95% Confidence Interval
Eye Bank (tvc)						
Referent Eye Bank		1.00			<0.0001	
		0.76	0.12	0.076		0.56 to 1.03
		0.93	0.17	0.688		0.65 to 1.32
		1.20	0.22	0.307		0.84 to 1.71
Range of n (604 to 2456)		2.16	0.41	<0.001		1.50 to 3.12
Central endothelial cell count						
Under 2500 cells/mm²	433	2.10	0.28	<0.001		1.61 to 2.72
2500 to 3249 cells/mm²	3539	1.45	0.12	<0.001		1.23 to 1.72
3250 or more cells/mm²	998	1.00			<0.0001	
Not advised	1977	1.51	0.28	0.026		1.05 to 2.17
Interstate transportation of donor cornea						
Same State	6650	1.00			<0.0001	
Different States	297	1.66	0.19			1.33 to 2.07
Recipient sex						
Female	3846	1.00			0.0007	
Male	3101	1.21	0.07			1.08 to 1.35
Indication for graft						
Failed previous graft	1580	1.27	0.10	0.002		1.09 to 1.49
Endothelial failure/bullous keratopathy	2052	1.25	0.10	0.004		1.07 to 1.45
Fuchs' endothelial dystrophy	3159	1.00				
Other	156	1.50	0.24	0.011		1.09 to 2.04
Raised intraocular pressure in past or at graft (tvc)						
No	5417	1.00			0.0001	
Yes	1530	1.35	0.11			1.16 to 1.57
Previous contralateral grafts						
None	5183	1.12	0.08	0.114		0.97 to 1.29
One	1438	1.00			0.0146	
Two or more	326	1.41	0.17	0.004		1.12 to 1.78
Type of graft						
DSAEK	3549	1.00			0.0001	
DSEK	2933	1.16	0.09	0.046		1.00 to 1.35
UT-DSEK	309	1.60	0.24	0.002		1.18 to 2.16
Not advised	156	1.78	0.29	<0.001		1.29 to 2.45
Graft size						
Less than 8.00 mm	704	1.53	0.14	<0.001		1.29 to 1.83
8.00 mm to 8.24 mm	1732	1.28	0.10	0.001		1.11 to 1.49
8.25 mm to 8.49 mm	641	1.01	0.10	0.902		0.83 to 1.24
8.50 mm or more	3363	1.00			<0.0001	
Not advised	507	1.09	0.13	0.452		0.87 to 1.36

Incision size						
Up to 5.00 mm	3228	1.00			0.0001	
More than 5.00 mm	1048	1.43	0.12	<0.001		1.21 to 1.68
Not advised	2671	1.17	0.08	0.028		1.02 to 1.34
Lens status pre and post-graft						
Phakic/pseudophakic	1589	1.00			0.0049	
Other	5358	1.26	0.10			1.07 to 1.48
Surgeon caseload and level of follow-up (tvc)						
Low caseload surgeons	2743	1.95	0.18	<0.001		1.62 to 2.34
High caseload, low follow-up	1533	1.32	0.12	0.002		1.11 to 1.57
High caseload, high follow-up	2671	1.00			<0.0001	
Graft era/year (tvc)						
Pre 2015	3274	1.59	0.16	<0.001		1.31 to 1.93
2015/2016	1308	1.00			<0.0001	
2017/2018	1257	1.23	0.12	0.041		1.01 to 1.50
2019	579	1.65	0.25	0.001		1.22 to 2.23
2020	529	6.17	1.37	<0.001		3.99 to 9.54
Post-graft rejection						
None	6529	1.00			<0.0001	
Any	416	1.71	0.13			1.48 to 1.98
Post-graft corneal neovascularisation						
No	6762	1.00			<0.0001	
Yes	185	2.52	0.26			2.07 to 3.08
Post-graft corneal oedema						
No	6446	1.00			0.0001	
Yes	501	1.37	0.11			1.17 to 1.59
Post-graft rise in intraocular pressure (tvc)						
No	6087	1.00			<0.0001	
Yes	860	0.48	0.05			0.39 to 0.58

Notes: tvc = time variant coefficient; the potential effect of contaminated storage media was also controlled for in this model.

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

4.7.1.1 Central endothelial cell count

Grafts performed using donor corneas with endothelial cell counts below 2500 cells/mm² had significantly poorer survival than those performed using donor corneas with 2500 to 3249 cells/mm² (p=0.001) or 3250 or more cells/mm² (p<0.001).

Grafts performed using donor corneas with endothelial cell counts of 3250 or more cells/mm² also had significantly better survival than those performed using donor corneas with endothelial cell counts of 2500 to 3249 cells/mm² (p<0.001).

4.7.1.2 Indication for graft

Grafts performed for Fuchs' endothelial dystrophy had significantly better survival than those performed for failed previous graft/s (p=0.002), endothelial failure/bullous keratopathy (p=0.004), or other indications (p=0.011).

4.7.1.3 Number of previous contralateral grafts

Grafts performed in recipients who had a history of multiple grafts performed in their contralateral eye exhibited significantly poorer survival than those with one prior contralateral graft (p=0.004).

4.7.1.4 Type of surgery

Grafts where the trephination of the donor cornea was specified to have been automated and the donor tissue thickness was not ultra-thin, had significantly better survival than those where the donor tissue was cut to be ultra-thin (p=0.002), and where the trephination technique was not specified (p<0.001).

Survival of grafts performed with manually dissected tissue of normal thickness was also significantly better than those where the trephination technique was not specified (p=0.006).

4.7.1.5 Graft size

Survival of grafts that were less than 8.00 mm was significantly poorer than those that were 8.25 mm to 8.49 mm (p=0.001), or 8.50 mm or larger (p<0.001).

Survival of grafts that were 8.00 mm to 8.24mm was significantly poorer than those that were 8.50 mm or larger (p=0.001).

4.7.1.6 Incision size

Grafts where the incision size was 5.00 mm or less had significantly better survival than those where it was larger than 5.00mm (p<0.001).

4.7.1.7 Number of DS(A)EK registered by surgeon and level of follow-up received

Grafts performed by surgeons with fewer than 139 DS(A)EK registered (<2% of the cohort) with the ACGR, had significantly poorer survival than those with 139 or more DS(A)EK registered, regardless of whether the high-caseload surgeons had high or low follow-up (both p<0.001).

Grafts performed by surgeons with 139 or more DS(A)EK registered with the ACGR and above average (>73%) levels of follow-up had significantly better survival than grafts performed by surgeons with 139 or more DS(A)EK registered with the ACGR, and below average (≤73%) levels of follow-up (p=0.002).

4.7.1.8 Graft era/year

Grafts performed in 2020 had significantly poorer survival than those performed in all prior eras/years (all p<0.001).

Grafts performed in 2015/2016 had significantly better survival than those performed prior to 2015 (p<0.001) or in 2019 (p=0.001).

4.8 Reasons for Graft Failure

Of the 5,091 followed grafts, 1,442 (28%) were known to have failed by the census date. This equates to 21% of the 6,947 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 4.14 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 4.14 Reasons for graft failure

Descemet's Stripping (Automated) Endothelial Keratoplasty Reasons for Graft Failure

Endothelial cell failure	555 (38%)
Primary graft failure	352 (24%)
Rejection	180 (12%)
Glaucoma	41 (3%)
Non herpetic infection	37 (3%)
Scarring	26 (2%)
Herpetic infection	13 (<1%)
Graft detachment	12 (<1%)
Trauma	10 (<1%)
Other specified*	47 (3%)
Unspecified	169 (12%)
Total	***1442 (100%)***

Other included: Descemet's folds/wrinkles (8), Corneal ulcer/perforation (7), epithelial/limbal stem cell failure (6), ICE syndrome (6), astigmatism (5), band keratopathy (2), corneal melt (2), phthisical eye (2), retinal detachment (2), contraction of graft (1), fibrosis (1), hyphaema (1), hypotony (1), iris adhesion (1), pellucid marginal degeneration (1), suprachoroidal haemorrhage (1).

Of the 352 grafts reported by surgeons to have been primary graft failures, 219 had no further information provided. Specific reasons given were: detachment or rupture of Descemet's membrane (71), endothelial failure (19), contaminated storage medium (11), surgical trauma (11), Descemet's folds (6), rejection (3), endophthalmitis (2), donor cornea split during pre-cut (1), epithelial defect (1), Fuchs' endothelial dystrophy in donor (1), fungal keratitis in donor (1), glaucoma (1), pellucid marginal degeneration (1), pupillary block (1), residual opacity (1).

4.9 Post-graft Changes in Best Corrected Visual Acuity

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 6,392 (92%) of registered Descemet's stripping (automated) endothelial keratoplasties. In 80% of cases (5,225), this was the sole desired outcome indicated. All analyses are conducted on data for **surviving** grafts. See section 1.4.7 for further explanation of the methods used to analyse visual acuity data.

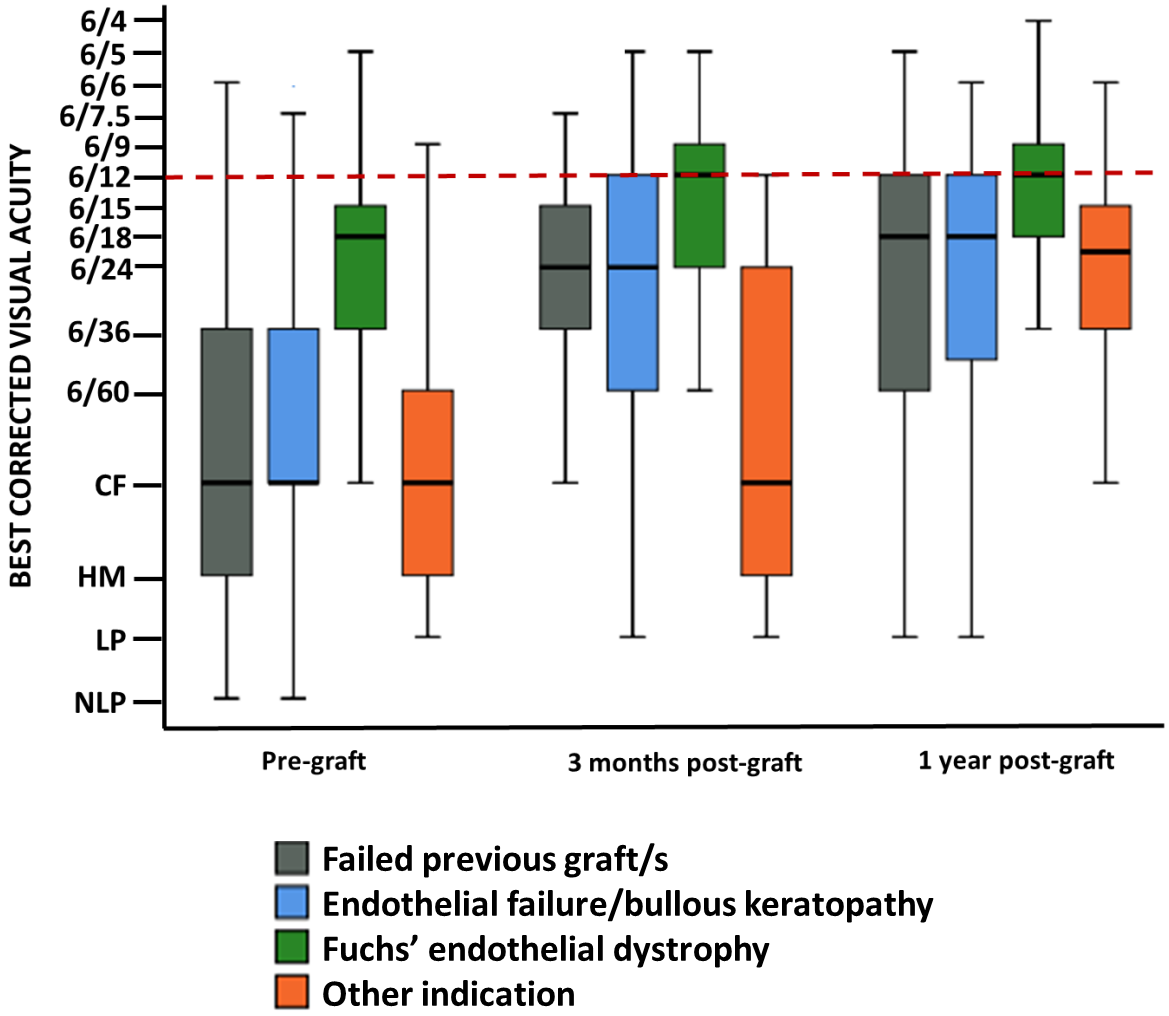
4.9.1 Descemet's stripping (automated) endothelial keratoplasty: One-year post-graft visual acuity change by indications for graft

Figure 4.9.1 shows the pre-graft best corrected visual acuity, and the three-month and one-year post-graft best corrected visual acuity, reported for eyes undergoing Descemet's stripping (automated) endothelial keratoplasty for each of the indication for graft groups. The central line within each box-and-whisker plot shows the median BCVA reported for the group, the box represents the inter-quartile range, while the whisker shows the range. Please note that outliers were included in the calculation of the box and whisker plots but are not shown in the figures. The dashed line indicates a BCVA of 6/12, which represents functional vision.

Median pre-graft BCVA was best for grafts for Fuchs' endothelial dystrophy (6/18). All other categories had median pre-graft BCVA of Count Fingers. At 3-months post-graft, there had been a significant improvement in BCVA for the three, individual, indication for graft groups (all $p<0.001$), but not for "other" indications ($p=0.584$). Grafts for failed previous graft/s and endothelial failure/bullous keratopathy had reached a median BCVA of 6/24, while grafts for Fuchs' endothelial dystrophy had a median BCVA of 6/12.

At one-year post-graft, the improvement in BCVA remained significant at the $p<0.001$ level for all individual indication groups and also reached this level of significance for "other" indications. Grafts for Fuchs' endothelial dystrophy maintained their vision of 6/12 at this time point, while median BCVA reached 6/18 for the other three groups.

Figure 4.9.1 Best corrected visual acuity pre-graft, and three-months and one-year post-graft



Number of grafts with BCVA available at each time point

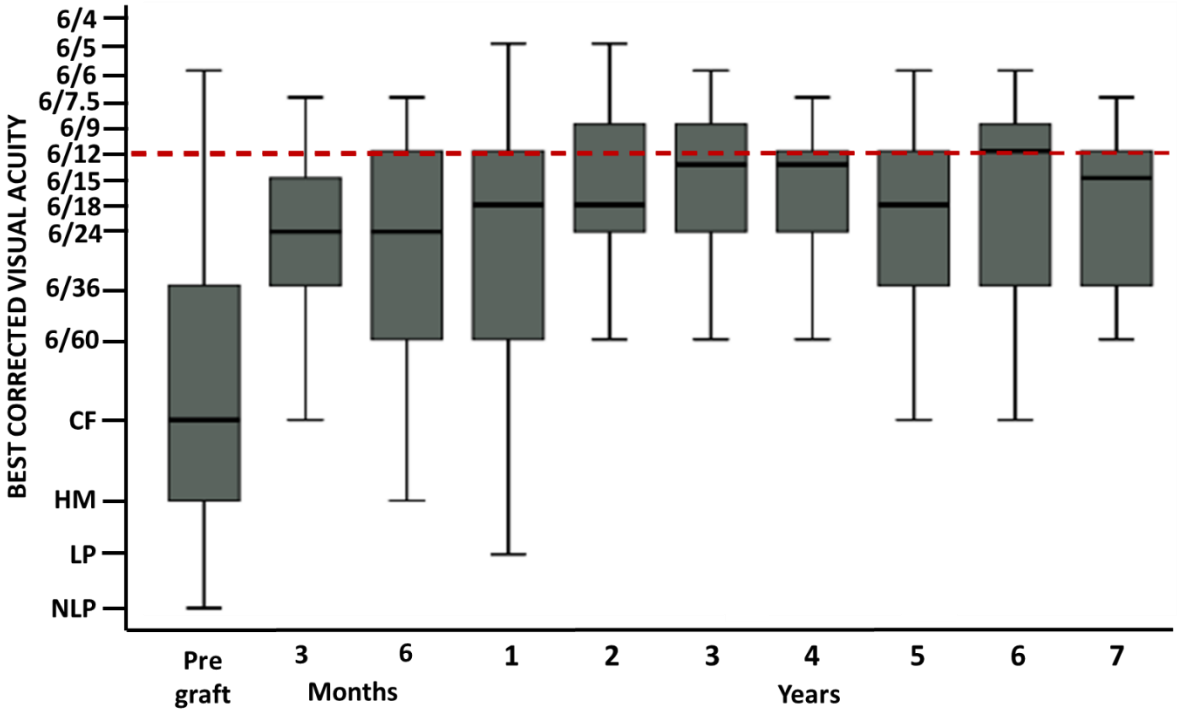
	Pre	3m	6m	1y	2y	3y	4y
Failed previous graft/s	1409	54	61	117	69	48	22
Endothelial failure/bullous keratopathy	1856	76	106	171	105	61	39
Fuchs' endothelial dystrophy	2951	115	155	272	212	151	77
Other	146	10	8	14	13	4	6

	5y	6y	7y	8y	9y	10y	11y
Failed previous graft/s	17	14	10	2	2	8	0
Endothelial failure/bullous keratopathy	32	17	10	5	0	5	0
Fuchs' endothelial dystrophy	78	53	45	26	13	10	0
Other	6	1	1	0	0	0	0

The figures on pages 174 to 177 look at the median BCVA achieved over time for individual indications for graft.

4.9.2 Descemet's stripping (automated) endothelial keratoplasty: Changes in best corrected visual acuity over time by individual indications for graft

Figure 4.9.2 Best corrected visual acuity for surviving Descemet's stripping (automated) endothelial keratoplasties performed for failed previous graft/s, over time



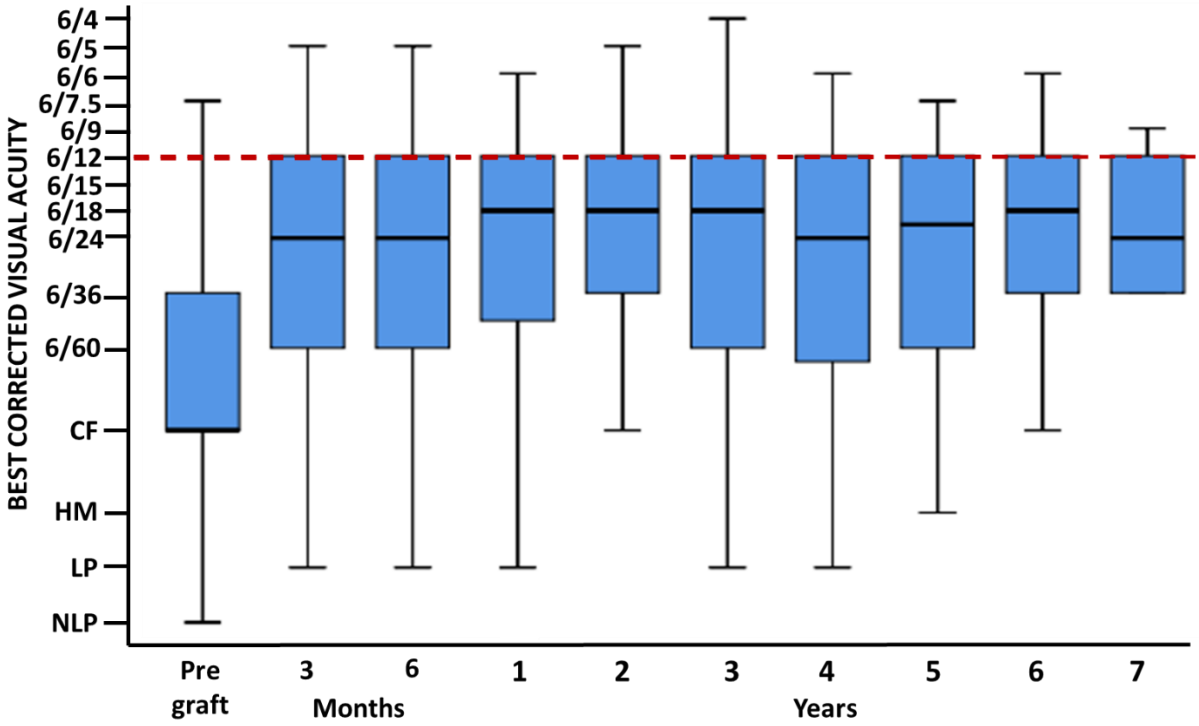
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y	6y	7y
1409	54	61	117	69	48	22	17	14	10

The median BCVA obtained following Descemet's stripping (automated) endothelial keratoplasty for failed previous graft improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). This difference was maintained at 6-months and 1-year but did not improve significantly again until 2-years post-graft ($p=0.014$). There were no significant changes in median BCVA after 2-years post-graft. The difference compared to pre-graft BCVA remained significant to 7-years post-graft (all $p<0.001$).

Surviving Descemet's stripping (automated) endothelial keratoplasties performed for failed previous graft/s, had a median BCVA below 6/12 up to 5-years post-graft. Median BCVA was 6/12 for the 14 surviving grafts that had data available at 6-years post-graft, but this had dropped back down to 6/15 for the 10 with data at 7 years.

Figure 4.9.3 Best corrected visual acuity for surviving Descemet's stripping (automated) endothelial keratoplasties performed for endothelial failure/bullous keratopathy, over time



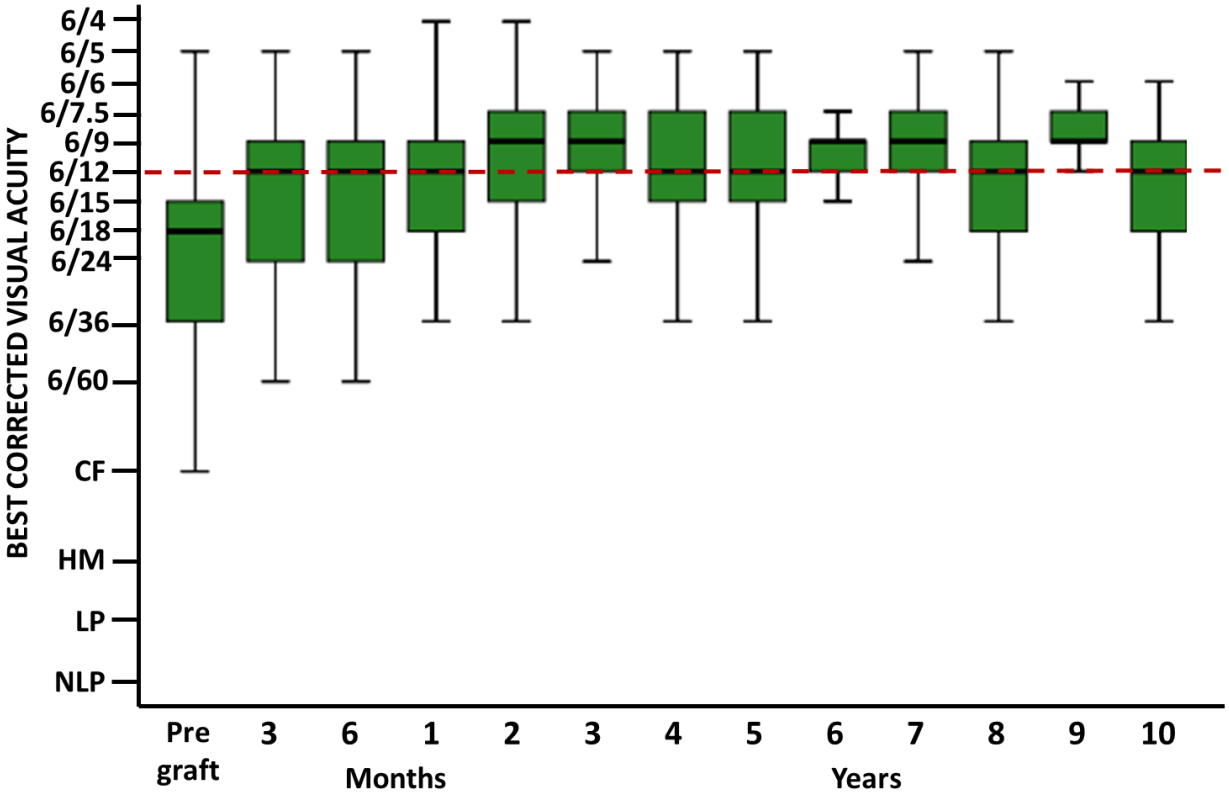
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y	6y	7y
1856	76	106	171	105	61	39	32	17	10

The median BCVA obtained following Descemet's stripping (automated) endothelial keratoplasty for endothelial failure/bullous keratopathy improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). This difference did not improve significantly again. The difference compared to pre-graft BCVA remained significant to 10-years post-graft (all $p<0.001$).

Descemet's stripping (automated) endothelial keratoplasties performed for endothelial failure/bullous keratopathy, which survived for 1-year, achieved a median BCVA of 6/18. The median BCVA never reached the 6/12 level, varying between 6/24 and 6/18 up to 7-years post-graft for surviving grafts performed for endothelial failure/bullous keratopathy.

Figure 4.9.4 Best corrected visual acuity for surviving Descemet's stripping (automated) endothelial keratoplasties performed for Fuchs' endothelial dystrophy, over time



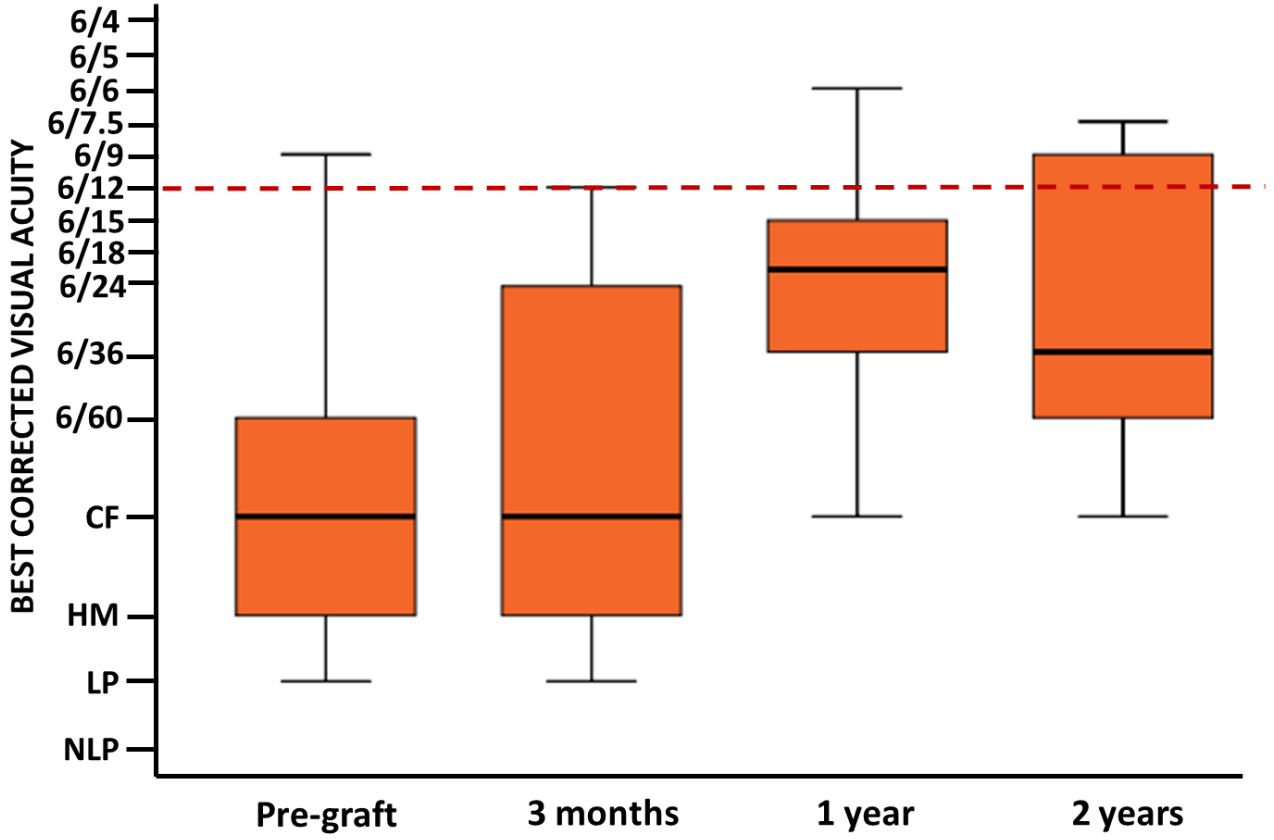
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y
2951	115	155	272	212	151	77	78	53	45	26	13	10

The median BCVA obtained following Descemet's stripping (automated) endothelial keratoplasty for Fuchs' endothelial dystrophy improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). This difference was maintained at 6-months but did not improve significantly again until 1-year post-graft ($p=0.018$) and again from 1-year to 2-years post-graft ($p<0.001$). There was a significant drop in median BCVA between 7-years and 8-years post-graft ($p=0.026$) but this significantly improved again between 8-years and 9-years post-graft ($p=0.028$). No other changes were significant compared to the previous time-point. The difference compared to pre-graft BCVA remained significant to 10-years post-graft (all $p<0.001$, except 10-years $p=0.009$).

Descemet's stripping (automated) endothelial keratoplasties performed for Fuchs' endothelial dystrophy, which survived for 3-months, achieved a median BCVA of 6/12. The median BCVA remained above the 6/12 level, varying between 6/9 and 6/12 up to 10-years post-graft for surviving grafts performed for Fuchs' endothelial dystrophy.

Figure 4.9.5 Best corrected visual acuity for surviving Descemet's stripping (automated) endothelial keratoplasties performed for other indications, over time



Number of grafts with data at each time point

Pre	3m	6m	1y	2y
146	10	8	14	13

The median BCVA obtained following Descemet's stripping (automated) endothelial keratoplasty for other indications for graft had not improved significantly compared to pre-graft levels by 3-months post-graft ($p=0.584$) but had by 1-year post-graft ($p<0.001$). The difference in median BCVA between 1-year and 2-years was not significant ($p=0.941$). The difference compared to pre-graft BCVA remained significant at 2-years post-graft ($p<0.001$).

Descemet's stripping (automated) endothelial keratoplasties performed for other indications for graft, which survived for 1-year, achieved a median BCVA of 6/18. The median BCVA at 2-years post-graft had dropped to 6/36 for surviving grafts performed for other indications.

5 Descemet's Membrane Endothelial Keratoplasty

This chapter presents analyses of the 3,215 Descemet's membrane endothelial keratoplasties (DMEK) registered with the ACGR. Kaplan-Meier survival analyses were conducted 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 found to be **significant** in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (3,215 registered and 1,756 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

Descemet's Membrane Endothelial Keratoplasty

Donor and Eye Banking Factors

	Registered (%)	Followed (%)
Eye bank		
	962 (30%)	420 (24%)
Eye banks are not identified due to	346 (11%)	199 (11%)
confidentiality constraints. See	1415 (44%)	859 (49%)
section 1.4.8 for further information.	348 (11%)	235 (13%)
	144 (4%)	43 (2%)
Age of donor		
0 to 39 years	67 (2%)	48 (3%)
40 to 49 years	100 (3%)	53 (3%)
50 to 59 years	555 (17%)	296 (17%)
60 to 69 years	1272 (40%)	687 (39%)
70 to 79 years	1003 (31%)	539 (31%)
80 years and older	218 (7%)	133 (8%)
Sex of donor		
Female	1213 (38%)	666 (38%)
Male	2002 (62%)	1090 (62%)
Storage media		
Optisol	1318 (41%)	907 (52%)
Organ culture	1897 (59%)	849 (48%)
Interstate transportation		
Same State	165 (5%)	62 (4%)
Different States	3050 (95%)	1694 (96%)

	Registered (%)	Followed (%)
Enucleation-to-storage time		
Within 1 hour	110 (353%)	48 (3%)
1 to 3 hours	1709 (18%)	922 (53%)
4 to 6 hours	591 (18%)	342 (19%)
7 to 9 hours	117 (4%)	75 (4%)
10 to 12 hours	67 (2%)	44 (3%)
13 to 15 hours	103 (3%)	49 (3%)
16 to 18 hours	85 (3%)	39 (2%)
More than 18 hours	108 (3%)	51 (3%)
Not advised	325 (10%)	186 (11%)
Storage to graft time - Organ culture		
Up to 2 weeks	416 (13%)	208 (12%)
2 to 3 weeks	861 (27%)	372 (21%)
More than 3 weeks	315 (10%)	144 (8%)
Not advised	305 (9%)	125 (7%)
Not applicable	1318 (41%)	907 (52%)
Cornea pre-cut by eye bank		
No	2805 (87%)	1517 (86%)
Yes	410 (13%)	239 (14%)
Total	***3215 (100%)***	***1756 (100%)***

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 (3,215 registered and 1,756 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

Table 5.2 Donor and eye banking factors, not significant in univariate analyses

Descemet's Membrane Endothelial Keratoplasty

Donor and Eye Banking Factors

	Registered (%)	Followed (%)
Cause of donor death		
Cardiovascular	684 (21%)	383 (22%)
Malignancy	1377 (43%)	743 (42%)
Trauma	185 (6%)	109 (6%)
Respiratory	277 (9%)	154 (9%)
Intracranial/cerebral haemorrhage	524 (16%)	280 (16%)
Other specified	155 (5%)	82 (5%)
Not advised/live donor*	13 (<1%)	5 (<1%)
Chi^2=2.77, df=5, p=0.735		
Donor type		
Eye donor only	2803 (87%)	1555 (89%)
Solid organ and/or bone/tissue donor	412 (13%)	201 (11%)
Chi^2=0.05, df=1, p=0.816		
Central corneal endothelial cell density		
<2500 cells/mm²	92 (3%)	46 (3%)
2500 to 2749 cells/mm²	337 (10%)	152 (9%)
2750 to 2999 cells/mm²	445 (14%)	218 (12%)
3000 to 3249 cells/mm²	493 (15%)	243 (14%)
3250 to 3499 cells/mm²	270 (8%)	141 (8%)
≥ 3500+ cells/mm²	145 (5%)	87 (5%)
Not advised	1433 (45%)	869 (49%)
Chi^2=3.76, df=5, p=0.585		
Death-to-enucleation time		
Up to 3 hours	143 (4%)	64 (4%)
4 to 6 hours	319 (10%)	173 (10%)
7 to 9 hours	473 (15%)	263 (15%)
10 to 12 hours	482 (15%)	277 (16%)
13 to 15 hours	482 (15%)	290 (17%)
16 to 18 hours	557 (17%)	337 (19%)
More than 18 hours	756 (24%)	351 (20%)
Not advised	3 (1%)	1 (<1%)
Chi^2=2.00, df=6, p=0.919		

	Registered (%)	Followed (%)
Storage to graft time - Optisol		
Within 2 days	185 (6%)	127 (7%)
2 to 3 days	128 (4%)	91 (5%)
3 to 4 days	174 (5%)	126 (7%)
4 to 5 days	260 (8%)	172 (10%)
More than 5 days	430 (13%)	295 (17%)
Not advised	141 (4%)	38 (2%)
Not applicable	1897 (59%)	907 (52%)
Chi²=5.44, df=4, p=0.245		
Deswelling-to-graft time – Organ culture		
Within 2 days	422 (13%)	180 (10%)
2 to 3 days	576 (18%)	267(15%)
More than 3 days	515 (16%)	209 (12%)
Not advised	384 (12%)	193 (11%)
Not applicable	1318 (41%)	907 (52%)
Chi²=4.44, df=2, p=0.109		
Total	***3215 (100%)***	***1756 (100%)***

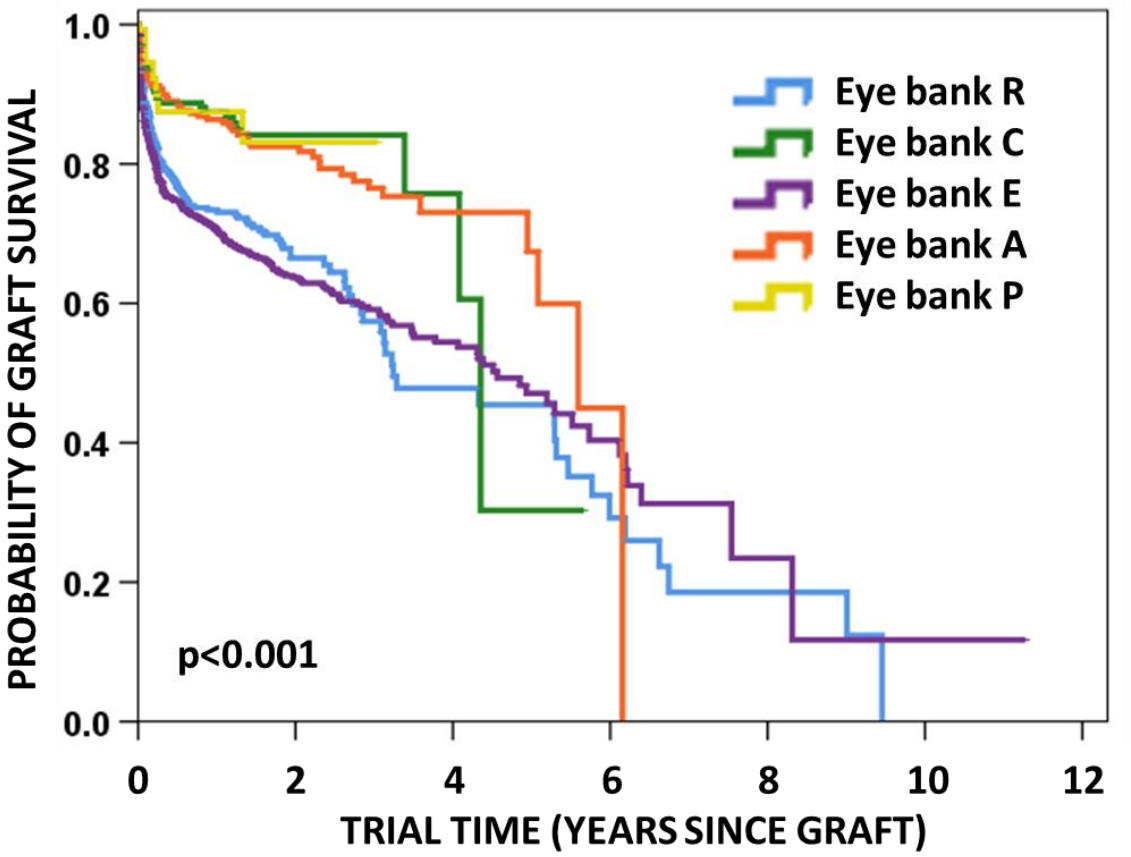
Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable.

*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.

5.1.1 Descemet's membrane endothelial keratoplasty 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. A significant difference was found across eye banks (Log Rank Statistic=40.72; df=4; p<0.001), with Eye Bank R and Eye Bank E having significantly poorer survival than Eye Bank C and Eye Bank A (all p<0.001). Eye Bank P also had significantly better survival than Eye Bank E (p=0.015). This variable was retained in the final multivariate model (see section 5.7).

Figure 5.1.1 Australian eye bank



Probability of graft survival (years post-graft)

	1	2	3	4	5	6
Eye Bank R	0.73	0.67	0.57	0.48	NA	NA
Eye Bank C	0.88	0.84	NA	NA	NA	NA
Eye Bank E	0.71	0.64	0.59	0.55	0.47	0.40
Eye Bank A	0.86	0.83	0.77	0.73	NA	NA
Eye Bank P	0.88	NA	NA	NA	NA	NA

Note: Further information is not provided due to confidentiality constraints (see section 1.4.8).

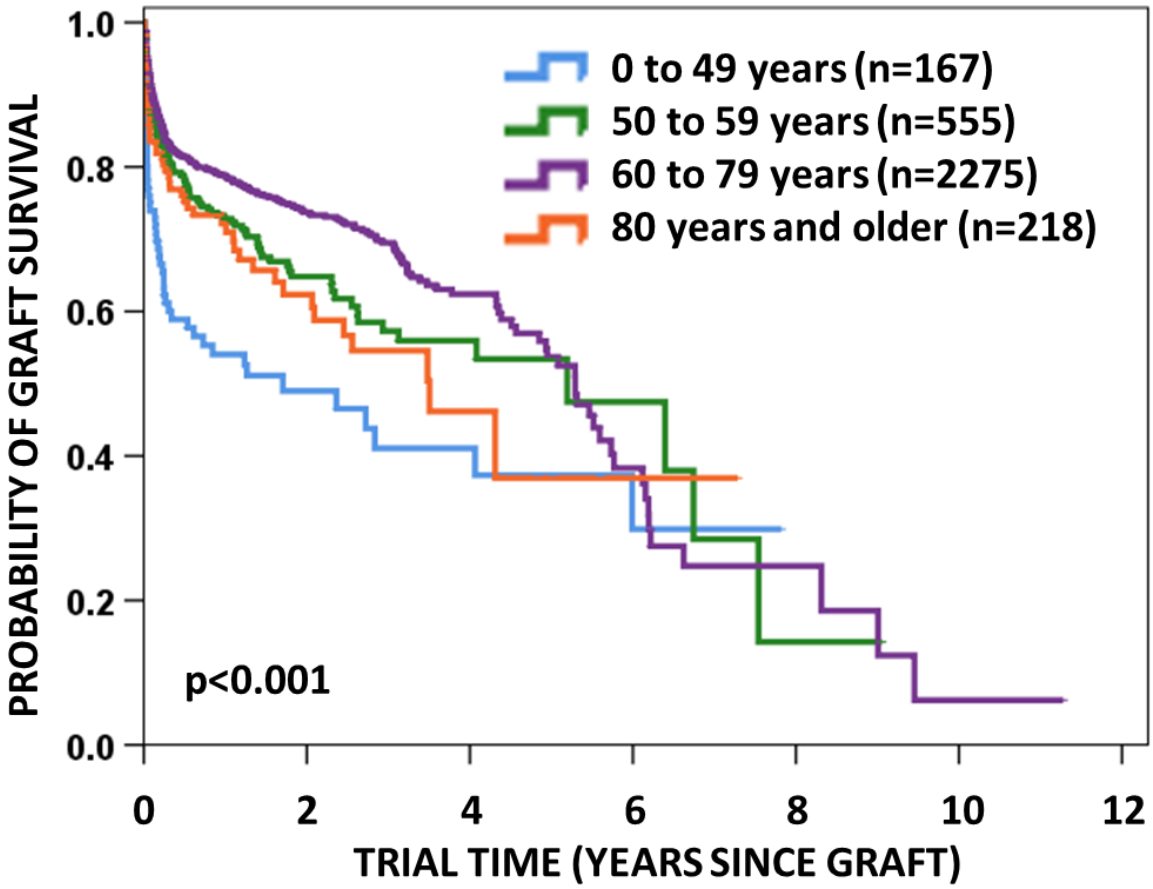
5.1.2 Descemet's membrane endothelial keratoplasty survival: influence of donor age (years)

Figure 5.1.2 shows the comparison of graft survival depending on donor age. Donors were initially stratified by 10-year age groups. Numbers of donors aged under 30 years or over 90 years were low, and so these data were combined with the adjacent age groups. A significant difference was found across groups (Log Rank Statistic=31.14; df=5; p<0.001).

Further analyses examined whether there were significant differences between adjacent age groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=30.89; df=3; p<0.001).

Survival for grafts performed with tissue from donors aged under 50 years was significantly poorer than those performed with tissue from donors aged 50 to 59 years (p=0.003), 60 to 79 years (p<0.0.001) and 80 years and older (p=0.036). Grafts performed with tissue from donors aged 60 to 79 years also had superior survival compared to those performed with tissue from donors aged 50 to 59 years (p=0.016), or 80 years and older (p=0.009). This variable was retained in the final multivariate model (see section 5.7).

Figure 5.1.2 Donor age group



Number at risk (years post-graft)

	1	2	3	4	5	6
0 to 49 years	40	21	14	11	8	4
50 to 59 years	166	74	46	23	13	5
60 to 79 years	721	380	190	84	48	19
80 years or older	60	36	20	10	2	2

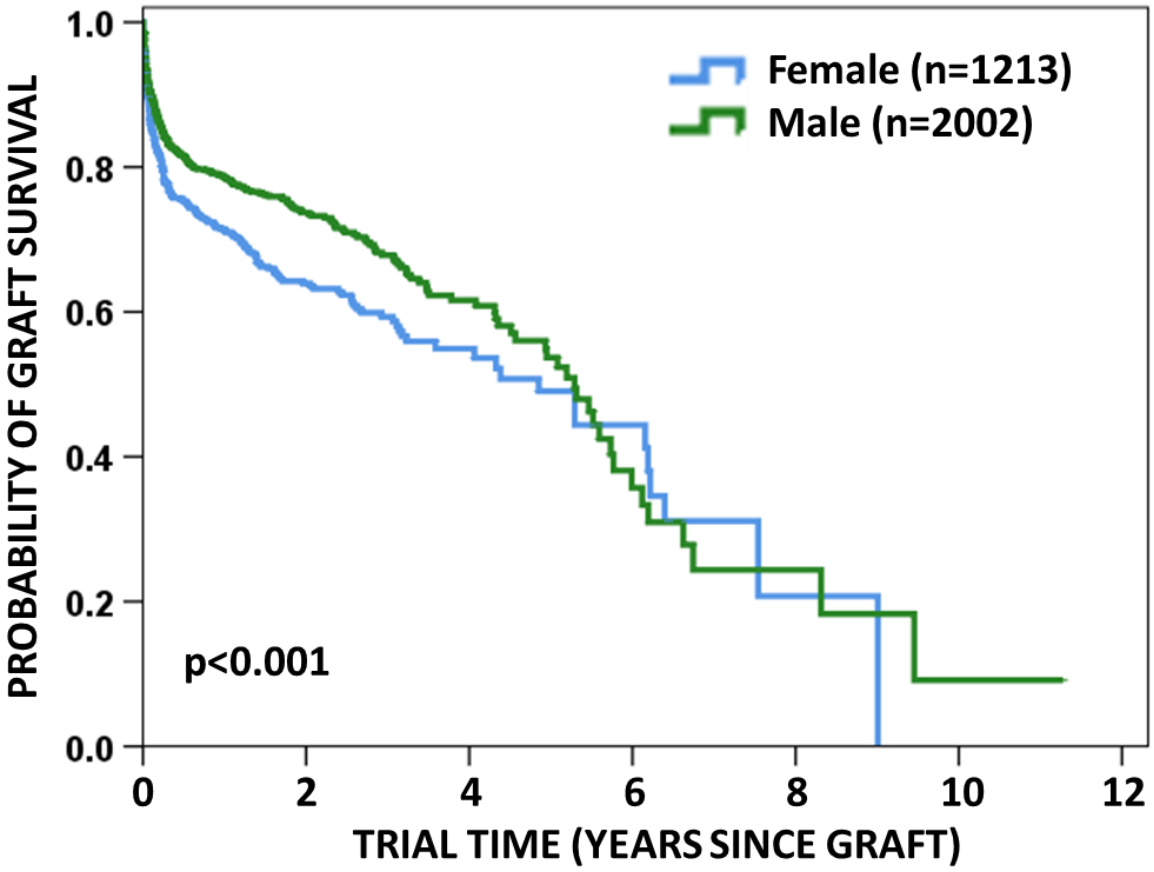
Probability of graft survival (years post-graft)

	1	2	3	4	5
0 to 49 years	0.54	0.49	NA	NA	NA
50 to 59 years	0.73	0.65	0.57	0.56	NA
60 to 79 years	0.79	0.74	0.70	0.62	0.54
80 years or older	0.72	0.62	0.55	NA	NA

5.1.3 Descemet's membrane endothelial keratoplasty survival: influence of donor sex

Almost two-thirds of corneal donors were male. Figure 5.1.3 shows the comparison of graft survival depending on donor sex (Log Rank Statistic=11.02; df=1; p=0.001). This variable was not included in the multivariate analysis (see section 5.7), as it is collinear with the variable analysing donor/recipient sex match/mismatch (see section 5.2.6), which was retained in the final multivariate model.

Figure 5.1.3 Donor sex



Number at risk (years post-graft)

	1	2	3	4	5	6
Female	359	186	97	44	26	15
Male	628	325	173	84	45	15

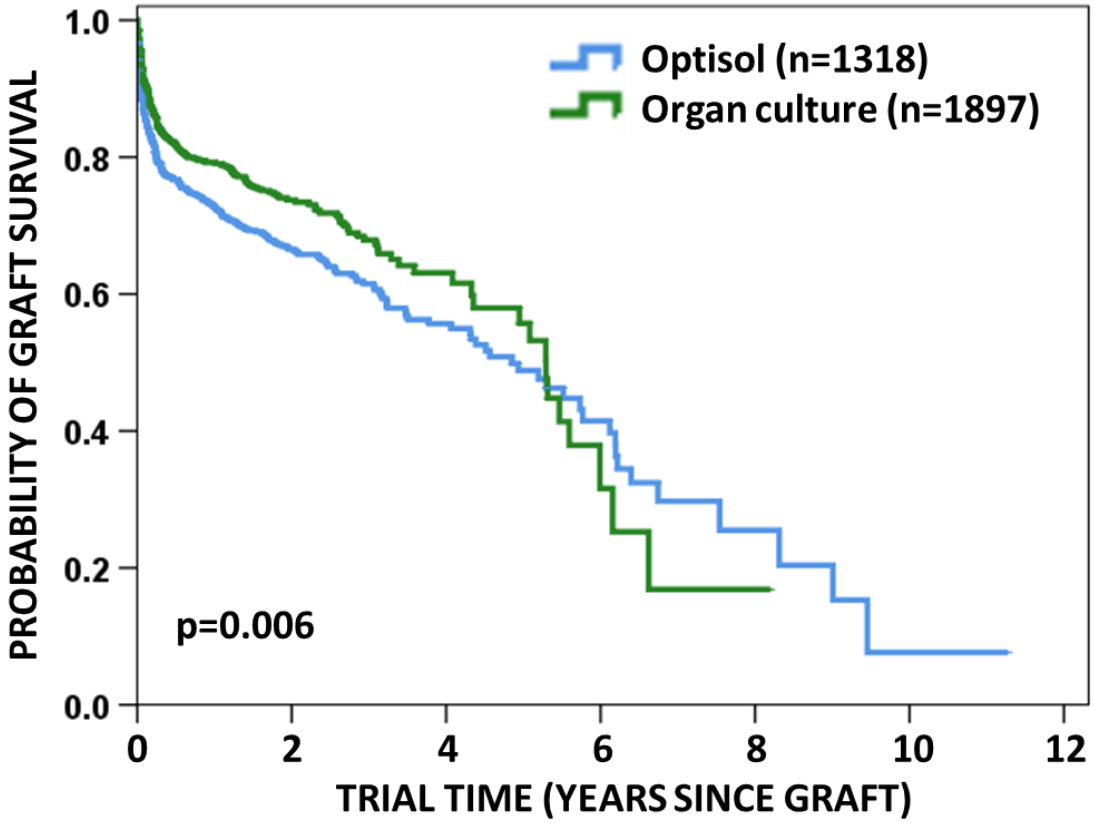
Probability of graft survival (years post-graft)

	1	2	3	4	5
Female	0.71	0.64	0.59	0.55	0.49
Male	0.79	0.74	0.68	0.62	0.54

5.1.4 Descemet's membrane endothelial keratoplasty survival: influence of storage media

Figure 5.1.4 shows the comparison of graft survival for corneas stored using Optisol compared to organ culture medium (see section 1.2 for further details about storage media). A significant difference in outcomes was found between media (Log Rank Statistic=7.58; df=1; p=0.006). However, this variable was not retained in the final multivariate model (see section 5.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 5.1.4 Storage media



Number at risk (years post-graft)

	1	2	3	4	5	6	7
Optisol	492	277	153	85	48	25	10
Organ culture	495	234	117	43	23	5	2

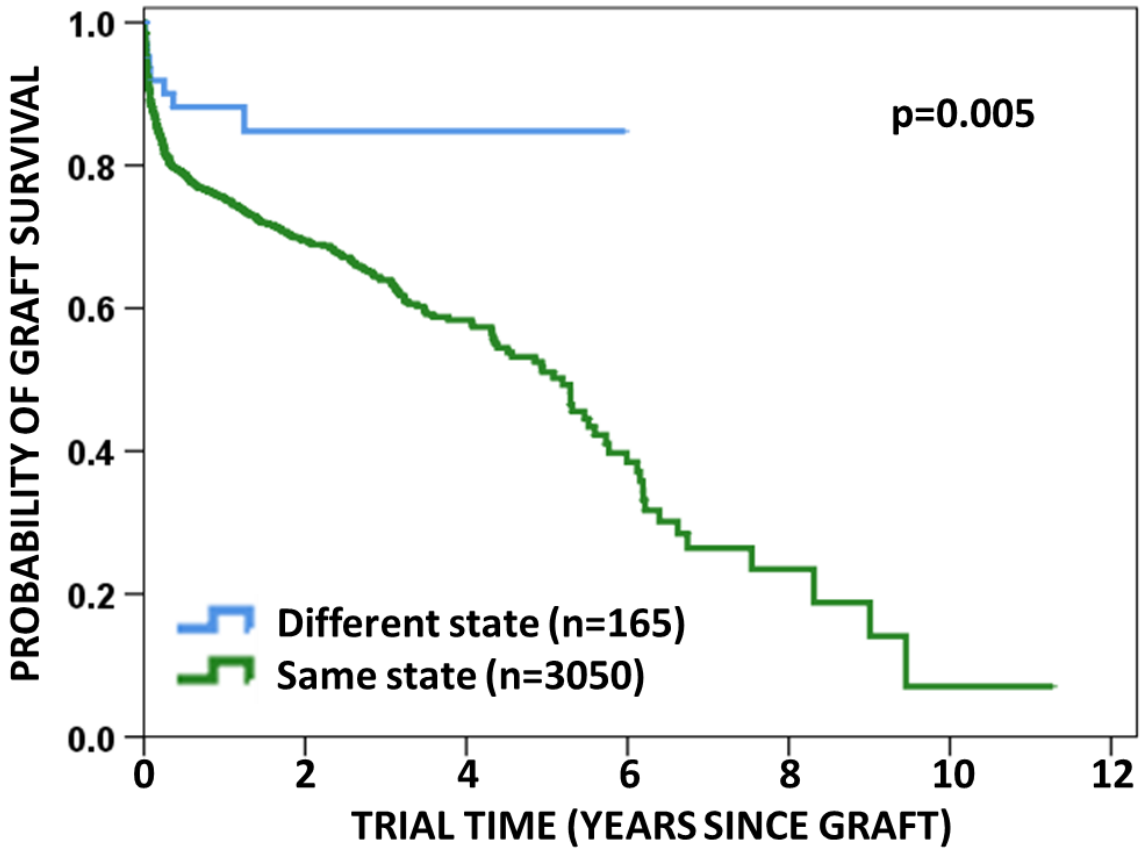
Probability of graft survival (years post-graft)

	1	2	3	4	5	6
Optisol	0.73	0.67	0.62	0.56	0.49	0.42
Organ culture	0.79	0.74	0.68	0.63	0.56	NA

5.1.5 Descemet's membrane endothelial keratoplasty survival: influence of interstate transportation

In the majority of transplants, donor corneas are sourced from the State in which the surgery occurs, however, in some cases corneas are transported interstate via air freight. Figure 5.1.5 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=7.78; df=1; p=0.005). However, 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 5.1.5 Interstate transportation



Number at risk (years post-graft)

	1	2	3	4	5	6	7
Different state	31	15	8	5	3	NA	NA
Same state	956	496	262	123	68	30	12

Probability of graft survival (years post-graft)

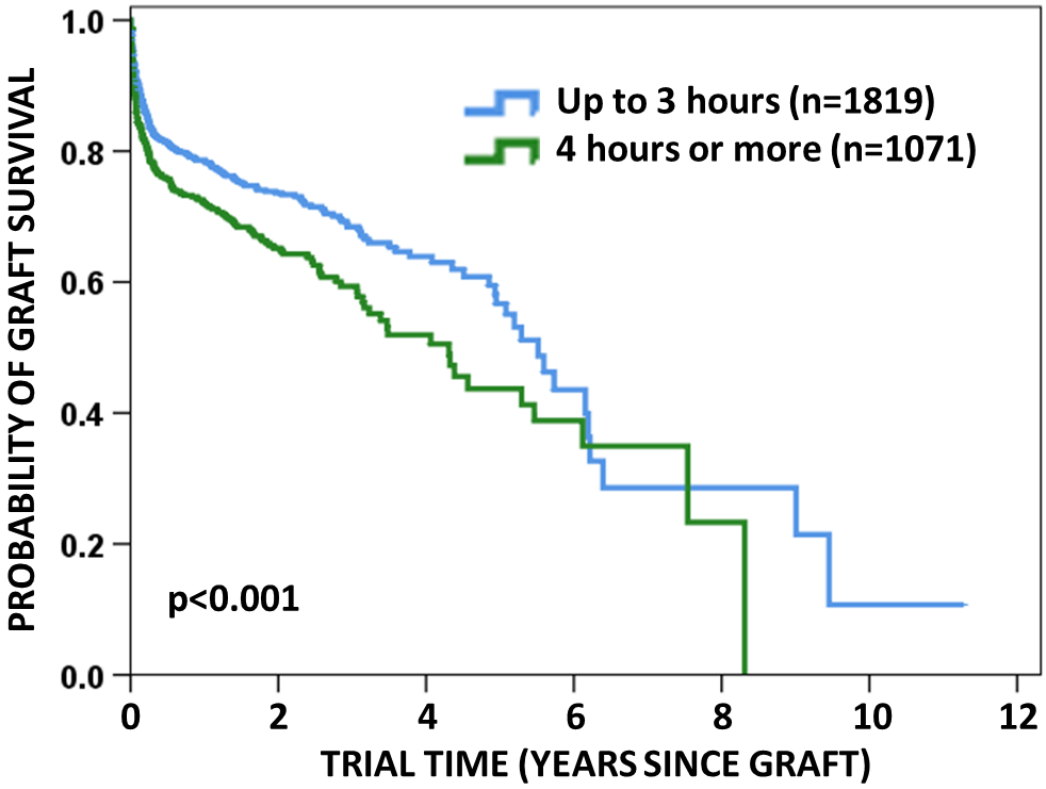
	1	2	3	4	5	6
Different state	0.88	NA	NA	NA	NA	NA
Same state	0.76	0.70	0.64	0.58	0.51	0.39

5.1.6 Descemet's membrane endothelial keratoplasty survival: influence of enucleation-to-storage time

Figure 5.1.6 shows a comparison of graft survival depending on time from enucleation of the donor cornea to initial storage in preservation media. Times were initially stratified into those that were stored immediately (within 1 hour of enucleation) and then in three-hourly groups. Due to low numbers in the categories above 18 hours, these groups were combined. A significant difference was found across time groups (Log Rank Statistic=18.81; df=7; p=0.009). Further analyses examined whether there were significant differences between adjacent time groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=10.93; df=1; p<0.001).

Data on this variable were not provided in 10% of cases and these were categorised as "not advised". A significant difference was still found across groups when this category was included (Log Rank Statistic=11.30; df=2; p=0.004). However, this variable was not retained in the final multivariate model (see section 5.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 5.1.6 Time from enucleation to storage



Number at risk (years post-graft)

	1	2	3	4	5	6
Up to 3 hours	578	291	159	76	38	13
4 or more hours	306	154	79	37	22	10

Probability of graft survival (years post-graft)

	1	2	3	4	5
Up to 3 hours	0.79	0.74	0.68	0.64	0.57
4 or more hours	0.72	0.65	0.59	0.52	0.44

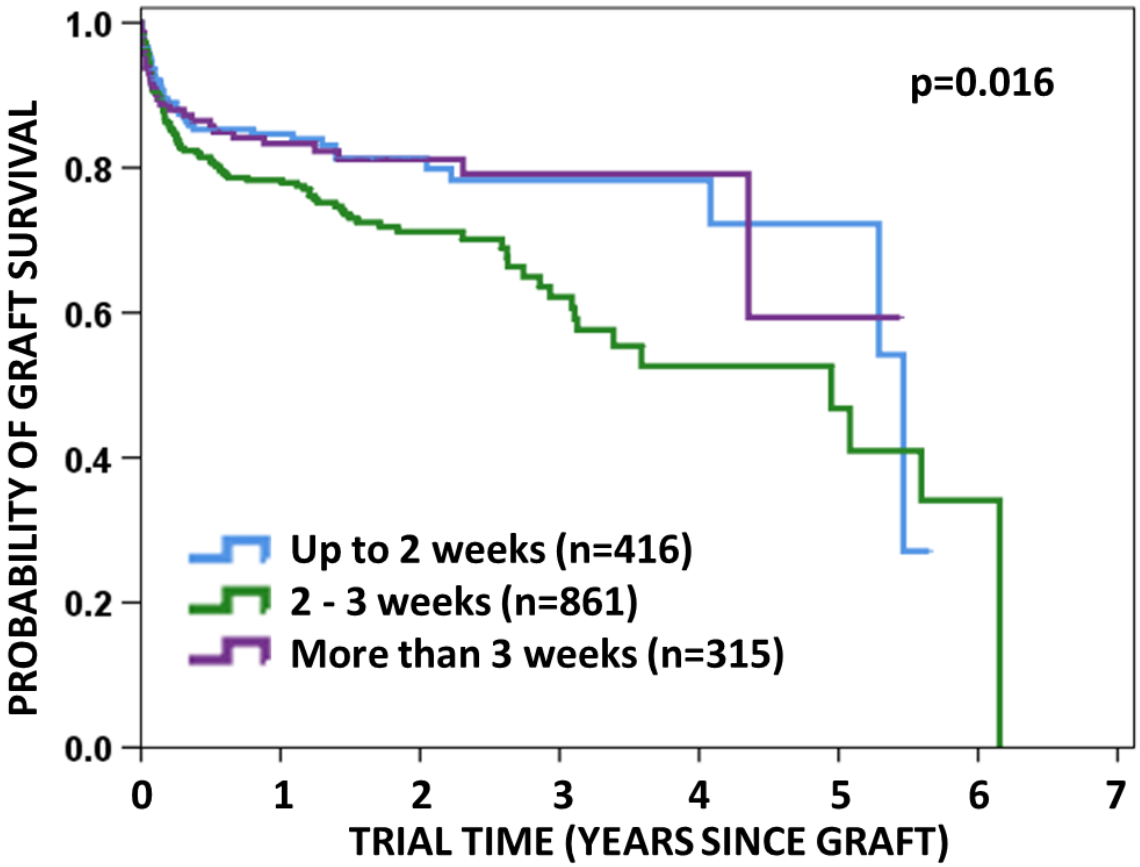
5.1.7 Descemet's membrane endothelial keratoplasty survival: influence of storage-to-graft time in organ culture

Figure 5.1.7 shows a comparison of graft survival depending on time from initial storage of the donor cornea in organ culture media to graft. Times were initially stratified into weekly groups, with those within the first week combined with those 1 to 2 weeks post-storage, due to low numbers. A significant difference was found across time groups (Log Rank Statistic=8.33; df=2; p=0.016).

This variable was not applicable for the 1318 corneas not stored in organ culture and the data for these grafts were excluded from the analysis. Data on this variable were not provided in 16% of grafts stored in organ culture (9% of all grafts) and these were categorised as "not advised". A significant difference was still found across groups when this category was included (Log Rank Statistic=16.15; df=3; p=0.001).

As this variable was not applicable to the 41% of grafts that were stored in Optisol, this variable was initially combined with the variable relating to storage media (see section 5.1.4) for the purpose of multivariate analysis. However, this variable was not retained in the final multivariate model (see section 5.7), suggesting that it is **not** an independent factor significantly affecting graft survival.

Figure 5.1.7 Time from storage to graft for organ culture media



Number at risk (years post-graft)

	1	2	3	4
Up to 2 weeks	124	59	31	13
2 – 3 weeks	211	90	43	15
More than 3 weeks	98	50	25	5

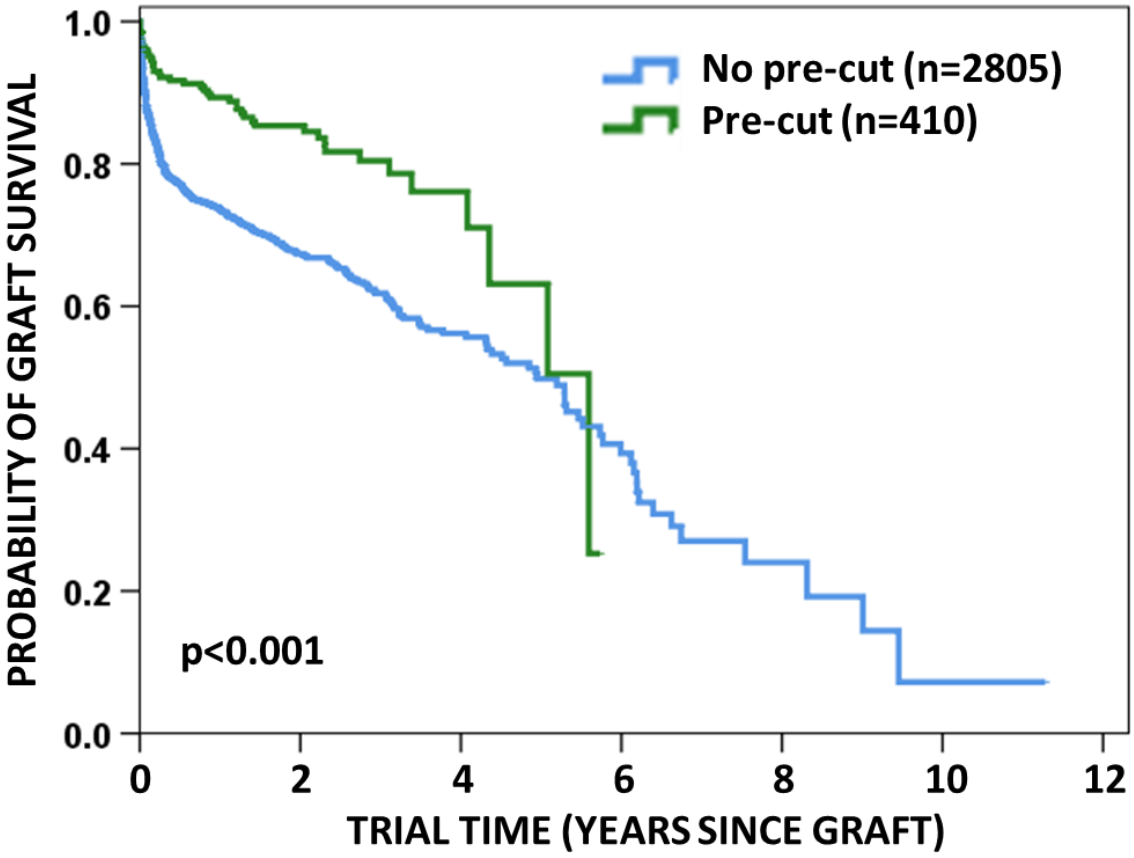
Probability of graft survival (years post-graft)

	1	2	3
Up to 2 weeks	0.85	0.81	0.78
2 – 3 weeks	0.78	0.71	0.62
More than 3 weeks	0.83	0.81	0.79

5.1.8 Descemet's membrane endothelial keratoplasty survival: influence of pre-cut of donor button by eye bank

Donor tissue for endothelial grafts is increasingly prepared (pre-cut) by eye banks. Figure 5.1.8 shows the comparison of graft survival between grafts that were pre-cut by the eye bank and those where the tissue was cut by the surgeon. A significant difference was found across groups (Log Rank Statistic=22.57; df=1; p<0.001). However, 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 5.1.8 Pre-cut of donor button by eye bank



Number at risk (years post-graft)

	1	2	3	4	5	6	7
No pre-cut	813	402	217	112	65	30	12
Pre-cut	174	109	53	16	6	NA	NA

Probability of graft survival (years post-graft)

	1	2	3	4	5	6
No pre-cut	0.74	0.67	0.62	0.56	0.50	0.39
Pre-cut	0.89	0.85	0.80	NA	NA	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 (3,215 registered and 1,756 followed) and the percentages, which should be summed vertically for each variable, total 100.

Table 5.3 Recipient factors, significant in univariate analyses

Descemet's Membrane Endothelial Keratoplasty

Recipient factors

	Registered (%)	Followed (%)
Indication for graft		
Failed previous graft	730 (23%)	438 (25%)
Endothelial failure/bullous keratopathy	506 (16%)	244 (14%)
Fuchs' endothelial dystrophy	1931 (60%)	1044 (59%)
Other*	48 (1%)	30 (2%)
Prior ipsilateral corneal graft/s		
None	2482 (77%)	1316 (75%)
One	501 (16%)	292 (17%)
Two	150 (5%)	94 (5%)
Three or more	82 (3%)	54 (3%)
Australian State where graft was performed		
	946 (29%)	406 (23%)
States are not identified due to	277 (9%)	175 (10%)
confidentiality constraints. See	1482 (46%)	884 (50%)
section 1.4.8 for further information.	330 (10%)	246 (14%)
	144 (4%)	45 (3%)
	36 (1%)	0 (0%)
Recipient age group		
0 to 49 years	173 (5%)	92 (5%)
50 to 59 years	334 (10%)	184 (11%)
60 to 69 years	881 (27%)	498 (28%)
70 to 79 years	1143 (36%)	616 (35%)
80 to 89 years	602 (19%)	327 (19%)
90 years and older	82 (3%)	39 (2%)
Recipient sex		
Female	1807 (56%)	999 (57%)
Male	1408 (44%)	757 (43%)
Donor/recipient sex match		
Female/female	670 (21%)	366 (21%)
Female/male	543 (17%)	300 (17%)
Male/female	1137 (35%)	633 (36%)
Male/male	865 (27%)	457 (26%)

	Registered (%)	Followed (%)
Neovascularisation pre-graft		
None	2875 (89%)	1606 (91%)
One quadrant	198 (6%)	92 (5%)
Two to four quadrants	142 (4%)	58 (3%)
Pre-graft inflammation/ recent steroid use		
No	2347 (73%)	1298 (74%)
Yes	824 (26%)	428 (24%)
Unknown	44 (1%)	30 (2%)
History raised IOP at graft or prior to graft		
IOP never raised	2760 (86%)	1502 (86%)
IOP raised in past and/or at graft	455 (14%)	254 (14%)
Prior contralateral corneal graft/s		
None	2084 (65%)	1117 (64%)
One	928 (29%)	505 (29%)
Two or more	203 (6%)	134 (8%)
Prior intraocular surgery of any kind		
No	881 (27%)	515 (29%)
Yes	1591 (49%)	796 (45%)
Not advised	10 (<1%)	5 (<1%)
Not applicable (repeat and/or prior concurrent)	733 (23%)	440 (25%)
	3215 (100%)	***1756 (100%)***

*Other included: trauma (35), ICE syndrome (8), band keratopathy (1), endophthalmitis (1), Fuchs' heterochromatic iridocyclitis (1), retro corneal membrane (1), and toxic shock syndrome (1).

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 (3,215 registered and 1,756 with follow-up provided) and the percentages, summed vertically, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

Table 5.4 Recipient factors, not significant in univariate analyses

Descemet's Membrane Endothelial Keratoplasty
Recipient Factors

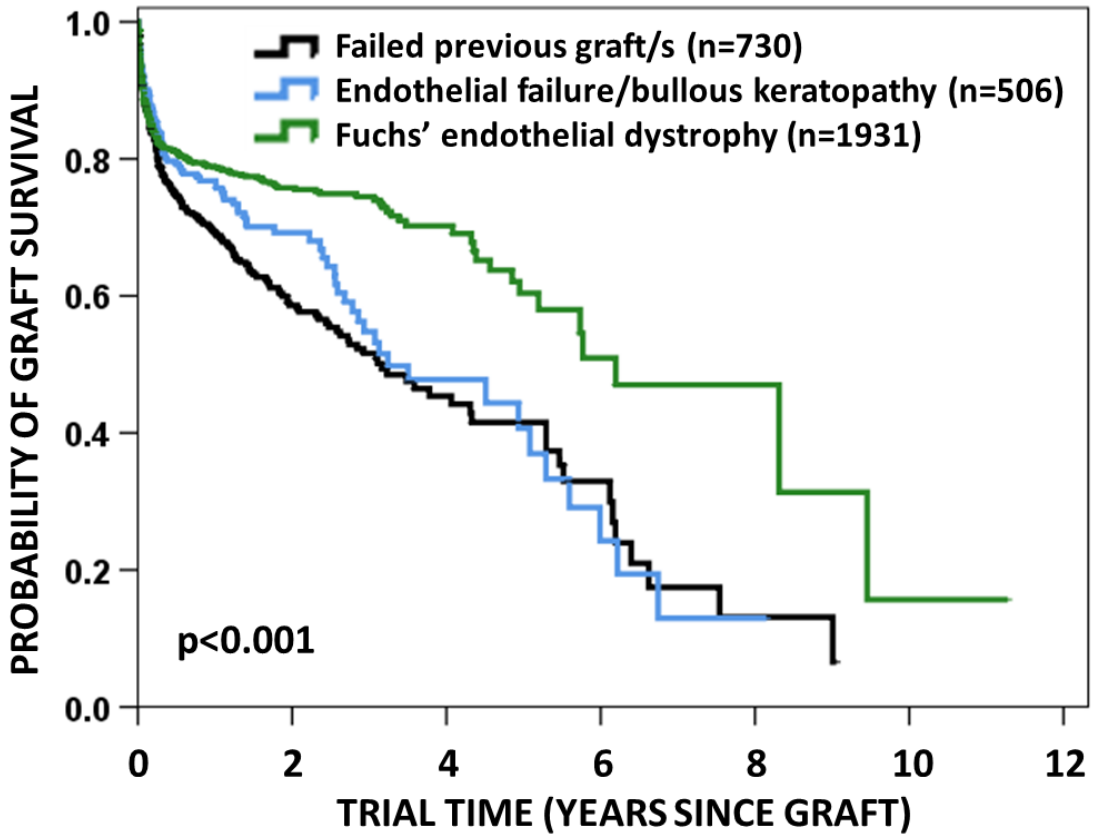
		Registered (%)	Followed (%)
Eye grafted			
Left		1587 (49%)	867 (49%)
Right		1627 (51%)	889 (51%)
Not advised		1 (<1%)	0 (0%)
Chi²=0.05, df=1, p=0.823			
	Total	***3215 (100%)***	***1756 (100%)***

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

5.2.1 Descemet's membrane endothelial keratoplasty survival: influence of indication for graft

Figure 5.2.1 shows the comparison of graft survival depending on indication for graft. All repeat grafts were analysed together, regardless of original pathology. Just 48 (<1%) first grafts were not for either Fuchs' endothelial dystrophy or endothelial failure/bullous keratopathy and these were excluded from the analysis. A significant difference was found across groups (Log Rank Statistic=35.87; df=2; p<0.001). Grafts performed for Fuchs' endothelial dystrophy had significantly better survival than those performed for failed previous grafts (p<0.001) or endothelial failure/bullous keratopathy (p=0.003). However, 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)

	1	2	3	4	5	6
Failed previous graft/s	237	128	73	40	23	12
Endothelial failure/bullous keratopathy	146	71	35	19	11	5
Fuchs' endothelial dystrophy	590	305	159	67	35	13

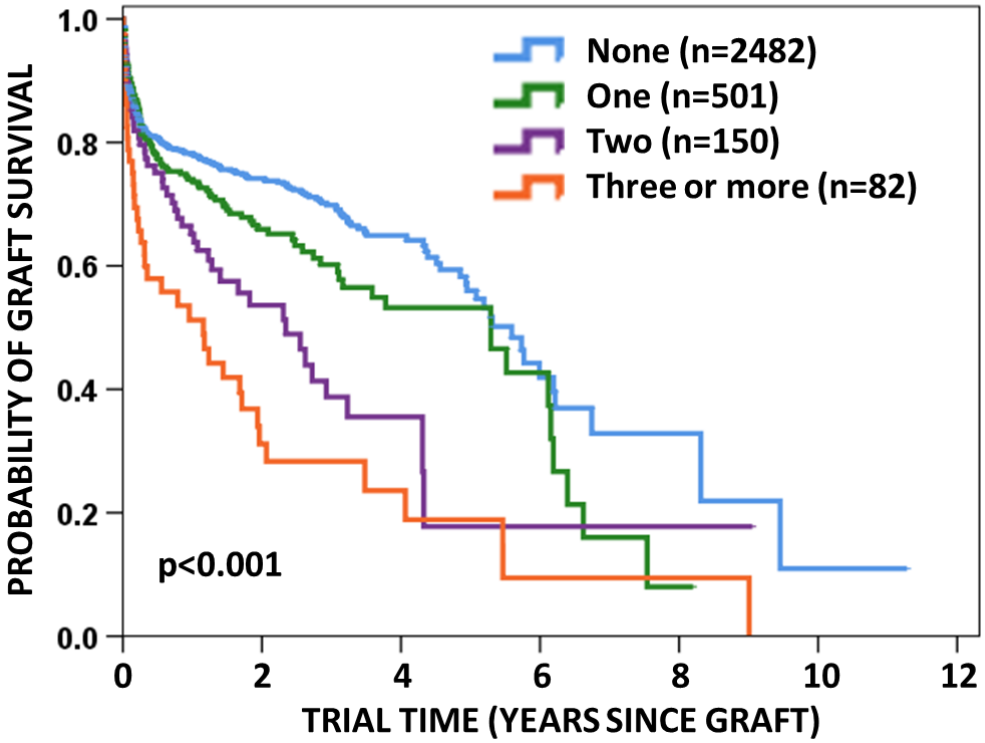
Probability of graft survival (years post-graft)

	1	2	3	4	5
Failed previous graft/s	0.69	0.59	0.52	0.45	0.42
Endothelial failure/bullous keratopathy	0.77	0.69	0.55	NA	NA
Fuchs' endothelial dystrophy	0.79	0.76	0.75	0.70	0.60

5.2.2 Descemet's membrane endothelial keratoplasty survival: influence of number of previous ipsilateral grafts

Survival was compared across groups based on the number of previous grafts in the same eye, as shown in Figure 5.2.2. Grafts performed in eyes with three or more prior grafts were grouped together due to low numbers. Previous grafts may not have been Descemet's membrane endothelial keratoplasties. The difference across groups was significant (Log Rank Statistic=55.89, df=3, p<0.001). Eyes with no prior grafts had significantly better survival than those with one (p=0.020), two, and three or more prior grafts (both p<0.001). Survival became significantly worse with each additional previous graft (one versus two, p=0.022; one versus three or more, p<0.001; two versus three or more, p=0.045). However, 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 5.2.2 Number of previous ipsilateral grafts



Number at risk (years post-graft)

	1	2	3	4	5	6
None	749	382	197	88	48	18
One	167	93	51	30	19	9
Two	49	25	15	5	2	2
Three or more	22	11	7	5	2	1

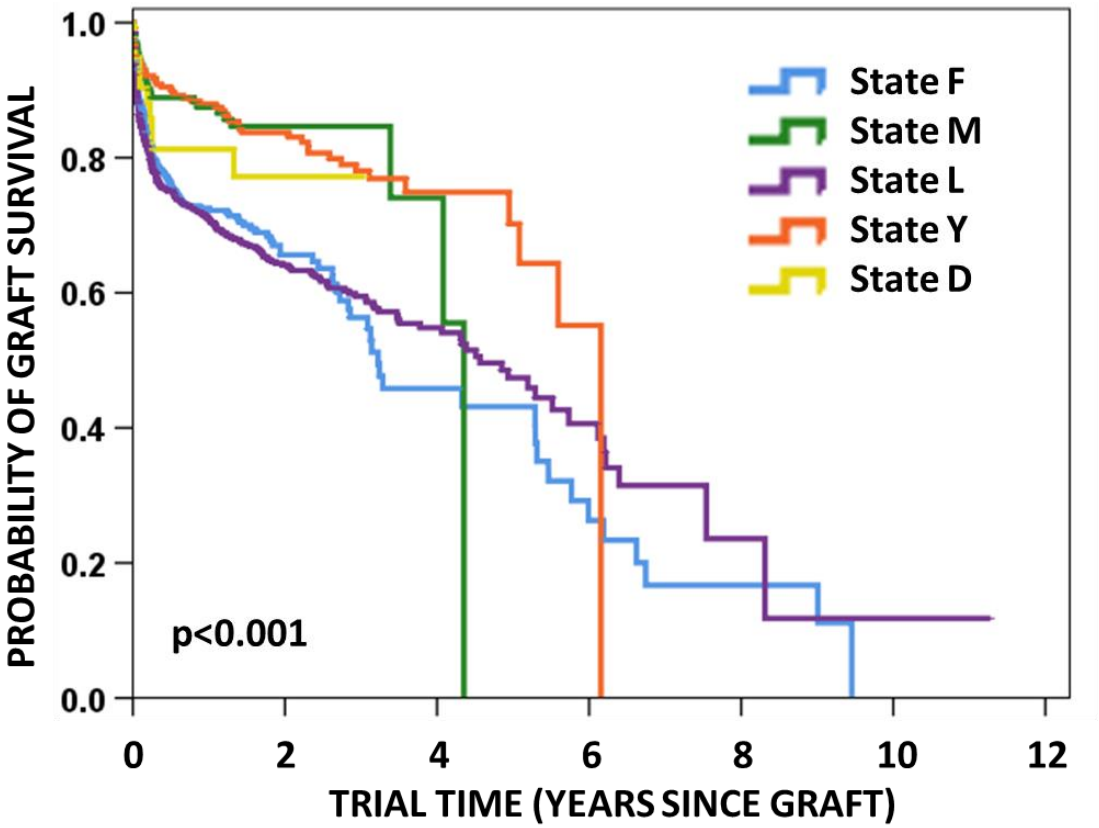
Probability of graft survival (years post-graft)

	1	2	3	4	5
None	0.78	0.74	0.70	0.65	0.56
One	0.74	0.66	0.60	0.53	NA
Two	0.65	0.54	NA	NA	NA
Three or more	0.51	NA	NA	NA	NA

5.2.3 Descemet's membrane endothelial keratoplasty survival: influence of Australian State where graft was performed

Figure 5.2.3 shows the comparison of graft survival depending on the Australian State in which the transplantation occurred. One State only had 36 DMEK registered, none of which had been followed-up, and these grafts were excluded from the analysis. A significant difference was found across groups (Log Rank Statistic=41.63; df=4; p<0.001), with State M and State Y having significantly better survival than State F and State L (all p<0.001). This variable was excluded from the multivariate analysis (see section 5.7) as it is collinear with the variables relating to eye bank (see section 5.1.1) and interstate transportation (see section 5.1.5). The variable relating to eye bank was retained in the final multivariate model.

Figure 5.2.3 Australian State where graft was performed



Probability of graft survival (years post-graft)

	1	2	3	4	5	6
State F	0.73	0.66	0.56	NA	NA	NA
State M	0.88	0.85	NA	NA	NA	NA
State L	0.71	0.64	0.60	0.55	0.47	0.41
State Y	0.88	0.84	0.78	0.75	NA	NA
State D	0.81	NA	NA	NA	NA	NA

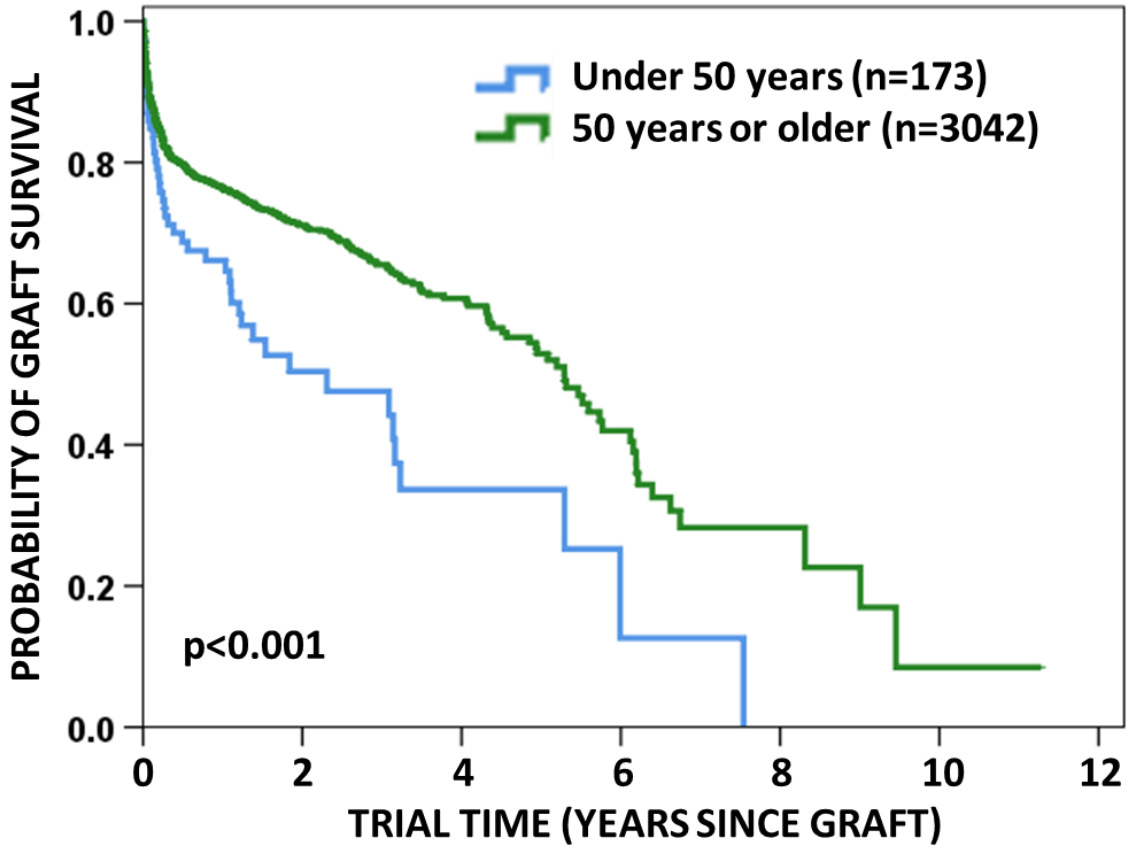
Note: Further information is not provided due to confidentiality constraints (see section 1.4.8).

5.2.4 Descemet's membrane endothelial keratoplasty survival: influence of recipient age (years)

Figure 5.2.4 shows the comparison of graft survival depending on the age of the corneal transplant recipient. Recipients were initially stratified by 10-year age groups. 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=22.95; df=5; p<0.001).

Further analyses examined whether there were significant differences between adjacent age groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=17.56; df=1; p<0.001). However, 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 5.2.4 Recipient age group



Number at risk (years post-graft)

	1	2	3	4	5	6	7
Under 50 years	45	19	14	8	6	1	1
50 years or older	942	492	256	120	65	29	11

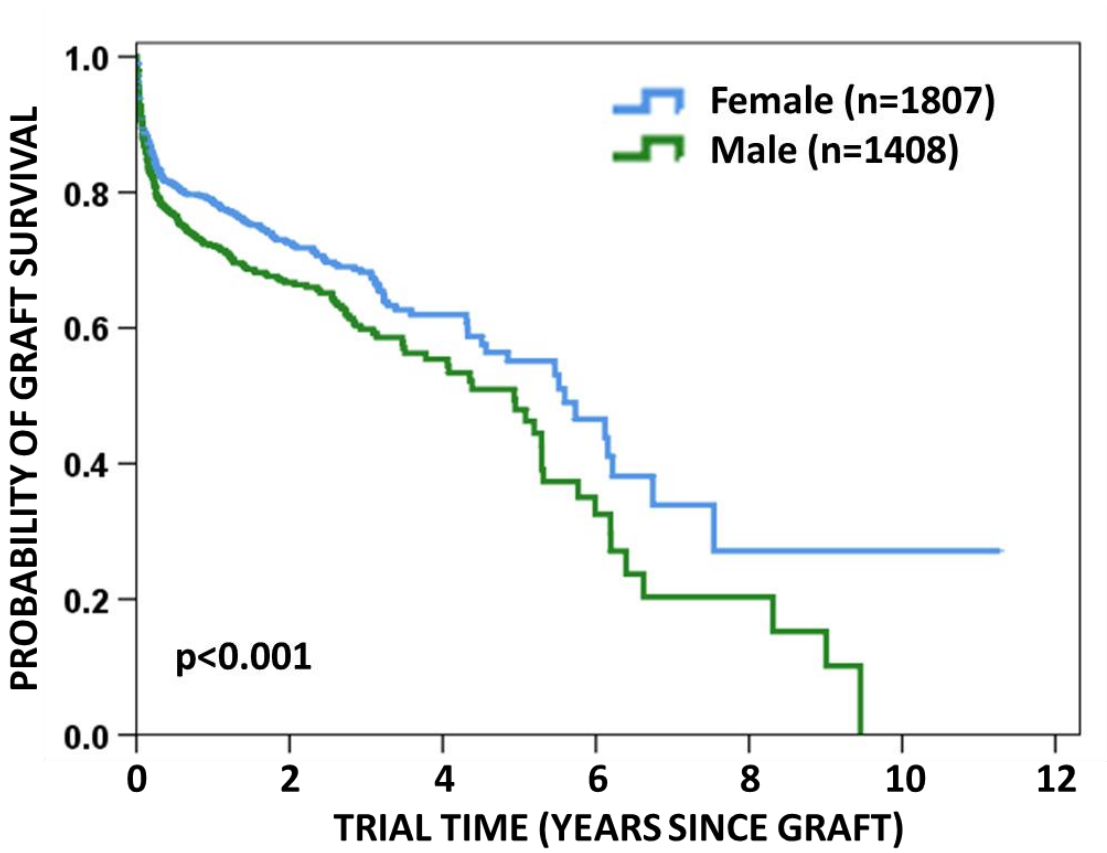
Probability of graft survival (years post-graft)

	1	2	3	4	5	6
Under 50 years	0.66	NA	NA	NA	NA	NA
50 years or older	0.76	0.71	0.66	0.61	0.53	0.42

5.2.5 Descemet's membrane endothelial keratoplasty survival: influence of recipient sex

Comparison of graft survival between male and female transplant recipients is shown in Figure 5.2.5 A significant difference was found between groups (Log Rank Statistic=10.65; df=1; p=0.001). This variable was not included in the multivariate analysis (see section 5.7), as it is collinear with the variable analysing donor/recipient sex match/mismatch (see section 5.2.6), which was retained in the final model.

Figure 5.2.5 Recipient sex



Number at risk (years post-graft)

	1	2	3	4	5	6
Female	584	304	165	71	39	17
Male	403	207	105	57	32	13

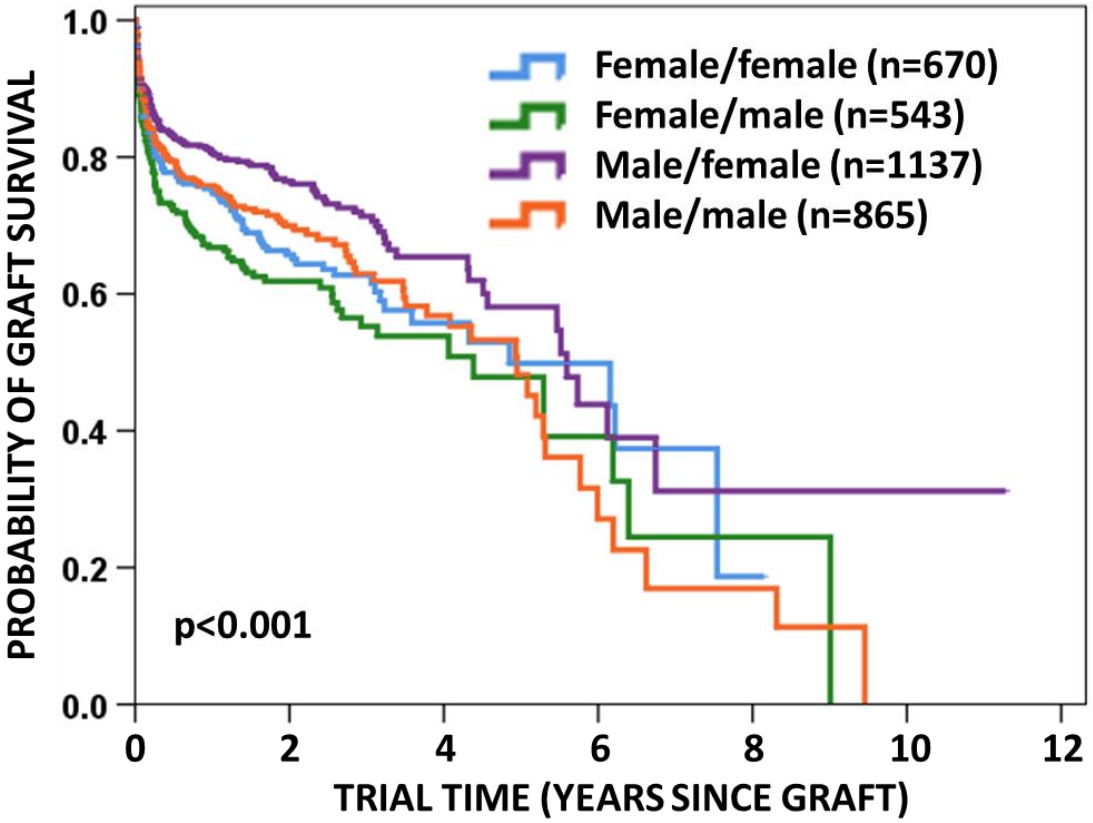
Probability of graft survival (years post-graft)

	1	2	3	4	5
Female	0.79	0.73	0.68	0.62	0.55
Male	0.72	0.67	0.60	0.55	0.48

5.2.6 Descemet's membrane endothelial keratoplasty survival: influence of donor/recipient sex match/mismatch

Comparison of graft survival across groups based on donor/recipient sex combinations is shown in Figure 5.2.6. A significant difference was found across groups (Log Rank Statistic=20.98; df=3; p<0.001). Grafts performed in females using male donor tissue had significantly better survival than those performed in females using female donor tissue (p=0.010), those performed in males using female donor tissue (p<0.001), and those performed in males using male donor tissue (p=0.007). This variable was retained in the final multivariate model (see section 5.7).

Figure 5.2.6 Donor/recipient sex match/mismatch



Number at risk (years post-graft)

	1	2	3	4	5	6
Female/female	202	103	56	25	13	8
Female/male	157	83	41	19	13	7
Male/female	382	201	109	46	25	9
Male/male	246	124	64	38	19	6

Probability of graft survival (years post-graft)

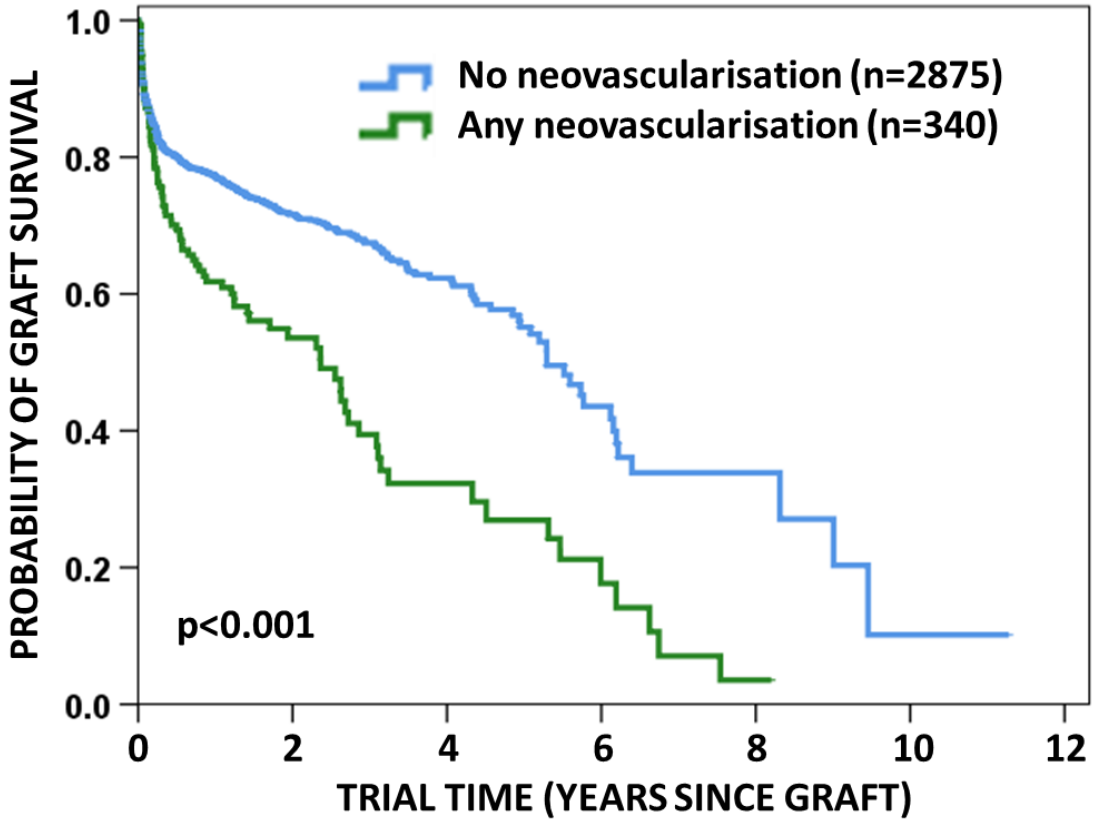
	1	2	3	4	5
Female/female	0.75	0.66	0.63	0.56	NA
Female/male	0.67	0.62	0.55	NA	NA
Male/female	0.81	0.77	0.71	0.65	0.58
Male/male	0.76	0.70	0.63	0.57	NA

5.2.7 Descemet's membrane endothelial keratoplasty survival: influence of pre-graft corneal neovascularisation

Figure 5.2.7 shows the comparison of graft survival between those recipients with corneal neovascularisation pre-graft and those without. Grafts were originally categorised based on the extent of neovascularisation, with eyes with two to four quadrants grouped together due to low numbers in the two most vascularised groups. The resulting comparison was significant. (Log Rank Statistic=29.61; df=2; p<0.001).

Further analysis examined where there was any significant difference in survival between those with a single quadrant of neovascularisation and those with multiple, with no significant difference detected (p=0.213). These two groups were thus combined, and the resulting comparison remained significant (Log Rank Statistic=27.45; df=1; p<0.001). However, 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 5.2.7 Pre-graft corneal neovascularisation



Number at risk (years post-graft)

	1	2	3	4	5	6	7
No neovascularisation	912	472	246	113	61	25	10
Any neovascularisation	75	39	24	15	10	5	2

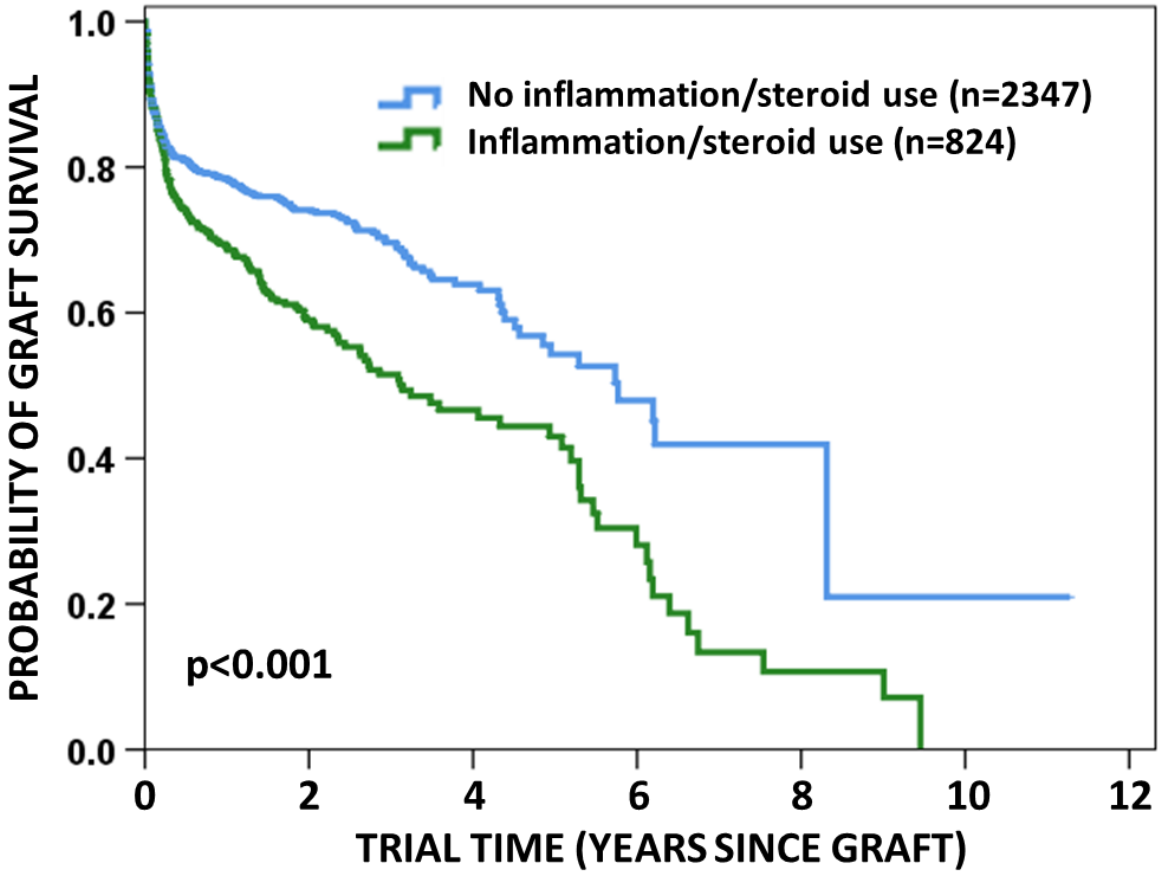
Probability of graft survival (years post-graft)

	1	2	3	4	5	6
No neovascularisation	0.77	0.72	0.68	0.62	0.55	0.44
Any neovascularisation	0.62	0.54	0.39	NA	NA	NA

5.2.8 Descemet's membrane endothelial keratoplasty survival: influence of pre-graft inflammation/steroid use

Figure 5.2.8 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=29.13; df=1; p<0.001). Data on this variable were not provided in 44 (<2%) cases and these were excluded from the analysis. However, 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 5.2.8 Pre-graft inflammation/steroid use



Number at risk (years post-graft)

	1	2	3	4	5	6
No inflammation/steroid use	730	378	193	83	41	18
Inflammation/steroid use	242	128	74	43	29	12

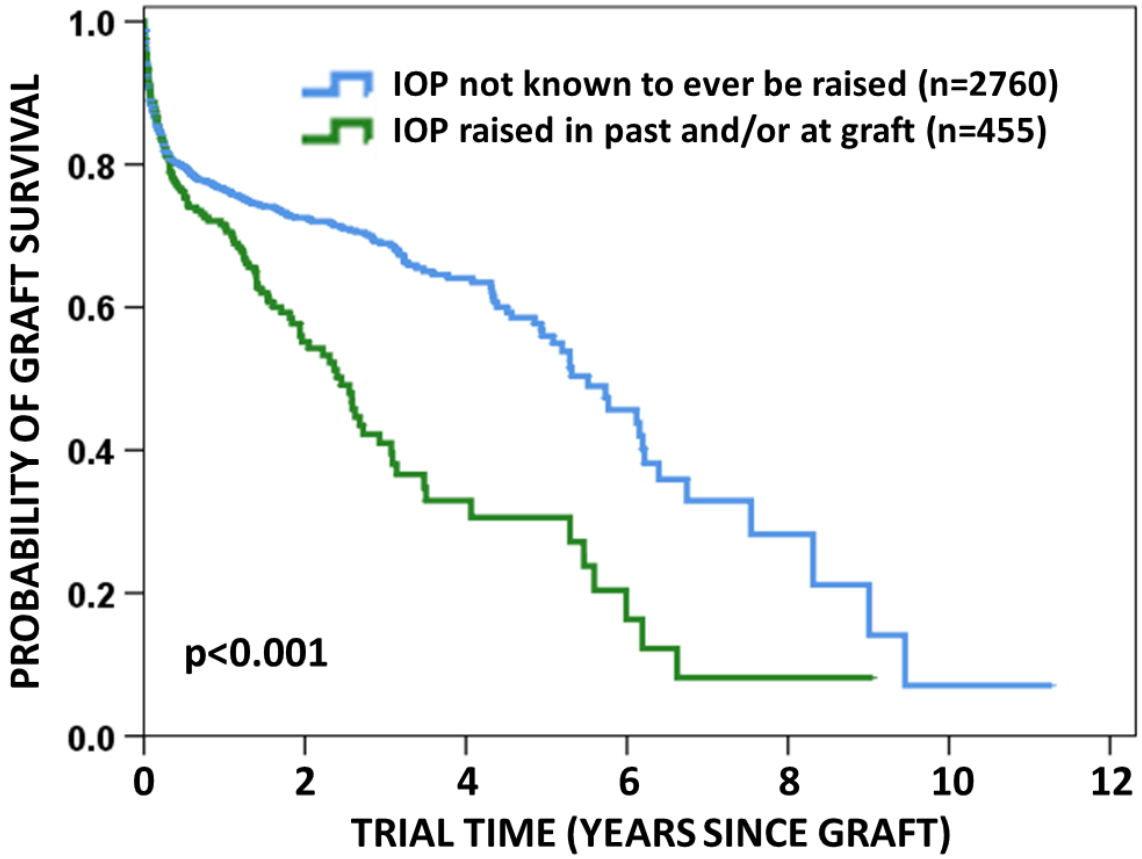
Probability of graft survival (years post-graft)

	1	2	3	4	5
No inflammation/steroid use	0.78	0.74	0.70	0.64	0.54
Inflammation/steroid use	0.69	0.59	0.52	0.47	0.43

5.2.9 Descemet's membrane endothelial keratoplasty survival: influence of history raised IOP at graft or prior to graft

Figure 5.2.9 shows the comparison of graft survival between groups based on whether the recipient had a history of raised intraocular pressure (Log Rank Statistic=28.86; df=1; p<0.001). This was irrespective of whether IOP was raised at the time of graft. However, 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 5.2.9 History of raised intraocular pressure at graft or prior to graft



Number at risk (years post-graft)

	1	2	3	4	5	6	7
IOP never raised	848	447	240	114	62	26	10
IOP raised	139	64	30	14	9	4	2

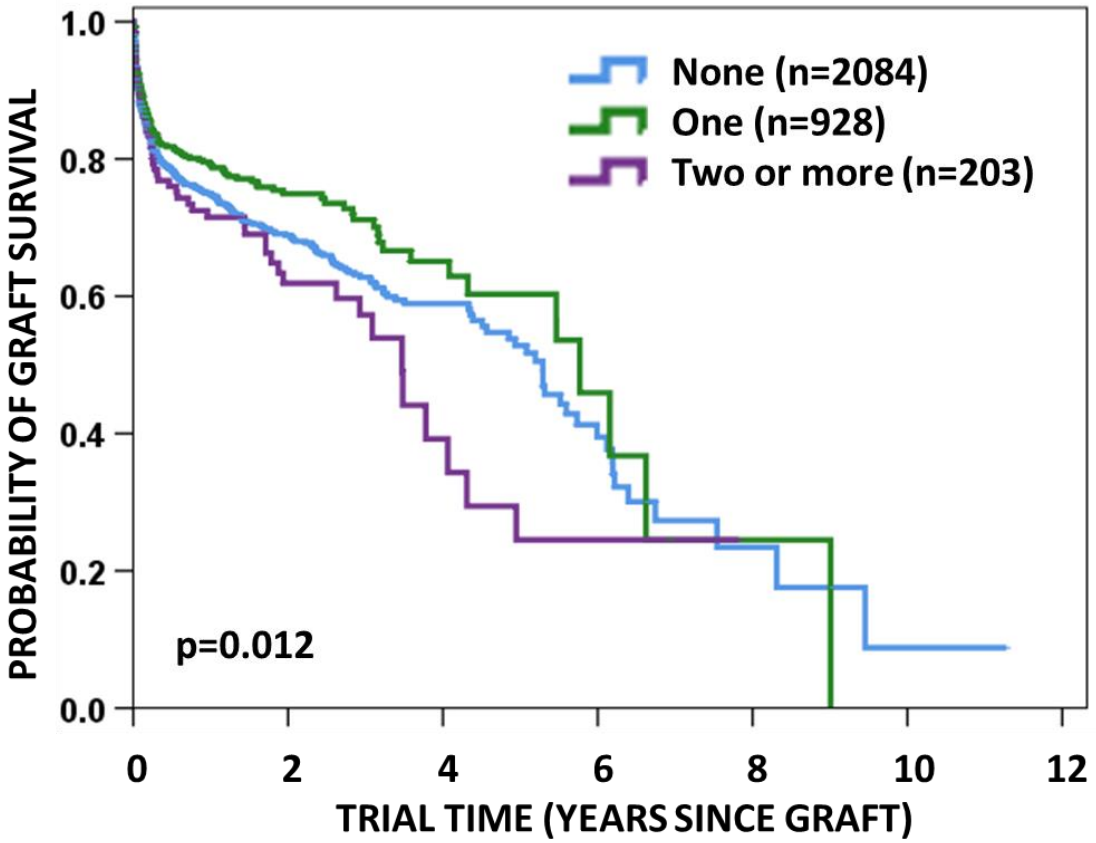
Probability of graft survival (years post-graft)

	1	2	3	4	5	6
IOP never raised	0.77	0.73	0.69	0.64	0.56	0.46
IOP raised	0.72	0.55	0.41	NA	NA	NA

5.2.10 Descemet's membrane endothelial keratoplasty survival: influence of previous contralateral corneal graft/s

Figure 5.2.10 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=8.86; df=2; p=0.012), with grafts performed in recipients with one previous graft in the contralateral eye having better survival than those with none (p=0.017), or two or more (p=0.006). However, 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 5.2.10 Previous contralateral corneal graft/s



Number at risk (years post-graft)

	1	2	3	4	5	6	7
None	631	333	171	88	53	22	10
One	285	137	78	32	13	6	1
Two or more	71	41	21	8	5	2	1

Probability of graft survival (years post-graft)

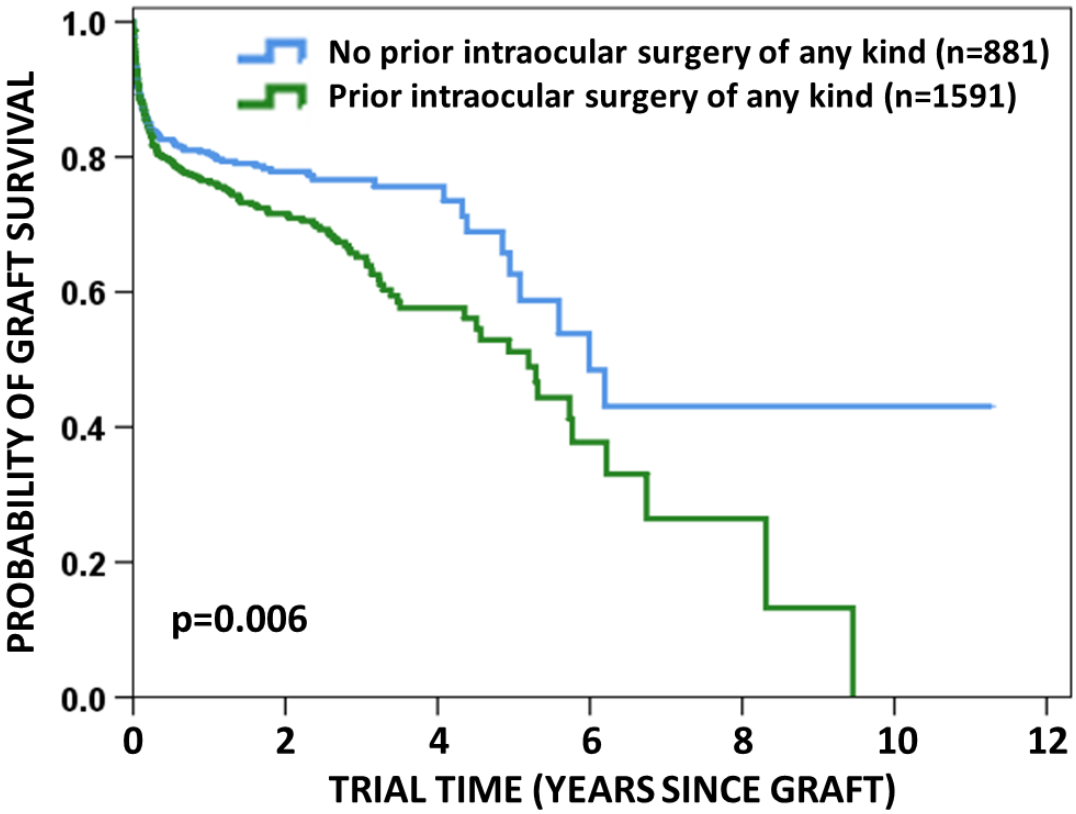
	1	2	3	4	5	6
None	0.75	0.69	0.63	0.59	0.53	0.40
One	0.79	0.75	0.71	0.65	NA	NA
Two or more	0.72	0.62	0.57	NA	NA	NA

5.2.11 Descemet's membrane endothelial keratoplasty survival: influence of prior intraocular surgery

The analysis on page 208 is of a sub-cohort of Descemet's membrane endothelial grafts which had **not** undergone a previous corneal transplant. Sub-cohort variables are excluded from multivariate analysis.

Data were not available for 10 grafts and these are excluded from the analysis. Figure 5.2.11 shows the comparison of graft survival between grafts where the recipient had undergone prior intraocular surgery (excluding prior graft) compared to those that had not (Log Rank Statistic=7.65; df=1; p=0.006). The nature of the variable means that a large percentage of the cohort (23%) are not included. While the type of prior surgery was not specified, in 62% of first grafts, the eye had undergone prior cataract extraction.

Figure 5.2.11 History of previous intraocular surgery in the ipsilateral eye



Number at risk (years post-graft)

	1	2	3	4	5	6
No prior surgery	300	163	89	39	19	9
Prior surgery	446	219	108	49	29	9

Probability of graft survival (years post-graft)

	1	2	3	4	5
No prior surgery	0.81	0.78	0.77	0.76	NA
Prior surgery	0.77	0.72	0.65	0.58	0.51

5.3 Graft Era/Year

Table 5.5 shows the number of grafts registered and followed based on single years combined. Grafts were initially stratified by yearly groups with all grafts performed prior to 2011 grouped together, due to low numbers. A significant difference was found across year groups (Log Rank Statistic=102.57; df=10; p<0.001).

Further analyses examined whether there were significant differences between adjacent year groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=94.97; df=3; p<0.001). The percentages, which should be summed vertically, total 100.

Table 5.5 Graft era/year

Descemet's Membrane Endothelial Keratoplasty
Graft Era/Year

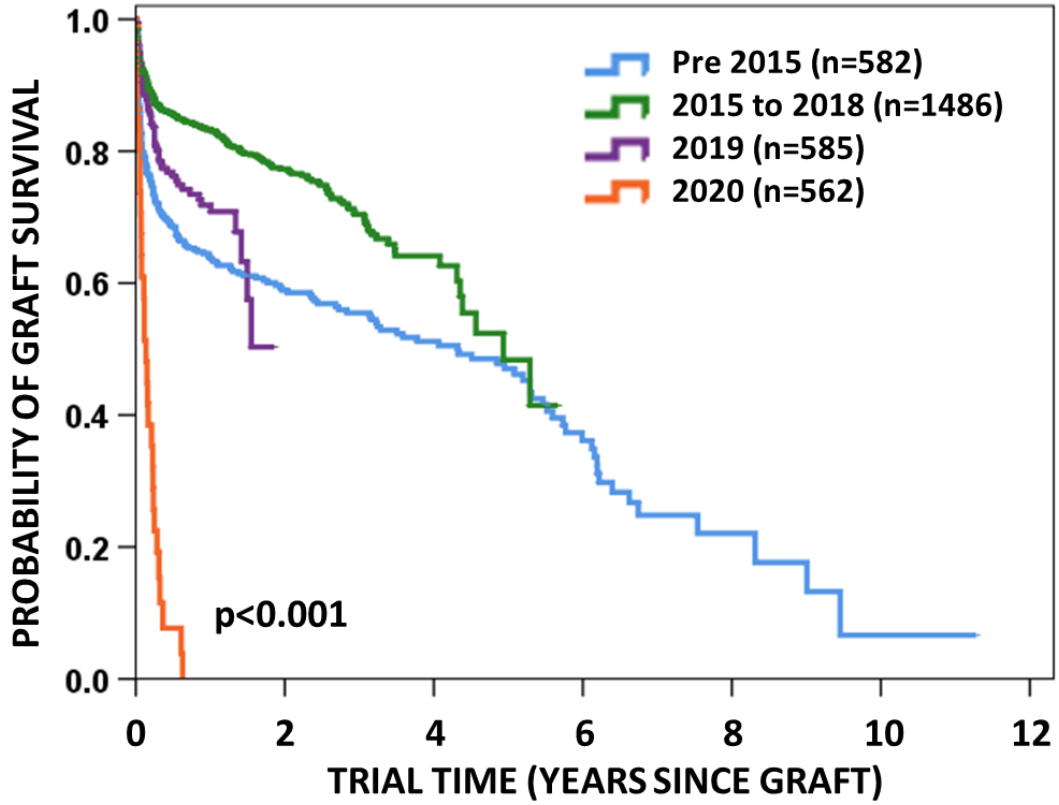
		Registered (%)	Followed (%)
Year of graft			
Pre 2015		582 (18%)	419 (24%)
2015 to 2018		1486 (46%)	1085 (62%)
2019		585 (18%)	214 (12%)
2020		562 (17%)	38 (2%)
	Total	***3215 (100%)***	***1756 (100%)***

See section 1.1 for a discussion of the impact that lag time to follow-up may have on survival depending on graft year/era. Comparisons amongst the percentages of grafts registered and followed in each category showed some differences. Level of follow-up reduces as time since graft reduces, with 72% of grafts performed prior to 2015 and 73% of grafts performed from 2015 to 2018 followed, compared to 37% of grafts performed in 2019, and just 7% of grafts performed in 2020. Of this last group, 82% were primary non-functioning grafts, failing within 3-months and recorded as such when a replacement graft was registered.

5.3.1 Descemet's membrane endothelial keratoplasty survival: influence of era of graft

Figure 5.3.1 shows the comparison of graft survival between eras of graft, stratified into the groups outlined in section 5.3 (Log Rank Statistic=94.97; df=3; p<0.001). Grafts performed in 2020 had significantly poorer survival than those performed in any of the three earlier time periods (all p<0.001). Grafts performed from 2015 to 2018 also had significantly better survival than those performed before this period or in 2019 (both p<0.001). Grafts performed in 2019 also had significantly better survival than those performed prior to 2015 (p=0.028). This variable was retained the final multivariate model (see section 5.7).

Figure 5.3.1 Graft Era/Year



Number at risk (years post-graft)

	1	2	3	4	5	6	7
Pre 2015	220	155	111	82	61	30	12
2015 to 2018	694	356	160	46	10	NA	NA
2019	73	NA	NA	NA	NA	NA	NA

Probability of graft survival (years post-graft)

	1	2	3	4	5	6
Pre 2015	0.64	0.59	0.56	0.51	0.47	0.36
2015 to 2018	0.83	0.77	0.70	0.64	NA	NA
2019	0.72	NA	NA	NA	NA	NA

Note: no grafts performed in 2020 had follow-up of one year by the census date and so this category is excluded from the above tables.

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 found to be **significant** in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (3,215 registered and 1,756 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

Descemet's Membrane Endothelial Keratoplasty

Surgery and Surgeon Factors

	Registered (%)	Followed (%)
Size of graft (diameter)		
Less than 8.00 mm	348 (11%)	191 (11%)
8.00 mm to 8.24 mm	1582 (49%)	925 (53%)
8.25mm to 8.49 mm	207 (6%)	117 (7%)
8.50 mm to 8.74 mm	505 (16%)	279 (16%)
8.75mm or more	440 (14%)	156 (9%)
Not advised	133 (4%)	88 (5%)
Size of incision		
Up to 2.25 mm	321 (10%)	122 (7%)
2.26 mm to 2.50 mm	625 (19%)	328 (19%)
2.51 mm to 2.75 mm	948 (29%)	568 (32%)
2.76 mm to 3.00 mm	180 (6%)	85 (5%)
3.01 mm to 4.00 mm	279 (9%)	93 (5%)
More than 4.00 mm	96 (3%)	55 (3%)
Not advised	766 (24%)	505 (29%)
Change in lens status		
Triple procedure	832 (26%)	502 (29%)
Always pseudophakic	2180 (68%)	1158 (66%)
Other	203 (6%)	96 (5%)
Use of IOL injector		
No	1557 (48%)	686 (39%)
Yes	744 (23%)	418 (24%)
Not advised	914 (28%)	652 (37%)
Use of Geuder technique		
No	1532 (48%)	685 (39%)
Yes	936 (29%)	549 (31%)
Not advised	747 (23%)	522 (30%)
Use of suture pull through technique		
No	2021 (63%)	916 (52%)
Yes	72 (2%)	9 (1%)
Not advised	1122 (35%)	831 (47%)
	Registered (%)	**Followed (%)**

Use of SF6 bubble		
No	1055 (33%)	217 (12%)
Yes	196 (6%)	118 (7%)
Not advised	1964 (61%)	1421 (81%)
Use of suture to wound		
No	882 (27%)	534 (30%)
Yes	1960 (61%)	901 (51%)
Not advised	373 (12%)	321 (18%)
Surgeon caseload and level of follow-up		
Fewer than 65 (2%) registered DMEK	772 (24%)	331 (19%)
65+ registered DMEK, <55% follow-up	1019 (32%)	361 (21%)
65+ registered DMEK, ≥55% follow-up	1424 (44%)	1064 (61%)
The centre effect		
Fewer than 65 (2%) registered DMEK	772 (24%)	331 (19%)
	684 (21%)	518 (29%)
	479 (15%)	147 (8%)
	326 (10%)	245 (14%)
	196 (6%)	105 (6%)
Individual surgeons are not identified	173 (5%)	40 (2%)
due to confidentiality constraints.	96 (3%)	75 (4%)
See section 1.4.8 for further information.	91 (3%)	43 (2%)
	90 (3%)	66 (4%)
	80 (2%)	26 (1%)
	78 (2%)	50 (3%)
	78 (2%)	59 (3%)
	72 (2%)	51 (3%)
Total	***3215 (100 %)***	***1756 (100 %)***

Note: 65 was selected as the cut-off point for high volume surgeons as this was 2% of all registered Descemet'smembrane endothelial keratoplasties. 55% was selected as the cut-off point for the follow-up categories as this was the average percentage of follow-up for all

Table 5.7 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 (6,947 registered and 5,091 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

Table 5.7 Surgery and surgeon factors, not significant in univariate analyses

Descemet's Membrane Endothelial Keratoplasty

Surgery and Surgeon Factors

	Registered (%)	Followed (%)
Use of glide inserter		
No	2623 (82%)	1348 (77%)
Yes	88 (3%)	50 (3%)
Not advised	504 (16%)	358 (20%)
Chi²=0.16, df=1, p=0.693		
Use of anterior chamber maintainer		
No	2640 (82%)	1375 (78%)
Yes	71 (2%)	19 (1%)
Not advised	504 (16%)	362 (21%)
Chi²=1.54, df=1, p=0.214		
Use of viscoelastic		
No	2608 (81%)	1352 (77%)
Yes	103 (3%)	42 (2%)
Not advised	504 (16%)	362 (21%)
Chi²=0.69, df=1, p=0.407		
Donor button folded		
No	2651 (82%)	1360 (77%)
Yes	75 (2%)	47 (3%)
Not advised	489 (15%)	349 (20%)
Chi²=2.95, df=1, p=0.086		
Descemet's membrane stripped		
No	523 (16%)	305 (17%)
Yes	2188 (68%)	1089 (62%)
Not advised	504 (16%)	362 (21%)
Chi²=0.284, df=1, p=0.594		
Total	**3215 (100%)**	**1756 (100%)**

5.4.1 Descemet's membrane endothelial keratoplasty survival: influence of graft size

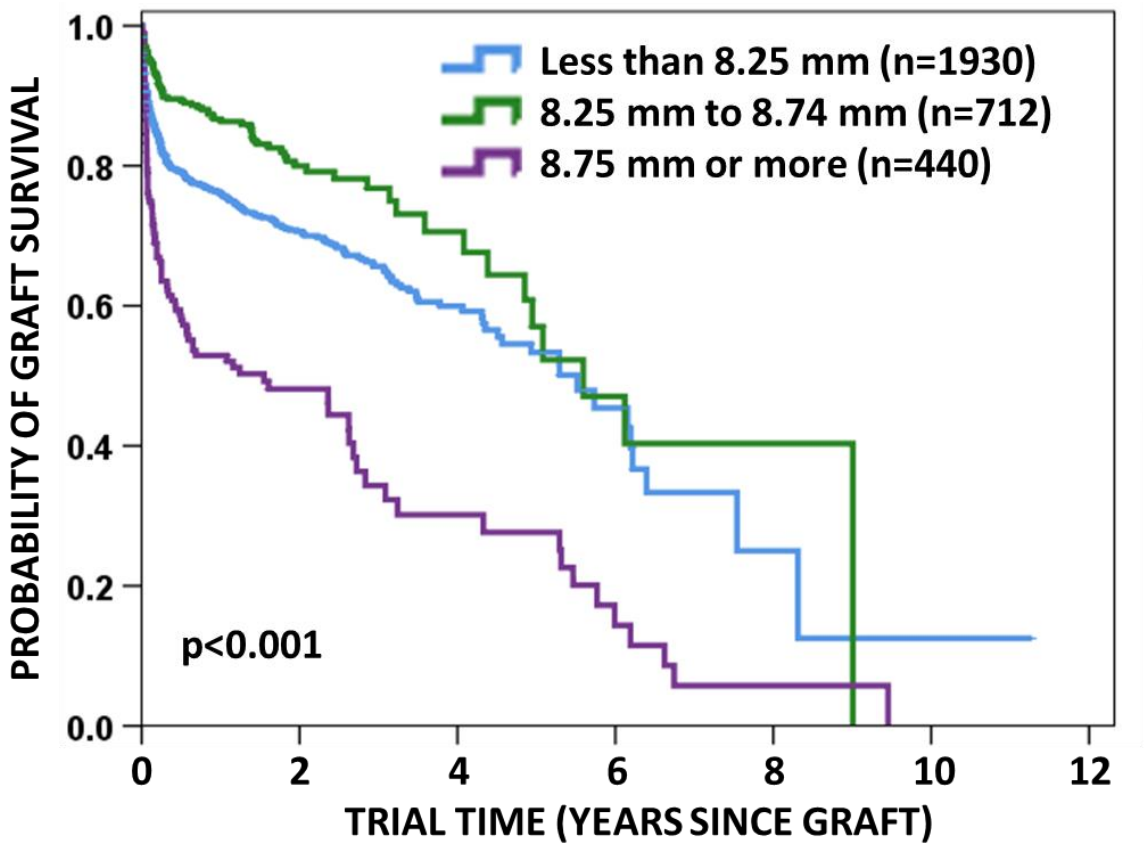
Figure 5.4.1 shows a comparison of graft survival depending on the size of the graft. Grafts were initially stratified in 0.25 mm incriments, with all grafts measuring under 8.00 mm analysed together, and all grafts measuring 8.75 mm and over analysed together. A significant difference was found across groups (Log Rank Statistic=68.81; df=4; p<0.001).

Further analyses examined whether there were significant differences between adjacent size groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=68.53; df=2; p<0.001).

Grafts measuring 8.75 mm or more had poorer survival than those measuring under 8.25 mm, or 8.25 mm to 8.74 mm (both p<0.001). Grafts that were under 8.25 mm also had poorer survival than those that were 8.25 mm to 8.74 mm (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=71.95; df=3; p<0.001). Graft size was thus categorised into these four groups for multivariate analysis. This variable was retained in the final multivariate model (see section 5.7).

Figure 5.4.1 Graft size



Number at risk (years post-graft)

	1	2	3	4	5	6
Less than 8.25 mm	638	351	195	86	43	17
8.25 mm to 8.74 mm	243	109	50	24	13	7
8.75 mm or more	66	30	17	12	11	5

Probability of graft survival (years post-graft)

	1	2	3	4	5
Less than 8.25 mm	0.76	0.71	0.66	0.60	0.53
8.25 mm to 8.74 mm	0.87	0.80	0.77	0.71	NA
8.75 mm or more	0.53	0.48	NA	NA	NA

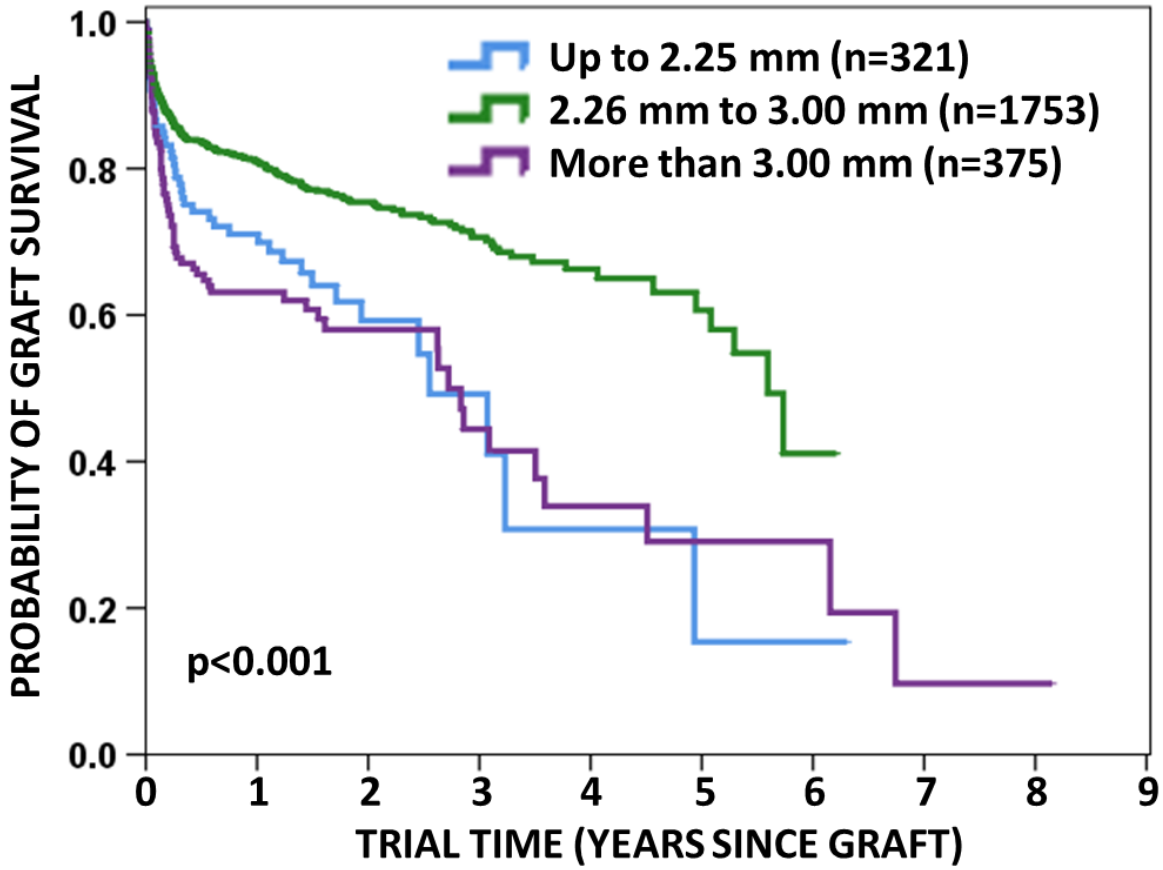
5.4.2 Descemet's membrane endothelial keratoplasty survival: influence of incision size

Figure 5.4.2 shows a comparison of graft survival depending on the size of the incision made to insert the donor lenticule, as reported by surgeons. Grafts were initially categorised in increments of 0.25 mm increases, with all grafts 2.25 mm and smaller, and all grafts over 4.00 mm, grouped together. A significant difference was found across groups (Log Rank Statistic=35.92; df=5; $p<0.001$).

Further analyses examined whether there were significant differences between adjacent size groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=32.36; df=2; $p<0.001$). Grafts with an incision size of 2.26 mm to 3.00 mm had significantly better survival than those either smaller or larger than this (both $p<0.001$).

Data on this variable were not provided in 24% 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=36.08; df=3; $p<0.001$). Incision size was thus categorised into these four groups for multivariate analysis. However, 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 5.4.2 Size of incision



Number at risk (years post-graft)

	1	2	3	4	5	6
Up to 2.25 mm	63	22	6	2	1	1
2.26 mm to 3.00 mm	588	297	159	55	24	2
More than 3.00 mm	63	33	15	9	4	4

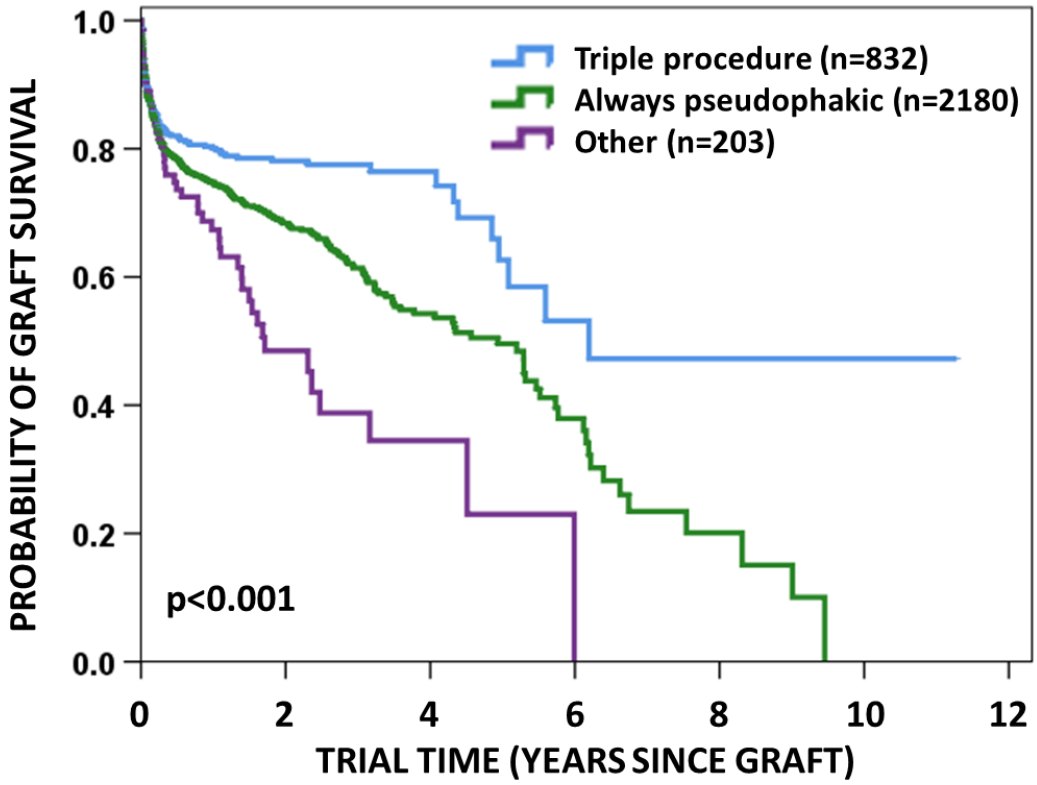
Probability of graft survival (years post-graft)

	1	2	3	4	5
Up to 2.25 mm	0.71	0.59	NA	NA	NA
2.26 mm to 3.00 mm	0.81	0.75	0.71	0.66	0.61
More than 3.00 mm	0.63	0.58	NA	NA	NA

5.4.3 Descemet's membrane endothelial keratoplasty survival: influence of change in lens status

Figure 5.4.3 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=29.21; df=2; p<0.001). Grafts performed in eyes in conjunction with cataract extraction and intraocular lens insertion (triple procedure) had significantly better survival than those performed in eyes that were already pseudophakic and remained so, or eyes that had any other combination of lens status pre- and post-graft (both p<0.001). Grafts performed in eyes that were already pseudophakic and remained so had significantly better survival than those in eyes with any other combination of lens status other than undergoing triple procedure (p<0.001). However, 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 5.4.3 Change in lens status



Number at risk (years post-graft)

	1	2	3	4	5	6	7
Triple procedure	287	158	86	37	18	9	4
Always Pseudophakic	650	333	175	86	52	21	8
Other	50	20	9	5	1	NA	NA

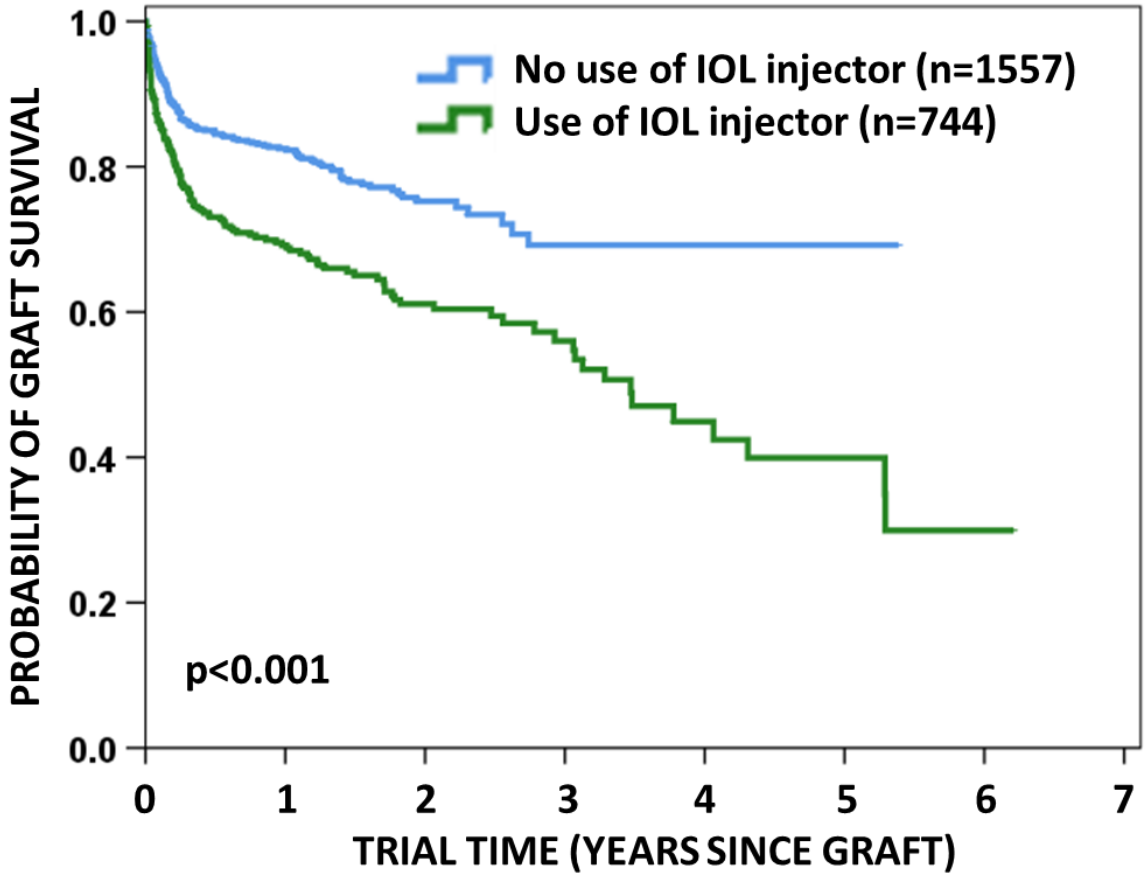
Probability of graft survival (years post-graft)

	1	2	3	4	5	6
Triple procedure	0.80	0.78	0.78	0.76	NA	NA
Always Pseudophakic	0.75	0.68	0.61	0.54	0.50	0.38
Other	0.67	0.49	NA	NA	NA	NA

5.4.4 Descemet's membrane endothelial keratoplasty survival: influence of use of IOL injector

Figure 5.4.4 shows the comparison for survival of grafts where an IOL injector was used in comparison with grafts where one was not. A significant difference was found across groups (Log Rank Statistic=24.12; df=1; p<0.001). Data on this variable were not provided in 28% 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=26.97; df=2; p<0.001). Use of IOL injector was thus categorised into these three groups for multivariate analysis. However, 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 5.4.4 Use of IOL injector



Number at risk (years post-graft)

	1	2	3	4
No use of IOL injector	399	126	35	5
Use of IOL injector	187	90	44	17

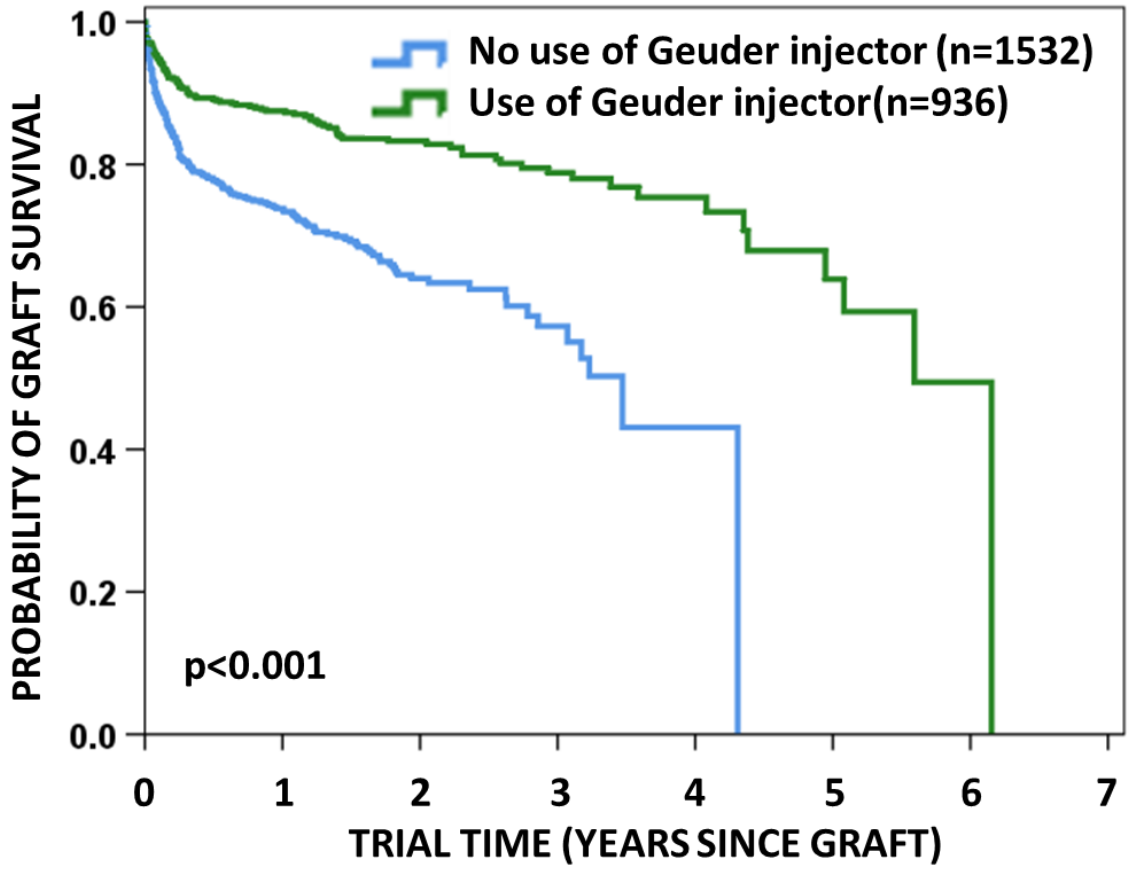
Probability of graft survival (years post-graft)

	1	2	3
No use of IOL injector	0.83	0.75	0.69
Use of IOL injector	0.69	0.61	0.56

5.4.5 Descemet's membrane endothelial keratoplasty survival: influence of use of Geuder injector

Figure 5.4.5 shows the comparison for survival of grafts where a Geuder injector was used in comparison with grafts where one was not. A significant difference was found across groups (Log Rank Statistic=40.07; df=1; p<0.001). Data on this variable were not provided in 23% 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=59.36; df=2; p<0.001). Use of Geuder injector was thus categorised into these three groups for multivariate analysis. This variable was retained in the final multivariate model (see section 5.7).

Figure 5.4.5 Use of Geuder injector



Number at risk (years post-graft)

	1	2	3	4	5
No use of Geuder injector	320	109	32	4	NA
Use of Geuder injector	387	199	112	39	15

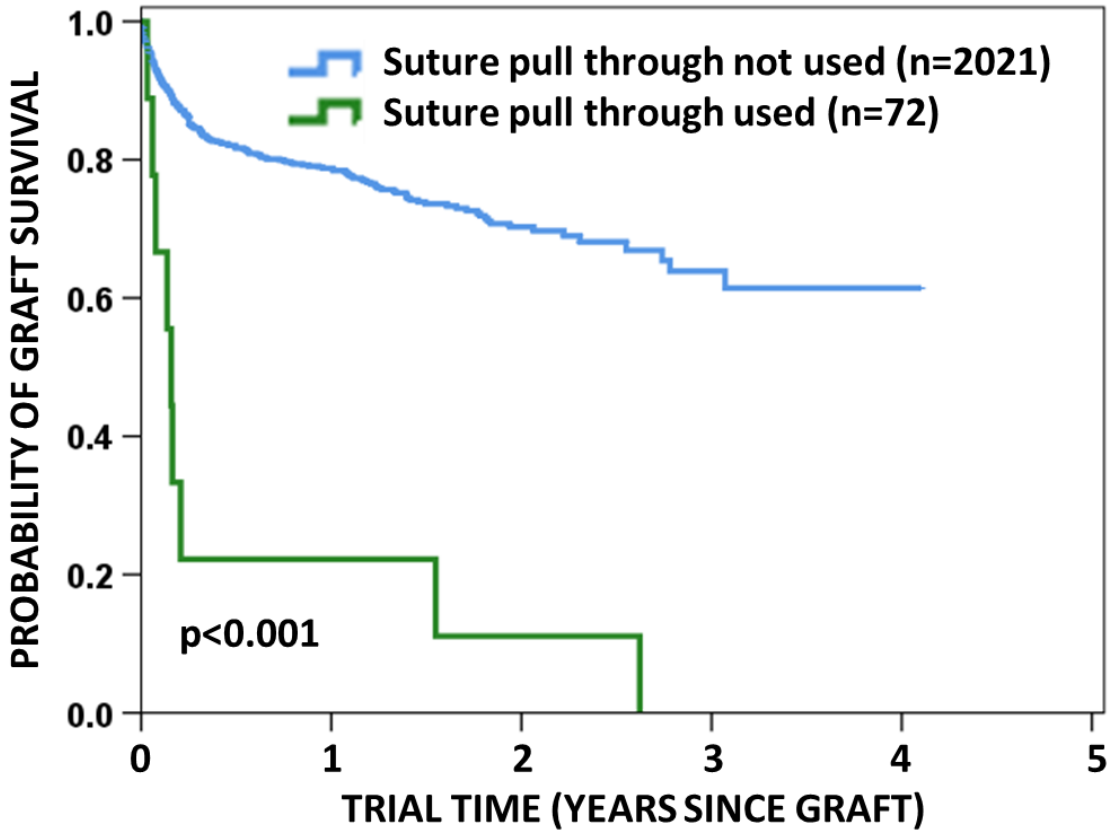
Probability of graft survival (years post-graft)

	1	2	3	4
No use of Geuder injector	0.74	0.64	0.57	NA
Use of Geuder injector	0.88	0.83	0.79	0.75

5.4.6 Descemet's membrane endothelial keratoplasty survival: influence of use of suture pull through technique

Figure 5.4.6 shows the comparison for survival of grafts where the suture pull through technique was used in comparison with grafts where it was not. A significant difference was found across groups (Log Rank Statistic=25.94; df=1; p<0.001). Data on this variable were not provided in 35% 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=21.82; df=2; p<0.001). Use of suture pull through technique was thus categorised into these three groups for multivariate analysis. However, 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 5.4.6 Suture pull through



Number at risk (years post-graft)

	1	2	3	4
No suture pull not used	479	135	32	1
Suture pull through used	2	1	NA	NA

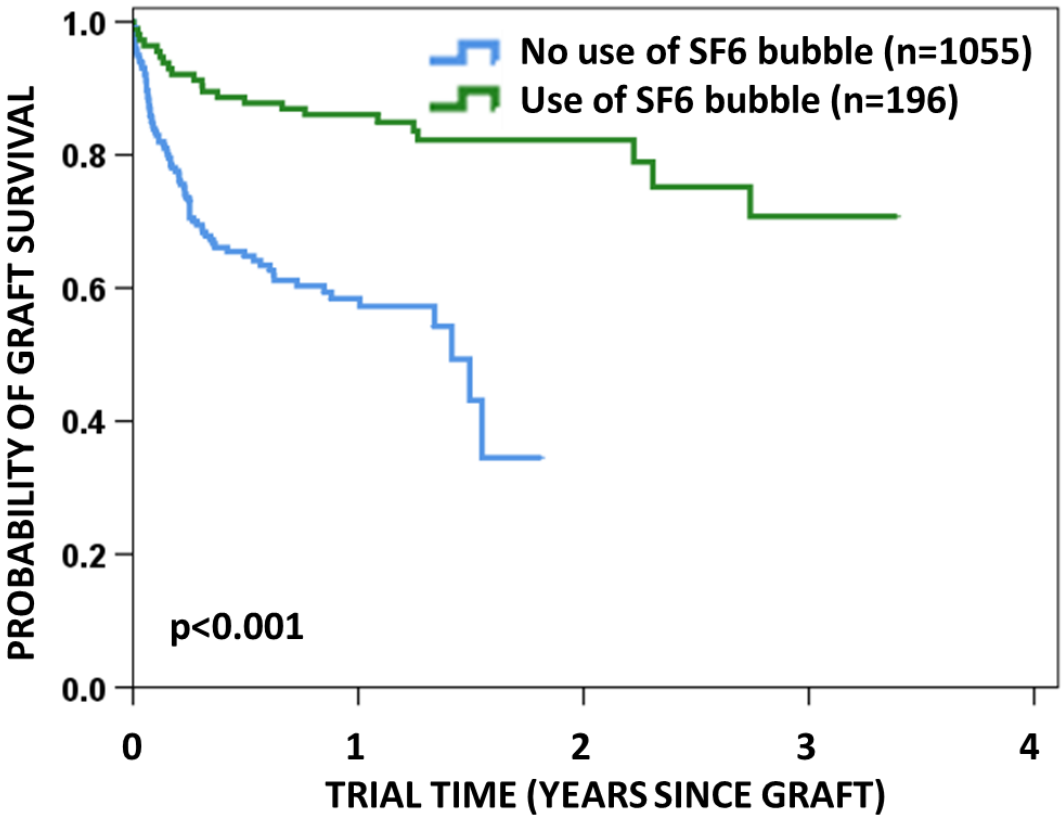
Probability of graft survival (years post-graft)

	1	2	3
No suture pull not used	0.79	0.70	0.64
Suture pull through used	NA	NA	NA

5.4.7 Descemet's membrane endothelial keratoplasty survival: influence of use of SF6 bubble

Figure 5.4.7 shows the comparison for survival of grafts where a SF6 bubble technique was used in comparison with grafts where one was not. A significant difference was found across groups (Log Rank Statistic=28.05; df=1; p<0.001). Data on this variable were not provided in 61% of cases. This variable was excluded from the multivariate analysis (see section 5.7) due to the high amount of missing data (61%).

Figure 5.4.7 Use of SF6 bubble



Number at risk (years post-graft)

	6m	1	2	3
No SF6 bubble	97	50	NA	NA
SF6 bubble	102	92	37	10

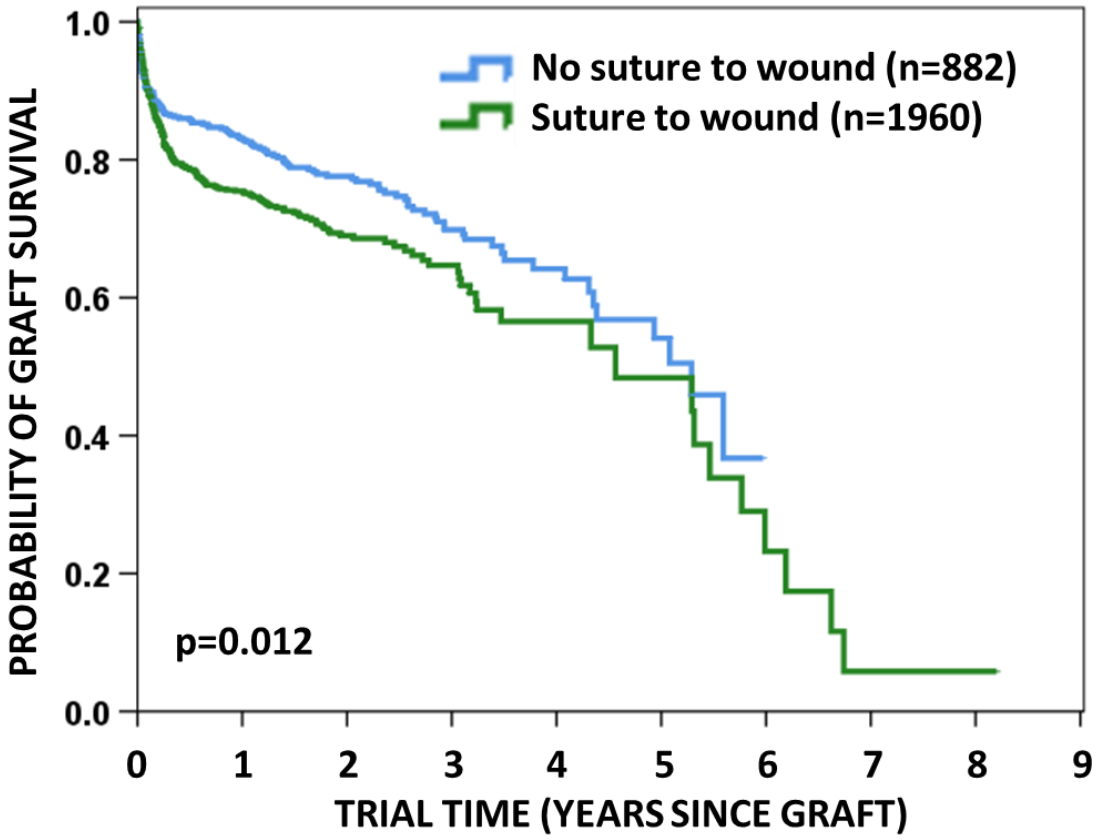
Probability of graft survival (years post-graft)

	6m	1	2
No SF6 bubble	0.65	0.58	NA
SF6 bubble	0.88	0.86	0.82

5.4.8 Descemet's membrane endothelial keratoplasty survival: influence of use of suture to close wound

Figure 5.4.8 shows the comparison for survival of grafts where a suture was used to close the wound in comparison with grafts where one was not. A significant difference was found across groups (Log Rank Statistic=6.26; df=1; p=0.012). Data on this variable were not provided in 12% 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=18.32; df=2; p<0.001). Use of suture to close the wound was thus categorised into these three groups for multivariate analysis. However, 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 5.4.8 Use of suture to close wound



Number at risk (years post-graft)

	1	2	3	4	5
No suture used to close wound	350	217	112	47	17
Suture used to close wound	470	176	76	21	10

Probability of graft survival (years post-graft)

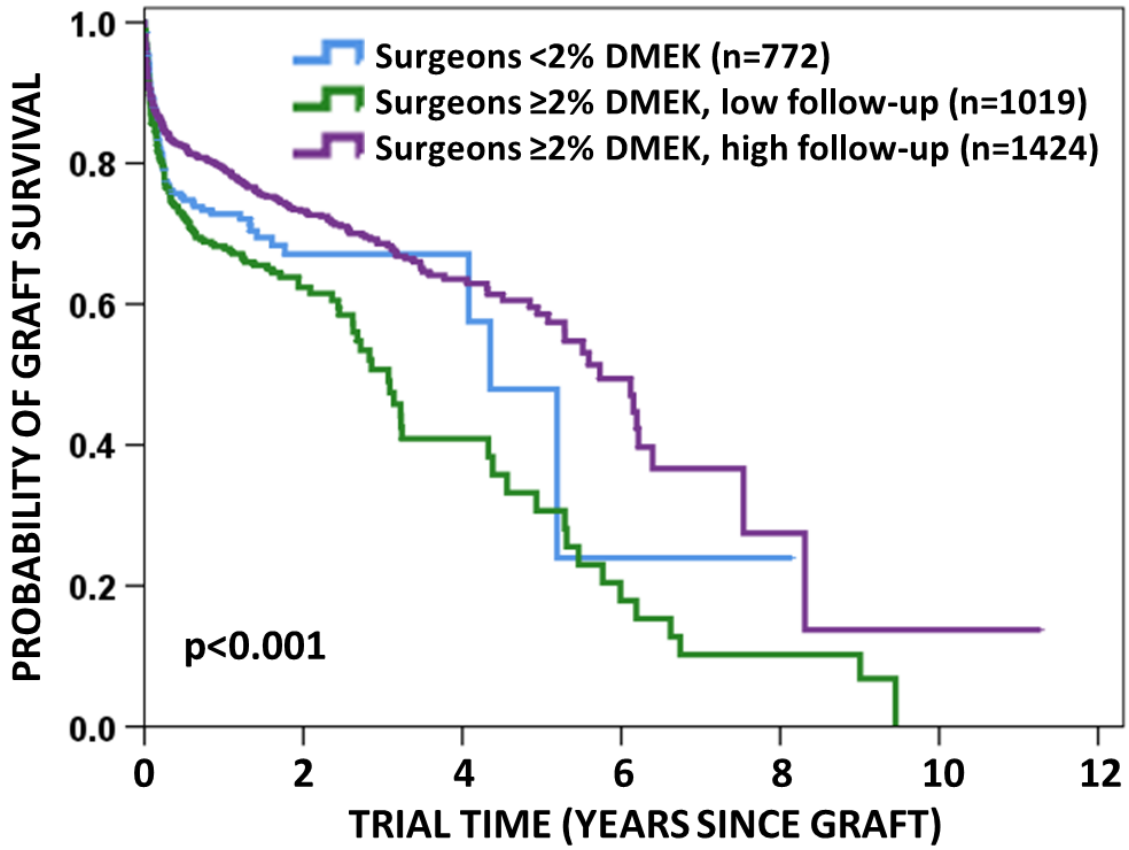
	1	2	3	4
No suture used to close wound	0.83	0.78	0.70	0.64
Suture used to close wound	0.76	0.69	0.65	0.57

5.4.9 Descemet's membrane endothelial keratoplasty survival: influence of surgeon volume grouped by level of follow-up

Figure 5.4.9 shows the comparison of graft survival between grafts performed by surgeons with 65+ (≥2%) registered Descemet's membrane endothelial keratoplasties with average or better (≥55%) follow-up, to those with lower than average follow-up (<55%), and to surgeons with fewer than 65 (<2%) registered Descemet's membrane endothelial keratoplasties (Log Rank Statistic=32.98; df=2; p<0.001).

Survival of grafts performed by high caseload surgeons with average or better follow-up was significantly better than that of grafts performed by high caseload surgeons with below average follow-up (p<0.001), and of grafts performed by low caseload surgeons (p=0.013). This variable was retained in the final multivariate model (see section 5.7).

Figure 4.4.9 Surgeon caseload and level of follow-up



Number at risk (years post-graft)

	1	2	3	4	5	6	7
<2% registered DMEK	163	52	21	9	3	1	1
≥2% DMEK, low follow-up	170	76	33	17	12	7	4
≥2% DMEK, high follow-up	654	383	217	102	56	22	7

Probability of graft survival (years post-graft)

	1	2	3	4	5	6
<2% registered DMEK	0.72	0.65	0.61	NA	NA	NA
≥2% DMEK, low follow-up	0.66	0.61	0.49	NA	NA	NA
≥2% DMEK, high follow-up	0.80	0.74	0.70	0.65	0.60	0.50

5.5 Operative procedures at the time of graft

Table 5.8 shows the number of grafts for which specified operative procedures were performed at the time of graft. This did not include cataract extraction, pseudophakic IOL insertion, or pseudophakic IOL extraction, as these were covered by the variable relating to change in lens (see section 5.4.3). The comparison of survival for grafts that had undergone another operative procedure at graft and those that had not was non-significant (Log Rank Statistic=0.12; df=1; p=0.725).

Table 5.8 Operative procedures at the time of graft

Descemet's Membrane Endothelial Keratoplasty

Operative Procedures at Time of Graft

	Number
Peripheral iridectomy	328
Vitrectomy	37
Pseudophakic IOL exchanged	11
Piggyback IOL inserted	10
Keratectomy	9
Pupilloplasty	7
Glaucoma tube inserted (Molteno: 3, iStent: 2, Baerveldt: 1)	6
Synechiolysis	6
Glaucoma tube repositioned	4
Glaucoma tube trimmed	3
Other*	28
Total operative procedures (number of grafts)	**449 (424)**

*Other included: biopsy (2), EDTA chelation (2), epithelial debridement (2), IOL repositioned (2), iridoplasty (2), removal of phakic IOL (2), removal of retrocorneal membrane (2), artificial iris segment inserted (1), Avastin injection (1), coreoplasty (1), iridectomy (1), relaxing incisions (1), removal of fibrous tissue (1), removal of piggyback IOL (1), removal of pupillary membrane (1), removal of residual lens material (1), removal of Salzmann nodule (1), removal of scar tissue (1), removal of unspecified corneal tissue (1), trabeculectomy (1), scleral patch graft (1).

5.6 Post-graft Events

Table 5.9 shows post-graft surgical procedures, as reported by follow-up practitioners. 520 Descemet's membrane endothelial keratoplasties were reported to have undergone a re-grafting procedure at the date last seen. Of these, 438 had not had additional post-graft operative procedures reported.

Table 5.9 Post-graft surgical procedures

Descemet's Membrane Endothelial Corneal Graft

Post-graft Surgical Procedures

	Number
Rebubbled	377
YAG laser	90
Trabeculectomy	30
Intravitreal/intracameral/conjunctival injection/s*	27
Cataract removal and IOL insertion	26
Vitrectomy	23
IOL repositioned/removed/exchange	13
Membrane peel	8
Insertion of piggyback lens	7
IOL insertion (cataract removed prior to graft)	6
Tube insertion (Baerveldt: 3, unspecified:2)	5
Keratectomy	5
Other**	52
Total number of surgical procedures (number of grafts)	***669 (544)***

*Avastin (19), Triamcinolone (2), Anti-VEGF (1), Eylea (1), Lucentis (1), unspecified steroid (1), unspecified (2).

** Other included: iridectomy (4), ptosis repair (4), blepharoplasty (3), cyclodiode laser (3), implantable contact lens (3), paracentesis (3), removal of scar (3), unspecified glaucoma surgery (3), bleb needling (2), PTK laser (2), removal of air bubble (2), removal of piggyback IOL (2), retinal detachment surgery (2), tarsorrhaphy (2), removal of chalazion (1), corneal collagen cross linking (1), corneal scraping (1), diabetic PRP laser (1), entropion repair (1), graft repositioned (1), iridoplasty (1), removal of cyst (1), removal of lid lesion (1), removal of pupilary membrane (1), selective laser trabeculoplasty (1), suturing of IOL (1), synechiolysis (1), vitrial tap (1).

Table 5.10 shows the occurrence of post-graft events, which were found to be **significant** in univariate analyses. Only 44 grafts had post-graft interface opacity reported, 10 had microbial keratitis, seven had herpetic infection, and six had uveitis, so the impact of these factors was not further analysed. Please note: post-graft data may be incomplete when follow-up is based on a registration for a replacement graft.

Table 5.10 Post-graft events, significant in univariate analyses

Descemet's Membrane Endothelial Keratoplasty

Post-graft Events

	Registered (%)	Followed (%)
Post-graft neovascularisation		
No	**3122 (97%)**	**1663 (95%)**
Yes	**93 (3%)**	**93 (5%)**
At least one rejection episode		
No	3136 (98%)	1677 (96%)
Yes	79 (2%)	79 (4%)
Total	***3215 (100 %)***	***1756 (100 %)***

Table 5.11 shows the occurrence of post-graft events, which were found to be **non-significant** in univariate analysis and the corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable. The sum of these numbers for each variable equals the total number of grafts (3,215 registered and 1,756 followed) and the percentages, which should be summed vertically for each variable, total 100.

Table 5.11 Post-graft events, not significant in univariate analyses

Descemet's Membrane Endothelial Keratoplasty

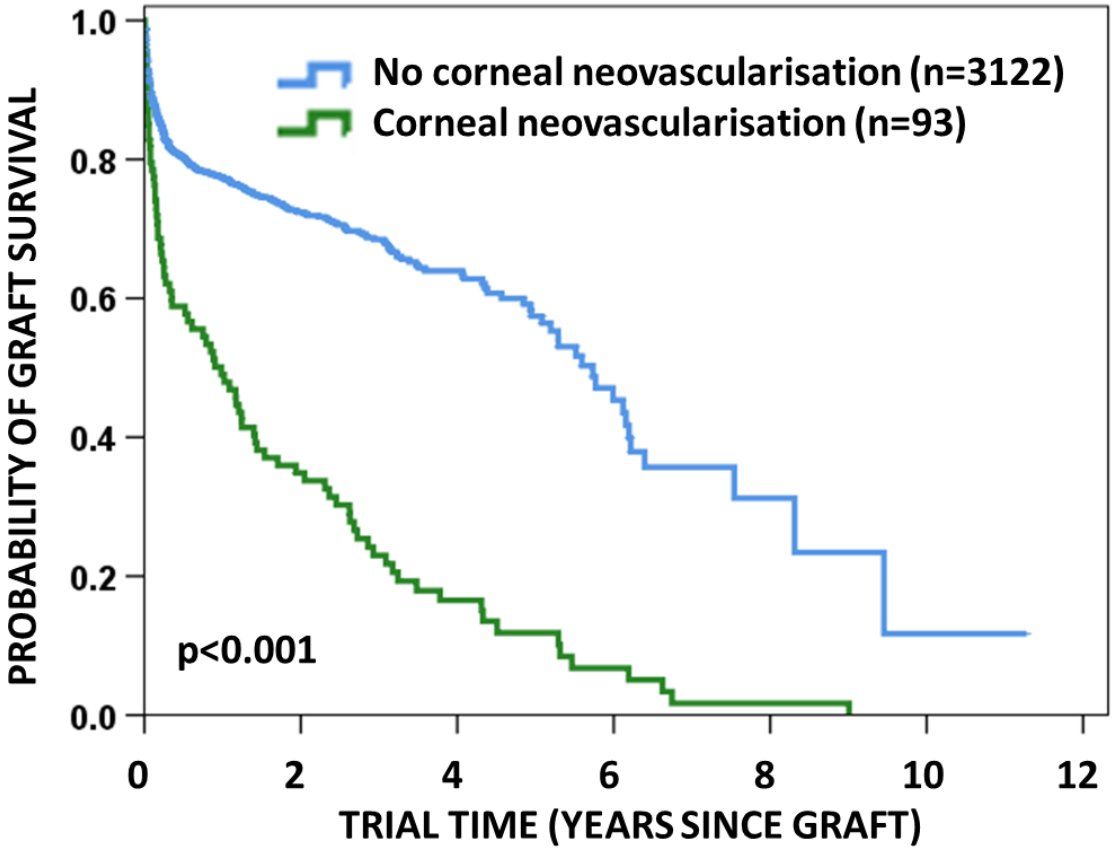
Post-graft Events

	Registered (%)	Followed (%)
Time to removal of sutures		
Sutures not removed or no date given	3032 (94%)	1573 (90%)
Within 2 months	112 (3%)	112 (6%)
More than 2 months	71 (2%)	71 (4%)
Chi²=0.034, df=1, p=0.854		
Post-graft oedema		
No	2911 (91%)	1452 (83%)
Yes	304 (9%)	304 (17%)
Chi²=0.000, df=1, p=0.987		
Post-graft rise in intraocular pressure		
No	3064 (95%)	1605 (91%)
Yes	151 (5%)	151 (9%)
Chi²=0.000, df=1, p=0.985		
Total	***3215 (100 %)***	***1756 (100 %)***

5.6.1 Descemet's membrane endothelial keratoplasty survival: influence of post-graft corneal neovascularisation

Figure 5.6.2 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=110.00, df=1, p<0.001). This variable was retained in the final multivariate model (see section 5.7).

Figure 4.6.1 Post graft corneal neovascularisation



Number at risk (years post-graft)

	1	2	3	4	5	6	7
No neovascularisation	942	480	251	116	64	26	11
Neovascularisation	45	31	19	12	7	4	1

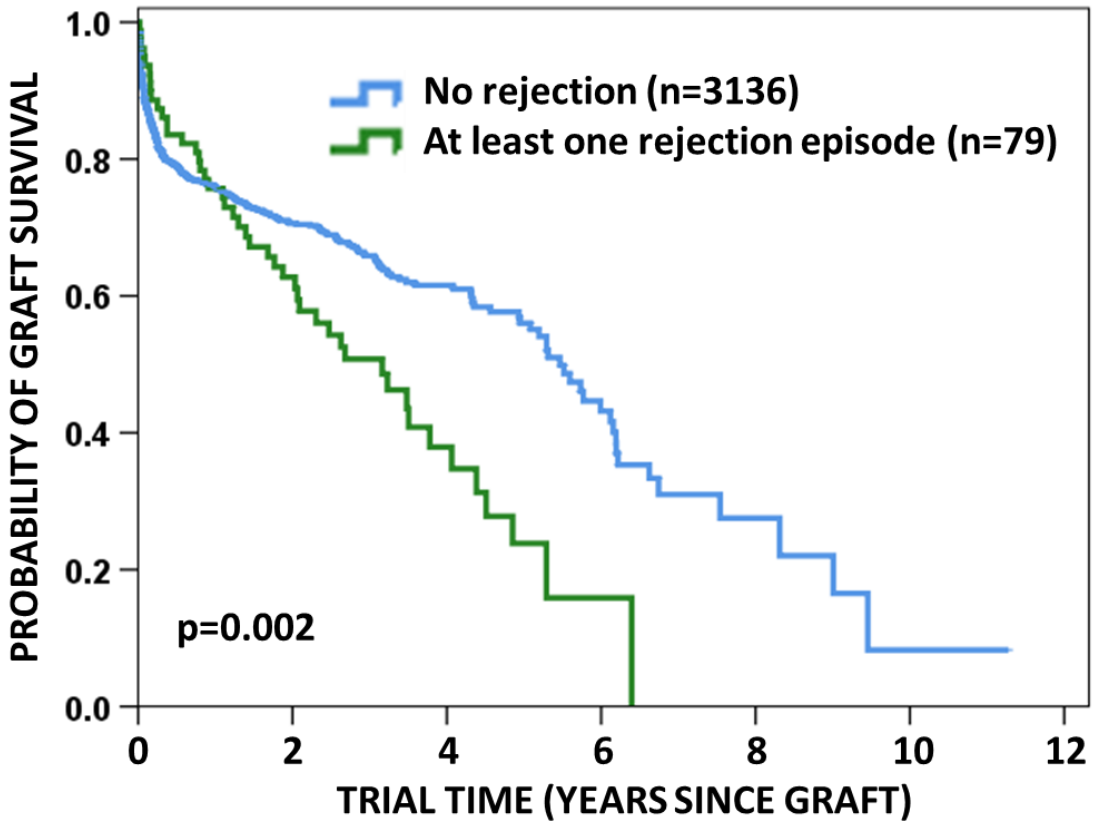
Probability of graft survival (years post-graft)

	1	2	3	4	5	6
No neovascularisation	0.77	0.72	0.69	0.64	0.57	0.45
Neovascularisation	0.49	0.35	NA	NA	NA	NA

5.6.2 Descemet's membrane endothelial keratoplasty survival: influence of post-graft rejection episodes

Figure 5.6.2 shows the comparison of graft survival for grafts with no rejection episodes compared to those with one or more rejection episodes. A significant difference was found between groups (Log Rank Statistic=9.25, df=1, p=0.002). However, 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 5.6.2 Post graft influence of post-graft rejection episodes



Number at risk (years post-graft)

	1	2	3	4	5	6	7
No rejection episode	930	473	245	115	66	29	12
Any rejection episode	57	38	26	13	5	1	NA

Probability of graft survival (years post-graft)

	1	2	3	4	5	6
No rejection episode	0.76	0.71	0.66	0.62	0.56	0.43
Any rejection episode	0.76	0.63	0.51	NA	NA	NA

5.7 Multivariate Analysis

A multivariate model was used to investigate the combined effect of variables on Descemet's membrane endothelial graft survival, adjusted for all other variables in the model (see section 1.4.6 for further information).

Table 5.12 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. Some variables that were found to be significant in the univariate analyses were excluded from the multivariate model as they were found to be collinear with (i.e. were highly correlated and produced the same effect on the outcome as) another variable in the model.

Table 5.12 Multivariate model

Descemet's Membrane Endothelial Keratoplasty

Multivariate Model

Not significant in univariate analysis

- Cause of donor death
- Eye only donor
- Central endothelial cell count
- Time from donor death to enucleation of donor tissue
- Time from storage of donor tissue to graft – Optisol
- Time in deswelling media for tissue stored in organ culture media
- Eye grafted
- Use of glide during insertion
- Use of anterior chamber maintainer
- Use of viscoelastic
- Donor lenticule folded
- Stripping of recipient Descemet's membrane by surgeon
- Other operative procedure at graft
- Time to removal of sutures
- Post-graft corneal oedema
- Post-graft rise in intraocular pressure

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

- The centre effect (collinear with surgeon experience and level of follow-up)
- Australian State in which graft was performed (collinear with eye bank and interstate transportation of donor cornea)
- Donor sex (collinear with donor/recipient sex match/mismatch)
- Recipient sex (collinear with donor/recipient sex match/mismatch)
- Use of SF6 bubble during insertion of donor button (missing data)

Significant in univariate analysis but not retained in multivariate model

- Use of suture to close wound
- Recipient age group
- Pre-graft inflammation and/or steroid use
- Pre-graft corneal neovascularisation
- Donor cornea pre-cut by eye bank
- Indication for graft
- Number of previous ipsilateral grafts
- Use of suture pull through technique
- Change in lens status from pre- to post-graft
- Raised intraocular pressure in past and/or at graft
- Any post-graft rejection
- Time from enucleation to storage of donor tissue
- Incision size
- Time from storage of donor tissue to graft – organ culture
- Use of IOL injector during insertion
- Interstate transportation of donor cornea
- Storage medium
- Number of pervious contralateral grafts

Significant in univariate analysis AND retained in multivariate model

- Eye bank
- Donor age group
- Donor/recipient sex match/mismatch
- Graft era/year
- Graft size
- Use of Geuder injector during insertion
- Surgeon caseload and level of follow-up
- Post-graft corneal neovascularisation

Table 5.13 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 first level of each categorical variable was taken as the referent, except where it made logical sense to use a different group.

The hazard ratios for a given variable are adjusted for all other variables in the model. This model included data from 3,215 Descemet's membrane endothelial keratoplasties, performed in 2,307 recipients. Where no valid response had been provided for one of the included variables, these cases were classified as "not advised" and these categories were included where 2% of cases were included in this group. The overall model was highly significant: (Chi^2=384.48, p<0.0001).

Table 5.13 Clustered multivariate model

	n	Hazard ratio	Standard Error	p-value	Global p-value	95% Confidence Interval
Eye Bank						
Referent Eye Bank		1.00			<0.0001	
		2.11	0.83	0.053		0.98 to 4.56
		2.13	0.75	0.031		1.07 to 4.24
		3.86	1.34	<0.001		1.96 to 7.62
Range of n (144 to 1415)		4.21	1.66	<0.001		1.94 to 9.12
Donor age group						
0 to 49	167	1.62	0.25	0.002		1.20 to 2.21
50 to 59	555	1.18	0.13	0.144		0.95 to 1.46
60 to 79	2275	1.00			0.0094	
80 or older	218	1.25	0.20	0.156		0.92 to 1.70
Donor/recipient sex match/mismatch						
Female/Female	670	1.44	0.17	0.002		1.15 to 1.80
Female/Male	543	1.65	0.21	<0.001		1.29 to 2.11
Male/Female	1137	1.00			0.0004	
Male/Male	865	1.26	0.14	0.039		1.01 to 1.58
Graft era/year (tvc)						
Pre 2015	582	2.13	0.40	<0.001		1.47 to 3.08
2015 to 2018	1486	1.00			<0.0001	
2019	585	1.70	0.25	<0.001		1.27 to 2.26
2020	562	4.33	0.88	<0.001		2.91 to 6.46
Graft size						
Less than 8.25mm	1930	1.50	0.21	0.004		1.14 to 1.97
8.25mm to 8.74mm	712	1.00			0.0011	
8.75mm or more	440	1.91	0.33	<0.001		1.35 to 2.69
Not advised	133	1.76	0.37	0.007		1.16 to 2.71
Geuder injector used						
No	1532	1.97	0.32	<0.001		1.43 to 2.71
Yes	936	1.00			0.0002	
Unknown	747	1.77	0.38	0.008		1.16 to 2.71
Surgeon caseload and level of follow-up						
Low caseload surgeons	772	1.70	0.23	<0.001		1.31 to 2.21
High caseload, low follow-up	1019	1.73	0.24	<0.001		1.31 to 2.28
High caseload, high follow-up	1424	1.00			<0.0001	
Post-graft corneal neovascularisation (tvc)						
No	3122	1.00			<0.0001	
Yes	93	1.98	0.31			1.46 to 2.69

Note: tvc = time variant coefficient

5.7.1 Significant differences in the Descemet's membrane endothelial keratoplasty multivariate model for categories with more than two groups following Holm-Bonferroni correction for multiple comparisons

5.7.1.1 Donor age group

Grafts performed using corneas from donors aged under 50 years of age had significantly poorer outcomes that those performed using corneas from donors aged 60 to 79 years (p=0.002).

5.7.1.2 Donor/recipient sex match/mismatch

Grafts performed in female recipients using corneas from male donors had significantly better outcomes that those performed in male recipients using corneas from female donors (p<0.001) and those performed in female recipients using corneas from female donors (p=0.002).

5.7.1.3 Graft era/year

Grafts performed from 2015 to 2018 had significantly better survival than those performed prior to 2015, in 2019, or in 2020 (all p<0.001).

Grafts performed in 2020 also had significantly poorer survival than those performed prior to 2015 (p=0.008) and in 2019 (p<0.001).

5.7.1.4 Graft size

Survival of grafts that were 8.24mm to 8.74 mm was significantly better than those that were 8.75 mm or larger (p<0.001), or less than 8.25 mm (p=0.004).

5.7.1.5 Use of Geuder injector

Grafts where a Gueder injector was used to insert the donor lenticule had significantly better survival than those where it was not (p<0.001).

5.7.1.6 Caseload of DMEK registered by surgeon and level of follow-up received

Grafts performed by surgeons with 65 or more (≥2% of the cohort) DMEK registered with the ACGR and above average (>55%) levels of follow-up had significantly better survival than grafts performed by surgeons with 65 or more DMEK registered with the ACGR, and below average (≤55%) levels of follow-up, and grafts performed by surgeons with fewer than 65 DS(A)EK registered with the ACGR (both p<0.001).

5.8 Reasons for Graft Failure

Of the 1,756 followed grafts, 564 (32%) were known to have failed by the census date. This equates to 18% of the 3,215 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 5.14 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 5.14 Reasons for graft failure

Descemet's Membrane Endothelial Keratoplasty
Reasons for Graft Failure

Primary graft failure	299 (53%)
Endothelial cell failure	157 (28%)
Rejection	29 (5%)
Graft detachment	12 (2%)
Non herpetic infection	10 (2%)
Scarring	6 (1%)
Other specified*	16 (3%)
Unspecified	35 (6%)
Total	***564 (100%)***

Other included: Descemet's folds/wrinkles (4), epithelial/limbal stem cell failure (2), trauma (2), wound dehiscence (2), anterior synechia (1), corneal melt (1), glaucoma (1), herpetic infection (1), phthisical eye (1), retained Descemet's membrane (1),

Of the 299 grafts reported by surgeons to have been primary graft failures, 134 had no further information provided. Specific reasons given were: detachment of Descemet's membrane (115), endothelial failure (17), surgical trauma (14), upside-down insertion (6), rejection (5), Descemet's folds (4), corneal ulcer (1), endophthalmitis (1), fungal keratitis (1), haemorrhage (1).

5.9 Post-graft Changes in Best Corrected Visual Acuity

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 3,031 (94%) of registered Descemet's membrane endothelial keratoplasties. In 91% of cases (2,789), this was the sole desired outcome indicated. All analyses are conducted on data for **surviving** grafts. See section 1.4.7 for further explanation of the methods used to analyse visual acuity data.

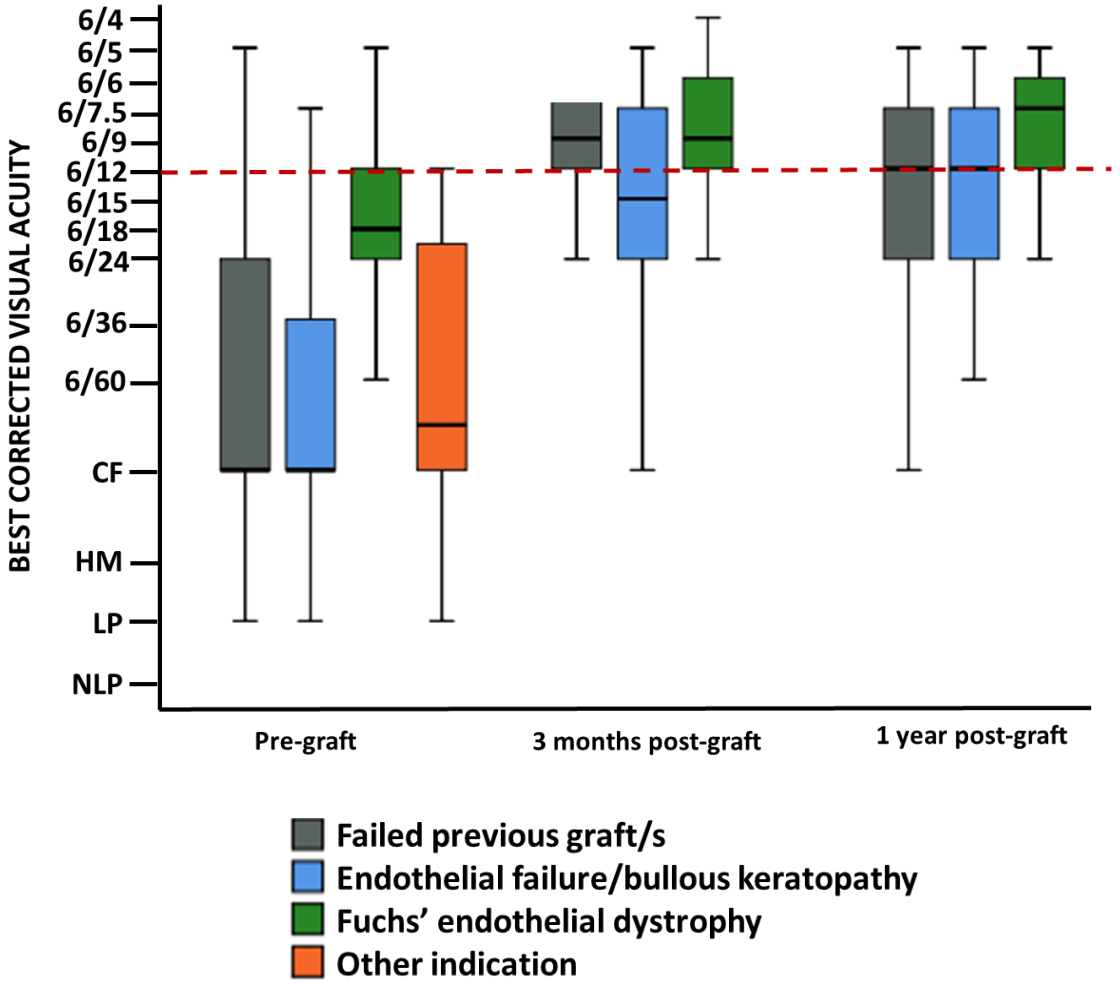
5.9.1 Descemet's membrane endothelial keratoplasty: One-year post-graft visual acuity change by indications for graft

Figure 5.9.1 shows the pre-graft best corrected visual acuity, and the three-month and one-year post-graft best corrected visual acuity, reported for eyes undergoing Descemet'smembrane endothelial keratoplasty for each of the indication for graft groups. The central line within each box-and-whisker plot shows the median BCVA reported for the group, the box represents the inter-quartile range, while the whisker shows the range. Please note that outliers were included in the calculation of the box and whisker plots but are not shown in the figures. The dashed line indicates a BCVA of 6/12, which represents functional vision.

Median pre-graft BCVA was best for grafts for Fuchs' endothelial dystrophy (6/18). Grafts performed for endothelial failure/bullous keratopathy, and repeat grafts, had median pre-graft BCVA of Count Fingers. At 3-months post-graft, there had been a significant improvement in BCVA for the three, individual, indication for graft groups (all $p<0.001$). There were an insufficient number of grafts performed for "other" indications with post-graft visual acuity data available to make any comparisons. Repeat grafts and grafts for Fuchs' endothelial dystrophy reached a median BCVA of 6/9, while grafts for endothelial failure/bullous keratopathy had reached a median BCVA of 6/15.

At one-year post-graft, the improvement in BCVA remained significant at the $p<0.001$ level for all individual indication groups. Grafts for Fuchs' endothelial dystrophy had a further improvement of median BCVA, reaching 6/7.5 at this time point. Median BCVA for grafts for endothelial failure/bullous keratopathy also improved further, reaching a median BCVA of 6/12, while that for repeat grafts dropped back to 6/12.

Figure 5.9.1 Best corrected visual acuity pre-graft, and three-months and one-year post-graft



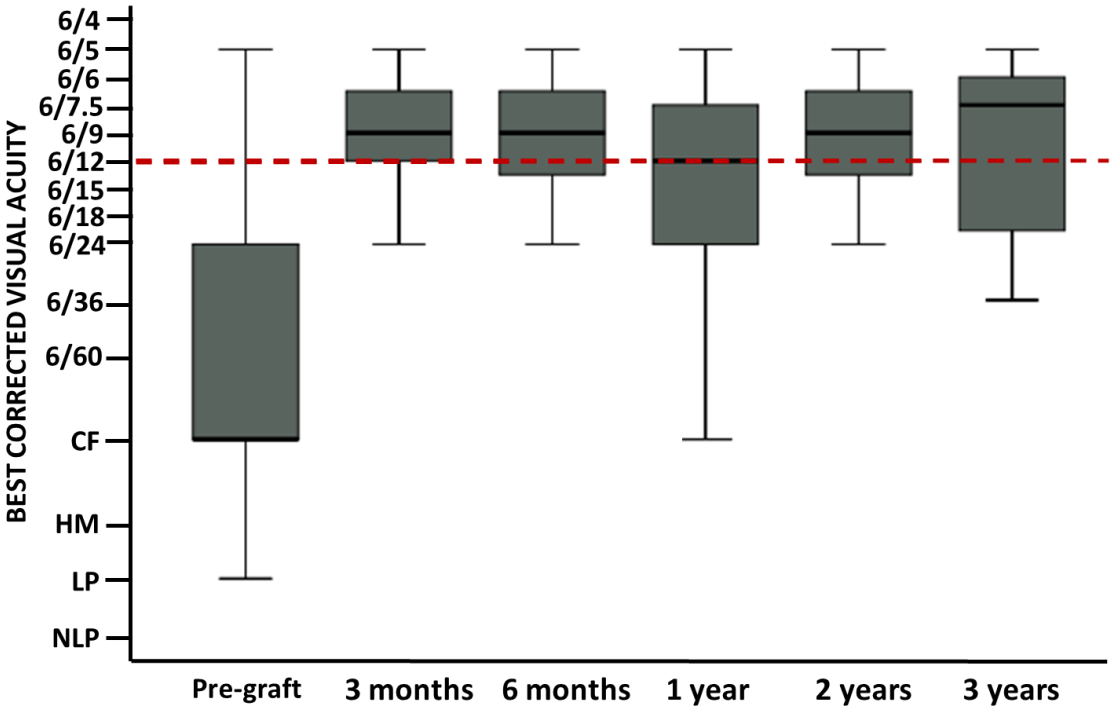
Number of grafts with BCVA available at each time point

	Pre	3m	6m	1y	2y	3y	4y	5y
Failed previous graft/s	684	27	23	53	31	15	7	3
Endothelial failure/bullous keratopathy	470	18	20	41	21	5	3	1
Fuchs' endothelial dystrophy	1824	85	69	156	74	49	11	10
Other	40	0	1	5	2	1	0	0

The figures on pages 240 to 242 look at the median BCVA achieved over time for individual indications for graft.

5.9.2 Descemet's membrane endothelial keratoplasty: Changes in best corrected visual acuity over time by individual indications for graft

Figure 5.9.2 Best corrected visual acuity for surviving Descemet's membrane endothelial keratoplasties performed for failed previous graft/s, over time



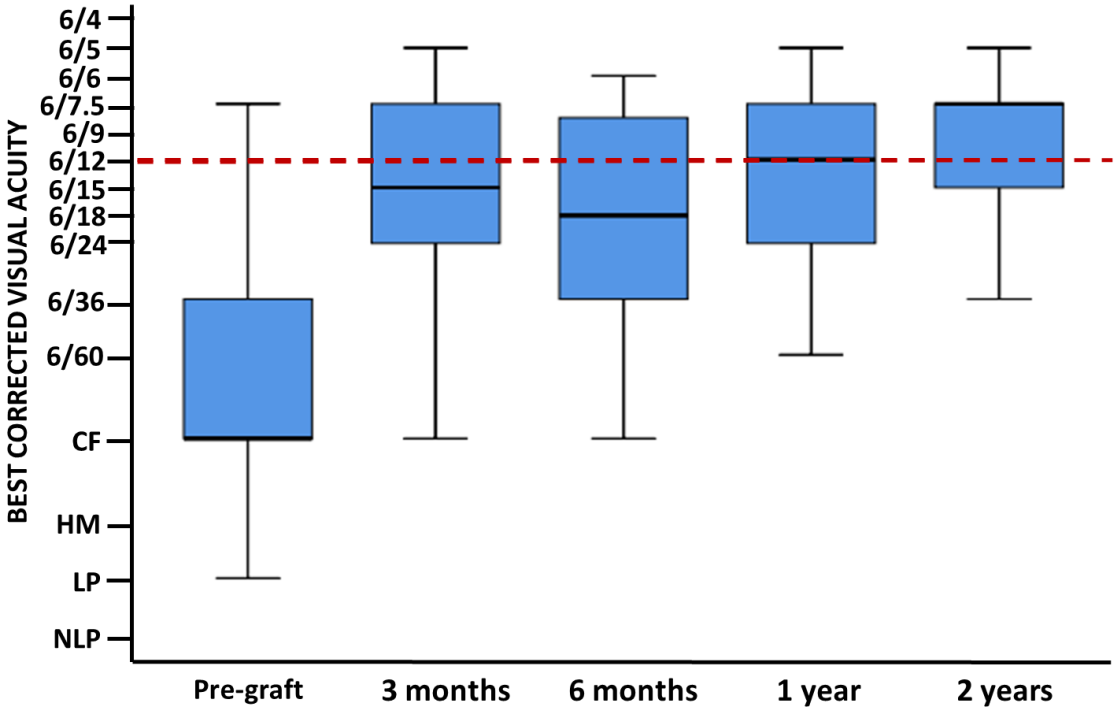
Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y
684	27	23	53	31	15

The median BCVA obtained following Descemet's membrane endothelial keratoplasty for failed previous graft/s improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). There were no significant changes in median BCVA after 3-months post-graft. The difference compared to pre-graft BCVA remained significant to 3-years post-graft (all $p<0.001$).

Surviving Descemet's membrane endothelial keratoplasties performed for failed previous graft/s, had a median BCVA of 6/9 by 3-months post graft. This dropped back to 6/12 at 1-year post-graft, which was the time point with the most post-graft BCVA data available. Median BCVA had improved again to 6/9 at 2-years and reached 6/7.5 for the 15 surviving grafts that had data available at 3-years post-graft.

Figure 5.9.3 Best corrected visual acuity for surviving Descemet's membrane endothelial keratoplasties performed for endothelial failure/bullous keratopathy, over time



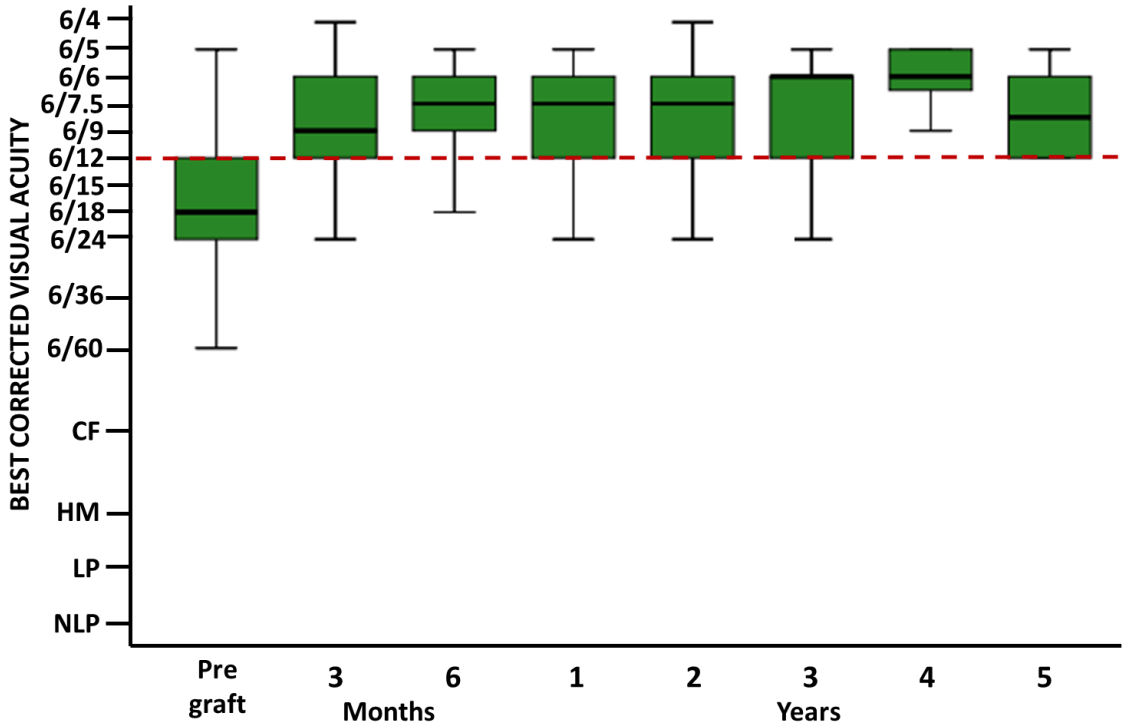
Number of grafts with data at each time point

Pre	3m	6m	1y	2y
470	18	20	41	21

The median BCVA obtained following Descemet's membrane endothelial keratoplasty for endothelial failure/bullous keratopathy improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). This difference did not improve significantly again. The difference compared to pre-graft BCVA remained significant to 2-years post-graft (all $p<0.001$).

Descemet's membrane endothelial keratoplasties performed for endothelial failure/bullous keratopathy, which survived for 1-year, achieved a median BCVA of 6/12. Median BCVA reached 6/7.5 for the 21 surviving grafts that had data available at 2-years post-graft.

Figure 5.9.4 Best corrected visual acuity for surviving Descemet's membrane endothelial keratoplasties performed for Fuchs' endothelial dystrophy, over time



Number of grafts with data at each time point

Pre	3m	6m	1y	2y	3y	4y	5y
1824	85	69	156	74	49	11	10

The median BCVA obtained following Descemet's membrane endothelial keratoplasty for Fuchs' endothelial dystrophy improved significantly compared to pre-graft levels by 3-months post-graft ($p<0.001$). This improvement was maintained up to 5-years post-graft (all $p<0.001$). There were no significant differences between adjacent yearly time points, though median BCVA at 4-years was significantly better than at 1-year post-graft ($p=0.010$).

Descemet's membrane endothelial keratoplasties performed for Fuchs' endothelial dystrophy, which survived for 3-months, achieved a median BCVA of 6/9. The median BCVA reached 6/7.5 at 6-months post-graft, and then reached 6/6 at 3-years. This level was maintained at 4-years but had dropped back down to 6/9 for the ten surviving grafts with data available at 5-years.

6 Deep Anterior Lamellar Keratoplasty

This chapter presents analyses of the 2,018 deep anterior lamellar keratoplasties (DALK) registered with the ACGR. Kaplan-Meier survival analyses were conducted 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 and eye banking factors, **all of which** were found to be **non-significant** in univariate analysis. The sum for each variable equals the total number of grafts (2,018 registered and 1,241 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable. As no donor and eye banking factors were found to be significant in univariate analysis, no Kaplan-Meier curves are shown in this section.

Table 6.1 Donor and eye banking factors, not significant in univariate analyses

Deep Anterior Lamellar Keratoplasty

Donor and Eye Banking Factors

	Registered (%)	Followed (%)
Eye bank		
	937 (46%)	393 (32%)
Eye banks are not identified due to confidentiality constraints. See section 1.4.8 for further information.	353 (18%)	312 (25%)
	429 (21%)	348 (28%)
	141 (7%)	77 (6%)
	157 (8%)	110 (9%)
Not advised (autograft)	1 (<1%)	1 (<1%)
Chi²=8.15, df=4, p=0.086		
Age of donor		
0 to 19 years	58 (3%)	38 (3%)
20 to 29 years	75 (4%)	47 (4%)
30 to 39 years	119 (6%)	70 (6%)
40 to 49 years	219 (11%)	129 (10%)
50 to 59 years	425 (21%)	240 (19%)
60 to 69 years	560 (28%)	350 (28%)
70 to 79 years	421 (21%)	268 (22%)
80 years and older	141 (7%)	99 (8%)
Chi²=5.33, df=7, p=0.620		
Sex of donor		
Female	842 (42%)	530 (43%)
Male	1176 (58%)	711 (57%)
Chi²=1.12, df=1, p=0.289		

	Registered (%)	Followed (%)
Donor type		
Eye donor only	1693 (84%)	1048 (84%)
Solid organ and/or bone/tissue donor	325 (16%)	193 (16%)
Chi²=1.33, df=1, p=0.249		
Cause of donor death		
Cardiovascular	449 (22%)	285 (23%)
Malignancy	731 (36%)	431 (35%)
Trauma	194 (10%)	105 (8%)
Respiratory	153 (8%)	107 (9%)
Intracranial/cerebral haemorrhage	345 (17%)	227 (18%)
Other specified	113 (6%)	69 (6%)
Not advised/live donor*	33 (2%)	17 (1%)
Chi²=3.48, df=5, p=0.626		
Central corneal endothelial cell density		
<2500 cells/mm²	179 (9%)	97 (8%)
2500 to 2749 cells/mm²	230 (11%)	125 (10%)
2750 to 2999 cells/mm²	302 (15%)	149 (12%)
3000 to 3249 cells/mm²	333 (17%)	188 (15%)
3250 to 3499 cells/mm²	230 (11%)	128 (10%)
3500+ cells/mm²	150 (7%)	82 (7%)
Not advised	594 (29%)	472 (38%)
Chi²=5.80, df=5, p=0.326		
Storage media		
Organ culture	1108 (55%)	570 (46%)
Optisol	904 (45%)	668 (54%)
Moist Pot	5 (<1%)	2 (<1%)
Frozen	1 (<1%)	1 (<1%)
Chi²=0.23 df=1, p=0.634		
Interstate transportation		
Same State	1959 (97%)	1200 (97%)
Different States	58 (3%)	40 (3%)
Not advised	1 (<1%)	1 (<1%)
Chi²=0.67, df=1, p=0.415		
Death-to-enucleation time		
Up to 3 hours	190 (9%)	141 (11%)
4 to 6 hours	277 (14%)	175 (14%)
7 to 9 hours	324 (16%)	181 (15%)
10 to 12 hours	352 (17%)	226 (18%)
13 to 15 hours	260 (13%)	176 (14%)
16 to 18 hours	257 (13%)	154 (12%)
More than 18 hours	353 (17%)	185 (15%)
Not Advised	5 (<1%)	3 (<1%)
Chi²=6.94, df=6, p=0.327		

	Registered (%)	Followed (%)
Enucleation-to-storage time		
Within 1 hour	56 (3%)	26 (2%)
1 to 3 hours	981 (49%)	562 (45%)
4 to 6 hours	226 (11%)	156 (13%)
7 to 9 hours	56 (3%)	35 (3%)
10 to 12 hours	42 (2%)	35 (3%)
13 to 15 hours	53 (3%)	42 (3%)
16 to 18 hours	47 (2%)	32 (3%)
More than 18 hours	62 (3%)	54 (4%)
Not advised	495 (25%)	299 (24%)
Chi²=3.13, df=7, p=0.873		
Storage-to-graft time - Optisol		
Within 5 days	440 (22%)	338 (27%)
More than 5 days	269 (13%)	198 (16%)
Not advised	195 (10%)	132 (11%)
Not applicable	1114 (55%)	573 (46%)
Chi²=0.04, df=1, p=0.843		
Storage-to-graft time - Organ culture		
Up to 2 weeks	233 (12%)	123 (10%)
2 to 3 weeks	396 (20%)	190 (15%)
More than 3 weeks	140 (7%)	81 (7%)
Not advised	339 (17%)	176 (14%)
Not applicable	910 (45%)	671 (54%)
Chi²=2.21, df=2, p=0.331		
Deswelling-to-graft time – Organ culture		
Within 2 days	204 (10%)	86 (7%)
2 to 3 days	203 (10%)	64 (5%)
Longer than 3 days	141 (7%)	47 (4%)
Not advised	560 (28%)	373 (30%)
Not applicable	910 (45%)	671 (54%)
Chi²=1.99, df=2, p=0.369		
Total	***2018 (100%)***	***1241 (100%)***

Note: Kaplan-Meier analyses did not include grafts where categorisation was not advised or not applicable. Categories with fewer than 2% of grafts were combined with adjacent groups or other logical combinations where possible or excluded when unable to be logically combined with another group.

*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.

6.2 Recipient Factors

Table 6.2 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 (2,018 registered and 1,241 followed) and the percentages, which should be summed vertically for each variable, total 100.

Table 6.2 Recipient factors, significant in univariate analyses

Deep Anterior Lamellar Keratoplasty Recipient Factors	Registered (%)	Followed (%)
Indication for graft		
Failed previous graft	86 (4%)	50 (4%)
Keratoconus	1510 (75%)	911 (73%)
Herpetic eye disease	97 (5%)	69 (6%)
Corneal degeneration	79 (4%)	45 (4%)
Corneal dystrophies	52 (3%)	34 (3%)
Non-herpetic infections	76 (4%)	54 (4%)
Corneal scars and opacities	50 (2%)	31 (2%)
Other*	68 (3%)	47 (4%)
Prior ipsilateral corneal grafts		
None	1930 (96%)	1190 (96%)
One or more	88 (4%)	51 (4%)
Australian State where graft was performed		
	940 (47%)	394 (32%)
States are not identified due to	346 (17%)	306 (25%)
confidentiality constraints. See	418 (21%)	334 (27%)
section 1.4.8 for further information.	149 (7%)	86 (7%)
	146 (7%)	103 (8%)
	19 (<1%)	18 (1%)
Recipient age group		
0 to 19 years	136 (7%)	80 (6%)
20 to 29 years	609 (30%)	365 (29%)
30 to 39 years	518 (26%)	322 (26%)
40 to 49 years	309 (15%)	180 (15%)
50 to 59 years	200 (10%)	127 (10%)
60 to 69 years	132 (7%)	91 (7%)
70 years or older	114 (6%)	76 (6%)
Pre-graft corneal neovascularisation		
None	1767 (88%)	1076 (87%)
One quadrant	100 (%)	64 (5%)
Two quadrants	79 (%)	52 (4%)
Three/four quadrants	72 (%)	49 (4%)
Pre-graft inflammation and/or steroid use		
No	1799 (89%)	1101 (89%)
Yes	184 (9%)	123 (10%)
Not advised	35 (2%)	17 (1%)

	Registered (%)	Followed (%)
Prior intraocular surgery in first grafts		
No	1784 (88%)	1099 (88%)
Yes	121 (6%)	82 (6%)
Not advised	25 (1%)	9 (<1%)
Not applicable (repeat and/or prior concurrent)	88 (4%)	51 (4%)
Total	***2018 (100%)***	***1241 (100%)***

* Other included: trauma (23), corneal perforation (7), interstitial keratitis (6), keratoglobus (6), irregular astigmatism (5), metabolic deposits (4), aniridia (2), descemetocoele (2), astigmatism (1), beta radiation (1), corneal necrosis (1), epithelial failure (1), limbal dermoid (1), mucopolysaccharidosis (1), neurotrophic keratopathy (1), Peter's Anomaly (1), pseudophakic bullous keratopathy (1), pterygium (1), Sjogren's syndrome (1), Stevens Johnson syndrome (1), Wegener's granulomatosis (1).

Table 6.3 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 (2,018 registered and 1,241 with follow-up provided) and the percentages, summed vertically, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

Table 6.3 Recipient factors, not significant in univariate analyses

Deep Anterior Lamellar Keratoplasty
Recipient Factors

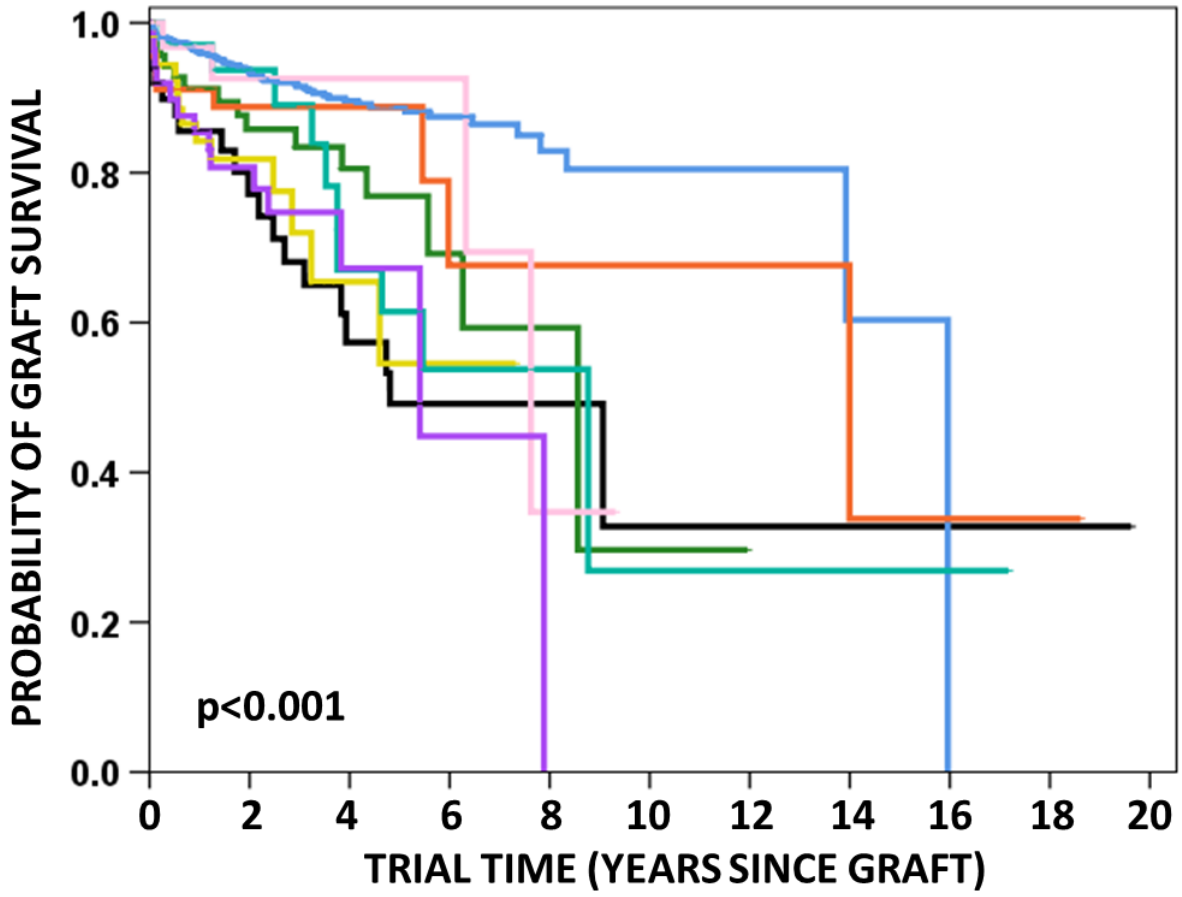
	Registered (%)	Followed (%)
Recipient sex		
Female	781 (39%)	498 (40%)
Male	1237 (61%)	743 (60%)
Chi²=1.86, df=1, p=0.173		
Donor/recipient sex match/mismatch		
Female/female	315 (16%)	198 (16%)
Female/male	527 (26%)	332 (27%)
Male/female	466 (23%)	300 (24%)
Male/male	710 (35%)	411 (33%)
Chi²=2.87, df=3, p=0.412		
Eye in which graft was performed		
Left	1023 (92%)	634 (51%)
Right	995 (92%)	607 (49%)
Chi²=0.28, df=1, p=0.595		
Prior contralateral corneal graft/s		
None	1666 (83%)	1053 (85%)
One or more	352 (17%)	188 (15%)
Chi²=0.31, df=1, p=0.581		
History of corneal collagen crosslinking		
No	1967 (97%)	1221 (98%)
Yes	51 (3%)	20 (2%)
Chi=0.23, df=1, p=0.629		
Total	***2018 (100%)***	***1241 (100%)***

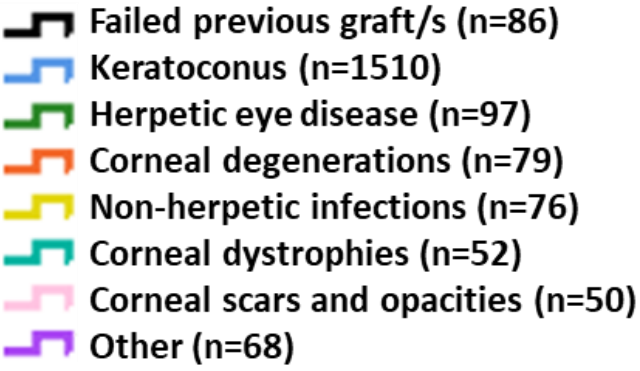
6.2.1 Deep anterior lamellar keratoplasty survival: influence of indication for graft

Figure 6.2.1 shows the comparison of graft survival depending on the indication for graft. A significant difference was found across groups (Log Rank Statistic=66.52; df=7; p<0.001).

Survival of grafts performed for keratoconus was significantly better than those performed for failed previous grafts, non-herpetic infections, other specified indications (all p<0.001), and herpetic infections (p=0.001). As the differences between groups for grafts performed for indications other than keratoconus were not significant, these were combined for the multivariate analysis. This variable was not retained in the final multivariate model (see section 6.7), however the variable relating to prior ipsilateral grafts was (see section 6.2.2).

Figure 6.2.1 Indication for graft





Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Failed previous graft	36	26	22	15	12	8	6	5	3	2
Keratoconus	783	507	329	231	159	105	72	38	22	13
Herpetic eye disease	58	46	33	27	16	9	6	2	1	1
Corneal degeneration	39	26	23	14	9	6	6	5	3	3
Non-herpetic infections	37	23	12	8	4	2	1	NA	NA	NA
Corneal dystrophies	30	22	17	12	10	6	3	2	1	1
Corneal scars & opacities	26	15	12	7	7	6	2	1	1	NA
Other	39	28	17	8	4	1	1	NA	NA	NA

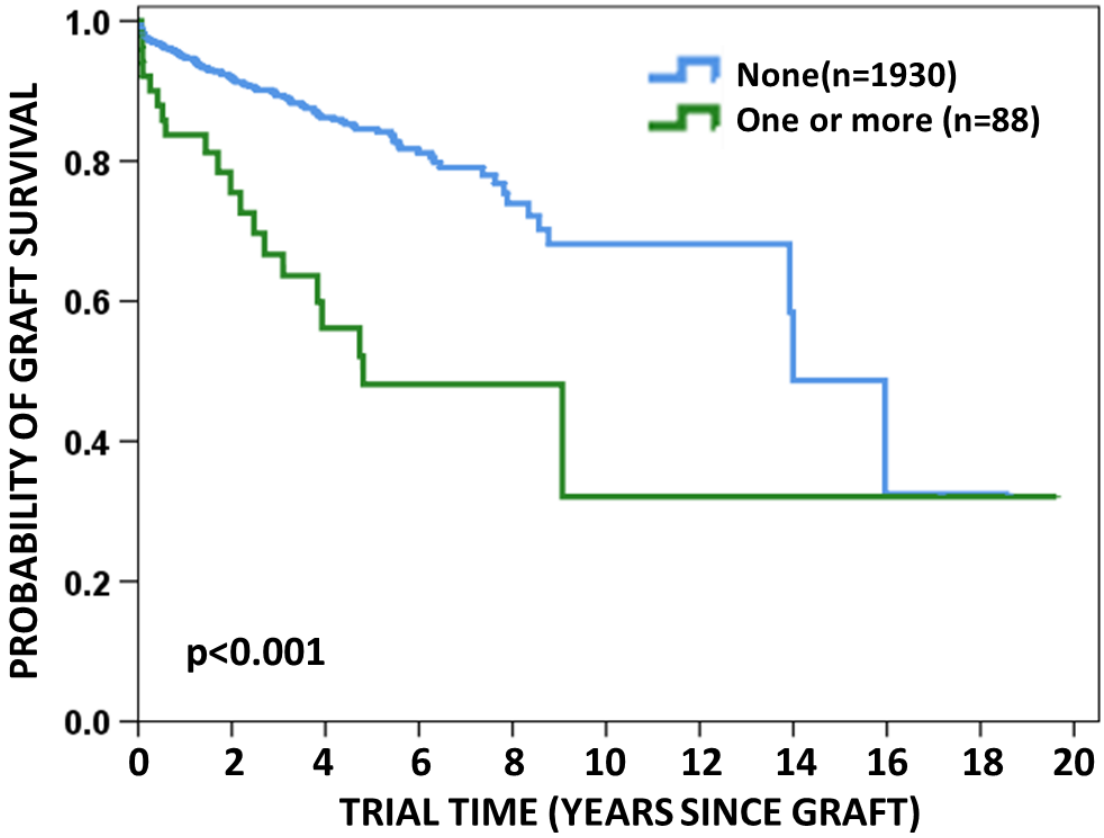
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9
Failed previous graft	0.86	0.77	0.68	NA	NA	NA	NA	NA	NA
Keratoconus	0.96	0.94	0.92	0.90	0.89	0.88	0.87	0.83	0.81
Herpetic eye disease	0.91	0.86	0.83	0.81	NA	NA	NA	NA	NA
Corneal degeneration	0.91	0.89	0.89	NA	NA	NA	NA	NA	NA
Non-herpetic infections	0.84	0.82	NA	NA	NA	NA	NA	NA	NA
Corneal dystrophies	0.97	0.94	NA	NA	NA	NA	NA	NA	NA
Corneal scars & opacities	0.97	NA	NA	NA	NA	NA	NA	NA	NA
Other	0.85	0.81	NA	NA	NA	NA	NA	NA	NA

6.2.2 Deep anterior lamellar keratoplasty survival: influence of previous ipsilateral graft/s

Figure 6.2.2 shows the comparison of graft survival between those recipients with previous graft/s in the ipsilateral eye compared to those without (Log Rank Statistic=23.36; df=1; p<0.001). This variable was retained in the final multivariate model (see section 6.7).

Figure 6.2.2 Previous graft/s in ipsilateral eye



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
None	1012	667	443	307	209	135	92	48	28	18
One or more	36	26	22	15	12	8	6	5	3	2

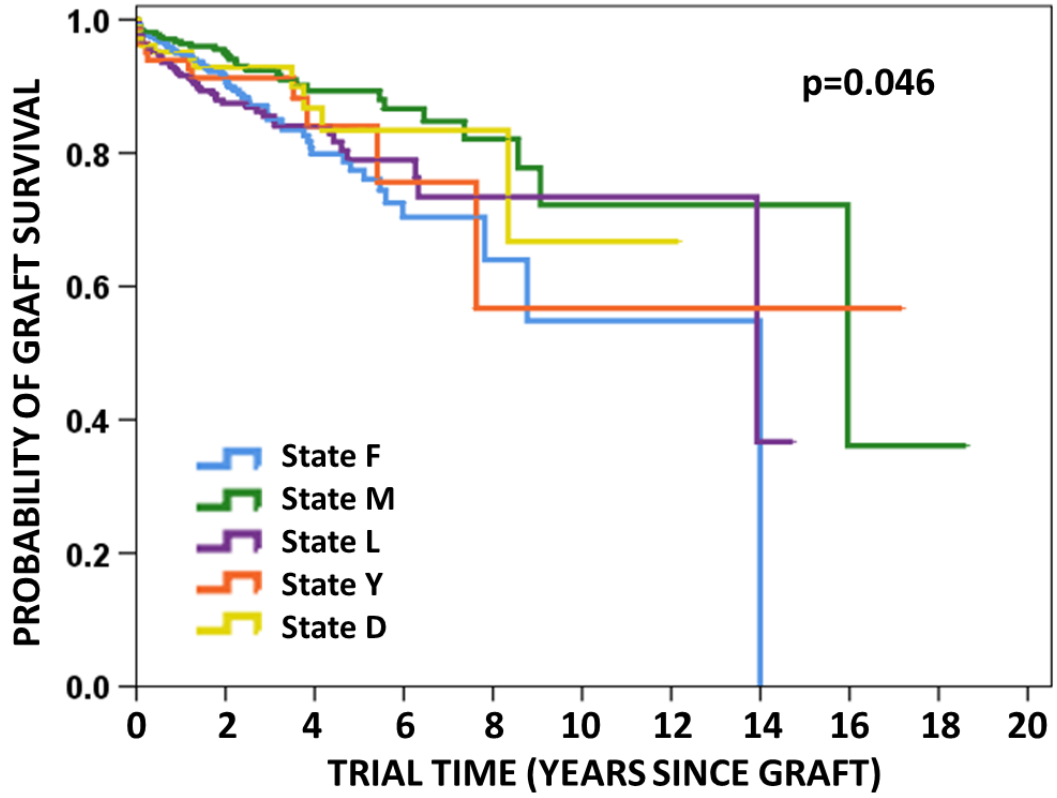
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9
None	0.95	0.92	0.89	0.86	0.85	0.81	0.79	0.74	0.68
One or more	0.84	0.76	0.67	NA	NA	NA	NA	NA	NA

6.2.3 Deep anterior lamellar keratoplasty survival: influence of Australian State where graft was performed

Figure 6.2.3 shows the comparison of graft survival depending on the Australian State in which the transplantation occurred. One State only had 19 DALK registered and these grafts were excluded from the analysis. A significant difference was found across groups (Log Rank Statistic=9.71; df=4; p=0.046), however, no individual comparison between groups were significant following Holm-Bonferroni correction. This variable was not retained in the final multivariate model (see section 6.7) suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.2.3 Australian state where graft was performed



Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8
State F	0.95	0.91	0.85	0.80	0.77	0.70	0.70	NA
State M	0.96	0.95	0.92	0.89	0.89	0.87	0.85	0.82
State L	0.92	0.88	0.86	0.84	0.79	0.79	0.73	NA
State Y	0.94	0.91	0.91	NA	NA	NA	NA	NA
State D	0.95	0.93	0.93	0.87	NA	NA	NA	NA

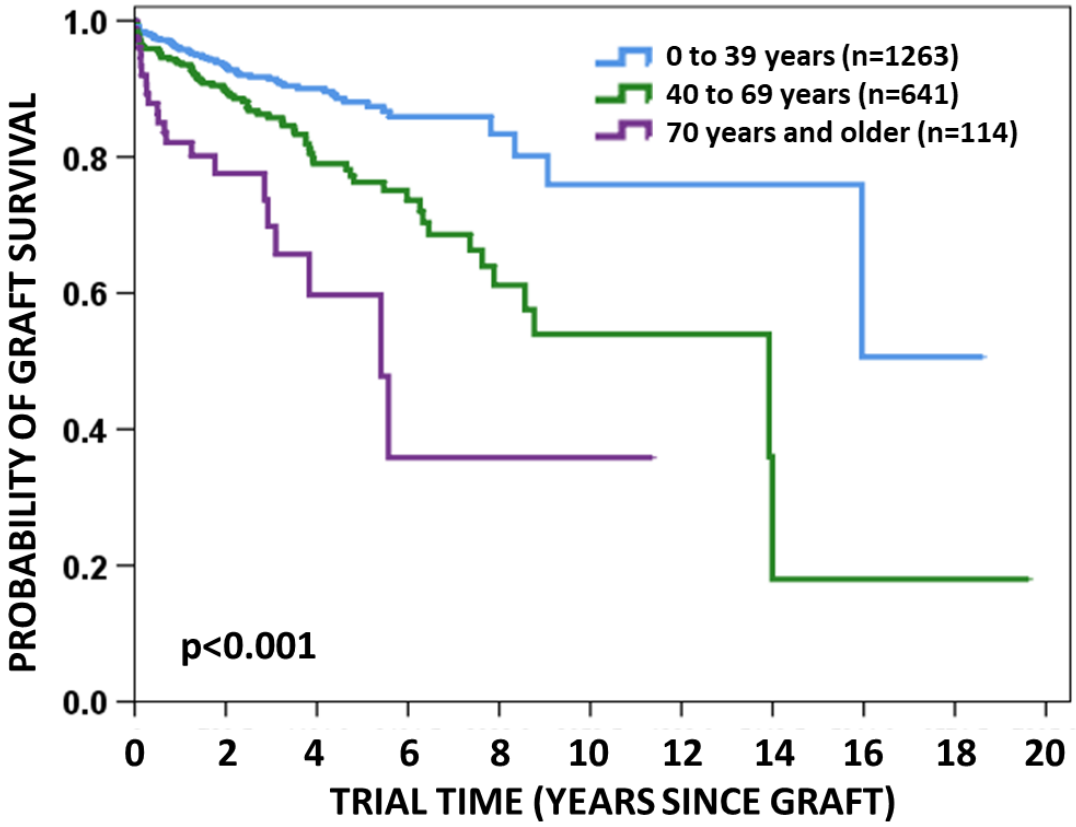
Note: Further information is not provided due to confidentiality constraints (see section 1.4.8).

6.2.4 Deep anterior lamellar keratoplasty 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. Recipients were initially stratified by 10-year age groups. Data for the "0-9 years" group was combined with the "10 to 19 years" group, and all recipients aged 70 years and older were grouped together for analysis, due to the low number of recipients in these groups. A significant difference was found across groups (Log Rank Statistic=49.08; df=6; p<0.001).

Further analyses examined whether there were significant differences between adjacent age groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=45.07; df=2; p<0.001). All comparisons between age groups were significantly different at the p<0.001 level, with the younger recipient group showing superior survival to the older group in each case. This variable was retained in the final multivariate model (see section 6.7).

Figure 6.2.4 Recipient age group



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9
0 to 39 years	654	429	287	207	140	90	60	32	19
40 to 69 years	345	236	160	105	76	50	36	20	11
70 years and older	49	28	18	10	5	3	1	1	1

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8
0 to 39 years	0.96	0.93	0.91	0.90	0.88	0.86	0.86	0.83
40 to 69 years	0.94	0.90	0.86	0.79	0.76	0.74	0.69	0.61

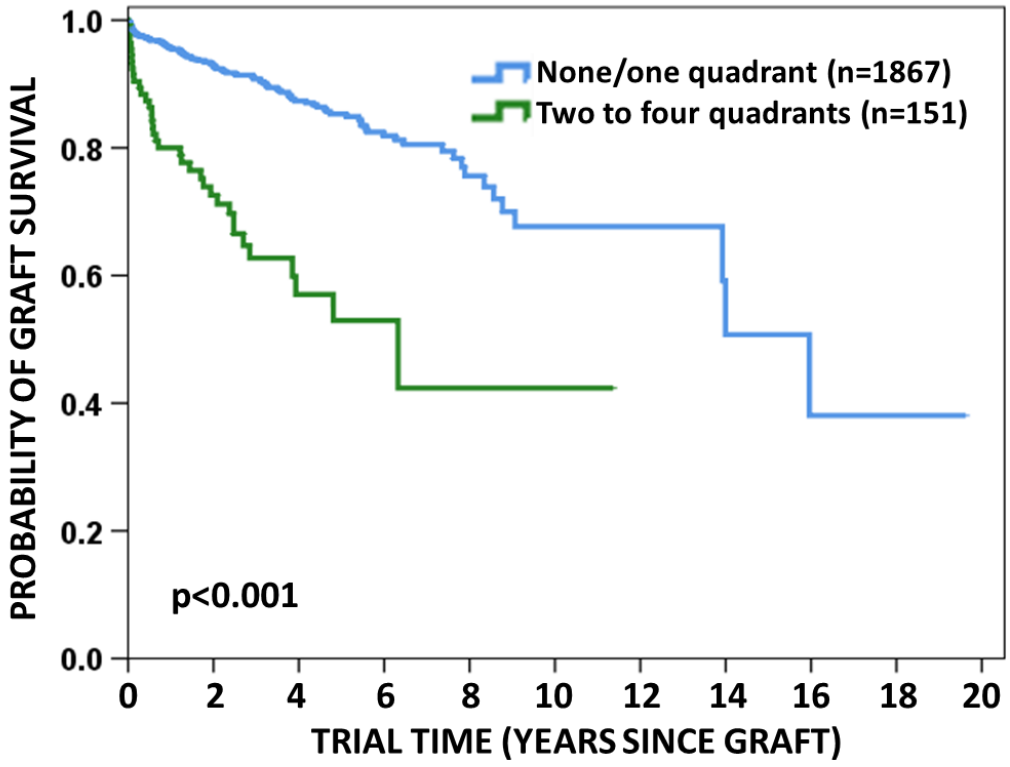
70 years and older	0.82	0.78	NA	NA	NA	NA	NA	NA

6.2.5 Deep anterior lamellar keratoplasty survival: influence of pre-graft corneal neovascularisation

Figure 6.2.5 shows the comparison of graft survival depending on the level of pre-graft corneal neovascularisation. Comparisons were initially made with neovascularisation split into single quadrant levels, with grafts performed in eyes with three and four quadrants combined due to low numbers in these groups. The comparison was significant (Log Rank Statistic=66.10; df=3; p<0.001).

Further analyses examined whether there were significant differences between adjacent groups. Recipients with avascular corneas pre-graft, or one quadrant of pre-graft neovascularisation, did not have significantly different graft survival (p=0.112). Recipients with two, three or four quadrants of pre-graft neovascularisation, did not have significantly different graft survival (p=0.996). These groups were therefore combined, and the comparison remained significant (Log Rank Statistic=64.06; df=1; p<0.001). This variable was retained in the final multivariate model (see section 6.7).

Figure 6.2.5 Pre-graft corneal neovascularisation



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
None/one quadrant	975	638	435	302	209	137	94	52	30	19
Two to four quadrants	73	55	30	20	12	6	1	1	1	1

Probability of graft survival (years post-graft)

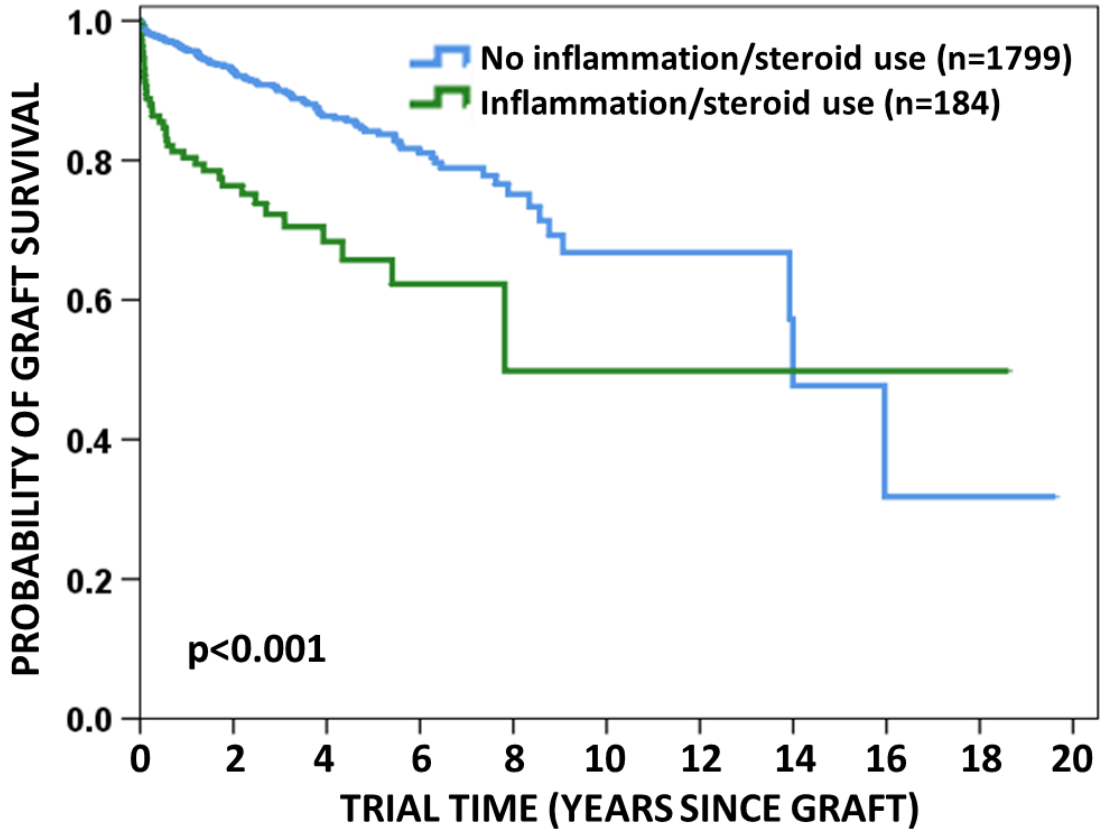
	1	2	3	4	5	6	7	8	9
None/one quadrant	0.96	0.93	0.91	0.78	0.85	0.82	0.81	0.76	0.70
Two to four quadrants	0.80	0.73	0.63	0.57	NA	NA	NA	NA	NA

6.2.6 Deep anterior lamellar keratoplasty survival: influence of pre-graft inflammation and/or recent steroid use

Figure 6.2.6 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=32.02; df=1; p<0.001).

Data were not available for 35 grafts; however, this was not a sufficient number to create an extra category (<2%) and these grafts were excluded from the analysis. This variable was not retained in the final multivariate model (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.2.6 Pre-graft inflammation and/or recent steroid use



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No inflammation/steroid use	942	613	418	286	198	127	87	48	28	18
Inflammation/steroid use	91	69	42	32	21	14	8	4	3	2

Probability of graft survival (years post-graft)

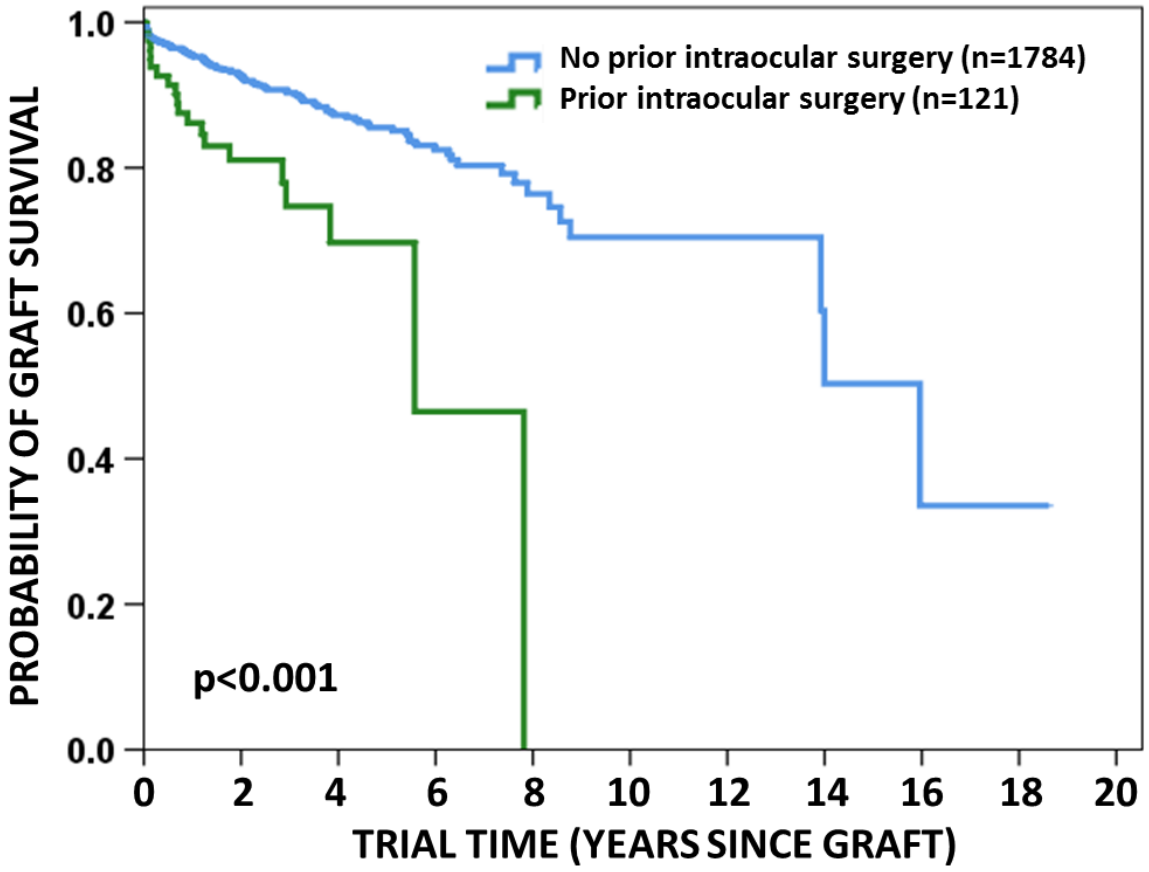
	1	2	3	4	5	6	7	8	9
No inflammation/steroid use	0.96	0.93	0.90	0.86	0.84	0.81	0.80	0.75	0.69
Inflammation/steroid use	0.80	0.76	0.72	0.68	0.66	NA	NA	NA	NA

6.2.7 Deep anterior lamellar keratoplasty survival: influence of prior intraocular surgery

The analysis on page 255 is of a sub-cohort of deep anterior lamellar grafts which had **not** undergone a previous corneal transplant. Sub-cohort variables are excluded from multivariate analysis.

Data were not available for 25 grafts and these are excluded from the analysis. Figure 6.2.7 shows the comparison of graft survival between grafts where the recipient had undergone prior intraocular surgery (excluding prior graft) compared to those that had not (Log Rank Statistic=18.78; df=1; p<0.001).

Figure 6.2.7 Prior intraocular surgery



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No prior surgery	941	622	417	292	202	132	89	47	28	18
Prior surgery	62	39	23	13	6	2	1	NA	NA	NA

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9
No prior surgery	0.95	0.93	0.90	0.87	0.86	0.83	0.80	0.76	0.70
Prior surgery	0.86	0.81	0.75	NA	NA	NA	NA	NA	NA

6.3 Graft Era/Year

Table 6.4 shows the number of grafts registered and followed based on single years combined. Grafts were initially stratified by yearly groups. Data for grafts performed prior to 2007 were combined due to low number of grafts registered in those years. A significant difference was found across year groups (Log Rank Statistic=33.72; df=14; p=0.002).

Further analyses examined whether there were significant differences between adjacent year groups. Further analyses examined whether there were significant differences between adjacent year groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=17.71; df=1; p<0.001). The percentages, which should be summed vertically, total 100.

Table 6.4 Graft era/year

Deep Anterior Lamellar Keratoplasty
Graft Era/Year

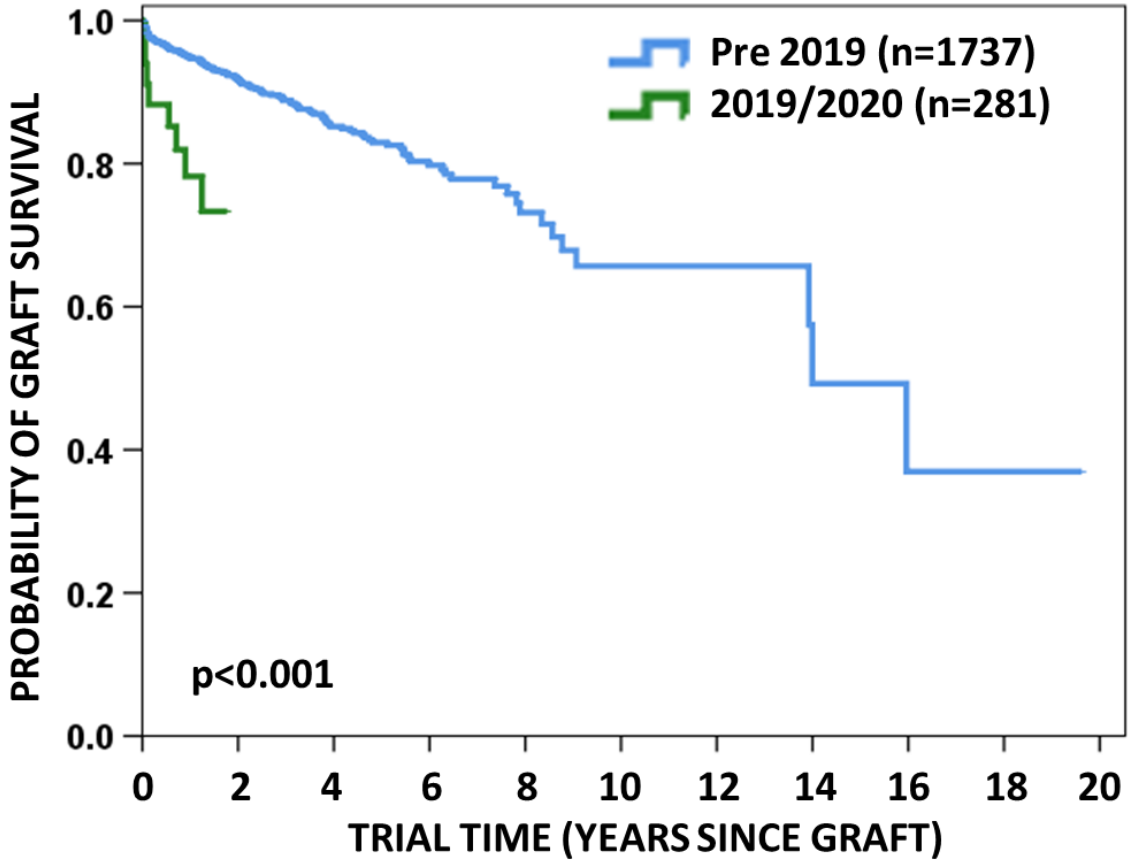
		Registered (%)	Followed (%)
Year of graft			
Pre 2019		1737 (86%)	1205 (97%)
2019/2020		281 (14%)	36 (3%)
	Total	***2018 (100%)***	***1241 (100%)***

See section 1.1 for a discussion of the impact that lag time to follow-up may have on survival depending on graft year/era. A comparison between the percentages of grafts registered and followed in each group showed a distinct difference. This difference was examined using a Chi^2 analysis and found to be significant (p<0.001). Follow-up was lower for grafts performed in more recent years.

6.3.1 Deep anterior lamellar keratoplasty survival: influence of era of graft

Figure 6.3.1 shows the influence of year of graft, stratified into the two groups outlined in Section 6.3. The difference in survival was significant (Log Rank Statistic=17.71; df=1; p<0.001). This finding is likely due to the lag time discussed in section1.1.1. This variable was retained in the final multivariate model (see section 6.7).

Figure 6.3.1 Graft Era



Number at risk (years post-graft)

	6 m	1	2	3	4	6	8	10	12
Pre 2019	1129	1028	693	466	322	143	53	20	9
2019/2020	29	20	NA	NA	NA	NA	NA	NA	NA

Probability of graft survival (years post-graft)

	6m	1	2	3	4	6	8	10
Pre 2019	0.97	0.95	0.92	0.89	0.85	0.80	0.73	0.66
2019/2020	0.88	0.78	NA	NA	NA	NA	NA	NA

6.4 Surgery and Surgeon Factors

Table 6.5 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 (2,018 registered and 1,241 followed) and the percentages, which should be summed vertically for each variable, total 100.

Table 6.5 Surgery and surgeon factors, significant in univariate analyses

Deep Anterior Lamellar Keratoplasty
Surgery and Surgeon Factors

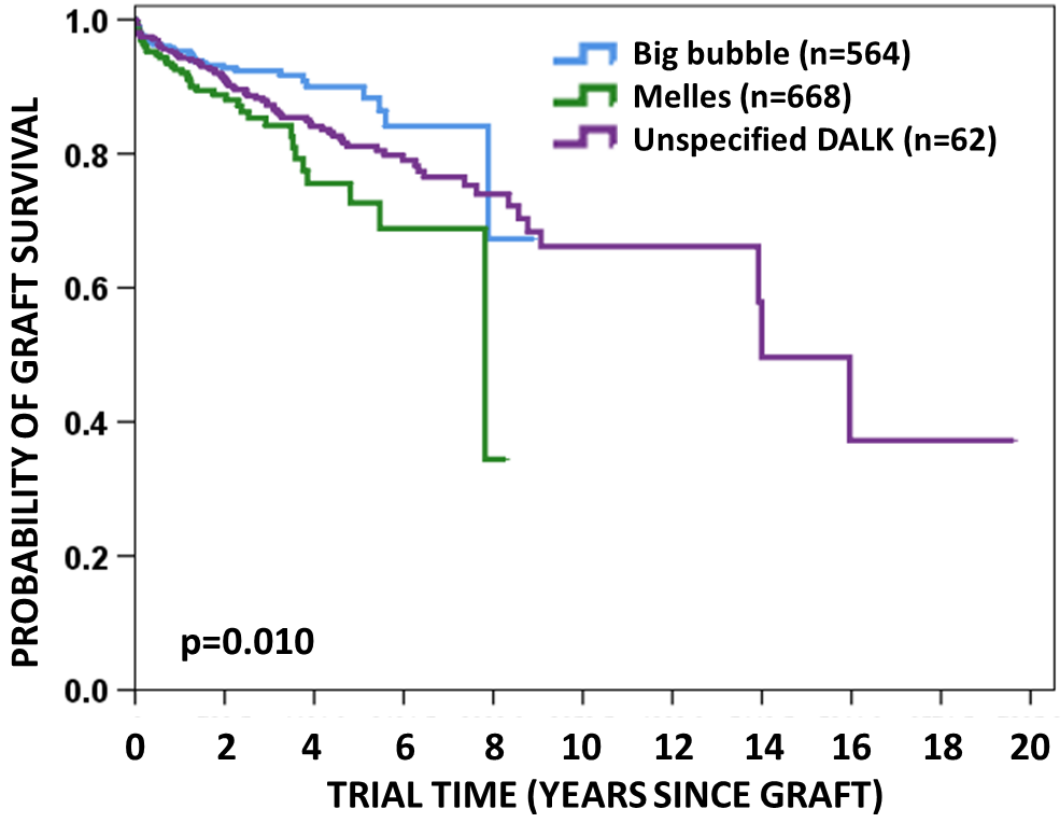
	Registered (%)	Followed (%)
Graft type		
Big bubble	564 (28%)	418 (34%)
Melles	668 (33%)	245 (20%)
Unspecified DALK	786 (39%)	578 (47%)
Graft size		
Less than 8.00 mm	215 (11%)	150 (12%)
8.00 mm to 8.49 mm	788 (39%)	582 (47%)
8.50 mm to 8.99 mm	497 (25%)	261 (21%)
9.00 mm or more	400 (20%)	153 (12%)
Unknown	118 (6%)	95 (8%)
Change in lens status		
Phakic post-graft	1885 (93%)	1150 (93%)
Other	133 (7%)	91 (7%)
Surgeon caseload and level of follow-up		
Fewer than 41 registered DALK	660 (33%)	466 (38%)
41+ registered DALK, <62% follow-up	589 (29%)	145 (12%)
41+ registered DALK, ≥62% follow-up	769 (38%)	630 (51%)
The centre effect		
Fewer than 41 registered DALK	660 (33%)	466 (38%)
	535 (27%)	115 (9%)
	115 (6%)	94 (8%)
	98 (5%)	94 (8%)
	94 (5%)	83 (7%)
Individual surgeons are not identified	91 (5%)	64 (5%)
due to confidentiality constraints.	79 (4%)	52 (4%)
See section 1.4.8 for further information.	74 (4%)	62 (5%)
	59 (3%)	39 (3%)
	56 (3%)	47 (4%)
	54 (3%)	47 (4%)
	54 (3%)	30 (2%)
	49 (2%)	48 (4%)
Total	***2018 (100%)***	***1241 (100%)***

41 was selected as the cut-off point for high caseload surgeons as this was 2% of all registered deep anterior lamellar keratoplasties. 62% was selected as the cut-off point for the follow-up categories as this was the average percentage of follow-up for all deep anterior lamellar grafts.

6.4.1 Deep anterior lamellar keratoplasty 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 and so a third category of "unspecified" also exists. The overall comparison of the three groups was significant (Log Rank Statistic=9.13; df=2; p=0.010) and is shown in Figure 6.4.1. A significant difference was found in the outcomes from the two different techniques (p=0.002) while survival of grafts where the technique used was not specified did not differ significantly compared to either specified technique (both p>0.05). This variable was not retained in the final multivariate model (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.4.1 Type of DALK technique



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
Big bubble	362	235	147	97	57	27	15	3	NA	NA	NA
Melles	193	118	72	39	23	12	6	1	NA	NA	NA
Unspecified DALK	493	340	246	186	141	104	76	49	31	20	13

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Big bubble	0.95	0.93	0.92	0.90	0.90	0.84	NA	NA	NA	NA
Melles	0.93	0.89	0.84	0.76	0.73	NA	NA	NA	NA	NA
Unspecified DALK	0.94	0.91	0.87	0.84	0.81	0.79	0.77	0.74	0.68	0.66

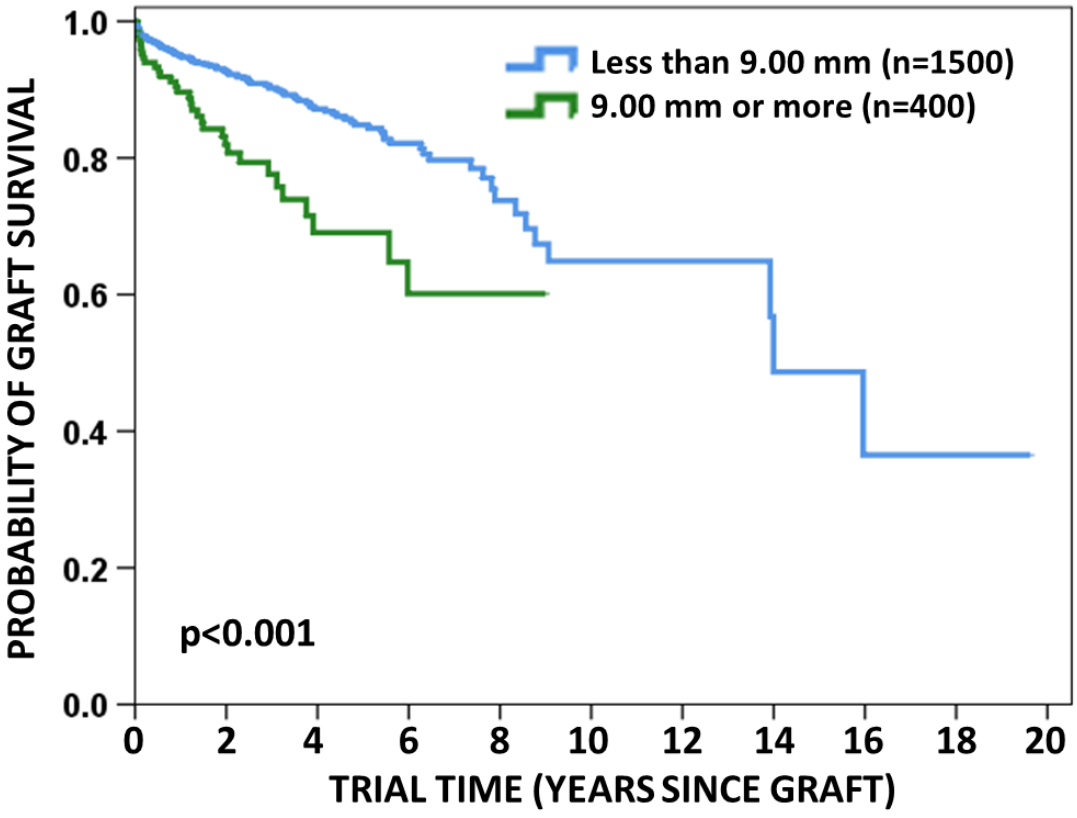
6.4.2 Deep anterior lamellar keratoplasty survival: influence of graft size

Figure 6.4.2 shows a comparison of graft survival depending on the size of the graft. Grafts were initially stratified in 0.50 mm incriments, with all grafts measuring under 8.00 mm analysed together, and all grafts measuring 9.00 mm and over analysed together. A significant difference was found across groups (Log Rank Statistic=17.90; df=3; p<0.001).

Further analyses examined whether there were significant differences between adjacent size groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=16.39; df=1; 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=16.29; df=2; p<0.001). This variable was not retained in the final multivariate model (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.4.2 Size of graft



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Less than 9.00 mm	848	573	387	270	183	115	77	41	27	19
9.00 mm or more	116	68	45	27	19	13	8	5	NA	NA

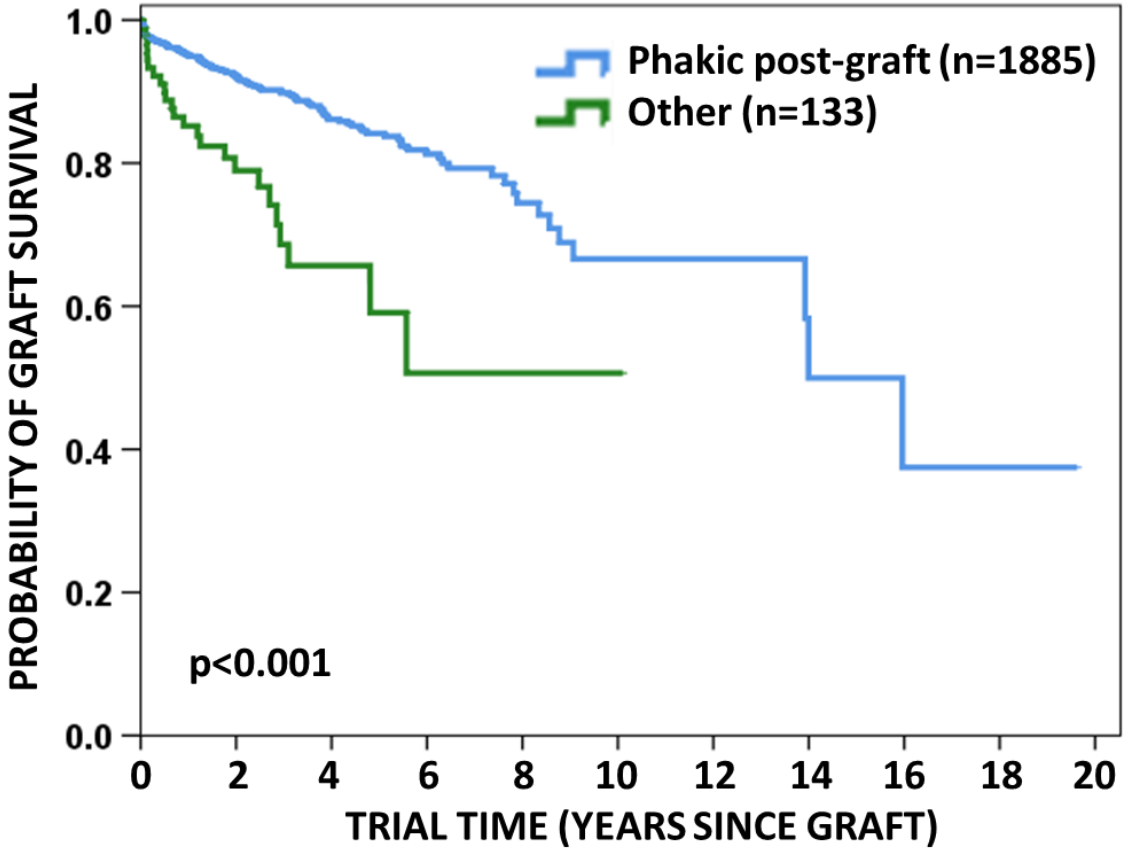
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9
Less than 9.00 mm	0.95	0.93	0.90	0.87	0.85	0.82	0.80	0.74	0.67
9.00 mm or more	0.90	0.82	0.78	0.69	NA	NA	NA	NA	NA

6.4.3 Deep anterior lamellar keratoplasty survival: influence of change in lens status

Figure 6.4.3 shows the comparison of graft survival stratified by the change of lens status from pre- to post-graft. “Phakic post-graft” 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=24.25; df=1; p=0.001). This variable was not retained in the final multivariate model (see section 6.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 6.4.3 Change in lens status



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
Phakic post-graft	982	649	441	306	212	139	96	52	30	19
Other	66	44	24	16	9	4	1	1	1	1

Probability of graft survival (years post-graft)

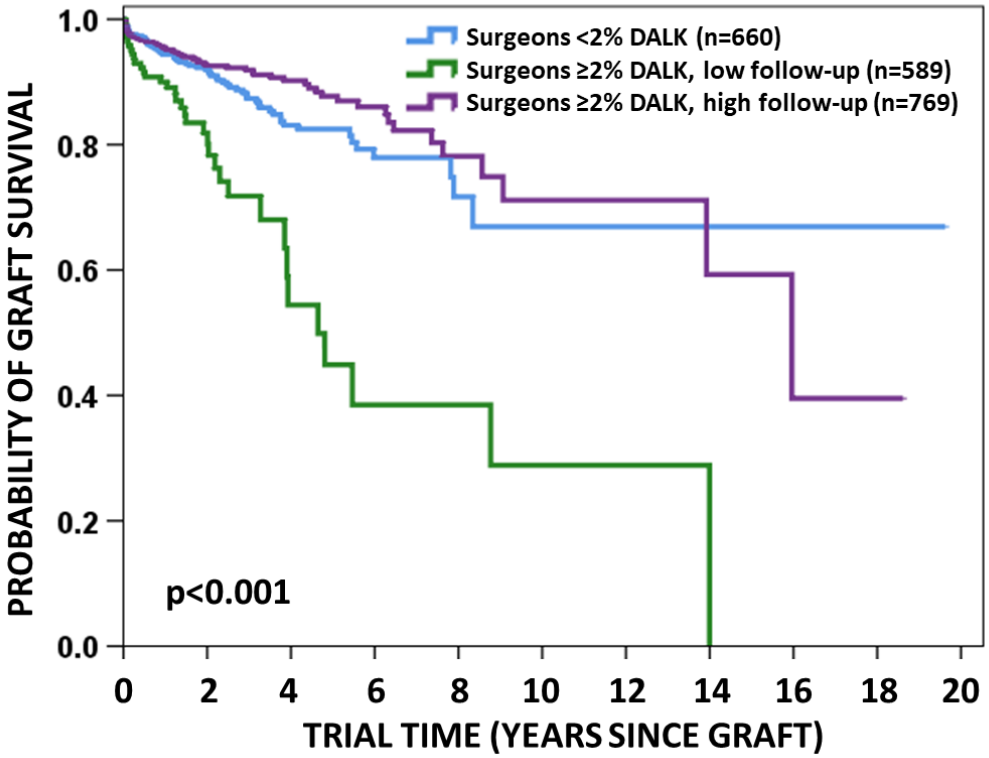
	1	2	3	4	5	6	7	8	9
Phakic post-graft	0.95	0.92	0.90	0.86	0.84	0.81	0.79	0.74	0.69
Other	0.85	0.79	0.69	NA	NA	NA	NA	NA	NA

6.4.4 Deep anterior lamellar keratoplasty survival: influence of surgeon caseload grouped by level of follow-up

Figure 6.4.4 shows the comparison of graft survival between grafts performed by surgeons with 41+ (≥2%) registered deep anterior lamellar keratoplasties with average or better (≥62%) follow-up, to those with lower than average follow-up (<62%), and to surgeons with fewer than 41 (<2%) registered deep anterior lamellar keratoplasties (Log Rank Statistic=169.39; df=2; p<0.001).

Survival of grafts performed by high caseload surgeons with lower than average follow-up was significantly worse than that of either of the other two groups (both p<0.001). There was no significant difference in survival between the surgeons with 41+ registered DALK and high follow-up, and the group comprising grafts performed by surgeons withlow caseloads. This variable was retained in the multivariate analysis (see section 6.7).

Figure 6.4.4 Surgeons caseload and level of follow-up



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
<2% registered DALK	404	284	192	137	91	57	36	20	8	5
≥2% DALK, low follow-up	105	46	24	12	9	6	6	5	3	2
≥2% DALK, high follow-up	539	363	249	173	121	80	55	28	20	13

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9
<2% registered DALK	0.94	0.92	0.87	0.83	0.83	0.78	0.78	0.72	NA
≥2% DALK, low follow-up	0.90	0.82	0.72	NA	NA	NA	NA	NA	NA
≥2% DALK, high follow-up	0.95	0.93	0.92	0.90	0.88	0.86	0.82	0.78	0.75

6.5 Operative procedures at the time of graft

As outlined in Table 6.6, a total of thirty-six DALK underwent additional operative procedures at the time of graft (excluding cataract extraction and/or pseudophakic IOL insertion as this was covered by the change in lens status variable in section 6.4.3). As this was less than 2% of the DALK cohort, this factor was not further analysed.

Table 6.6 Operative procedures at the time of graft

Deep Anterior Lamellar Keratoplasty

Operative Procedures at Time of Graft

	Number
Tarsorrhaphy	9
Peripheral iridectomy	6
Corneal ring segments removed	3
Conjunctival flap	3
Pterygium excision	3
Amniotic membrane transplant	2
Intravitreal injection/s	2
Vitrectomy	2
Iris adhesion released	1
Keratectomy	1
Limbal dermoid removed	1
Lipoma removed	1
Phakic IOL inserted	1
Pseudophakic IOL exchanged	1
Trabeculectomy	1
Total operative procedures (number of grafts)	**39 (36)**

6.6 Post-graft Events

Table 6.7 shows post-graft surgical procedures, as reported by follow-up practitioners. 123 deep anterior lamellar keratoplasties were reported to have undergone a re-grafting procedure at the date last seen. Of these 92 had not had additional post-graft operative procedures reported.

Table 6.7 Post-graft surgical procedures

Deep Anterior Lamellar Keratoplasty

Post-Graft Surgical Procedures

	Number
Cataract removal/IOL insertion	164
Cataract removal without IOL insertion	4
IOL exchange/reposition/piggyback lens	9
Wound repair/re-sutured	62
PRK laser	39
Re-bubbled	33
YAG laser	33
Keratotomy	24
Suture adjustment	16
Intravitreal/intracameral/conjunctival injection/s*	15
Trabeculectomy	14
Tarsorrhaphy	13
PRK	10
Relaxing incision	9
Concurrent graft**	8
Vitrectomy	8
LASIK	6
Phakic IOL inserted	6
Wedge resection	5
Other***	74
Total number of surgical procedures (number of grafts)	***552 (321)***

*Avastin (7), silicone oil (2), air (1), Botulinum toxin (1), Eylea (1), Perfluoropropane - C3F8 (1), Triamcinolone (1), unspecified - conjunctival (1),

**Descemet's membrane endothelial keratoplasty (2), Descemet's stripping endothelial keratoplasty (2), limbal/conjunctival (2), lamellar patch (2).

*** Other included: conjunctival flaps (4), compression sutures (4), corneal collagen cross-linking (4), keratectomy (4), removal of cyst (3), Baerveldt tube inserted (2), corneal diathermy (2), corneal laser regularisation (2), cryotherapy (2), pterygium repair (2), punctal plug insertion (2), removal of folds/wrinkles in membrane (2), removal of interface fluid (2), retinal detachment surgery (2), trichiasis surgery (2), Baerveldt tube replaced (1), Blepheroplasty (1), cyclodiode laser (1), drainage of double anterior chamber (1), ectropion repair (1), entropion surgery (1), epithelial debridement (1), enhancement of PRK (1), enucleation (1), evisceration (1), extension of tarsorrhaphy (1), fine needling (1), glaucoma surgery - unspecified (1), interface revision (1), IOL removed (1), iridotomy (1), lash epilation (1), limbal renal lever (1), membrane peel (1), non-specified glaucoma drainage device inserted (1), paracentesis (1), periotomy (1), ptosis surgery (1), punctal cautery (1), reformation of graft-host junction (1), removal of BCC (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), rotation of graft (1), strabismus surgery (1), trabeculoplasty (1), trauma related lensectomy (1).

Table 6.8 shows the occurrence of post-graft events, which were 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 6.8 Post-graft events, significant in univariate analyses

Deep Anterior Lamellar Keratoplasty Post-graft Events	Registered (%)	Followed (%)
Post-graft neovascularisation		
No	1885 (93%)	1108 (89%)
Yes	133 (7%)	133 (11%)
Post-graft microbial keratitis		
No	1966 (97%)	1189 (96%)
Yes	52 (3%)	52 (4%)
Post-graft rise in intraocular pressure		
No	1912 (95%)	1135 (91%)
Yes	106 (5%)	106 (9%)
Total	***2018 (100 %)***	***1241 (100 %)***

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 (2,018 registered and 1,241 with follow-up provided) and the percentages, summed vertically, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

Only sixteen DALK had post-graft herpetic infection reported and a further eight had uveitis reported. These factors were not further analysed.

Table 6.9 Post-graft events, not significant in univariate analyses

Deep Anterior Lamellar Keratoplasty

Post-graft Events

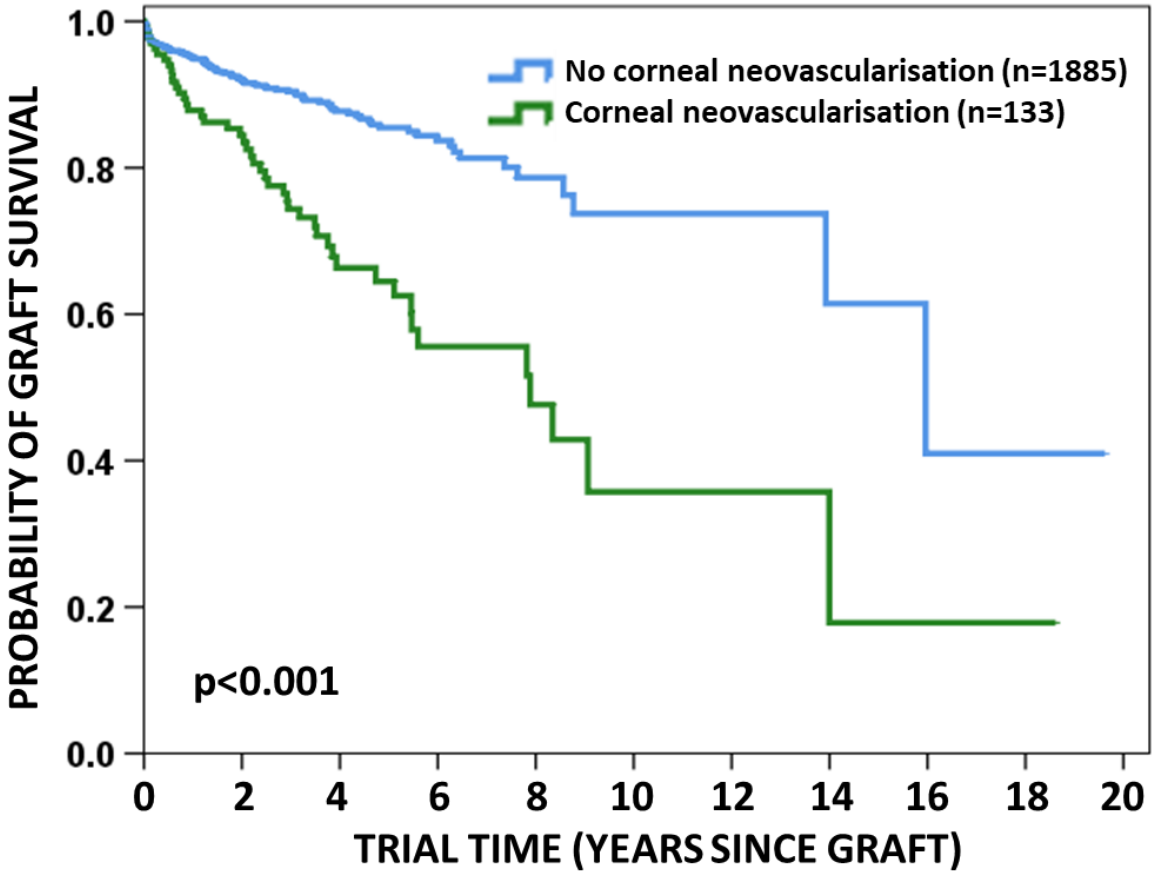
	Registered (%)	Followed (%)
At least one rejection episode		
No	1933 (96%)	1156 (93%)
Yes	85 (4%)	85 (7%)
Chi²=0.115, df=1, p=0.735		
Time to removal of sutures		
Within 12 months	166 (8%)	166 (13%)
13 to 18 months	188 (9%)	188 (15%)
19 to 24 months	114 (6%)	114 (9%)
More than 2 years	97 (5%)	97 (8%)
Not yet removed/not advised*	1453 (72%)	676 (54%)
Chi²=5.20, df=3, p=0.158		
Post-graft oedema		
No	1970 (98%)	1193 (96%)
Yes	48 (2%)	48 (4%)
Chi²=1.67, df=1, p=0.197		
Post-graft interface opacity		
No	1907 (95%)	1130 (91%)
Yes	111 (6%)	111 (9%)
Chi²=1.14, df=1, p=0.285		
Total	***2018 (100 %)***	***1241 (100 %)***

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

6.6.1 Deep anterior lamellar keratoplasty survival: influence of post-graft corneal neovascularisation

Figure 6.6.1 shows the survival of grafts where post-graft corneal vascularisation was reported, compared to those that did not have any post-graft corneal neovascularisation. A significant difference was found between groups (Log Rank Statistic=36.83; df=1; p<0.001). This variable was retained in the final multivariate model 9see section 6.7).

Figure 6.6.1 Post-graft corneal neovascularisation



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No neovascularisation	937	603	396	278	187	122	80	41	25	16
Neovascularisation	111	90	69	44	34	21	17	12	6	4

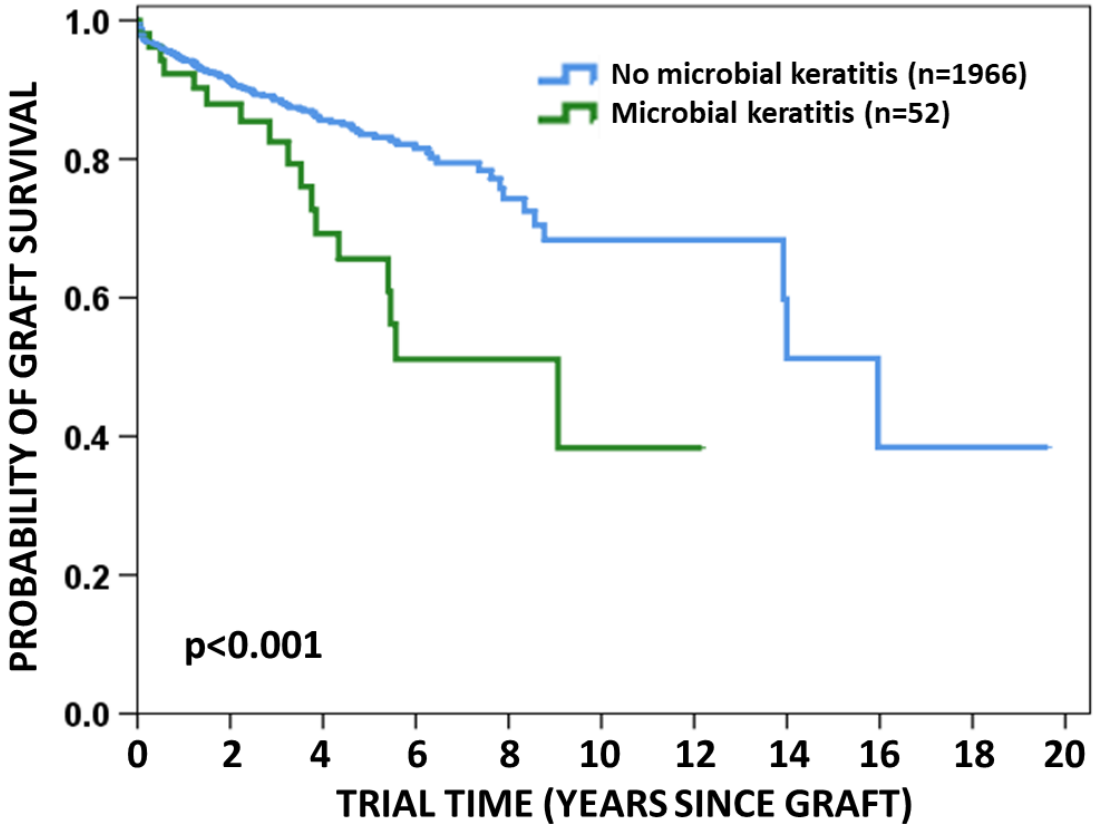
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9
No neovascularisation	0.95	0.92	0.91	0.88	0.87	0.84	0.82	0.79	0.74
Neovascularisation	0.88	0.84	0.74	0.66	0.65	0.56	NA	NA	NA

6.6.2 Deep anterior lamellar keratoplasty survival: influence of post-graft microbial keratitis

Figure 6.6.2 shows the influence of post-graft microbial keratitis on graft survival. A significant difference was found between groups (Log Rank Statistic=10.41; 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 6.6.2 Post-graft microbial keratitis



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No microbial keratitis	1001	657	437	302	207	135	92	48	27	19
Microbial keratitis	47	36	28	20	14	8	5	5	4	1

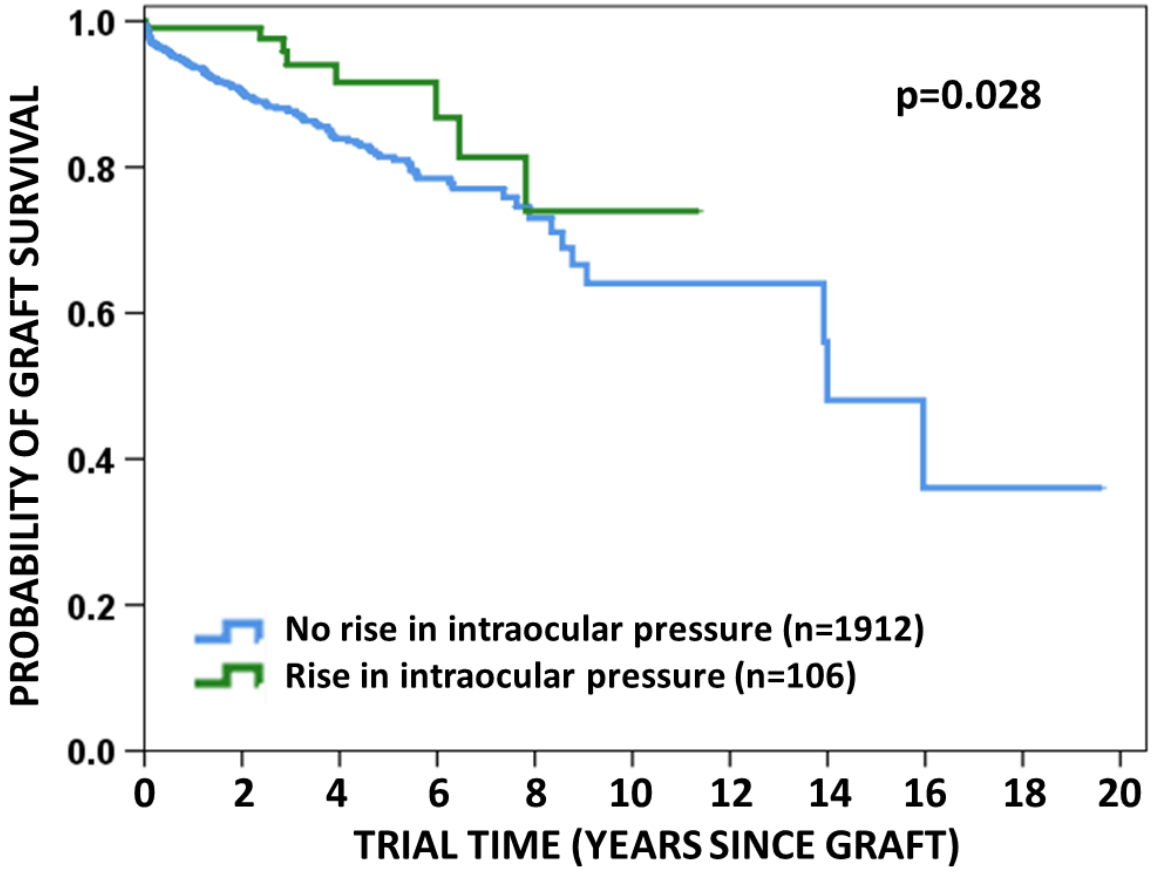
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9
No microbial keratitis	0.94	0.91	0.89	0.86	0.84	0.82	0.80	0.74	0.68
Microbial keratitis	0.92	0.88	0.83	0.69	NA	NA	NA	NA	NA

6.6.3 Deep anterior lamellar keratoplasty survival: influence of post-graft rise in intraocular pressure

Figure 6.6.3 shows the influence of post-graft rise in intraocular pressure on graft survival. A significant difference was found across groups (Log Rank Statistic=4.83; df=1; p=0.028). This variable was retained in the final multivariate model (see section 6.7).

Figure 6.6.3 Post-graft rise in intraocular pressure



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No rise in IOP	947	616	416	284	193	125	83	45	26	18
Rise in IOP	101	77	49	38	28	18	14	8	5	2

Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9
No rise in IOP	0.94	0.91	0.88	0.84	0.82	0.79	0.77	0.73	0.67
Rise in IOP	0.99	0.99	0.94	0.92	0.92	NA	NA	NA	NA

6.7 Multivariate Analysis

A multivariate model was used to investigate the combined effect of variables on deep anterior lamellar graft survival, adjusted for all other variables in the model (see section 1.4.6 for further information).

Table 6.10 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 collinear with (i.e. were highly correlated and produced the same effect on the outcome as) another variable in the model.

Table 6.10 Multivariate model

Deep Anterior Lamellar Keratoplasty

Multivariate Model

Not significant in univariate analysis

- Donor age group
- Donor sex
- Eye bank
- Interstate transportation of donor cornea
- Eye only donor
- Cause of donor death
- Central endothelial cell count
- Storage medium
- Time from donor death to enucleation of donor tissue
- Time from enucleation to storage of donor tissue
- Time from storage of donor tissue to graft – Optisol
- Time from storage of donor tissue to graft – organ culture
- Time in deswelling media for tissue stored in organ culture media
- Recipient sex
- Donor/recipient sex match/mismatch
- Eye grafted
- Any pervious contralateral graft/s
- Prior corneal collagen cross linking
- Any post-graft rejection
- Time to removal of sutures
- Post-graft corneal oedema
- Post-graft interface opacity

Significant in univariate analysis but excluded from multivariate model due to collinearity

- The centre effect (collinear with surgeon experience and level of follow-up)

Significant in univariate analysis but not retained in multivariate model

- Change in lens status from pre- to post-graft
- Pre-graft inflammation and/or steroid use
- Type of DALK procedure
- Australian State in which graft was performed
- Post-graft microbial keratitis
- Indication for graft - graft performed for keratoconus
- Graft size

Significant in univariate analysis AND retained in multivariate model

- Any prior ipsilateral graft/s
- Pre-graft corneal neovascularisation
- Recipient age group
- Graft era/year
- Surgeon caseload and level of follow-up
- Post-graft corneal neovascularisation
- Post-graft rise in intraocular pressure

Table 6.11 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, except where it made logical sense to use a different group. The hazard ratios for a given variable are adjusted for all other variables in the model. This model included data from 2,018 deep anterior lamellar keratoplasties, performed in 1,824 recipients.

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: ($Chi^2=187.44$, $p<0.0001$).

Table 6.11 Clustered multivariate model

	n	Hazard Ratio	Standard error	p-value	Global p-value	95% confidence interval
Number of prior ipsilateral grafts						
None	1930	1.00			0.0394	
One or more	88	1.65	0.40			1.02 to 2.65
Pre-graft corneal neovascularisation						
None/one quadrant	1767	1.00			<0.0001	
Two/three/four quadrants	251	2.50	0.51			1.67 to 3.73
Recipient age group						
0 to 39 years	1263	0.26	0.07	<0.001		0.16 to 0.43
40 to 69 years	641	0.40	0.10	<0.001		0.25 to 0.67
70 years or older	114	1.00			<0.0001	
Surgeon caseload and level of follow-up						
Low caseload surgeons	660	0.36	0.08	<0.001		0.23 to 0.55
High caseload, low follow-up	589	1.00			<0.0001	
High caseload, high follow-up	769	0.34	0.08	<0.001		0.22 to 0.53
Graft era						
Pre 2019	1737	1.00			0.0004	
2019/2020	281	3.66	1.35			1.77 to 7.56
Post-graft corneal neovascularisation						
No	1885	1.00			<0.0001	
Yes	133	2.20	0.39			1.56 to 3.11
Post-graft rise in intraocular pressure						
No	1912	1.00			0.0010	
Yes	106	0.30	0.11			0.15 to 0.61

6.7.1 Significant differences in the deep anterior lamellar keratoplasty multivariate model for categories with more than two groups following Holm-Bonferroni correction for multiple comparisons

6.7.1.1 Recipient age group

Significantly poorer survival was shown for the 70 years and over age group, compared to those aged 0 to 39 years or 40 to 69 years (both $p<0.001$).

Significantly poorer survival was shown for the 40 to 69 years age group, compared to those aged 0 to 39 years ($p=0.011$).

6.7.1.2 Volume of DALK registered by surgeon and level of follow-up received

Grafts performed by surgeons with 41 or more DALK registered (>2% of the cohort) with the ACGR, and below average (≤62%) levels of follow-up had significantly poorer survival than those performed by surgeons with 41 or more DALK registered with the ACGR, and above average (>62%) levels of follow-up, and surgeons with fewer than 41 DALK registered (both $p<0.001$).

6.8 Reasons for Graft Failure

Of the 1,241 followed grafts, 161 (13%) were known to have failed by the census date. This equates to 8% of the 2,018 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 6.12 shows the reasons for failure given.

Table 6.12 Reasons for graft failure

Deep Anterior Lamellar Corneal Grafts
Reasons for Graft Failure

Scarring	21 (13%)
Primary graft failure	20 (12%)
Non herpetic infection	17 (11%)
Astigmatism	12 (7%)
Trauma	9 (6%)
Endothelial cell failure	8 (5%)
Recurrence of corneal dystrophy	8 (5%)
Corneal ulcer/perforation	7 (4%)
Herpetic infection	6 (4%)
Rejection	6 (4%)
Corneal melt	5 (3%)
Corneal neovascularisation	5 (3%)
Other	8 (5%)
Unspecified	29 (18%)
Total	***161 (100%)***

Other included: graft detachment (3), epithelial/limbal stem cell failure (3), lipid keratopathy (1), recurrent inflammation (1).

Of the 20 grafts reported by surgeons to have been primary graft failures, 10 had no further information provided. Specific reasons given were: detachment or rupture of Descemet's membrane (10), corneal oedema (1), residual opacity (1), and fungal keratitis (1).

6.9 Post-graft Changes in Best Corrected Visual Acuity

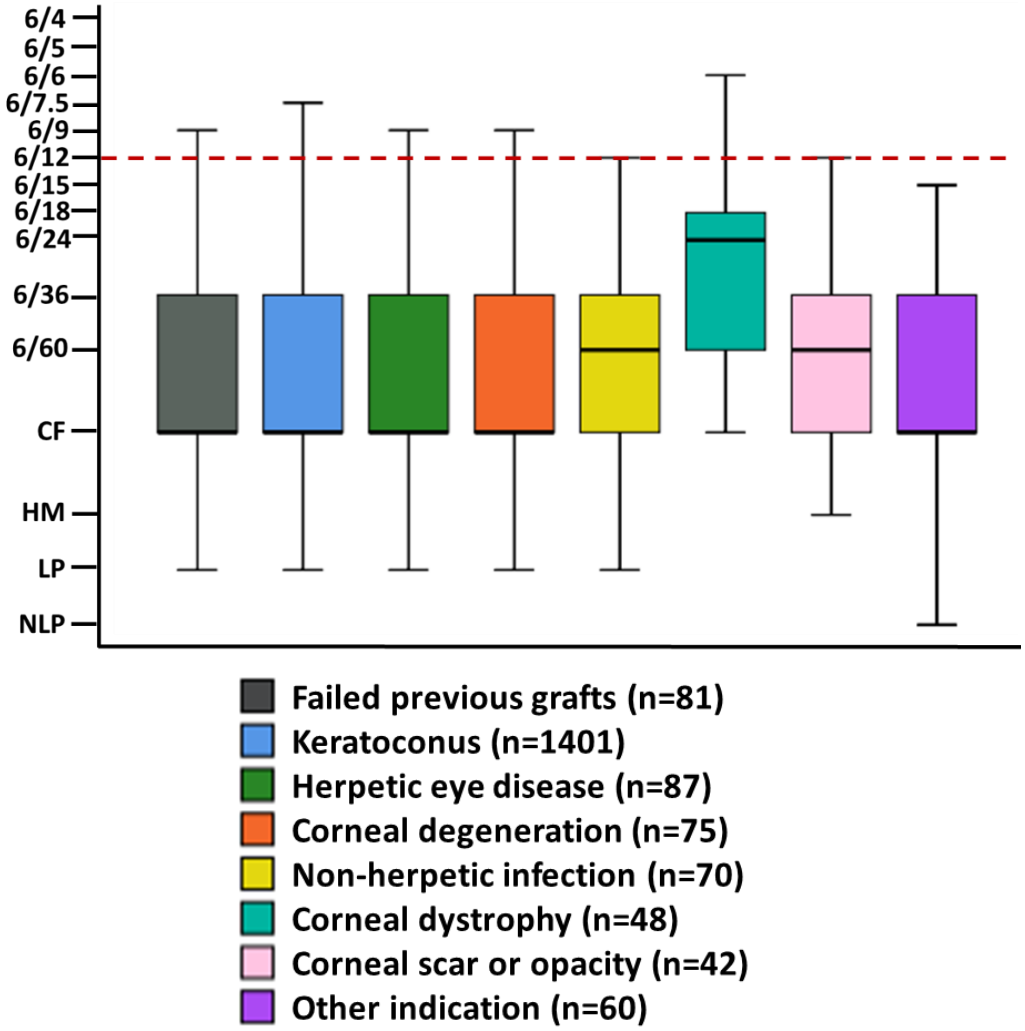
Post-graft best corrected visual acuity (BCVA) is an important outcome for many corneal graft recipients. A desire for improved visual acuity was specified as a reason for graft in 1854 (92%) of registered deep anterior lamellar keratoplasties. In 87% of cases (1746), this was the sole desired outcome indicated. All analyses are conducted on data for **surviving** grafts. See section 1.4.7 for further explanation of the methods used to analyse visual acuity data.

6.9.1 Deep anterior lamellar keratoplasty: Pre-graft visual acuity by indication

Figure 6.9.1 shows the pre-graft BCVA, reported for eyes undergoing deep anterior lamellar keratoplasty for each of the indication for graft groups. The central line within each box-and-whisker plot shows the median BCVA reported for the group, the box represents the inter-quartile range, while the whisker shows the range. Please note that outliers were included in the calculation of the box and whisker plots but are not shown in the figures. The dashed line indicates a BCVA of 6/12, which represents functional vision.

Median pre-graft BCVA was poor for all indication groups. Those performed for failed previous graft/s, keratoconus, herpetic eye disease, corneal degeneration, and other indications had a median pre-graft BCVA of Count Fingers. Those performed for non-herpetic infection or corneal scars and opacities had slightly better levels at 6/60, while the best pre-graft BCVA was in eyes with corneal dystrophies, at 6/24.

Figure 6.9.1. Pre-graft best corrected visual acuity

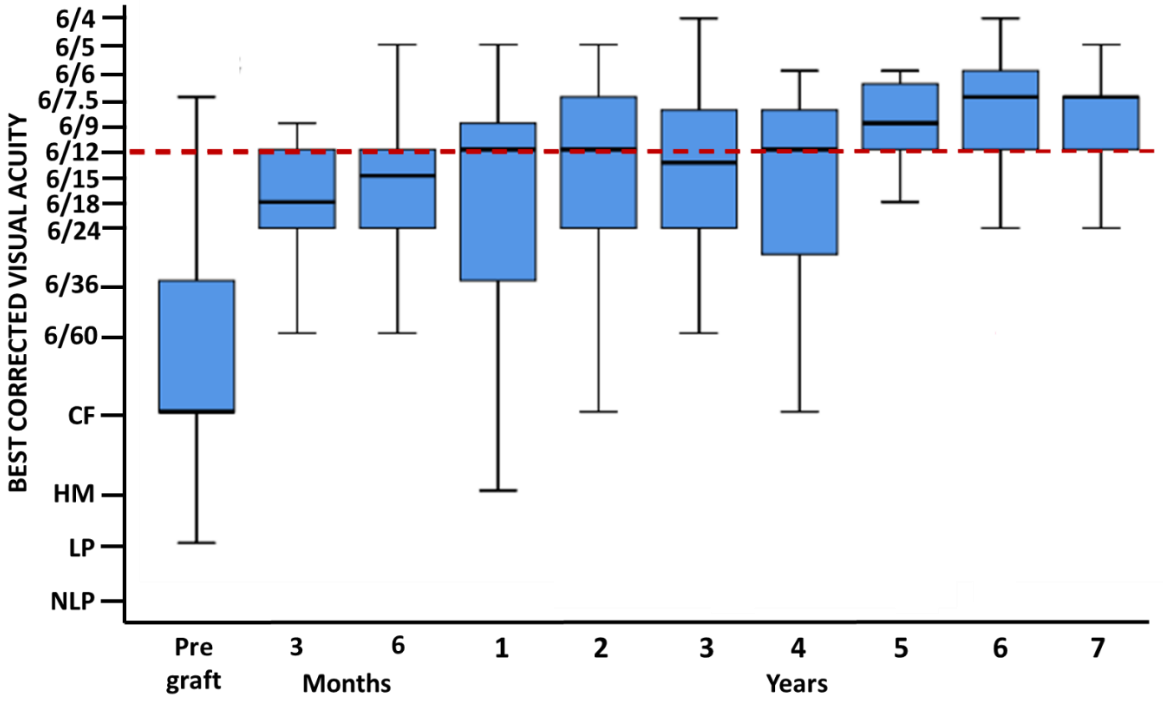


Deep Anterior Lamellar Keratoplasty

6.9.2 Deep anterior lamellar keratoplasty: Post-graft visual acuity in surviving grafts performed for keratoconus, over time

Figure 6.9.2 shows the change in median BCVA over time for deep anterior lamellar keratoplasty performed for keratoconus. The median BCVA improved significantly compared to the pre-graft level (Count Fingers), reaching 6/15 by 6-months post-graft ($p<0.001$). It further improved to 6/12 by 1-year post-graft, however this was not a significant improvement compared to 6-months, $p=0.185$. The group retained this 6/12 level, or better, to 7-years post-graft.

Figure 6.9.2 Change in BCVA for deep anterior lamellar keratoplasties, surviving at time of measurement for keratoconus, over time

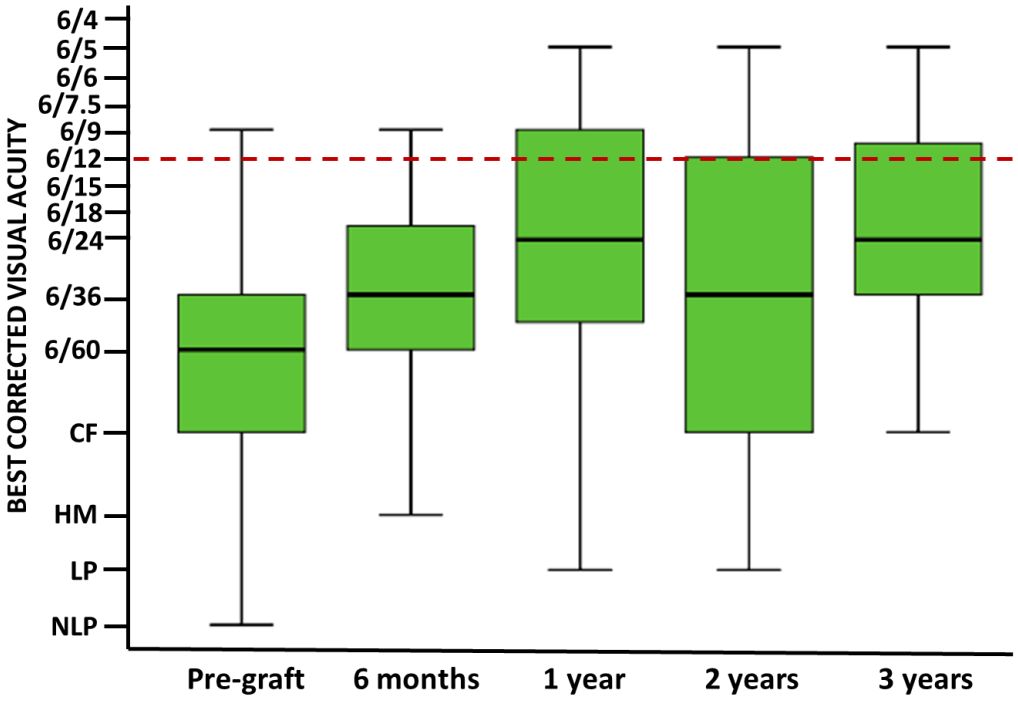


	Pre	3m	6m	1y	2y	3y	4y	5y	6y	7y	8y
Keratoconus	1401	14	43	130	85	44	23	16	20	19	5

6.9.3 Deep anterior lamellar keratoplasty: Post-graft visual acuity in surviving grafts performed for indications other than keratoconus, over time

Due to the low number of grafts for individual indications with visual acuity data available, changes in BCVA post-graft were only able to be examined individually for those grafts performed for keratoconus. All other indications for graft were analysed together. Figure 6.9.3 shows the change in median BCVA over time for these grafts. The median BCVA improved significantly compared to the pre-graft level (6/60), reaching 6/36 by 6-months post-graft (p=0.015). It further improved to 6/24 by 1-year post-graft, however this was not a significant improvement compared to 6-months, p=0.171. The group varied between 6/24 and 6/36 up to 3-years post-graft. While never reaching the 6/12 level, this improvement remained significant compared to pre-graft levels (p<0.001, p=0.005, and p<0.001, respectively).

Figure 6.9.3 Change in BCVA for deep anterior lamellar keratoplasties, surviving at time of measurement for indications other than keratoconus, over time



Number of grafts with BCVA data available at each time point

	Pre	3m	6m	1y	2y	3y	4y
Failed previous graft/s	81	1	2	7	1	0	1
Herpetic eye disease	87	1	3	10	8	5	4
Corneal degeneration	75	1	1	4	2	4	1
Non-herpetic infections	70	2	5	5	7	3	0
Corneal dystrophy	48	1	1	3	2	0	0
Corneal scar/opacity	42	1	1	4	2	0	0
Other	60	0	2	7	4	3	0
Total	463	7	15	40	26	15	6

7 Traditional Lamellar Keratoplasty

This chapter presents analyses of the 1,670 traditional lamellar keratoplasties (TLK) registered with the ACGR. Kaplan-Meier survival analyses were conducted 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.

7.1 Donor and Eye Banking Factors

Table 7.1 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 (1,670 registered and 1,248 followed) and the percentages, which should be summed vertically for each variable, total 100.

Table 7.1 Donor and eye banking factors, significant in univariate analyses

Traditional Lamellar Keratoplasty

Donor and Eye Banking Factors

	Registered (%)	Followed (%)
Eye bank		
	938 (56%)	677 (54%)
Eye banks are not identified due to	225 (13%)	180 (14%)
confidentiality constraints. See	183 (11%)	141 (11%)
Section 1.4.8 for further information.	141 (8%)	88 (7%)
	133 (8%)	117 (9%)
Not advised	50 (3%)	45 (4%)
Storage media		
Optisol	392 (23%)	290 (23%)
Organ Culture	221 (13%)	130 (10%)
Moist Pot	826 (49%)	638 (51%)
Superseded media	180 (11%)	154 (12%)
Frozen	30 (2%)	17 (1%)
Not advised	21 (1%)	19 (2%)
Interstate transportation		
Same State	1531 (92%)	1127 (90%)
Different States	89 (5%)	76 (6%)
Not advised	50 (3%)	45 (4%)
Death-to-enucleation time		
Up to 3 hours	182 (11%)	143 (11%)
4 to 6 hours	323 (19%)	253 (20%)
7 to 9 hours	354 (21%)	271 (22%)
10 to 12 hours	328 (20%)	253 (20%)
13 to 15 hours	186 (11%)	133 (11%)
16 to 18 hours	117 (7%)	77 (6%)
More than 18 hours	137 (8%)	80 (6%)
Unknown	43 (3%)	38 (3%)
Total	***1670 (100%)***	***1248 (100%)***

Table 7.2 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 (1,670 registered and 1,248 with follow-up provided) and the percentages, summed vertically for each variable, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

Table 7.2 Donor and eye banking factors, not significant in univariate analyses

Traditional Lamellar Keratoplasty

Donor and Eye Banking Factors

	Registered (%)	Followed (%)
Age of donor		
0 to 29 years	51 (3%)	43 (3%)
30 to 39 years	44 (3%)	35 (3%)
40 to 49 years	81 (5%)	64 (5%)
50 to 59 years	198 (12%)	144 (12%)
60 to 69 years	430 (26%)	317 (25%)
70 to 79 years	532 (32%)	392 (31%)
80 years and older	300 (18%)	223 (18%)
Not advised	34 (2%)	30 (2%)
Chi^2=7.00, df=6, p=0.321		
Sex of donor		
Female	700 (42%)	518 (42%)
Male	923 (55%)	687 (55%)
Not advised	47 (3%)	43 (3%)
Chi^2=0.146, df=1, p=0.702		
Donor type		
Eye donor only	1540 (92%)	1159 (93%)
Solid organ and/or bone/tissue donor	130 (8%)	89 (7%)
Chi^2=1.90, df=1, p=0.168		
Cause of donor death		
Cardiovascular	557 (33%)	418 (34%)
Malignancy	401 (24%)	294 (24%)
Trauma	92 (6%)	71 (6%)
Respiratory	185 (11%)	140 (11%)
Intracranial/cerebral haemorrhage	268 (16%)	198 (16%)
Other specified	81 (5%)	64 (5%)
Not advised/live donor*	86 (5%)	63 (5%)
Chi^2=6.56, df=5, p=0.256		
Central corneal endothelial cell density		
<2500 cells/mm^2	59 (4%)	34 (3%)
2500 to 2999 cells/mm^2	110 (7%)	79 (6%)
3000+ cells/mm^2	62 (4%)	40 (3%)
Not advised	1439 (86%)	1095 (88%)
Chi^2=0.719, df=2, p=0.698		

	Registered (%)	Followed (%)
Enucleation-to-storage time		
Within 1 hour	162 (10%)	141 (11%)
1 to 3 hours	718 (43%)	501 (40%)
4 to 6 hours	170 (10%)	126 (10%)
7 to 9 hours	68 (4%)	49 (4%)
10 to 18 hours	63 (4%)	55 (4%)
More than 18 hours	80 (5%)	64 (5%)
Not advised	409 (24%)	312 (25%)
Chi²=5.47, df=5, p=0.361		
Storage-to-graft time - Optisol		
Within 5 days	155 (9%)	121 (10%)
More than 5 days	163 (10%)	118 (9%)
Not advised	74 (4%)	51 (4%)
Not applicable	1278 (77%)	958 (77%)
Chi²=1.90, df=1, p=0.168		
Storage-to-graft time – Organ culture		
Up to 2 weeks	60 (4%)	40 (3%)
2 to 3 weeks	67 (4%)	39 (3%)
More than 3 weeks	54 (3%)	26 (2%)
Not advised	40 (2%)	25 (2%)
Not applicable	1449 (87%)	1118 (90%)
Chi²=4.43, df=2, p=0.109		
Storage-to-graft time – Moist pot		
Within 2 days	102 (6%)	83 (7%)
2 to 7 days	116 (7%)	96 (8%)
8 to 14 days	116 (7%)	86 (7%)
15 to 21 days	100 (6%)	62 (5%)
More than 3 weeks	122 (7%)	98 (8%)
Not advised	270 (16%)	213 (17%)
Not applicable	844 (51%)	610 (49%)
Chi²=5.71, df=4, p=0.222		
Deswelling-to-graft time – Organ culture		
Within 2 days	66 (4%)	41 (3%)
More than 2 days	56 (3%)	21 (2%)
Not advised	99 (6%)	68 5(%)
Not applicable	1449 (87%)	1118 (90%)
Chi²=0.47, df=1, p=0.495		
Total	***1670 (100%)***	***1248 (100%)***

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

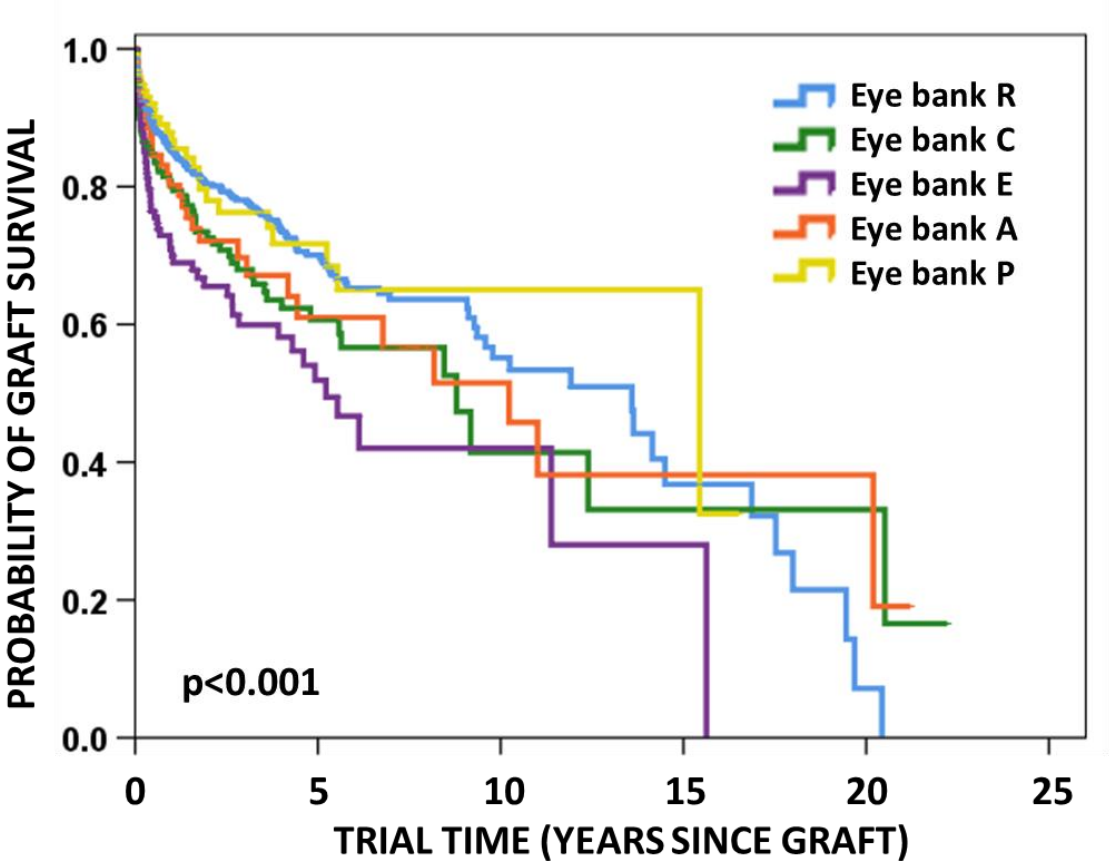
* ACGR advised that cause of death was not yet determined but there were no medical contraindications and the eye had been cleared for release, by the Medical Director, in accordance with EBAANZ guidelines.

Traditional Lamellar Keratoplasty

7.1.1 Traditional lamellar keratoplasty survival: influence of Australian eye bank

Donor corneas are retrieved, processed, stored and distributed by five eye banks around Australia. Figure 7.1.1 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=19.31; df=4; p<0.001), with grafts performed in State E having poorer survival than those performed State R (p<0.001) and State P (p=0.003). Data on this variable were not provided in 3% of cases, primarily registered with the ACGR 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=21.01; df=5; p<0.001). This variable was not retained in the final multivariate model (see section 7.7) suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 7.1.1 Australian eye bank



Probability of graft survival (years post-graft)

	1	2	4	6	8	10
Eye bank R	0.85	0.80	0.74	0.65	0.64	0.55
Eye bank C	0.80	0.73	0.64	0.57	NA	NA
Eye bank E	0.70	0.66	0.58	NA	NA	NA
Eye bank A	0.80	0.72	0.67	NA	NA	NA
Eye bank P	0.88	0.78	0.72	NA	NA	NA

Note: Further information is not provided due to confidentiality constraints (see section 1.4.8).

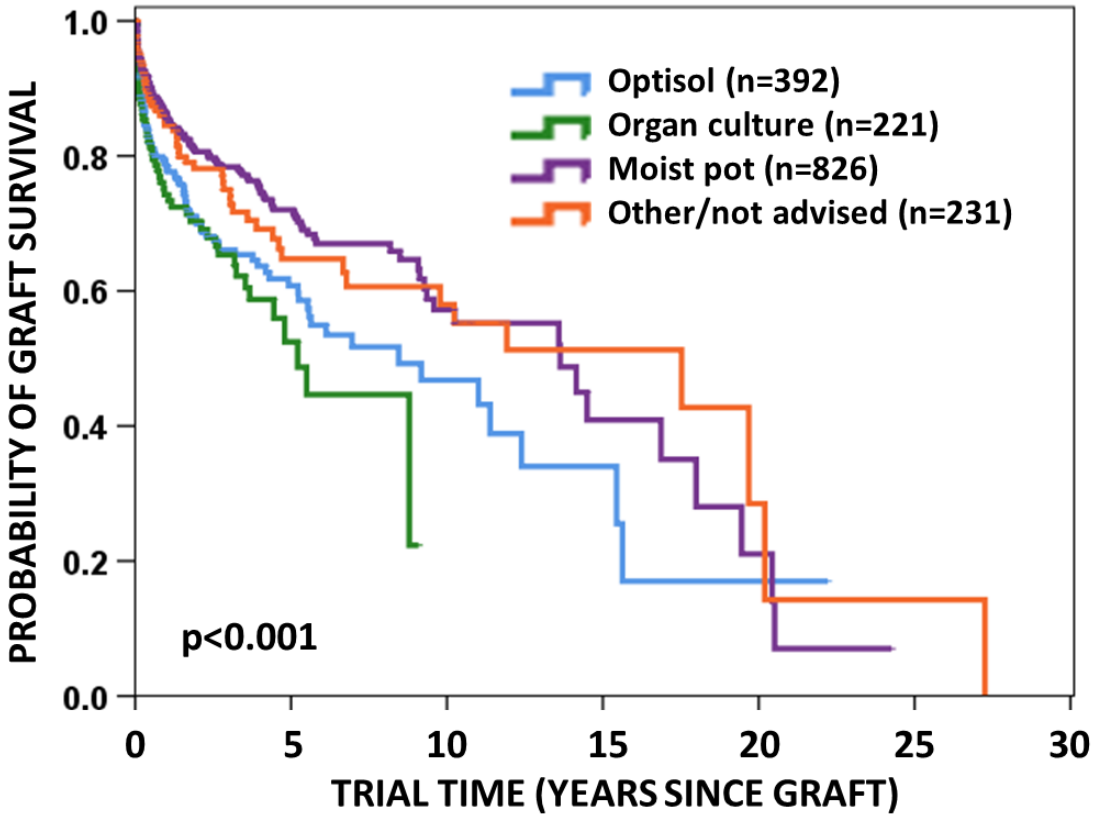
7.1.2 Traditional lamellar keratoplasty survival: influence of storage media

Figure 7.1.2 shows the comparison of graft survival for corneas stored using hypothermic techniques (split into Optisol and superseded media) compared to organ culture medium and moist pot (see section 1.2 for further details about storage media). Initially, data were not analysed for 30 grafts where the donor eye was frozen, and 21 grafts where the eye bank did not specify which medium was used.

A significant difference in outcomes was found between media (Log Rank Statistic=21.60; df=3; p<0.001). All the grafts where the storage media was not advised had been performed prior to 2002, as had two-thirds of those in which the tissue was frozen. Further analyses revealed that there were no differences in survival for grafts stored in superseded media, grafts performed with corneas that had been frozen, and grafts where the storage media was not advised (p=0.675). These groups were therefore combined, with the resulting comparison retaining significance (Log Rank Statistic=20.70; df=3; p<0.001).

Survival of grafts performed with tissue stored in a moist pot was significantly better than those stored in either Optisol or organ culture (both p<0.001). The nature of this variable means that tissue stored in Optisol and organ culture are more likely to be from more recent years. See section 7.3 for a discussion of the effect of graft era on survival. This variable was not retained in the final multivariate model (see section 7.7), suggesting that it is **not** an independent factor significantly affecting graft survival

Figure 7.1.2 Storage media



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14
Optisol	178	117	74	40	23	17	8	4
Organ culture	83	61	30	10	5	NA	NA	NA
Moist pot	403	284	164	92	62	31	21	14
Other/not advised	117	87	52	34	25	21	13	9

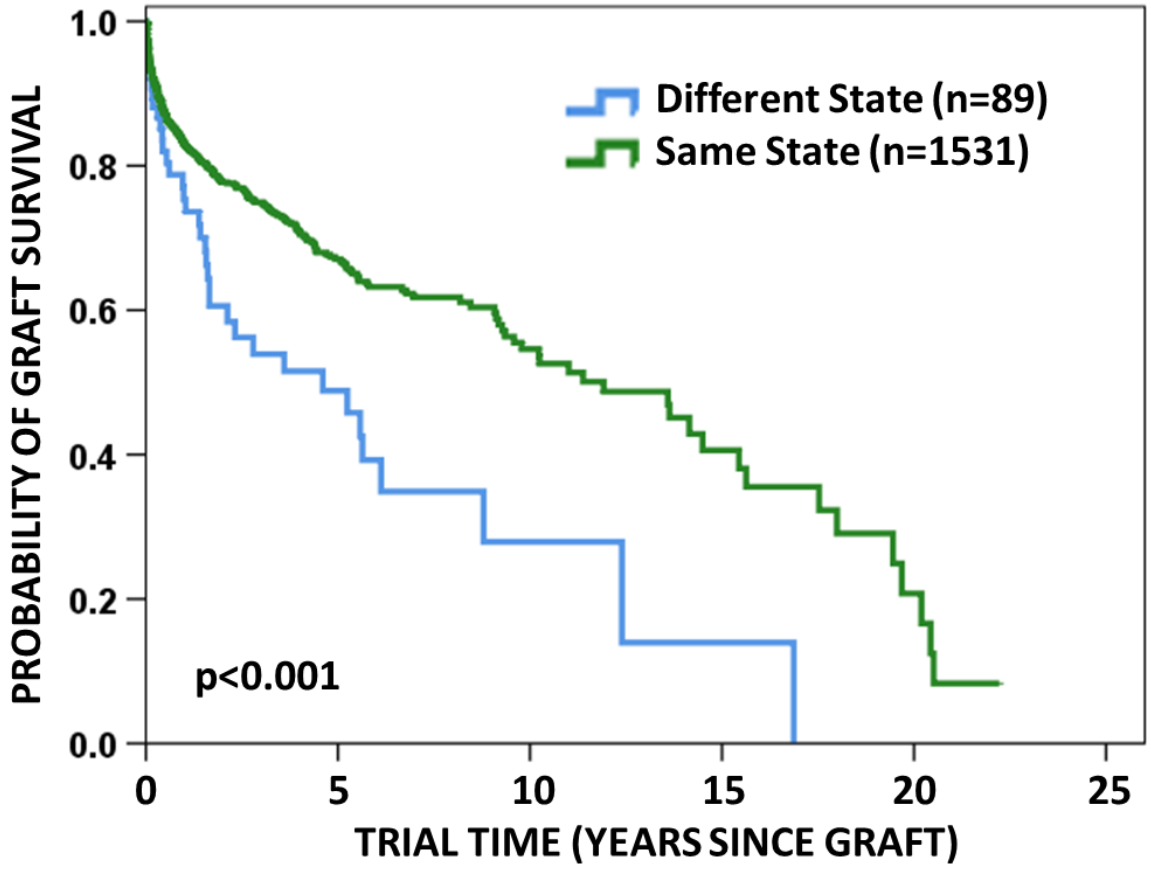
Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12
Optisol	0.79	0.70	0.64	0.55	0.52	NA	NA
Organ culture	0.74	0.70	0.59	NA	NA	NA	NA
Moist pot	0.86	0.81	0.75	0.67	0.67	0.57	0.55
Other/not advised	0.85	0.78	0.69	0.65	0.61	0.58	NA

7.1.3 Traditional lamellar keratoplasty survival: influence of interstate transportation

In most 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 7.1.3 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. A significant difference was found between groups (Log Rank Statistic=14.68; df=1; p<0.001). Data for this variable were not available for the 3% of cases where the donor State was not advised (see section 7.1.1). 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=16.13; df=2; p<0.001). This variable was not retained in the final multivariate model (see section 7.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 7.1.3 Interstate transportation



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14	16
Different State	44	29	20	9	7	4	2	1	1
Same State	711	500	286	156	97	57	34	22	14

Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12	14
Different State	0.75	0.61	0.52	NA	NA	NA	NA	NA
Same State	0.83	0.78	0.71	0.63	0.62	0.55	0.49	0.45

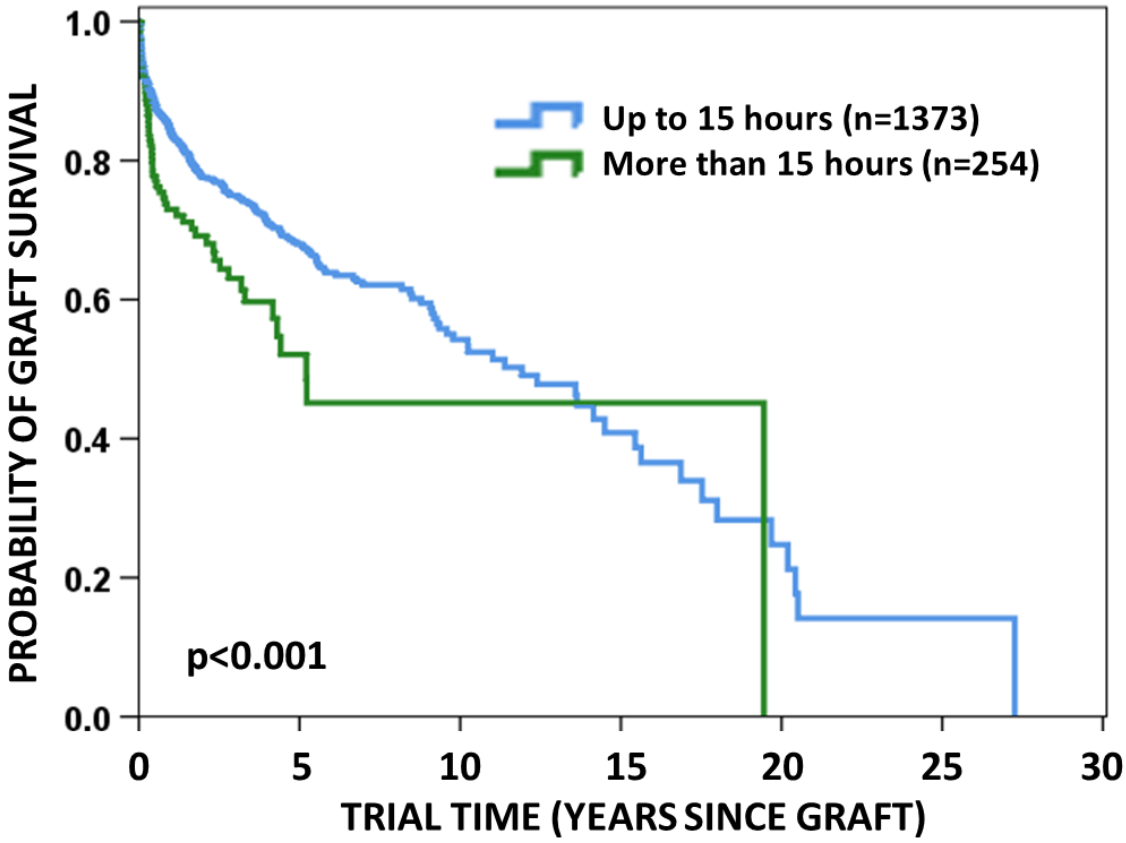
7.1.4 Traditional lamellar keratoplasty survival: influence of death-to-enucleation time

Donor corneas are retrieved as soon as possible following donor death. Retrieval is recommended within the first 18 hours and 92% of donor eyes were enucleated within this time-frame. Times are rounded down to the nearest hour and the median time from donor death to enucleation was 9 hours (range 0-42 hours).

Figure 7.1.4 shows a comparison of graft survival depending on time from donor death to enucleation. Times were initially stratified into three-hourly groups. Very few enucleations occur within the hour following donor death and so these were combined with those performed between 1 to 3 hours. A significant difference was found across time groups (Log Rank Statistic=14.37; df=6; p=0.026). Further analyses examined whether there were significant differences between adjacent time groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=10.74; df=1; p=0.001).

Data on this variable were not provided in 3% of cases and 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=10.64; df=2; p=0.005). This variable was retained in the final multivariate model (see section 7.7).

Figure 7.1.4 Time from donor death to enucleation



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14	16
Up to 15 hours	671	469	284	163	105	63	40	25	17
More than 15 hours	88	63	28	9	6	2	1	1	1

Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12	14
Up to 15 hours	0.84	0.78	0.71	0.64	0.62	0.54	0.49	0.45
More than 15 hours	0.73	0.69	0.60	NA	NA	NA	NA	NA

7.2 Recipient Factors

Table 7.3 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 (1,670 registered and 1,248 followed) and the percentages, which should be summed vertically for each variable, total 100.

Table 7.3 Recipient factors, significant in univariate analyses

Traditional Lamellar Keratoplasty

Recipient Factors

	Registered (%)	Followed (%)
Indication for graft		
Failed previous graft	253 (15%)	184 (15%)
Beta radiation	234 (14%)	172 (14%)
Pterygium	225 (13%)	190 (15%)
Corneal ulcers	200 (12%)	150 (12%)
Keratoconus	107 (6%)	74 (6%)
Scleral necrosis	97 (6%)	71 (6%)
Herpetic eye disease	88 (5%)	64 (5%)
Limbal dermoid	85 (5%)	70 (6%)
Corneal degenerations	69 (4%)	54 (4%)
Glaucoma	53 (3%)	28 (2%)
Cancer	50 (3%)	34 (3%)
Non-herpetic infections	42 (2%)	32 (3%)
Trauma	35 (2%)	30 (2%)
Other*	132 (8%)	95 (8%)
Australian State where graft was performed		
	942 (56%)	680 (54%)
	210 (13%)	167 (13%)
States are not identified due to	173 (10%)	133 (11%)
confidentiality constraints. See	164 (10%)	106 (8%)
section 1.4.8 for further information.	123 (7%)	108 (9%)
	57 (3%)	53 (4%)
	1 (<1%)	1 (<1%)
Recipient age		
0 to 9 years	70 (4%)	61 (5%)
10 to 19 years	50 (3%)	37 (3%)
20 to 29 years	111 (7%)	86 (7%)
30 to 39 years	157 (9%)	134 (11%)
40 to 49 years	173 (10%)	136 (11%)
50 to 59 years	207 (12%)	167 (13%)
60 to 69 years	300 (18%)	216 (17%)
70 to 79 years	353 (21%)	254 (20%)
80 and older years	249 (15%)	157 (13%)

	Registered (%)	Followed (%)
Pre-graft neovascularisation		
None	1090 (65%)	796 (64%)
One quadrant	160 (10%)	119 (10%)
Two quadrants	193 (12%)	152 (12%)
Three quadrants	69 (4%)	60 (5%)
Four quadrants	158 (9%)	121 (10%)
Pre-graft inflammation and/or steroid use		
No	905 (54%)	678 (54%)
Yes	681 (41%)	511 (41%)
Not advised	84 (5%)	59 (5%)
History of raised intraocular pressure		
No raised IOP	1477 (88%)	1117 (90%)
Raised IOP	193 (12%)	131 (11%)
Active herpetic infection at graft		
No	1515 (91%)	1142 (92%)
Yes	56 (3%)	40 (3%)
Not advised	99 (6%)	66 (5%)
Prior ipsilateral corneal graft/s		
None	1383 (83%)	1040 (83%)
One	189 (11%)	140 (11%)
Two	64 (4%)	46 (4%)
Three or more	34 (2%)	22 (2%)
Prior contralateral corneal graft/s		
None	1523 (91%)	1138 (91%)
One	105 (6%)	77 (6.2%)
Two or more	42 (3%)	33 (3)
Total	***1670 (100%)***	***1248 (100%)***

*Other included: wound dehiscence (19), corneal dystrophy (18), corneal scar/opacity (17), decemetocoele (17), pseudophakic bullous keratopathy (10), scleromalacia (8), interstitial keratitis (5), keratoglobus (5), band keratopathy (3), lipid keratopathy (3), not advised (3), amyloidosis (2), aniridic keratopathy (2), corneal thinning (2); ectodermal dysplasia (2), epithelial defect (2), scleral fistula (2), aphakia (1), atopic keratoconjunctivitis (1), autograft repair (1), corneal membrane change (1), corneal thickening (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).

Table 7.4 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 (1,670 registered and 1,248 with follow-up provided) and the percentages, summed vertically, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided for each variable.

Table 7.4 Recipient factors, not significant in univariate analyses

Traditional Lamellar Keratoplasty

Recipient Factors

	Registered (%)	Followed (%)
Recipient sex		
Female	670 (40%)	506 (41%)
Male	1000 (60%)	742 (59%)
Chi²=1.04, df=1, p=0.307		
Donor/recipient sex match/mismatch		
Female/female	292 (17%)	217 (17%)
Female/male	408 (24%)	301 (24%)
Male/female	359 (21%)	273 (22%)
Male/male	564 (34%)	414 (33%)
Not advised	47 (3%)	43 (3%)
Chi²=1.06, df=3, p=0.787		
Eye in which graft was performed		
Left	**866 (52%)**	**643 (52%)**
Right	803 (48%)	604 (48%)
Not advised	1 (<1%)	1 (<1%)
Chi²=0.04, df=1, p=0.851		
Prior intraocular surgery in first grafts		
No	923 (55%)	718 (58%)
Yes	424 (25%)	300 (24%)
Not advised	36 (2%)	22 (2%)
Not applicable (repeat and/or prior concurrent)	287 (17%)	208 (17%)
Chi²=0.27, df=1, p=0.601		
Total	***1670 (100%)***	***1248 (100%)***

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

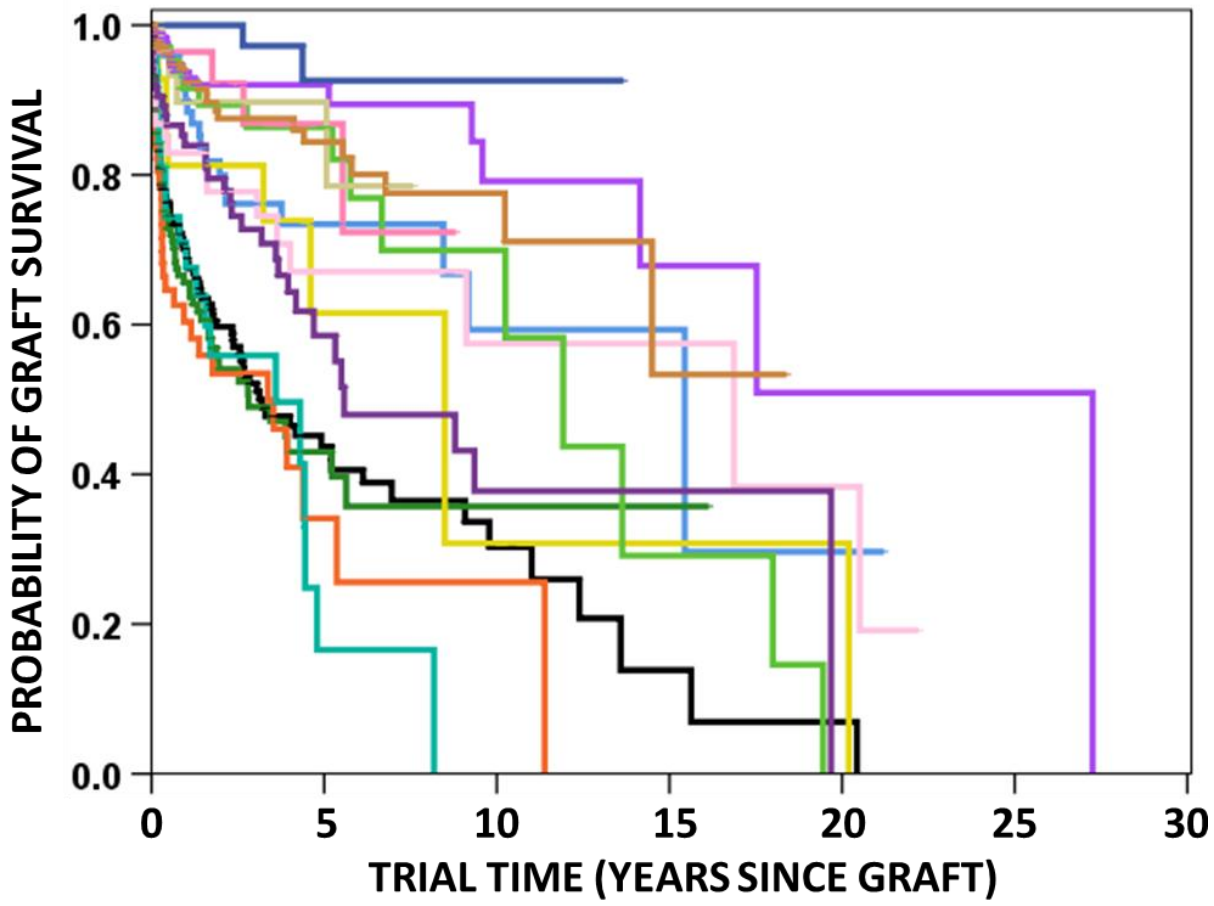
7.2.1 Traditional lamellar keratoplasty survival: influence of indication for graft

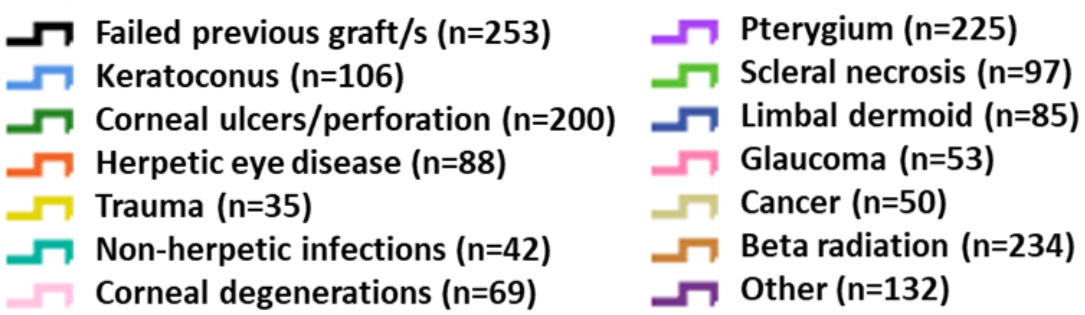
Figure 7.2.1 shows the comparison of graft survival depending on indication for graft. All repeat grafts were analysed together, regardless of original pathology. A significant difference was found across groups (Log Rank Statistic=207.53; df=13; p<0.001).

Grafts performed for keratoconus, limbal dermoid, pterygium, scleral necrosis, effects of beta radiation, glaucoma or cancer all had better survival than those performed for failed previous graft/s corneal ulcers, herpetic eye disease, and non-herpetic infections. Grafts performed for keratoconus, limbal dermoid, pterygium, scleral necrosis, or effects of beta radiation, all had better survival than those performed for failed previous graft/s.

Grafts performed for limbal dermoid or pterygium also had better survival than those performed for corneal degenerations. Grafts performed for limbal dermoid or beta radiation had better survival than those performed for trauma. Grafts performed 'other' indications had poorer survival than those performed for limbal dermoid, pterygium, beta radiation (all comparisons p<0.001). Indication for graft was retained in the final multivariate model (see section 7.7).

Figure 7.2.1 Indication for graft





Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9
Failed previous graft/s	107	72	50	38	30	25	15	13	13
Keratoconus	58	42	33	24	20	18	15	11	9
Corneal ulcers/perforation	69	37	26	21	15	7	7	6	3
Herpetic eye disease	27	21	15	7	4	3	3	3	3
Trauma	19	17	14	6	5	2	2	2	1
Non-herpetic infection	20	11	9	6	2	1	1	1	NA
Corneal degeneration	38	26	24	19	14	10	10	9	7
Pterygium	120	81	63	46	37	31	27	23	18
Scleral necrosis	44	34	28	25	22	13	8	6	6
Limbal dermoid	54	40	33	25	18	13	8	6	5
Glaucoma	24	21	11	8	7	3	1	1	NA
Cancer	22	15	10	8	8	4	1	NA	NA
Beta radiation	117	82	69	59	43	34	30	24	15
Other	62	50	38	28	18	12	11	10	9

Probability of graft survival (years post-graft)

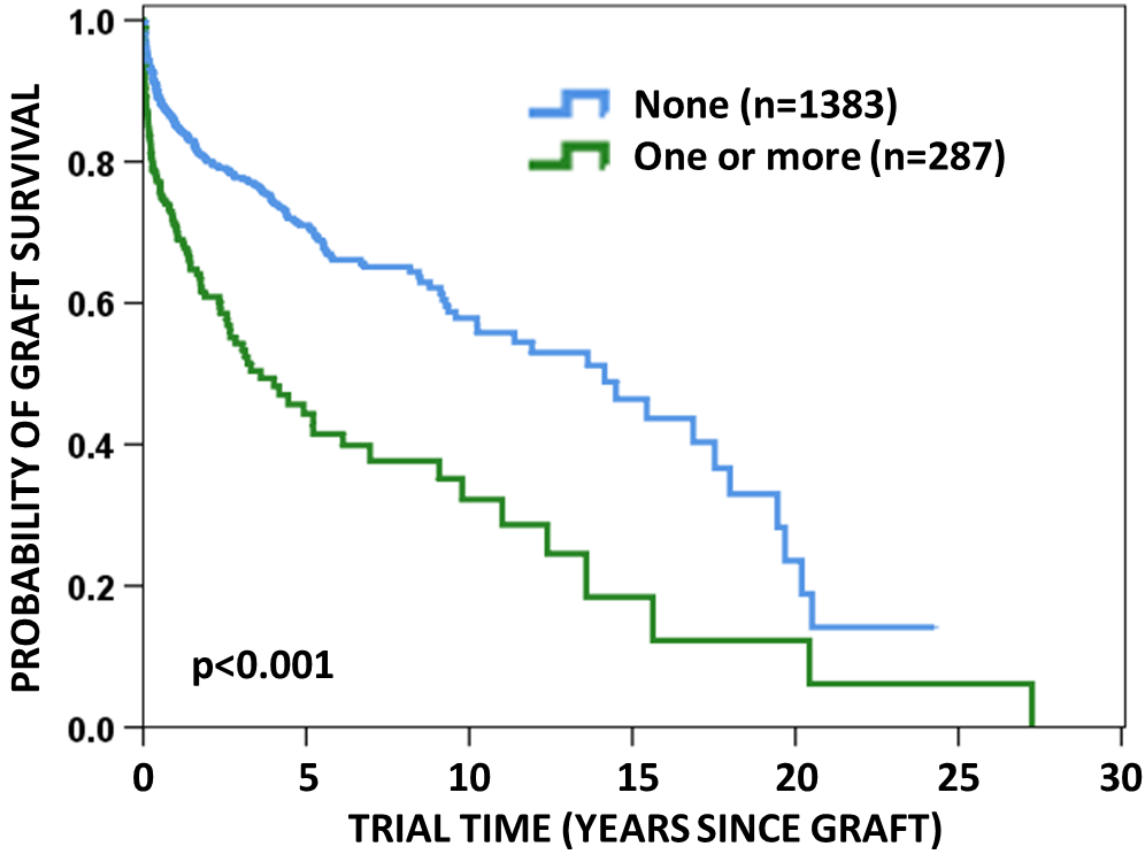
	1	2	3	4	5	6	7	8
Failed previous graft/s	0.70	0.60	0.52	0.48	0.44	0.41	NA	NA
Keratoconus	0.90	0.80	0.76	0.73	0.73	NA	NA	NA
Corneal ulcers/perforation	0.66	0.54	0.49	0.43	NA	NA	NA	NA
Herpetic eye disease	0.60	0.54	NA	NA	NA	NA	NA	NA
Non-herpetic infection	0.68	NA	NA	NA	NA	NA	NA	NA
Corneal degeneration	0.83	0.78	0.78	NA	NA	NA	NA	NA
Pterygium	0.94	0.92	0.92	0.92	0.92	0.89	0.89	0.89
Scleral necrosis	0.92	0.89	0.86	0.86	0.86	NA	NA	NA
Limbal dermoid	1.00	1.00	0.97	0.97	NA	NA	NA	NA
Glaucoma	0.96	0.92	NA	NA	NA	NA	NA	NA
Cancer	0.90	NA	NA	NA	NA	NA	NA	NA
Beta radiation	0.93	0.88	0.88	0.88	0.84	0.80	0.78	0.78
Other	0.84	0.80	0.73	0.64	NA	NA	NA	NA

7.2.2 Traditional lamellar keratoplasty survival: influence of number of previous ipsilateral graft/s

Figure 7.2.2 shows the comparison of graft survival stratified by the number of prior ipsilateral graft/s the recipient was known to have had at the time of graft. Comparisons were initially made with the number of previous grafts split into single categories, where there were enough data, and the comparison was significant (Log Rank Statistic=56.09; df=3; p<0.001).

Further analyses examined whether there were significant differences between adjacent groups. Recipients with one, two, or three or more previous ipsilateral grafts, did not have significantly different graft survival (p=0.291). These groups were therefore combined, and the comparison remained significant (Log Rank Statistic=49.95; df=1; p<0.001). This variable was not included in the multivariate analysis (see section 7.7) as it was collinear with indication for graft (see section 7.2.1) which was retained in the final multivariate model.

Figure 7.2.2 Previous ipsilateral graft/s



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10	12	14	16
None	656	465	364	276	210	149	122	100	74	59	34	24	16
One or more	125	84	59	44	33	27	17	15	15	10	8	3	2

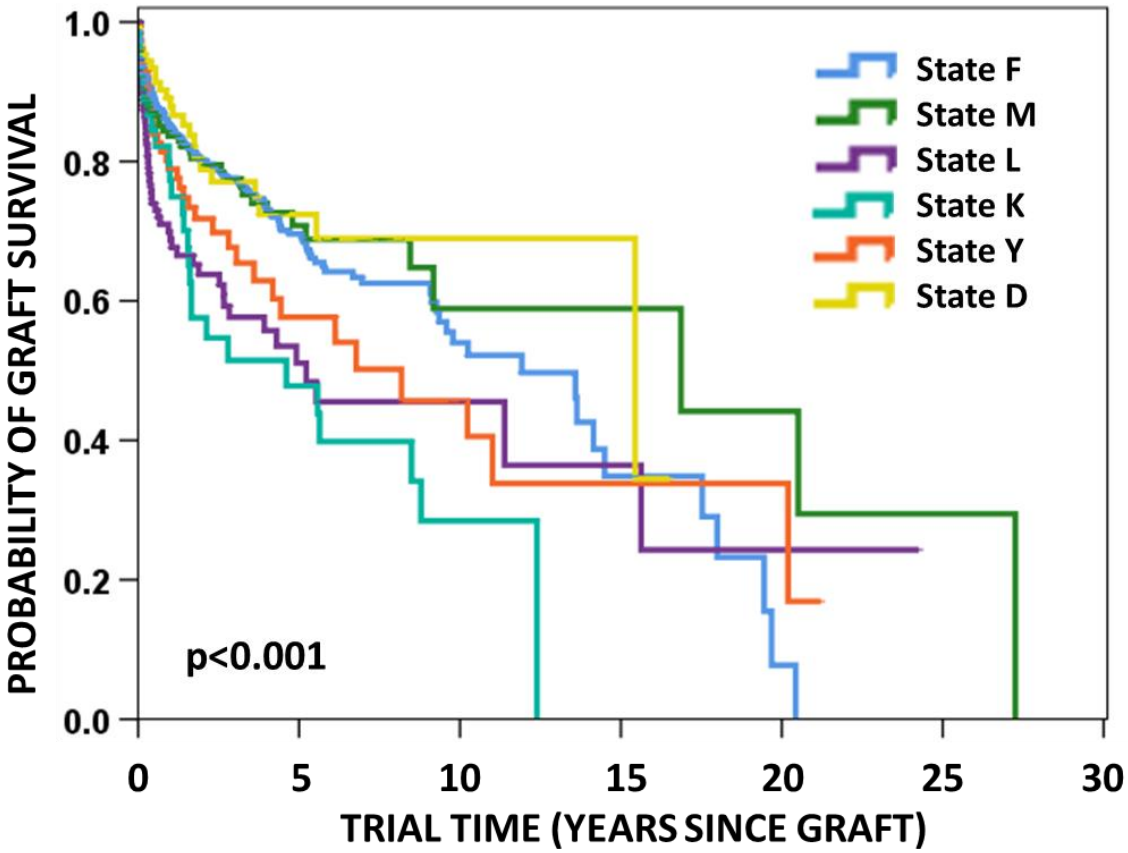
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10	12	14
None	0.85	0.80	0.78	0.74	0.71	0.66	0.65	0.65	0.62	0.58	0.53	0.41
One or more	0.71	0.61	0.54	0.49	0.44	0.42	NA	NA	NA	NA	NA	NA

7.2.3 Traditional lamellar keratoplasty survival: influence of Australian State where graft was performed

Figure 7.2.3 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=29.69; df=5; p<0.001), with grafts performed in State F, State M or State D having better survival than those performed in State K (all p≤0.001) and State L (all p≤0.002). This variable was excluded from the multivariate analysis (see section 7.7) as it was collinear with the variables relating to eye bank (see section 7.1.1), interstate transportation (see section 7.1.3), and the centre effect (see section 7.4.3), the last of which was retained in the final multivariate model.

Figure 7.2.3 Australian State where graft was performed



Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9	10	11
State F	0.85	0.80	0.78	0.73	0.70	0.64	0.63	0.63	0.63	0.54	0.52
State M	0.84	0.80	0.78	0.74	0.71	0.69	0.69	NA	NA	NA	NA
State L	0.69	0.64	0.58	0.56	0.51	NA	NA	NA	NA	NA	NA
State K	0.77	0.58	NA	NA	NA	NA	NA	NA	NA	NA	NA
State Y	0.79	0.72	0.68	0.63	0.58	NA	NA	NA	NA	NA	NA
State D	0.89	0.79	0.77	0.72	0.72	NA	NA	NA	NA	NA	NA

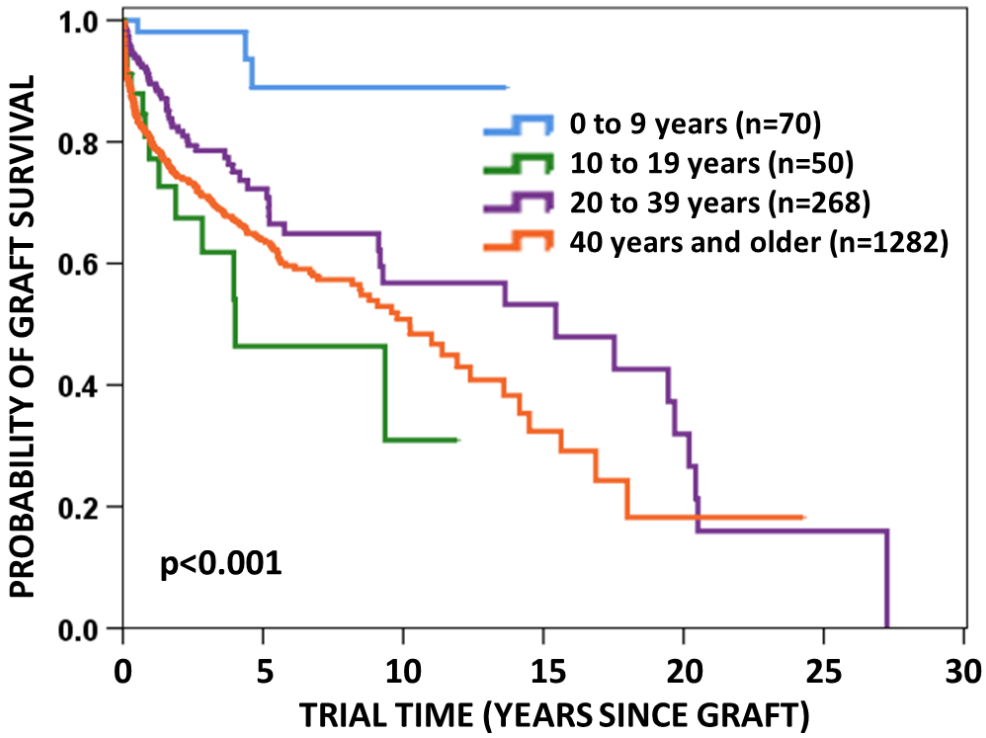
Note: Further information is not provided due to confidentiality constraints (see section 1.4.8).

7.2.4 Traditional lamellar keratoplasty survival: influence of recipient age (years)

Figure 7.2.4 shows the comparison of graft survival depending on the age of the corneal transplant recipient. Recipients were initially stratified by 10-year age groups. Data for all recipients aged 80 years and older were grouped together for analysis, due to the low number of recipients aged 90 or older. A significant difference was found across groups (Log Rank Statistic=31.69; df=8; p<0.001).

Further analyses examined whether there were significant differences between adjacent age groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=25.16; df=3; p<0.001). Survival of grafts in recipients aged 0 to 9 years was significantly better than in the three older age groups (all p≤0.002), while those in recipients aged 20 to 39 years had significantly better survival than in recipients aged 40 years and older (p=0.005) or 10 to 19 years (p=0.024). This variable was retained in the final multivariate model (see section 7.7).

Figure 7.2.4 Recipient age group



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14
0 to 9 years	48	35	26	12	6	4	3	NA
10 to 19 years	21	13	7	5	3	2	NA	NA
20 to 39 years	158	111	60	39	30	20	18	12
40 years and older	554	390	227	120	76	43	21	15

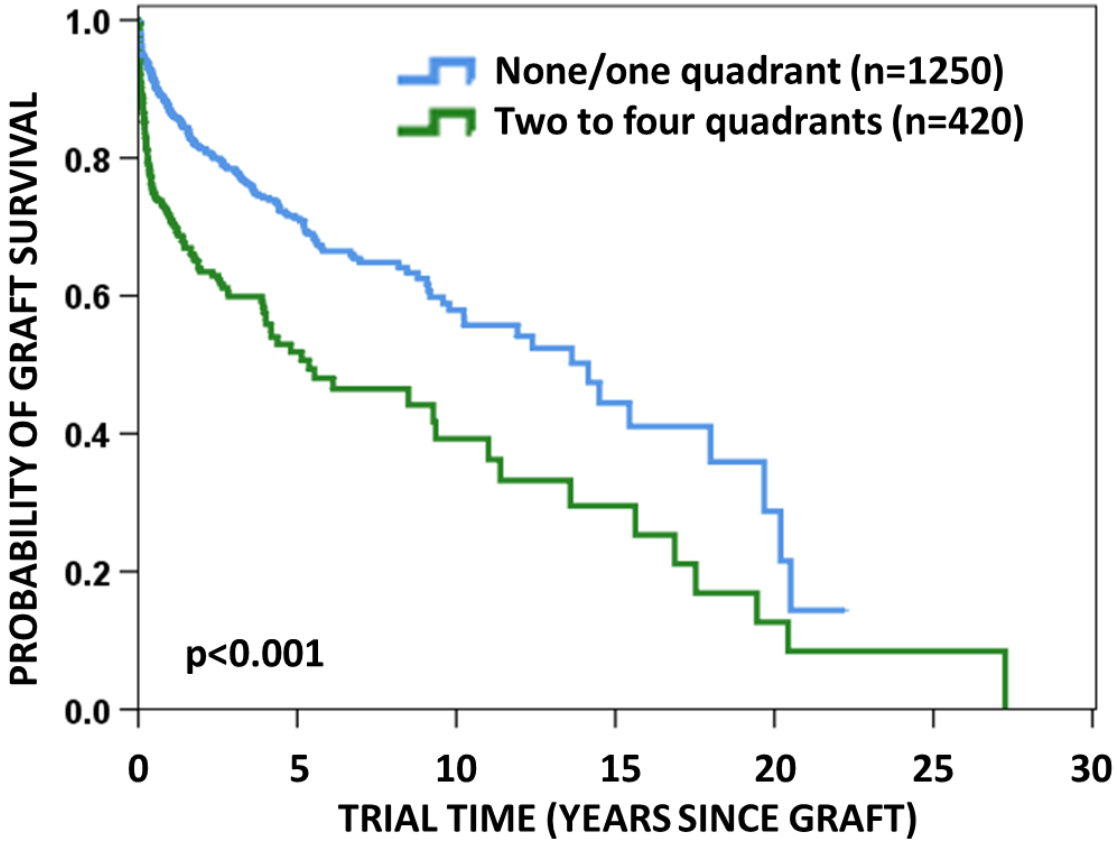
Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12
0 to 9 years	0.98	0.98	0.98	NA	NA	NA	NA
10 to 19 years	0.77	NA	NA	NA	NA	NA	NA
20 to 39 years	0.90	0.82	0.75	0.65	0.65	0.57	NA
40 years and older	0.80	0.74	0.67	0.60	0.57	0.51	0.43

7.2.5 Traditional lamellar keratoplasty survival: influence of pre-graft corneal neovascularisation

Figure 7.2.5 shows the comparison of graft survival depending on the level of pre-graft corneal neovascularisation. Comparisons were initially made with neovascularisation split into single quadrant levels and the comparison was significant (Log Rank Statistic=49.07; df=4; p<0.001). Further analyses examined whether there were significant differences between adjacent groups. Recipients with avascular corneas pre-graft, or one quadrant of pre-graft neovascularisation, did not have significantly different graft survival (p=0.565). Recipients with two, three or four quadrants of pre-graft neovascularisation, did not have significantly different graft survival (p=0.130). These groups were therefore combined, and the comparison remained significant (Log Rank Statistic=42.60; df=1; p<0.001). This variable was retained in the final multivariate model (see section 7.7).

Figure 7.2.5 Pre-graft corneal neovascularisation



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14	16
None/one quadrant	598	432	250	143	90	56	32	20	12
Two to four quadrants	183	117	70	33	25	13	NA	NA	NA

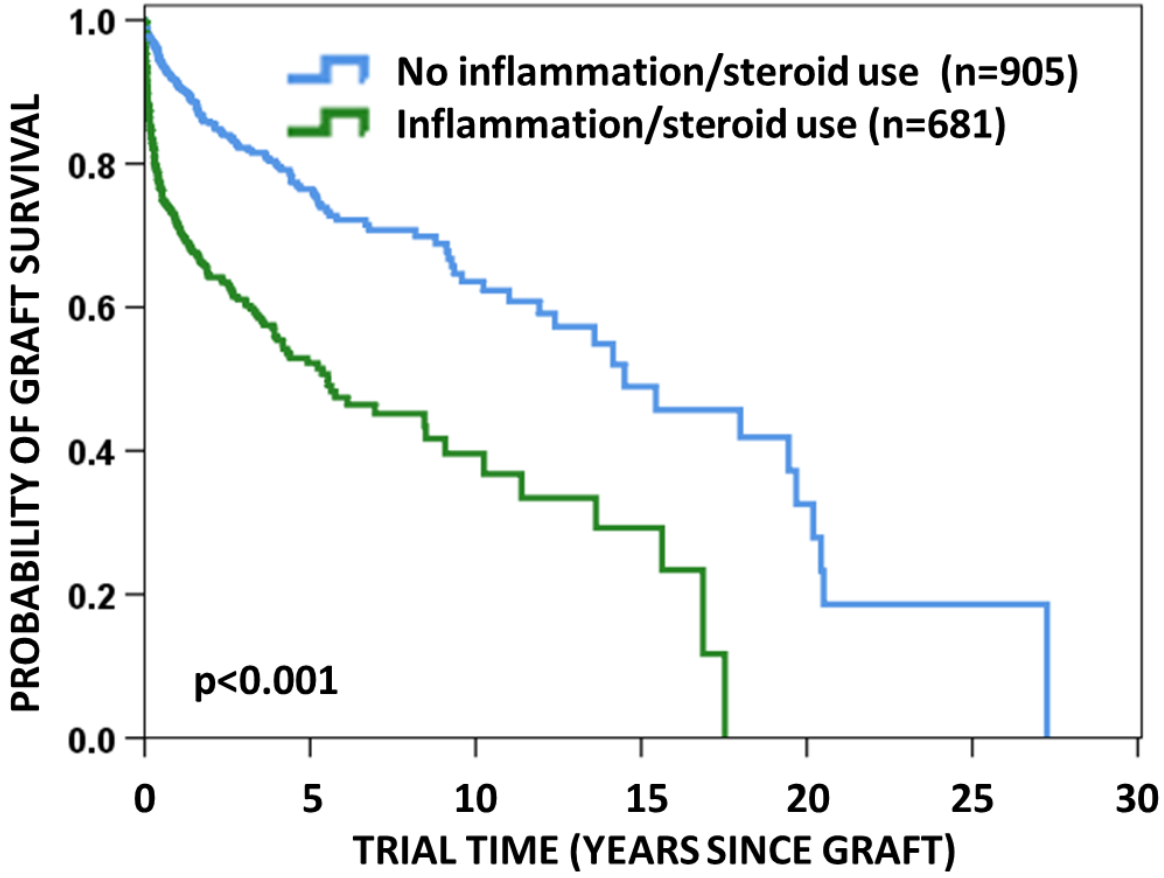
Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12	14
None/one quadrant	0.87	0.81	0.74	0.67	0.65	0.58	0.54	0.50
Two to four quadrants	0.71	0.64	0.58	0.48	0.47	NA	NA	NA

7.2.6 Traditional lamellar keratoplasty survival: pre-graft inflammation and/or recent steroid use

Figure 7.2.6 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=82.15; df=1; 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=82.82; 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 final multivariate model (see section 7.7).

Figure 7.2.6 Pre-graft inflammation and/or recent steroid use



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14	16
No inflammation/steroid use	469	330	197	118	80	54	33	20	14
Inflammation/steroid use	271	188	104	49	31	14	8	6	4

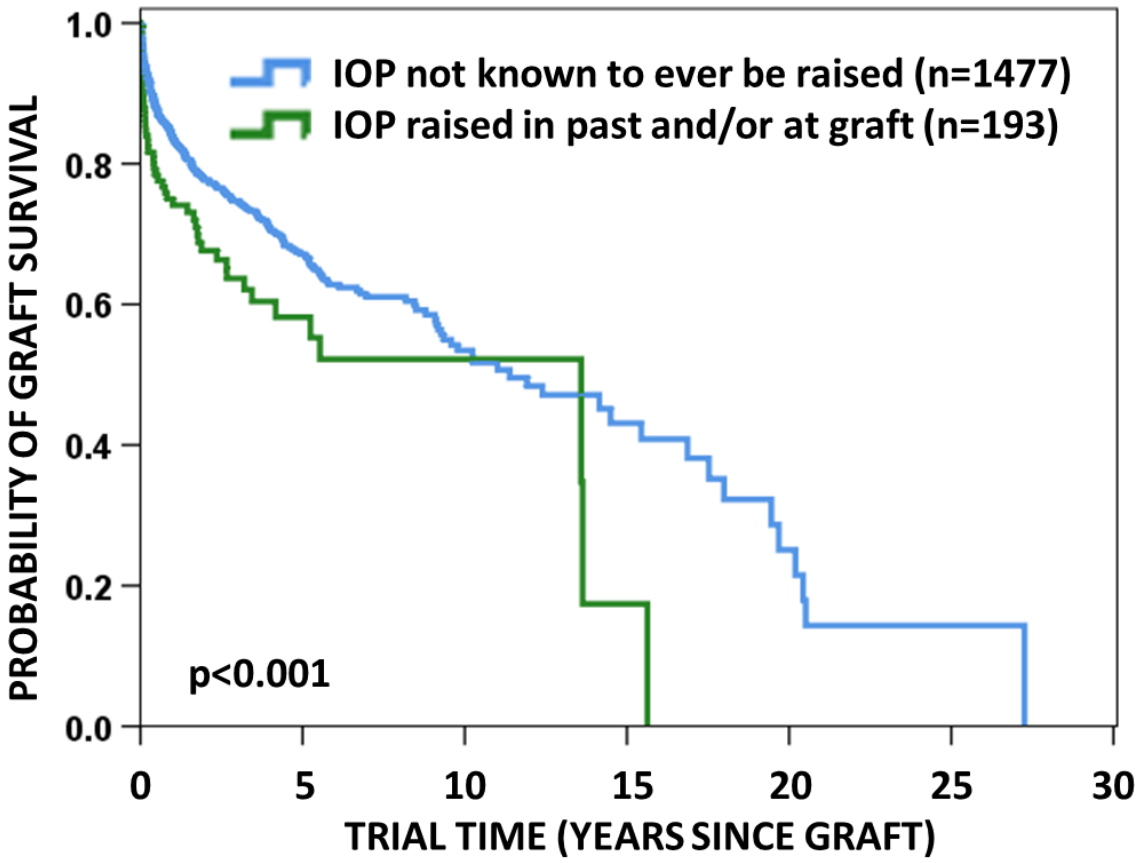
Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12	14
No inflammation/steroid use	0.91	0.86	0.80	0.72	0.71	0.64	0.59	0.55
Inflammation/steroid use	0.72	0.64	0.56	0.47	0.45	NA	NA	NA

7.2.7 Traditional lamellar keratoplasty survival: influence of history of raised intraocular pressure (IOP)

Figure 7.2.7 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=8.19; df=1; p=0.004). This variable was not retained in the final multivariate model (see section 7.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 7.2.7 History of raised intraocular pressure



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14	16
No raised IOP	697	492	289	162	108	65	39	26	18
Raised IOP	84	57	31	14	7	4	3	1	NA

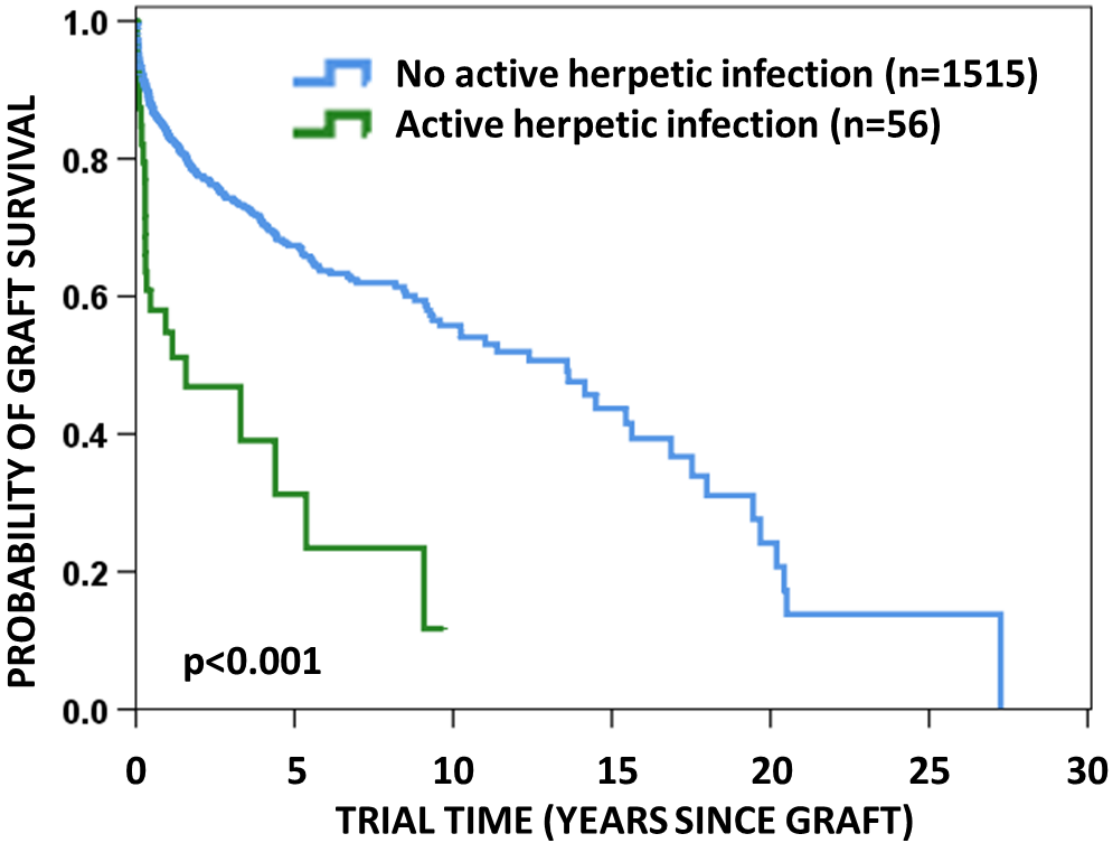
Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12	14
No raised IOP	0.84	0.78	0.71	0.63	0.61	0.54	0.48	0.47
Raised IOP	0.74	0.68	0.60	NA	NA	NA	NA	NA

7.2.8 Traditional lamellar keratoplasty survival: influence of active herpetic infection at time of graft

Figure 7.2.8 shows the comparison of graft survival between grafts with an active herpetic infection at the time of graft and those without. (Log Rank Statistic=31.04; df=1; 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=31.6; df=2; p<0.001). Active herpetic infection was thus categorised into these three groups for multivariate analysis. This variable was not retained in the final multivariate model (see section 7.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 7.2.8 Presence of active herpetic eye disease at time of graft



Number at risk (years post-graft)

	3m	6m	1	2	5	10	15	20
No active herpetic infection	959	844	724	507	226	68	22	7
Active herpetic infection	30	20	16	8	4	NA	NA	NA

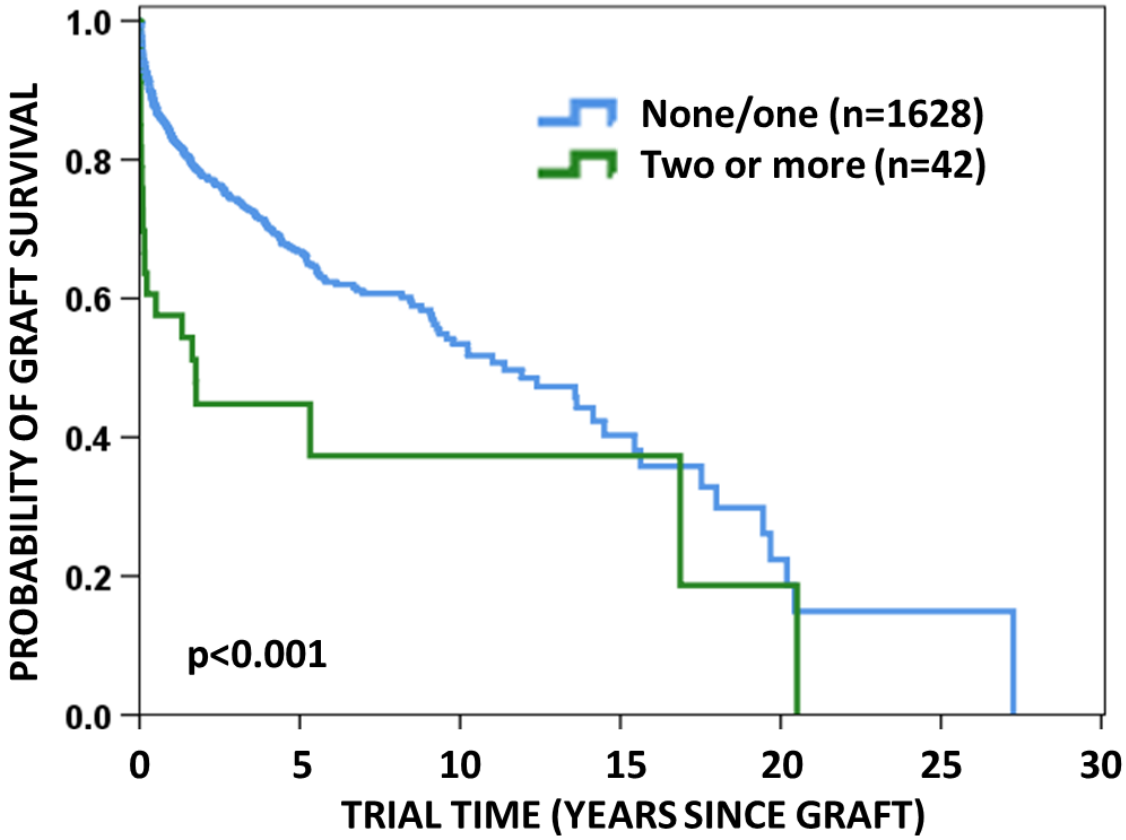
Probability of graft survival (years post-graft)

	3m	6m	1	2	5	10	15
No active herpetic infection	0.91	0.88	0.84	0.78	0.67	0.56	0.44
Active herpetic infection	0.79	0.58	NA	NA	NA	NA	NA

7.2.9 Traditional lamellar keratoplasty survival: influence of number of previous contralateral graft/s

Figure 7.2.9 shows the comparison of graft survival stratified by the number of prior contralateral graft/s the recipient was known to have had at the time of graft. Comparisons were initially made with the number of previous grafts split into single categories, where there were enough data, and the comparison was significant (Log Rank Statistic=14.44; df=2; p<0.001). Further analyses examined whether there were significant differences between adjacent groups. Recipients with no or one previous ipsilateral graft did not have significantly different graft survival (p=0.885). These groups were therefore combined, and the comparison remained significant (Log Rank Statistic=14.41; df=1; p<0.001). This variable was not retained in the final multivariate model (see section 7.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 7.2.9 Number of previous contralateral grafts



Number at risk (years post-graft)

	3m	6m	1	2	5	10	15	20
None/one	1026	897	762	535	237	67	20	6
Two or more	20	20	19	14	6	2	2	1

Probability of graft survival (years post-graft)

	3m	6m	1	2	5	10	15
None/one	0.92	0.88	0.83	0.78	0.67	0.53	0.40
Two or more	0.61	0.61	NA	NA	NA	NA	NA

7.3 Graft Era/Year

Table 7.5 shows the number of grafts registered and followed, based on single years combined. Grafts were initially stratified by yearly groups. Data for grafts performed in 1985, 1986 and 1987 were combined due to low number of grafts registered in those years. This was also the case for grafts performed in 1988 and 1989. A significant difference was found across year groups (Log Rank Statistic=76.25; df=32; p<0.001).

Further analyses examined whether there were significant differences between adjacent year groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=37.43; df=3; p<0.001). The percentages, which should be summed vertically, total 100.

Table 7.5 Graft era/year

Traditional Lamellar Keratoplasty
Graft Era/Year

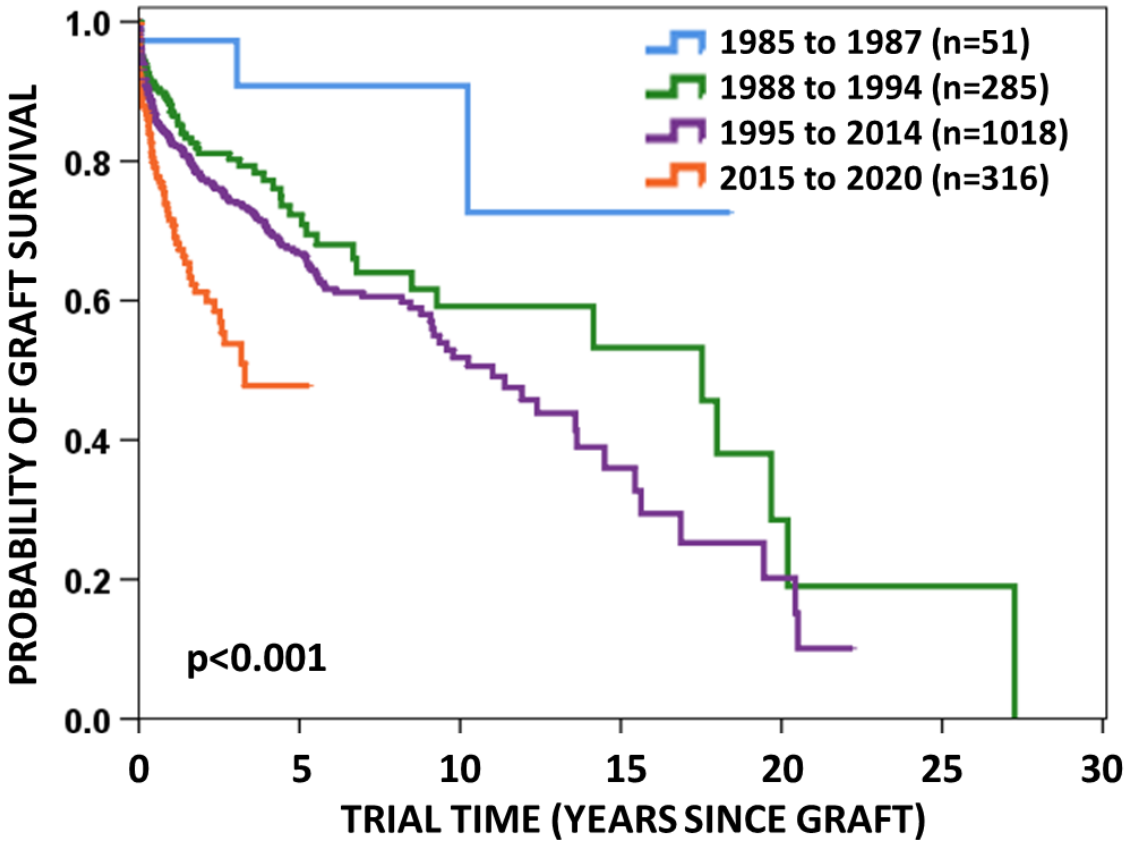
	Registered (%)	Followed (%)
Year of graft		
1985 to 1987	51 (3%)	43 (3%)
1988 to 1994	285 (17%)	242 (19%)
1995 to 2014	1018 (61%)	799 (64%)
2015 to 2020	316 (19%)	164 (13%)
Total	***1670 (100%)***	***1248 (100%)***

See section 1.1 for a discussion of the impact that lag time to follow-up may have on survival depending on graft year/era. A comparison between the percentages of grafts registered and followed in each group showed a distinct difference. This difference was examined using a Chi^2 analysis and found to be significant (p<0.001). Follow-up was lower for grafts performed in more recent years.

7.3.1 Traditional lamellar keratoplasty survival: influence of era of graft

Figure 7.3.1 shows the comparison of graft survival between year of graft, stratified into the groups determined in section 7.3 (Log Rank Statistic=37.43; df=3; p<0.001). Grafts performed between 2015 and 2020 had significantly poorer survival than those performed in the earlier eras (all p<0.001). These findings are likely, at least in part, due to the lag time discussed in section 1.1. Grafts performed from 1985 to 1987 had significantly better survival than those performed from 1995 to 2014 (p=0.005). This variable was not retained in the final multivariate model (see section 7.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 7.3.1 Graft Era



Number at risk (years post-graft)

	1	2	3	4	6	8	10	12	14
1985 to 1987	25	21	15	13	10	7	5	4	3
1988 to 1994	153	106	89	72	38	27	19	14	10
1995 to 2014	512	375	296	225	128	81	45	24	14
2015 to 2020	91	47	23	10	NA	NA	NA	NA	NA

Probability of graft survival (years post-graft)

	1	2	3	4	6	8	10	12
1985 to 1987	0.97	0.97	NA	NA	NA	NA	NA	NA
1988 to 1994	0.88	0.81	0.80	0.77	0.68	NA	NA	NA
1995 to 2014	0.83	0.77	0.74	0.71	0.62	0.61	0.52	0.46
2015 to 2020	0.72	0.61	0.54	0.48	NA	NA	NA	NA

7.4 Surgery and Surgeon Factors

Table 7.6 shows the number of grafts within each of the variable sub-groups, for the surgery and surgeon factors that were found to be **significant** in univariate analyses. The sum of these numbers for each variable equals the total number of grafts (1,670 registered and 1,248 followed) and the percentages, which should be summed vertically for each variable, total 100.

Table 7.6 Surgery and surgeon factors, significant in univariate analyses

Traditional Lamellar Keratoplasty

Surgery and Surgeon Factors

	Registered (%)	Followed (%)
Size of graft (diameter)		
4.00 mm or less	144 (9%)	97 (8%)
4.01 mm to 5.00 mm	116 (7%)	82 (7%)
5.01 mm to 6.00 mm	199 (12%)	145 (12%)
6.01 mm to 7.00 mm	189 (11%)	148 (12%)
7.01 mm to 8.00 mm	294 (18%)	221 (18%)
8.01 mm to 9.00 mm	188 (11%)	146 (12%)
More than 9.00 mm	113 (7%)	91 (7%)
Not advised	427 (26%)	318 (25%)
Change in lens status		
Phakic post-graft	1235 (74%)	960 (77%)
Other	435 (26%)	288 (23%)
The centre effect		
Fewer than 34 (2%) registered TLK	974 (58%)	722 (58%)
	133 (8%)	128 (10%)
	126 (8%)	71 (6%)
	93 (6%)	84 (7%)
	71 (4%)	65 (5%)
Individual surgeons are not identified	51 (3%)	16 (1%)
due to confidentiality constraints.	50 (3%)	25 (2%)
See section 1.4.8 for further information.	49 (3%)	40 (3%)
	45 (3%)	25 (2%)
	43 (3%)	43 (3%)
	35 (2%)	29 (2%)
Total	***1670 (100%)***	***1248 (100%)***

Table 7.7 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 (1,670 registered and 1,248 followed) and the percentages, which should be summed vertically for each variable, total 100. The corresponding non-significant log-rank statistic from the Kaplan-Meier survival analysis is also provided.

Table 7.7 Surgery and surgeon factors, not significant in univariate analyses

Traditional Lamellar Keratoplasty

Surgery and Surgeon Factors

	Registered (%)	Followed (%)
Surgeon caseload and level of follow-up		
Fewer than 34 (2%) registered TLK	974 (58%)	722 (58%)
34+ registered TLK, <75% follow-up	272 (16%)	137 (11%)
34+ registered TLK, ≥75% follow-up	424 (25%)	389 (31%)
Chi²=1.25, df=2, p=0.534		
Total	***1670 (100%)***	***1248 (100%)***

34 was selected as the cut-off point for high caseload surgeons as this was 2% of all registered traditional lamellar keratoplasties. 75% was selected as the cut-off point for the follow-up categories as this was the average percentage of follow-up for all traditional lamellar grafts.

7.4.1 Traditional lamellar keratoplasty survival: influence of graft size

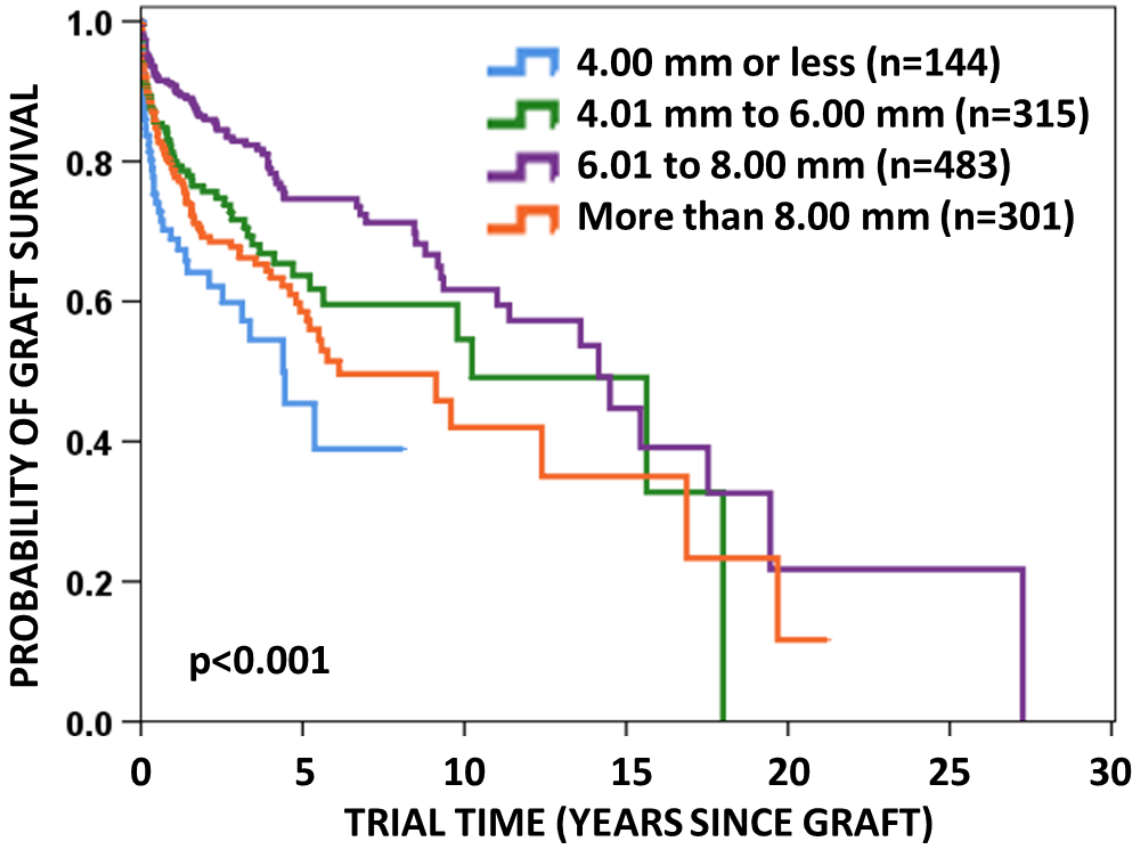
Figure 7.4.1 shows a comparison of graft survival depending on the size of the graft, based on the donor button diameter, as reported by surgeons. Grafts were initially categorised in increments of 1.00 mm increases, with all grafts 4.00 mm or less, and all grafts more than 9.00 mm, grouped together. A significant difference was found across groups (Log Rank Statistic=37.50; df=6; p<0.001).

Further analyses examined whether there were significant differences between adjacent size groups. Where no significant difference was found, these groups were combined, with the resulting analysis remaining significant (Log Rank Statistic=34.02; df=3; p<0.001).

Survival of grafts sized 6.01 mm to 8.00 mm was significantly better than those 4.00 mm or less (p<0.001), 4.01 mm to 6.00 mm (p=0.002), and more than 8.00 mm (p<0.001). Survival of grafts of 4.00 mm or less was also significantly worse than those that were 4.01 mm to 6.00 mm (p=0.012).

Data on this variable were not provided in 26% 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=33.97; df=4; p<0.001). Graft size was thus categorised into these five groups for multivariate analysis. This variable was retained in the final multivariate model (see section 7.7).

Figure 7.4.1 Graft size



Number at risk (years post-graft)

	1	2	3	4	6	8	10	12	14
4.00 mm or less	51	32	24	16	6	2	NA	NA	NA
4.01 mm to 6.00 mm	130	92	65	51	24	15	11	5	3
6.01 mm to 8.00 mm	256	182	144	113	75	52	33	22	13
More than 8.00 mm	152	103	89	65	31	16	10	6	4

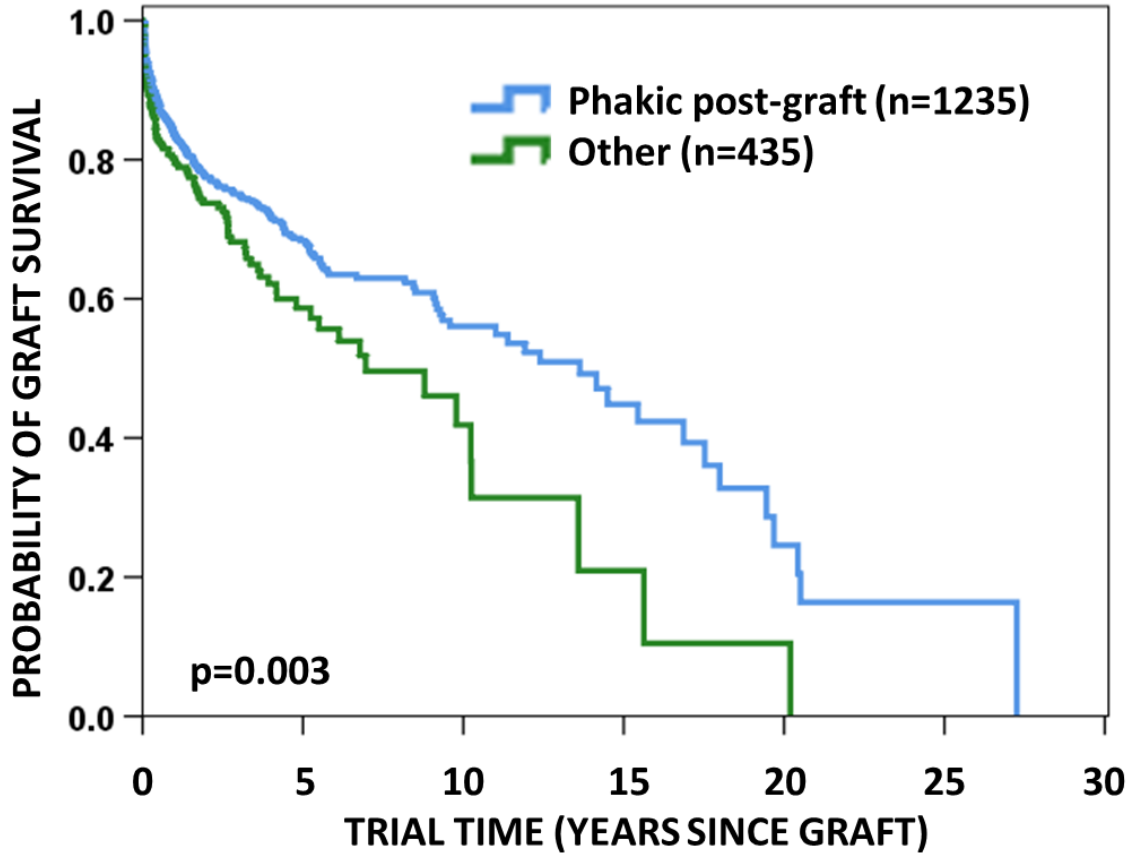
Probability of graft survival (years post-graft)

	1	2	3	4	6	8	10	12
4.00 mm or less	0.69	0.64	0.60	NA	NA	NA	NA	NA
4.01 mm to 6.00 mm	0.81	0.76	0.72	0.67	0.60	NA	NA	NA
6.01 mm to 8.00 mm	0.91	0.86	0.83	0.79	0.75	0.71	0.62	0.57
More than 8.00 mm	0.79	0.69	0.68	0.64	0.52	NA	NA	NA

7.4.2 Traditional lamellar keratoplasty survival: influence of change in lens status

Figure 7.4.2 shows the comparison of graft survival stratified by the change of lens status from pre- to post-graft. “Phakic post-graft” 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=8.99; df=1; p=0.003). This variable was not retained in the final multivariate model (see section 7.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 7.4.2 Change in lens status



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14	16
Phakic post-graft	601	427	258	143	99	60	38	25	17
Other	180	122	62	33	16	9	4	2	1

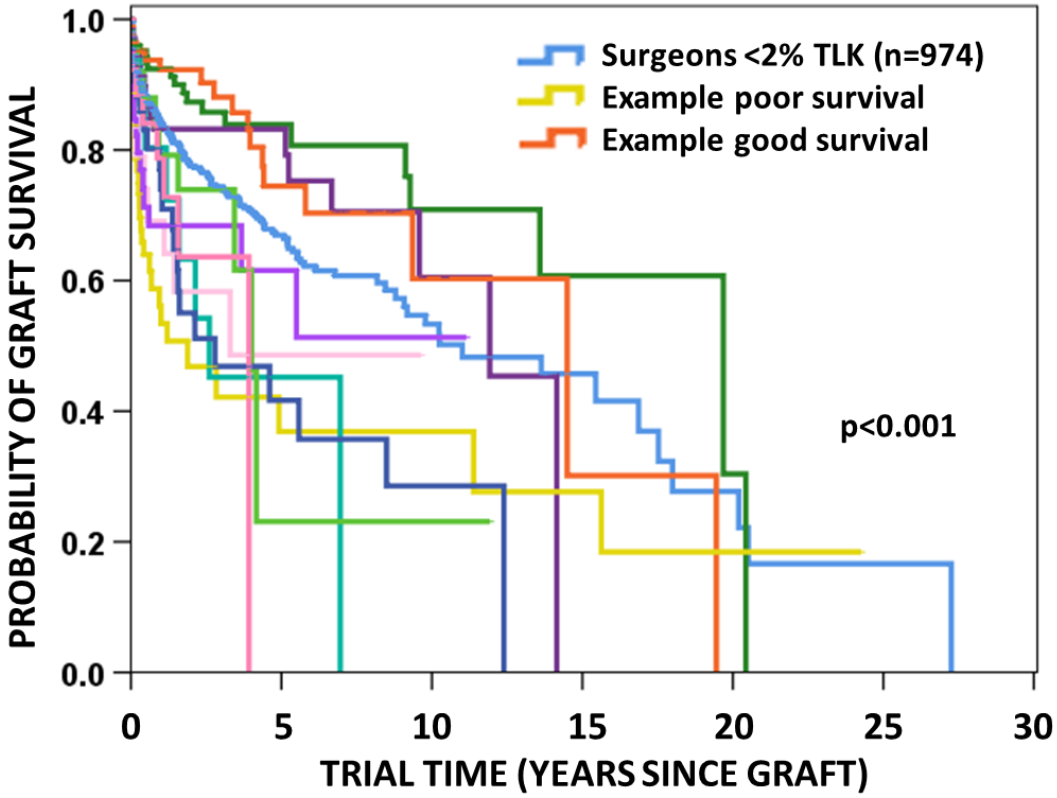
Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12	14
Phakic post-graft	0.84	0.77	0.72	0.64	0.63	0.56	0.52	0.49
Other	0.80	0.74	0.62	0.56	NA	NA	NA	NA

7.4.3 Traditional lamellar keratoplasty survival: influence of the centre effect

Figure 7.4.3 shows the comparison of graft survival between grafts performed by individual surgeons with 34+ (≥2%) registered traditional lamellar keratoplasties to surgeons with fewer than 34 (<2%) registered traditional lamellar keratoplasties (Log Rank Statistic=60.18; df=10; p<0.001). High caseload individual surgeons had between 35 and 133 traditional lamellar keratoplasties registered. Follow-up ranged from 31% to 100%. The surgeon used as the example of poor survival had a follow-up rate of 92%, while the surgeon used as an example of good survival had a follow-up rate of 90%. Low caseload surgeons had a follow-up rate of 74%. This variable was retained in the final multivariate model (see section 7.7).

Figure 7.4.3 The centre effect



Probability of graft survival (years post-graft)

	1	2	3	4	5	6	8	10	12
<2% registered TLK	0.84	0.78	0.74	0.71	0.67	0.62	0.61	0.53	0.48
Example poor survival	0.53	NA	NA	NA	NA	NA	NA	NA	NA
Example good survival	0.92	0.92	0.88	0.80	0.75	NA	NA	NA	NA

Note: Further information is not provided due to confidentiality constraints (see section 1.4.8).

7.5 Operative procedures at the time of graft

Table 7.8 shows the number of grafts for which specified operative procedures were performed at the time of graft. This did not include cataract extraction, pseudophakic IOL insertion, or pseudophakic IOL extraction, as these were covered by the variable relating to change in lens (see section 7.4.2). The comparison of survival for grafts that had undergone another operative procedure at graft and those that had not was non-significant (Log Rank Statistic=0.03; df=1; p=0.873).

Table 7.8 Operative procedures at the time of graft

Traditional Lamellar Keratoplasty

Operative Procedures at Time of Graft

	Number
Pterygium excision	70
Conjunctival flap (Gunderson: 11, unspecified: 27)	38
Glaucoma tube inserted (Baerveldt: 17, unspecified: 3)	20
Tarsorrhaphy	18
Vitrectomy	18
Limbal dermoid removed	10
Peripheral iridectomy	10
Conjunctival graft	8
Tumor removed	7
Amniotic membrane transplant	6
Excimer laser	5
Scleral necrosis removed	5
Other*	82
Total operative procedures (number of grafts)	**297 (271)**

*Other included: conjunctival resection (4), glaucoma tube repositioned (4), scleral patch graft (4), sclerectomy (4), Beta radiation (3), cryotherapy (3), removal of corneoscleral tissue (3), scleral debridement (3), anterior chamber washout (2), corneal glueing (2), keratectomy (2), peritomy (2), punctal plugs (2), pupilloplasty (2), removal of corneal scar (2), removal of lesion (2), trabeculectomy (2), Visumax laser (2), Alphacor exchanged (1), cleansing of corneal ulcer (1), cone recession (1), conjunctival biopsy (1), division of iris adhesions (1), epikeratoplasty (1), integrated implant (1), iris repositioned (1), iris resection (1), keratoprosthesis inserted (1), laceration repair (1), mucousal membrane graft (1), muscle disinsertion (1), removal and reapplication of lateral vectus (1), removal of conjunctiva from cornea (1), removal of foot of IOL (1), removal of corneal abscess (1), removal of prolapsed iris (1), removal of pupillary inflammatory membrane (1), removal of scleral buckle (1), removal of superior limbus (1), removal of radiation burn tissue (1), repair of scleral defect (1), reposition of IOL (1), retinectomy (1), revision of trabeculectomy (1), rotation of conjunctival flap (1), scleral resection (1), stent pulled back (1), synechiolysis (1), tarsorrhaphy revision (1), thermal keratoplasty (1), unspecified operation (1), vitreous clearance (1).

7.6 Post-graft Events

Table 7.9 shows post-graft surgical procedures, as reported by follow-up practitioners. 236 traditional lamellar keratoplasties were reported to have undergone a re-grafting procedure (separate to subsequent concurrent graft/s) at the date last seen. Of these, 117 had not had additional post-graft operative procedures reported.

Table 7.9 Post-surgical procedures

Traditional Lamellar Keratoplasty

Post-graft Surgical Procedures Excluding Re-graft

	Number
Cataract removal and IOL insertion	125
Cataract removal without IOL insertion	5
IOL insertion (cataract removed prior to graft)	7
Trabeculectomy	96
Concurrent subsequent graft (10 PK, 9 patch, 6 limbal/conjunctival, 3 DSAEK)	28
YAG laser	17
Wound repair/re-sutured	16
Tarsorrhaphy	15
Enucleation	12
Conjunctival flap (7 Gunderson, 3 unspecified)	10
Vitrectomy	9
Relaxing incision	8
Suture adjustment	8
Evisceration	7
PRK laser	7
Pterygium excision	7
Corneal debridement/scraping	5
Other*	68
Total post-graft surgical procedures (number of grafts)	**450 (362)**

*Other included: keratotomy (4), LASIK (4), punctal cautery (4), amniotic membrane transplant (3), refractive keratoplasty (3), wedge resection (3), Baerveldt tube inserted (2), cryotherapy (2), intravitreal Eylea (2), keratectomy (2), lash epilation (2), piggyback IOL inserted (2), ptosis repair (2), removal of band keratopathy (2), removal of conjunctival tumour (2), corneal collagen cross linking (1), conjunctival recession (1), cry flap refashioned (1), cyclodiode laser (1), dacryocystorhinostomy with tube inserted (1), debulking of conjunctival flap (1), drainage of interface (1), entropion surgery (1), exenteration (1), Gunderson flap removal (1), intravitreal Avastin (1), intravitreal Lucentis (1), IOL exchanged (1), iridoplasty (1), iridotomy (1), iridectomy (1), Molteno tube inserted (1), phakic IOL inserted (1), PTK laser (1), removal of calcified plaque (1), removal of conjunctival cyst (1), removal of giant cell granuloma (1), removal of gold weight from eyelid (1), removal of haematoma under graft (1), removal of limbal lesions and mucous glands (1), reposition of Baerveldt tube (1), scleral buckle inserted (1), severing of pedical flap (1), silicone oil exchanged (1).

Table 7.10 shows the occurrence of post-graft events, found to be **significant** in univariate analyses. Table 6.11 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 (1,670 registered and 1,248 with follow-up provided) and the percentages, summed vertically, total 100. The result of the Kaplan-Meier survival analysis is also provided.

Only 23 TLK had a post-graft herpetic infection, 20 had post-graft oedema, 15 had post-graft uveitis, and seven had post-graft steroid use or inflammation reported. Thus, the impact of these factors was not further analysed. Please note: post-graft data may be incomplete when follow-up is based on a registration for a replacement graft.

Table 7.10 Post-graft events, significant in univariate analyses

Traditional Lamellar Keratoplasty

Post-graft Events

	Registered (%)	Followed (%)
Post-graft microbial keratitis		
No	1617 (97%)	1195 (96%)
Yes	53 (3%)	53 (4%)
At least one rejection episode		
No	1632 (98%)	1210 (97%)
Yes	38 (2%)	38 (3%)
Total	***1670 (100 %)***	***1248 (100 %)***

Table 7.11 Post-graft events, not significant in univariate analyses

Traditional Lamellar Keratoplasty

Post-graft Events

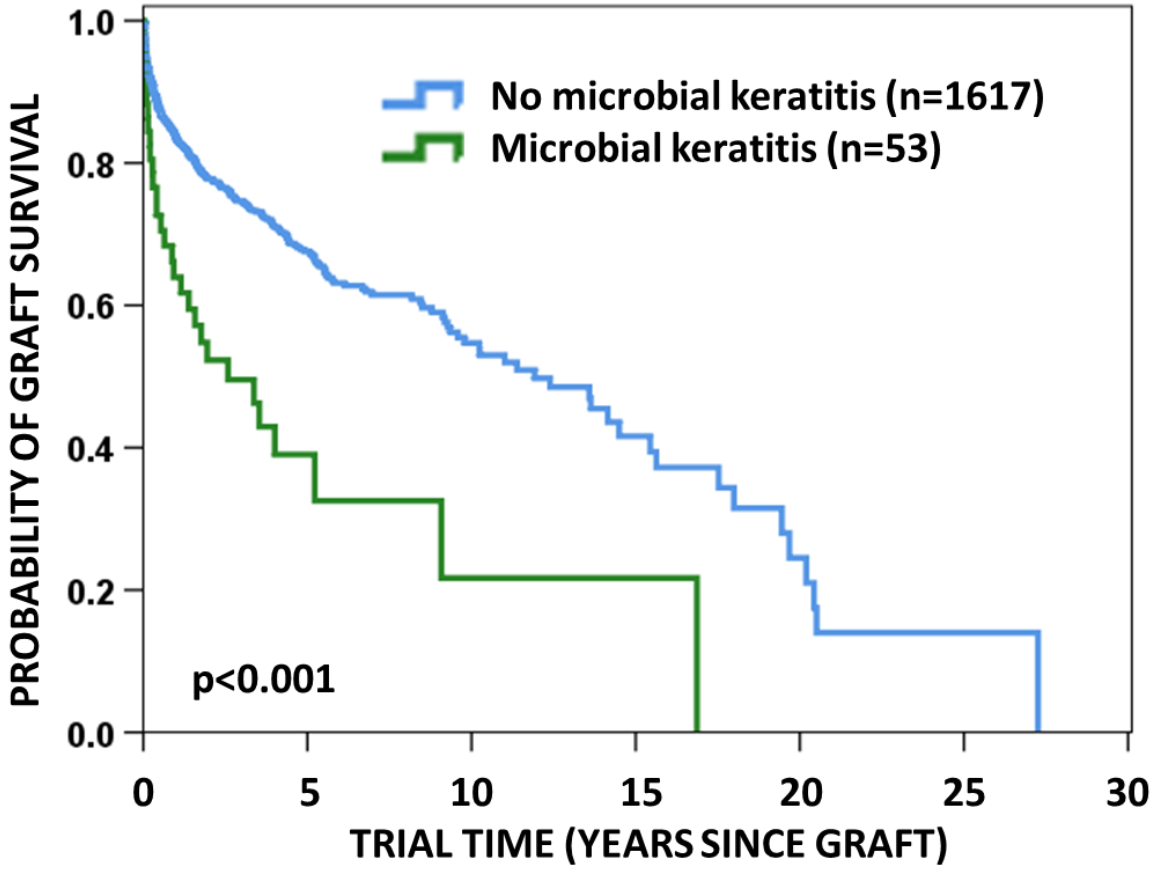
	Registered (%)	Followed (%)
Time to removal of sutures		
Within 6 months	240 (14%)	240 (19%)
7 to 12 months	100 (6%)	100 (8%)
13 to 18 months	77 (5%)	77 (6%)
19 to 24 months post-graft	37 (2%)	37 (3%)
More than 2 years	34 (2%)	34 (3%)
Not yet removed/not advised*	1182 (71%)	760 (61%)
Chi^2=1.69, df=4, p=0.792		
Post-graft neovascularisation		
No	1511 (90%)	1090 (87%)
Yes	159 (10%)	158 (13%)
Chi^2=2.09, df=1, p=0.149		
Post-graft rise in intraocular pressure		
No	1586 (95%)	1164 (93%)
Yes	84 (5%)	84 (7%)
Chi^2=2.00, df=1, p=0.158		
Total	***1670 (100 %)***	***1248 (100 %)***

* Grafts with no ROS date advised were excluded from the analysis. Some failed grafts had ROS dates provided which were after the date of failure and thus not included in analysis.

7.6.1 Traditional lamellar keratoplasty survival: influence of post-graft microbial keratitis

Figure 7.6.1 shows the comparison of graft survival for grafts where the eye was reported to have had microbial keratitis post-graft to those without. A significant difference was found between groups (Log Rank Statistic=23.22; df=1; p<0.001). It was not retained in the final multivariate model (see section 7.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 7.6.1 Post-graft microbial keratitis



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14	16
No microbial keratitis	752	528	309	171	112	67	41	26	17
Microbial keratitis	29	21	11	5	3	2	1	1	1

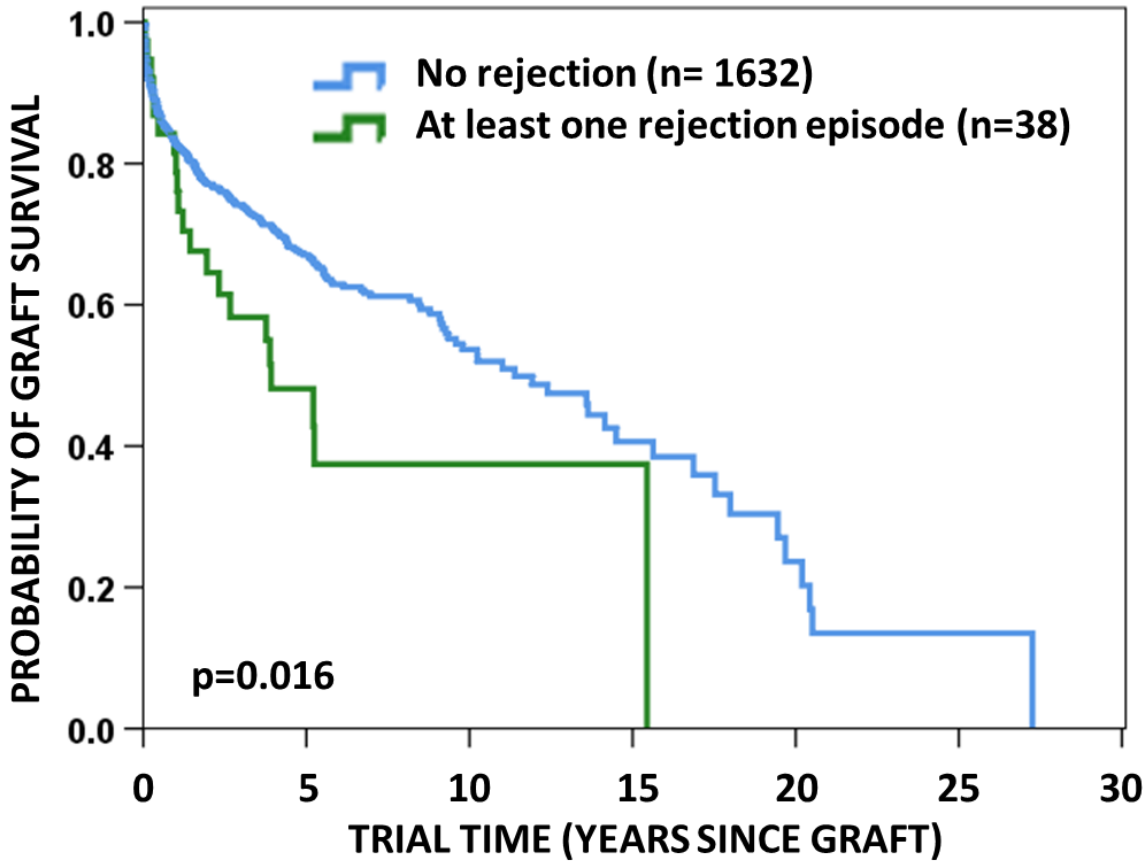
Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12	14
No microbial keratitis	0.84	0.78	0.71	0.63	0.62	0.55	0.50	0.50
Microbial keratitis	0.64	0.52	NA	NA	NA	NA	NA	NA

7.6.2 Traditional lamellar keratoplasty survival: influence of any graft rejection

Figure 7.6.2 shows the comparison of graft survival depending on whether the eye underwent at least one rejection episode. A significant difference was found between groups (Log Rank Statistic=5.85; df=1; p=0.016). This variable was not retained in the final multivariate model (see section 7.7), suggesting that this is **not** an independent factor significantly affecting graft survival.

Figure 7.6.2 Any graft rejection



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14	16
No rejection	751	528	306	170	109	66	40	26	18
Any rejection	30	21	14	6	6	3	2	1	NA

Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12	14
No rejection	0.83	0.77	0.71	0.63	0.61	0.54	0.49	0.44
Any rejection	0.82	0.65	NA	NA	NA	NA	NA	NA

7.7 Multivariate Analysis

A multivariate model was used to investigate the combined effect of variables on Descemet's membrane endothelial graft survival, adjusted for all other variables in the model (see section 1.4.6 for further information).

Table 7.12 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. Some variables that were found to be significant in the univariate analyses were excluded from the multivariate model as they were found to be collinear with (i.e. were highly correlated and produced the same effect on the outcome as) another variable in the model.

Table 7.12 Multivariate model

Traditional Lamellar Keratoplasty

Multivariate Model

Not significant in univariate analysis
- Donor age group
- Donor sex
- Eye only donor
- Cause of donor death
- Central endothelial cell count
- Time from donor death to enucleation of donor tissue
- Time from enucleation to storage of donor tissue
- Time from storage of donor tissue to graft – Optisol
- Time from storage of donor tissue to graft – organ culture
- Time from storage of donor tissue to graft – moist pot
- Time in deswelling media for tissue stored in organ culture media
- Eye grafted
- Recipient sex
- Donor/recipient sex match/mismatch
- Surgeon experience and level of follow-up
- Other operative procedure at graft
- Post-graft corneal neovascularisation
- Post-graft rise in intraocular pressure
- Time to removal of sutures

Significant in univariate analysis but excluded from multivariate model due to collinearity
- Australian State in which graft was performed (collinear with the centre effect)
- Prior ipsilateral graft (collinear with indication for graft)

Significant in univariate analysis but not retained in multivariate model
- Raised intraocular pressure in past and/or at graft
- Post-graft microbial keratitis
- Active herpetic infection at time of graft
- Interstate transportation of donor cornea
- Change in lens status pre- to post-graft
- Storage medium
- Eye Bank
- Graft era
- Previous contralateral graft(s)
- Any post-graft rejection

Significant in univariate analysis AND retained in multivariate model
- Time from donor death to enucleation of donor tissue
- Indication for graft
- Recipient age group
- Pre-graft corneal neovascularisation
- Pre-graft inflammation and/or steroid use
- Graft size
- The centre effect

Table 7.13 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 first level of each categorical variable was taken as the referent, except where it made logical sense to use a different group. The hazard ratios for a given variable are adjusted for all other variables in the model. This model included data from 1,670 traditional lamellar keratoplasties, performed in 1,495 recipients.

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: ($Chi^2=252.61$, $p<0.0001$).

Table 7.13 Clustered multivariate model

	n	Hazard Ratio	Standard error	p-value	Global p-value	95% confidence interval
Time from donor death to enucleation						
Up to 15 hours	1373	1.00			0.0165	
More than 15 hours	254	1.53	0.25	0.007		1.12 to 2.08
Not advised	43	1.42	0.46	0.281		0.75 to 2.66
Indication for graft						
Failed previous graft	253	4.65	1.30	<0.001		2.68 to 8.05
Pterygium	241	1.00			<0.0001	
Scleral necrosis	97	2.20	0.78	0.025		1.11 to 4.39
Corneal ulcers/perforation	200	4.51	1.37	<0.001		2.49 to 8.18
Keratoconus	107	2.34	0.85	0.019		1.15 to 4.75
Herpetic eye disease	88	5.70	1.87	<0.001		2.99 to 10.85
Limbal dermoid	85	0.44	0.41	0.376		0.07 to 2.69
Trauma	35	2.51	1.01	0.023		1.14 to 5.53
Corneal degeneration	69	2.10	0.82	0.058		0.97 to 4.51
Non-herpetic infections	42	6.90	2.31	<0.001		3.58 to 13.31
Glaucoma	53	1.29	0.74	0.658		0.42 to 3.97
Cancer	50	1.40	0.82	0.563		0.44 to 4.44
Beta radiation	234	1.56	0.53	0.196		0.80 to 3.04
Other	132	3.35	1.08	<0.001		1.78 to 6.29
Recipient age group						
0 to 9	70	0.30	0.18	0.049		0.09 to 1.00
10 to 19	50	1.00			0.0026	
20 to 39	268	0.43	0.11	<0.001		0.56 to 0.71
40+	1282	0.43	0.10	<0.001		0.27 to 0.70
Pre-graft corneal neovascularisation						
None/one quadrant	1250	1.00			0.0005	
Two/three/four quadrants	420	1.60	0.22			1.23 to 2.09
Pre-graft inflammation and/or steroid use						
No	905	1.00			0.0007	
Yes	681	1.65	0.22	<0.001		1.27 to 2.15
Not advised	84	1.39	0.36	0.204		0.34 to 2.31
Graft size						
Up to 4.00 mm	144	1.73	0.38	0.012		1.13 to 2.66
4.01 mm to 6.00 mm	315	1.60	0.31	0.014		1.10 to 2.32
6.01 mm to 8.00 mm	483	1.00			0.0068	
8.01 mm or larger	301	1.76	0.29	0.001		1.27 to 2.43
Not advised	427	1.50	0.27	0.024		1.06 to 2.14
The centre effect						
< 34 (2%) TLK registered	974	1.00			0.0032	
10 HV surgeons (lowest HR	93	0.71	0.19	0.203		0.42 to 1.20
highest HR)	43	2.63	0.61	<0.001		1.67 to 4.15
Range of n (35 to 133)						

7.7.1 Significant differences in the traditional lamellar keratoplasty multivariate model for categories with more than two groups following Holm-Bonferroni correction for multiple comparisons

7.7.1.1 Time from donor death to enucleation

Grafts performed with donor tissue that was enucleated more than 15 hours post-mortem had significantly poorer survival than those performed with tissue enuclead within 15 hours (p=0.007).

7.7.1.2 Indication for graft

Grafts performed for pterygium had significantly better survival than those performed for herpetic eye disease, non-herpetic infections, failed previous graft/s, corneal ulcers, or those performed for “other” specified indications (all p<0.001).

Grafts performed for damage from beta radiation had significantly better survival than those performed for herpetic eye disease, non-herpetic infections, failed previous graft/s, or corneal ulcers (all p<0.001).

Grafts performed for scleral necrosis had significantly better survival than those performed for non-herpetic infections (p<0.001).

7.7.1.3 Recipient age group

Grafts performed in recipients aged 10 to 19 years had significantly poorer survival than those performed in recipients aged 20 to 39 years or 40 years or older (both p<0.001).

7.7.1.4 Pre-graft inflammation and/or steroid use

Grafts with a history of inflammation or steroid use in the two-weeks prior to graft had significantly poorer survival than those with no history of inflammation of steroid use in this time (p<0.001).

7.7.1.5 Graft size

Grafts that were 8.01 mm or larger had significantly poorer survival than those that were 6.01 mm to 8.00 mm in size (p=0.001).

7.8 Reasons for Graft Failure

Of the 1,248 followed grafts, 353 (28%) were known to have failed by the census date. This equates to 21% of the 1,670 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 7.14 shows the reasons for failure given.

Table 7.14 Reasons for graft failure

Traditional Lamellar Keratoplasty
Reasons for Graft Failure

Corneal melt	51 (14%)
Non-herpetic infection	40 (11%)
Corneal ulcer/perforation	39 (11%)
Primary graft failure	18 (5%)
Scarring	18 (5%)
Endothelial cell failure	15 (4%)
Herpetic infection	13 (4%)
Rejection	12 (3%)
Scleral necrosis	12 (4%)
Recurrent pterygium	11 (3%)
Cancer	11 (3%)
Astigmatism	10 (3%)
Other specified*	42 (12%)
Unspecified	61 (17%)
Total	***353 (100%)***

*Other included: wound leak (8), epithelial defect (5), vascularisation (5), ectasia (3), glaucoma (3), keratoconus (3), trauma (3), Stevens-Johnson syndrome (2), Wegener's granulomatosis (2), atopic keratoconjunctivitis (1), band keratopathy (1), cataract (1), corneal thinning (1), descemetocoele (1), keratoglobus (1), ocular pemphigoid (1), symblepharon (1).

Of the 18 grafts reported by surgeons to have been primary graft failures, nine had no further information provided. Specific reasons given were: corneal melt (4), persistent wound leak (2), effects of beta-radiation (1), perforation (1) and surgical trauma (1).

7.9 Post-graft Changes in Best Corrected Visual Acuity

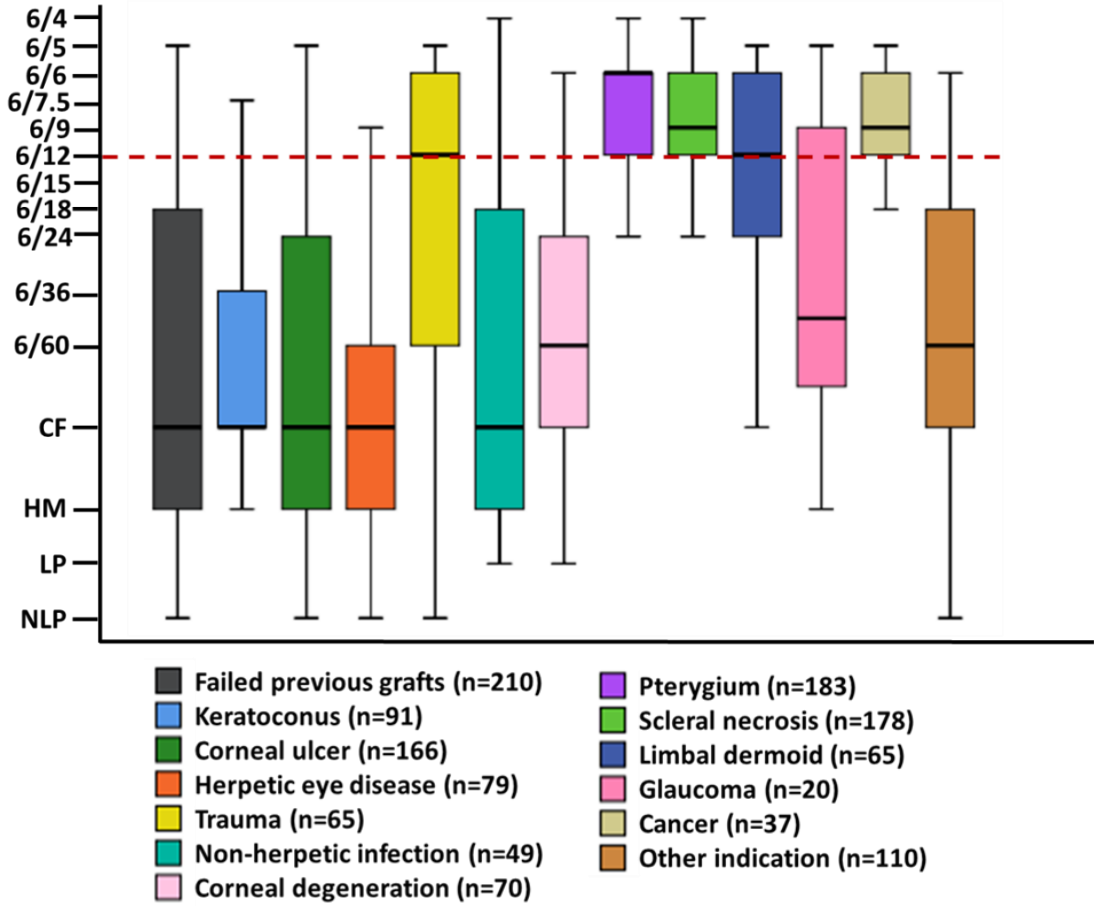
Post-graft best corrected visual acuity (BCVA) is an important outcome for many corneal graft recipients. A desire for improved visual acuity was specified as a reason for graft in 340 (20%) of registered traditional lamellar keratoplasties. In 12% of cases (207), this was the sole desired outcome indicated. These percentages were much lower than for any other type of grafts, with traditional lamellar keratoplasties most often (74% of those with a reason for graft provided) performed for structural repair (see section 2.1.4). All analyses are conducted on data for **surviving** grafts. See section 1.4.7 for further explanation of the methods used to analyse visual acuity data.

7.9.1 Traditional lamellar keratoplasty: Pre-graft visual acuity by indication

Figure 7.9.1 shows the pre-graft BCVA, reported for eyes undergoing traditional lamellar keratoplasty for each of the indication for graft groups. The central line within each box-and-whisker plot shows the median BCVA reported for the group, the box represents the inter-quartile range, while the whisker shows the range. Please note that outliers were included in the calculation of the box and whisker plots but are not shown in the figures. The dashed line indicates a BCVA of 6/12, which represents functional vision.

Median pre-graft BCVA was poor for grafts for failed previous graft/s, keratoconus, corneal ulcer, herpetic eye disease, non-herpetic infection corneal degeneration, other indications, and glaucoma (range 6/48 to Count Fingers). In contrast, it was 6/12 or better for trauma, pterygium, scleral necrosis, limbal dermoid and cancer. Visual improvement was listed as a reason for graft in 32% of the grafts in the indication groups with poor pre-graft BCVA, compared to 14% of the grafts in the indication groups with good pre-graft BCVA.

Figure 7.9.1. Pre-graft best corrected visual acuity

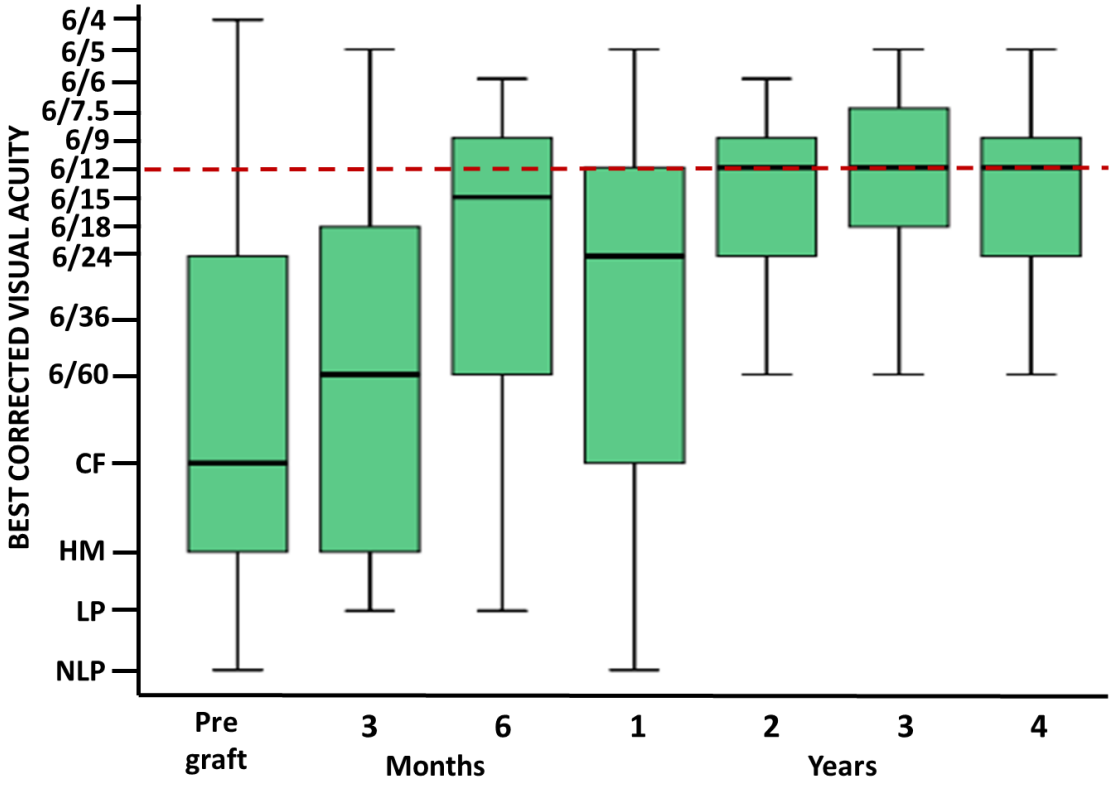


Traditional Lamellar Keratoplasty

7.9.2 Traditional lamellar keratoplasty: Post-graft visual acuity in surviving grafts with poor pre-graft best corrected visual acuity, over time

Due to the low number of grafts for individual indications with visual acuity data available, indications for graft were combined for analysis. Figure 7.9.2 shows the change in median BCVA over time for all indications for graft that had pre-graft median BCVA of 6/48 or worse (see section 7.9.1). The median BCVA improved significantly compared to the pre-graft level (Count Fingers), reaching 6/15 by 6-months post-graft (p<0.001). It further improved to 6/12 by 2-years post-graft, however this was not a significant improvement compared to 6-months, p=0.190. The group retained this 6/12 level to 4-years post-graft.

Figure 7.9.2 Change in BCVA for traditional lamellar keratoplasties, surviving at time of measurement for indications with poor pre-graft BCVA (<6/36), over time



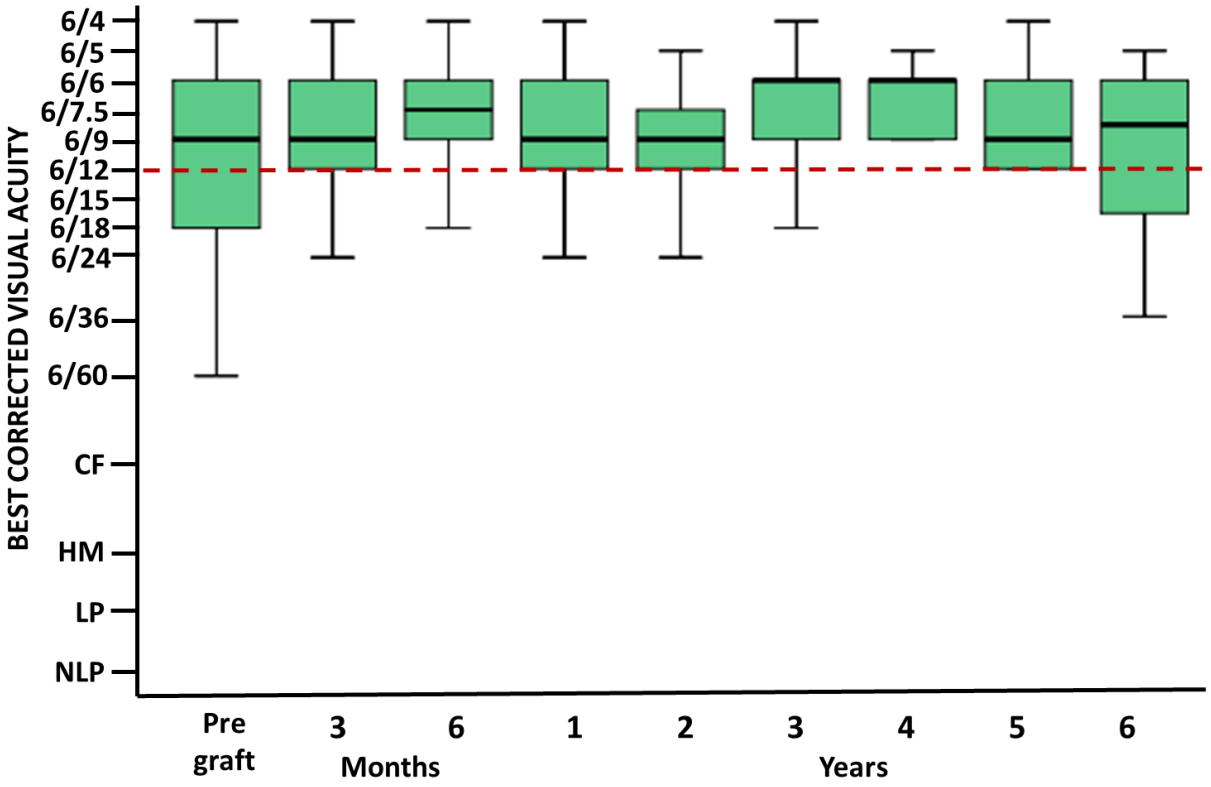
Number of grafts with BCVA data available at each time point

	Pre	3m	6m	1y	2y	3y	4y	5y
Failed previous graft/s	210	9	14	8	8	7	2	3
Keratoconus	91	4	2	8	5	2	5	2
Corneal ulcers	166	15	9	14	7	3	2	2
Herpetic eye disease	79	3	3	4	3	1	1	0
Non-herpetic infections	49	4	2	5	1	2	1	0
Corneal degeneration	70	2	5	6	3	4	6	1
Glaucoma	20	2	0	1	0	1	1	0
Other	110	5	4	9	4	1	4	1
Total	795	44	39	55	31	21	22	9

7.9.3 Traditional lamellar keratoplasty: Post-graft visual acuity in surviving grafts with good pre-graft best corrected visual acuity, over time

Figure 7.9.3 shows the change in median BCVA over time for all indications for graft that had pre-graft median best corrected visual acuity of 6/12 or better (see section 7.9.1). The median BCVA improved significantly compared to the pre-graft level (6/9), reaching 6/7.5 by 6-months post-graft (p=0.036). It dropped back to 6/9 at 1-year post-graft, but this difference was not significant (p=0.878). Between 1-year and 6-years post-graft the median BCVA varied between 6/9 and 6/6, however no between year comparisons were significant (all p>0.05).

Figure 7.9.3 Change in BCVA for traditional lamellar keratoplasties, surviving at time of measurement for indications with good pre-graft BCVA (≥6/12), over time



	Pre	3m	6m	1y	2y	3y	4y	5y	6y	7y
Trauma	65	9	3	1	4	6	0	2	1	1
Pterygium	183	26	31	25	10	9	6	4	2	5
Scleral necrosis	178	23	11	16	6	7	3	5	4	2
Limbal dermoid	65	11	4	6	3	4	3	1	4	1
Cancer	37	4	2	5	3	1	1	0	1	0
Total	528	73	51	53	26	27	13	12	12	9

8 Post-graft Factors Affecting Visual Acuity

Surgeons reported additional factors affecting visual acuity in the grafted eye. These are shown in Table 8.1 and include factors that were present at any point post-graft. In some cases (e.g. cataract or opacity/scar) further interventions may have subsequently resolved the issue, so that they were no longer present at the time of last reported follow-up. Percentages given are of the number of followed grafts.

Table 8.1 Factors affecting visual acuity in the grafted eye at any time post-graft

	PK	DS(A)EK	DMEK	DALK	TLK
Glaucoma*	2934 (13%)	991 (19%)	172 (10%)	51 (4%)	89 (7%)
Macular degeneration	1929 (9%)	347 (7%)	66 (4%)	6 (<1%)	44 (4%)
Opacity/scar	1500 (7%)	362 (7%)	94 (5%)	110 (9%)	102 (8%)
Anisometropia	2593 (12%)	67 (1%)	9 (<1%)	34 (3%)	46 (4%)
Cystoid macular oedema	1144 (5%)	150 (3%)	59 (3%)	6 (<1%)	12 (<1%)
Cataract	1517 (7%)	26 (<1%)	8 (<1%)	95 (8%)	83 (7%)
Myopia	818 (4%)	64 (1%)	16 (<1%)	36 (3%)	24 (2%)
Amblyopia	596 (3%)	59 (1%)	14 (<1%)	37 (3%)	43 (3%)
Retinal detachment	406 (2%)	84 (2%)	13 (<1%)	8 (<1%)	10 (<1%)
Diabetic retinopathy	140 (<1%)	41 (<1%)	8 (<1%)	5 (<1%)	7 (<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.

In addition, major astigmatism (defined as 5 dioptres or more) was reported at some time post-graft in 6,843 (31%) penetrating keratoplasties, 134 (3%) Descemet's stripping (automated) endothelial keratoplasties, 33 (2%) Descemet's membrane endothelial keratoplasties, 232 (19%) deep anterior lamellar keratoplasties, and 121 (10%) traditional lamellar keratoplasties.

In followed grafts performed for keratoconus, 2,624 penetrating keratoplasties (39%) were reported to have major astigmatism **at any time post-graft**, compared to 189 deep anterior lamellar keratoplasties (21%). This difference was statistically significant, $Chi^2=114.92$, $p<0.001$. Of these, 1,427 penetrating keratoplasties (22%) were reported to have major astigmatism **at last follow-up**, compared to 135 deep anterior lamellar keratoplasties (15%). This difference was also statistically significant, $Chi^2=19.97$, $p<0.001$.

The specific amount of astigmatism at the time of last follow-up, in dioptres, was provided for 2,413 penetrating keratoplasties (1,016 in grafts performed for keratoconus) and 139 deep anterior lamellar keratoplasties (115 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 ($p=0.316$).

Surgeons reported whether graft recipients used visual aids (glasses and/or contact lens) to attain the best corrected visual acuity at the time of follow-up.

Table 8.2 shows the proportion of followed grafts for each graft type for which the recipient was reported to have worn glasses and/or a contact lens **at any point post-graft**. It also shows the proportions of followed recipients for each graft type who had an IOL in place **at time of last follow-up**. 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 8.2 Post-graft visual correction

	PK	DS(A)EK	DMEK	DALK	TLK
IOL	11832 (54%)	4913 (97%)	1696 (97%)	245 (20%)	376 (30%)
Glasses	10731 (49%)	2478 (49%)	826 (47%)	483 (39%)	381 (31%)
Contact lens	1382 (6%)	35 (<1%)	40 (2%)	91 (7%)	27 (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 8.3 shows the combinations of visual aids used following the different types of graft.

Table 8.3 Post-graft visual correction combinations

	PK	DS(A)EK	DMEK	DALK	TLK
None	4828 (22%)	105 (2%)	38 (2%)	555 (45%)	611 (49%)
IOL only	5675 (26%)	2486 (49%)	878 (50%)	138 (11%)	240 (19%)
Glasses & IOL	5830 (26%)	2397 (47%)	780 (44%)	98 (8%)	133 (11%)
Glasses only	4343 (20%)	68 (1%)	20 (1%)	359 (29%)	237 (19%)
Contact lens only	665 (3%)	4 (<1%)	0 (0%)	60 (5%)	15 (1%)
Glasses & contact lens	390 (2%)	1 (<1%)	2 (<1%)	22 (2%)	9 (<1%)
Contact lens & IOL	159 (<1%)	18 (<1%)	14 (<1%)	5 (<1%)	1 (<1%)
All three	168 (<1%)	12 (<1%)	24 (1%)	4 (<1%)	2 (<1%)

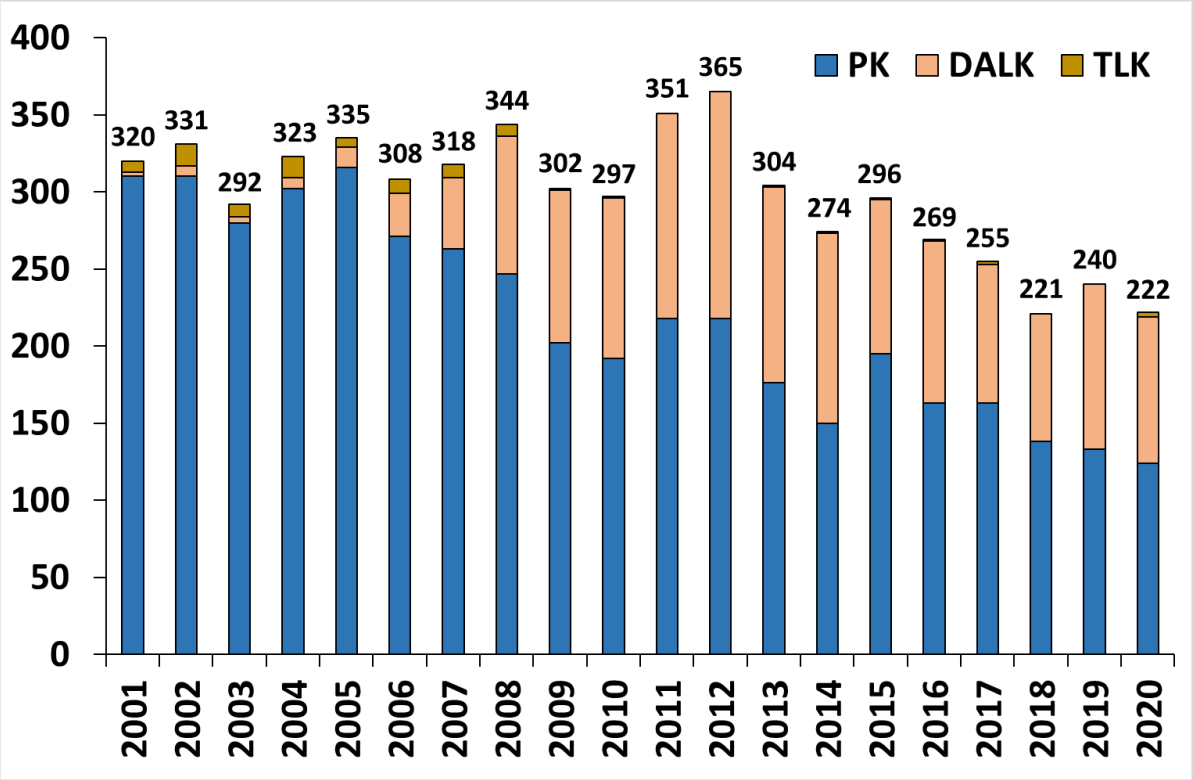
9 Comparisons Across Graft Types

This chapter presents the results of analyses that compare the outcomes of different types of grafts, performed for the same indications, across the same time period.

9.1 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 9.1.1. Traditional lamellar keratoplasties are rarely performed for keratoconus anymore, and the small number that have been registered since 2001 (when the first DALK was registered for this indication) are excluded from all further analyses in this section due to the low numbers.

Figure 9.1.1 Number of grafts performed each year, for keratoconus, 2001 to 2020

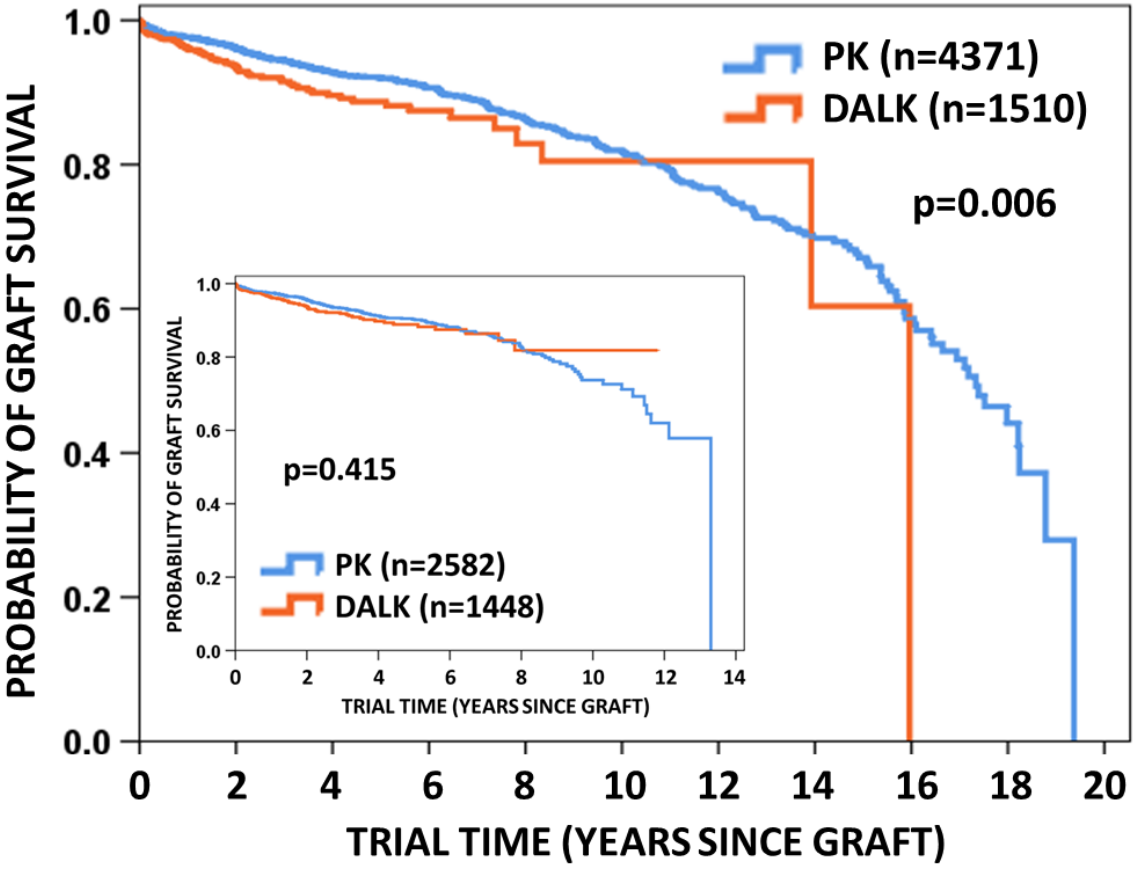


There has been a decrease in the total number of grafts for keratoconus, including both penetrating keratoplasties and deep anterior lamellar keratoplasties, over the past 10 years. This decrease in the combined number of grafts registered from 2011-2020, compared to the previous decade from 2001-2010, was statistically significant ($p<0.001$). The reduced numbers were most apparent in recipients under 40 years at the time of corneal transplantation.

9.1.1 Survival of grafts for keratoconus: influence of type of graft

Figure 9.1.2 shows the comparison of survival between penetrating keratoplasties and deep anterior lamellar keratoplasties performed for keratoconus since the year 2001. The difference in survival was significant (Log Rank Statistic=7.53; df=1; p=0.006), however when survival since 2006 was examined (see inset panel in Figure 9.1.2) the difference was non-signficiant (Log Rank Statistic=0.66; df=1; p=0.415).

Figure 9.1.2 Type of graft for keratoconus, 2001 to 2020 (inset 2006 to 2020)



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14	16	18
PK	2997 (1649)	2233 (1227)	1342 (699)	902 (397)	592 (201)	393 (81)	262 (18)	149	72	18
DALK	783 (744)	507 (479)	231 (216)	105 (94)	38 (28)	13 (7)	5 (NA)	3	NA	NA

Probability of graft survival (years post-graft)

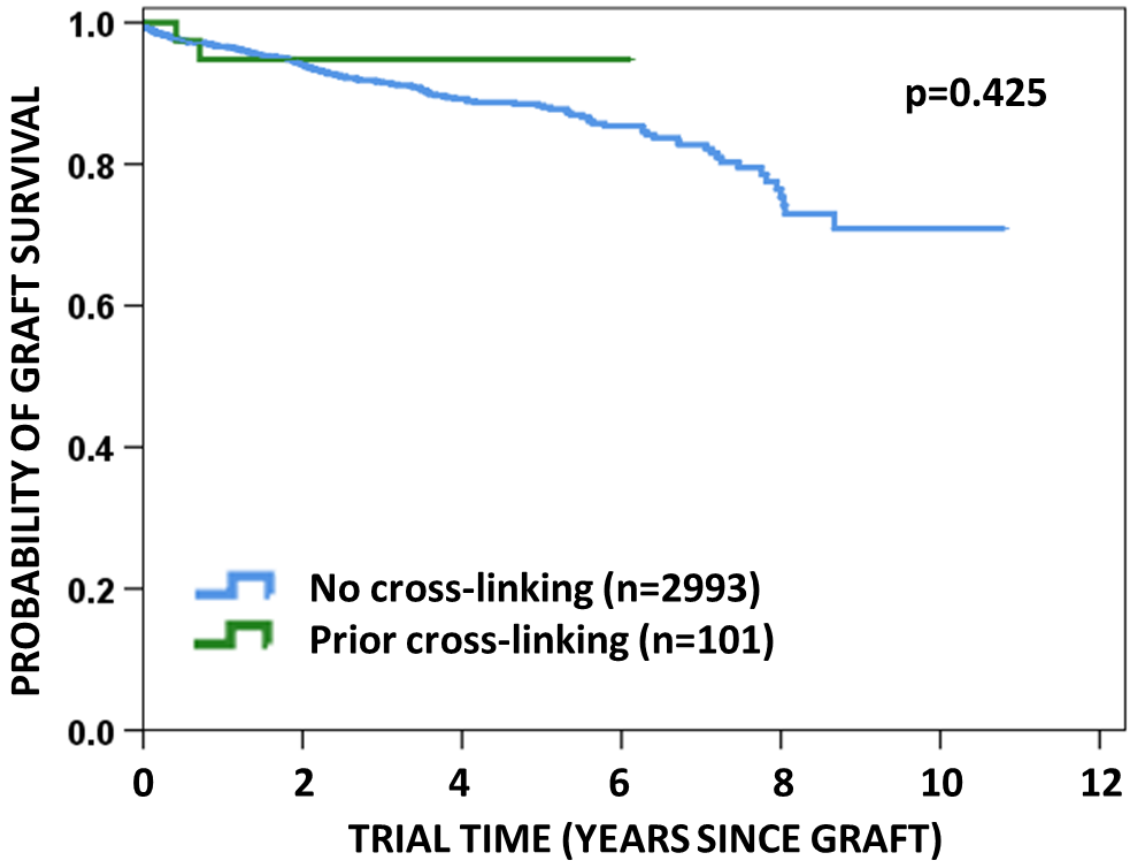
	1	2	4	6	8	10	12	14	16
PK	0.98 (0.97)	0.96 (0.96)	0.93 (0.91)	0.91 (0.88)	0.86 (0.83)	0.82 (0.74)	0.76	0.70	0.59
DALK	0.96 (0.96)	0.94 (0.94)	0.90 (0.90)	0.88 (0.88)	0.83 (0.82)	NA (NA)	NA	NA	NA

Note: Figures provided in brackets are for the subset of data for grafts performed from 2006 to 2020

9.1.2 Survival of grafts for keratoconus: influence of history of corneal collagen cross-linking

Corneal collagen cross-linking was introduced in Australia as a procedure to halt or delay the progression of keratoconus in the early 2000s and the first report to the ACGR of a graft being performed in an eye that had undergone the procedure was in 2010. Since then a total of 170 grafts have been performed in an eye known to have had cross-linking. Of these, 101 were in eyes undergoing a first graft for keratotocnus. Figure 9.1.3 shows the comparison of survival for first grafts performed for keratoconus where the eye did or did not have a reported history of corneal collagen cross-linking. There was no significant difference in survival (Log Rank Statistic=0.64; df=1; p=0.425).

Figure 9.1.3 History of corneal collagen cross-linking, 2010 to 2020



Number at risk (years post-graft)

	1	2	3	4	5	6	7	8	9	10
No cross-linking	1677	1145	767	539	368	229	146	68	20	6
Prior cross-linking	35	26	16	10	5	1	NA	NA	NA	NA

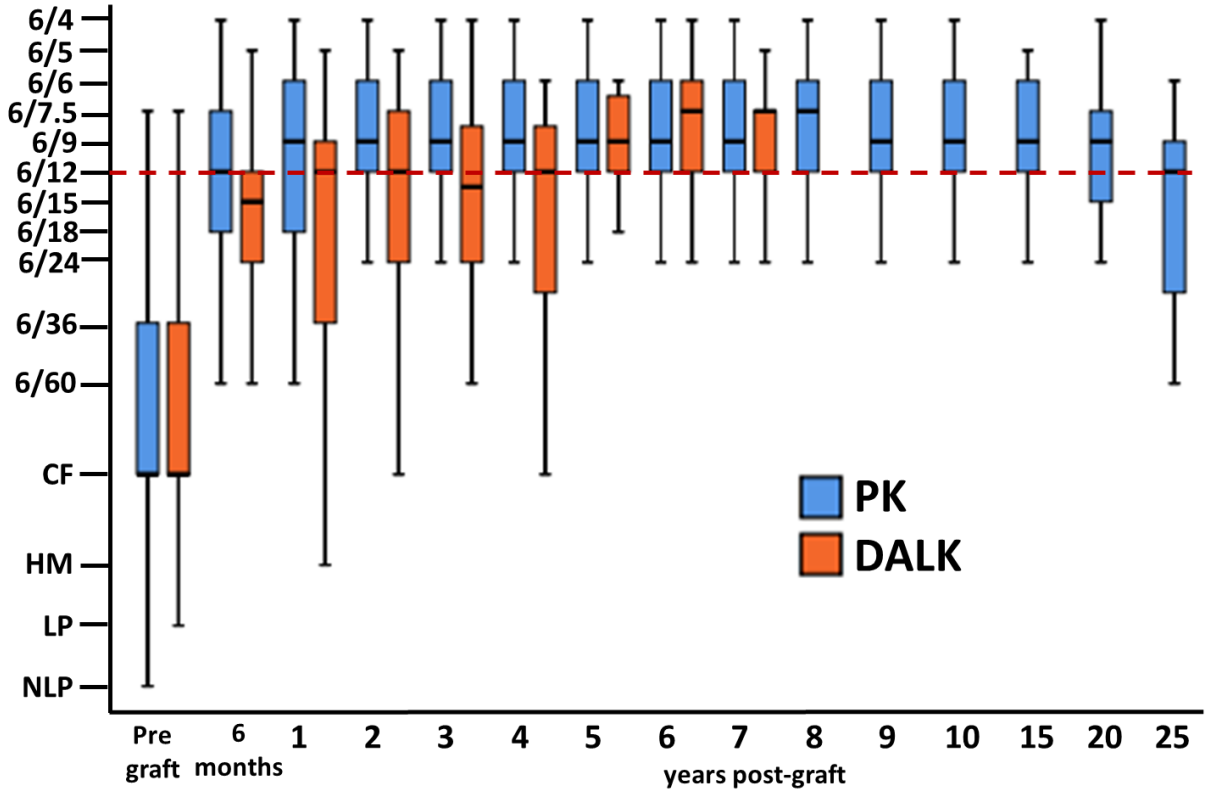
Probability of graft survival (years post-graft)

	1	2	3	4	5	6	7	8	9
No cross-linking	0.97	0.94	0.92	0.89	0.88	0.85	0.83	0.77	0.71
Prior cross-linking	0.95	0.95	NA	NA	NA	NA	NA	NA	NA

9.1.3 Best corrected visual acuity in surviving grafts performed for keratoconus

Figure 9.1.4 shows the best corrected visual acuity reported for grafts performed for keratoconus, 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. This analysis included data for grafts registered since the inception of the ACGR in 1985. See section 1.4.7 for further explanation of the methods used to analyse visual acuity data.

Figure 9.1.4 BCVA in surviving grafts performed for keratoconus



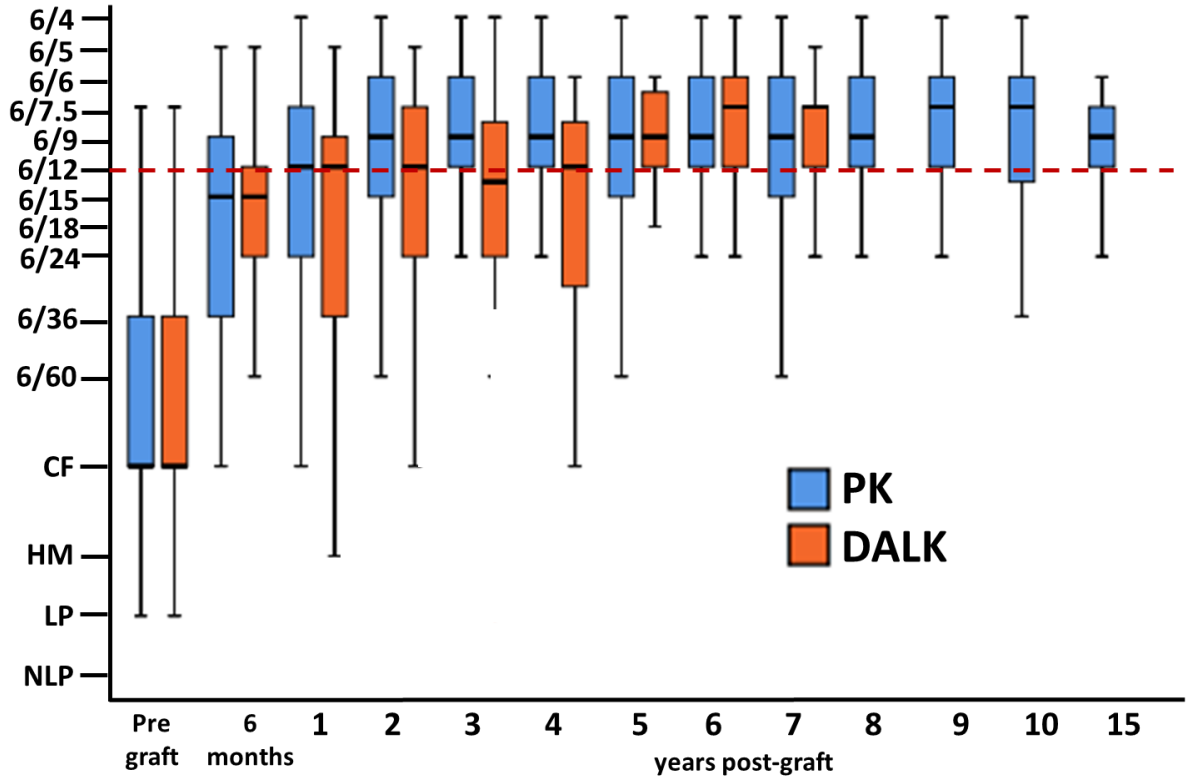
	Pre	6m	1y	2y	3y	4y	5y
PK	6845	481	1006	666	390	285	235
DALK	1401	43	130	85	44	23	16

	6y	7y	8y	9y	10y	15y	20y	25y
PK	208	163	113	123	91	67	22	16
DALK	20	19	5	0	1	0	0	0

There was no significant difference between the groups in BCVA pre-graft (p=0.160). BCVA in both groups improved significantly post-graft (see sections 3.9.2 and 6.9.2 for further discussion) with the attained BCVA significantly better in PK compared to DALK at each time-point analysed from 6-months up to 4-years post-graft (all p<0.001). There were no significant differences in median BCVA between the groups at 5-, 6- or 7-years post-graft (all p≥0.500).

Figure 9.1.5 shows the best corrected visual acuity reported for grafts performed for keratoconus, pre-graft and at various time-points post-graft, excluding penetrating keratoplasties performed prior to 2001. 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 9.1.5 BCVA in surviving grafts performed for keratoconus, 2001 to 2020



	Pre	6m	1y	2y	3y	4y	5y
PK	4167	75	408	384	192	126	116
DALK	1401	43	130	85	44	23	16

	6y	7y	8y	9y	10y	15y
PK	87	82	36	56	31	17
DALK	20	19	5	0	1	0

There was no significant difference between the groups in BCVA pre-graft (p=0.076). The attained BCVA was significantly better in PK compared to DALK at 2-years (p=0.006), 3-years (p=0.008), and 4-years (p=0.026) post-graft. There were no significant differences in median BCVA between the groups at 6- or 12-months, or at 5-, 6- or 7-years post-graft.

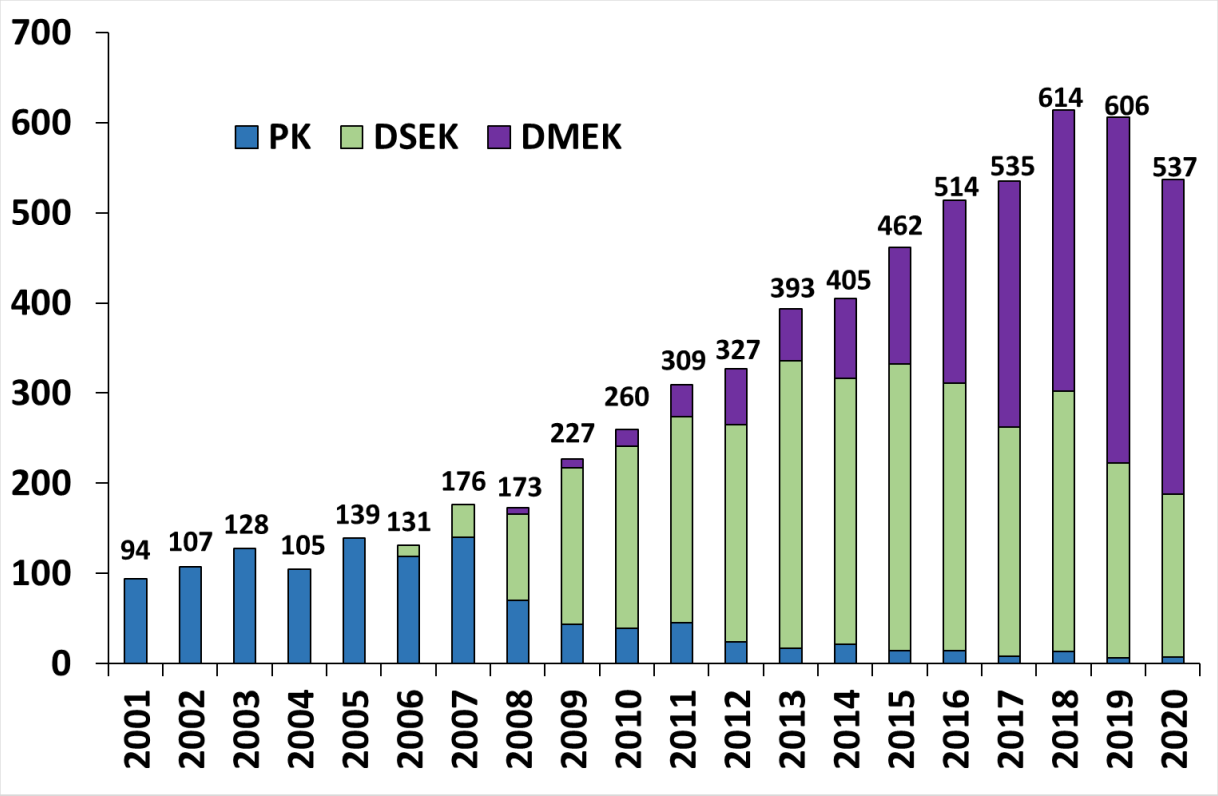
9.2 Fuchs' Endothelial Dystrophy

Two types of graft are primarily performed for Fuchs' endothelial dystrophy: Descemet's stripping (automated) endothelial keratoplasty and Descemet's membrane endothelial keratoplasty. 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 increased steadily over the following decade (as shown in Figure 9.2.1), so was the more common technique used to treat this condition just two years later. The use of DMEK was less pronounced in the early years following its introduction in 2008 but has continued to increase, particularly in the last five years, and it is now the most often registered technique, outnumbering DS(A)EK almost 2-to-1 in 2020.

The transition to endothelial keratoplasty has led to a corresponding large increase in recent years, with significant increases over each five-year time period compared to the last (all $p<0.001$). While 2020 did not see a further increase in registered graft numbers compared to previous years, these numbers may have been affected by a reduction in elective surgery in Australia during the COVID-19 pandemic.

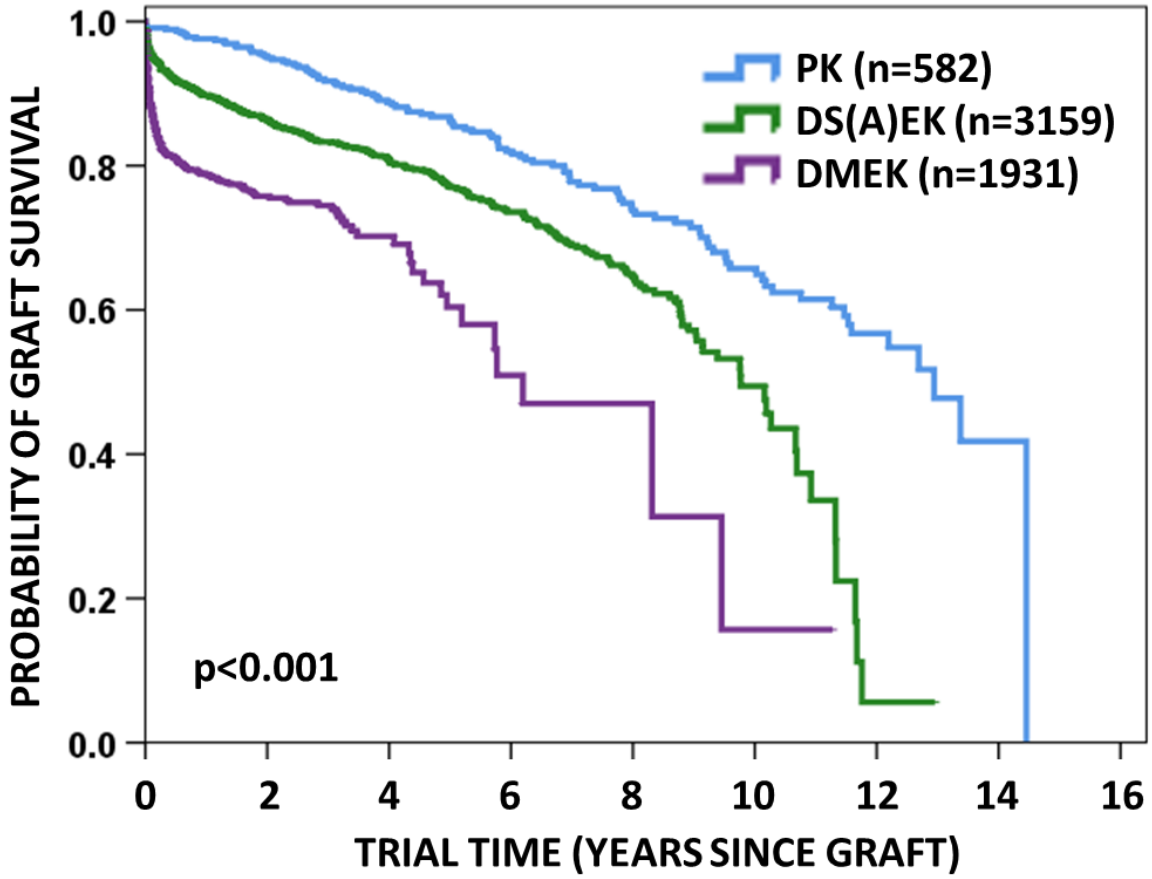
Figure 9.2.1 Number of grafts performed each year, for Fuchs' endothelial dystrophy, 2001 to 2020



9.2.1 Survival of grafts for Fuchs' endothelial dystrophy: influence of type of graft

Figure 9.2.2 shows the comparison of survival between penetrating keratoplasties, Descemet's stripping (automated) endothelial keratoplasties, and Descemet's membrane endothelial keratoplasties performed for Fuch's endothelial dystrophy since the year 2006. The difference in survival was significant (Log Rank Statistic=128.90; df=2; p<0.001) with each comparison significant at the p<0.001 level. When early failures (within 3-months of graft) were removed from the analysis, the difference remained significant (Log Rank Statistic=18.76; df=2; p<0.001), with the comparisons between penetrating keratoplasties and each of the endothelial keratoplasties still significant at the p<0.001 level, while the difference between DS(A)EK and DMEK became non-significant (p=0.142).

Figure 9.2.2 Type of graft for Fuchs' endothelial dystrophy, 2006 to 2020



Number at risk (years post-graft)

	1	2	4	6	8	10	12	14
PK	448	376	278	210	143	82	34	1
DS(A)EK	1852	1441	761	373	149	31	1	NA
DMEK	590	305	67	13	3	1	NA	NA

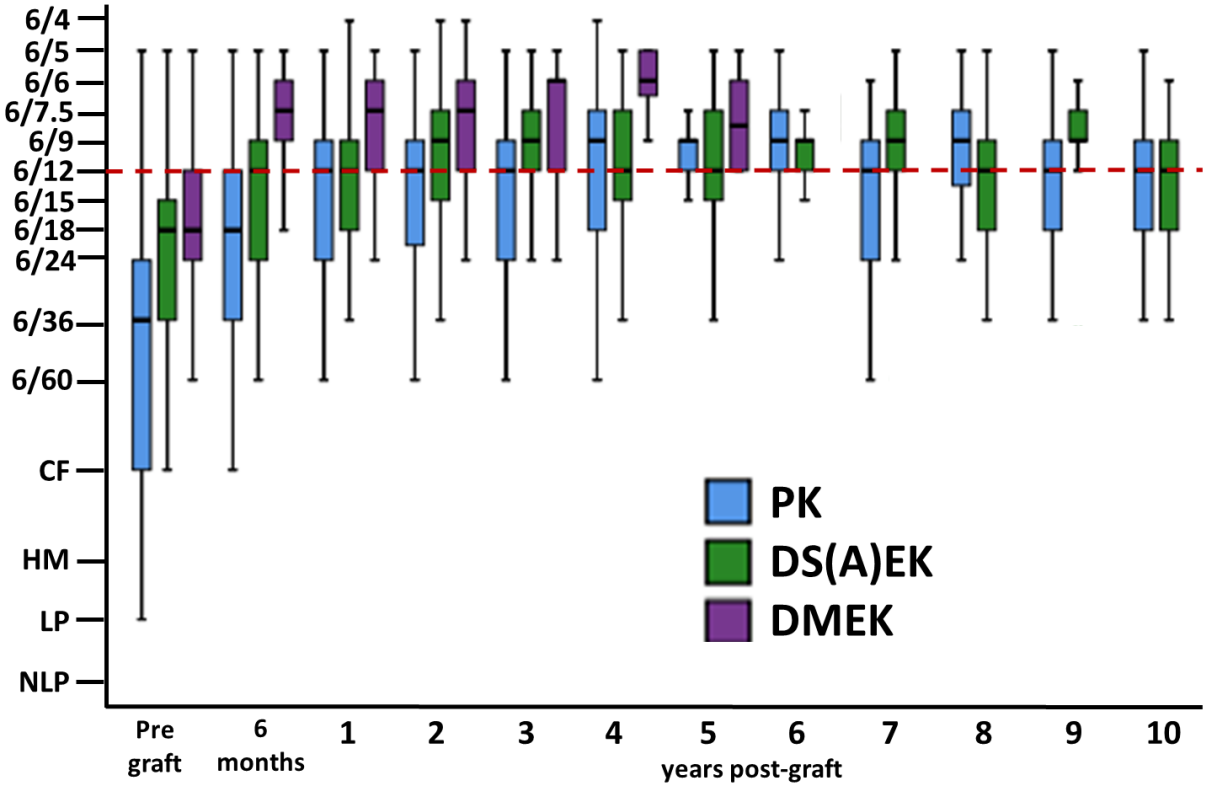
Probability of graft survival (years post-graft)

	1	2	4	6	8	10	12
PK	0.98	0.95	0.89	0.82	0.74	0.66	0.57
DS(A)EK	0.90	0.86	0.81	0.74	0.65	0.49	NA
DMEK	0.79	0.76	0.70	NA	NA	NA	NA

9.2.2 Best corrected visual acuity in surviving grafts performed for Fuchs' endothelial dystrophy

Figure 9.2.3 shows the best corrected visual acuity reported for grafts performed for Fuchs' endothelial dystrophy, 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. These analyses included data for grafts registered since the inception of the ACGR in 1985. See section 1.4.7 for further explanation of the methods used to analyse visual acuity data.

Figure 9.2.3 BCVA in surviving grafts performed for Fuchs' endothelial dystrophy



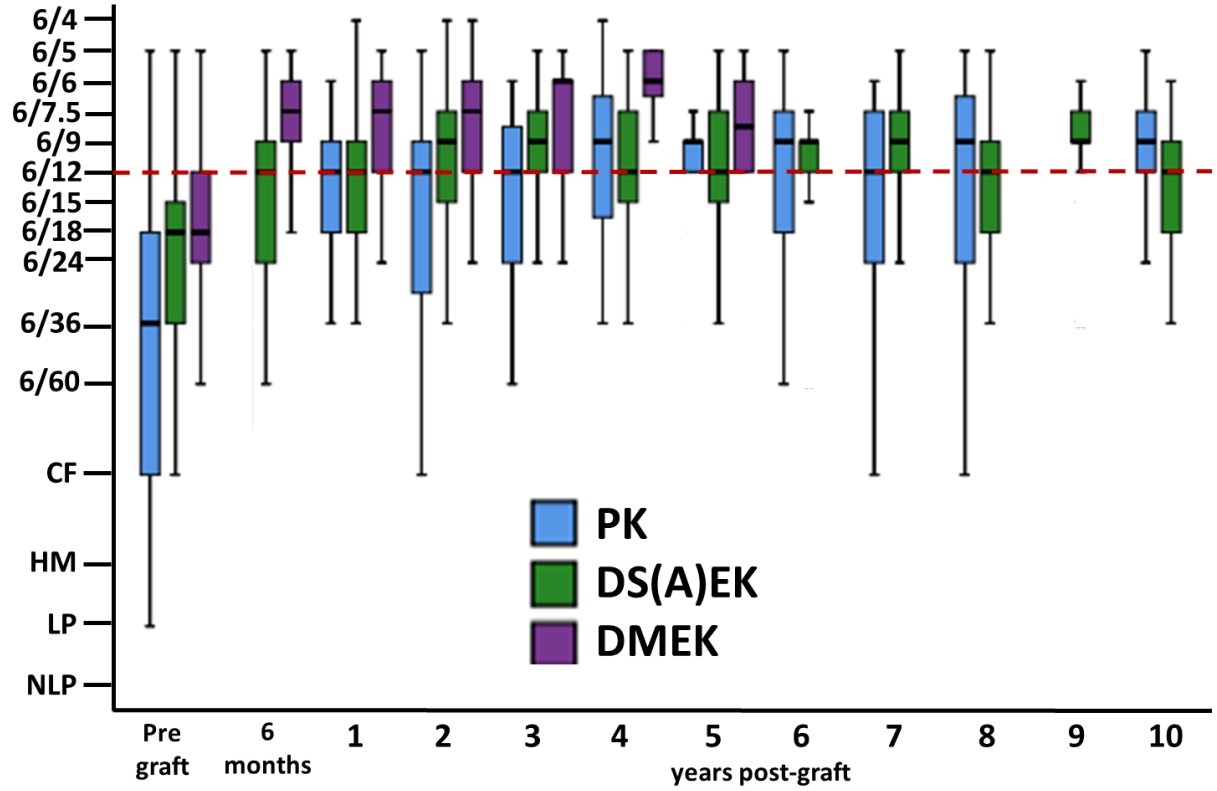
	Pre	6m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y
PK	1816	114	211	167	117	78	62	73	59	43	30	31
DS(A)EK	2951	155	272	212	151	77	78	53	45	26	13	10
DMEK	1824	69	156	74	49	11	10	4	0	0	0	0

There were significant differences in BCVA pre-graft, with pre-graft BCVA worse in PK, compared to DS(A)EK and DMEK, and worse in DS(A)EK compared to DMEK (all $p<0.001$). BCVA in all groups improved significantly post-graft (see sections 3.9.2, 4.9.2, and 5.9.2 for further discussion) with the attained BCVA significantly better in DMEK compared to PK and DS(A)EK at each time-point analysed from 6-months up to 4-years post-graft (all $p<0.001$). Significantly better vision was also exhibited following DS(A)EK compared to PK at 6-months ($p=0.010$), 2-years ($p<0.001$), 3-years ($p=0.027$), and 7-years ($p=0.011$) post-graft. All other comparisons were non-significant.

Comparisons Across Graft Types

Figure 9.2.4 shows the best corrected visual acuity reported for grafts performed for Fuchs' endothelial dystrophy, pre-graft and at various time-points post-graft, excluding penetrating keratoplasties performed before 2006. 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 9.2.4 BCVA in surviving grafts performed for Fuchs' endothelial dystrophy, 2006 to 2020



	Pre	6m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y
PK	556	7	38	55	27	23	17	22	17	19	6	10
DS(A)EK	2951	155	272	212	151	77	78	53	45	26	13	10
DMEK	1824	69	156	74	49	11	10	4	0	0	0	0

All comparisons between DS(A)EK and DMEK were the same as discussed on the previous page. Pre-graft BCVA was still worse in PK, compared to DS(A)EK and DMEK (both $p<0.001$). The attained BCVA was significantly better in DMEK compared to PK and at each time-point analysed from 1-year up to 4-years post-graft (all $p<0.001$, except at 4-years when $p=0.006$). Significantly better vision was also exhibited following DS(A)EK compared to PK at 2-years post-graft ($p=0.001$). All other comparisons were non-significant.

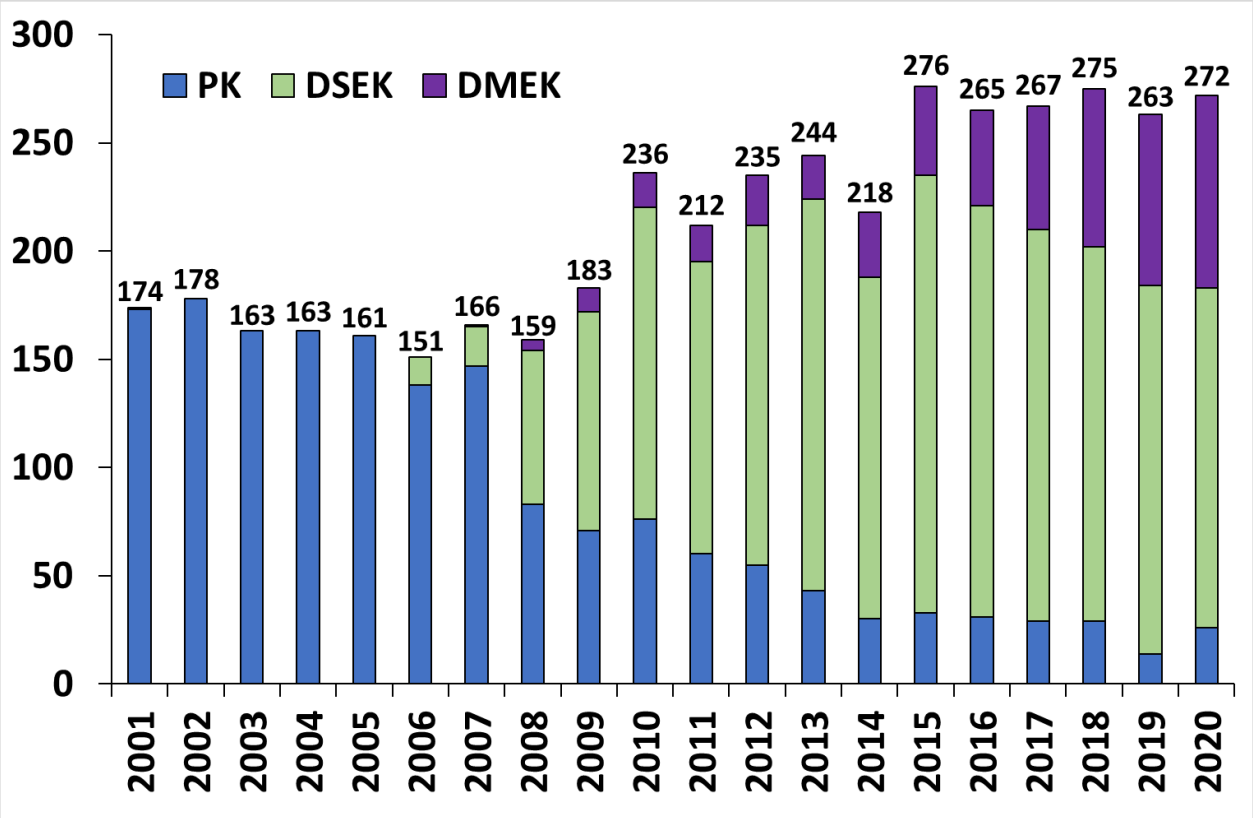
9.3 Endothelial Failure/Bullous Keratopathy

Two types of graft are primarily performed for endothelial failure/bullous keratopathy, these being Descemet's stripping (automated) endothelial keratoplasty and Descemet's membrane endothelial keratoplasty. Penetrating keratoplasty is now only performed for this indication in approximately 10% of cases.

The DS(A)EK technique was introduced in Australia in 2006 and its use in treating endothelial failure/bullous keratopathy increased steadily over the following five years, at which point it stabalised (as shown in Figure 9.3.1). The use of DMEK was also introduction in 2008 but the use of this technique in the treatment of endothelial failure/bullous keratopathy has only increased in the last five years, with DS(A)EK remaining the technique of choice at an approximate ration of 2-to-1.

While the number of grafts being registered for endothelial failure/bullous keratopathy has increased since the introduction of endothelial keratoplasty, the proportion of registered grafts for this indication has decreased from 17.4% to 14.5% when comparing the cohorts for 2001 to 2005 and 2016 to 2020 ($p<0.001$). However, the large increases in first grafts performed for Fuchs' endothelial dystrophy, as discussed in section 9.2, contributes to this, and when these grafts are excluded, the proportion of the remaining cohort that were for endothelial failure/bullous keratopathy does not differ significantly across these time groups (19.7% vs 20.9%, $p=0.150$).

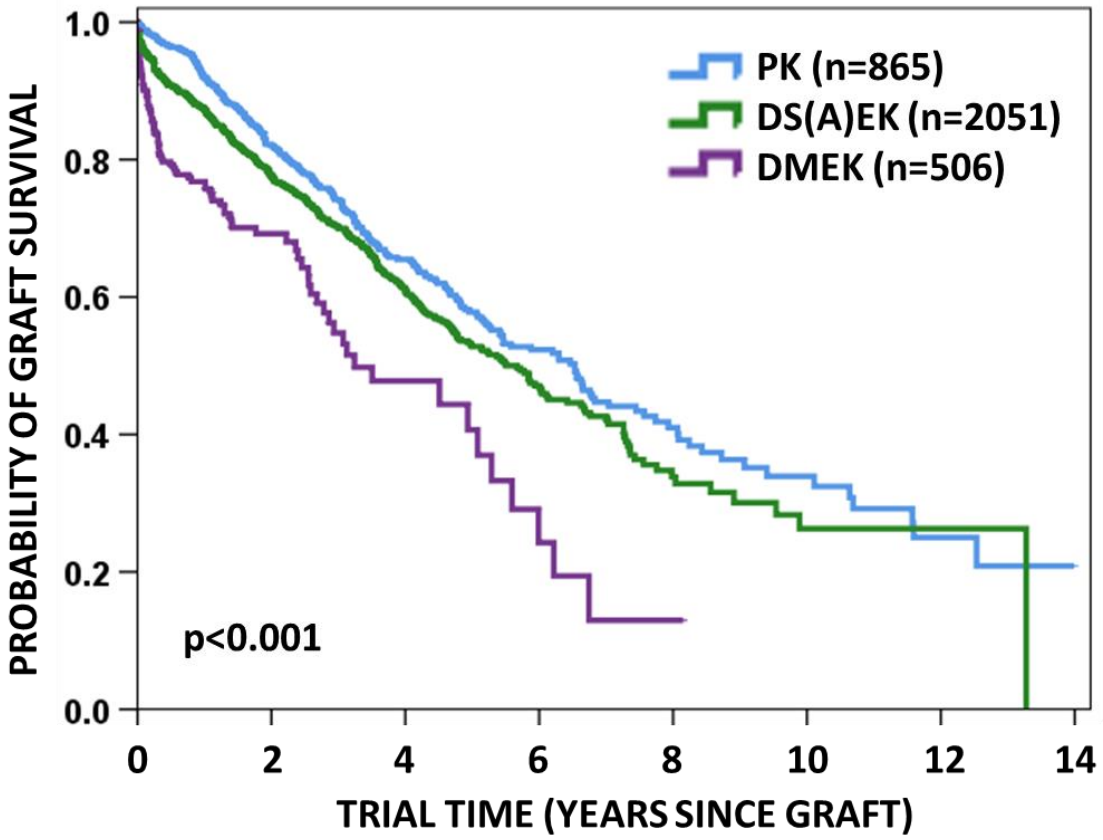
Figure 9.3.1 Number of grafts performed each year, for endothelial failure/bullous keratopathy, 2001 to 2020



9.3.1 Survival of grafts for endothelial failure/bullous keratopathy: influence of type of graft

Figure 9.3.2 shows the comparison of survival between penetrating keratoplasties, Descemet's stripping (automated) endothelial keratoplasties, and Descemet's membrane endothelial keratoplasties performed for endothelial failure/bullous keratopathy since the year 2006. The difference in survival was significant (Log Rank Statistic=38.45; df=2; p<0.001) with DMEK having poorer survival than the other graft types (both p<0.001) and DS(A)EK significantly poorer survival than PK (p=0.011). When early failures (within 3-months of graft) were removed from the analysis, the difference remained significant (Log Rank Statistic=8.43; df=2; p=0.015), with the comparisons between DMEK and the other two graft types remaining significant (PK: p=0.005, DS(A)EK: p=0.009), while the difference between DS(A)EK and PK became non-significant (p=0.465).

Figure 9.3.2 Type of graft for endothelial failure/bullous keratopathy, 2006 to 2020



Number at risk (years post-graft)

	1	2	4	6	8	10	12
PK	547	399	221	111	47	24	8
DS(A)EK	1033	704	299	122	36	11	1
DMEK	146	71	19	5	1	NA	NA

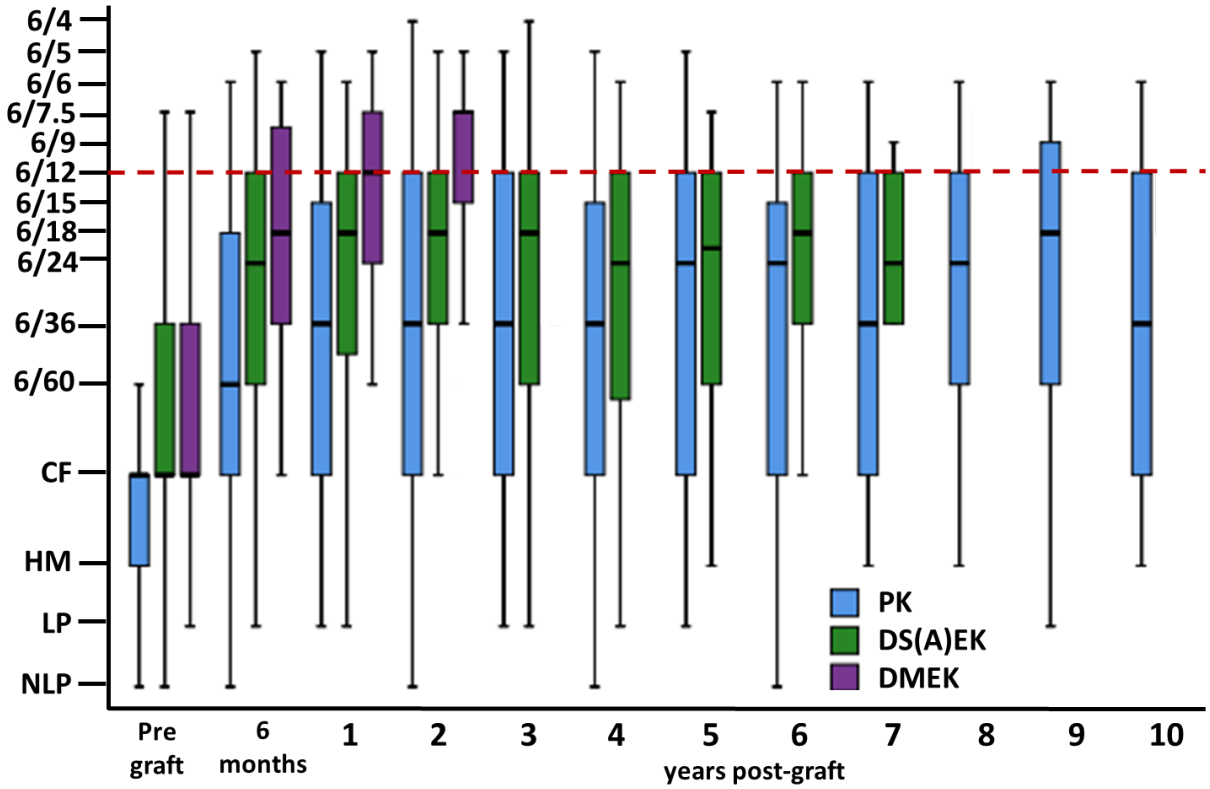
Probability of graft survival (years post-graft)

	1	2	4	6	8	10
PK	0.92	0.82	0.66	0.52	0.41	0.34
DS(A)EK	0.87	0.78	0.61	0.47	0.34	NA
DMEK	0.77	0.69	NA	NA	NA	NA

9.3.2 Best corrected visual acuity in surviving grafts performed for endothelial failure/bullous keratopathy

Figure 9.3.3 shows the best corrected visual acuity reported for grafts performed for endothelial failure/bullous keratopathy, 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. This analysis included data for grafts registered since the inception of the ACGR in 1985. See section 1.4.7 for further explanation of the methods used to analyse visual acuity data.

Figure 9.3.3 BCVA in surviving grafts performed for endothelial failure/bullous keratopathy



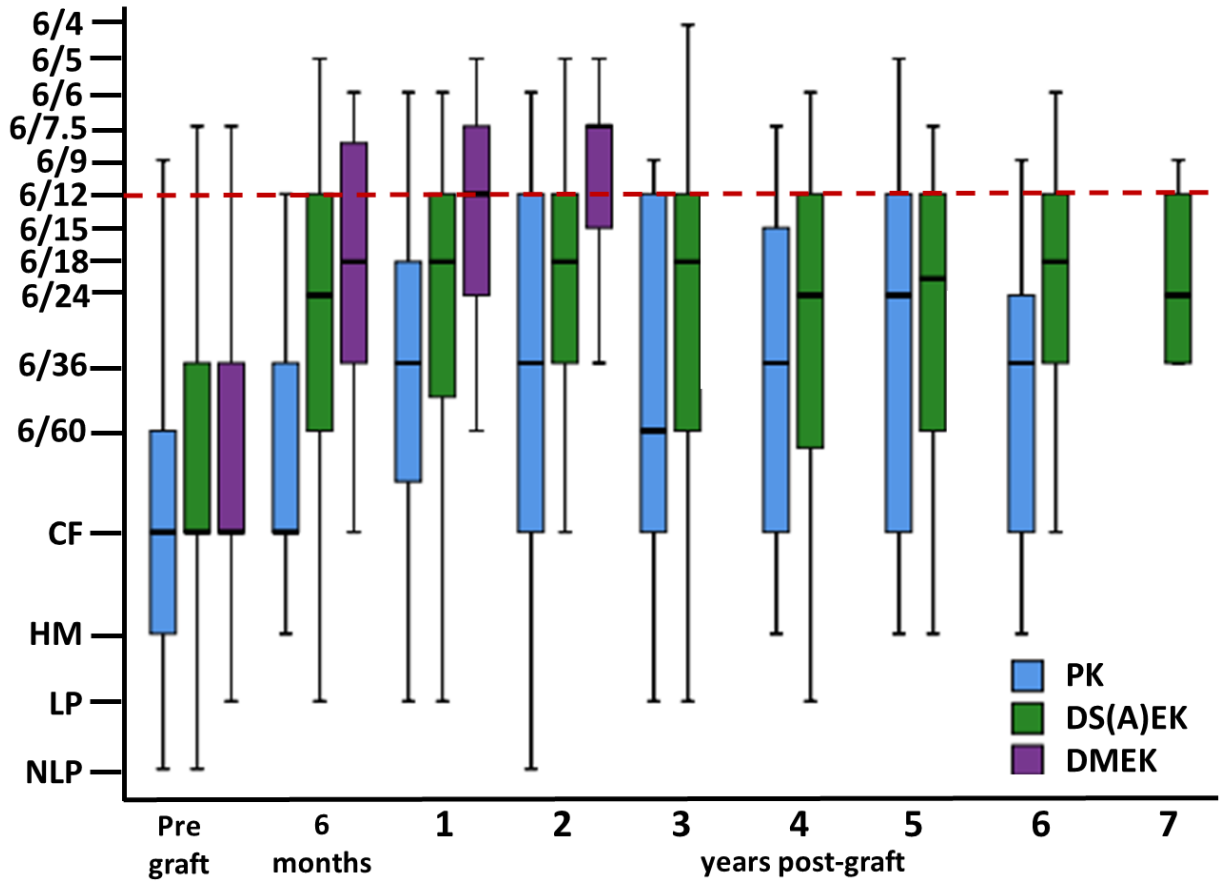
	Pre	6m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y
PK	3717	283	460	253	153	105	74	57	45	39	22	17
DS(A)EK	1856	106	171	105	61	39	32	17	10	5	0	5
DMEK	470	20	41	21	5	3	1	0	0	1	0	0

There were significant differences in BCVA pre-graft, with pre-graft BCVA worse in PK, compared to DS(A)EK and DMEK (both $p<0.001$), and worse in DS(A)EK compared to DMEK ($p=0.004$). BCVA in all groups improved significantly post-graft (see sections 3.9.2, 4.9.2, and 5.9.2 for further discussion) with the attained BCVA significantly better in DMEK compared to PK at 6-months, 1-year, and 2-years post-graft (all $p<0.001$). Significantly better vision was also exhibited following DMEK compared to DS(A)EK at 1-year and 2-years post-graft (both $p<0.001$), and DS(A)EK compared to PK at 6-months, 1-year (both $p<0.001$), and 2-years ($p=0.002$) post-graft. All other comparisons were non-significant.

Comparisons Across Graft Types

Figure 9.3.4 shows the best corrected visual acuity reported for grafts performed for endothelial failure/bullous keratopathy, pre-graft and at various time-points post-graft, excluding penetrating keratoplasties performed before 2006. 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 9.3.4 BCVA in surviving grafts performed for endothelial failure/bullous keratopathy, 2006 to 2020



	Pre	6m	1y	2y	3y	4y	5y	6y	7y
PK	807	13	56	60	29	24	14	11	6
DS(A)EK	1856	106	171	105	61	39	32	17	10
DMEK	470	20	41	21	5	3	1	0	0

All comparisons between DS(A)EK and DMEK were the same as discussed on the previous page. Pre-graft BCVA was again worse in PK compared to DS(A)EK and DMEK (both $p<0.001$) The attained BCVA was significantly better in DMEK compared to PK at 6-months ($p=0.001$), 1-year, and 2-years post-graft (both $p<0.001$). Significantly better vision was also exhibited following DS(A)EK compared to PK at 6-months ($p<0.001$), 1-year ($p=0.003$), 2-years ($p=0.009$), and 6-years ($p=0.049$) post-graft. All other comparisons were non-significant.

10 Summary

Up to 31st March 2021, 40,864 grafts were registered with the Australian Corneal Graft Registry. 31,460 (77%) of these had follow-up received by the census date. There has been a shift away from full-thickness penetrating keratoplasties in favour of partial-thickness endothelial keratoplasty techniques, resulting in approximately even numbers of each being registered in the 2019 calendar year.

10.1 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). For traditional lamellar keratoplasty (TLK), grafts performed with corneas where the donor eye had been enucleated more than 15 hours after donor death exhibited poorer survival.

Donor age group was retained in multivariate analysis relating to penetrating keratoplasty (PK) and Descemet's membrane endothelial keratoplasty, with grafts performed using tissue from younger donors exhibiting better survival for PK but poorer survival for DMEK.

For Descemet's stripping (automated) endothelial keratoplasty (DS(A)EK), pre-graft central endothelial cell density was a significant independent risk factor with grafts performed using donor tissue with <2500 cells/mm² exhibiting poorest survival and those with ≥3250 cells/mm² exhibiting the best 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/mm² also exhibited poorest survival in the significant univariate analysis.

There were differences in survival between grafts performed with tissue provided by various eye banks for DS(A)EK and DMEK. Interstate transportation of the donor cornea was found to be an independent risk factor in the final DS(A)EK model.

10.2 Recipient Factors

Indication for graft was a significant independent factor for PK, DS(A)EK and TLK. Survival was best for PK performed for keratoconus, followed by those for Fuchs' endothelial dystrophy, and worst for those performed for corneal ulcers or multiple previous failed grafts. DS(A)EK survival was best in grafts performed for Fuchs' endothelial dystrophy, while superior survival was found for TLK performed for pterygium, complications from beta-radiation, and scleral necrosis. Though indication for graft was not retained in the DALK model as an independent predictor of survival, a history of prior ipsilateral graft/s was and was found to have a deleterious effect.

Recipient age group was a significant factor for DALK and TLK, with poorer survival in DALK recipients aged 70 or older and best survival in those aged under 40 years, and poorer survival in TLK recipients aged 10 to 19 years.

Recipient sex was an independent risk factor for DS(A)EK, with male recipients exhibiting poorer graft survival. This was also the case for DMEK but was combined with donor sex in the final model as the combined effect was stronger, with the best survival observed in female recipients receiving male donor corneas when compared to female donors in either sex recipient.

Pre-graft corneal neovascularisation was an independent risk factor for PK, DALK and TLK, as was inflammation and/or use of steroids within the two weeks prior to graft for PK and TLK. A history and/or current episode of raised intraocular pressure was also a risk factor for PK and DS(A)EK. A history of multiple prior contralateral grafts was an independent risk factor for DS(A)EK but a history of any prior contralateral grafts was a protective factor for PK.

An independent risk factor for DS(A)EK was ultra-thin trephination of the donor lenticule, and those where the trephination technique was not advised also had poorer survival.

10.3 Graft Era/Year

Graft year/era was a significant independent risk factor for survival of PK, DALK, DS(A)EK and DMEK. Survival tended to be worse in earlier cohorts for PK, DS(A)EK and DMEK, and then saw improvement before dropping off again in the more recent years. Poorest outcomes were observed in the 2019 and 2020 cohorts for all graft types. 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.

10.4 Surgical factors

The size of the graft was found to be a significant independent risk factor for graft failure for PK, DS(A)EK, DMEK and TLK. For PK best survival was found for grafts 7.75 to 8.49 mm, with worse survival in both smaller and larger grafts. For TLK optimal survival was found for grafts sized 6.01 to 8.00 mm, with poorest survival in those larger than 8.00 mm. For both DS(A)EK and DMEK poorer survival was found in grafts smaller than 8.25 mm, and for DS(A)EK an incision size larger than 5.00 mm was also an independent risk factor for failure.

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, those undergoing a triple procedure (graft, cataract extraction and IOL insertion) had the best survival. Those who were aphakic post-graft had the poorest survival for PK and eyes which underwent additional surgery at the time of graft, excluding triple procedures, exhibited poorer survival. DMEK performed using a Geuder injector to insert the donor lenticule exhibited better survival.

The caseload of a surgeon, analysed in conjunction with their level of follow-up information provided to the ACGR, was a significant risk factor in PK, DS(A)EK, DMEK and DALK. Surgeons who had performed 2% or more of the registered grafts in the relevant cohort, and had better than average levels of follow-up provided, had significantly better documented outcomes than those with fewer registered grafts, or with lower levels of follow-up. The exception to this finding was for DALK, where there was no difference between high caseload surgeons with high follow-up and low caseload surgeons. For PK and DALK, low caseload surgeons also had better outcomes than high caseload surgeons with low levels of follow-up, while for DS(A)EK high caseload surgeons with low follow-up also had better outcomes than low caseload surgeons. For TLK the centre effect was retained in the final model.

10.5 Post-graft factors

The occurrence of post-graft rejection was an independent risk factor for failure in both PK and DS(A)EK. Post-graft rejection occurred most frequently following penetrating keratoplasty and very few lamellar grafts underwent more than one post-graft rejection episode (see table 10.1).

Table 10.1 Number of post-graft rejection episodes stratified by graft type

	None	One	Two	Three or more
PK	22387 (83%)	3324 (12%)	765 (3%)	448 (2%)
DS(A)EK	6539 (94%)	367 (5%)	38 (<1%)	12 (<1%)
DMEK	3137 (98%)	74 (2%)	3 (<1%)	2 (<1%)
DALK	1934 (96%)	73 (4%)	9 (<1%)	3 (<1%)
TLK	1621 (97%)	33 (2%)	4 (<1%)	1 (<1%)

Post-graft corneal neovascularisation was associated with poorer survival for PK, DALK, DS(A)EK and DMEK. The presence of post-graft corneal oedema had an independent detrimental effect on the survival of both PK and DS(A)EK. In addition, post-graft microbial keratitis resulted in poorer survival for PK. Lower risk was associated with raised intraocular pressure post-graft for PK, DALK and DS(A)EK.

Summary

10.6 Comparisons Across Graft Types

Primary non-functioning grafts were reported most often following DMEK (9%), and DS(A)EK (5%). They were rarely reported following TLK, DALK (both 1%) or PK (<1%). Comparisons of 5-year PNF rates from 2006 to 2010 and 2016 to 2020, show that for DS(A)EK, the primary non-function rate has reduced from 8% to 5%, whereas for DMEK, the rate has decreased from 12% to 7%.

Survival of PK and DALK performed for keratoconus since the introduction of DALK shows a significant difference, with superior survival for PK, however this difference becomes non-significant when the first five years of DALK are excluded. There was no significant difference between groups in pre-graft BCVA but eyes that had undergone a PK had significantly better BCVA at 2- to 4- years than those that underwent DALK. Both groups saw a significant improvement in BCVA post graft, reaching 6/12 by 1-year.

While PK are not often now performed for Fuchs' endothelial dystrophy, the survival of those performed for this indication since the introduction of endothelial keratoplasty in 2006 is significantly better than that of either DS(A)EK or DMEK. The survival of DS(A)EK was also superior to DMEK, however, this difference became non-significant when primary non-functioning early graft failures (within 3 months of graft) were removed from the analysis. There were significant differences in the pre-graft BCVA across groups, with the poorest recorded in those undergoing PK and the best in those undergoing DMEK. All graft types resulted in a significant improvement in BCVA post graft, reaching 6/12 by 1-year, with the best vision reported following DMEK, for which the median BCVA was 6/7.5 by 6-months post graft.

The survival of PK performed for endothelial failure/bullous keratopathy since 2006 was also found to be superior to that of DS(A)EK and DMEK. Following removal of primary non-functioning early graft failures, this significant difference remained compared to DMEK but not DS(A)EK, which also had superior survival to DMEK. There were significant differences in the pre-graft BCVA across groups, with the poorest recorded in those undergoing PK and the best in those undergoing DMEK. Both endothelial keratoplasty groups reported significantly better BCVA than PK at 6-month, 1-year and 2-years post-graft. Only DMEK reached a post-graft BCVA of 6/12 which was attained by 1-year post-graft.

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Publications

CURRENT REGISTRATION AND FOLLOW-UP FORMS USED BY THE AUSTRALIAN CORNEAL GRAFT REGISTRY

Registry No. Registry use only	THE AUSTRALIAN CORNEAL GRAFT REGISTRY REGISTRATION FORM	Date Rec'd Registry use only

OPERATING SURGEON (surname and initial): _____ STATE:

CONSULTANT (if different): _____

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 ☐

CONFIRMATION OF CONSENT (please tick) *I have gained consent from the corneal graft recipient to:*

Forward their data to the Australian Corneal Graft Registry (ACGR) ☐

Allow the ACGR to perform confidential linkage with the National Death Index to determine if recipients have died ☐

AT WHICH ADDRESS SHOULD THE ACGR SEEK FOLLOW-UP? : _____

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 non-function ☐ Detachment ☐ Rejection ☐ Endothelial failure ☐ Other:	Date of failure: / /

Immediately **prior** to the graft, the eye to be grafted was (please circle): **Phakic** **Aphakic** **Pseudophakic**

Number 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): R: L:

Please tick applicable boxes

Does the patient have any of the following:	Yes	No	Unknown
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)			

Please select applicable boxes

Presence of vessels in the recipient cornea:	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: _____

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

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 ☐ Yes ☐ Other tissue/bone donor ☐

Cause of donor death:

OFFICE USE ONLY

TIMES AND DATES (please fill in as many as are known using a **24 hour** clock)

Donor death:	Time :	Date / /		
Enucleation of eye:	Time :	Date / /		
Storage of cornea:	Time :	Date / /		
De-swelling commenced:	Time :	Date / /		

STORAGE METHOD (please tick)
Optisol ☐
Organ culture ☐
Moist pot ☐

Endothelial cell count (per mm²): _____ Pre-cut tissue: No ☐ Yes ☐

Registry No. Registry use only	THE AUSTRALIAN CORNEAL GRAFT REGISTRY **PENETRATING** GRAFT FOLLOW-UP FORM		Date Rec'd 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:	Office use only
1.	
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		RECURRENT HERPETIC DISEASE		OEDEMA	
CATARACT DEVELOPED SINCE GRAFT		MICROBIAL KERATITIS/ABSCESS		UVEITIS	
INTERFACE/STROMAL HAZE OR OPACITY		SIGNIFICANT RISE IN IOP	→	STEROID INDUCED?	Y 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		PSEUDOPHAKIC IOL INSERTION		PHAKIC IOL INSERTION	
IOL REMOVAL		IOL EXCHANGE		YAG LASER/CAPSULOTOMY	
PIGGY-BACK IOL		TARSORRHAPHY		VITRECTOMY		TRABECULECTOMY	

OTHER (please specify): _____

HAS ANY REFRACTIVE SURGERY BEEN PERFORMED ON THE GRAFTED EYE? Yes | No

(please tick as many as apply)

SUTURE ADJUSTMENT		RELAXING INCISION		**EXCIMER LASER** LASIK	
COMPRESSION SUTURES		WEDGE RESECTION		LASEK	
				PRK	
				PTK	

OTHER (please specify): _____

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)		GRAFTED EYE	CONTRALATERAL EYE
SNELLEN ACUITY **WITH PINHOLE**:		GRAFTED EYE	CONTRALATERAL EYE

FACTORS AFFECTING VISUAL ACUITY IN GRAFTED EYE (please tick all that apply)

ANISOMETROPIA MAJOR ASTIGMATISM (≥5D) Dioptres: _____

K-Reading: _____

CATARACT		CME		MYOPIA		RETINAL DETACHMENT	
GLAUCOMA		ARMD		AMBLYOPIA		DIABETIC RETINOPATHY	
OPACITY/SCAR		APHAKIA		OTHER (please specify):			

IF GRAFTED FOR PAIN, HAS PAIN BEEN RELIEVED? Yes | No

CENTRAL GRAFT PACHYMETRY _____ ENDOTHELIAL CELL COUNT (per mm²) _____

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. Registry use only	THE AUSTRALIAN CORNEAL GRAFT REGISTRY **LAMELLAR** GRAFT FOLLOW-UP FORM		Date Rec'd 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:	Office use only
1.	
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 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		RECURRENT HERPETIC DISEASE		OEDEMA	
CATARACT DEVELOPED SINCE GRAFT		MICROBIAL KERATITIS/ABSCESS		UVEITIS	
INTERFACE/STROMAL HAZE OR OPACITY		SIGNIFICANT RISE IN IOP	→	STEROID INDUCED?	Y 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		PSEUDOPHAKIC IOL INSERTION		PHAKIC IOL INSERTION	
IOL REMOVAL		IOL EXCHANGE		YAG LASER/CAPSULOTOMY	
PIGGY-BACK IOL		TARSORRHAPHY		VITRECTOMY		TRABECULECTOMY	

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) ☐ FAILED WITHIN 28 DAYS Yes / No

INTERFACE OPACITY ☐ DOUBLE ANTERIOR CHAMBER ☐

COMPLETE GRAFT DETATCHMENT ☐ PARTIAL GRAFT DETACHMENT ☐

RE-BUBBLED Yes / No NO. OF REBUBBLES: _____ SUCCESSFUL RE-ATTACHMENT 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) ☐ GRAFTED EYE ☐ CONTRALATERAL EYE ☐

SNELLEN ACUITY **WITH PINHOLE**: GRAFTED EYE ☐ CONTRALATERAL EYE ☐

FACTORS AFFECTING VISUAL ACUITY IN GRAFTED EYE (please tick all that apply)

ANISOMETROPIA ☐ MAJOR ASTIGMATISM (≥5D) ☐ Dioptres: _____ K-reading: _____

CATARACT		CME		MYOPIA		RETINAL DETACHMENT	
GLAUCOMA		ARMD		AMBLYOPIA		DIABETIC RETINOPATHY	
OPACITY/SCAR		APHAKIA		OTHER (please specify):			

IF GRAFTED FOR PAIN, HAS PAIN BEEN RELIEVED? Yes / No

CENTRAL GRAFT PACHYMETRY ☐ ENDOTHELIAL CELL COUNT (per mm²) ☐

OTHER COMMENTS:

_____

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Current Forms