



Archived at the Flinders Academic Commons:

<http://dspace.flinders.edu.au/dspace/>

'This is the peer reviewed version of the following article:

Lowe MT, Keane MC, Coster DJ, Williams KA. The outcome of corneal transplantation in infants, children, and adolescents. *Ophthalmology*. 2011 Mar;118(3):492-7. doi: 10.1016/j.ophtha.2010.07.006.

© 2011. This manuscript version is made available under the CC-BY-NC-ND 4.0 license <http://creativecommons.org/licenses/by-nc-nd/4.0/>

which has been published in final form at

DOI:

<http://dx.doi.org/10.1016/j.ophtha.2010.07.006>

Copyright © 2011 American Academy of Ophthalmology.

Published by Elsevier Inc. All rights reserved.

1

2

3 **The Outcome of Corneal Transplantation in Infants, Children and**  
4 **Adolescents**

5 *Marie T. Lowe, BSc,<sup>1</sup> Miriam C. Keane, BPsych (Hons),<sup>1</sup> Douglas J. Coster, FRANZCO,<sup>1</sup>*  
6 *Keryn A. Williams PhD,<sup>1</sup> on behalf of all contributors to The Australian Corneal Graft*  
7 *Registry*

8

9

10 **Footnotes and Financial Disclosures**

11 <sup>1</sup> Department of Ophthalmology, Flinders University, Adelaide, Australia

12

13 **Financial Support**

14 This work was supported by the Australian Organ and Tissue Donation and Transplantation  
15 Authority, Canberra, Grant number 01 572 36019 and by the Australian National Health &  
16 Medical Research Council (NHMRC). The funding organizations had no role in the design or  
17 conduct of this research.

18

19 **Conflict of Interest**

20 No authors had any financial/conflicting interest to disclose.

21

22 Correspondence: Keryn A. Williams, Department of Ophthalmology, Flinders Medical  
23 Centre, Bedford Park, SA 5042, Australia.

24 Email: keryn.williams@flinders.edu.au

25

**1 Abstract**

2 **Objective:** To examine factors affecting penetrating corneal graft survival and visual  
3 outcomes in patients under the age of 20 years.

4 **Design:** Large prospective, cohort study.

5 **Participants:** Records of 14,865 followed penetrating corneal grafts in 11,929 patients were  
6 searched to identify 765 grafts in 640 patients aged less than 20 years of age at time of graft.

7 **Methods:** Records submitted to the Australian Corneal Graft Registry by 381 ophthalmic  
8 surgeons and 253 follow-up practitioners from May 1985 to June 2009 were analysed using  
9 Kaplan-Meier survival plots and Cox proportional hazards regression analysis.

10 **Main Outcomes Measures:** Probability of corneal graft survival and Snellen acuity at time of  
11 most recent follow-up and at defined intervals post-graft.

12 **Results:** Infants (<5 years) exhibited poorer graft survival than children aged 5 to 12 years.  
13 Adolescents (13-19 years) exhibited better corneal graft survival than other age groups; 86%  
14 of grafts in adolescents were for keratoconus. Factors significantly affecting corneal graft  
15 survival in pediatric patients included indication for graft, graft inflammation, history of intra-  
16 ocular surgery, vascularisation, rejection episodes, post graft operative procedures and  
17 refractive surgery. Fourteen percent of pediatric grafts failed, of which 65% failed within 2  
18 years post graft. Forty four percent of failures were due to unknown causes (18) or  
19 irreversible rejection (30).

20 **Conclusions:** Corneal grafts for keratoconus in adolescents show excellent survival. Infants  
21 exhibit poor graft survival and visual outcomes, especially those transplanted for Peters'  
22 anomaly. Corneal graft survival and visual outcomes vary more by indication for graft than  
23 recipient age. The major reason for graft failure is irreversible rejection. Corneal  
24 transplantation improves overall bilateral vision in pediatric patients.

25 **Financial Disclosures (s):** The author(s) have no proprietary or commercial interest in any of

1 the materials discussed in this article.

2

1 The frequency of pediatric keratoplasty has increased and its success rate has improved over  
2 the past twenty years.<sup>1,2</sup> Better outcomes have been credited to improvements in postoperative  
3 care and developments in corneal microsurgery,<sup>3</sup> although the results of penetrating  
4 keratoplasty in children are still not as good as those reported for adults.<sup>1,4</sup> The infant cornea  
5 is less rigid and is thinner than in adults, making keratoplasty technically more difficult.<sup>2,5-6</sup>  
6 Other factors impacting upon outcomes in children include possible positive vitreous pressure  
7 and increased fibrinous reactions after surgery, an increased risk of infection and rejection  
8 associated with frequent loosening of sutures, and the inability of young children to  
9 communicate the occurrence of post-operative symptoms.<sup>1,4</sup>

10 A key factor in predicting the success of penetrating keratoplasty in pediatric patients  
11 is indication for graft, which changes with increasing recipient age.<sup>6</sup> Patients under five years  
12 are commonly grafted for a congenital opacity such as Peters' anomaly, whereas adolescents  
13 are more likely to undergo a penetrating keratoplasty for conditions such as keratoconus.<sup>1,4,7</sup>  
14 Geographical location has an impact on the types of indications that are prevalent in a  
15 community, with regions such as China and Saudi Arabia showing a higher occurrence of  
16 congenital hereditary endothelial dystrophy (CHED) than Australia and New Zealand.<sup>2,4,8</sup>  
17 Generally, older children and adolescents exhibit better graft survival rates than do infants.<sup>6</sup>

18 Using data collected within the large, prospective cohort of the Australian Corneal  
19 Graft Registry, we investigated independent risk factors affecting graft survival, and visual  
20 outcomes in 765 penetrating corneal grafts performed on 640 patients in a pediatric cohort,  
21 and analysed variations in outcomes between the very young and the group of adolescents.  
22 The Registry approach has the advantage that it describes outcomes obtained in the real  
23 world, in a wide variety of practice settings and not solely in an academic environment.

## 1 **Patients and Methods**

### 2 **Patients**

3 The Australian Corneal Graft Registry, established in May 1985, measures visual outcomes  
4 and corneal graft survival for patient undergoing corneal transplantation in Australia. It  
5 contains records of penetrating (full-thickness), lamellar (partial thickness) and limbal  
6 (epithelial stem cell) corneal grafts, of which 95% are penetrating. The study period for these  
7 analyses was May 1985 to June 2009. At the census date, the Register held records of 19,387  
8 penetrating corneal grafts of which 14,865 (77%) had been followed on at least one occasion.  
9 The number of follow-ups recorded per graft ranged from 1 to 10 over a 24 year period. Of  
10 11,929 individual patients (as distinct from grafts) with archival follow-up, 2,936 (20%) had  
11 had more than one registered graft in the ipsilateral and/or contralateral eye. Of the 957  
12 records for recipients under the age of 20 years at time of graft (identified as the pediatric  
13 cohort), 765 (80%) had follow-up data available. The majority of penetrating grafts in  
14 pediatric patients 705 (74%) were performed by 20 of the 381 contributing surgeons.  
15 Australia has a network of nationally-licensed Eye Banks, and there is essentially no waiting  
16 list for corneal transplantation, which is performed at a time convenient for the recipient and  
17 the surgeon. Consent for information to be lodged with the register was handled by individual  
18 contributors. The host institutional Clinical Research Ethics Committee provided approval for  
19 the operations of the Register, which were carried out in accordance with the Declaration of  
20 Helsinki.

21

### 22 **Data Collection**

23 Contributing surgeons submit records to the Registry as soon as possible after performing  
24 corneal graft surgery and follow-up is requested at intervals of 12 months until graft failure or  
25 until death or loss to follow-up of the patient. Missing data are routinely sought by direct

1 correspondence with the surgeon. Data verification is inherent in the structure of the database,  
2 which contains internal logic checks, but all records, once entered, are independently verified  
3 by a second individual against the record provided by the contributing surgeon. All  
4 information submitted is amalgamated and de-identified prior to analysis.

5

#### 6 **Definition of specified events before and after corneal transplantation**

7 Information on graft recipient, donor, eye bank, operative procedure, post-operative course  
8 and visual acuity was collected as previously described.<sup>7,9-10</sup> A history of past inflammation  
9 was recorded if the individual was reported to have had such an episode, if the patient had had  
10 one or more previous grafts in the same (ipsilateral) eye, if any intraocular surgery had ever  
11 been performed on the grafted eye, or if there was a history of the use of topical  
12 glucocorticosteroids in that eye in the two weeks immediately preceding the graft. Vessel  
13 ingrowth into the cornea at the time of graft was scored on a scale of 0-4, with 0 representing  
14 no growth in any quadrant extending to the graft-host junction, 1 being growth in 1 quadrant,  
15 2 being growth in 2 quadrants, 3 being vessel ingrowth in 3 quadrants and 4 being vessel  
16 ingrowth in 4 quadrants. No distinction was made between superficial or deep vessels, patent  
17 or ghost vessels, or single or multiple vessel leashes. After corneal transplantation, the  
18 presence of even one vessel leash extending into the graft was considered enough to classify  
19 that graft as vascularized. The intraocular pressure (IOP) was considered to be raised if a  
20 reading of 25 mm of mercury or greater was made by applanation tonometry, but the final  
21 decision was at the discretion of the ophthalmologist. Presenting diseases, indications for graft  
22 (including failed previous graft), post-operative complications and reasons for graft failure  
23 were coded using the ICD.9.CM system (US Department of Health and Human Services).  
24 Information was collected on both recipient bed size and donor button size, but for the  
25 purpose of examining the influence of graft size, the former was used. Primary graft non-

1 functions were defined as grafts that never thinned and cleared in the immediate post-  
2 operative period. The trial time for such grafts was arbitrarily adjusted to one day. Any  
3 existing graft that was replaced by another in the same eye, irrespective of graft clarity and for  
4 whatever reason, was classified as a failed graft. In all other cases, graft failure was defined as  
5 oedema and irremediable loss of clarity in a previously thin, transparent graft. The day of  
6 failure was the first day the patient was seen with an oedematous, opaque graft that  
7 subsequently failed to thin and clear. Rejection was defined as the development of a rejection  
8 line (epithelial or endothelial) or a unilateral anterior chamber reaction with corneal infiltrates  
9 and spreading corneal oedema in a previously thin, transparent graft.

10

### 11 **Statistical Analysis**

12 Kaplan-Meier survival functions were constructed to provide a graphical record of graft  
13 survival, using the log-rank statistic to test significance.<sup>11-13</sup> Variables were considered  
14 statistically significant if  $p < 0.05$ . Trial time was calculated for surviving grafts as the time  
15 between the date of graft and the date at which the patient was last seen. For failed grafts, trial  
16 time was calculated as the time between the date of graft and the date of failure. No  
17 exclusions were applied. Kaplan-Meier plots were also used to identify the variables of  
18 interest to be included in Cox proportional hazards regression analysis. This model was used  
19 to investigate the joint effects of a subset of variables on penetrating corneal graft failure in  
20 recipients under 20 years of age. In order to control for potential inter-graft and/or inter-eye  
21 dependence in this multivariate analysis, the model was adjusted to allow for clustering by  
22 individual patient.<sup>14</sup> The best model was found by a non-automatic backward elimination  
23 process, removing variables not appearing to be predictors of graft failure. The model  
24 excluded variables with  $p > 0.05$  (or global  $p > 0.05$  for categorical variables) in a stepwise  
25 manner, beginning with the removal of the least significant variable in the model and



1 continuing until all variables met the required significance level. Some variables that were  
2 significant in univariate analyses were judged to be collinear, and were omitted from the final  
3 model. The first group of each categorical variable was used as the referent. In all other cases,  
4 the absence of the variable was the referent. SPSS v15 (SPSS Inc, Chicago, IL, USA) was  
5 used to construct Kaplan-Meier plots and multivariate analysis was performed using Stata  
6 version 9 (StatCorp LP, Texas, USA).

7

## 1 **Results**

### 2 **Factors Influencing Corneal Graft Survival in Univariate Analysis**

3 The pediatric cohort was subdivided into infants (<5 years of age at the time of graft),  
4 children (aged 5-12 years at graft), and adolescents (aged 13-19 years at graft). Infants fared  
5 worse than older children in terms of graft survival (Fig 1). Children aged 5-12 years showed  
6 comparable corneal graft survival rates to adults ( $\geq 20$  years at graft), whereas adolescents  
7 displayed better corneal graft survival than did any other age group (Fig 1).

8 Indications for penetrating keratoplasty in the pediatric cohort and (for comparative  
9 purposes) the adult cohort are presented in Table 1. Infants received a corneal graft primarily  
10 for Peters' anomaly (44%) or corneal deformity (21%). The major indications for corneal  
11 transplantation in children aged 5-12 years were keratoconus (35%) and corneal scar or  
12 opacity (27%). Keratoconus accounted for 86% of grafts in adolescents. Corneal graft  
13 survival stratified by indication for graft is shown in Figure 2. Grafts for Peters' anomaly did  
14 not fare well: of 32 grafts in 19 patients, 14 grafts failed. Co-morbidities/conditions that may  
15 have influenced graft or visual outcomes in patients with Peters' anomaly included bilateral  
16 corneal transplantation, amblyopia, graft neovascularization and occurrence of graft rejection.

17 A history of failed previous graft from any cause exerted a significant negative  
18 influence on subsequent graft survival (Fig 3A). We investigated the ophthalmic history more  
19 closely in those 62 pediatric recipients who had undergone more than one graft in the  
20 ipsilateral eye. In 17 instances, the presenting condition was keratoconus, in 11 instances was  
21 Peters' anomaly, and in 6 instances was congenital glaucoma. There were three cases each of  
22 bacterial keratitis and failed previous graft (not due to rejection), and two cases each of  
23 corneal amyloid, irreversible graft rejection, herpetic keratitis, interstitial keratitis and  
24 keratomalacia. The remaining 12 cases comprised one case each of trauma, corneal burn,  
25 congenital staphyloma, corneal perforation, endophthalmitis, endothelial cell failure,

1 Goldenhaars bilateral syndrome, penetrating injury, sclerocornea, corneal ulcer and two of  
2 uncertain etiology.

3 Corneal graft survival was significantly reduced in eyes in which there was corneal  
4 neovascularisation prior to graft (Fig 3B), inflammation at graft (Fig 3C), a history of  
5 previous surgery (Fig 3D) or post graft operative procedure (Fig 3E), and in grafts that had  
6 suffered one or more rejection episodes (Fig 3F). Another significant factor affecting graft  
7 survival was graft size. Of the 736 grafts with a host-bed size recorded, 602 (82%) had a  
8 diameter between 7.5 mm and 8.5 mm. Corneal grafts performed with a host-bed size in this  
9 range exhibited a better survival rate than those that were smaller or larger ( $p<0.0001$ ). Graft  
10 survival was significantly better in phakic than in aphakic or pseudophakic eyes ( $p<0.0001$ ).

11 Post-operatively, graft survival was significantly reduced if the graft became  
12 vascularised ( $p<0.0001$ ). However, survival was positively associated with the need for  
13 refractive surgery to the graft ( $p<0.0001$ ). Other factors significantly affecting corneal graft  
14 survival in univariate analysis included early suture removal. Suture removal in less than 6  
15 months from the time of transplantation was associated with significantly poorer graft  
16 survival than later suture removal ( $p<0.0001$ ).

17 Neither cause of donor death ( $p=0.36$ ) nor donor age stratified into less than 65 years  
18 or 65 years and over (Fig 4;  $p=0.39$ ) exerted any significant effect on corneal graft survival in  
19 the pediatric cohort. We next examined the influence of graft era in Kaplan-Meier analysis by  
20 stratifying recipients according to the calendar year in which the graft was performed.  
21 Irrespective of whether we stratified in three or five year blocks from the Registry's inception  
22 to the census date for these analyses, graft survival did not differ significantly amongst the  
23 strata:  $p=0.82$  and  $p=0.56$ , respectively (data not shown).

24

25 **Factors Influencing Corneal Graft Survival in Multivariate Analysis**

1 Multivariate analysis indicated that seven variables: indication for graft; ocular inflammation  
2 at the time of graft; history of past intraocular surgery; corneal vascularization at graft;  
3 occurrence of rejection episode; need for operative procedure post-graft; and refractive  
4 surgery to the graft, were independent predictors of corneal graft failure in the pediatric cohort  
5 (Table 2).

6

### 7 **Reasons for Corneal Graft Failure**

8 Reasons for corneal graft failure in the pediatric cohort are shown in Table 3. Half of all grafts  
9 performed in infants failed, whereas only 20% of corneal grafts in children aged 5-12 years  
10 and 10% of those performed in adolescents failed. Of 11 corneal grafts that failed as a result  
11 of corneal endothelial cell failure, 2 had intraocular lenses in place in the grafted eye. Sixty-  
12 five percent (71) of grafts that failed did so within the first two post-operative years.  
13 Irreversible immunological rejection accounted for 27% of all failures.

14

### 15 **Visual Outcomes after Corneal Transplantation**

16 At the time of most recent follow-up, 283 (37%) eyes were corrected with a spectacle lens, 88  
17 (11%) with a contact lens and 37 (5%) eyes had an intraocular lens *in situ*. No visual  
18 correction had been prescribed in 357 (48%) cases. Best-corrected Snellen acuity recorded at  
19 last follow-up, stratified by age at graft, is shown in Figure 5. No pre-graft visual acuity was  
20 recorded in 46 (59%) infants, 32 (43%) children and 170 (27%) adolescents. Visual acuity  
21 was affected by indication for graft, with the majority (75%) of patients grafted for  
22 keratoconus displaying better than 20/40 vision at the most recent follow-up, while a large  
23 proportion (71%) of patients grafted for any other reason achieved visual outcomes of 20/50  
24 or worse (Fig 6). Adolescents generally achieved excellent acuity in the grafted eye.  
25 Amblyopia was recorded in 62 (8%) grafted eyes in the total pediatric cohort, 26 (51%) of

1 whom were infants. Although its presence did not significantly influence graft survival  
2 ( $p=0.88$ ), amblyopia had a major influence on visual outcomes: a visual acuity of 20/200 or  
3 worse was achieved by 30 (48%) amblyopic, grafted eyes.

4       Because of the potential for bias in the use of snapshot visual acuity, measured at the  
5 time of most recent follow-up,<sup>15</sup> we re-examined visual outcomes in the total pediatric cohort  
6 using interval visual acuity. The cohort was stratified into two groups: those with best-  
7 corrected Snellen acuity of 20/40 or better (Fig 7A), and those with best-corrected Snellen  
8 acuity that was poorer than 20/40, or that could not be measured because the recipient was  
9 pre-verbal (Fig 7B). The number and percentage of grafts in each group was then plotted  
10 against interval, specified time zero as at graft, less than one year post-graft, one year post-  
11 graft, and then at further yearly intervals. Only 2 percent of eyes grafted exhibited a pre-graft  
12 Snellen acuity of better than 20/40. By approximately 2 years post graft, the percentage of  
13 grafts with a visual acuity of 20/40 or better reached 70% of those followed and lingered  
14 between 60-80% at each interval. The majority of grafts were performed on eyes with a pre-  
15 graft Snellen acuity of worse than 20/40 (65%). Post graft, the percentage of grafts with a  
16 visual acuity of worse than 20/40 reduced substantially (20-40%). A large proportion (33%)  
17 of grafts had no pre-graft Snellen acuity recorded.

18       Finally, we examined overall vision in pediatric patients by comparing pre-graft visual  
19 acuity in the operated eye and the contralateral eye against post-graft visual acuity in the  
20 operated eye (Fig 8A). Post-operative Snellen acuity in the *contralateral* eye was not  
21 recorded. At the time of corneal transplantation, the majority (59%) of pediatric patients with  
22 recorded visual outcomes had a Snellen acuity of 20/40 or better in the contralateral eye. Of  
23 these, 72% presented with 20/200 or worse Snellen acuity in the eye to be grafted. At the time  
24 of most recent follow-up, 46% of eyes in the cohort had achieved 20/40 vision or better in  
25 both eyes (Fig 8B). In thirteen (3%) patients, Snellen acuity was recorded as 20/40 or better in

1 both the ipsilateral and contralateral eye, immediately before graft. The indication for corneal  
2 transplantation was keratoconus in 12 of these eyes, and corneal perforation in the remaining  
3 case. In a further two patients, Snellen acuity was recorded as 20/40 or better in the operated  
4 eye immediately before graft, and both of these grafts were also performed for keratoconus.  
5 Post-operatively, all of these grafts achieved the same or better visual acuity as pre-  
6 operatively.

7

## 1 **Discussion**

2 A number of groups have reported on the outcomes of penetrating keratoplasty in pediatric  
3 recipients (see Vanathi *et al* for review<sup>1</sup>). We stratified our cohort into infants, children and  
4 adolescents on the basis of convention. Infants received corneal grafts primarily for  
5 developmental disorders, adolescents for keratoconus, and the children in the middle of the  
6 age range, for a mixture of indications. Our findings are broadly similar to those of others, in  
7 that children under 13 years of age exhibited poorer graft survival rates than did adults  
8 ( $p < 0.0001$ ).<sup>1,4</sup> We further found that infants aged under 5 years fared worse than older  
9 children, with graft survival at 16 years post-operatively being less than 40% in infants  
10 compared to 70% in the 5-12 year age group.

11 In pediatric recipients as in adults,<sup>7,9-10</sup> excellent graft survival rates were achieved  
12 following penetrating keratoplasty for keratoconus. Over 85% of penetrating grafts performed  
13 in adolescents aged 13-19 years were performed for this indication, and 75% of these eyes  
14 achieved a best-corrected Snellen acuity of at least 20/40 and exhibited Kaplan-Meier graft  
15 survival rates of over 90% at ten years post-operatively. A small number of patients (n=14)  
16 with keratoconus and a best-corrected Snellen acuity of 20/40 or better underwent corneal  
17 transplantation. All experienced good outcomes.

18 A high rate of corneal graft failure was noted in infants aged less than 5 years.  
19 Developmental disorders may have affected graft survival in this age group.<sup>2</sup> Almost half of  
20 the infants suffered from Peters' anomaly, a common congenital corneal disorder worldwide,<sup>1</sup>  
21 and almost half of these grafts failed. Similar findings have been reported by others.<sup>16,17</sup> A  
22 proportion of our patients with Peters' anomaly had co-morbidities that were likely to have  
23 influenced graft or visual outcomes. Children aged 5-12 years showed a broad spectrum of  
24 indications for graft, reflected in a moderately good graft survival of 70% at 22 years post  
25 graft.

1 The probability of corneal graft survival in pediatric patients, as in all age groups, reduced  
2 over time.<sup>7,9-10</sup> However, some factors, including the indication for corneal transplantation,  
3 inflammation of the eye, history of previous surgery, graft vascularisation, and failed previous  
4 graft, affected survival time more than others. The major reason for graft failure in patients  
5 under 20 years of age was irreversible rejection. This presented as the predominant reason for  
6 failure in infants (29%) and adolescents (27%). However, given the difficulty of diagnosing  
7 graft rejection in children, it is possible that some rejections were missed, and that other  
8 corneal pathology may have been classified as rejection, when in fact it was not. In children  
9 aged 5-12, corneal edema attributed to corneal endothelial cell failure was the major reason  
10 for graft failure (33%). Patterns of practice change over time, and we thus examined the  
11 influence of era of the surgery on graft survival: no significant influence was apparent, and  
12 recent outcomes were no better than outcomes reported from early years of the Registry's  
13 operation.

14 Univariate and multivariate analyses indicated that the 107 pediatric patients who  
15 underwent refractive surgery to the graft (suture adjustment, compression sutures, relaxing  
16 incisions, excimer laser procedures) in the post-operative period exhibited better graft survival  
17 than the remainder of the cohort. This factor was also noted in a previous study by these  
18 authors in a cohort of all penetrating grafts.<sup>7</sup> The likely explanation is that ophthalmologists  
19 select pediatric patients with stable grafts and no other risk factors for failure for such  
20 procedures. In contrast, more invasive post-operative procedures such as removal of cataract,  
21 insertion of an IOL and YAG laser capsulotomy, performed in 110 grafted eyes, exerted a  
22 detrimental effect on graft survival: 56% of grafts undergoing these procedures subsequently  
23 failed.

24 Visual outcomes in the pediatric cohort were clearly associated with the indication for  
25 graft. Post-graft Snellen acuity was available for only 45% of recipients with Peters' anomaly



1 because of the difficulty in assessing visual performance in preverbal children.<sup>17</sup> However,  
2 78% of grafted eyes presented with 20/200 or worse Snellen acuity at the time of most recent  
3 follow-up. In contrast, 82% of grafts for keratoconus achieved a post-operative Snellen acuity  
4 of 20/40 or better. Although amblyopia did not significantly influence graft survival, it had a  
5 major influence on visual outcomes, as seen in other studies.<sup>18</sup> Prior to penetrating  
6 keratoplasty, 78% of patients for whom information was available presented with 20/200 or  
7 worse best-corrected Snellen acuity (without pinhole) in the pre-grafted eye. Post-operatively,  
8 74% achieved 20/40 or better Snellen acuity in the grafted eye. Although the number of grafts  
9 followed reduced over time, the percentage of grafts displaying 20/40 or better Snellen acuity  
10 in the grafted eye remained steady at between 60 to 80% up to 15 years post graft. The impact  
11 of good bilateral vision on the educational and social future of children of all ages is  
12 substantial.<sup>18</sup> Investigation of visual outcomes in both eyes following corneal transplantation  
13 in at least one eye showed an improvement in overall bilateral vision: the percentage of  
14 patients with initially poor vision overall (less than 20/50 in both eyes) was reduced from  
15 41% to 12% of the cohort.

16 In conclusion, we assessed graft and visual outcomes in 765 corneal grafts in 640  
17 pediatric patients in a national registry of corneal transplantation. Disease registries are  
18 increasingly being used to fill evidence-gaps that may not be amenable to randomised  
19 controlled clinical trials.<sup>19</sup> Strengths of the approach include the ability to follow large  
20 numbers of patients who have undergone a surgical intervention “in the real world”, and in  
21 the longer term. We report, as have others,<sup>1</sup> that penetrating corneal transplants in infants  
22 exhibit relatively poor survival and visual outcomes. Almost half of these grafts were  
23 performed for Peters’ anomaly. In contrast, corneal grafts in adolescents aged 13-19 years  
24 were mostly performed for keratoconus, and graft survival and visual outcomes were  
25 excellent. Corneal transplantation in children aged 5-12 is performed for a wide variety of

1 indications for graft, and outcomes are broadly similar to outcomes in adults. However,  
2 overall, improvement in vision following penetrating keratoplasty in the total pediatric cohort  
3 is substantial, which suggests that the procedure is of benefit in pediatric patients.

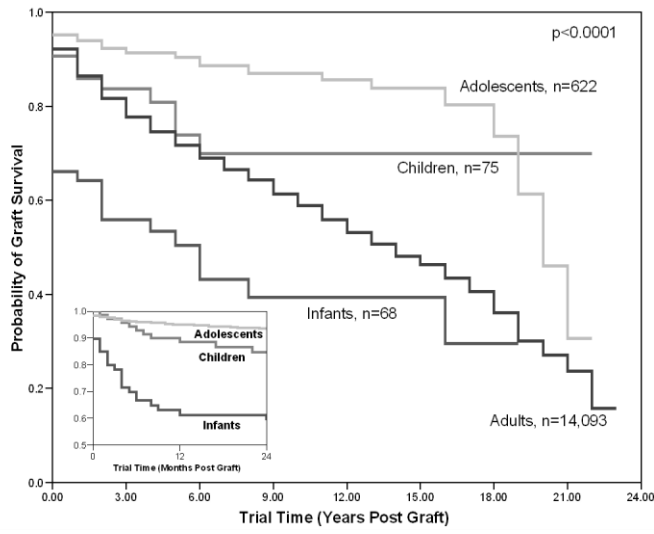
4

## 1 **References**

- 2 1. Vanathi M, Panda A, Vengayil S, et al. Pediatric keratoplasty. *Surv Ophthalmol*  
3 2009;54:245-71.
- 4 2. Hong JX, Xu JJ, Sheng MJ, et al. Pediatric penetrating keratoplasty in Shanghai: a  
5 retrospective multiple centre study from 2003 to 2007. *Chinese Medical Journal*  
6 2008;121:1911-4.
- 7 3. McClellan K, Lai T, Grigg J, et al. Penetrating keratoplasty in children: visual and  
8 graft outcomes. *Br J Ophthalmol* 2003;87:1212-4.
- 9 4. Al-Ghamdi A, Al-Rajhi A, Wagoner MD. Primary pediatric keratoplasty: Indications,  
10 graft survival, and visual outcome. *J AAPOS* 2007;11:41-7.
- 11 5. Aasuri MK, Garg P, Gokhle N, Gupta S. Penetrating keratoplasty in children. *Cornea*  
12 2000;19:140-4.
- 13 6. Huang PT. Penetrating keratoplasty in infants and children. *J AAPOS* 2007;11:5-6.
- 14 7. Williams KA, Lowe MT, Bartlett CM, L Kelly & DJ Coster eds. *The Australian*  
15 *Corneal Graft Registry 2007 Report*. Adelaide: Flinders Press; 2007:1-194.  
16 *The Australian Corneal Graft Registry 2007 Report*. Available at:  
17 [http://dspace.flinders.edu.au/dspace/bitstream/2328/1723/3/FINAL%20COMPILED%](http://dspace.flinders.edu.au/dspace/bitstream/2328/1723/3/FINAL%20COMPILED%20REPORT%202007.pdf)  
18 [20REPORT%202007.pdf](http://dspace.flinders.edu.au/dspace/bitstream/2328/1723/3/FINAL%20COMPILED%20REPORT%202007.pdf). Accessed December 16, 2009.
- 19 8. Patel HY, Ormonde S, Brookes NH, et al. The indications and outcome of pediatric  
20 corneal transplantation in New Zealand: 1991-2003. *Br J Ophthalmol* 2005;89:404-8.
- 21 9. Williams KA, Roder D, Esterman A, et al. Factors predictive of corneal graft survival:  
22 report from the Australian Corneal Graft Registry. *Ophthalmology* 1992;99:403-14.
- 23 10. Williams KA, Muehlberg SM, Wing SJ, et al. *The Australian Corneal Graft Registry*  
24 *1990-1992 report*. *Aust NZ J Ophthalmol* 1993;21 (suppl):1-48.
- 25 11. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am*

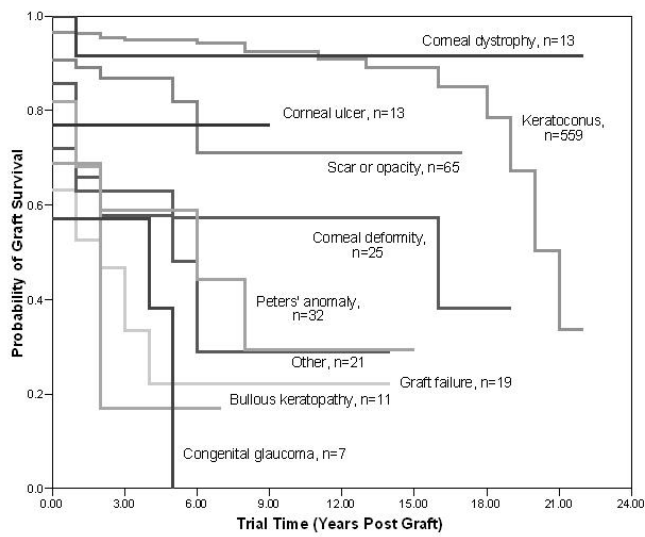
- 1 Stat Assoc 1958;53:475-81.
- 2 12. Peto R, Pike MC, Armitage P, et al. Design and analysis of randomised clinical trials  
3 requiring prolonged observations of each patient. I Introduction and design. Br J  
4 Cancer 1976;34:585-612.
- 5 13. Peto R, Pike MC, Armitage P, et al. Design and analysis of randomised clinical trials  
6 requiring prolonged observation of each patient. II Analysis and examples. Br J  
7 Cancer 1977;35:1-39.
- 8 14. Williams RL. A note on robust variance estimation for cluster-correlated data.  
9 Biometrics 2000;56:645-6.
- 10 15. DiLoreto DA Jr, Bressler NM, Bressler SB, Schachat AP. Use of best and final visual  
11 acuity outcomes in ophthalmological research. Arch Ophthalmol 2003;121:1586-90.
- 12 16. Rao KV, Fernandes M, Gangopadhyay N, et al. Outcome of penetrating keratoplasty  
13 for Peters anomaly. Cornea 2008;27:749-53.
- 14 17. Yang LL, Lambert SR, Drews-Botsch C, et al. Long-term visual outcome of  
15 penetrating keratoplasty in infants and children with Peters anomaly. J AAPOS  
16 2009;13:175-80.
- 17 18. James DM and Stojanovik V. Communication skills in blind children: a preliminary  
18 investigation. Child Care Health Dev 2006;33:4-10.
- 19 19. Dreyer NA, Garner S. Registries for robust evidence. JAMA 2009;302: 790-1.
- 20

1 Figure 1.



2

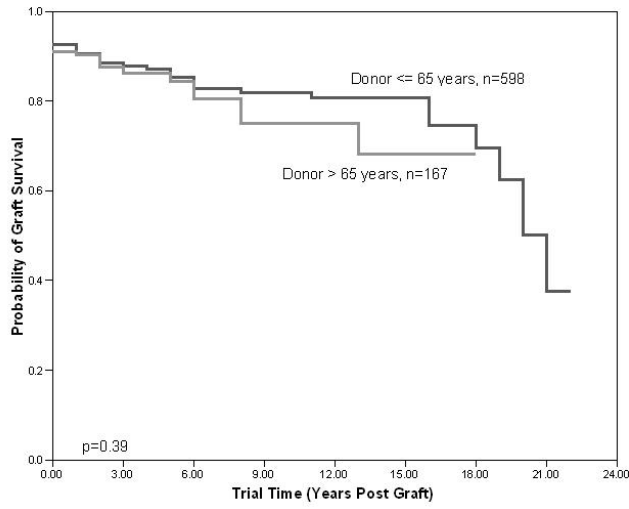
3 Figure 2.



4

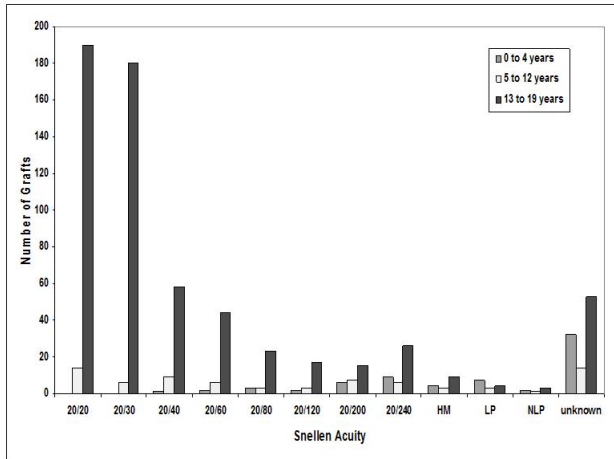
5

1 Figure 4.



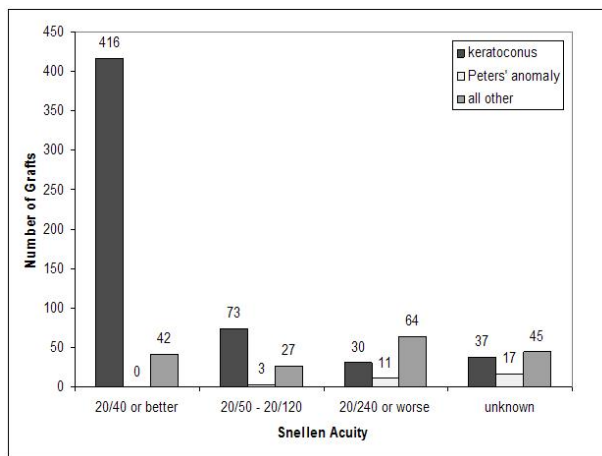
2

3 Figure 5.



4

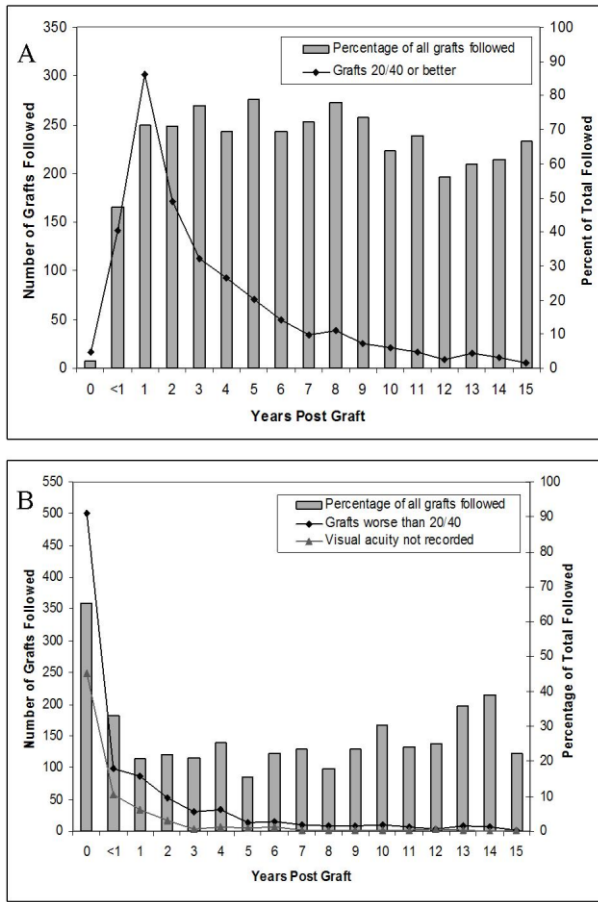
5 Figure 6.



6

7

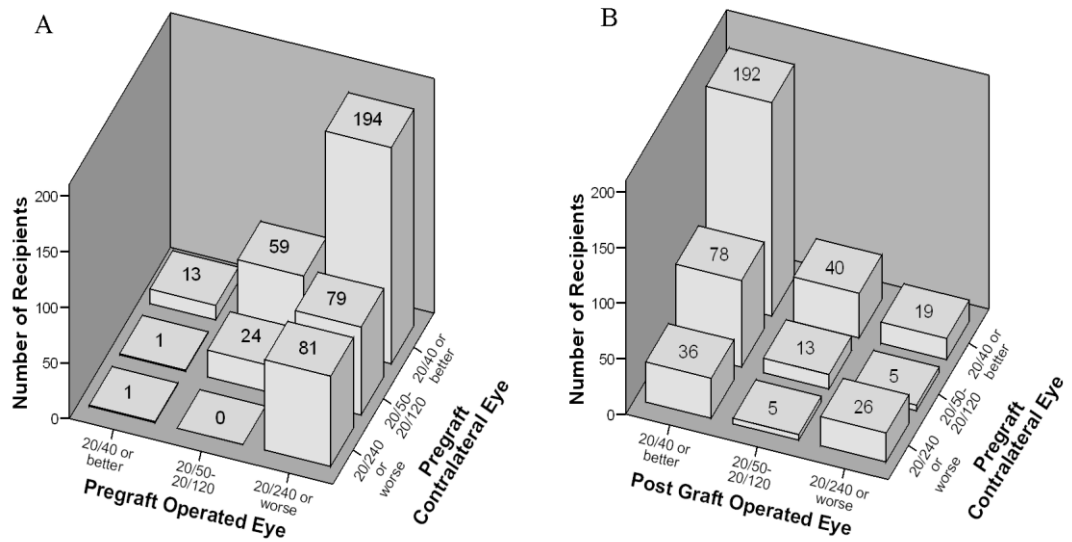
1 Figure 7.



2

3

Figure 8.



4

Table 2. Cox Proportional Hazards Analysis Showing Significant Independent Risk Factors  
for Corneal Graft Failure

<b>Contributing Variable</b>	<b>Hazard Ratio</b>	<b>Standard Error</b>	<b>P</b>	<b>Global P</b>	<b>95% Confidence Intervals</b>
Indication for graft:					
Keratoconus	1.00			0.008	
Peters' Anomaly	2.41	0.74	0.004		1.32 – 4.40
Other	2.10	0.55	0.005		1.24 – 3.52
Inflammation at time of graft	1.90	0.50	0.014		1.14 – 3.16
Previous intra-ocular surgery	1.69	0.43	0.041		1.02 – 2.79
Corneal vascularisation at graft	1.87	0.42	0.005		1.21 – 2.90
One or more rejection episodes	3.53	0.70	<0.001		2.40 – 5.21
Operative procedure post graft	4.09	0.95	<0.001		2.60 – 6.44
Refractive surgery post graft	0.12	0.12	0.033		0.02 – 0.84



Table 3. Reasons for Corneal Graft Failure

Reason for Graft Failure	Number of Failed Grafts (percent)			
	Age at graft in years			
	<i>0-4</i>	<i>5-12</i>	<i>13-19</i>	<i>Total</i>
Graft rejection	10 (29%)	4 (27%)	16 (27%)	30 (27%)
Corneal endothelial cell failure	3 (9%)	5 (33%)	3 (5%)	11 (10%)
Graft rupture/injury	0 (0%)	0 (0%)	9 (15%)	9 (8%)
Infection	2 (6%)	2 (13%)	4 (6%)	8 (7%)
Glaucoma	2 (6%)	0 (0%)	4 (6%)	6 (6%)
Primary non-function	2 (6%)	0 (0%)	3 (5%)	5 (4%)
Graft neovascularisation	1 (3%)	1 (7%)	1 (2%)	3 (3%)
Astigmatism	0 (0%)	0 (0%)	3 (5%)	3 (3%)
Keratoconus	0 (0%)	0 (0%)	2 (3%)	2 (2%)
Endophthalmitis	1 (3%)	0 (0%)	1 (2%)	2 (2%)
Other*	5 (15%)	1 (7%)	7 (11%)	13 (12%)
Unknown	8 (23%)	2 (13%)	8 (13%)	18 (16%)
Total	34 (100%)	15 (100%)	61 (100%)	110 (100%)

\* Includes hypotony, atrophy of globe, retinal detachment, iridocyclitis, epithelial defect or failure, corneal scar or opacity, phthisis, corneal degeneration, dystrophy or deformity, microphthalmos and Peters' anomaly