

# CORNEAL TRANSPLANTATION FOR KERATOCONUS

## A SUMMARY OF RESULTS FROM THE AUSTRALIAN CORNEAL GRAFT REGISTRY

### What is keratoconus?

Keratoconus is a disease which affects the cornea, the front window-like layer of the eye. The cornea becomes thinner, and this leads to a change in its shape. This affects vision, most often through high levels of irregular astigmatism. The cause of keratoconus is unknown, though there is evidence that genetics play a role in some cases.

It is hard to know exactly how many people keratoconus affects as mild cases may go undiagnosed; however, estimates suggest somewhere between 1 and 5 people in every 2000 have the condition. Both eyes are usually affected, though the severity may vary. Diagnosis usually occurs in adolescence or the early 20s, when individuals notice a change in their vision.

### What is the Australian Corneal Graft Registry?

The Australian Corneal Graft Registry (ACGR) operates an Australia-wide register of corneal transplants. The purpose of the ACGR is to collect information to inform clinical practice and identify risk factors for poor patient outcomes. Started in May 1985, by the beginning of 2023 the ACGR had over 44,000 registered grafts.

At the time of graft, the ACGR collects information on the corneal donor, the graft recipient, and the details of the surgery. The surgeons then regularly provide the ACGR with follow-up information. They tell us if the graft is surviving, what the patient's vision is, and about any complications or additional treatments the patient has had since the graft. They do this for as long as possible - until the graft fails, the patient is known to have died, or they have not been seen for several years.

The team at the ACGR uses specialist techniques to analyse this information. They aim to identify if there are factors that increase the chance that a graft will fail, or might affect the vision of the recipient. The results are then sent back to surgeons, so that they can use the information to improve their practices, and the related outcomes for their patients.

### Corneal transplantation for keratoconus in Australia

Keratoconus is the leading indication for primary corneal transplantation (first grafts) registered with the Australian Corneal Graft Registry (ACGR) since it was started in 1985. In the early 2000s, two-in-five first grafts were for keratoconus; however, this reduced to less than one-in-five for the 2017 to 2021 period (Figure 1). Over this time, the average number of first grafts for keratoconus registered annually has reduced by almost 100 per year (Figure 2).

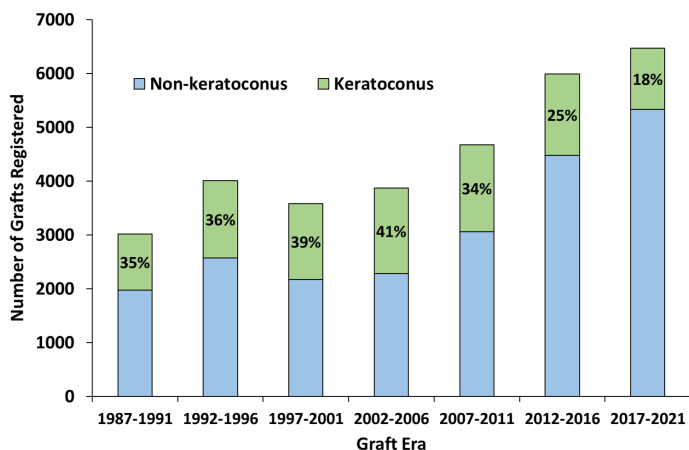


Figure 1 - Number of first grafts registered for keratoconus versus other indications, split into five-year time periods, 1987 to 2021. Percentages shown indicate the proportion of grafts that were for keratoconus.

### Treatments for keratoconus

The treatment required for keratoconus depends on the stage and progression of the disease. In mild cases, it can be managed with spectacles or contact lenses, and for a large proportion of people it will stabilise without any further intervention needed. Corneal collagen crosslinking is a procedure that can be used to assist in preventing progression of mild to moderate keratoconus.

In advanced cases (estimated at 1 in 5), the shape of the cornea can make it difficult and uncomfortable for people with keratoconus to wear contact lenses. They may also experience other complications such as corneal scarring. When this occurs, a corneal transplant may be performed

Another change has been a shift from full-thickness, penetrating keratoplasty (PK), where the whole cornea is replaced, to partial thickness, deep anterior lamellar keratoplasty (DALK). In DALK the front part of the cornea is replaced, while the back part is left alone, as it is not affected by keratoconus. This type of operation can't always be performed, for instance if scarring is very bad, and in some cases a PK may still be the best option. PK are now performed in about 60% of cases.

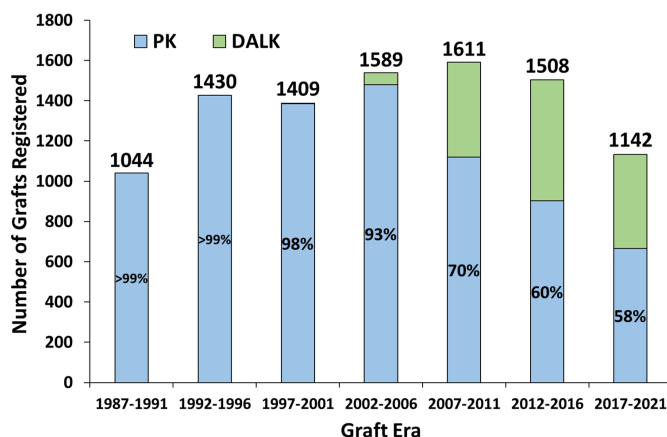
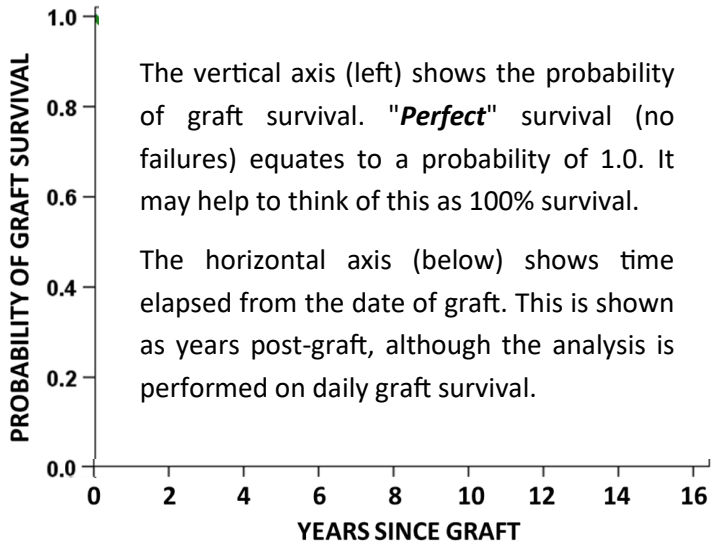


Figure 2 - Combined total of first penetrating keratoplasty (PK) and deep anterior lamellar keratoplasty (DALK) performed for keratoconus, registered during five-year time periods, 1987 to 2021. Percentages shown indicate the proportion of grafts that were PKs.

## What is a Kaplan-Meier survival curve?

Kaplan-Meier survival analysis is used by the ACGR to evaluate the likelihood of graft survival over time. This type of analysis uses all data available, for however long a graft has been followed, regardless of whether it has failed or not.



The numbers of grafts being followed at given times after graft are shown in the tables below the curves. They are referred to as the **number at risk** at these time points. At time zero, all grafts in the group are at risk, as this corresponds to the day the graft was performed. At the furthestmost point on the right-hand side of any curve, the grafts that have been followed the longest are at risk.

Grafts stop having their data included at some point along the curve for two reasons: either they fail or they are **censored**. Being censored means that is as long as they have been followed for so far, but they are surviving at that time. Because the curves are showing survival of grafts, failures cause the curves to drop downwards, whereas censoring doesn't because those grafts are still surviving.

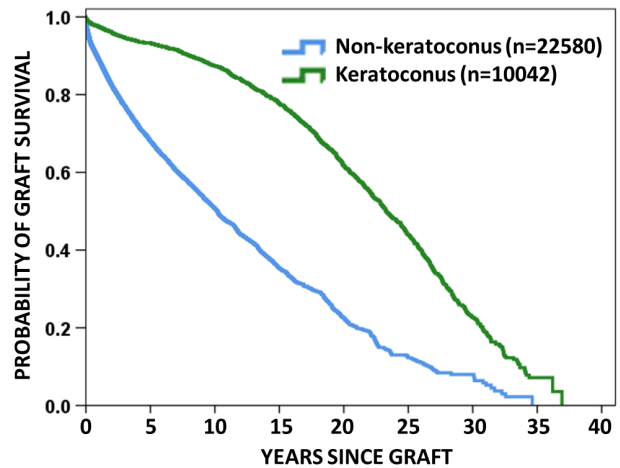
How much the curve drops down will depend on how many other, surviving, grafts are also still being followed at that point. If there are not a lot of grafts, it will look more dramatic. A sudden drop at the far right of a given curve may merely mean, for example, that one of only two grafts that have 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 group have failed or will fail by this time point.

## Survival of first grafts for keratoconus

For as long as a corneal transplant continues to provide good vision, and relieve pain if that was an issue, it is described as surviving. When this is no longer the case, it is said to have failed. The most common reasons that corneal grafts for keratoconus fail are endothelial rejection and/or failure, and recurrent keratoconus and/or astigmatism. In these cases, a repeat graft may be necessary.

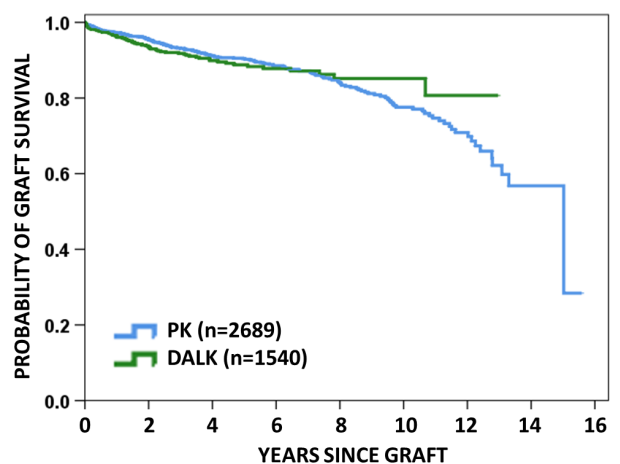
As well as being the most common indication for a corneal graft, transplants for keratoconus have the best outcomes in terms of length of survival (Figure 3).



	1	5	10	15	20	25	30	35
Non-KC	13321	4536	1406	449	155	50	16	NA
KC	7178	3282	1795	1096	629	319	101	6

**Figure 3 - Survival of first grafts for keratoconus compared to first grafts performed for other indications. Those performed for keratoconus have superior survival with an average (median) of over 20 years, compared to approximately 10 years for those performed for other indications.**

The average (median) survival of first grafts for keratoconus is more than 20 years, compared to 10-year survival for first grafts performed for other indications. Over the last 15 years, PK and DALK have had similar survival profiles (Figure 4).



	1	2	4	6	8	10	12	14
PK	1839	1385	824	502	305	169	68	11
DALK	818	562	276	150	77	30	5	NA

**Figure 4 - Survival of first penetrating keratoplasties (PK) for keratoconus compared to first deep anterior lamellar keratoplasties (DALK) for keratoconus, performed from 2007 up to 2021. Survival is similar regardless of graft type.**

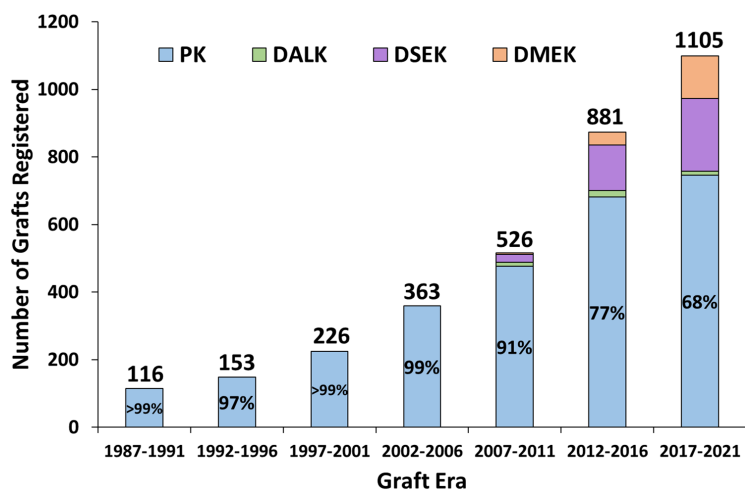
## Repeat grafts in eyes with keratoconus

Repeat grafts, where the original indication for graft was keratoconus, are also registered with the ACGR. This could have been the first repeat graft, or subsequent grafts.

Sometimes the original graft is still improving the shape of the eye so that the astigmatism is under control, but a second problem has occurred where the endothelial cells at the back of the cornea aren't functioning properly. This can also affect vision.

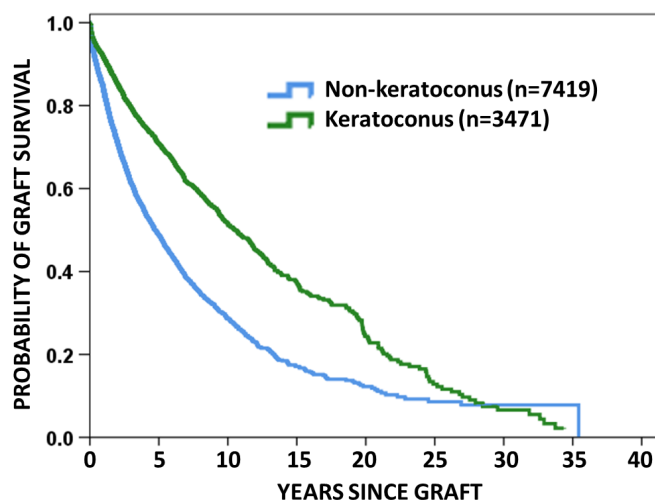
From 2008, some repeat grafts were endothelial keratoplasties (DSEK/DMEK). In these cases, the front of the original graft is left in place and only the thin layer of endothelial cells on the back of the cornea is replaced.

Most repeat grafts are still PK, while DALK are rarely done as repeat grafts for this group. More than 30% of repeat grafts are now DSEK/DMEK. There has been a continual increase in the number of repeat grafts in eyes originally grafted for keratoconus registered annually, doubling approximately every decade (Figure 5).



**Figure 5 - Combined total of repeat penetrating keratoplasty (PK), deep anterior lamellar keratoplasty (DALK), Descemet's stripping endothelial keratoplasty (DSEK) and Descemet's membrane endothelial keratoplasty (DMEK), where the original graft was for keratoconus, registered during five-year time periods, 1987 to 2021. Percentages shown indicate the proportion of grafts that were PKs.**

As with first grafts, repeat grafts where the original graft was for keratoconus have better survival than those with other original indications; this time an average (median) of approximately 10 years compared to 5 years (Figure 6).



	1	5	10	15	20	25	30	35
Non-KC	4211	1219	329	93	37	12	2	1
KC	2280	936	351	143	63	21	8	NA

**Figure 6 - Survival of repeat grafts where the original graft was for keratoconus compared to repeat grafts with other original indications. Those performed for keratoconus have superior survival with an average (median) of approximately 10 years.**

## Bilateral grafts for keratoconus

As keratoconus is a bilateral condition, sometimes people can need corneal grafts in both eyes. These may be performed months or even years apart. For grafts performed in recipients who have previously had a single graft in the opposite eye, survival is similar compared to those with no graft in the other eye.

Somewhat poorer, but still excellent, survival is observed for grafts where the recipient had multiple previous grafts in the opposite eye.

### Funding, ethics and data security

The Australian Corneal Graft Registry is based at Flinders University in South Australia. It is funded by the Australian Government Organ and Tissue Authority (DonateLife).

The operations of the ACGR are overseen by the Southern Adelaide Clinical Human Research Ethics Committee.

The ACGR is a declared quality assurance activity under the Commonwealth Qualified Privilege Scheme.

Assistance with updating the database is provided by the Australian Institute of Health and Welfare through linkage with the National Death Index.

All records are de-identified prior to analysis.



## Visual outcomes following transplants for keratoconus

Figure 8 shows the best corrected visual acuity (BCVA) in the grafted eye at various time points for first grafts that were surviving. Prior to grafting, the average (median) BCVA allowed the person to count fingers (CF). This level of BCVA is worse than 6/60 vision, which is considered legally blind.

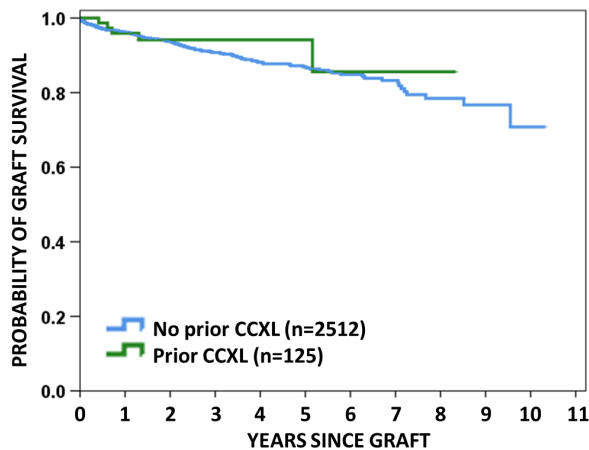
The level for vision to be considered fully functional, for instance to be able to drive a car, is 6/12. While some people had vision at or above this level when they had their graft, it's possible they could only achieve this by wearing contact lenses, which might have become too uncomfortable.

Following the graft, BCVA improved to the 6/12 level for more than half of people with a surviving graft at each yearly time point up to 20-years post-graft. Two-thirds of people still reported wearing spectacles or a contact lens to achieve their BCVA post-graft.

Vision following second grafts also improved up to the 6/12 level by 1-year post-graft for the majority of eyes with surviving transplants. This remained the case up to 10-years after the graft, though there was more variation in the results than for first grafts (Figure 9). Vision following subsequent grafts was also shown to improve, but not to the same level, and again with greater variation in results.

### Corneal collagen cross-linking (CCXL)

An alternative treatment to transplantation which may be offered in the earlier stages of keratoconus is corneal collagen cross-linking (CXL). This is a procedure where the eye is treated with riboflavin and ultra-violet light to make the cornea more stable and less likely to become further misshapen. For some people this may mean the disease does not progress to needing a corneal graft, while for others it may just delay the need for a time. Some surgeons also use CXL prior to performing a graft, to stabilise the section of the cornea that is left in place, to which the graft will be sutured. This treatment does not have any evident effect on the survival of grafts (Figure 10).



	1	2	3	4	5	6	7	8	9	10
No CCXL	1413	984	666	450	299	193	117	67	24	2
CCXL	65	39	24	17	13	8	4	2	NA	NA

Figure 10 - Survival of first grafts for keratoconus where the eye had previously undergone treatment with corneal collagen cross-linking (CCXL) first grafts for keratoconus where it had not, for grafts performed 2007 to 2021. No impact of CCXL on the survival of grafts was detected.

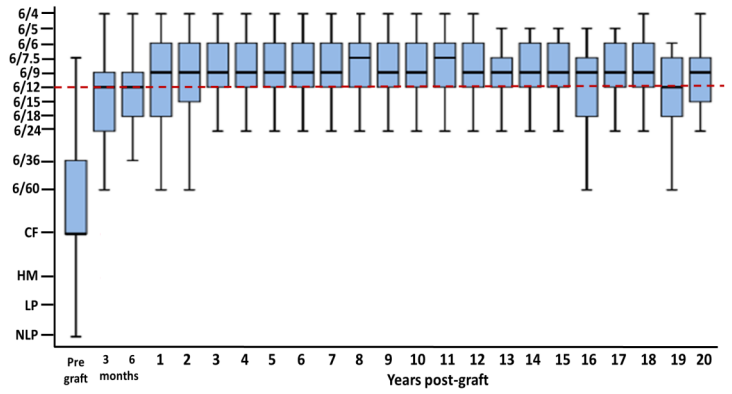


Figure 8 - Box and whisker plot showing best corrected visual acuity in eyes undergoing first grafts for keratoconus, before graft and at yearly time points afterwards for surviving grafts. The box indicates the interquartile range (middle 50%) of values, with the central line showing the median value. Functional vision of 6/12 is indicated by the red dashed line.

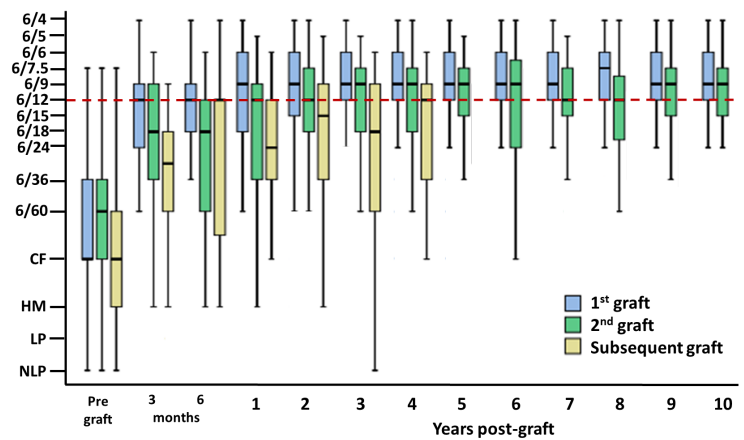


Figure 9 - Box and whisker plot showing best corrected visual acuity in eyes undergoing first, second, and subsequent grafts for keratoconus, before graft and at yearly time points afterwards for surviving grafts. Functional vision of 6/12 was less likely to be achieved in the majority of cases when the eye had undergone more than a single previous graft.

### Acknowledgements

We acknowledge the surgeons and eye banks who have contributed registration data to the ACGR since its inception and we recognise the ongoing efforts of surgeons to provide follow-up information on a regular basis.

We thank the corneal graft recipients who agreed to have their data included in the ACGR.

We thank the members of the ACGR Community Engagement Group, both past and present, for their valuable insight and input.

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