

Changing Trends in Corneal Transplantation in Aotearoa/New Zealand, 1991 to 2020: Effects of Population Growth, Cataract Surgery, Endothelial Keratoplasty, and Corneal Cross-Linking for Keratoconus

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Purpose: The purpose of this study was to identify trends in the primary indication for keratoplasty in New Zealand/Aotearoa (NZ) after significant population growth, increase in the number of cataract surgeries per population, widespread adoption of endothelial keratoplasty, and introduction of corneal cross-linking for keratoconus.

Methods: Statistical analysis of the New Zealand National Eye Bank's prospective database of all keratoplasties was performed between January 1991 and January 2020. Indications for keratoplasty were isolated for the primary diagnosis.

Results: In total, 6840 corneas were transplanted with mean 236 ± 57.5 transplants/year, increasing from 2.55 to 6.06 per 100,000 NZ population/year. Over the past decade, the number of transplant recipients aged 60 years or older has increased and recipients aged 20 to 39 years have plateaued. In 2019, for the first time, regrant became the most common indication (30.9%), followed by keratoconus (27.9%) and corneal dystrophy (18.8%), with a steady decline in bullous keratopathy. Proportions of the keratoplasty technique changed dramatically: penetrating keratoplasty fell from 91.4% in 2006 to 55.0% in 2019, Descemet's stripping endothelial keratoplasty increased from 0% to 29.5%, anterior lamellar keratoplasty increased from 2.5% to 5.7%, and Descemet membrane endothelial keratoplasty increased from 0% to 9.1%.

Conclusions: Keratoplasty trends in Aotearoa/NZ have changed considerably because of the evolution of phacoemulsification and keratoplasty techniques. Unlike proportions observed overseas, NZ still performs penetrating keratoplasties in over half of all transplants. Corneal cross-linking may be having an early effect of reducing keratoplasty rates for keratoconus.

Key Words: cornea, corneal transplantation, eye bank, keratoconus, corneal cross-linking

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The New Zealand National Eye Bank (NZNEB) was established in 1989 to acquire, store, and distribute donated corneal tissues for all New Zealand/Aotearoa (NZ). All NZNEB operations adhere to the Eye Bank Association of Australia and New Zealand Standards. Since 1991, the NZNEB has maintained a comprehensive prospective database in relation to indications for keratoplasty through information provided by ophthalmic surgeons. Tissues provided by the NZNEB are predominantly sourced from within NZ but are also imported from overseas during times of shortage.¹

Over the past decade, 2 major changes in surgical techniques for corneal diseases may have influenced trends in indication for keratoplasty in NZ. First, surgical techniques for corneal transplantation have greatly evolved, specifically a dramatic rise in endothelial keratoplasty,^{2–4} with Descemet's stripping (automated) endothelial keratoplasty (DS(A)EK) and Descemet membrane endothelial keratoplasty (DMEK) being widely adopted in NZ since 2007. Second, corneal cross-linking (CXL) for keratoconus, first reported in 2003,⁵ was also introduced to NZ in 2007, with the aim of slowing or stopping disease progression, preserving vision, and reducing the need for corneal transplantation. Progressive disease eligible for CXL treatment in NZ is defined as 1 or more of the following changes: an increase of 1.00 diopter (D) or more in the steepest keratometry (K_{MAX} measurement on tomography), an increase of 1.00 D or more in the manifest cylinder, or an increase of 0.50 D or more in manifest refraction spherical equivalent to over 12 months. Although the procedure has been provided since 2007, access was

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initially limited because of both public service and medical insurance funding constraints. Between 2009 and 2015, approximately 50 CXL procedures per year were performed in Auckland's public hospital sector, which is NZ's largest city, and since then, access has rapidly increased country-wide. In 2019, the public sector performed 238 CXL procedures in the Auckland region and that year a total of approximately 700 to 750 CXL procedures were performed in NZ. To date, including procedures in both public and private practice, we estimate that a minimum of 3000 eyes with keratoconus have received CXL treatment in NZ. It has been reported that approximately 10 years after keratoconus diagnosis, those with progressive disease typically undergo transplant surgery.⁶ It has therefore been postulated that approximately 10 years after the implementation of CXL in NZ, an impact might be noted on keratoplasty rates for keratoconus.⁷ In addition, an increasing trend in ophthalmic surgery per se, that is, the rapidly rising number of cataract surgeries per 100,000 population in recent years,⁸ may also affect corneal transplantation rates in relation to bullous keratopathy.

Because the NZNEB serves the whole country, we have previously reported on various aspects of the indications for surgery and trends in corneal transplantation in NZ during the period 1991 to 2015.^{7,9,10} New Zealand has a public-funded health care system with universal access, similar to but preceding the United Kingdom National Health Service. Most of the surgery is performed in the public sector; however, the NZNEB collects data from both the public and private health sectors.^{7,9,10} There are some cases in NZ where the donor tissue is imported directly by surgeons, and therefore, these are not included in the NZNEB database. The exact number imported directly is difficult to establish but is estimated to represent no more than 5% to 10% of all transplants in NZ in this study period. Ultimately, the NZNEB database includes most of the keratoplasty performed in NZ.

The aim of this study was to identify trends (1991–2020) in the primary indication for keratoplasty based on the following: 1) significant population growth, 2) dramatic increase in the number of cataract surgeries, 3) widespread adoption of endothelial keratoplasty, 4) introduction of CXL for keratoconus, and 5) how these NZ trends compare with those observed worldwide.^{2–4,11}

MATERIALS AND METHODS

This study adhered to the tenets of the Declaration of Helsinki and the National Ethics Advisory Committee guidelines¹² and met the criteria for exemption from formal review by the NZ Health and Disability Ethics Committee.¹³

As part of a large, longitudinal, prospective study, the electronic records of the NZNEB were analyzed for the period January 1991 to January 2020 for recipient demographics, clinical indications, and type of corneal transplantation planned at the time of booking surgery.

Data are entered into the NZNEB database in a prospective manner by the NZNEB staff. Recipient demographics, ocular history, associated ocular conditions, and the

preoperative diagnoses, that is, indications for keratoplasty, are recorded at the time of wait listing with NZNEB for transplant surgery. Information regarding the surgery performed is collected from surgeons at the time of operation in the form of a paper pro forma and the data forwarded to NZNEB to update the electronic database. Missing data were subsequently sought from surgeons by the way of follow-up correspondence. Although all donor information is also entered at the time of donor tissue procurement, this was not considered as part of this study.

For analysis, where there was more than 1 clinical diagnosis identified, the priority scheme suggested by Brady et al¹⁴ was applied, and all other diagnoses were removed. In particular, the diagnosis of regraft (repeat keratoplasty) was given priority over all other diagnoses. National census data for NZ were used to normalize trends by population growth.¹⁵ For continuous variables, the results are expressed as mean \pm SD, median, and range.

RESULTS

A total of 6840 corneas were transplanted between January 1, 1991, and January 1, 2020 (mean 236 \pm 57.5 transplants/year, range 89–348), with an increasing number of transplants performed per year (Fig. 1A). In relation to the NZ population,¹⁵ the number of corneal transplants performed each year increased from 2.55/100,000 population/year to 6.06/100,000 population/year, as illustrated in Figure 1B. The overall number of transplants performed per year with the primary indication of keratoconus slowly increased with time but remained relatively stable when normalized per 100,000 NZ population. The major contributor to the rise in total transplants/100,000 population in the past 15 years was the rising rates of regraft and corneal dystrophy [98.9% of which was classified as Fuchs endothelial corneal dystrophy (FECD)] as the primary indication.

Most of the corneal transplants were performed in the public-funded health care system (mean 72.1%, range 60.8–85.4), with the remainder performed in the private health sector. The relative proportion of surgeries performed in the public health sector has been slowly increasing over the past 30 years: 66.8% of transplants were performed in public between 1991 and 2000, 72.9% between 2001 and 2010, and 75.2% between 2011 and 2020. During the decade 2010 to 2019, most of the corneal transplants were performed in the regions with tertiary ophthalmology care: Auckland region (54.6%), Wellington (17.5%), and Christchurch (13.2%). This is similar to the decade 2000 to 2009 (47.2%, 14.5%, and 9.9%, respectively).

In total, 54.3% of transplant recipients were male (n = 3716) and 44.6% were female (n = 3050). The mean age of transplant recipient was 50.1 \pm 21.6 years. Recipient sex and age were not specified in 1.1% (n = 74) and 0.7% (n = 48) of transplants, respectively. Overall, the age range was relatively bimodal with the most common recipient age group 20 to 29 years (17.9%), followed by 70 to 79 years (15.5%), 30 to 39 years (14.3%), and 60 to 69 years (13.9%). The trend in corneal transplantation over time by recipient age is displayed in

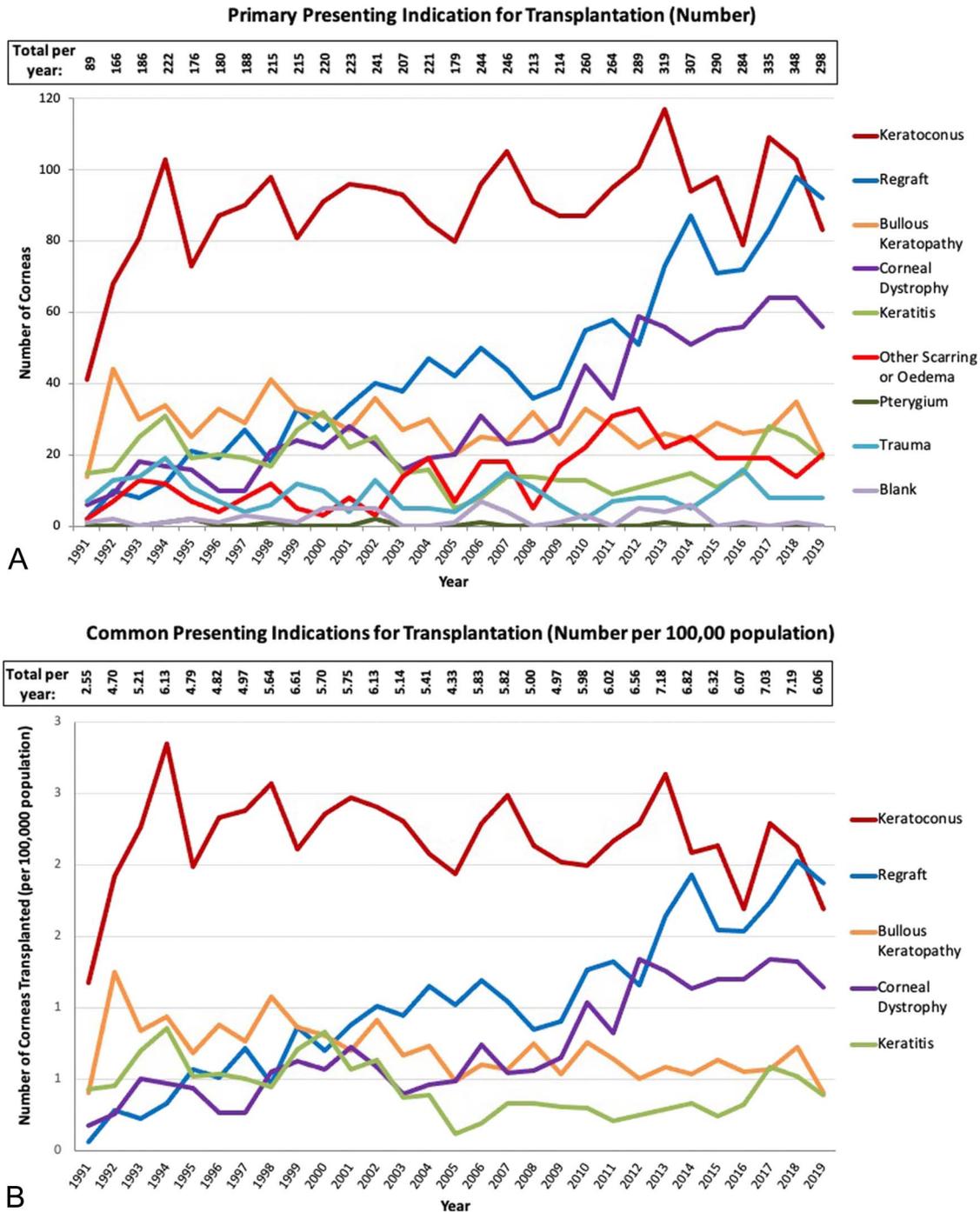


FIGURE 1. Total corneal transplants performed each year grouped by primary indication for surgery, represented by (A) absolute number and (B) common primary presenting indications per 100,000 NZ population. The number of transplants over time showed an increasing trend for absolute number and number per population, as well as for regrant and corneal dystrophy indications. By contrast, transplants performed for bullous keratopathy and keratoconus decreased when normalized by population growth. (The full color version of this figure is available at www.corneajrnl.com.)

Figure 2, highlighting that since 2007, more transplants were performed for patients aged 60+ years, whereas the absolute number of transplant recipients aged 20 to 39 years has remained steady in the past 10 years.

Historically, keratoconus was the most common presenting indication for corneal transplantation in NZ (Fig. 3), but 2019 was the first year where regrant became the most common indication at 30.9% of all corneas

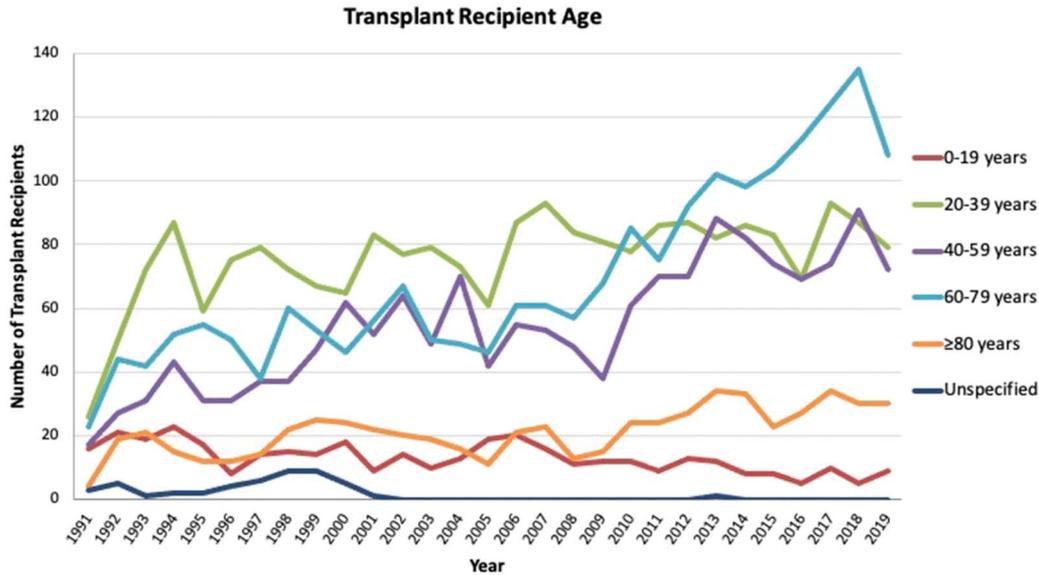


FIGURE 2. Number of transplant recipients by recipient age group. Graph shows an increasing number of transplants for older recipients over time, with a plateau in transplants for patients aged 20 to 39 years and a decreasing trend for recipients aged 0 to 19 years. (The full color version of this figure is available at www.corneajrnl.com.)

transplanted, followed by keratoconus at 27.9% and corneal dystrophy at 18.8%, of which 92.8% were for FECD. There has been a steady rise in the percentage of transplants being performed for corneal dystrophy and overall a steady decrease for bullous keratopathy and keratitis as the presenting indication.

Overall, FECD was specified in 83.9% of all corneal dystrophy cases during the study period; however, in the past 15 years, FECD was specified in 98.9%, and in 2019,

it was 92.8% of all corneal dystrophies. Earlier in the study period, there was incomplete or nonspecific recording about the type of corneal dystrophy as the primary indication for transplantation. The surgeon reporting on corneal dystrophy as an indication had the following 2 subcategories: “Fuchs endothelial corneal dystrophy” (the majority) and “Other.” When assessing these “Other” classifications (n = 143, 16.1%), the authors found that 34 descriptions (23.8%) were not detailed and 18 cases

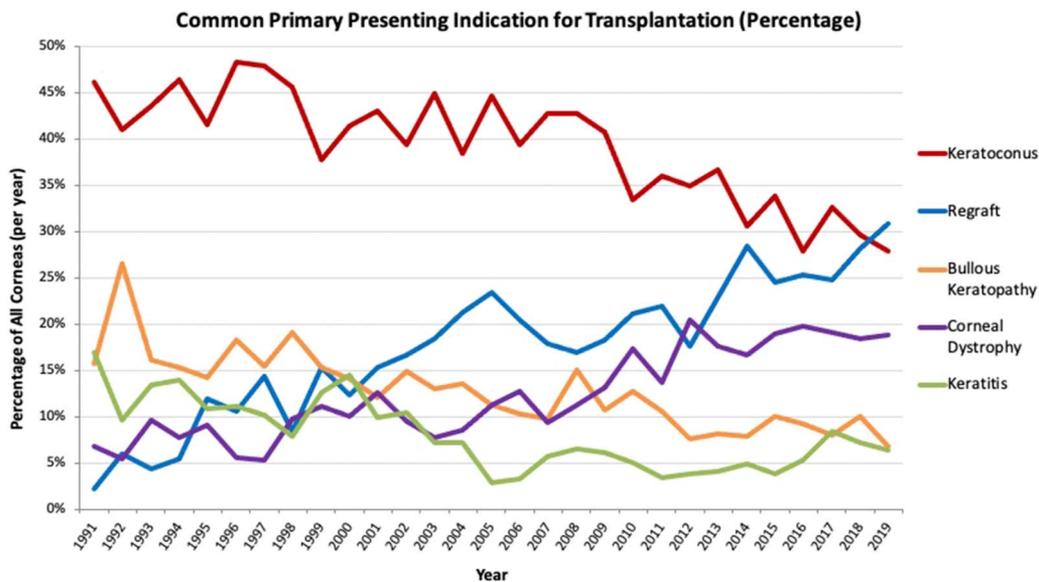


FIGURE 3. Common primary presenting indications for corneal transplantation as a percentage of all corneas transplanted each year. Graph shows an increasing trend in the proportion of regrafts and corneal dystrophy, with a decreasing number of transplants performed for keratoconus and bullous keratopathy. (The full color version of this figure is available at www.corneajrnl.com.)

(12.6%) might be variations on FECD (eg, “reduced endothelial cell count,” “idiopathic bullous keratopathy,” and “endothelial dystrophy”).

Although the number of corneal transplants performed each year in NZ has been steadily increasing (Fig. 4A), the number of penetrating keratoplasties (PK) has decreased because of the increased utility of deep anterior/ anterior lamellar keratoplasty ((D)ALK) and the introduction of endothelial keratoplasty to NZ. As a percentage of all

transplants performed per year (Fig. 4B), the proportion of techniques used changed dramatically between 2007 and 2010; PK comprised 91.4% of all transplants in 2006 and fell to 56.9% by 2010, whereas DS(A)EK increased from 0% to 31% and (D)ALK increased from 2.5% to 9.2%. By 2019, 55.0% were PK, 29.5% were DS(A)EK, 5.7% were (D)ALK, and 9.1% were DMEK.

Aside from the addition of the DMEK technique in NZ in 2015, the proportion of surgical techniques used for

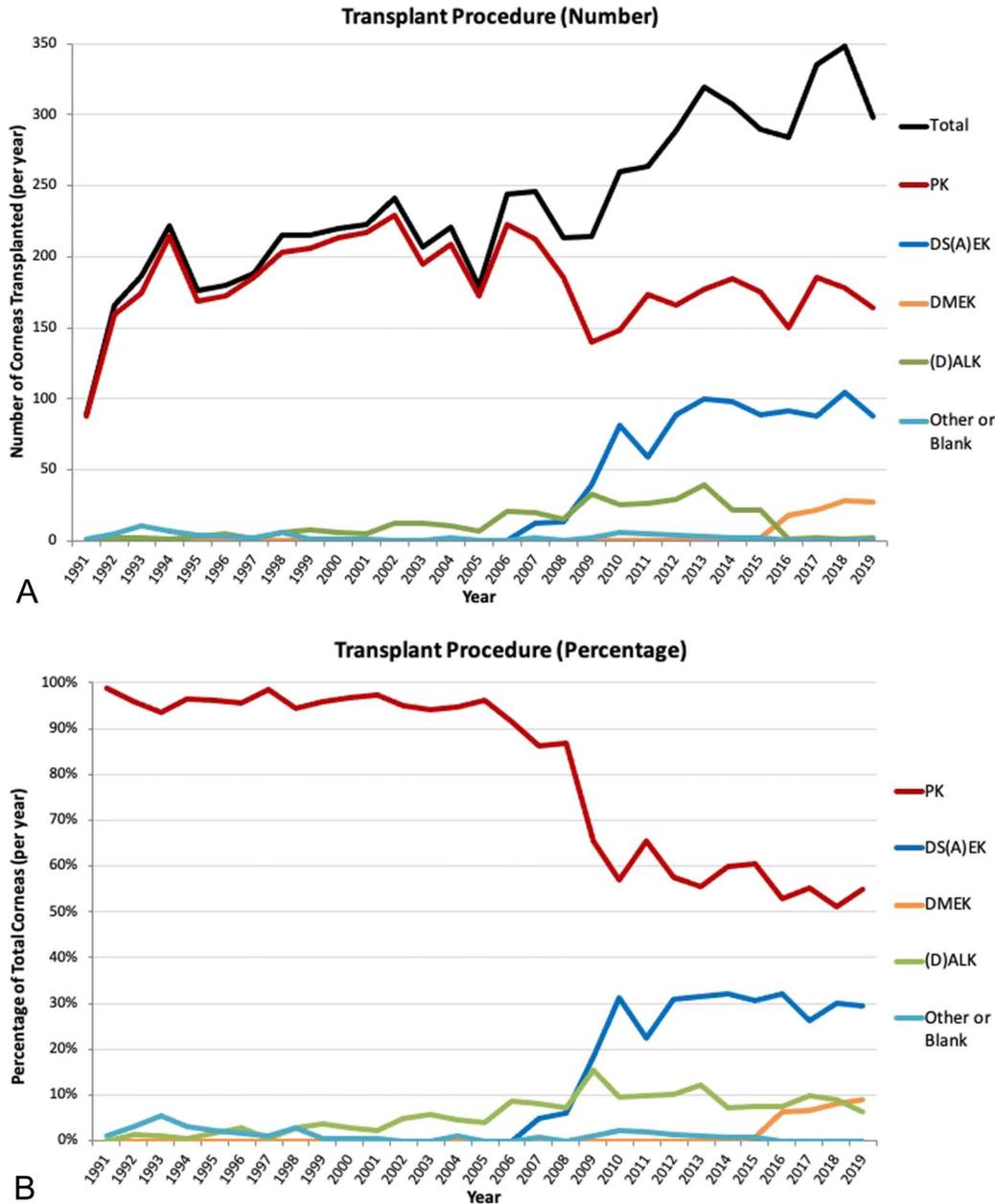


FIGURE 4. Corneal transplants performed per year, grouped by procedure represented (A) as total numbers and (B) as a percentage of corneal transplants performed each year. Graphs show an increase in the total number of transplants being performed, with a rise in lamellar and endothelial grafts and a decrease in the number and percentage of penetrating keratoplasties over the past 5 to 10 years compared with previous years. (The full color version of this figure is available at www.corneajrnl.com.)

TABLE 1. Keratoplasty Technique Used for Each Indication (n, %) Between 2010 and 2020

	Penetrating Keratoplasty (Total n = 1703)	Descemet's Stripping (Automated) Endothelial Keratoplasty (Total n = 888)	Descemet Membrane Endothelial Keratoplasty (Total n = 98)	(Deep) Anterior Lamellar Keratoplasty (Total n = 266)	Patch/Other/Blank (Total n = 44)
Regraft (total n = 738)	508 (68.8%)	205 (27.8%)	19 (2.6%)	6 (0.8%)	0 (0%)
Keratoconus (total n = 965)	748 (77.5%)	1 (0.1%)	0 (0%)	209 (21.7%)	7 (0.7%)
Bullous keratopathy (total n = 273)	89 (32.6%)	174 (63.4%)	10 (3.7%)	0 (0%)	0 (0%)
Fuchs endothelial corneal dystrophy (total n = 514)	20 (3.9%)	431 (83.9%)	63 (12.2%)	0 (0%)	0 (0%)
Other corneal dystrophy (total n = 28)	14 (50.0%)	8 (28.6%)	1 (3.6%)	5 (17.9%)	0 (0%)
Keratitis (total n = 160)	120 (75.0%)	0 (0%)	0 (0%)	21 (13.1%)	19 (11.8%)
Trauma (total n = 80)	66 (82.5%)	9 (11.3%)	0 (0%)	1 (1.3%)	4 (5.0%)
Pterygium (total n = 1)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other scarring/oedema (total n = 220)	122 (55.5%)	57 (25.9%)	5 (2.3%)	23 (10.5%)	13 (5.9%)
Other/blank (total n = 264)	259 (98.1%)	3 (1.1%)	0 (0%)	1 (0.4%)	1 (0.4%)

corneal transplants has remained stable over the past decade. Isolating the data to the decade 2010 to 2019, Table 1 displays the keratoplasty techniques used for each indication. Of note, the main surgical technique used for regrafts or keratoconus as the primary indication is penetrating keratoplasty, and the main technique used for bullous keratopathy or corneal dystrophy is DS(A)EK.

To illustrate the effect of CXL on keratoplasty rates as indicated for keratoconus, piecewise analysis (Fig. 5) was performed on 10 years of data before the implementation of CXL and all data 10 years after the introduction of CXL to NZ. The mean number of primary keratoplasties performed for keratoconus in the decade before the introduction of CXL was 2.30/100,000 population/year. Analyzing the data 10

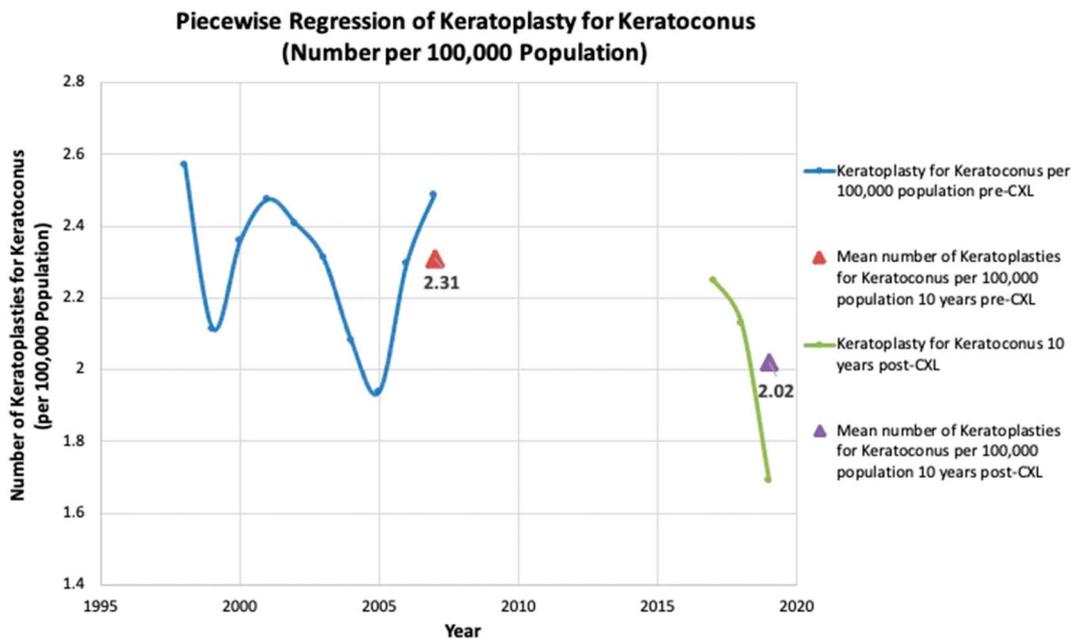


FIGURE 5. Piecewise analysis of keratoplasty performed for keratoconus per 100,000 population. For the 10 years before the introduction of CXL, the blue line represents annual keratoplasty rates for keratoconus and the red triangle is the decade’s mean (2.31 transplants/100,000 population/year). From 10 years after the introduction of CXL, the annual keratoplasty rate for keratoconus is represented by the green line, and the purple triangle is the mean (2.02 transplants/100,000 population/year). (The full color version of this figure is available at www.corneajrnl.com.)

years after the introduction of CXL shows a reduction in primary keratoplasty performed for keratoconus with mean 2.02/100,000 population/year; however, this did not reach statistical significance ($P = 0.079$).

DISCUSSION

This study aimed to assess the trends in corneal transplantation performed in Aotearoa/New Zealand (NZ) over the period 1991 to 2020 (29 years), normalized by NZ population data and isolating for the primary indication. The NZ population was estimated to be 3,495,800 in 1991 and increased to 4,922,200 by the end of 2019.¹⁶ The number of corneal transplants performed per population more than doubled increasing from 2.55/100,000 population/year to 6.06/100,000 population/year, a similar trend to that observed overseas.¹⁷ However, in addition to NZ's dramatic 41% increase in population, 3 additional factors might have significantly influenced trends in keratoplasty: increased number of cataract surgeries with improving phacoemulsification technology, introduction of endothelial keratoplasty with lower clinical threshold for surgery, and the use of CXL for keratoconus that might obviate future keratoplasty in many cases.

Previous studies in NZ have shown that the indications for corneal transplantation in NZ were dominated by keratoconus,^{7,9} possibly due to higher prevalence^{18–20} and severity²¹ of keratoconus in NZ Māori and Pasifika ethnicities. The proportion of NZ Māori and Pasifika ethnicities in the overall NZ population has increased from 15.9% in 1991 to 19.9% in 2018,¹⁶ yet regrant became the most common indication for corneal transplantation in 2019, followed by keratoconus and corneal dystrophy. We also observed the most common recipient age range increasing from 60 to 79 years, compared with 20 to 39 years for the period 1991 to 2010.⁷ Both of these observations may be due to several factors including the effect of CXL on preventing progression to keratoplasty, the rise in endothelial keratoplasty for corneal dystrophy (0% in 1991, 4.8% in 2007, and 38.6% in 2019), and/or patients undergoing repeat transplantation for keratoplasty endothelial exhaustion.

Bullous keratopathy as an indication for transplantation has continued to decrease in NZ. This is likely due to improved techniques for cataract surgery with fewer complications. The implementation of the New Zealand Cataract Risk Stratification system in the Auckland District Health Board, which is the largest teaching center for ophthalmology vocational registrars [residents], has been successful in lowering intraoperative complications from 8.4%²² to 3.0%²³ and may likely be a contributing factor in reducing the number of patients who proceed to transplantation for bullous keratopathy in Auckland.

Before 2006, over 90% of all transplants performed were PK. By 2009, this decreased dramatically because of the rise in the number of (D)ALK and DS(A)EK being performed. This mirrors what has been observed in South Korea,² Canada,⁴ Germany,³ and the United States.²⁴ However, although lamellar versus penetrating surgery now approaches 50:50, PK currently remains the most common

form of transplantation in NZ, unlike other countries,^{3,4,24} possibly due to the prevalence of early presentation with advanced keratoconus.

Interestingly, the introduction of DMEK to NZ in 2015 did not significantly affect the proportion of DS(A) EKs being performed, unlike observations in Spain,¹⁷ Canada,⁴ and Germany.³ This may be, in part, due to the NZNEB precutting DS(A)EK tissue but does not yet prepare DMEK tissue, and there are fewer surgeons in NZ who perform DMEK surgery; during the study period, there were 9 surgeons who performed DMEK ($n = 99$ surgeries) compared with 19 surgeons who performed DS(A)EK ($n = 954$ surgeries).

A Canadian study found a significant decrease in the proportion of total corneal transplants performed for keratoconus but no change in the absolute numbers of grafts performed for keratoconus, and therefore, was believed to represent an increasing demand for endothelial keratoplasty rather than a decrease in requirement for keratoconus²⁵; however, this study did not normalize data to account for population growth. Normalizing the number of transplants per year and per population in NZ and performing piecewise analysis suggest that we are beginning to see the beneficial effects of CXL on keratoconus-related transplantation. Although this did not reach statistical significance, which is likely, in part, due to the limited data 10 years after the implementation of CXL ($n = 3$ years) and fewer CXL procedures performed early on, it shows the trend toward a reduction in primary keratoplasty for keratoconus. This is also supported by the observation that the number of transplant recipients aged 20 to 39 years began leveling off in 2010. The percentage of patients with keratoconus who have received CXL is difficult to estimate because the true prevalence of keratoconus in NZ, as elsewhere, is not precisely known, and there is no unifying CXL database in NZ. Previous studies on keratoconus in NZ have assessed demographics, tomographic features, and disease severity of sample populations of high school students,¹⁸ tertiary care centers,^{26,27} and optometrists.^{27,28} Although not absolutely conclusive, these studies support the widely held suspicion that keratoconus is more common in both New Zealand and the Māori and Pasifika populations. Currently, CXL for keratoconus exceeds keratoplasty for keratoconus in NZ by at least a factor of 8 but ultimately a longer study period since the introduction of CXL is required to fully investigate the long-term effects on keratoplasty rates.

A limitation of the data set is the incomplete or nonspecific reporting on the type of corneal dystrophy. Most of these blank or nonspecific descriptions occurred early in the data set and could be affecting the trends in FECD as the primary indication for transplantation, but based on more complete data from recent years, FECD is likely to be at least 92.8% of all corneal dystrophy cases. Some tissue for corneal transplantation in NZ is sourced by surgeons directly from eye banks overseas, which is estimated to be 5% to 10% of all keratoplasty performed in this study period. This is not included in the NZNEB database and is another limitation of this study; indications and keratoplasty types not included might be different from those included and is a future area of

interest. Although the exact number of imported corneas each year is unknown, the NZNEB database includes most of the keratoplasty performed in NZ.

This study found that the trends in corneal transplantation performed in Aotearoa/NZ over the period January 1991 to January 2020, normalized by NZ population data and isolating for the primary indication, has changed considerably in the past 15 years with the evolution of phacoemulsification and keratoplasty techniques and the development of CXL. The number of transplants being performed per population is increasing, with regrant being the number 1 indication in 2019, surpassing keratoconus. The proportion of transplants being performed does not fully align with other countries, possibly due to the ethnic composition and the burden of keratoconus in NZ, but the beneficial effect of CXL on keratoplasty rates for keratoconus is beginning to emerge.

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