The Australian Corneal Graft Registry: 35 Years in Sight

Presented by Miriam Keane, PhD, Executive Director, ACGR

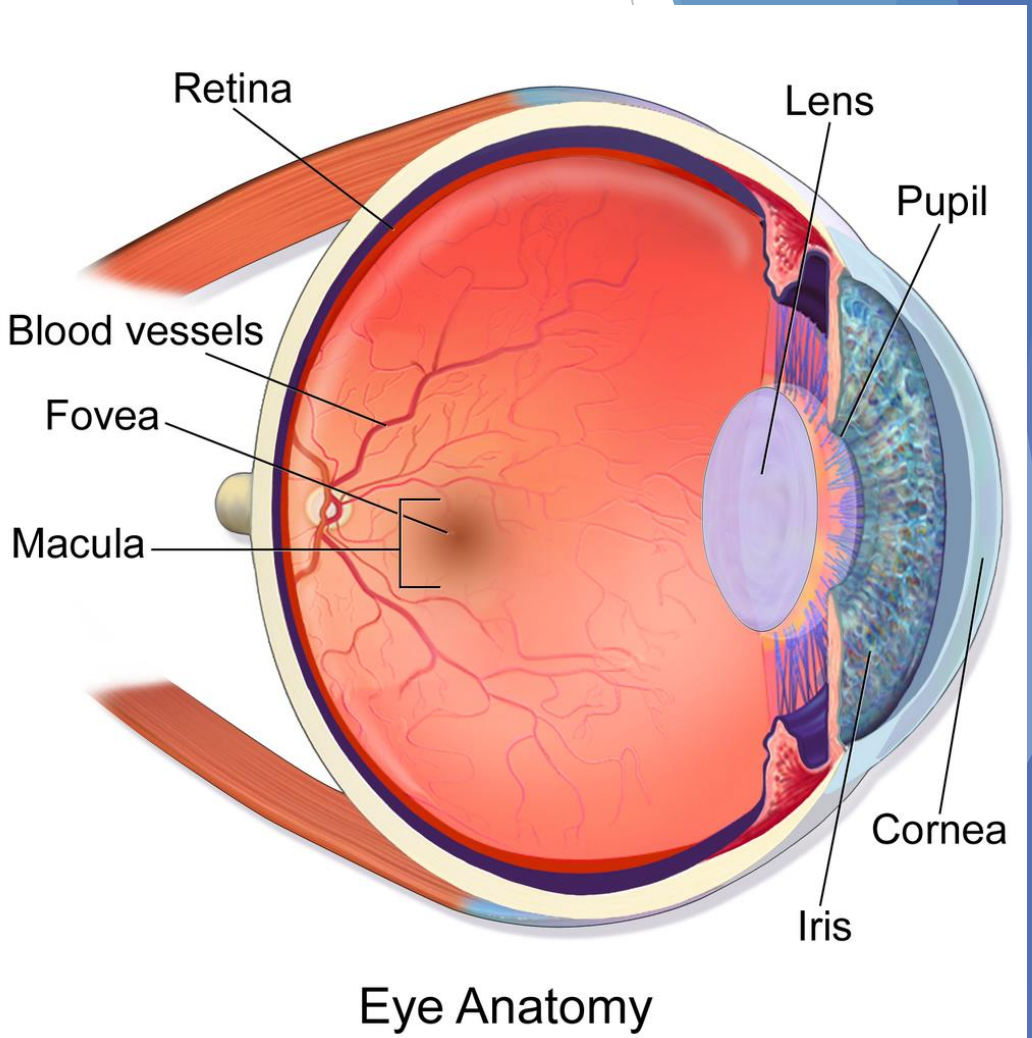
As part of the College of Medicine and Public Health

Medicine and Bioscience Seminar Series

28th August 2019

The Cornea

- Clear window at front of eye
- Function can be affected by:
  - Disease
  - Trauma
  - Infection
- These may cause:
  - Poor vision
  - Pain/discomfort
  - Structural issues



Corneal Transplantation

- AKA corneal graft
- AKA keratoplasty
- Replaces diseased or damaged cornea with tissue from a donor
- Performed for over 100 years
- Evolution of multiple techniques

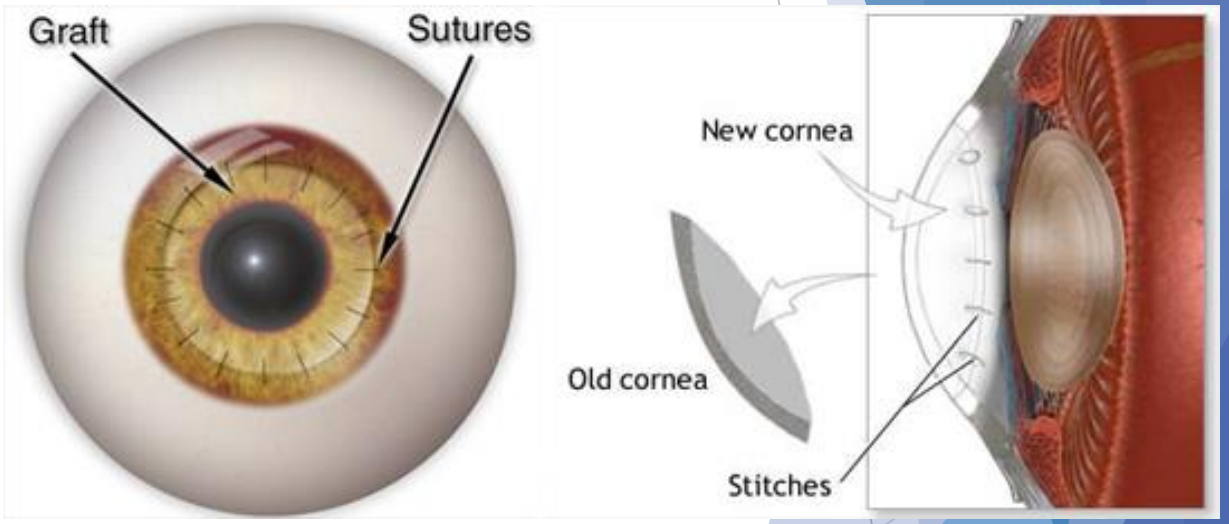


Image source: drdulay.com/corneal-transplant-surgery

Corneal Transplantation

- Multiple layers
- Different layers affected by different diseases
- Full-thickness replacement (Penetrating Keratoplasty)
- Partial replacement (Lamellar Keratoplasty):
  - Epithelium
  - Endothelium

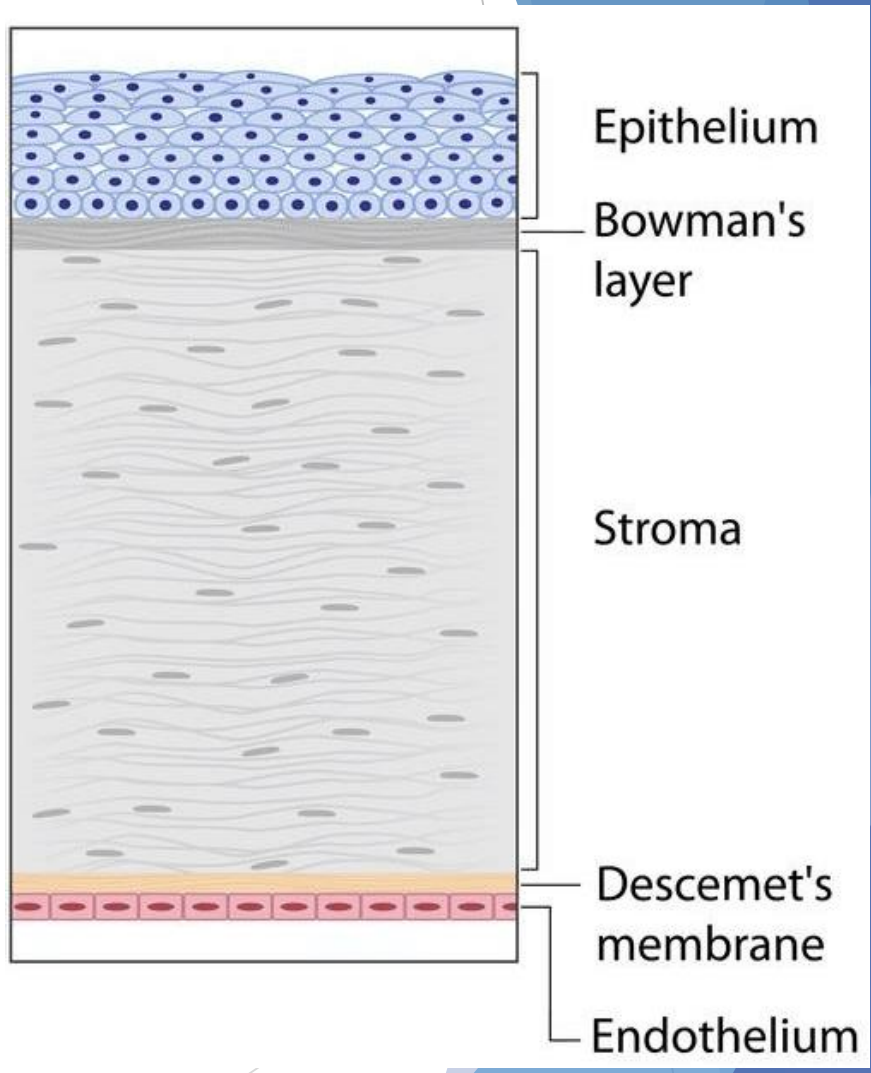


Image credit: alilamedicalimages.com

Corneal Transplantation

- B) Penetrating Keratoplasty(PK)
- C) Lamellar keratoplasty (LK)
- D) Deep Anterior Lamellar Keratoplasty (DALK)
- E) Descemet's Stripping Endothelial Keratoplasty (DSEK) + variations (DSAEK, UT-DSEK)
- F) Descemet's Membrane Endothelial Keratoplasty (DMEK)

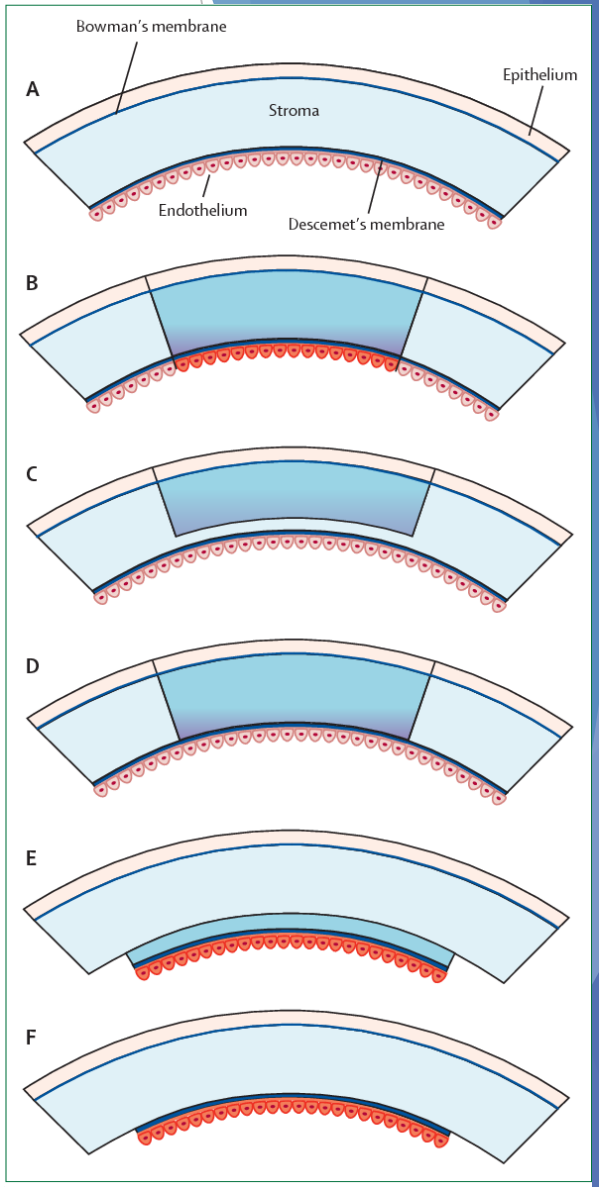
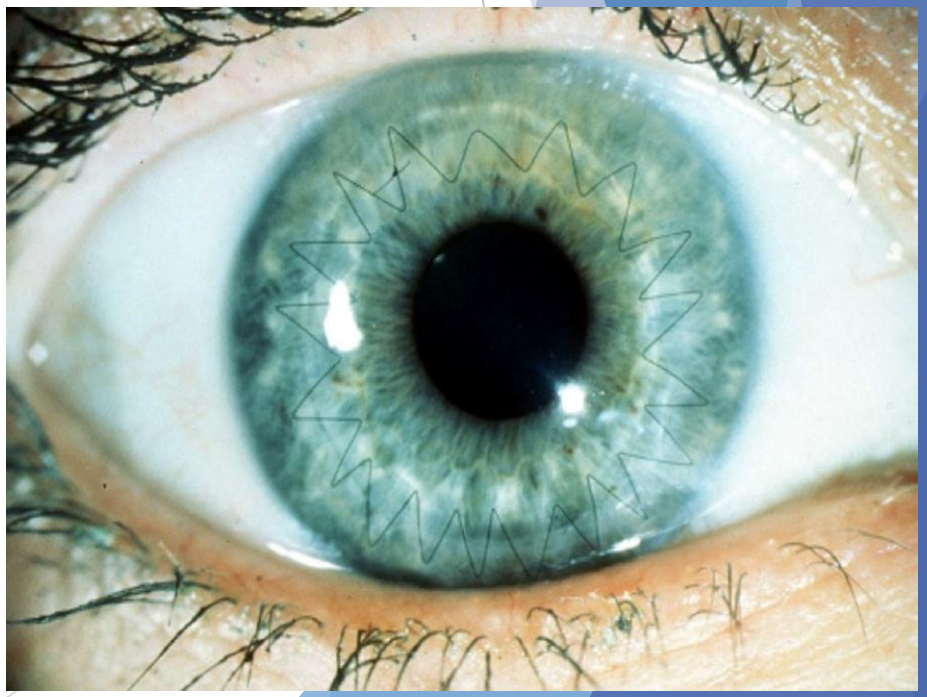


Image source: Tan, Donald T. H. et al. "Corneal transplantation." *The Lancet* 379 (2012): 1749-1761.

The Australian Corneal Graft Registry

- Corneal transplant outcomes register
- Research tool
- Established in May 1985 (2020 will be our 35th birthday)
  - Emeritus Professors Keryn Williams and Doug Coster
- Used to inform data collection internationally



The Australian Corneal Graft Registry

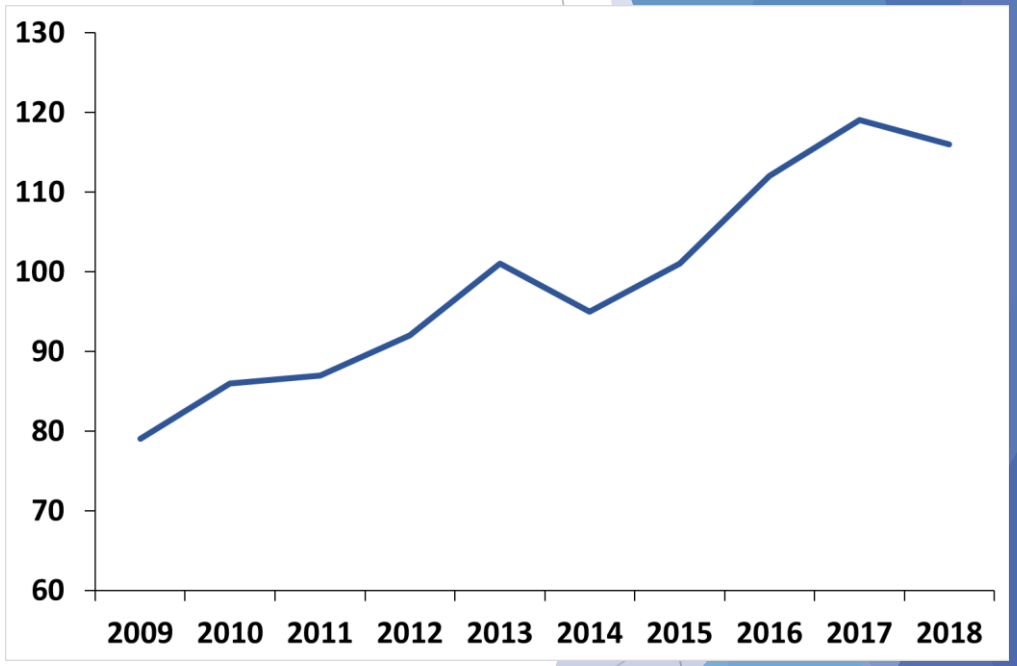
- The goals of the ACGR:
  - To measure graft survival and visual outcomes after corneal transplantation
  - To investigate risk factors for graft failure
  - To examine changing patterns of practice
  - To return amalgamated, de-identified results to all contributing surgeons, eye banks and other interested parties

Data Collection – Registration

- At time of corneal graft
  - Eye Banks around Australia:
    - Provide demographic data on donor
    - Forward Registration form to surgeon
  - Surgeon
    - Obtains patient consent for inclusion
    - Provide demographic data on recipient
    - Outline eye health history of recipient
    - Detail the surgery performed

Data Collection - Registration

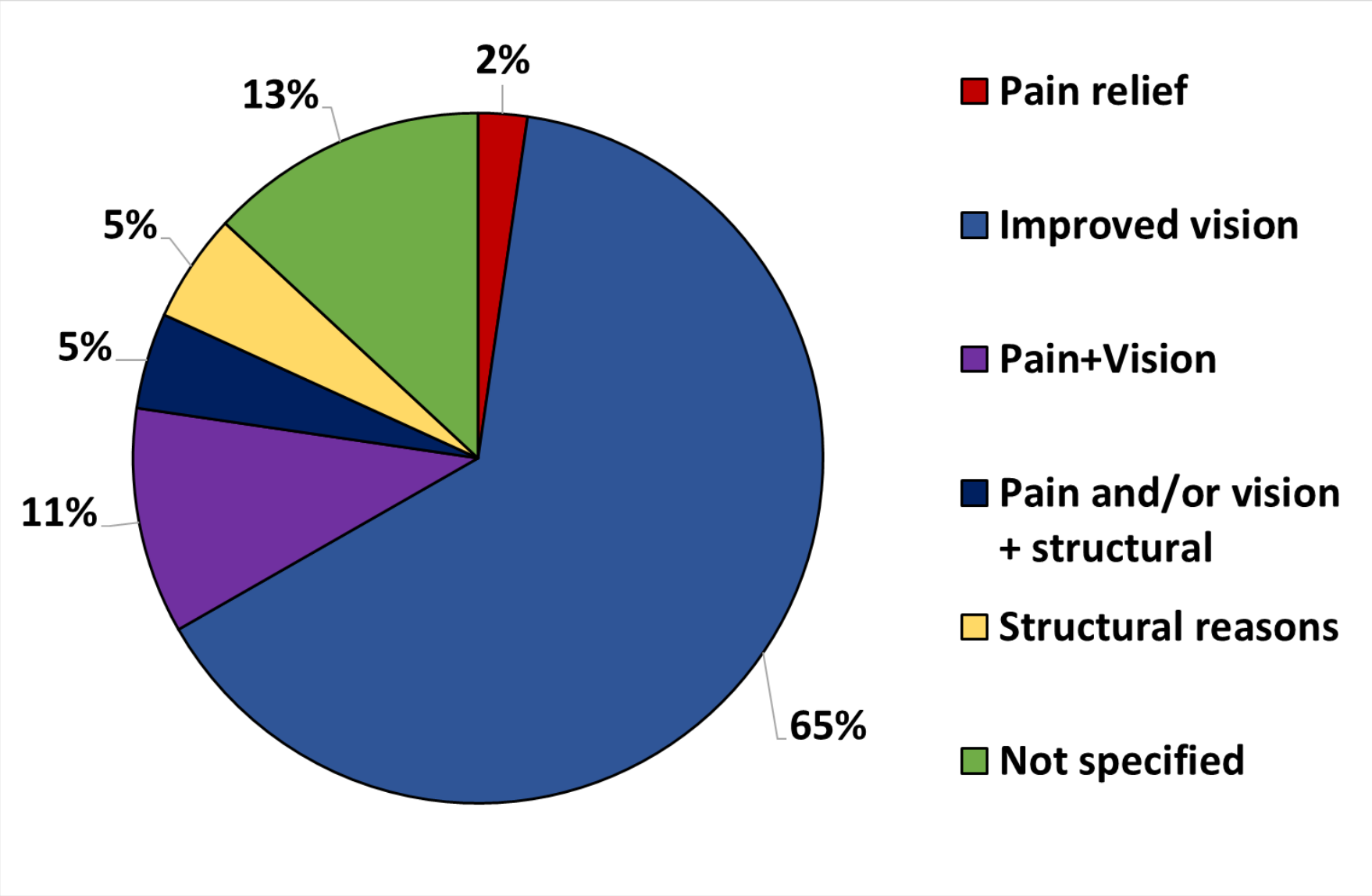
- Surgeons all around Australia provide data
- Number of operating surgeons varies per year
  - Steady increase in last 10 years
  - Approximately 120 current operating surgeons



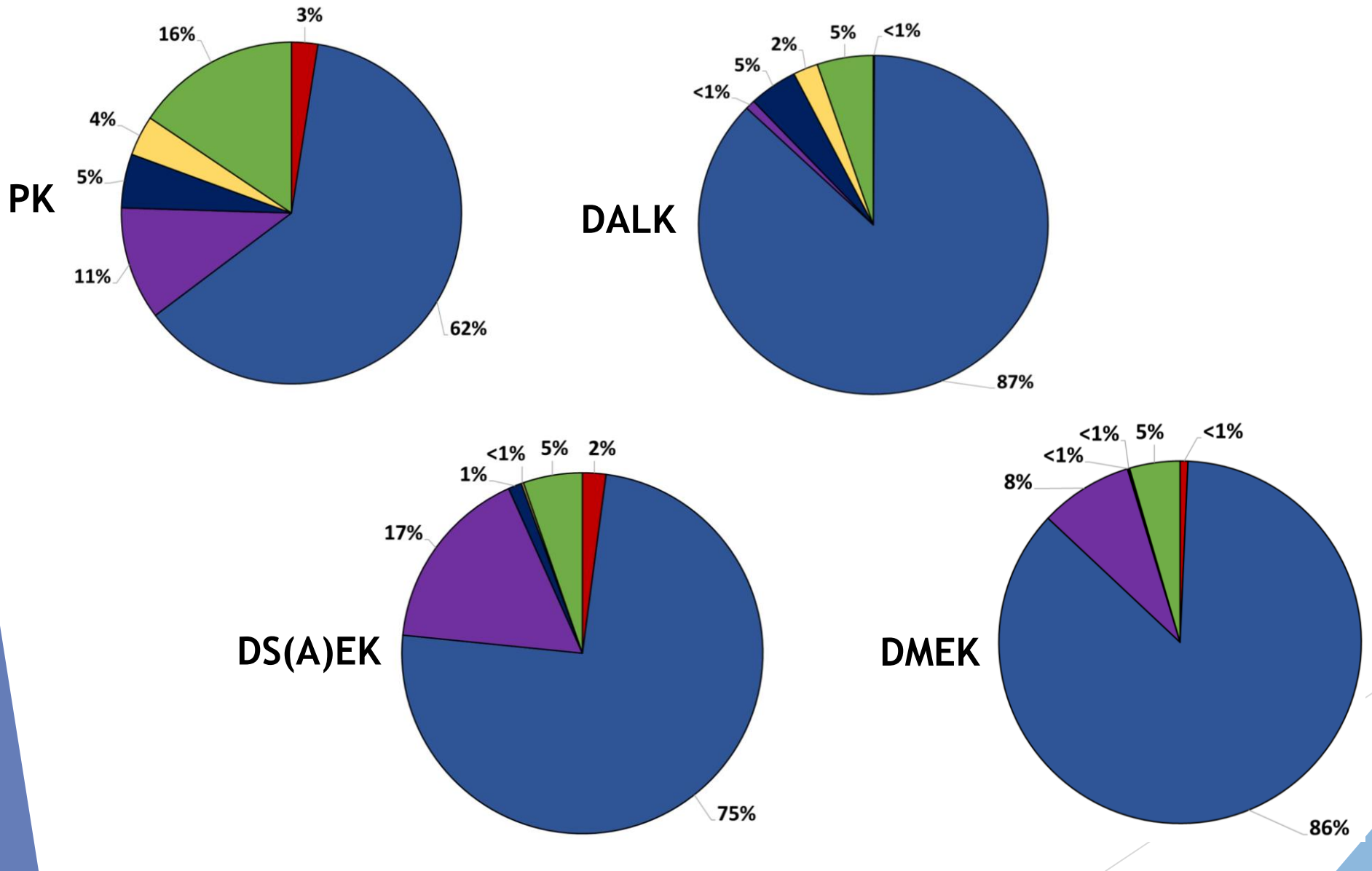
Data Collection – Follow-up

- Requested by ACGR
  - March and September
  - 1 to 3 yearly intervals between follow-ups
- Over 900 contributors to date
- Exact date patient last seen by practitioner
- Report on outcomes
  - Graft survival
  - Complications
  - Visual outcomes
  - Further surgery

Reasons for Corneal Transplantation



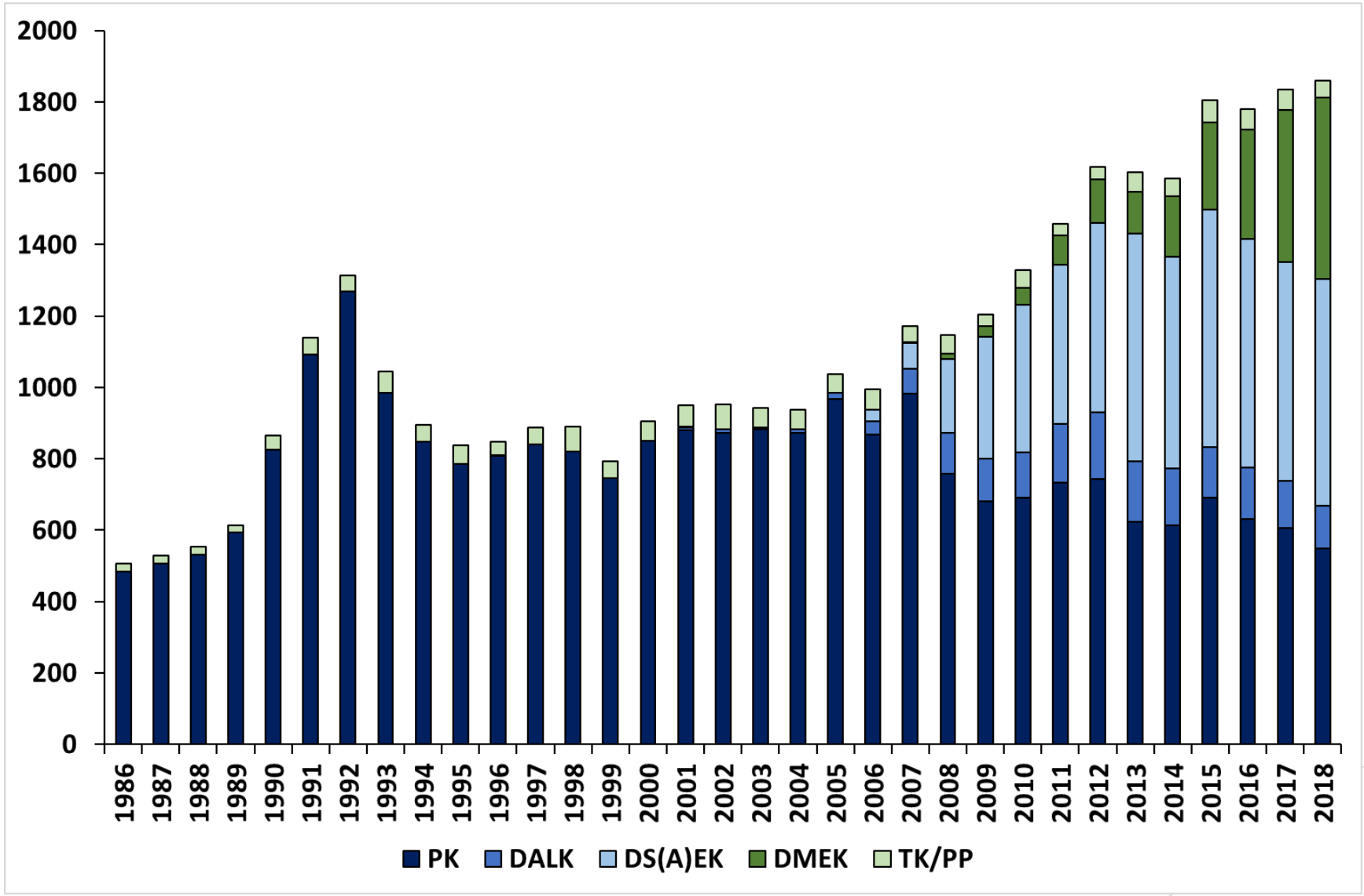
Reasons for Corneal Transplantation



Data Analyses

- Survival
  - Kaplan Meier Survival Curves
  - Cox Proportional Hazards Regression
- Rejection
  - Presence of any/repeat episodes
  - Time to first episode
- Best Corrected Visual Acuity
  - Level of BCVA
  - Time to 6/12 attainment
  - Improvement
- Improvement in pain

Number and Type of Graft Over Time



The ACGR Database 1985 to 2018

	Registered
PK	25801
TK	1389
DALK	1740
DS(A)EK	5831
DMEK	2065
Total	37099

The ACGR Database 1985 to 2018

	Registered	Followed
PK	25801	82%
TK	1389	78%
DALK	1740	61%
DS(A)EK	5831	70%
DMEK	2065	51%
Total	37099	77%

The ACGR Database 1985 to 2018

	Registered	Followed	Failed
PK	25801	82%	24%
TK	1389	78%	22%
DALK	1740	61%	7%
DS(A)EK	5831	70%	19%
DMEK	2065	51%	19%
Total	37099	77%	22%

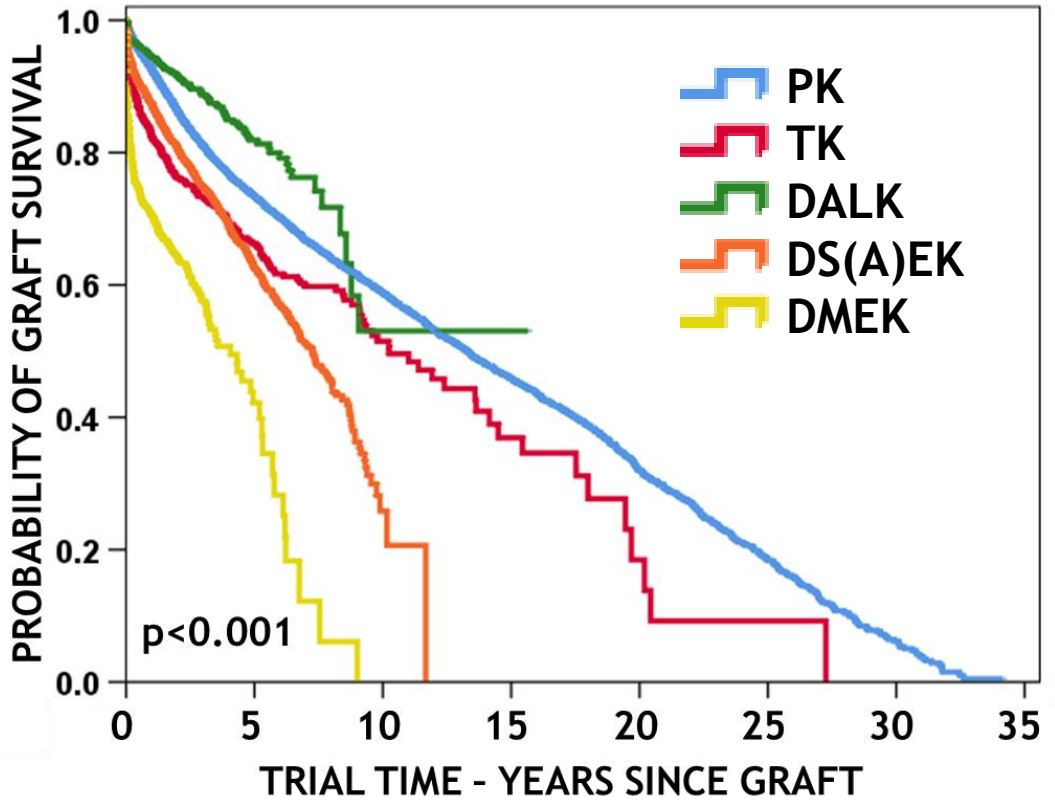
The ACGR Database 1985 to 2018

	Registered	Followed	Failed	Primary non-function
PK	25801	82%	24%	<1%
TK	1389	78%	22%	1%
DALK	1740	61%	7%	<1%
DS(A)EK	5831	70%	19%	5%
DMEK	2065	51%	19%	11%
Total	37099	77%	22%	2%

Primary non-function: graft didn't clear and begin healing as expected

Graft Survival - Graft Type

- Kaplan Meier survival curve
  - Likelihood of survival (0 to 1)
  - From time since event
  - 1 = every case surviving
  - 0 = every case followed for that length of time has failed
  - A curve reaching 0 doesn't mean that all cases have failed, just those with the longest follow-up
- Great variation in numbers per group
- Different lengths of follow-up



	1 Year	5 Years	10 Years
PK	17649	6754	2707
LK	670	209	57
DALK	898	150	7
DS(A)EK	2970	584	10
DMEK	560	24	NA

Factors Affecting Graft Survival - Evolving Techniques

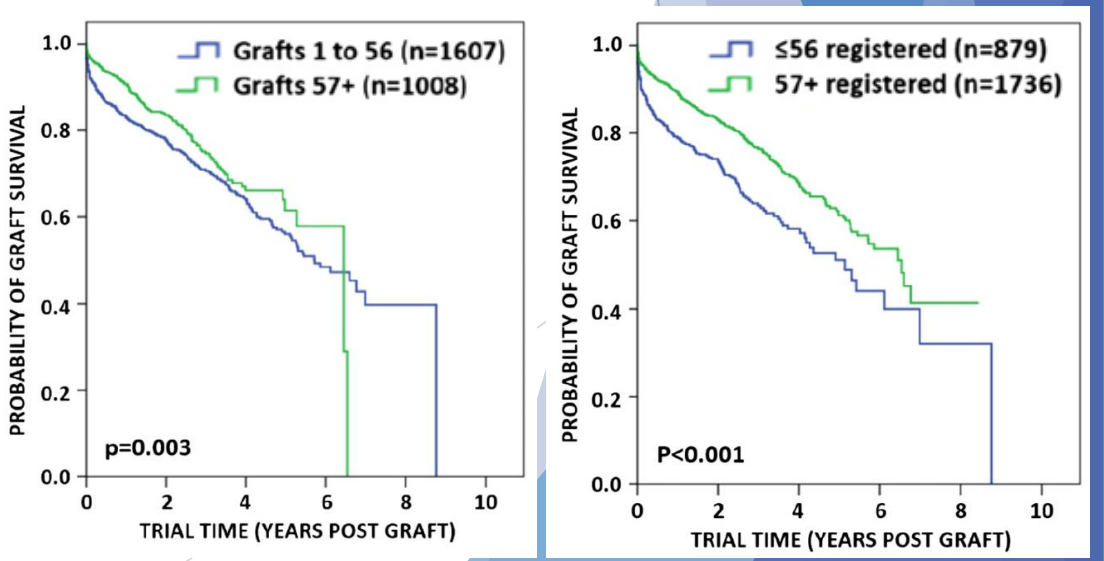
- Surgeon learning curve
  - Time and experience that a surgeon requires to achieve an optimal level of competence with a technique
    - Reduction in frequency of adverse events
    - Decrease in time taken to complete procedure
- Later grafts
  - Significantly better survival
  - Significantly lower PNFG
- For high-volume, experienced surgeons
  - Better outcome vs. low volume
  - Not significant between 1-56 & 57+

Clinical & Experimental Ophthalmology
RANZCO
Clinical and Experimental Ophthalmology 2017; 45: 575–583 doi: 10.1111/ceo.12921

Original Article

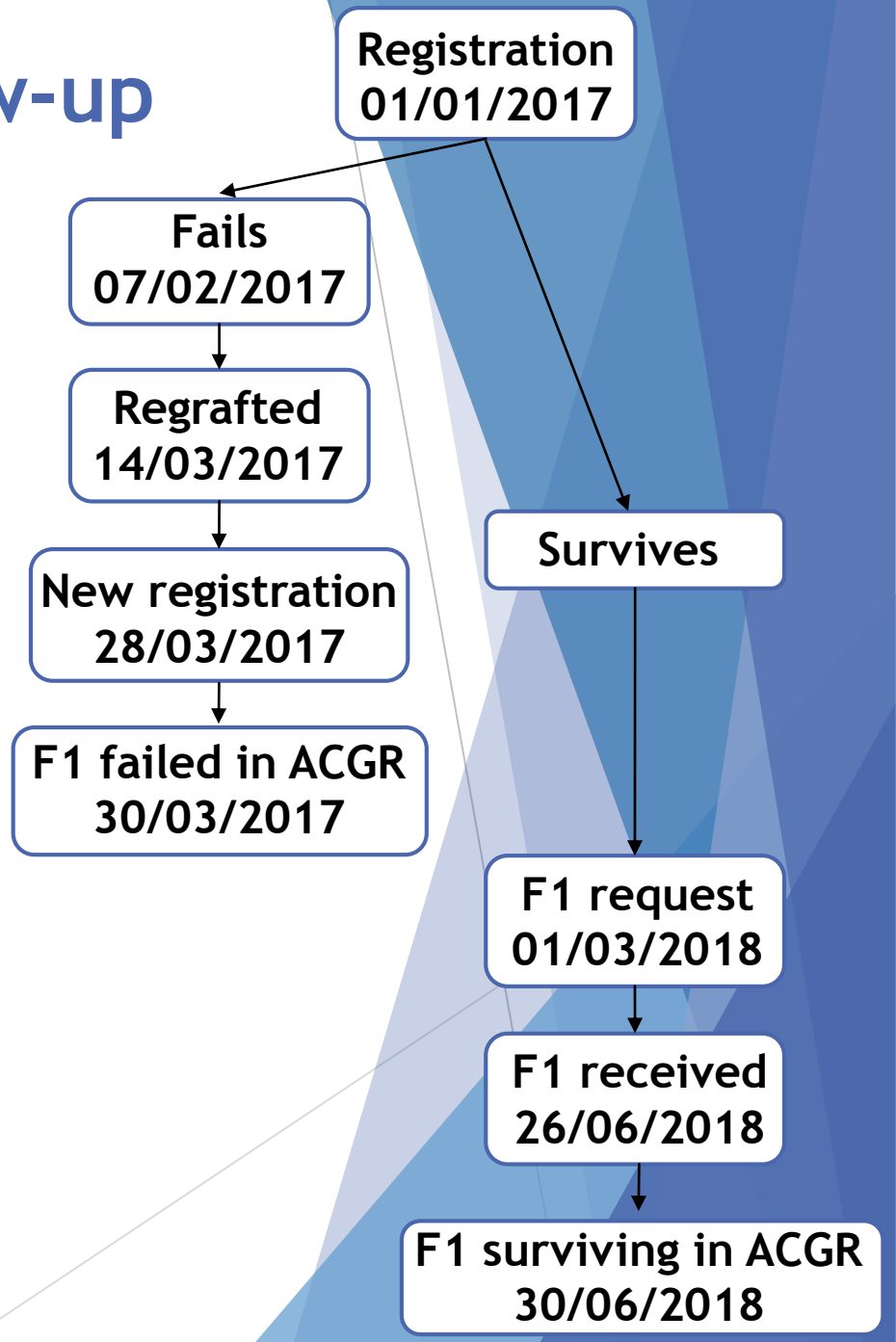
Is there evidence for a surgeon learning curve for endothelial keratoplasty in Australia?

Miriam C Keane PhD, Richard AD Mills FRANZCO PhD, Douglas J Coster FRANZCO DSc, Keryn A Williams PhD and on behalf of Contributors to the Australian Corneal Graft Registry
Department of Ophthalmology, Flinders University, Adelaide, Australia

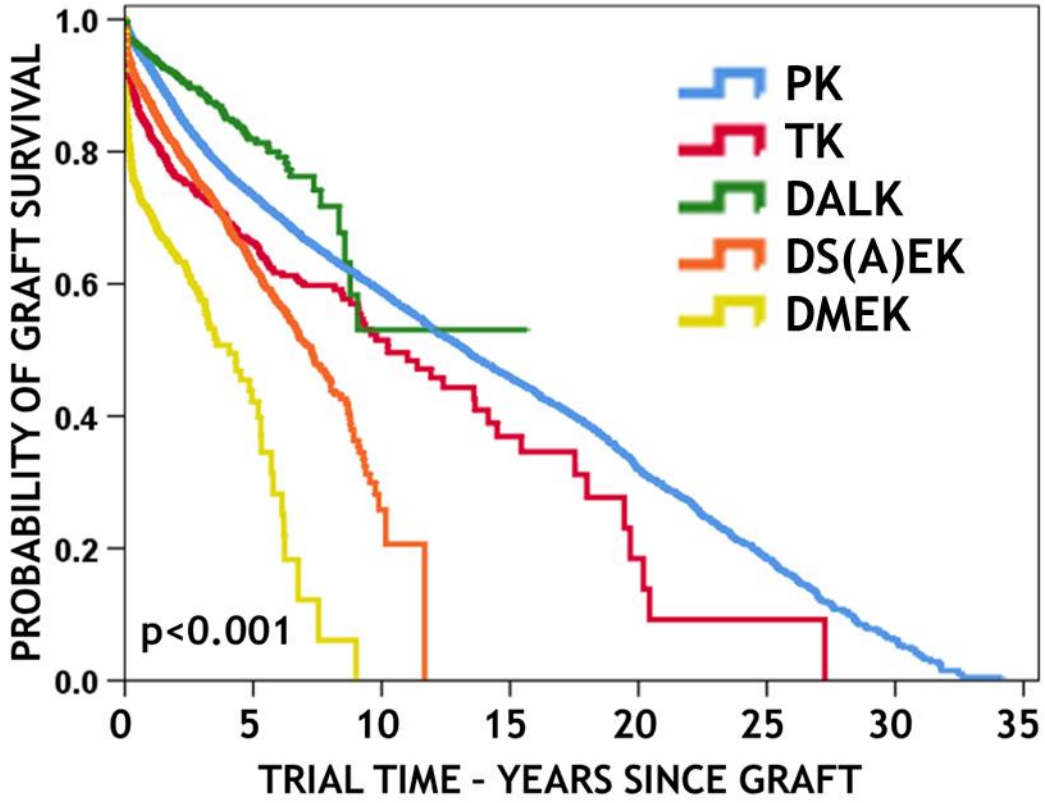


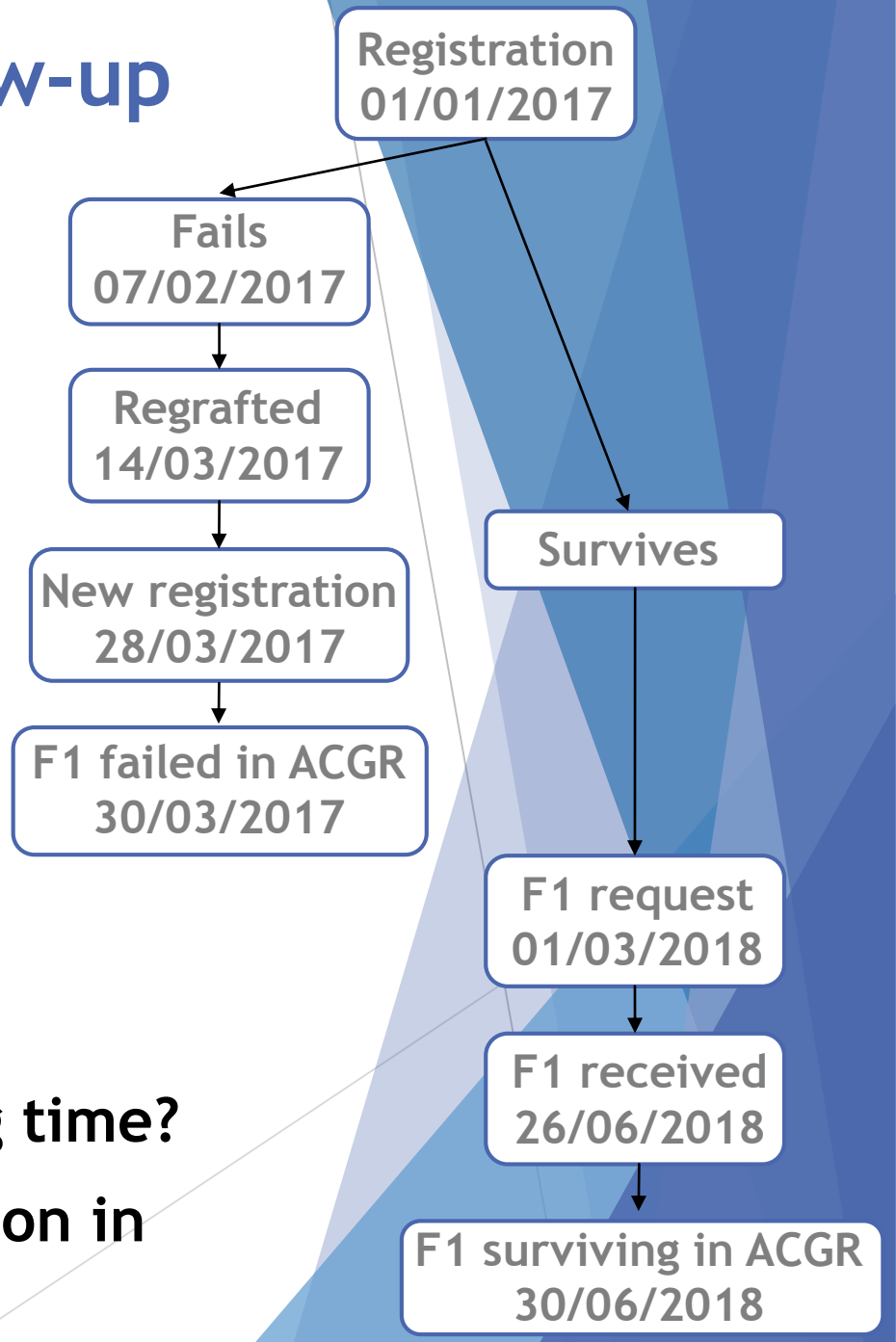
Factors Affecting Graft Survival – Follow-up

- Dependant on graft era – lag time
- Most pronounced for most recent grafts
  - If eye regrafted, prior graft failed
  - First follow-up request at 1 year
  - Prior to this most followed grafts are failures
- Primary non-functioning grafts
  - Higher proportions in EK (<1% vs. 5% vs. 11%)



Factors Affecting Graft Survival - Follow-up





- May affect differences seen in other variables
  - Poorer outcomes in new techniques due to lag time?
  - Certain groups for other variables more common in later eras due to changes in practices?

Factors Affecting Graft Survival - Indication for Graft

- Keratoconus (25%)
  - Treatment with PK or DALK

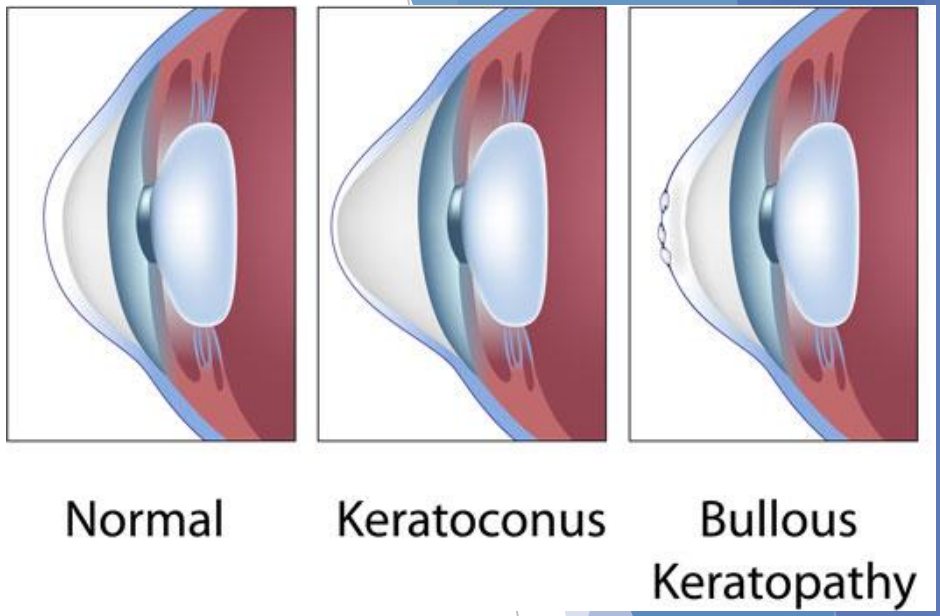


Image source: www.lasikmanchester.com

- Fuchs' Endothelial Corneal Dystrophy (16%)
  - Treatment with PK or EK

- Pseudophakic Bullous Keratopathy (15%)
  - Treatment with PK or EK

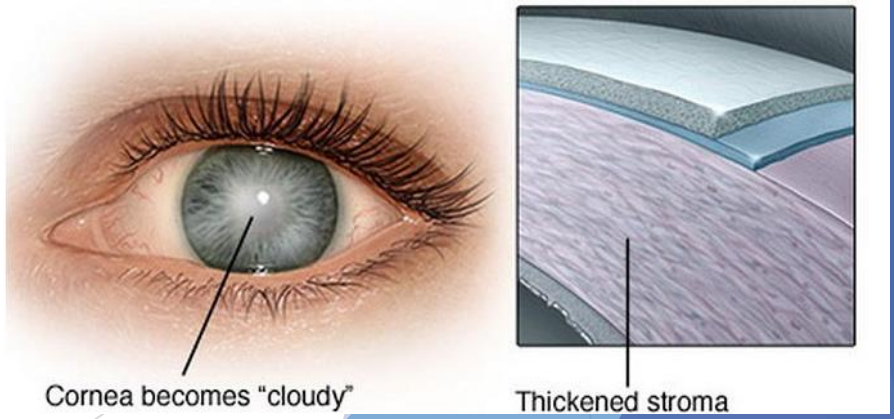
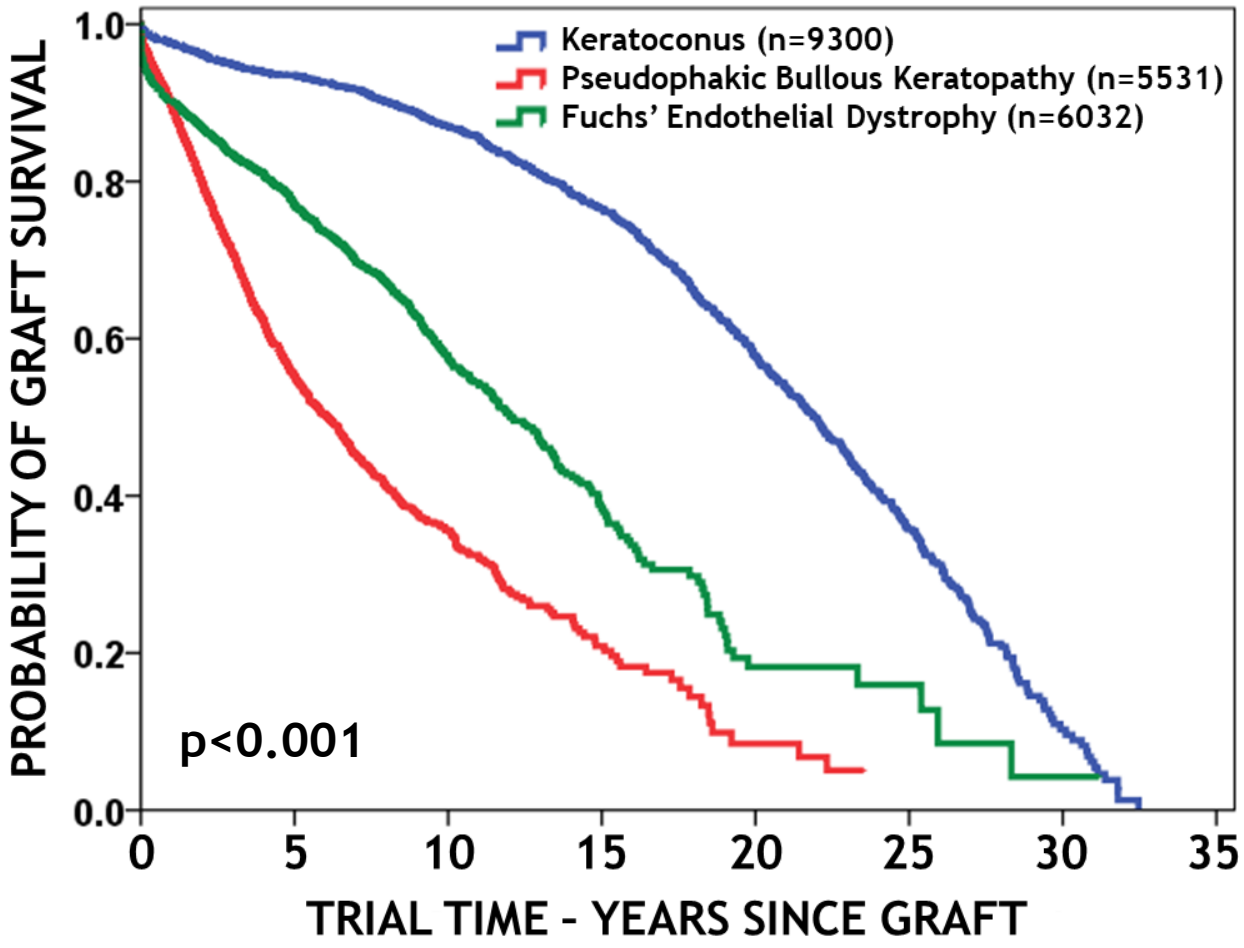


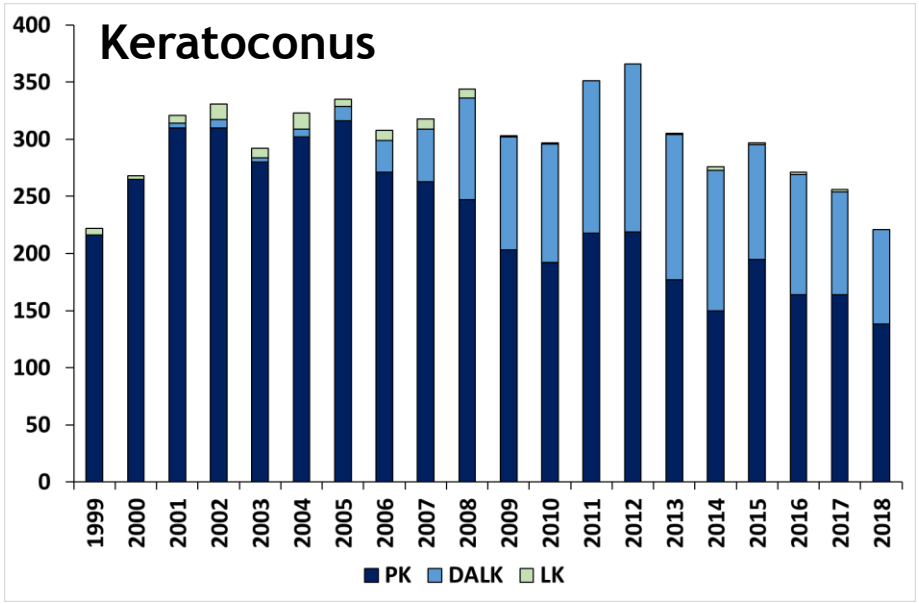
Image source: mittlemaneye.com

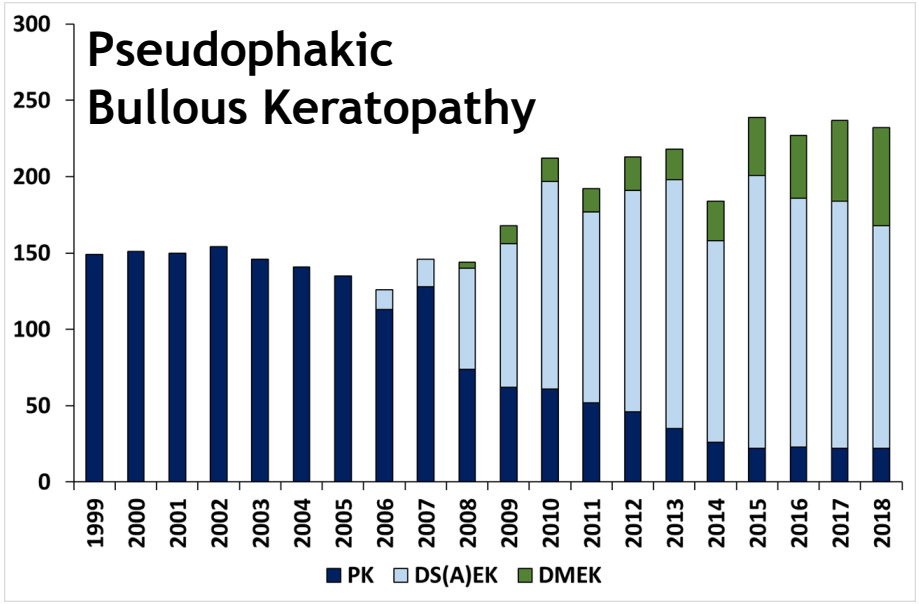
Factors Affecting Graft Survival - Indication

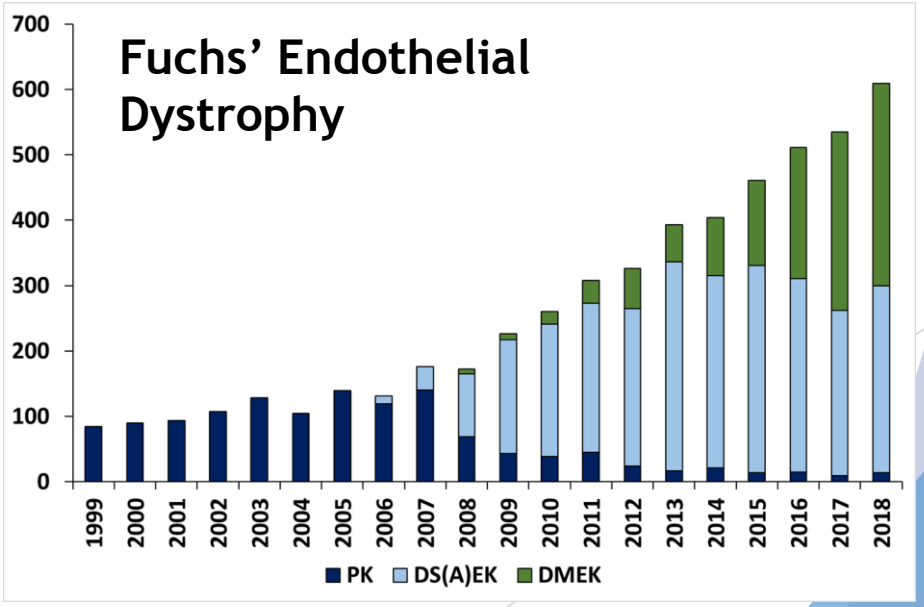


	1 Year	5 Years	10 Years	15 Years	20 Years	25 Years	30 Years
Keratoconus	6554	2729	1322	741	372	136	15
Pseudophakic Bullous Keratopathy	3234	766	162	35	6	NA	NA
Fuchs' Endothelial Dystrophy	3472	1228	336	80	15	5	1

Graft Type by Graft Year by Indication





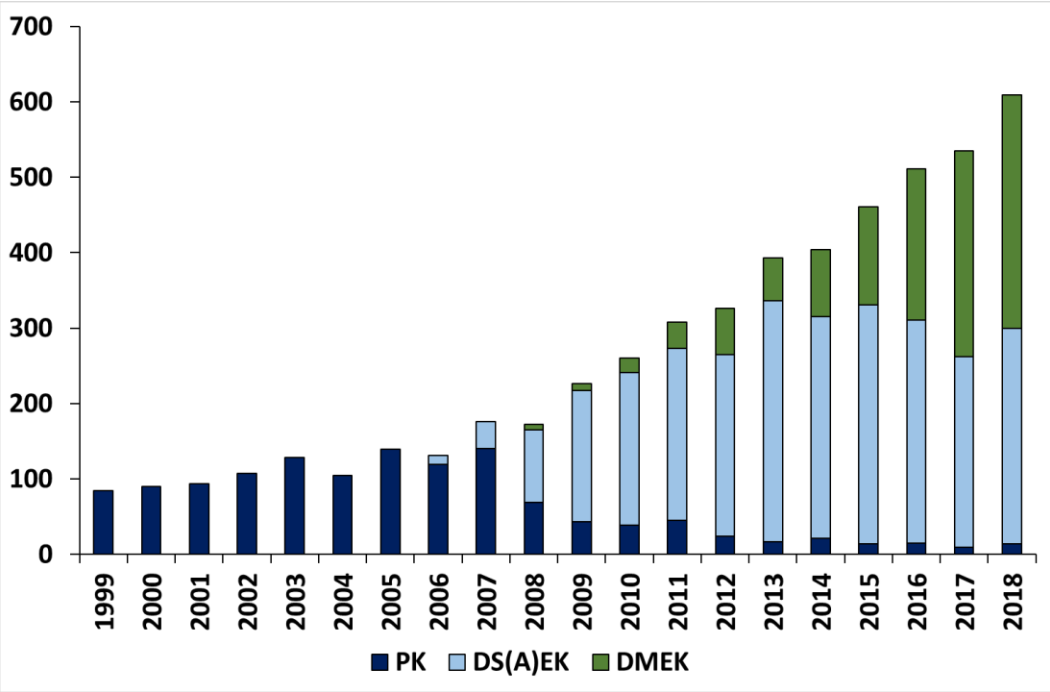


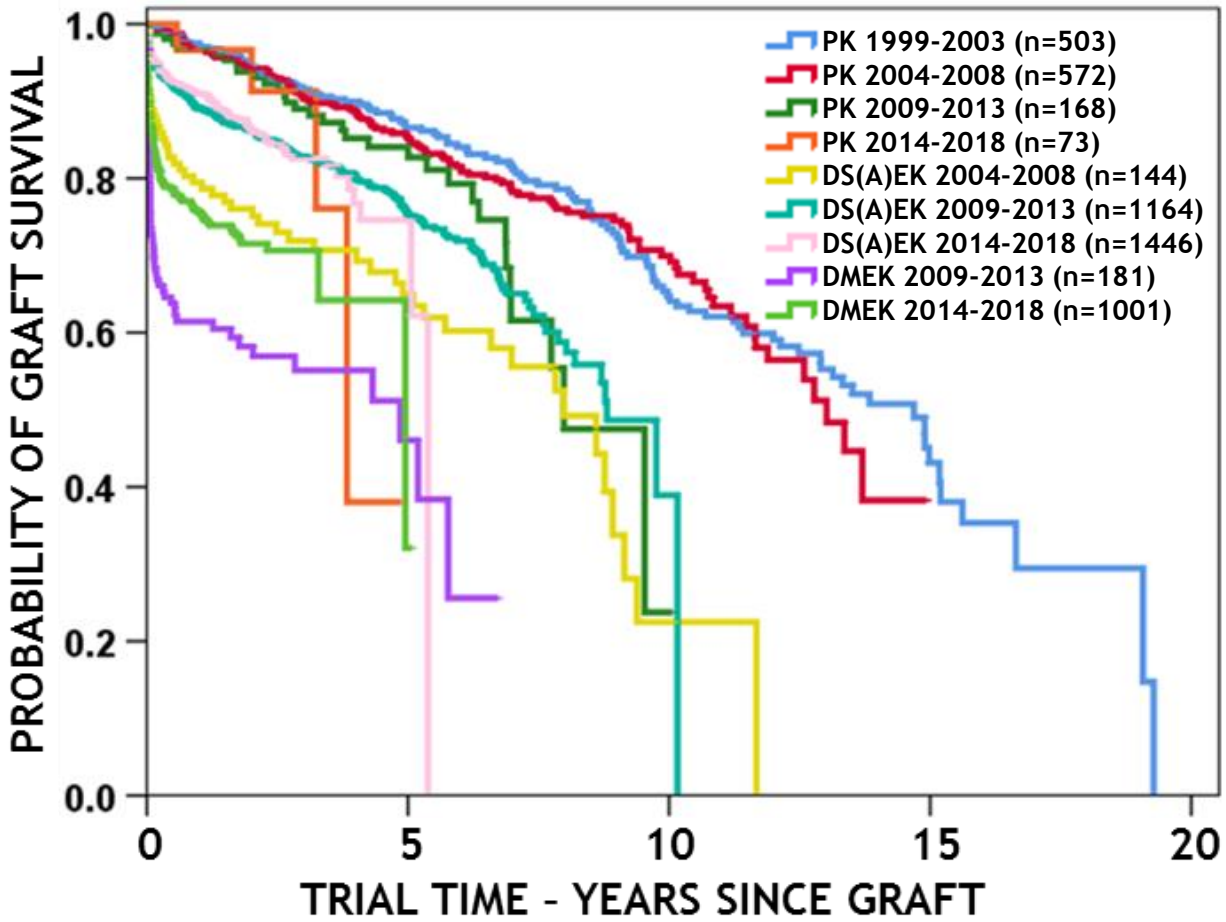
Factors Affecting Graft Survival

- Graft type
- Graft era
- Indication for graft

- Combination?

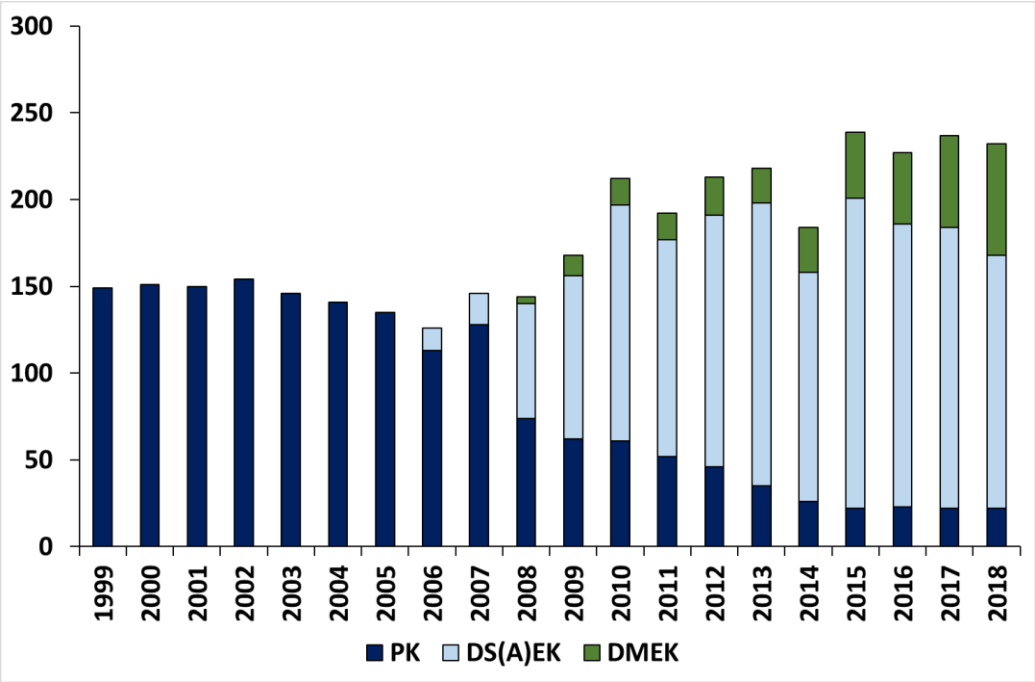
Fuchs' Endothelial Dystrophy

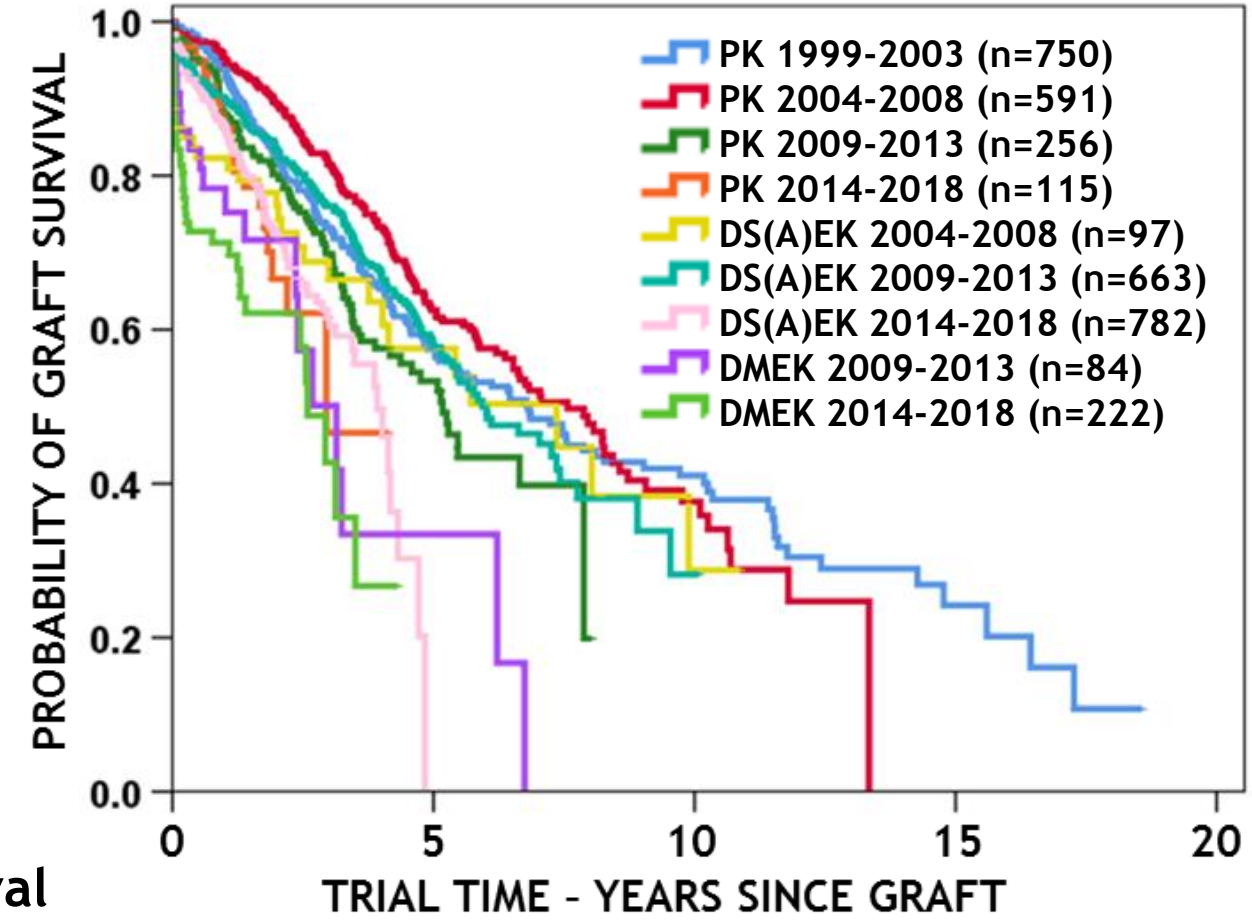




- PK vs. DSAEK vs. DMEK - quite separate
- PK cohorts have similar survival
- DS(A)EK cohorts similar since 2009
- DMEK recent cohort better survival

Pseudophakic Bullous Keratopathy





- PK vs. DS(A)EK vs. DMEK – some overlap
- Most recent cohorts have poorest survival
- PK 2004-2008 better than 1999-2003
- DS(A)EK 2009-2013 better than 2004-2008

Factors Affecting Graft survival - Disease Severity

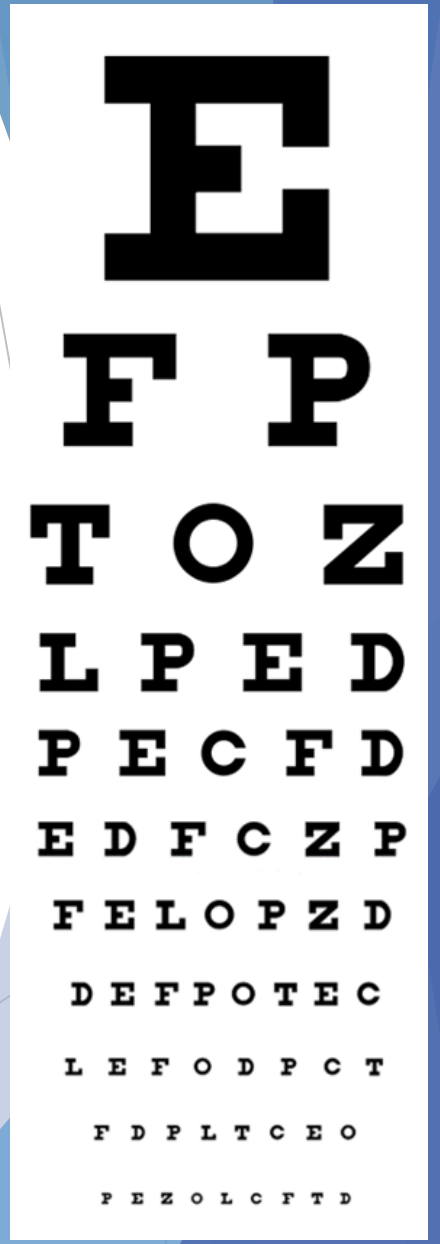
- Percentage of grafts for pain - Fuchs'

	1999-2003	2004-2008	2009-2013	2014-2018
PK	22%	19%	25%	32%
DS(A)EK	NA	20%	10%	10%
DMEK	NA	NA	10%	3%
Total	22%	19%	12%	8%

- Median pre-graft vision - Fuchs'

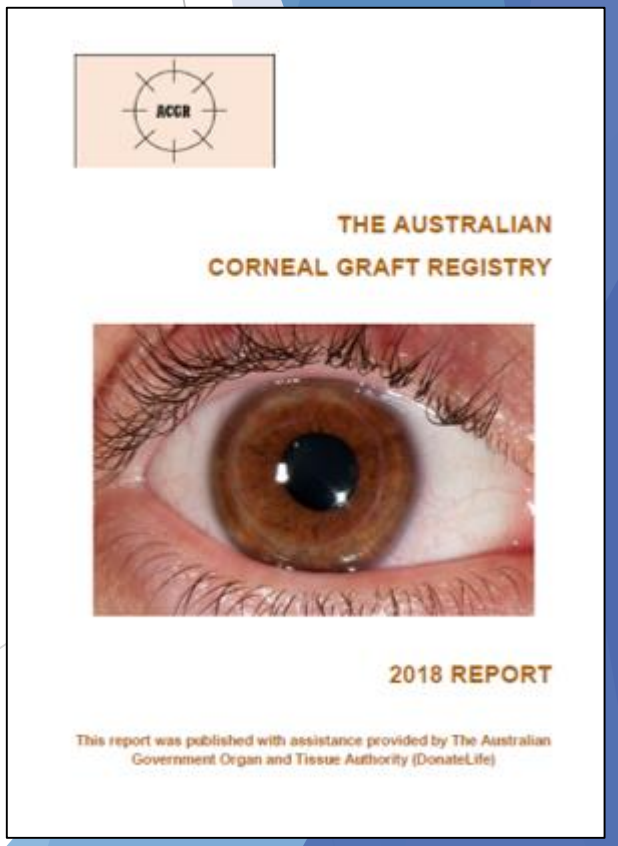
	1999-2003	2004-2008	2009-2013	2014-2018
PK	6/36	6/36	6/36	6/60
DS(A)EK	NA	6/36	6/24	6/18
DMEK	NA	NA	6/24	6/18
Total	6/36	6/36	6/24	6/18

- Highlights the difficulty of comparing like with like



Comparing Like with Like?

- Individual analyses split by graft type
- Outcomes for individual indications for graft
- Comparing pre and post visual outcomes
- Multivariate analyses
- What we aim to do in our major reports
  - Latest report in 2018
  - Analysed data collected to 31st July 2017



Results from The Australian Corneal Graft Registry 2018 Report

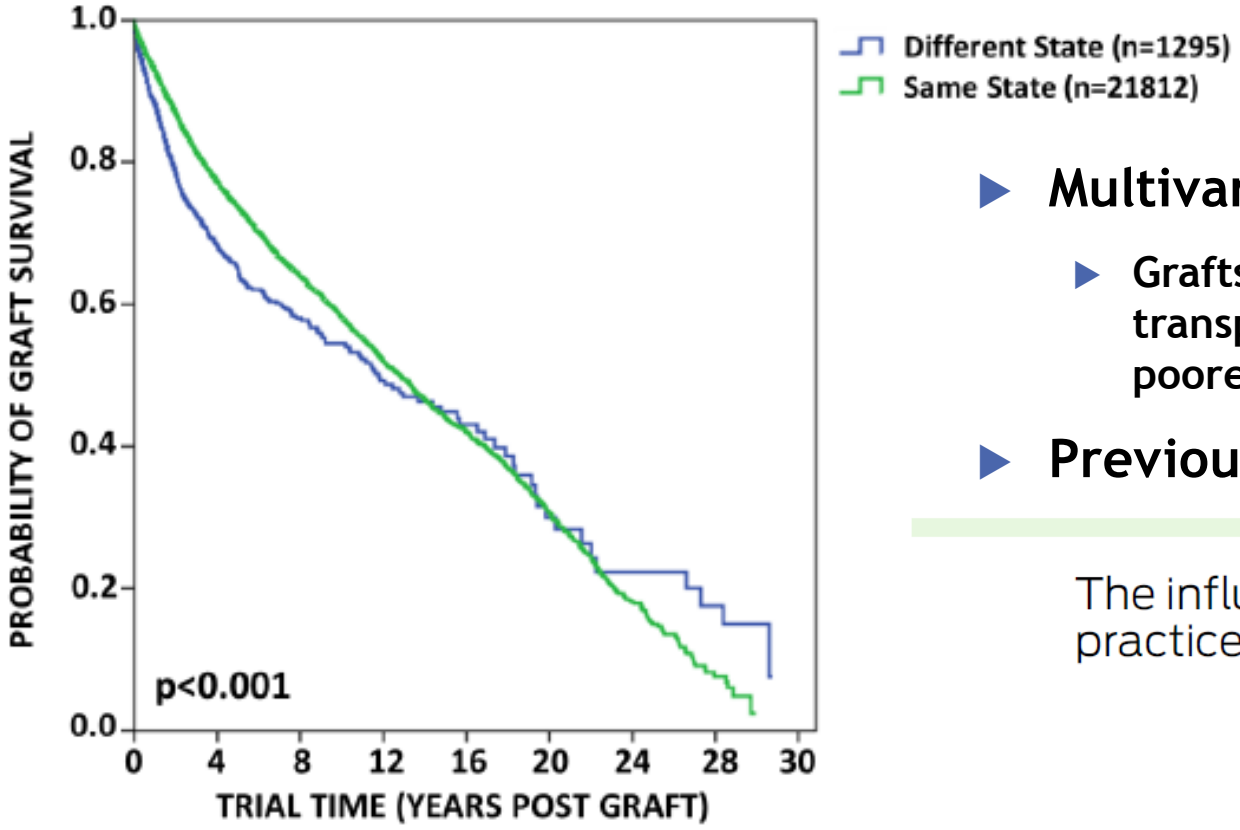
Results from The ACGR 2018 Report

- PK multivariate analysis results
  - Indication for graft
  - Donor age group
  - Donor/recipient sex match/mismatch
  - Interstate transportation of donor corneas
  - Pre-graft raised intraocular pressure
  - Pre-graft inflammation and/or steroid use
  - Pre-graft corneal neovascularisation
  - Graft size
  - Number of previous grafts in other eye
  - Lens status pre/post graft
  - Graft era
  - Volume of PK registered by surgeon and level of follow-up
  - Post-graft corneal neovascularisation
  - Post-graft herpetic infection
  - Post-graft microbial keratitis
  - Post-graft rise in intraocular pressure
  - Post-graft rejection episode/s

Results from The ACGR 2018 Report

- PK multivariate analysis results
  - Indication for graft
  - Donor age group
  - Donor/recipient sex match/mismatch
  - Interstate transportation of donor cornea
  - Pre-graft raised intraocular pressure
  - Pre-graft inflammation and/or steroid use
  - Pre-graft corneal neovascularisation
  - Graft size
  - Number of previous grafts in other eye
  - Lens status pre/post graft
  - Graft era
  - Volume of PK registered by surgeon and level of follow-up
  - Post-graft corneal neovascularisation
  - Post-graft herpetic infection
  - Post-graft microbial keratitis
  - Post-graft rise in intraocular pressure
  - Post-graft rejection episode/s

PK – Interstate Transportation of Cornea



- **Multivariate confirmed**
  - **Grafts performed with corneas transported interstate had significantly poorer survival (p<0.001)**
- **Previously reported by us**

Research

The influence of Australian eye banking practices on corneal graft survival

Miriam C Keane BPsych(Hons), PhD, Research Associate[1]
Marie T Lowe BSc, Research Assistant[1]
Douglas J Coster MB BS, DSc, FRANZCO, Emeritus Professor[1]
Graeme A Pollock PhD, MPH, Director, Lions Eye Donation Service[2]
Keryn A Williams PhD, Professor[1]

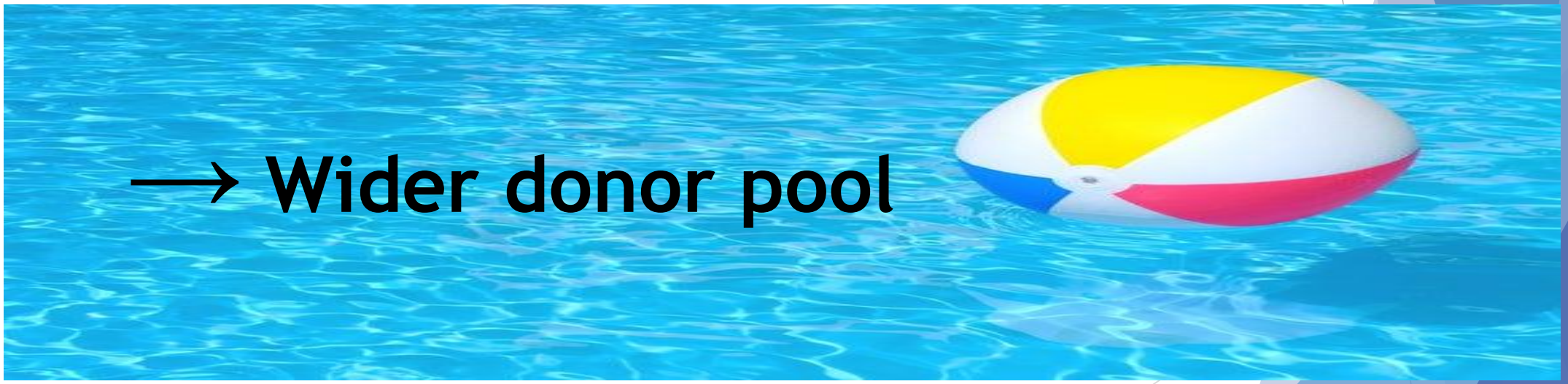
1 Department of Ophthalmology, Flinders University, Adelaide, SA.
2 Centre for Eye Research Australia, University of Melbourne, Melbourne, VIC.
miriam.keane@flinders.edu.au

MJA 2013; 199: 275–279
doi: 10.5694/mja12.11584

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

Negative Results Also a Positive

- Older donors provide viable corneas
- Cause of donor death does not affect graft survival
- Time from donor death to enucleation of eye extended
  - Up to 24 hours



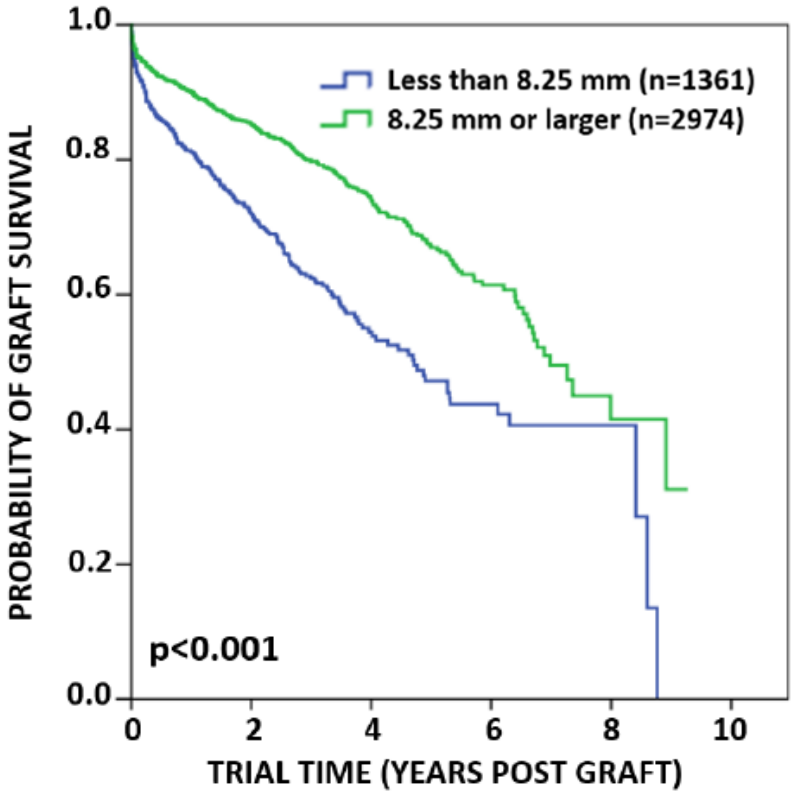
Results from The ACGR 2018 Report

- DS(A)EK multivariate analysis results
  - Indication for graft
  - Donor age group
  - Central endothelial cell count
  - Australian State where performed
  - Pre-graft raised intraocular pressure
  - Recipient sex
  - Graft size
  - Incision size
  - Graft Year
  - Lens status pre/post graft
  - Volume of PK registered by surgeon and level of follow-up
  - Post-graft corneal neovascularisation
  - Post-graft rise in intraocular pressure
  - Post-graft rejection episode/s

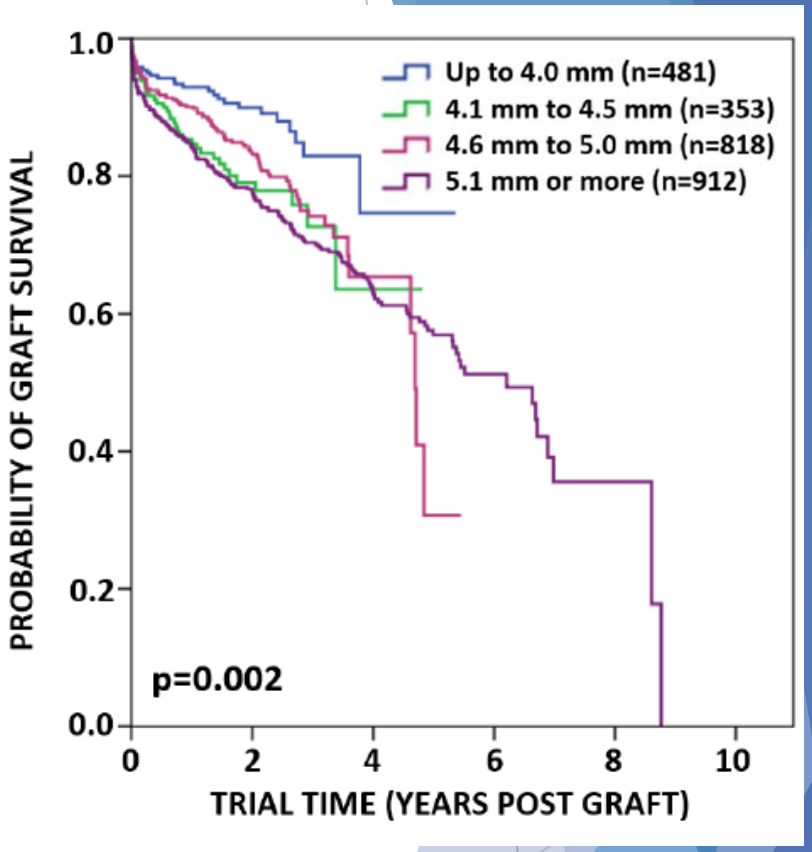
Results from The ACGR 2018 Report

- DS(A)EK multivariate analysis results
  - Indication for graft
  - Donor age group
  - Central endothelial cell count
  - Australian State where performed
  - Pre-graft raised intraocular pressure
  - Recipient sex
  - Graft size
  - Incision size
  - Graft Year
  - Lens status pre/post graft
  - Volume of PK registered by surgeon and level of follow-up
  - Post-graft corneal neovascularisation
  - Post-graft rise in intraocular pressure
  - Post-graft rejection episode/s

DS(A)EK – Graft and Incision Sizes



- Hazard ratio for smaller grafts 1.63
- Largest incision group has poorest survival
- Steady reduction in % in this group
  - 100% pre 2011, 20% since 2014
- May be uncontrollable factors involved



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

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

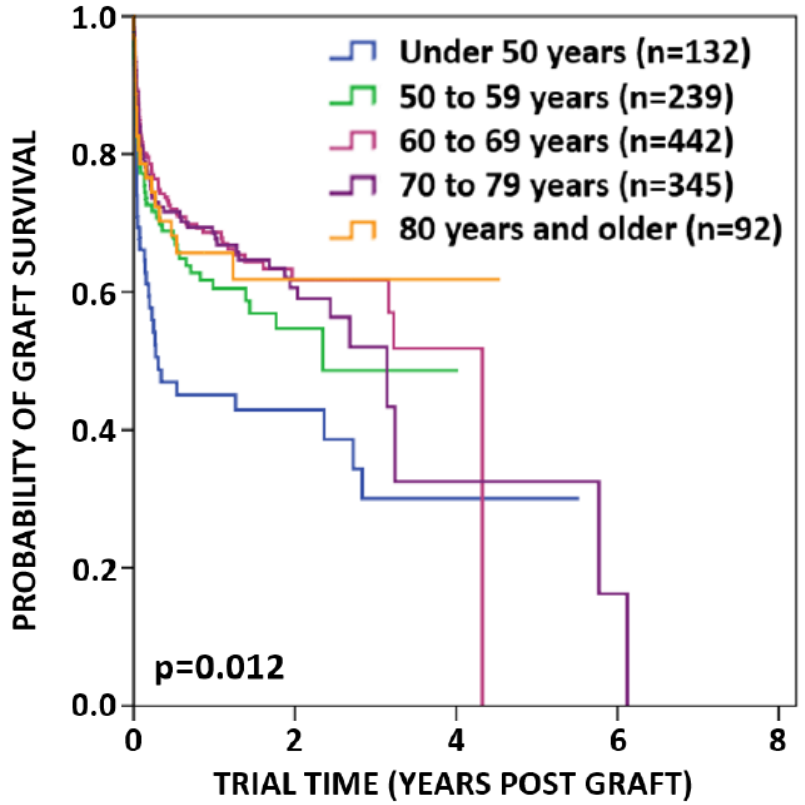
Results from The ACGR 2018 Report

- DMEK multivariate analysis results
  - Donor age group
  - Cornea pre-cut by eye bank
  - Recipient age group
  - Graft year
  - Australian State where performed

Results from The ACGR 2018 Report

- DMEK multivariate analysis results
  - Donor age group
  - Cornea pre-cut by eye bank
  - Recipient age group
  - Graft year
  - Australian State where performed

Results from The ACGR 2018 Report



	1	2	3	4	5
Under 50 years	23	11	6	1	1
50 to 59 years	51	16	4	1	NA
60 to 69 years	102	37	13	1	NA
70 to 79 years	81	41	7	3	2
80 years and older	19	9	2	1	NA

- <50 significantly poorer
  - 60 - 69 and 70 - 79
  - More recent analyses also found a difference for <50 vs. 50 - 59
- No significant differences between other groups
- Adds evidence to reports of surgeon experience
- Only 1% of DMEK donors in 2018 were under 50
  - Down from 15-17%

The Future

- Current publications being written on
  - Infections
  - Corneal dystrophies
- Annual feedback with stakeholders
- Community engagement
- New techniques continue to be developed
- Continued increase in grafts?
  - Increase in data
  - Increase in analyses
  - Increase in impact

Acknowledgments

- DonateLife – The Australian Government Organ and Tissue Authority
- Contributing surgeons, eye banks and follow-up practitioners

- Our team
  - Miriam Keane – Executive Director
  - Nora Coffey – Project Officer
  - Vicky Jones – Administrative Officer
  - Keryn Williams – Scientific Director
  - Richard Mills – Medical Director

Australian Corneal Graft Registry

Phone: 08 8204 5321

Email: miriam.keane@flinders.edu.au

2018 report: http://hdl.handle.net/2328/37917