

The Belgian Endothelial Surgical Transplantation of the Cornea Study

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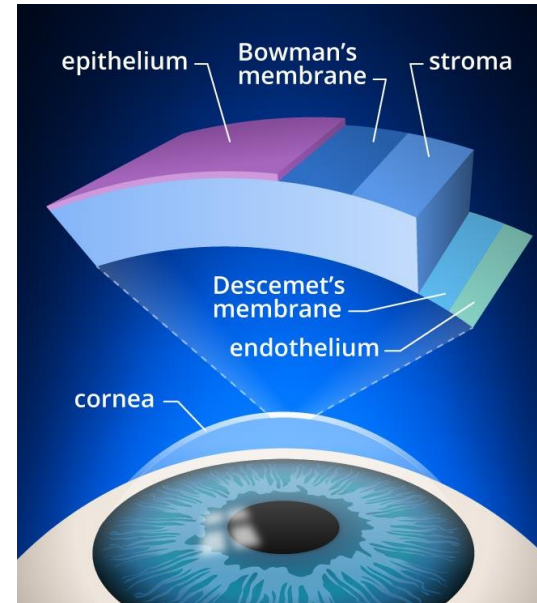
4th KCE Clinical Trials Symposium
Brussels 25th of May 2023

Introduction



Building a clinical trial from scratch

- Like many of us, COVID 19 gave me some time to think and read
- Pick something fascinating – this enthusiasm has to sustain you
- In surgery we strive for technical perfection of what is.
- In research and innovation we work on what will be.



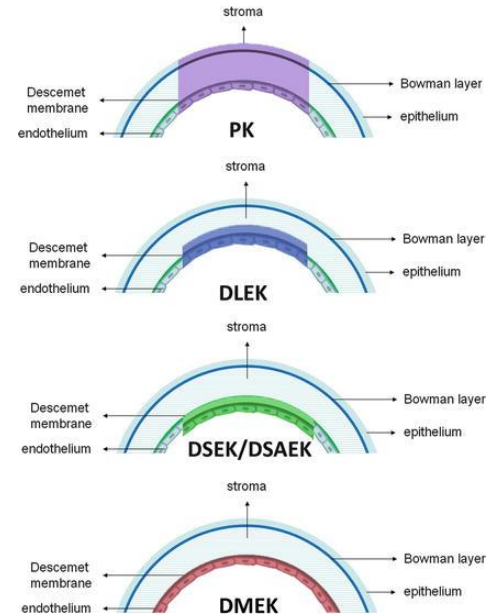
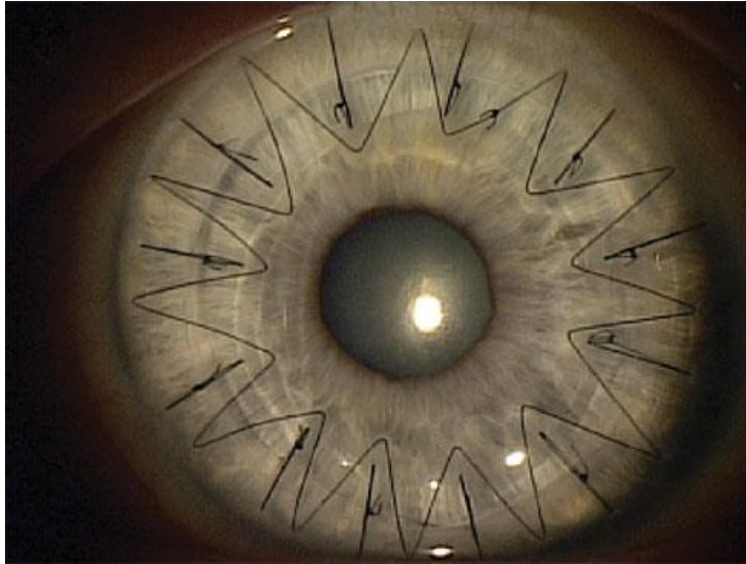
Rationale



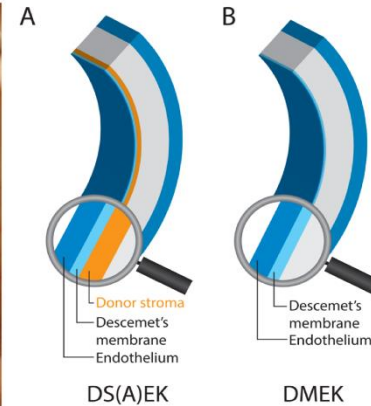
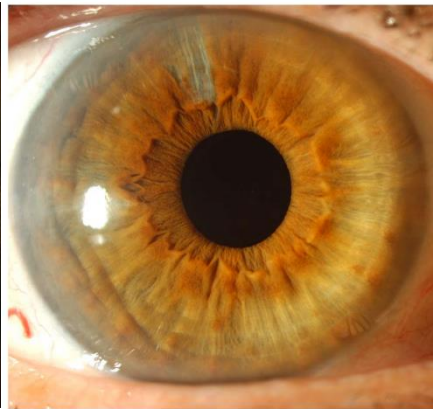
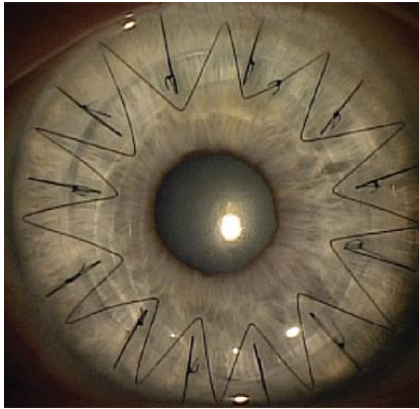
Two main diseases:

- Fuchs endothelial dystrophy (FECD) 80%
- Pseudophakic bullous keratopathy (PBK) 20% (Increase in IOL exchanges and multi surgery)

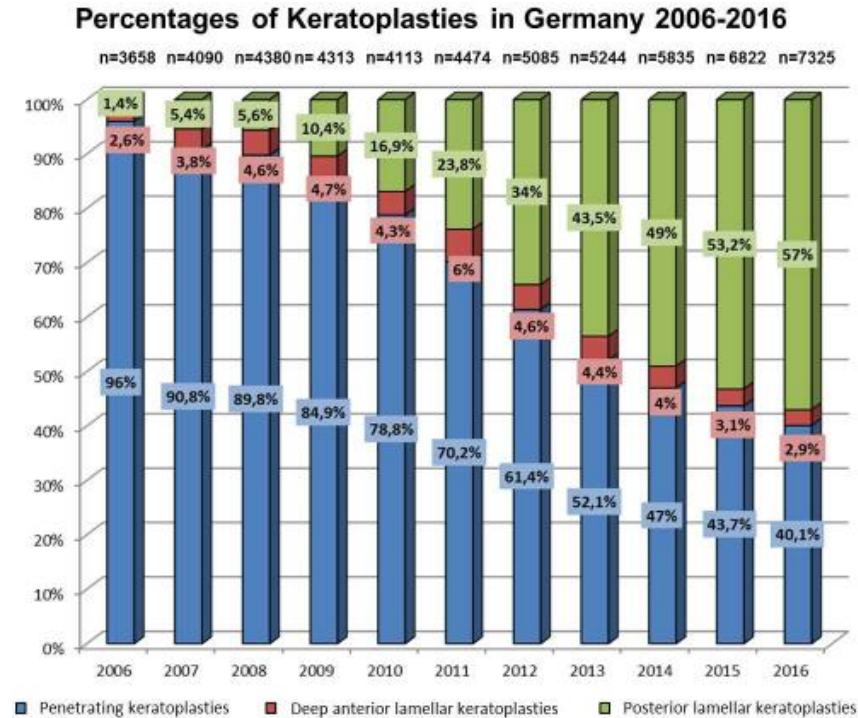
Evolution in corneal transplantation



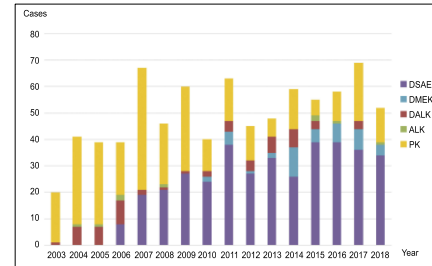
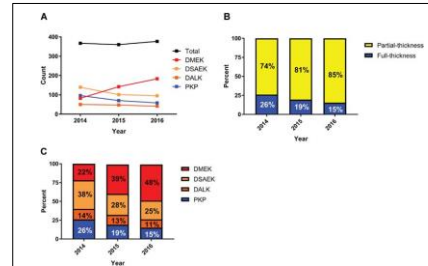
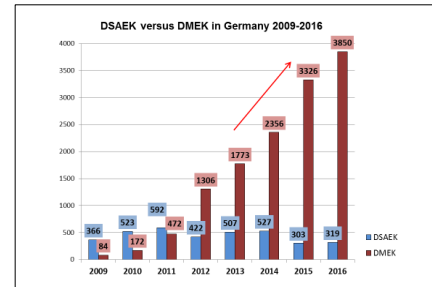
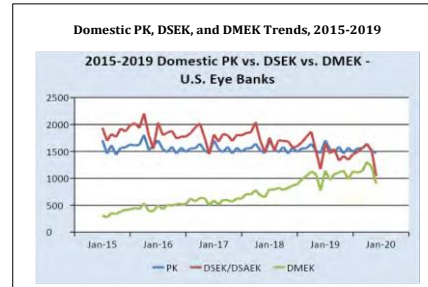
A short history of corneal transplants



Question



Question



Pros and Cons

	UT- DSAEK	DMEK
Composition	Endothelium, Descemet membrane and stoma	Endothelium and Descemet membrane
Thickness	Variable 70-200µm	10-15µm
Surgery	Technically straightforward	More difficult, longer learning curve
Complications	Lower[10]	Higher (rebubble or intervention)[10]
Endothelial Cell Density	No difference	No difference
BCVA	Reported to be lower (disputed)	Reported to be higher (disputed)
Recovery time	Slower	Faster
Cost of surgery	?	?
Donor tissue efficiency	1:1 donor: recipient.	Possibility for split graft 1:2 donor: recipient.[11]
Rejection risk	More donor APCs 7.9% rejection over 5 years [12]	Fewer donor APCs 2.5% rejection over 5 years [13, 14]

But hasn't this been studied?



Descemet Endothelial Thickness Comparison Trial

A Randomized Trial Comparing Ultrathin Descemet Stripping Automated Endothelial Keratoplasty with Descemet Membrane Endothelial Keratoplasty

Winston Chamberlain, MD, PhD,¹ Charles C. Lin, MD,² Ariana Austin, MS,³ Nicholas Schubach,¹ Jameson Clover,¹ Stephen D. McLeod, MD,¹ Francis C. Porco, PhD, MPH,^{1,2} Thomas M. Lietman, MD,^{2,3,6} Jennifer Rose-Nussbaumer, MD^{1,2}



Descemet Membrane Endothelial Keratoplasty versus Ultrathin Descemet Stripping Automated Endothelial Keratoplasty

A Multicenter Randomized Controlled Clinical Trial

Suryan L. Durrer, MD,¹ Mor M. Dickman, MD, PhD,^{1,2} Robert P.L. Wisse, MD, PhD,³ Stamatios Nibacht, MD,⁴ Robert H.J. Wijdh, MD,⁵ Marjolijn C. Bartels, MD, PhD,⁶ Mei L. Tang, MD,¹ Frank J.H.M. van den Biggelaar, PhD,¹ Pieter J. Kruijt, MD, PhD,⁶ Rudy M.M.A. Nuijts, MD, PhD^{1,2}

- Do your literature review.
- Three RCTs reported from 2019 and 2022 – US/UK/The Netherlands
- No pragmatic RCT design, cherry picking of cases, little inclusion of bullous keratopathy (n=1), small numbers, DSAEK procedure not reflective of “real world”

The Question

Which corneal transplantation technique, DSAEK or DMEK, provides the best clinical and patient reported outcomes in real-life patients in Belgium?

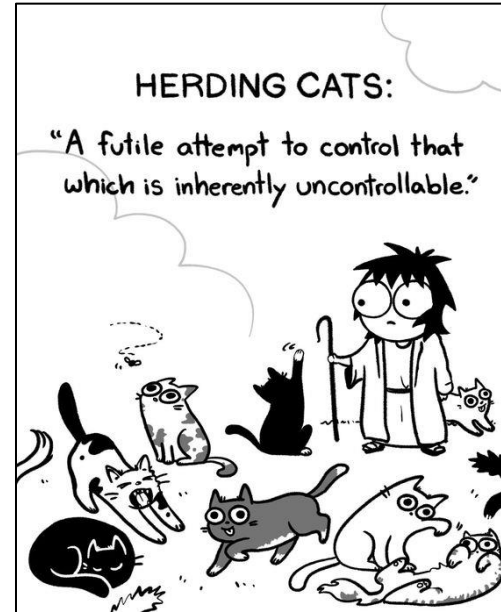
A pragmatic Clinical Trial

First – Get an Acronym



The Belgian Endothelial Surgical Transplantation of the Cornea Study:
The “BEST” Cornea Study

Building a consortium



Suddenly it gets real

KCE TRIALS PROGRAMME



Trials Board decision letter

2020 Investigator-led call, Trials Board Meeting 12 January 2021

15 January 2021

Dear Sorcha Ní Dhubhghaill,

Project no and title: INV20-1254, The Belgian Endothelial Surgical Transplant of the Cornea (BEST Cornea)
Study: Clinical and Patient-Reported Outcomes of Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) versus Descemet Membrane Endothelial Keratoplasty: A Randomised, Multicentre, Parallel Group Pragmatic Trial in Corneal Endothelial Decompensation., status Research Outline

Decision: Invited to Submit a Full Research proposal (FRP)

The Belgian Endothelial Surgical Transplantation of the Cornea Study: The “BEST” Cornea Study



KCE-201254: A Randomised Multicentric Parallel Group
Pragmatic trial of Descemet Stripping Automated Endothelial
Keratoplasty (DSAEK) versus Descemet Membrane Endothelial
Keratoplasty (DMEK) in Corneal Endothelial Decompensation



Study Objectives

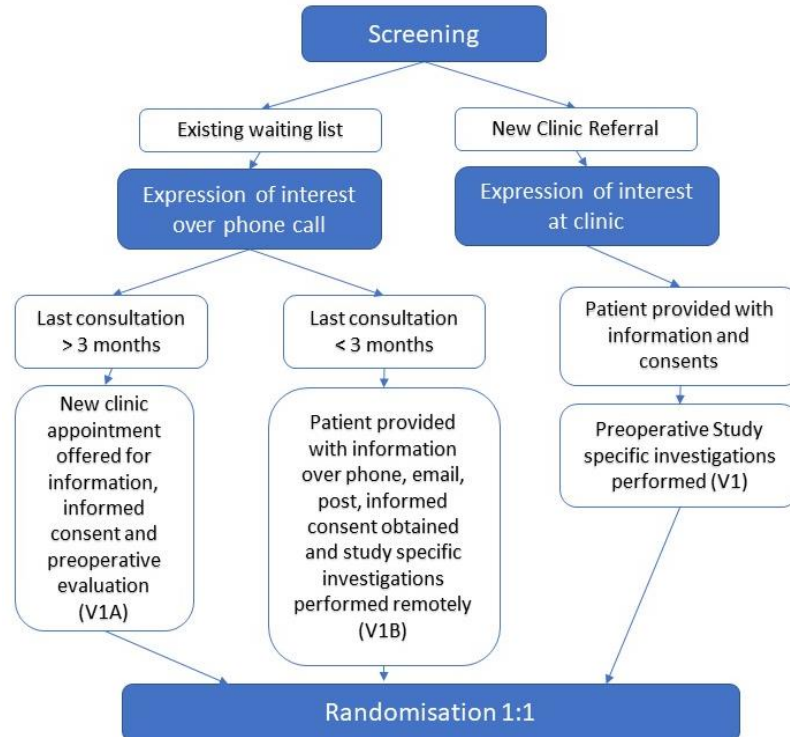
Primary endpoints

This study's primary outcome is to report on the change in BCVA, represented in LogMAR units, compared with baseline at **12 months** after DSAEK and DMEK.

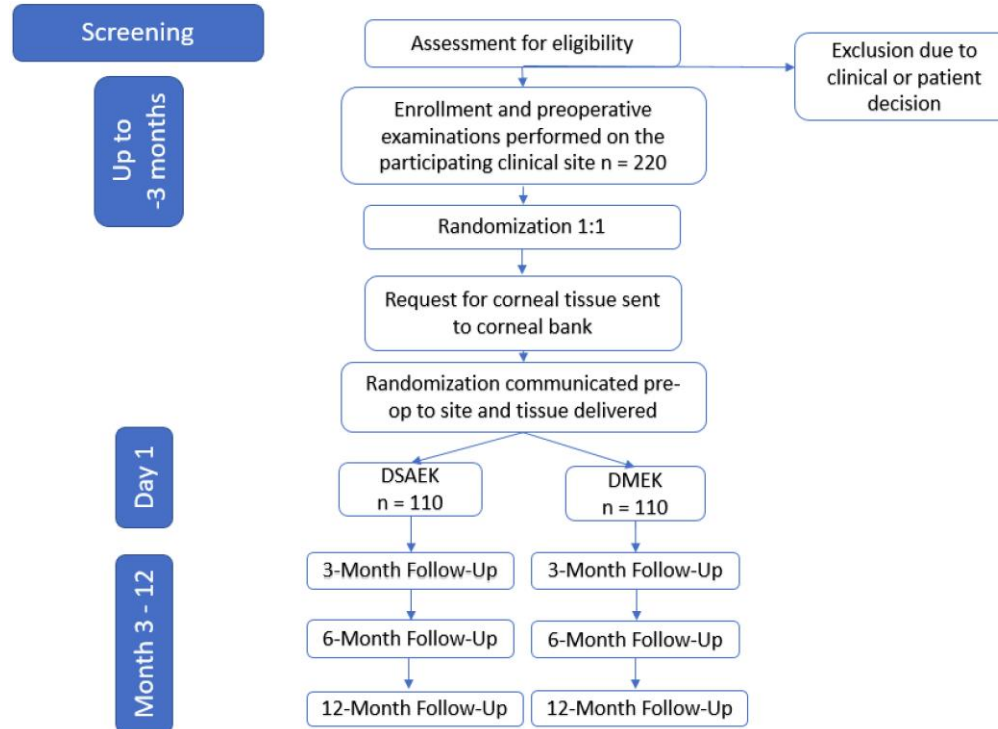
Secondary endpoints

- Change in BCVA at 3 and 6 months between DSAEK and DMEK;
- Change in UCVA at 3, 6, and 12-months between DSAEK and DMEK;
- Change in refraction at 3, 6, and 12-months between DSAEK and DMEK;
- Proportion of patients to achieve 0.2 LogMAR visual acuity or less (i.e., better vision) at 3, 6, and 12 months;
- Change in quality of life determined by the EQ-5D-5L questionnaire instrument at 3, 6, and 12 months between DSAEK and DMEK;
- Change in vision related quality of life determined by the VFQ25 item questionnaire instrument at 3, 6, and 12-months between DSAEK and DMEK;
- **Endothelial Cell Count (ECC) between DSAEK and DMEK at 3, 6, and 12 months;**
- Change in Central Corneal Thickness from baseline (pachymetry) at 3, 6, and 12 months;
- Complications and adverse events between DSAEK and DMEK (e.g. iatrogenic glaucoma, primary graft failure, rebubbling etc).

Adaptation for waiting lists



Flow Chart Overview of BEST Cornea



Developing a full protocol



UZA Sponsor CTC/Ophthalmology Team



Veerle Van
Gerwen
Project Manager
Study/Research
Coordinator BEST
Cornea



Ann Deconinck
Project Manager
BEST Cornea



Iris Verhaegen
Clinical Trial
Coordinator



Kristien Wouters
Statistician



Kim Claes
Data Manager



Elke Smits
Head of Science
and Innovation



Sofie Grenier
Administrative
Assistant



Debbie Smet
Administrative
Assistant



Dr Barbara De
Bruyn
ASO - UZA



Mathias Allegaert
Data Monitor



Lynsey Verhoeven
Data Monitor



Dafne Balemans
Data Monitor

Cornea Bank Collaboration



Prof Dr Manon Huizing
Head of Cell/tissue bank
UZA



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Koppen
Medical Director
Cornea Bank
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Nezahat Bostan
Cornea bank
technician UZA



Francisca Leandro
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Prof Dr Bernard
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QA Manager
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Prof Dr Hilde Beele
Head of Cell/tissue bank



Sarah Glorieux
Cornea bank
UZ Gent



Prof Dr Kristel Van Landuyt
Head of Biobank UZL

And many other
cornea bank
colleagues
including:
Nadine Ectors and
all the bank
technicians

TSC International Experts



Dr Silke Oellerich PhD
Head of R+D
Netherlands Institute for
Innovative Ophthalmic Surgery
(NIIOS)



Dr Robert Wisse MD O
Head Corneal Research Group
Utrecht University Hospital
The Netherlands

- 11 Surgical sites
- 14 Participating surgeons
- 4 Cornea banks collaborating
 - CHU DSAEK
 - UZA DMEK
 - UZG and UZL observation and support



Postoperative Medications

BEST Cornea Postoperative Eyedrop Protocol							Version 0.1
All study patients (DSAEK and DMEK) follow the same calendar							
Medication	Recommended dosing scheme						Duration
Combination of 2 medications together or apart (Dexamethasone 0.1% + antibiotic e.g. chloramphenicol or tobramycin)	08:00	12:00	16:00	18:00	20:00	22:00	Postop weeks 1 -4 (inclu
Non-steroidal anti-inflammatory Drug (NSAID)	08:00	12:00	16:00		20:00		Postop weeks 1 -4 (inclu
Topical dexamethasone 0.1%	08:00	12:00	16:00	18:00	20:00		Postop Month 2
Topical dexamethasone 0.1%	08:00		16:00	18:00	20:00		Postop Month 3
Topical dexamethasone 0.1%	08:00		16:00		20:00		Postop Month 4
Topical dexamethasone 0.1%	08:00				20:00		Postop Month 5
Topical dexamethasone 0.1%	08:00						Postop Month 6
AFTER 6 MONTHS OF TREATMENT CONVERT TO TOPICAL Fluorometholone 0.1% FML®							
Fluorometholone 0.1%	08:00		16:00		20:00		Postop month 7 - 8 (inclu
Fluorometholone 0.1%	08:00				20:00		Postop month 9 - 10 (inclu
Fluorometholone 0.1%	08:00						Postop month 11 - 12 (inclu
After 12 months, long term therapy with Fluorometholone 0.1% FML® once a day is recommend but is the decision of patient/physician							

Study Calendar

Belgian Endothelial Surgical Transplant of the Cornea Study Calendar						Version 1.0	
All study patients (DSAEK and DMEK) follow the same calendar							
Study Visits	V1	V1A	V1B	V2	V3	V4	V5
Visit Type	Screening / Inclusion				Post op 3 months	Post op 6 months	Post op 12 months
Timing of visit	Up to 3 months prior to day of surgery			Day 0	Month 3	Month 6	Month 12
Eligibility screening	x	x	x				
Discussion of surgery	x	x	x				
Informed consent	x	x	x				
Randomisation	x*	x*	x*				
Protocol assessments							
Baseline Characteristics	x	x	x				
Surgery				x			
Surgeon questionnaire				x			
UCVA	x	x	x		x	x	x
BCVA	x	x	x		x	x	x
Subjective Refraction	x	x	x		x	x	x
Central Corneal Thickness	x	x	x		x	x	x
EQ-5D-5L questionnaire	x	x	x		x	x	x
VFQ 25 questionnaire	x	x	x		x	x	x
Endothelial Cell Count					x	x	x
Adverse events					Continuous reporting		

x in bold refers to **standard of care** and is not considered as specifically associated with the study

* Randomisation to the DSAEK/DMEK group is performed after the patient is included and then relayed to the corneal bank.

And the Trial Begins...

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Other official information and services: www.belgium.be

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BEST CORNEA: A randomised multicentric parallel group pragmatic trial of Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) versus Descemet Membrane Endothelial Keratoplasty (DMEK) in corneal endothelial decompensation (KCE-201254)

[Summary \(French or Dutch\)](#)

Losing vision at an older age can have a major impact on our ability to look after ourselves, to manage our medical needs, and to preserve our independence and dignity. One of the eye's structures that can become affected is the inner layer of the cornea known as the endothelium. Corneal endothelial dysfunction is a disease that usually affects the elderly. It gradually blurs vision and, if left untreated, can result in a painful and blind eye. Corneal transplantation is the only way to treat this disease. Thankfully, surgical techniques have made major leaps forward in the past decade by replacing the classic thick corneal graft with very thin layers in order to selectively replace the diseased tissue through minimally invasive microsurgery.

Clinical Trial Registration

 U.S. National Library of Medicine

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The Belgian Endothelial Surgical Transplant of the Cornea (BESTCornea)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT05436665

[Recruitment Status](#) ⓘ : Not yet recruiting
[First Posted](#) ⓘ : June 29, 2022
[Last Update Posted](#) ⓘ : July 5, 2022
See [Contacts and Locations](#)

Sponsor:
University Hospital, Antwerp

Collaborator:
Belgium Health Care Knowledge Centre

Information provided by (Responsible Party):
University Hospital, Antwerp

Dashboard as of yesterday



That's the study

- Many thanks for your attention

