

## **Supplementary Online Content**

Gain P, Jullienne R, He Z et al. Global survey of corneal transplantation and eye banking.

eTable 1. The 11 International Congresses Where Corneal Surgeons and Eye Banking Professionals Were Interviewed Face-to-Face.

eTable 2. Grading Used to Determine the Supply/Demand Balance of Each Country and Seven-Group Classification of the Balance Between Procurement and Transplantation Activities.

eFigure: World Map Showing the Leading Indication for Corneal Transplantation Reported by 98 Countries.

eResults

eDiscussion

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. The 11 international congresses where corneal surgeons and eye banking professionals were interviewed face-to-face.**

Congress name	Year (city, country)	Continents chiefly represented
Association for Research in Vision and Ophthalmology	2012 (Fort Lauderdale, USA) 2013 (Seattle, USA)	All
French Society of Ophthalmology	2012 (Paris, France) 2013 (Paris, France)	Europe, North and Central Africa
African symposium hosted by the French Society of Ophthalmology	2012 (Paris, France)	Africa
European Association for Vision and Eye Research	2012 (Nice, France)	Europe
European Cornea Conference	2012 (Cork, Eire)	Europe
European Eye Bank Association	2012 (Zagreb, Croatia)	Europe, Australia
Afro-Asian Council of Ophthalmology	2012 (Istanbul, Turkey)	Africa, Asia
EuCornea	2012 (Milan, Italy) 2013 (Amsterdam, Netherlands)	Europe, USA

**eTable 2. Grading used to determine the supply/demand balance of each country and seven-group classification of the balance between procurement and transplantation activities.**

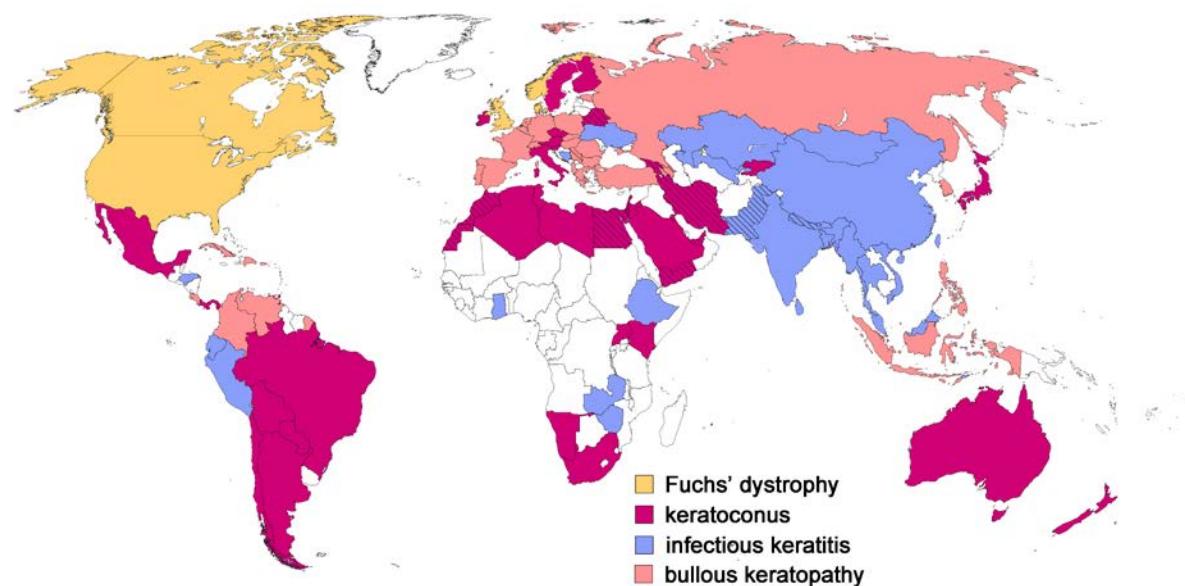
Keratoplasty/million inhab	Interpretation	Points
0-1	Absent or negligible <sup>a</sup>	0
1-5	Very low	1
5-10	Lower half	2
10-19	Between median numbers of CT <sup>b</sup>	3
19-50	Upper half	4
>50	Very high	5
Procurements/million inhab	interpretation	points
0	Absent	0
>0-4	Almost negligible	1
>4-15	Insufficient	2
>15-30	Around the worldwide median <sup>c</sup>	3
>30-60	Sufficient	4
>60	Very high	5
Exports		
	Bonus for significant exports	+1
Overall grading	Characteristics	
null	Absolutely no procurement/grafting activity recensed	0
embryonic	Marginal activity	1 and 2
not sufficient	Significant activity but demand very far from met	3, 4, and 5
adequate	Demand partly met	6 and 7
almost sufficient	With moderate changes, national needs could be met	8 and 9
self sufficient (non-exporter)	Meets needs of its population	10
exporter	Meets needs of its population AND has an active, constant export programme	11

a. deemed null; mostly isolated humanitarian missions

b. the median number of CTs for all countries was 10; and, for the subgroup of countries doing CT, was 19/million inhab.

c. the global median was 25 for the 82 countries that performed procurement

**eFigure:** World map showing the leading indication for corneal transplantation reported by 98 countries



Hatched bars indicate countries for which we deemed the data of questionable robustness. The boundaries and names shown on this map do not imply the expression of any opinion whatsoever by the authors regarding the legal status of any country or territory or its authorities or regarding the delimitation of frontiers or boundaries.

## **eResults**

### **Transplantation**

On a regional basis, considering all the countries (performing CT or not), the median rate per million inhabitants was: Africa 0, Asia 4, Middle East 16, South America 19, Europe 30, Oceania 58, and North and Central America 43.

List of the 31 countries performing less than 5.10-6 CTs per capita (by alphabetic order): Afghanistan, Albania, Bangladesh, Bhutan, Bosnia and Herzegovina, Burkina Faso, Burma, Burundi, Cambodia, China, East Timor, Ethiopia, Guatemala, Ghana, Haiti, Indonesia, Iraq, Ivory Coast, Kenya, Kyrgyzstan, Mongolia, Nigeria, Papua New Guinea, Peru, Philippines, Senegal, Tanzania, Uganda, Uzbekistan, Vietnam, Zambia.

List of the 32 countries performing no CTs (by alphabetic order): Angola, Benin, Botswana, Cameroon, Central African Republic, Chad, Democratic Republic of the Congo, Eritrea, Gabon, Gambia, Guinea, Guinea Bissau, Jamaica, Kosovo, Laos, Lesotho, Liberia, Macedonia, Madagascar, Malawi, Mali, Mauritania, Mozambique, Niger, Republic of the Congo, Rwanda, Sierra Leone, Somalia, South Sudan, Sudan, Swaziland, Togo.

#### Type of keratoplasty

Twenty-four countries (25%) reported that lamellar grafts made up 1-10% of their activity, and seven (7%) reported that lamellar grafts made up 50% or more of their activity. The highest ratios of lamellar grafts were 73%, 70%, 60% and 60% in Singapore, Denmark, Switzerland, and Norway respectively.

#### Indications

Ninety-eight countries reported their indications. The leading reported indication was keratoconus (a frequent corneal disease affecting young people, which slowly deforms the cornea) in 40 countries (41%), secondary bullous keratopathy (an iatrogenic corneal oedema following some cataract or refractive operations) in 29 countries (30%), sequelae of infectious keratitis in 24 countries (24%), Fuchs' dystrophy (a primary disease affecting the posterior endothelial layer of the cornea and leading to permanent oedema) in five countries (5%) (eFigure). Given the number of grafts performed in each country, although we did not obtain the exact distribution of each indication, we can assume that Fuchs' dystrophy was the leading indication worldwide (first in the USA, Canada, the UK, Denmark, and Norway, which performed 39% of all grafts (71831/184675)), followed by keratoconus (first in countries performing 27% (48850) of all grafts), sequelae of infectious keratitis (20%, 36450), and secondary bullous keratopathy (15%, 27034) (data missing for only 506 grafts). Of the 116 transplant-performing countries, 100 reported their top three indications. For four countries totalling 68561 transplants the top three were bullous keratopathy/Fuchs'/regraft, for 40 countries (67335 transplants in total) they were bullous keratopathy/keratoconus/infectious keratitis, for 15 countries (19253) they were bullous keratopathy/keratoconus/Fuchs', and for seven countries (7474) they were bullous keratopathy/keratoconus/regraft.

### **Cornea procurement and eye banking**

By continent, the number of corneas procured for a number of corresponding eye banks was distributed as follows: 1273/11 (=116) in Africa, 54378/396 (=137) in Asia, 57809/118

(=490) in Europe, 10057/25 (=402) in the Middle East, 125558/110 (=1141) in North and Central America, 2292/6 (=382) in Oceania and 32163/77 (=418) in South America. Considering the 82 countries where corneas were procured, on a regional basis, the rate of procurement per million inhabitants was: Africa 3, Asia 16, Middle East 47, Europe 80, South America 84, Oceania 85, and North and Central America 253. In proportion to the population of all countries studied (n=148), on a regional basis, it was: Africa 1, Asia 14, Middle East 32, Europe 78, South America 82, Oceania 70, and North and Central America 231.

### **Cornea exports**

In addition to the USA, Sri Lanka and Italy, the other exporting countries were the Philippines, the Netherlands, the Czech Republic, France, Australia, and Colombia (by decreasing number of exported corneas ranging from 588 to 17). Unlike the other exporters, the Philippines exported more than half of its procured corneas, while performing only 4 CTs per million inhabitants.

### **Procurement methods and storage**

Forty countries procured corneas exclusively (n=34) or mostly (n=6) by corneo-scleral rim excision, representing 50% of corneas worldwide, while 24 countries procured corneas exclusively (n=20) or mostly (n=4) by enucleation, representing 14% of corneas. Twelve countries, which procured 36% of corneas, used both techniques. There was no data for six countries, representing less than 1% of corneas. Sixty-eight of the 82 countries reported the maximum authorised time between death and procurement, with a median of 12 hours (6-72). This post-mortem time and the rate of CPs per million inhabitants were unrelated (Spearman's Rho = 0.19). For the top four cornea-procuring countries, the maximum time was 6 hours in India (40000 CPs, 35/m/inhab), 12 hours in the USA (117000, 366), 12 hours in Italy (15000, 248), and 24 hours in Brazil (27000, 135). Eighty-three percent of corneas were stored hypothermically and 17% were processed in organ culture, mainly in Europe, Australia, and New Zealand. Ninety-two percent of corneas were procured from non heart-beating donors (the remainder from multi-organ donors). In 18 countries (68% of all procured corneas), eye banks' pre-cut corneas were available for lamellar keratoplasty (USA, Brazil, Iran, China, Italy, UK, Spain, Japan, Australia, The Netherlands, Dominican Republic, Sweden, Czech Republic, Singapore, Denmark, New Zealand, Greece, Paraguay).

## **eDiscussion**

Infectious keratitis (IK) is the most frequent blinding corneal disease in most developing countries, and 80% of IK cases can be treated preventively or curatively.<sup>1</sup> This is true of trachoma<sup>2</sup>, endemic to 53 countries<sup>3</sup> with the highest corneal-blindness rates. However, IK is not always the leading indication of CT in these countries because its post-transplant prognosis can be poor. IK is the third-ranking indication (by number of countries and of transplant patients), so ophthalmologists likely keep their limited donor corneas for patients with keratoconus, which mostly affects young working people and has a consistently excellent long-term visual prognosis.

In affluent countries, the top two indications are iatrogenic bullous dystrophies (irreversible corneal oedema after some eye operations) or Fuchs' dystrophy, a frequent disease which threatens 4% of people aged over 40 in the USA but typically only decompensates from 60-70 years onwards. Notably, the latter disease is the leading indication of CT in only five countries, but as one of these is the USA it is also the leading indication overall by number of CTs. It is also notable that regrafts are also a leading indication in these countries. Several factors limit donor-cornea lifetime: reduction at varying speeds of the number of endothelial cells, immune rejection,<sup>4</sup> and initial disease reoccurrence. Actively fighting these phenomena is another way to reduce tissue demand.

We identified 284000 procured corneas. The 100000 non-transplanted corneas (35%) reflect how tissues are selected by eye banks. Although the complexity of controls and resources for surgery probably differ between countries, minimum standards exist. They are based mainly on serological testing of donor blood (HIV and hepatitis B and C, at least) and on *in situ* counting of endothelial cells under a microscope. As these cells cannot divide, a minimum level (around 2000 cells/mm<sup>2</sup>) is essential to avoid primary failure and ensure acceptable graft survival over time. In affluent countries that use the organ-culture technique at 31°C for long-term tissue storage, there are more controls, including microbiological analysis to reduce the risk of direct transmission of bacteria or fungi liable to cause endophthalmitis. Any additional quality control reduces the proportion of eligible corneas.



## **eReferences**

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