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### Title

Challenges of ophthalmic care in the developing world.

### Permalink

<https://escholarship.org/uc/item/2cv076tg>

### Journal

JAMA ophthalmology, 132(5)

### ISSN

2168-6165

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### Publication Date

2014-05-01

### DOI

10.1001/jamaophthalmol.2014.84

Peer reviewed



Published in final edited form as:

*JAMA Ophthalmol.* 2014 May ; 132(5): 640–644. doi:10.1001/jamaophthalmol.2014.84.

## Challenges of Ophthalmic Care in the Developing World

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### Abstract

Global blindness exacts an enormous financial and social cost on developing countries. Reducing the prevalence of blindness globally requires a set of strategies that are different from those typically employed in developed countries. This was the subject of the 2013 Knapp symposium at the American Ophthalmological Society Annual Meeting, and this article summarizes the presentations of epidemiologists, health care planners, and ophthalmologists. It explores a range of successful strategies from the multinational Vision 2020 Initiative to disease-specific schemes in cataract, trachoma control, infectious corneal ulceration, cytomegalovirus retinitis, and retinopathy of prematurity. In each example, the importance of an attitudinal set towards the public health becomes clear. There is reason for optimism in the struggle against global blindness, in large measure because of innovative programs like those described here.

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Poor people in the developing world suffer far more blindness and visual impairment than wealthier populations. This is largely due to the persistence of diseases that no longer occur in wealthy countries, like trachoma, xerophthalmia and Onchocerciasis (“river blindness”); from diseases particularly prevalent and un- or under-treated, like corneal infections and HIV-related CMV retinitis; and from a lack of access to ophthalmic services for those conditions that occur commonly among both rich and poor populations (e.g. glaucoma, diabetes, retinopathy of prematurity and un-operated cataract). As a result, rates of blindness (defined by the World Health Organization as vision of less than 20/400 in the better eye) in wealthy countries are commonly below 0.5 percent; sometimes much lower. Blindness rates in many poor countries exceed 1–2 percent. Reduced (but not officially “blinding”) acuity

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None of the other authors had conflicts of interest to disclose.

(20/60 to 20/100) that can seriously impair personal functioning, including employment, is at least 6 times more common than blindness. As a result, roughly 30 million people, mostly in the poorer countries of the world are (to a large degree unnecessarily) blind, and 200 million more are unable to participate fully in the workforce.

Research into the cause and prevention of three major blinding diseases, xerophthalmia, river blindness (*Onchocerciasis*), and trachoma, have yielded cost-effective programs that can virtually eliminate these entities through population-based public health interventions. Only a tiny portion of afflicted individuals require the attention of an ophthalmologist, since these three diseases are entirely preventable through periodic mass dosing of the populations at risk (a single, large-dose vitamin A supplement, twice a year to children 6 months-5 years of age in deficient populations; a single annual dose of ivermectin to individuals in communities infected with *Onchocerca volvulus*; and a single dose of azithromycin once or twice a year (with other components of the “SAFE” strategy) to communities harboring endemic trachoma. These programs are largely carried out by community-based health workers requiring minimal training.

Other major causes of avoidable blindness stem from the lack of access to effective ophthalmic services, such as cataract surgery, the screening for, and treatment of, diabetic retinopathy, or retinopathy of prematurity. Systematic approaches to deliver high quality, efficient and low-cost cataract surgery have sprung up around the world, dramatically increasing cataract surgical rates where they have been instituted. This has begun to blunt the rise in blindness rates anticipated from the growth and aging of the world’s population.

“Newer” blinding problems disproportionately afflict the developing world, such as CMV retinitis and retinopathy of prematurity, partly because of the dearth of skilled ophthalmic examiners capable of making early diagnoses and acting upon them. New, low cost, innovative techniques for imaging the retina may soon allow relatively low-skilled, but well trained technicians to capture these images and forward them digitally to referral centers for diagnosis and appropriate referral.

Vision 2020, *The Right to Sight*, an advocacy and organizing initiative of the International Agency for the Prevention of Blindness (IAPB) and the World Health Organization (WHO), leads the global fight against avoidable blindness. But a good deal more can and needs to be done. This white paper highlights what some of these efforts might be, and the important role that ophthalmology must continue to play in advancing our understanding and approaches to preventing ocular disease, and developing innovative approaches for providing ophthalmic services to underserved populations.

## The Vision 2020 Initiative

Recognizing that at least 75% of blindness was unnecessary and could be reduced dramatically, the WHO and IAPB together launched the ambitious initiative Vision 2020: The Right to Sight in 1999. Its goal was to eliminate avoidable blindness by the year 2020 in order to give all people in the world the right to sight.<sup>1</sup> The IAPB is the peak body that brings together all the non-government organizations working on eye care and blindness and WHO represents the world’s governments. Together they have been working with national

partners to develop national eye care plans and institute and implement sustainable eye care programs. Vision 2020 focuses on effective disease control, human resource development and the development of the appropriate infrastructure and resources. It also recognizes the need for affordable and accessible eye services that provide quality outcomes and that are provided equitably.

There has been a revolution in the provision of cataract surgery with modern small incision IOL surgery being done at increasing rates around the world. Equally tremendous progress is being made in the management of childhood blindness including xerophthalmia, trachoma and onchocerciasis. Increasingly, fashionable low-cost spectacles are available through outreach refraction services that are being built both by eye care programs and by private practice.

Co-ordination and integration of services from the primary, secondary and tertiary level has been seen as the key to effective eye care services. Many areas use outreach or visiting services so well developed in the Aravind model<sup>2</sup> and by the LV Prasad Eye Institute.<sup>3</sup> The latter builds on “vision centers” at a village level that provide basic eye care including refraction services, with good supervision and referral links to secondary district level facilities where cataract surgery can be performed. These in turn are linked to regional tertiary eye care centers that provide more advanced services, training and supervision.

Blindness has a dramatic economic impact on the individual, their family and their community.<sup>4</sup> Many have recognized that blindness causes poverty and poverty causes blindness. Equally, many of the individual eye care interventions have been shown to be extremely cost effective with a four-fold return for every dollar spent developing eye care in developing countries.<sup>5</sup>

The good news is that we are actually making extraordinary progress in reducing the amount of blindness world wide.<sup>6</sup> A recent analysis finds that the age-adjusted prevalence of blindness from all causes has dropped some 58% over the last 20 years. This clearly shows we know what to do, we know how to do it and when we do it, it works. We are on the right track. Equally, however there is still much work that needs to be done to eliminate unnecessary blindness. In May 2013, the World Health Assembly approved a new five-year action plan to continue this work so that we can aspire to reach the goal of Vision 2020.<sup>7</sup>

## **Cataract blindness--a systems approach**

Cataract accounts for 20 million blind people world-wide but disproportionately over 50% of blindness in developing countries.<sup>8</sup> In many ways this is just the tip of the iceberg since these numbers do not include those who are blind only in one eye from cataract or the much larger number of those who would benefit from cataract surgery in carrying out their day-to-day activities but are not yet legally blind. The reality is that in developing countries, the Cataract Surgical Rate (CSR or number of cataract surgeries performed per million people per year) varies from less than 200 to over 6,000.<sup>9</sup> While differing incidence (thus the magnitude of the problem) could explain some of this, it is mostly influenced by the effectiveness of strategies or lack of them for stimulating demand, delivery of services while assuring good outcomes, and patient satisfaction.<sup>10</sup>

There are proven effective interventions for cataract surgeries such as low cost manual small incision surgery with a rigid IOL implant to more expensive phacoemulsification surgery with foldable lens, both of which, when done well, result in excellent visual recovery. These have been time tested and used in many settings. So the current situation is not for want of a clinical solution but due to issues in effective implementation. While some of the reasons for the current situation might be attributed to inadequate resources such as too few ophthalmologists, especially in Sub Saharan Africa, even in these resource-poor settings, contrary to what one would expect, the ophthalmologist's output is much lower than what it could be, ranging from 25 to 350 surgeries per ophthalmologist per year. Such low productivity is widespread even when the number of ophthalmologists is adequate.

While efforts are ongoing to build more hospitals and equip them, not enough is being done to build the right teams and put in place processes that on one hand would work on the **demand** side to ensure that all those who can benefit from cataract surgery actually seek it, and on the other hand ensure the right enabling conditions that would result in efficient delivery of cataract services with good outcomes to responsibly take care of the **supply** side.

While there is a convincing case to significantly enhance the resource base – infrastructure, equipment, ophthalmologists and other ophthalmic workers, there must be an equal emphasis on management<sup>11</sup> to build the right processes and the organizational capability for maximal cost-effective resource utilization. Patient access, affordability and availability of surgical consumables and pharmaceuticals are all part of this. From a strategic perspective two of the most critical challenges are low cataract surgical output and less than desirable outcomes. Future solutions will need to address these big challenges.

The Aravind Eye Care system was founded on the concept that the major hurdles to eliminating needless blindness from cataracts were a low patient demand from the rural poor, challenges in acquiring adequate equipment, and acquiring appropriate human resources and supplies. To address these problems, the founders built our institution on principles that would minimize these bottlenecks. Its business model addresses both the demand and supply sides of the problem.

In developing countries where only a small fraction of those who need eye care services are actually getting them, the focus has to be on non-consumers and how to attract them. Simultaneously hospital systems need to be geared up to serve the demand efficiently; the HR policies should bring out the best in the hospital staff; systems need to be in place for continuous review and improvement - all leading to excellence in outcomes and high levels of patient satisfaction. Quality eye care is the goal that Aravind adopted from the beginning.

## Trachoma Prevention and Treatment

The leading infectious cause of blindness worldwide, trachoma is caused by repeated episodes of infection with *Chlamydia trachomatis*. Trachoma continues to be endemic in many of the poorest and most remote areas of Africa, Asia, and the Middle East. Communities with trachoma are often those with the fewest resources to take on health issues, and trachoma strikes the most vulnerable members of those communities, women

and children. Trachoma affects an estimated 40 million people and an estimated 7.6 million are blind or severely visually impaired.<sup>12</sup>

The clinical signs of trachoma are the result of the immunopathologic response to *C. trachomatis*. As a result of multiple infections over time, the conjunctiva of older children and young adults develop tarsal scarring.<sup>13,14</sup> Significant scarring can cause rolling inward of the lid margin (entropion) and inturned eye lashes (trichiasis) usually in middle aged adults. Lid surgery is required to correct the inturned eye lashes and prevent visual loss from corneal damage. The most effective method for prevention of these late manifestations of trachoma is to eliminate the active disease in children.

WHO recommends the use of the multifaceted “SAFE” strategy for trachoma control. This approach includes Surgery for trichiasis cases, Antibiotics to treat the community pool of infection, Face cleanliness to reduce transmission, and Environmental change to sustain reduction in transmission. There is epidemiological evidence to support each component of the SAFE strategy, which must be implemented on a community-wide basis. The implementation of the full strategy is critically important, as the temptation is strong to follow a more medically oriented model of concentration on provision of surgery and antibiotics with less attention to the hygiene and environmental components. Provision of mass drug administration to entire districts where trachoma is endemic, rather than individual case management, is the approach to reducing the pool of infection. Azithromycin is effective as a single, oral dose of 20mg/kg up to 1 gm. The cost of azithromycin treatment originally put it out of reach for trachoma control programs, but the manufacturer instituted a generous donation program that makes the drug available free of charge for approved trachoma programs.

Several countries are close to being verified as having eliminated trachoma, including Morocco, Ghana and Oman with other countries in the final stages of mopping up the last remaining trachoma endemic districts. The challenges lie with countries with large, highly endemic populations like Ethiopia, Southern Sudan, and Nigeria, and where no activities are happening such as Somalia and Democratic Republic of Congo. There is an understandable urgency to speed up the elimination process. The initial hope that a few rounds of mass drug administration with azithromycin would be sufficient has proved not to be true in most settings, and the realization that a longer-term commitment to the full SAFE has been a hard transition. There is reason for optimism that blinding trachoma can be eliminated as a public health problem, but sustained effort will be needed to achieve the endpoint by the goal year of 2020.

## Corneal Blindness and Infectious Keratitis

Despite recent developments and new treatments, infectious corneal ulcers remain the fourth leading cause of blindness worldwide<sup>8</sup>. The incidence of ulcers is approximately 10-fold higher in the developing world than in the US<sup>15</sup>, so any important reductions in global incidence will almost certainly require changes in poorer rural areas around the world.

Ophthalmologists have made major changes in their pattern of antibiotic use in the past two decades. Topical 4<sup>th</sup>-generation fluoroquinolones have broad-spectrum activity with

excellent corneal penetration, and are readily available commercially. Large studies have demonstrated that *in vitro* susceptibility is associated with *in vivo* clinical outcomes such as visual acuity, suggesting that antibiotic choice does affect outcome<sup>16</sup>. However, it has been extremely difficult to show that the new antimicrobial agents such as fluoroquinolones have better outcomes than the previous fortified aminoglycosides and cephalosporins; in fact, many cornea specialists treat their most severe cases with the same older fortified treatments that were widely used 20 years ago.

The use of adjunctive anti-inflammatory agents has been explored. While there is a suggestion that topical corticosteroids may benefit certain cases, any benefit is at best marginal<sup>17</sup>. In fact, the most consistent conclusion from large corneal ulcer treatment trials is that once ulcers are present, choice of treatment has only a modest effect. Infiltrate size at presentation is almost identical to eventual scar size. While acuity may, on average, improve about 4-lines from presentation, by far the largest predictor of eventual acuity is still the presenting acuity<sup>17</sup>. Some investigators have utilized deep anterior lamellar keratoplasty (DALK) in active ulcers, although others are concerned about the high rates of infection in the graft. Corneal transplantation after resolution of infection remains a viable intervention, and tissue availability is increasing worldwide. However, transplants are expensive, and introduce new problems such as surgical skill, post-transplant infection, rejection, glaucoma, and irregular astigmatism.

Our inability to improve results significantly after presentation suggests that prevention is the best way to reduce corneal ulcer blindness and a series of studies in Nepal, Bhutan, Myanmar, and India show this is possible<sup>18</sup>. In each study, community-level health care workers actively ensured villagers received topical antimicrobial ointment within 18 hours of a corneal abrasion. Three of the studies found no ulcers in treated abrasions. The fourth found two small ulcers, presumably due to fungus in abrasions treated only with antibiotic ointment<sup>18</sup>. Each study suggested the incidence of ulcers was reduced more than 80%. While encouraging, the efficacy of community-level prophylaxis and other prevention measures needs to be confirmed in community-randomized clinical trials. These results should not be generalized to corneal abrasions in developed countries, where injuries tend to be less severe, and where microbial flora are different.

It is difficult to see how blindness from corneal ulcers worldwide can be reduced dramatically with treatment of the ulcers themselves; cases often present too late to prevent the corneal scarring that causes blindness. However, prevention of ulcers at the community-level may be possible. As with xerophthalmia, trachoma, and river blindness, community-level, or *in vivo* interventions may be necessary to make a large impact on the incidence of infectious corneal ulcers.

## CMV Retinitis

Cytomegalovirus (CMV) retinitis is an opportunistic infection affecting immunocompromised individuals, most commonly those with HIV/AIDS. Retinal infection leads to necrosis and irreversible loss of vision. Retinitis usually progresses slowly in untreated eyes, leaving a substantial window of opportunity to provide treatment and prevent vision loss.<sup>19</sup>



CMV retinitis remains an important cause of blindness in developing countries where HIV/AIDS is prevalent. Rates are highest in southeast Asia, where CMV retinitis has been found in roughly one-third of patients with CD4 counts less than 50 cells/ $\mu$ L.<sup>20</sup> Infection often leads to blindness. For example, CMV retinitis was the leading cause of irreversible bilateral blindness in a hospital-based study in northern Thailand.<sup>21</sup>

Treatment of CMV retinitis is relatively straightforward. Systemic treatments such as oral valganciclovir are used routinely in industrialized countries, but are much too expensive for the developing world. In resource-poor settings, repeated intravitreal injections with ganciclovir are typically performed.<sup>22</sup> Treatment is relatively inexpensive, costing only \$0.57 per injection.<sup>20</sup>

Given the slow progression of disease and the availability of effective treatment, CMV retinitis is an ideal candidate for disease screening. However, screening is generally not performed in those areas of the world where CMV retinitis is most common. The lack of screening means that retinitis is often at an advanced stage by the time of diagnosis. In order to diagnose infection earlier, efforts should be directed at increasing both the supply of screening examinations and also the demand for screening--both from patients and physicians. Several strategies could be effective, including training HIV providers in indirect ophthalmoscopy, as well as telemedicine approaches.

Telemedicine is a promising strategy for enhancing access to CMV retinitis screening. A non-physician could be trained to take fundus photographs of HIV patients who meet a CD4 threshold, and the photographs could in turn be assessed by trained graders. Telemedicine diagnosis of diabetic retinopathy has been adopted in several settings in the United States, and has been shown to be cost-effective in a developing country setting.<sup>23</sup> The cost of current fundus cameras (\$30,000) is a barrier, so less expensive cameras should be encouraged. One promising approach is the development of inexpensive smartphone attachments that allow retinal photography--though the quality of the resulting photographs and ease of use of such a system remains in to be determined.

CMV retinitis remains a significant problem in southeast Asia and other places with prevalent HIV/AIDS. Screening programs are virtually non-existent. Novel screening strategies, including those that utilize new technologies, could greatly expand the number of patients screened for CMV retinitis, and reduce the incidence of blindness in this population.

## Retinopathy of prematurity in the developing world

Retinopathy of prematurity (ROP) is a retinal neovascular disease of premature infants. Despite major advances in management, it continues to be a leading cause of childhood blindness throughout the world. From a societal perspective, the burden of infancy-acquired blindness is enormous. The relationship between supplementary oxygen and ROP was identified in the 1950s, and resulted in rigid oxygen curtailment within neonatal intensive care units (NICUs)<sup>24</sup>. Although this led to a dramatic decrease in ROP incidence, there was worsening of infant mortality from respiratory and neurological disorders. More recently, the oxygen requirements of premature infants have been more thoroughly characterized.



Continuous pulse oximetry monitoring is routinely performed within the developed world, although optimal oxygen saturation levels remain somewhat controversial<sup>25</sup>.

With more preterm infants surviving due to improved neonatal care in developing countries, the number of ROP cases internationally has increased dramatically<sup>26</sup>. Meanwhile, there are enormous challenges regarding availability of medical care in the developing world. For example, high levels of supplemental oxygen are administered to infants in NICUs that lack air-oxygen blenders, continuous pulse oximetry, or adequate nursing care. Furthermore, ROP screening by trained ophthalmologists may be unavailable. Therefore, even large infants in the developing world can be at risk for blinding ROP.

Traditional ROP screening performed at the NICU bedside is logistically-difficult and time-consuming. These examinations require specialized training and are typically performed by retinal or pediatric ophthalmologists, who are often unavailable in rural or medically-underserved areas. Infants need multiple examinations at regular intervals, requiring coordination of care between ophthalmologists and NICU staff. The precise documentation of findings using hand-drawn sketches is qualitative and subjective. These challenges create difficulties even within developed economies, which are far worse in developing countries.

Telemedicine could address these challenges in the developing world. Using this approach, trained neonatal personnel could capture images and clinical data from infants, which would subsequently be interpreted by a remote ROP expert. This might improve the quality, accessibility, and cost of ROP care internationally. Telemedicine is accurate, more cost-effective, and faster than standard ophthalmoscopy for ROP management<sup>27</sup>.

Similar information technologies can address challenges regarding ROP training in the developing world<sup>28</sup>. For example, in 2010 the Armenian Eye Care Project trained ophthalmologists with no prior experience to manage ROP. Images were taken using a wide-angle camera and reviewed remotely by experts in the United States to improve diagnostic skills. There was 95% agreement for diagnosis of treatment-requiring ROP among 151 infants in this study<sup>29</sup>.

There are enormous challenges for ROP care and training within the developing world. Telemedicine and tele-education are promising approaches in which information and communication technology may be applied to address these challenges.

## Conclusions

Clearly strategies for reducing the global burden of blindness require a global vision, but local implementation. These strategies share a public health focus and an empirical realism. But there is great reason for optimism because these strategies are beginning to show their effectiveness as have been described in this paper, and portend a future with much, much less global blindness.

## Acknowledgments

Dr. Chiang is an unpaid member of the Scientific Advisory Board for Clarity Medical Systems (Pleasanton, CA).

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Table 1

## Ophthalmologist productivity by country

Country	Popln. in millions	Cat. Surgeries per year	CSR	No. of Oph.	Per Ophthalmologist		Productivity
					Population	Cat. Surgeries	
<b>Target Productivity: Cataract surgeries per Ophthalmologist per year</b>							
Brazil	199.7	580,000	2,900	4,194	47,619	138	18%
Bolivia	10.2	9,500	930	133	76,981	72	10%
Colombia	47.5	83,000	1,752	1,796	26,455	46	6%
Cuba	11.6	31,000	2,708	1,244	9,328	25	3%
Ecuador	14.9	26,000	1737	453	32,906	57	8%
México	116.4	200,000	1720	4,190	27,778	48	6%
Paraguay	6.6	9,000	1350	103	64,390	88	12%
Perú	29.7	47,000	1600	677	43,844	69	9%
Venezuela	29.7	108,000	3650	1,402	21,190	77	10%

Population Source: U.S. Bureau of the Census, International Data Base: Estimate for 2011

Performance & data on Ophthalmologists: Courtesy – Van Lausung (Feb 2012)