

Bridging the valley of death between research and implementing a systematic diabetic retinopathy screening program in low- and medium-income countries

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Translating research findings to routine clinical practice is fraught with obstacles. The gap between the end of a research project and the implementation of its results is often termed the “valley of death.” In this perspective, we highlight the barriers and potential solutions in translating research on diabetic retinopathy care pathways to implementation in the clinic. This gap analysis applies to all countries around the world, though it predominantly applies to low- and middle-income countries.

Key words: Diabetic retinopathy screening, low- and middle-income countries, translating research into clinical practice

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There are many obstacles in the translation of basic research to clinical knowledge and from clinical knowledge to implementation of related health policies or innovations into routine health services, and this is often referred to as the “valleys of death.”^[1]

Global health research is now a priority for many international and national funding agencies and charities, primarily focusing on improving health outcomes in low- and middle-income countries (LMICs). Many of these research programs are between researchers in high-income and LMICs or between the LMICs to ensure that the outputs are translated to clinical practice to benefit the health of people in LMICs. These research collaborations are also central to improve research capacity and capability to address the local needs. Several barriers prevent the translation of evidence-based research to implementation in clinical practice in LMICs.^[2] Anticipating and addressing these barriers from the beginning of the research project is vital to successfully translate and implement the research evidence.

In this communication, we provide a perspective on the translation of research on screening for diabetic retinopathy (DR) into clinical practice from the lessons learned out of conducting research in this area in India.

Untreated complications of DR such as diabetic macular edema and proliferative DR are common causes of permanent

visual loss in the working-age group that incurs a high societal and economic burden. As these conditions are asymptomatic in the early stages and are treatable, people with diabetes require regular retinal screening by ophthalmoscopy or digital photography. Currently, there are no other accurate ways of identifying sight-threatening diabetic retinopathy (STDR). Systematic screening for STDR and prompt treatment has been proven to reduce the risk of visual impairment in people with diabetes in some high-income countries.^[3] However, very few countries have been able to introduce and sustain DR screening programs at a population level due to several challenges.^[4] This is of particular concern in LMICs. These countries are most affected by the diabetes epidemic; yet, they have limited resources to implement a DR care pathway, from screening to treatment. Therefore, there has been a significant investment in research to identify means to implementing DR screening in LMICs such as India. Many grant-funded research projects on setting up a DR care pathway initiate an initial burst of protocol-based screening activities utilizing fixed resources from these grants resulting in collaborative publications which provide new knowledge. Examples include high-quality publications on DR screening, artificial intelligence, population-based studies on the prevalence and incidence of DR, and qualitative studies. However, systematic screening for DR in clinical practice is still an unmet need.

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While the research to identify people at risk of blindness are most welcome, we highlight here the valley of death between these – the evidence generated by research and the ability to scale up and sustain a systematic DR care pathway.

We present key issues and potential solutions for scalability and sustainability of systematic DR care pathway in LMICs borne out of the lessons learned from our conducting research in India, funded by the Global Challenges Research Fund and UK Research and Innovation.^[5]

The Complexity of Diabetic Retinopathy Screening

Screening for DR is complex and costly, unlike many other screening programs. People with diabetes have to be screened regularly during their lifetime. Below are some of the barriers.

Retinal camera

The retinal cameras used for screening are costly. Despite the availability of less expensive hand-held retinal cameras, obtaining high-quality retinal images with these cameras is still a challenge. It reduces their diagnostic accuracy in the mobile retinal screening environment.^[6,7] There is a move to task sharing with nontechnical staff capturing the retinal images, but these staff also need training and continual retraining.^[8] There is also a keen interest in the use of nonmydriatic retinal photography. However, in LMICs, where the cataract is still the most common cause of adult blindness, dilating pupil is necessary to obtain quality retinal images paramount for effective DR screening.^[9] Thus, the current practice of opportunistic screening for DR using a nonmydriatic retinal camera and artificial intelligence to grade retinal images is inferior to standard mydriatic retinal photography captured by experienced technicians and graded by trained graders. Therefore, research findings do not mirror current practice in LMICs. A change in practice requires significant buy-in from multiple stakeholders. For example, setting up a national guideline on DR screening is one way forward.^[10,11]

Treatment

Studies have shown that a DR care pathway from screening to treatment should be in place before any screening is done so that screen-positive patients can access treatment. However, this does not always happen in practice in most LMICs due to several challenges. Currently, DR screening is mainly delivered opportunistically; patients identified with STDR are only informed of their condition, and the treatment decision is left to the patients. Many patients are asymptomatic when they screen positive, so they need to be educated about their risk to lose vision in the future. One of the reasons a defined DR care pathway does not translate into practice could be an inadequate public health care system. It results in out-of-pocket spending (OOPS) for treatment by the patient even though the DR screening episode could be free.

Public-private partnership

In India and several similar LMICs, the public health facilities are not sufficiently equipped by infrastructure and/or trained workforce.^[12] To improve the health care delivery system and overcome the limitations of financial, technical, and human resources, public-private partnerships should be considered for future health reforms.

Operational research

This partnership should extend to operational research in addition to patient care. A long-term benefit will be derived when the local investigators are involved and build the available resources and context into the research methodology. Therefore, there is an unmet need to find solutions to bridge the valley of death early so that a scale-up plan is in place before the research project is completed. Building this infrastructure often commences only after the research project is completed.

Finally, DR screening is not a health priority in LMICs. Hence, it is challenging to convince policymakers about future planning to reduce the risk of blindness in the tsunami of people with diabetes coming our way when the government is tackling immediate priorities such as maternal and child health and communicable diseases.

Solutions

Potential solutions to bridging this valley of death and facilitating a sustainable state-wide DR care pathway based on research findings in a local setting include the following:

Translatable research projects

A key issue that results in the valley of death is the design and/or conduct of the project. The research project should be designed with the help of local key stakeholders to ensure that all required elements for the future implementation of any intervention are included. The outcomes should lead to translation. For example, if the prevalence of DR is higher in urban than rural areas, research on implementation should be focused first in urban areas. Although the researchers may do genetic studies or multiomics to understand the difference in urban versus rural prevalence, these projects do not result in immediate translation.

Government engagement

Implementation of research outputs incurs health care costs. In the absence of robust public health, mainly primary health system, the people are subjected to OOPS, often catastrophic health expenditure. This is unlike the health systems in affluent countries where primary care infrastructure is well developed. Systematic DR screening initiated by nongovernmental agencies is challenging. An easy-to-maintain Diabetes Health Card that mandates the care providers to complete a minimal dataset might be the first step for systematic screening for diabetes complications in LMICs. The government has stable resources for long-term use. People with diabetes and DR need life-long care. Hence, the Government engagement is crucial for the successful scalability and sustainability of DR screening programs. This will likely resolve the lack of follow-on research funding that leads to the demise of the immediate impact of such research projects.

However, government buy-in is often challenging, and this is the major hurdle for the scalability and sustainability of DR care programs. This resistance is mainly because policy makers are not aware of the long-term cost-benefit of these programs through well-developed strategic plans and business cases. Lobbying at national or local government levels must be initiated early in the research projects with a well-developed long-term strategic plan, ideally over 10 years. This strategy will also enable the government to develop policies and programs to reflect the local unmet needs for a systematic DR care pathway,

from screening to treatment. Government-level policies and financial planning are crucial for successful implementation. It is a top-down requirement that considers possible and unforeseen political and/or economic national risks.

Community engagement

People engagement must be an integral part of all screening activities, in this case, people with diabetes. It is necessary for the people and the community to understand that DR screening is not a one-off episode. Opportunistic DR screening provides a false sense of security. Because of poor public awareness of the need for life-long screening for DR to reduce diabetes-related blindness, the public demand for DR screening services is low. Therefore, advocacy and public education must be integral to all screening programs and include local stakeholders.

From the patient's perspective education and self-management support programs are needed to educate patients about the purpose of screening, including the need for dilation of the pupils, which can cause blurred vision and photosensitivity, and that a person should accompany them to the screening site.

As patients with diabetes have many appointments to keep, including foot examinations and blood glucose, blood lipids, and blood pressure tests, telephone calls, text messages, and reminder letters should be sent to inform them of DR screening. Most patients are also in the working age group and may have time and financial constraints.

In India, accredited social health activists (ASHAs) have long been the link between the community and primary care; they form an essential asset to impart knowledge to the community.^[13]

For example, in Kerala, there are 27,500 ASHAs, that is, approximately one ASHA for every 1000 people. Although similar resources may not be available in all other Indian states or other LMICs, increasing knowledge of similar health workers generate confidence in the community. Further, public awareness programs such as media, public engagement meetings, and population-based screening may also be deployed. However, costs should be borne in mind, especially if a successful awareness program increases demand that outstrips the available capacity. We need to build increased community knowledge and confidence in the public health system. A good public-private partnership helps.

Development and maintenance of electronic health records

DR screening must be done at frequent intervals; the re-call system can only be achieved by local registers maintained at each provider center. DR screening in LMICs is usually cross-sectional. Building on or maintaining a diabetes research register may be a stepping stone to develop a re-call system for DR screening. There are few national guidelines for personalized screening intervals, but these work well only if patients return to the same provider. Most countries have a register for noncommunicable diseases as part of an international drive to tackle these diseases. However, a majority of these registers are incomplete and/or maintained on nonviable systems. An electronic patient record system is more ideal for the ever-growing number of people with diabetes who require periodic screening for their entire life. The electronic register enables the re-call of these patients for rescreening,

and at the same time, it gives freedom to the patients to seek care at places of their convenience.

Capacity building to improve infrastructure

LMICs could benefit by adopting newer and less expensive technologies than those used in high-income countries. However, there is a need for an additional trained health workforce to use these newer technologies effectively. Along with the infrastructure, there is an acute shortage of technical personnel in all LMICs, including India. Widespread use of smartphones and tablets throughout developing countries often leapfrogs wired infrastructure. Therefore, prioritizing the accessibility of applications via wireless platforms is essential. However, technical support and maintenance costs would continue to challenge. In the future, artificial intelligence such as deep learning may ease this burden in LMICs. However, it must be borne in mind that these tools may only aid or augment the pathway but is unlikely to replace this infrastructure requirement. Policy makers should make the cameras and laser devices are available in public hospitals.

Multidisciplinary staff capability building

Well-trained ophthalmologists are the most ideal for efficient management at every level of the entire DR care pathway. However, the demand far outweighs the number of ophthalmologists available globally, including even in high-income countries. In England and Wales, the DR screening program is a stand-alone service where all patients with diabetes are referred by the General Practitioner (GP) to undergo mydriatic retinal photography by screeners, and the images are graded by graders. Primary, secondary, and arbitration grading ensure quality assurance of the system. Patients with ungradable images and those that require referral due to a clinical indication are referred to secondary care for management in medical retina clinics. This robust pathway has been effective in identifying and treating STDR, and the GP only receives the screening outcome. Although this service is an ideal example where multidisciplinary teams serve as a more appropriate service model, such elaborate stand-alone service is not feasible in countries with limited resources. Direct replication of this DR care pathway in LMICs is unpractical. More effective and efficient use of existing multidisciplinary team members within existing infrastructure must be deployed within each clinical setting without overburdening the caregivers.

Capital costs

The DR screening and treatment involve substantial capital costs for equipment such as retinal cameras, optical coherence tomography, retinal lasers, and intravitreal injections of antivascular endothelial growth factors and IT infrastructure. National or state-level budgets in LMICs do not usually have sufficient reserve to accommodate high capital costs. Therefore, international aid and donations from various agencies are ideal opportunities that can bridge the funding gap. At the same time, the government must budget for the maintenance and replacement costs of the equipment.

Recurring costs

The initial capital costs to conduct the research do not mirror the funding required in clinical practice. There are several recurring expenses such as maintaining the IT infrastructure, the cost of retinal image transfer to a centralized reading-grading centre, and finally, the grading of retinal images. Development

and maintenance of the electronic health record also add to the recurring cost. The government has to be the long-term guardian of the electronic database, including data protection and patient confidentiality.

One size does not fit all

A country such as India will require several DR screening models to achieve universal coverage. Much of the research on DR screening is done by ophthalmologists, but due to the lack of ophthalmologists, DR screening should also be the physicians' responsibility who offer holistic care. The newer technology and the trained manpower to use these technologies would release the ophthalmologists to manage patients with DR. Other systems may require ophthalmology–diabetes physician tie-ups. These should be built into research projects to enable immediate translation.

Treatment of screen-positive patients

Although DR screening should ideally be the responsibility of the doctor who manages the diabetes care, our research on DR care pathways in India shows a complete breakdown in the pathway between identifying a screen positive patient and treatment of STDR. Screening for DR will be meaningless unless this is modelled into any new DR care pathway. Therefore, opportunistic screening for DR is not useful unless people with STDR are treated. It calls for significant partnerships between the treating diabetologist and ophthalmologist. It is important to impress the patients on the need for regular follow-up and care. This gap between identifying a patient with STDR and treatment is the biggest challenge in LMICs and will remain so unless the public health policies are in place to bring these patients for timely care.

Initiation with a pilot phase

In a populous and resource-constraint country like India, seeking national or government implementation of a DR screening program, based on available research evidence, may not be possible due to the need for a significant investment. Therefore, pilot DR systematic screening programs may be set up in different regions in India to provide evidence for a future nationwide program plan.

Conclusion

In conclusion, the valley of death should be prevented by aligning research projects to the local needs. Research projects will help identify the most appropriate care model, mitigate risks, dispel myths, and alleviate uncertainties linked to operational issues or about the disease and its treatment options in the short term. However, public health financing, health system strengthening, and improving public awareness are required to implement a minimally resourced but efficient DR care model. Public–private partnerships and involving several stakeholders to share these risks may be useful in the long term. National policies on blindness or diabetes may also ensure constant government buy-in to ascertain scalability, sustainability, and continuity.

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Conflicts of interest

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References

- Butler D. Translational research: Crossing the valley of death. *Nature* 2008;453:840-2.
- Piyasena MMPN, Murthy GVS, Yip JLY, Gilbert C, Peto T, Premarathna M, *et al.* A qualitative study on barriers and enablers to uptake of diabetic retinopathy screening by people with diabetes in the Western Province of Sri Lanka. *Trop Med Health* 2019;47:34-44.
- Scanlon PH. The contribution of the English NHS diabetic eye screening programme to reductions in diabetes-related blindness, comparisons within Europe, and future challenges. *Acta Diabetol* 2021;58:521-30.
- Vujosevic S, Aldington SJ, Silva P, Hernández C, Scanlon P, Peto T, *et al.* Screening for diabetic retinopathy: New perspectives and challenges. *Lancet Diabetes Endocrinol* 2020;8:337-47.
- Sivaprasad S, Raman R, Conroy D, Mohan V, Wittenberg R, Rajalakshmi R, *et al.* for the ORNATE India project group. The ORNATE India project: United Kingdom-India research collaboration to tackle visual impairment due to diabetic retinopathy. *Eye (Lond)* 2020;34:1279-86.
- Natarajan S, Jain A, Krishnan R, Rogye A, Sivaprasad S. Diagnostic accuracy of community-based diabetic retinopathy screening with an offline artificial intelligence system on a smartphone. *JAMA Ophthalmol* 2019;137:1182-8.
- Nderitu P, Nunez do Rio JM, Rasheed R, Raman R, Rajalakshmi R, Bergeles B, *et al.* Deep learning for gradability classification of handheld, non-mydratric retinal images. *Sci Rep* 2021;11:9469.
- World Health Organization, PEPFAR and UNAIDS. Task shifting: Rational redistribution of tasks among health workforce teams: Global recommendations and guidelines. 2007. [Last accessed on 2021 May 3]. Available from: <https://apps.who.int/iris/handle/10665/43821>.
- Das T, Keeffe J, Sivaprasad S, Rao GN. Capacity building for universal eye health coverage in South East Asia beyond 2020. *Eye (Lond)* 2020;34:1262-70.
- Raman R, Ramasamy K, Rajalakshmi R, Sivaprasad S, Natarajan S. Diabetic retinopathy screening guidelines in India: All India Ophthalmological Society diabetic retinopathy task force and Vitreoretinal Society of India consensus statement. *Indian J Ophthalmol* 2021;69:678-88.
- Das T, Takkar B, Sivaprasad S, Thanksphong T, Taylor H, Wiedemann P, *et al.* Recently updated global diabetic retinopathy screening guidelines: Commonalities, differences, and future possibilities. *Eye (Lond)* 2021. <https://doi.org/10.1038/s41433-021-01572-4>.
- Gilbert CE, Babu RG, Gudlavalleti AS, Anchala R, Shulka R, Pant HB, *et al.* Eye care infrastructure and human resources for managing diabetic retinopathy in India: The India 11-city 9-state study. *Indian J Endocrinol Metab* 2016;20(Suppl 1):S3-10.
- Abdullah AS, Rawal LB, Choudhury SR, Baral S, Jiang L, Sha T, *et al.* Use of community health workers to manage and prevent non communicable diseases: Policy options based on the findings of the COACH study. New Delhi: World Health Organization Regional Office for South-East Asia; 2019.