

Retinoblastoma outcomes: a global perspective



Retinoblastoma is the most common paediatric eye cancer, and is typically curable through early diagnosis and protocol-based management. In fact, advanced medical care delivery in high-income regions has provided excellent rates of survival, and globe and vision salvage.^{1,2} Unfortunately, these outcomes are not true to medical systems in middle-income and low-income regions.^{3,4} Low-income or middle-income countries in Asia and Africa contribute a large majority of retinoblastoma cases, including many advanced retinoblastoma tumours at presentation, resulting in dismal patient outcomes. In *The Lancet Global Health*, the systematic review and meta-analysis by Emily Wong and colleagues⁵ provides strong evidence that overall survival, globe salvage, and visual outcomes are compromised due to disparities in socioeconomic and related health-care factors. It also emphasises the need for targeted health-care policies to improve retinoblastoma outcomes.

The incidence of retinoblastoma is known to vary with the size of the population and the birth rate.⁶ However, there is also a disparity related to the existence and abilities of national tumour registries. For example, high-income nations, such as Japan, the USA, and some in Europe, have robust national retinoblastoma registries not found in low-income countries in Asia and Africa. Therefore, only mathematical means (based on population at risk and the livebirth rate) can be used to estimate the incidence of retinoblastoma in regions without robust registries. That said, current estimates suggest that more than half of all retinoblastoma cases come from the Asia Pacific region and nearly a quarter come from Africa.^{3,7} Of individual countries, India has the highest retinoblastoma incidence (~2000 cases per year), which is nearly 50% more than China (~1000 cases per year) and 6 times more than the USA (~325 cases per year).⁶ Delay in diagnosis is more common in low-income countries, resulting in children presenting with advanced retinoblastoma (ie, combinations of proptosis, red eye, orbital cellulitis, and extraocular retinoblastoma) and thus poorer outcomes.^{3,4}

Wong and colleagues explored the reasons for delayed presentation and found that low awareness among parents, an inability to pay for care, and a scarcity of ophthalmic examination resources at paediatricians'

offices all contributed to delayed recognition of retinoblastoma symptoms. In addition, remote tertiary care facilities, gender bias, religious beliefs, and social stigma can delay or obstruct early diagnosis and prompt treatment. By contrast, high-income countries have improved medical and retinoblastoma care in the setting of a declining birth rate. As such, more resources are available for fewer patients in those countries. It is often assumed that retinoblastoma incidence must be on the decline in high-income countries, but recent data suggest a rise in the incidence of familial retinoblastoma.⁸ Hence, there is still room for increased retinoblastoma sensitisation around the world.

The risks for death can also be economically stratified. The major cause of retinoblastoma mortality in high-income countries is second malignancies, whereas most children die from extraocular retinoblastoma and systemic metastasis in low-income countries.⁹ Treatment has shifted towards vision salvage and rehabilitation in resource-rich countries, whereas resource-poor countries still struggle to provide access to primary treatment to save lives. Another example is the use of intra-arterial and intravitreal chemotherapy, which might have prompted a trend towards conservative management of retinoblastoma in resource-poor countries, but these treatments require costly equipment, specialised pharmacies, and multiple hospital visits. Wong and colleagues underscore that these treatments are beyond the capabilities of many areas in low-income countries, where even pathological evaluations of enucleated retinoblastoma eyes for high-risk histopathological features (necessary for prescribing adjuvant chemotherapy to prevent tumour recurrence and systemic metastasis) is typically unavailable or delayed.

Reducing retinoblastoma deaths across the world is a huge challenge. Despite knowing that early detection and prompt enucleation is typically curative, it is incredibly difficult to provide that basic care when tens of countries have no eye cancer specialist. The Eye Cancer Foundation and the International Council of Ophthalmology have been working together to support fellowship training of retinoblastoma specialists for unserved countries and underserved areas.¹⁰ Eye cancer specialists around the world have written

Lancet Glob Health 2022

Published Online
January 27, 2022
[https://doi.org/10.1016/S2214-109X\(21\)00598-2](https://doi.org/10.1016/S2214-109X(21)00598-2)

See Online/Articles
[https://doi.org/10.1016/S2214-109X\(21\)00555-6](https://doi.org/10.1016/S2214-109X(21)00555-6)

For more on The Eye Cancer Foundation and the International Council of Ophthalmology see <https://www.eyecancercure.com/the-international-council-of-ophthalmology-highlights-fellowship-partnership-with-ecf.html>

open-access eye cancer surgical texts targeted to help ophthalmologists and young specialists offer adequate eye cancer care.¹¹ The community of eye cancer, paediatric, and radiation oncology specialists, together with social service agencies, can foster a synchronised multistep approach involving public awareness, professional training, infant eye screening (positive family history), and medico-economic development.

A key point highlighted by Wong and colleagues is the multicentre, international retinoblastoma registries, which can serve as a great method to pool real-world data for this rare form of cancer.^{1,2,4} Data can be used to answer crucial questions regarding treatment strategies and to guide government policies.^{4,12} Wong and colleagues report that retinoblastoma treatment outcomes have improved globally but the prevailing disparity between high-income and low-income countries must be addressed. Together we have an opportunity to save both life and sight.

PTF and AST have received funding for travel expenses and processing charges from The Eye Cancer Foundation, and PTF is on the Data Safety Monitoring Board and Advisory Board for the Ophthalmic Oncology Task Force Registries.

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- 1 Tomar AS, Finger PT, Gallie B, et al. A multicenter, international collaborative study for American Joint Committee on Cancer staging of retinoblastoma: part I: metastasis-associated mortality. *Ophthalmology* 2020; **127**: 1719–32.
- 2 Tomar AS, Finger PT, Gallie B, et al. A multicenter, international collaborative study for American Joint Committee on Cancer staging of retinoblastoma: part II: treatment success and globe salvage. *Ophthalmology* 2020; **127**: 1733–46.
- 3 Fabian ID, Abdallah E, Abdullahi SU, et al. Global retinoblastoma presentation and analysis by national income level. *JAMA Oncol* 2020; **6**: 685.
- 4 Tomar AS, Finger PT, Gallie B, et al. Global retinoblastoma treatment outcomes: association with national income level. *Ophthalmology* 2021; **128**: 740–53.
- 5 Wong ES, Choy RW, Zhang Y, et al. Global retinoblastoma survival and globe preservation: a systematic review and meta-analysis of associations with socioeconomic and health-care factors. *Lancet Glob Health* 2022; published online Jan 27. [https://doi.org/10.1016/S2214-109X\(21\)00555-6](https://doi.org/10.1016/S2214-109X(21)00555-6).
- 6 Usmanov RH, Kivelä T. Predicted trends in the incidence of retinoblastoma in the Asia-Pacific region. *Asia Pac J Ophthalmol (Phila)* 2014; **3**: 151–57.
- 7 Munier FL, Beck-Popovic M, Chantada GL, et al. Conservative management of retinoblastoma: challenging orthodoxy without compromising the state of metastatic grace. "Alive, with good vision and no comorbidity". *Prog Retin Eye Res* 2019; **73**: 100764.
- 8 Stacey AW, Bowman R, Foster A, et al. Incidence of retinoblastoma has increased: results from 40 European countries. *Ophthalmology* 2021; **128**: 1369–71.
- 9 Chantada GL, Qaddoumi I, Canturk S, et al. Strategies to manage retinoblastoma in developing countries. *Pediatr Blood Cancer* 2011; **56**: 341–48.
- 10 Torres-Netto EA, Gabel-Obermaier C, Gabel P, et al. Twenty years of International Council of Ophthalmology fellowships: description of the programme and the impact on more than 1100 awardees. *Br J Ophthalmol* 2021; **105**: 1318–24.
- 11 Chaugule SS, Honavar SG, Finger PT. Surgical ophthalmic oncology: a collaborative open access reference. Geneva: Springer Nature, 2019.
- 12 Tomar AS, Finger PT, Gallie B, et al. Retinoblastoma seeds: impact on American Joint Committee on Cancer clinical staging. *Br J Ophthalmol* 2021; published online Aug 2. <https://doi.org/10.1136/bjophthalmol-2021-318892>.