Glaucoma is a chronic, age-related, optic neuropathy which causes progressive and irreversible damage to retinal ganglion cells. It is the second leading cause of irreversible blindness in developed countries. It impacts 2% of the population over 40 and 4% over 80 years of age. In its early stages glaucoma is asymptomatic, and there are effective and well tolerated treatments to halt or reduce disease progression. The insidious and irrevocable nature of the disease make early detection paramount to reduce the functional, societal, and fiscal consequences associated with it. The world population is increasing and so too is the aging population. Therefore, the global burden of glaucomatous disease is set to essentially double from 76 million in 2020 to 140 million in 2040. Worryingly, up to 70% of patients who have the disease are unaware that they are affected by it. It would therefore seem reasonable to conclude that population screening for glaucoma would be an extremely useful asset to mitigate the global health burden associated with it.

In 1968, ten principles of screening were established by Junger and Wilson which have remarkably endured the test of time. Before a decision to undertake population-based screening is made, the disease in question should pose a significant health problem, the natural history of disease progression should be known, and early signs of the disease should be evident with a test that is acceptable and reproducible within a population. There should be an appropriate treatment for the disease alongside a consensus on who to treat. Crucially, the cost effectiveness of the screening should also be considered to ensure that limited health care resources are utilised appropriately and represent good value for money. Glaucoma is a disease entity which abides by almost all of the Junger and Wilson criteria.

A recent systematic review published in JAMA Ophthalmology in January 2022, expanded upon previous recommendations (published in 2013) made to the US Preventative Services Taskforce on the harms and benefits of screening for glaucoma in adults, and aimed to provide an update on these proposals.
A total of 83 studies were included, consisting of a total of n = 75,887 patients. The review concluded that there was limited direct evidence for glaucoma screening, with no association with benefits. They stated that screening can identify patients with glaucoma and that treatment of glaucoma was associated with a lower risk of glaucomatous progression, but the evidence related to screening and associated improvement in visual outcomes, quality of life, and function was inadequate. Cost-effectiveness outcomes were not considered in this USA-based report.

The authors evaluated three different methods of diagnosing glaucoma including Optical Coherence Tomography (OCT) scanning, perimetry utilising a Humphrey Visual Field (HVF) analyser and intraocular pressure (IOP) with tonometry. They concluded that there is no accepted test or combination of tests that should be used in a population screening for glaucoma.

A similar evaluation published by the UK National Screening Committee (NSC) concluded that they cannot recommend population screening for primary open angle glaucoma (POAG) in adults due to inadequate supporting evidence. They stated that there is “an insufficient evidence base for a simple, safe, precise and validated screening test with known distribution of test values and agreed suitable cut-off levels”\(^5\). The overall prevalence of glaucoma in the general population is relatively low and there are concerns relating to overdiagnoses and over treatment, especially when many patients will not progress to visual impairment. The possibility of conducting a randomised controlled trial in the UK to evaluate the practicality and cost-effectiveness of population screening for glaucoma has been formally assessed and it was concluded that it was not the best use of research resources\(^6\).

In contrast, a study from Finland suggested population screening for glaucoma of older adults may be cost-effective\(^7\). Another study examining the cost and the detection rate of glaucoma screening in an at-risk population reported a recognition rate of 4.1%, but this was associated with a cost of $1,410 per case detected\(^8\). A recent study from Malmo, Sweden demonstrated that population screening may reduce bilateral low vision and blindness caused by glaucoma by approximately 50% over a 30-year period\(^9\).

In Ireland, most glaucoma diagnoses are opportunistic, relying solely on patient presentation to their optician and subsequent referral to an ophthalmologist based on abnormal IOP, disc, or perimetric findings. One of the greatest barriers to glaucoma screening is its cost effectiveness, but with the introduction of newer technologies this may change. Two promising future screening modalities include machine learning and genetic risk profiling in terms of polygenic risk scores (PRS).
Machine learning, and specifically deep learning systems, have been shown to replicate human grading of optic nerve head (ONH) analysis from fundal photographs for referrable and suspect cases of glaucoma. Fundal photography is an inexpensive and a reproducible method of ONH imaging that is quick and requires a basic level of training to obtain. Furthermore, incorporating fundal photography with OCT of the ganglion cell layer and the optic nerve head can augment the algorithm’s diagnostic predictability and overcome limitations associated with human labelling. It is a modality that can be utilised in conjunction with telehealth to limit in-person visits to tertiary care centres. It may also mitigate the screening requirement of IOP measurement and for undertaking time consuming visual field analysis.

Both genetic and environmental factors play an important role in the development and progression of glaucoma. The number of genes discovered that are associated with glaucomatous progression has recently skyrocketed owing to advances in genome wide association studies (GWAS). Polygenic risk scores are promising and exciting new screening and risk stratification tools in complex multifactorial diseases such as glaucoma. They can create individual profiles by aggregating multiple risk alleles and their effect sizes. The screening can incorporate glaucoma specific endophenotypes, including IOP and vertical cup to disc ratio (VCDR), to augment prediction accuracy for diagnosing glaucoma, and for identifying those at risk of rapid disease progression.

Currently glaucoma does not meet the criteria for screening, but it is a global health issue of major concern. The conditions for screening are lacking both in a standardised test and in the cost effectiveness of screening. However, both the acceptance of a standardised test and the cost effectiveness of said tests are dynamic processes which will undoubtedly evolve over time. Both machine learning and PRS are exciting novel prospects which will likely revolutionise the screening process and will be symbiotic with one another. If whole population screening proves to be too onerous of an undertaking, targeted screening of high-risk groups (persons over 60, positive family history, diabetics, and persons other than white race) may be an appropriate intermediary step. As ophthalmologists and public health physicians, it behoves us to develop new screening techniques, as the single biggest risk factor for blindness from glaucoma is late presentation.

**Corresponding Author:**
Professor Colm O’Brien,
Mater Misericordiae University Hospital,
Eccles Street,
D07 R2WY,
Ireland.
E-Mail: cobrien@mater.ie
References: