

# Is Screening for Glaucoma Necessary? A Policy Guide and Analysis

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Glaucoma is the second leading cause of preventable blindness in the World<sup>1</sup>, and gravely affects quality of life.<sup>2</sup> It affects approximately 60 million people worldwide; 1-2% of the population over 40 years and 10% of people aged over 70.<sup>3</sup> It has been estimated that the toll of bilateral blindness due to primary glaucoma will increase to 11 million people by 2020.<sup>1</sup> In developed countries, at least half of glaucoma patients are unaware of their disease and this estimate is likely to be higher in developing countries. World Glaucoma Week: WGW (<http://www.wgweek.net/>) is recognized annually on the second week of March (this year, March 9-15) in order to create and maintain global awareness and initiative for glaucoma control.

According to the World Health Organization (WHO), glaucoma is an emerging cause of blindness in Iran.<sup>4</sup> Estimated prevalence rates in Iran are 0.5% for those under 50 years and up to 5% in older populations.<sup>3,5</sup> These figures are comparable to other population-based studies in Asia and are lower in comparison to those of Middle-Eastern countries.<sup>1</sup>

Health actions are broadly categorized in four major groups of primordial, primary, secondary and tertiary prevention. Classic ophthalmic examples for these categories, in the same order include sanitation improvement and environmental hygiene to reduce Chlamydia trachomatis-infested flies as a part of strategies for trachoma control, tight control of blood sugar in diabetic patients to prevent retinopathy, access to and delivery of cataract surgery, and provision of black pupil contact lenses for patients with blind disfigured eyes. Parenthetically, it is

noteworthy that these designations are relative and may change based on what one considers as the attributing health condition.

The popular expression for secondary prevention is "screening" which itself means separation and sorting. Why "secondary"? Because the disease is already present, and we are trying to diagnose it at an asymptomatic "pre-clinical" phase (see below). Why "prevention"? Because there is potential to avoid undesirable outcomes. In this sense, one should take care not to confuse screening with surveys, as the former is a health measure and the latter is a research effort for the generation of epidemiological evidence.

We are on the merge of being able to diagnose glaucoma at early and even subclinical phases with certainty. Optic nerve imaging and nerve-fiber layer thickness analysis in terms of data capture and analytical algorithms have advanced tremendously in recent years. But in order to apply a diagnostic test for glaucoma screening, it should be practical as well as accurate for the given population; i.e. demonstrate near perfect negative predictive value (i.e. no glaucoma missed) and a positive predictive value of better than 20% (i.e. at least one true glaucoma in 5 referrals). These performance indicators are predicated on the intrinsic susceptibility and selectivity of the test, such as sensitivity and specificity, respectively, as well as the disease prevalence.

Chronic glaucomas (open and closed angle) classically fulfill screening criteria. They have a long natural course with a latent "pre-clinical" phase of reportedly 5 to 14 years,<sup>6,7</sup> the major

pathogenic factor, i.e. high intraocular pressure, is treatable, they are diagnosable, and the significance of their public health impact has been documented.

While our resources are limited, health issues and the required actions are almost infinite. Here is where economic evaluation helps us with rational priority setting. These evaluations function in two dimensions including what to screen and how to screen.<sup>8</sup> Limited studies, mostly in developed nations, addressed glaucoma screening cost-effectiveness. Advanced modeling and a variety of vision-related quality of life indices were used to estimate the gains over a 20 year time span as compared to that of the existing scenario in the target health care system.<sup>9-13</sup> The hypothetical screening staff were either optometrists or technicians, and screening tests comprised of ophthalmoscopy, tonometry and perimetry<sup>14</sup> in the population over 40 years. Unanimously, all evaluations concluded that population-based screening is not cost-effective. Projected incremental cost-effectiveness ratios (ICER) for developed countries exceeded predetermined thresholds for one additional quality-adjusted life year (QALY) gained; for instance, the ICER in the UK was more than £30,000 per QALY, which is very costly.<sup>10</sup> Corresponding figures are £15,000 per QALY for photography-based diabetic retinopathy screening by technicians<sup>15</sup> and £16,500 for amblyopia screening at 3 years of age.<sup>16</sup>

Results of economic evaluations depend on the socio-economical context, healthcare infrastructure (existing feasible alternatives and access to providers) and epidemiological factors. In the UK, an ICER of £20,000/QALY or less is considered cost-effective, and is judged as an effective use of public resource.<sup>17</sup> For developing countries like Iran where there is neither an established threshold nor estimates on cost-effectiveness, WHO proposes using the gross domestic product (GDP). In this sense, the average GDP per capita in Iran over the past five years was about \$10,000.<sup>18</sup> Therefore, glaucoma screening would be highly cost-effective for an ICER less than \$10,000/QALY, relatively cost-effective if it is between 1-3 times the GDP per

capita, and not cost-effective for an ICER more than \$30,000/QALY.<sup>19</sup>

Considering the relatively lower glaucoma prevalence in Iran, one may infer that population-based screening for chronic glaucoma is not cost-effective either. But as mentioned, other contextual factors like the screening personnel, applied diagnostic technology, existing health system capacity, etc. influence these evaluations.

A more frugal alternative is "targeted screening" in which people at higher baseline risk of the disease are chosen. Established risk factors can form the framework for this approach. In case of chronic glaucoma, these include age and family history (race may not be applicable to Iran). The estimated odds ratio per decade of increase in age is 1.6 for Asians.<sup>20</sup> The prevalence of open angle glaucoma in the under 55 age group is less than 1%, while it is significantly greater in individuals older than 70 years (3% in Asians).<sup>3,5,21</sup> Figures for Whites follow the same pattern. The adjusted odds ratio of first degree family history of glaucoma is 3 and the lifetime risk is 9 times more for siblings and offspring.<sup>22,23</sup> In the UK, it is predicted that glaucoma screening might be cost-effective in a 50-year-old cohort at a prevalence of 4% with a 10 year screening interval.<sup>10</sup>

What do ophthalmologists routinely do? They perform "opportunistic case finding"!<sup>24</sup> It has been reported that half of the patients with a recent diagnosis of glaucoma had undergone an eye examination in the preceding 12 months but still had been missed.<sup>25</sup> On the other hand, it has been shown that glaucoma is more common in clinical populations.<sup>26</sup> This opportunity for "clinical screening" should be well embraced by clinicians. It is emphasized that this is intended to detect glaucoma in subjects with no complaint of visual loss and in non-specific referrals like dry eye syndrome, etc.<sup>15</sup> This capacity can be hugely extended to primary eye care services such as optometry and general practices.

#### PRELIMINARY POLICY STATEMENTS

Population-based screening for chronic glaucoma may not be currently cost-effective for Iran.

Targeted screening in families who had a glaucoma case in first degree relatives older than 50 years is recommendable.

Social marketing and occasional campaigns (on World Glaucoma Week, for instance) should be performed to create awareness and encourage people to seek care.

Clinical screening should be approached on multiple levels; optometrists, general/family physicians, and ophthalmologists should rule out glaucoma in their referrals. For this purpose, required guidelines and equipment should be developed and supplied.

Alternative screening programs should be tested and evaluated in population labs. Specifically, teleophthalmology and modern information technology tools and protocols should be explored.

The future is bright, as personalized (molecular and genomic-based) medicine may soon provide us with constitutional probabilities for a wide spectrum of health conditions including glaucoma. Alternatively, biomarkers may help us assess risks for glaucoma or directly diagnose it at clinical and population levels; then we can consider our approach towards glaucoma screening more precisely.

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### Conflicts of Interest

None.

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