Glaucoma in Asia: regional prevalence variations and future projections

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ABSTRACT

Purpose To evaluate glaucoma prevalence and disease burden across Asian subregions from 2013 to 2040.

Methods We conducted a systematic review and meta-analysis of 23 population-based studies of 1318 primary open angle glaucoma (POAG) cases in 66 800 individuals and 691 primary angle closure glaucoma (PACG) cases in 72 767 individuals in Asia. Regions in Asia were defined based on United Nations’ (UN) classification of macro-geographic regions. PubMed, Medline and Web of Science databases were searched for population-based glaucoma prevalence studies using standardised criteria published to 31 December 2013. Pooled glaucoma prevalence for individuals aged 40–80 years was calculated using hierarchical Bayesian approaches. Prevalence differences by geographic subregion, subtype and habitation were examined with random effects meta-regression models. Estimates of individuals with glaucoma from 2013 to 2040 were based on the UN World Population Prospects.

Results In 2013, pooled overall glaucoma prevalence was 3.54% (95% credible interval (CrI) 1.83 to 6.28). POAG (2.34%, 95% CrI 0.96 to 4.55) predominated over PACG (0.73%, 95% CrI 0.18 to 1.96). With age and gender adjustment, PACG prevalence was higher in East than South East Asia (OR 5.55, 95% CrI 1.52 to 14.73), and POAG prevalence was higher in urban than rural populations (OR 2.11, 95% CrI 1.57 to 2.38). From 2013 to 2040, South Central Asia will record the steepest increase in number of glaucoma individuals from 17.06 million to 32.90 million compared with other Asian subregions. In 2040, South-Central Asia is also projected to overtake East Asia for highest overall glaucoma and POAG burden, while PACG burden remains highest in East Asia.

Conclusions Across the Asian subregions, there was greater glaucoma burden in South-Central and East Asia. Sustainable public health strategies to combat glaucoma in Asia are needed.

INTRODUCTION

Glaucoma is a leading cause for irreversible visual impairment and blindness worldwide.1 Asia alone accounts for almost 60% of the world’s total glaucoma cases.2–5 In view of the disproportionate burden of glaucoma and the rapid ageing trends in Asia, there is a pressing need for public healthcare readiness to specifically address the growing number of people with glaucoma in Asia.

Because specific subtypes of glaucoma require different strategies for screening, prevention and treatment (eg, prophylactic laser iridotomy is needed to prevent primary angle closure glaucoma (PACG)), accurate and up-to-date estimates of glaucoma prevalence and trends are needed. Previous reviews and meta-analyses of glaucoma in Asian populations3–6 were based on studies conducted nearly a decade ago with scant population-based data.7–10 These studies also varied in age group structure, sample size, glaucoma examination methods and diagnostic criteria, making accurate comparisons of glaucoma prevalence between different populations challenging. More importantly, considering the magnitude of the glaucoma burden in Asia, there is still a significant lack of knowledge on various glaucoma subtypes across different Asian subregions. A recent meta-analysis only reported the trend of PACG in Asia, but did not provide estimates for primary open angle glaucoma (POAG) and other glaucoma subtypes.11

Our group recently reported on global glaucoma prevalence, as well as continent-specific glaucoma prevalence in Africa, North America, Latin America, Europe and Asia. Similarly, we found that glaucoma burden disproportionally affected people residing in Asia compared with other regions of the world.5 Nevertheless, our earlier study did not evaluate the variation of glaucoma prevalence across different Asian subregions. Furthermore, estimates of secondary glaucoma were also not calculated in our earlier work, as secondary glaucoma data were largely not available in Western and African population-based studies. Hence, to accurately assess subregional variations in the prevalence of glaucoma overall or its subtypes, a further analysis that takes into consideration differences in regional population structures is needed.

In this systematic review and meta-analysis, we aimed to estimate the prevalence and future projection of glaucoma, including its subtypes, in different subregions across Asia using the hierarchical Bayesian (HB) approach. The HB models account for different sources of heterogeneity in population characteristics, allowing a flexible modelling structure,16 17 and provide robust estimates for regions with limited data. Detailed findings across Asian subregions will provide useful and in-depth information for the design of sustainable public health strategies across Asia.

METHODS

Sources and methods of literature search

We conducted a systematic review and meta-analysis according to the Meta-analysis of Observational Studies in Epidemiology.18 We searched the electronic databases of PubMed, Medline and Web of Science for relevant published research articles, letters, review articles and abstracts. We conducted the literature search from 23 October 2013 and
updated to 31 December 2013 for articles dating from January 1960. The literature search used a combination of the following words either as title words or medical subject headings (MeSH):

Irrelevant and duplicate articles were excluded on the basis of the titles and abstracts. Reference lists of all short-listed articles were checked to identify other studies. This strategy identified all articles used in previous reviews.1 4 6 8 9

Study inclusion and exclusion criteria
Study inclusion was based on the guidelines for glaucoma prevalence surveys by Foster et al15 and Quigley et al.20 We identified studies fulfilling all the following criteria: (1) population-based study of POAG, PACG or secondary glaucoma from a defined geographic region in Asia; (2) clear definition of random or clustered sampling procedure; (3) response rate ≥70%; (4) visual field testing with either automated static or frequency doubling perimetry at least among glaucoma suspects; (5) optic disc evaluation by an ophthalmologist; (6) anterior chamber angle evaluation by gonioscopy at least among glaucoma suspects; and (7) glaucoma defined using the International Society for Geographical & Epidemiological Ophthalmology (ISGEO) criteria20 or similar to the ISGEO scheme based on evidence for structural or functional features of glaucomatous optic neuropathy, independent of intraocular pressure.

Studies with the following characteristics were excluded: (1) hospital-based or clinic-based studies or audits; (2) comprising invited volunteers, self-reported glaucoma diagnosis or specific groups of individuals; (3) populations of Asian ancestry not residing in Asia (eg, Asian descents in Europe or the Americas); (4) non-English articles; and (5) studies reporting number of eyes rather than individuals with glaucoma.

Two investigators (EWC and Y-CT) independently selected the studies and applied the inclusion and exclusion criteria. Disagreements were resolved by consensus or adjudication by the senior author (C-YC).

Data extraction
The following information was extracted from each study: study location, year of publication, year of study conducted, response rate, age groups, gender, habitation type, geographic subregion and the prevalence of POAG, PACG and secondary glaucoma. Habitation type was defined as rural, urban or mixed, according to the descriptors of the population studied in the published articles. Geographic subregion in Asia was defined according to the United Nations (UN) classification of macro-geographic subregions: East Asia, South East Asia, South-Central Asia and West Asia.21 Secondary glaucoma was defined based on clinical findings indicating the following entities: pseudoexfoliation, rubecoid, steroid-induced, traumatic and pigment dispersion glaucoma. We excluded aphakic or anaphakic glaucoma as there is uncertainty of the anterior chamber angle status, and whether glaucoma was primary or secondary to cataract surgery. If age group or gender-specific data were not available in the published articles, respective authors were contacted for request of stratified data. For this purpose, authors from eight studies were contacted; of these, four responded with requested data.

Statistical analyses
We constructed HB models to perform meta-analysis to determine the prevalence of POAG, PACG, secondary glaucoma and all glaucoma combined in Asia. In this study, ‘all glaucoma combined’ refers to the combined group of POAG, PACG and secondary glaucoma. This approach has also been adopted and described in existing literature.9 18 22 In total, there were 23 studies included in the analyses and provided overall prevalence data for the glaucoma subtypes (POAG, PACG and secondary glaucoma). Among them, gender-specific and age group-specific prevalence were extracted from 20 studies (except Meiktila, Qatar and Yazd studies) for the glaucoma subtypes (POAG and PACG), that is, each study had age group-specific and gender-specific prevalence breakdown data. For the South-Central Asia subregion, as there were no currently available population-based studies from Central Asia, the calculation was extrapolated to the whole subregion, based on studies from South Asia.

Meta-analysis can be naturally described in a hierarchical structure in the HB model. In the HB approach, the logit of prevalence was modelled using a normal distribution with mean of a linear combination of covariates that varies across studies (ie, age, gender, geographic subregion, habitation type). The overall age ranges of different studies were mapped to the same age range (ie, 40–80) to ensure the pooled prevalence was comparable between various subregions or rural/urban habitation, by centring the lower bound of age range to 40 and upper bound to 80.22 For each study, we calculated the difference between the lower age bound of each study and the defined lower age bound of 40, and vice versa for the upper age bound difference. For example, for a study with an age range of 35–90, the lower age bound difference would be −5 and the upper age bound difference would be +10. After calculating these two differences respectively across the included studies, two additional parameters were estimated in the model for the lower and upper age bound differences, respectively. At the same time, censoring of studies with age range outside 80 years but without specified upper limit (eg, 80+) was also taken into account in our model.

In the estimation of pooled prevalence, the overall prevalence data from 23 studies were used to model Asian subregions (East, South-Central, South East and West) and habitation types (rural/urban/mixed). Subregion and habitation-type covariates were individually added into the model with the aforementioned two age mapping parameters and one age-censoring parameter. Random effects were specified for subregions and habitation-type covariates to borrow information from other covariate-specific groups, which is especially useful in estimating for groups with small sample size. Some studies provide several data sets (ie, >1 age group, or habitation type, within the same study). Under such circumstances, the inherent variability within the same study also needs to be taken into account when pooling data with other studies. Hence, the effect of within-study variability was also added into the model as a random effect. Other parameters were treated as fixed effects.

In the same model, the number of people with glaucoma was projected by subregions in Asia according to UN classification. The population projection data in World Population Prospects of the UN 2010 consist of the latest results of national population consensus and demographic surveys from countries worldwide and also consider mortality rate and fertility rate in its projection of world population number.23 These data were incorporated in the aforementioned prevalence model by multiplying the prevalence parameters. Specifically, the projected number of individuals with glaucoma was first given by the
RESULTS

The selection process to identify relevant studies is shown in figure 1. A total of 3,132 published articles based on abstracts and titles were identified. After initial abstract review, 74 potentially eligible unduplicated articles were retrieved for detailed evaluation. Of these, we applied the inclusion and exclusion criteria and identified 30 articles from 23 population-based studies reporting glaucoma prevalence in Asia for inclusion in the meta-analysis (see online supplementary tables S1 and S2). In brief, there were 10 studies from East Asia (China,[28–33] Japan,[34–38] South Korea,[39–40] and Mongolia[41]), 9 studies from South-Central Asia (India,[42–43] Nepal,[44] Iran[45] and Sri Lanka[46–48]), 5 studies from South East Asia (Singapore,[49–50] Myanmar,[51–52] and Thailand[53]) and 1 study from West Asia (Qatar).[54] POAG data were extracted from 23 articles, of which 20 consisted of data stratified by age and 17 comprised data stratified by both age and gender. PACG data were extracted from 24 articles, of which 19 consisted of data stratified by age and 16 comprised data stratified by both age and gender. Data on secondary glaucoma data were extracted from 15 articles. In all, the included data involved 1,318 POAG cases in 66,800 individuals, 691 PACG cases in 72,767 individuals and 103 secondary glaucoma cases in 38,029 individuals.

Pooled glaucoma prevalence across Asia

Pooled estimates of glaucoma in people aged 40–80 years in 2013 stratified by glaucoma subtypes and geographic subregions are shown in table 1 and online supplementary figure S1. The pooled prevalence of glaucoma overall was 3.54% (95% CrI 1.83 to 6.28) in adult Asians. Among the glaucoma subtypes, the prevalence of POAG was highest (2.34%; 95% CrI 0.96 to 4.55), followed by PACG (0.73%; 95% CrI 0.18 to 1.96) and secondary glaucoma (0.47%; 95% CrI 0.09 to 1.48).

The prevalence of glaucoma overall was similar across subregions, ranging from 3.40% in West Asia to 3.70% in East Asia (table 1). A significant difference in glaucoma prevalence between subregions was observed only for PACG. East Asia had the highest prevalence of PACG (1.07%; 95% CrI 0.28 to 2.74) compared with the rest of the other Asian subregions (table 1).
Bayesian meta-regression showed that the OR of PACG was 5.55 (95% CrI 1.52 to 14.73) in East Asia compared with South East Asia after adjusting for age and gender (table 2).

### Association of age, gender and habitation type with glaucoma subtype

Based on the Bayesian meta-regression model (table 2), for each decade increase in age, the odds of POAG increased by 54% (95% CrI 40% to 70%), and the odds of PACG increased by 121% (95% CrI 92% to 157%). After adjusting for age, men were more likely to have POAG (OR 1.37, 95% CrI 1.17 to 1.59) and less likely to have PACG (OR 0.54, 95% CrI 0.41 to 0.71) compared with women.

In addition, POAG was more prevalent in urban areas (2.24%) compared with rural areas (1.53%), while PACG appeared more prevalent in rural areas (0.73%) (figure 2). However, Bayesian meta-regression analysis showed that only POAG was significantly more prevalent in people living in urban areas (OR 2.11, 95% CrI 1.57 to 2.38) compared with people living in rural areas after adjusting for age and gender.

### Number of people with glaucoma across Asia

The number of people with glaucoma in Asia in 2013 was 51.32 million (table 1). For various glaucoma subtypes, the figure estimates in 2013 were 33.45 million for POAG, 11.74 million for PACG and 6.13 million for secondary glaucoma. East Asia had the highest number of people with glaucoma (25.20 million), followed by South-Central Asia (17.06 million) and South East Asia (6.92 million).

The number of people with glaucoma in Asia is estimated to increase by 16.0% to 59.51 million in 2020, and by 57.6% to 80.87 million in 2040 (table 3 and online supplementary table S3). These increments would be mainly attributable to the drastic increase in South-Central Asia region (see online supplementary figure S2). Specifically, South-Central Asia would eventually surpass East Asia and would consist the highest number of people with POAG (23.25 million), secondary glaucoma (4.28 million) and overall glaucoma (32.90 million) in the year 2040. Nevertheless, East Asia would continue to remain as the region with the highest number of PACG (9.13 million) in the year 2040 (table 3).

### DISCUSSION

Our systematic review and meta-analysis provided a comprehensive evaluation of glaucoma epidemiology and trends across Asia, the world’s most populous and fastest-growing continent. Our results suggest a significant current and future glaucoma burden in Asia, particularly affecting East and South-Central Asia regions. In 2013, the overall prevalence of glaucoma was 3.54%. POAG was the predominant glaucoma subtype, accounting for 65.2% of all glaucoma. There was a higher PACG risk in individuals residing in East Asia, and higher POAG risk in urban compared with rural habitations. Among the subregions, South-Central Asia will record the steepest increase in number of glaucoma individuals from 17.06 million to 32.90 million, from 2013 to 2040. These findings have implications on the prioritisation and implementation of future public health initiatives for glaucoma in different countries and regions across Asia.

We estimated a higher overall prevalence of POAG (2.34%) and PACG (0.73%) in Asians compared with earlier reviews. Quigley and Broman estimated that the prevalence of POAG and PACG were 0.98% and 0.60%, respectively, in Asians aged 40 years and older in 2010. Rudnicka and colleagues found a...
pooled POAG prevalence of 1.4% in Asians. These analyses likely underestimated the actual glaucoma prevalence, as these were based predominantly on population studies with non-standardised glaucoma diagnostic procedures and criteria, for example, lacking visual field testing, or relying only on intraocular pressure to diagnose glaucoma. Accurate glaucoma assessment involves a complete evaluation of structural (ie, glaucomatous optic disc changes) and functional damage (ie, visual field defects). Gonioscopy is essential to differentiate between POAG and PACG, while alternative assessment techniques, for example, van Herrick, fail to identify a significant number of PACG cases. In this analysis, we imposed strict study inclusion criteria and excluded several studies pooled in earlier meta-analyses with non-standardised study designs or criteria and excluded several studies pooled in earlier meta-analyses focusing only on PACG prevalence. However, our calculations differ from an earlier analysis by Tham et al. The principal reason is that this analysis included two additional studies, that is, Aravind and Yazd, both of which are large studies with >7100 participants cumulatively. The Yazd study was not published at the time the global analysis was conducted; nevertheless, its inclusion indicates that our analysis is likely more representative of the diverse populations across Asia. Furthermore, discrepancies in estimates between this study and Tham et al may also be due to the additional information of population structure across Asian subregions that was incorporated in the analysis of this current work. In this regard, Tham et al previously assumed a constant prevalence for entire Asia (ie, without taking into account regional variation in population structure across the Asian subregions). This was particularly observed for PACG estimates, which showed greater variation in prevalence across the subregions, compared with POAG (table 1). Thus, the overall estimate for PACG was slightly different from that in Tham et al, while that for POAG was largely similar.

We found that POAG was associated with urban habitations. This possibly suggests evidence for a broader effect of urban environments on POAG risk across Asia, consistent with more limited data from two Indian populations. The higher prevalence of myopia in urban areas could partially explain the increased risk. However, the role of hypertension and diabetes, two major risk factors for POAG, as well as other less consistent risk factors such as diet, physical activity, pollution and psychological stressors, need to be explored. With increased urbanisation in Asia projected for the future, glaucoma prevalence could continue increasing, particularly in countries with higher rates of urbanisation, for example, China and India.

Not surprisingly, East and South-Central Asia harbour the highest glaucoma burden in 2013. These regions comprise the two most highly populated Asian countries, that is, China and India, which account for 61% of Asia’s population. Overall glaucoma prevalence rates for East Asia are attributed to the high prevalence of PACG in China, and high POAG prevalence in Japan and South Korea in the form of normal tension glaucoma. The overall and region-specific glaucoma prevalence in Asia of 1.09% (95% CrI 0.43 to 2.32), which was slightly higher than the estimate in the current analysis (0.73%).

### Table 2: ORs for POAG and PACG in terms of age, gender, geographic subregion and habitation type from Bayesian meta-regression model

<table>
<thead>
<tr>
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<th>Unadjusted</th>
<th>Age and gender adjusted</th>
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<tbody>
<tr>
<td></td>
<td>POAG</td>
<td>PACG</td>
</tr>
<tr>
<td>Age, decade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.54 (1.40 to 1.70)*</td>
<td>2.21 (1.92 to 2.57)*</td>
<td>1.50 (1.39 to 1.63)*‡</td>
</tr>
<tr>
<td>Gender, male</td>
<td>1.47 (1.16 to 1.86)*</td>
<td>0.59 (0.44 to 0.79)*</td>
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<tr>
<td>Geographic subregion</td>
<td></td>
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<tr>
<td>South-East</td>
<td>Reference</td>
<td>Reference</td>
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<tr>
<td>0.88 (0.39 to 1.76)</td>
<td>2.05 (1.18 to 5.61)*</td>
<td>0.88 (0.32 to 1.98)</td>
</tr>
<tr>
<td>East</td>
<td>1.03 (0.43 to 2.05)</td>
<td>1.51 (0.53 to 3.22)</td>
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<tr>
<td>South-Central</td>
<td></td>
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<tr>
<td>Rural</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Urban</td>
<td>1.72 (1.06 to 2.58)*</td>
<td>0.76 (0.37 to 1.36)</td>
</tr>
<tr>
<td>Mixed</td>
<td>2.08 (0.59 to 5.34)</td>
<td>1.28 (0.39 to 3.38)</td>
</tr>
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Data are OR (95% credible intervals). *Significant results are indicated. †Adjusted for gender only. ‡Adjusted for age only. §Age-specific data not available for Western Asia.

PACG, primary angle closure glaucoma; POAG, primary open angle glaucoma.

Figure 2: Pooled prevalence estimates (40–80 years) of primary open angle glaucoma (POAG), primary angle closure glaucoma (PACG), secondary glaucoma and all glaucoma stratified by habitation type (rural/urban/mixed). Estimates were calculated from meta-analysis model.
burdens are higher than previous projections for Asia and India. There is a substantial increase of people with glaucoma (57.6%) in our projection up to 2040. The increase in overall number of people with glaucoma is principally due to the ageing transition in population structure, that is, improved life expectancy and disproportionate increase in elderly individuals over time. While East Asia had the highest number of people with glaucoma in 2013, South-Central Asia will eventually surpass East Asia and record the highest number of people with POAG, secondary glaucoma and overall glaucoma in 2040. These future changes in trend over time may be attributed to the disproportionate projected population expansion in South-Central Asia compared with stable (or near zero) population growth and declining fertility in East Asia in the coming years.65

The strengths of this study include measures to reduce inaccuracies associated with a large number of heterogeneous study populations within a meta-analysis. First, we used the HB approach, which provides robust estimates of disease prevalence. Second, studies included in our meta-analysis were based on standardised glaucoma evaluation methods and diagnostic criteria, lending greater accuracy to calculated estimates. In addition, better representation across Asia in the meta-analysis is evidenced by pooling more recent studies from varied ethnicities, including those not previously analysed (ie, South Korea, Iran, Nepal, Sri Lanka and Qatar).48–51 55 56 58

There are limitations to this analysis. First, the lack of age-specific and gender-specific data from several studies allowed fewer studies to be included in the Bayesian meta-regression, particularly for secondary glaucoma. Second, prevalence estimates for West Asia used data from the Qatar Eye Study only. Third, prevalence estimates for South-Central Asia were derived from South Asian population-based studies due to the unavailability of data in Central Asia. However, considering the geographic proximity between South and Central Asia, and the larger demographic of South Asia in that subregion, it may be reasonable to extrapolate the estimates of South Asia to the entire subregion in order to provide the best available estimate for this subregion.

**SUMMARY**

Our analysis provides the basis to guide rationalisation and implementation of sustainable healthcare infrastructure to screen, monitor, treat and rehabilitate people affected with glaucoma across Asia. Our findings point to a particular need in East Asia and South-Central Asia, which will harbour the highest number of people with glaucoma. It is also well recognised that there are significant challenges faced in these resource-poor regions. The lack of an acceptable screening technique, limitations in access to care and available medical expertise need to be sufficiently addressed to ensure the success of any public health programme.

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**Contributors** EWC and XL contributed equally to the article. EWC and Y-CT reviewed the literature. XL and JL checked and analysed the data. EWC and Y-CT drafted the manuscript. C-YC planned the study. C-YC, TYW and TA did the critical revision.

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