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Brad Guo, Yiran Tan, Stephen Nygaard, Cesar Carrillo, Kham Od Nouansavanh, Kitar Souksamone, Robert J Casson

Prevalence of glaucoma in the Lao People's Democratic Republic: the Vientiane Eye Study

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23 November 2021

Prevalence and causes of visual impairment and blindness in Lao People's Democratic Republic

The Vientiane Eye Study

Yiran Tan;^{1,2} Brad Guo;^{1,2} Stephen Nygaard; ² Cesar Carillo; ¹ Kham Od Nouansavanh;³ Kitar Souksamone; ³ Robert Casson; ^{1,2}

Affiliations:

¹Department of Ophthalmology, Royal Adelaide Hospital, Port Road, SA 5000, Australia.

² Discipline of Ophthalmology and Visual Sciences, University of Adelaide, Adelaide, SA 5000, Australia.

³ National Ophthalmology Centre (NOC), Vientiane Province, Lao PDR

Corresponding author: Prof. Robert Casson Royal Adelaide Hospital, Port Rd, Adelaide, SA 5000. Email: casson.robert@gmail.com Telephone: (08) 7074 0000

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This paper has not been presented previously in any meeting.

KEYWORDS: Visual impairment; blindness; prevalence; Lao; Vientiane

ABSTRACT

Objective: To determine the prevalence and causes of visual impairment and blindness in Vientiane Province, the Lao People's Democratic Republic (Lao PDR). **Design:** Population-based, cross-sectional study.

Participants: Random, stratified, cluster sampling of inhabitants 40 years of age and older from urban and rural areas of Vientiane Province was performed; 1264 eligible participants were identified.

Methods: The ophthalmic examination included presenting and pinhole Snellen visual acuity with an illiterate E chart, slit-lamp examination of the anterior segment, and dilated stereoscopic fundus examination. The principal cause of visual impairment was recorded.

Main Outcome Measures: Visual impairment and blindness were defined by both presenting and corrected visual acuity (VA) based on the better eye according to World Health Organization (WHO) criteria: VA < 6/12 for mild impairment, VA < 6/18 for moderate impairment, VA < 6/60 for severe impairment, and VA < 3/60 for blindness.

Results: Comprehensive ophthalmic examinations were performed on 1264 participants (77.8%). Population-weighted prevalence of presenting bilateral blindness was 1.4% and bilateral visual impairment was 22.4% for persons 40 years of age and older. After pinhole correction, the corresponding prevalence of blindness was 1.3% and that of visual impairment was 12.6%. Cataract was the leading cause of presenting bilateral blindness (52.9%), whereas uncorrected refractive error was the predominant cause of presenting visual impairment (40.3%).

Conclusions: Visual impairment and blindness remain major public health problems in Lao PDR. There is an ongoing need to fund ophthalmic care resources and community education programs to improve access to health care in this region.

Background

Vision impairment remains a major global health problem. An estimated 340 million people worldwide are at least moderately visually impaired by World Health Organization (WHO) criteria. At least 2.2 billion people worldwide have a vision impairment, of whom almost half are preventable or curable. The leading causes of vision impairment or blindness are cataract (94 million), uncorrected refractive error (88.4 million) and glaucoma (7.7 million).¹

South East Asia has a particularly severe burden of blindness.²

Lao People's Democratic Republic (<u>Lao</u>PDR) is a landlocked country in South East Asia with an estimated population of 6.3 million.³ Lao<u>PDRs</u> is served by 1 tertiary and 10 secondary eye care facilities. In 1996, 29% of disabilities in Lao PDR were attributed to visual impairment.⁴ <u>TA key objective of he</u> WHO's Universal Eye Health: Global Action Plan <u>emphasizedhighlighted</u> the need f<u>orer</u> generating evidence on the magnitude and causes of visual impairment.⁵ However, robust epidemiologic data from many Asian regions, including the Lao PDR, remain scarce.

To provide updated data on the prevalence and causes of visual impairment in Lao PDR, we conducted a large-scale, population-based ophthalmic survey in urban and rural areas of Vientiane Province. Here, we report the prevalence and causes of visual impairment after best spectacle correction in this region.

Patients and Methods

Sampling Procedure

The Vientiane Eye Study (VES) was a population-based, cross-sectional ophthalmic survey of inhabitants in urban and rural areas of the Lao PDR. The principle aim of this project was to estimate the prevalence and causes of visual impairment among persons 40 years and older in this region.

Commented [RC1]: Reference: GBD 2019 Blindness and Vision Impairment Collaborators. and Vision Loss Expert Group of the Global Burden of Disease Study. "Trends in prevalence of blindness and distance and near vision impairment over 30 years: an analysis for the Global Burden of Disease Study." *The Lancet. Global health* vol. 9,2 (2021): e130-e143. doi:10.1016/S2214-109X(20)30425-3

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The study was conducted within Vientiane Province, an area covering 15, 927 square kilometres and divided into 11 districts. The province has an approximate population of 419 090 people and is served by a centrally located eye hospital. Participants were selected using a randomised, stratified, cluster sampling process. A sampling frame consisting of a list of all villages in the Vientiane Province along with their populations was obtained from the Ministry of Health. Based <u>on</u> data from neighbouring regions, the <u>prevalence of</u> combined blindness and visual impairment of-was estimated to be 13%. Allowing for an estimated design effect of 2.0 and an expected participation rate of 80%, a total sample size of 1610 persons \geq 40 was calculated to obtain a precision of 20% with 95% confidence interval (CI).

The primary sampling unit occurred at the village level. The sampling frame comprised the 491 villages in the province of which 181 (36.9%) were categorised as urban. Members of our team Investigator (SN) and health care workers from the National Ophthalmology Centre (NOC) enumerated the selected villages before commencinged of the survey. Four urban and four rural sites were randomly selected. Households were selected by random compact sampling and all persons in the household \geq 40 years of age were invited to participate. Sampling in each village continued until the required sample size had been reached. All participants within a village were well known to the village chief, and eligible participants were identifiable readily.

Data Collection

Data collection was carried out between June 2016 to June 2018. A single survey team conducted the entire study. Each team member was assigned specific tasks and was well trained in the appropriate area. All equipment and personnel were transported to each survey site, and the data collection occurred on site. Examinations were performed at the OPH, the village community hall, or at participants' residence if distance from the site was prohibitive. Specific observations such <u>as</u> intraocular pressure (IOP) and the grading of cataracte were performed by <u>one4 experienced</u> team members to limit or eliminate interobserver variability.

Demographic details and a medical and ophthalmic history were obtained from each patient in their own language by qualified health care workers who used a standardized questionnaire. Each participant then received a comprehensive Commented [RC2]: What's this?

ophthalmic examination that included presenting and best-corrected visual acuity (VA); autorefraction (Nikon, Retinomax, Tokyo, Japan); Goldmann applanation tonometry (Haag-Streit AT 900, Koeniz, Switzerland); pupil reflex examination; slitlamp examination of the segment; static and dynamic gonioscopy using a Sussman Four Mirror Gonioscope (Ocular, Bellevue, WA); ocular biometry (Quantel Medical Axis II PR, Clermont-Ferrand, France); pachymetry (Quantel Medical Pocket II); slitlamp lens assessment using the WHO Cataract Grading System; and stereoscopic fundus examination. If more than 90° of the posterior trabecular meshwork (TM) was visible, the pupil was dilated with tropicamide 1% and phenylephrine 2.5%. Eyes with \leq 180° of posterior TM visible were deemed "occludable" and dilated with tropicamide 0.5% only and kept under observation for 4 hours; if not possible, they were not dilated. All instruments were recalibrated when moved to another examination site. Eyes presenting with VA less than 6/12 were assigned a principalle cause of visual impairment by an experienced ophthalmologist (CC). In difficult cases, at least ≥ 2 experienced ophthalmologists reached a consensus on the principal cause of visual impairment.

One well-qualified and experienced health care worker performed all of the VA testing in the patients' own language. VA was measured in each eye separately using a front-illuminated illiterate E LogMAR acuity chart. The presenting VA was measured with the participant's' <u>wearing their</u> habitual spectacles, if any. Best-corrected visual acuity was measured as pinhole vision using a multi-fenestrated occluder. Testing for counting fingers (CF), hand movement (HM), perception of light (PL), or no perception of light (NPL) was performed on those with <u>VAvision</u> worse than 3/60. The VA was intermittently re-examined by the attending ophthalmologists for quality assurance, and all borderline cases of blindness (6/60 < VA < CF) were checked by an ophthalmologist. In case of discrepancy between the recorded VA and the clinical findings, the VA was repeated, and the best result was recorded.

Definition

Blindness and vision impairment were defined based on the International Classification of Diseases 11th Revision (ICD-11).⁶ WHO presenting blindness was defined as unaided VA (or with spectacles if worn) less than 3/60 in the better eye, and best-corrected blindness was defined as pinhole VA less than 3/60 in the better

eye. Visual impairment was classified as either mild, moderate or severe according to the WHO visual impairment classification. Mild presenting visual impairment was defined as VA less than 6/12 but 6/18 or more in the better eye unaided (or with spectacles if worn). Moderate presenting visual impairment was defined as VA less than 6/18 but 6/60 or more in the better eye unaided (or with spectacles if worn). Severe presenting visual impairment was defined as VA less than 6/18 but 6/60 or more in the better eye unaided (or with spectacles if worn). Severe presenting visual impairment was defined as VA less than 6/60 but 3/60 or more in the better eye unaided (or with spectacles if worn). Field defects were not taken into consideration. Pinhole VA was considered best-corrected VA for the purposes of the study (aphakic patients used a +10-dioptre sphere (DS) lens and pinhole).

Ethics

The VES was approved by Lao PDR Ministry of Health and had ethical approval from the Central Adelaide Local Health Network Human Research Ethics Committee. Consent for participation was obtained from the head of each village before commencement of the survey. Written informed consent was obtained from all participants, in their native language. The study was conducted in accordance with the Declaration of Helsinki. Treatment of minor ailments was provided free of charge at the examination sites. Participants blind from cataracts and those requiring essential treatment were offered referral to the NOC, Vientiane Province.

Statistics

Prevalence was calculated as ratio estimates using appropriate weights for each of the sampled villages. Bootstrapping was used to overcome the problem of variance estimation in clusters where only the 1 primary sampling unit (village) was selected. Univariate analyses were performed to determine whether age, gender, medical comorbidities, tobacco use, and locality were significantly related to blindness. Age was grouped into the following subgroups: 40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years or older. Medical comorbidities included history of diabetes, hypertension, coagulopathy and autoimmune disorders. A multivariate logistic regression model was constructed to investigate the combined predictors of blindness. Estimates of prevalence and statistical analyses were performed using a commercially available statistical software package (Stata v.15.1 for Windows, **Commented [RC3]:** < 6/18 or < 6/12? Is 6/18 mild or moderate?

College Station, TX). Odds ratios and 95% confidence intervals (CIs) for the predictors were calculated. All *P* values were 2-sided and were considered statistically significant when the values were less than 0.05.

Results

A total of 1625 participants were sampled and 1264 completed the full ophthalmic examination (60.9% female and 39.1% male). The overall participation rate was 77.8%, and the mean age was 57.6 years (<u>s</u>Standard deviation (SD), 11.2 years). 64.6% of participants lived in a rural area. The demographic characteristics and age distribution of subjects in the VES are shown in Table 1 and Table 2, respectively.

The prevalence estimates of presenting_WHO defined blindness in the 40 years or older population in Vientiane Province was 1.4% (95% CI, 0.8 -2.0; 17 participants). The prevalence estimates for combined WHO visual impairment (including mild, moderate, and severe) was 22.4%. The prevalence estimates of blindness based on best-corrected visual acuity (BCVA) was 1.3% (95% CI, 0.8 – 1.8; 16 participants). The prevalence estimates of visual impairment based on BCVA was 12.6%. Age-specific prevalence rates of presenting and best corrected visual impairment are shown in Table 3 and Table 4, respectively.

The causes of WHO defined-blindness and visual impairment are shown in Table 5. Seventeen participants were blind in both eyes, of whom 1 was correctable with refraction. Cataract was the leading cause of bilateral blindness in 53% of participants. Maculopathy, including age_-related macular degeneration (1/17) and myopic macular degeneration (2/17), was the cause of 18% of blindness in both eyes. Two participants (12%) were blind because of glaucoma; one from primary angle_-closure glaucoma (PACG) and another from primary open_-angle glaucoma (POAG). A further two participants (12%) were blind due to corneal opacification of unspecified aetiology. Uncorrected refractive error was the leading cause of visual impairment (40%), followed by cataract (33%), maculopathy (7%), glaucoma (5%), pterygium (2%) and non-glaucomatous optic neuropathy (2%).

The odds of developing visual impairment and blindness increased with age. In the univariate analysis, age (OR, 16.9; P < 0.001) was the only risk factor found to have a statistically significant association with blindness (Figure 6). In the **Commented [RC4]:** Do we have CI for this estimate?

Commented [RC5]: CI?

multivariable analysis, age, gender and hypertension were all found to be independently associated with the odds of visual impairment, including blindness (Figure 7).

Discussion

The VES is the first population-based, cross-sectional eye study conducted in Lao PDR. We found that the population-weighted prevalence of bilateral blindness and visual impairment among the adult population aged 40 years of age and older in Vientiane Province was 1.4% and 22.4%, respectively. As expected, the prevalence estimate of blindness and visual impairment in Lao PDR were higher when compared to developed countries in the Asia-Pacific, including Japan^{7,8}, Singapore⁹, China¹⁰⁻¹² and Australia^{13,14}; but significantly lower than the neighbouring Myanmar¹⁵. Notably, our study found higher proportion of visual impairment (22.4%) when compared to the overall prevalence of blindness (1.4%). This observation can be explained by changes to the definition of visual impairment under ICD 11 to include mild visual impairment, which was defined as Snellen VA between 6/12 and 6/18.6 Age was a significant predictor of visual impairment and blindness based on the multi-variable analysis (p<0.001). Over 40% of participants surveyed aged 70 years or older were found to suffer from visual impairment or blindness. This trend is observed in all other epidemiological studies and reflects the predominantly agerelated causes of visual impairment and potential limitations in access to ophthalmic care among the elderly population^{7,9-11,15-18}. Gender was another strong predictor of visual impairment, with females being 1.9 times more likely to have visual impairment compared to male counterparts. This apparent disparity can be explained by both socioeconomic and cultural factors. For example, in many developing communities, women consistently face barriers due to limited experience in travelling outside their community and limitations in financial decision-making power.¹ It is important therefore to recognise gender inequity as an ongoing barrier to the delivery of sustainable eye care. Participants with a history of hypertension also had a slightly higher risk of having visual impairment (OR, 1.18, 95% CI 1.01 to 1.38), though the statistical significance is borderline (p<0.05) compared to other risk factors such as gender and age.

Cataract was the leading cause of blindness in the current study population. This trend is observed in many developing countries including, Mongolia¹⁹, India²⁰, **Commented [yt6]:** Would it be beneficial to include summary table of all the major epidemiology studies conducted in the Asia Pacific? – with region, design, rurality, population sampled, prevalence of blindness/visual impairment. I was thinking of just including the larger studies published in BJO/Ophthalmology

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Commented [yt8]: From Table 7 (multivariable analysis), HTN had p value of 0.037. Do we need to go into more detail to provide a justification for this? No. I think we can leave this as is. Malaysia²¹ and rural parts of China.²² Cataract surgery remains one of the most costeffective healthcare interventions to combat the global burden of eye disease.²³ Treatment for cataract, however, requires a number of key resources, including a trained surgeon, specialized equipment and <u>a well-trained eye health care</u> <u>workerseperating space</u>; all of which are in limited supply across the developing world. Lao PDR has no private sector entities to provide <u>service on eye health</u> care; hence, the majority of cataract surgeries are performed at the NOC.⁴ During 2011, <u>the</u> provincial cataract surgical rate (CSR) in Lao PDR ranged from 364 to 889 cases per million population per annum²⁴, which is low when compared to Vietnam (1362)²⁵ and India (4425)²⁶. Furthermore, <u>the</u> surgical refusal rate among Laotians is also high (30%), which highlights the potential for fatalism and a fear of surgery as possible barriers to the delivery of eye care in the community.⁴

Uncorrected refractive error is the leading cause of moderate to severe visual impairment in the world.²⁷ In Vientiane province, uncorrected refractive error accounted for 40% of <u>the</u> visual impairment; <u>cases</u>. 25% of participants wore spectacles at time of assessment, the large majority (69%) of which lived in urban areas. The undertreatment of refractive error is likely to reflect limitations in the availability of optometricy and refractive services across the country and highlights potential underprovision of medical resources in poor and remote regions.

Maculopathy was the third most common cause of presenting visual impairment and the second most common cause of blindness in this study. Three participants were blind due to bilateral maculopathy, one from severe age-related macular degenerated (AMD), and two from untreated myopic macular degeneration. While AMD is the most common cause of blindness in many developed countries, the prevalence of AMD remains relatively low in Asian countries such as China, Myanmar, Japan and Sri Lanka.^{7,8,15,22,28} Low rate of AMD in Lao PDR is likely related its young population, with only 4% of the total population being aged 65 years and above.³ TheOur finding s-offer myopic macular degeneration (11.8%) as a cause of bilateral blindness was comparable to results from predominantly Chinese populations^{12,22,29} but significantly higher compared to neighbouring <u>rural</u> Myanmar¹⁵. With comparable rates of myopia between Laos and Myanmar, the observed difference may be explained by unknown genetic or environmental factors.

Glaucoma is the second leading cause of blindness in those aged 50 years and older, affecting 3.6 million people worldwide. Approximately 60% of the world's

Commented [yt9]: I'm slightly unsure as to how we can explain the higher rates of myopic macular degeneration in this population, especially compared to Myanmar where there were none. Does Myanmar have the same prevalence of high myopia? Commented [RC10]: Reference? glaucoma disease is are found in people of Asian descent.³⁰ Our study observed a surprisingly low glaucoma prevalence estimate of 1.54%, which is probably explained by the relatively young median age of our study cohort.³¹ Corneal opacification (of unspecified cause) was responsible for blindness in 2 participants, both of whom did not have clinical features of trachoma.

<u>A</u><u>The</u> key strength of this study was the robust design, which consisted of randomly selected sample of participants from a variety of locations across Vientiane Province. Prior to VES, data on national blindness and visual impairment in Lao PDR were limited to a <u>r</u>Rapid <u>a</u>Assessment of <u>a</u>Avoidable <u>b</u>Blindness (RAAB) survey conducted by the NOC.³² A limitation of our study is the lack of subjective refraction, which would have further improved the visual acuity <u>beyond pinhole improvement</u> <u>inef</u> some participants. The effect of this limitation is likely to cause a <u>slight</u> overestimation of the prevalence of visual impairment. Furthermore, visual fields were not considered in the visual impairment data. It is possible that a proportion of participants with glaucoma may have fulfilled WHO criteria for visual impairment based on visual field defects. Also, there may be a possibility of systematic bias due to participants with symptomatic eye disease or inflexible work arrangements having difficulty attending this study.

In conclusion, VES provides the first robust population-based data on the prevalence and causes of visual impairment in Lao PDR. Cataract and uncorrected refractive errors were the leading causes of blindness and visual impairment and remain the leading public health concerns in the country. The results of VES highlights the need for ongoing funding of ophthalmic care resources and community education programs to improve access to health care in this region.

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Commented [yt12]: For blindness due to corneal opacification (2 cases) – our survey didn't list a specific cause for these. Hence, I've left the discussion fairly brief here.

TABLES AND FIGURES

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Variable	Overall (n = 1,264)
Age (years) <i>mean (SD)</i> Age <i>n (%)</i>	57.6 (11.2)
40 - 49	345 (27.3)
50 – 59	421 (33.3)
60 – 69	270 (21.4)
≥70	228 (18.0)
Gender <i>n (%</i>)	
Male	494 (39.1)
Female	770 (60.9)
Rural <i>n</i> (%)	816 (64.6)
Region n (%)	
Somsavan	267 (21.1)
Na Lao	235 (18.6)
Simano	228 (18.0)
Hon	182 (14.4)
Sikaithong	167 (13.2)
Kudsambath	140 (11.1)
Nongtha Thai	37 (2.9)
Thong Pong	8 (0.6)
Smoker n (%)	237 (18.8)
Hypertension n (%)	405 (32.0)
Diabetes n (%)	124 (9.8)

Table 2. Age and gender distribution of study participants. Data are n (%).

Age Group (years)	Female	Male	Total
	(n = 770)	(n = 494)	(n = 1,264)

40 – 49	241 (31.3)	104 (21.1)	345 (27.3)
50 – 59	253 (32.9)	168 (34)	421 (33.3)
60 – 69	155 (20.1)	115 (23.3)	270 (21.4)
70+	121 (15.7)	107 (21.7)	228 (18)

Table 3. Age-specific prevalence of visual impairment in the VES by WHO presenting visual acuity. Data provided as (%) (95% CI)

	Age Categories (Yrs)				
Visual impairment	40 – 49	50 – 59	60 - 69	70+	Total
Mild	3.76 (-1.93, 9.44)	7.67 (1.13, 14.21)	13.07 (3.74, 22.39)	10.89 (2.91, 18.88)	8.34 (1.81, 14.86)
Moderate	1.95 (0.16, 3.74)	5.89 (3.19, 8.60)	16.93 (13.06, 20.80)	37.72 (28.63, 46.82)	12.94 (8.98, 16.91)
Severe	0.00	0.28 (-0.33, 0.89)	0.87 (-0.69, 2.42)	4.57 (2.16, 6.98)	1.11 (0.31, 1.90)
Total visual impairment	5.71 (0.92, 10.49)	13.84 (8.67, 19.01)	30.87 (21.40, 40.33)	53.18 (39.69, 66.68)	22.39 (14.67, 30.10)
Age-specific blindness	0.34 (-0.42, 1.10)	0.77 (0.05, 1.50)	0.43 (-0.34, 1.21)	5.42 (1.43, 9.42)	1.42 (0.83, 2.01)
Total visual impairment	6.05 (0.53, 11.56)	14.61 (9.41, 19.82)	31.30 (22.47, 40.13)	58.61 (47.10, 70.12)	23.81 (16.48, 31.14)

Table 4. Age-specific prevalence of visual impairment in the VES by best-corrected(pinhole) visual acuity in the better-seeing eye. Data provided as (%) (95% CI)

		Age Categories (Yrs)				
Visual impairment	40 – 49	50 - 59	60 - 69	70+	Total	
Mild	0.54 (-0.28, 1.35)	2.17 (0.42, 3.93)	7.01 (0.89, 13.12)	14.95 (6.97, 22.94)	5.07 (1.60, 8.55)	
Moderate	0.68 (0.06, 1.30)	1.96 (1.34, 2.59)	7.33 (3.48, 11.18)	23.92 (16.59, 31.25)	6.74 (4.60, 8.88)	
Severe	0.00	0.28 (-0.33, 0.89)	0.87 (-0.69, 2.42)	2.65 (0.40, 4.90)	0.76 (-0.08, 1.60)	
Total visual impairment	1.21 (0.72, 1.71)	4.42 (2.74, 6.09)	15.20 (8.28, 22.12)	41.52 (29.85, 53.19)	12.57 (8.27, 16.86)	
Age-specific blindness	0.34 (-0.42, 1.10)	0.77 (0.05, 1.50)	0.00	5.42 (1.43, 9.42)	1.33 (0.84, 1.82)	
Total visual impairment or blindness	1.55 (0.41, 2.69)	5.19 (3.53, 6.85)	15.20 (8.28, 22.12)	46.95 (35.79, 58.10)	13.90 (9.71, 18.09)	

Table 5. Causes of WHO-Defined Visual Impairment and Blindness

Cause	Visual Impairment	Blindness
	n (%)	n (%)

Refractive Error	125 (40.3)	1 (5.9)
Cataract	101 (32.6)	9 (52.9)
Maculopathy	23 (7.4)	3 (17.7)
Glaucoma	14 (4.5)	2 (11.8)
Pterygium	7 (2.3)	0
Optic neuropathy	7 (2.3)	0
Corneal opacification	5 (1.6)	2 (11.8)
Other	9 (2.9)	0
Undetermined	19 (6.1)	0
Total	310	17

Table 6. Results from logistic regression model investigating the association

 between participant characteristics and the odds of blindness.

Variable	OR (95% CI)	P-value
Age		<0.001
40-49	Reference	
50 – 59	2.29 (0.57, 9.16)	0.243
60-69	1.28 (0.62, 2.62)	0.502
≥70	16.87 (7.24, 39.29)	<0.001
Gender		
Male	Reference	
Female	1.15 (0.41, 3.21)	0.784
Location		
Rural	Reference	
Urban	0.56 (0.17, 1.86)	0.341
Smoker		
No	Reference	
Yes	0.95 (0.41, 2.21)	0.899
History of hypertension		
No	Reference	
Yes	1.93 (0.92, 4.06)	0.082
History of diabetes		
No	Reference	
Yes	2.86 (0.70, 11.66)	0.144

Table 7. Results from logistic regression model investigating the association between participant characteristics and the odds of visual impairment, including blindness.

	Unadjusted	Unadjusted		
Variable	OR (95% CI)	P-value	OR (95% CI)	P-value
Age		<0.001		<0.001
40 - 49	Reference		Reference	
50 – 59	2.66 (1.32, 5.34)	0.006	2.73 (1.29, 5.75)	0.008
60 - 69	7.08 (3.37, 14.88)	<0.001	7.67 (3.60, 16.33)	<0.001
≥70	22.01 (10.51, 46.08)	<0.001	24.86 (10.72, 57.67)	<0.001
Gender				
Male	Reference		Reference	
Female	1.24 (0.98, 1.57)	0.070	1.90 (1.47, 2.47)	<0.001
Location				
Rural	Reference		Reference	
Urban	1.35 (0.62, 2.96)	0.448	1.57 (0.68, 3.66)	0.293
Smoker		0.455		0.302
No	Reference		Reference	
Yes	0.95 (0.67, 1.36)	0.795	1.33 (0.83, 2.14)	0.241
Unknown	1.44 (0.55, 3.77)	0.459	1.01 (0.14, 7.30)	0.995
Hypertension		⊲0.001		0.010
No	Reference		Reference	
Yes	1.99 (1.71, 2.32)	⊲0.001	1.18 (1.01, 1.38)	0.037
Unknown	0.90 (0.58, 1.38)	0.620	0.25 (0.05, 1.35)	0.108
Diabetes		0.088		0.642
No	Reference		Reference	
Yes	1.65 (1.05, 2.59)	0.029	1.05 (0.63, 1.72)	0.863
Unknown	1.16 (0.76, 1.78)	0.481	1.36 (0.68, 2.70)	0.381

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