• Investigation •

# Prevalence of strabismus in the adult Iranian population: findings of the Persian Eye Cohort Study

*Motahhareh Sadeghi[1,2], Shayan Shojaei[3], Mehdi Yaseri[4], Fateme Jafari[1,2], Mohammad Reza Soleimani[5], Kourosh Shahraki[6], Yousef Alizadeh[7], Mohammad Mirzaei[8], Mohammad Reza Shoja[9], Gholam Reza Khataminia[10], Ali Esmaeili Nadimi[11], Alireza Ansari-Moghaddam[6], Farahnaz Joukar[12], Fahimeh Khalili[13], Amir Houshang Mehrparvar[14], Sara Saki[15], Fateme Alipour[1,2]*

[1]Translational Ophthalmology Research Center, Tehran University of Medical Sciences, Tehran 1336616351, Iran
[2]Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran 1336616351, Iran
[3]Cardiovascular Disease Research Institute, Tehran Heart Center, Tehran University of Medical Sciences, Tehran 1411713138, Iran
[4]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran 1417613151, Iran
[5]Department of Ophthalmology, Rafsanjan University of Medical Sciences, Rafsanjan 7713961151, Iran
[6]Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan 4346398167, Iran
[7]Department of Ophthalmology, Amiralmomenin Hospital, Guilan University of Medical Sciences, Rasht 4139638459, Iran
[8]Department of Ophthalmology, Tabriz University of Medical Sciences, Tabriz 5166614766, Iran
[9]Department of Ophthalmology, Shahid Sadoughi University of Medical Sciences, Yazd 8916978477, Iran
[10]Department of Ophthalmology, Jundishapur University of Medical Sciences, Ahvaz 1579461357, Iran
[11]Non-Communicable Diseases Research Center, Rafsanjan University of Medical Sciences, Rafsanjan 7717933777, Iran
[12]Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht 4144895655, Iran
[13]Liver and Gastrointestinal Diseases Research Center, Tabriz University of Medical Sciences, Tabriz 5166614766, Iran
[14]Shahid Sadoughi University of Medical Sciences, Yazd 8916978477, Iran
[15]Pediatric Gastroenterology Department, Stanford University, Stanford, CA 95032, USA
**Correspondence to:** Motahhareh Sadeghi and Fateme Alipour. Translational Ophthalmology Research Center, Tehran University of Medical Sciences, Tehran 1336616351, Iran. mt.sadeghi@gmail.com; Alipour@tums.ac.ir

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## Abstract

● **AIM:** To investigate the prevalence of strabismus and its associated factors in the adult Iranian population.

● **METHODS:** The Persian Eye Cohort Study (PECS) is a branch of the Prospective Epidemiological Research Studies of the Iranian Adults (PERSIAN) Cohort Study, designed at Tehran University of Medical Sciences, Farabi Eye Hospital, Tehran, Iran. A web-based questionnaire was utilized to recruit Iranian citizens aged 31–73y, collecting demographic, socioeconomic, and lifestyle data, as well as family, drug, past medical, and ocular history.

● **RESULTS:** Totally 49 349 participants were enrolled in this study, including 21 939 males (44.5%) and 27 410 females (55.5%). A total of 636 patients (1.29%) were positive for strabismus, 358 (0.73%) had exotropia (constant and intermittent), which was nearly twice as prevalent as esotropia (0.37%) and vertical deviation (0.29%; $P<0.001$). Our study demonstrated an esotropia-to-exotropia ratio of 0.51. Anisometropia and amblyopia were detected in 27.8% and 32% of the strabismic population. Considering the residence type, strabismus was more prevalent among residents of urban areas (1.39% *vs* 0.96%). And comparing our six major ethnic groups in the study, the Arabs had the highest prevalence of strabismus in general (5.64%, $P<0.001$), where the Azari and the Guilak had the lowest (0.5% and 0.99%, $P=0.66$ and 0.68, respectively).

● **CONCLUSION:** In this population-based cohort study in different regions in Iran, we report the general prevalence of strabismus and its subtypes, as well as the effect of different risk factors associated with strabismus.

● **KEYWORDS:** Persian Eye Cohort; adult strabismus; amblyopia; risk factors; prevalence

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## INTRODUCTION

Strabismus, the disorder of ocular misalignment, can affect visual acuity and visual function by causing amblyopia and decreasing binocularity and depth perception. In addition, the significant influence of the abnormal appearance of strabismus on the mental well-being and social interactions of strabismic children and adults cannot be underestimated. The central pathogenesis of strabismus is still unclear; however, maternal smoking, prematurity, refractive errors, and ethnicity have been reported as risk factors for strabismus[1]. Therefore, evaluating the prevalence of strabismus and its risk factors is essential from a public health perspective. Epidemiological information on strabismus prevalence, particularly from population-based surveys, assists in recognizing the magnitude and burden of the disorder and preparing health and screening systems that provide appropriate preventive and curative services.

Most cohorts on the prevalence and incidence of strabismus are reported in pediatric populations[2-3], but few population-based studies have focused on strabismus in adults, reporting a prevalence of 1%–4% in different countries and populations[4-13], and the worldwide prevalence is calculated 1.8% in a recent systematic review[14]. Regarding the Iranian population, only one previous strabismus survey has included the adult population (3248 individuals aged over 1y), which reported a prevalence of 4.3%, with no statistically significant relationship with age, gender, and refractive errors[15], and one amblyopia survey including individuals aged 3–93, reporting 2.73%[16].

To the best of our knowledge, there has been no comprehensive population-based study on the prevalence of strabismus, its risk factors, and epidemiological characteristics in the Iranian adult population. Considering the medical, economic, and psychosocial impacts of this disorder, it is necessary to collect relevant data to generate plans for screening, preliminary diagnosis, and prompt intervention.

The purpose of this report from this cohort is to determine the prevalence of strabismus and its risk factors in different medical, nutritional, and socioeconomic situations, in Iranian residents aged between 31 and 73, selected from six geographically distinct regions of Iran, to assess the impact of ophthalmic disorders, and use them to improve the quality of ophthalmic care and eye health in different geographic areas of Iran.

## PARTICIPANTS AND METHODS

**Ethical Approval** The study was approved by the ethics committees of the Ministry of Health and Medical Education and the Tehran University of Medical Sciences (IR.TUMS.DDRI.REC.1396.1). It was performed in accordance with the Declaration of Helsinki, and informed consent was obtained from all participants or their legal caretakers.

The Prospective Epidemiological Research Studies of Iranian Adults (PERSIAN) Cohort, designed by the Central Committee of the Ministry of Health and Medical Education, is a national, multicenter, prospective, cross-sectional study. The PERSIAN Eye Cohort Study (PECS) is a branch of the PERSIAN Cohort Study, designed at Tehran University of Medical Sciences, Farabi Eye Hospital, Tehran, Iran, to investigate the prevalence and risk factors for non-communicable ocular diseases in the Iranian population. The study was conducted in six peripheral cohort regions representing major Iranian ethnicities, with no discernible demographic or socioeconomic disparities between regions and the Iranian general population. A web-based questionnaire was utilized to recruit Iranian citizens aged 31–73, collecting demographic, socioeconomic, and lifestyle data, as well as family, drug, past medical, and ocular history.

The PERSIAN Cohort Study was performed in two stages. During the first stage, a comprehensive ophthalmic examination was carried out by expert optometrists. Documentation was performed according to our web-based checklist, including data on uncorrected visual acuity, best-corrected visual acuity, dry objective refraction for adults, and cyclo-refraction for the pediatric population using tropicamide 1% and an automated refractometer. Additionally, the presence of relative afferent pupillary defect, eyelid lesions, and intraocular pressure (measured using an applanation tonometer) was recorded. Ocular alignment was assessed before the administration of cycloplegic and mydriatic drops.

Refractive error was classified into three groups, based on the spherical equivalent (SE) in diopters (myopia, hyperopia, and emmetropia), and astigmatism more than 1 diopter was considered positive and was further categorized into three groups, with the rule, against the rule, and oblique astigmatism. Anisometropia was considered positive when there was a difference of more than 1.5 diopters in the SE between the two eyes, subdivided into two groups: anisometropia in the same direction, and antimetropia. Amblyopia is defined as a difference of two or more lines in best corrected vision between the two eyes, or visual acuity of less than 20/30 in the worse eye, with no apparent structural ocular pathology that could be attributed to poor vision. Strabismus, defined as ocular misalignment, was documented by the optometrists as esotropia, exotropia, vertical deviation, or orthotropia (no strabismus). The alternate cover test and cover/uncover test

**Table 1 Prevalence of different types of strabismus**

| Parameters | *n* | % | 95%CI | | % in strabismus | 95%CI | |
|---|---|---|---|---|---|---|---|
| | | | Lower | Upper | | Lower | Upper |
| Orthotropia | 48708 | 98.71 | 98.61 | 98.81 | | | |
| Strabismus | 636 | 1.29 | 1.19 | 1.39 | | | |
| Exotropia | 358 | 0.73 | 0.65 | 0.80 | 56.38 | 52.50 | 60.20 |
| Esotropia | 181 | 0.37 | 0.32 | 0.42 | 28.46 | 25.06 | 32.06 |
| Vertical deviation | 143 | 0.29 | 0.25 | 0.34 | 22.52 | 19.40 | 25.89 |
| Nystagmus | 47 | 0.10 | 0.07 | 0.13 | 2.36 | 1.39 | 3.77 |

CI: Confidence interval.

were employed to evaluate ocular deviation. The presence or absence of nystagmus was also recorded.

Those who met at least one of the following criteria were referred to an ophthalmologist for further evaluation in the second stage of ocular examination: positive medical history of diabetes, positive family history of glaucoma, intraocular pressure more than 20 mm Hg, positive pupillary defect, best corrected vision less than 20/25, detection of strabismus, positive scissor motion sign in retinoscopy, eyelid abnormalities, moderate to severe dry eye symptoms, and poor red reflex. At this stage, a more comprehensive ocular evaluation, including assessment of eyelids and lacrimal system, extraocular muscles and strabismus, conjunctiva, cornea and anterior chamber, red reflex, pupillary evaluation, and fundoscopy, was performed by the ophthalmologist.

Participants were classified into four distinct groups based on their highest level of education: illiterate, low education, high school diploma, and higher education. Similarly, they were categorized into two groups based on their current place of residence, rural or urban areas. To estimate the wealth score index (WSI), the multiple correspondence analysis (MCA) was employed. The WSI provides insight into the economic status based on various indicators and factors. The details and specifics of this analysis can be found in the Persian Cohort Protocol.

**Statistical Analysis** All statistical analyses were conducted using Stata (StataCorp. 2021. Stata Statistical Software: Release 17, College Station, TX: StataCorp LLC). Quantitative data were reported as mean and standard deviation when continuous, and median and range when non-continuous; Categorical data were reported as frequencies and percentages. The estimates were accompanied by their corresponding 95% confidence interval. The Kolmogorov–Smirnov (K–S) test was used to evaluate data normality. In order to assess the impact of different variables on strabismus, cluster sampling and probability design effects were taken into account during logistic regression analysis within a multilevel framework. The correlations are reported as odds ratio (OR) and a *P*-value of less than 0.05 was considered to be statistically significant.

## RESULTS

**Study Population** Among 65 580 patients who participated in the PECS from six centers, 49 349 patients (75.3% of the total population) had strabismus-related data, including 21 939 males (44.5%) and 27 410 females (55.5%). The mean age at the time of the study was 49.9±9.2y (ranged from 31 to 73).

**Strabismus, Refractive Error, and Amblyopia** A total of 636 patients (1.29%) were positive for strabismus, 358 (0.73%) had exotropia (constant and intermittent), which was nearly twice as prevalent as esotropia (0.37%) and vertical deviation (0.29%; $P<0.001$). Our study demonstrated an esotropia-to-exotropia ratio of 0.51. Nystagmus was positive in 47 participants (0.1%). Table 1 reviews the prevalence of different strabismus categories in our population.

Generally, the prevalence of refractive error (non-emmetropic SE) was higher in the strabismic compared to the non-strabismic population (51.9% *vs* 41.7%). In the strabismic population, the prevalence of hyperopic SE (29%) was higher than myopic (21.9%). In subgroup analysis, in exotropic participants, hyperopia was more prevalent (34.4% *vs* 20.2%), while in esotropic participants, myopia was more prevalent (26.6% *vs* 24.3%). However, none of these differences were significant.

Oblique astigmatism was the most prevalent type in all analysis groups, followed by against the rule and with the rule astigmatism; however, this difference was only significant in exotropic participants (71.1%, $P=0.009$).

Anisometropia was detected in 11.4% and 27.8% of the non-strabismic and strabismic populations, respectively, and the difference was not statistically significant ($P=0.518$). In strabismus subgroups, the prevalence of anisometropia was 32.6% in exotropic participants, 28.9% in esotropic participants, and 11.9% in those with vertical deviation. Anisometropia in the same direction was more prevalent in all subgroups, but the difference was not statistically significant.

The prevalence of amblyopia among strabismic participants was 32%, compared to 4.9% in non-strabismic participants ($P<0.001$). Amblyopia was significantly more prevalent in exotropia and esotropia compared to vertical deviation (37%, 36.8%, and 4.7% respectively, $P<0.001$).

**Table 2 Prevalence of refractive errors in different types of strabismus and nystagmus**

| Parameters | Spherical equivalent | | | | | | Astigmatism | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Emmetropia | | Myopia | | Hyperopia | | Oblique | | WTR | | ATR | |
| | % | 95%CI | % | 95%CI | % | 95%CI | % | 95%CI | % | 95%CI | % | 95%CI |
| Ortho | 58.4 | 57.9–58.8 | 15.3 | 14.9–15.6 | 26.4 | 26–26.8 | 80.4 | 80.1–80.8 | 5.7 | 5.5–6 | 13.8 | 13.5–14.1 |
| OR | 1.38 | | 0.8 | | 0.78 | | 1.16 | | 0.69 | | 0.97 | |
| *P* | <0.001 | | 0.019 | | 0.015 | | 0.114 | | 0.018 | | 0.746 | |
| | | | <0.001 | | | | | | 0.052 | | | |
| XT | 45.3 | 40–50.7 | 20.2 | 16.2–24.8 | 34.4 | 29.5–39.7 | 71.1 | 66.1–75.8 | 10 | 7.1–13.6 | 18.8 | 14.9–23.3 |
| OR | 0.62 | | 1.61 | | 1.17 | | 0.72 | | 1.85 | | 1.12 | |
| *P* | <0.001 | | <0.001 | | 0.255 | | 0.009 | | 0.001 | | 0.418 | |
| | | | <0.001 | | | | | | 0.002 | | | |
| ET | 49.1 | 41.6–56.6 | 26.6 | 20.4–33.6 | 24.3 | 18.3–31.1 | 76.2 | 69.3–82.1 | 6.5 | 3.5–11 | 17.3 | 12.1–23.5 |
| OR | 0.72 | | 0.98 | | 1.65 | | 1.05 | | 1.25 | | 0.86 | |
| *P* | 0.037 | | 0.909 | | 0.005 | | 0.783 | | 0.474 | | 0.474 | |
| | | | 0.016 | | | | | | 0.632 | | | |
| Ver | 60.7 | 52.3–68.7 | 18.5 | 12.7–25.7 | 20.7 | 14.6–28.2 | 73.7 | 65.7–80.6 | 4.5 | 1.9–9.1 | 21.8 | 15.4–29.4 |
| OR | 1.22 | | 0.78 | | 0.97 | | 1.07 | | 0.84 | | 0.97 | |
| *P* | 0.259 | | 0.242 | | 0.89 | | 0.737 | | 0.668 | | 0.9 | |
| | | | 0.45 | | | | | | 0.897 | | | |
| Nys | 32.6 | 20–47.3 | 37.2 | 24–52.1 | 30.2 | 18.1–44.9 | 72.1 | 57.6–83.7 | 16.3 | 7.6–29.3 | 11.6 | 4.6–23.6 |
| OR | 0.35 | | 1.3 | | 3.14 | | 0.63 | | 3.25 | | 0.8 | |
| *P* | 0.001 | | 0.433 | | 0.001 | | 0.177 | | 0.005 | | 0.649 | |
| | | | <0.001 | | | | | | 0.017 | | | |

Ortho: Orthotropia; XT: Exotropia; ET: Esotropia; Ver: Vertical deviation; Nys: Nystagmus; SE: Spherical equivalent; WTR: With the rule; ATR: Against the rule; OR: Odds ratio; CI: Confidence interval.

**Table 3 Prevalence of amblyopia and anisometropia in different types of strabismus and nystagmus**

| Parameters | Amblyopia | | | Anisometropia | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Same direction | | | Antimetropia | | |
| | % | 95%CI | | % | 95%CI | | % | 95%CI | |
| | | Lower | Upper | | Lower | Upper | | Lower | Upper |
| Ortho | 4.9 | 4.7 | 5.1 | 69.2 | 67.8 | 70.5 | 30.8 | 29.5 | 32.2 |
| OR | 9.48 | | | | | | 1.13 | | |
| *P* | <0.001 | | | | | | 0.518 | | |
| XT | 37 | 30.9 | 43.3 | 72.8 | 63.1 | 81.1 | 27.2 | 18.9 | 36.9 |
| OR | 0.08 | | | | | | 0.82 | | |
| *P* | <0.001 | | | | | | 0.416 | | |
| ET | 36.8 | 27.2 | 47.2 | 70 | 54.8 | 82.4 | 30 | 17.6 | 45.2 |
| OR | 0.1 | | | | | | 0.91 | | |
| *P* | <0.001 | | | | | | 0.785 | | |
| Ver | 4.7 | 1.3 | 12 | 64.3 | 38.5 | 84.9 | 35.7 | 15.1 | 61.5 |
| OR | 1.68 | | | | | | 1.13 | | |
| *P* | 0.385 | | | | | | 0.824 | | |
| Nys | 48 | 29.5 | 66.9 | 75 | 40.8 | 94.4 | 25 | 5.6 | 59.2 |
| OR | 0.06 | | | | | | 0.72 | | |
| *P* | <0.001 | | | | | | 0.687 | | |

Ortho: Orthotropia; XT: Exotropia; ET: Esotropia; Ver: Vertical deviation; Nys: Nystagmus; OR: Odds ratio; CI: Confidence interval.

Tables 2 and 3 provide additional information on the prevalence of SE, astigmatism, amblyopia, and anisometropia.

**Other Related Risk Factors of Strabismus** The prevalence of strabismus was slightly higher in male participants (1.35%) than in female participants (1.24%). The female gender had a negative relationship with the prevalence of exotropia, considered a protective factor (*P*=0.051), which remained significant in the multivariate analysis (OR 0.74, *P*=0.008). However, it was not the same for esotropia or vertical deviation. Different types of strabismus demonstrated a gradual

increase in prevalence with age, where participants older than 65y were more commonly diagnosed with strabismus, which was statistically significant in both exotropia ($P$=0.004) and esotropia ($P$<0.001). Although in multivariate analysis, it was only a statistically significant risk factor for esotropia (OR 2.56, $P$<0.001).

Strabismus was more prevalent in the illiterate population in general ($P$<0.001), and in subgroups; however, the difference was statistically significant only in exotropia ($P$=0.026). Participants with low WSI scores were most commonly diagnosed with strabismus ($P$<0.001). This trend of decreasing strabismus prevalence with increasing WSI score was observed in all three subgroups of strabismus; however, the difference was only significant in exotropia ($P$=0.005). Higher levels of education and higher WSI scores have shown a significant protective effect against exotropia which remained statistically significant in the multivariable analysis (OR 0.59 with $P$=0.04, and OR 0.68 with $P$=0.012, respectively).

Considering the residence type, strabismus was more prevalent among residents of urban areas (1.39% *vs* 0.96%). In strabismus subgroups, exotropia was significantly more common in urban areas than in rural or suburban areas (0.79% *vs* 0.52%, $P$=0.011), as well as vertical deviation ($P$=0.019). Living in rural areas was a significant protective factor against exotropia and vertical deviation, which remained statistically significant in multivariable analysis (OR 0.56, $P$<0.001; OR 0.54, $P$=0.015).

Comparing our six major ethnic groups in the study, the Arabs had the highest prevalence of strabismus in general (5.64%, $P$<0.001), where the Azari and the Guilak had the lowest (0.5% and 0.99%, $P$=0.66 and 0.68, respectively). The Arabs showed the highest prevalence of different types of strabismus, which was statistically significant in exotropia and esotropia in multivariate analysis (OR 3.71, $P$<0.001 and OR 12.78, $P$<0.001, respectively). In the same way, being Zaboli had a positive correlation with esotropia (OR 1.95, $P$=0.022). On the other hand, the Azari were demonstrated to have a significantly lower prevalence of vertical deviation (OR 0.04, $P$=0.031).

Regarding study centers, the Hoveizeh center reported the highest strabismus (5.74%), followed by the Zahedan center (1.89%; $P$<0.001). These two centers also had the highest prevalence in each type of strabismus [exotropia 2.42%, 0.29% ($P$<0.001), esotropia 2.22%–0.33% ($P$<0.001), vertical deviation 2.42%, 0.29% ($P$<0.001)].

Details on the prevalences and confidence intervals of each variable and multivariate analysis are provided in Table 4 and Table 5, respectively.

**Nystagmus** Nystagmus was found in 47 participants (0.1%), and myopia was the most common type of SE refractive error (37.2%, $P$<0.001). Oblique astigmatism was the most common type of astigmatism (72.1%, $P$=0.017). Anisometropia and amblyopia were found in 25.6% and 48% ($P$<0.001).

The prevalence of nystagmus in male participants was nearly twice females (0.13% *vs* 0.07%, $P$=0.02), and female gender was found to be a protective factor against nystagmus in multivariate analysis (OR 0.34, $P$<0.001). There was no significant difference in nystagmus prevalence across the age categories in univariate analysis; however, in multivariate analysis, age had a negative correlation with nystagmus in participants aged 55–64 and >65y (OR 0.43, $P$=0.049, and OR 0.12, $P$=0.043, respectively). Furthermore, in the low WSI score group, 0.16% had the diagnosis of nystagmus, while only 0.05% in the high WSI score group had nystagmus ($P$=0.009). The prevalence of nystagmus was higher in illiterate participants (0.17%) and lower in participants with higher educational levels (0.02%), being significant in multivariate analysis.

Comparing nystagmus prevalence among ethnic groups, the Arabs demonstrated the highest prevalence (0.22%, $P$=0.044), and the Balouch were found to be less likely to be diagnosed with nystagmus. Regarding study centers, the Ahvaz center had the highest reported prevalence, followed by the Guilan center ($P$<0.001).

Details of the multivariate analysis of nystagmus are provided in Table 5.

## DISCUSSION

**Prevalence of Strabismus** Most published studies on the prevalence of strabismus and amblyopia are in pediatric populations. Our study is among the few adult population-based studies in the Middle East region. This cohort included 49 349 adult individuals with comprehensive ophthalmologic examination, and we detected an overall strabismus prevalence of 1.29%, which is in line with most previous studies reporting a range of 1% to 4.3% in different regions[4-6,8,11,15,17].

Several factors might have influenced the prevalence of strabismus in our study population. This is a two-stage study, in which well-trained optometrists are responsible for primary strabismus examination. Regardless, small-angle strabismus or intermittent deviations might have been overlooked. In addition, the protocol of the present study includes ocular alignment examination only with corrective glasses on, which might have caused under-detection of the accommodation-related strabismus (accommodative esotropia). Nearly 30 percent of the total PECS data is excluded due to incomplete examination and registration, due to the emergence of the COVID-19 pandemic. On the other hand, the national program for screening children for amblyopia and strabismus has been developed in recent years; therefore, adult participants included in our study have not undergone a proper evaluation in childhood, especially in less developed areas. In addition,

**Table 4 Prevalence rates of different types of strabismus and nystagmus, characterized by gender, age, residence, education status, WSI category, ethnicity, and center**

| Parameters | Strabismus | | | Exotropia | | | Esotropia | | | Vertical deviation | | | Nystagmus | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % | 95%CI | | % | 95%CI | | % | 95%CI | | % | 95%CI | | % | 95%CI | |
| | | Lower | Lower | | Lower | Upper | | Lower | Upper | | Lower | Upper | | Lower | Upper |
| Sex | | | | | | | | | | | | | | | |
| M | 1.35 | 1.20 | 1.51 | 0.78 | 0.67 | 0.90 | 0.38 | 0.30 | 0.47 | 0.27 | 0.21 | 0.35 | 0.13 | 0.09 | 0.19 |
| F | 1.24 | 1.11 | 1.38 | 0.68 | 0.59 | 0.79 | 0.36 | 0.29 | 0.43 | 0.30 | 0.24 | 0.37 | 0.07 | 0.04 | 0.10 |
| *P* | | 0.043 | | | 0.051 | | | 0.415 | | | 0.977 | | | 0.02 | |
| Age, y | | | | | | | | | | | | | | | |
| <44 | 1.01 | 0.87 | 1.17 | 0.53 | 0.43 | 0.65 | 0.32 | 0.24 | 0.41 | 0.26 | 0.19 | 0.34 | 0.11 | 0.07 | 0.17 |
| 45-54 | 1.29 | 1.12 | 1.47 | 0.76 | 0.64 | 0.90 | 0.32 | 0.25 | 0.42 | 0.27 | 0.20 | 0.36 | 0.11 | 0.07 | 0.17 |
| 55-64 | 1.45 | 1.26 | 1.67 | 0.86 | 0.71 | 1.03 | 0.37 | 0.28 | 0.49 | 0.34 | 0.25 | 0.45 | 0.08 | 0.04 | 0.14 |
| >65 | 2.14 | 1.68 | 2.70 | 1.02 | 0.71 | 1.42 | 0.83 | 0.56 | 1.20 | 0.38 | 0.21 | 0.65 | 0.03 | 0 | 0.15 |
| *P* | | <0.001 | | | 0.004 | | | | | | 0.341 | | | 0.588 | |
| Residence | | | | | | | | | | | | | | | |
| Urban | 1.39 | 1.27 | 1.51 | 0.79 | 0.70 | 0.88 | 0.37 | 0.32 | 0.44 | 0.32 | 0.26 | 0.38 | 0.08 | 0.06 | 0.12 |
| Rural | 0.96 | 0.79 | 1.15 | 0.52 | 0.40 | 0.66 | 0.34 | 0.24 | 0.46 | 0.20 | 0.13 | 0.29 | 0.13 | 0.08 | 0.22 |
| *P* | | <0.001 | | | 0.011 | | | 0.111 | | | 0.019 | | | 0.252 | |
| Education | | | | | | | | | | | | | | | |
| Illiterate | 2.31 | 2.00 | 2.65 | 1.23 | 1.00 | 1.48 | 0.61 | 0.46 | 0.80 | 0.66 | 0.50 | 0.86 | 0.17 | 0.10 | 0.28 |
| Low | 1.19 | 1.03 | 1.37 | 0.70 | 0.58 | 0.84 | 0.39 | 0.30 | 0.50 | 0.20 | 0.14 | 0.28 | 0.10 | 0.06 | 0.16 |
| Diploma | 1.01 | 0.88 | 1.16 | 0.60 | 0.50 | 0.72 | 0.24 | 0.18 | 0.32 | 0.20 | 0.14 | 0.27 | 0.08 | 0.05 | 0.13 |
| Higher | 1.07 | 0.82 | 1.37 | 0.51 | 0.34 | 0.72 | 0.38 | 0.24 | 0.57 | 0.31 | 0.19 | 0.48 | 0.02 | 0 | 0.08 |
| *P* | | <0.001 | | | 0.026 | | | 0.459 | | | 0.138 | | | 0.071 | |
| WSI | | | | | | | | | | | | | | | |
| Low | 1.70 | 1.51 | 1.90 | 1.01 | 0.86 | 1.17 | 0.43 | 0.34 | 0.54 | 0.39 | 0.30 | 0.50 | 0.16 | 0.11 | 0.23 |
| Moderate | 1.14 | 0.99 | 1.32 | 0.64 | 0.52 | 0.78 | 0.34 | 0.25 | 0.44 | 0.23 | 0.17 | 0.32 | 0.08 | 0.05 | 0.14 |
| High | 1.04 | 0.89 | 1.19 | 0.54 | 0.44 | 0.65 | 0.34 | 0.26 | 0.43 | 0.25 | 0.18 | 0.33 | 0.05 | 0.02 | 0.09 |
| *P* | | <0.001 | | | 0.005 | | | 0.586 | | | 0.319 | | | 0.009 | |
| Ethnicity | | | | | | | | | | | | | | | |
| Fars | 0.76 | 0.63 | 0.89 | 0.43 | 0.34 | 0.54 | 0.19 | 0.13 | 0.26 | 0.16 | 0.11 | 0.23 | 0.08 | 0.05 | 0.13 |
| Azari | 0.50 | 0.39 | 0.64 | 0.29 | 0.20 | 0.39 | 0.19 | 0.12 | 0.28 | 0.03 | 0.01 | 0.08 | 0.07 | 0.04 | 0.13 |
| Balouch | 1.45 | 1.06 | 1.93 | 1.07 | 0.74 | 1.49 | 0.24 | 0.11 | 0.47 | 0.14 | 0.05 | 0.33 | 0.10 | 0.03 | 0.28 |
| Arab | 5.64 | 4.92 | 6.43 | 2.18 | 1.75 | 2.70 | 2.18 | 1.75 | 2.70 | 2.35 | 1.89 | 2.88 | 0.22 | 0.10 | 0.42 |
| Zaboli | 2.17 | 1.80 | 2.60 | 1.44 | 1.14 | 1.80 | 0.37 | 0.23 | 0.57 | 0.36 | 0.22 | 0.55 | 0 | 0 | 0 |
| Guilak | 0.99 | 0.78 | 1.24 | 0.72 | 0.54 | 0.94 | 0.23 | 0.14 | 0.36 | 0.04 | 0.01 | 0.11 | 0.18 | 0.10 | 0.31 |
| Others | 1.53 | 0.94 | 2.36 | 1.19 | 0.68 | 1.94 | 0.34 | 0.12 | 0.81 | 0.09 | 0.01 | 0.40 | 0 | 0 | 0 |
| *P* | | <0.001 | | | <0.001 | | | <0.001 | | | 0.016 | | | 0.044 | |
| Center | | | | | | | | | | | | | | | |
| Rafsanjan | 0.62 | 0.47 | 0.80 | 0.03 | 0.01 | 0.09 | 0.20 | 0.12 | 0.31 | 0.03 | 0.01 | 0.09 | 0.05 | 0.02 | 0.11 |
| Hoveizeh | 5.74 | 5.01 | 6.54 | 2.42 | 1.95 | 2.97 | 2.22 | 1.78 | 2.75 | 2.42 | 1.95 | 2.97 | 0.23 | 0.11 | 0.42 |
| Guilan | 1.03 | 0.83 | 1.27 | 0.05 | 0.02 | 0.12 | 0.24 | 0.15 | 0.37 | 0.05 | 0.02 | 0.12 | 0.16 | 0.09 | 0.27 |
| Tabriz | 0.50 | 0.39 | 0.64 | 0.04 | 0.02 | 0.09 | 0.18 | 0.12 | 0.27 | 0.04 | 0.02 | 0.09 | 0.08 | 0.04 | 0.14 |
| Zahedan | 1.89 | 1.63 | 2.17 | 0.29 | 0.20 | 0.41 | 0.33 | 0.23 | 0.45 | 0.29 | 0.20 | 0.41 | 0.07 | 0.03 | 0.14 |
| Yazd | 0.65 | 0.48 | 0.86 | 0.22 | 0.13 | 0.35 | 0.15 | 0.08 | 0.26 | 0.22 | 0.13 | 0.35 | 0.08 | 0.03 | 0.17 |
| *P* | | <0.001 | | | <0.001 | | | <0.001 | | | <0.001 | | | <0.001 | |

WSI: Wealth score index; M: Male; F: Female; CI: Confidence interval.

the late manifestation of many types of strabismus, such as decompensated phoria or intermittent deviations, as well as acquired restrictive or paralytic strabismus, could have affected the prevalence of strabismus in adults, as stated in previous studies[5-6,17].

Globally, esotropia has been reported to be the most common type of strabismus in European populations, and exotropia in Asian and Australian populations[11,13,17]. This difference can be

**Table 5 Multivariate analysis results of risk factors**

| Parameters | XT | | | | ET | | | | Vertical deviation | | | | Nystagmus | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | OR | 95%CI | | *P* | OR | 95%CI | | *P* | OR | 95%CI | | *P* | OR | 95%CI | | *P* |
| | | Lower | Upper | | | Lower | Upper | | | Lower | Upper | | | Lower | Upper | |
| Sex | | | | | | | | | | | | | | | | |
| M | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - |
| F | 0.74 | 0.59 | 0.92 | 0.008 | 0.93 | 0.67 | 1.28 | 0.652 | 0.99 | 0.68 | 1.44 | 0.97 | 0.34 | 0.18 | 0.62 | <0.001 |
| Age, y | | | | | | | | | | | | | | | | |
| <44 | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - |
| 45–54 | 1.29 | 0.98 | 1.7 | 0.071 | 0.95 | 0.64 | 1.39 | 0.775 | 0.99 | 0.64 | 1.52 | 0.958 | 0.79 | 0.4 | 1.55 | 0.492 |
| 55–64 | 1.33 | 0.98 | 1.79 | 0.064 | 1.17 | 0.77 | 1.77 | 0.465 | 1.24 | 0.78 | 1.97 | 0.356 | 0.43 | 0.19 | 1 | 0.049 |
| >65 | 1.44 | 0.93 | 2.223 | 0.099 | 2.56 | 1.53 | 4.31 | <0.001 | 1.21 | 0.6 | 2.41 | 0.594 | 0.12 | 0.01 | 0.94 | 0.043 |
| Residence | | | | | | | | | | | | | | | | |
| Urban | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Rural | 0.56 | 0.41 | 0.77 | <0.001 | 0.74 | 0.5 | 1.1 | 0.134 | 0.54 | 0.33 | 0.89 | 0.015 | 0.76 | 0.38 | 1.51 | 0.432 |
| Education | | | | | | | | | | | | | | | | |
| Illiterate | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Low | 0.84 | 0.63 | 1.14 | 0.263 | 1.18 | 0.78 | 1.8 | 0.432 | 0.64 | 0.39 | 1.03 | 0.065 | 0.42 | 0.19 | 0.93 | 0.034 |
| Diploma | 0.73 | 0.52 | 1.01 | 0.062 | 0.86 | 0.52 | 1.41 | 0.548 | 0.82 | 0.48 | 1.39 | 0.459 | 0.29 | 0.12 | 0.71 | 0.007 |
| Higher | 0.59 | 0.36 | 0.98 | 0.04 | 1.1 | 0.58 | 2.09 | 0.766 | 0.94 | 0.47 | 1.9 | 0.866 | 0.08 | 0.01 | 0.67 | 0.02 |
| WSI | | | | | | | | | | | | | | | | |
| Low | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Moderate | 0.74 | 0.57 | 0.96 | 0.023 | 1 | 0.69 | 1.46 | 1 | 0.75 | 0.49 | 1.15 | 0.186 | 0.58 | 0.29 | 1.17 | 0.127 |
| High | 0.68 | 0.51 | 0.92 | 0.012 | 1.23 | 0.82 | 1.86 | 0.317 | 0.95 | 0.59 | 1.5 | 0.815 | 0.41 | 0.17 | 1.01 | 0.052 |
| Ethnicity | | | | | | | | | | | | | | | | |
| Fars | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Azari | 0.58 | 0.28 | 1.2 | 0.142 | 1.06 | 0.61 | 1.82 | 0.84 | 0.04 | 0 | 0.75 | 0.031 | 0.73 | 0.31 | 1.73 | 0.473 |
| Balouch | 1.14 | 0.56 | 2.34 | 0.715 | 1.31 | 0.57 | 3 | 0.53 | 0.34 | 0.1 | 1.17 | 0.088 | 0.65 | 0.18 | 2.39 | 0.518 |
| Arab | 3.71 | 1.78 | 7.73 | <0.001 | 12.78 | 8.27 | 19.75 | <0.001 | 1.38 | 0.04 | 44.55 | 0.855 | 1.45 | 0.56 | 3.71 | 0.442 |
| Zaboli | 1.72 | 0.89 | 3.3 | 0.105 | 1.95 | 1.1 | 3.44 | 0.022 | 0.88 | 0.37 | 2.1 | 0.778 | 1 | | | |
| Guilak | 1.48 | 0.73 | 3.01 | 0.279 | 1.46 | 0.79 | 2.72 | 0.231 | 0.1 | 0.01 | 1.37 | 0.084 | 1.73 | 0.76 | 3.97 | 0.194 |
| Others | 2.11 | 1.03 | 4.33 | 0.041 | 1.98 | 0.69 | 5.6 | 0.2 | 0.19 | 0.02 | 2.39 | 0.199 | 1 | | | |

WSI: Wealth score index; XT: Exotropia; ET: Esotropia; M: Male; F: Female; CI: Confidence interval; OR: Odds ratio.

explained by the genetic factors playing roles in different types of strabismus[18]. Adult population-based studies have reported the same pattern[4-6,10]. Multiple studies on Iranian children have reported a prevalence of 2%–3% of strabismus, with exotropia being the predominant type[19]. An all-ages population-based study in rural areas of Iran reported the prevalence of exotropia and esotropia to be 3.87% and 0.43%, respectively[15]. Likewise, in the present study, exotropia (intermittent and constant) was the predominant type of strabismus population, with an exotropia/esotropia ratio of 2 ($P$<0.001).

**Refractive Error, Anisometropia, and Amblyopia** In our non-strabismic population, the prevalence of emmetropic SE was 58.4%, followed by hyperopia (26.4%), and myopia (15.3%). The prevalence of myopia and hyperopia is slightly higher than what has been previously reported in the Iranian pediatric population[19-20], which can be explained by the myopia progression process in younger adults, as well as an increase in hyperopia in early presbyopic ages, as demonstrated by Rozema *et al*[21] in the Tehran Eye Study. Details of the distribution of SE among different age groups of the PECS are discussed elsewhere[22]. In strabismic participants, SE was mostly emmetropic, with emmetropia being a protective factor against exotropia and esotropia (OR 0.62 and 0.72, $P$<0.04). In a Meta-analysis of the relationship between refractive errors and strabismus, published in 2016 by Tang *et al*[23], both myopia and hyperopia were risk factors for strabismus when adjusted for age, gender, and refraction, in the way that myopia had a high correlation with exotropia (OR 2.63), while hyperopia was a risk factor for esotropia (OR 22.95). On the other hand, there was no significant correlation between myopia and esotropia, nor between hyperopia and exotropia. Lee *et al*[7] reported an increased risk of exotropia with an increased degree of myopia. Although the prevalence of myopia and hyperopia in exotropia and esotropia was

somehow different from previous studies, a positive correlation was found between myopia and exotropia, and hyperopia and esotropia (OR 1.61 and 1.65, respectively), with myopia being a significant risk factor for exotropia and hyperopia a considerable risk factor for esotropia ($P$<0.001 and 0.005). It is stated that this association might explain the higher prevalence of exotropia in Asian populations, where the prevalence of myopia is significantly higher[23].

The correlation between strabismus and astigmatism has been reported differently. Fieß *et al*[5] and Lee *et al*[7] reported an increase in strabismus prevalence in astigmatic refractive error, while in the Meta-analysis in 2016, the adjusted OR for astigmatism and strabismus was not significant[23]. Oblique astigmatism was the most prevalent type in all strabismus subgroups.

Anisometropia is a well-recognized risk factor for disruption of normal binocular vision, particularly when left uncorrected, contributing to the development of amblyopia and strabismus[5,7]. The prevalence of anisometropia in our non-strabismic population was 11.4%, which is higher than what has been previously reported in Iranian pediatric populations (2%–4%)[19-20]. The explanation can be found in the report of refractive error details of the PECS, where anisometropia prevalence increases significantly by age, from 5% in those <45y to 28% in those >65 years of age[22]. As expected, the prevalence of anisometropia was higher in our strabismic participants (27.8%). In all subgroups, anisometropia in the same direction (both eyes hyperopic, or both eyes myopic) was the most common type, but the difference was not significant.

Amblyopia may serve either as a precursor to, or a consequence of, strabismus. The prevalence of amblyopia was significantly higher in the strabismic, compared to the non-strabismic population (32% *vs* 4.9%, $P$<0.001). The prevalence of amblyopia among our non-strabismic adults was in line with a Meta-analysis in 2020, reporting 3.29% in adults over 20y, and a previous rural study in Iran, reporting 2.73%[9,16], higher than reported prevalence of 1.27%–1.46% in pediatric populations[24]. The reported prevalence of adult amblyopia in strabismus is variable from 15% to 70%, depending on unilateral or alternating strabismus, and age groups[4,8,25]. A significant positive correlation has been documented between amblyopia and strabismus, especially in the contexts of esotropia and exotropia (OR 0.11). However, we did not specify unilateral or alternating strabismus.

**Other Related Risk Factors** Gender has not been shown to significantly influence the prevalence of strabismus[4-5,23,26], and the same results are demonstrated in our general strabismic population; However, in our population, females were less frequently diagnosed with exotropia (OR 0.74, $P$=0.008). Likewise, female gender was identified as an independent protective factor against nystagmus (OR 0.34, $P$<0.001, respectively).

In our population, there was an increasing prevalence of strabismus and its subgroups with increased age, and it was both statistically significant in exotropia and esotropia, which can be explained by the increasing rate of decompensated phoria or acquired deviations in the elderly, earlier detection of strabismus and amblyopia, and effective treatments in later generations. Being above 65y was a risk factor for both exotropia and esotropia. The same results were demonstrated in the US database and Japan cohort, in which a higher proportion of participants aged above 65–75y were diagnosed with strabismus[27-28]. However, after multivariate analysis, it was only significant for esotropia (OR 2.56, $P$<0.001). In the previous rural cohort in Iran, the increase in the prevalence of exotropia with age compared to esotropia was attributed to the fact that exotropia, especially intermittent exotropia, tends to manifest at later ages in life[15]. The same pattern has also been reported in Japan[6]. However, some countries have reported an inverse pattern, where the prevalence of strabismus decreased in older individuals[5].

Detection and treatment of strabismus need knowledge and attention to health, cosmesis, and social communications, as well as financial support. The effects of socioeconomic status on the prevalence of strabismus have not specifically been reported elsewhere; as expected, we observed a higher prevalence of strabismus in participants with lower socioeconomic status, as reported previously[15]. It is expected that higher education leads to increased diagnosis and treatment and decreased prevalence in adults. However, this protective effect was proved to be significant in multivariate correlation analysis only in exotropia (OR 0.68, $P$=0.012).

We demonstrated that living in rural areas can decrease the prevalence of strabismus (multivariate analysis, OR 0.56 and $P$<0.001 for exotropia, OR 0.54 and $P$=0.015 for vertical deviation). Theoretically, living outside the city has its protective factors, including increased outdoor activity and distant viewing, less screen time, increased sunlight exposure, fewer pollutants in the air, and healthier dietary intake. However, not all have shown a significant protective effect on the prevalence of strabismus.

Genetics is stated to have various effects on the prevalence of different types of strabismus[18]. Thus, our study here is the first one to evaluate the effects of our local ethnic groups on the prevalence of strabismus. Comparing six major ethnicities in the present population, the Arabs had the highest prevalence of general strabismus, followed by the Zaboli. Population-based studies in the Arab population have also reported a higher prevalence of strabismus. Although the Arab's data were excluded the most, by reducing the effect of confounding

factors using multivariate analysis, the Arabs had the highest risk for exotropia and esotropia (OR 3.71 and 12.78, respectively, $P$<0.001).

Categorizing strabismus prevalence in study centers, the Hoveizeh center reported the highest (5.74%, $P$<0.001), followed by the Zahedan center (1.89%, $P$<0.001), in general strabismus prevalence and strabismus subgroups. The increased numbers can be attributed to multiple potential factors, including genetics and ethnic predominance in the area, environmental factors, as both centers are placed in the southern part of the country, which is remote from central healthcare establishments, and socioeconomic considerations as well, which limit the ability to seek timely diagnosis and appropriate treatment.

Nystagmus was the other ocular condition evaluated in this study. The prevalence of nystagmus was 0.1% in our study population, which is in line with previous studies[29-30]. There is limited published data on the clinical aspects of nystagmus in adult populations. As stated above, myopia was the most common type of SE in nystagmus, along with oblique astigmatism, similar to our normal and other Asian populations, and opposite to what has been reported in European populations[30]. The prevalence of amblyopia and anisometropia was 48% and 25%, which followed the pattern of strabismic participants. Furthermore, in this cohort, the female gender was an independent protective factor for nystagmus. However, due to limited data, we were not able to categorize nystagmus based on etiology and type.

**Strengths and Limitations** Our study holds several notable strengths that contribute to its reliability and validity. The study adopts a population-based design, ensuring the findings can be generalized to the wider population. Moreover, the study benefits from a relatively large sample size, allowing for more robust statistical analysis and increasing the precision of the results. The methods employed for sampling and examination are standardized, minimizing biases and enhancing the study's internal validity. Another key strength of our study is its territory-wide coverage, encompassing different districts of Iran. This extensive geographic representation enhances the generalizability of the findings to the entire region. All study participants were also invited to PERSIAN cohort facilities, where they underwent comprehensive ophthalmological examinations. The utilization of a single clinic setting ensures consistency in the examination techniques and tools throughout the study, thereby maintaining a high level of sensitivity and specificity in the diagnosis of strabismus.

It is important to interpret the results considering certain limitations. The two-stage protocol of ocular examination might cause an underdiagnosis of smaller deviations in the first stage. Family history data is unavailable in our cohort, which can provide a clue to genetic risk factors. In addition, prior strabismus surgery and strabismus evaluation without corrective glasses are not included, which might have led to underestimation of the strabismus prevalence. However, we are reporting the strabismus still present in the adult population, considering the fact that many are already treated in childhood, and many are acquired and not treated yet. It is crucial to note that the study design is a first-phase report of a cohort, which means that it is not possible to establish a causal relationship between variables. The findings provide associations rather than causation. In addition, out of the total 65 580 included patients in the study, only 49 349 individuals had a complete strabismus-related data sheet, causing a smaller population size for risk factor analysis. The data exclusion was most prominent in the Arab ethnic group; this might have been the cause of higher prevalences. However, we tried to lessen the effects of this confounding factor in multivariate analyses. It is noteworthy that the information on the participants' records was collected by personnel with different education statuses, increasing the possibility of error bias and affecting the results of ophthalmologic examinations. Moreover, since the history of treated strabismus is not included in the study, it could have resulted in an underestimation of the prevalence of strabismus. Lastly, due to the limited number of cases for each type of strabismus and no data on the cause of strabismus, congenital *vs* acquired, the interpretation of the associated risk factors for each group should be done with caution. This limitation was due to insufficient statistical power.

In conclusion, in this population-based cohort study in different regions in Iran, we report the general prevalence of strabismus and its subtypes, as well as the effect of different risk factors associated with strabismus.

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