Prevalence of Glaucoma in the United States: The 2005–2008 National Health and Nutrition Examination Survey

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PURPOSE. To estimate the prevalence of glaucoma in the US population based on optic nerve head photography, to estimate the prevalence of glaucoma awareness, and to identify demographic and ocular risk factors for being unaware of having glaucoma.

METHODS. The study included 57,466 men and women 40 years of age and older participating in the National Health and Nutrition Examination Survey (NHANES) 2005–2008. Each participant had 45° photographs of the macula and optic disc of both eyes. Fundus photographs were first graded by a reading center, and those with a cup-to-disc ratio (CDR) ≥ 0.6 were regraded by three glaucoma specialists to determine the presence or absence of glaucoma. Analyses were performed using NHANES weights to account for the complex multistage probability sampling design.

RESULTS. The estimated overall prevalence of glaucoma in the US civilian, noninstitutionalized population 40 years of age and older was 2.1% (95% confidence interval [CI], 1.7%–2.6%). Glaucoma affected 2.9 million individuals, including 1.4 million women; 1.5 million men; 2.3 million people 60 years of age and older; and 0.9 million blacks, Mexican Americans, and people of other races. The prevalence of glaucoma was highest in non-Hispanic blacks, followed by non-Hispanic whites, Mexican Americans, and others. Over half of participants with glaucoma were unaware that they had the disease.

CONCLUSIONS. The prevalence of glaucoma based on optic nerve fundus photography assessment in the general US population 40 years of age and older was 2.1%. Approximately half of glaucoma cases were previously undiagnosed. Studies to determine whether and how to identify undiagnosed glaucoma are an important next step.

Keywords: cup-to-disc ratio, glaucoma, National Health and Nutrition Examination Survey (NHANES), optic disc, prevalence

Glaucoma is the second leading cause of blindness and a major source of morbidity and disability in the United States. Several population-based surveys have estimated the prevalence of glaucoma in general population samples in the United States.1–5 but most surveys were restricted to specific regional or ethnic populations and were not generalizable to the overall US population. A 2004 meta-analysis pooled data from population-based studies and estimated the prevalence of primary open-angle glaucoma (POAG) in the US population 40 years and older at 1.86% (95% confidence interval, 1.75%–1.96%),2 while another meta-analysis in 2014 estimated the prevalence to be 3.29 (95% confidence interval [CI], 1.83–5.53).6 These estimates, however, were limited by sparse data on blacks and Latinos and lacked information on other minorities.

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional survey that used a stratified multistage probability design to obtain representative health data of the civilian, noninstitutionalized US population.7 The NHANES oversamples elderly participants and certain age and minority groups, making it well suited to estimate glaucoma prevalence in the United States. Previous estimates of glaucoma prevalence using NHANES data were based only on self-report of a glaucoma diagnosis,8–10 which is prone to recall bias and underdiagnosis as glaucoma has a long asymptomatic phase.11 Others have attempted to estimate glaucoma prevalence based on NHANES data12; however, these estimates have been limited by use of cup-to-disc ratio, which does not take into account more nuanced changes of the optic nerve such as disc size, localized notching, or disc hemorrhage.

During the 2005–2006 and 2007–2008 NHANES cycles, fundus photography and visual field testing using frequency-doubling technology (FDT) were performed as part of the physical examination of people aged 40 years or older. The objective of this study is to estimate the prevalence of glaucoma in the general US population using fundus photography in...
NHNES 2005–2008. In addition, we assess the risk factors associated with confirmatory defects on FDT visual field testing, the prevalence of glaucoma awareness, and the risk factors for being unaware of having glaucoma.

METHODS

Study Population
The NHANES is conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention. We restricted our analysis to NHANES 2005–2008 participants 40 years of age or older (n = 7081). We excluded 1355 participants with no fundus photographs or with ungradable photograph quality. The final sample included 5746 participants who had at least one eye that could be evaluated for glaucoma using optic nerve photos (2883 men and 2863 women).

The NCHS Institutional Review Board approved the NHANES, and written informed consent was obtained from all participants. The present study involved an additional review of optic nerve photos of NHANES participants by investigators at Johns Hopkins University and the Johns Hopkins School of Medicine, and the NCHS Institutional Review Boards approved this review.

Data Collection
The NHANES included a standardized questionnaire administered at home by a trained interviewer and an extensive examination in a mobile examination center (MEC) that included a physical exam, specialized measurements, and laboratory tests. Demographic data included age, sex, race/ethnicity, education, income, and specific questions related to access to health care and health insurance coverage. Educational attainment was defined as less than high school if the participant reported having less than 12 years of schooling or equivalent. Poverty was defined as having a poverty-to-income ratio (PIR) ≤ 1.0, where PIR is a ratio of family income to poverty threshold as defined by the United States Census Bureau. Access to health care and health insurance coverage at the time of survey were assessed via the questions “Is there a place you usually go when you are sick or need advice about your health?” and “Are you covered by health insurance or some other kind of health care plan?” We categorized health insurance as private insurance only, government insurance only, a combination of private and government, or no health insurance. Self-reported glaucoma status was ascertained via the question “Have you ever been told by an eye doctor that you have glaucoma, sometimes called high pressure in your eyes?” Because availability of government insurance, specifically Medicare, is affected by age, we analyzed insurance status separately for those <65 and those ≥65 years old.

Optic Disc Grading
Each NHANES participant had nonmydriatic 45° photographs taken of the macula and optic disc of both eyes (CR6-45NM; Canon USA, Melville, NY, USA). Initial grading of the photographs, including cup-to-disc ratio (CDR), was performed (Canon USA, Melville, NY, USA). Initial grading of the photographs was also evaluated for the presence of macular disease including macular edema, panretinal photocoagulation, focal photocoagulation, artery or vein occlusion, diabetic retinopathy, age-related macular degeneration, chorioretinal abnormalities, macular hole, and retinal detachment. All images with a CDR ≥ 0.6 on initial grading (1201 images of 1073 eyes from 549 participants) were reviewed and regraded by three glaucoma specialists (PG, MVB, and DSF) at the Wilmer Eye Institute of the Johns Hopkins University School of Medicine. For this analysis, we assumed that participants with CDR < 0.6 in both eyes did not have glaucoma (this value is close to the optimal cutoff point for defining glaucomatous optic neuropathy in population-based glaucoma risk factor analysis).14 As a consequence, all glaucoma cases in the analysis were derived from participants who had at least one eye with CDR ≥ 0.6 on initial grading.

The nonstereo color images of participants with CDR ≥ 0.6 as determined by the reading center were transferred to a tablet-based review system (TruthMarker, IDx, LLC; Iowa City, IA, USA), and three glaucoma specialists regraded each image to determine image quality (excellent, good, fair, poor, ungradable), vertical CDR (0.0–1.0 in increments of 0.1), notching of the neuroretinal rim (none, inferior, superior, both), excavation of the optic cup (no, maybe, yes, unable), optic disc hemorrhage (no, maybe, yes, unable), tilting of the disc (no, yes), and relative disc size (small, average, large). Each glaucoma specialist then determined likelihood of glaucoma (no, possible, probable, definite, unable) based on clinical judgment of all features of disc appearance. The results were adjudicated where necessary.

To evaluate the reliability of the CDR determined by the reading center, 180 participants with CDR < 0.6 in both eyes (423 images of 360 eyes of 180 participants) were randomly sampled. Among the 180 participants, 2 participants had missing grading on CDR; 157 participants had CDR < 0.6 in both eyes in the initial and second readings; and 21 participants were classified as having a CDR ≥ 0.6 in at least one eye on the reading at Johns Hopkins University. Among all regraded participants, the kappa for agreement between the Johns Hopkins University and University of Wisconsin readings on CDR categorization was 0.76.

Definition of Glaucoma
Using the appearance of the optic nerve on fundus photography, three glaucoma specialists judged the presence of glaucoma in each eye (no, possible, probable, definite, unable). Glaucoma was defined if the consensus assessment by the three glaucoma specialists was probable or definite in at least one eye. Disagreements were adjudicated using the algorithm detailed in the Supplementary Material.

Frequency Doubling Technology Perimetry
The methodology for performing FDT perimetry on NHANES participants has been previously described.15 Briefly, each NHANES participant with at least light-perception vision who did not have an infection underwent a 19-point suprathreshold screening test using the N-30-5 pattern on a Matrix FDT (Carl Zeiss Meditec, Dublin, CA, USA). Participants were required to successfully and reliably complete two such tests. The NHANES protocol defined a test as unreliable if the false-positive rate was greater than 33%, if there were more than 33% fixation losses by blind spot testing, or if the technician administering the test noted an error of some kind. The result for a particular eye was deemed unreliable if either of the two tests was unreliable by these criteria.

The NHANES protocol defines visual field loss as the presence of at least two field locations in the first test abnormal at the <1% threshold level and at least two field locations in the second test abnormal at the <1% threshold level with at least one abnormal field location being the same on both tests. An abnormal FDT was defined as any outcome of that test that would have resulted in the patient’s being referred on for further evaluation. This included the test not being done, a
Table 1. Characteristics of Study Participants by Glaucoma Status in the National Health and Nutrition Examination Survey 2005–2008

| Characteristic          | Overall, n = 5746 (95% CI) | No Glaucoma, n = 5574 (95% CI) | Glaucoma, n = 172 (95% CI) | P Value Glaucoma vs. No Glaucoma |
|-------------------------|----------------------------|--------------------------------|----------------------------|---------------------------------|
| Age, mean               | 56.7 (55.9, 57.5)          | 57.0 (56.2, 57.8)               | 68.8 (66.3, 71.3)           | <0.001                          |
| Female sex              | 53.2 (51.9, 54.5)          | 53.3 (52.0, 54.6)               | 46.7 (36.8, 56.9)           | 0.20                            |
| Race/ethnicity          |                            |                                |                            |                                 |
| White                   | 75.8 (71.1, 79.9)          | 75.9 (71.3, 80.0)               | 70.2 (58.2, 80.0)           | 0.05                            |
| Black                   | 10.2 (7.9, 13.2)           | 10.1 (7.8, 13.0)                | 17.7 (11.0, 27.3)           |                                 |
| Mexican American        | 5.6 (4.2, 7.4)             | 5.6 (4.2, 7.4)                  | 4.8 (2.7, 8.4)              |                                 |
| Other                   | 8.4 (6.5, 10.8)            | 8.4 (6.5, 10.8)                 | 7.2 (4.0, 12.7)             |                                 |
| Poverty PIR < 1         | 9.8 (8.5, 11.3)            | 9.7 (8.4, 11.3)                 | 12.2 (8.6, 17.0)            | 0.22                            |
| Education < high school | 19.8 (17.4, 22.4)          | 19.7 (17.4, 22.2)               | 26.8 (17.0, 39.5)           | 0.12                            |
| Lack access             | 8.7 (7.6, 10.0)            | 8.8 (7.7, 10.1)                 | 5.8 (3.7, 9.0)              | 0.05                            |
| Insurance               |                            |                                |                            |                                 |
| Private only            | 48.4 (44.5, 52.3)          | 48.9 (44.9, 52.9)               | 26.5 (18.6, 36.4)           | <0.001                          |
| Private and gov.        | 20.4 (17.6, 23.5)          | 19.8 (17.1, 22.9)               | 45.0 (36.6, 53.8)           |                                 |
| Government only         | 18.5 (16.7, 20.5)          | 18.4 (16.6, 20.4)               | 23.8 (15.7, 34.4)           |                                 |
| None                    | 12.7 (10.6, 15.0)          | 12.8 (10.8, 15.2)               | 4.6 (2.3, 9.2)              |                                 |
| Insurance for age < 65  |                            |                                |                            | 0.49                            |
| Private only            | 64.2 (59.8, 68.4)          | 64.2 (59.7, 68.4)               | 68.3 (48.5, 83.2)           |                                 |
| Private and gov.        | 6.8 (5.2, 8.9)             | 6.9 (5.3, 9.0)                  | 2.3 (0.5, 11.1)             |                                 |
| Government only         | 11.9 (10.1, 13.9)          | 11.8 (10.0, 13.9)               | 16.2 (6.2, 36.2)            |                                 |
| None                    | 17.1 (14.3, 20.2)          | 17.1 (14.3, 20.3)               | 13.2 (5.7, 27.8)            |                                 |
| Insurance for age ≥ 65  |                            |                                |                            | 0.50                            |
| Private only            | 7.7 (6.2, 9.4)             | 7.7 (6.1, 9.5)                  | 8.0 (3.7, 16.5)             |                                 |
| Private and gov.        | 55.3 (50.8, 59.8)          | 54.8 (50.1, 59.5)               | 64.0 (52.1, 74.5)           |                                 |
| Government only         | 35.7 (31.5, 40.1)          | 36.2 (31.8, 40.9)               | 27.2 (17.7, 39.2)           |                                 |
| None                    | 1.3 (1.0, 1.7)             | 1.3 (0.9, 1.8)                  | 0.8 (0.1, 6.3)              |                                 |
| Abnormal FDT results    | 14.6 (13.2, 16.0)          | 13.9 (12.6, 15.4)               | 44.6 (35.8, 53.8)           | <0.001                          |
| Glaucoma by self-report | 5.0 (4.3, 5.7)             | 4.1 (3.5, 4.8)                  | 45.0 (36.6, 53.7)           | <0.001                          |

* Data are means (95% confidence intervals) or percentages (95% confidence intervals).

Statistical Analysis

The reference population used in this study was the civilian, noninstitutionalized population 40 years of age and older who resided in the United States during 2005 to 2008. NHANES used a complex, stratified multistage probability sampling design. Continuous and categorical demographic and clinical variables were compared across glaucoma status categories using Student’s t-tests or χ² tests. We estimated the prevalence and number of people with glaucoma in the United States overall and in subgroups defined by age, sex, and race/ethnicity. We also modeled the prevalence of glaucoma as a function of age using restricted cubic splines with knots at 50, 60, and 70 years of age to provide a smooth yet flexible description of the association.

The association between demographic variables and disc size (small, medium, large) was evaluated using multinomial logistic regression models. The association between demographic variables and other disc morphology variables was evaluated using multivariable logistic regression models. The left and right eyes were assessed and reported separately. The kappa statistics for agreement between the left and right eyes were 0.49, 0.09, 0.41, 0.50, and 0.07 for disc size, hemorrhage, excavation, notch, and tilt, respectively. All models were adjusted for age, sex, and race/ethnicity, and separate models were fitted for the association of self-reported glaucoma, optic disc grading, defined glaucoma, and CDR ≥ 0.6 with disc morphology variables. We also modeled the association between demographic variables and disc morphology with previous diagnosis of glaucoma using multivariable logistic regression models.

Results

We identified 172 cases of glaucoma based on optic disc appearance in the study population. Characteristics of those who did and did not have gradable fundus photos are described in detail in Supplementary Table S1. Participants with glaucoma were more likely to be older and to have a combination of private and government insurance, abnormal FDT test results, and a self-report of a physician diagnosis of glaucoma and were less likely to have no insurance (Table 1).
The weighted estimate of the overall prevalence of glaucoma in the US civilian noninstitutionalized population aged 40 years and older was 2.1% (95% CI, 1.7%–2.6%; Table 2), affecting 2.91 million people (1.36 million women and 1.55 million men; Table 3). The prevalence increased with age, was higher in men than in women (2.4% vs. 1.9%), and was higher in blacks compared to other ethnicities. The age-related increase in prevalence was evident in men and women and almost all race and ethnicity groups, albeit weaker for Mexican Americans after age 60 (Fig., Supplementary Fig. S1).

The associations of participant characteristics with individual morphologic optic disc features were evaluated among the 729 participants whose optic images were reviewed at Johns Hopkins University (Table 4; Supplementary Table S2). The associations were mostly consistent between left and right eye. Non-Hispanic blacks, other races, and participants with CDR ≥ 0.6 were less likely to have a small disc size. Disc hemorrhage, excavation, and notching were more likely to occur in participants who were older, had CDR ≥ 0.6, or had glaucoma. The prevalence of tilted disc was lower in participants with CDR < 0.6, but was not statistically associated with glaucoma diagnosis.

Among the 172 participants with glaucoma, only 78 reported a previous diagnosis of glaucoma (43.7%, Table 5). Those who were unaware of glaucoma status were more likely to be younger, to have a small disc, and to have an abnormal FDT result and were less likely to have notching or disc hemorrhages compared with those with a self-reported diagnosis. Among 5551 participants without glaucoma, 271 reported a previous diagnosis of glaucoma (3.9%, Table 6). Those who reported a previous diagnosis of glaucoma were older and more likely to be non-Hispanic black, to have an abnormal FDT test, and to have notch of the optic nerve. They were also less likely to be educated and to have private insurance only or no insurance compared with participants who correctly self-identified as not having glaucoma. The positive and negative predictive values of self-report of a glaucoma diagnosis were 18.5% and 98.8%, respectively.
| No. cases/total no. | Small vs. Normal Disc Size | Large vs. Normal Disc Size | Disc Hemorrhage | Excavation | Any Notch | Tilted |
|---------------------|----------------------------|-----------------------------|-----------------|------------|-----------|--------|
| 108/708             | 45/708                      | 8/706                       | 274/701         | 44/708     | 19/708    |
| Age, with 10y increase | 0.87 (0.73, 1.03)           | 0.62 (0.38, 1.00)           | 1.63 (0.88, 3.02)| 1.80 (1.52, 2.14)| 3.47 (2.25, 5.34) | 0.78 (0.51, 1.20) |
| Sex                 |                            |                             |                 |            |           |        |
| Male                | 1.00, reference             | 1.00, reference             | 1.00, reference | 1.00, reference | 1.00, reference | 1.00, reference |
| Female              | 1.77 (1.03, 3.02)           | 0.91 (0.45, 1.85)           | 1.21 (0.59, 2.48)| 0.72 (0.45, 1.17) | 0.78 (0.56, 1.67) | 5.08 (0.88, 29.43) |
| Race/ethnicity      |                            |                             |                 |            |           |        |
| White               | 1.00, reference             | 1.00, reference             | 1.00, reference | 1.00, reference | 1.00, reference | 1.00, reference |
| Black               | 0.20 (0.10, 0.38)           | 1.62 (0.68, 3.84)           | 0.20 (0.02, 2.51)| 0.84 (0.58, 1.22) | 0.99 (0.54, 1.81) | 0.95 (0.34, 2.61) |
| Mexican American    | 0.53 (0.25, 1.10)           | 0.89 (0.35, 2.24)           | 1.31 (0.14, 12.71)| 0.75 (0.45, 1.27) | 1.51 (0.41, 5.56) | 0.22 (0.04, 1.13) |
| Other               | 0.32 (0.10, 0.99)           | 1.29 (0.29, 5.80)           | 0.35 (0.03, 4.55)| 0.47 (0.26, 0.83) | 1.90 (0.52, 6.92) | 2.00 (0.48, 8.25) |
| Glaucoma by self-report† |                        |                             |                 |            |           |        |
| No                  | 1.00, reference             | 1.00, reference             | 1.00, reference | 1.00, reference | 1.00, reference | 1.00, reference |
| Yes                 | 0.50 (0.24, 1.04)           | 2.36 (0.92, 6.08)           | 8.24 (3.77, 17.97)| 3.77 (1.95, 7.28) | 10.94 (4.44, 26.94) | 1.20 (0.35, 4.41) |
| Glaucoma by optic disc grading† |                      |                             |                 |            |           |        |
| No                  | 1.00, reference             | 1.00, reference             | 1.00, reference | 1.00, reference | 1.00, reference | 1.00, reference |
| Yes                 | 0.71 (0.32, 1.58)           | 1.83 (0.66, 5.10)           | 7.55 (3.63, 15.70)| 745.06 (88.14, 6297.95) | - | 0.74 (0.19, 2.80) |
| Vertical CDR ≥ 0.6† |                        |                             |                 |            |           |        |
| No                  | 1.00, reference             | 1.00, reference             | 1.00, reference | 1.00, reference | 1.00, reference | 1.00, reference |
| Yes                 | 0.11 (0.06, 0.19)           | 7.64 (1.50, 39.02)          | 14.85 (1.04, 211.09)| 37.11 (17.85, 77.21) | - | 0.40 (0.15, 1.01) |

* Age, sex, and ethnicity are assessed together in the main model. Among 729 total subjects with glaucoma grading, 708 participants had disc size and notch grading, 706 participants had disc hemorrhage evaluation, and 701 had excavation evaluation. Data are odds ratios (95% confidence intervals).
† Each glaucoma indicator was included in separate models adjusted for age, sex, and ethnicity.
DISCUSSION

The overall prevalence of glaucoma in a representative sample of the US population 40 years of age and older based on fundus photographs was 2.1% (95% CI, 1.7%–2.6%), representing 2.9 million cases if applied to the entire US population. This includes 1.4 million cases in women, 1.5 million cases in men, 2.3 million cases among people 60 years of age and older, and 0.9 million cases among blacks, Mexican Americans, and others. The prevalence of glaucoma was highest in non-Hispanic blacks, followed by non-Hispanic whites, Mexican Americans, and others. Consistent with other studies,1,16–18 we found that 55.0% of people with glaucoma identified by masked evaluation of optic nerve photos were unaware of their disease status.

Our estimates of the prevalence of glaucoma overall and among non-Hispanic whites were similar to those from a meta-analysis of population-based studies in the United States,2 but were lower than those in the more recent meta-analysis that presented global estimation of glaucoma prevalence.6 Our study and the two meta-analyses differed in the prevalence estimates for non-Hispanic blacks and Mexican Americans, as data were scarce and the estimates in the meta-analysis were derived from single studies. Our estimate of glaucoma among non-Hispanic blacks (3.7%) was lower than that of blacks in the Baltimore Eye Survey (5.6%),1 the only study of blacks in the United States, and of that in the Barbados Eye Study (10.8%)16 and the St. Lucia Study (8.8%),19 the two major studies of blacks outside the United States. Our estimate of the prevalence of glaucoma among Mexican Americans (1.9%) was similar to that of Proyecto Ver (2.0%),4 but lower than that of the Los Angeles Latino Eye Study (4.7%).5 In addition, we did not find an exponential increase of glaucoma prevalence with age in Mexican Americans as observed in other ethnic groups and in the two studies of Latinos in the United States.1,5 Possible explanations include different demographic and genetic characteristics of participants across

| | Self-Report Glaucoma, n = 78 | Self-Report Nonglaucoma, n = 91 | P Value |
|---|---|---|---|
| Age, y | 73.5 (71.5, 75.4) | 64.9 (61.8, 68.0) | <0.001 |
| Female sex, % | 45.3 (35.2, 55.8) | 47.9 (33.5, 62.6) | 0.74 |
| Race/ethnicity, % | | | 0.33 |
| White | 73.0 (60.4, 82.7) | 69.0 (53.7, 81.0) | 0.03 |
| Black | 17.8 (11.3, 26.9) | 16.5 (8.7, 29.0) | 0.04 |
| Mexican American | 2.7 (1.0, 7.4) | 6.6 (3.8, 11.4) | 0.05 |
| Other | 6.5 (2.5, 15.9) | 7.9 (2.7, 20.7) | 0.46 |
| Poverty PIR < 1, % | 13.5 (8.7, 20.4) | 10.4 (5.9, 17.7) | 0.48 |
| Education < high school, % | 27.3 (13.0, 48.5) | 26.3 (15.5, 40.9) | 0.92 |
| Lack access, % | 6.5 (1.8, 20.5) | 5.4 (2.5, 11.1) | 0.84 |
| Insurance, % | | | 0.31 |
| Private only | 18.8 (9.1, 34.7) | 33.3 (22.9, 45.6) | 0.03 |
| Private and gov. | 54.6 (39.5, 68.9) | 37.9 (28.9, 47.9) | 0.03 |
| Government only | 22.1 (11.5, 38.2) | 24.1 (13.9, 38.4) | 0.03 |
| None | 4.6 (1.5, 13.1) | 4.7 (2.0, 10.9) | 0.03 |
| Insurance for age < 65, % | | | 0.31 |
| Private only | 61.7 (29.6, 86.0) | 70.3 (47.0, 86.3) | 0.03 |
| Private and gov. | 10.3 (1.9, 40.8) | 0 | 0.03 |
| Government only | 7.0 (1.7, 24.2) | 18.9 (6.6, 43.6) | 0.03 |
| None | 21.1 (5.7, 54.1) | 10.9 (4.2, 25.4) | 0.03 |
| Insurance for age ≥ 65, % | | | 0.54 |
| Private only | 10.8 (3.7, 27.4) | 4.7 (1.7, 12.3) | 0.03 |
| Private and gov. | 62.8 (45.2, 77.5) | 67.2 (50.4, 80.5) | 0.03 |
| Government only | 24.9 (12.5, 45.5) | 28.1 (15.6, 45.2) | 0.03 |
| None | 1.5 (0.2, 11.4) | 10.9 (4.2, 25.4) | 0.03 |
| Abnormal FDT result | 65.8 (52.9, 76.7) | 26.9 (18.5, 37.4) | <0.001 |
| Disc size†, % | | | 0.25 |
| Small | 8.6 (4.2, 16.7) | 17.1 (8.7, 30.6) | 0.03 |
| Average | 84.9 (72.9, 92.1) | 73.2 (60.0, 83.3) | 0.03 |
| Large | 6.5 (2.1, 18.2) | 9.7 (4.0, 21.9) | 0.03 |
| Disc hemorrhage†, % | 8.5 (3.3, 20.0) | 0 | 0.03 |
| Excavation†, % | 91.0 (74.7, 97.2) | 84.6 (75.2, 90.8) | 0.40 |
| Any notch†, % | 41.1 (29.8, 53.4) | 11.5 (6.0, 21.1) | 0.001 |
| Tilted†, % | 3.9 (1.2, 12.1) | 1.6 (0.4, 7.1) | 0.37 |

* Data are means (95% confidence intervals) or percentages (95% confidence intervals).
† Right eye.

Out of the 172 glaucoma patients identified through fundus photograph, 169 self-reported glaucoma status in questionnaire.
TABLE 6. Participant Characteristics and Disc Morphology by Self-Reported Glaucoma Status Among People Without Glaucoma Determined in Fundus Photographs in the National Health and Nutrition Examination Survey 2005–2008*

|                                                                 | No Glaucoma in Fundus Photograph                                                                 |
|-----------------------------------------------------------------|---------------------------------------------------------------------------------------------|
|                                                                | Self-Report Nonglaucoma, n = 5280                                                          | Self-Report Glaucoma, n = 271                                                               | P Value |
| Age, y                                                          | 56.6 (55.9, 57.4)                                                                          | 65.2 (62.8, 67.6)                                                                          | <0.001  |
| Female sex, %                                                   | 53.2 (51.7, 54.6)                                                                          | 56.3 (47.7, 64.6)                                                                          | 0.48    |
| Race/ethnicity, %                                               |                                                                                             |                                                                                             | 0.02    |
| White                                                           | 76.1 (71.6, 80.1)                                                                          | 74.3 (65.1, 81.7)                                                                          |         |
| Black                                                           | 9.9 (7.6, 12.7)                                                                             | 14.4 (9.6, 20.9)                                                                           |         |
| Mexican American                                               | 5.6 (4.2, 7.3)                                                                             | 4.5 (2.2, 9.0)                                                                             |         |
| Other                                                           | 8.4 (6.6, 10.7)                                                                             | 6.9 (3.7, 12.6)                                                                            |         |
| Poverty PIR < 1, %                                              | 9.6 (8.3, 11.2)                                                                             | 11.3 (7.9, 15.8)                                                                           | 0.32    |
| Education < high school, %                                      | 19.2 (17.0, 21.7)                                                                           | 26.7 (20.5, 33.8)                                                                          | 0.008   |
| Lack access, %                                                  | 8.9 (7.8, 10.1)                                                                             | 6.8 (4.0, 11.3)                                                                            | 0.27    |
| Insurance, %                                                    |                                                                                             |                                                                                             | <0.001  |
| Private only                                                    | 49.7 (45.7, 53.7)                                                                           | 32.1 (23.5, 42.1)                                                                          |         |
| Private and gov.                                                | 19.2 (16.6, 22.3)                                                                           | 34.6 (26.9, 43.2)                                                                          |         |
| Government only                                                 | 18.0 (16.1, 20.0)                                                                           | 26.9 (20.3, 34.8)                                                                          |         |
| None                                                            | 13.1 (10.9, 15.6)                                                                           | 6.3 (3.3, 11.9)                                                                            |         |
| Insurance for age < 65, %                                       |                                                                                             |                                                                                             | 0.31    |
| Private only                                                    | 64.3 (59.7, 68.6)                                                                           | 62.8 (51.0, 73.3)                                                                          |         |
| Private and gov.                                                | 6.9 (5.3, 9.0)                                                                             | 6.8 (2.5, 17.4)                                                                            |         |
| Government only                                                 | 11.6 (9.8, 13.7)                                                                            | 19.7 (11.3, 32.0)                                                                          |         |
| None                                                            | 17.2 (14.5, 20.5)                                                                           | 10.7 (4.8, 22.0)                                                                           |         |
| Insurance for age ≥ 65, %                                       |                                                                                             |                                                                                             | 0.37    |
| Private only                                                    | 7.8 (6.3, 9.6)                                                                             | 6.5 (2.9, 14.0)                                                                            |         |
| Private and gov.                                                | 54.7 (50.0, 59.4)                                                                           | 57.7 (48.5, 66.7)                                                                          |         |
| Government only                                                 | 36.3 (31.9, 41.0)                                                                           | 53.0 (24.6, 42.5)                                                                          |         |
| None                                                            | 1.2 (0.8, 1.7)                                                                             | 2.7 (1.1, 6.7)                                                                             |         |
| Abnormal FDT result                                             | 13.2 (11.9, 14.7)                                                                           | 28.5 (22.8, 35.0)                                                                          | <0.001  |

* Data are means (95% confidence intervals) or percentages (95% confidence intervals).

studies and variations in sample selection, measurement techniques including potential small subgroup size despite oversampling of minority populations, and diagnostic criteria. Participants in NHANES were sampled from across the United States, while participants from other studies were recruited from specific regions. In addition, we relied on fundus photographs to identify glaucoma, while other studies also used information from intraocular pressure, visual acuity, and/or visual field testing for diagnosis.1,4,5,16–18 Compared to participants who self-report a previous diagnosis of glaucoma, those with undiagnosed glaucoma tended to be younger and were less likely to have visual field defects or clear optic disc changes such as a focal notch or a disc hemorrhage. Older individuals were more likely to have had more visits to an eye doctor and therefore may have been more likely to have the disease detected during these exams. Our results suggest that systematic eye exams with fundus evaluation may identify nonsymptomatic cases who are unaware of the disease and thus may benefit from treatment and clinical follow-up at earlier stages in the natural history of the disease.
Several limitations need to be considered in the interpretation of our findings. First, we relied exclusively on fundus photographs for glaucoma assessment. We did not consider information on FDT perimetry because of its poor diagnostic performance in visual field–naive people. Fundus photographs, however, are subject to variability in interpretation and measurement error. In order to minimize this we had three glaucoma experts independently grade all optic nerve images, and final diagnosis was based on a standardized algorithm for decision making. In addition, participants with small optic discs (which are more common in non-Hispanic whites and females) may develop a pathologic appearance of the disc only after the appearance of visual field defects.

Second, we have likely underestimated the prevalence of glaucoma since we assumed that all participants with a CDR < 0.6 in the initial reading at the University of Wisconsin were free of glaucoma. However, in our reliability analysis of 180 participants selected at random among those with CDR < 0.6 based on the initial reading from Wisconsin, 21 people were reclassified as CDR ≥ 0.6 after interpretation of the images by three glaucoma specialists. We identified three glaucoma cases (all non-Hispanic whites with small discs) among these 21 participants, but these numbers could not be incorporated into the overall prevalence estimates because the probabilities obtained from 180 participants were statistically unstable. These findings, however, emphasize that future studies should seek a more robust grading of CDR, especially when the nerve is small. In our analysis, this misclassification will likely result in an underestimation of glaucoma prevalence. Also, in addition to the higher prevalence of self-reported glaucoma among participants with missing or ungradable fundus photographs, participants with advanced visual defects and other subgroups at high risk of glaucoma may be more likely to refuse participation in NHANES. This selection bias may lead to further underestimation of glaucoma prevalence, particularly among older individuals, since people with advanced glaucoma may more likely be institutionalized due to visual limitations. As a consequence, our estimates likely underestimate the prevalence of glaucoma and should be interpreted as lower bounds of its prevalence in the US population 40 years of age and older.

Third, although our sample size was large overall, the sample size in some subgroups was small and subject to greater random variability, which may explain the lack of exponential increase of glaucoma prevalence with age in Hispanic participants. The sample size for the evaluation of the associations between glaucoma and disc morphology characteristics was also smaller, resulting in large variance of the estimates. Finally, we could not distinguish among various types of glaucoma, which is classified mainly based on the anatomic structure of the anterior chamber. Future studies with more detailed anatomic assessment are needed to estimate the prevalence of different clinical forms of glaucoma in the US population.

The strengths of our study include the use of a large nationally representative sample with oversampling of elderly participants and minorities for more accurate subgroup estimation, rigorous quality control procedures in data collection, and the use of expert evaluation of fundus images for glaucoma assessment.

Data from NHANES 2005–2008 suggest that the lower bound estimate is 2.9 million people in the United States who have glaucoma, of whom 1.6 million are undiagnosed. This is the first time that glaucoma prevalence in the United States has been estimated based on expert assessment of fundus photographs, with more reliable estimates than those from self-reported surveys. With the aging of the US population, it is projected that the number of glaucoma patients in the United States will increase by 28% per decade, and the socioeconomic and health burden associated with glaucoma will continue to escalate. As a consequence, developing effective and practical screening algorithms for glaucoma is a clinical research priority and a requirement for disease control in the population.
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