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Relationship of Incident Glaucoma versus Physical Activity and Fitness in Male Runners

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Abstract

Purpose—To assess the dose–response relationship of vigorous physical activity (running distance, km/d) or cardiorespiratory fitness (meters-per-second pace during a 10-km footrace) to the risk for incident glaucoma.

Design—Prospective epidemiologic cohort study.

Methods—Participant-reported, physician-diagnosed incident glaucoma was compared with distance run per week and 10-km footrace performance in a cohort of 29,854 male runners without diabetes followed prospectively for 7.7 yr. The survival analyses were adjusted for age, hypertension, current and past cigarette use, and intakes of meat, fish, fruit, and alcohol.

Results—Two hundred incident glaucoma cases were reported during follow-up. The risk for reported glaucoma decreased 37% per meter-per-second increment in a 10-km race performance ($P = 0.005$). Relative to the least fit men (i.e., slowest, ≤ 3.5 m/s), the risk for incident-reported glaucoma declined 29% in those who ran 3.6–4.0 m/s ($P = 0.06$), 54% for those who ran 4.1–4.5 m/s ($P = 0.001$), 51% for those who ran 4.6–5.0 m/s ($P = 0.04$), and glaucoma was nonexistent among the 781 men who exceeded 5.0 m/s ($P = 0.03$). The risk for incident, reported glaucoma decreased 5% per kilometer-per-day run at baseline ($P = 0.04$), which remained significant when adjusted for the 10-km race performance (5% reduction per kilometer-per-day, $P = 0.04$), and both body mass index and race performance ($P = 0.04$). Baseline hypertension was unrelated to the incident glaucoma.

Conclusions—These data provide preliminary evidence that vigorous physical activity may reduce glaucoma risk, which, in the absence of medical record validation, could represent ocular hypertension in addition to frank glaucoma. Additional follow-up with validation is needed to identify the type of glaucoma affected.

INTRODUCTION

Glaucoma is an increase in intraocular pressure (IOP) that results in a progressive optic neuropathy, which is characterized by optic disk cupping and permanent visual field impairment due to ganglion cell loss and optic nerve atrophy [1,5]. It is estimated that glaucoma affects 2.5 million Americans [1]. Risk factors for glaucoma are age, family history, African American race, diabetes, hypertension, myopia, and IOP > 22 mm Hg [1].

There is a dearth of published reports on the association between incident glaucoma and physical activity among the many prospective cohorts. One possible explanation is that glaucoma is unrelated to physical activity despite being associated with lower IOP [5,11,14].

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IOP decreases transiently with aerobic exercise in proportion to intensity and duration [2,9, 15,24]. Running has been shown specifically to acutely decrease IOP [13] in proportion to its intensity [16]. There are also several studies suggesting that exercise training may chronically reduce IOP: one showing an IOP difference of 1.1 mm Hg ($P < 0.05$) at the end of a 10-wk aerobic conditioning program compared with maintained sedentary lifestyle [31]; two others reporting additional 0.93- and 1.1-mm Hg IOP reductions in subjects participating in a 3-month supervised exercise program versus nonparticipating controls [27,28]; and an uncontrolled study suggesting that IOP decreased 4.6 mm Hg after 3 months of aerobic conditioning and returned to baseline levels once training ended [23]. Cross-sectionally, subjects who participate in moderate or vigorous exercise have lower IOP than sedentary subjects [28], and steel workers actively engaged in heavy work requiring moderate or severe exertion have lower IOP than those with sedentary jobs [29].

The dearth of published associations between incident glaucoma and physical activity may also be because institutional-, geographical-, gender-, and occupational-based cohorts may not include a sufficient proportion of men and women who regularly engage in high doses of intense physical activity for its detection. The National Runners' Health Study was created specifically to test the health benefits and risks associated with running [35–40]. Although physical activity is not generally associated with visual health, prospective follow-up of this cohort has shown that men who ran an average of 64 km/wk had 35% lower risk for cataracts than those averaging less than 16 km/wk and that cataract risk decreased in association with 10-km race performance (a measure of cardiorespiratory fitness) [40]. In addition, we have shown that men's and women's risk for incident age-related macular degeneration decreased 10% per kilometer-per-day increment in usual running distance and that those who ran ≥ 4 km/d were at 42% to 54% lower risk than those who ran < 2 km/d [35]. In this article, we extend these analyses to incident, self-reported, physician-diagnosed glaucoma in relation to the dose of vigorous physical activity (specifically running distance, km/d) and cardiorespiratory fitness (i.e., as measured by meters-per-second pace during a 10-km footrace). The dose–response relationship of eye diseases to vigorous activity, in conjunction with those of other risk factors, is directly relevant to the formulation of public health policy to promote greater physical activity [10].

SUBJECTS AND METHODS

The design and methods of the National Runners' Health Study are described elsewhere [35–40]. Briefly, recruitment of this cohort took place between 1991 and 1994 (primarily 1993) by national distribution by mail of a two-page questionnaire to runners identified through subscription lists to a running magazine and as participants of footrace events. The questionnaire solicited information on demographics, running history, weight history, smoking habits, prior history of heart attacks and cancer, and medications for blood pressure, thyroid, cholesterol, and diabetes. We estimate that approximately 15% of the participants who received questionnaires responded to our survey (the number is approximate because we do not know the number of survey questionnaires actually distributed and the proportion of individuals who received multiple questionnaires). The study protocol was approved by the University of California Berkeley Committee for the Protection of Human Subjects, and all participants signed committee-approved informed consents.

Follow-up questionnaires were sent by mail requesting information on current running levels, body weight, and medical condition. Multiple follow-up survey questionnaires were sent, and telephone calls were made until an *a priori* determined response rate of 80% of the 54,956 participants of the National Runners' Health Study provided follow-up information or were known deceased. Participants were asked, “Since 1991, have you been diagnosed by a physician for any of the following conditions (provide year of diagnosis if yes),” with glaucoma as one of the listed conditions.

Running distances were reported in usual miles run per week at baseline. There were strong correlations between repeated questionnaires for self-reported running distance ($r = 0.89$) [34]. Although other leisure time physical activities were not recorded for this cohort, data from runners, recruited after 1998 (when the question was added to the survey), show that running represents (mean $\pm$ SD) $91.5 \pm 19.1\%$ and $85.2 \pm 24.0\%$ of all vigorously intense activity in men and women, respectively, and $73.5 \pm 23.7\%$ and $69.4 \pm 25.7\%$ of total leisure time physical activity, respectively.

Height and weight were also obtained by self-report. Elsewhere, we have described the strong correlations between self-reported and clinically measured heights ($r = 0.96$) and weights ($r = 0.96$) [34]. Baseline body mass index (BMI_{baseline}) was computed as the baseline weight in kilograms divided by the square of the baseline height in meters. Participants also reported their weights when they most recently started running 12 or more miles per week, from which we calculated $BMI_{\text{preexercise}}$ using the baseline height. Thus, BMI_{baseline} represents the standardized baseline body weights, and $BMI_{\text{preexercise}}$ represents the standardized body weights when the participant began running. Intakes of meat, fish, and fruit were based on the questions “During an average week, how many servings of beef, lamb, or pork do you eat,” “...serving of fish do you eat,” and “...pieces of fruit do you eat.” Alcohol intake was estimated from the corresponding questions for 4-oz (112 mL) glasses of wine, 12-oz (336 mL) bottles of beer, and mixed drinks and liqueurs. Alcohol was computed as 10.8 g per 4-oz glass of wine, 13.2 g per bottle of beer, and 15.1 g per mixed drink. Correlations between these responses and values obtained from 4-d diet records in 110 men were $r = 0.65$ for alcohol intake, $r = 0.46$ for red meat, $r = 0.38$ for fruit, and $r = 0.19$ for fish.

More than 80% of the follow-up participants also reported their best 10-km performance time during the previous 5 yr. For this report, baseline cardiorespiratory fitness was defined as speed in meters-per-second (m/s) of the participant’s best 10-km race during the previous 5 yr (reported as finish time in min). Published data support the use of running performance to approximate maximal oxygen consumption ($VO_{2\text{max}}$) [6], which, as a fitness measure, has been found to be significantly associated with multiple health outcomes [36–40].

Statistical analyses

Cox proportional hazard model (JMP software version 5.0; SAS Institute, Cary, NC) was used to estimate the dose–response relationships of incident glaucoma to baseline body weight, usual distance run, and cardiorespiratory fitness. Age, education, baseline hypertension, and reported weekly intakes of alcohol, meat, fish, and fruit were used as covariates. A quadratic term was included for age to accommodate the accelerated risk for glaucoma with growing older (quadratic term significant at $P < 0.0001$).

RESULTS

The analyses excluded 115 men who reported being diagnosed with glaucoma before, or in the year of their baseline survey. We also excluded 175 men for preexisting diabetes at baseline because they were at considerably greater risk for developing glaucoma than those without diabetes (7 incident glaucoma, relative risk 5.3 compared to nondiabetics, $P = 0.0006$ when adjusted for age). The remaining 29,739 men were primarily White (95.1%), the rest self-identified as Hispanic (2%), Asian (1.2%), Black (0.7%), Native American (0.4%), or mixed ethnicity (0.6%). There were 200 men who reported incident glaucoma during the (mean $\pm$ SD) 7.7 ± 1.8 yr of the cohort’s follow-up. Twenty-five thousand men provided their best 10-km performance times during the previous 5 yr (84.1% of the follow-up sample), including 160 who developed glaucoma. The men reporting 10-km performance times tended to be slightly younger (difference $\pm$ SE: -1.2 ± 0.2 yr), leaner (-0.5 ± 0.1 kg/m²), and to run more (1.4 ± 0.1 km/d) compared with those lacking performance times. Results for the 12,068 female

runners are not presented because only 39 were diagnosed with glaucoma, which were too few for meaningful analyses.

The 200 men reporting incident glaucoma were older than the 29,539 unaffected men (mean $\pm$ SE: 53.64 ± 0.73 vs 44.86 ± 0.06 yr, $P < 0.0001$). When adjusted for age, ANCOVA showed that those developing glaucoma did not differ from unaffected men in their baseline education, BMI, or intakes of alcohol, meat, fish, fruit, or aspirin, percent smokers, or hypertensive medication use (Table 1).

Table 2 shows that when adjusted for age, current and past smoking, baseline hypertension medication use, and diet, greater cardiorespiratory fitness at baseline, as measured by 10-km race performance time, was associated with significantly lower risk for incident glaucoma during follow-up. Each 1-m/s increment in performance was associated with a 36.7% reduction in the risk ($P = 0.007$). Borderline significance was obtained when adjusted for baseline BMI ($P = 0.06$), suggesting that some of the risk reduction may be attributable to the current leanness of the runners. This is not simply due to leaner people choosing to run faster because adjustment for pre-exercise BMI did not affect the reduction in risk. Figure 1 shows that relative to the slowest men (≤ 3.5 m/s), the risk for incident glaucoma declined 29% in those who ran 3.6–4.0 m/s ($P = 0.06$), 54% for those who ran 4.1–4.5 m/s ($P = 0.001$), 51% for those who ran 4.6–5.0 m/s ($P = 0.04$), and was essentially nonexistent among the 781 men who exceeded 5 m/s ($P = 0.03$). When analyzed by fitness categories, adjustment for BMI had little effect on the decline in risk with 10-km performance, nor did adjustment for the participants' reported usual running distance (km/d).

Included in Figure 1 are the probabilities above individual *bars* for the test of whether faster 10-km performance decreased the risk for reported incident glaucoma. For example, men who exceeded 3.5 m/s were at significantly lower risk than slower men ($P = 0.004$) and those who exceeded 4 m/s were at significantly lower risk than men who ran 3.6–4 m/s ($P = 0.04$). These probabilities show a significant dose–response relationship through at least 4.0 m/s.

Usual running distance was also significantly predictive of incident glaucoma (Table 3), even when adjusted for both baseline BMI and 10-km performance (all $P = 0.05$). Figure 2, which presents the risk reduction for incident glaucoma versus reported running distance, shows declining risk with greater distance.

DISCUSSION

Our findings suggest that faster 10-km race performance (presumably reflecting cardiorespiratory fitness) and longer running distances predict lower risk for incident, participant-reported, physician-diagnosed glaucoma. Although the greatest risk reduction was between men who ran ≥ 5 versus < 3.5 m/s, there were statistically and clinically significant risk reductions for incremental performance differences even among the slower runners (i.e., 3.6–4 vs ≤ 3.5 m/s; Fig. 1). This is our third report suggesting that vigorous physical activity may reduce the risks of age-related eye diseases [35,40]. Our success in demonstrating fewer vision problems in physically active and fit men may be due to the statistical power we achieved by targeting active individuals, in addition to the large sample size. Additional follow-up will be required to test whether physical activity and cardiorespiratory fitness lower glaucoma risk in women and whether other vigorous physical activities provide the same benefits as running, although we have no reason to expect that this would not be the case.

Our findings are consistent with several studies that report reduced IOP with training [23,27, 28,31]; however, these studies tended to be small and are unlikely to have the statistical power required to be definitive. Sargent et al. [32] did not obtain significant reductions in IOP after 6 months of training when compared with controls. Some [28,29], but not all [8], cross-

sectional comparisons between active and sedentary individuals show lower IOP among the most active or athletic. If chronic IOP reductions show the same pattern as transient IOP changes after exercise, then exercise may need to be intense to lower IOP. Qureshi et al. [30] reported that exercising at 40%, 60%, and 80% of maximal HR produced reduction in IOP of 0.9 ± 0.04 , 3.5 ± 0.07 , and 4.5 ± 0.7 mm Hg, respectively, after exercise. IOP reductions were greater during running than during walking (mean $\pm$ SD: -5.1 ± 1.8 vs -3.2 ± 1.9 mm Hg) and took longer to return to pre-exercise levels after running (56 ± 11.2 vs 31 ± 8.0 min) in healthy sedentary men [25]. Initial IOP and glaucoma status also affect response, i.e., greater post-exercise IOP reductions are reported in open-angle glaucoma patients than in healthy controls after walking (-7.7 ± 1.3 vs -2.4 ± 0.3 mm Hg), jogging (-10.9 ± 2.1 vs -3.9 ± 0.6 mm Hg), and running (-12.9 ± 2.1 vs -4.0 ± 0.4 mm Hg) [26].

The decrease in glaucoma risk with faster 10-km footrace performance was weakened when adjusted for running distance (Table 2), although the effect was small (Fig. 1). Vigorous physical activity increases cardiorespiratory fitness to a greater degree than moderately intense physical activity [33]. Cardiorespiratory fitness levels among nonathletic individuals and changes in cardiorespiratory fitness with training are, in part, inherited [4]. Sixty-four percent of the variation in IOP has been attributed to additive genetic effects [21]. Although we are aware of no data linking genetic determination of IOP and cardiorespiratory fitness, co-segregation of their separate genetic influences could contribute to their association independent of physical activity. Figure 1 adds additional support to our prior position [36] that low levels of cardiorespiratory fitness should be recognized as a clinically important health diagnostic that warrants routine screening in the population at large.

The mechanisms by which long-term exercise might lower IOP, thereby reducing glaucoma risk, are not known. Various explanations for the IOP decrease with acute, dynamic exercise have been proposed including changes in episcleral venous pressure, plasma lactate levels, blood pH, plasma osmolarity, and hormones [15,17,19,20,26,27]. Vigorous physical activity and greater cardiorespiratory fitness are associated with improved insulin resistance [36] and lower blood pressure [36], both of which have been associated with lower IOP [12].

In our sample, the 177 men with diabetes had 5.3-fold increase in risk for incident glaucoma than men without diabetes. Although this is larger than the 1.5-fold risk increase in primary open-angle glaucoma from meta-analyses of cross-sectional studies of patients with diabetes versus those without [3], and the 1.6-fold risk increase in patients with diabetes versus those without for a cohort followed prospectively [7], the 5.3-fold increase was based on only seven incident cases. On average, patients with diabetes have higher IOP than those without. Moreover, baseline diabetes has been associated with greater increases in IOP after 4 yr of follow-up in the Barbados Eye Study [12], and greater increases in primary open-angle glaucoma after 13 yr of follow-up of the Nurses' Health Study [22]. We found no association between the risk for incident glaucoma and hypertension, BMI, and other adiposity measures, which is consistent with the fact that they are less established as risk factors. Baseline blood pressures might have provided a stronger association but were not obtained, and the effect may also have been dampened by the high proportion of patients with hypertension taking blood pressure medications (76%). Although the prevalence of glaucoma is four- to five-fold greater in blacks than in whites [1], confounding between race and running distance would not account for the reported association; that is, less than 1% of the runners were black, and their exclusion did not change the results (analyses not displayed).

Current public health guidelines for physical activity focus on the motivation of sedentary individuals to become moderately active, while acknowledging the additional benefits that may accrue for more vigorous exercise [10]. Moderate-intensity exercises (e.g., walking) are those activities requiring three- to six-fold the energy expenditure of sitting at rest, whereas vigorous

exercise (e.g., running) are those activities requiring greater expenditure [10]. The current guidelines specifically recommend walking 30 min/d on 5 d/wk, which may be substituted with shorter durations of more vigorous exercise. Recent population data in the United States estimate that 50.7% of men and 47.9% of women already satisfy these minimum guideline levels [10].

The average energy expenditure of the least active men in Figure 2 (≤ 2 km/d) includes those men who satisfy guideline activity levels [10]. Thus, our analyses pertain to apparent health benefits of substantially exceeding current guideline levels. Elsewhere, we have described other apparent health benefits for men in this cohort that substantially exceed guideline levels, i.e., 30% lower odds for hypertension [36], 47% lower odds for hypercholesterolemia [36], 68% lower odds for diabetes [36], 33% lower risk for benign prostatic hyperplasia [37], 52% lower risk for gallbladder disease [38], 45% lower risk for gout [39], 35% lower risk for cataracts [40], and 42%–54% lower risk for age-related macular degeneration [35]. Given these benefits, plus the fact that one-half of the American population already exercises at guideline levels, we believe that public health recommendations should emphasize the benefits of further increasing physical activity among those already active and include visual health among the possible health benefits.

Limitations

The primary limitation of this study is the absence of clinical validation or medical record verification of self-reported, physician-diagnosed glaucoma. Pasquale et al. [22], reporting on the validity of self-reported, physician-diagnosed glaucoma, found that 25% were diagnoses with primary open-angle glaucoma with vision field loss, 26% with optic disk cupping or elevated IOP, and 19% with other glaucomas or glaucoma suspects. The diagnoses were denied by 9% of participants and refuted by 2% of their physicians (the remaining 19% refused record review or were unreachable). Thus, the associations we report could include reductions in ocular hypertension with running distances and 10-km performance. We did not collect information on whether the participant was under current eye care and, therefore, cannot exclude detection bias. Concern about ascertainment bias is warranted given the insidious nature of the condition, which is more likely to be diagnosed during a routine eye examination or in response to another condition rather than on the basis of its symptoms. However, underestimation or overestimation of the incidence of glaucoma would not account for the observed associations unless it varied systematically with 10-km performance or running distance. We do not believe that our findings are due to more frequent medical checkups leading to greater detection in the least fit and least active men. In fact, the Health Professionals Follow-up Study reported that their more vigorously active participants had more routine medical checkups than less active men [18]. Theoretically, visual field loss before the diagnosis of glaucoma could contribute to slower performance time rather than the converse; however, minor peripheral vision loss is generally unnoticed and usually does not impair function.

We also acknowledge that these analyses are based on self-reported usual distance run and 10-km performance, which are subject to error and do not take into account changes in physical activity or fitness that occurred during follow-up. These analyses do not include other physical activities that may contribute to the dose of overall vigorous activity. In addition, factors other than cardiorespiratory fitness contribute to 10-km performance times, e.g., training regimen. Finally, we acknowledge that runners may differ genetically, socioeconomically, psychologically, and with respect to various health behaviors from other individuals that may affect the generalizability of these results. We expect, however, that the biological processes that relate glaucoma to physical activity and cardiorespiratory fitness are similar in runners and nonrunners.

Our analyses provide preliminary evidence that vigorous activity may help prevent or delay glaucoma. Proof of this hypothesis will require randomized, controlled, clinical trials, animal studies, and a better understanding of those physiological processes leading to glaucoma that may be affected by vigorous physical activity. Whether the reduction in risk applies to the lower doses of moderate-intensity exercise currently advocated remains to be determined.

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REFERENCES

1. American Academy of Ophthalmology, Glaucoma Panel. Primary Open-Angle Glaucoma. Preferred Practice Pattern Committee. San Francisco (CA): American Academy of Ophthalmology; 2000. p. 1-36.
2. Avunduk AM, Yilmaz B, Sahin N, Kapicioglu Z, Dayanir V. The comparison of intraocular pressure reductions after isometric and isokinetic exercises in normal individuals. *Ophthalmologica* 1999;213:290–294. [PubMed: 10516516]
3. Bonovas S, Peponis V, Filioussi K. Diabetes mellitus as a risk factor for primary open-angle glaucoma: a meta-analysis. *Diabet Med* 2004;21:609–614. [PubMed: 15154948]
4. Bouchard C, Lesage R, Lortie G, et al. Aerobic performance in brothers, dizygotic and monozygotic twins. *Med Sci Sports Exerc* 1986;18:639–646. [PubMed: 3784876]
5. Collaborative Normal-Tension Glaucoma Study Group. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. *Am J Ophthalmol* 1998;126:487–497. [PubMed: 9780093]
6. Cooper KH. A means of assessing maximal oxygen intake: correlation between field and treadmill testing. *JAMA* 1968;203:201–204. [PubMed: 5694044]
7. Ellis JD, Evans JM, Ruta DA, et al. Glaucoma incidence in an unselected cohort of diabetic patients: is diabetes mellitus a risk factor for glaucoma. *Br J Ophthalmol* 2000;84:1218–1224. [PubMed: 11049943]
8. Era P, Parssinen O, Kallinen M, Suominen M. Effect of bicycle ergometer test on intraocular pressure in elderly athletes and controls. *Acta Ophthalmol Scand* 1993;71:301–307.
9. Harris A, Malinovsky V, Martin B. Correlates of acute exercise induced ocular hypotension. *Invest Ophthalmol Vis Sci* 1994;35:3852–3857. [PubMed: 7928182]
10. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation* 2007;116:1081–1093. [PubMed: 17671237]
11. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M. Early manifest glaucoma. Trial group reduction of intraocular pressure and glaucoma progression: results from the early manifest glaucoma trial. *Arch Ophthalmol* 2002;120:1268–1279. [PubMed: 12365904]
12. Hennis A, Wu SY, Nemesure B, et al. Hypertension, diabetes, and longitudinal changes in intraocular pressure. *Ophthalmology* 2003;110:908–914. [PubMed: 12750088]
13. Karabatakis VE, Natsis KI, Chatzibalis TE, et al. Correlating intraocular pressure, blood pressure, and heart rate changes after jogging. *Eur J Ophthalmol* 2004;14:117–122. [PubMed: 15134108]
14. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002;120:701–713. [PubMed: 12049574]
15. Kieler RA, Teraslinna P, Rowe DG, Jackson J. Standardised aerobic and anaerobic exercise: differential effects on intraocular tension, blood pH, and lactate. *Invest Ophthalmol Vis Sci* 1975;14:782–785.

16. Kiuchi Y, Mishima HK, Hotehama Y, Furumoto A, Hirota A, Onari K. Exercise intensity determines the magnitude of IOP decrease after running. *Jpn J Ophthalmol* 1994;38:191–195. [PubMed: 7967212]
17. Leighton DA, Philips CI. Effect of moderate exercise on the ocular tension. *Br J Ophthalmol* 1970;54:599–605. [PubMed: 5458251]
18. Leitzmann MF, Giovannucci EL, Rimm EB, et al. The relation of physical activity to risk for symptomatic gallstone disease in men. *Ann Intern Med* 1998;128:417–425. [PubMed: 9499324]
19. Marcus DF, Krupin T, Podos SM, Becker B. The effect of exercise on intraocular pressure. II. Rabbits. *Invest Ophthalmol Vis Sci* 1970;9:753–757.
20. Martin B, Harris A, Hammel T, Malinovsky V. Mechanisms of exercise-induced ocular hypotension. *Invest Ophthalmol Vis Sci* 1999;40:1011–1015. [PubMed: 10102302]
21. Pärssinen O, Era P, Tolvanen A, Kaprio J, Koskenvuo M, Rantanen T. Heritability of intraocular pressure in older female twins. *Ophthalmology* 2007;114:2227–2231. [PubMed: 17640733]
22. Pasquale LR, Kang JH, Manson JE, Willett WC, Rosner BA, Hankinson SE. Prospective study of type 2 diabetes mellitus and risk of primary open-angle glaucoma in women. *Ophthalmology* 2006;113:1081–1086. [PubMed: 16757028]
23. Passo MS, Goldberg L, Elliot DL, Van Buskirk EM. Exercise training reduces intraocular pressure among subjects suspected of having glaucoma. *Arch Ophthalmol* 1991;109:1096–1098. [PubMed: 1867551]
24. Price EL, Gray LS, Humphries L, Zweig C, Button NF. Effect of exercise on intraocular pressure and pulsatile ocular blood flow in a young normal population. *Optom Vis Sci* 2003;80:460–466. [PubMed: 12808407]
25. Qureshi IA. Effects of mild, moderate and severe exercise on intraocular pressure of sedentary subjects. *Ann Hum Biol* 1995;22:545–553. [PubMed: 8815781]
26. Qureshi IA. The effects of mild, moderate, and severe exercise on intraocular pressure in glaucoma patients. *Jpn J Physiol* 1995;45:561–569. [PubMed: 7474535]
27. Qureshi IA. Effects of exercise on intraocular pressure in physically fit subjects. *Clin Exp Pharmacol Physiol* 1996;23:648–652. [PubMed: 8886483]
28. Qureshi IA. Does physical fitness influence intraocular pressure? *J Pak Med Assoc* 1997;47:81–84. [PubMed: 9131859]
29. Qureshi IA, Wu XD, Xi XR, Yang J, Huang YB. Resting intraocular pressure of steel factory workers is related to their physical fitness. *Ind Health* 1997;35:259–263. [PubMed: 9127559]
30. Qureshi IA, Xi XR, Huang YB, Wu XD. Magnitude of decrease in intraocular pressure depends upon intensity of exercise. *Korean J Ophthalmol* 1996;10:109–115. [PubMed: 9055540]
31. Qureshi IA, Xi XR, Wu XD, Zhang J, Shiarkar E. The effect of physical fitness on intraocular pressure in Chinese medical students. *Zhonghua Yi Xue Za Zhi (Taipei)* 1996;58:317–322. [PubMed: 9037846]
32. Sargent RG, Blair SN, Magun JC, et al. Physical fitness and intraocular pressure. *Am J Optom Physiol Opt* 1981;58:460–466. [PubMed: 7270654]
33. Swain DP. Moderate or vigorous intensity exercise: which is better for improving aerobic fitness? *Prev Cardiol* 2005;8:55–58. [PubMed: 15722695]
34. Williams PT. Vigorous exercise and the population distribution of body weight. *Int J Obes Relat Metab Disord* 2004;28:120–128. [PubMed: 14569277]
35. Williams PT. Prospective study of incident age-related macular degeneration in relation to vigorous physical activity during 7-year follow-up. *Invest Ophthalmol Vis Sci* 2009;50:101–106. [PubMed: 18566466]
36. Williams PT. Vigorous exercise, fitness and incident hypertension, high cholesterol, and diabetes. *Med Sci Sports Exerc* 2008;40:998–1006. [PubMed: 18461008]
37. Williams PT. Effects of running distance and performance on incident benign prostatic hyperplasia. *Med Sci Sports Exerc* 2008;40:1733–1739. [PubMed: 18799982]
38. Williams PT. Independent effects of cardiorespiratory fitness, vigorous physical activity, and body weight on gallbladder disease risk during 7.6 years of follow-up. *Am J Gastroenterol* 2008;103:2239–2247. [PubMed: 18637096]

39. Williams PT. Effects of diet, physical activity and performance and body weight on incident gout in ostensibly healthy, vigorously active men. *Am J Clin Nutr* 2008;87:1480–1487. [PubMed: 18469274]
40. Williams PT. Independent effects of vigorous physical activity and fitness on incident cataract during 7.6-year follow-up. *Invest Ophthalmol Vis Sci* 2009;50:95–100. [PubMed: 18408175]

FIGURE 1.

Relative risk of incident glaucoma by 10-km race performance relative to the slowest performing men, adjusted for age, education, hypertension medication use, current and past cigarette use, and intakes of meat, fish, fruit, and alcohol. Significance levels relative to the slowest men are coded *P < 0.05, †P < 0.01, ‡P < 0.005. Significance levels relative to all faster performing men are presented above the bars and to the left of the arrows (e.g., men who exceeded 4 m/s had significantly lower risk for incident glaucoma than those who ran 3.6-4 m/s at P = 0.04). Additional adjustment for usual running distance and baseline BMI where indicated.

FIGURE 2.

Relative risk of incident glaucoma by running distance (km/d) relative to the men averaging ≤ 2 km/d, adjusted for age, education, hypertension medication use, current and past cigarette use, and intakes of meat, fish, fruit, and alcohol. Significance levels relative to all longer distanced runners are presented above the bars and to the left of the arrows (e.g., men who exceeded 6 km/d had significantly lower risk for incident glaucoma than those who ran 4.1–6 km/d, at $P = 0.02$). Asterisk (*) signifies that men who exceeded 6 km/d had significantly lower risk relative to men who ran ≤ 6 km/d ($P \leq 0.02$) with or without adjustment for BMI or fitness. Additional adjustment for 10-km performance and baseline BMI where indicated.

TABLE 1

Age-adjusted baseline characteristics of men affected and unaffected by incident glaucoma during the 7.7-yr follow-up

	Mean or Percent $\pm$ SE		Difference $\pm$ SE	Significance (<i>P</i>)
	Affected	Unaffected		
Education (yr)	16.90 $\pm$ 0.17	16.74 $\pm$ 0.02	0.16 $\pm$ 0.17	0.35
BMI (kg/m ²)	24.43 $\pm$ 0.18	24.13 $\pm$ 0.02	0.30 $\pm$ 0.18	0.10
BMI _{baseline} (kg/m ²)	25.06 $\pm$ 0.25	24.60 $\pm$ 0.03	0.46 $\pm$ 0.25	0.07
Alcohol (mL/wk)	78.33 $\pm$ 8.08	84.24 $\pm$ 0.80	-5.91 $\pm$ 8.08	0.46
Meat (servings/wk)	2.82 $\pm$ 0.19	2.83 $\pm$ 0.02	-0.01 $\pm$ 0.19	0.96
Fish (servings/wk)	1.65 $\pm$ 0.10	1.54 $\pm$ 0.01	0.10 $\pm$ 0.10	0.31
Fruit (servings/wk)	10.78 $\pm$ 0.63	10.79 $\pm$ 0.06	-0.01 $\pm$ 0.63	0.98
Aspirin (tablets/wk)	2.37 $\pm$ 0.35	2.64 $\pm$ 0.03	-0.28 $\pm$ 0.35	0.43
Smokers (%)	0.93 $\pm$ 0.82	1.52 $\pm$ 0.08	-0.60 $\pm$ 0.82	0.47
Hypertensive medications (%)	5.45 $\pm$ 1.63	5.06 $\pm$ 0.16	0.40 $\pm$ 1.63	0.81

TABLE 2

Relative risk (95% confidence interval) of incident self-reported, **physician-diagnosed** glaucoma per meter-per-second increment in 10-km race performance (our measure of cardiorespiratory fitness) from survival analyses.

	Unadjusted for Running Distance (km/d)	Adjusted for Running Distance (km/d)
Unadjusted for BMI	0.633 (0.456–0.882) <i>P</i> = 0.007	0.740 (0.517–1.062) <i>P</i> = 0.10
Adjusted for BMI _{preexercise}	0.625 (0.444–0.886) <i>P</i> = 0.008	0.720 (0.494–1.051) <i>P</i> = 0.10
Adjusted for BMI _{baseline}	0.704 (0.493–1.010) <i>P</i> = 0.06	0.800 (0.549–1.171) <i>P</i> = 0.25

Analyses adjusted for age (age and age²), present and past smoking history, hypertension, and reported weekly intakes of meat, fish, fruit, and alcohol. Additional adjustment for running distance and BMI as indicated.

TABLE 3

Relative risk (95% confidence interval) of incident, self-reported, physician-diagnosed glaucoma per kilometer-per-day increment in running distance (physical activity) from survival analyses.

	Unadjusted for cardiorespiratory fitness (10-km performance, m/s)	Adjusted for cardiorespiratory fitness (10-km performance, m/s)
Unadjusted for BMI	0.949 (0.902–0.997) <i>P</i> = 0.04	0.934 (0.876–0.994) <i>P</i> = 0.03
Adjusted for BMI _{preexercise}	0.950 (0.902–0.999) <i>P</i> = 0.04	0.937 (0.878–0.998) <i>P</i> = 0.04
Adjusted for BMI _{baseline}	0.953 (0.903–1.003) <i>P</i> = 0.07	0.937 (0.878–0.999) <i>P</i> = 0.05

Analyses adjusted for age (age and age²), present and past smoking history, hypertension, and reported weekly intakes of meat, fish, fruit and alcohol. Additional adjustment for meters-per-second and BMI as indicated.