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ARTICLE

Visual impairment and ten-year mortality: the Liwan Eye Study

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Abstract

Objectives To explore associations between visual impairment (VI) and mortality in an adult population in urban China.

Methods The Liwan Eye Study was a population-based prevalence survey conducted in Guangzhou, Southern China. The baseline examination was carried out in 2003. All baseline participants were invited for the 10-year follow-up visit. VI was defined as the visual acuity of 20/40 or worse in the better-seeing eye with habitual correction if worn. Correctable VI was defined as the VI correctable to 20/40 or better by subjective refraction, and non-correctable VI was defined as the VI correctable to worse than 20/40. Mortality rates were compared using the log-rank test and Cox proportional hazards regression models.

Results Of the 1399 participants (mean age: 65.3 ± 9.93 years; 56.4% female) with available baseline visual acuity measurement, 320 participants (22.9%) had VI. After 10 years, 314 (22.4%) participants died. Visually impaired participants had a significantly increased 10-year mortality compared with those without VI (40.0% vs. 17.2%, $P < 0.05$). After adjusting for age, gender, income, educational attainment, BMI, history of diabetes and hypertension, both VI (HR, 1.55; 95% CI, 1.14–2.11) and non-correctable VI (HR, 2.72; 95% CI, 1.86–3.98) were significantly associated with poorer survival, while correctable VI (HR, 0.99; 95% CI, 0.66–1.49) was not an independent risk factor for 10-year mortality.

Conclusions Our findings that VI, particularly non-correctable VI, predicting poorer survival may imply the underlying mechanism behind VI-mortality association and reinforce the importance of preventing and treating disabling ocular diseases to prevent premature mortality in the elderly.

Introduction

Visual impairment (VI) poses a significant global public health burden among older populations and has a profoundly negative effect on quality of life [1–5], self-reported health [6], and the ability to live independently [7, 8]. A recent systematic review and meta-analysis reported that 1.3 billion people around the world are visually impaired and 36 million were suffering from blindness in 2015 [9]. It is estimated that the number of people with VI and blindness across the world is set to triple within the next few decades, with the number of people affected by moderate to severe VI expected to rise to 550 million, and blindness to 115 million by 2050 [9].

A growing body of scientific evidence has indicated that VI is an independent risk factor for mortality [10–26]. However, there have been few studies that have addressed this issue in Chinese adults, who have different risk profiles of ocular diseases, systemic comorbidities, as well as health care systems [15, 18, 19, 25–27]. The Chinese Longitudinal Healthy Longevity Survey [18], the Tanjong Pagar study [19] and the Southern Harbin eye study [15] have reported significantly increased risk of all causes of mortality among visually impaired persons. However, the Beijing eye study has not found an independent relationship between VI and 5-year [25] or 10-year mortality rates [26]. Understanding the relationship between VI and mortality may provide an

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insight into the management of VI and its impact on severe life event such as mortality. Therefore, the purpose of the present study was to investigate the relationship between VI and 10-year mortality rates in an adult population in southern urban China.

Patients and methods

Study population

The Liwan eye study is a population-based study carried out in the Liwan district of Guangzhou, Southern China in 2003. Detailed information about the Liwan eye study had been described elsewhere [28]. In brief, participants were identified using cluster random sampling, and those aged ≥50 years who were residents of the selected study cluster for >6 months were considered eligible for participation. Eligible participants were invited for a comprehensive eye examination at a temporary research clinic established in the community. At baseline, 1405 (75.4%) of 1864 eligible participants completed eye examinations and questionnaires. A 5-year follow-up examination was conducted in 2009, and a 10-year follow-up examination was conducted from 2013 to April 2014. All baseline and follow-up studies followed the same testing protocol.

Ethical approval for the study was obtained from the Zhongshan University Ethics Review Board and the Research Governance Committee of Moorfields Eye Hospital, London. The study was conducted in accordance with the tenets of the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from all participants.

Measurements

Presenting visual acuity (PVA) was measured with an Early Treatment Diabetic Retinopathy Study visual acuity chart with participants wearing their habitual correction. Best-corrected visual acuity (BCVA) in each eye was measured in participants with PVA < 20/40 in either eye. VI was defined as PVA < 20/40 in the better-seeing eye. Participants with VI were further categorized into two groups: correctable and non-correctable VI. Correctable VI was defined as the VI correctable to 20/40 or better after subjective refraction, and non-correctable VI was defined as the VI correctable to worse than 20/40 by subjective refraction.

A comprehensive examination of the anterior segment and posterior segment was performed using a slit-lamp (TopconSL-8Z [Topcon, Tokyo, Japan] with a Nikon D1 digital image system [Nikon, Tokyo]) and a 78-diopter lens at 16 times magnification by an experienced ophthalmologist (MH). A principal cause of VI or blindness was assigned by the same experienced ophthalmologist using a 15-item diagnostic checklist.

A short questionnaire was administered to collect details of ophthalmic history, general medical history, family income level, and educational attainment. Diabetes and hypertension were defined based on self-reported history of diagnosis or previous medication use. Height and weight were measured using a standard calibrated scale. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in centimetres and was divided into three groups: underweight (BMI < 18.5 kg/m^2), normal or overweight (18.5–30.0 kg/m^2), or obese (BMI > 30.0 kg/m^2). Educational attainment was based on the highest level of education attained and was divided into: did not complete high school and high school or greater. Family income level was classified as: <1000 RMB or more than 1000 RMB per month.

Mortality data

Confirmation of death during the 10-year follow-up period was obtained from the Chinese Centre for Disease Control and Prevention (CDC). After providing the CDC with a list of names, date of birth, gender and last known address for participants who did not show up at the 10-year follow-up examination. Researchers from the CDC then provided a corresponding list of matched deaths including date of death and cause of death. In addition to CDC death index, we also contacted participants who did not return at the 10-year follow-up visit by phones or home visit to improve the reliability of the identification of deaths. Those who did not show at the follow-up examination and were not found to have records of deaths were considered as survivors. Of note, most of them (94.4%) could be contacted, which implied their survival status. Therefore, the potential bias on the identification of deaths in the present study was trivial.

Statistical analysis

All statistical analyses were performed using Stata (Version 10; Stata Corp, College Station, TX). The student's *t* test was used to compare continuous variables, while Pearson's Chi-Square test or Fisher's exact test was used for the comparison of categorical data. Survival time was calculated for each participant from the date of baseline examination through to date of death or April 30, 2014, whichever came first. The log-rank test was used to compare different groups with respect to their survival distributions. The association between VI and 10-year mortality was assessed using the Cox proportional hazards regression model, after adjusting for age, gender, family income, educational attainment, BMI and medical history of

Table 1 Characteristics of participants categorized by presenting visual acuity at baseline examination.

Basic factors	No visual impairment, *N* (%)	Visual impairment, *N* (%) (PVA < 20/40)			*P* value
		Correctable (BCVA ≥ 20/40)	Non-correctable (BCVA < 20/40)	Total	
Total number (%)	1079 (77.1)	188 (13.5)	132 (9.43)	320 (22.9)	
Age (year)					<0.001
50–59	442 (41.0)	31 (16.5)	1 (0.76)	32 (10.0)	
60–69	336 (31.1)	45 (23.9)	22 (16.7)	67 (20.9)	
+70	301 (27.9)	112 (59.6)	109 (82.7)	221 (69.1)	
Gender					0.026
Female	594 (55.1)	106 (56.4)	89 (67.4)	195 (60.9)	
Education					<0.001
No more than primary middle school	808 (83.1)	114 (68.7)	53 (53.0)	167 (62.8)	
Income					0.003
<1000 (RMB)	554 (72.4)	103 (76.3)	75 (89.3)	178 (81.3)	
Body mass index (BMI)					0.201
Normal/overweight (18.5–30.0 kg/m^2)	676 (90.7)	114 (87.0)	60 (90.9)	174 (88.3)	
Under weight (<18.5 kg/m^2)	42 (5.64)	14 (10.7)	5 (7.58)	19 (9.64)	
Obese (>30.0 kg/m^2)	27 (3.62)	3 (2.29)	1 (1.52)	4 (2.03)	
Hypertension					0.552
Yes	405 (40.7)	75 (43.4)	50 (45.5)	125 (44.2)	
Diabetes					0.004
Yes	90 (9.07)	21 (12.1)	21 (18.9)	42 (14.7)	

PVA presenting visual acuity, *BCVA* best corrected visual acuity.

diabetes and hypertension. We adjusted for these variables recognized widely as potential confounder for mortality [29–33]. Hazard ratios (HR) and 95% CI were given. A Proportional Hazard test was used to check the assumption of cox proportional hazards model. A p value of <0.05 was defined to indicate statistical significance. All variables included in the Cox proportional hazards regression models were found to be valid (all P values > 0.05).

Results

At baseline, PVA measurements were available for 1399 (99.6%) of the 1405 participants. Of the 1399 participants, 320 (22.9%) had VI. Table 1 shows the baseline characteristics of participants categorized by the status of VI.

Compared to participants without VI, visually impaired participants were older, female, more likely to have diabetes, had a lower level of educational attainment and lower family income (all p values < 0.05). There were no statistically significant differences between groups for other baseline characteristics.

By the end of April 2014 (median follow-up length: 9.38 years; range: 0.15–10.2 years), 314 (22.4%) of the 1399 participants had died. At baseline, those who died tended to be older, male, underweight, have a lower level of educational attainment and lower family income (all p values < 0.05). No differences were found in those with a medical history of hypertension and/or diabetes (Table 2).

Among the 320 visually impaired participants, 128 (40.0%) participants died during 10-year follow-up period. The 10-year mortality rate was significantly higher in participants with VI than in those without VI (40.0 % vs. 17.2%, log-rank $P < 0.05$). The significant association between VI and poorer survival rate was observed in the crude model (HR, 2.69; 95% CI, 2.15–3.36), and this association became weaker but still statistically significant after adjusting for age and sex (HR, 1.84; 95% CI, 1.43–2.35). After further adjusting for BMI, education level, family income, history of diabetes and hypertension, as compared with participants without VI, those with VI were significantly likely to have poorer survival (HR, 1.55; 95% CI, 1.14–2.11). When dividing visually impaired participants into those with correctable and non-correctable VI, the presence of non-correctable VI was significantly associated with a 172% greater risk of 10-year mortality in the multivariable adjusted model (HR, 2.72; 95% CI, 1.86–3.98), while correctable VI was not an independent risk factor for 10-year mortality after adjusting for confounding factors (HR, 0.99; 95% CI, 0.66–1.49) (Table 3). The multivariate-adjusted survival curves stratified by VI status are shown in Fig. 1.

Table 2 Distribution of basic characters associated with mortality at baseline in Liwan Eye study.

Basic factors	Died, *N* (%)	Alive, *N* (%)	*P* value
Total number (%)	314 (22.4)	1085 (77.6)	
Age (year)			<0.001
50–59	23 (7.32)	451 (41.6)	
60–69	67 (21.3)	336 (31.0)	
+70	224 (71.4)	298 (27.4)	
Gender			<0.001
Female	148 (47.1)	641 (59.1)	
Education			<0.001
No more than primary middle school	161 (67.9)	814 (81.3)	
Income			0.001
<1000 RMB	179 (82.9)	553 (72.0)	
Body mass index (BMI)			0.004
Normal/overweight (18.5–30.0 kg/m^2)	167 (85.2)	683 (91.6)	
Under weight (<18.5 kg/m^2)	23 (11.7)	38 (5.09)	
Obese (>30.0 kg/m^2)	6 (3.06)	25 (3.35)	
Hypertension			0.328
Yes	114 (44.2)	416 (40.8)	
Diabetes			0.155
Yes	33 (12.7)	99 (9.72)	

Discussion

This present study found that those with VI had a poorer survival rate relative to those without VI, even after adjusting for age, gender, BMI, education level, family income, history of diabetes, and hypertension. Furthermore, we found that VI due to refractive error was not an independent risk factor for long-term survival, while there was nearly a threefold higher risk of mortality for those with non-correctable VI which was independent of confounding factors.

The association between VI and mortality has been consistently reported in Western populations [10–26]. However, growing evidence suggests that Chinese adults have a different ocular diseases' spectrum, risk factors for ocular diseases, and systemic comorbidities relative to Western populations [27]. The association between VI and mortality in Chinese adults remains inclusive. In our study, we observed that the 10-year mortality rate among participants with VI were significantly higher than those without VI. This association became attenuated after adjusting for other potential confounders but remained statistically greater. Our findings are comparable to several studies which also included Chinese adults. The Chinese Longitudinal Healthy Longevity Survey [18] concluded that VI was an independent predictor of 3-year mortality. The Southern Harbin eye study [15], based on a northern Chinese population, reported a significant association between VI and 4-year mortality. Similarly, in a Chinese population in Singapore [19], VI was independently associated with an increased risk of mortality. On the contrary, the Beijing eye study did not find an independent relationship between VI and 5-year [25] or 10-year mortality [26]. These disparate findings may be due to differences in study design, methodology, geographic environment, study population, and definitions. Firstly, the inclusion criteria (age ≥40 vs. ≥50 years old) and the demographic characteristics (rural and urban vs. urban) of participants in the Beijing Eye Study were different from our study. Secondly, the Beijing Eye Study investigated VI based on BCVA, instead of PVA in our study, as a risk factor of mortality. Thirdly, logistic regression model, instead of Cox proportional hazards regression model was used in the Beijing Eye Study. Finally, the discrepancy in the selection of confounding factors might also explained the conflicting results between the Beijing Eye Study and the present study.

There are several possible explanations for the association of VI and mortality. Growing evidence has suggested that the association between VI and increased risk of mortality is due to functional disability attributable to poor VA. Zheng et al. [34] suggests that VI increases the risk of mortality directly and indirectly through its adverse impact on mental wellbeing. The presence of VI has been reported to be associated with psychosocial conditions including social isolation [35], cognitive impairment [36], loss of independence [37], need for community support [38, 39], reduced social interaction [40], and depression [36]. Furthermore, many studies indicate that VI is strongly related to increased risk of accidents, falls, and fractures [36, 41, 42], which directly increase the risk of mortality. On the other hand, VI may be a marker of systemic aging and frailty. It has been proposed that VI related to ocular diseases and several systemic conditions may share a common underlying pathogenesis [43, 44]. In the present analysis, we found VI due to refractive error was not significantly associated with mortality, while non-correctable VI predicted an increased risk of mortality. Our findings imply that functional disabilities caused by poorer visual acuity may only explain a small proportion of the VI-mortality association. The poorer survival among visually impaired participants is more likely to suggest that aging and frailty associated with ocular diseases, such as cataract and age-related macular degeneration, which is corroborated by previous studies [36, 45, 46]. Further studies are needed to explore the underlying mechanisms between VI and poor survival.

Results from the present study have relevant public health implications for the management of VI. Firstly, the consistent association between VI and mortality reported in our study and previous studies reinforces the importance of vision screening and preventive strategies for

Table 3 Cox proportional hazards regression models between presenting visual acuity in the better-seeing eye and 10-year mortality.

	HR (95% CI)		
	Crude	Age and gender adjusted	Multivariable adjusted[a]
Visual acuity			
PVA ≥ 20/40	Reference	Reference	Reference
VI (PVA < 20/40)	2.69 (2.15, 3.36)	1.84 (1.43, 2.35)	1.55 (1.14, 2.11)
Correctable VI	1.66 (1.22, 2.27)	1.29 (0.94, 1.78)	0.99 (0.66, 1.49)
Non-correctable VI	4.44 (3.49, 5.94)	2.81 (2.08, 3.81)	2.72 (1.86, 3.98)

HR hazard ratio, *CI* confidence interval, *PVA* presenting visual acuity, *VI* visual impairment.

[a]Adjusted for age, gender, body mass index, educational attainment, family income, history of diabetes and hypertension.

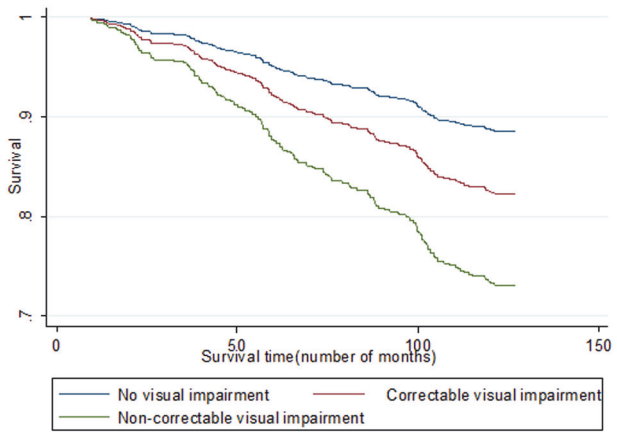

Fig. 1 Surval curves for visual impairment and 10-year mortality. Survival curves were adjusted for age, sex, history of diabetes and hypertension, body mass index, educational attainment and family income. Blue, red and green curves indicate the surivial curve for no visual impairment, correctable and non-correctable visual impairment, respectively.

ocular disease in the elderly. Secondly, some studies have shown that correction of VI can improve survival rate in older adults [47–49]. Rehabilitation of reversible VI, such as performing cataract surgery, may potentially improve long-term survival rates, although this would require further confirmation.

There are several strengths of our study. Firstly, the Liwan Eye Study is a population-based cohort study that uses a standard protocol. Secondly, VA was performed by an experienced optometrist to ensure measurement reliability. Finally, the Cox proportional hazards regression model used in the current study has an advantage over traditional logistic regression model on survival analysis because the censored time was considered. One limitation of this study was that the baseline questionnaire collection was not able to capture all potential confounding factors due to pragmatic reasons in the field work, therefore it was not possible to investigate the confounding effects on some confirmed risk factors on mortality, such as smoking and cardiovascular disease [50, 51]. Another limitation in the present study was the missing information on the specific cause of mortality for half of the participants. More studies are needed to explore the association between VI and specific cause of mortality. Finally, the current study only explored high contrast visual acuity, which tests only one component of visual function. Further studies are needed to assess the effect of other visual function, such as visual field and contrast sensitivity, on mortality.

In conclusion, we found a strong association between VI and mortality in an urban Chinese population, particularly for non-correctable VI. Our study found the significant association between VI and mortality, highlighting the importance of preventing and treating VI to prevent premature mortality. Further studies exploring the mechanisms underlying VI-mortality association are needed.

Summary

What was known before

- Many studies indicated that visial impairment was an independent risk factor for mortality.However, there have been few studies that have addressed this issue in Chinese adults who have different disease profile.

What this study adds

- VI, particularly non-correctable VI, was an independent risk factor for mortality in this adult population in urban China

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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References

1. Bekibele CO, Gureje O. Impact of self-reported visual impairment on quality of life in the Ibadan study of ageing. Br J Ophthalmol. 2008;92:612–5.
2. Brown GC. Vision and quality-of-life. Trans Am Ophthalmol Soc. 1999;97:473–511.
3. Chia EM, Mitchell P, Rochtchina E, Foran S, Wang JJ. Unilateral visual impairment and health related quality of life: the Blue Mountains Eye Study. Br J Ophthalmol. 2003;87:392–5.
4. Chia EM, Wang JJ, Rochtchina E, Smith W, Cumming RR, Mitchell P. Impact of bilateral visual impairment on health-related quality of life: the Blue Mountains Eye Study. Investig Ophthalmol Vis Sci. 2004;45:71–76.
5. Varma R, Wu J, Chong K, Azen SP, Hays RD, Los Angeles Latino Eye Study G. Impact of severity and bilaterality of visual impairment on health-related quality of life. Ophthalmology. 2006;113:1846–53.
6. Wang JJ, Mitchell P, Smith W. Vision and low self-rated health: the Blue Mountains Eye Study. Investig Ophthalmol Vis Sci. 2000;41:49–54.
7. Christ SL, Zheng DD, Swenor BK, Lam BL, West SK, Tannenbaum SL, et al. Longitudinal relationships among visual acuity, daily functional status, and mortality: the Salisbury eye evaluation study. JAMA Ophthalmol. 2014;132:1400–6.
8. Yeung P, Towers A, La Grow S, Philipp M, Alpass F, Stephens C. Mobility, satisfaction with functional capacity and perceived quality of life (PQOL) in older persons with self-reported visual impairment: the pathway between ability to get around and PQOL. Disabil Rehabil. 2015;37:113–20.
9. Bourne RRA, Flaxman SR, Braithwaite T, Cicinelli MV, Das A, Jonas JB, et al. Magnitude, temporal trends, and projections of the global prevalence of blindness and distance and near vision impairment: a systematic review and meta-analysis. Lancet Glob Health. 2017;5:e888–97.
10. Tournier M, Moride Y, Ducruet T, Moshyk A, Rochon S. Depression and mortality in the visually-impaired, community-dwelling, elderly population of Quebec. Acta Ophthalmol. 2008;86:196–201.
11. Siantar RG, Cheng CY, Gemmy Cheung CM, Lamoureux EL, Ong PG, Chow KY, et al. Impact of Visual Impairment and Eye diseases on Mortality: the Singapore Malay Eye Study (SiMES). Sci Rep. 2015;5:16304.
12. Pedula KL, Coleman AL, Hillier TA, Ensrud KE, Nevitt MC, Hochberg MC, et al. Visual acuity, contrast sensitivity, and mortality in older women: Study of osteoporotic fractures. J Am Geriatr Soc. 2006;54:1871–7.
13. Knudtson MD, Klein BE, Klein R. Age-related eye disease, visual impairment, and survival: the Beaver Dam Eye Study. Arch Ophthalmol. 2006;124:243–9.
14. Lopez D, McCaul KA, Hankey GJ, Norman PE, Almeida OP, Dobson AJ, et al. Falls, injuries from falls, health related quality of life and mortality in older adults with vision and hearing impairment-is there a gender difference? Maturitas. 2011;69:359–64.
15. Li Z, Sun D, Liu P, Zhang L, Bai J, Cui H. Visual impairment and mortality in a rural adult population (the Southern Harbin eye study). Ophthalmic Epidemiol. 2011;18:54–60.
16. Khanna RC, Murthy GV, Giridhar P, Krishnaiah S, Pant HB, Palamaner Subash Shantha G, et al. Cataract, visual impairment and long-term mortality in a rural cohort in India: the Andhra Pradesh Eye Disease Study. PLoS ONE. 2013;8:e78002.
17. Jacobs JM, Hammerman-Rozenberg R, Maaravi Y, Cohen A, Stessman J. The impact of visual impairment on health, function and mortality. Aging Clin Exp Res. 2005;17:281–6.
18. Gu D, Zhou J, Yong V, Sautter J, Saito Y. Age differential effects of severity of visual impairment on mortality among older adults in China. J Appl Gerontol. 2013;32:876–88.
19. Foong AW, Fong CW, Wong TY, Saw SM, Heng D, Foster PJ. Visual acuity and mortality in a chinese population. The Tanjong Pagar Study. Ophthalmology. 2008;115:802–7.
20. Thiagarajan M, Evans JR, Smeeth L, Wormald RP, Fletcher AE. Cause-specific visual impairment and mortality: results from a population-based study of older people in the United Kingdom. Arch Ophthalmol. 2005;123:1397–403.
21. Lee DJ, Gomez-Marin O, Lam BL, Zheng DD. Visual acuity impairment and mortality in US adults. Arch Ophthalmol. 2002;120:1544–50.
22. Cacciatore F, Abete P, Maggi S, Luchetti G, Calabrese C, Viati L, et al. Disability and 6-year mortality in elderly population. Role of visual impairment. Aging Clin Exp Res. 2004;16:382–8.
23. McCarty CA, Nanjan MB, Taylor HR. Vision impairment predicts 5 year mortality. Br J Ophthalmol. 2001;85:322–6.
24. Kulmala J, Era P, Tormakangas T, Parssinen O, Rantanen T, Heikkinen E. Visual acuity and mortality in older people and factors on the pathway. Ophthalmic Epidemiol. 2008;15:128–34.
25. Xu L, Wang YX, Wang J, Jonas JJ. Mortality and ocular diseases: the Beijing Eye Study. Ophthalmology. 2009;116:732–8.
26. Wang YX, Zhang JS, You QS, Xu L, Jonas JB. Ocular diseases and 10-year mortality: the Beijing Eye Study 2001/2011. Acta Ophthalmol. 2014;92:e424–8.
27. Zhou Q, Friedman DS, Lu H, Duan X, Liang Y, Yang X, et al. The epidemiology of age-related eye diseases in Mainland China. Ophthalmic Epidemiol. 2007;14:399–407.
28. He M, Foster PJ, Ge J, Huang W, Zheng Y, Friedman DS, et al. Prevalence and clinical characteristics of glaucoma in adult Chinese: a population-based study in Liwan District, Guangzhou. Investig Ophthalmol Vis Sci. 2006;47:2782–8.
29. Lear SA, Hu W, Rangarajan S, Gasevic D, Leong D, Iqbal R, et al. The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study. Lancet. 2017;390:2643–54.
30. Spoerri A, Schmidlin K, Richter M, Egger M, Clough-Gorr KM. Swiss National C. Individual and spousal education, mortality and life expectancy in Switzerland: a national cohort study. J Epidemiol Community Health. 2014;68:804–10.
31. Wade KH, Carslake D, Sattar N, Davey Smith G, Timpson NJ. BMI and Mortality in UK Biobank: revised estimates using mendelian randomization. Obesity. 2018;26:1796–806.
32. Bragg F, Holmes MV, Iona A, Guo Y, Du H, Chen Y, et al. Association Between Diabetes and Cause-Specific Mortality in Rural and Urban Areas of China. JAMA. 2017;317:280–9.

33. Argulian E. Hypertension and mortality in the elderly: further insights. JAMA Intern Med. 2013;173:325.
34. Zheng DD, Christ SL, Lam BL, Arheart KL, Galor A, Lee DJ. Increased mortality risk among the visually impaired: the roles of mental well-being and preventive care practices. Investig Ophthalmol Vis Sci. 2012;53:2685–92.
35. Carabellese C, Appollonio I, Rozzini R, Bianchetti A, Frisoni GB, Frattola L, et al. Sensory impairment and quality of life in a community elderly population. J Am Geriatr Soc. 1993;41:401–7.
36. Karpa MJ, Mitchell P, Beath K, Rochtchina E, Cumming RG, Wang JJ, et al. Direct and indirect effects of visual impairment on mortality risk in older persons. Arch Ophthalmol. 2009;127: 1347–53.
37. Salive ME, Guralnik J, Glynn RJ, Christen W, Wallace RB, Ostfeld AM. Association of visual impairment with mobility and physical function. J Am Geriatr Soc. 1994;42:287–92.
38. Wang JJ, Mitchell P, Smith W, Cumming RG, Attebo K. Impact of visual impairment on use of community support services by elderly persons: the Blue Mountains Eye Study. Investig Ophthalmol Vis Sci. 1999;40:12–19.
39. Hong T, Mitchell P, Burlutsky G, Fong CS, Rochtchina E, Wang JJ. Visual impairment and subsequent use of support services among older people: longitudinal findings from the Blue Mountains Eye Study. Am J Ophthalmol. 2013;156:393–9.
40. Tolman J, Hill RD, Kleinschmidt JJ, Gregg CH. Psychosocial adaptation to visual impairment and its relationship to depressive affect in older adults with age-related macular degeneration. Gerontologist. 2005;45:747–53.
41. Dhital A, Pey T, Stanford MR. Visual loss and falls: a review. Eye (Lond). 2010;24:1437–46.
42. Klein BE, Klein R, Knudtson MD, Lee KE. Frailty, morbidity and survival. Arch Gerontol Geriatr. 2005;41:141–9.
43. Grauslund J, Green A, Sjolie AK. Blindness in a 25-year follow-up of a population-based cohort of Danish type 1 diabetic patients. Ophthalmology. 2009;116:2170–4.
44. Brown MM, Brown GC, Sharma S, Hollands H, Landy J. Quality of life and systemic comorbidities in patients with ophthalmic disease. Br J Ophthalmol. 2002;86:8–11.
45. Zhu Z, Wang W, Keel S, Zhang J, He M. Association of Age-Related Macular Degeneration With Risk of All-Cause and Specific-Cause Mortality in the National Health and Nutrition Examination Survey, 2005 to 2008. JAMA Ophthalmol. 2019;137:248–57.
46. Zhu Z, Wang L, Young CA, Huang S, Chang BH, He M. Cataract-Related Visual Impairment Corrected by Cataract Surgery and 10-Year Mortality: the Liwan Eye Study. Investig Ophthalmol Vis Sci. 2016;57:2290–5.
47. Fong CS, Mitchell P, Rochtchina E, Teber ET, Hong T, Wang JJ. Correction of visual impairment by cataract surgery and improved survival in older persons: the Blue Mountains Eye Study cohort. Ophthalmology. 2013;120:1720–7.
48. Blundell MS, Hunt LP, Mayer EJ, Dick AD, Sparrow JM. Reduced mortality compared with national averages following phacoemulsification cataract surgery: a retrospective observational study. Br J Ophthalmol. 2009;93:290–5.
49. McGwin G Jr, Owsley C, Gauthreaux S. The association between cataract and mortality among older adults. Ophthalmic Epidemiol. 2003;10:107–19.
50. Dehghan M, Mente A, Zhang X, Swaminathan S, Li W, Mohan V, et al. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. Lancet. 2017;390:2050–62.
51. Pan A, Wang Y, Talaei M, Hu FB. Relation of smoking with total mortality and cardiovascular events among patients with diabetes mellitus: a meta-analysis and systematic review. Circulation. 2015;132:1795–804.