# BMJ Open Protocol for Shenzhen-working-age cohort study (SZ-working age): a prospective observational cohort study on eye health and myopia

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**Introduction** The widespread use of digital devices in modern workplaces has led to a rise in visual health problems, such as myopia and dry eye syndrome, among the working-age population. This study aims to investigate the incidence of eye disorders, associated risk factors and relevant biomarkers in Shenzhen, addressing a crucial gap in the research on visual health in rapidly urbanising Chinese cities.

**Methods** This prospective observational cohort study, conducted from September 2024 to December 2029, will recruit 3000 full-time employees aged 18-65 in Shenzhen through multistage sampling across five job sectors. Data collection will include questionnaire surveys, standardised scale assessments, ophthalmic examinations, ophthalmic imaging and biomarker testing. Annual follow-ups will track the incidence of high myopia and dry eye, as well as associated factors and biomarker changes. Data accuracy will be ensured through double entry and continuous quality control.

Ethics and dissemination The study has been approved by the Ethics Committee of Shenzhen Eye Hospital (2024KYPJ012; 04 February 2024). The results will be presented at professional conferences and submitted for publication in peer-reviewed journals.

Trial registration number National Health Information Platform (MR-44-24-026548).

Visual health concerns have increasingly

of workplace performance and overall work

productivity.<sup>5</sup> Moreover, frequent exposure

#### INTRODUCTION

**ABSTRACT** 

come to the forefront in modern work environments. With the extensive integration of digital technology and screen-based devices in workplaces, there has been a significant rise in prolonged screen use and near-vision tasks among the working-age population.<sup>2</sup> Notably, neglecting eye health in the workplace can significantly reduce productivity<sup>3</sup>, for instance, one prospective, non-interventional, cross-sectional study in the USA reported that symptomatic dry eye disease led to approximately 30% impairment

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Focusing on the working-age population fills a critical gap in eye health research, especially as the prevalence of screen use and near-vision tasks continues to rise in modern workplaces.
- ⇒ This study investigates the incidence of eye disorders, associated risk factors and biomarkers in the working-age population. All variables will be repeatedly collected through active follow-up, allowing for comprehensive tracking of changes in eye health
- ⇒ The large-scale, multistage sampling ensures diverse occupational representativeness.
- ⇒ As an observational study, it identifies associations but cannot establish causality. Potential recall and reporting biases may arise from self-reported guestionnaire data.

Protected by copyright, including for uses related to text and data mining, to digital screens and poor workplace ergonomics can lead to chronic issues, such as dry eye syndrome, visual fatigue and aggravated myopia progression, ultimately diminishing quality of life. <sup>6</sup> Collectively, these factors pose a substantial threat to the visual health of the working-age population. Unlike older adults, individuals in this age group need to maintain optimal visual health not only to ensure high work efficiency but also to prevent the potential impact of eye diseases on their quality of life. Consequently, it is of significant public health and societal importance to thoroughly investigate the factors influencing & visual health in occupational settings and to explore effective prevention and intervention strategies.

While previous studies have investigated various factors affecting visual health, these studies have largely focused on specific subgroups or geographic regions, with inherent methodological limitations and varying conclusions. For example, a study in the Netherlands found that increased axial



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length and high myopia were significantly associated with visual impairment, but its conclusions were primarily based on older populations and specific regions, making it difficult to generalise to other groups or areas with rapidly rising myopia rates.8 In China, particularly in rapidly developing cities like Shenzhen, research on visual health among the working-age population remains sparse. Existing studies predominantly concentrate on students and the elderly, 9-12 with limited attention to the visual health challenges faced by individuals at the peak of their careers. Additionally, many of these studies focus only on individual factors rather than the complex interplay between workplace environments, lifestyle habits and near-vision activities. Given these research gaps, there is a critical need for more extensive and systematic studies to provide a clearer understanding of how various occupational and lifestyle factors interact to affect eye health in the working-age population.

We have integrated biomarker detection into our screening process, offering an opportunity to analyse the potential impact of systemic health conditions on eye health in ways previous studies have not. While international research has started to investigate the links between eve diseases and overall health through biomarker analysis-such as the connection between diabetes and diabetic retinopathy,<sup>13</sup> and the roles of inflammatory and oxidative stress markers in conditions like dry eye and retinal diseases 14 15—these studies have seen limited application within China's working-age population. Given that much of the research in China still lacks a systemic, multidimensional approach to understanding these links, our study aims to fill this gap by examining biomarkers in conjunction with visual health data. Our study seeks to build on this by conducting biomarker analysis via blood sample collection, with a particular focus on identifying potential risk factors for vision health and eye diseases, including metabolic, inflammatory and tumour markers.

This study aims to conduct a comprehensive visual health survey to assess the incidence of eve disorders and their associated risk factors among the working-age population in Shenzhen. Particular attention will be given to the incidence of myopia, high myopia and dry eye syndrome, along with their potential risk factors. Employing a prospective observational cohort design, this study integrates a variety of data collection tools, including advanced ophthalmic imaging technologies and detailed questionnaires. Focusing on Shenzhen, a city emblematic of China's rapid urban development, this research addresses a significant gap in the current literature on visual health among the working-age population in major Chinese urban centres. The findings of this study are expected to inform the development of more targeted workplace health guidelines, such as optimising screen usage, enhancing workstation ergonomics and improving indoor lighting conditions. Additionally, these findings will provide a scientific basis for companies and policymakers to design and implement visual health management programmes, including regular eye

examinations and visual health education, aimed at mitigating the long-term impact of visual health issues on employee productivity and quality of life.

## METHODS AND ANALYSIS Study objectives

The SZ-working-age study aims to advance eye health and myopia research by collecting and analysing high-quality data from ophthalmic examinations, questionnaires and biological samples of the working-age population. The specific objectives of the study include the following.

- ► Collecting comprehensive data on the eye health of the working-age population.
- ► Enhancing epidemiological data through the use of questionnaires, standardised assessments, venous blood sample testing and family medical history collection.
- ► Estimating the incidence of ocular surface diseases and myopia, with a focus on high myopia and pathological myopia.
- ► Identifying risk factors and biomarkers related to eye health in this population.
- ▶ Developing risk prediction tools for ocular surface diseases and high myopia.

## **Patient and public involvement**

Patients and the public are not involved in the design and recruitment of this project.

#### SZ-working-age sample

Shenzhen, as China's first special economic zone, has attracted a large number of immigrants from other regions across the country and even overseas. According to the statistical yearbooks and census data released by the Shenzhen Municipal Bureau of Statistics, Shenzhen has a total population of approximately 17.79 million, with the working-age population (18-65 years) accounting for more than 70%. 16 This suggests that the working age population in Shenzhen is estimated to be between 12 million and 13 million. Common eye health conditions among the working-age population include dry eye, myopia and others. 6 17 Given that the incidence of high myopia is relatively low among common eye diseases, we used high myopia as the outcome parameter to calculate the sample size. In urbanised Asian regions, the overall myopia rate among the working-age population has already exceeded 80%, with the proportion of high myopia being around 10%. 18 This means that approximately 7% of the working-age population in Shenzhen suffers from high myopia. Based on the expected incidence, we used the following formula to calculate the sample size:

$$n = \left[ \frac{Z_{1-\alpha/2} \sqrt{2q(1-q)} + Z_{\beta} \sqrt{p_1(1-p_1) + p_2(1-p_2)}}{p_1 - p_2} \right]^2$$

where  $p_1$  and  $p_2$  represent the incidence of the outcome of interest in the exposed and non-exposed groups, respectively, with q being the mean of  $p_1$  and  $p_2$ 

. The expected incidence of the outcome of interest in the exposed group  $(p_1)$  is 7%  $(p_1 = 0.07)$ . Assuming a risk ratio of 2.0, the expected incidence in the non-exposed group  $(p_2)$  is calculated as 3.5%  $(p_2 = 0.035)$ . The significance level ( $\alpha$ ) is set at 5%, and the power (1- $\beta$ ) is set at 80%. Substituting these values into the formula:

Calculate q:

$$q = \frac{0.07 + 0.035}{9} = 0.0525$$

Compute SD:

$$\sqrt{2q(1-q)} = \sqrt{2 \times 0.0525 \times (1-0.0525)} = \sqrt{0.0995} \approx 0.3154$$

$$\sqrt{p_1(1-p_1) + p_2(1-p_2)} = \sqrt{(0.07 \times 0.93) + (0.035 \times 0.965)} = \sqrt{0.0651 + 0.0338} = \sqrt{0.0999} \approx 0.3164$$

Calculate numerator:

$$(1.96 \times 0.3154) + (0.84 \times 0.3145) = 0.6182 + 0.2642 = 0.8824$$

Calculate denominator:

$$p_1 - p_2 = 0.07 - 0.035 = 0.035$$

Final computation:

$$n = \left(\frac{0.8824}{0.035}\right)^2 = \left(25.21\right)^2 \approx 636$$

Given the exposure prevalence of 25%, the required total sample size is:

$$n_{total} = \frac{636}{0.25} = 2544$$

As this study is a prospective cohort study, there is a possibility of participant loss to follow-up. To compensate for potential sample attrition, we adjusted the sample size accordingly. Based on the epidemiological research experience, we assumed a follow-up retention rate of 90%. The adjusted sample size was calculated using the following formula:

$$n_{adjusted} = \frac{n_{total}}{follow\ ub\ rate} = \frac{2544}{0.9} \approx 2827$$

To ensure the robustness of our study, we ultimately decided to increase the sample size to 3000 participants, enhancing the statistical power and minimising potential bias due to loss to follow-up.

This study uses a multistage sampling method to recruit participants from various job positions in Shenzhen, China. In the first stage, we selected five distinct types of job positions spanning the manufacturing, services, finance, information technology and education sectors. In the second stage, we will recruit participants from these 5 job positions, targeting a total of 3000 employees, with 600 participants from each position. In developing the employee sampling framework, the research team established a data collaboration protocol with enterprise human resources departments to obtain anonymised comprehensive employee rosters. These rosters consolidated key demographic variables, including age, gender, department affiliation and employment start dates. A sampling weight system was constructed based on Shenzhen's most recent population census data, enabling

stratified calibration of the target working-age population across age-gender composition and industry-specific tenure distribution. 19

The third phase implemented a trilevel systematic stratification strategy. Primary stratification was conducted according to the departmental functions, followed by secondary stratification based on age-gender cohorts divided at 5-year intervals, culminating in tertiary stratification by employment duration. Within each stratified subgroup, participant selection was executed through systematic random sampling using fixed-interval sampling to establish the initial sample pool. The recruitment process ensures procedural integrity through three coordinated mechanisms: first, enterprise human resources departments distribute personalised study invitations via internal encrypted communication systems, each containing unique registration codes and privacy protection specifications. Second, an anonymous opt-out channel is implemented through a secure web portal, where potential participants can decline involvement by clicking a 'Decline' button, with all associated metadata automatically purged within 48 hours of receipt. Third, standardised replacement protocols automatically engage subsequent candidates from the original sampling sequence to address non-response cases. All randomisation procedures were operationalised using a Mersenne Twister algorithm-based random number generator.

The recruitment process is expected to start in 5 September 2024 and conclude in December 2029. Before participating in the study, each individual will be required to sign an informed consent form to ensure that they fully understand the study's purpose. understand the study's purpose, procedures and potential risks. The inclusion criteria are: (1) age between 18 and 65 years; (2) full-time employment in the specified job positions; (3) willingness to participate in the survey with written informed consent; (4) ability to cooperate and complete data collection; (5) effective communication with interviewers and (6) at least 6 months of employment in Shenzhen. The exclusion criteria are: (1) temporary or part-time employment; (2) presence of severe mental illnesses; (3) severe ocular diseases that significantly impair visual function or interfere with study measurements, such as advanced glaucoma, retinal detachment or severe corneal disease and (4) individuals with high myopia or pathological myopia will not be excluded, but their baseline status will be recorded for stratified analysis.

## **Primary outcome**

The primary outcome of the SZ-working-age study is the incidence of high myopia and pathological myopia among the working-age population.

#### **Secondary outcomes**

Secondary outcomes include various eye health indicators and related factors that may contribute to the progression of myopia and ocular surface diseases.

- Incidence of ocular surface diseases, such as dry eye syndrome.
- ► Changes in visual function, including best-corrected visual acuity and contrast sensitivity.
- Structural and vascular changes in the retina and choroid.
- ▶ Work-related visual strain and fatigue.
- ▶ Quality of life and psychological well-being.

## **Exposure variables**

To investigate the risk factors for high myopia and ocular surface diseases, this study examines multiple exposures, including occupational, lifestyle and biological factors. Occupational exposures encompass job type, work environment, screen time, digital device use and work-related stress. Lifestyle factors, such as outdoor activity, sunlight exposure, sleep quality and dietary habits, are also considered. Additionally, biological and genetic factors, including family history of myopia and systemic health conditions, are analysed for their role in disease development. Biomarkers from venous blood samples, such as inflammatory markers and oxidative stress indicators, are also assessed. By integrating multiple exposures, this study aims to develop a comprehensive risk prediction model for high myopia and ocular surface diseases, contributing to early detection and intervention strategies.

#### Standardised questionnaire survey

All participants are invited to undergo a free physical examination related to data collection at the health departments within their workplaces. Table 1 summarises the various data collection methods of the SZ-working-age study, including the standardised questionnaire survey, standardised scale assessments, basic ophthalmic examination and ophthalmic imaging examination. Participants will first complete the questionnaires and self-assessment scales electronically via a secure online platform prior to their on-site visit. On the day of the physical examination, participants will undergo a brief review of their questionnaire responses and complete the scales that require face-to-face evaluation by professionals. The standardised questionnaire survey aims to gather comprehensive information on various aspects that may affect eye health and overall health status. The survey includes multiple sections, such as demographic information, lifestyle habits, sleep patterns, work patterns, history of systemic diseases, history of eye diseases, family medical history, drug allergy history and other relevant factors. This standardised questionnaire will be administered face-to-face by trained general practitioners.

#### **Standardised scale assessments**

A range of standardised scales is used to thoroughly evaluate different facets of participants' daily functioning, mental health, quality of life, work-related stress and social support. The Lawton Instrumental Activities of Daily Living Scale<sup>20</sup> is used to evaluate participants' ability to carry out essential daily tasks, including managing

finances, shopping, meal preparation, housekeeping, telephone use, medication management, transportation and responding to emergencies. Each task is rated based on the participant's performance, typically using a scale from 0 to 3: 0 indicates complete dependence on others, 1 indicates a need for significant assistance, 2 suggests a need for minimal help and 3 represents full independence. Cognitive function is evaluated using the minimental state examination (MMSE) and the Montreal cognitive assessment (MoCA).<sup>21</sup> The MMSE is a widely  $\tau$ used tool for screening cognitive impairment, assessing five key domains: orientation, memory, attention and calculation, language and visuospatial skills. Scores range from 0 to 30, with 0 indicating severe cognitive impairment and 30 representing normal cognitive function. A ? score below 24 typically suggests cognitive impairment, with lower scores reflecting a more pronounced decline. The MoCA assesses a broader array of cognitive domains, including executive function and visuospatial abilities. It also offers more detailed evaluations of language fluency, short-term memory and more complex tasks involving attention and concentration. MoCA is particularly sensitive to mild cognitive impairment (MCI), making it especially useful for detecting subtle cognitive changes that might go unnoticed with the MMSE. A score below 26 on the MoCA often signals MCI, with lower scores indicating an increased likelihood of cognitive decline.

The beck depression inventory (BDI)<sup>22</sup> and the generalised anxiety disorder 7 (GAD-7)<sup>23</sup> scale are used to assess the symptoms of depression and anxiety, respectively. The BDI measures depression severity through 21 questions, each addressing a specific symptom of depression, such as low mood, insomnia, changes in appetite, fatigue and pessimism about the future. Each question is rated on a scale from 0 to 3, where 0 indicates no symptoms and 3 indicates the most severe symptoms. The total score ranges from 0 to 63, with higher scores reflecting ≥ greater levels of depression. Depression severity is classified into four categories based on the total score: 0-13 as minimal depression, 14-19 as mild depression, 20-28 as moderate depression and 29-63 as severe depression. The GAD-7 measures the frequency of anxiety symptoms through seven questions, each capturing a core symptom of generalised anxiety disorder, such as excessive worry, difficulty controlling anxiety, sleep disturbances, irritability and muscle tension. Each question is rated on a scale of 0–3, with 0 indicating 'not at all', 1 indicating 'several days', 2 indicating 'more than half the days' and 3 indicating 'nearly every day'. The total score ranges from **3** 0 to 21, with higher scores indicating more severe anxiety. Anxiety severity is classified as mild (5-9), moderate (10-14) and severe (15-21) based on the total score. The 36-item short form survey<sup>24</sup> assesses participants' quality of life across eight domains: physical functioning, bodily pain, general health perceptions, vitality, social functioning, emotional role functioning and mental health. Sleep quality is assessed using the Pittsburgh sleep quality index (PSQI)<sup>25</sup> and the insomnia severity index (ISI).<sup>26</sup>



| /leasurements                         | Variables  |
|---------------------------------------|--|
| Standardised questionnaire            | survey   |
| Demographics                          | National ID, name, date of birth, age, gender, ethnicity, marital status, education level, occupation income level, type of residence and family structure                         |
| Lifestyle                             | Eating habits, physical activity level, smoking status, drinking habits, BMI, recreational activities and time spent using electronic devices                                      |
| Sleep habits                          | Sleep duration, bedtime, sleep interruptions, early awakening and daytime fatigue  |
| Environmental exposure                | Air quality, noise exposure, living conditions and exposure to secondhand smoke  |
| Work patterns                         | Working hours, intensity, environment, posture, location and career development  |
| Occupational disease exposure history | Dust, radiation, chemical exposure, physical hazards, toxic substances, biological hazards and repetitive actions leading to musculoskeletal pressure                              |
| Occupational exhaustion               | Workload, job autonomy, WLB, occupational exhaustion and job satisfaction  |
| Health awareness                      | Frequency of regular health checkups, vaccination status and health knowledge level  |
| Disease management                    | Chronic disease management, accessibility of medical services and health insurance   |
| Systemic disease history              | Hypertension, diabetes, coronary heart disease, chronic obstructive pulmonary disease, liver disease, nervous system diseases and autoimmune diseases                              |
| History of eye diseases               | Myopia, hyperopia, astigmatism, dry eye, cataract, glaucoma, macular degeneration, retinal detachment, diabetic retinopathy and pathological myopia                                |
| Family history                        | Hypertension, diabetes, coronary heart disease, cerebrovascular disease, cancer, mental illness Alzheimer's disease, Parkinson's disease and hereditary eye diseases               |
| Drug allergy history                  | Allergies to penicillin, sulfa drugs, cephalosporins, aminoglycosides, tetracyclines, anaesthetics, NSAIDs and vaccine components  |
| Others                                | Surgical history, trauma history, sedentary behaviour and self-assessed health status  |
| andardised scale assessr              | nents  |
| ADL                                   | Lawton IADL scale  |
| Cognitive function                    | MMSE, MoCA   |
| Depression and anxiety                | BDI, GAD-7   |
| Quality of life                       | SF-36  |
| Sleep quality                         | PSQI, ISI  |
| Work stress                           | PSS, JCQ   |
| Occupational burnout                  | MBI  |
| Visual function                       | NEI VFQ, VF questionnaire  |
| Visual fatigue                        | CVS-Q  |
| WLB                                   | WLB scale  |
| Social support assessment             | Duke-UNC FSSQ, MSPSS   |
| asic ophthalmic examinati             | on   |
| Routine examination                   | Uncorrected visual acuity, corrected visual acuity and intraocular pressure  |
| Refractive error                      | Myopic, hyperopic, astigmatism, astigmatic axis and anisometropia  |
| Optical biometry                      | Corneal curvature radius (horizontal and vertical), central corneal thickness, anterior chamber depth, lens thickness and axial length   |
| Tear secretion measurement            | Tear secretion volume, tear film breakup time, degree of conjunctival hyperaemia and dry eye score   |
| Slit-lamp examination                 | Corneal epithelial integrity, KP, anterior chamber flare and cell count, lens transparency and vitreous opacities  |
| F                                     | Eye movements, nystagmus, strabismus angle, binocular fusion ability and diplopia  |
| Eye movement                          |  |
| Colour vision examination             | Type of colour vision deficiency (red–green colour blindness, blue–yellow colour blindness and total colour blindness), colour vision fatigue test and colour vision recovery time |

Continued

| Table 1 Continued              |  |  |
|--------------------------------|--|--|
| Measurements                   | Variables  |  |
| Ophthalmic imaging examination |  |  |
| OCT                            | Macular central foveal thickness, retinal nerve fibre layer thickness, macular retinal thickness, retinal layer structure, optic disc cupping depth and optic disc structure   |  |
| OCTA                           | Retinal blood flow density, macular blood flow density, optic disc blood flow density, non-<br>perfusion area size, microaneurysms, neovascularisation, choroidal blood flow density, vascular<br>complexity index and retinal vascular distribution       |  |
| Fundus photography             | Optic disc colour and morphology, retinal vascular morphology, macular morphology, cup-to-disc ratio, arteriovenous crossing and macular central foveal reflex   |  |
| UWF imaging                    | Retinal periphery condition, retinal lesion distribution, retinal vascular morphology, retinal pigment changes, peripheral retinal haemorrhages and retinal tears or breaks  |  |
| Anterior segment OCT           | Corneal epithelial thickness, anterior chamber depth, anterior chamber angle structure, anterior surface curvature of the lens, anterior chamber angle and lens structure  |  |
| Corneal topography             | Central corneal curvature, corneal thickness map, corneal shape symmetry, corneal surface smoothness and corneal morphology  |  |
| Visual field examination       | Type of visual field defect, contrast sensitivity, light sensitivity threshold, visual field indices, central visual field clarity and peripheral visual field integrity   |  |
| Biomarker testing              |  |  |
| Metabolic function             | Fasting blood glucose, glycated haemoglobin, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides and insulin   |  |
| Liver and kidney function      | Alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, direct bilirubin, albumin, globulin, albumin–globulin ratio, gamma-glutamyl transferase, lactate dehydrogenase, blood urea nitrogen, creatinine and uric acid |  |
| Vitamins/micronutrients        | 25-hydroxyvitamin D, cobalamin and ferritin  |  |
| Inflammatory/immune            | C reactive protein, high-sensitivity C reactive protein and homocysteine   |  |
| Tumour biomarkers              | Alpha-fetoprotein, carcinoembryonic antigen and carbohydrate antigen 19-9  |  |

ADL, activities of daily living; BDI, beck depression inventory; BMI, body mass index; CVS-Q, computer vision syndrome questionnaire; FSSQ, functional social support questionnaire; GAD-7, generalised anxiety disorder; IADL, instrumental activities of daily living; ISI, insomnia severity index; JCQ, job content questionnaire; KP, keratic precipitates; MBI, Maslach burnout inventory; MMSE, mini-mental state examination; MoCA, Montreal cognitive assessment; MSPSS, multidimensional scale of perceived social support; NEI VFQ, National Eye Institute Visual Function Questionnaire; NSAIDs, non-steroidal anti-inflammatory drugs; OCT, optical coherence tomography; OCTA, optical coherence tomography angiography; PSQI, Pittsburgh sleep quality index; PSS, perceived stress scale; SF-36, 36-item short form survey; SZ-working age, Shenzhen-working age; UWF, ultrawidefield; VF, visual function; WLB, work-life balance; WLB, work-life balance.

The PSQI comprises 19 self-reported questions and 5 additional questions rated by others, evaluating participants' overall sleep quality over the past month. The scale is divided into seven components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. The ISI measures the severity of insomnia symptoms through seven self-reported questions, addressing difficulty falling asleep, staying asleep, early awakening, concerns about sleep problems, daytime impairment and worries about insomnia. Each question is scored on a 0-4 scale, with a total score ranging from 0 to 28. Insomnia severity is categorised based on the total score: subthreshold (0-7), mild (8-14), moderate (15-21) and severe insomnia (22-28). Higher scores indicate more severe insomnia symptoms.

The perceived stress scale (PSS)<sup>27</sup> and the job content questionnaire (JCQ)<sup>28</sup> are used to evaluate work-related stress. The PSS measures an individual's subjective perception of stress over the past month through ten questions,

Protected by copyright, including for uses related to text and data mining, Al training, and each rated on a five-point Likert scale, ranging from 'never' (0 points) to 'very often' (4 points). Total scores range from 0 to 40, with higher scores indicating greater perceived stress. The ICQ assesses three key aspects of the work environment: job demands (such as workload and pace), decision latitude (including skill use and ated using a series of questions, typically rated on a Likert scale from 1 to 4 or 1 to 5. Higher scores in each dimension signify greater intensity in that area. For example, higher job demand scores indicate greater work pressure higher decision latitude scores real and higher social and higher social support scores suggest stronger workplace support. Occupational burnout is assessed using the Maslach burnout inventory (MBI),<sup>29</sup> which evaluates three key dimensions: emotional exhaustion, depersonalisation and reduced personal accomplishment, providing a comprehensive view of burnout. Emotional exhaustion measures the extent to which an individual

feels emotionally drained and fatigued by their work, with higher scores indicating greater exhaustion. Depersonalisation reflects a sense of detachment or a cold attitude towards colleagues or clients, with higher scores signifying a more negative or indifferent response in interpersonal interactions. Reduced personal accomplishment assesses how individuals perceive their effectiveness and success at work, with lower scores pointing to dissatisfaction or a sense of underachievement. The MBI consists of 22 items, each rated on a Likert scale from 0 (never) to 6 (daily), representing the participant's level of agreement with each statement. Scores for each dimension are calculated separately: higher scores in emotional exhaustion and depersonalisation indicate greater burnout, while lower scores in personal accomplishment suggest a stronger sense of burnout. Based on these scores, burnout is classified as low, moderate or high. Typically, an emotional exhaustion score above 27 is considered high, 17-26 is moderate and 16 or below is low. For depersonalisation, a score above 13 is categorised as high, 7–12 as moderate and 6 or below as low. In the reduced personal accomplishment dimension, a score of 33 or below indicates high burnout, 34-39 is moderate and 40 or above reflects low burnout.

Visual function is assessed using the National Eye Institute Visual Function Questionnaire (NEI VFQ-25) and the visual function questionnaire (VF-14).<sup>30</sup> These tools evaluate the impact of visual impairment on participants' daily activities and overall quality of life. The NEI VFQ-25 includes 25 items that cover various vision-related aspects, such as overall vision status, visual function in everyday tasks, near and distance vision and the influence of vision on social activities, mental health, role performance, mobility and driving. The VF-14, on the other hand, specifically addresses the impact of visual impairment on particular daily activities, comprising 14 items that assess participants' difficulty in tasks like reading, driving, watching television and other visually demanding activities. Both questionnaires use a 100-point scale, with higher scores reflecting better visual function. The computer vision syndrome questionnaire (CVS-Q)<sup>31</sup> is designed to assess the symptoms of visual fatigue resulting from prolonged use of computers and other digital devices. It asks participants to report symptoms they experience while using electronic screens, such as dry eyes, stinging, headaches, blurred vision and eye fatigue. Each symptom is rated by its frequency ('never', 'occasionally' or 'often') and intensity ('mild' or 'severe'). When symptoms occur more frequently and with greater intensity, visual fatigue is deemed more severe. The total score determines the overall level of visual fatigue, categorised as mild, moderate or severe. A higher CVS-Q score indicates more severe visual fatigue and a greater impact of eye discomfort on daily activities.

The work-life balance scale (WLB)<sup>32</sup> is designed to comprehensively assess participants' ability to balance their work and personal life, reflecting the degree of conflict or harmony between these two areas. The scale

includes multiple items that explore how work interferes with personal life, how personal life impacts work, the participant's ability to disconnect from work and their capacity to enjoy a fulfilling personal life outside of work. Each item is rated on a Likert scale, ranging from 'strongly disagree' to 'strongly agree'. Higher scores indicate greater harmony and balance between work and life, while lower scores suggest more conflict. The total score categorises WLB into low, moderate or night recommendate or night recommendate and personal demands, whereas a low score may indicate the need for additional support or adjustments. Social to Duke-UNC functional social support questionnaire (FSSQ)<sup>33</sup> and the multidimensional scale of perceived social support (MSPSS).34 These tools are designed to measure the perceived availability and adequacy of social support, particularly from family, friends and significant others. The FSSQ consists of eight items that assess emotional and instrumental support on a scale from 1 to 5, with higher scores indicating greater perceived support. The MSPSS includes 12 items that measure the strength of support from the same sources. The combined scores from both scales provide a comprehensive reflection of the participants' overall level of perceived social support.

#### **Basic ophthalmic examination**

Ophthalmic examinations are performed in a controlled environment by trained optometrists and ophthalmologists. Visual acuity, both uncorrected and corrected, is evaluated using a standardised Snellen eye chart (Snellen Chart, Good-Lite, USA). Intraocular pressure is measured with a calibrated non-contact tonometer (NT-530P, NIDEK Co., Japan). Refractive errors, including myopia, hyperopia, astigmatism and anisometropia, are measured using an autorefractor (PRK-7000, Potec Co., South Korea). Subjective refraction is then conducted with a phoropter (VT-10, Topcon, Japan), involving two main steps: spherical and cylindrical power adjustments. Initially, the optometrist adjusts the spherical power based on the autorefractor's preliminary data, asking the patient to read letters of varying sizes from a visual acuity chart while fine-tuning the prescription based on visual feedback to achieve optimal corrected vision. The cylindrical power is then adjusted to address any astigmatism present. An optical biometer (IOLMaster 700, Carl Zeiss Meditec AG, Germany) is used to measure corneal curvature radius, central corneal thickness, anterior chamber depth, lens thickness and axial length. The participant is first seated in front of the device, with their head securely positioned on the headrest and chin rest to ensure stability during the measurement. The operator then adjusts the biometer to align with the participant's eye, ensuring that the line of sight is properly centred. During the measurement process, the device automatically performs multiple scans to minimise errors and ensure data accuracy. The results are then compiled and processed by the device's internal

software. Finally, the clinician reviews these parameters to support the subsequent diagnosis.

A slit-lamp biomicroscope (SL-D701, Topcon, Japan) is used to evaluate the corneal epithelium's integrity, detect keratic precipitates (KP), assess anterior chamber flare and cell count and examine the transparency of the lens and vitreous for any opacities. The participant is seated with their head securely positioned on the headrest and chin rest to maintain stability throughout the examination. Prior to beginning, the ophthalmologist adjusts the slit-lamp's illumination intensity and angle to suit the specific requirements of the exam. A focused beam of light is directed onto the corneal surface to inspect the epithelium for any defects. The clinician closely examines for KP, which often signals intraocular inflammation, particularly in the iris or ciliary body.<sup>35</sup> The light beam's direction and intensity are then adjusted to evaluate lens clarity, checking for any opacities or signs of cataracts. Finally, a deeper light beam is used to assess the vitreous for transparency. Tear secretion volume is measured using Schirmer test strips (Schirmer Tear Test, Bausch & Lomb, USA), while tear film breakup time is assessed with fluorescein staining and a slit lamp. Conjunctival hyperaemia and tear film quality are evaluated with an eye surface analyser (Keratograph 5M, OCULUS, Germany), which also examines meibomian gland function and captures high-resolution images of the eye surface. The dry eye score is calculated based on the combined results of these tests. All procedures are conducted in a controlled environment to minimise external factors that could influence tear production.

An eye-tracking system (Tobii Pro Spectrum, Tobii Technology, Sweden) is employed to assess the range of eye movements, nystagmus, strabismus angle, binocular fusion ability and the presence of diplopia. Before the test begins, the system is calibrated for each participant by having them fixate on several points displayed on the screen. The system then adjusts its tracking parameters based on the participant's pupil position and corneal reflection to ensure precise measurements. During the test, the participant follows a moving target on the screen, while the system records the amplitude and speed of eye movements in horizontal, vertical and diagonal directions, which helps evaluate the function of the extraocular muscles and overall eye movement capabilities. By tracking both eyes as they focus on the same target, the system can accurately assess the strabismus angle. Additionally, by guiding the participant to fixate on targets at varying distances and angles, the system can detect the presence of double vision and identify the conditions under which it occurs. Colour vision testing uses Ishihara plates (Ishihara Test, Kanehara Trading Inc., Japan) to detect red-green colour blindness and other colour vision deficiencies. The test features a series of patterns made up of coloured dots with distinct contrast. Each pattern contains numbers or shapes that the individual must identify based on what they perceive, providing an effective means of detecting both the presence and severity of

red-green colour blindness. In addition to the Ishihara test, the Farnsworth-Munsell 100 Hue Test (Farnsworth-Munsell 100 Hue Test, X-Rite, USA) is employed for a more comprehensive assessment of colour vision. This test involves arranging colours in a continuous sequence based on subtle variations in hue, requiring participants to correctly order the colours. This method not only identifies colour vision deficiencies but also evaluates the individual's ability to distinguish fine gradations of colour. To assess colour vision fatigue, the procedure includes  $\tau$ cycles of repeated colour stimulation and rest. Initially, the participant is exposed to a series of colour patterns or hue tests until symptoms of visual fatigue appear, such as a diminished ability to differentiate between colours. Afterwards, the participant is given a rest period to allow their ? eyes to recover, followed by another colour vision test. The recovery time, or the duration needed for the participant to regain normal colour vision, is recorded to evaluate the effects of colour vision fatigue. The assessment of night vision, glare sensitivity and stereopsis is performed in a darkened room to simulate nighttime or low-light conditions. Night vision and glare sensitivity are evaluated using a mesotest (Mesotest II, Oculus, Germany), where the participant identifies targets in low-light settings while the device introduces varying levels of glare to assess visual performance under bright light interference. The results include the measurements of night vision acuity and the degree of performance decline in glare conditions. Stereopsis is tested with the Randot Stereo Test (Stereo Optical Co., USA), during which the participant wears polarised glasses to view images with depth variations and reports the hidden 3-D patterns.

## **Ophthalmic imaging examination**

Ophthalmic imaging examinations include optical coherence tomography (OCT), optical coherence tomography angiography (OCTA), fundus photography, ultrawidefield imaging (UWF), anterior segment OCT, corneal topography and visual field examination. The OCT is used to measure macular central foveal thickness, retinal nerve fibre layer thickness, macular retinal thickness and to evaluate retinal layer structure and optic disc morphology. Imaging is performed using a spectraldomain OCT device (Cirrus HD-OCT 5000, Carl Zeiss Meditec, Germany). Participants are seated comfortably with their eyes aligned to the machine's optical axis. After proper focus, scans are taken of the macula and optic **o** disc. Standardised settings and scanning protocols are applied to ensure consistent image quality. The images **3** are automatically analysed by the software, with manual adjustments made when necessary to ensure accuracy. The procedure typically takes 5–10 min per eye.

OCTA is a non-invasive imaging technique that visualises blood flow in the retina and choroid without the need for contrast agents. By detecting the movement of red blood cells within blood vessels, it produces high-resolution, 3-D vascular images, making it particularly valuable for evaluating eye microcirculation. We use a

training, and

swept-source OCTA device (Towardpi, China), which provides faster scanning speeds, higher image resolution and a broader field of retinal scanning. First, it features an A-scan speed of up to 400 000 scans/s, far exceeding the 70 000–100 000 scans/s typical of standard OCTA devices, greatly reducing imaging time and minimising artefacts. Second, with an axial resolution of 3.8 microns and a lateral resolution of 10 microns, the device ensures high imaging precision, allowing clinicians to clearly observe the microvascular structures of the retina and choroid. Moreover, the device supports a wider scanning range, with OCTA scans adjustable from 3×3 mm to 12×12 mm, covering a maximum field of 24×20 mm and providing a wide-angle view of up to 120° of the fundus, significantly enhancing the assessment of retinal pathologies. The device also supports multiple scanning modes, with OCTA scans for the retina and anterior segment ranging from 3×3 mm to 12×12 mm and 6×6 mm to 16×12 mm, respectively. The number of scan lines can be adjusted from 512 to 1280, ensuring comprehensive imaging of different ocular regions. OCTA measures several critical blood flow parameters, including retinal blood flow density, macular blood flow density and optic disc blood flow density. Through these analyses, clinicians can assess perfusion, identify non-perfusion areas, detect microaneurysms and monitor neovascularisation. Additionally, OCTA evaluates vascular complexity, revealing changes

in the microvascular network's morphology. Fundus photography is employed to capture detailed documentation of the optic disc colour and morphology, retinal vascular structure, macular appearance, cup-to-disc ratio and other key fundus characteristics. This imaging is conducted using a widefield fundus camera (CLARUS 500, Carl Zeiss Meditec, Germany). During the procedure, participants are instructed to fixate on a target, while a series of high-resolution images are taken. The CLARUS 500 provides true-colour imaging and captures a 133° widefield view of the retina, enabling comprehensive examination of both central and peripheral retinal areas. The procedure is non-invasive and typically takes about 5 min to complete. Images are carefully reviewed for clarity and precision, with reimaging performed if needed to ensure the highest quality diagnostic results. UWF retinal imaging is performed using the UWF imaging system (Optos Daytona, Optos Ltd., UK), which captures a broad view of the peripheral retina without the need for pupil dilation, offering a more comprehensive image than traditional fundus photography. Using low-intensity, multiwavelength lasers (including red and green light) to scan the retina, the system captures up to 200° of the retinal area in a single image, spanning from the macula to the far periphery. This enables clinicians to clearly detect peripheral retinal abnormalities, such as retinal tears, detachment and peripheral haemorrhages. Beyond providing a detailed view of retinal structures, UWF also delivers valuable information on vascular morphology, highlighting conditions like arterial narrowing, venous tortuosity and abnormal vascular

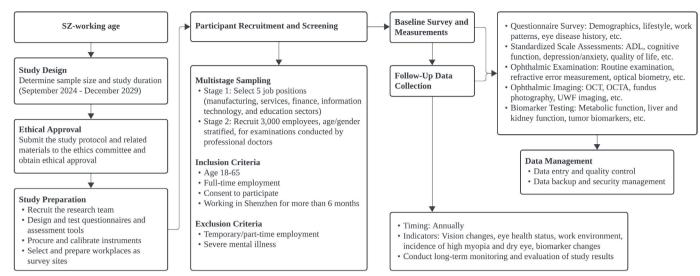
dilation. During the procedure, the patient is positioned in front of the device, with head and chin adjustments for stability. They are instructed to focus on a specific light inside the device and remain still as the system quickly captures high-resolution images, documenting various layers and regions of the retina.

Anterior segment OCT is used to assess corneal thickness, corneal epithelial thickness, anterior chamber depth, anterior chamber angle structure and the curvature of the lens surface. The examination is performed  $\boldsymbol{\tau}$ using a swept-source OCT device (CASIA2, Tomey Corporation, Japan). Participants are positioned similarly to retinal OCT, with scans specifically targeting the anterior segment of the eye. The CASIA2 produces detailed crosssectional images of the cornea and anterior chamber, ? aiding in the evaluation of conditions, such as angle-closure glaucoma. Each eye takes approximately 10 min to scan, ensuring precise measurement and comprehensive documentation of the anterior segment structures. Corneal topography assesses the distribution of corneal refractive power, the axis of corneal astigmatism and any irregularities on the corneal surface. Imaging is conducted using a Placido-ring-based corneal topographer (Pentacam HR, Oculus, Germany). Participants are instructed to keep their eyes wide open, while the device captures detailed surface maps of the cornea. The visual field examination assesses the type and extent of visual field defects, as well as contrast sensitivity and light sensitivity thresholds. This test is performed using an automated perimetry device (Humphrey Field Analyser 3, Carl Zeiss Meditec, Germany) and is conducted monocularly, with each eye tested individually for 10-15 min. During the exam, light stimuli are randomly presented in the participant's peripheral vision. Participants are instructed to press a button whenever they detect a stimulus while maintaining focus on a central fixation point. The device records the minimum light stimulus the participant can perceive, determining their light sensitivity threshold. Additionally, contrast sensitivity is evaluated by adjusting the brightness and contrast of the light stimuli.

## **Biomarker testing**

Fasting samples 2-mL ethylenediblood (one aminetetraacetic acid (EDTA) anticoagulant tube, one 5-mL EDTA anticoagulant tube, one 5-mL coagulationpromoting tube and one 5-mL lithium-heparinised tube) are collected from participants after at least 8 hours of overnight fasting. The laboratory analyses include & comprehensive assessments of hepatic and kidney function, serum lipids, tumour biomarkers and other relevant indicators (table 1). After analysis, blood specimens in the 5-mL EDTA anticoagulant or lithium-heparinised tubes are centrifuged at 3000 rpm for 10 min at 4 °C to separate plasma, white blood cells and red blood cells. All aliquoted samples are stored at -80 °C for future use.

Participants will receive a detailed schedule of the on-site visit in advance, including estimated time blocks for each procedure, to facilitate informed consent and



**Figure 1** Flowchart of SZ-working-age cohort study. ADL, activities of daily living; OCT, optical coherence tomography; OCTA optical coherence tomography angiography; SZ-working age, Shenzhen-working age; UWF, ultrawidefield.

personal planning. The total duration of the on-site visit is carefully planned to not exceed 3–4 hours. Breaks are mandatory after every 60–90 min of testing, with hydration and light snacks provided postblood collection to mitigate physical strain. Following the examination, participants will be provided with meal vouchers as well as reimbursement for travel expenses.

#### Follow-up and monitoring

As shown in figure 1, the study follows an annual follow-up strategy, where the content of each follow-up is identical to the baseline survey. This comprehensive process includes the assessments of vision changes, eye health, work environment and the incidence of high myopia and dry eye, conducted through face-to-face interviews and ophthalmic examinations. Additionally, long-term monitoring is implemented to continuously evaluate study outcomes, ensuring both data quality and consistency over time.

## **Data quality assurance**

The Shenzhen Eye Hospital is responsible for overseeing and validating the entire project to ensure its integrity and reliability. Research investigators undergo annual training at the hospital to maintain consistency and standardisation in data collection. This training covers the study's objectives, proper administration of questionnaires, standardised measurement techniques and the importance of adhering to uniform procedures throughout the study. Each investigator is provided with detailed manuals outlining the procedures for administering questionnaires, conducting standardised scale assessments, performing ophthalmic examinations and managing data. After each survey, trained investigators thoroughly review the questionnaires for completeness and logical consistency. Any missing data are collected, and errors are corrected when participants receive their medical examination reports. Data from each questionnaire are

then independently entered into a secure database by two data entry personnel using EpiData software (V.3.2), ensuring that all information is double checked for accuracy and validity.

## **Statistical analysis**

All statistical analyses will be performed using SPSS 25.0 (IBM Corp.) and R (V.4.0.2, R Foundation for Statistical Computing). Descriptive statistics will be used to summarise the baseline characteristics of participants, including mean±SD for normally distributed continuous variables, median±IQR for skewed continuous variables and frequencies for categorical variables. For comparisons between groups, independent t-tests or Mann–Whitney U tests will be used for continuous variables depending on data normality, assessed using the Shapiro–Wilk test. Categorical variables will be compared using  $\chi^2$  tests.

To evaluate the incidence of high myopia and pathological myopia, Kaplan-Meier survival analysis will be conducted, and differences between groups will be conducted, and differences between groups will be assessed using the log-rank test. Cox proportional hazards regression models will be used to identify risk factors associated with myopia progression. For secondary outcomes, multivariate regression models will be applied to assess associations among eye health indicators, work-related visual strain and systemic biomarkers, adjusting for potential confounders, such as age, sex, occupation and baseline refractive status. Repeated measures analysis, including generalised estimating equations or mixedeffects models, will be used to analyse longitudinal data. For continuous variables with different measurement units, data will be standardised using z-score normalisation to ensure comparability in multivariate models. For biomarkers with skewed distributions, log transformation will be applied to approximate normality before statistical modelling.

Missing data will be assessed using Little's Missing Completely at Random (MCAR) test. If data are determined to be MCAR, complete case analysis will be employed. For data classified as Missing at Random, multiple imputation will be performed using predictive mean matching for continuous variables and logistic regression for categorical variables. In the event that data are suspected to be Missing Not at Random, sensitivity analyses will be conducted to assess the robustness of findings. A two-sided p<0.05 will be considered statistically significant.

#### **ETHICS AND DISSEMINATION**

The SZ-working-age study has been registered with the National Health Information Platform (MR-44-24-026548). Ethical approval has been granted by the Ethics Committee of Shenzhen Eye Hospital (2024KYPJ012). All study procedures adhere to ethical guidelines, and written informed consent is obtained from all participants after they receive a thorough explanation of the study's aims, potential benefits, procedures and confidentiality measures regarding their personal information. Although there are currently no plans to make the collected data publicly accessible, the study promotes international collaboration and data sharing through specific agreements. Research findings will be disseminated via presentations at professional conferences and submissions to peer-reviewed scientific journals. All published results will be based on aggregated data to ensure the anonymity of individual participants.

## **Strengths and limitations**

The SZ-working age is a prospective observational cohort study designed to investigate eye health and the incidence of high myopia among the working-age population. Its key strengths include a large-scale, multistage sampling method, which ensures the representativeness and diversity of the sample. The study population encompasses individuals from various occupational sectors, including manufacturing, services, IT and education, with stratification by age and gender, enhancing the generalisability of the findings. A distinguishing feature of this study is its focus on the eye health of the working population, addressing a critical research gap. Given the unique visual demands and environmental stressors faced by this group, the study aims to identify occupation-related risk factors and support the development of targeted prevention and intervention strategies.

The study integrates a series of standardised assessment tools and ophthalmic examinations to ensure both data accuracy and reproducibility. A key feature is the use of cutting-edge OCTA equipment, which provides wide-angle scans of the retina with high-resolution imaging. This advanced device, which has not been used in the previous eye health studies, offers significant improvements over the equipment typically used in community screenings. It not only detects subtle

changes in retinal microvasculature with greater precision but also captures a broader field of view, enabling a more comprehensive assessment of retinal and choroidal blood flow. This technological advancement enhances the study's capacity to detect early microvascular changes and other eye health issues, facilitating earlier diagnosis and intervention.

The annual follow-up design offers a valuable opportunity for dynamic monitoring of vision changes and eye health, enabling the observation of long-term trends and developments. By maintaining continuous follow-up, the study can track eye health changes in real time and evaluate the long-term effects of work environments and lifestyle factors on eye health. This ongoing data collection provides crucial evidence to inform public health interventions and support the development of relevant policies.

However, the study has some limitations. First, as an observational study, it cannot establish causality but can only identify associations. Second, the study population primarily consists of healthy working-age individuals, which may limit the generalisability of the findings to those with pre-existing eye conditions or other health issues. Additionally, since data collection relies on questionnaires and self-reports, there is a potential risk of recall and reporting biases. Despite these limitations, the study provides valuable data and insights into the eye health of the working-age population, contributing to further research and the development of public health policies in this area.

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