THE UNIVERSITY *of* EDINBURGH

The national and subnational disease burden of age-related eye diseases in China

Peige Song, BMed, MMed, MSc

THE UNIVERSITY *of* EDINBURGH

Doctor of Philosophy

The University of Edinburgh

2019

Declaration

I, Peige Song, hereby declare that the following thesis has been composed solely by me. The work has not been previously submitted, in whole or in part, for any other degree or professional qualification. Except where the due acknowledgement is made, the work is entirely executed by myself.

Date:22/02/2019

Abstract

Background

In the past decades, China has experienced one of the fastest ageing processes in the world. Alongside the demographic transition, there is a dramatic increase in age-related disability. Currently, vision loss is the leading cause of age-related disability in developing countries. Age-related eye diseases (AREDs), mainly including age-related macular degeneration (AMD), glaucoma, cataract and diabetic retinopathy, are primarily degenerative diseases in older people, whose burden is expected to increase with demographic ageing. This thesis aims to estimate the prevalence and burden of AREDs in China.

Methods

I searched three Chinese and three English bibliographic databases, namely China National Knowledge Infrastructure (CNKI), Wanfang, Chinese Biomedicine Literature Database (CBM-SinoMed), PubMed, Embase and Medline for studies of the prevalence of age-related macular degeneration (AMD), cataract, glaucoma, and diabetic retinopathy (DR) in China. For diseases where a single study could contribute multiple stratum-specific (e.g. age-specific and sex-specific) data points, a multilevel mixed-effects meta-regression was applied to generate the stratum-specific prevalence estimates of disease. For diseases where only study-level prevalence estimates were available, a random-effects meta-analysis was conducted to generate the pooled prevalence. By applying the estimated stratum-specific prevalence (or pooled prevalence) to the corresponding population data, available from the United Nations Population Division (UNPD), the national number of affected people was determined. By taking the geographic effects, the national number of cases was finally distributed into the six geographic regions (East China, North China, Northeast China, Northwest China, South Central China, Southwest China) in China.

Results

For estimating the prevalence and burden of AMD, 25 eligible studies were identified in the systematic review. The prevalence of any AMD ranged from 2.44% (95% CI: 1.85-3.22) in people aged 45-49 years to 18.98% (95% CI: 15.05-23.66) in people aged 85-89 years.

Prevalence of early AMD ranged from 1.79% (95% CI: 1.05-3.02) to 10.05% (95% CI: 6.17-15.97), and, in the case of late AMD, from 0.38% (95% CI: 0.16-0.97) to 3.88% (95% CI: 1.68-9.13). In late AMD, the prevalence of geographic atrophy (GA) was 0.15% (95% CI: 0.05-0.47) in people aged 45-49 years and 1.09% (95% CI: 0.35-3.36) in those aged 85-89 years, and the prevalence of neovascular AMD (NVAMD) ranged between 0.24% (95% CI: 0.11-0.50) and 2.79% (95% CI: 1.33-5.77). In people aged 45-89 years, the number of people with any AMD was 12.01 million (95% CI: 9.29-15.46) in 1990 and 26.65 million (95% CI: 20.62-34.27) in 2015. Within the same period, the number of people with early AMD increased from 9.44 million (95% CI: 7.74-11.15) to 20.91 million (95% CI: 17.16-24.68), and those with late AMD rose from 2.58 million (95% CI: 1.56-4.30) to 5.74 million (95% CI: 3.46-9.59). In late AMD, the number of people living with GA ranged from 0.87 million (95% CI: 0.40-1.83) in 1990 to 1.93 million (95% CI: 0.89-4.08) in 2015, and NVAMD from 1.71 million (95% CI: 1.16-2.47) to 3.81 million (95% CI: 2.57-5.51). It is projected the number of people with any AMD in 2050 will be 55.19 million (95% CI: 43.04-70.30). Among different regions, the South Central owed the most AMD cases (5.50 million in 2000 and 7.52 million in 2010), whereas North-West China the least (0.66 million in 2000 and 0.95 million in 2010).

For estimating the prevalence and burden of glaucoma, 30 studies met the inclusion criteria in the systematic review. In males, the prevalence of POAG ranged from 0.74% (95% CI: 0.48-1.14) in individuals aged 45-49 years to 3.02% (95% CI: 1.92-4.73) in those aged 85-89 years. The prevalence of POAG in females was slightly lower than that in males across the whole age spectrum from 45 to 89 years, ranging from 0.54% (95% CI: 0.35-0.84) to 2.24% (95% CI: 1.41-3.53). For PACG, the prevalence increased from 0.48% (95% CI: 0.39-0.60) in males aged 45-49 years to 3.44% (95% CI: 2.66-4.45) in males aged 85-89 years. The prevalence of PACG was consistently higher in females than in males, ranging from 0.91% (95% CI: 0.74-1.11) in females aged 45-49 years to 6.33% (95% CI: 4.98-8.02) in females aged 85-89 years. The pooled prevalence of secondary glaucoma was 0.15% (95% CI: 0.10-0.23). In people aged 45-89 years, the number of people affected by POAG increased from 2.35 million (95% CI: 1.54-3.60) in 1990 to 5.22 million (95% CI: 3.40-7.98) in 2015, PACG from 3.22 million (95% CI: 2.70-3.84) to 7.14 million (95% CI: 5.97-8.53), and secondary glaucoma from 0.34 million (95% CI: 0.23-0.53) to 0.76 million (95% CI: 0.51-1.17). In 2015, more than half (54.42%) of the glaucoma cases were PACG, followed by POAG (39.79%) and secondary glaucoma (5.79%). By 2050, the number of all glaucoma cases in China will be 25.16 million (95% CI: 18.96-33.86). %). In both 2000 and 2010, East China owed the most POAG cases (1.02 million in 2000 and 1.39 million in 2010) and PACG cases (1.24 million in 2000 and 1.68 million in

2010), whereas Northwest China the least (POAG: 0.19 million in 2000 and 0.27 million in 2010; PACG: 0.32 million in 2000 and 0.46 million in 2010).

For estimating the prevalence and burden of cataract and cataract blindness, 55 studies met the eligibility criteria and were included in the systematic review and meta-analysis. In males, the prevalence of any cataract (including post-surgical cases) ranged from 6.71% (95% CI: 5.06-8.83) in people aged 45-49 years to 73.01% (95% CI: 65.78-79.2) in elderly aged 85-89 years. In females, the prevalence of any cataract increased from 8.39% (95% CI: 6.36-10.98) in individuals aged 45-49 years to 77.51% (95% CI: 71.00-82.90) in those aged 85-89 years. For age-related cataract (ARC, including post-surgical cases), in males, the prevalence rates ranged from 3.23% (95% CI: 1.51-6.80) in adults aged 45-49 years to 65.78% (95% CI: 46.72-80.82) in those aged 85-89 years. The prevalence of ARC in females was 4.72% (95% CI: 2.22-9.76) in the 45-49 years age group and 74.03% (95% CI: 56.53-86.21) in the 85–89 years age group. The pooled prevalence rate of cataract blindness (including post-surgical cases) by best corrected visual acuity (BCVA) <0.05 among middle-aged and older Chinese was 2.30% (95% CI: 1.72-3.07), and those of cataract blindness by BCVA <0.10 and cataract blindness by presenting visual acuity (PVA) <0.10 were 2.56% (95% CI: 1.94-3.38) and 4.51% (95% CI: 3.53-5.75) respectively. In people aged 45-89 years, the number of any cataract cases was 50.75 million (95% CI: 42.17-60.37) in 1990 and 111.74 million (95% CI: 92.94-132.84) in 2015, and that of ARC rose from 35.77 million (95% CI: 19.81-59.55) in 1990 to 79.04 million (95% CI: 44.14-130.85) in 2015. By 2050, it is projected that the number of people (45-89 years of age) affected by any cataract will be 240.83 million (95% CI: 206.07-277.35), and that of those with ARC will be 187.26 million (95% CI: 113.17-281.23). During 2000 and 2010, South Central China consistently owed the most cases of any cataract (23.50 million in 2000 and 31.79 million in 2010), whereas Northwest China the least (3.37 million in 2000 and 4.87 million in 2010).

For estimating the prevalence and burden of DR. A total of 31 studies provided information on the prevalence of DR and 21 explored potential risk factors for DR. The pooled prevalence of any DR, nonproliferative DR (NPDR) and proliferative DR (PDR) was 1.14% (95% CI: 0.80-1.52), 0.90% (95% CI: 0.56-1.31) and 0.07% (95% CI: 0.02-0.14) in general population; In people with DM, the pooled prevalence rates were 18.45% (95% CI:14.77-22.43), 15.06% (95% CI:11.59-18.88) and 0.99% (95% CI: 0.40-1.80) for any DR, NPDR and PDR, respectively. The prevalence of any DR in DM patients peaked between 60 and 69 years of age, and increased steeply with the duration of DM. DM patients residing in rural China were at a higher risk to have DR than those in urban areas. In addition, insulin treatment, elevated

FBG level and higher HbA1c concentration were confirmed to be associated with a higher prevalence of DR in people with DM, with meta-ORs of 1.99 (95% CI: 1.34-2.95), 1.33 (95% CI: 1.12-1.59) and 1.15 (95% CI: 1.09-1.20) respectively. In 2010, a total of 13.16 million (95% CI: 8.95-18.00) Chinese aged 45 years and above were living with DR, among whom the most were in South Central China (3.71 million) and the least were in Northwest China (0.87 million).

Conclusions

This thesis presents a comprehensive estimation of the prevalence and burden of AREDs in China. With the dramatic ageing trend in the next three decades, the prevalence and burden of AREDs will continue to increase. More elaborate epidemiological studies are still required for better estimation of the disease burden of AREDs. Primary and secondary prevention, treatment and effective government response are urgently needed to optimise public health strategies for mitigating this important health problem.

Lay Summary

Age-related eye diseases (AREDs), primarily including age-related macular degeneration, cataract, glaucoma, and diabetic retinopathy, are degenerative diseases in older people. Visual impairment caused by AREDs is associated with decreased mobility and physical performance, diminished quality of life, increased risks of falls and accidents, fractures, etc. Globally, there are 285 million people with visual impairment, among whom 40 million are blind. Tellingly, 65% of those with visual impairment and 82% of those with blindness are over 50 years. With a rapid demographic shift towards ageing, increasing prevalence of diabetes and wide usage of electronic devices, an upward trend in the prevalence of AREDs is expected worldwide, this is also true for the most populous country China, where the number of older population aged over 60 years is projected to be 440 million and account for more than 30% of the total population by 2050. Although global estimates of visual impairment revealed the proportions of AREDs as causes of visual impairment and blindness in general population, the limited numbers of surveys hampered their ability exploring the variations of AREDs prevalence within specific countries, in addition, there is still no subnational estimate of AREDs in China up to date. An in-depth analysis in exploring the epidemiology of AREDs across China is essential, as a means of informing public health policymaking and health resource allocating at both the national and local levels. In this study, I systematically searched and reviewed all publicly available information on the epidemiology of AREDs in China. By using meta-analysis and meta-regression approaches, I estimated the prevalence of AREDs and the number of people with AREDs in the general Chinese population, at both national and subnational levels.

Acknowledgements

This PhD was funded by the China Scholarship Council (CSC) and the University of Edinburgh. I deeply appreciated their financial support.

First and foremost, I offer my deepest gratitude to my supervisors, Dr Kit Yee Chan, Dr Evropi Theodoratou and Professor Igor Rudan, for their constant guidance, support and encouragement over the past four years. I highly admire their expertise in the field of global health. I am greatly indebted to Professor Igor Rudan, whom I have spent so much time closely working with. He has become a role model for me of being an excellent scientist. Without his inspiration and investment, I couldn't have got through this PhD process.

My special thanks also go to Dr Evropi Theodoratou and Professor Harry Campbell for recruiting me in the first place and leading me to such a fantastic research journey. Much gratitude also goes to Professor Harish Nair and Dr Veronique Vitart for offering me valuable suggestions on improving the quality of this project. I would also like to thank my dissertation committee, Professor Alex Tsai, Dr Jonine Figueroa and Professor Harry Campbell, to whom I owe a debt of gratitude for their time and constructive comments.

I am truly grateful to my dear friends and colleagues in Edinburgh for being sources of emotional support, especially Xue, Luciana, Anna, Sarah, Rachael, Tomi and all the dear Chinese peers for their warm accompany during a hard time of my life. I also miss all my friends in my home country for their constant friendship. I would like to thank the anonymous peer reviewer for the four publications presented in this thesis.

Finally, I would like to thank my parents and husband for their endless love and support. Like I always believe, life will definitely get better and I look forward to us being together.

Abbreviations

AFR	African region
ALT	Argon Laser Trabeculoplasty
AMD	Age-related macular degeneration
AMR	region of the Americas
ARC	age-related cataract
ARED	age-related eye disease
AREDS	Age-Related Eye Disease Study Grading System
BCVA	best corrected visual acuity
BMI	body mass index
BUN	blood urea nitrogen
CARMS	Clinical Age-Related Maculopathy Grading System
CBM-SinoMed	Chinese Biomedicine Literature Database
CHARLS	China Health and Retirement Longitudinal Study
CHERG	Child Health Epidemiology Reference Group
CI	confidence interval
CMA	China Medical Association
CNKI	China National Knowledge Infrastructure
COPD	chronic obstructive pulmonary disease
DALY	Disability Adjusted Life Year
DBP	diastolic blood pressure
DM	diabetes mellitus
DMO	diabetic macular oedema
DR	diabetic retinopathy
EMR	Eastern Mediterranean region
ETDRS	Early Treatment of Diabetic Retinopathy Study
EUR	European region
EUREYE	European Eye Study
FBG	fasting blood glucose
FP	fundus photography
GA	geographic atrophy
GADM	Global Administrative Areas
GATHER	Guidelines for Accurate and Transparent Health Estimates Reporting

GBD	Global Burden of Disease
HbA1c	haemoglobin A1c
HDL	high-density lipoprotein
HIC	high-income countries
IC	International Classification and Grading system
ICD	International Classification of Disease
ICDRDSS	International Clinical Diabetic Retinopathy Disease Severity Scale
IOP	intraocular pressure
KDM	known diabetes mellitus
LIC	low-income countries
LOCS	Lens Opacities Classification
MCMC	Markov Chain Monte Carlo
MIC	middle-income countries
MOOSE	Meta-analysis of Observational Studies in Epidemiology
NASA	National Aeronautics and Space Administration
NCD	non-communicable disease
NCOFD	National Conference on Ocular Fundus Diseases
NDM	newly detected diabetes mellitus
NHS	National Health Service
NOFDG	National Ocular Fundus Diseases Group
NPDR	non-proliferative diabetic retinopathy
NVAMD	neovascular age-related macular degeneration
OCCGS	Oxford Clinical Cataract Classification System
OR	odds ratio
PACG	primary angle-closure glaucoma
PBG	postprandial blood glucose
PDR	proliferative diabetic retinopathy
PHCM	primary health care management
POAG	primary open angle glaucoma
PPS	probability-proportional-to-size
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PS	posterior subcapsular
PSU	primary sampling unit
PVA	presenting visual acuity
RGC	retinal ganglion cell

RR	risk ratio
SBP	systolic blood pressure
Scr	serum creatinine
SEAR	south-east Asian region
SLT	Selective Laser Trabeculectomy
STROBE	Reporting of Observational Studies in Epidemiology
T1DM	type 1 diabetes mellitus
T2DM	type 2 diabetes mellitus
TC	total cholesterol
TFN-α	Tumour necrosis factor alpha
TFR	total fertility rate
TG	triglyceride
Ucr	urine creatinine
UN	United Nations
UNPD	United Nation's Population Division
UP	urine protein
US	United States
UV	ultraviolet
UVB	ultraviolet B
VEGF	vascular endothelial growth factor
VTDR	vision-threatening diabetic retinopathy
WARMGS	Wisconsin age-related maculopathy grading system
WCGS	Wisconsin Cataract Grading System
WHO	World Health Organization
WHOSCGS	WHO Simplified Cataract Grading System
WHR	waist-to-hip ratio
WPR	Western Pacific region
YLDs	Years Lived with Disability

Contents

List of tables

List of figures

Chapter 1 General Introduction

1.1 Background

Over the course of the past two centuries and into the 21st century, the world has been undergoing unprecedented demographic transitions, both in developed and developing countries (Bongaarts, 2009, Lee, 2003, Rechel et al., 2013, Shetty, 2012). For most developed countries, the shift to an ageing society was completed during the last century (Lee, 2003, World Health Organization, 2011a, Rechel et al., 2013, United Nations, 2015a), whereas demographic transitions began later, and are still underway in the developing world (Bongaarts, 2009, World Health Organization, 2011a, Guilmoto and Jones, 2015, Shetty, 2012). The world's most populous country, China, has benefited from its large population in terms of both economic and social development, yet the population is ageing (Banister et al., 2012, Guilmoto and Jones, 2015, Mai et al., 2013). As a consequence, diseases associated with ageing have become a significant cause of concern for the whole society, and will bring great challenges to the Chinese health systems as well as to individuals (World Health Organization, 2011a, Banister et al., 2012, Beard et al., 2016).

Among all common age-related diseases, chronic and degenerative diseases have long occupied policy priorities and public attention, such as dementia, stroke, diabetes and other cardiovascular diseases (Beard et al., 2016, Prince et al., 2015, Prospective Studies Collaboration, 2002). However, age-related eye diseases (AREDs), primarily including age-related macular degeneration, cataract, glaucoma, and diabetic retinopathy, despite also being degenerative diseases (Gohdes et al., 2005, Li et al., 2011, Wong et al., 2006a), are relatively neglected in policy and by the public (Voleti and Hubschman, 2013, McCarty et al., 2001b, Li et al., 2011). Visual impairment caused by AREDs is associated with decreased mobility and physical performance, diminished quality of life, increased risks of falls and accidents, fractures, etc. (Klein and Klein, 2013, Ng et al., 2007). According to the World Health Organization (WHO) estimates, there were 285 million individuals globally living with visual impairment. Of these, 40 million were blind in 2010, among whom 80% could have been prevented or treated (Pascolini and Mariotti, 2011, Stevens et al., 2013). Eye diseases are largely seen in elderly populations, with 65% of those with visual impairment and 82% of those with blindness being over 50 years old (Pascolini and Mariotti, 2011, Chader and Taylor, 2013).

With rapid demographic shifts towards ageing, increasing prevalence of diabetes and wide usage of electronic devices, an upward trend in the prevalence of AREDs worldwide is expected (Voleti and Hubschman, 2013, Pizzarello et al., 2004). This is also true for China, where the number of people aged over 60 years is projected to be 440 million, and account for more than 30% of the total population by 2050 (Banister et al., 2012). However, our understanding of the burden of AREDs in elderly is surprisingly limited (Wong et al., 2006a, Klein and Klein, 2013). Although global estimates of visual impairment revealed the proportion of AREDs as causes of visual impairment and blindness (Pascolini and Mariotti, 2011), no national epidemiological survey has revealed the epidemiology and variations of AREDs in China (Zhou et al., 2007). Furthermore, there exists no up-to-date sub-national estimate of AREDs in China.

In this study, I will estimate the burden of AREDs in China from 1990 to 2015, with a projection to the year 2050. Furthermore, I will also explore the different distribution of the burden of AREDs at both the national and sub-national levels. The difference in the prevalence by demographic and geographic factors will also be investigated.

This chapter starts with a brief overview of the global demographic transition, and the transitions in health associated with ageing populations. Then, the chapter focuses on ageing vision, with an emphasis on common AREDs. In addition, as a background setting for this study, special attention is paid to the Chinese context. Finally, the systematic review and meta-analysis method is explained as a prevailing approach to disease burden estimation.

1.2 Demography of ageing

1.2.1 Ageing as a global phenomenon

The global population is getting older, indicative of improvements in health and economics (United Nations, 2015a, Kinsella and Phillips, 2005, Rechel et al., 2013). The WHO defines ‘elderly’ as any person aged 65 years and above. Although this cut-off has been widely accepted in many developed countries, its usefulness is questionable in many developing countries, where a cut-off age of 60 years may be more appropriate (Juni, 2015, World Health Organization, 2002). According to this study context, the cut-off of 60 years is adopted across the whole thesis.

Generally, without considering the migration factor, the dynamic of the demographic structure is mainly driven by three factors: fertility rate, mortality rate and life expectancy (Kinsella and Phillips, 2005, United Nations, 2015a, World Health Organization, 2015b, Bongaarts, 2009). The total fertility rate (TFR), which refers to the average number of children a woman would bear over the course of her lifetime according to a given set of age-specific fertility rates throughout her childbearing years (normally between the ages of 15 and 49 years), is one of the important determinants of population's age structure (He et al., 2016, United Nations, 2015a). The decline of TFR is occurring almost everywhere in the world, and this trend steadily lowers the proportion of children and young people in a population, thus leading to a relative increase in the proportion in older age groups. According to the estimates and future projections from the United Nations (UN), TFR has dramatically decreased from 4.9 children per woman in 1950 to 2.5 in 2015, and is expected to decline to 2.2 in 2050. In most areas (**Figure 1.1**), TFR has already dropped below or near the general replacement-level (2.1 children per woman) for maintaining the current population size, except in Africa (Wilson, 2004, He et al., 2016, United Nations, 2004).

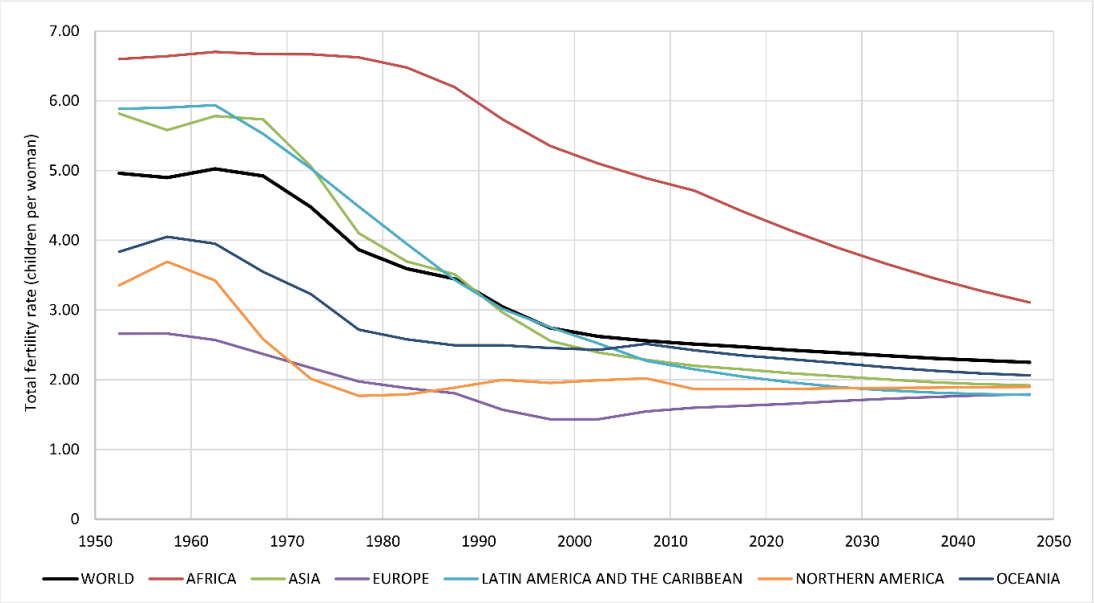


Figure 1.1. Total fertility rate by region: 1950-2050 (data source: (United Nations, 2015b))

Note: The classification of world regions is based on the United Nations Statistics Division, Department of Economic and Social Affairs regional groupings. The projections are based on the medium scenario (United Nations, 2015b).

In addition to TFR, the size and age composition of a population is also influenced by mortality to a large extent (United Nations, 2015a, United Nations, 2004, Guilmoto and Jones, 2015, Kinsella and Phillips, 2005). Mortality levels and trends determine the proportion of the population that eventually survives to old age. In parallel to the decline in fertility, mortality has also declined considerably over the past decades (United Nations, 2015a, Bongaarts, 2009, Guilmoto and Jones, 2015). Life expectancy (at birth) refers to the average number of years a newborn infant would live if prevailing patterns of mortality at the time of birth were to stay the same throughout their life (United Nations Population Fund, 2012). By summarising the information of mortality pattern across all age groups - children and adolescents, adults and the elderly - life expectancy at birth can be seen as a reflection of the overall mortality level in a population (World Health Organization, 2017b, Bongaarts, 2009). The improvement of life expectancy at birth can be driven by mortality reduction in different age groups (United Nations, 2015a, World Health Organization, 2015b). In countries where child mortality rates have been reducing at a stable level, reduction in mortality among elderly persons has become an important contribution of population ageing (United Nations Population Fund, 2012). Changes in life expectancy at birth according to the contribution of mortality decline at different age groups is shown in **Figure 1.2**, which presents different driving patterns of improvement in life expectancy between 1995-2000 and 2010-2015 for the whole world and its six regions. At the global level, mortality reduction in older population accounted for one-quarter of the total gain in the life expectancy at birth, while in North America this share was as high as 71%.

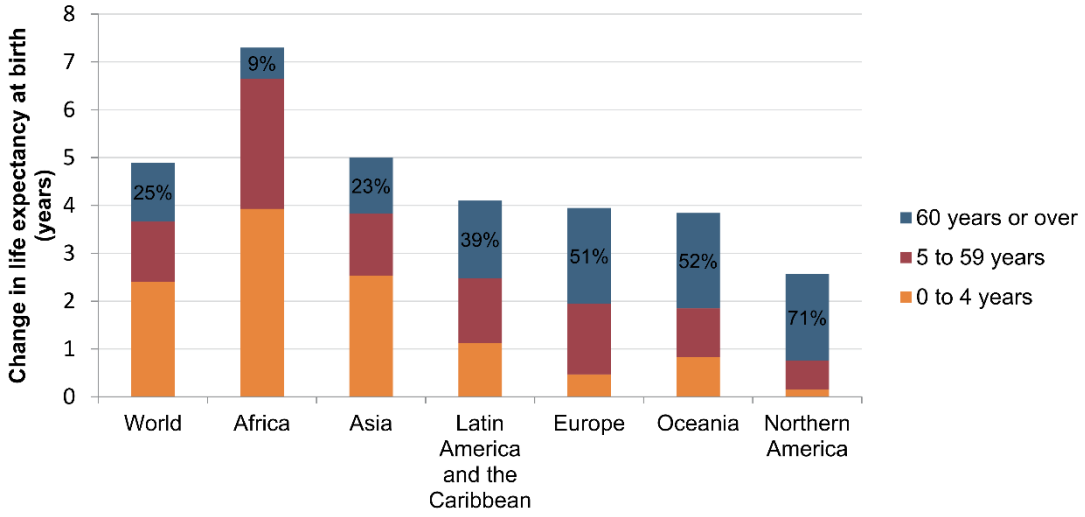


Figure 1.2. Contribution of mortality reduction at different age groups to improvements in the life expectancy at birth between 1995-2000 and 2010-2015, for the world and six regions (source: (United Nations, 2015a))

Globally, from 1950 to 2015, life expectancy at birth has risen by more than 23 years, from 46.8 years to 70.5 years. Such increases in life expectancy are a result of advances in economic development, nutrition, education, sanitation and medical care (Guilmoto and Jones, 2015, World Health Organization, 2015b, Lunenfeld and Stratton, 2013). In addition, it is projected that the global life expectancy at birth will keep increasing to 77.1 years by 2050. All regions have experienced an increase in life expectancy since 1950. Of all the six regions, Asia has made the largest gains in survival, with life expectancy having increased by 30 years - from 42.1 years in 1950 to 71.6 years in 2015. Largely due to the lower development levels in many African countries, the African region showed the shortest life expectancy over the same period (**Figure 1.3**) (World Health Organization, 2011b, United Nations, 2015a).

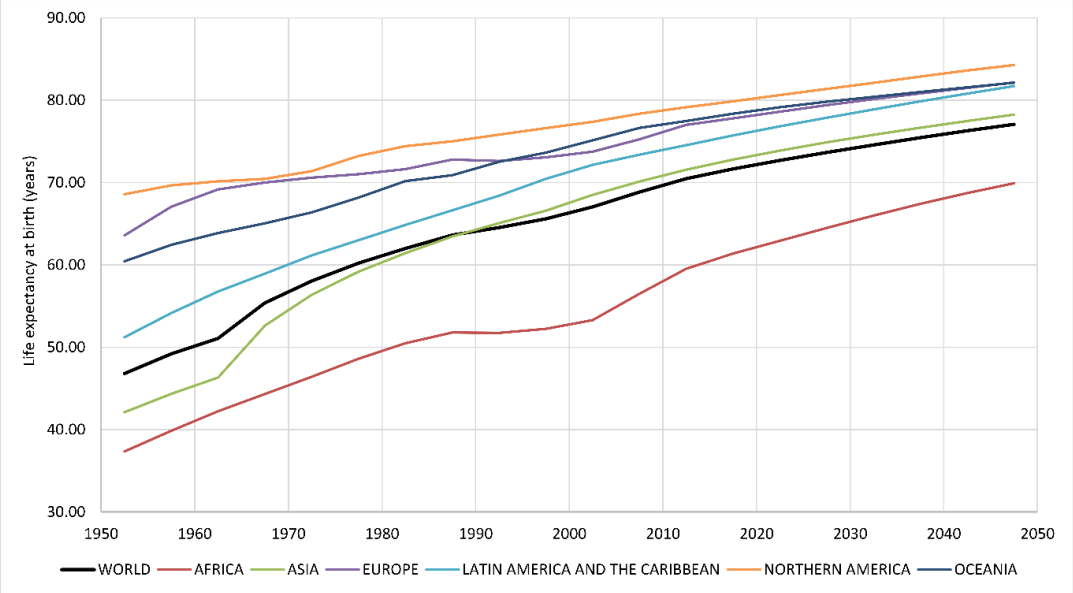


Figure 1.3. Life expectancy at birth by region: 1950-2050 (both sexes, data source: (United Nations, 2015b))

Note: The classification of world regions is based on the United Nations Statistics Division, Department of Economic and Social Affairs regional groupings. The projections are based on the medium scenario (United Nations, 2015b).

The remarkable increase in life expectancy accompanied by falling fertility rates has reshaped the age structure by shifting the majority of the population from younger to older age groups

(Bongaarts, 2009, Kinsella and Phillips, 2005). Worldwide, the number of individuals aged 60 years and above is growing faster than any other age group. **Figure 1.4** shows the population pyramids in 1950, 2000 and 2050, which illustrate the changes in the size and age structure of the global population over time. Over the last half-century, the proportion of children aged 0-14 years has steadily declined from 34.4% in 1950 to 26.1% in 2015. In the following three decades, the proportion of children is projected to drop to 21.3%. In 2050, for the first time in human history, the older population will surpass the younger (United Nations, 2015b).

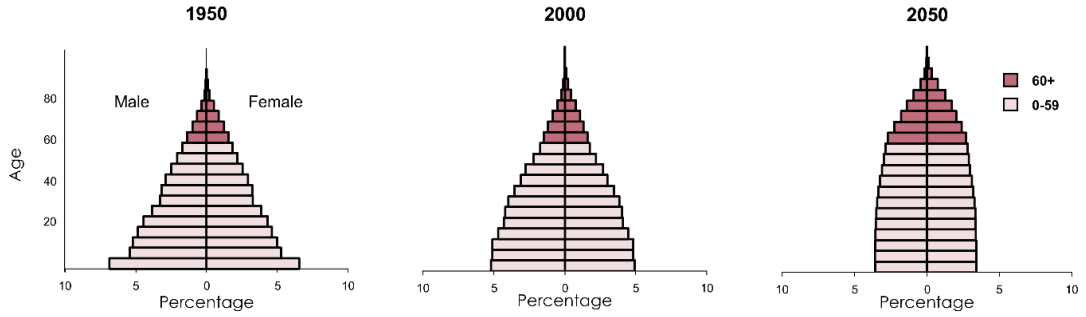


Figure 1.4. World population pyramid, 1950-2050 (source: (United Nations, 2002))

In 2015, there were 7.3 billion people, among whom 12.3% (901 million) were aged 60 years or over. According to the projections by the United Nation's Population Division (UNPD) (United Nations, 2015b), the share of older people is expected to increase in the years to come, causing almost every society in the world to face the implications of population ageing (**Figure 1.5**). From 2015 to 2050, the global population is projected to increase to 9.7 billion. In this timeframe, the population aged 60 years and above will increase by 123.2%, to 2.1 billion, accounting for 21.5% of the total world population. Geographically, this ageing process is especially advanced in Europe and North America, where more than one in five persons were 60 years or older in 2015 already. By 2050, older persons are expected to account for more than one-third of the population in Europe and more than one-fourth in North America. The ageing process is also occurring rapidly in Latin America and the Caribbean, Asia and Oceania, where nearly one-fourth of the population will be elderly in 2050. Despite being at the earlier stages of demographic transition, the African region will almost double its proportion of older population to around 10% by 2050 (World Health Organization, 2015b, United Nations, 2015b).

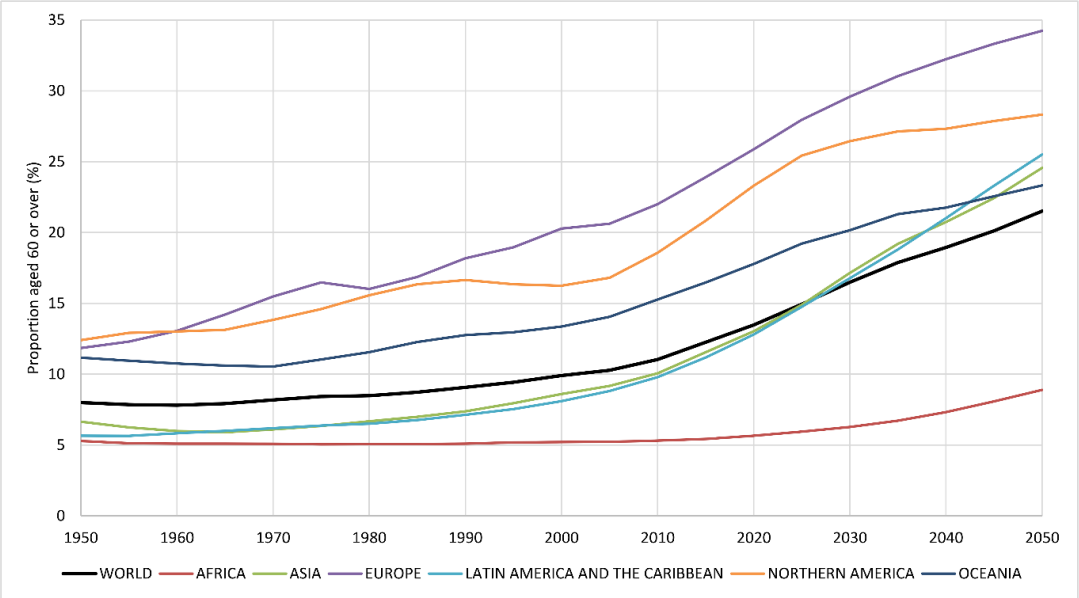


Figure 1.5. Proportion of people aged 60 years or over by region, 1950-2050 (both sexes, data source: (United Nations, 2015b))

Note: The classification of world regions is based on the United Nations Statistics Division, Department of Economic and Social Affairs regional groupings. The projections are based on the medium scenario (United Nations, 2015b).

This global ageing process is not only an issue of changing proportions of younger and older persons in a population. As population ageing continues to take place, the number of people aged 80 years and over is growing even faster than the number of older population overall (United Nations, 2005). As a larger proportion of old people survive to more advanced ages, this progressive demographic ageing of the older population itself has become a notable issue of concern, and it is essential to differentiate among the age groups of older people (United Nations, 2002). **Figure 1.6** shows the age distribution of the older population itself as estimated by the UNPD from 1950 to 2050. It shows how the share of the oldest among the old persons (those over 80 years) within the older population was 7% in 2013, but it is projected to reach 20% in 2050. In terms of absolute numbers, there were 14.2 million people aged 80 years and over worldwide in 1950. Since then, the number of the oldest persons increased by 782.1% to 125.3 million in 2015, and is projected to increase by another 246.8% over the next three decades, reaching nearly 434.4 million in 2050 (United Nations, 2015b). Undoubtedly, the twenty-first century is expected to be the century of human population ageing (United Nations, 2004).

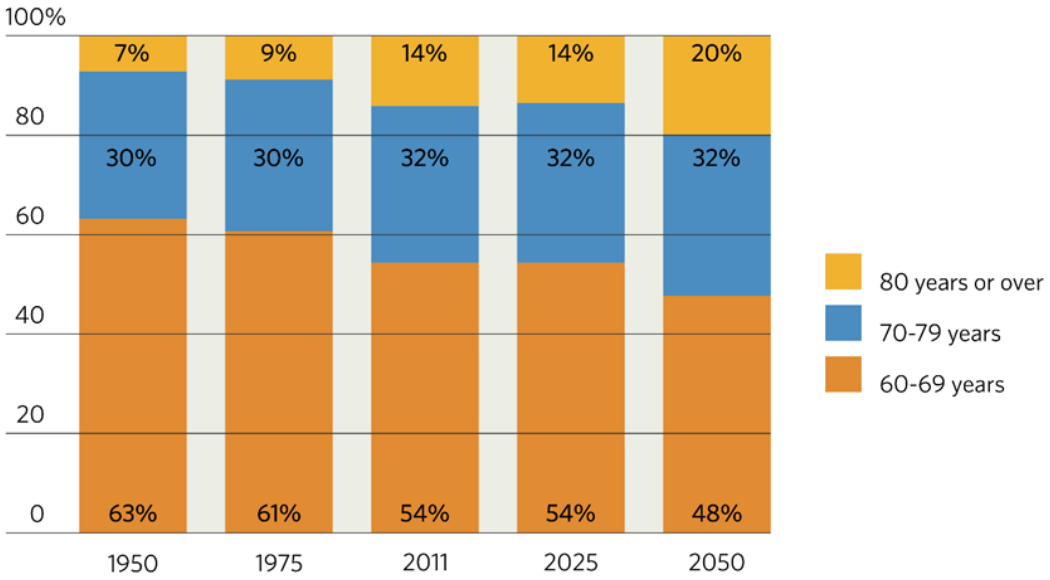


Figure 1.6. Share of the global older population by age group, 1950-2050 (source: (United Nations Population Fund, 2012))

1.2.2 Ageing in China

The People's Republic of China, which was established in 1949, is the most populous country in the world. In the global context, China has not been spared from population ageing process and it is facing numerous challenges at a relatively early stage of development (United Nations, 2015a, Smith and Majmundar, 2012). In the past decades, largely due to improved health care and living standards, China has experienced one of the fastest demographic transitions in the world, which can also be regarded as the combination impact of low fertility, rising life expectancy and the cumulative effect of past changes in the birth and death rates (Banister et al., 2012, Li, 2015a, Department of Ageing and Life Course, 2015).

Of all of the determinants of demographic structure, the decline in total fertility rate is the key factor in the population dynamics of the Chinese population. From 1950 to 1995, the total fertility rate fell from approximately 6 children per woman to under 2, and from 2000 it started to hover around 1.5 children per woman (**Figure 1.7**). This decline, which has been especially rapid in the period of 1970-1980, was mainly reinforced by the "later, longer, fewer" (later marriage and age at first birth, longer inter-birth intervals, and fewer births) campaign, which was then followed by the formal introduction of the one-child policy in 1979. Due to the central and local government efforts leading up to its strict adoption, most parents in urban areas had only one child. However, in most rural areas where son preference was prevalent, this policy

was only partially implemented and rural parents with a first-born daughter were allowed to have a second child after five years (Choukhmane et al., 2013, Hesketh et al., 2005, Zeng and Hesketh, 2016). In the long run, the total fertility rate in China fell below the replacement level of 2.1 children per woman from the early 1990s (He et al., 2016). After a gradual decline until 1995, the total fertility rate has stabilised at near 1.7 children per woman (Hesketh et al., 2005). According to the UNPD estimates, the total fertility rate in China was 1.6 children per woman in 2015 and is projected to reach 1.7 by 2050 (United Nations, 2015b). From 2015, the one-child policy was formally replaced by a universal two-child policy, which allows almost all Chinese couples to have two children. However, in contemporary China, the impact of the new policy on the improvement of the total fertility rate level may be less than expected (Zeng and Hesketh, 2016, Attané, 2016).

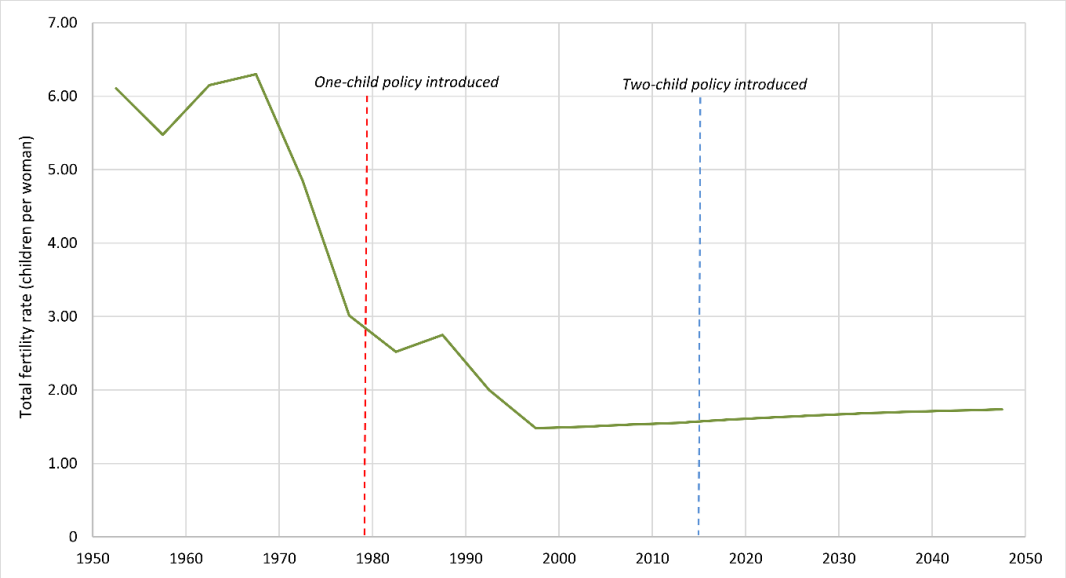


Figure 1.7. Total fertility rate in Mainland China: 1950-2050 (data source: (United Nations, 2015b))

Note: The projections are based on the medium scenario (United Nations, 2015b).

While longevity gains have occurred globally, prolonging of lifespan as a result of a highly compressed process of mortality decline has also obviously played an important role in China's ageing process (Li, 2015a, Department of Ageing and Life Course, 2015). Since 1950, life expectancy at birth for both sexes in China has successfully increased by more than 30 years, from 43.4 years to 75.4 years in 2015 (**Figure 1.8**). This is almost 9 years higher than the average level of less developed countries (67.0 years in 2015), and only about 3 years lower than the average level of the more developed countries (78.3 years in 2015) (Guilmoto

and Jones, 2015, United Nations, 2015b). Although remarkable improvement in life expectancy has occurred in both sexes, Chinese women were advantaged relative to Chinese men in terms of survival rates. The life expectancy at birth for women was 3 years higher than that for men in 2015 (77.0 vs. 74.0 years). With this trend continuing in the next three decades, the national life expectancy at birth is projected to increase to 82.5 years, and the sex difference will shrink to 1.7 years (83.4 in females vs. 81.7 in males) by 2050 (United Nations, 2015b).

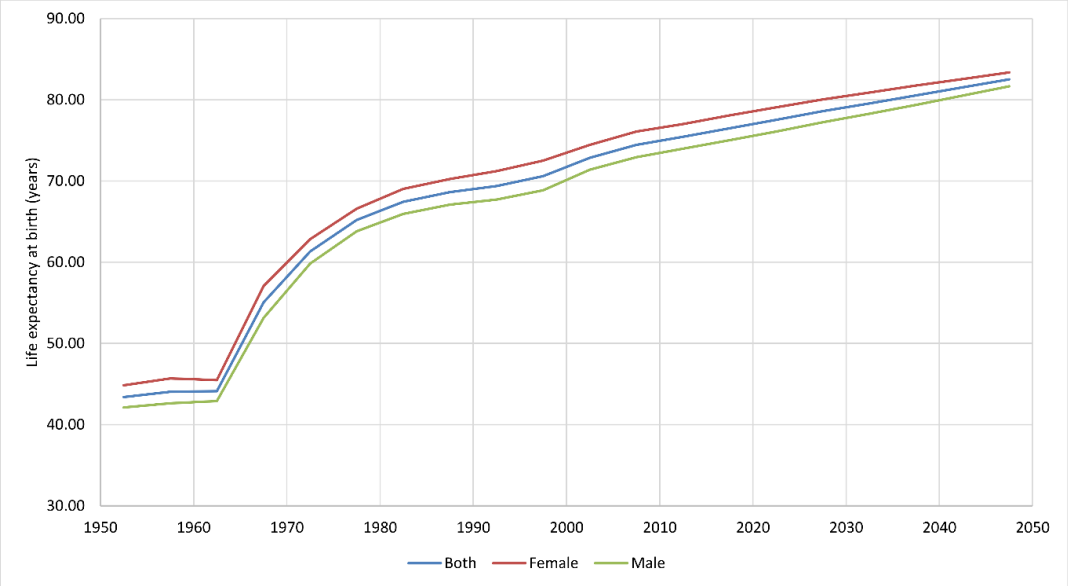


Figure 1.8. Life expectancy at birth in Mainland China: 1950-2050 (data source: (United Nations, 2015b))

Note: The projections are based on the medium scenario (United Nations, 2015b).

As a combined result of early and steep fertility decline, long-term sub-replacement fertility, and greater longevity, a significant change in China's population age structure has occurred (**Figure 1.9**). The low level of fertility rates brought the decline in the number of young people, whereas the improved life expectancy increased the number of older people within the society (Lee and Reher, 2011, Lee, 2003). In 1950, the proportion of children aged 0-14 years was 34.3%, and that of people aged 60 or over was 7.5%, shaping a typical population pyramid with a broad base of young people. During the last few decades, characterised by a large economic growth, the proportion of children aged 0-14 years has rapidly declined to 17.2%, whereas that of people aged 60 or more grew to 15.2% in 2015. As a consequence, China's population pyramid shape has shifted from "triangular" to "irregular". According to the UNPD estimates, the proportion of older population will surpass that of younger population by 2020 in China, 30 years ahead of the global trend (United Nations, 2015b). Furthermore, in the

coming decades up to 2050, the proportion of children aged 0-14 years is projected to drop to 13.5%, and those aged 60 and over are set to form a larger share of the population (36.5%), with the population pyramid moving to an olive shape (United Nations, 2015b, Zhang et al., 2012).

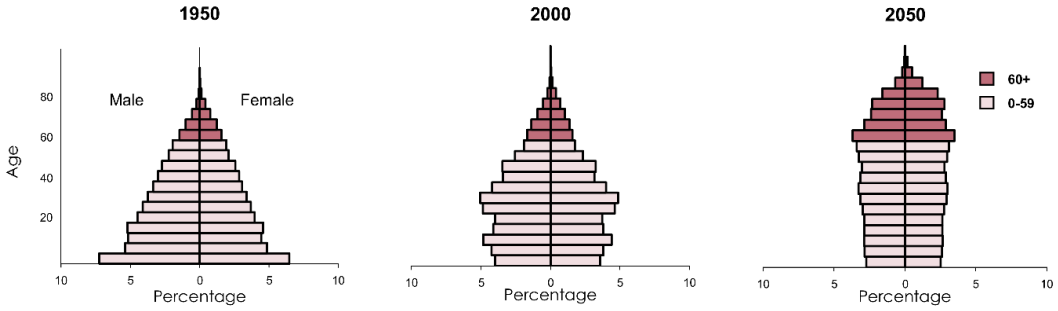


Figure 1.9. China population pyramid, 1950-2050 (source: (United Nations, 2002))

Over a period of roughly half a century, China has completed its demographic transition from a low rate of natural increase, due to high fertility and high mortality, to a low rate of natural increase as a result of low fertility and low mortality (Lee and Reher, 2011). If the current demographic transitions continue, it is estimated that by 2025 China will be surpassed by India in overall population size and become the second most populous country in the world. However, the ageing process is more rapid in China than in India, or even in most other developing countries worldwide (Guilmoto and Jones, 2015, Department of Ageing and Life Course, 2015, Mai et al., 2013). According to UNPD estimates, the total population was 1.4 billion at the end of 2015, of which 209.2 million were older people aged 60 years and over, or 15.2% of the total population. The share of older people is expected to continue to increase almost continuously in the coming years (**Figure 1.10**), and by 2050, one in three Chinese persons will be 60 years or older.

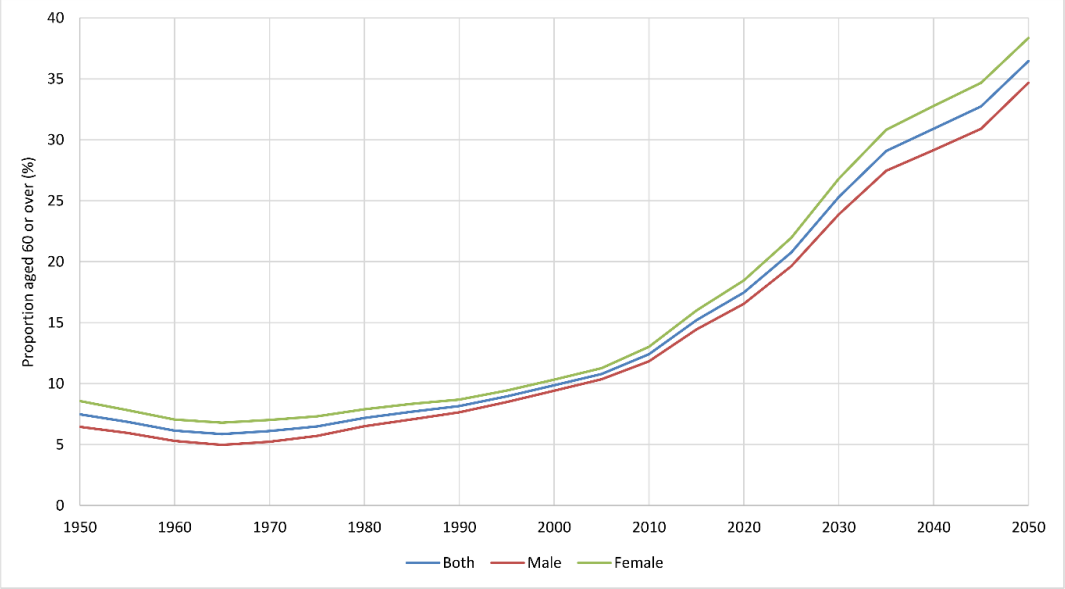


Figure 1.10. Proportion of people aged 60 years or over in Mainland China: 1950-2050 (data source: (United Nations, 2015b))

Note: The projections are based on the medium scenario.

Population ageing is now a prominent phenomenon across the whole country, largely due to improved survival of the elderly. Consequently, the group of the oldest among the old population, those aged 80 years or more, have gone through remarkable growth - from 0.3% in 1950 to 1.6% in 2015 of the total population. This is expected to reach 8.9% in the next three decades until 2050 (United Nations, 2015b). As the fastest growing segment of the older population, the 80+ years accounted for only 3.7% of the older population in 1950, and then increased to 10.7% in 2015 (**Figure 1.11**). This trend is expected to accelerate in the next three decades, with the share of 80+ years within the older population projected to be five times as large as it is at present by the year 2050. With an overall size of 120.6 million, China will inevitably face large challenges linked to the ageing population by 2050, with almost one in four older people being 80 years and older. Over time, this pronounced upward shift in the age structure is prone to generate a substantial increase in the demand for both formal and informal medical and long-term care services in China.

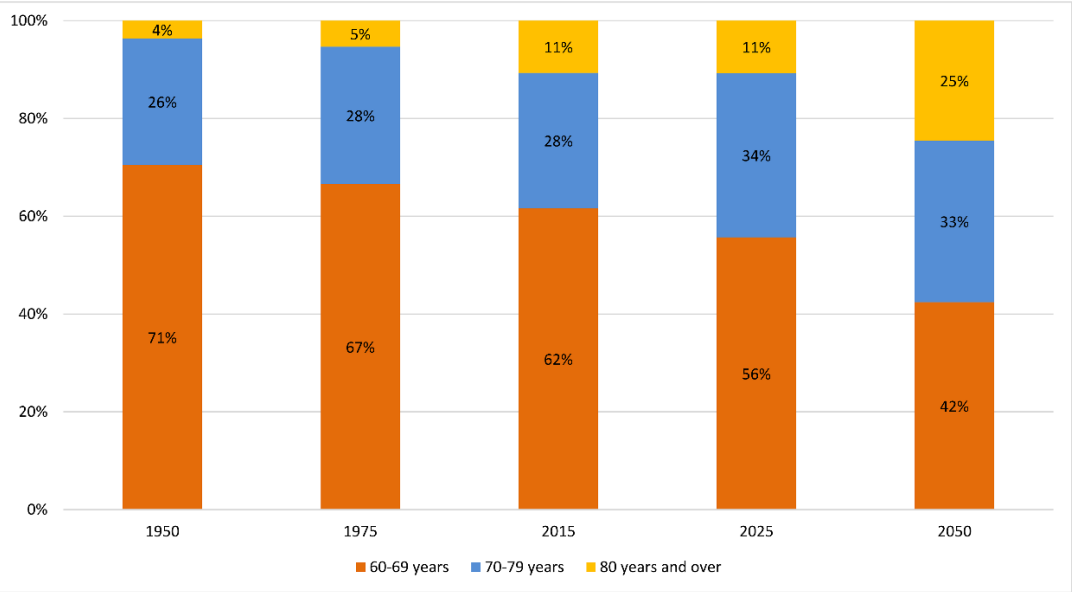


Figure 1.11. Share of the older population by age group in Mainland China, 1950-2050 (data source:(United Nations, 2015b))

China is an unevenly developed country and, as such, disparities remain between the urban and the rural, the rich and the poor. These disparities contribute to varying patterns in lifestyle, morbidity and mortality rates across regions (Woo et al., 2002, Peng et al., 2010). With the nationwide ageing trend, the proportion of older population has increased from 7.1% to 12.1% in urban areas, and from 7.8% to 13.7% in rural areas between 1982 to 2005. Due to rapid urbanisation and inner labour migration, this urban-rural disparity is likely to grow (Wang et al., 2005, Cai et al., 2012). It is estimated that the proportion of the older population will reach 14.8% in urban areas and 21.8% in rural areas by the year 2030 (Cai et al., 2012). In addition, people living in rural areas and the poor are generally more disadvantaged in terms of survival and health (Yu et al., 2012, Peng et al., 2010, Zhang et al., 2012). This exacerbates the challenge of dealing with population ageing in rural and less developed areas. In such circumstances, the increasing degenerative disease burden and social implications associated with ageing have become one of the most important agendas for the Chinese government. As a result, studies estimating the burden of degenerative diseases are necessary and timely to inform policy making (Woo et al., 2002, Department of Ageing and Life Course, 2015).

1.3 Health transition

1.3.1 Global Health transition

The previous section explained the demographic transition occurring both globally and in the context of China between 1950 and 2015, with projections until the year 2050. In parallel with this phenomenon of demographic ageing, a fundamental epidemiological transition has also been taking place across the world - albeit with considerable variations between different populations (Kinsella and Phillips, 2005, McCracken and Phillips, 2012, Omran, 2005). Health transition, which is also referred as a combination of demographic and epidemiological transitions, is a broad set of changes in the patterns and causes of morbidity (illness) and mortality (death) (Kinsella and Phillips, 2005, World Health Organization, 2011a, McCracken and Phillips, 2012). As initially categorized by Omran (Omran, 2005), health transition involves a sequence of three stages (**Table 1.1**). The first stage, the 'Age of Pestilence and Famine', is marked by fluctuating mortality at high levels and high prevalence of infectious and parasitic diseases, such as tuberculosis, influenza and diarrhoea. The second stage, the 'Age of Receding Pandemics', is a transitional phase characterised by decreasing mortality, a decline in the prevalence of infectious diseases and an increase in the prevalence of chronic degenerative diseases. Gradually, the second stage gives way to the third stage, the 'Age of Degenerative and Man-Made Diseases'. In this stage, mortality continues to decline until it stabilises at a low level, and the major causes of death are chronic degenerative diseases and man-made diseases, such as cardiovascular disease, diabetes and cancer. Since Omran's concept, another widely acknowledged and adopted stage, the 'Age of Delayed Degenerative Diseases', has been added to this transition theory. During this fourth stage, major degenerative causes of death in the third stage remain as prevalent killers, but more concentrated in the older population (Olshansky and Ault, 1986).

Table 1.1. The four stages of health transition

Stage	Life expectancy	Mortality	Morbidity
Stage 1			
Age of Pestilence and Famine	20~40 years	Extremely high mortality	Epidemic infectious diseases, nutritional disorders
Stage 2			

Stage	Life expectancy	Mortality	Morbidity
Age of Receding Pandemics	30~50 years	Declining mortality	Infectious diseases and malnutrition
Stage 3			
Age of Degenerative and Man-Made Diseases	>50 years	Lower mortality with a peak in older people	Non-communicable diseases and injuries
Stage 4			
Age of Delayed Degenerative Diseases	up to 80-85 years	Rapid declining mortality in advanced age	Degenerative diseases concentrated in advanced ages

At the global level, population ageing has emerged as a significant trend in almost every country. Improved longevity has brought non-communicable diseases (NCDs) to the fore as the most important source of global disease burden, responsible for 56.3% in 2015, with this projected to rise substantially to almost two thirds in 2030 (World Health Organization, 2015a). Generally, health transition is highly associated with modernisation and urbanisation, especially improvements in the standard of living and education (Defo, 2014, Omran, 2005). Health transition firstly emerged in industrialized countries, almost a century ago. For most developed countries, this transition has stabilised at the fourth stage (Santosa et al., 2014). Evidence from the Global Burden of Disease (GBD) project (**Figure 1.12**) suggests that, when measured by the Disability Adjusted Life Years (DALYs) - a summary measure of the overall burden of disease - 86.6% of all the disease burden was caused by NCDs in high-income countries in 2015. This share will become even larger in the next decade (Alwan, 2011, Institute for Health Metrics and Evaluation, 2015, Mathers and Loncar, 2006, GBD 2015 DALYs and HALE Collaborators, 2016). However, the emergence of NCDs is not limited to affluent countries. The proportion of the total burden of disease in middle-income countries attributable to NCDs was 68.8% in 2015, and has a larger potential to increase remarkably to 76.2% by 2030. Even in the poorest low-income countries, NCDs are predicted to be an increasingly important cause of morbidity and mortality, where the proportion of disease burden will increase from 42.4% in 2015 to more than half of all the disease burden in 2030 (World Health Organization, 2011a, World Health Organization, 2015a).

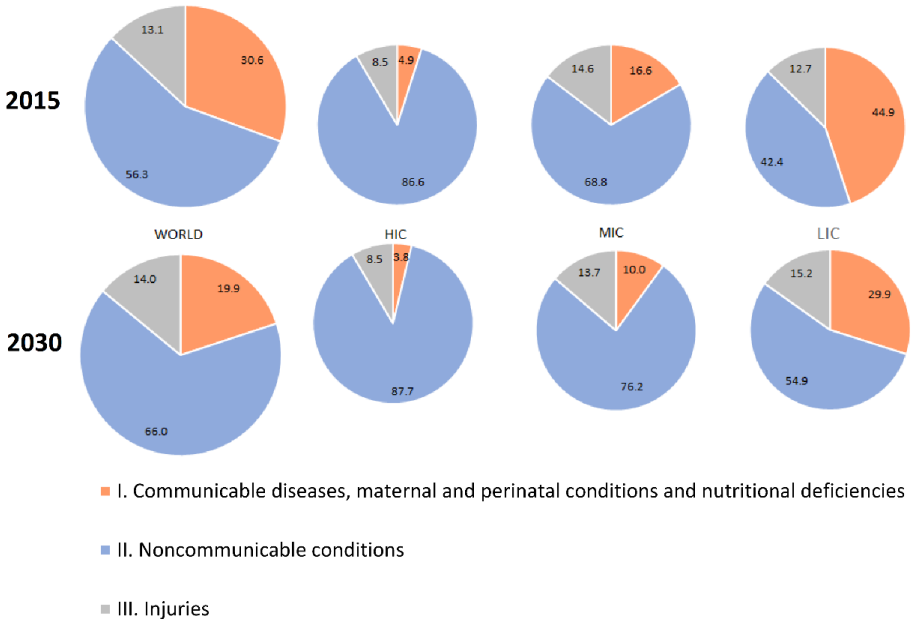


Figure 1.12. Share of disease burden by broad cause and the World Bank income group: 2015 and 2030 (data source: (World Health Organization, 2015a))

Note: HIC, high-income countries; MIC, middle-income countries; LIC, low-income countries (World Health Organization, 2015a).

Susceptibility to NCDs increases with age, and with the trend in worldwide population ageing, the rise in the burden of NCDs presents important challenges for global health in the 21st century. According to the GBD estimates, NCDs have become the dominant causes of disease burden in older population irrespective of their economic status (Beard et al., 2016, Prince et al., 2015). As shown in **Figure 1.13**, almost 90% of the total disease burden in people aged 60 years and older was attributable to NCDs in 2015, and its predominant order did not vary greatly by the income group. In the next decade, it is projected that this predominant contribution of NCDs in the older population will become even more pronounced. By 2030, the share of NCDs attributable to the total disease burden will be more than 90% in every region of the world, even in low-income countries. However, older people in those settings die or are disabled at a relatively younger age than those in high-income countries. Historically, despite the fact that health transition is increasingly placing the greatest burden of disease on non-communicable conditions, which are more associated with older population, NCDs in poor settings receive low priority in health policies and financing. The potential challenges of NCDs to economies, health care systems, informal care and individuals may be much larger

in the middle- and lower-income countries than in other well-developed economies (Yu et al., 2012, World Health Organization, 2011a, Sousa et al., 2009).

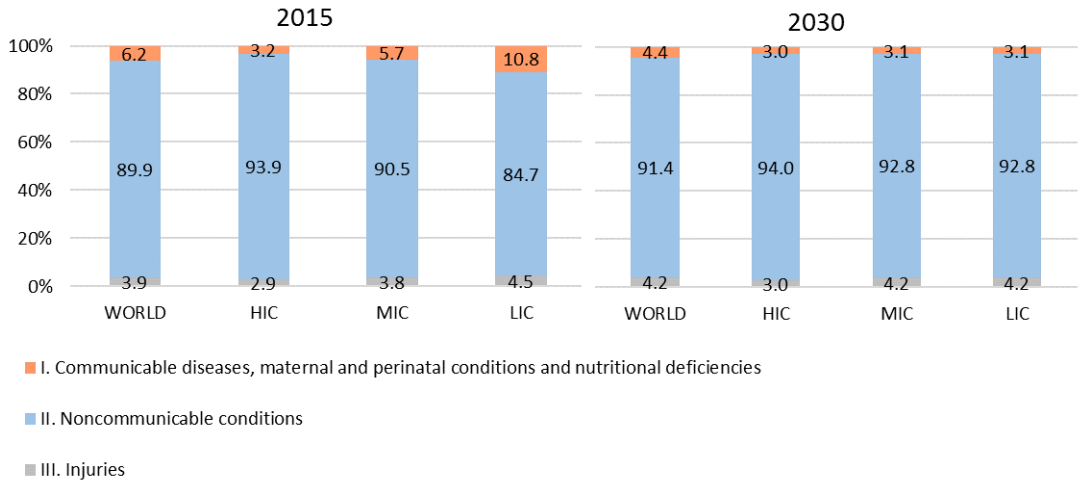


Figure 1.13. Disease burden in older population by broad cause and world bank income group: 2015 and 2030 (data source: (World Health Organization, 2015a))

Note: HIC, high-income countries; MIC, middle-income countries; LIC, low-income countries (World Health Organization, 2015a).

1.3.2 Health transition in ageing China

As stated in the previous section, NCDs have replaced communicable diseases as the most important contributing factor to the global disease burden, regardless of development levels. Compared with other low- and middle-income countries, China is catching up quickly with the high-income countries in terms of its disease burden profile. It is widely acknowledged that China has already stepped into the fourth stage of health transition (Santosa et al., 2014). According to the GBD estimates, NCDs showed a strikingly increasing trend in the share of disease burden in China in the last two decades (**Figure 1.14**). In 2015, 81.3% of the disease burden was contributed by NCDs, which was much higher than the contemporary global level of 56.3%, and only slightly lower than that of high-income countries (86.6%). The older population has seen an increasing share of NCDs as the source of disease burden during the last two decades, although at a relatively slower pace. From the beginning of the 21st century, the share of total burden of disease attributable to NCDs started to fluctuate around 93%.

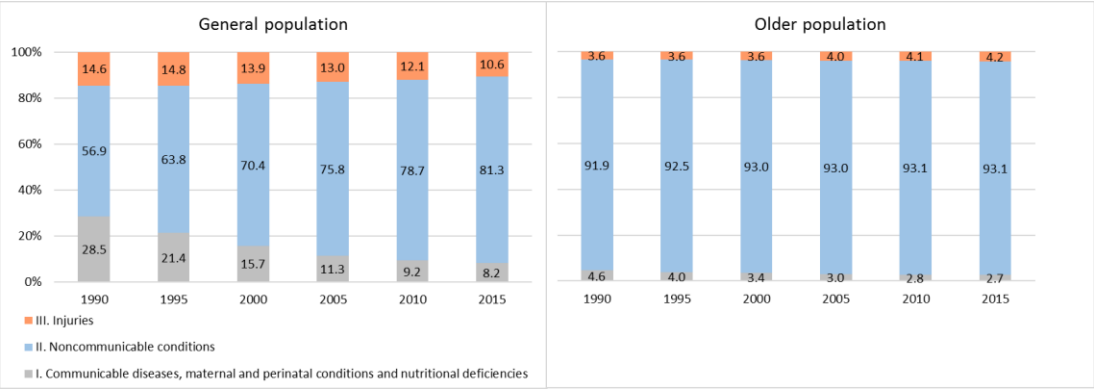


Figure 1.14. Share of disease burden by broad cause in China from 1990 to 2015: in general population and older population (data source: (Institute for Health Metrics and Evaluation, 2015))

Figure 1.15 presents the change in leading causes of disease burden measured by DALYs from 1990 to 2015. In general population, lower respiratory infections, cerebrovascular disease and neonatal preterm birth were the three leading causes of disease burden in 1990; by 2015, no communicable diseases, maternal and perinatal conditions, or nutritional deficiencies remained at the list of leading causes. Instead, during this period, the disease burden due to a subset of NCDs increased significantly, including ischaemic heart disease, low back and neck pain and sensor organ disease. Due to the limitation of GBD data availability, the group of people aged 70 years and over (instead of 60 years and over due to the availability of GBD data) was chosen to illustrate the decomposition of disease burden in older population (Institute for Health Metrics and Evaluation, 2015). From 1990 to 2015, for people aged 70 years and older, the top ten causes of disease burden were exclusively NCDs, with cerebrovascular disease, ischemic heart disease, sense organ disease, Alzheimer disease, lung cancer, low back and neck pain all climbing up the ranks. Although a few data are available to allow projections of the future disease burden in China, along with the trends in urbanisation, rising incomes and longevity, it appears inevitable that NCDs will keep rising, with age-related diseases being the fastest-growing group.

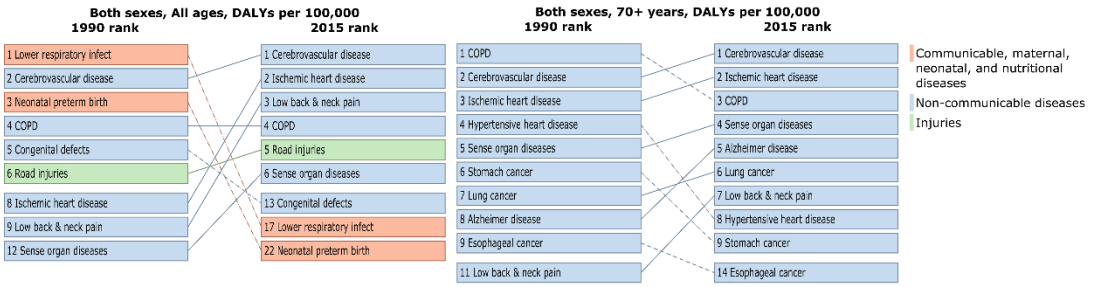


Figure 1.15. Leading causes of disease burden in China from 1990 to 2015: in general population and people aged 70 years and over (source: (Institute for Health Metrics and Evaluation, 2015))

Health transition in China has promoted NCDs into the leading source of the disease burden. Among these long-term diseases, conditions with severe disability rates, or of long duration, may confer an even larger burden than those that have no impact on life, or are of shorter duration (World Health Organization, 2008, GBD 2015 Disease and Injury Incidence and Prevalence Collaborators, 2016). With advancing age, sensory and motor performance decreases. The incidence of disabilities related to mobility and independence grows, while decreasing people's ability to live in full health. To a large extent, this phenomenon is particularly prevalent in the oldest age groups, despite the benefits from longevity (World Health Organization, 2011c, Motl and McAuley, 2010). In China, the fast-growing number of older persons and the increasing disease burden attributable to NCDs have left a relatively high proportion of older people with disabilities. With the ageing trend, this number is expected to continuously grow. It was reported that there were 9.4 million completely disabled and more than 18.9 million partially disabled older people in 2006 (Wang, 2009). The Years Lived with Disability (YLDs) is an indicator calculated by multiplying the prevalence of a disorder by the short- or long-term loss of health associated with that disability (GBD 2015 Disease and Injury Incidence and Prevalence Collaborators, 2016). When assessed by YLDs, the top causes of disability in the general Chinese population in 1990 were lower back and neck pain, sensory organ diseases and skin diseases. Over more than two decades, lower back and neck pain and sensory organ diseases remained the top two causes of disability, whereas the third leading cause - skin diseases - were replaced by depressive disorders in 2015 (**Figure 1.16**). In older people (aged 70 years and over due to the availability of GBD data), the spectrum of leading causes of disability was different, with sensory organ disease identified as the leading cause, and lower back and neck pain the second in both 1990 and 2015. In this group, the third leading cause of disability was chronic obstructive pulmonary disease (COPD) in 1990, which was then replaced by Alzheimer disease in 2015.

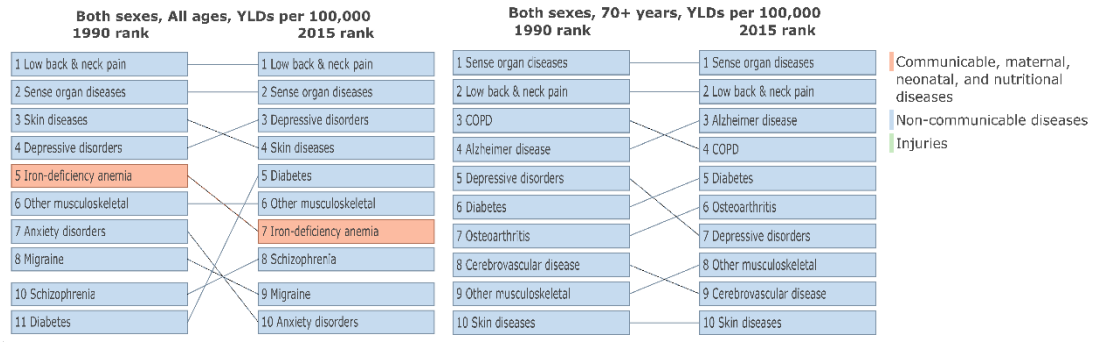


Figure 1.16. Leading causes of disability in China from 1990 to 2015: in general population and people aged 70 years and over (source: (Institute for Health Metrics and Evaluation, 2015)).

In the coming few decades, the older Chinese population is likely to rise to a historically unprecedented level. Rising disability burden and corresponding long-term care needs will become the most important challenges for the society (Woo et al., 2002, Department of Ageing and Life Course, 2015). The opposite is true for China where, unlike in the developed world - which firstly became richer, and then older - the population is ageing while the economy is still growing. Thus, it is important to realise that there will only be limited resources to support the upcoming long-term care needs for older people in the Chinese context (Woo et al., 2002, Zhang et al., 2012). These challenges should be placed as foci for investment in health infrastructure. The Chinese central government has initiated policies to encourage private and foreign investment in building nursing homes and care homes. However, it is still a common perception that these profit-driven institutions will serve primarily older people from wealthier families, and thus the informal care pattern, usually from family members, will still be the predominant pattern of long-term care in China (Zimmer and Kwong, 2003, Chu and Chi, 2008).

1.4 Ageing and the eye

1.4.1 Introduction

The classical sensory function senses of the human body include vision, hearing, smell, taste, and touch (Correia et al., 2016). Among these five senses, visual sense has often been considered as the most important (Wang et al., 2014a). Sight is essential for determining directions, identifying people and objects, adjusting movement and social behaviour and, thus,

deemed as essential for conducting daily activities. When vision is impaired or absent, a person's ability to function will be largely affected (Leo et al., 1999). In addition, although vision loss is not a life-threatening condition, it is widely regarded as highly associated with disability, placing a huge burden on caregivers and society (West et al., 2002, Li et al., 2011). As the lifespan increases globally, there is a dramatic increase in age-related disability, including especially eye-related diseases. Currently, vision loss is the leading cause of age-related disability in developing countries, where 94 million older people are affected (**Figure 1.17)**. This may also be the situation in China, where sense organ diseases are the leading causes of disability in older population, as noted in the previous section (Atal et al., 2016, Institute for Health Metrics and Evaluation, 2015). With the unprecedented rate of growth of the older population, combating preventable vision loss must be listed as one of the leading public health priorities. Furthermore, there is a continuing need for an up-to-date understanding of the magnitude and characteristics of vision loss. In this section, the nature, burden and impacts of vision loss will be presented, with an emphasis on age-related eye conditions.

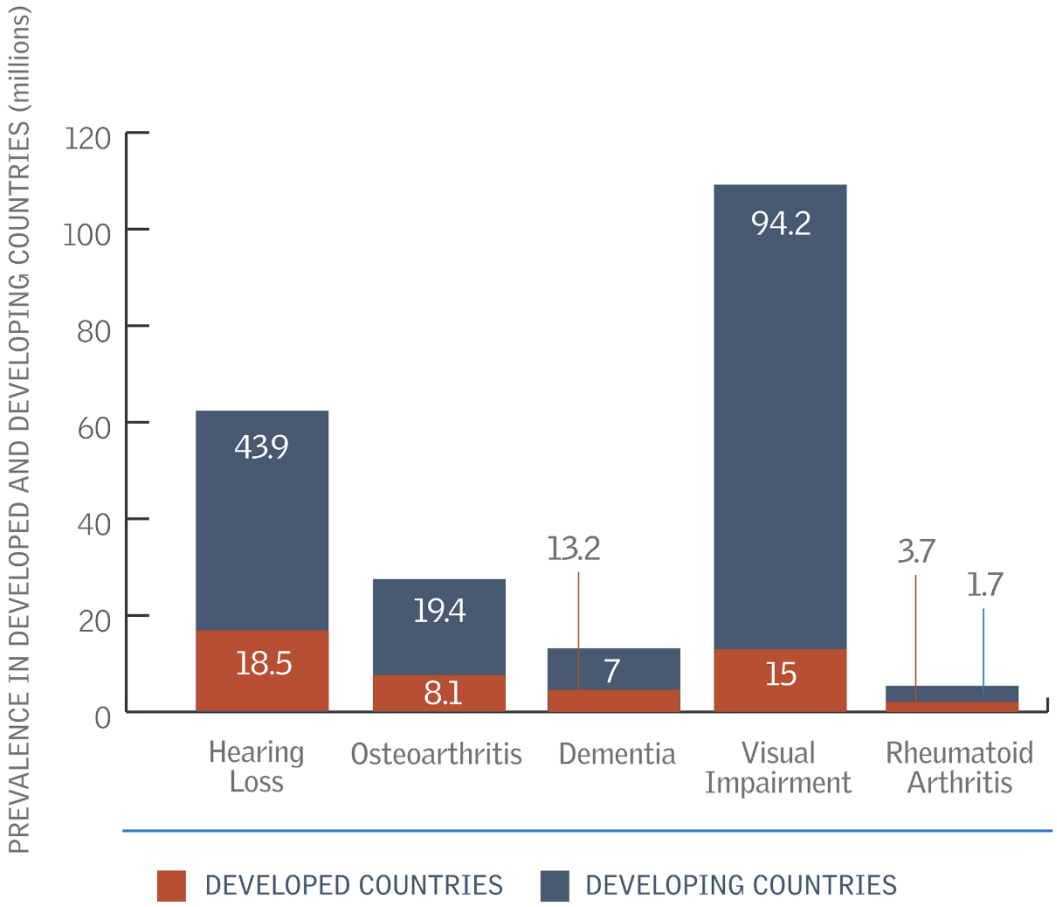


Figure 1.17. Global prevalence of moderate and severe disability in older people in 2011 (source: (International Federation on Ageing, 2012))

1.4.2 Ageing effects on the eye

The human eye is the organ of sight. It serves as an important tool in many activities during daily life, collecting information from surrounding environments (Agarwal et al., 2002). As one of the most important and sensitive organs in the body, the eye contains several incredibly complex structures. Each part is essential for clear vision, and any damage may lead to severe visual impairment, or even blindness (World Health Organization, 2014b, Fairchild, 2013). **Figure 1.18** shows the schematic diagram of the horizontal cross-section of a human eye, highlighting the important parts such as the cornea, iris, pupil, lens, retina, fovea and optic nerve. These structures are separated by three chambers, namely, the anterior, posterior and vitreous chambers (Myers, 2003).

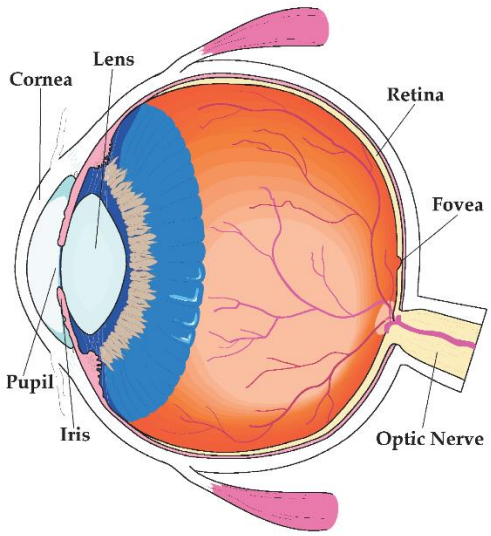


Figure 1.18. Anatomy of the human eye with some key structures labelled (source: (Fairchild, 2013))

Compromised function of the eye is becoming increasingly prevalent with ageing. Advancing age has been revealed as one important factor that increases the chance of developing age-related eye diseases (Lin et al., 2016, Chader and Taylor, 2013). At the biological level, the ageing process is associated with gradual accumulation of a wide variety of molecular and cellular damages, ultimately leading to impairment of anatomic and physiological functions

(Tosato et al., 2007, Michael and Bron, 2011). **Figure 1.19** presents several age-related dysfunctions of major structures and the corresponding diseases.

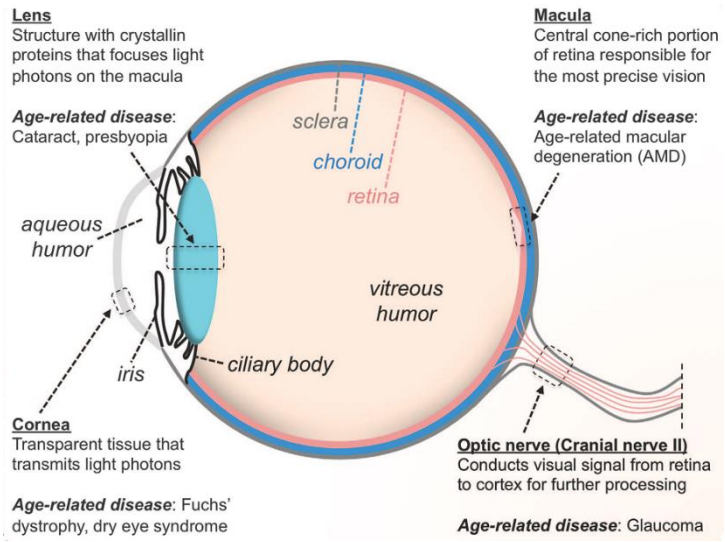


Figure 1.19. Major age-related eye diseases and the affected structures (source: (Lin et al., 2016)).

The cornea is the front transparent outer coating through which, as the principle refractive element of the eye that is responsible for nearly two-thirds of the eye's refractive power, incoming light rays pass and move through into the anterior chamber (Myers, 2003, Agarwal et al., 2002). With ageing, the functioning of the corneal endothelium, the innermost layer of cells in the cornea, begins to deteriorate. Since the endothelium cannot be regenerated, the overall endothelial cell density reduces during this process, resulting in a fluid buildup in the cornea, known as corneal swelling (Fuchs' Endothelial Dystrophy) (Cerulli and Missiroli, 2008). In addition, ageing itself is associated with decreased tear production, making dry eye syndrome more prevalent in older people (Sharma and Hindman, 2014, Mathers, 2000).

The iris is a thin, circular and multi-level structure. Iris colour, which varies due to the amount of pigments formed by melanocytes, gives a specific characteristic to eye colour. The centre of the iris is the pupil, which regulates the amount of light entering the inner globe of the eye. Pupil varies with different illumination levels. Its size is controlled by dilator and sphincter muscles of the iris. Pupil size increases in the dark and decreases in the bright light chamber (Myers, 2003, Agarwal et al., 2002). With ageing, the iris becomes less reactive and more difficult to dilate, while pupil size also diminishes, so that less light enters the eye (Salvi et al., 2006).

The lens is located directly behind the iris and the pupil. It is a biconvex transparent structure that provides around a third of the eye's refractive power, and works together with the cornea to reflect light into the retina. Similar to the cornea, the lens is adjustable to focus light rays. Ciliary muscles control the shape and curvature of the lens through the accommodation process, focusing on different objects that are either nearby, or at a distance. The lens becomes "fatter" to increase optical power when focusing on near objects, and becomes "flatter" to decrease optical power when focusing on distant objects (Fairchild, 2013, Agarwal et al., 2002). In the lens, a decline of accommodation initiates in infancy. At younger ages, accommodation for near sight is achieved by ciliary muscle contraction, which relaxes zonular tension and changes the lens to become more globular. Over time, lens fibre and zonules stiffen, gradually restricting the rate and amplitude of accommodative power, a process known as presbyopia (Michael and Bron, 2011, Bron et al., 2000). During ageing, the accumulation of yellow pigments in the lens also decreases the transmission of blue light. The loss of the ultraviolet (UV) ray filter function thus increases phototoxic lesions of the retina (Lin et al., 2016, Bron et al., 2000). Furthermore, ageing brings opacities in the lens, ultimately leading to lens opacification or even cataract (Zhang et al., 2016, Michael and Bron, 2011).

After the lens, light rays pass through the vitreous humour and reach the retina. The retina is the most important part of the eye, which lies on the inner surface of the eye. The retina is responsible for the transduction of light energy into neural signals by means of photoreceptors, the only neurons that are directly sensitive to light (Lin et al., 2016, Agarwal et al., 2002). The human eye contains two types of photoreceptors: rods and cones. There are approximately 126 million photoreceptors in the retina - 120 million rods and 6 million cones. Rods support the black and white vision and mainly function in low light, and are spread evenly in the retina, except at the fovea. Cones provide daytime vision and the perception of colour, their density reaching the peak in the centre of the retina, namely, macular (Agarwal et al., 2002). The fovea is located near the centre of the macula. It is a small pit that contains the largest amount of cones. The macula is the only part of the retina where neuronal and vascular circuits bend sideways, so the photoreceptors can receive light rays directly. Therefore, the macula is responsible for clear central vision, while the fovea provides sharpest detailed vision. The peripheral parts of the retina, which are composed predominately of rods, are responsible for providing grainier or peripheral vision (Fairchild, 2013, Agarwal et al., 2002). With ageing, oxidative damage accumulates within the retina, resulting in age-related retinal dysfunction, or even visual loss, together with pupillary miosis and reduced crystalline lens light transmission. The macula is especially susceptible to environmental stressors. Due to fewer cell layers, the progressive damage of the macula is a common disease, known as age-related

retinal disorders -including age-related macular degeneration (Bonnel et al., 2003, Gao and Hollyfield, 1992).

The last key structure after the retina is the optic nerve, which is responsible for transferring visual signals from the retina to the vision centres in the brain via electrical impulses. The optic nerve is small and nearly unmyelinated from infancy, and then grows rapidly and becomes medullated (Tezel et al., 2007, Agarwal et al., 2002). The optic nerve lies in the back of the retina and is composed of the axons of retinal ganglion cell and glial cells. In the area of the retina where the optic nerve leaves the eye, a blind spot exists - because of the absence of photoreceptors (Fairchild, 2013, Agarwal et al., 2002). With advancing ages, the leptomeninges and fibrous septa become broader, resulting in a progressive loss of ganglion cells and, thereafter, vision damage. Moreover, in the case of glaucoma, intraocular fluid in the cavity behind the eye's lens drains too slowly, or stops draining altogether, leading to damages in the optic nerve and vision loss (Burgoyne and Morrison, 2001, Weinreb and Khaw, 2004).

1.4.3 Visual impairment

1.4.3.1 Definition and classification

Visual impairment generally refers to any condition of the eye or visual system that cannot be corrected to within normal limits. According to the International Classification of Disease (ICD) 10th version, visual function is classified into four levels: normal vision, moderate visual impairment, severe visual impairment and blindness. Moderate visual impairment is defined as best corrected visual acuity of equal to or greater than 6/60 but less than 6/18, and severe visual impairment as best corrected visual acuity of equal to or greater than 3/60 but less than 6/60 (Stevens et al., 2013). Blindness is defined as best corrected visual acuity of less than 3/60 in the better eye or visual field loss in each eye to less than 10° from fixation. Furthermore, moderate visual impairment and severe visual impairment are grouped into the category "low vision", and low vision combined with blindness represents all visual impairment (Dandona and Dandona, 2006, World Health Organization, 2014b).

1.4.3.2 Burden of visual impairment

In 2010, approximately 285 million people globally were visually impaired, of whom 246 million were suffering from low vision and 39 million people were blind (Pascolini and

Mariotti, 2011). Geographically, more than 90% lived in developing countries. **Figure 1.20** provides a closer look at the global distribution of visually impaired people. The most populous countries harboured a large burden of visual impairment. China reported that there were 75 million visually impaired people in 2010, representing more than one-fourth of all the global visual impairment cases. Approximately 80% of visual impairments can be prevented or corrected. However, if no preventive actions are taken and the current trends remain unchanged, the number of blind people is projected to increase four times by 2020 in China. In addition, visual impairments are more common among older people than in any other age groups. Of all visually impaired people globally, about 65% were aged 50 and older, although this age group only comprised about 20% of the world's population (Pascolini and Mariotti, 2011). As the population of older people continues to grow in China, the number of people suffering from vision-related disability will also increase accordingly.

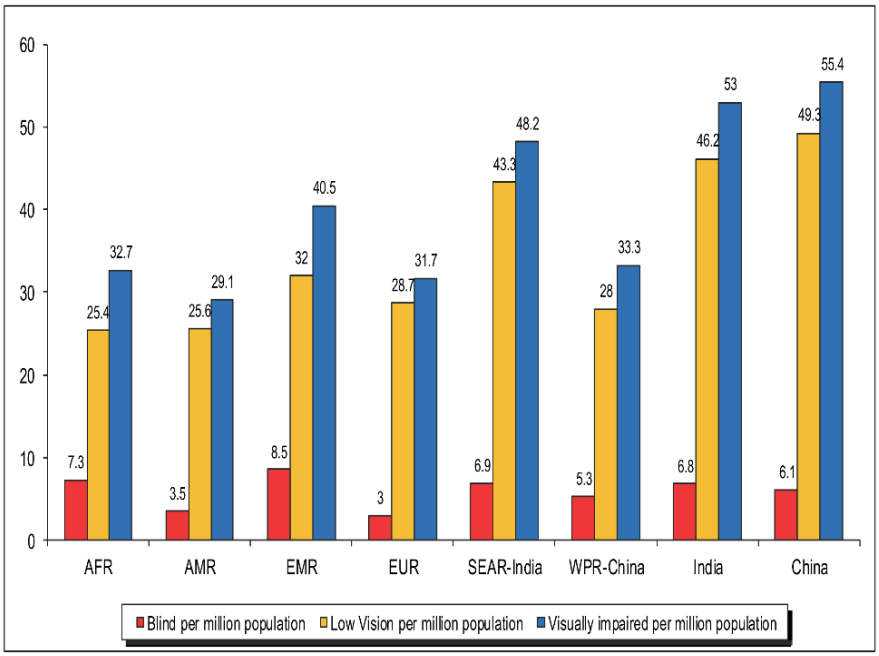


Figure 1.20. Number of people (in thousands) visually impaired and corresponding proportion of the global impairment by WHO region and country (source: (Pascolini and Mariotti, 2011))

Note: AFR, African region; AMR, region of the Americas; EMR, Eastern Mediterranean region; EUR, European region; SEAR, south-east Asian region (without India); WPR, Western Pacific region (without China).

Historically, visual impairment and blindness have been one of the most feared disabilities known to mankind (Loo et al., 2009, Saaddine et al., 2003). Epidemiological studies indicate that visual impairment results in higher rates of falls, hip fracture, poor nutrition, medical errors, and mortality, especially among older people. Furthermore, visual impairments trigger depression and suicidal ideation (Rees et al., 2010, Lam et al., 2008). All these serious events place affected people at a vulnerable status of health and wellbeing, while also having a "snowball effect" on their families, caregivers and the community (Lamoreux et al., 2008, Cacciatore et al., 2004). In addition to causing excess diseases and mortality, visual impairments also lead to tremendous economic burden, especially when indirect costs are taken into account (International Federation on Ageing, 2012, John and David, 2013). Globally, the direct costs of vision loss were $2.3 trillion in 2010, whereas the indirect costs, such as lost productivity and provision of informal and family care reached $652 billion. With an increasing elderly population in many countries, it seems likely that more people will be at risk of visual impairment. It is projected that this total cost will increase to $2.8 trillion for direct costs and $760 billion for indirect costs by 2020 (International Federation on Ageing, 2012). The social and economic implications of visual impairment represent serious public health, social and economic concerns. It is, therefore, vital that the prevention and management of visual diseases becomes a major public health and clinical priority (Dandona and Dandona, 2006, Pizzarello et al., 2004, World Health Organization, 2017a). Indeed, proven cost-effective preventive and curative interventions are available for prevention of avoidable visual impairment, such as low-cost medicines, intra-ocular lens implants and other treatments, and ophthalmic interventions (International Federation on Ageing, 2012, Pizzarello et al., 2004).

1.4.3.3 Causes of visual impairment

In 1999, the WHO and the International Agency for the Prevention of Blindness launched the Global Initiative for the Elimination of Avoidable Blindness, widely known as Vision 2020: The Right to Sight. Their aim was to halt and reverse the estimated doubling of avoidable visual impairment globally between 1990 and 2020 (Pizzarello et al., 2004). The initial framework identified five conditions as immediate priorities: cataract, trachoma, onchocerciasis, childhood blindness and refractive errors and low vision, all of which are preventable or treatable. However, over time, significant shifts have occurred in the pattern of causes of visual impairment, which also varies from country to country, necessitating a more up-to-date and geography-based approach to national, supra-national, continental and global prevention strategies and local programs (World Health Organization, 2014b, Bourne et al., 2013).

Globally, the most common causes of visual impairment in 2010 were identified as uncorrected refractive error (43%), cataract (33%), glaucoma (2%), age-related macular degeneration (1%), diabetic retinopathy (1%) and a large proportion of undetermined causes (18%). The major causes of blindness were cataract (51%), glaucoma (8%), age-related macular degeneration (5%) and the undetermined causes (21%). This new spectrum has promoted a redefinition of the Vision 2020 scheme (Pascolini and Mariotti, 2011), which should include the blindness prevention as well as the rehabilitation and education of persons with irreversible and unavoidable visual impairment (World Health Organization, 2013).

In China, no national statistic on the main causes of visual impairment has been available until recently. Local epidemiological surveys have identified different spectrums (Huang et al., 2009, Xu et al., 2006, Li et al., 2008). In the latest five-year National Plan for Eye Health, cataract, uncorrected refractive error, diabetic retinopathy, glaucoma, age-related macular degeneration, and retinopathy of prematurity were listed as program priorities, most of which were age-related conditions (National Health and Family Planning Commission of the People's Republic of China, 2016).

1.4.4 Age-related macular degeneration

1.4.4.1 Definition and classification

Age-related macular degeneration (AMD) is a degenerative disease of the macula that becomes more clinically apparent with advanced age (Jager et al., 2008, Lim et al., 2012). It is most common among elderly people living in developed countries (Lim et al., 2012, Wong et al., 2014). AMD develops slowly and asymptomatically in its early stages, but can lead to progressive loss of central vision at late or advanced stages (Coleman et al., 2008). Accompanying this central vision loss, motion sensitivity, contrast sensitivity, visual acuity and delayed dark adaption are also affected (Kuyk and Elliott, 1999, Faria et al., 2015, Owsley et al., 2016).

AMD is characterised by the formation of drusen (extracellular deposits of lipid and protein between the retinal pigment epithelium and Bruch’s membrane) and pigmentary abnormalities in the macula (hyper- or hypo- pigmentation of the retinal pigment epithelium) (Coleman et al., 2008, Jager et al., 2008). Drusen can be classified into small (<63um in diameter), medium (63-124um in diameter), and larger (>124um in diameter) by diameter of the optic disc, and also into hard (with discrete margins and uniform colouring) and soft (with indistinct edges,

usually large and confluent) by appearance of edges (Jager et al., 2008, Klein et al., 1992). Drusen size, number and degree of confluence are associated with the development of AMD, providing the basis of AMD classification. However, the presence of a limited number of small, hard drusen is ubiquitous in older people and can be considered a part of normal ageing (Jager et al., 2008, Coleman et al., 2008). The presence of soft drusen, particularly when the drusen is large, can be considered indicative of AMD (Bird et al., 1995).

Multiple schemes have been adopted for the grading of AMD, by affected area, type and size of drusen, the extent of geographic atrophy (GA) and the occurrence of aberrant choroidal neovascularization (Klein et al., 1991, Bird et al., 1995, Group, 2005, Seddon et al., 2006). Widely adopted classification systems include the Wisconsin age-related maculopathy grading system (WARMGS), which divides AMD into six semi-quantitative stages based on the presence and severity of drusen and pigmentary irregularities (Klein et al., 1991). In 1995, the International Classification and Grading System Study group developed a more standardised but complicated classification system (Bird et al., 1995). Thereafter, this classification has been simplified in some epidemiological studies, such as the Rotterdam study and the European Eye Study (EUREYE) (Vingerling et al., 1995, Augood et al., 2006). More recently, the Age-related Eye Disease Study group adopted a new classification system to provide reliable detection of change indicating progression to advanced AMD (Group, 2005). In 2006, another modification of the AREDS grading system was published, known as the Clinical Age-Related Maculopathy Grading System (CARMS) (Seddon et al., 2006). To standardise all previous classification systems, the Beckman Initiative for Macular Research Classification Committee suggested a more clinically useful AMD classification in 2013 (Ferris III et al., 2013). In China, the widely adopted classification system is "Age-related Macular Degeneration Clinical Diagnosis Standard", proposed by the China Medical Association in 1986 (CMA1986). Unlike the above-mentioned classification systems which classify AMD into early and late stages, the CMA1986 system broadly classifies AMD into "dry" and "wet", where "dry" includes both early AMD and GA and "wet" refers to neovascular AMD (NVAMD) (China Medical Association, 1987). Although these schemes share many similar features, a universal classification of the AMD subtype for either clinical or research purposes is still lacking (Hunter et al., 2014, Klein et al., 2014).

Despite the aforementioned complicated grading schemes, the clinical course of AMD can be broadly divided into two stages: early and late (advanced) (De Jong, 2006, Gottlieb, 2002, Lim et al., 2012). Early AMD is characterised by soft drusen and/or pigmentary changes of the retinal pigment epithelium and retina, without visible choroidal vessels (Gottlieb, 2002, De

Jong, 2006). Late AMD includes two types: GA (geographic atrophy) and NVAMD. Typical symptoms in late AMD include decreased night vision and progressive loss of central vision (Rickman et al., 2013). GA is characterised by the development of one or more sharply delineated areas of chorioretinal atrophy near the fovea but without involving the foveal centre. In the last stage of GA when the atrophy expands into the foveal centre, the central vision will be lost (Holz et al., 2001, Holz et al., 2007). NVAMD is characterised by the formation of abnormal blood vessels growth from the tiny blood vessels into the choroid. This choroid breaks Bruch's membrane and spreads into the macular. The new blood vessels are very fragile, leaking blood and fluid with subsequent fibrous scarring. This process can result in rapid and severe loss of vision (Nowak, 2006, Jager et al., 2008).

Moreover, in major epidemiological studies, AMD can also be divided into two broad categories: dry (non-exudative) and wet (exudative) (Jager et al., 2008, Lim et al., 2012). Dry AMD is the most common form of AMD, accounting for about 90% of all the diagnosed cases (Evans and Syed, 2013, Damico et al., 2012). Dry AMD is formed from drusen deposit, pigment disruption and eventually GA (Rickman et al., 2013). GA is the end-stage form of dry AMD, when the deterioration of the retina has reached the most significant level. However, dry AMD progresses slowly, and only a minority of dry AMD progresses to GA (Cook et al., 2008). Confusingly, dry AMD includes both early AMD and GA (**Figure 1.21**), even though the clinical difference is considerable (Gehrs et al., 2006, Rickman et al., 2013, Cook et al., 2008). Wet AMD, which is also known as neovascular and exudative AMD, is a result of the neovascularization of the choriocapillaris (Nowak, 2006, Gehrs et al., 2006). The wet AMD is the most severe form that may lead to rapid vision loss in absence of treatment, although it accounts for only about 10% of all advanced AMD cases, approximately 90% of the severe loss of central vision manifest wet AMD (Chen et al., 2010, Bressler, 2002).

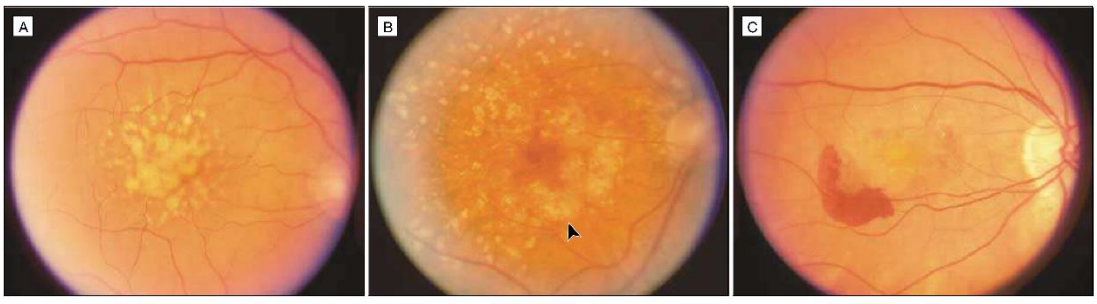


Figure 1.21. Age-related macular degeneration (source: (Gottlieb, 2002))

Note: A, early age-related macular degeneration; B, Late dry age-related macular degeneration. C, Wet age-related macular degeneration.

1.4.4.2 Burden and impact

AMD is the leading cause of blindness and visual impairment globally, especially in developed countries (Lim et al., 2012, Kawasaki et al., 2010). Conservatively, 14 million people were blind or severely visually impaired because of AMD in 2002, according to WHO estimates (Gehrs et al., 2006). Previous studies that adopted standardised classification protocols, and were based on fundus photography, have illustrated different prevalence estimates (Augood et al., 2006, Vingerling et al., 1995, Mitchell et al., 1995). According to the latest synthesis of global AMD prevalence in 2014, the prevalence of early, late, and any AMD was 8.01%, 0.37%, and 8.69% in people aged 45 to 85 years. Correspondingly, 170 million had some form of AMD worldwide, this represents 2.3% of the global population and 18.9% of the older population, and was equivalent to more than half of the contemporary US population (Wong et al., 2014, United Nations, 2015b). Given the global ageing trend, the prevalence of AMD is projected to keep increasing, and the number of people with AMD is also likely to reach to 196 million by 2020, and 288 million by 2040, with an overall increasing rate of 68.8%. Likewise, the number of people with early AMD will increase from 154 million in 2014 to 177 million in 2020 and, finally, reach 260 million in 2040, with an increasing rate of 68.4%. However, the severe form of late AMD will show a much faster rate of growth over this period (92.6%), from 10 million in 2014 to almost 19 million in 2040 (Wong et al., 2014). This increasing burden raises important issues such as the impact on health-related quality of life, specialised assistance and services, and economic burden, both at individual and government levels.

Although AMD is not a life-threatening disease and early AMD has limited impact, visual impairment from late AMD often significantly diminishes patients' quality of life, psychological well-being and ability to function independently, such as seeing fine details, reading, watching, driving or even recognising people (Soubrane et al., 2007, Bonastre et al., 2002, Lamoureux et al., 2010). Up to one-third of affected individuals will experience various degrees of disability and depression, even when only one eye is affected (Casten et al., 2004, Mitchell and Bradley, 2006). Moreover, the decreased mobility performance of this type of vision loss is also remarkable, with the consequences especially profound among older people. Consequently, AMD is significantly associated with increased incidence of falls and other injuries, resulting in an increasing economic and social burden on the individuals, caregivers

and community (Hassan et al., 2002, Brody et al., 2001, Lamoureux et al., 2010, Bonastre et al., 2002).

The impacts of AMD, especially the associated visual loss, are not only limited to individuals but also affect whole communities. In addition to the devastating effects on individual life, the economic burden arising in the affected population is also relatively high (Bonastre et al., 2002, Brown et al., 2005). Despite the global ageing trend, AMD will not manifest in every country to the same extent, with the developed ageing entity suffering a heavier economic burden (Velez-Montoya et al., 2014). Multiple studies have been conducted to evaluate the economic burden of AMD around the world (Cruess et al., 2007, Cruess et al., 2008). For Canada, the annual cost for an individual with bilateral wet AMD was $ 11,334 in 2006, which was more than eight times higher than the annual cost of individuals free from wet AMD ($ 1,412) (Cruess et al., 2007). Another study indicated that the annual societal cost for an individual with bilateral wet AMD was € 12,445 in Germany, € 7,879 in Canada, € 7,349 in France, €5,732 in Spain, and € 5,300 in the United Kingdom in 2004. Almost half (23%-63%) of the abovementioned societal costs were direct medical costs. Therefore, the direct cost of bilateral wet AMD on treatments and health professionals in these countries was estimated to be €268 - €1311million (Cruess et al., 2008). In China, an economic analysis of wet AMD has indicated that the cost was $4,856 per affected eye annually, whereas the cost of the whole disease course can reach to $33,999 in 2013 (Zhang et al., 2015). However, for a developing country whose gross national income per capita ($7,930 in 2015) was only a fraction of that in developed countries, these costs are a huge burden for both individuals and families (World Bank, 2015). Furthermore, with the rising number of individuals with AMD, the economic burden is projected to rise as well.

1.4.4.3 Risk factors

AMD is a multifactorial disease. A number of risk factors for AMD have been identified, including demographics (e.g. age, sex and ethnicity), environmental factors (e.g. cigarette smoking, light exposure, cardiovascular diseases) and genetics (e.g. complement factor H polymorphisms) (Chen et al., 2010, Smith et al., 2001, Cook et al., 2008). Some of these risk factors are described below.

Demographic factors

As the disease term implies, the association between ageing and AMD is consistently strong (Wong et al., 2014, Lim et al., 2012, Bonastre et al., 2002). With the increase in age, the

prevalence of AMD increases exponentially. Compared with subjects younger than 60 years, subjects aged between 60-80 years showed a three-fold increase in the risk of developing late AMD (VanNewkirk et al., 2000). For those 75+ years old, the Beaver Dam Eye Study revealed a much higher prevalence of both NVAMD (5.2% vs.0.1%) and GA (2.1% vs. 0%) in people aged 75 years and over than those aged 43-54 years (Klein et al., 1992).

Female sex has also been suggested as a risk factor for AMD, but existing evidence and strength of association is inconsistent (Klein et al., 1997b, Klein et al., 2007). Pooled data from the Beaver Dam Eye Study, the Rotterdam study of the elderly, and the Blue Mountains Eye Study indicated that females have a higher prevalence of AMD when compared with males (odds ratio [OR]: 1.15), this possibly due to the lack of protective effects of oestrogens in postmenopausal women (Smith et al., 1997). However, no such significant sex differences in the prevalence of AMD were reported in other synthesis studies (Smith et al., 2001, Rudnicka et al., 2012, Chakravarthy et al., 2010).

Among different ethnic groups, AMD prevalence was found to vary. In the ten-year follow-up of the Beaver Dam Eye Study, both iris and hair colour were associated with the development of AMD. Compared with individuals with blue eyes, those with brown eyes were more likely to have soft indistinct drusen (risk ratio [RR]: 1.53), but less likely to develop pigment epithelial depigmentation (RR: 0.58). Furthermore, individuals with brown hair were at lower risk of developing pigmentary abnormalities than those with blond hair (RR: 0.73), indicating an ethnic difference (Tomany et al., 2003). In the Baltimore Eye study, large drusen (>125um) were found to be more prevalent in older whites than in older blacks (15% vs. 9%). As such, pigmentary abnormalities were also more common in older whites than in older blacks (7.9% vs. 0.4%). The overall prevalence of AMD was 2.1% for older whites but 0% for older blacks (Friedman et al., 1999). However, the results from the National Health and Nutrition Examination Survey III did not show significant difference among non-Hispanic whites, non-Hispanic blacks and Mexican-Americans (Klein et al., 1999). Outside the United States, two meta-analyses of AMD prevalence in people of European and Asian ancestry indicated similar prevalence of late AMD in people aged 40-79 years (0.59 vs. 0.56%), however, the prevalence of early signs was relatively higher in Europeans than in Asians (8.8% vs. 6.8%) (Kawasaki et al., 2010, Rudnicka et al., 2012).

Environmental factors

Cigarette smoking has been consistently implied as a risk factor for AMD in numerous studies, with both onset and disease progression of AMD strongly associated with smoking (Cano et

al., 2010, Smith et al., 2001, Chakravarthy et al., 2010, Thornton et al., 2005). Pooled findings from the Beaver Dam Eye Study, the Rotterdam study of the elderly, and the Blue Mountains Eye Study summarised the dramatic influence that cigarette smoking has on the incidence of AMD. Current smokers had increased incidence of GA and late AMD (GA and NVAMD) when compared with non-smokers, with ORs of 2.83 (95% confidence interval [CI]: 1.15-6.93) and 2.35 (95% CI: 1.30-4.27) respectively. Of particular interest, former smokers were not more likely to develop late AMD, GA or NVAMD than non-smokers in the same synthesised analysis, indicating the benefits of smoking cessation (Smith et al., 2001). In addition, the pack-year smoking of cigarettes was found to have a strong association with the risk of developing AMD in white people, and the OR increased with the amount smoked. Individuals with more than 40 pack-years of cigarettes smoking showed an OR of 3.43 (95% CI 1.28-9.20) for GA and 2.49 (95% CI: 1.06-5.82) for NVAMD. Smoking cessation was associated with reduced OR of AMD, with the risk in those who had stopped smoking for more than 20 years was comparable to non-smokers (Khan et al., 2006b, Cano et al., 2010).

Exposure to light can cause damage to the retina. Excessive exposure to sunlight or ultraviolet radiation has been found to be associated with AMD in some studies (Fletcher et al., 2008, Cruickshanks et al., 2001, Tomany et al., 2003, Khan et al., 2006a, Tomany et al., 2004, McCarty et al., 2001a, Reibaldi et al., 2016). The Beaver Dam Eye Study suggested that leisure time spent outdoors in, both, the teens (13-19 years) and thirties (30-39 years) was significantly associated with the five-year incidence of early AMD (OR: 2.09 [95% CI: 1.19-3.65]) but not of late AMD (Cruickshanks et al., 2001). In its ten-year follow-up, individuals who experienced the summer sun more than five hours per day in teens (13-19 years) and thirties (30-39 years) at the baseline examination were more likely to develop increased retinal pigment (RR: 3.17 [95% CI: 1.24-8.11]) and early AMD (RR: 2.14 [95% CI: 0.99-4.61]) (Tomany et al., 2004). In addition, the different risks of developing AMD in individuals with different iris and hair colours implied the melanin's protective effects on sunlight's direct oxidative damage (Tomany et al., 2003). However, despite this strong evidence, other epidemiological studies failed to confirm this positive association between sunlight exposure and AMD, partly because of difficulties in quantifying the exposure to sunlight (Khan et al., 2006a, McCarty et al., 2001a).

Cardiovascular disease and its risk factors may also be risk factors for AMD, although the evidence for this has not been consistent (Klein et al., 1993, Klein et al., 1997a, Delcourt et al., 2001, Smith et al., 2001, Erke et al., 2014). Five population-based studies, namely, the Singapore Malay Eye Study, Singapore Indian Eye Study, Singapore Chinese Eye Study,

Singapore Cardiovascular Cohort Study, and Singapore Prospective Study Program were synthesised in order to analyse the latest data on cardiovascular risk factors and AMD. The pooled data showed hypertension (OR: 1.24 [95% CI: 1.04-1.47), lower total cholesterol (OR: 0.77 [95% CI: 0.62-0.95]), higher HDL cholesterol (OR: 1.34 [95% CI: 1.06-1.69]), and higher body mass index (OR: 1.28 [95% CI: 1.01-1.62]) were significantly associated with the presence of AMD (Shin et al., 2014). However, other studies showed that neither a history of stroke nor heart attack was positively associated with the incidence or progression of AMD (Klein et al., 2003).

Genetic factors

Over the last decades, increasing evidence has supported the role of genetic polymorphisms in AMD. Initial evidence came from twin and family studies. Studies found that, compared with first-degree relatives of individuals without AMD, the first-degree relatives of patients with AMD were more likely to develop this disorder at a younger age, and had a higher risk to develop a late AMD during their lifetime (Heiba et al., 1994, Klein et al., 2001, Seddon et al., 1997). More recent studies reveal a number of underlying genetic modifiers in AMD, with variants at chromosome 1q32 and 10q26 being among the most convincing ones (Chen et al., 2010, Swaroop et al., 2007). Further variants at other loci, such as APOE, LIPC, C2/BF genes, also made a substantial contribution to the genetic risk for AMD (Swaroop et al., 2007).

1.4.5 Glaucoma

1.4.5.1 Definition and classification

Glaucoma is a common and heterogeneous group of optic neuropathies characterised by both glaucomatous optic neuropathy (structural damage) and the gradual loss of visual field (functional loss) in at least one eye (Foster et al., 2002, Weinreb et al., 2014, Quigley, 2011). The development of glaucomatous optic neuropathy is a result of the loss of the retinal ganglion cells (RGCs) axons and the corresponding support vasculature. When loss of optic nerve tissue is significant, visual field loss occurs. The defects of vision loss in glaucoma are opposite to that in age-related macular degeneration, which usually leads to reduced peripheral visual acuity before affecting the central vision (Quigley et al., 1982, Quigley, 2011, Barton and Hitchings, 2013).

There are a number of classificatory systems for glaucoma, for example, according to its aetiology (primary and secondary), age of onset (infantile, juvenile, and adult), occurrence type (acute and chronic), intraocular pressure (IOP) (normal tension and high tension), and angle structure (open angle and angle closure) (Foster et al., 2002, Myint, 2013, Baker, 2008). Primary glaucoma is a set of conditions that solely cause glaucoma in the absence of other ocular or systemic pathology, and it is often, although not always associated with IOP elevation. The most common primary glaucoma includes primary open angle glaucoma (POAG) and normal tension glaucoma (Barton and Hitchings, 2013, Foster et al., 2002, Weinreb and Khaw, 2004, Kwon et al., 2009). In contrast, secondary glaucoma is mainly caused by other separate pathological processes, especially IOP elevation. Common secondary glaucoma includes pigmentary dispersion glaucoma, exfoliative glaucoma, neovascular glaucoma, and traumatic glaucoma (Barton and Hitchings, 2013, Whitmore et al., 2005).

Anatomically, glaucoma can be further classified as open-angle versus closed angle glaucoma by the appearance of the iridocorneal angle. Open-angle glaucoma can be either primary or secondary, in the absence of significant iridotrabecular contact. POAG can be diagnosed in the context of an open iridocorneal angle (with or without IOP elevation) and no underlying secondary cause. Secondary open-angle glaucoma is much less frequent than POAG, and it can be diagnosed in the presence of an open iridocorneal angle and an underlying cause for IOP elevation (Whitmore et al., 2005, Foster et al., 2002). Angle-closure glaucoma occurs with clinically visible anatomical obstruction to aqueous outflow in the iridocorneal drainage angle, the iris, therefore, blocks aqueous outflow and leads to elevated IOP. It can also be primary or secondary (Congdon and Friedman, 2003). In primary angle-closure glaucoma (PACG), pupil block is the commonest cause of angle closure, other anatomical features may also play a role, such as peripheral iris thickness and conformation, anterior placement of the lens-iris diaphragm. In secondary angle-closure glaucoma, the underlying cause can close the angle by local iris directly or pathological changes in the iridocorneal angle result to the closure of the angle (secondary pupillary block) (Foster et al., 2002, Congdon and Friedman, 2003). The simplified classification of Glaucoma is shown in **Figure 1.22**.

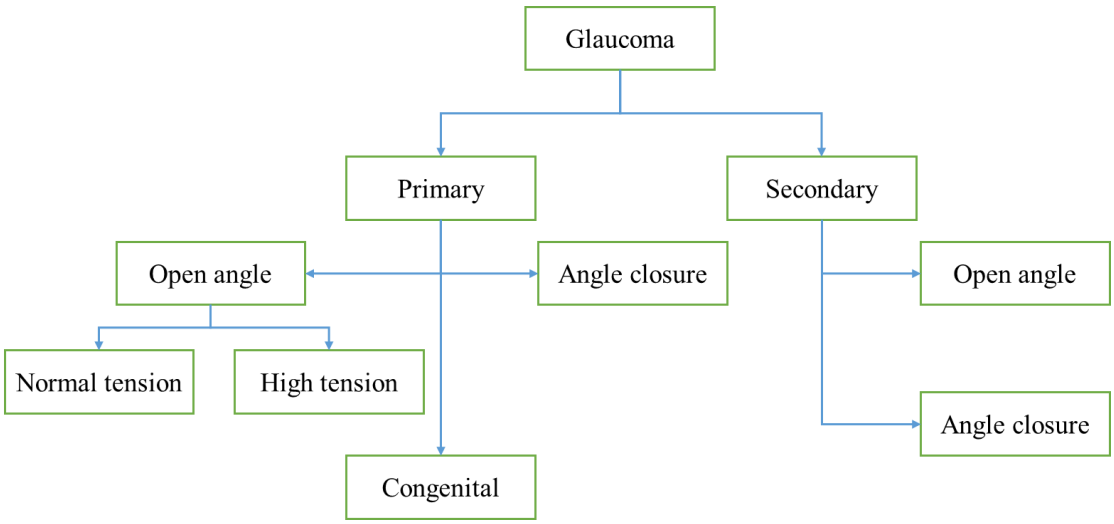


Figure 1.22. Simplified classification of Glaucoma.

1.4.5.2 Burden and impact

Glaucoma is the second leading cause of blindness worldwide, after cataracts. However, the public health impact of glaucoma may be even greater than that of cataracts because of the irreversible blindness it causes (World Health Organization, 2013, World Health Organization, 2014a). In 2010, approximately 60.5 million people were suffering from different kinds of primary glaucoma, among whom 44.7 were from POAG and 15.7 from PACG. With the global ageing trend, the population affected by glaucoma is also expected to increase. By 2020, around 79.6 million people will live with primary glaucoma, among whom 58.6 million will with POAG whereas 21.0 million with PACG. Compared with POAG, PACG is generally associated with a higher risk of blindness. In 2010, 4.5 million people with POAG and 3.9 million people with PACG were bilaterally blind, and these numbers are projected to rise to 5.9 million and 5.3 million by 2020 respectively (Quigley and Broman, 2006). By 2040, the number of people with POAG or PACG is projected to keeping rising to 111.8 million (Tham et al., 2014).

Glaucoma affects people disproportionally, the distribution of glaucoma shows large variation in respect to age, sex and ethnicity. Globally, people residing in Africa are more likely to have POAG and those in Asia are more likely to have PACG (Tham et al., 2014, Quigley and Broman, 2006). For China alone, the number of people with POAG was 8.3 million in 2010, accounting for almost one-fifth of the total POAG cases worldwide. However, almost half of the global PACG cases (7.5 million) resides in China (Foster and Johnson, 2001). Although PACG comprised only 47% of primary glaucoma (POAG and PACG), given the fact that

PACG appears to be more visually damaging, it seems the public health impact arising from PACG will be much larger (Foster and Johnson, 2001). Among 1.7 million people bilaterally blind from glaucoma in China, 91% were caused by PACG (Foster and Johnson, 2001, Congdon and Friedman, 2003).

Similar to any other ocular disease with potential blindness outcomes, glaucoma is associated with diminished quality of life and psychological disturbances, such as anxiety and depression (Ramulu, 2009, Varma et al., 2011). In extreme situations where severe visual impairment or blindness results, the associated consequences will be catastrophic to both affected individuals and their families (Zhou et al., 2013, Zhou et al., 2014, Ramulu, 2009, Rouland et al., 2005). As glaucoma is primarily a disease of the elderly, its social and economic burden will also increase as life expectancy and the total number of the older population continue to increase. The direct medical costs of glaucoma mainly include ocular hypotensive medication, physician and hospital visits, and glaucoma-related procedures. Direct non-medical costs consist of transportation, and nursing home care. Finally, indirect costs mainly refer to lost productivity, which includes both the productivity lost at work and productivity costs borne by caregivers (Varma et al., 2011). In the United States, the direct medical cost of glaucoma was $2.9 billion for 2 million US citizens, accounting for 17.8% of the total medical cost of major visual disorders in 2004 (Rein et al., 2006). In Australia, this cost was AUS$144.2 million for 300,000 Australian citizens affected by glaucoma (Taylor et al., 2006). According to recent economic studies, patients with glaucoma are more likely to receive medications rather than surgeries as their first-line therapy (Rouland et al., 2005, Bateman et al., 2002, Jampel et al., 2003). As new expensive anti-glaucoma medications become available on the market, the direct medical cost of glaucoma is also expected to rise accordingly (Rouland et al., 2005). Although the economic burden of glaucoma is still unknown in China, given the fact that treatment costs are directly related to the severity of glaucoma and PCAG is most prevalent in China, it is plausible to expect the existence of a larger social and economic burden.

1.4.5.3 Risk factors

Identifying risk factors for developing glaucoma is of special importance as it will help to identify those at high risk, therefore early medical detection and treatment can be initiated accordingly. In recent years, substantial evidence has emerged as to the risk factors for glaucoma, among which elevated IOP remains the sole known modifiable one. Other non-modifiable risk factors for glaucoma include age, ethnicity, central corneal thickness, and family history, etc. (Quigley, 2011).

Elevated IOP remains the most important primary and prognostic risk factor for POAG (Palmberg, 2001, Stewart et al., 2000), although POAG can occur with or without ocular hypertension. The reduction of IOP can slow the progression of glaucoma and has become the primary focus of glaucoma treatment (Barton and Hitchings, 2013, Crowston and Weinreb, 2005). In the Barbados Eye Study, individuals with elevated IOP (>21mmHg) were eleven times more likely to have POAG than those with normal IOP (≤21 mmHg) (Leske et al., 1995). However, elevated IOP alone cannot explain the formation of glaucoma, because a considerable proportion of glaucoma patients do not present IOP elevation. Moreover, recurrence of glaucoma after treatment indicates that some other IOP-independent risk factors may also play a role (Yanagi et al., 2011).

Ageing is also proven as a crucial risk factor for glaucoma. In ageing eyes, increased accumulation of extracellular material will present in both the trabecular meshwork and uveoscleral outflow pathway, leading to a reduction of the aqueous humour outflow. Older age is also a measure of the length of exposure to other risk factors. In the Early Manifest Glaucoma Trial, individuals aged 68 years and over were 1.5 times more likely to develop early glaucoma than those younger than 68 years (Leske et al., 2003).

A number of studies have indicated that an African-derived race is associated with higher risk of developing POAG than other ethnicities, whereas PACG is more common among the Chinese (Quigley and Broman, 2006, Tham et al., 2014). The reasons are probably the differences in the anterior chamber and angle anatomy, as African descendants generally have larger optic discs with a smaller neuroretinal rim, and thinner cornea thickness (Boland and Quigley, 2007). However, Chinese are more likely to have shallower central anterior chamber depth, and some other nonpupil-block mechanisms may also contribute to the formation of PACG significantly (He et al., 2006, Congdon and Friedman, 2003).

A positive family history of glaucoma is another well-established risk factor. Siblings and offspring of glaucoma sufferers are more likely to have a higher IOP (Wolfs et al., 1998). In the Baltimore Eye Survey, the association between POAG and family history was even stronger in a sibling (OR: 3.7) than a parent (OR: 2.2) or child (OR: 1.1) (Tielsch et al., 1994). Although the POAG pedigrees do not show a simple Mendelian pattern of inheritance, a polygenic or multifactorial influence has been suggested (Wiggs, 2007).

1.4.6 Cataract

1.4.6.1 Definition and classification

Cataract is defined as a clouding or loss of transparency due to opacification of the crystalline lens. Lenticular opacities lead to scattered light, thus impinging the amount of light rays to the retina. Common syndromes of cataract include reduced visual acuity, blurry vision, monocular diplopia, loss of contrast and increased sensitivity to glare (Asbell et al., 2005). At the end stages, a cataract can affect a large part of the lens' central area, resulting in impeded central vision, sight loss or even blindness (Solomon and Donnenfeld, 2003, Brian and Taylor, 2001).

Cataract is most commonly seen in older people. Over the last two decades, epidemiological studies of cataract have been supported by the development of a number of grading systems to classify and grade lens opacities, including the Oxford Clinical Cataract Classification System (OCCGS) (Sparrow et al., 1986), the comprehensive Lens Opacities Classification System (LOCS) (Chylack et al., 1988, Chylack et al., 1989, Chylack et al., 1993), the Wisconsin Cataract Grading System (Wisconsin system) (Leske et al., 1988), and the Age-Related Eye Disease Study Grading System (AREDS) (Group, 2001). These lens classification systems were based on a comparison between the clinical appearance of the lens (or the lens photographs) and a series of standard photographs, however, various assessment methods and cut-offs in different grading systems make between-study comparison complicated and difficult. Recently, a consensus has been partially reached on the WHO Simplified Cataract Grading System (WHOSCGS) (Thylefors et al., 2002). All above-mentioned systems have demonstrated their advantages in previous epidemiological studies. However, the complicated grading methods that largely rely on the training and reliability of the grades may make combining results from different studies very difficult, and introduce additional variability.

Although the aetiology of cataract is not fully understood, cataracts can be broadly divided into a number of subtypes from an etiological perspective: age-related, congenital, traumatic, complicated, drug-induced cataracts, etc. (World Health Organization, 1993, Gupta et al., 2014). Of these, age-related cataract is the most common form which mainly affects individuals aged fifty years and over (Asbell et al., 2005, Michael and Bron, 2011). Congenital cataract is the rarest form of cataract, which presents in utero or at birth. Traumatic cataract refers to cataract that is caused by blunt or penetrating ocular trauma. Complicated types occur mainly secondary to other ocular disorders, such as uveitis and myopia. Finally, drug-induced cataract is induced by exposure drugs, such as oral, topical, or inhaled steroids (Shiels and

Hejtmancik, 2013, Gupta et al., 2014). According to the study context, only the age-related cataract will be discussed and analysed in the thesis.

Age-related cataract may occur everywhere in the lens. Depending on the different locations where cataract may occur, an age-related cataract can be divided into three main types, namely: cortical; nuclear; and posterior subcapsular cataract, with these different forms occurring independently or in combination (Michael and Bron, 2011, Vinson, 2006, Taylor, 1999). Cortical cataract is the clouding of lens cortex, which is comprised of the new fibres between the adult nucleus and the capsule. It is generated by deterioration of the architecture of the young fibre cells of the lens. This form of cataract is most common in diabetic patients. Visual damage depends on the location of opacification (Asbell et al., 2005, Michael and Bron, 2011). A nuclear cataract occurs in the centre of the lens, or nucleus. Post-translational modification to the structure of the crystallins in the centre of the lens results in a reduction of lens' transparency. It is generally regarded as a result of oxidation and progresses slowly. The nucleus gradually becomes harder and opaque, associated with yellowing of the lens, with this sclerosis progressing relatively slowly over the years. In its early stages, it does not significantly affect vision or increase the refractive power of the lens (myopic shift). However, with continued progression, colour discrimination and vision will eventually be lost (Asbell et al., 2005). A posterior subcapsular cataract occurs from the anterior to the posterior capsule. In this form of cataract, lens fibres migrate to the posterior pole of the lens, and the accumulation finally forms a granular layer of enlarged and hydrated cells between the back of the lens and capsule. Although posterior subcapsular cataract is less prevalent and often occurs in combination with cortical or nuclear cataracts in their late stages, it has a profoundly debilitating effect on vision and a more severe degree of blurring and glare due to the central area of the lens being affected. This form of cataract is most common in diabetic patients and long-term steroid users (Vinson, 2006).

1.4.6.2 Burden and impact

Cataract is the leading cause of blindness. According to the latest WHO statistics in 2010, cataract was responsible for more than half of all cases of blindness and two-thirds of all individuals with visual impairment worldwide. Of these, over 20 million are visually disabled because of the presence of cataract (World Health Organization, 2013). Since cataract is primarily an age-related disease, it is estimated that its burden will increase corresponding with ageing, and become an emerging public health concern (World Health Organization, 2014b). There is still no estimate of the global prevalence of age-related cataract, this largely

due to the difficulty of combining prevalence data from different population groups, especially in cases where different grading systems were adopted. In a synthesised analysis using data from two population-based studies in Australia (the Blue Mountains Eye Study and Melbourne Visual Impairment Project), it was estimated that, in 2001, there were 1.7 million Australians with clinically significant age-related cataract in either eye, and up to 320,000 with cataract surgery history. As populations age, it is estimated that these two figures would keep growing by two-thirds during the next two decades, reaching to 2.7 million and over 500,000 in 2021, respectively (Rochtchina et al., 2003). In China, different epidemiological surveys have been conducted across the nation, demonstrating various prevalence estimates ranging from less than 10% to more than 50% (Sheng et al., 2016, Zhou and Jia, 2011). By taking a low-medium estimate of 18%, it was speculated that there was around 30 million affected older population in 2010 (Bao et al., 2008, Li et al., 2009, Zhao et al., 2001, United Nations, 2015b). However, only 6.26 million of the population were diagnosed with cataracts in 2012 in China, thus this difference of estimates implies a serious rate of under-diagnosis (Li, 2016).

At an individual level, vision loss arising from cataract is the leading cause of morbidity, functional impairment and diminished quality of life in older people. From a clinical perspective, a cataract can be regarded as a conquered disease because of the highly effective surgery that is available. Yet, for older people who are referred to receive surgical treatment, complications still exist - in spite of the guarantee of positive vision outcome associated with treatment. Perioperative complications include lens capsular tear, loss of nuclear material into the vitreous, vitreal loss, and others. Postoperative complication includes endophthalmitis. Even after a long term, there is still a probability of developing retinal detachment and cystoid macular oedema (Abdelkader et al., 2015).

However, the accessibility of cataract surgical services varies between countries, and in many countries the availability of cataract extraction is limited (Brian and Taylor, 2001, Nirmalan et al., 2004). In China, where economic development is heavily uneven across the country, cataract still accounts for a large amount of vision loss in older people (Zhao et al., 2010). The burden of disability due to cataract can be further compounded by inequality in health care. A critical indicator to reflect how a cataract is being eliminated is the cataract surgery rate, which refers to the number of cataract surgeries per million people per year (Zhu et al., 2014). In China, it was estimated that the cataract surgery rate was only 446 per million per year, almost the lowest in Asia and comparable to some West African countries - where well-developed ophthalmic infrastructures are insufficient (He et al., 2007, Shen et al., 2013, Zhang et al., 2010a). This low speed of eliminating cataract, in conjunction with a population that is

increasing in both size and age, will inevitably escalate the health and economic burden of cataract on society. This will especially affect rural and poor areas, where access to appropriate ophthalmological care is limited due to many significant barriers (e.g. lack of knowledge and concern over the poor quality of local services) (Zhao et al., 2010, He et al., 2007, Lam et al., 2009). In the latest national eye health plan (2016-2020), the central government has listed improving cataract surgery rate and its coverage as one priority to eliminate cataract significantly (National Health and Family Planning Commission of the People's Republic of China, 2016).

Although several studies have demonstrated a high success rate (over 90%) of good clinical outcomes in both developed and developing countries, this is not the case for China. In a survey covering nine provinces, 17.7% of the cataract-operated eyes had visual acuity less than 20/200 (Zhao et al., 2010). Currently, cataract surgery has become the most commonly performed surgical procedure. Yet, given the large number of individuals undergoing this surgery, a failure rate of 17.7%, or even at the best 10%, will translate into a large number of individuals who suffer from the poor surgical outcomes and complications.

The economic burden of cataract for a society extends beyond the disability. In the United States, cataract ranks as the second costliest vision problem, only inferior to refractive error (John and David, 2013). The direct medical cost of cataract mainly stems from the surgical procedure, which nears $ 12 billion in 2015 (Ianchulev et al., 2016). In Australia, cataract has become the largest contributor to the allocated health system expenditure, reaching $459 million in 2009 (Access Economics, 2010). Until recently, there were no national estimates of the economic burden of cataract for China, this being largely due to the difficulty of quantifying the costs in a nation with large variation in costs of cataract management between rural and urban populations, and in different provinces (Zhang et al., 2010a, Fang et al., 2010).

1.4.6.3 Risk factors

Research on the aetiology of cataract is of merit in expanding our understanding of the mechanisms by which cataract develops. More practically, it can also provide useful clues on preventions of cataract. Multiple factors have been suggested to have contributions to the development of cataract (**Table 1.2**), including demographics (age, sex, ethnicity), environmental factors (UV exposure, lifestyle, specific health problems) and genetic factors (Asbell et al., 2005, Taylor, 1999).

Table 1.2. Summary of risk factors for age-related cataract (source: (Asbell et al., 2005))

Risk factor	Cataract type	Evidence
Demographic factors		
Age	Cortical, Nuclear, posterior subcapsular (PS)	Conclusive for nuclear and cortical cataract formation; but less strong for PS
Female sex	Cortical, nuclear	Robust for slightly increased risk of cortical; weaker for nuclear
Ethnicity	Cortical, less nuclear, PS	Robust for increased risk of cortical in black people; some evidence for higher risk of nuclear and PS in white people; limited for excess PS in Chinese
Environmental factors		
Ultraviolet B	Cortical	Robust with dose-response relation for cortical
Cigarette smoking	Nuclear, PS	Robust with dose-response relation for nuclear; some evidence for PS
Diabetes	Cortical, PS	Robust; risk related to duration and control of diabetes; associated with cataract surgery at an early age
Steroid use	PS	Robust; associated with high doses and long-term use; inhaled administration also a likely factor
Low socioeconomic status, educational attainment, income	Cortical, nuclear, PS	Strong, linking markers of low socioeconomic status with all types
Genetic factors		
	Cortical, nuclear	Robust for genetic component to both cortical and nuclear in white people; could be the source of racial variation

1.4.7 Diabetic retinopathy

1.4.7.1 Definition and classification

Diabetic retinopathy (DR), one of the major complications of diabetes mellitus, is a chronic, progressive disease caused by pathological changes of the neurovascular retina. Like all other diabetic complications, DR develops with the progression of diabetes and, thus, is more common in older diabetic patients. In early stages, vascular occlusion and dilations occur, while in late stages, there is a proliferation of new blood vessels and fibrous tissues (World Health Organization, 2006, Cheung et al., 2010).

Different sets of classification systems have been developed for describing the severity of retinopathy and macular oedema (Early Treatment Diabetic Retinopathy Study Research Group, 1991b). The most widely applied system is the Early Treatment of Diabetic Retinopathy Study (ETDRS) severity scale. This scale is based on the grading of stereo photographs of 7 fields, and classifies DR into 13 complex levels ranging from level 10 (absence of retinopathy) to level 85 (severe vitreous haemorrhage or retinal detachment involving the macula) (Early Treatment Diabetic Retinopathy Study Research Group, 1991b, Wu et al., 2013). This scale has shown satisfactory reproducibility and validity and, thus, is regarded as the "golden standard" for grading the severity of DR. However, the fine granularity makes it rather complicated to be utilised in daily clinical practice (Ting et al., 2016, Wu et al., 2013). In April 2002 the Global Diabetic Retinopathy Group at the International Congress of Ophthalmology produced a simplified international clinical diabetic retinopathy and diabetic macular oedema disease severity scale (Wilkinson et al., 2003). This new scale classifies DR into five stages based on severity, with the first three stages as low risk, the fourth as severe non-proliferative diabetic retinopathy (NPDR) and the fifth as proliferative diabetic retinopathy (PDR). DMO is simply classified as apparently present or apparently absent (Wilkinson et al., 2003). Compared with the ETDRS scale, this classification system is much more user-friendly and easy to adopt in clinical settings (Wu et al., 2013, Ting et al., 2016).

In accordance with the international clinical diabetic retinopathy and diabetic macular oedema disease severity scale, DR is generally divided into NPDR and PDR according to the presence of new blood vessel growth within the retina in epidemiological studies (**Figure 1.23**) (Mohamed et al., 2007, Ting et al., 2016). NPDR is characterised by damage to retinal endothelium and the resultant capillary occlusion, with common clinical features including microaneurysms, haemorrhages and cotton wool spots in the retinal periphery. PDR occurs

with further retinal ischemia and is characterised by the proliferation of neovascularization on the interface between the retina and the vitreous cavity. These fragile blood vessels may rupture and result in vitreous haemorrhage, subsequent fibrosis and tractional retinal detachment. Diabetic macular oedema (DMO), which is frequently the principal cause of vision loss due to DR, can occur in any stage of DR. DMO is characterised by increased vascular permeability and the deposition of hard exudates at the central retina. Severe NPDR, PDR and DMO together are categorised as vision-threatening DR (VTDR) (Porta and Bandello, 2002, Mohamed et al., 2007).

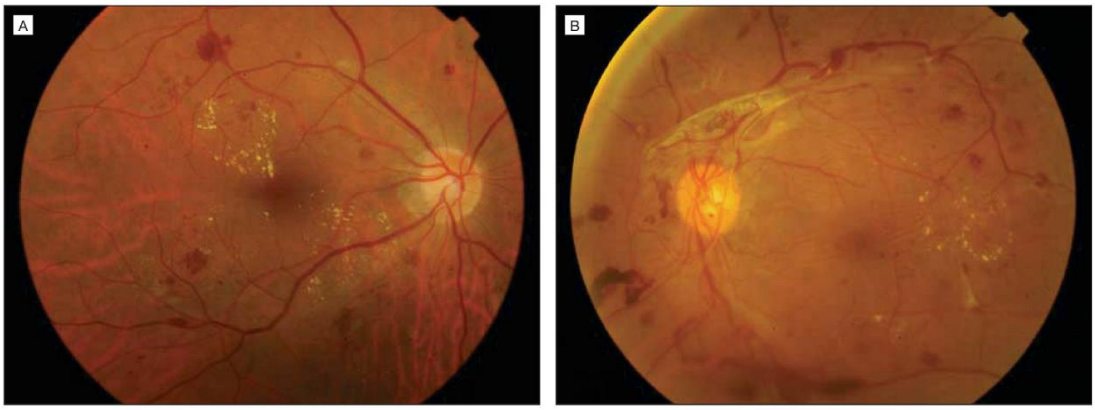


Figure 1.23. Diabetic Retinopathy (source: (Mohamed et al., 2007))

Note: A, Moderate NPDR with microaneurysms, retinal haemorrhages, and macular oedema characterised by increased vascular permeability and deposition of hard exudates at the central retina; B, PDR with new vessels and fibrous tractional bands arising from the optic disc.

1.4.7.2 Burden and impact

Diabetes has been proven to be associated with a range of ocular diseases, but the main cause of blindness that is directly linked to diabetes is DR. It was estimated that at least 75% of the patients suffering from diabetes for more than 20 years will have some kind of DR (World Health Organization, 2006). In 2010, there were 285 million adults with diabetes globally, and this figure is expected to increase to 439 million by 2030. During this period, the increasing rate of the number of adults with diabetes is especially high in developing countries in comparison to developed countries (69% vs. 20%) (Shaw et al., 2010). Among people with diabetes, the overall prevalence of diabetic retinopathy is more than one-third. In 2010, approximately 93 million people were living with DR, among whom 76 million were with

NPDR, 17 million with PDR and 21 million with DMO. The number of people living with VTDR has also reached 28 million (Yau et al., 2012). Considering these global trends, and the lack of proper action taken, another global estimate indicated an even larger burden, where the number of people with DR will increase from 126.6 million in 2010 to 191.0 million by 2030, and the number with VTDR will also grow from 37.3 million to 56.3 million (Zheng et al., 2012). The WHO estimated that DR was the fifth leading cause of visual impairment worldwide in 2010 (Pascolini and Mariotti, 2011, Stefánsson et al., 2000). Given that DR can be largely prevented with existing screening and treatment approaches, the WHO placed DR as one of the priority eye conditions that can be partly prevented or treated (World Health Organization, 2014b, Pizzarello et al., 2004). In China, approximately 114 million adults aged 18 years or older were living with diabetes in 2010, which accounts for 40% of the worldwide diabetic population (Xu et al., 2013). Previous synthesised analysis of the prevalence of DR in China revealed that the prevalence of DR, NPDR and PDR was 23.0%, 19.1% and 2.8% in diabetic patients respectively (Liu et al., 2012). Extrapolating these prevalence rates to the population of diabetes cases in China, approximately 26 million diabetic patients were living with DR in China in 2010, among whom 22 million were with NPDR and 4 million were with PDR. These numbers are expected to escalate with an ageing population in the foreseeable future.

DR is the leading cause of visual impairment in the working-age population. At the individual level, visual and functional impairments associated with DR have been shown to reduce health-related quality of life and increase dependency in activities of daily living to a large extent, resulting in anxiety and depression (Lamoureux et al., 2004, Sharma et al., 2005). At the societal level, DR is also notably associated with high direct (medical care) and indirect costs (reduced productivity). In the United States, the direct costs for DR were $493 million in 2004 and, given the reduction of work function associated with DR and its affected population, indirect costs were expected to account for a larger proportion of the total cost (John and David, 2013, Rein et al., 2006). In Germany, in the year 2002, the medical cost of DR covered by the German statutory health insurance was €2.23 billion, and the societal cost was €3.51billion (Happich et al., 2008). In China, although the economic burden has not been estimated, the annual costs of screening and grading alone were estimated to more than £540 million in 2015 (Li, 2015b).

1.4.7.3 Risk factors

Risk factors for DR have been previously examined in many epidemiological and clinical studies, with consistent factors including the duration of diabetes; the level of glycemia; the presence of high blood pressure; dependence on insulin; pregnancy; levels of selected serum lipids; nutritional and genetic factors (Klein, 2007). However, considerable variation still exists in the consistency and strength of this evidence, especially in cases where the stages of DR are different (Yau et al., 2012).

Duration of diabetes is a prerequisite of DR. Once being diagnosed, DR is generally more prevalent in the older-onset group than in the younger-onset group (Klein et al., 1984b, Klein et al., 1984a), and patients with type 1 diabetes have a higher prevalence of DR compared with those with type 2 diabetes (Ting et al., 2016). It was estimated that the OR of DR increased by 1.07±0.2 per year of duration of diabetes (Wong et al., 2008b).

Multiple studies have consistently shown poor glycemic control to be an independent risk factor for the development and progression of DR (Varma et al., 2007, Wong et al., 2006b, UK Prospective Diabetes Study Group, 1998, van Leiden et al., 2003). Elevated haemoglobin A1c (HbA1c) reflects poorly controlled diabetes, and it was estimated that a 1% increase in HbA1c was associated with a 22% increase in the prevalence of DR (Varma et al., 2007). Even in patients with a good HbA1c level of 7.0%, the absolute risk of retinal laser treatment was as high as 7.9 per 1000 patient-years (Varma et al., 2007, UK Prospective Diabetes Study (UKPDS) Group, 1998). This implies the importance of optimal glycemic control in diabetic patients.

High blood pressure is also an independent risk factor for the development of RD in both type 1 and type 2 diabetic patients. In the Los Angeles Latino eye study, the OR of DR was 1.26 for every 20 mm Hg increase in blood pressure (Varma et al., 2007). The decreased systolic blood pressure of 10 mm can bring a declined risk of DR and the need for laser treatment by more than one-third (Cheung et al., 2010).

Genetic predispositions are also of etiological importance for DR. Previous twin studies and familial aggregation studies have indicated significant familial clustering, with siblings and relatives of diabetic patients with DR having demonstrated a two to three-fold risk of DR compared with relatives of diabetic patients without DR (Diabetes Control and Complications Trial Research Group, 1997, Leslie and Pyke, 1982). As the severity of DR increases, the degree of familial clustering also increases. It was estimated that heritability was as high as

27% for DR and 52% for PDR (Hietala et al., 2008, Cho and Sobrin, 2014). Numerous genes have been studied for association with DR through linkage analysis, candidate gene association studies and genome-wide association studies, but more efforts are still needed to ascertain these associations in future studies.

1.5 Systematic review and meta-analysis

1.5.1 Systematic review

Synthesis of evidence (literature review) is necessary to summarise available evidence in a specific research area, and it can be conducted both qualitatively (literature review) and quantitatively through appropriate statistical methods (meta-analysis). A conventional literature review has been conducted to collect and summarise the available evidence in a narrative way, and thus it may be particularly prone to unsystematic bias in presenting a comprehensive and sound overview of the given evidence (Cook et al., 1997, Impellizzeri and Bizzini, 2012). In light of this shortcoming, review methods have been advanced in the 1970s to systematically examine the existing evidence from all available primary studies, known as a systematic review with meta-analysis (Cook et al., 1997, Haidich, 2011).

Systematic review refers to an approach that identifies all relevant empirical evidence in a specific research area. It is a transparent process for identifying, appraising, summarising and (if appropriate) synthesising all the available evidence in specific research areas (Kitchenham, 2004, Cook et al., 1997). Compared with the conventional literature review, a systematic review is becoming increasingly popular in contemporary research contexts. High-quality systematic reviews should be conducted systematically and easily replicated with pre-defined and reproducible methods. Possible methods for reducing bias include clear study objectives and methods, comprehensive search for relevant studies, independent reviewers to validate included studies, and systematic presentation of the results (Moher et al., 2009, Cooper, 2016).

Typically, the process of systematic review involves defining a particular research topic, and then conducting the literature review with a transparent and replicable search strategy. The comprehensive search of literature is the key feature of a systematic review, which aims to identify as much relevant evidence as possible. In this process, the search for relevant studies should not only be limited to published studies, but also include unpublished studies (grey literature), such as government reports, theses, etc., to reduce the potential effect of publication bias. Further efforts should also be made to contact the authors for clarification on some key

issues, if this is deemed necessary. Then, the articles are assessed based on preset inclusion and exclusion criteria. For those that meet the inclusion criteria, full-text papers are assessed in detail. Data extraction will then be performed to extract key findings (Kitchenham, 2004, Moher et al., 2009, Higgins and Green, 2008). A number of guidelines have been developed to standardise the systematic review process and its reporting format, including the guidance for conducting a systematic review, published by the Cochrane Collaboration (Higgins and Green, 2008), the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) by the Centre for Review and Dissemination at the University of York (Moher et al., 2009), the Meta-analysis of Observational Studies in Epidemiology (MOOSE) statement by the MOOSE group (Stroup et al., 2000), and the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement by the GATHER working group (Stevens et al., 2016). Given the study context in this thesis, the PRISMA guidelines and GATHER statement are adopted in reporting the disease burden estimates of AREDs in China.

A systematic review is especially useful in disease burden research, especially for diseases that are not cost-effective to be included in national surveillance systems or large-scale surveys. For disease burden studies that adopt the systematic review approach, epidemiological studies (case-control, cross-sectional or cohort studies) have typically been used to evaluate the long-term exposures that may cause disease or death, or summarise the frequency of diseases (e.g. incidence, prevalence) (Lopez et al., 2006, Wong et al., 2014, Tham et al., 2014). For this kind of research, randomly designed trails are of limited utility because of ethical concerns (Stroup et al., 2000). With an increasing amount of epidemiological research, it has become possible to critically appraise both published and unpublished literature. For observational studies, the lack of a control group may limit the ability to control potential confounding variables, and thus generate considerable bias (Impellizzeri and Bizzini, 2012).

1.5.2 Meta-analysis

1.5.2.1 Introduction

With attempts to reduce individual subjectivity, a systematic review with statistical aggregation of data is generally referred to as a quantitative systematic review, namely, a meta-analysis (Egger et al., 2008, Impellizzeri and Bizzini, 2012). A systematic review with meta-analysis refers to a complete process of identifying, appraising, synthesising and combining evidence from multiple independent studies (Copetti et al., 2013, Lau et al., 1997). If correctly performed, meta-analysis can be used to summarise results from many types of studies.

Typically, meta-analysis is used to synthesise results from randomised controlled trials, where small sample size studies cannot provide stable estimates, but the approach of meta-analysis pooling a group of individual studies can achieve a more powerful and reliable inference. However, the difference in study design, sample size and other characteristics - such as the investigated population, or the outcome measurement - may also lead to the variability or heterogeneity between individual studies (Haidich, 2011, Lau et al., 1997).

Unlike meta-analyses of randomised controlled trials, which are largely based on the assumption that the overall effect of an experiment is unbiased and can provide causation, meta-analysis for observational studies is based on the assumption that the variation arises from multiple confounding factors, biases, or both. For meta-analysis of observational studies, exploration of possible sources of heterogeneity is the main aim for providing insights, rather than the overall combination of studies, which is often biased (Egger et al., 2008, Stroup et al., 2000, Impellizzeri and Bizzini, 2012, Barendregt et al., 2013). In some cases, the study characteristics can be used to conducted sub-group analysis, or as covariates in meta-regression models (Thompson and Higgins, 2002).

1.5.2.2 Heterogeneity assessment

An important part of meta-analysis is testing the heterogeneity of the combining studies. This is generally defined as the variability in the underlying effect size between studies that cannot be solely explained by chance (within-study variation) (Haidich, 2011, Borenstein et al., 2009). The significance of the heterogeneity is generally tested by using a Cochran's Q statistic, which assumes that the study effects follow a normal distribution (Higgins et al., 2003). However, the statistical power for testing heterogeneity is generally low, due to a small number of included studies, which implies a higher-than-expected probability of false negative result. To compensate for this shortcoming, a higher level of cut-off significance is generally adopted (e.g. $p<0.10$ instead of the classic $p<0.05$). In circumstances where the Q statistic is significant, the potential causes of heterogeneity could be further investigated by subgroup analysis or meta-regression, and the reduction of between-study variance represents the amount of variation explained by the covariates (Huedo-Medina et al., 2006).

Several approaches have been developed to estimate the magnitude of the between-study variance, τ^2. One popular approach is the DerSimonian-Laird method. However, in circumstances where the included studies are few, the estimation of τ^2 may not be an approximation for the population estimate (Huedo-Medina et al., 2006). Another popular

statistic for measuring the heterogeneity is the I^2 parameter, which represents the percentage of total variation across all included studies that is due to heterogeneity rather than chance (Higgins et al., 2003, Higgins and Thompson, 2002).

$$I^2 = \left(\frac{Q - df}{Q}\right) * 100\%$$

Where Q is Cochran's heterogeneity statistic and df denotes the degrees of freedom.

Compared with the τ^2, the magnitude of I^2 is independent from the number of included studies, but it may be influenced by the precision of the studies. As a result, I^2 can be classified into three categories by cut-off values of 25% and 75%, which suggest low, moderate and high heterogeneity respectively (Huedo-Medina et al., 2006, Higgins et al., 2003).

In the process of meta-analysis, the investigation of heterogeneity is crucial before deciding the statistical methods for polling results, and whether the result should be interpreted by groups. The selection of the analysis model should be based on the research context and characteristics of the included studies. In cases where heterogeneity is highly suspected, three approaches are recommended (West et al., 2010, Higgins and Green, 2008, Huedo-Medina et al., 2006):

1) Categorise the included studies into different homogeneous subgroups and then summarise, using fixed-effect models;
2) Accommodate heterogeneity by using random-effects models;
3) Explore possible sources of heterogeneity by using meta-regression.

1.5.2.3 Classical meta-analytic approach

Broadly speaking, two main models are available for frequentist meta-analytic approach, namely, fixed-effect model and random-effects model. The fixed-effect model is based on the assumption that all included studies come from the same population, so that variance across studies is solely attributed to sampling variability and no between-study variation exists (Borenstein et al., 2009). The pooled result is thus calculated as a weighted average of all included evidence. The fixed-effect model assumes the included study effects follow a normal distribution.

$$\widehat{\theta_i} \sim N(\theta, \sigma_i^2)$$

Where θ is the true value of the effect size and σ_i^2 is the variance in studies i=1, 2,…, k.

In contrast, the random-effects model assumes that the included studies are only a sample from an unknown population and thus between-study variance should be taken into account, too.

$$\widehat{\theta_i} \sim N(\theta_i, \sigma_i^2)$$

In this model, the distribution of θ_i has a mean of θ and a heterogeneity variance of τ^2, in some circumstances, the distribution of θ_i is a normal distribution.

$$\theta_i \sim N(\theta, \tau^2)$$

Meta-regression is another preferable method to conduct analysis in circumstances where one or more confounding factors are associated with the effect size. Meta-regression can be used to explain the source of heterogeneity. Its advantage over the sub-group analysis is a more compelling assessment of heterogeneity (Thompson and Higgins, 2002). In meta-regression, variables at study-level can attribute to a proportion of the total heterogeneity. Both fixed and random-effects models can be applied in meta-regression, but the latter is more realistic and appropriate in most cases (Borenstein et al., 2009).

$$\widehat{\theta_i} \sim N(\theta_i, \sigma_i^2)$$

$$\theta_i \sim N(\theta, \sum_{j=1}^{m} \beta_j, \tau^2)$$

Where β_{ij} is the jth variable in a model where m study-level covariates are included.

1.5.2.4 Bayesian meta-analytic approach

Bayesian methods have been widely adopted in meta-analysis approach (Dixon-Woods et al., 2005, Van Houwelingen et al., 2002, Wong et al., 2014), in contrast to the frequentist paradigm, which relies solely on the likelihood from the collected data. Bayesian statistics attribute the results to a posterior probability distribution based on a prior probability distribution (external evidence about the effect of interest) and the likelihood (evidence from the collected data) (Copetti et al., 2013). The prior probability distribution may come from results in previous studies or purely from experts' beliefs, which may yield a variety of prior distributions. The choice of prior distribution should be made with caution, because the choice can affect the results to a considerable extent. For example, if an unreliable prior distribution dominates the

likelihood, an inaccurate or over-influenced posterior distribution cannot be avoided (Sutton and Abrams, 2001). The two sources of evidence (likelihood function and prior distribution) combinedly contribute to the posterior probability of the effect of interest.

$$P(\varphi|data) \approx P(\varphi)P(data|\varphi)$$

$P(\varphi|data)$ is the posterior distribution based on the prior distribution $P(\varphi)$ and the likelihood based on the observed data $P(data|\varphi)$.

The choice of prior distribution is a major source of controversy in Bayesian meta-analysis approach, so in many circumstances, prior distributions are defined as "non-informative" or "reference" to reflect a position of prior ignorance - i.e., prior distributions can be broadly distributed over a wide range of values. In these situations, Bayesian meta-analysis often yields very similar results as the classical frequentist meta-analysis, because the posterior estimate will only rely on the likelihood function. However, this "non-informative" approach should also be used with caution because all values within the pre-set broad range are equally likely, and even the choice of "non-informative" prior may have considerable effects on the results of the analysis (Lambert et al., 2005, Sutton and Abrams, 2001). Although the application of Bayesian approaches has increased in recent decades, it is still limited when compared with the classical frequentist meta-analyses (Copetti et al., 2013)

In Bayesian models where many study-level covariates are included, high-dimensional integration may be needed. Common methods for calculating the posterior distribution in a Hierarchical Bayesian model include Markov Chain Monte Carlo (MCMC) approach, which simulates high dimensional joint probability distributions. In addition, Gibbs Sampling is also used in this practice (Brooks, 1998, Spiegelhalter et al., 1996).

1.6 Rationale for proposed research

As discussed in preceding sections, the older population in China is expected to increase substantially. This is expected to lead to several age-related health problems that will grow in importance over time. From a public health perspective, investigating the disease burden of AREDs is of significant importance, because it is a key indicator of eye care plan at both the national level and the local level. However, the study of AREDs in China has been somewhat overlooked when compared with other diseases of ageing. There remains a lack of knowledge and awareness of the burden of AREDs among policymakers and the general public in China.

Furthermore, although vision-threatening conditions have been revealed and cost-effective approaches may also exist, many affected individuals remain unaware of the need to seek ophthalmic screening and medical treatment. Finally, the lack of well-trained professional ophthalmologists, especially in resource-poor areas, is perpetuated. These factors may contribute to the continued increase of the AREDs burden in the foreseeable future.

To date, no blind surveillance system or national investigation on AREDs exists to provide the disease burden estimates for AREDs in China. Furthermore, most Chinese epidemiological studies on AREDs are local investigations, which can only represent the disease burden in particular circumstances. The approach of systematic review and meta-analysis has emerged as a popular and useful tool in collecting the existing local surveys and understanding the epidemiology of ARMDs. Therefore, a systematic review and meta-analysis is adopted in this thesis to provide a better approximation of the AREDs burden in China at the national level, or even the sub-national level.

1.7 Research aims and objectives

The main aim of this thesis is to quantify the disease burden of AREDs in China. This aim will be achieved through the following specific objectives:

1) To quantify the prevalence and disease burden of four major AREDs (AMD, glaucoma, cataract and DR) from 1990 to 2015, by using existing survey data;
2) To identify individual and cluster-level factors underlying the prevalence of AREDs and to explore the relative importance of variations at different scales;
3) To predict the prevalence and disease burden of AREDs from 2020 to 2050 (if possible);
4) To estimate the disease burden of AREDs at sub-national level, by applying the corresponding population data and risk factor characteristics.

1.8 Outline of this thesis

Chapter 2 describes the overall methods of this thesis; Chapters 3-6 demonstrate the prevalence and burden of AMD, glaucoma, cataract and DR respectively. Finally, Chapter 7 discusses the main findings of the thesis and highlights the important issues arisen from this work that may inform policymaking.

Chapter 2 Overall methods

Overall, the study approach in this thesis could be classified into five stages (**Figure 2.1**):

- Stage 1- Systematic review;
- Stage 2- Meta-analysis and meta-regression of prevalence data;
- Stage 3- Estimation of the national number of cases;
- Stage 4- Identification of potential correlates of or risk factors for AREDs;
- Stage 5- Estimation of the regional number of cases.

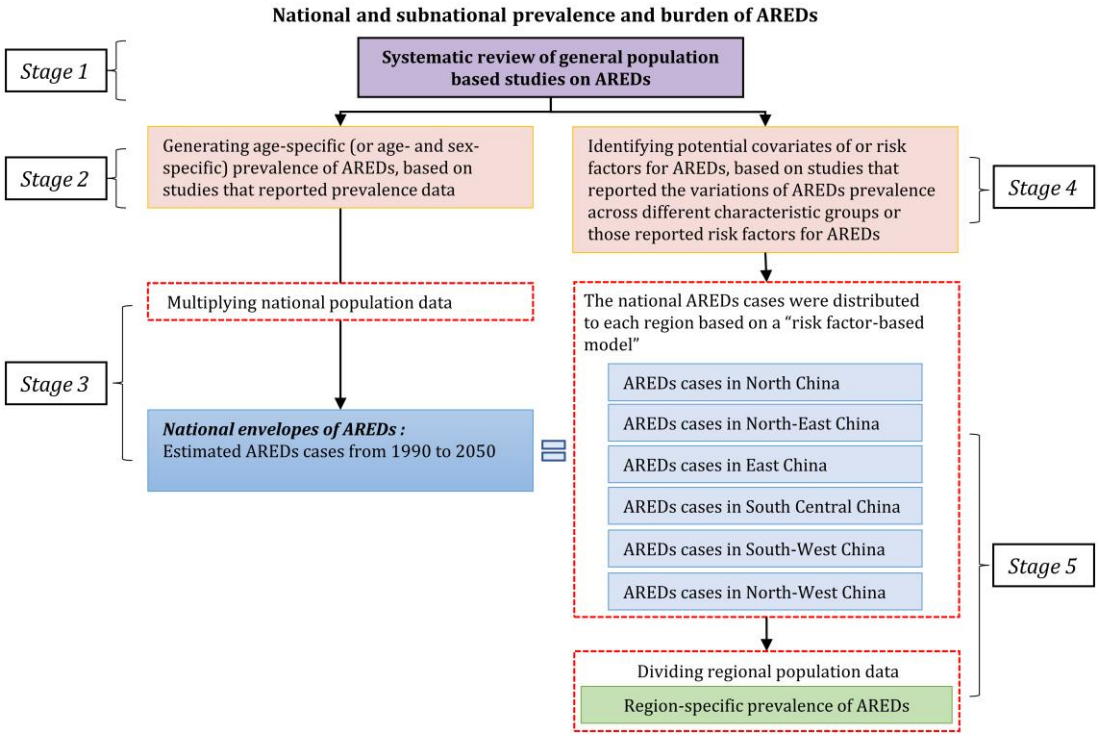


Figure 2.1. Overall study design flowchart

2.1 Systematic review

2.1.1 Literature search

To derive studies that reported prevalence data on AREDs in China, four systematic reviews were separately carried out for AMD, glaucoma, cataract and DR (see Chapters 3-6 for more details). In Chinese scientific society, the Chinese bibliographic databases consist of a large

sheer volume of studies that are important data sources for understanding the epidemiology of diseases in China (Xia et al., 2008, Cohen et al., 2015). Therefore, three major Chinese bibliographic databases, namely China National Knowledge Infrastructure (CNKI), Wanfang database, Chinese Biomedicine Literature Database (CBM-SinoMed) were selected for the literature search. Searchable databases in the CNKI platform include China Academic Journals Full-text Database (1994 onwards, 63904806 records in total), China Doctoral Dissertations Full-text Database (1984 onwards, 364992 records in total), China Masters' Theses Full-text Database (1984 onwards, 3508873 records in total), China Proceedings of Conference Full-text Database (1953 onwards, 2303841 records in total), International Proceedings of Conference Full-text Database (1981 onwards, 788716 records in total), China Core Newspapers Full-text Database (2000 onwards, 16540597 records in total), and China Yearbooks Full-text Database (1949 onwards, 31496104 records in total). Wanfang database and CBM-SinoMed are similar platforms which cover different ranges of literature (Xia et al., 2008). PubMed, Embase and Medline were also searched to identify English-language articles that reported the epidemiology of AREDs in Chinese population. In the literature search, different search strategies were respectively developed for each disease and bibliographic database. Both peer-reviewed articles and grey literature (conference proceedings, master and doctoral dissertations) were searched. The reference lists of included studies and relevant reviews (if any) were additionally searched for any potentially eligible studies.

All identified records from bibliographic databases were imported into NoteExpress (version 3.2.0.7103) for screening. After removing duplicate records within and between databases, the screening process was conducted in two stages to select studies that reported data of interest: title and abstract screening followed by a full-text review. Generally, only studies that were published from January 1, 1990 onwards and conducted in China (including Mainland China, Hong Kong, Macao and Taiwan) were included. The specific selection criteria were not unified for the systematic reviews of each disease. For example, in the systematic reviews of AMD, glaucoma and cataract, only individual studies that were conducted in the general Chinese population were included. This was done to guarantee the generality of prevalence estimation. Given the disease nature of DR, only individual studies that were conducted in people with diabetes were eligible. Other selection criteria are detailed in the following chapters.

The process of systematic review was conducted in accordance with the PRISMA guidelines and GATHER statement (Moher et al., 2009, Stevens et al., 2016).

2.1.2 Data extraction and quality assessment

Relevant data were extracted from the included studies using a pilot tested and refined data extraction table. Generally, the extracted data included the following parts:

(1) Characteristics of the study, including authors, year of publication, study setting, year of investigation, sampling method, study design, disease assessment;
(2) Characteristics of the investigated sample, including sample size, age structure (age range, mean or median age, or midpoint of the age range), sex (male, female or mixed) and residence (urban, rural or mixed);
(3) Prevalence data. Throughout this study, the prevalence of AREDs was defined based on the number of affected individuals, rather than the number of affected eyes. Wherever a study reported prevalence data by stratum (e.g. age group, sexes, geographic locations), multiple data points were extracted for different strata from the single study.
(4) Data on risk factors. In studies where risk factors for AREDs were reported using multivariate logistic regression, the definition and effect (OR and corresponding 95% CI) of each risk factor were extracted.

According to the Reporting of Observational Studies in Epidemiology (STROBE) guideline, quality of the included studies was assessed in terms of five core components-sample population, sample size, participation rate, outcome assessment, and analytical methods. Each bias component was scored as 2 for low risk, 1 for moderate risk and 0 for high risk and unclear. The quality of each study was represented by the total score (**Table 2.1**) (Von Elm et al., 2007, Song et al., 2018).

Table 2.1. Quality score scale for assessing the risk of bias

Bias type	Low risk (score=2)	Moderate risk (score=1)	High risk (score=0)
Selection (sample population)	1) Sample from the general population, not a select group; 2) Consecutive unselected population; 3) Rationale for case and control selection explained.	1) Sample selected from large population but selection criteria not defined; 2) Sample selection ambiguous but may be representative; 3) Rationale for cases and controls not explained; 4) Eligibility criteria not explained;	1) Highly select population making it difficult to generalise finding; 2) Sample selection ambiguous and sample unlikely to be representative.

Bias type	Low risk (score=2)	Moderate risk (score=1)	High risk (score=0)
		5) Analysis to adjust for sampling strategy bias.	
Selection (sample size)	1) Sample size calculation performed and adequate.	1) Sample size calculation performed and reasons for not meeting sample size given; 2) Sample size calculation not performed but all eligible persons studied.	1) Sample size estimation unclear or only sub-sample studied.
Selection (participation rate)	1) High response rate (>85%).	1) Moderate response rate (70-85%).	1) Low response rate (<70%); 2) Response rate not reported.
Performance bias (outcome assessment)	1) Diagnosis using consistent criteria and direct examination.	1) Assessment from administrative database or register; 2) Assessment from hospital record or interviewer.	1) Assessment from non-validated data or generic estimate from the overall population.
Performance bias (analytical methods to control for bias)	1) Analysis appropriate for the type of sample (subgroup analysis/regression etc.).	1) Analysis does not account for common adjustment.	1) Data confusing.

2.2 Meta-analysis and meta-regression

As above stated, the extracted prevalence data were organised in a hierarchical structure. To take into account the wide variety of strata (e.g. age, sex and setting) reported in the literature, meta-regression approaches were adopted to construct stratum-specific prevalence of AREDs. Given that:

$$\text{prevalence} = \text{p} = \frac{number\ of\ affected\ cases}{number\ of\ examined\ sample}$$

Then, the prevalence estimates were stabilised by using the logit link,

$$\text{logit}(p) = \ln\left(\frac{p}{1-p}\right) = \ln odds = \alpha + \beta_1 * x_1 + \beta_2 * x_2 + \cdots \beta_n * x_n$$

Thus,

$$odds = \frac{p}{1-p} = e^{\alpha+\beta_1*x_1+\beta_2*x_2+\cdots\beta_n*x_n}$$

And,

$$\text{prevalence} = \text{p} = \frac{e^{\alpha+\beta_1*x_1+\beta_2*x_2+\cdots\beta_n*x_n}}{1+e^{\alpha+\beta_1*x_1+\beta_2*x_2+\cdots\beta_n*x_n}}$$

Given the disease nature of AREDs, age is the most important factor of interest, therefore the abovementioned equations were generally adopted to construct the relation of prevalence and age (the base equation). In situations where sex was a statistically significant factor for the development of disease after controlling the effect of age, sex could also be added into the base equations to generate the age- and sex-specific prevalence estimates. Similarly, this approach could also be used to develop regional prevalence estimates, if geographic characteristics (e.g., latitudes, longitudes and locations) statistically influenced the development of AREDs.

However, this meta-regression approach might not be applicable to all cases. For diseases where only study-level prevalence data were available, a random-effects (DerSimonian and Laird method) meta-analysis was conducted to calculate the pooled prevalence and 95% CI (Barendregt et al., 2013, Higgins and Green, 2008). To evaluate the robustness of the pooled prevalence, a leave-one-out sensitivity analysis was conducted by removing one study at one time (Wallace et al., 2009). Potential publication bias was assessed by visual inspection of funnel plots. When the number of individual studies was ten and more, Egger's regression test for funnel plot asymmetry and Begg’s rank correlation test were additionally performed to examine the existence of publication bias (Egger et al., 1997, Begg and Mazumdar, 1994, Peters et al., 2006).

2.3 Estimation of the national number of cases

At this stage, the stratum-specific (e.g. age-specific, or age- and sex-specific) prevalence was applied to the corresponding stratum-specific population data, available from the UNPD

(United Nations Population Division) (United Nations, 2015b). This was done for the years 1990, 2000, 2010, 2015. To account for the uncertainty in demographic projections, UNPD developed different scenarios by combining multiple assumptions for fertility, mortality and international migration. The main scenarios in UNPD population projections are the low, medium, and high variants, among which the medium (or standard) variant is the most likely scenario with medium fertility, normal mortality and normal international migration, whereas the low and high variants reasonably represent the corresponding lower and upper limits of population projections. The disparity among those three scenarios is caused by different levels of fertility, where the total fertility rates in the low and high scenarios are respectively one-half child less and one-half child more than that in the medium scenario. Therefore, differences in population size in the low, medium, and high scenarios from 2015 to 2050 are only presented in people under 35 years of age (United Nations, 2015b). Given the study topic of AREDs, the target samples in this study are mainly middle-aged and older Chinese ($\geqslant$45 years), therefore only the most likely scenario (the medium variant) was taken to generate the projections of AREDs cases. In the projections of national number of cases for the years 2020, 2030, 2040 and 2050, I applied the stratum-specific (e.g. age-specific, or age- and sex-specific) prevalence to the corresponding stratum-specific population data in the middle variant scenario. Throughout this thesis, the burden of disease refers to the number of affected cases. The national number of people living with AREDs in one specific year was set as the "national envelope" and therefore provided a basis for the subsequent "risk factor-based model" of regional distribution.

2.4 Identification of potential correlates of or risk factors for AREDs

The effects of different variables on AREDs prevalence were examined using the meta-analysis of risk factor approach or the meta-regression approach. Among studies that reported the epidemiology of AREDs, some might explored potential risk factors for AREDs by using multivariate logistic regression. In the data extraction stage, those data on risk factors were collected and grouped by definitions. For factors that had been investigated in at least three individual studies, a random-effects (DerSimonian Laird method) meta-analysis was performed to evaluate the overall effect of a specific factor and its statistical significance. However, when the extracted data on potential risk factors were not sufficient for conducting the abovementioned meta-analysis of risk factors, a meta-regression approach, as described in

stage 2, was used to explore the potential correlates of AREDs. Common correlates that could be examined in the meta-regression approach included study-level or stratum-level characteristics, for example, sex, year of investigation, study setting, geography (latitudes, longitudes, or features associated with geographic locations). The specific approaches adopted in each systematic review varied and can be found in the following chapters.

2.5 Estimation of the regional number of cases

In this study, the subnational number of cases was generated for the six geographic regions in China, namely, East China, North China, Northeast China, Northwest China, South Central China, Southwest China (**Table 2.2** and **Figure 2.2**) (Zhang et al., 2013, National Bureau of Statistics, 2012, National Bureau of Statistics, 2002). As stated in stage 4, the identification of potential correlates of or risk factors for AREDs could be conducted using the meta-regression approach or the meta-analysis of risk factor approach. In the meta-regression approach, the prevalence estimates in each geographic region could be directly generated by taking their corresponding geographic features., The sum of regional cases should be adjusted to ensure that the regional burden of AREDs (number of cases) exactly fit the "national envelope". This was done by multiplying the regional number of cases by an "adjustment index", which was calculated as follows:

$$\text{Adjustment index} = National\ number\ of\ cases / Sum\ of\ regional\ number\ of\ cases$$

In the meta-analysis approach, a "risk factor-based model", as initially proposed by the Child Health Epidemiology Reference Group (CHERG), and has, since, been adopted widely in disease burden research (Rudan et al., 2004, Fowkes et al., 2013, Adeloye et al., 2015), was carried out to split the "national envelope" into the six regions. First, the prevalence of risk factors, as identified in stage 4, at the national level and in each of the six geographic regions was obtained. The data sources varied according to the type of risk factors. Second, the regional number of cases was calculated using the following equation:

$$N_{region} = (Pop_{region}) * (Prev_{AREDs_{nation}}) * (1 + \sum_{RF_1}^{RF_n} [(Prev_{RF_{region}} - Prev_{RF_{nation}}) * (OR_{RF_{nation}} - 1)])$$

Where N_{region} refers to the number of cases in each of the six geographic regions, Pop_{region} indicates the regional population size, $Prev_{AREDs_{nation}}$ is the estimated prevalence of AREDs

at the national level (stage 2), $Prev_{RF_{region}}$ is the prevalence of a risk factor in one region and $Prev_{RF_{nation}}$ is the national prevalence of a specific risk factor. $OR_{RF_{nation}}$ is the estimated OR of a specific risk factor (stage 4). Finally, the regional number of cases was adjusted by multiplying the "adjustment index".

Table 2.2. The six geographical regions in China

Region	Included provinces
North China	Beijing Municipality, Hebei province, Inner Mongolia Autonomous Region, Shanxi province, Tianjin Municipality;
Northeast China	Heilongjiang province, Jilin province, Liaoning province;
East China	Anhui province, Fujian province, Jiangsu province, Jiangxi province, Shandong province, Shanghai Municipality, Zhejiang province;
South Central China	Guangdong province, Guangxi Zhuang Autonomous Region, Hainan province, Henan province, Hubei province, Hunan province;
Southwest China	Chongqing Municipality, Guizhou province, Sichuan province, Tibet Autonomous Region, Yunnan province;
Northwest China	Gansu province, Ningxia Hui Autonomous Region, Qinghai province, Shaanxi province, Xinjiang Uyghur Autonomous Region;

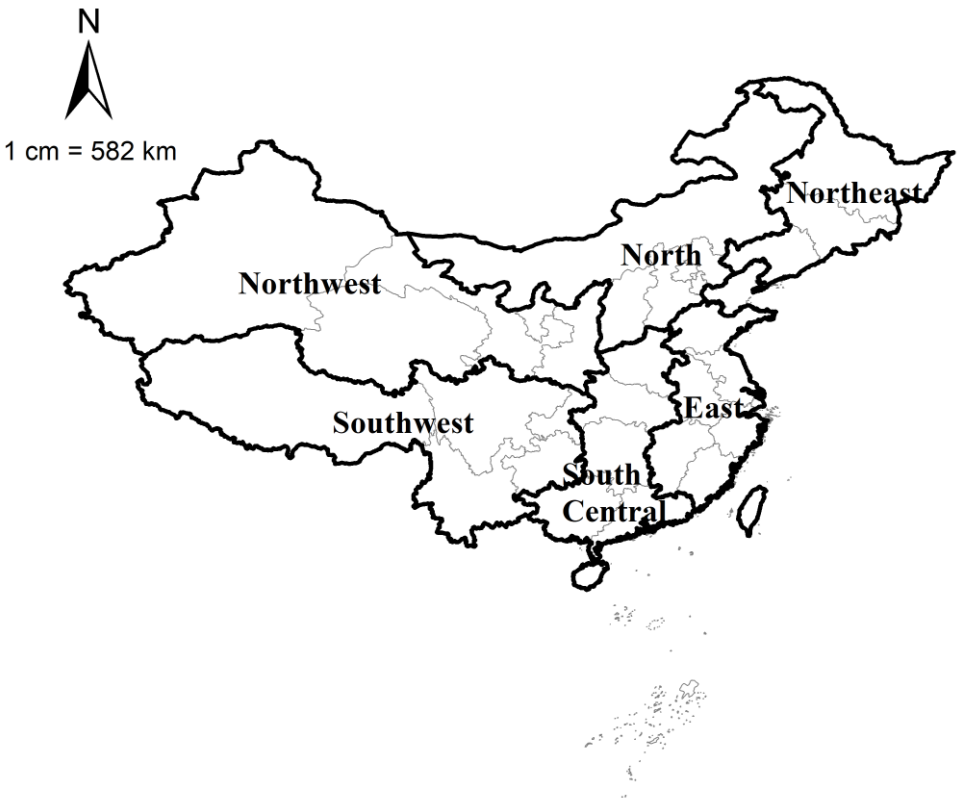


Figure 2.2. The six geographical regions in China

2.6 Ethical self-assessment

This study was based on publicly available and published information, thus no ethical approval was needed. A level-one ethical self-assessment was carried out by Dr Kit Yee Chan, based on institutional policy (see **Appendix table 1**).

Chapter 3 The national and subnational prevalence and burden of age-related macular degeneration in China

3.1 Summary

In this chapter, I applied the systematic review and meta-regression approach, as described in Chapter 2, to estimate the age-specific prevalence of AMD and its subtypes, namely early AMD and late AMD (GA and NVAMD). Overall, the prevalence of AMD and its subtypes all increased with advancing age. By applying the age-specific population data in China, the national numbers of people affected by AMD and its subtypes in China were demonstrated from 1990 to 2050. For any AMD, its prevalence was additionally lower in rural settings and decreased with increasing latitudes. Therefore, the regional prevalence and burden of any AMD were generated by taking the effects of age, setting and latitude.

The work presented in this chapter has been published in the Journal of Global Health cited as "Song, P., Du, Y., Chan, K. Y., Theodoratou, E., Rudan, I., & on behalf of the Global Health Epidemiology Research Group (GHERG). (2017). The national and subnational prevalence and burden of age-related macular degeneration in China. Journal of Global Health, 7(2), 020703. http://doi.org/10.7189/jogh.07.020703".

I was fully involved in all aspects of this project, including study design, development of search strategies, systematic review, data extraction, data analysis, interpretation of findings. I prepared the first draft of manuscript for publication, which has been subsequently revised for several rounds according to the comments from anonymous peer reviewers and the journal editors during the publishing process. The specific contributions of co-authors are as follows: Rudan, I. conceptualised and designed the study, Du, Y. conducted the dual systematic review and data extraction, Rudan, I., Chan, K. Y. and Theodoratou, E. critically reviewed the manuscript and approved the final manuscript.

3.2 Background

Age-related macular degeneration (AMD), a degenerative disease of the macula, is a leading cause of severe and irreversible loss of vision globally, and most notably in developed countries (Lim et al., 2012, Jager et al., 2008, Wong et al., 2014). In 2010, it was estimated that AMD was the third most common cause of blindness, and the fourth leading cause of visual impairment worldwide (Pascolini and Mariotti, 2011). Although AMD is not a life-threatening disorder, up to one-third of the affected individuals will experience various degrees of disability and depression during the course of the disease, even when only one eye is affected (Casten et al., 2004, Mitchell and Bradley, 2006). Moreover, AMD is notably associated with falls and other injuries, resulting in increased economic and social burden for the individual, caregiver and community to bear (Hassan et al., 2002, Brody et al., 2001, Lamoureux et al., 2010, Bonastre et al., 2002). Ageing is consistently documented as the most important risk factor for AMD (Wong et al., 2014, Lim et al., 2012, Bonastre et al., 2002). In addition, other factors, such as cigarette smoking, female sex, ethnicity, and genetic predisposition may also play a role (Thornton et al., 2005, Wong et al., 2014, Swaroop et al., 2007). The combined effect of continuous exposure to different risk factors and different demographic ageing speed resulted in the global epidemic of AMD showing substantial variation across different ethnic groups and geographic regions (Wong et al., 2014, Rudnicka et al., 2012, Kawasaki et al., 2010, Reibaldi et al., 2016).

The clinical course of AMD can be broadly divided into two stages: early and late (advanced) (De Jong, 2006, Gottlieb, 2002, Lim et al., 2012). Early AMD is characterised by soft drusen and/or pigmentary changes, but many early cases do not progress to the advanced form (Gottlieb, 2002, De Jong, 2006). Late AMD includes two types: geographic atrophy (GA) and neovascular (exudative) AMD (NVAMD). Compared with early AMD, late AMD is far less frequent but most damaging to the sight (Rickman et al., 2013). According to the latest global estimate of AMD prevalence, both early and late AMD were most frequent in populations of European ancestry (11.20% and 0.50%). Early AMD is least common in Asians (6.81%) while late AMD is least common in populations of African ancestry (0.28%) (Wong et al., 2014). With Asia having the largest share of the world's population, and understanding that AMD is an age-driven disorder, it was estimated that Asia had the greatest number of people with AMD in 2014 (59 million). Furthermore, this number is expected to increase at the fastest pace in Asia in comparison to other regions - to 113 million by 2040. China, the most populous country in the world, is experiencing the most rapid ageing trend among all developing countries. It

has been estimated that more than one-third of Chinese people living in China will be aged 60 years and over by 2050 (United Nations, 2015b). It is, therefore, important to have an up-to-date summary of the magnitude and distribution of AMD in the general population to inform stakeholders and guide eye-related health policy-making and health services allocation in China.

In the last two decades, an increasing number of epidemiological studies of AMD have been conducted in China. The estimates were, however, contingent upon the characteristics of individual studies: the age structure of the study sample, case definition and classification of AMD (Li et al., 2009, Zhou et al., 2007, Zhang et al., 2015). Another important feature of AMD is that its prevalence is likely to be associated with geographic factors. In the most recent global geo-epidemiology analysis of AMD, both latitude and longitude were inversely correlated with AMD prevalence, providing a new clue to study the geographic distribution of AMD (Reibaldi et al., 2016).

Until recently, there were no systematic estimates of AMD prevalence in China. With that said, the sheer volume of data available on the prevalence of AMD in Chinese bibliographical databases makes it possible to summarise the prevalence and burden of AMD from a modelling perspective (Fung, 2008, Xia et al., 2008). Moreover, the large territory area with great variation of latitude and longitude in China provides a good opportunity to explore the influence of geographic factors within the same country. In this study, I undertook a comprehensive systematic review, in both Chinese and English databases, to retrieve population-based studies of AMD prevalence in China from 1990 onwards. Based on the existing evidence, I estimated and projected the prevalence and burden of AMD and its sub-types. The aims of this study were to 1) ascertain the AMD prevalence in China by using epidemiological modelling; 2) estimate and project the overall prevalence and number of people living with AMD at the national level from 1990 to 2050; 3) estimate the regional prevalence and number of people with AMD from 2000 to 2010.

3.3 Methods

3.3.1 Systematic review

For developing epidemiological models to estimate the prevalence of AMD and its subtypes in the general population, a systematic review was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines and the

Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement (Moher et al., 2009, Stevens et al., 2016).

3.3.1.1 Search strategy

To ensure that all possible informative studies are included, a comprehensive literature search (title, abstract and keywords) was conducted in order to identify relevant studies. First, three Chinese bibliographic databases and three English bibliographic databases were searched from inception to 17 September 2016. These were the China National Knowledge Infrastructure (CNKI), Wanfang, Chinese Biomedicine Literature Database (CBM-SinoMed), PubMed, Embase and Medline. The source of studies in the three Chinese databases included journal articles, abstracts, dissertations and conference proceedings, whereas those in the three English databases included journal articles only. A combination of search terms for prevalence (prevalence, incidence, mortality, morbidity, epidemiology), AMD (age-related macular degeneration, age-related maculopathy, retina* macula* age related degeneration, retina* macular degeneration, macular degeneration) and China (China, Chinese, Hong Kong, Macau, Taiwan) was adopted for the comprehensive search. The final search strategy is presented in **Appendix table 2**. Note that the search strategy for the different bibliographic databases was slightly different based on the database's specific search features. Snowball searching of reference lists of publications retrieved in the first step was then conducted to further identify studies of interest. Only studies published since 1990 were retrieved and no language restrictions were imposed.

3.3.1.2 Inclusion and exclusion criteria

Only population-based studies that quantified the prevalence of AMD were included in this study. This is because studies conducted at institutional sites tend to have poor representativeness of the surrounding general population, especially for affected people living in poor and rural areas where access to health is not universal. Studies that relied on self-reported diagnosis were also excluded, due to recall bias. Studies that only reported the number of eyes affected by AMD, rather than the number of affected individuals, were also excluded because no prevalence of AMD could be derived from such studies. Duplicate publications of the same study were compared and the study providing more details was retained. Some additional criteria were also applied to ensure the quality of included studies. The detailed selection criteria are shown in **Table 3.1**.

Table 3.1. Selection criteria of studies on AMD prevalence in China in the systematic review

Inclusion criteria
1) Community-based study of AMD in China (including Hong Kong, Macao and Taiwan);
2) Studies conducted to examine the epidemiology of AMD;
3) Studies reported numerical prevalence measure of AMD.
Exclusion criteria
1) Multiple publications of the same study;
2) Studies with no professional assessment methods or relied on self-reported diagnoses;
3) Studies that were conducted in a group of people with characteristics that were clearly unrepresentative, e.g. those with visual impairment, diabetic patients;
4) Studies with inconsistencies between reported methods and presented results.

3.3.1.3 Study selection and data extraction

Before reviewing the retrieved records, duplicates were removed manually. Records were screened for relevance in two stages: screening of titles and abstracts followed by the retrieval and check of full-text articles. All non-English or non-Chinese language documents were reviewed after translation into English by Google Translate. The quality of each included study was assessed in terms of five core components-sample population, sample size, participation rate, outcome assessment, and analytical methods. Each bias component was scored as 2 for low risk, 1 for moderate risk and 0 for high risk and unclear. The quality of each study was represented by the total score (**Table 2.1**) (Von Elm et al., 2007, Song et al., 2018). For studies that fulfilled the criteria, three main categories of data were extracted: characteristics of the study, characteristics of the investigated population, and prevalence estimates of AMD and its subtypes. The data extraction tables were pilot tested on ten randomly selected included studies and refined accordingly before the final extraction.

The final data extraction table included:

1) Characteristics of the study: authors, publication year, study setting, year of survey, sampling method, study design (cross-sectional or cohort), AMD assessment method, and AMD grading system;

2) Characteristics of the investigated population: number of the sample, population type (urban, rural or mixed), sex (male, female or mixed), and age (age range, mean or median age, or midpoint of the age range);
3) Prevalence data: number of people with AMD and the number of participants who had been tested, by age group, sex, setting and AMD subtype where available.

The geographic indicators of interest (latitude, longitude and average annual insolation) were assigned to each study accordingly. The latitude and longitude data were obtained using Google Maps GPS coordinates (http://www.gps-coordinates.net/). The average annual insolation data (i.e., the amount of solar radiation incident on the surface of the earth) on the horizontal surface, expressed in $kWh/m^2/day$, was obtained from the National Aeronautics and Space Administration (NASA) Atmospheric Science Data Centre (http://eosweb.larc.nasa.gov/sse/). When study settings were defined as larger regions, such as at provincial, or regional levels, the mean centre point of the setting was calculated and the corresponding geographic data of the centre point was used. Studies that reported raw prevalence data in more than one geographic area (e.g. a single study presented prevalence of AMD for three different cities) were recorded separately for each geographic area. For studies that reported aggregated AMD prevalence data for different geographic areas, the average geographic data of the different areas were calculated and recorded. For studies with missing data of survey year, three years were subtracted from the published year to impute the survey year, which was based on the average time from survey to publication in studies with available data (see **Appendix table 3**). In studies where censoring age groups were reported, e.g. older than 80 years, the missing age band was taken as the same width as other age groups in the same study.

The classification systems used to define AMD and its subtypes include the Wisconsin age-related maculopathy grading system (WARMGS) (Klein et al., 1991), the International Classification and Grading system (IC) (Bird et al., 1995), the Clinical Age-Related Maculopathy Grading System (CARMS) (Seddon et al., 2006), and the "Age-related Macular Degeneration Clinical Diagnosis Standard" proposed by the China Medical Association in 1986 (CMA1986) (China Medical Association, 1987). For studies adopting different classification systems, the prevalence of any AMD, early AMD, late AMD, which included GA and NVAMD, was extracted or calculated (if necessary) separately according to the definitions below:

1) Early AMD: any soft drusen (distinct or indistinct) and pigmentary abnormalities, or large soft drusen 125 μm or more in diameter with a large drusen area (>500 μm diameter circle) or large soft indistinct drusen in the absence of signs of late-stage disease;
2) Late AMD: the presence of geographic atrophy or pigment epithelial detachment, subretinal haemorrhage or visible subretinal new vessel, or subretinal fibrous scar or laser treatment scar.

3.3.2 Statistical analysis

3.3.2.1 Epidemiological modelling of AMD prevalence

Due to high heterogeneity between studies that reported prevalence rates for any AMD, early AMD, late AMD, GA and NVAMD (**Appendix table 4**), random-effects models were adopted throughout the analysis. In the data3 extraction process, data were stratified by age, sex and setting. Some studies provided more than one data point. To take this hierarchical data structure into account, a multilevel mixed-effect meta-regression was conducted (Hox et al., 2010, Viechtbauer, 2010). Given that:

$$\text{Prevalence} = \text{p} = \frac{Number\ of\ cases}{Samle\ size}$$

Then, the binomial distribution of prevalence rates was transferred to the normal distribution by using the logit link:

$$\text{logit}(p) = \log_e\left(\frac{p}{1-p}\right) = \log_e(odds) = \alpha + \beta_1 * x_1 + \beta_2 * x_2 + \cdots \beta_n * x_n$$

Estimates were back transformed and expressed as conventional prevalence:

$$\text{p} = \frac{e^{\alpha+\beta_1*x_1+\beta_2*x_2+\cdots\beta_n*x_n}}{1+e^{\alpha+\beta_1*x_1+\beta_2*x_2+\cdots\beta_n*x_n}}$$

3.3.2.2 Estimation of national number of people with AMD from 1990 to 2015

To develop the overall "envelope" of AMD cases in China from 1990 to 2015, five models were first developed to establish the prevalence of any AMD, early AMD, late AMD, GA and NVAMD as a function of age:

$$\text{logit}(p) = \alpha + \beta_1 * (age)$$

Thus, the prevalence of AMD is:

$$\text{p} = \frac{e^{\alpha+\beta_1*(age)}}{1 + e^{\alpha+\beta_1*(age)}}$$

The total number of AMD cases ("envelope") in China was calculated by multiplying the age-specific prevalence of AMD for each 5-year age group estimated in the above models with the corresponding 5-year population subgroups in China, available from the United Nations Population Division (UNPD) (United Nations, 2015b). This was performed for any AMD, early AMD, late AMD, GA and NVAMD separately in the years 1990, 2000, 2010 and 2015.

3.3.2.3 Effects of demographic and geographic factors on the prevalence of AMD

To investigate whether study-level demographic and geographic factors might affect the prevalence of AMD, variables of interest were added into the multilevel mixed-effect meta-regression to test the significance (Higgins and Green, 2008). As a rule, at least seven data points should be available for each variable (Vittinghoff and McCulloch, 2007). These variables included sex, setting, latitude, longitude and average annual insolation. Investigation year was also tested so as to assess if there were any significant time trends. All variables that individually associated AMD prevalence in univariable analyses were included in the subsequent multivariable regression model, where variables that were not statistically significant were removed, starting from the one with the highest p value.

3.3.2.4 Projection of national number of people with AMD from 2020 to 2050

For the projection to the year 2050, age-specific prevalence rates of AMD were assumed to be constant over the next 34 years, the number of individuals with AMD from 2020 to 2050 was calculated by multiplying the age-specific prevalence rates to the corresponding UNPD Prospects data in the medium scenario (United Nations, 2015b).

3.3.2.5 Estimation of regional number of people with AMD from 2000 to 2010

Based on the final multivariable regression models that take the effects of demographic and geographic factors into consideration, the estimated national AMD cases were distributed into six geographical regions, namely, East China, North China, Northeast China, Northwest China, South Central China, Southwest China (**Table 2.2** and **Figure 2.2**) (Zhang et al., 2013, National Bureau of Statistics, 2012, National Bureau of Statistics, 2002). This method was initially proposed by the Child Health Epidemiology Reference Group (CHERG), and has, since, been adopted widely in disease burden research (Rudan et al., 2004, Fowkes et al., 2013, Adeloye et al., 2015). First, AMD prevalence in each geographic region was calculated, based on the final regression equation. Second, the regional number of people with AMD was estimated by multiplying the regional AMD prevalence and corresponding population for the years 2000 and 2010, where regional population data were available from the fifth and sixth census (National Bureau of Statistics, 2002, National Bureau of Statistics, 2012). Finally, the regional AMD cases were adjusted to fit the national AMD "envelope".

The overall study design is shown in **Figure 3.1**. Non-dichotomous variables were analysed as continuous. A two-sided p value less than 0.05 was regarded as statistically significant for all analyses. All statistical analyses were performed in R Studio (version 1.0.136) built on R (version 3.3.0). All included studies in the analysis were mapped by ArcGIS software (Version 10.1). The China base map was obtained as a shapefile from the Global Administrative Areas (GADM) database (GADM, 2015, version 2.0; www.gadm.org).

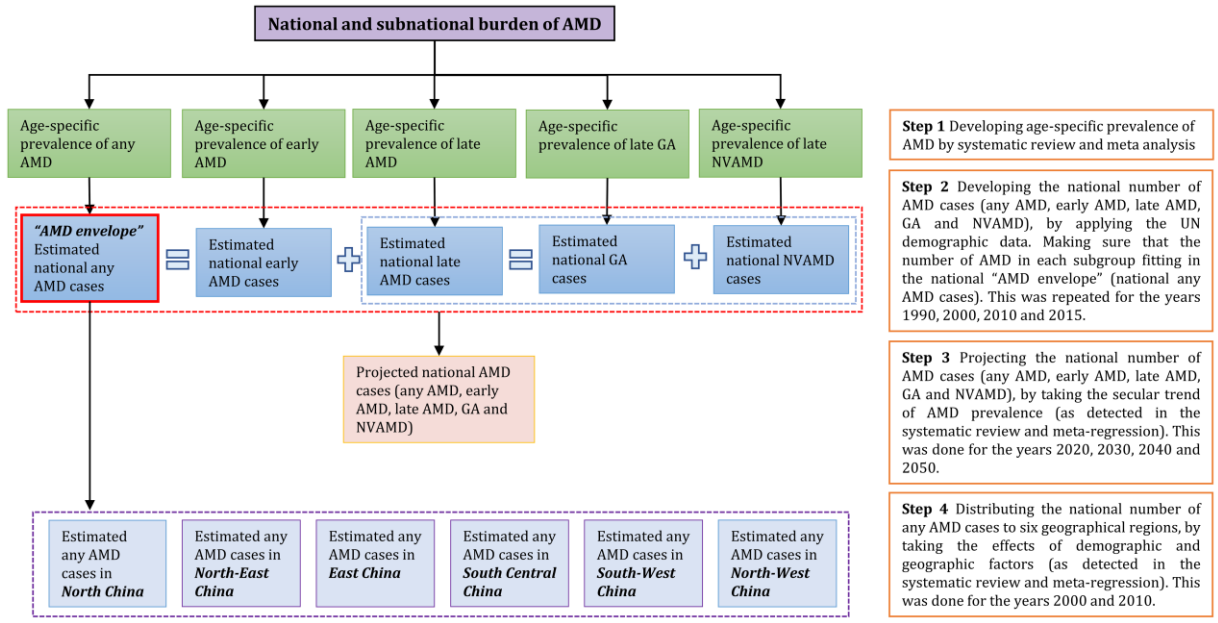


Figure 3.1. Overall study design flowchart for the prevalence and burden of AMD study in China

3.4 Results

3.4.1 Summary of systematic review

Figure 3.2 shows the process of systematic review for studies included in the final meta-analysis. In brief, the initial search identified 2016 citations. After removing 750 duplications, 986 apparently irrelevant citations by title and abstract review, and 15 citations with no sufficient information on methods and results, 265 papers were reviewed at the full-text level to assess their eligibility. Ultimately, 25 AMD prevalence studies were included in the final analysis.

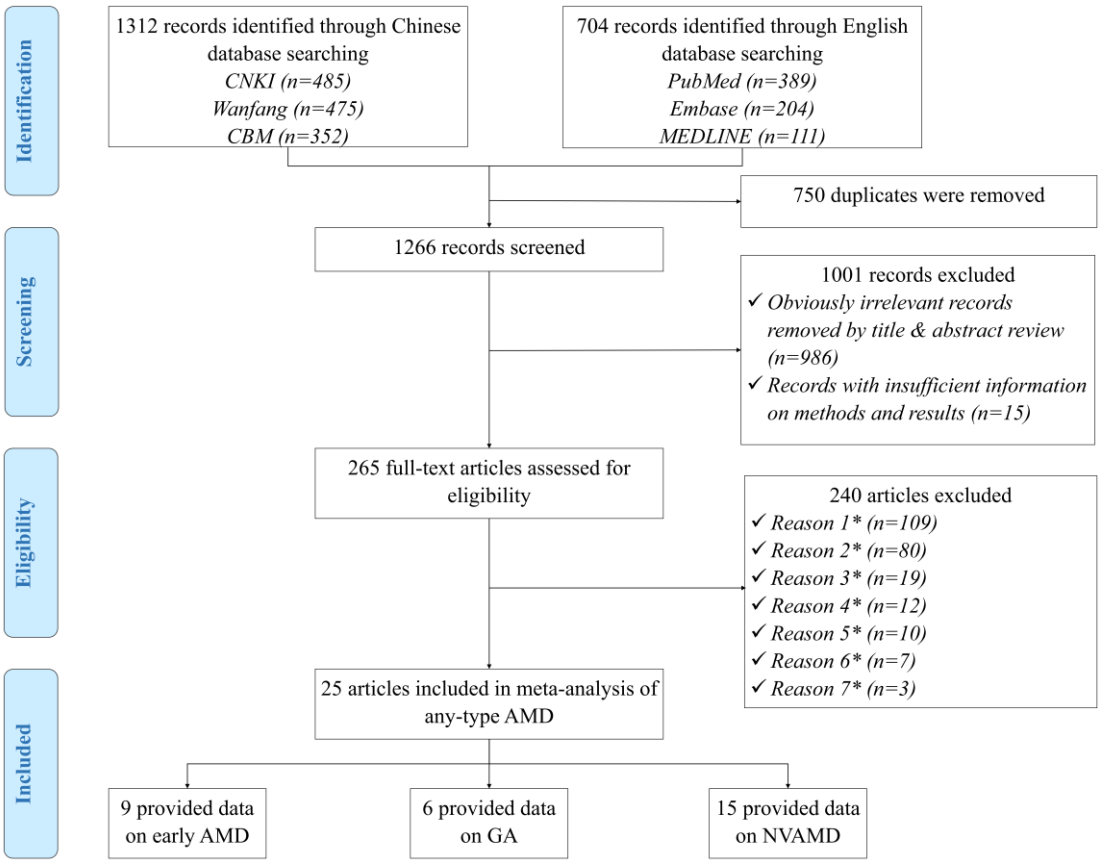


Figure 3.2. Systematic review flow diagram of studies on AMD prevalence in China

*Note: *Reason 1-Articles with no numerical measures of AMD prevalence; *Reason 2-Studies that were not population-based; *Reason 3-Multiple publications of the same study; *Reason 4-Studies that were not based in China; *Reason 5-Studies that had no professional assessment methods or relied on self-reported diagnoses; *Reason 6-Studies that were conducted in people with unrepresentative characteristics of general population (hypertensive patients, people with reduced vision, etc.); *Reason 7- Articles with inconsistency between reported methods and presented results.*

A full list of included studies is shown in **Appendix table 5**, the included data involved 3016 AMD cases in a total of 43420 examined individuals. **Table 3.2** shows the main characteristics of the studies. The detailed characteristics and quality score of every study can be found in **Appendix table 6** and **Appendix table 7**. All included studies were cross-sectional studies that assessed AMD by using fundus imaging. Almost half of the retained studies were published in the past six years (44.0%), with CMA1986 the most widely adopted grading system (48.0%), followed by WARMGS (24.0%) and CARMS (20.0%). All the included

studies were with an overall quality score of at least 6. The geographic distribution of the 25 included studies is demonstrated in **Figure 3.3**.

Table 3.2 Main characteristics of the included studies on AMD prevalence in China (n=25)

Characteristic		Number of studies (%)
Year published		
	1990-1999	7 (28.0)
	2000-2009	7 (28.0)
	2010-2016	11 (44.0)
Setting		
	Urban	7 (28.0)
	Rural	9 (36.0)
	Mixed	9 (36.0)
Sample size		
	600-1000	5 (20.0)
	1001-2000	5 (20.0)
	2001-3000	7 (28.0)
	3001-5000	4 (16.0)
	5001-8000	4 (16.0)
Grading system		
	CMA1986	12 (48.0)
	WARMGS	6 (24.0)
	CARMS	5 (20.0)
	IC	1 (4.0)
	Other	1 (4.0)
Quality score		
	10	6 (24.0)
	9	8 (32.0)
	8	4 (16.0)
	7	2 (8.0)
	6	5 (20.0)

Note: CAM 1986, the "Age-related Macular Degeneration Clinical Diagnosis Standard" proposed by the China Medical Association in 1986; WARMGS, the Wisconsin age-related maculopathy system; CARMS, the Clinical Age-Related Maculopathy Grading System; IC, the

International Classification and Grading system; Other, definition in the "Ophthalmology" (7th version).

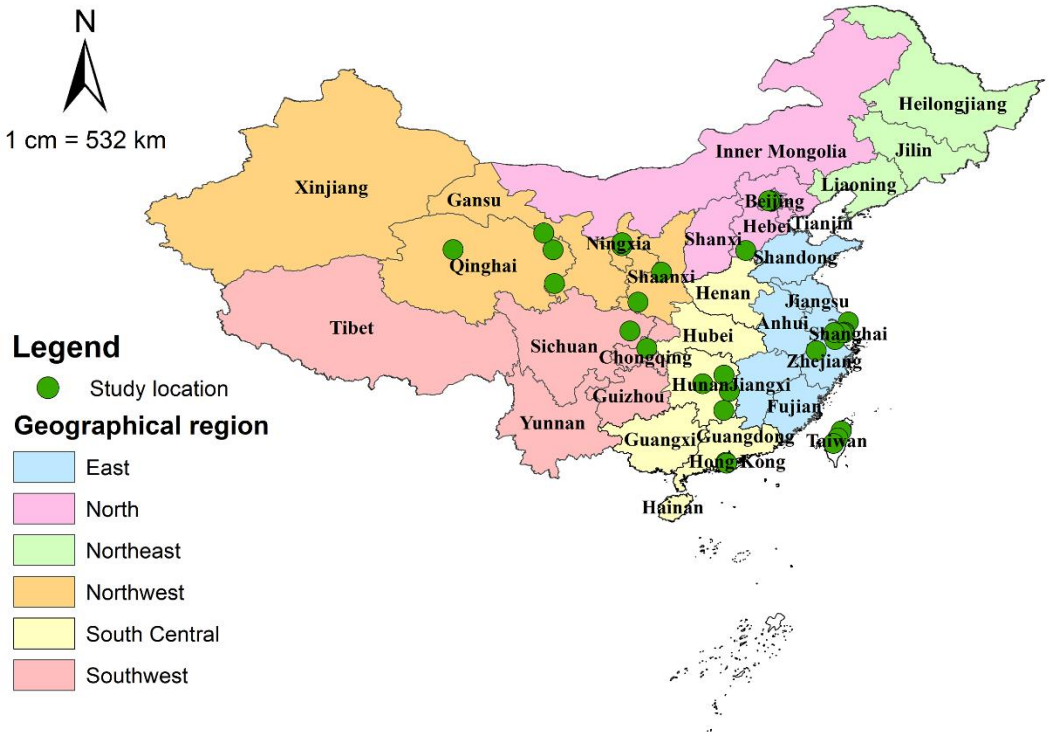


Figure 3.3. Geographic distribution of the included studies on AMD prevalence in China

3.4.2 Age-specific prevalence of AMD

In each model (**Figure 3.4**), a substantial number of data points were available for constructing the relationship between AMD prevalence and age. The age spectrum ranged from around 35 years to less than 90 years. However, for GA and NVAMD, few data points were available at younger ages (30-40 years). In this study, to ensure that the estimated prevalence was comparable, the lower bound of age range was set as 45 years and the upper bound as 89 years where data were available for model construction at all AMD subtype groups.

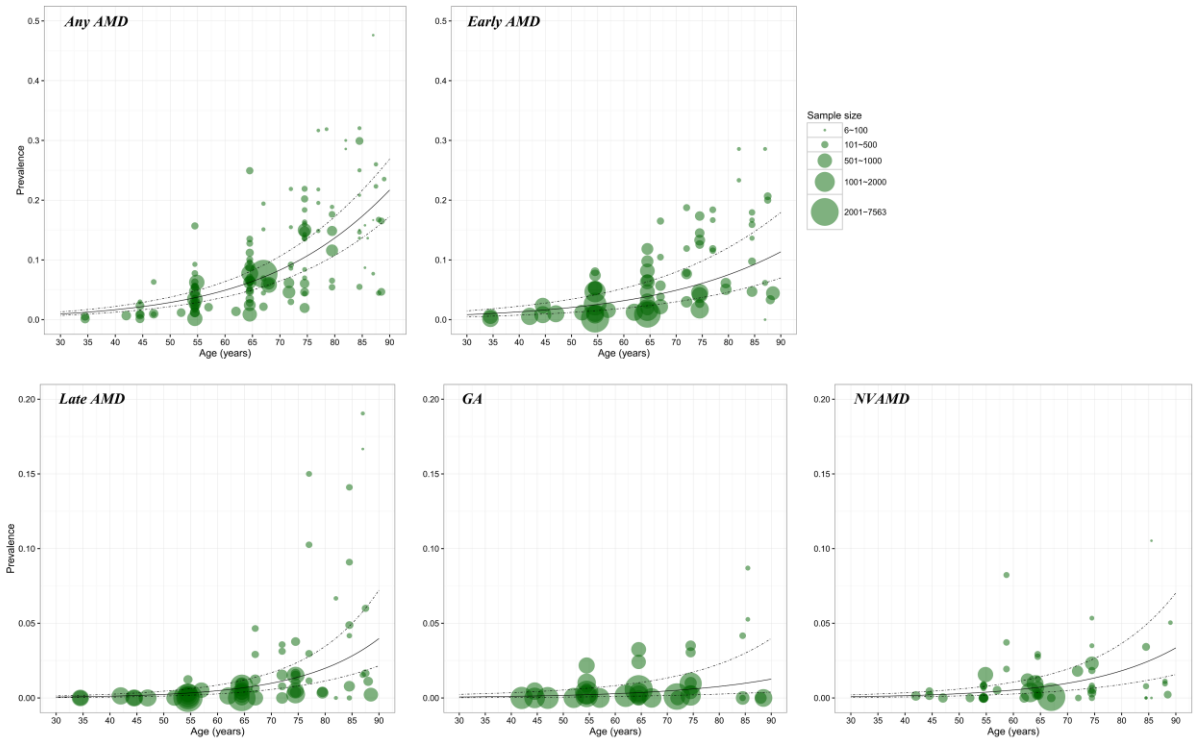


Figure 3.4. Prevalence of AMD and its subtypes by age in retained studies

Note: The size of each bubble is proportional to the sample size. There were 124 data points for constructing the relation between prevalence and age for any AMD, 67 for early AMD, 67 for late AMD, 35 for GA and 54 for NVAMD.

The estimated age-specific prevalence of any AMD, early AMD, late AMD, GA and NVAMD is shown in **Figure 3.5** and **Table 3.3**. The prevalence of any AMD ranged from 2.44% (95% CI: 1.85-3.22) in people aged 45-49 years to 18.98% (95% CI: 15.05-23.66) in people aged 85-89 years. Prevalence of early AMD ranged from 1.79% (95% CI: 1.05-3.02) to 10.05% (95% CI: 6.17-15.97), and, in the case of late AMD, from 0.38% (95% CI: 0.16-0.97) to 3.88% (95% CI: 1.68-9.13). In late AMD, the prevalence of GA was 0.15% (95% CI: 0.05-0.47) in people aged 45-49 years and 1.09% (95% CI: 0.35-3.36) in those aged 85-89 years, and the prevalence of NVAMD ranged between 0.24% (95% CI: 0.11-0.50) and 2.79% (95% CI: 1.33-5.77).

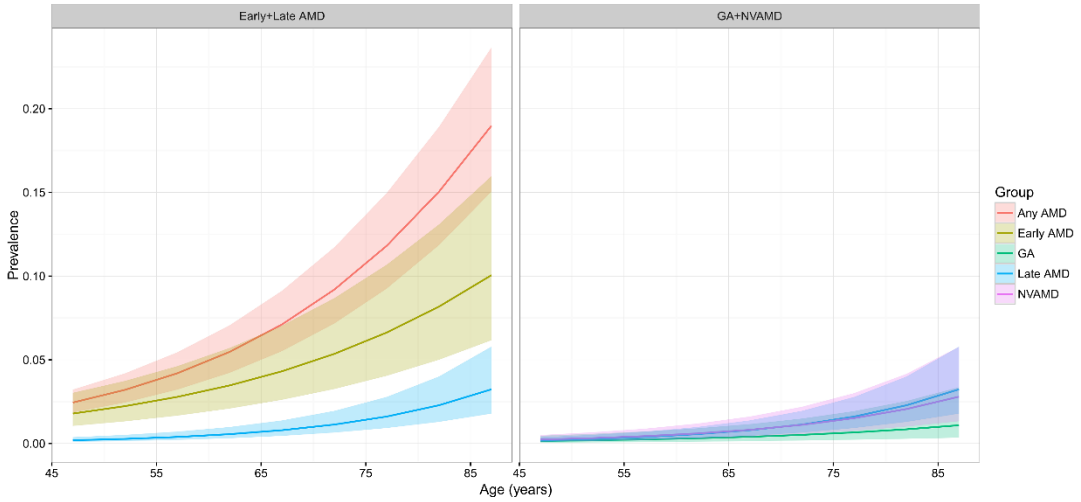


Figure 3.5. Estimated age-specific prevalence of AMD and its subtypes in China, with 95% confidence intervals

Table 3.3. Estimated age-specific prevalence of AMD and its subtypes in China

Age group	Any AMD	Early AMD	Late AMD	GA	NVAMD
45-49 years	2.44 (1.85-3.22)	1.79 (1.05-3.02)	0.38 (0.16-0.97)	0.15 (0.05-0.47)	0.24 (0.11-0.50)
50-54 years	3.21 (2.45-4.19)	2.23 (1.32-3.74)	0.51 (0.22-1.24)	0.19 (0.06-0.58)	0.32 (0.16-0.67)
55-59 years	4.20 (3.22-5.45)	2.78 (1.67-4.62)	0.68 (0.30-1.60)	0.24 (0.08-0.72)	0.44 (0.22-0.89)
60-64 years	5.47 (4.23-7.06)	3.47 (2.09-5.71)	0.91 (0.41-2.09)	0.31 (0.11-0.90)	0.60 (0.30-1.19)
65-69 years	7.11 (5.52-9.12)	4.31 (2.61-7.05)	1.22 (0.55-2.76)	0.40 (0.14-1.15)	0.82 (0.41-1.60)
70-74 years	9.20 (7.17-11.72)	5.36 (3.26-8.68)	1.63 (0.74-3.67)	0.52 (0.18-1.48)	1.11 (0.56-2.19)
75-79 years	11.81 (9.26-14.96)	6.63 (4.05-10.68)	2.18 (0.98-4.94)	0.66 (0.23-1.93)	1.52 (0.76-3.01)
80-84 years	15.05 (11.85-18.92)	8.18 (5.01-13.09)	2.91 (1.29-6.70)	0.85 (0.28-2.54)	2.06 (1.01-4.16)
85-89 years	18.98 (15.05-23.66)	10.05 (6.17-15.97)	3.88 (1.68-9.13)	1.09 (0.35-3.36)	2.79 (1.33-5.77)

Note: Data are % (95% CI).

3.4.3 National number of people with AMD from 1990 to 2015

By applying the age-specific prevalence of AMD to the national population in 1990, 2000, 2010 and 2015, the number of people living with AMD in China was estimated (**Appendix table 8**). During this period, the national prevalence of any AMD slightly decreased by 0.41%, from 5.26% (95% CI: 4.07-6.76) in 1990 to 5.24% (95% CI: 4.05-6.73) in 2015. This declining trend was also witnessed in early AMD and late AMD, with decreasing rates of 0.50% and 0.07% respectively. In late AMD, GA also showed a decreasing trend within this time frame, whereas the prevalence of NVAMD increased slightly (**Table 3.4**). Despite this decreasing prevalence trend during 1990-2015, the overall number of people with any AMD or its subtypes all increased dramatically due to the rapidly ageing population. The national number of people with any AMD increased by 121.80%, from 12.01 million (95% CI: 9.29-15.46) in 1990 to 26.65 million (95% CI: 20.62-34.27) in 2015. Within the same period, the number of people with early AMD increased from 9.44 million (95% CI: 7.74-11.15) to 20.91 million (95% CI: 17.16-24.68), and those with late AMD rose from 2.58 million (95% CI: 1.56-4.30) to 5.74 million (95% CI: 3.46-9.59), which yielded increasing rates of 121.60% and 122.55% respectively. In late AMD, increase in the number of people living with GA was similar to those with NVAMD (121.99% vs. 122.84%), which ranged from 0.87 million (95% CI: 0.40-1.83) to 1.93 million (95% CI: 0.89-4.08), and 1.71 million (95% CI: 1.16-2.47) to 3.81 million (95% CI: 2.57-5.51) throughout this time frame respectively (**Table 3.4**). In 2015, the age group that contributed the most cases of any AMD, early AMD, late AMD, GA and NVAMD was 60-64 years (**Figure 3.6**).

Table 3.4. Estimated prevalence and number of people living with AMD in China from 1990 to 2015, by AMD type

AMD type	Prevalence of AMD (%, 95% CI)				Number of people with AMD (million, 95% CI)				Relative rate of change (%, 1990-2015)	
	1990	2000	2010	2015	1990	2000	2010	2015	Prevalence	AMD cases
Any AMD	5.26 (4.07-6.76)	5.16 (3.99-6.64)	5.24 (4.05-6.73)	5.24 (4.05-6.73)	12.01 (9.29-15.46)	16.31 (12.62-20.99)	22.43 (17.36-28.85)	26.65 (20.62-34.27)	-0.41	+121.80
Early AMD	4.13 (3.39-4.88)	4.05 (3.33-4.79)	4.11 (3.37-4.85)	4.11 (3.37-4.85)	9.44 (7.74-11.15)	12.81 (10.51-15.13)	17.60 (14.45-20.78)	20.91 (17.16-24.68)	-0.50	+121.60
Late AMD	1.13 (0.68-1.88)	1.11 (0.67-1.85)	1.13 (0.68-1.88)	1.13 (0.68-1.88)	2.58 (1.56-4.30)	3.50 (2.11-5.86)	4.83 (2.91-8.07)	5.74 (3.46-9.59)	-0.07	+122.55
GA	0.38 (0.17-0.80)	0.37 (0.17-0.79)	0.38 (0.17-0.80)	0.38 (0.17-0.80)	0.87 (0.40-1.83)	1.18 (0.54-2.50)	1.62 (0.75-3.43)	1.93 (0.89-4.08)	-0.33	+121.99
NVAMD	0.75 (0.51-1.08)	0.74 (0.50-1.06)	0.75 (0.50-1.08)	0.75 (0.51-1.08)	1.71 (1.16-2.47)	2.32 (1.57-3.36)	3.21 (2.16-4.64)	3.81 (2.57-5.51)	+0.05	+122.84

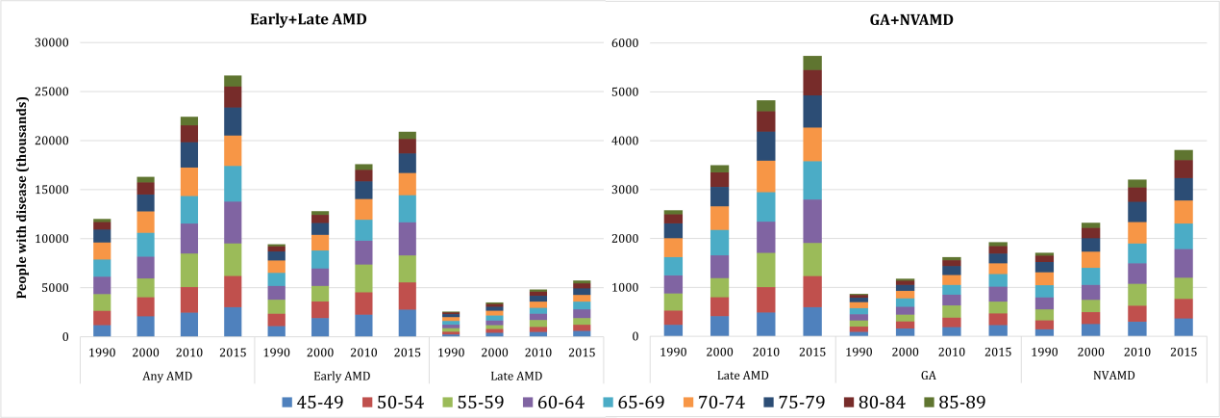


Figure 3.6. Estimation of the national number of people with AMD and contributing age groups in China from 1990 to 2015, by AMD type

3.4.4 Effects of demographic and geographic factors on the prevalence of AMD

Findings from the univariable meta-regression analyses (**Table 3.5**) showed that age, setting and latitude were significantly associated with the prevalence of any AMD. For early AMD, age, sex, setting and latitude also had a significant influence on the prevalence. For late AMD, age and latitude were found to be significantly associated with the prevalence. However, in late AMD, only age was found to be significantly associated with the prevalence of GA, and age, sex, latitude and insolation were significantly associated with the prevalence of NVAMD. For any AMD and all subtypes, the investigation year was identified to have no influence on prevalence rates and increased age was the only constantly significant risk factor.

Table 3.5. Meta-regression of AMD prevalence (logit form), univariable analyses

Variable	Number of studies	β (95 % CI)	p value
Any AMD			
Intercept	25	[-2.489] ([-2.764]-[-2.215])	<0.001
Age	25	0.056 (0.052- 0.060)	<0.001
Sex-male[$]	19	0.069 ([-0.004]-0.141)	0.063
Setting-rural	16	[-0.829] ([-1.304]-[-0.354])	<0.001
Latitude	25	[-0.076] ([-0.119]-[-0.033])	<0.001
Longitude	25	0.023 ([-0.017]-0.064)	0.262
Insolation	25	[-0.551] ([-1.132]-0.030)	0.063

Variable	Number of studies	β (95 % CI)	p value
Investigation year	25	[-0.014] ([-0.045]-0.017)	0.370
Early AMD			
Intercept	10	[-2.982] ([-3.528]-[-2.436])	<0.001
Age	10	0.045 (0.039-0.052)	<0.001
Sex-male[$]	7	0.197 (0.054-0.339)	0.007
Setting-rural	7	[-1.037] ([-1.833]-[-0.241])	0.011
Latitude	10	[-0.127] ([-0.181]-[-0.072])	<0.001
Longitude	10	0.052 ([-0.033]-0.137)	0.233
Insolation	10	[-0.864] ([-2.155]-0.428)	0.190
Investigation year	10	0.003 ([-0.103]-0.109)	0.954
Late AMD			
Intercept	10	[-4.548] ([-5.308]-[-3.787])	<0.001
Age	10	0.071 (0.055-0.088)	<0.001
Sex-male[$]	7	0.321 ([-0.053]-0.696)	0.093
Setting-rural	7	[-0.229] ([-1.715]-1.257)	0.763
Latitude	10	[-0.167] ([-0.247]-[-0.086])	<0.001
Longitude	10	0.045 ([-0.078]-0.169)	0.472
Insolation	10	0.066 ([-1.915]-2.046)	0.948
Investigation year	10	0.054 ([-0.090]-0.198)	0.464
GA			
Intercept	6	[-5.517] ([-6.557]-[-4.478])	<0.001
Age	6	0.050 (0.028-0.072)	<0.001
Sex-male[$]	2	0.089 ([-0.449]-0.627)	0.746
Setting-rural	4	1.261 ([-0.734]-3.255)	0.215
Latitude	6	[-0.048] ([-0.274]-0.179)	0.681
Longitude	6	[-0.115] ([-0.280]-0.050)	0.173
Insolation	6	[-1.522] ([-3.914]-0.871)	0.213
Investigation year	6	0.081 ([-0.105]-0.266)	0.394
NVAMD			
Intercept	15	[-4.756] ([-5.360]-[-4.152])	<0.001
Age	15	0.063 (0.046-0.079)	<0.001
Sex-male[$]	6	0.376 (0.070-0.682)	0.016
Setting-rural	9	0.433 ([-0.827]-1.693)	0.501
Latitude	15	0.074 ([-0.061]-0.209)	0.282

Variable	Number of studies	β (95 % CI)	p value
Longitude	15	[-0.078] ([-0.142]-[-0.014])	0.017
Insolation	15	0.973 (0.290-1.656)	0.005
Investigation year	15	[-0.057] ([-0.133]-0.020)	0.149

Note: [$] the estimate of sex effect was based on studies that provided AMD prevalence for both males and females; coefficients represent log odds ratios (ORs).

Although most studies provided multiple data points of prevalence rates, these data were mainly stratified by age groups. For AMD subtype groups (early AMD, late AMD, GA and NVAMD), and after controlling the difference of age structures, insufficient data were available for conducting multivariable meta-regression that simultaneously included all statistically significant factors identified in the univariable analyses. Thus, here the multivariable regression model was only conducted and reported for any AMD. The formula generated from the multivariable regression is shown below:

$$\text{logit}(p) = -4.230 + 0.056 * age + (-0.6013) * setting_{rural} + 0.053 * setting_{urban} + (-0.060) * latitude + u_i$$

Where p indicates the prevalence of any AMD; $setting_{rural}$=1 for rural setting and =0 otherwise; $setting_{urban}$=1 for urban setting and =0 otherwise; $latitude$ refers to the absolute value of latitude; u_i=variance of the study level random effect.

3.4.5 Projection of national number of people with AMD from 2020 to 2050

No secular trend of the prevalence of any AMD, early AMD, late AMD, GA and NVAMD was observed in the included studies, thus age-specific prevalence was assumed as constant for the projection analysis. By applying the age-specific prevalence of AMD to the national population in 2020, 2030, 2040 and 2050, the numbers of people with AMD were projected (**Appendix table 8**). Unlike the slightly fluctuating trend of AMD prevalence from 1990 to 2015, the prevalence rates of all subtypes of AMD will increase notably during 2020 and 2050. In 2020, the prevalence of any AMD will be 5.39% (95% CI: 4.18-6.93) and is expected to increase by 41.66%, reaching to 7.64% (95% CI: 5.96-9.73) in 2050. Among all subtypes of AMD, NVAMD will show the greatest increasing rate of 57.48%, from 0.78% (95% CI: 0.52-1.12) in 2020 to 1.22% (95% CI: 0.83-1.75) in 2050, whereas the increasing rate of early AMD

will be the smallest (38.45%), from 4.23% (95% CI: 3.47-4.99) to 5.21% (95% CI: 4.31-6.08) during this period (**Table 3.6**).

From 2020 to 2050, the number of cases of any AMD in China will rise by 76.72%, from 31.23 million (95% CI: 24.18-40.14) to 55.19 million (95% CI: 43.04-70.30). The increasing rate of late AMD cases will be greater than that of early AMD cases (91.12% vs. 72.70%), with the number of people affected by early AMD increasing from 24.47 million (95% CI: 20.10-28.87) in 2020 to 42.26 million (95% CI: 35.15-49.05) in 2050, and those affected by late AMD from 6.76 million (95% CI: 4.08-11.28) to 12.92 million (95% CI: 7.89-21.26). In late AMD, the number of people with GA will increase by 80.78%, from 2.26 million (95% CI: 1.04-4.78) in 2020, to 4.09 million (95% CI: 1.89-8.59) in 2050. Furthermore, the number of those with NVAMD will grow even further (96.45%), from 4.50 million (95% CI: 3.04-6.50) to 8.84 million (95% CI: 6.00-12.66) (**Table 3.6**). From 2020 to 2050, the age groups to contribute the most cases will shift from 65-69 years to 80-84 years for any AMD, late AMD, GA and NVAMD, and from 65-69 years to 75-79 years for early AMD (**Figure 3.7**).

Table 3.6. Projected prevalence and number of people living with AMD in China from 2020 to 2050, by AMD type

AMD type	Prevalence of AMD (%, 95% CI)				Number of people with AMD (million, 95% CI)				Relative rate of change (%, 2020-2050)	
	2020	2030	2040	2050	2020	2030	2040	2050	Prevalence	AMD cases
Any AMD	5.39 (4.18-6.93)	6.15 (4.77-7.88)	6.75 (5.25-8.62)	7.64 (5.96-9.73)	31.23 (24.18-40.14)	40.40 (31.36-51.78)	50.22 (39.07-64.18)	55.19 (43.04-70.30)	+41.66	+76.72
Early AMD	4.23 (3.47-4.99)	4.78 (3.94-5.62)	5.21 (4.31-6.08)	5.85 (4.87-6.79)	24.47 (20.10-28.87)	31.42 (25.90-36.90)	38.78 (32.10-45.28)	42.26 (35.15-49.05)	+38.45	+72.71
Late AMD	1.17 (0.70-1.95)	1.37 (0.83-2.26)	1.54 (0.94-2.54)	1.79 (1.09-2.94)	6.76 (4.08-11.28)	8.98 (5.45-14.87)	11.45 (6.97-18.9)	12.92 (7.89-21.26)	+53.28	+91.21
GA	0.39 (0.18-0.83)	0.45 (0.21-0.94)	0.50 (0.23-1.04)	0.57 (0.26-1.19)	2.26 (1.04-4.78)	2.95 (1.36-6.20)	3.69 (1.71-7.76)	4.09 (1.89-8.59)	+44.92	+80.78
NVAMD	0.78 (0.52-1.12)	0.92 (0.62-1.32)	1.04 (0.71-1.50)	1.22 (0.83-1.75)	4.50 (3.04-6.50)	6.03 (4.09-8.67)	7.76 (5.26-11.13)	8.84 (6.00-12.66)	+57.48	+96.45

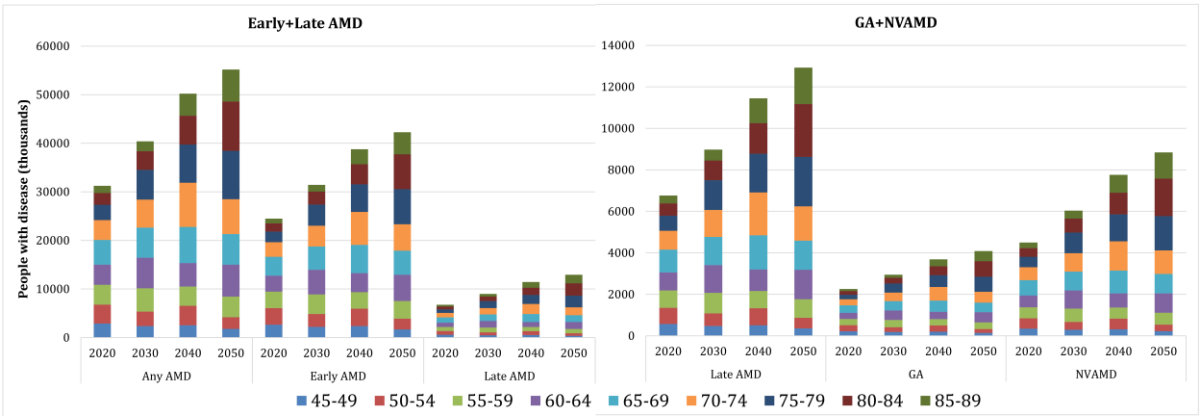


Figure 3.7. Projection of the national number of people with AMD and contributing age groups in China from 2020 to 2050, by AMD type

3.4.6 Regional number of people with any AMD from 2000 to 2010

The total numbers of AMD cases in China in 2000 and 2010 were distributed across the six geographical regions according to the final multivariable model that took into account three main factors: age, setting and latitude (**Appendix table 9**). In 2000, the national prevalence of AMD in China was 5.16% (95% CI: 3.99-6.64), with the regional prevalence estimates ranging from 2.69% (95% CI: 1.67-4.29) in North-East China to 6.64% (95% CI: 5.12-8.52) in South Central China. In 2010, the prevalence was still the highest in South Central China (6.74% [95% CI: 5.20-8.65]) and the lowest in North-East China (2.65% [95% CI: 1.66-4.20]), with the overall prevalence in Chinese population increasing to the level of 5.24% (95% CI: 4.05-6.73). During 2000 to 2010, the overall prevalence of AMD increased by 1.44%, and the most marked increase was in Southwest China (6.51%) while the prevalence rate of AMD declined by 1.37% in North-East China (**Table 3.7**).

Table 3.7. Estimated prevalence and number of people living with any AMD in China from 2000 to 2010, by geographical region

Region	Prevalence of any AMD (%, 95% CI)		Number of people with any AMD (million, 95% CI)		Relative rate of change (%, 2000-2010)	
	2000	2010	2000	2010	prevalence	AMD cases
North China	3.28 (2.35-4.55)	3.36 (2.42-4.64)	1.23 (0.88-1.70)	1.82 (1.31-2.51)	+2.40	+48.18

Region	Prevalence of any AMD (%, 95% CI)		Number of people with any AMD (million, 95% CI)		Relative rate of change (%, 2000-2010)	
	2000	2010	2000	2010	prevalence	AMD cases
North-East China	2.69 (1.67-4.29)	2.65 (1.66-4.20)	0.76 (0.47-1.21)	1.11 (0.69-1.76)	-1.37	+46.70
East China	5.46 (4.39-6.74)	5.57 (4.49-6.86)	5.32 (4.29-6.57)	7.33 (5.91-9.04)	+1.99	+37.67
South Central China	6.64 (5.12-8.52)	6.74 (5.20-8.65)	5.50 (4.24-7.05)	7.52 (5.80-9.64)	+1.54	+36.74
South-West China	5.68 (4.50-7.11)	6.05 (4.81-7.56)	2.85 (2.26-3.56)	3.70 (2.94-4.62)	+6.51	+29.97
North-West China	3.29 (2.44-4.43)	3.40 (2.53-4.55)	0.66 (0.49-0.89)	0.95 (0.71-1.28)	+3.23	+44.65
China	5.16 (3.99-6.64)	5.24 (4.05-6.73)	16.31 (12.62-20.99)	22.43 (17.36-28.85)	+1.44	+37.50

Estimates of the number of people living with AMD in different regions are shown in **Table 3.7** and **Figure 3.8**. With the ageing trend of the Chinese population, the total number of people living with AMD in China increased by 37.50%, from 16.31million (95% CI: 12.62-20.99) in 2000 to 22.43 million (95% CI: 17.36-28.85) in 2010. In 2000, more than one-third (33.72%) of Chinese AMD cases were found living in South Central China (5.50 million [95% CI: 4.24-7.05]) and only 4.05% were in North-West China (0.66 million [95% CI: 0.49-0.89]). In 2010, this distribution of AMD cases remained the same across the six geographical regions, with most (33.53%) of the AMD cases in South Central China (7.52 million [95% CI: 4.24-7.05]) and the least (4.24%) in North-West China (0.95 million [95% CI: 0.71-1.28]). From 2000 to 2010, the most striking increases in the number of AMD cases were in North China (48.64%) and North-East China (47.06%), and the least in South-West China (29.97%). In 2010, the age groups that contributed the most AMD cases was 55-59 years in all of the six geographic regions.

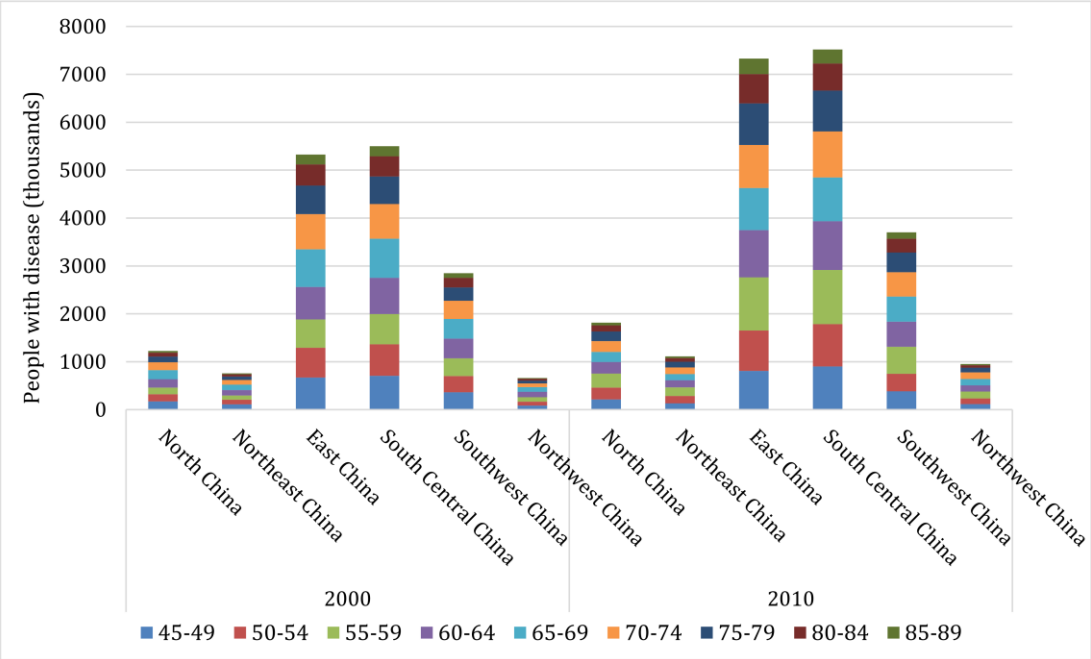


Figure 3.8. Estimation of the regional number of people with any AMD and contributing age groups in China from 2000 to 2010

3.5 Discussion

3.5.1 Statement of principal findings

In this systematic review and meta-analysis, data-driven estimates and projections of AMD prevalence and burden in China were presented, both at the national level and at the regional levels. The results from this synthesised population-based data show that the burden of AMD in China is substantial. From 1990 to 2015, the prevalence of AMD fluctuated at around 5.2%, which translates to a total of 26.65 million affected individuals in 2015. By 2050, the prevalence of AMD is expected to increase to 7.64%, with the corresponding number of affected individuals to 55.19 million. Substantial regional variation was found across the country, with AMD prevalence being the highest in South Central China and the lowest in the North-East. In terms of the total number of AMD cases, the greatest burden was in the South Central area, and the smallest in North-West China.

3.5.2 Strengths and limitations

To the best of my knowledge, this study is the first attempt to estimate the prevalence and the burden of AMD in China and to make future projections. The comprehensive search strategies and strict inclusion and exclusion criteria ensured a well-designed analysis. Furthermore, the current study provided estimates of the prevalence and the number of affected AMD cases by AMD subtype, with this additional information being of particular clinical and public health relevance. Indeed, such information offers valuable, detailed insights into the burden of AMD in China. Critically, this study used the best available data to portray a complete picture of the public health burden of AMD in different regions. Therefore, it can serve as the basis for health policy making and resource allocation for AMD prevention and treatment initiatives. From a global perspective, this study complements the most recent Global AMD study, where insufficient data were available for national estimates and projections (Wong et al., 2014).

However, this study is not free from limitations. First, significant heterogeneity existed between all of the included studies, despite the strict inclusion and exclusion criteria applied. Like any meta-analysis, the findings of this study are only as good as the included primary investigations. Included studies did not come from across the country, thus the ability to generate provincial estimates of AMD prevalence and cases may be limited. Second, one NVAMD-like disease, polypoidal choroidal vasculopathy, is markedly more common in Asians (Wong et al., 2014, Liu et al., 2007, Lee et al., 2009), and taking into consideration that most population-based studies may have limited ability to distinguish between these two diseases (as suggested previously (Wong et al., 2014)), the prevalence and burden of NVAMD in the current study may be overestimated. In addition, as suggested by a previous meta-analysis, studies using fundus imaging with classifications, rather than the internationally recognised grading systems, are more likely to diagnose late AMD (Rudnicka et al., 2012). In this study, almost half of the included studies adopted the grading system proposed by the Chinese Medical Association, which may also have contributed to the peculiarly elevated prevalence rate of late AMD. A further point to raise is that only a limited set of variables were included and explored in the meta-regression analysis. This means that there could have also been further explanatory variables that may influence the presence of AMD. Moreover, the included demographic and geographic variables were mainly aggregate level data, and although efforts were made to extract data stratified by age, sex and location, the variation at the individual level may still be hidden. This may include smoking exposure, the habit of wearing sunglasses, and others. A further limitation of the study is that the estimates of

regional prevalence and burden of AMD were based on the assumption that the pooled prevalence estimate for a specific region was homogeneous across all included provinces within this region, but this is quite unrealistic. Additionally, for regions that contributed only a few, or no actual AMD prevalence data points to the model, the model-based estimates may diverge quite considerably from the true prevalence. Finally, as reported in both previous reviews and substantiated in the current study, the prevalence of AMD and all its subtypes was stable over time (Rudnicka et al., 2012, Wong et al., 2014). Based on this assumption, the projections of the national prevalence and burden of AMD were actually based on the model-based age-specific prevalence and demographic changes during the next three decades. Thereby, the uncertainty of these projections may be largely dependent on the accuracy of age-specific prevalence model and the UNPD population projection. Bearing these limitations in mind, estimates presented in the current study should be interpreted judiciously.

3.5.3 Interpretation of findings

In this study, the overall prevalence of AMD among the Chinese population was lower than the estimates in the Global AMD study, which reported an overall AMD prevalence of 6.86% in people living in Asia (Wong et al., 2014). In the Global AMD study, the prevalence estimates for Asia were based on eleven studies conducted across Asia, among which, six came from South Asia (India, Singapore, and Thailand), three from China and two from Japan. Given the fact that AMD prevalence increases with decreasing latitude, as detected in both this study and a previous global geo-epidemiology study of AMD (Reibaldi et al., 2016), it is not surprising that the overall prevalence of AMD in the current study is lower than that in Asia - as estimated by the Global AMD study. Moreover, the eleven studies in the Global AMD study were each published in the 21st century, whereas those included in this study distributed from 1990 to 2014. Although no secular trend of AMD was detected in either the Global AMD study or this study, the difference of the estimated AMD prevalence in these two studies can still be partly explained by the difference of ageing demographic structure (Wong et al., 2014, Reibaldi et al., 2016, Rudnicka et al., 2012).

In line with previous population-based investigations and synthesised analysis (Kawasaki et al., 2010, Wong et al., 2014, Klein et al., 2007), this study confirms two common notions of AMD with strong evidence. First, AMD is a degenerative and progressive disease, with the prevalence of AMD dramatically increasing with age, and with age also found to be the only constant risk factor in the presence of any AMD and all its subtypes. Second, the prevalence of early AMD was found to be much higher than that of late AMD. This finding, however,

should not be misinterpreted as late AMD contributing a smaller burden. Rather, most individuals with early AMD may not go on to develop the late-stage disease, and late AMD is a much more severe disease than early AMD (Rudnicka et al., 2012, Lamoureux et al., 2010). In this study, the prevalence of late AMD in Chinese people in 2015 was found to be even higher than that of people living in Europe (1.13% vs. 0.75), the continently highest prevalence of both early and late AMD as revealed by the Global AMD study (Wong et al., 2014). In view of the large population size in China, this striking finding highlights an urgent need for action on the prevention and treatment of late AMD, given its clinical significance. Compared with GA, the group of NVAMD represents a larger burden in Chinese population because the prevalence and number of people with NVAMD were estimated as around twice higher than those of GA. This phenomenon has been reported in some individual investigations (Owen et al., 2003, Eye Diseases Prevalence Research Group, 2004a), although it has not been universally acknowledged (Rudnicka et al., 2012). This finding is still of particular importance for the secondary prevention, especially for NVAMD, whose progress to sight loss could be slowed considerably by current treatment approaches - such as the use of anti-vascular endothelial growth factor agents (Cook et al., 2008, Brechner et al., 2011).

In this study, AMD was found to be more prevalent in urban populations than in rural populations, with possible explanations for this disparity being the difference in environments (e.g. UV exposure), as well as lifestyles (e.g. education, profession and level of physical activity). While it is not possible to say precisely what the determinants are, this study clearly shows that people living in rural areas with a self-sustained economy are less likely to be affected by AMD (Cheung et al., 2013, Ye et al., 2014).

A gradient of decreasing prevalence of AMD was noted in increasing latitude, which suggests that the special climate and environmental factors in geographical areas approximating the equator may accelerate the development of AMD. One common hypothesis is that AMD is associated with the amount of insolation (Reibaldi et al., 2016). However, the indicator of average annual insolation was only found to be significantly associated with late AMD in this present study. There are two possible reasons for this. First, annual insolation data were averaged over a 22-year period (July 1983 - June 2005), which may represent a considerable time-lag (Wild et al., 2005, Shi et al., 2008). Second, the relation between insolation and the prevalence of AMD may not be a monotone function, the global geo-epidemiology study of AMD revealed higher prevalence rates of AMD in locations with insolation ≤ 3 kWh/m^2/day compared with those with insolation >3 kWh/m^2/day (Reibaldi et al., 2016). Although this interesting relation was not studied further because of limited data availability, the negative

relation between latitude and AMD prevalence is an interesting hypothesis to explore in future Chinese AMD epidemiological studies.

Male sex was indicated as a risk factor for early AMD and NVAMD in the univariable regression analysis of this study. This is in contrast to previous reviews and individual investigations of populations of European ancestry, where females were reported to have a higher risk of developing NVAMD (Rudnicka et al., 2012, Eye Diseases Prevalence Research Group, 2004a, Klein et al., 1997b). However, this study is underpowered to further confirm the observed sex difference in multivariable regression analysis. In the multivariable analysis of the prevalence of any AMD, no evidence of sex difference was found after adjusting for *a priori* demographic and geographic variables. This finding is consistent with the previous Global AMD study (Wong et al., 2014).

Variation in AMD prevalence and burden was noted in different geographic locations in China. The variation was mainly driven by the different demographic structures and the intrinsic environmental characteristics of these regions. According to the estimates for the six regions, AMD epidemics continue to be concentrated in the most populous South Central China. Taken together, these findings are of a particular public health interest in national health service allocation. Based on this study, more epidemiological investigations are required in order to make the regional estimates of subtypes of AMD in the future.

3.5.4 Implications for policy, practice and future research

This work has important implications both in academic and public health areas. Future epidemiological studies of AMD in China would benefit from greater standardisation and improved design, ideally adopting internationally recognised grading systems and presenting results for different subtypes. In addition, as AMD is a priority eye disease that may lead to severe visual impairment or even blindness, its potential burden on individuals and health systems is particularly large in resource-limited settings (Lim et al., 2012, Jager et al., 2008, Gottlieb, 2002). Thus, localised epidemiological surveys should be conducted in socio-economically disadvantaged provinces, such as Tibet. From the national perspective, the public health impact of AMD is not only limited to the number of affected people, but also brings about multiple diagnostic and treatment challenges arising from this condition (Brown et al., 2005, Soubrane et al., 2007). It is prudent to address the importance of primary prevention, such as smoking cessation (Khan et al., 2006b, Thornton et al., 2005), lifestyle

modification, antioxidant therapy (Wong et al., 2011), and the use of hats and sunglasses (Tomany et al., 2004). In the meanwhile, the treatment of NVAMD is already available (although rather expensive) (Damico et al., 2012, Takeda et al., 2007, Brechner et al., 2011). Given the remarkable potential economic burden on the society, government efforts must be taken to ensure the availability of health services to address AMD from the points of diagnosis and treatment, and even prevention when available.

3.6 Conclusions

To conclude, this systematic review and meta-analysis provides the first comprehensive and up-to-date estimate of AMD prevalence and burden in China. The results from this study indicate that the burden of AMD is substantial in China, with great variance among different subtypes and geographic regions. In the next decade and beyond, the ageing demographic will make this burden even larger. Improved epidemiological studies are still needed to inform optimal implementation of eye care programmes in China.

Chapter 4 The national and subnational prevalence and burden of glaucoma in China

4.1 Summary

In this chapter, I applied the systematic review and meta-regression approach to estimate the age- and sex-specific prevalence of POAG and PACG respectively. The national numbers of people living with POAG and PACG were generated for the years 1990, 2000, 2010, 2015, 2020, 2030, 2040 and 2050 by applying the national demographic data. For secondary glaucoma, the meta-analysis approach, rather than the meta-regression approach, was adopted because only study-level prevalence estimates were available. Although not precisely enough, the national number of people with secondary glaucoma was also generated under the assumption that the prevalence of secondary glaucoma was, and will still be constant during 1990-2050. By using the meta-regression approach, as described in Chapter 2, males were found to have a higher risk of developing POAG, but a lower risk of developing PACG than females. In addition, the prevalence of POAG and PACG varied geographically, where urban dwellers were at a higher risk of developing POAG than rural dwellers, and people in Northeast China were more likely to have PACG than people in East China. By taking the abovementioned geographic variation, the regional numbers of people living with POAG and PACG were respectively estimated.

The work presented in this chapter has been published in the Journal of Global Health cited as "Song, P., Wang, J., Bucan, K., Theodoratou, E., Rudan, I., Chan, K. Y., & on behalf of the Global Health Epidemiology Research Group (GHERG). (2017). National and subnational prevalence and burden of glaucoma in China: A systematic analysis. Journal of Global Health, 7(2), 020705. http://doi.org/10.7189/jogh.07.020705".

I conducted all aspects of research work in this project, including designing and conceptualising the study, developing search strategy, systematic review, extracting data, analysing data, interpreting findings and preparing the first draft of manuscript for publication. The specific contributions of co-authors are as follows: Rudan, I. conceptualised and designed

the study, Wang, J. conducted the dual systematic review and data extraction, Bucan, K., Theodoratou, E., Rudan, I., and Chan, K. Y. critically reviewed the manuscript and approved the final manuscript. During the publishing process, the manuscript was additionally revised for several rounds according to the comments from anonymous peer reviewers and the journal editors.

4.2 Background

Glaucoma, the second leading cause of blindness, is an optic neuropathy characterised by progressive structural and functional changes of the optic nerve, leading to a typical appearance of the optic disc and visual field damage if untreated (Weinreb et al., 2014, Weinreb and Khaw, 2004, Foster et al., 2002, Congdon and Friedman, 2003, Pascolini and Mariotti, 2011). People with glaucoma-induced visual impairment generally suffer from decreased vision-related quality of life (including reduced vision-dependent mobility, increased incidence of falls), and place a huge burden on caregivers and communities (Ramulu, 2009, Rouland et al., 2005, Varma et al., 2011, Traverso et al., 2005). Glaucoma is often associated with a long and asymptomatic initial phase, and is usually unnoticed until its later stages, when extensive and irreversible damage has occurred (Quigley, 1996, Topouzis et al., 2008). In the late stage of the disease, the effects of medical and surgical treatment can be unsatisfactory, underscoring the importance of early detection and treatment (Weinreb et al., 2014, Nduaguba and Lee, 2006, Weinreb and Khaw, 2004). As glaucoma has an uncertain prognosis, it requires lifelong management and follow-up to prevent further loss of vision (Rulli et al., 2013, Weinreb et al., 2014, Schwartz, 2005). The recognition of glaucoma's pervasive nature and adverse impact on both individuals and society, and the documentation of the magnitude and distribution of glaucoma is of pronounced importance to inform clinicians and researchers, and will guide policymakers in health services allocation (Traverso et al., 2005, Quigley and Broman, 2006, Tham et al., 2014).

Globally, 64.3 million individuals, or 3.5% of the world's population, have glaucoma; of these, about 5.7 million people are visually impaired and 3.1 million are blind (Pascolini and Mariotti, 2011, Tham et al., 2014). Of the many subtypes of glaucoma, primary open-angle glaucoma (POAG) is the most common in nearly all regions, accounting for more than two-thirds (68.6%) of all glaucoma cases (Tham et al., 2014, Quigley and Broman, 2006). Geographically, POAG is believed to be particularly prevalent in Africa (4.2%), and least prevalent in Asia (2.3%); however, more than half (53.4%) of the global POAG cases are in Asia due to the relatively

large population size of this region (Tham et al., 2014, Chan et al., 2016). Compared with POAG, primary angle-closure glaucoma (PACG) is a less common subtype, but is more visually damaging (Wong et al., 2006a). PACG also disproportionally affects the global population; it is least common in North America (0.3%), but is the predominant type of glaucoma in Asian populations (1.1%) (Tham et al., 2014). More than three quarters (76.7%) of the global PACG cases are in Asia (Tham et al., 2014, Chan et al., 2016). Given the positive association of glaucoma prevalence and advanced age, glaucoma is expected to become an even larger public health concern in the coming decades (United Nations, 2015a, Shetty, 2012, Wong et al., 2006a). This dramatic increase of glaucoma burden is also expected to be the case for the largest developing country - China - where rapid ageing of the population is underway (Foster and Johnson, 2001, World Health Organization, 2015b, Woo et al., 2002).

The last three decades have seen a proliferation of population-based studies in China. The mounting volume of data on the prevalence of glaucoma in Chinese bibliographical databases allows me to explore the burden of glaucoma in China from a modelling approach (Xia et al., 2008, Fung, 2008, Song et al., 2016). However, epidemiological studies on glaucoma to date have been restricted to specific demographic and geographic features in China, and are therefore not generalisable to the overall Chinese population (Wang et al., 2010b, Song et al., 2011, Sun et al., 2012, Cheng et al., 2013a). Because of the uncertainty and variation surrounding the epidemiological surveys on glaucoma, a systematic synthesis of the prevalence of glaucoma in China is particularly needed. The first study to pool the prevalence of primary glaucoma in China was published in 2013, which revealed an overall prevalence of 0.7% for POAG, and 1.4% for PACG (Cheng et al., 2013a). The meta-analysis was based on 14 articles from 12 population-based studies published before 2009. No study has yet systematically appraised research into the prevalence of primary glaucoma in China published over the last nine years. Furthermore, considering that different subtypes of glaucoma may require different strategies for screening, prevention and treatment, there is a pressing need for a more updated effort to provide finer quantification of the relative magnitude across the main types of glaucoma, namely, POAG, PACG and secondary glaucoma, which is missing in the 2013 study (Chan et al., 2016).

To fill the gaps in the evidence matrix, in this study I used a comprehensive systematic review to synthesise the best available evidence from 1990 onwards. Based on the retained evidence, the prevalence and burden of glaucoma and its subtypes were assessed at both the national and subnational levels. The aims of this present study were: 1) to estimate glaucoma prevalence in China by using epidemiological modelling; 2) to estimate and project the overall prevalence

and number of people with glaucoma at the national level from 1990 to 2050; and 3) to estimate the regional prevalence and number of people with glaucoma from 2000 to 2010.

4.3 Methods

4.3.1 Systematic review

The comprehensive systematic review was conducted and reported in line with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines and the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement (Moher et al., 2009, Stevens et al., 2016).

4.3.1.1 Search strategy

A systematic literature search was performed to identify all relevant articles that have reported the prevalence of glaucoma in the general Chinese population. The searched databases included three Chinese and three English electronic databases: China National Knowledge Infrastructure (CNKI), Wanfang, Chinese Biomedicine Literature Database (CBM-SinoMed), PubMed, Embase, and Medline. The search strategy combined controlled vocabularies (e.g. Medical Subject Heading terms) and free text terms of prevalence (prevalence, incidence, mortality, morbidity, epidemiology), glaucoma and China (China, Chinese, Hong Kong, Macau, Taiwan); the specific search strategies for each database were adapted to fit their specific features (**Appendix table 10**). The searches were restricted to studies that were published between January 1990 and August 2017. No language restrictions were applied to the searches or search results. The reference lists of all included full-text articles were also scrutinised in detail to identify additional data sources.

4.3.1.2 Inclusion and exclusion criteria

The inclusion and exclusion criteria adopted in this study were developed based on the examination guidelines for glaucoma-related population-based studies (Foster et al., 2002, Quigley et al., 1993, Tham et al., 2014). To be included in this systematic review, studies had to be population-based and report the prevalence of glaucoma. I excluded studies that were hospital-based or conducted in a population that was not representative of the general population. Reviews, commentaries, studies that only adopted qualitative methods and studies that reported the number of eyes with glaucoma instead of the number of individuals were also

excluded because they were not able to provide numerical estimates of glaucoma prevalence. Studies that did not include clear assessment methods of glaucoma or relied on self-reported diagnosis were also excluded. Although different case definitions and examination methods exist in identifying glaucoma cases, a remarkable similarity of glaucoma prevalence was noted across surveys despite variations in survey methodology and glaucoma definition (Rudnicka et al., 2006, Kapetanakis et al., 2016, Tham et al., 2014, Eye Diseases Prevalence Research Group, 2004b). In this systematic review, studies were not excluded on the basis of their specific definitions of glaucoma or adopted instrumentation; the assessment of glaucoma should be independent of intraocular pressure (IOP) measurements, but rely on structural or functional evidence of glaucomatous optic neuropathy evaluated by optic disc evaluation or visual field testing (Tham et al., 2014, Foster et al., 2002). Therefore, studies were eligible to contribute data if the following standardised assessments were carried out in suspected cases of glaucoma: anterior chamber angle/depth evaluation by slit-lamp examination or gonioscopy, optic disc evaluation by ophthalmologists using slit-lamp biomicroscopy or fundus photography and visual field testing with automated static perimetry.

4.3.1.3 Study selection and data extraction

Search results from the six bibliographic databases were merged together and duplicate references were removed within and between the databases. All records were screened in two stages: screening of titles and abstracts, followed by the retrieval and screening of full-text articles. For multiple articles that reported results of the same individual study, those with the most comprehensive or most recent data were kept. Disagreements were resolved by consensus through discussion. According to the STROBE guideline, the quality of each included study was assessed in terms of sample population, sample size, participation rate, outcome assessment, and analytical methods. Each of the five bias components was scored as 2 for low risk, 1 for moderate risk and 0 for high risk and unclear. The total score represented the overall quality of each study (**Table 2.1**) (Von Elm et al., 2007, Song et al., 2018).

For the purpose of this study, glaucoma was classified into three main types: POAG, PACG and secondary glaucoma. Relevant data on different subtypes of glaucoma were separately extracted from the studies included. The pilot tested and refined extraction table included three modules:

1) Characteristics of the study: author(s), publication year, study setting (urban, rural or mixed), study location, geographic region, survey year, sampling method, study

design (cross-sectional or cohort), whether anterior chamber angle/depth evaluation, IOP measurement, optic disc evaluation and visual field testing were conducted;

2) Characteristics of the investigated population: number of the sample, sex (male, female or mixed), and age (age range, mean or median age, or midpoint of the age range);
3) Prevalence estimates: the number of participants who had been tested and the number of people with glaucoma, by age group, sex, setting and glaucoma subtype, where available.

The sites where the studies were classified into six geographic regions following definitions of National Bureau of Statistics of China: East China, North China, Northeast China, Northwest China, South Central China, and Southwest China (**Table 2.2** and **Figure 2.2**) (National Bureau of Statistics, 2002, National Bureau of Statistics, 2012). Missing data on survey years were imputed for two studies by subtracting three years from the published year, which was based on the average time from survey to publication in studies with available data (see **Appendix table 11**). In case of censoring age groups, e.g. older than 80 years, the same width as other age groups in the same study was used to impute the missing age band.

4.3.2 Statistical analysis

4.3.2.1 Epidemiological modelling of glaucoma prevalence

Prevalence of POAG, PACG and secondary glaucoma was stabilised by using the logit transformation (Barendregt et al., 2013). In this study, random-effects models were used throughout because of significant heterogeneity in the reported prevalence of POAG, PACG and secondary glaucoma between studies (**Appendix table 12**). For POAG and PACG, one individual study might have contributed multiple outcome measurements in the data extraction stage; to take into account the occurrence of different data points from the same study, a multilevel mixed-effect logistic regression approach was adopted (Hox et al., 2010, Viechtbauer, 2010). Before constructing epidemiological models of the prevalence for POAG and PACG, the association of prevalence estimates and each individual variable, i.e., age, sex (male and female), setting (urban, rural and mixed), geographic region, and survey year, was explored using a univariable meta-regression; this was done for POAG and PACG separately. Age and sex were found to be the only common factors that were significantly associated with prevalence estimates of both POAG and PACG. For the purpose of estimating the national prevalence of POAG and PACG, an age- and sex-adjusted model was developed. Given that:

$$\text{prevalence} = \text{p} = \frac{glaucoma\ cases}{number\ of\ participants}$$

Then, the prevalence estimates were stabilised by a logit link,

$$\text{logit(p)} = \ln(\frac{p}{1-p}) = \ln(odds) = \alpha + \beta_1 * x_1 + \beta_2 * x_2 + \cdots$$

The prevalence of glaucoma was established as a function of age and sex:

$$\text{logit(p)} = \alpha + \beta_1 * Age + \beta_2 * Sex$$

Therefore,

$$odds = \frac{p}{1-p} = e^{(\alpha+\beta_1*Age+\beta_2*Sex)}$$

And,

$$\text{prevalence} = \text{p} = \frac{e^{(\alpha+\beta_1*Age+\beta_2*Sex)}}{1+e^{(\alpha+\beta_1*Age+\beta_2*Sex)}}$$

Finally, the age- and sex-specific prevalence of POAG and PACG was generated based on the above-mentioned model. The lower bound of age range was set as 45 years and the upper bound as 89 years because enough data were available for model construction in this broad age range.

For secondary glaucoma, 12 individual studies provided prevalence estimates. Therefore the overall prevalence of secondary glaucoma was derived from the study-specific estimates using a random-effects meta-analysis model (DerSimonian and Laird method) (Higgins and Green, 2008). To evaluate the robustness of pooled prevalence, a leave-one-out sensitivity analysis was conducted by removing one study at one time (Wallace et al., 2009). Potential publication bias was assessed by visual inspection of funnel plots, Egger's regression test for funnel plot asymmetry and Begg's rank correlation test (Egger et al., 1997, Begg and Mazumdar, 1994, Peters et al., 2006).

4.3.2.2 Estimation of national number of people with glaucoma from 1990 to 2015

The national number of people with glaucoma (glaucoma "envelopes") from 1990 to 2015 was derived by multiplying the prevalence of glaucoma with the population in China, available from the United Nations Population Division (UNPD) (United Nations, 2015b). For POAG and PACG, the numbers of age- and sex-specific cases were calculated by using their age- and sex-specific prevalence for each 5-year age group estimated in the above models. In view of the limited data availability, the age- and sex-specific prevalence of secondary glaucoma was not estimated, thus the overall prevalence pooled from 12 studies were used (**Appendix figure 8**). This was performed for the years 1990, 2000, 2010 and 2015 consecutively.

4.3.2.3 Projection of national number of people with glaucoma from 2020 to 2050

For the projection of people with glaucoma to the year 2050, the prevalence of POAG, PACG and secondary glaucoma was assumed to be constant over the next 33 years. This assumption was partly supported by the multivariable meta-regression model, where no significant changes of POAG and PACG prevalence with survey year were observed after adjusting the effects of age and sex. Bases on the same procedures adopted in the estimation of national population with glaucoma from 1990 to 2015, the numbers of people with glaucoma from 2020 to 2050 were projected by taking UNPD Prospects data, which took into account mortality rates and fertility rates in its population projection (United Nations, 2015b).

4.3.2.4 Effects of demographic and geographic factors on the prevalence of POAG and PACG

To investigate whether the prevalence of POAG and PACG varied across different strata of the population, the associations of prevalence estimates and variables of interest were assessed by multivariable meta-regression, adjusting the effects of age and sex. Before model fitting, all variables were tested for correlation to avoid multicollinearity. The variables were selected based on knowledge, previous studies and the availability of data in this present study, which included setting (urban, rural and mixed), geographic region, and survey year. As a rule, at least seven data points should be available for each variable (Vittinghoff and McCulloch, 2007).

4.3.2.5 Estimation of regional number of people with POAG and PACG from 2000 to 2010

The regional population with glaucoma was estimated at an envelope condition. This method was initially proposed by the Child Health Epidemiology Reference Group (CHERG) and has been widely adopted in disease burden research (Rudan et al., 2004, Fowkes et al., 2013, Adeloye et al., 2015). The national glaucoma cases were set as the glaucoma envelope, for POAG and PACG separately. Then the "POAG envelope" and the "PACG envelope" were split into the six subnational regions according to the different distributions of risk factors identified in the multivariable meta-regression models. This was conducted for the years 2000 and 2010, where regional population data were available from the fifth and sixth censuses of China (National Bureau of Statistics, 2002, National Bureau of Statistics, 2012).

The overall study design is shown in **Figure 4.1**. All analyses were performed using R, version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria). The China base map was obtained as a shapefile from the Global Administrative Areas (GADM) database (GADM, 2015, version 2.0; www.gadm.org) and all maps were drawn by ArcMap version 10.1 (Environmental Systems Research Institute, Redlands, CA). A two-sided p-value of less than 0.05 indicated statistically significant difference for all analyses.

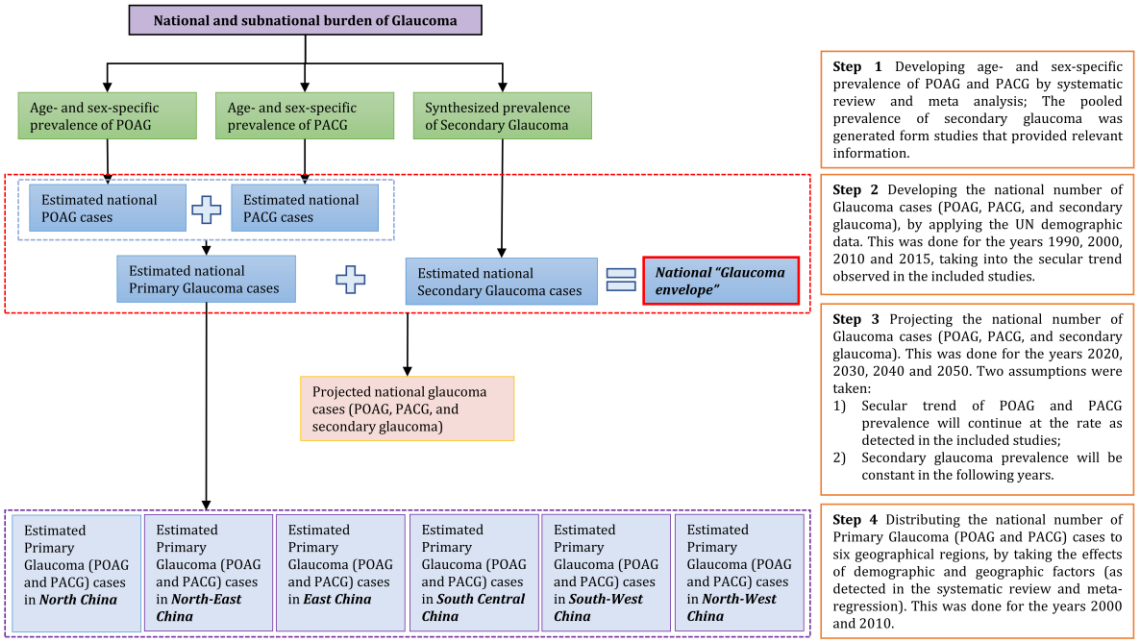


Figure 4.1. Overall study design flowchart for the prevalence and burden of glaucoma study in China

4.4 Results

4.4.1 Summary of systematic review

The initial search identified a total of 10609 citations for screening, after elimination of duplicates, 5387 records remained. After screening titles and abstracts, 623 potentially relevant full-text articles were reviewed for eligibility, of which 30 reported the prevalence of glaucoma and were included in the systematic review (**Figure 4.2**). A full list of the included studies is shown in **Appendix table 13**.

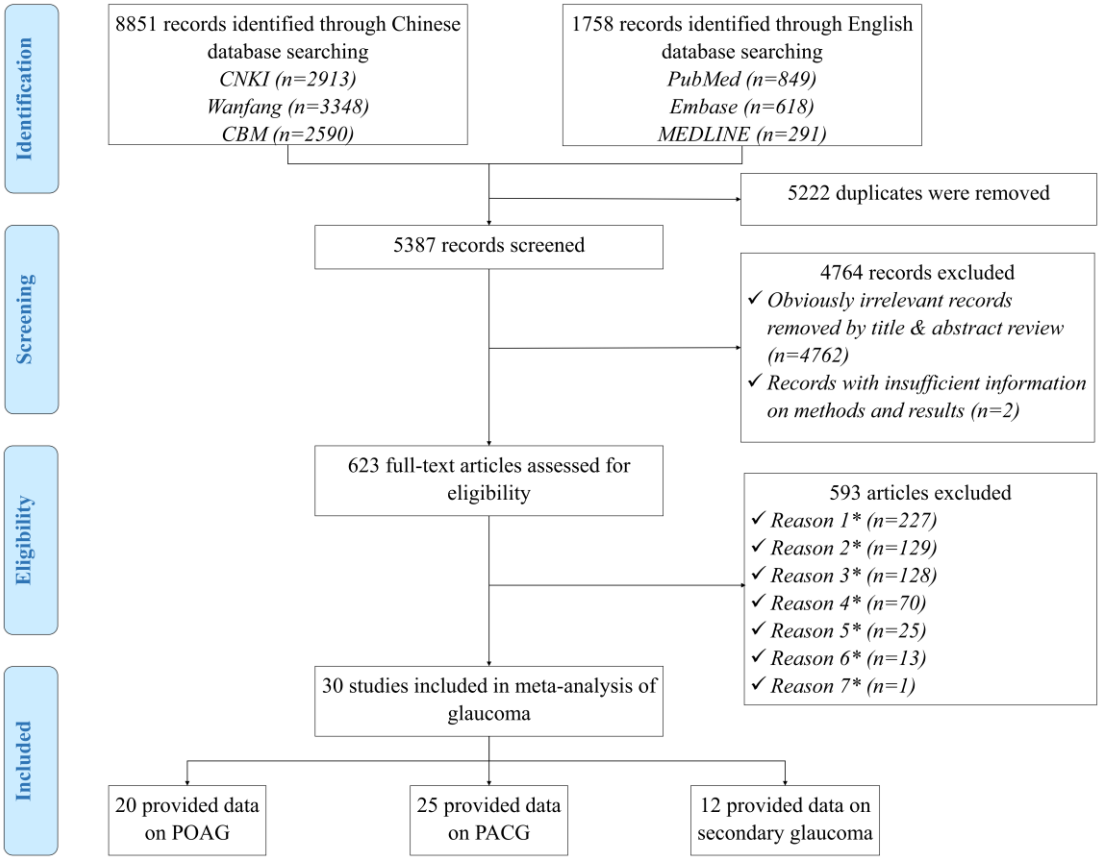


Figure 4.2. Systematic review flow diagram of studies on glaucoma prevalence in China

*Note: *Reason 1-Studies that were not population-based; *Reason 2-Studies that were conducted in people with unrepresentative characteristics of general population (diabetic patients, people with reduced vision, etc.); *Reason 3-Articles with no numerical measure of glaucoma prevalence; *Reason 4-Studies that relied on self-reported diagnoses or didn't conduct standardised assessments (anterior chamber angle/depth evaluation by slit-lamp*

*examination or gonioscopy, optic disc evaluation by ophthalmologists using slit-lamp biomicroscopy or fundus photography and visual field testing with automated static perimetry) in at least glaucoma suspects; *Reason 5-Multiple publications of the same study; *Reason 6-Studies that were not based in China; *Reason 7-Articles with inconsistency between reported methods and presented results.*

The 30 studies, published between 1995 and 2016, reported the prevalence of glaucoma with a geographical distribution covering all the six regions in China (**Figure 4.3**). The included studies were all cross-sectional, of which 20 studies reported the prevalence of POAG, 25 focused on PACG and 12 on secondary glaucoma. The detailed characteristics and quality score of every study are listed in **Appendix table 14** and **Appendix table 15**, and the main characteristics of the 30 studies are summarised in **Table 4.1**. More than half of the 30 studies were published in the past seven years, underlining the necessity for conducting my revision of the estimate. The included studies were generally larger, with the majority (60%, n=18) being conducted in rural areas. Anterior chamber angle/depth evaluation, IOP measurement and optic disc evaluation were mostly undertaken in all participants, whereas visual field testing was largely used in glaucoma suspects. More than half of the included studies were with a quality score of nine or above.

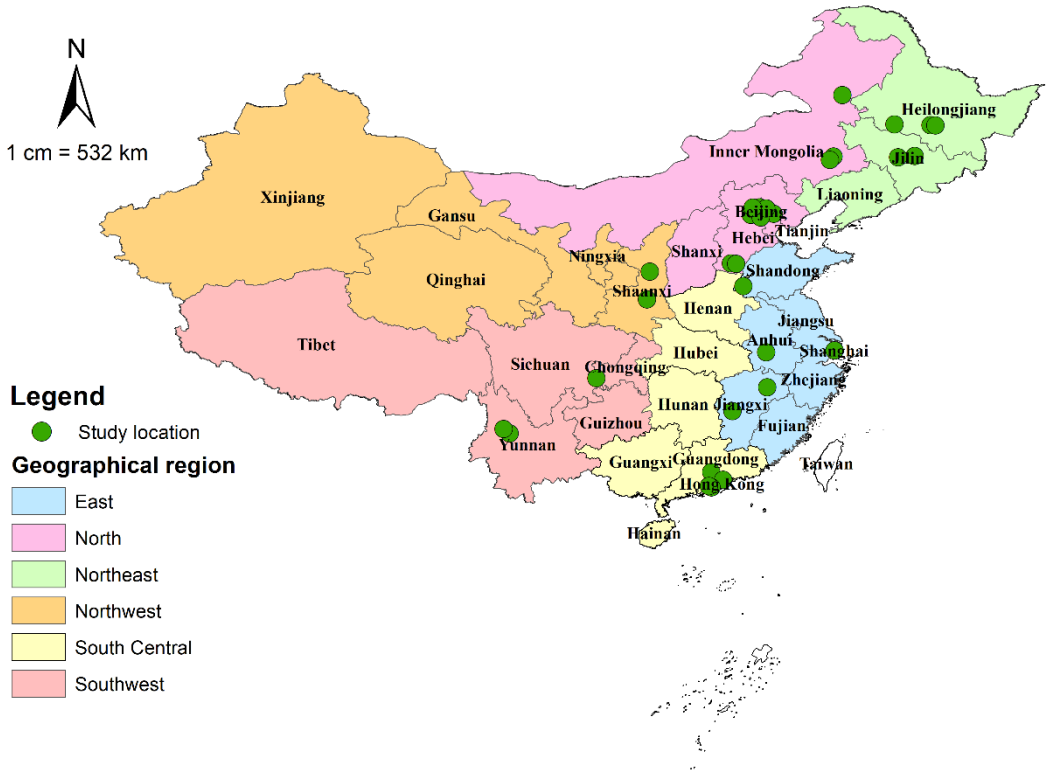


Figure 4.3. Geographical distribution of the included studies on glaucoma prevalence in China (n=30)

Table 4.1. Main characteristics of the included studies on glaucoma prevalence in China (n=30)

Characteristic		Number of studies (%)
Year published		
	1990-1999	2 (6.7)
	2000-2009	12 (40.0)
	2010-2017	16 (53.3)
Setting		
	Urban	6 (20.0)
	Rural	18 (60.0)
	Mixed	6 (20.0)
Sample size		
	500-1500	6 (20.0)
	1501–2500	7 (23.3)
	2501–5000	9 (30.0)
	>5000	8 (26.7)
Geographic regions		
	North China	12 (40.0)
	Northeast China	5 (16.7)
	East China	4 (13.3)
	South Central China	4 (13.3)
	Southwest China	3 (10.0)
	Northwest China	2 (6.7)
Anterior chamber angle/depth evaluation		
	In all participants	28 (93.3)
	In glaucoma suspects	2 (6.7)
IOP measurement		
	In all participants	29 (96.7)
	In glaucoma suspects	1 (3.3)
Optic disc evaluation		
	In all participants	28 (93.3)
	In glaucoma suspects	2 (6.7)

Characteristic	Number of studies (%)
Visual field testing	
In all participants	4 (13.3)
In glaucoma suspects	26 (86.7)
Quality score	
10	4 (13.3)
9	15 (50.0)
8	8 (26.7)
7	3 (10.0)

4.4.2 Age- and sex-specific prevalence of POAG and PACG

Based on a substantial number of data points from the included studies, the sex-specific relationship between age and the prevalence of POAG and PACG was constructed (**Figure 4.4**). The informative data points covered a wide age spectrum from the mid-30s to the 9th decade, with the majority concentrating between the mid-40s to the mid-80s. Therefore, in the estimation of age- and sex-specific prevalence of POAG and PACG, the age range was set as from 45 years to 89 years.

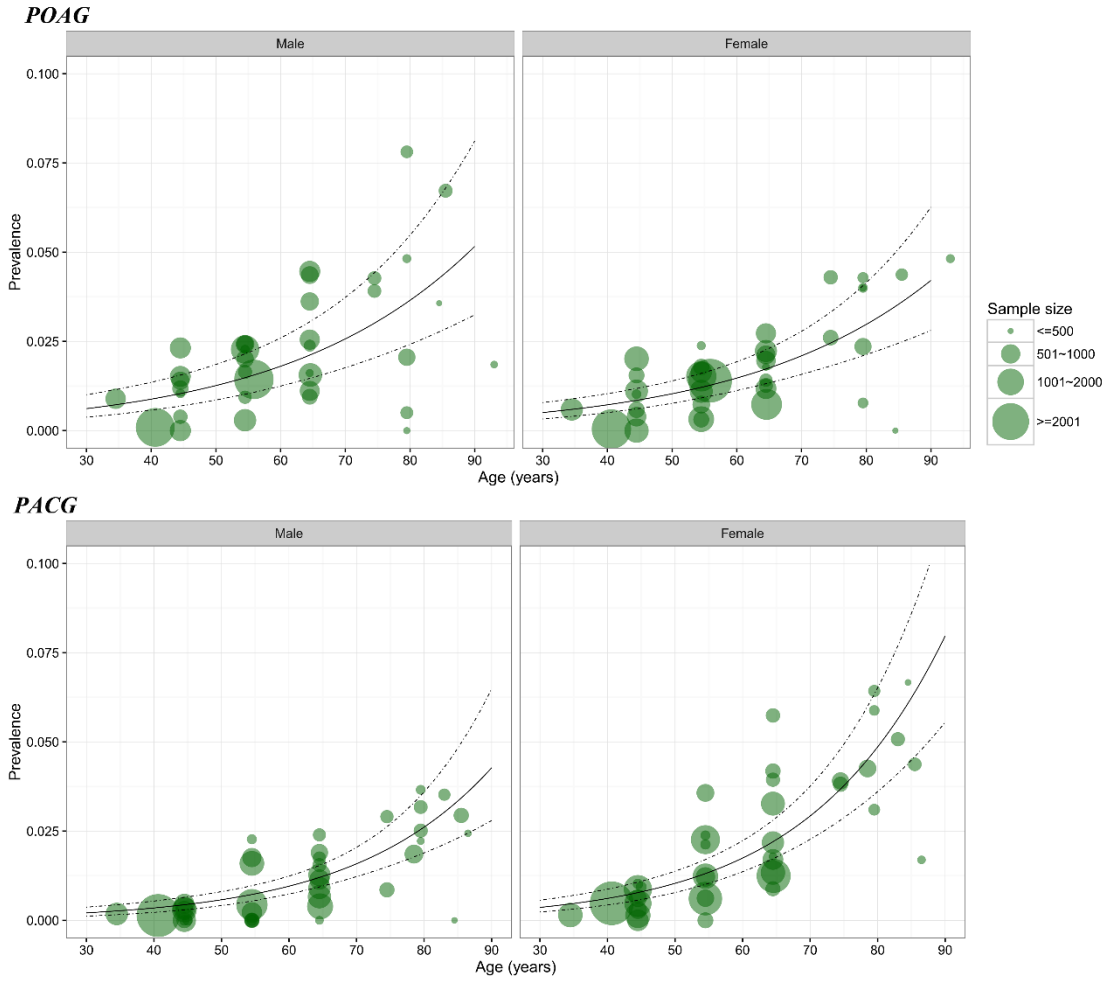


Figure 4.4. Age- and sex-specific prevalence of POAG and PACG based on the informative data points from the included studies

Note: The size of each bubble is proportional to the sample size. Overall, there were 86 data points for constructing the sex-specific relation between age and prevalence for POAG, and 103 for PACG.

Table 4.2 and **Figure 4.5** show the estimated age- and sex-specific prevalence of POAG and PACG respectively. Generally, the prevalence of POAG and PACG both increased steadily with advanced age, and this positive relationship between age and prevalence rate was similar between sexes, but more pronounced for PACG. In males, the prevalence of POAG ranged from 0.74% (95% CI: 0.48-1.14) in individuals aged 45-49 years to 3.02% (95% CI: 1.92-4.73) in those aged 85-89 years. The prevalence of POAG in females was slightly lower than that in males across the whole age spectrum from 45 to 89 years, ranging from 0.54% (95% CI: 0.35-0.84) to 2.24% (95% CI: 1.41-3.53). In contrast, the prevalence of PACG was consistently

higher in females than in males. In females, the prevalence of PACG ranged from 0.91% (95% CI: 0.74-1.11) in those aged 45-49 years to 6.33% (95% CI: 4.98-8.02) in those aged 85-89 years. In males, the prevalence of PACG increased from 0.48% (95% CI: 0.39-0.60) in people aged 45-49 years to 3.44% (95% CI: 2.66-4.45) in elderly aged 85-89 years.

Table 4.2. Estimated sex-specific prevalence of POAG and PACG in China, by age group

Age group	Prevalence of POAG (%, 95% CI)		Prevalence of PACG (%, 95% CI)	
	Male	Female	Male	Female
45-49 years	0.74 (0.48-1.14)	0.54 (0.35-0.84)	0.48 (0.39-0.60)	0.91 (0.74-1.11)
50-54 years	0.88 (0.57-1.34)	0.65 (0.42-0.99)	0.62 (0.51-0.75)	1.16 (0.98-1.38)
55-59 years	1.05 (0.69-1.60)	0.77 (0.51-1.18)	0.79 (0.66-0.94)	1.49 (1.28-1.74)
60-64 years	1.25 (0.83-1.90)	0.92 (0.61-1.41)	1.01 (0.86-1.20)	1.90 (1.65-2.20)
65-69 years	1.50 (0.98-2.27)	1.10 (0.72-1.68)	1.30 (1.09-1.54)	2.43 (2.10-2.81)
70-74 years	1.79 (1.17-2.72)	1.32 (0.86-2.02)	1.66 (1.38-1.99)	3.10 (2.64-3.64)
75-79 years	2.13 (1.38-3.27)	1.57 (1.02-2.43)	2.12 (1.73-2.59)	3.94 (3.28-4.73)
80–84 years	2.54 (1.63-3.93)	1.87 (1.20-2.92)	2.70 (2.15-3.39)	5.00 (4.06-6.16)
85-89 years	3.02 (1.92-4.73)	2.24 (1.41-3.53)	3.44 (2.66-4.45)	6.33 (4.98-8.02)

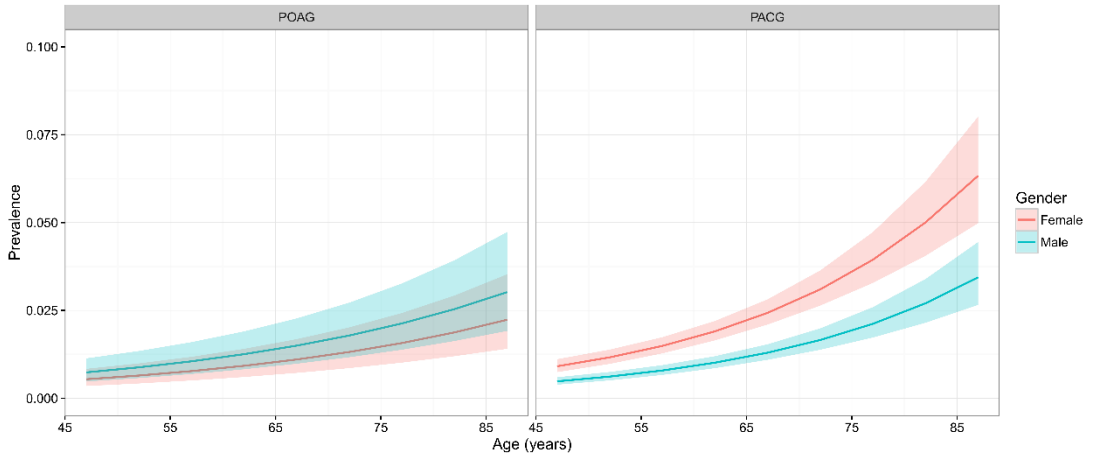


Figure 4.5. Estimated age- and sex-specific prevalence of POAG and PACG in China, with 95% confidence intervals

4.4.3 Pooled prevalence of secondary glaucoma during 1990 and 2017

Based on the random-effects meta-analysis, the prevalence of secondary glaucoma was pooled as 0.15% (95% CI: 0.10-0.23) in the general Chinese population (**Figure 4.6**). After removing each study at one time, the pooled prevalence of secondary glaucoma ranged from 0.14% (95% CI: 0.09-0.23) to 0.16% (95% CI: 0.11-0.25) (**Figure 4.7**). No single study was found to significantly influence the pooled prevalence of secondary glaucoma. Potential publication bias was detected by visual evaluation of the funnel plot and Egger's test ($t= -5.323$, $p< 0.001$), whereas Begg's test indicated that no publication was evident ($z= 0.274$, $p= 0.783$) (**Figure 4.8**).

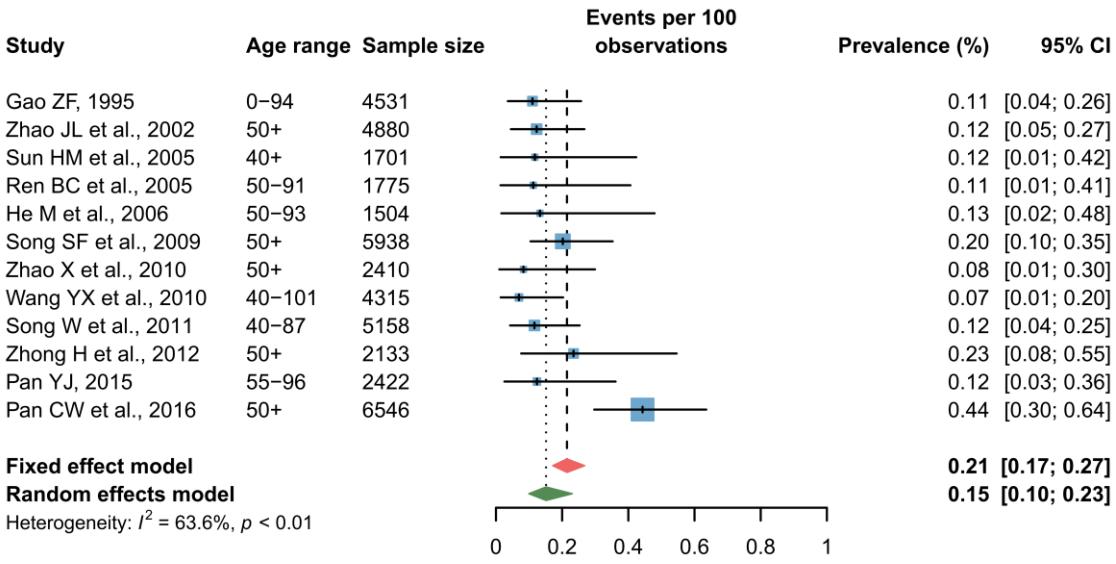


Figure 4.6. Pooled prevalence of secondary glaucoma in the general Chinese population (n=12)

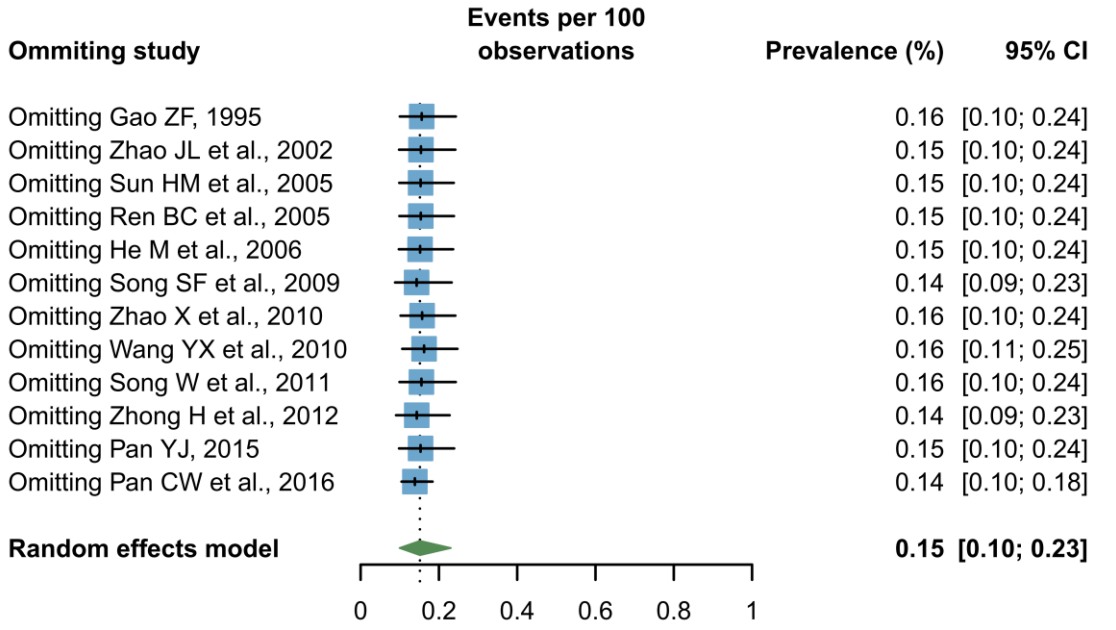


Figure 4.7. Leave-one-out sensitivity analysis of the influence of single study on the pooled prevalence of secondary glaucoma

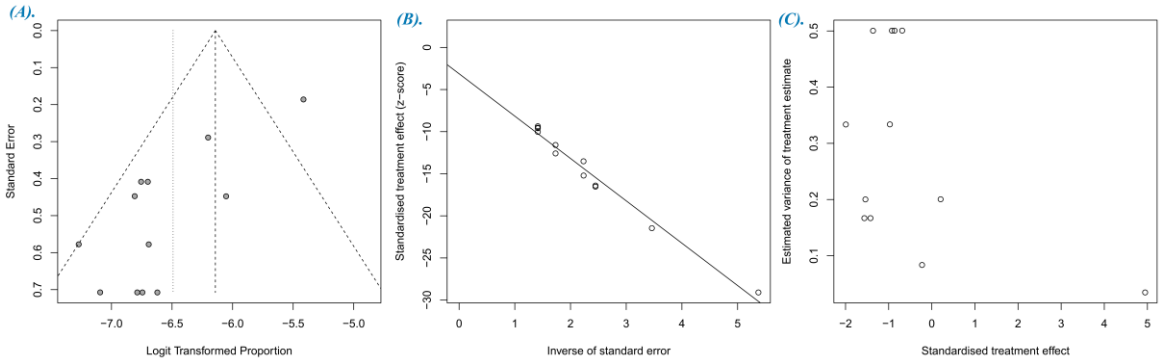


Figure 4.8. Publication bias of the studies on the prevalence of secondary glaucoma in the general population and people with DM

Note: (A) Funnel plot; (B) Egger's test; (C) Begg's test.

4.4.4 National number of people with glaucoma from 1990 to 2015

By extrapolating the estimated age- and sex-specific prevalence of POAG and PACG to UNPD data, the numbers of people with POAG and PACG were generated (**Appendix table 16**). For secondary glaucoma, its pooled prevalence was assumed as constant over the time frame of this research. At the national level, the overall prevalence of glaucoma was listed in **Table 4.3**. From 1990 to 2015, the prevalence of all glaucoma ranged from 2.59% (95% CI: 1.96-3.49) to 2.58% (95% CI: 1.94-3.47), indicating a slightly relative decreasing rate of 0.39%. For different subtypes of glaucoma, the overall prevalence of POAG ranged from 1.03% (95% CI: 0.67-1.58) in 1990 to 1.02% (95% CI: 0.67-1.57) in 2015, which yielded a relative decreasing rate of 0.97%. Similarly, the prevalence of PACG decreased by 0.71%, from 1.41% (95% CI: 1.18-1.68) in 1990 to 1.40% (95% CI: 1.17-1.68) in 2015.

Table 4.3. Estimated prevalence and number of people with glaucoma in China from 1990 to 2015, by glaucoma type

Glaucoma type	Prevalence of glaucoma (%, 95% CI)				Number of people with glaucoma (million, 95% CI)				Relative rate of change (%, 1990-2015)	
	1990	2000	2010	2015	1990	2000	2010	2015	Prevalence	Cases
POAG	1.03 (0.67-1.58)	1.01 (0.66-1.55)	1.03 (0.67-1.57)	1.02 (0.67-1.57)	2.35 (1.54-3.60)	3.21 (2.09-4.91)	4.39 (2.86-6.72)	5.22 (3.40-7.98)	-0.97	+122.13
PACG	1.41 (1.18-1.68)	1.38 (1.16-1.65)	1.40 (1.17-1.68)	1.40 (1.17-1.68)	3.22 (2.70-3.84)	4.37 (3.66-5.23)	6.01 (5.03-7.18)	7.14 (5.97-8.53)	-0.71	+121.74
Secondary glaucoma	0.15 (0.10-0.23)				0.34 (0.23-0.53)	0.47 (0.32-0.73)	0.64 (0.43-0.99)	0.76 (0.51-1.17)	-	+123.53
All glaucoma	2.59 (1.96-3.49)	2.55 (1.92-3.44)	2.58 (1.94-3.47)	2.58 (1.94-3.47)	5.92 (4.47-7.97)	8.05 (6.07-10.87)	11.04 (8.32-14.89)	13.12 (9.88-17.68)	-0.39	+121.62

Note: All glaucoma includes POAG, PACG and secondary glaucoma.

With the ageing of Chinese population during 1990-2015, the total number of people living with glaucoma increased dramatically (**Table 4.3**). The number of people with all glaucoma in China was 5.92 million (95% CI: 4.47-7.97) in 1990 and 13.12 million (95% CI: 9.88-17.68) in 2015, indicating an overall increasing rate of 121.62% throughout this period. This increasing trend was also witnessed in different subtypes of glaucoma. For POAG, the affected cases increased by 122.13%, from 2.35 million (95% CI: 1.54-3.60) in 1990 to 5.22 million (95% CI: 3.40-7.98) in 2015. Similarly, the number of people with PACG increased by 121.74%, ranging from 3.22 million (95% CI: 2.70-3.84) in 1990 to 7.14 million (95% CI: 5.97-8.53) in 2015. Even for secondary glaucoma, whose overall prevalence was assumed as constant, the number of affected people also increased by 123.53% during 1990 to 2015, from 0.34 million (95% CI: 0.23-0.53) to 0.76 million (95% CI: 0.51-1.17). In 2015, more than half (54.42%) of the glaucoma cases were PACG, followed by POAG (39.79%) and secondary glaucoma (5.79%). From 1990 to 2015, the age group that contributed the most cases shifted from 55-59 years to 60-64 years for both POAG and PACG (**Figure 4.9**).

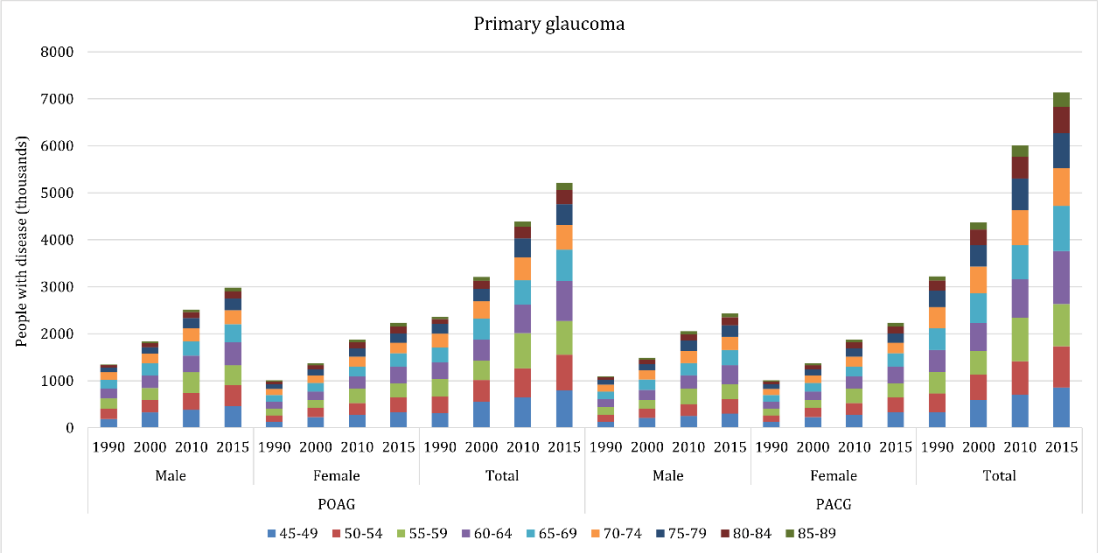


Figure 4.9. Estimated sex-specific number of people with POAG and PACG in China from 1990 to 2015, with contributing age groups

4.4.5 Projection of national number of people with glaucoma from 2020 to 2050

In the projection analysis, the age- and sex-specific prevalence estimates of POAG and PACG, and the overall prevalence estimate of secondary glaucoma were all assumed as constant. By applying these estimates to the medium scenario UNPD data up to the year 2050, the numbers of people with glaucoma were projected (**Appendix table 16** and **Table 4.4**). Unlike the slight declining trend of glaucoma prevalence between 1990 and 2015, from 2020 to 2050, the overall prevalence of all glaucoma is expected to increase from 2.64% (95% CI: 1.99-3.55) to 3.48% (95% CI: 2.63-4.69), which is a 32% increase. For different subtypes of glaucoma, the prevalence of POAG will also increase during this period, but at a lower rate (27%). In 2020, the prevalence of POAG is projected to be 1.05% (95% CI: 0.68-1.60), and then reach 1.33% (95% CI: 0.86-2.04) in 2050. The prevalence of PACG will show a greater increasing rate between 2020 and 2050, from 1.44% (95% CI: 1.21-1.72) to 2.01% (95% CI: 1.66-2.42), i.e. by 40%.

Table 4.4. Projected prevalence and number of people with glaucoma in China from 2020 to 2050, by glaucoma type

Glaucoma type	Prevalence of glaucoma (%, 95% CI)				Number of people with glaucoma (million, 95% CI)				Relative rate of change (%, 2020-2050)	
	2020	2030	2040	2050	2020	2030	2040	2050	Prevalence	Cases
POAG	1.05 (0.68-1.60)	1.14 (0.75-1.75)	1.21 (0.79-1.86)	1.33 (0.86-2.04)	6.06 (3.95-9.27)	7.51 (4.90-11.50)	9.04 (5.89-13.86)	9.59 (6.23-14.72)	+26.67	+58.25
PACG	1.44 (1.21-1.72)	1.64 (1.37-1.95)	1.79 (1.49-2.14)	2.01 (1.66-2.42)	8.36 (7.00-9.98)	10.75 (9.00-12.84)	13.30 (11.08-15.97)	14.49 (12.01-17.48)	+39.58	+73.33
Secondary glaucoma	0.15 (0.10-0.23)				0.87 (0.58-1.33)	0.99 (0.66-1.51)	1.12 (0.74-1.71)	1.08 (0.72-1.66)	-	+24.14
All glaucoma	2.64 (1.99-3.55)	2.93 (2.22-3.93)	3.15 (2.38-4.24)	3.48 (2.63-4.69)	15.28 (11.53-20.58)	19.26 (14.56-25.84)	23.47 (17.71-31.54)	25.16 (18.96-33.86)	+31.82	+64.66

Note: All glaucoma includes both primary glaucoma and secondary glaucoma.

The projected number of people living with glaucoma in China is also shown in **Table 4.4**. Between 2020 and 2050, the number of all glaucoma cases in China is expected to increase from 15.28 million (95% CI: 11.53-20.58) to 25.16 million (95% CI: 18.96-33.86), i.e. by 65%. The increasing rates for POAG and PACG will also be notable within the same period. The number of people with POAG is expected to increase from 6.06 million (95% CI: 3.95-9.27) to 9.59 million (95% CI: 6.23-14.72), and those with PACG from 8.36 million (95% CI: 7.00-9.98) to 14.49 million (95% CI: 12.01-17.48), which will translate into the rates of increase between 2020 and 2050 of 58% and 73%, respectively. Due to the forecasted trend in population ageing over the next three decades, the number of secondary glaucoma cases is anticipated to also increase slightly, from 0.87 million (95% CI: 0.58-1.33) in 2020 to 1.08 million (95% CI: 0.72-1.66) in 2050; i.e. an increase by 24.14%. During this period, PACG will remain the predominant subtype of glaucoma in China, followed by POAG and secondary glaucoma. From 2020 to 2050, the age group in which most POAG cases will be concentrated will shift from 65-69 years to 75-79 years, and the age group for PACG will shift from 65-69 years to 80-84 years (**Figure 4.10**).

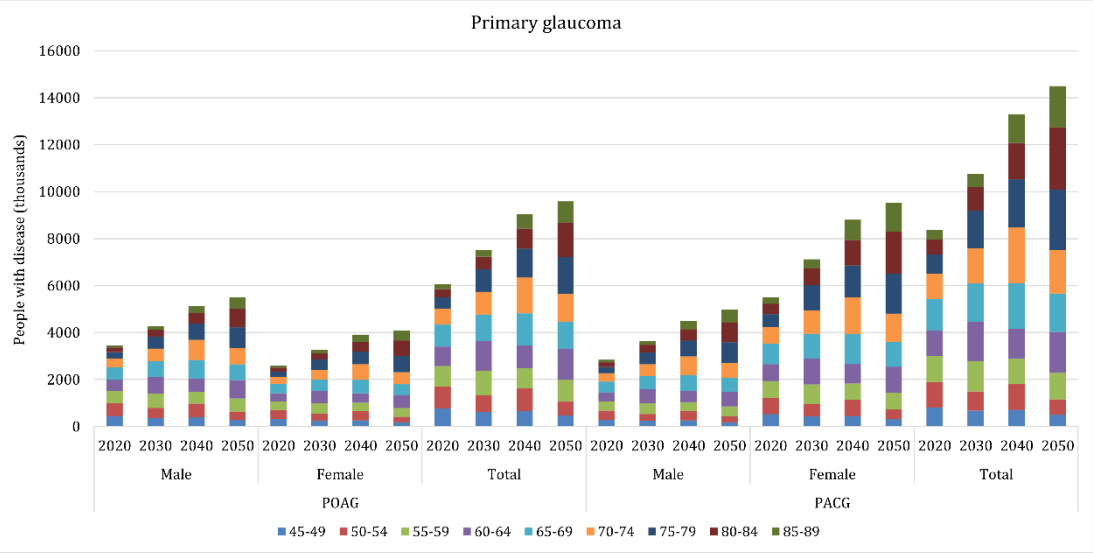


Figure 4.10. Projected sex-specific number of people with POAG and PACG in China from 2020 to 2050, with contributing age groups

4.4.6 Effects of demographic and geographic factors on the prevalence of POAG and PACG

Based on univariable and multivariable meta-regression models (**Table 4.5**), the effects of selected demographic and geographic factors on the risk of POAG and PACG were assessed. The univariable meta-regression indicated that age, sex and study setting were significantly associated with POAG, while PACG was associated with age, sex and geographic region. No evidence for secular trends was observed. After adjusting for age and sex in a multivariable meta-regression, the odds ratio (OR) for each increase in age by 10 years was 1.43 (95% CI: 1.33-1.55) for POAG, and 1.65 (95% CI: 1.51-1.80) for PACG. Males still showed a higher risk of POAG (1.36 [95% CI: 1.17-1.59]), but a lower risk of PACG (0.53 [95% CI: 0.46-0.60]) in comparison with females. People living in urban areas were more likely to have POAG compared with those in rural areas, with an OR of 1.54 (95% CI: 1.02-2.35). Among the six geographic regions, people in Northeast China were at a higher risk (1.77 [95% CI: 1.07-2.94]) of having PACG than people in East China.

Table 4.5. Odds ratios for POAG and PACG in terms of age, sex, setting and geographic region from multilevel univariable and multivariable meta-regression models, with 95% confidence intervals

Variable	Unadjusted		Age and sex-adjusted	
	POAG	**PACG**	**POAG**	**PACG**
Age (per decade increase)	1.38 (1.30-1.47)*	1.58 (1.49-1.67)*	1.43 (1.33-1.55)*	1.65 (1.51-1.80)*
Sex$				
Female	Reference	Reference	Reference	Reference
Male	1.39 (1.19-1.62)*	0.53 (0.46-0.60)*	1.36 (1.17-1.59)*	0.53 (0.46-0.60)*
Setting				
Rural	Reference	Reference	Reference	Reference
Urban	1.68 (1.13-2.51)*	0.90 (0.64-1.28)	1.54 (1.02-2.35)*	0.82 (0.54-1.23)
Mixed	0.93 (0.37-2.33)	1.13 (0.67-1.90)	2.18 (0.68-6.99)	0.64 (0.25-1.62)
Geographic region				
East	Reference	Reference	Reference	Reference
North	1.44 (0.45-4.61)	1.81 (0.93-3.52)	1.29 (0.36-4.69)	1.23 (0.77-1.97)
Northeast	1.48 (0.31-7.02)	2.87 (1.37-6.01)*	1.41 (0.26-7.74)	1.77 (1.07-2.94)*
Northwest	0.80 (0.10-6.33)	1.87 (0.79-4.41)	0.44 (0.05-4.07)	1.38 (0.76-2.49)
South Central	2.14 (0.45-10.14)	1.54 (0.72-3.28)	-	0.89 (0.51-1.53)

Variable	Unadjusted		Age and sex-adjusted	
	POAG	PACG	POAG	PACG
Southwest	1.48 (0.37-6.00)	1.51 (0.69-3.29)	0.94 (0.17-5.16)	1.24 (0.70-2.22)
Investigation year (per decade increase)^	1.07 (0.58-1.98)	0.76 (0.50-1.15)	1.47 (0.51-4.25)	1.18 (0.92-1.50)

*Note: * statistically significant; $ the effect of sex was estimated based on studies that reported sex-specific glaucoma prevalence; ^ the secular trend was evaluated based on studies that were conducted after the year 2000.*

4.4.7 Regional number of people with POAG and PACG from 2000 to 2010

By taking the effects of age, sex and setting, the national POAG cases were distributed to the six geographic regions in China (**Table 4.6** and **Figure 4.11**; **Appendix table 17** for more details). In 2000, the overall prevalence of POAG was 1.01% (95% CI: 0.66-1.55) in China, ranging from 0.96% (95% CI: 0.60-1.53) in Southwest China to 1.08% (95% CI: 0.75-1.54) in Northeast China. In 2010, the overall prevalence of POAG in China rose to 1.03% (95% CI: 0.67-1.57), and the regions with the highest prevalence of POAG were Northeast China (1.05% [95% CI: 0.71-1.54]) and East China (1.05% [95% CI: 0.69-1.59]), and that with the lowest POAG prevalence was Northwest China (0.98% [95% CI: 0.62-1.53]). From 2000 to 2010, the prevalence of POAG has risen in China, with an exception of Northeast China, where the prevalence of POAG decreased by 2.47%. The most marked increasing rate was observed in Southwest China (3.68%). In both 2000 and 2010, the distribution of POAG cases across the six geographic regions was similar, with the most cases in East China and the least in Northwest China. From 2000 to 2010, the greatest increase rate was in North China (46.13%), and the least in Southwest China (26.51%). In 2010, the age groups that contributed the most POAG cases was 55-59 years across the six regions, except Northwest China, where people aged 45-49 years owed the largest share of POAG cases.

Table 4.6. Estimated prevalence and number of people with POAG in China from 2000 to 2010, by geographic region

Region	Prevalence of POAG (%, 95% CI)		Number of people with POAG (million, 95% CI)		Relative rate of change (%, 2000-2010)	
	2000	2010	2000	2010	Prevalence	Cases
North China	1.01 (0.67-1.53)	1.02 (0.68-1.54)	0.38 (0.25-0.57)	0.55 (0.37-0.83)	+1.00	+46.13
Northeast China	1.08 (0.75-1.54)	1.05 (0.71-1.54)	0.30 (0.21-0.43)	0.44 (0.30-0.64)	-2.47	+45.03
East China	1.04 (0.69-1.58)	1.05 (0.69-1.59)	1.02 (0.67-1.54)	1.39 (0.91-2.10)	+1.00	+36.34
South Central China	1.01 (0.65-1.56)	1.01 (0.65-1.57)	0.83 (0.53-1.29)	1.13 (0.73-1.75)	+0.72	+35.65
Southwest China	0.96 (0.60-1.53)	1.00 (0.63-1.59)	0.48 (0.30-0.77)	0.61 (0.38-0.97)	+3.68	+26.51
Northwest China	0.97 (0.62-1.51)	0.98 (0.62-1.53)	0.19 (0.12-0.30)	0.27 (0.18-0.43)	+1.00	+41.49
China	1.01 (0.66-1.55)	1.03 (0.67-1.57)	3.21 (2.09-4.91)	4.39 (2.86-6.72)	+1.05	+36.97

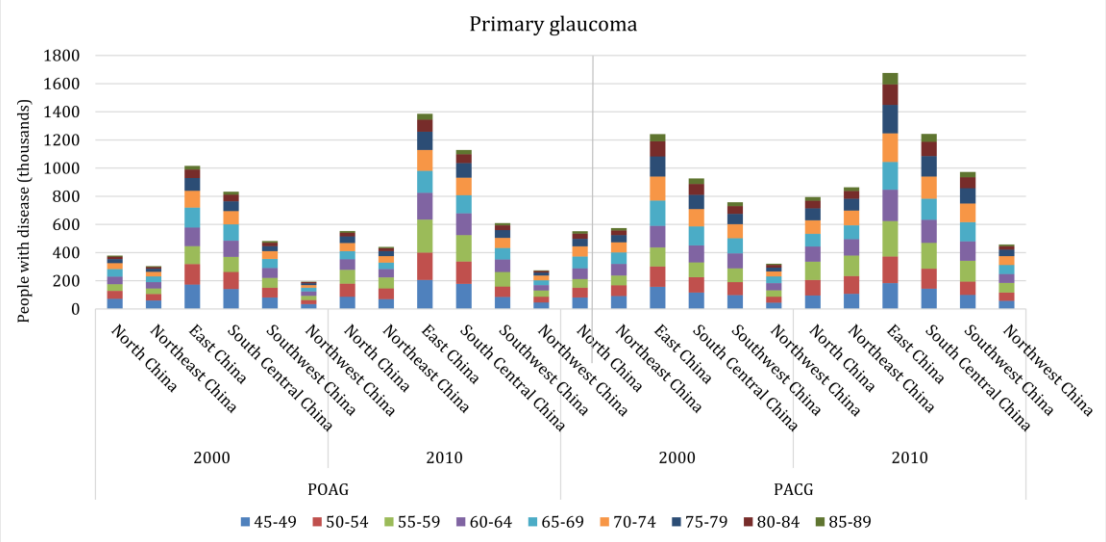


Figure 4.11. Estimation of the regional number of people with primary glaucoma and contributing age groups in China from 2000 to 2010

The number of people with PACG in China was distributed based on the multivariable meta-regression model of PACG and features of the six geographic regions (**Table 4.7** and **Figure 4.11**; **Appendix table 18** for more details). In 2000, the overall prevalence of PACG in China

was 1.38% (95% CI: 1.16-1.65), with the highest regional prevalence estimate in Northeast China (2.04% [95% CI: 1.82-2.26]) and lowest in South Central China (1.12% [95% CI: 0.95-1.32]). In 2010, the national prevalence of PACG rose by 1.30%, reaching to 1.40% (95% CI: 1.17-1.68), and the region with the highest prevalence of PACG was still Northeast China (2.06% [95% CI: 1.84-2.30]) and that with the lowest PACG prevalence was still South Central China (1.11% [95% CI: 0.94-1.31]). Within this time frame, the prevalence of PACG decreased in North China, East China and South Central China, but increased in Northeast China, Southwest China and Northwest China. The region with the greatest increasing rate of PACG prevalence was Southwest China (5.06%), and that with the greatest decreasing rate was South Central China (-0.52%). From 2000 to 2010, East China consistently harboured the largest share of PACG cases, while Northwest China has had the smallest share. Overall, the number of people with PACG increased from 4.37 million (95% CI: 3.66-5.23) to 6.01 million (95% CI: 5.03-7.18), which is a 37% increase over this period. This increase was also witnessed in every region, being the most marked in Northeast China (51%) and the least in Southwest China (28%). In 2010, the age groups that contributed the most POAG cases was 55-59 years across all the six geographic regions.

Table 4.7. Estimated prevalence and number of people with PACG in China from 2000 to 2010, by geographic region

Region	Prevalence of PACG (%, 95% CI)		Number of people with PACG (million, 95% CI)		Relative rate of change (%, 2000-2010)	
	2000	2010	2000	2010	Prevalence	Cases
North China	1.48 (1.42-1.53)	1.47 (1.41-1.52)	0.55 (0.53-0.57)	0.79 (0.76-0.82)	-0.47	+44.00
Northeast China	2.04 (1.82-2.26)	2.06 (1.84-2.30)	0.57 (0.51-0.64)	0.86 (0.77-0.96)	+1.27	+50.59
East China	1.27 (0.99-1.63)	1.27 (0.99-1.63)	1.24 (0.97-1.59)	1.68 (1.30-2.15)	-0.03	+34.94
South Central China	1.12 (0.95-1.32)	1.11 (0.94-1.31)	0.93 (0.79-1.09)	1.24 (1.05-1.46)	-0.52	+33.99
Southwest China	1.51 (1.22-1.87)	1.59 (1.28-1.97)	0.76 (0.61-0.94)	0.97 (0.78-1.20)	+5.06	+28.20
Northwest China	1.60 (1.26-2.03)	1.63 (1.27-2.07)	0.32 (0.25-0.41)	0.46 (0.36-0.58)	+1.58	+42.31
China	1.38	1.40	4.37	6.01	+1.30	+37.31

Region	Prevalence of PACG (%, 95% CI)		Number of people with PACG (million, 95% CI)		Relative rate of change (%, 2000-2010)	
	2000	2010	2000	2010	Prevalence	Cases
	(1.16-1.65)	(1.17-1.68)	(3.66-5.23)	(5.03-7.18)		

4.5 Discussion

4.5.1 Statement of principal findings

Based on rigorous systematic review of existing evidence on glaucoma prevalence in China, this study offers a comprehensive estimate of the prevalence and burden of glaucoma in China at both national and subnational levels, and compares the relative magnitude of three main subtypes of glaucoma, i.e., POAG, PACG and secondary glaucoma, in the general mainland Chinese population. From 1990 to 2015, the prevalence of glaucoma fluctuated at around 2.6%, corresponding to 5.92 million and 13.12 million people with glaucoma in the years 1990 and 2015, respectively. By 2050, the prevalence of glaucoma will rise to 3.48%, which equivalents to a total of 25.16 million affected people. Substantial evidence demonstrated that PACG was the predominant subtype of glaucoma in the general Chinese population, followed by POAG and secondary glaucoma. The geographic variations in the prevalence of POAG and PACG were also assessed, with urban dwellers at a higher risk of developing POAG than rural dwellers, and people living in Northeast China being more prone to PACG than people in East China. Because of the uneven population distribution in China, from 2000 to 2010, East China consistently had the largest share of both POAG and PACG cases, and Northwest China the least.

4.5.2 Strengths and limitations

To the best of my knowledge, this study is the most up-to-date and comprehensive systematic review and meta-analysis to explore and present the national and subnational prevalence and burden of glaucoma in China. The principal strengths of this study are a reasonable coverage of the Chinese population, a comprehensive literature search, and a stringent approach to selecting studies for inclusion. Ultimately, this systematic review was built upon 30 individuals studies, which was more than double the number of studies included in the first systematic review on glaucoma in China (Cheng et al., 2013a). With a wide geographical scope covering all the six geographic regions of China, the included studies ensured a sufficient

power to conduct the estimates for both the whole nation and subnational regions. Furthermore, with the aim of limiting between-study heterogeneity due to methodological variations, the assessments of glaucoma in the studies included were based on structural or functional evidence of glaucomatous optic neuropathy, rather than IOP measurements, which in part guaranteed a very good detection ability of early-stage glaucoma. In addition, POAG in this study included persons with IOP at all levels (Tham et al., 2014, Foster et al., 2002). Moreover, the prevalence and burden of secondary glaucoma in China was developed for the first time, which added new evidence to the epidemiology of glaucoma both domestically and globally.

Despite the strengths of this study, there are also multiple limitations. First, given the diversity of studies included in study design, targeted population, methods and settings, a relatively high degree of heterogeneity among studies included was observed. Although the estimates of POAG and PACG prevalence were generated based on meta-regression, by taking the effects of age, sex and geographic factors together, some factors other than chance may also be attributable to the observed variance, but could not be fully controlled. In this study, a key issue was that I didn't choose to exclude studies based on consensus criteria for the definitions and grading systems of glaucoma, but rather relied on the examinations. This is because previous studies suggested a remarkable similarity among surveys with different survey methods and glaucoma definitions (Rudnicka et al., 2006, Kapetanakis et al., 2016, Tham et al., 2014, Eye Diseases Prevalence Research Group, 2004b). This approach for defining eligible studies has been widely adopted in previous systematic reviews on glaucoma prevalence, but it might still be influenced by the inherent subjectivity of interpreting ophthalmic images (Chan et al., 2016, Tham et al., 2014, Kapetanakis et al., 2016, Rudnicka et al., 2006). Second, compared with primary glaucoma, secondary glaucoma has been under-examined in epidemiological studies (Chan et al., 2016, Tham et al., 2014, Yamamoto et al., 2005). In this study, despite the extensive efforts to identify all the available evidence without language restrictions, the number of eligible studies that provided the estimate of secondary glaucoma prevalence was still not sufficient. Given that there was moderate heterogeneity between studies that reported the prevalence of secondary glaucoma, I acknowledge issues about the appropriateness of roughly reporting an overall prevalence of secondary glaucoma. Third, the projections of glaucoma were only based on the assumption that the prevalence estimates will be constant, thus, changes in the number of people with glaucoma only reflect changes in demographic features of the next three decades. Although this assumption has been commonly adopted in the projection of disease burden, the power of projection analysis beyond the period of studies conducted is limited (Tham et al., 2014, Wong et al., 2014, Chan et al., 2016). Forth, only the effects of age, sex, setting and geographic region were assessed

in subgroup analyses by using both univariable and multivariable meta-regression; however, other relevant factors that were not obtained from the included studies may have also had a role. In addition, all these factors were aggregate level data, thus hampering the opportunity to explore the differences in effects at the individual level, or interaction between factors(Welch et al., 2017, Song et al., 2017a). Fifth, the estimates of glaucoma prevalence were generated at the regional level at best. Any estimates at the provincial level were not possible, owing to the limited availability of data in each province. Taken collectively, the results presented in this study should be interpreted with caution.

4.5.3 Interpretation of findings

The overall estimated prevalence of POAG in this study was slightly higher than that in the previous systematic review (1.0% vs. 0.7%) (Cheng et al., 2013a). The disparity between these two estimates might be explained by the combined effect of the different age and sex structures, and the different geographic features of the participants included in these two systematic reviews. Surprisingly, despite the substantial variation in the studies that were included as the basis for both reports, and further differences in adopted methods of meta-analysis, the prevalence of PACG in these two studies was almost identical - both at the level of 1.4%. This similarity in PACG prevalence supports the current understanding of the magnitude of PACG in China.

The prevalence estimates of POAG and PACG were notably associated with advanced age in both sexes; this strong positive relationship matches the natural history of primary glaucoma, which was described in many previous studies. This association confirms the commonly accepted notion that primary glaucoma is an age-related disease (Eye Diseases Prevalence Research Group, 2004b, Gabelt and Kaufman, 2005, Quigley, 2011, Foster et al., 2000, Friedman et al., 2008, Xu et al., 2008). With increasing longevity, a striking increase in the prevalence and burden of glaucoma is likely, especially for primary glaucoma.

The distribution patterns of POAG and PACG by sex were opposite, with POAG being the predominant subtype of glaucoma in males, and PACG in females. The female predilection for PACG has been widely acknowledged in previous studies, and could be linked to the aetiology of disease, differences in biological factors and environmental exposures between sexes (Friedman et al., 2008, Xu et al., 2008, Vajaranant et al., 2010, Cheng et al., 2013a, Cheng et al., 2014). However, the evidence of sex effect on POAG is still conflicting (Rudnicka et al., 2006, Kapetanakis et al., 2016, Vajaranant et al., 2010, Tham et al., 2014).

The findings in the present study disagree with the first systematic review of glaucoma prevalence in China, where a male predilection for POAG was not reported (Cheng et al., 2013a). The discrepancy between these two studies might be explained by the inadequate study power to confirm associations. Further studies are still needed to explore the different effects of sex on the development of glaucoma, especially POAG, and for deciding different public health policies.

In view of the general understanding that secondary glaucoma is caused by other ocular or systematic disorders that may lead to an increase in intraocular pressure, rather than a normal degenerative process with ageing, it was expected that no effects of age, sex or geographic factors would be seen (Quigley, 2011, Yamamoto et al., 2005). Only a pooled overall prevalence was generated for secondary glaucoma, with no separate subgroup analysis. In this study, the prevalence of secondary glaucoma was largely lower than that for East Asia (0.15% vs. 0.39%) (Chan et al., 2016). However, this relatively lower prevalence of secondary glaucoma, presented in this study, still needs to be confirmed with new data. There is little doubt that secondary glaucoma is less frequent in comparison with primary glaucoma; however, the disease burden caused by secondary glaucoma should never be underestimated or neglected, bearing in mind its visually destructive effects (Foster et al., 2000, Quigley, 2011).

In China, PACG was estimated to be responsible for the largest share of glaucoma, followed by POAG and secondary glaucoma. This finding confirms previous studies, which concluded that Chinese people might be more likely to develop PACG than any other ethnic groups in the world (Eye Diseases Prevalence Research Group, 2004b, He et al., 2006). Mechanisms underlying this phenomenon are controversial, but may be associated with the difference of anterior chamber and angle anatomy among races (Wong et al., 2006a, Congdon et al., 2002, Leung et al., 2010). In addition, given that PACG is more common in females than males, and females have a longer life expectancy than males, the burden of PACG is considerably concerning (United Nations, 2015b). The visual damages of PACG are more severe than of the other main subtypes of glaucoma, presenting an even greater public health challenge with a considerable social and economic impact (Foster and Johnson, 2001, Wong et al., 2006a).

The higher prevalence of POAG in urban than in rural settings is in agreement with findings from studies conducted in China, and also with many other regions across the world (Tham et al., 2014, Cheng et al., 2013a, Chan et al., 2016). The reasons for this are not certain, but may be partly related to a higher myopia prevalence in urban areas, and to other potential risk

factors for POAG that vary greatly between urban and rural areas. Hypertension, diabetes, diet, physical activity and air pollution may also play a role (Tham et al., 2014, Chan et al., 2016, Kwon et al., 2009, Bonovas et al., 2004). With rapid urbanisation, the prevalence and burden of POAG may continue to increase in China (Gong et al., 2012, Zhang and Song, 2003). For PACG, people in Northeast China had the highest prevalence. An explanation for this geographic variation is an evolutionary modification of shallower anterior chambers that resist corneal freezing (Qu et al., 2011, Casson et al., 2007). However, these geographic variations might also be a product of differences in the studies included among regions. Future studies should be undertaken to assess geographical risk factors for glaucoma in more detail, to improve locally relevant policy-making on glaucoma.

4.5.4 Implications for policy, practice and future research

The findings of this study add insight to the knowledge of the epidemiology of glaucoma and have clear policy implications for China. Together with ageing demography, glaucoma, especially primary glaucoma, will place an ever-increasing burden on the already stretched health-care services in China, unless proactive preventive strategies are put in place. Despite advances in medical treatment, a cost-effective approach for detecting and diagnosing glaucoma is still lacking (Barton and Hitchings, 2013, Hernández et al., 2008a, Hernández et al., 2008b, Vaahtoranta‐Lehtonen et al., 2007). Indeed, a strong need remains for the development of an appropriate prevention and treatment framework to counter the growing burden of glaucoma in China, especially in rural and poor areas where medical resources are unevenly distributed. National and local efforts are also needed for the formulation of better medical systems and effective public health strategies informed by evidence, such as reallocating medical resources, improving access to health care, and health education on the importance of early examination.

In the meantime, the need to scale up reliable data on glaucoma epidemiology in places where primary data have never been available has been highlighted in the present study. This is essential for both researchers and policymakers to improve understanding of the magnitude and distribution of this problem and the main risk factors. For a comprehensive assessment of glaucoma epidemiology in China, more robust evidence from studies using consistent methods across populations and further reviews of the prevalence of glaucoma are needed to corroborate the statements in the present study more reliably.

4.6 Conclusions

In conclusion, this contemporary systematic review and meta-analysis suggests a substantial burden of glaucoma in China, with considerable variation among the different age groups, sexes, study settings and geographic regions. PACG is the predominant subtype of glaucoma in the general Chinese population, followed by POAG and secondary glaucoma. In the next three decades, the prevalence and burden of glaucoma will continue to increase with the current ageing trend. More elaborate epidemiological studies are needed to optimise public health strategies for mitigating this important health problem.

Chapter 5 The national and subnational prevalence and burden of cataract and cataract blindness in China

5.1 Summary

In this chapter, a systematic review was first conducted to derive all studies that reported the prevalence of cataract in China. Due to the vast heterogeneity in case definitions, the reported prevalence of cataract in China varied greatly between studies. After comparing the various definitions across studies, I chose the most commonly adopted definitions of cataract, ARC and cataract blindness. This was done to guarantee the possibility of subsequent quantitative syntheses, but might, in turn, restrict the ability of international comparison. By using the meta-regression approach, the age- and sex-specific prevalence of cataract and ARC was estimated. The prevalence of cataract blindness, however, was pooled by a random-effects meta-analysis because only study-level prevalence estimates were available. The national numbers of people with cataract and ARC were calculated by applying the age- and sex-specific prevalence to the corresponding demographic data in the years 1990-2050. Similar to the case of secondary glaucoma, as described in Chapter 4, the number of people with cataract blindness was also generated by multiplying the population size from 1990-2050. This was done under the assumption that the prevalence of cataract blindness stayed and will continue to be constant during 1990-2050. By taking the effects of age, sex and geography, the national cataract cases were finally distributed into the six geographic regions in China.

The work presented in this chapter has been published in the Journal of Global Health cited as "Song, P., Wang, H., Theodoratou, E., Chan, K. Y., & Rudan, I. (2018). The national and subnational prevalence of cataract and cataract blindness in China: a systematic review and meta-analysis. Journal of Global Health, 8(1), 010804. http://doi.org/10.7189/jogh.08-010804".

I fully participated in the whole process of this project, including study conceptualisation and design, development of search strategy, systematic review, data extraction, data analysis and interpretation. I prepared the first draft of manuscript, which has been subsequently revised according to the comments from co-authors and anonymous peer reviewers during the

publishing process. The specific contributions of co-authors are as follows: Rudan, I. conceptualised and designed the study, Wang, H. conducted the dual systematic review and data extraction, Theodoratou, E., Chan, K. Y. and Rudan, I. critically reviewed the manuscript and approved the final manuscript.

5.2 Background

Cataract, defined as any opacity of the crystalline lens in the eye that affects clear vision, is a common condition in later life (Asbell et al., 2005, Kanski and Bowling, 2011, Liu et al., 2017). If left untreated, cataract can eventually progress to severe visual impairment or even blindness (Brian and Taylor, 2001, Pascolini and Mariotti, 2011). Compared with the general population, people with cataract are more likely to have substantially reduced vision-related quality of life and increased risk of comorbidity and mortality (Broman et al., 2002, Polack et al., 2007, Song et al., 2014, Hu et al., 2001, Nemet et al., 2010, Liu et al., 2017). Surgery is cost-effective and successful in restoring cataract-related vision loss (Busbee et al., 2002, Busbee et al., 2003, Lansingh et al., 2007). However, in many resource-deprived areas, especially remote and poor areas in developing countries, barriers in access to appropriate preventative eye care and surgical treatments still exist, presenting an enormous problem to the society in terms of social and economic burden (Nirmalan et al., 2004, Rabiu, 2001, Yin et al., 2009, Khanna et al., 2011). Based on aetiology, cataract can be broadly classified as age-related, congenital, traumatic, secondary and drug-induced, etc., with age-related cataract (ARC) being the predominant subtype (Asbell et al., 2005, Liu et al., 2017).

Despite the fact that cataract can be easily, safely and cost-efficiently treated with a standard procedure, cataract still remains the second leading cause of visual impairment and the first of blindness globally (Age-Related Eye Disease Study Research Group, 2001b, Liu et al., 2017, Pascolini and Mariotti, 2011). According to the latest estimates in 2010, 94 million people were visually impaired and 20 million were blind because of cataract, accounting for one third (33%) of all individuals with visual impairment and more than half (51%) of blind cases worldwide (Pascolini and Mariotti, 2011). Cataract is a multifactorial disease, with ageing being the major risk factor by far (Asbell et al., 2005, Liu et al., 2017). As people live longer, the prevalence of cataract is expected to rise correspondingly, posing challenges for health systems. From the public health perspective, understanding the magnitude of cataract and cataract blindness is the first step in prevention and treatment, and can provide a basis for evidence-based policy making and public health resources allocation (Klein and Klein, 2013).

Despite this, a comprehensive review of data regarding the prevalence and burden of cataract on a global basis has never, to the best of my knowledge, been documented previously. This may largely due to the difficulty of combining prevalence data from different national, regional, racial and ethnic groups, especially in cases where inconsistent definitions of cataract were adopted and a universally recognised standardisation was lacking.

Similarly, in the largest developing country, China, few national-representative investigations have been conducted to provide precise estimates of the prevalence of cataract or cataract blindness in the general Chinese population. Nevertheless, a growing number of population-based studies on the epidemiology of cataract have been conducted across the nation during the past decades, which have reported an overall cataract prevalence of from less than 10% to more than 50% in various samples (Sheng et al., 2016, Zhou and Jia, 2011, Fung, 2008, Xia et al., 2008). The substantial variations might largely come from the disparities of cataract definitions (e.g. with reduced visual acuity or not, different cut-offs for defining reduced visual acuity), as well as the different characteristics of individual studies (e.g. the age structure of the investigated population and the geographic location of the study sites) (Wong et al., 2006a, Zhou and Jia, 2011, Guan et al., 2012, Wang et al., 2014b). Until recently, no information has been compiled for the prevalence of cataract and cataract blindness in China, and the magnitude of the national number of people with cataract and cataract blindness in general Chinese population remains unclear. As Chinese population is progressively ageing, an increasing burden of cataract and cataract blindness is also expected (United Nations, 2015a, Zhang et al., 2012, Woo et al., 2002, Mai et al., 2013). If nothing else alters, the corresponding increased demand for cataract surgery will present new challenges for the Chinese health system.

In view of uncertainties about the prevalence of cataract and cataract blindness in China, I conducted a comprehensive systematic review, in both Chinese and English databases, to retrieve all population-based studies that reported the prevalence of cataract or cataract blindness in China from 1990 onwards. By using standardised definitions of cataract and cataract blindness, I quantitatively summarised the prevalence of cataract and cataract blindness in China. Furthermore, the geographic patterns and secular trend of cataract/cataract blindness prevalence were also examined to add insights to the public health domain, assisting both researchers and policymakers to prioritise health-care resources needed. The principal aims of this study were: 1) to determine the prevalence and number of people affected by cataract and cataract blindness at the national level from 1990 to 2015; 2) to project the prevalence and number of people with cataract and cataract blindness at the national level till

2050; and 3) to examine regional differences in the prevalence of cataract and the number of affected people from 2000 to 2010.

5.3 Methods

5.3.1 Systematic review

This systematic review and meta-analysis conforms to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines and the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement (Moher et al., 2009, Stevens et al., 2016).

5.3.1.1 Search strategy

Three Chinese and three English bibliographic databases, including China National Knowledge Infrastructure (CNKI), Wanfang, Chinese Biomedicine Literature Database (CBM-SinoMed), PubMed, Embase, and Medline, were searched using a comprehensive search strategy to identify all relevant articles on the prevalence of cataract or cataract blindness in general Chinese population published from January 1990 onwards. Search terms that related to cataract ("cataract" or "cataracts"), prevalence ("incidence", "prevalence", "morbidity", "mortality", "epidemiology") and China ("China", "Chinese", "Hong Kong", "Macau", "Taiwan") were combined in forms of controlled vocabularies (e.g. Medical Subject Heading terms) and free text terms. No language restrictions were placed in the search or in the selection process. The complete search strategies are described in **Appendix table 19**, which were conceived and adapted to fit features of different bibliographic databases. To supplement the database searches, reference lists of all included articles were also scrutinised to identify additional data sources.

5.3.1.2 Inclusion and exclusion criteria

To be included in the systematic review, studies needed to be population-based primary studies, reporting the prevalence of cataract or cataract blindness in Chinese population of a defined age and sex structure. Herein, the prevalence of cataract or cataract blindness should be calculated based on the number of affected individuals, rather than the number of affected eyes. Definitions of cataract/cataract blindness and measurements of visual acuity should be clearly stated. To avoid potentially biased information, I excluded hospital-based studies, studies that

were conducted among populations of Chinese origin but residing outside China, and those confined to a specific population that was not representative of the general population (people with a specific health condition, people covered by health insurance, etc.). Narrative reviews, case reports, commentaries, editorials, conference proceedings and studies without primary data or explicit methodologies were additionally excluded. Furthermore, studies that reported prevalence rates based on self-reported data were also excluded because an underestimation was very likely. For multiple articles that reported duplicated or overlapping data of the same single study, the one with the most representative results or largest sample size was kept.

During the systematic review process, the definition of cataract was found to vary dramatically among studies (**Appendix table 20**): some studies defined cataract as the presence of lens opacities without diminished visual acuity, whereas other studies documented cataract in people with reduced visual acuity, which was determined by either best corrected visual acuity (BCVA) or presenting visual acuity (PVA) (Wang et al., 2014b, Zhou and Jia, 2011, Li et al., 1999, Guan et al., 2012). The cut-offs of reduced visual acuity in different studies varied widely from 0.50 decimal Snellen (6/12) to 0.70 decimal Snellen (6/9) (Zhou and Jia, 2011, Wang et al., 2014b), and those for defining blindness ranged from 0.05 decimal Snellen (6/120) to 0.10 decimal Snellen (6/60) (Li et al., 1999, Guan et al., 2012). To ensure maximum comparability across studies and the ability to synthesise data from various studies, only studies that adopted a standardised definition of cataract or cataract blindness were eligible for the meta-analysis. Herein the standardised definitions of cataract and cataract blindness refer to the definitions that were most widely taken in Chinese epidemiological surveys (**Table 5.1**). In summary, cataract could be unilateral or bilateral, with reduced visual acuity (BCVA $\leq$0.70), and include pseudophakia/aphakia. Cataract was further categorised as any cataract (including all subtypes of cataract without further sub-classifications) or ARC (being explicitly indicated as the age-related subtype of cataract). Cataract blindness must be bilateral and include operated cases. Since it is generally impossible to obtain the preoperative visual acuity of an operated eye, if one person's both eyes were operated on for cataract, he/she was presumed to have been bilaterally cataract blind preoperatively; or if only one eye was operated on for cataract and the fellow eye was blind because of cataract at the time of examination, then this person was also presumed to have bilateral cataract blindness (Guan et al., 2012, Sapkota et al., 2006, Nirmalan et al., 2002). Those basic assumptions about cataract blindness should be compiled into the included studies that reported the prevalence of cataract blindness. According to different cut-offs of visual acuity for defining blindness, cataract blindness was categorised as cataract blindness by BCVA <0.05, by BCVA <0.10 and by PVA <0.10 respectively.

Table 5.1. The standardised definitions of cataract and cataract blindness in the systematic review

Cataract
1) Lens opacities presenting in at least one eye (unilateral or bilateral); 2) With BCVA ≤0.70 in the cataract-affected eye; 3) Including pseudophakia/aphakia.
Cataract blindness
1) being blind in the better-seeing eye caused by cataract; 2) Including pseudophakia/aphakia.

5.3.1.3 Study selection and data extraction

All duplicate records within and between different bibliographic databases were identified and eliminated before conducting the formal systematic review. After screening the titles and abstracts of all retained records, the full texts of potentially relevant articles were retrieved and further appraised for inclusion against the eligibility criteria. All discrepancies were resolved through discussions until consensuses were reached. The quality of each included study was assessed based on the STROBE guideline (**Table 2.1**), where five bias components- sample population, sample size, participation rate, outcome assessment, and analytical methods were scored respectively. For each component, low risk was scored as 2, moderate risk as 1 and high risk and unclear as 0. The total score of the five components represented the overall quality of each study (Von Elm et al., 2007, Song et al., 2018).

Finally, relevant data were extracted from the eligible articles by using a pilot tested and refined extraction table, which included three main categories:

1) Characteristics of the study: authors, publication year, study setting, survey year, sampling method, study design (cross-sectional or cohort), case definition and assessment method;
2) Characteristics of the investigated population: sample size, population type (urban or rural), sex (male or female), and age (age range, mean or median age, or midpoint of the age range);
3) Prevalence data: the number of people with cataract/cataract blindness and the number of participants who had been tested, by age group, sex, setting and cataract/cataract blindness subtype where possible.

In cases where stratified prevalence estimates were not available by sex and setting, and only the overall estimates were reported, sex or setting were labelled as "mixed". Studies were grouped into six geographic regions according to their study sites. Those geographic regions included North China, Northeast China, East China, South Central China, Southwest China and Northwest China, which were delineated by the National Bureau of Statistics of China (**Table 2.2** and **Figure 2.2**) (National Bureau of Statistics, 2002, National Bureau of Statistics, 2012, Song et al., 2017c, Song et al., 2017b). If people in different geographic areas were examined in the same study, prevalence data were extracted for each geographic area separately, where available. For four studies where the years of survey were not specified, three years were subtracted from their publication years to impute the survey years, which was based on the average time lag from survey to publication in studies that provided such information (see **Appendix table 21**). For studies that reported censoring age groups, e.g. older than 80 years, less than 50 years, the missing age band was imputed by taking the same width as other age groups in the same study.

5.3.2 Statistical analysis

5.3.2.1 Epidemiological modelling of cataract prevalence and pooled prevalence of cataract blindness

Before synthesising the abstracted data, unadjusted prevalence of cataract (any cataract and ARC) and cataract blindness (by BCVA <0.05, by BCVA <0.10 and by PVA <0.10) was firstly calculated on the basis of crude numerators and denominators derived from individual studies. In this study, random-effects meta-analysis was performed throughout because sizeable heterogeneity of reported prevalence in different studies was suggested (**Appendix table 22**).

For cataract, multiple outcome measurements were available within a single study. To accommodate for this hierarchical data structure (clustering of different stratum-specific prevalence rates from the same study), a multilevel mixed-effects meta-regression model was fitted (Hox et al., 2010, Viechtbauer, 2010). Before constructing models for estimating the prevalence of cataract, the associations of prevalence rates and study-level variables of interest, i.e., age, sex (male and female), setting (urban, rural and mixed), geographic region and survey year were first explored using univariable meta-regression. This was done for any cataract and ARC separately. Age and sex were identified as variables that were commonly associated with the prevalence of both any cataract and ARC (**Table 5.2**).

Table 5.2. The Unadjusted odds ratios for any cataract and ARC in terms of demographic and geographic factors from univariable meta-regression models, with 95% confidence intervals

Variable	Any cataract		ARC	
	Number of studies	OR (95% CI)	Number of studies	OR (95% CI)
Age (per decade increase)	35	3.34 (3.29-3.40)*	10	2.74 (2.65-2.84)*
Sex$				
Female	29	Reference	10	Reference
Male	29	0.79 (0.77-0.80)*	10	0.67 (0.64-0.71)*
Setting				
Mixed	10	Reference	2	Reference
Rural	14	1.35 (0.86-2.12)	5	1.19 (0.20-7.12)
Urban	13	0.76 (0.49-1.20)	4	1.71 (0.25-11.61)
Geographic region				
East	15	Reference		
North	6	0.48 (0.22-1.05)^		
Northeast	2	0.87 (0.30-2.49)		
Northwest	5	0.74 (0.34-1.63)		
South Central	4	1.56 (0.71-3.43)		
Southwest	3	1.08 (0.44-2.61)		
Survey year (per decade increase)	35	1.27 (0.85-1.89)	10	0.50 (0.15-1.65)

*Note: * statistically significant ($p<0.05$); ^ $p<0.1$; $ the effect of sex was estimated based on studies that reported sex-specific cataract prevalence; the effect of geographic region on the prevalence of ARC was not conducted because of the deficiency of available information.*

For the purpose of producing the national "envelopes" (total number of cases) of any cataract and ARC, the age- and sex-specific prevalence estimates of any cataract and ARC were developed. Given that:

$$\text{Prevalence} = \text{p} = \frac{Number\ of\ cases}{Samle\ size}$$

Then, the prevalence rates were transformed using a logit link (Barendregt et al., 2013):

$$\text{logit}(p) = \log_e\left(\frac{p}{1-p}\right) = \log_e(odds) = \alpha + \beta_1 * x_1 + \beta_2 * x_2 + \cdots \beta_n * x_n$$

Given age and sex were the prespecified variables:

$$\text{logit}(p) = \alpha + \beta_1 * (age) + \beta_2 * (sex)$$

Thus, the prevalence of any cataract/ARC was:

$$\text{p} = \frac{e^{\alpha+\beta_1*(age)+\beta_2*(sex)}}{1 + e^{\alpha+\beta_1*(age)+\beta_2*(sex)}}$$

For cataract blindness, the stratum-specific prevalence rates were not universally available in the included studies. Therefore, the pooled prevalence, with 95% confidence intervals (CIs), was obtained from a random-effects meta-analysis model (DerSimonian and Laird method) with inverse-variance weighting. The variance of prevalence was also stabilised with the logit transformation (Barendregt et al., 2013). To check whether a single study disproportionally influenced the pooled results, the sensitivity analysis was conducted by removing one study at a time to run the meta-analysis without it (Wallace et al., 2009). I also assessed the publication bias by visual inspection of funnel plots test (Egger et al., 1997). Due to the small number of studies that reported the prevalence of cataract blindness, Egger's regression test for funnel plot asymmetry and Begg's rank correlation test were not performed (Egger et al., 1997, Begg and Mazumdar, 1994, Peters et al., 2006)

5.3.2.2 Estimation of the national number of people with cataract and cataract blindness from 1990 to 2015

The total number of people affected by cataract ("cataract envelope", including post-surgical cases) in China was generated by applying the modelled age- and sex-specific prevalence for each 5-year age group to the corresponding population subgroup in China, available from the United Nations Population Division (UNPD) (United Nations, 2015b). This was performed for any cataract and ARC respectively in the years 1990, 2000, 2010 and 2015.

For cataract blindness, the age- and sex-specific prevalence estimates were not specifically constructed, the overall number of people affected by cataract blindness (including post-surgical cases) was, therefore, estimated by multiplying the pooled prevalence of cataract blindness by the national population. This was conducted for the three subgroups of cataract

blindness determined by different definitions of blindness (by BCVA <0.05, by BCVA <0.10 and by PVA <0.10) from 1990 to 2015.

5.3.2.3 Projection of the national number of people with cataract and cataract blindness from 2020 to 2050

To derive the projected number of people with cataract/cataract blindness (including post-surgical cases) for the period 2020-2050, the age- and sex-specific prevalence of cataract and the pooled prevalence of cataract blindness were assumed to stay constant over time. For cataract, this assumption was supported by the univariable meta-regression models, where no significant association between survey year and the prevalence of cataract (both any cataract and ARC) was detected (**Table 5.2**). The national number of people living with cataract and cataract blindness from 2020 to 2050 was projected by following the same approach as used for deriving the national number of cataract and cataract blindness cases from 1990 to 2015. The demographic projection was taken from the UNPD medium variant population scenario, which was underpinned by assumptions about future fertility and mortality (United Nations, 2015b, Lee and Zhou, 2017).

5.3.2.4 Effects of demographic and geographic factors on the prevalence of cataract

Where appropriate (at least seven contributing estimates should be available for each variable (Vittinghoff and McCulloch, 2007)), the effects of demographic (i.e., age, sex) and geographic features (i.e., setting, geographic region) on the prevalence of cataract were initially assessed by univariable meta-regression models. The effect of survey year on the prevalence of cataract was also explored by introducing the survey year into the models. Finally, all variables with p values of less than 0.1 in univariable meta-regression models were entered into the multivariable meta-regression.

5.3.2.5 Estimation of the subnational number of people with cataract from 2000 to 2010

To generate the number of people with cataract in the six geographic regions, an “envelope” approach was adopted. This “envelope” approach was previously endorsed by the Child Health Epidemiology Reference Group (CHERG), and has, since, been widely advocated in the

disease burden domain (Rudan et al., 2004, Fowkes et al., 2013, Song et al., 2016, Song et al., 2017b, Song et al., 2017c, Bourne et al., 2017). First, based on the final multivariable meta-regression that took the effects of demographic and geographic features into account, cataract prevalence in each geographic region was calculated respectively. Then the regional cases of cataract were estimated by multiplying the regional cataract prevalence by their corresponding population. Finally, the regional cataract cases were adjusted to fit into the national "cataract envelope". This was done for the years 2000 and 2010, where the regional population data could be derived from the fifth and sixth censuses respectively (National Bureau of Statistics, 2002, National Bureau of Statistics, 2012).

The overall study design is shown in **Figure 5.1**. All statistical analyses were done with R, version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria) with the packages meta (version 4.8-4), metafor (version 2.0-2) and ggplot2 (version 2.2.1) (R Core Team, 2013). A two-sided p-value of less than 0.05 was regarded as indicative of statistically significant, unless otherwise specified. All maps were created using ArcMap version 10.1 (Environmental Systems Research Institute, Redlands, CA, USA), based on the China base map (in shapefile format) obtained from the Global Administrative Areas (GADM) database (GADM, 2015, version 2.0; www.gadm.org).

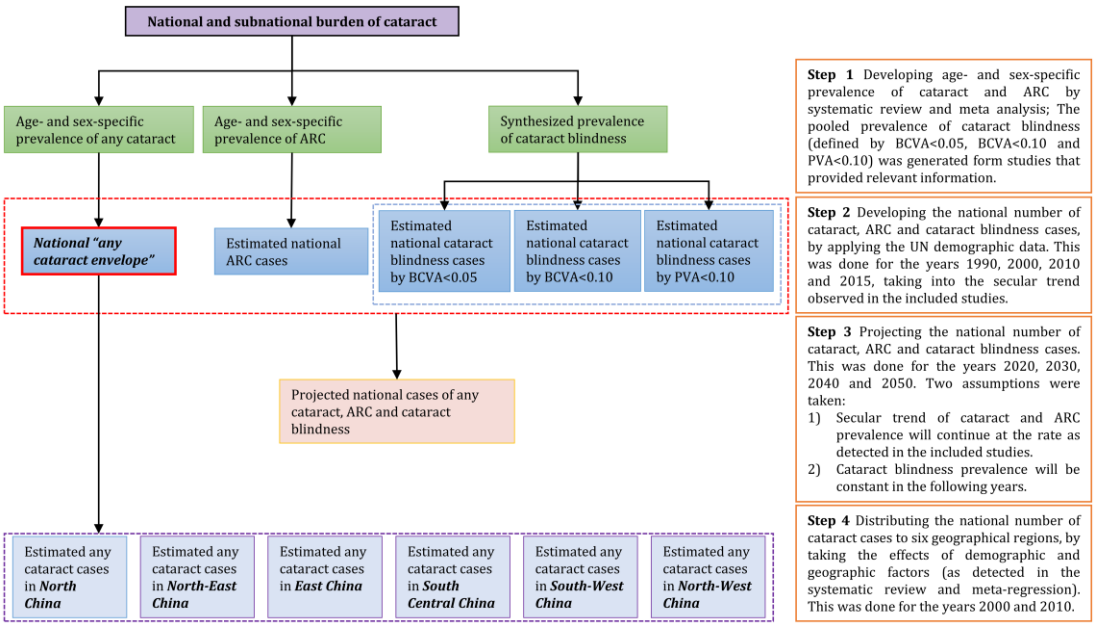


Figure 5.1. Overall study design flowchart for the prevalence and burden of cataract and cataract blindness study in China

5.4 Results

5.4.1 Summary of systematic review

The initial literature search yielded a total of 16345 citations. After removing 8181 duplicates, the titles and abstracts of 8164 unique records were screened for relevance. Of these, 1414 potentially relevant articles were reviewed in full-text form and 1359 were subsequently excluded. Finally, 55 studies met the eligibility criteria and were included in the systematic review and meta-analysis. The review process is summarised in **Figure 5.2** as a PRISMA flowchart. A list of the included studies is available in **Appendix table 23**.

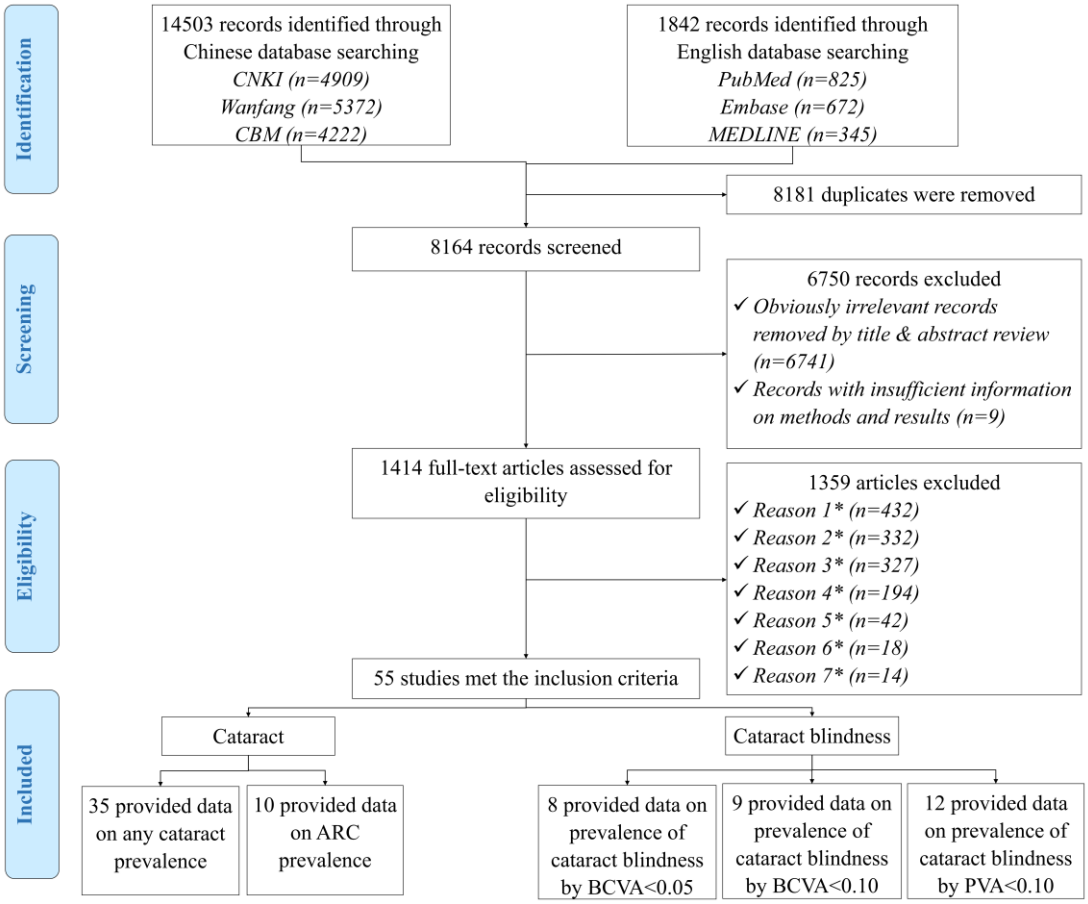


Figure 5.2. Systematic review flow diagram of studies on cataract and cataract blindness prevalence in China

*Note: *Reason 1-Studies that were conducted in in people with unrepresentative characteristics of general population (hypertensive patients, people with reduced vision, etc.);*

**Reason 2-Studies that were not population-based; *Reason 3-Studies that relied on self-reported diagnoses of cataract or cataract blindness; *Reason 4-Articles with no numerical prevalence measure of cataract or cataract blindness; *Reason 5-Studies that didn't adopt the standardised definitions of cataract and cataract blindness; *Reason 6-Multiple publications of the same study; *Reason 7-Studies that were not based in China.*

Table 5.3 summarises the main characteristics of the 55 included studies. All those studies were cross-sectional in design, among which the majority were published in this decade (from 2010 onwards). Most studies were relatively large, with more than 2000 participants. Almost all studies provided sex-specific data, enabling the exploration of sex difference in cataract prevalence. Of the included studies, 35 studies examined the prevalence of any cataract, ten provided prevalence data on ARC; eight studies focused on the prevalence of cataract blindness by BCVA<0.05, nine on the prevalence of cataract blindness by BCVA<0.10, and 12 on the prevalence of cataract blindness by PVA<0.10. The diverse geographical areas covered by the included studies are shown in **Figure 5.3**, and the detailed characteristics and quality assessments of all included studies are demonstrated in **Appendix table 24** and **Appendix table 25**.

Table 5.3. Main characteristics of the included studies on cataract and cataract blindness in China (n=55)

Characteristic	Number of studies provided prevalence data on (%)*				
	Any cataract (n=35)	**ARC (n=10)**	**Cataract blindness by BCVA<0.05 (n=8)**	**Cataract blindness by BCVA<0.10 (n=9)**	**Cataract blindness by PVA<0.10 (n=12)**
Year published					
1990-1999	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
2000-2009	10 (28.6)	6 (60.0)	4 (50.0)	0 (0.0)	4 (33.3)
2010-2017	25 (71.4)	4 (40.0)	4 (50.0)	9 (100.0)	7 (58.3)
Setting					
Urban	11 (31.4)	3 (30.0)	3 (37.5)	0 (0.0)	4 (33.3)
Rural	12 (34.3)	4 (40.0)	3 (37.5)	5 (55.6)	5 (41.7)
Mixed	10 (28.6)	2 (20.0)	1 (12.5)	4 (44.4)	2 (16.7)
Both	2 (5.7)	1 (10.0)	1 (12.5)	0 (0.0)	1 (8.3)
Sex					
Mixed	4 (11.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Characteristic	Number of studies provided prevalence data on (%)*				
	Any cataract (n=35)	**ARC (n=10)**	**Cataract blindness by BCVA<0.05 (n=8)**	**Cataract blindness by BCVA<0.10 (n=9)**	**Cataract blindness by PVA<0.10 (n=12)**
Both	31 (88.6)	10 (100.0)	8 (100.0)	9 (100.0)	12 (100.0)
Sample size					
≤2000	7 (20.0)	4 (40.0)	1 (12.5)	1 (11.1)	1 (8.3)
2001-5000	11 (31.4)	2 (20.0)	5 (62.5)	1 (11.1)	6 (50.0)
5001–10000	12 (34.3)	3 (30.0)	2 (25.0)	5 (55.6)	4 (33.3)
>10000	5 (14.3)	1 (10.0)	0 (0.0)	2 (22.2)	1 (8.3)
Geographic region$					
North China	6 (17.1)	3 (20.0)	2 (25.0)	2 (15.4)	2 (16.7)
Northeast China	2 (5.7)	1 (6.7)	1 (12.5)	1 (7.7)	0 (0.0)
East China	15 (42.9)	3 (20.0)	2 (25.0)	7 (53.8)	4 (33.3)
South Central China	4 (11.4)	2 (13.3)	0 (0.0)	1 (7.7)	1 (8.3)
Southwest China	3 (8.6)	2 (13.3)	2 (25.0)	1 (7.7)	5 (41.7)
Northwest China	5 (14.3)	4 (26.7)	1 (12.5)	1 (7.7)	0 (0.0)
Quality score					
10	10 (28.6)	1 (10.0)	3 (37.5)	7 (77.8)	5 (41.7)
9	9 (25.7)	3 (30.0)	2 (25.0)	1 (11.1)	4 (33.3)
8	3 (8.6)	2 (20.0)	1 (12.5)	0 (0.0)	2 (16.7)
7	10 (28.6)	3 (30.0)	1 (12.5)	1 (11.1)	1 (8.3)
6	3 (8.6)	1 (10.0)	1 (12.5)	0 (0.0)	0 (0.0)

*Note: *Some studies reported the prevalence estimates of any cataract, ARC, cataract blindness by BCVA<0.05, cataract blindness by BCVA<0.10 and cataract blindness by PVA<0.10 simultaneously, therefore the sum of the number of studies exceeded 55. $ Some studies covered more than one geographic region, therefore the sum of coved geographic regions exceeded the sum of studies.*

Figure 5.3. Geographical distribution of the included studies on cataract and cataract blindness prevalence in China (n=55)

5.4.2 Age- and sex-specific prevalence of cataract and pooled prevalence of cataract blindness

For cataract, a substantial number of data points from the included studies guaranteed my ability to construct the relation between age and prevalence (**Figure 5.4**). The age range covered by informative data points for any cataract was wider than that for ARC. To ensure the comparability of the estimated prevalence of any cataract and ARC, the age range in this study was set as from 45 to 89 years, where the most informative data points concentrated. The effect of sex on the prevalence of cataract was also assessed based on studies that provided sex-specific cataract prevalence (**Table 5.2**).

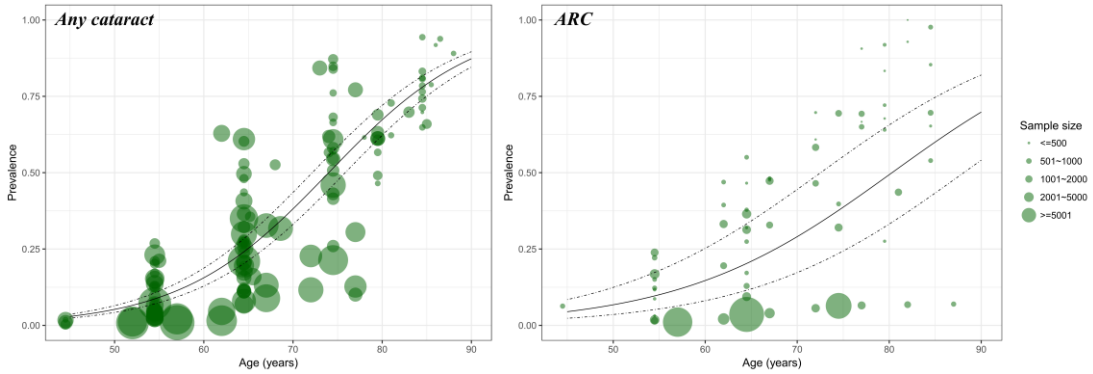


Figure 5.4. Age-specific prevalence of cataract and ARC based on informative data points from the included studies

Note: The size of each bubble is proportional to the sample size. For cataract, there were 143 data points for constructing the relation between age and prevalence; For ARC, there were 66.

Table 5.4 and **Figure 5.5** demonstrate the estimated age- and sex-specific prevalence of any cataract and ARC. Generally, the prevalence of any cataract and ARC was higher in females than in males, and both showed a steady rise with advanced age. In males, the prevalence of any cataract ranged from 6.71% (95% CI: 5.06-8.83) in people aged 45-49 years to 73.01% (95% CI: 65.78-79.2) in elderly aged 85-89 years. In females, the prevalence of any cataract increased from 8.39% (95% CI: 6.36-10.98) in individuals aged 45-49 years to 77.51% (95% CI: 71.00-82.90) in those aged 85-89 years. In the case of ARC, the prevalence rates ranged from 3.23% (95% CI: 1.51-6.80) in males aged 45-49 years to 65.78% (95% CI: 46.72-80.82) in those aged 85-89 years. The prevalence of ARC in females was consistently higher than that in males, ranging from 4.72% (95% CI: 2.22-9.76) in the 45-49 years age group to 74.03% (95% CI: 56.53-86.21) in the 85–89 years age group.

Table 5.4. Estimated sex-specific prevalence of any cataract and ARC in China, by age group

Age group	Prevalence of any cataract (%, 95% CI)		Prevalence of ARC (%, 95% CI)	
	Male	Female	Male	Female
45-49 years	6.71 (5.06-8.83)	8.39 (6.36-10.98)	3.23 (1.51-6.80)	4.72 (2.22-9.76)
50-54 years	10.16 (7.91-12.97)	12.59 (9.86-15.95)	5.25 (2.48-10.76)	7.59 (3.64-15.17)
	15.11	18.49	8.42	12.00

Age group	Prevalence of any cataract (%, 95% CI)		Prevalence of ARC (%, 95% CI)	
	Male	**Female**	**Male**	**Female**
55-59 years	(12.06-18.77)	(14.88-22.73)	(4.07-16.64)	(5.91-22.84)
60-64 years	21.89 (17.86-26.53)	26.30 (21.69-31.50)	13.24 (6.58-24.87)	18.46 (9.46-32.92)
65-69 years	30.60 (25.45-36.29)	35.97 (30.31-42.05)	20.22 (10.47-35.45)	27.31 (14.78-44.88)
70-74 years	40.97 (34.69-47.55)	46.92 (40.36-53.59)	29.60 (16.23-47.71)	38.41 (22.33-57.50)
75-79 years	52.20 (45.07-59.25)	58.18 (51.10-64.94)	41.10 (24.30-60.28)	50.86 (32.25-69.24)
80–84 years	63.22 (55.73-70.12)	68.65 (61.59-74.93)	53.67 (34.67-71.65)	63.21 (44.05-78.94)
85-89 years	73.01 (65.78-79.20)	77.51 (71.00-82.90)	65.78 (46.72-80.82)	74.03 (56.53-86.21)

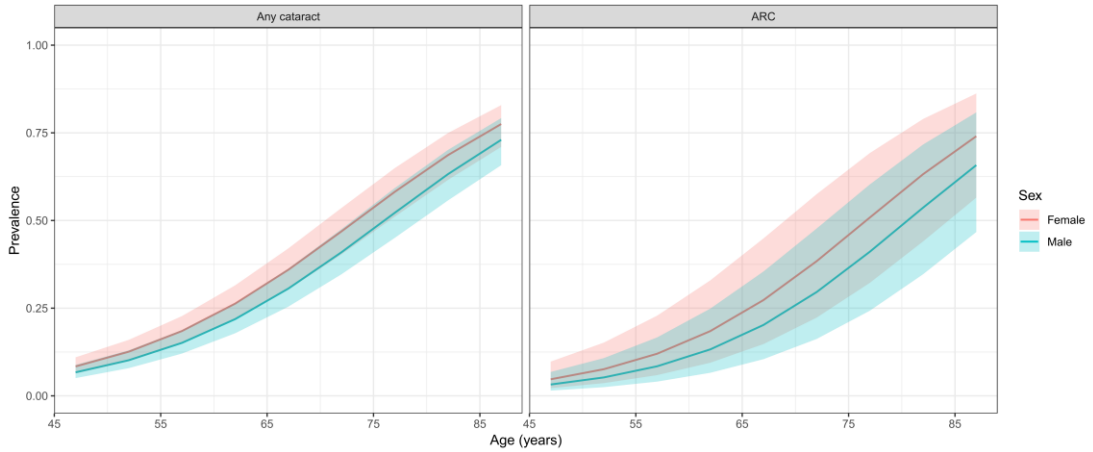


Figure 5.5. Estimated age- and sex-specific prevalence of any cataract and ARC in China, with 95% confidence intervals

For cataract blindness, the pooled prevalence estimates by random-effects meta-analyses are shown in **Figure 5.6**. Overall, the pooled prevalence of cataract blindness by BCVA <0.05 was 2.30% (95% CI: 1.72-3.07) and that of cataract blindness by BCVA <0.10 was 2.56% (95% CI: 1.94-3.38). At a more relaxed threshold level for defining blindness, the pooled prevalence of cataract blindness by PVA <0.10 was 4.51% (95% CI: 3.53-5.75). According to the leave-one-out sensitivity analysis, no single study had a substantial influence on the overall

prevalence of cataract blindness, where the pooled prevalence of cataract blindness by BCVA<0.05 ranged from 2.11% (95% CI: 1.59-2.81) to 2.45% (95% CI: 1.82-3.30), that of cataract blindness by BCVA<0.10 from 2.38% (95% CI: 1.98-2.87) to 2.67% (95% CI: 2.00-3.55), and that of cataract blindness by PVA<0.10 from 4.28% (95% CI: 3.32-5.49) to 4.81% (95% CI: 3.81-6.06) (**Figure 5.7**). The asymmetrical shape of funnel plots revealed some evidence of potential publication bias (**Figure 5.8**).

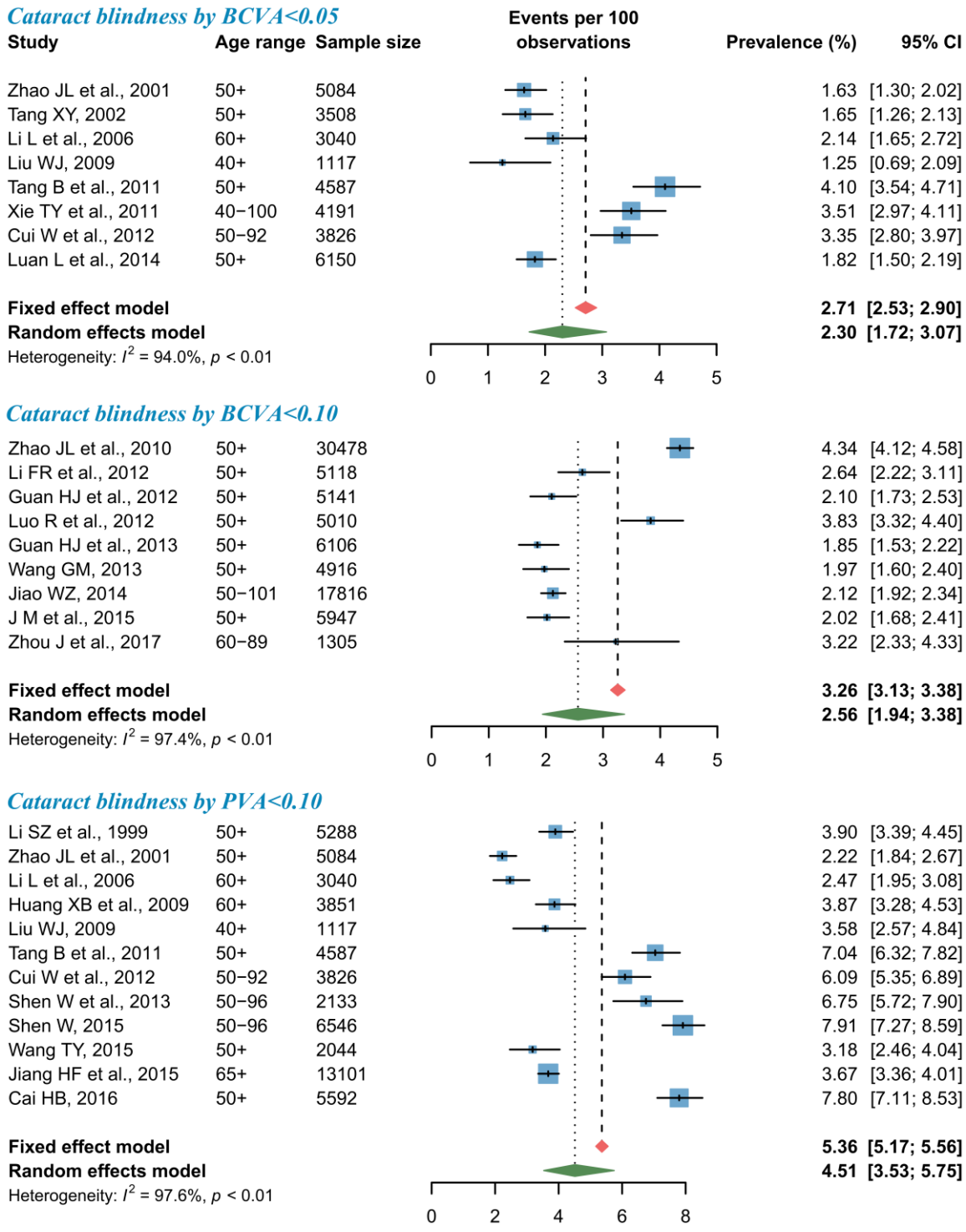


Figure 5.6. Forest plots of cataract blindness prevalence in China

Note: Data were pooled by a random-effects model; the size of the blue shaded areas is proportional to the weight of each study.

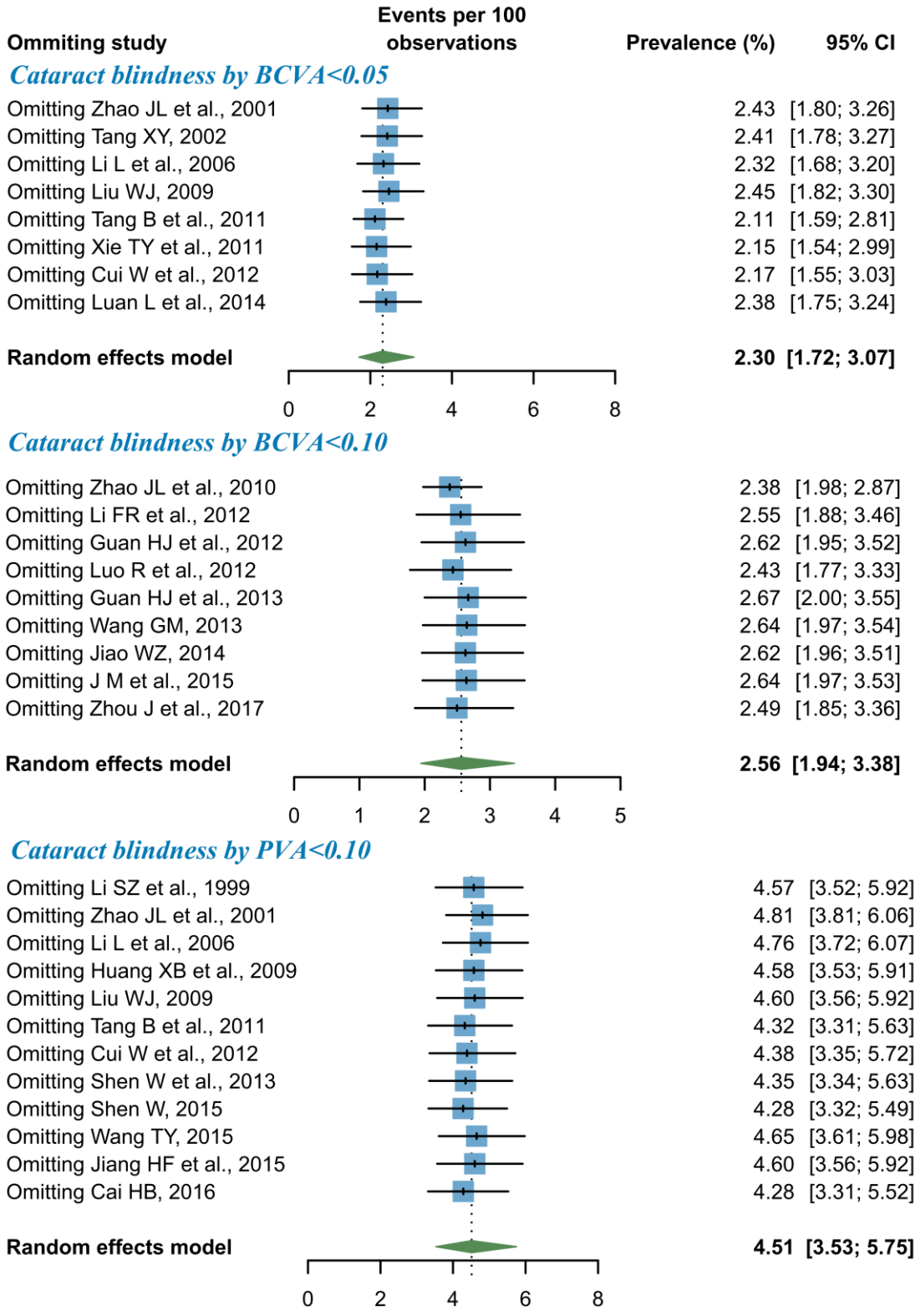


Figure 5.7. Leave-one-out sensitivity analysis of the influence of single study on the pooled prevalence of cataract blindness in China

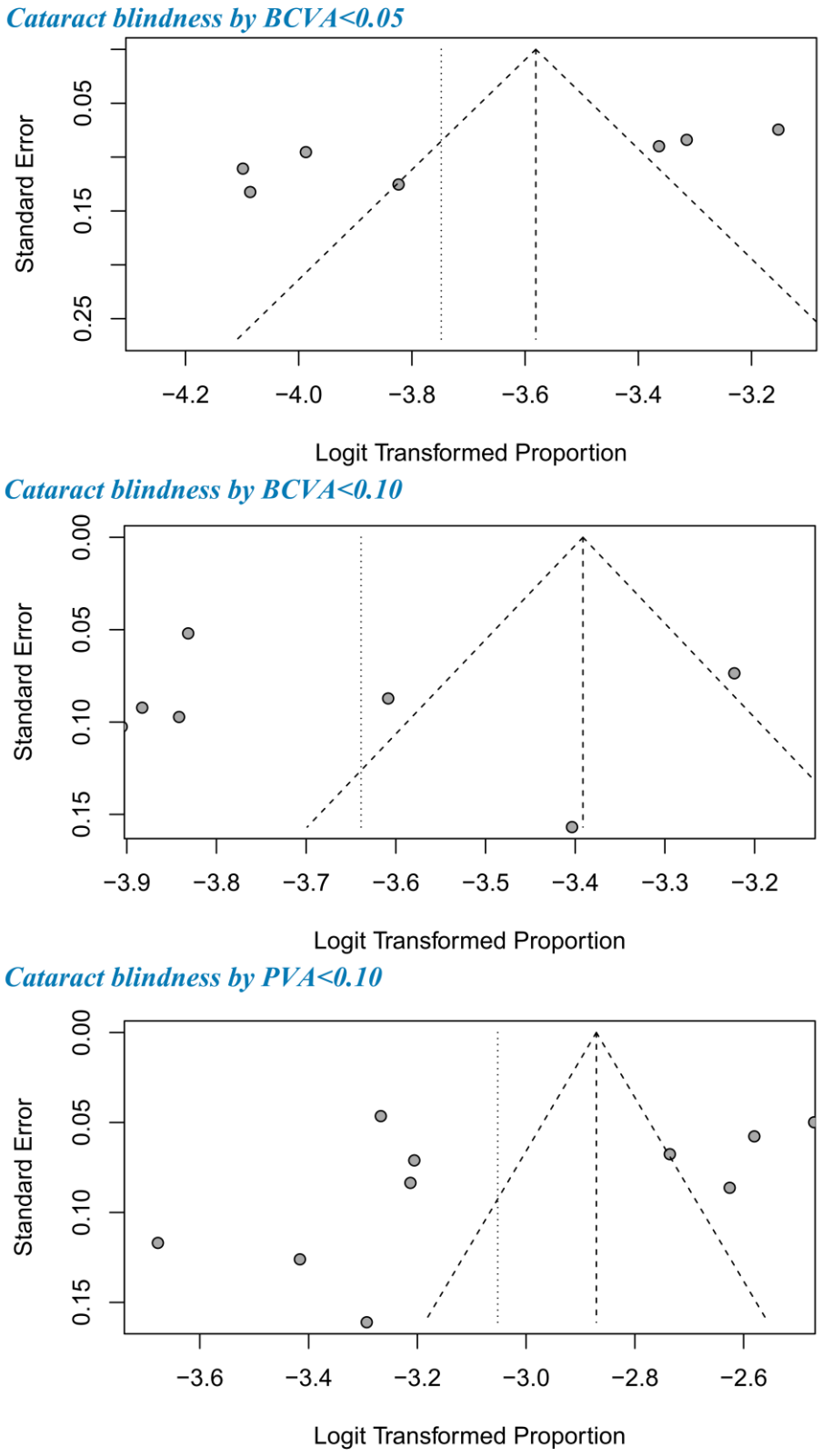


Figure 5.8. Funnel plot for the assessment of publication bias of the studies on the prevalence of cataract blindness in China

5.4.3 National number of people with cataract and cataract blindness from 1990 to 2015

For cataract, the numbers of people with any cataract and ARC were computed by applying the age- and sex-specific prevalence rates to the correspondingly stratified national population aged 45-89 years in the years 1990, 2000, 2010 and 2015 (**Table 5.5** and **Appendix table 26**). At the national level, the prevalence of any cataract in people aged 45-89 years slightly decreased by 1.13%, from 22.21% (95% CI: 18.46-26.42) in 1990 to 21.96% (95% CI: 18.26-26.10) in 2015. During this period, the prevalence of ARC in people 45-89 years of age ranged from 15.65% (95% CI: 8.67-26.06) to 15.53% (95% CI: 8.67-25.71), indicating an overall decreasing rate of 0.79%. Despite the gentle decline in prevalence estimates within this time frame, there was a considerable increase in the national number of people with cataract. In people aged 45-89 years, the number of any cataract cases was 50.75 million (95% CI: 42.17-60.37) in 1990 and 111.74 million (95% CI: 92.94-132.84) in 2015, and that of ARC cases rose from 35.77 million (95% CI: 19.81-59.55) in 1990 to 79.04 million (95% CI: 44.14-130.85) in 2015, which yielded overall increasing rates of 120.19% and of 120.96% respectively throughout this period. In 2015, around 71% of the cataract cases were the age-related subtype, and the age group that contributed the most cases was 60-64 years for both any cataract and ARC (**Figure 5.9**).

Table 5.5. Estimated prevalence and number of people with cataract and cataract blindness in China from 1990 to 2015

Type	Prevalence (%, 95% CI)				Relative rate of change
	1990	2000	2010	2015	(%, 1990-2015)
Any cataract	22.21 (18.46-26.42)	21.62 (17.97-25.72)	21.96 (18.26-26.11)	21.96 (18.26-26.10)	-1.13
ARC	15.65 (8.67-26.06)	15.27 (8.51-25.31)	15.53 (8.67-25.71)	15.53 (8.67-25.71)	-0.79
Cataract blindness (BCVA<0.05)	2.3 (1.72-3.07)				-
Cataract blindness (BCVA<0.10)	2.56 (1.94-3.38)				-
Cataract blindness (PVA<0.10)	4.51 (3.53-5.75)				-
Type	**Number of people with disease (million, 95% CI)**				**Relative rate of change**
	1990	**2000**	**2010**	**2015**	**(%, 1990-2015)**
Any cataract	50.75 (42.17-60.37)	68.33 (56.79-81.29)	94.07 (78.24-111.84)	111.74 (92.94-132.84)	+120.19
ARC	35.77 (19.81-59.55)	48.26 (26.89-79.99)	66.54 (37.15-110.14)	79.04 (44.14-130.85)	+120.96
Cataract blindness (BCVA<0.05)	5.26 (3.93-7.02)	7.27 (5.44-9.70)	9.85 (7.37-13.15)	11.71 (8.75-15.62)	+122.72
Cataract blindness (BCVA<0.10)	5.85 (4.43-7.72)	8.09 (6.13-10.68)	10.97 (8.31-14.48)	13.03 (9.87-17.20)	+122.72
Cataract blindness (PVA<0.10)	10.31 (8.07-13.14)	14.25 (11.16-18.17)	19.32 (15.12-24.63)	22.95 (17.97-29.26)	+122.72

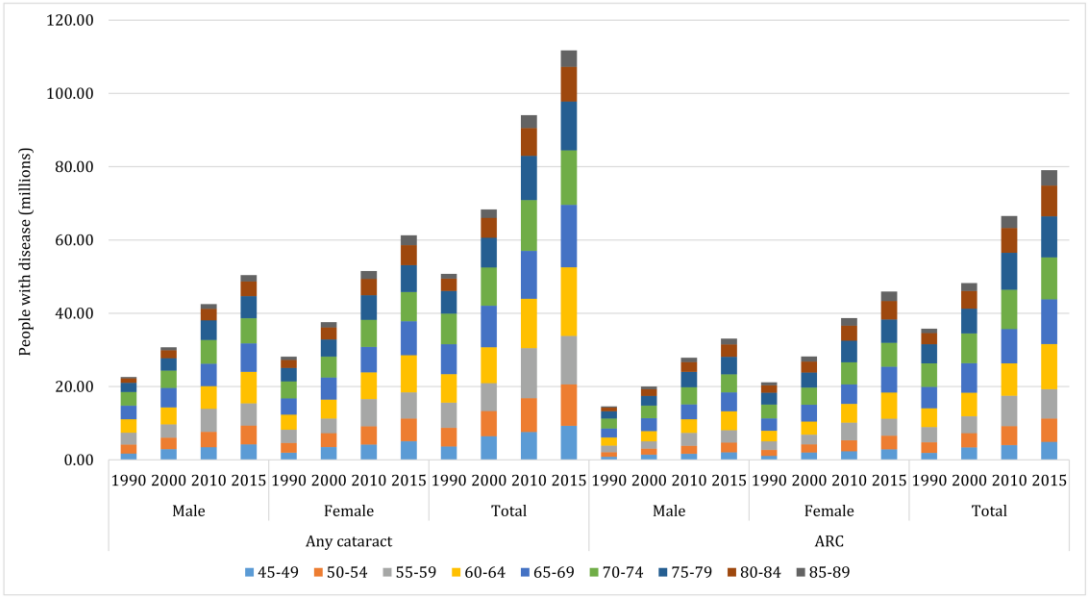


Figure 5.9. Estimated sex-specific number of people with any cataract and ARC in China from 1990 to 2015, with contributing age groups

For cataract blindness, the overall prevalence was assumed to be constant over the period 1990-2015, but even so, an increasing trend in cataract-blind cases was witnessed (**Table 5.5**). From 1990 to 2015, the number of people with cataract blindness by BCVA<0.05 (aged 45-89 years) increased from 5.26 million (95% CI: 3.93-7.02) to 11.71 million (95% CI: 8.75-15.62), and those with cataract by BCVA<0.10 rose from 5.85 million (95% CI: 4.43-7.72) to 13.03 million (95% CI: 9.87-17.20). By using the cut-off of PVA<0.10 for defining blindness, the number of people with cataract blindness (aged 45-89 years) ranged from 10.31 million (95% CI: 8.07-13.14) to 22.95 million (95% CI: 17.97-29.26) within the same time frame.

5.4.4 Projection of national number of people with cataract and cataract blindness from 2020 to 2050

For cataract, the projection of national affected cases from 2020 to 2050 was based on the assumption that the age- and sex-specific prevalence of any cataract and ARC would remain constant over time. By extrapolating the estimated age- and sex-specific prevalence of any cataract and ARC to the UNPD data, the numbers of people with any cataract and ARC were projected up to the year 2050 (**Table 5.6** and **Appendix table 26**). Given the demographic

changes over the next three decades, the prevalence of any cataract in people aged 45-89 years is expected to increase from 22.78% (95% CI: 18.98-27.03) to 33.34% (95% CI: 28.53-38.40), and that of ARC from 16.21% (95% CI: 9.07-26.72) to 25.93% (95% CI: 15.67-38.94) between the years 2020 and 2050, which will indicate increasing rates of 46% and 60% respectively. In people aged 45-89 years, the total number of affected cases is projected to keep increasing, with the number of those with ARC at a higher rate than those with any cataract (100% vs. 83%). In 2020, the total number of people with any cataract (aged 45-89 years) will be 131.92 million (95% CI: 109.91-156.49), and this figure is projected to increase to 240.83 million (95% CI: 206.07-277.35) by the year 2050. Among them, the number of people with ARC is projected to grow relatively rapidly from 93.83 million (95% CI: 52.52-154.69) in 2020 to 187.26 million (95% CI: 113.17-281.23) in 2050. By then, ARC will account for 78% of all cataract cases in China, and the age group where most cases concentrate will be 75-79 years for any cataract and 80-84 years for ARC (**Figure 5.10**).

Table 5.6. Projected prevalence and number of people with cataract and cataract blindness in China from 2020 to 2050

Type	Prevalence (%, 95% CI)				Relative rate of change
	2020	2000	2010	2050	(%, 2020-2050)
Any cataract	22.78 (18.98-27.03)	26.64 (22.40-31.27)	29.33 (24.88-34.12)	33.34 (28.53-38.40)	+46.35
ARC	16.21 (9.07-26.72)	19.53 (11.15-31.32)	22.17 (13.02-34.38)	25.93 (15.67-38.94)	+59.98
Cataract blindness (BCVA<0.05)	2.30 (1.72-3.07)				-
Cataract blindness (BCVA<0.10)	2.56 (1.94-3.38)				-
Cataract blindness (PVA<0.10)	4.51 (3.53-5.75)				-
Type	**Number of people with disease (million, 95% CI)**				**Relative rate of change**
	2020	**2030**	**2040**	**2050**	**(%, 2020-2050)**
Any cataract	131.92 (109.91-156.49)	175.01 (147.16-205.46)	218.41 (185.24-254.01)	240.83 (206.07-277.35)	+82.56
ARC	93.83 (52.52-154.69)	128.33 (73.24-205.78)	165.08 (96.98-255.97)	187.26 (113.17-281.23)	+99.57
Cataract blindness (BCVA<0.05)	13.32 (9.96-17.78)	15.11 (11.30-20.17)	17.12 (12.81-22.86)	16.61 (12.42-22.17)	+24.75
Cataract blindness (BCVA<0.10)	14.82 (11.23-19.57)	16.82 (12.75-22.21)	19.06 (14.44-25.17)	18.49 (14.01-24.41)	+24.75
Cataract blindness (PVA<0.10)	26.11 (20.44-33.29)	29.63 (23.19-37.78)	33.58 (26.28-42.81)	32.58 (25.50-41.53)	+24.75

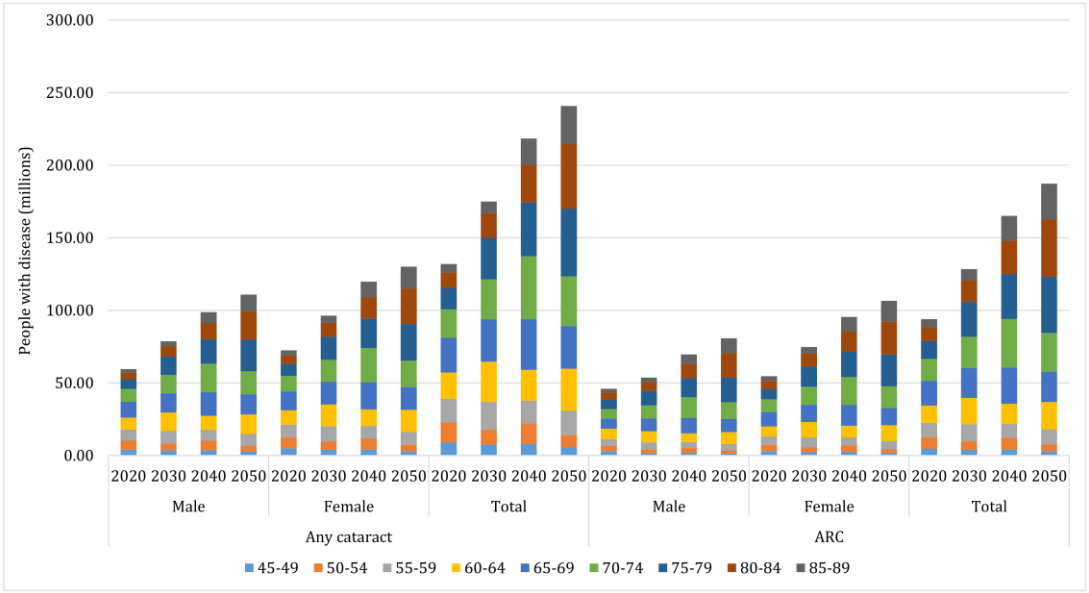


Figure 5.10. Projected sex-specific number of people with any cataract and ARC in China from 2020 to 2050, with contributing age groups

For cataract blindness (**Table 5.6**), the number of people with cataract blindness by BCVA<0.05 (aged 45-89 years) is projected to rise from 13.32 million (95% CI: 9.96-17.78) in 2020 to 16.61 million (95% CI: 12.42-22.17) in 2050, while those with cataract by BCVA<0.10 (aged 45-89 years) from 14.82 million (95% CI: 11.23-19.57) to 18.49 million (95% CI: 14.01-24.41) during this period. When applying a less stringent cut-off of PVA<0.10 for blindness, the number of people with cataract blindness (aged 45-89 years) is expected to grow from 26.11 million (95% CI: 20.44-33.29) in 2020 to 32.58 million (95% CI: 25.50-41.53) in 2050.

5.4.5 Effects of demographic and geographic factors on the prevalence of cataract

Results from the univariable meta-regression analyses revealed that age and sex were significantly associated with the prevalence of both any cataract and ARC, with older people and females having higher prevalence rates. No secular trend or urban-rural difference in the prevalence of any cataract or ARC were revealed (**Table 5.2**). In addition, a weaker association was seen for the geographic distribution of any cataract prevalence, where people living in North China were suggested to be with a relatively lower prevalence than those in East China ($p<0.1$).

For the purpose of constructing a multivariable regression model, insufficient data were available for ARC. Therefore, a multivariable regression model that took the effects of age, sex and geographic region simultaneously was only developed for any cataract:

$$\text{logit}(p) = -6.740 + 0.091 * Age + (-0.242) * Gender_{male} + U_{region} + u_i$$

Where p indicates the prevalence of any cataract; Age refers to the absolute value of age, $Gender_{male}$=1 for males and =0 for females; U_{region} represents the region-level effect, which equals to 0 for East China, -0.269 for North China, 0.486 for Northeast China, -0.075 for Northwest China, 0.636 for South Central China and 0.125 for Southwest China; u_i=variance of the study level random effect.

5.4.6 Regional number of people with any cataract from 2000 to 2010

Based on the final formula for developing the age- and sex-specific prevalence of any cataract in different regions, the national cases of any cataract in the years 2000 and 2010 were respectively allocated into the six geographic regions in China (**Table 5.7**; see **Appendix table 27** for more details). In 2000, the prevalence of any cataract in people aged 45-89 years was 21.62% (95% CI: 17.97-25.72) in China, varying from 15.05% (95% CI: 11.39-19.43) in North China to 28.38% (95% CI: 23.80-32.92) in South Central China. In 2010, the national prevalence of any cataract in people aged 45-89 years rose to 21.96% (95% CI: 18.26-26.11). The region with the highest prevalence of any cataract was still South Central China (28.50% [95% CI: 23.91-33.07]) and that with the lowest prevalence of any cataract was still North China (15.03% [95% CI: 11.39-19.43]). During 2000-2010, the prevalence of any cataract slightly increased by 1.57%, with the most pronounced increase occurring in Southwest China (7.31%). Northeast China was the only region with a declining rate in the prevalence of any cataract (0.11%) during this period.

Table 5.7. Estimated prevalence and number of people with any cataract in China from 2000 to 2010, by geographic region

Region	Prevalence of any cataract (%, 95% CI)		Number of people with any cataract (million, 95% CI)		Relative rate of change (%, 2000-2010)	
	2000	2010	2000	2010	Prevalence	Cases
North China	15.05 (11.39-19.43)	15.03 (11.39-19.43)	5.62 (4.26-7.26)	8.13 (6.16-10.50)	-0.11	+44.53
Northeast China	24.14 (15.86-33.25)	24.57 (16.20-33.80)	6.80 (4.47-9.37)	10.30 (6.79-14.16)	+1.77	+51.34
East China	19.36 (18.85-20.32)	19.53 (19.05-20.49)	18.89 (18.39-19.83)	25.72 (25.09-26.98)	+0.88	+36.17
South Central China	28.38 (23.80-32.92)	28.50 (23.91-33.07)	23.50 (19.70-27.26)	31.79 (26.67-36.88)	+0.41	+35.25
Southwest China	20.24 (14.75-26.47)	21.72 (16.01-28.02)	10.14 (7.39-13.26)	13.28 (9.79-17.13)	+7.31	+30.94
Northwest China	16.83 (12.88-21.51)	17.33 (13.34-22.01)	3.37 (2.58-4.31)	4.87 (3.75-6.18)	+3.00	+44.30
China	21.62 (17.97-25.72)	21.96 (18.26-26.11)	68.33 (56.79-81.29)	94.07 (78.24-111.84)	+1.57	+37.67

As demonstrated in **Table 5.7** and **Figure 5.11**, a total of 68.33 million (95% CI: 56.79-81.29) people aged 45-89 years were affected by any cataract in 2000. Among them, more than one-third (34%) were living in South Central China (23.50 million [95% CI: 19.70-27.26]) and only 5% were in Northwest China (3.37 million [95% CI: 2.58-4.31]). With the demographic ageing trend in China, the national number of people (aged 45-89 years) with any cataract reached to 94.07 million (95% CI: 78.24-111.84) by 2010. At the regional level, the number of people with any cataract was still the largest in South Central China (31.79 million [95% CI: 26.67-36.88]) and the smallest in Northwest China (4.87 million [95% CI: 3.75-6.18])- equivalent to 34% and 5% of the national cases of any cataract in 2010 respectively. Over the decade from 2000 to 2010, the number of people with any cataract increased by 38% at the national level. For the six geographic regions, the most marked increase was seen in Northeast China (51%) and the least in Southwest China (31%). In 2010, the age group that contributed the most cases of any cataract was 55-59 years in North China, Northeast China and South Central China, 65-69 years in Southwest China, and 70-74 years in East China and Northwest China.

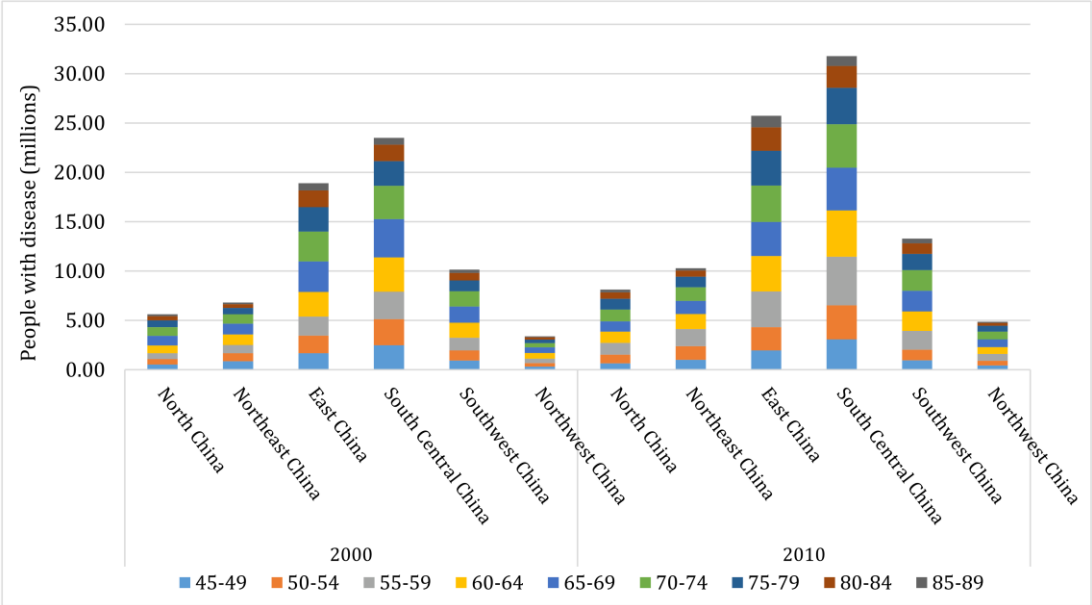


Figure 5.11. Estimated regional number of people with any cataract and contributing age groups in the years 2000 and 2010

5.5 Discussion

5.5.1 Statement of principal findings

By using all published evidence on the prevalence of cataract and cataract blindness in general Chinese population, this systematic review and meta-analysis, for the first time, provides the most comprehensive figures for the prevalence of cataract and cataract blindness in China at both the national and subnational levels. The data-driven estimates show that the number of people affected by cataract and cataract blindness in China is dramatic. From 1990 to 2015, more than one in five (around 22%) people aged 45-89 years were affected by any cataract, representing a total of 50.75 million and 111.74 million cases in the years 1990 and 2015 respectively. Among them, around 71% were with the age-related subtype of cataract. For cataract blindness, the pooled prevalence varied substantially according to different cutoffs for defining blindness, from 2.30% for cataract blindness by BCVA <0.05 to 4.51% for cataract blindness by PVA <0.10. As the Chinese population ages, the prevalence of cataract and the number of affected people will correspondingly increase in years to come. By the year 2050, the national cases of any cataract in people aged 45-89 years are projected to more than double to 240.83 million, giving a prevalence of one-third (33.34%). At that time, ARC will account for 78% of all cataract cases in China. Moreover, substantial geographic variations were also

highlighted in the prevalence of any cataract, which was the highest in South Central China and the lowest in North China during 2000-2010. Meanwhile, in terms of the number of people affected by any cataract, the largest share of cases was in South Central China, while the smallest in Northwest China.

5.5.2 Strengths and limitations

This systematic review and meta-analysis provides the first and most complete description of the prevalence of cataract and cataract blindness in China, which can be used as the basis for the formulation of public-health strategies to ease the burden of cataract and cataract blindness. The strengths of this study include comprehensive and reproducible search strategies incorporated both Chinese and English databases, a dual review process and rigorous selection criteria, which reduced the potential for information bias due to selection and methodological heterogeneity to a minimum. During the systematic review process, only studies that were conducted in general Chinese population were included, thus the generalisability of the whole results presented in this study was largely ensured. With an aim of enhancing the comparability of prevalence estimates from different individual studies, standardised definitions of cataract and cataract blindness based on the available evidence were specified, which made the quantitative synthesis of prevalence rates possible. Moreover, the included studies that reported the prevalence of any cataract were sufficient and with a large geographical diversity, guaranteeing my ability to synthesise the prevalence of any cataract at the subnational level in China.

However, this study is still subject to several potential limitations. First, despite my extensive efforts on minimising variations by means of strict eligibility criteria and unified definitions, meta-analyses of observational studies are generally vulnerable to bias and confounders inherent in the component studies (Egger et al., 1998). Second, in this study, the prevalence of cataract was estimated based on multilevel mixed-effects meta-regression models, by taking the effects of both demographic and geographic features into account. However, the examined demographic and geographic features were cluster-level data, any differences in effects at the individual level might be hidden. Other potential risk factors for cataract, such as economic status, smoking and diabetes, could not be included in the models owing to the absence of relevant information. As a further limitation, the prevalence of cataract could only be estimated at the regional level at best, adequate estimates at the provincial level were not attainable because insufficient studies were from each province in China. For cataract blindness, the roughly pooled estimates of prevalence were based on scant epidemiological evidence, and

the limited availability of data points restricted further exploration of heterogeneity and bias by sub-group meta-analysis or meta-regression, therefore several key differences pertinent to variations in risk factors, such as age and sex, might have been obscured. In terms of the cataract blindness prevalence, the assumption that all cataract-operated eyes were blind preoperatively might lead to an overestimation. Third, although the standardised definitions of cataract and cataract blindness served as a basis for this meta-analysis, on the other hand, cataract was not defined primarily based on any specific grading systems of cataract, but rather according to lens opacity in conjunction with reduced visual acuity. This approach, however, does not accord with modern grading systems, such as the Lens Opacities Classification System (LOCS), the Wisconsin Cataract Grading System (WCGS) and the Age-Related Eye Disease Study (AREDS) system, consequently the comparison of the estimates in this study with studies in other western countries would be difficult (Rochtchina et al., 2003, Congdon et al., 2004, Chylack et al., 1989, Leske et al., 1988, Chylack et al., 1993, Group, 2001, Mitchell et al., 1997). Of particular note, the cataract/cataract blindness cases referred to people who were suffering from cataract/cataract blindness and those who had already been operated. The currently prevalent cases of cataract/cataract blindness were not able to be estimated with this research approach. Therefore, the national and subnational prevalence of cataract and cataract blindness presented in this study could only be compared with studies (both domestic and international) that adopted similar definitions of cataract and cataract blindness, hindering the generalisation of my results to some extent. Fourth, in the projection analysis, the prevalence of cataract and cataract blindness was assumed to remain constant over time. In fact, any changes in risk exposure in the future might increase or decrease the incidence of cataract, and implementation of preventive care might substantially delay the onset of cataract or cataract blindness. The rise of prevalence and number of affected people as indicated in this study mainly relied on the UNPD demographic statistics, and therefore could be argued to be a reflection of population ageing. With the above limitations in mind, several findings in this study should be interpreted with considerable caution.

5.5.3 Interpretation of findings

In a synthesised analysis for estimating the prevalence of cataract in the United States (US), it was estimated that 20.5 million (17.2%) Americans older than 40 years had cataract in either eye in 2000, including those who had pseudophakia/aphakia (Congdon et al., 2004). In this study, a higher cataract prevalence of 22% was observed in Chinese people aged 45-89 years, corresponding to 68 million people living with cataract in the year 2000. The higher prevalence

of cataract in China compared with that in Americans seems to stand by previous statements that cataract is more prevalent in Asians than in Western populations (Vashist et al., 2011, Das et al., 1994, Liu et al., 2017). When compared with studies using comparable measurements of cataract blindness, the prevalence of cataract blindness by PVA<0.10 was noted to be slightly higher in China (4.5%) than in Nepal (4.1%) (Sapkota et al., 2006). Given the large population size in China, this prevalence rate of cataract blindness actually represents a large group of people who need surgery (if they have not received) and extensive care from both household and community (World Health Organization, 2017a, Brian and Taylor, 2001).

As revealed in this study and many previous studies, the prevalence of any cataract and ARC grows dramatically with advanced age and reaches the highest in older people. The prominent role of ageing as a cause of cataract has also been reinforced in this study, with increased age being the constant risk factor for both any cataract and ARC (Liu et al., 2017, Asbell et al., 2005, Michael and Bron, 2011, Abraham et al., 2006, McCarty et al., 1999, Vashist et al., 2011). After age-adjustment, females were found to exhibit a greater tendency to develop cataract and ARC than males, which accords with a large body of evidence across racial groups (Abraham et al., 2006, McCarty et al., 1999, Vashist et al., 2011, Liu et al., 2017). Although the mechanism behind sex disparity in cataract formation has not been fully clarified, the protective effect of hormone therapy in cataract development as suggested in previous studies offers a clue for future research (Asbell et al., 2005, Lai et al., 2013, Zetterberg and Celojevic, 2015). Taken the effects of ageing population and women's greater longevity together, the numbers of people living with any cataract and ARC in China will both more than double from 2015 to 2050 based on my projection analysis. Cataract, therefore, will continue to be a leading public health concern and pose wide-ranging effects on its social, economic and health systems.

In view of the geographic patterns of cataract in China, the variations in the prevalence of cataract in different geographic regions could be speculated as a combined result of different distributions of risk factors across the whole country. It has long been suggested that cataractogenesis is a multifactorial process, where individual factors, environmental factors and genetic factors all play a role (Asbell et al., 2005, Liu et al., 2017). Risk factors with robust evidence on cataract mainly include advanced age, female sex, smoking, excessive ultraviolet B (UVB) exposure, diabetes, etc. (Ye et al., 2012, Kelly et al., 2005, Liu et al., 2017, Asbell et al., 2005, Robman and Taylor, 2005). As revealed by my analysis, the geographic region with the highest prevalence of cataract was South Central China in the years of 2000 and 2010. A possible reason is the relatively lower latitude (as a surrogate for a higher UVB exposure level) in south China, but it is still not absolutely clear whether any other factors have

contributed to this because relevant information was not universally examined in included studies.

With rapidly ageing populations in China, the question of how best to care for older people with functional impairment is an ever-present concern (World Health Organization, 2017a, Brian and Taylor, 2001, Woo et al., 2002). The large cases of cataract and cataract blindness, and the uneven distribution across the nation, suggest that efforts to ameliorate the current and future burden of cataract are urgently needed. In China, the cataract surgical rate (cataract operations per million population per year) has been reported to be 446 in 2004, which was almost the lowest among Asian countries (World Health Organization, 2017a, Shen et al., 2013, China Disabled Person's Federation (CDPF), 2005). This might be resulted by the shortage of qualified eye care practitioners and health resources, in the meanwhile, the uncertain prognosis might also hider affected people to approach such operations (He et al., 2007, World Health Organization, 2017a, Fang et al., 2010). The estimates presented in this study should be interpreted with the most recent cataract surgical rate in China (if available) to better inform policymakers and healthcare providers for adequate preparation for the increasing burden of cataract.

5.5.4 Implications for policy, practice and future research

Our data also have important implications for adding new evidence into research. In the past decades, despite the advance in diagnostic and surgical techniques, uncertainties and discrepancy in the definitions and assessments of cataract still largely remain in epidemiological studies (Asbell et al., 2005, Liu et al., 2017). Until improved large-scale data using comparable definitions and assessments of cataract become available, the systematic review and meta-analysis approach will still be an important option for providing inputs by synthesising available evidence. This is also the case in China, where improvement in the quality of population-level information on the prevalence of cataract should be a priority for the national statistical agency, notably detailed age categories, classification of different subtypes of cataract, international grading systems, should be adopted as are often the cases. With the emergence of high-quality epidemiological studies on cataract in the foreseen future, reliable prevalence estimates of cataract, and its subtypes could be well achieved. Further, although no confirmed methods to prevent cataract formation are being advocated, well-established risk and protective factors demonstrate possible pathways for slowing cataract

progression, such as smoking cessation, wearing hats and sunglasses (Liu et al., 2017, Asbell et al., 2005). Given the impact of cataract, the need for further research on preventing and delaying disease is still highlighted.

5.6 Conclusions

In conclusion, the first and most comprehensive estimates of the prevalence of cataract and cataract blindness in China were provided in this study, at both the national and subnational levels. The prevalence of cataract varied considerably among different demographic and geographic groups. In the coming decades, cataract and cataract blindness will continue to be a leading public-health issue in China. Future work should be prioritised on the promotion of high-quality epidemiological studies on cataract.

Chapter 6 The national and subnational prevalence and burden of diabetic retinopathy in China

6.1 Summary

The study approach in this chapter is greatly different from those in Chapters 3-5, which included both secondary data analysis (systematic review and meta-analysis) and primary data analysis. For developing the overall prevalence of DR in both the general population and people with DM, a systematic review and meta-analysis was first conducted. Given the disease course of DR, age- and DM duration-specific prevalence of DR was further generated by using sub-group meta-analysis. To develop the national number of DR cases, the number of DM patients should be provided as the basis. For this purpose, the 2011 national baseline survey of China Health and Retirement Longitudinal Study, a nationally representative survey of Chinese people aged 45 years and older, was used to calculate the national prevalence of DM for the year 2010. After developing the national envelope of DR (national DR cases) in 2010, the regional number of DR cases was generated by the "risk-factor based model", as described in Chapter 2. The risk factors that were taken into the regional distribution model included rural setting, insulin treatment, elevated FBG level and higher HbA1c concentration.

The work presented in this chapter has been published in the Journal of Global Health cited as "Song, P., Yu, J., Chan, K. Y., Theodoratou, E., & Rudan, I. (2018). Prevalence, risk factors and burden of diabetic retinopathy in China: a systematic review and meta-analysis. Journal of Global Health, 8(1), 010803. http://doi.org/10.7189/jogh.08.010803.

I was involved in the whole process of this project, including study conceptualisation and design, development of search strategy, systematic review, data extraction, data analysis and interpretation of findings. I prepared the first draft of manuscript for publication, which has been subsequently revised according to the comments from anonymous peer reviewers and journal editors during the publishing process. The specific contributions of co-authors are as follows: Rudan, I. conceptualised and designed the study, Yu, J. conducted the dual systematic review and data extraction, Chan, K. Y., Theodoratou, E., and Rudan, I. critically reviewed the manuscript and approved the final manuscript.

6.2 Background

Diabetic retinopathy (DR), the primary retinal vascular complication of diabetes mellitus (DM), is a leading cause of vision impairment and blindness in the working-age population (Cheung et al., 2010, Yau et al., 2012, Frank, 2004, Kempen et al., 2004). In the early course of the disease, DR is generally asymptomatic. If left untreated, DR can seriously impair vision, and eventually progress to blindness (Frank, 2004, Cheung et al., 2010). Apart from its devastating visual effects that might lead to reduced mobility, depression and lower quality of life, DR is also associated with a higher risk of systemic vascular complications, imposing a noteworthy burden on individuals, households, communities and societies (Saaddine et al., 2008, Mazhar et al., 2011, Sharma et al., 2005). DR is a progressive disease that can be broadly divided into two stages according to its severity: nonproliferative and proliferative. Nonproliferative DR (NPDR) is characterised by microaneurysms, cotton-wool spots, intraretinal microvascular abnormalities, hard exudates and venous beading, whereas proliferative DR (PDR) is hallmarked by neovascularization of the optic disc or elsewhere, pre-retinal and vitreous haemorrhage (Wu et al., 2013, Cheung et al., 2010). Taken individually, PDR is less common but more sight-threatening than NPDR (Cheung et al., 2010, Frank, 2004, Yau et al., 2012, Sivaprasad et al., 2012, Wu et al., 2013).

Although available diagnostic and therapeutic advancements, such as optimum management of DM and early detection of DR, can substantially reduce the risk of visual deterioration, DR remains an important cause of visual impairment and blindness globally (Early Treatment Diabetic Retinopathy Study Research Group, 1991a, Group, 1981, Wilkinson et al., 2003, Leasher et al., 2016, Pascolini and Mariotti, 2011, Klein, 2007, Mohamed et al., 2007). In 2010, 3.7 million people were visually impaired and 0.8 million were blind because of DR, accounting for 1.9% of all visually impaired cases and 2.6% of all blind cases worldwide (Leasher et al., 2016). With DM having reached epidemic proportions worldwide, estimating the prevalence of DR in both the general population and those with DM is imperative for driving better health policy making and improved programming (Klein, 2007, Leasher et al., 2016). By pooling data from 35 population-based studies across the world, the Global DR Study estimated that the prevalence of any DR, PDR and vision-threatening DR (severe retinopathy and macular oedema) were 34.6 %, 7.0 % and 10.2 % respectively among individuals with DM, translating to approximately 93 million people with any DR, 17 million with PDR and 28 million with vision-threatening DR worldwide in 2010 (Yau et al., 2012). Unless substantial improvements occur in the prevention and treatment of DR, the prevalence

and burden of DR will continue to escalate as the global population ages and the epidemic of DM expands (Zheng et al., 2012, Shaw et al., 2010, Guariguata et al., 2014). In addition, evaluation of risk factors for DR is of special importance in optimal clinical management. Similar to other common complications of DM, DR is a sentinel indicator of the progression of DM, thus its prevalence, not surprisingly, associated with the duration and severity of DM (Kempen et al., 2004, Yau et al., 2012, Williams et al., 2004). In the Global DR Study, longer DM duration has been recognised as a key risk factor for DR in people with DM, as well as higher levels of haemoglobin A1c (HbA1c) and blood pressure. Moreover, individuals with type 1 DM (T1DM) are more likely to develop DR than those with type 2 DM (T2DM) (Kempen et al., 2004, Yau et al., 2012).

Despite mounting concerns about the emergence of DM as a major public health problem in the largest developing country, China, epidemiological data on DR in Chinese population are still rather scarce or inconsistent (Wong et al., 2006a, Sivaprasad et al., 2012, Liu et al., 2012, Xu et al., 2013). Thus far, there is still no national population-based data on the prevalence and burden of DR in China, and the existing surveys on DR are restricted to local characteristics, study methodologies, ascertainment and classification of DR, limiting direct comparisons between individual studies (Liu et al., 2012). A systematic review and meta-analysis by Liu and colleagues, dating back to 2012, has provided the first overview of the DR prevalence in China. Based on 19 individual studies, their meta-analysis suggested that the pooled prevalence rates of any DR, NPDR and PDR in general Chinese population were 1.3%, 1.1%, and 0.1% and those in people with DM were 23.0%, 19.1%, and 2.8% respectively (Liu et al., 2012). Thereafter, a growing body of epidemiological data on DR has become available in China, yet virtually none of them has been systematically appraised, underscoring the need for an updated analysis (Xia et al., 2008, Fung, 2008). Moreover, the effects of major risk factors for DR are still discrepant and inconclusive among the Chinese population, which need to be systematically evaluated in an evidence-based fashion.

To fill the gaps outlined above, I conducted a comprehensive systematic review, in both Chinese and English databases, to retrieve studies that reported the epidemiology of DR in China from 1990 onwards. Based on the existing evidence, I aimed to: (1) pool the overall prevalence of DR in both general Chinese population and people with DM; (2) estimate the effects of demographic and geographic variables on the prevalence of DR in people with DM; (3) assess the major risk factors for DR in people with DM; and (4) quantify the national and subnational burden of DR in 2010.

6.3 Methods

6.3.1 Systematic review

This systematic review and meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement (Moher et al., 2009, Stevens et al., 2016).

6.3.1.1 Search strategy

Three Chinese and three English electronic bibliographic databases, namely China National Knowledge Infrastructure (CNKI), Wanfang, Chinese Biomedicine Literature Database (CBM-SinoMed), PubMed, Embase, and Medline, were searched to locate all relevant publications that reported the epidemiology of DR in China. My comprehensive search strategies combined terms of diabetic retinopathy, epidemiology (incidence, prevalence, morbidity, mortality, epidemiology) and China (China, Chinese, Hong Kong, Macau, Taiwan) using both controlled vocabularies (e.g. Medical Subject Heading terms) and free text words. Search queries were optimised to fit the specific features of each database, and the full search strategies are detailed in **Appendix table 28**. To supplement the electronic database search, reference lists of eligible publications and related reviews were also scanned to identify other potentially pertinent studies. The literature search was limited to studies published between January 1990 and December 2017. No language restrictions were imposed on searches or search results.

6.3.1.2 Inclusion and exclusion criteria

To be included in the systematic review and meta-analysis, studies had to be population-based and reported the prevalence of DR or risk factors for DR. Depending on how the study population was sought, the identified population-based studies can be classified into three categories: community-based, primary health care management (PHCM)-based and registry-based. Community-based studies derived their study sample from the general population (e.g. cluster sampling of households), whereas PHCM-based and registry-based studies derived their study sample from all the primary care settings or primary care systems in a defined geographical area. Thus, both PHCM-based and registry-based studies attempted to capture

all, or at least a random sample, of people with DM in a defined geographical area. For the purpose of pooling prevalence rates of DR, the included studies must be community-based, and of particular note, include both newly detected and physician-diagnosed DM cases simultaneously (to avoid overestimation); To assess the risk factors for DR in people with DM, the included studies could be community-based, PHCM-based or registry-based, where DM cases could be either newly detected or physician-diagnosed, or both. To avoid suspected bias inherent to univariate analysis, the estimation of odds ratios (ORs) in studies that reported the risk factors for DR must be based on a multivariate study design.

Studies that were conducted in the T1DM group were excluded, whereas those focused on people with T2DM were retained. Studies that contained both T1DM and T2DM cases were not excluded if the proportion of people with T1DM was small (<10%). For studies where the type of DM was not specified but all other criteria were fulfilled, it was assumed that those studies contained both T2DM cases and a small proportion of T1DM cases. Otherwise, the type of DM could be speculated by the age at diagnosis of DM (if available), where people diagnosed before 30 years were deemed as with T1DM and those after 30 years were T2DM (Klein et al., 1984b, Yau et al., 2012). To be eligible for inclusion, studies must have undertaken fundus photography (FP) to ascertain DR and provided numerical estimates of DR prevalence. Reviews, commentaries and studies where the prevalence rates were calculated based on the number of eyes with DR rather than the number of affected individuals were excluded.

6.3.1.3 Study selection and data extraction

After deleting duplicate records within and between different bibliographic databases, the remaining titles and abstracts were reviewed to identify potentially eligible articles that required a full appraisal. In cases of multiple publications from the same study or overlapping data, preference was given to the most recent one or the one with the most inclusive information. Consensus was achieved for any discrepancies in study eligibility through discussion. For each included study, the quality was assessed from five aspects: sample population, sample size, participation rate, outcome assessment, and analytical methods. Each of the five components could be scored as 2 for low risk, 1 for moderate risk and 0 for high risk and unclear. The total score of those five components represented the overall quality of each study (**Table 2.1**) (Von Elm et al., 2007, Song et al., 2018).

With a predefined data-collection form, the following information was extracted from the included studies, where possible:

1) Characteristics of the study: author(s), publication year, study year, study type (community-based, PHCM-based or registry-based), sampling method, study design (cross-sectional or cohort), study setting (urban, rural or mixed) and location, geographic region, DR assessment method and grading system;
2) Characteristics of the sample (general population and people with DM): number of the sample, age (age range, mean or median age), sex (male, female or mixed), DM definition, DM classification (T1DM or T2DM, newly detected or physician-diagnosed), and duration of DM;
3) Prevalence data: the number of people with DR and the number of participants who had been tested for DR, by age, DM duration, sex, setting and DR subtype;
4) Risk factor data: definition of risk factor, OR and corresponding confidence intervals (CIs).

According to the definitions from National Bureau of Statistics of China, the geographic regions where the studies were carried out were classified into six categories: East China, North China, Northeast China, Northwest China, South Central China, and Southwest China (see **Table 2.2** and **Figure 2.2**) (National Bureau of Statistics, 2002, National Bureau of Statistics, 2012). Missing values for the median year of study were imputed by subtracting three years (the average time-lag from investigation to publication in studies with available data, see **Appendix table 29**) from their publication years, and this was done for six individual studies. In this study, I further classified DR as NPDR and PDR. Therefore, relevant data were extracted from the included studies for different subtypes of DR respectively, wherever available.

6.3.2 Statistical analysis

6.3.2.1 Pooling prevalence of DR in China

The crude prevalence of DR was firstly computed for each study and then double-arcsine transformed by using the Freeman-Tukey method (Freeman and Tukey, 1950, Barendregt et al., 2013, Nyaga et al., 2014). Heterogeneity among eligible studies was assessed with the Cochran's Q statistic and I^2 index (the proportion of total variability due to true between-study heterogeneity beyond chance) (Higgins et al., 2003, Higgins and Thompson, 2002). A p-value

of less than 0.1 showed the presence of heterogeneity, and I^2 values of less than 25% corresponded to mild heterogeneity, of from 25% to 50% reflected moderate heterogeneity, and of greater than 50% represented high heterogeneity, respectively (Higgins et al., 2003, Higgins and Thompson, 2002, Higgins and Green, 2008). Because of the substantial heterogeneity noted between individual studies, a random-effects (DerSimonian and Laird method) meta-analysis was used to adjust for variability and pool the study-specific prevalence rates (Barendregt et al., 2013, Higgins and Green, 2008). For each meta-analysis, a leave-one-out sensitivity analysis was developed to assess the robustness of the pooled results. By removing one study at a time to run the meta-analysis without it, the sensitivity analysis could test whether single studies had disproportionally excessive influence on the pooled results (Wallace et al., 2009). Publication bias was checked by visual inspection of funnel plots, and tested for significance with Egger's regression test for funnel plot asymmetry and Begg's rank correlation test (Egger et al., 1997, Begg and Mazumdar, 1994, Peters et al., 2006). The prevalence rates of any DR, NPDR and PDR in both the general population and people with DM were pooled with this approach respectively.

6.3.2.2 Subgroup meta-analysis and meta-regression of DR prevalence in people with DM

For the prevalence of any DR in people with DM, potential sources of heterogeneity were investigated using subgroup meta-analysis and meta-regression. In subgroup meta-analysis, the prevalence of any DR was estimated for different age groups and DM duration groups. This was done because age- and DM duration-specific prevalence of any DR in people with DM was universally provided by the included studies. Moreover, the individual associations between prevalence of any DR and study-level variables were evaluated by univariable meta-regression using the unrestricted maximum likelihood method. The prespecified variables included sex (male vs. female), setting (urban, rural and mixed), geographic region and study year. Because only a few variables were individually significant, a multivariable meta-regression was not subsequently performed.

6.3.2.3 Meta-analysis of risk factors for DR in people with DM

To investigate the risk factors for any DR in people with DM, a random-effects meta-analysis was employed a priori because of anticipated variation in study populations, geography and study design. As a rule, I only included risk factors that were investigated in at least three studies using multivariate design, and the definitions of the same risk factor should be similar

across all included studies. Finally, 11 factors (advanced age, male sex, DM duration, insulin treatment, fasting blood glucose [FBG], 2-hour postprandial blood glucose [2h-PBG], glycated HbA1c, total cholesterol [TC], triglyceride [TG], body mass index [BMI], systolic blood pressure [SBP]) met the pre-set criteria and were included in meta-analysis.

6.3.2.4 Estimation of national and subnational burden of DR in 2010

At the final stage, the national number of cases with any DR ("any DR envelope") was estimated by multiplying the age-specific prevalence of any DR in people with DM with the corresponding number of people with DM in China. For this purpose, the 2011 national baseline survey of China Health and Retirement Longitudinal Study (CHARLS) was used to provide prevalence estimates of DM in China for the year 2010. CHARLS is a nationally representative survey of Chinese people aged 45 years and older. In CHARLS, samples were drawn by using a four-stage, stratified, cluster sampling procedure: First, all counties in 28 provinces of China (except Tibet province, Hainan province and Ningxia Hui Autonomous Region) were stratified by geographic region, setting (urban and rural) and economic level (per capita statistics on the gross domestic product). Among them, 150 counties were randomly chosen by a probability-proportional-to-size (PPS) sampling technique (**Figure 6.1**). Second, three primary sampling units (PSU, communities in urban areas or administrative villages in rural areas) were randomly selected from each of those 150 counties. Third, all the dwellings within the 450 chosen PSU were outlined on Google Earth maps using the specifically designed "CHARLS-GIS" software, among which at least 24 households were randomly selected. Fourth, in the selected households, if there were more than one member aged 45 years, one such member was randomly selected, and his/her spouse was also interviewed.

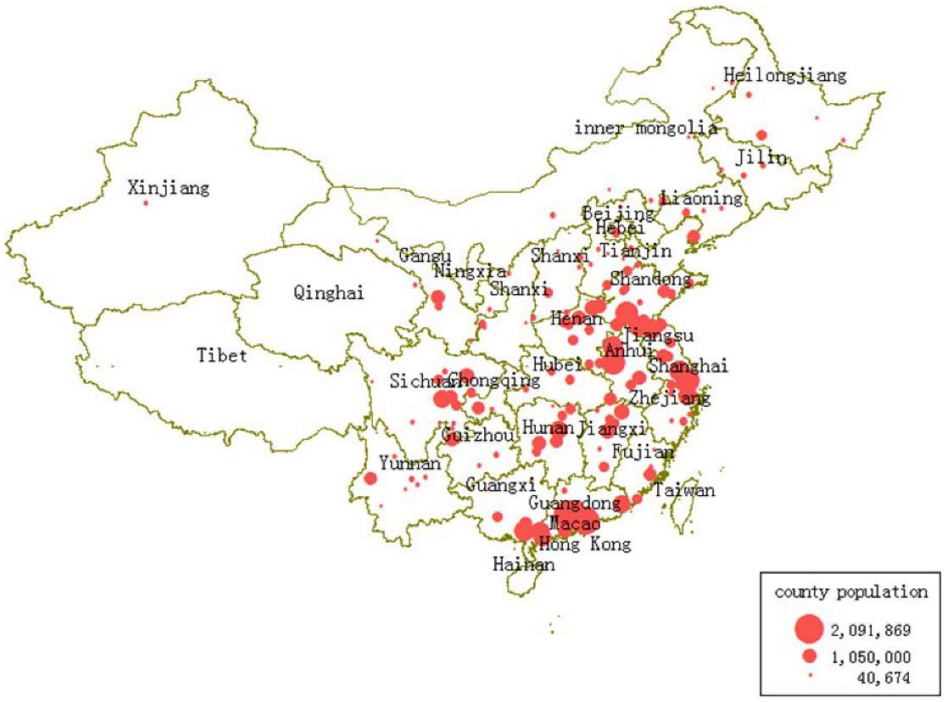


Figure 6.1. Geographic distribution of the sampled counties in CHARLS 2011 (source: (Zhao et al., 2013))

The study design and implement of CHARLS have been previously published and detailed (Zhao et al., 2013, Zhao et al., 2012). Overall, the household response rate was 80.5%, and 17,708 individual participants in 10,257 households successfully completed at least one module of the survey. In the household interview, the participants' information on demographics (i.e. age, sex, residence), socioeconomic status (i.e. educational attainment, marital status, income and expenditure), medical history and health-related behaviours (i.e. smoking, drinking) was collected by a structured questionnaire. Among all participants, 13978 (78.9%) took part in anthropometric and physical-performance module and 11847 (66.9%) provided venous blood samples (8ml each individual). DM was defined as a self-reported physician-diagnosed diabetes, or a fasting blood glucose (FBG) $\geqslant$126 mg/dl, or a random blood glucose $\geqslant$200 mg/dl, or a HbA1c concentration of 6.5% or above, or currently taking antidiabetic medications. People who had already been diagnosed with DM or were taking antidiabetic medications were classified as the diagnosed DM phenotype, and those who were not with diagnosed DM before the investigation but had an FBG $\geqslant$126 mg/dl, or a random blood glucose $\geqslant$200 mg/dl, or a HbA1c concentration of 6.5% or above were classified as the newly detected DM phenotype. All calculations in CHARLS 2011 took into account the complex survey design and adopted the blood weight with household and individual response

adjustment. The weighted mean FBG, mean HbA1c and prevalence of DM were stratified by age, sex, setting and geographic region. The flow diagram for selecting subjects in DM prevalence analysis is shown in **Figure 6.2**.

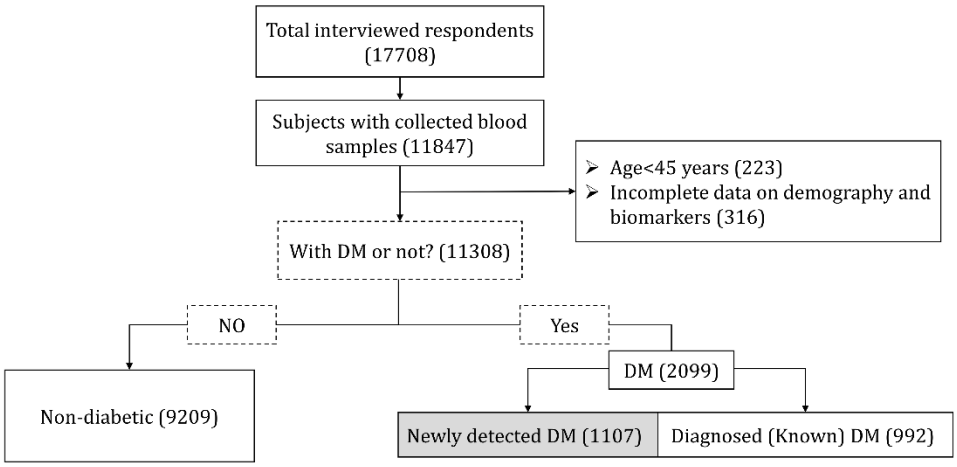


Figure 6.2. Flow chart for subjects included in the analysis of DM prevalence

The number of people with DM was estimated with the prevalence of DM and the corresponding population size, available from the United Nations Population Division (UNPD) (United Nations, 2015b). Then the national number of people with any DR ("any DR envelope") was distributed into six geographical regions in China (East China, North China, Northeast China, Northwest China, South Central China, Southwest China, see **Table 2.2** and **Figure 2.2** for more details) by taking the effects of major risk factors on the prevalence of any DR in those regions (Fowkes et al., 2013, Rudan et al., 2004). Four statistically significant risk factors (advanced age, rural setting, elevated FBG level and higher HbA1c concentration) were chosen because they were all objective indicators. DM duration and insulin treatment, although being significantly associated with the prevalence of any DR, were not selected because they were highly subject to the diagnosis and treatment of DM, socioeconomic circumstances or geography, and therefore might introduce bias in my estimation of DR burden at the subnational level.

The overall study design is shown in **Figure 6.3**. A two-sided p-value of less than 0.05 indicated statistical significance except for the Q statistics, in which a significance level of less than 0.1 was specified. All statistical analyses were done with R version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria) and STATA version 14.0 (STATA Corporation, College Station, TX, USA). All maps were drawn by ArcMap version 10.1 (Environmental

Systems Research Institute, Redlands, CA) using the China base map obtained from the Global Administrative Areas (GADM) database (GADM, 2015, version 2.0; www.gadm.org).

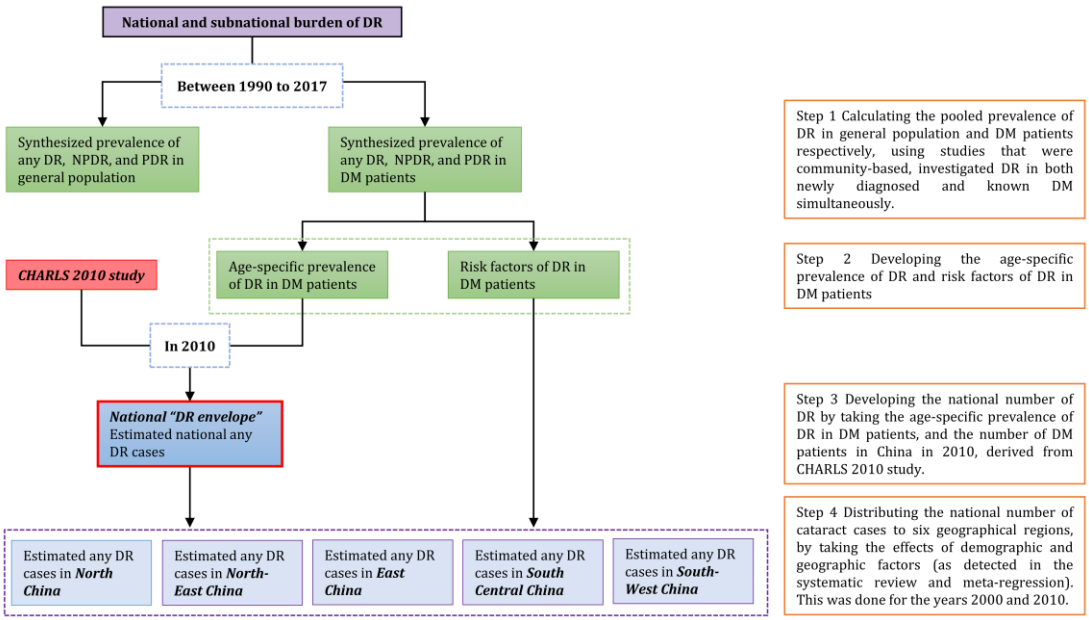


Figure 6.3. Overall study design flowchart for the prevalence, risk factor and burden of DR study in China

6.4 Results

6.4.1 Summary of systematic review

The initial search strategy yielded 9982 records. After removal of 4644 duplicates, a total of 5338 records were reviewed for relevance by titles and abstracts, of which 1147 were assessed in full-text form. Finally, 41 articles met eligibility criteria and were included in the systematic review. Of these, 31 studies provided information on the prevalence of DR and 21 explored potential risk factors for DR. The process of study selection is summarised in **Figure 6.4** according to the PRISMA guidelines. A full list of the included studies is shown in **Appendix table 30**.

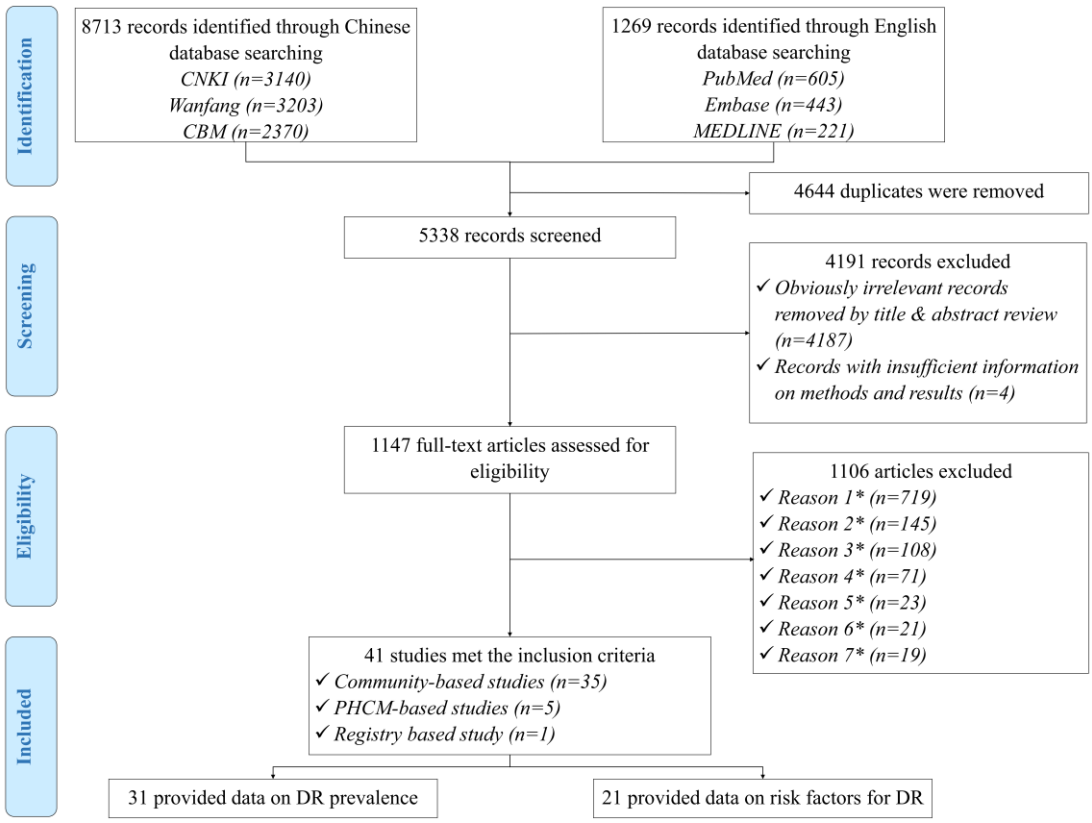


Figure 6.4. Systematic review flow diagram of studies on the prevalence of and risk factors for DR in China

*Note: PHCM, Primary Health Care Management; *Reason 1-Studies that were not community-based, PHCM-based or registry-based; *Reason 2-Articles with no numerical measure of DR prevalence or didn't report risk factor for DR in people with DM; *Reason 3-Studies with no clear assessment methods or grading systems of DR; *Reason 4-Studies that were specifically conducted in people with unrepresentative characteristics (hypertensive patients, people with reduced vision, etc.); *Reason 5-Studies that didn't include both newly detected and diagnosed DM cases; *Reason 6-Multiple publications of the same study; *Reason 7-Studies that were not based in China.*

All included studies were cross-sectional in design and assessed DR by using FP. **Table 6.1** summarises the main characteristics of all included studies, and **Appendix table 31** lists the detailed characteristics of every study. The quality assessments of the included studies are in **Appendix table 32**. For the 31 studies that reported the prevalence of DR and the 21 studies on risk factors for DR, the majority were published after 2010, implying the necessity for an updated analysis of the epidemiology of DR in China. The studies on the prevalence of DR were all community-based investigations, covering all the six geographic regions across China

(see **Figure 6.5**). For those on risk factors for DR, more than half were community-based (71%, n=15), whereas more than one third were conducted in East China (38%, n=8). There were no studies from Northwest China on which to base estimates of risk factors for DR (see **Figure 6.5**).

Table 6.1. Main characteristics of the included studies on the prevalence of and risk factors for DR in China

Characteristic		Number of studies (%)	
		Studies on DR prevalence (n=31)	Studies on risk factors for DR (n=21)
Year published			
	1990-1999	4 (12.9)	1 (4.8)
	2000-2009	7 (22.6)	5 (23.8)
	2010-2017	20 (64.5)	15 (71.4)
Study design			
	Community-based	31 (100.0)	15 (71.4)
	PHCM-based	0 (0.0)	5 (23.8)
	Registry-based	0 (0.0)	1 (4.8)
Setting			
	Urban	12 (38.7)	15 (71.4)
	Rural	7 (22.6)	3 (14.3)
	Mixed	12 (38.7)	3 (14.3)
Sex			
	Mixed	13 (41.9)	3 (14.3)
	Both	18 (58.1)	18 (85.7)
Sample size of DM			
	≤200	6 (19.4)	2 (9.5)
	201-500	12 (38.7)	5 (23.8)
	501–1000	9 (29.0)	6 (28.6)
	>1000	4 (12.9)	8 (38.1)
Grading system			
	ICDRDSS	12 (38.7)	11 (52.4)
	ETDRS	6 (19.4)	7 (33.3)
	NOFDG	3 (9.7)	1 (4.8)
	NCOFD	9 (29.0)	2 (9.5)

Characteristic	Number of studies (%)	
	Studies on DR prevalence (n=31)	**Studies on risk factors for DR (n=21)**
CBM	1 (3.2)	0 (0.0)
Geographic regions		
North China	11 (35.5)	7 (33.3)
Northeast China	5 (16.1)	3 (14.3)
East China	5 (16.1)	8 (38.1)
South Central China	4 (12.9)	2 (9.5)
Southwest China	1 (3.2)	1 (4.8)
Northwest China	5 (16.1)	0 (0.0)
Quality score		
10	3 (9.7)	1 (4.8)
9	7 (22.6)	7 (33.3)
8	8 (25.8)	4 (19.0)
7	8 (25.8)	6 (28.6)
6	5 (16.1)	3 (14.3)

Note: 11 studies reported both prevalence of DR and risk factors for DR, therefore the sum of the number of studies exceeded 41. PHCM, Primary Health Care Management; ICDRDSS, International Clinical Diabetic Retinopathy Disease Severity Scale; ETDRS, Early Treatment of Diabetic Retinopathy Study; NOFDG, National Ocular Fundus Diseases Group; NCOFD, National Conference on Ocular Fundus Diseases; CBM, China Medical Board.

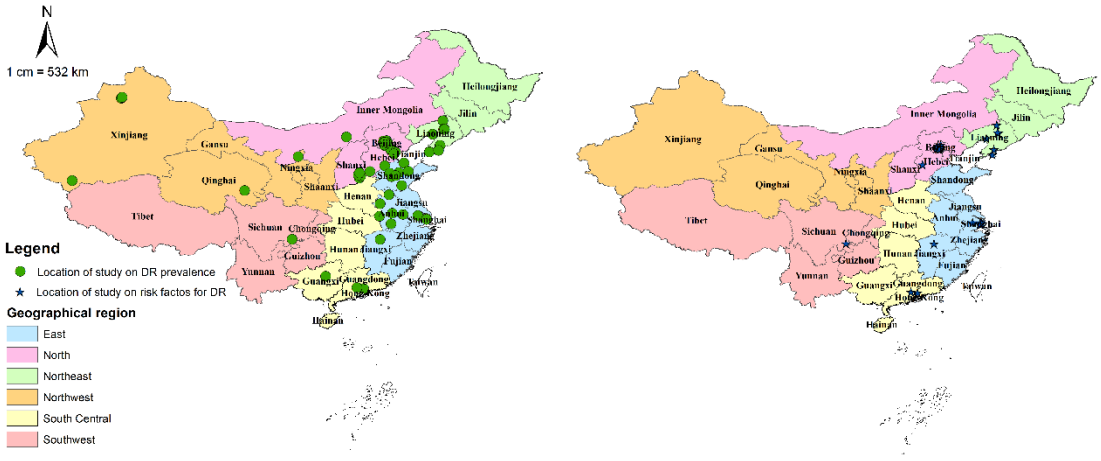


Figure 6.5. Geographical distribution of included studies on prevalence of and risk factors for DR in China

6.4.2 Pooled prevalence of DR in China during 1990 and 2017

By using random-effects meta-analysis, the pooled prevalence of any DR in general Chinese population was 1.14% (95% CI: 0.80-1.52), and that in people with DM was 18.45% (95% CI:14.77-22.43) (**Figure 6.6**). According to the leave-one-out sensitivity analysis (**Figure 6.7**), the pooled prevalence of any DR in general population varied from 1.08% (95% CI: 0.76-1.46) to 1.19% (95% CI: 0.86-1.58), and that in people with DM ranged from 17.67% (95% CI: 14.12-21.53) to 19.01% (95% CI: 15.38-22.94), no single study significantly influenced the overall pooled prevalence in the meta-analysis. No publication bias was evident based on the visual evaluation of the funnel plot, Egger's test and Begg's test (**Figure 6.8**).

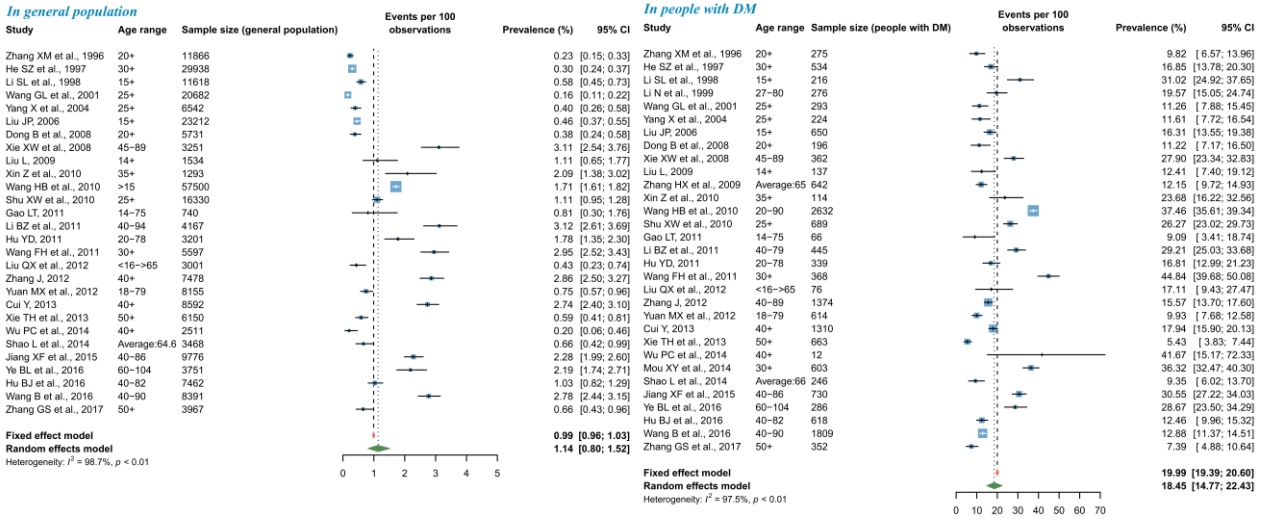


Figure 6.6. Pooled prevalence of any DR in general population and in people with DM by random-effects meta-analysis

Note: There were 28 studies for synthesising the prevalence of any DR in general population and 31 in people with DM.

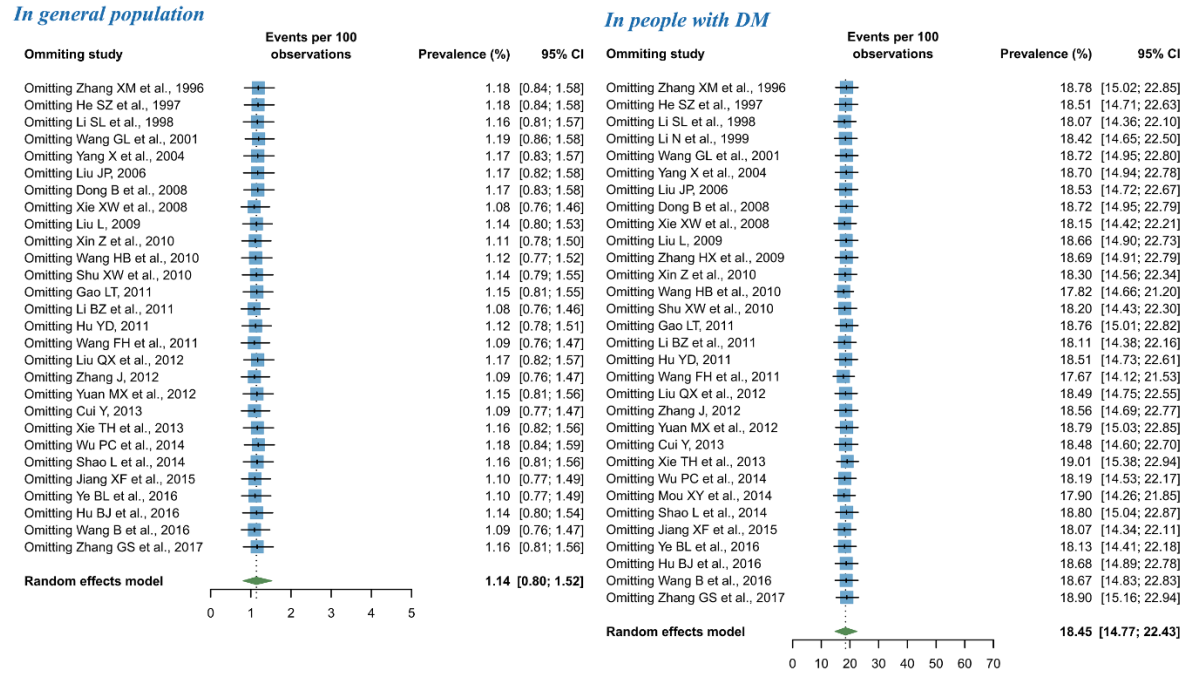


Figure 6.7. Leave-one-out sensitivity analysis of the influence of single study on the pooled prevalence of any DR in general population and people with DM

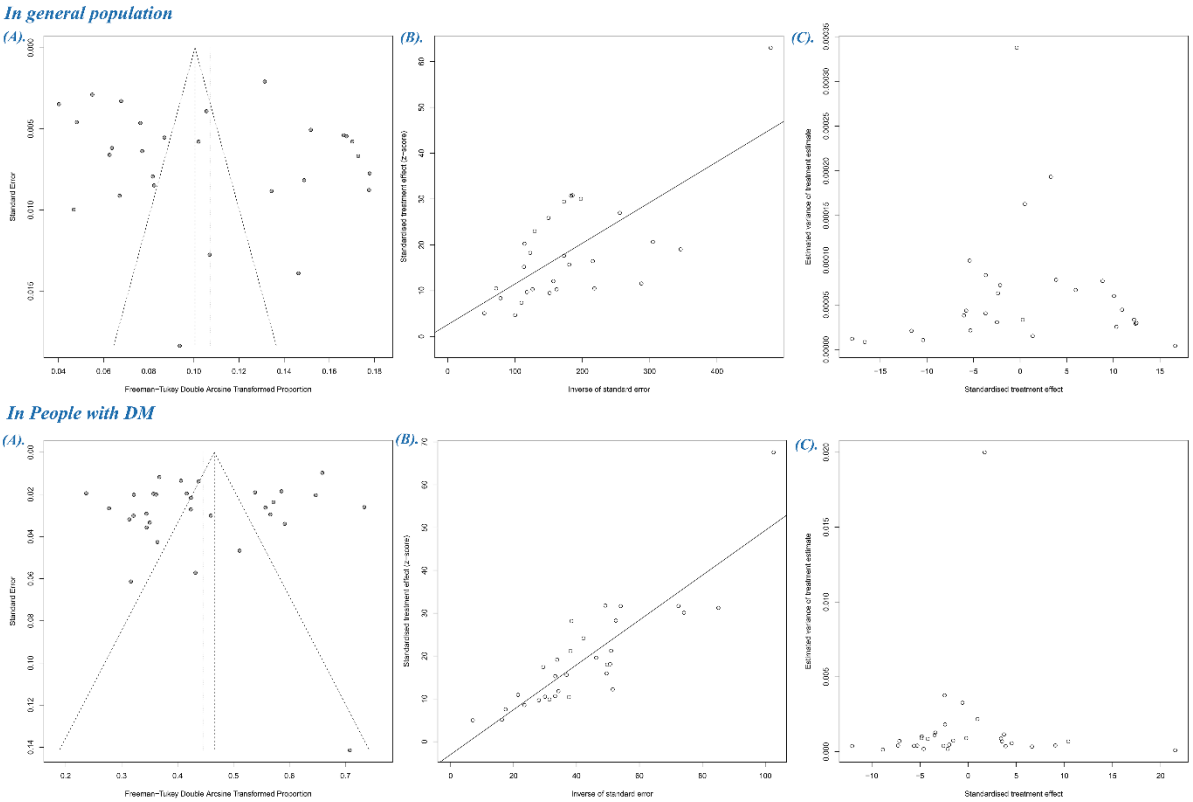


Figure 6.8. Publication bias of the studies on the prevalence of any DR in general population and people with DM

Note: (A) Funnel plot; (B) Egger's test (studies on DR prevalence in general population: t= 0.703, p= 0.488; studies on DR prevalence in people with DM: t= -1.128, p= 0.269); (C) Begg's test (studies on DR prevalence in general population: z= 0.553, p= 0.580; studies on DR prevalence in people with DM: z=- 0.493, p= 0.622).

For NPDR, the pooled prevalence in general population was 0.90% (95% CI: 0.56-1.31), and that in people with DM was 15.06% (95% CI:11.59-18.88) by use of random-effects meta-analysis (**Figure 6.9**). The leave-one-out sensitivity analysis suggested that no individual study significantly influenced the overall pooled prevalence in the meta-analysis (**Figure 6.10**), where the pooled prevalence of NPDR in general population ranged from 0.79% (95% CI:0.49-1.14) to 0.99% (95% CI: 0.63-1.42) and that in people with DM from 13.92% (95% CI:11.20-16.87) to 15.85% (95% CI: 12.48-19.53). Among studies that reported the prevalence of NPDR in general population, potential publication bias was revealed by the asymmetrical shape of funnel plot, Egger's test and Begg's test, whereas no publication bias was suggested for studies that reported the prevalence of NPDR in people with DM (**Figure 6.11**).

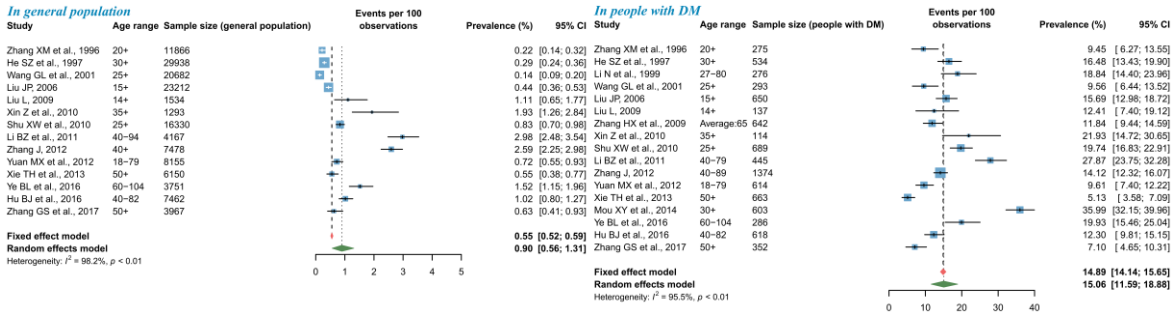


Figure 6.9. Pooled prevalence of NPDR in general population and in people with DM by random-effects meta-analysis

Note: There were 14 studies for synthesising the prevalence of NPDR in general population and 17 in people with DM.

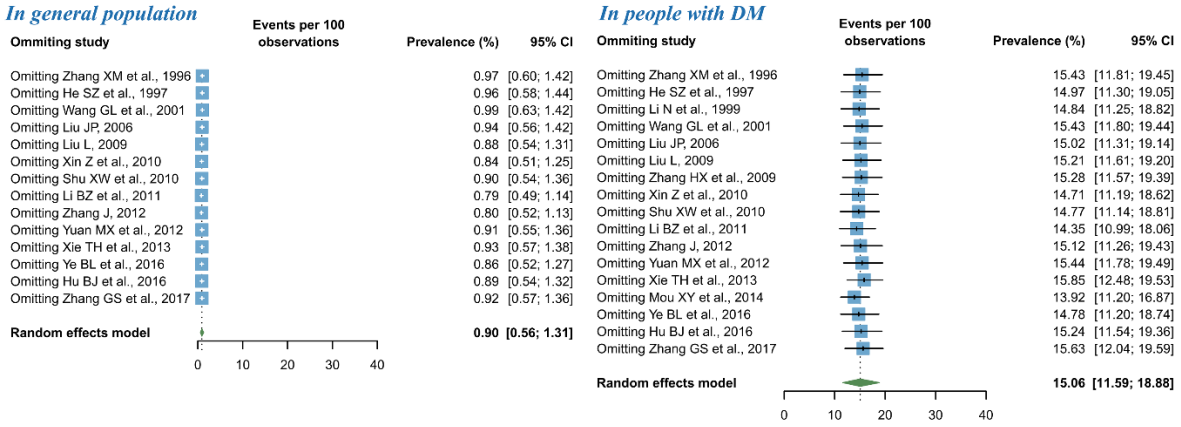


Figure 6.10. Leave-one-out sensitivity analysis of the influence of single study on the pooled prevalence of NPDR in general population and people with DM

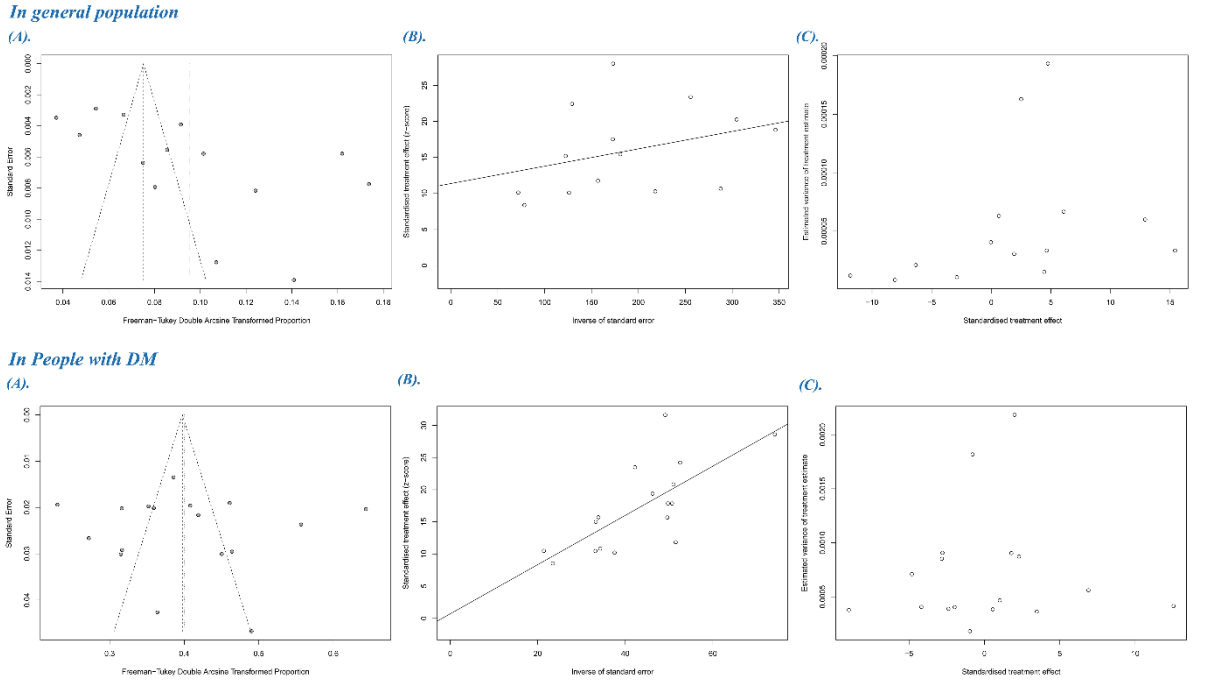


Figure 6.11. Publication bias of the studies on the prevalence of NPDR in general population and people with DM

Note: (A) Funnel plot; (B) Egger's test (studies on DR prevalence in general population: t= 2.858, p= 0.014; studies on DR prevalence in people with DM: t= 0.162, p= 0.873); (C) Begg's test (studies on DR prevalence in general population: z= 2.135, p= 0.033; studies on DR prevalence in people with DM: z= 0.494, p= 0.621).

As shown in **Figure 6.12**, the pooled prevalence of PDR from random-effects meta-analysis was 0.07% (95% CI: 0.02-0.14) in general population and 0.99% (95% CI: 0.40-1.80) in

people with DM. The subsequent sensitivity analysis showed that the pooled prevalence of PDR was not affected unduly by a single study, where the pooled prevalence rates ranged from 0.05% (95% CI: 0.01-0.10) to 0.08% (95% CI: 0.03-0.16) in general population, and from 0.76% (95% CI: 0.30-1.39) to 1.07% (95% CI: 0.43-1.95) in people with DM (**Figure 6.13**). For studies that reported the prevalence of PDR in general population, visual inspection of the funnel plot and Begg's test demonstrated some evidence of significant publication bias, which was not confirmed by the Egger's test. No publication bias was detected in the meta-analysis of PDR prevalence in people with DM (**Figure 6.14**).

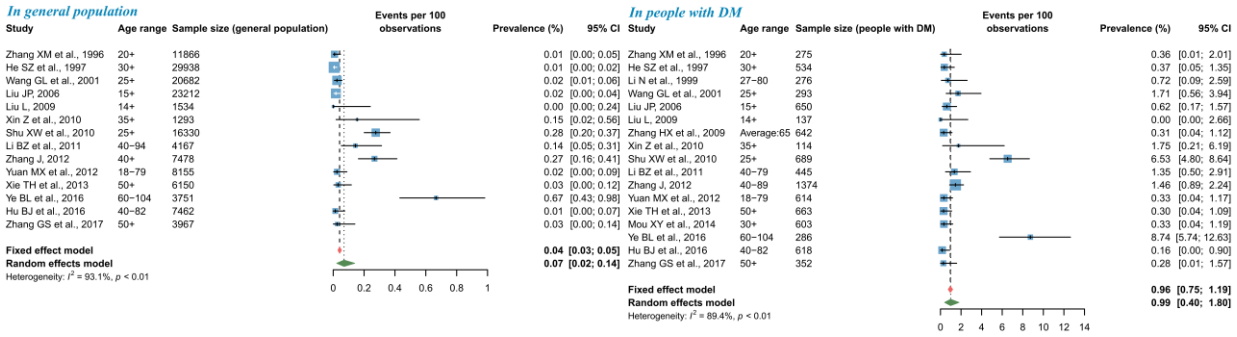


Figure 6.12. Pooled prevalence of PDR in general population and in people with DM by random-effects meta-analysis

Note: There were 14 studies for synthesising the prevalence of PDR in general population and 17 in people with DM.

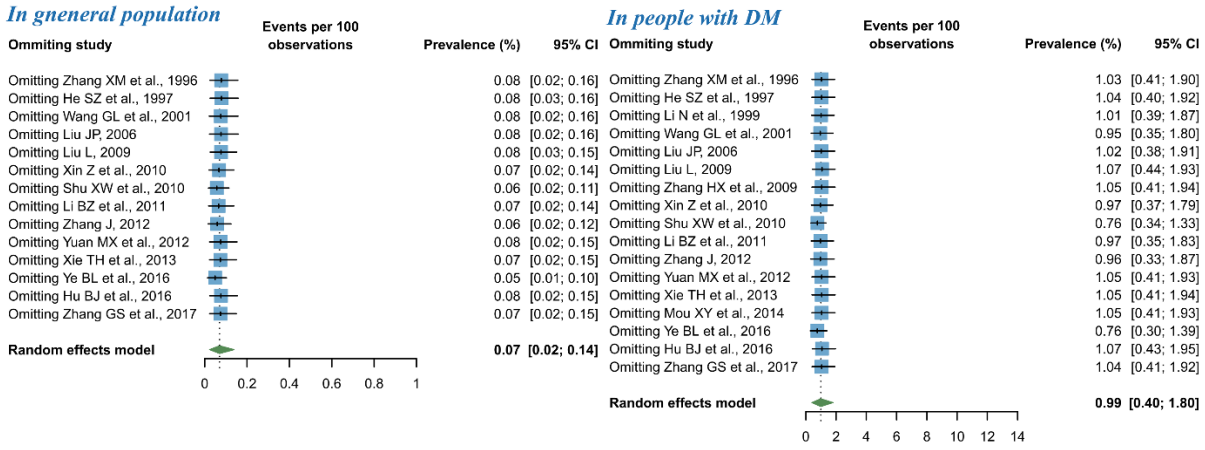


Figure 6.13. Leave-one-out sensitivity analysis of the influence of single study on the pooled prevalence of PDR in general population and people with DM

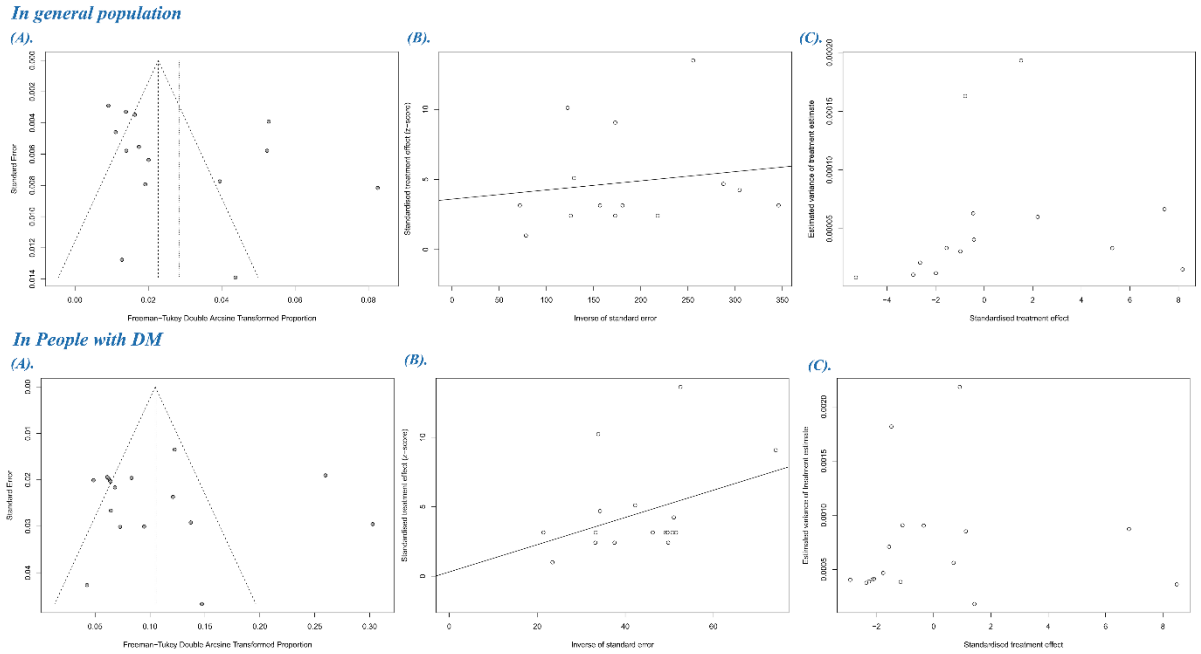


Figure 6.14. Publication bias of the studies on the prevalence of PDR in general population and people with DM

Note: (A) Funnel plot; (B) Egger's test (studies on DR prevalence in general population: t= 1.4635, p= 0.169; studies on DR prevalence in people with DM: t= 0.11095, p= 0.9131); (C) Begg's test (studies on DR prevalence in general population z= 2.1351, p= 0.03276; studies on DR prevalence in people with DM: z= 1.2358, p= 0.2165).

6.4.3 Subgroup meta-analysis and meta-regression of DR prevalence in people with DM

The age-specific prevalence of any DR in people with DM was derived based on subgroup meta-analysis (**Figure 6.15**). The following age categories were adopted: 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years and 80 years and older. Before the age of 70 years, the prevalence of any DR in people with DM kept rising from 12.55% (95% CI: 4.93-22.52) in adults aged 30-39 to 20.44% (95% CI: 15.04-26.36) in those were 60-69 years old. Then the prevalence of any DR in people with DM started to decrease, until 11.22% (95% CI: 2.57-23.12) in elderly aged 80 years and above. The detailed process of synthesising the prevalence of any DR in people with DM in each age category can be found in **Appendix figure 14**.

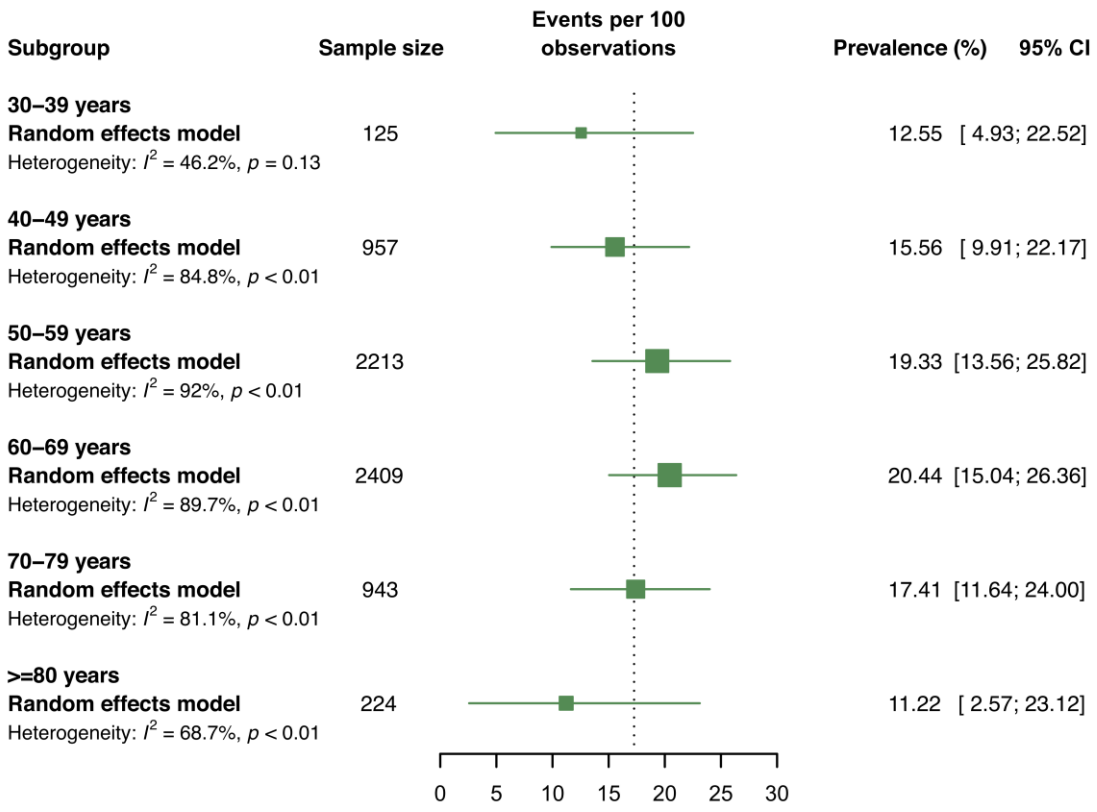


Figure 6.15. Age-specific prevalence of any DR in people with DM by random-effects meta-analysis

Note: The numbers of individual studies contributing to the synthesis of prevalence in each age group are 4 (for 30-39 years), 10 (for 40-49 years), 15 (for 50-59 years), 16 (for 60-69 years), 10 (for 70-79 years) and 9 (for 80-89 years) respectively.

By pooling the prevalence of any DR in strata of DM duration group, it was revealed that the prevalence of any DR in people with DM substantially increased with the duration of DM. Four different DM duration groups were used: 0 year (newly detected), 1-4 years, 5-9 years and 10 years and longer. According to the subgroup meta-analysis (**Figure 6.16**), the DM duration-specific prevalence of any DR ranged from 9.00% (95% CI: 5.15-13.75) in people with newly detected DM to 55.52% (95% CI: 47.90-63.02) in those who had been diagnosed with DM for 10 years and longer. The process of synthesising the prevalence of any DR in each DM duration group is detailed in **Appendix figure 15**.

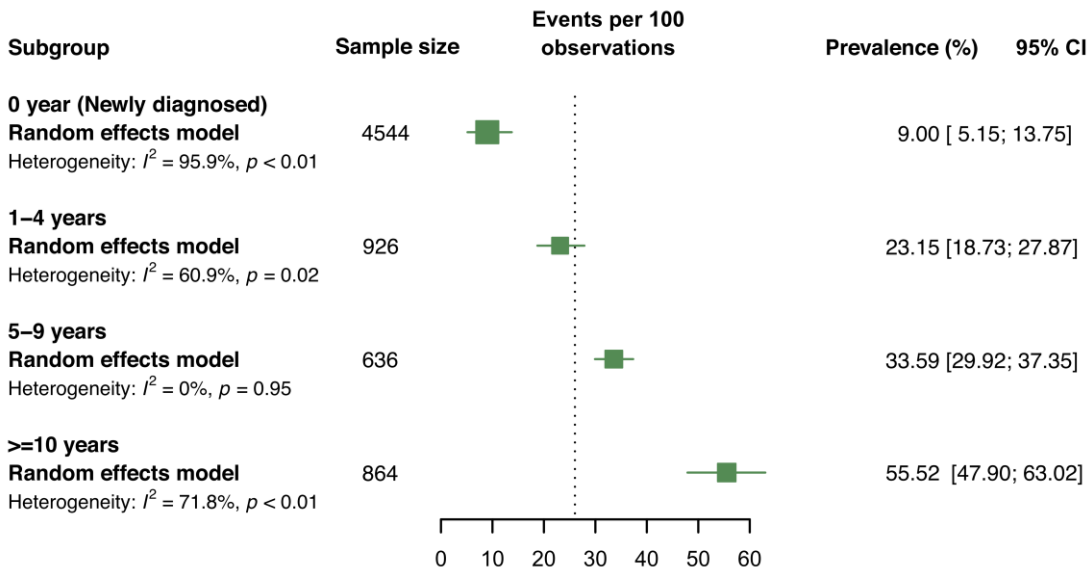


Figure 6.16. The prevalence of any DR by DM duration group, using random-effects meta-analysis

Note: The numbers of individual studies contributing to the synthesis of prevalence in each DM duration group are 13 (for newly diagnosed), 7 (for 1-4 years), 8 (for 5-9 years) and 9 (for ⩾10 years) respectively

According to the univariable meta-regression (**Table 6.2**), DM patients living in rural areas were more likely to have any DR than those in urban areas, with an OR of 1.22 (95% CI: 1.10-1.35). However, no evidence of sex difference, geographical variation or a secular trend in the prevalence of any DR in individuals with DM was observed.

Table 6.2. Odds ratios for any DR in terms of setting, geographic region and study year from univariable meta-regression models, with 95% confidence intervals

Variable		Number of studies	OR (95% CI)	z value	P value
Sex[$]					
	Female	18	Reference	Reference	Reference
	Male		0.98 (0.88-1.08)	-0.47	0.639
Setting					
	Urban	12	Reference	Reference	Reference
	Rural	7	1.22 (1.10-1.35)	3.74	<0.001
	Mixed	12	1.01 (0.93-1.10)	0.24	0.810

Variable	Number of studies	OR (95% CI)	z value	P value
Geographic region				
North China	11	Reference	Reference	Reference
Northeast China	5	0.96 (0.82-1.13)	-0.48	0.632
East China	5	0.99 (0.85-1.17)	-0.07	0.946
South Central China	4	0.95 (0.80-1.13)	-0.55	0.582
Southwest China	1	0.94 (0.69-1.28)	-0.39	0.699
Northwest China	5	0.97 (0.82-1.15)	-0.34	0.735
Study year (per decade)	31	1.01 (0.93-1.09)	0.22	0.826

Note: $ the effect of sex was estimated based on studies where sex-specific prevalence was available;

6.4.4 Synthesised effect size of risk factors for DR in people with DM

A total of 21 studies described the risk factors for any DR in people with DM by multivariate logistic regression (**Appendix table 33**). Risk factors for any DR were reported in various ways, among which 11 were with consistent definitions and sufficient information, and therefore were included in evidence synthesis (**Table 6.3**). Advanced age was found to be negatively associated with any DR, which was partly in line with my estimates on the age-specific prevalence of any DR, where the prevalence of any DR started to decrease from 70 years onwards. In accordance with the estimated DM duration-specific prevalence of any DR in subgroup meta-analysis, longer DM duration was additionally recognised as a significant risk factor for any DR. DM patients receiving insulin treatment were almost two times more likely to have any DR than those who were not treated by insulin (OR 1.99 [95% CI: 1.34-2.95]). Moreover, elevated FBG level and higher HbA1c concentration were all identified as important risk factors for any DR, with ORs per unit increase of 1.33 (95% CI: 1.12-1.59) and 1.15 (95% CI: 1.09-1.20) respectively. Individual forest plots of meta-analyses for each risk factor can be found in **Appendix table 34**.

Table 6.3. Synthesised effect size of 11 risk factors for any DR in people with DM

Risk factor	Number of studies	OR (95% CI)	z value	P value
Risk factor 1-Advanced age (per year increase)	4	0.96 (0.93-1.00)	2.26	0.024
Risk factor 2-Male	5	1.41 (0.88-2.27)	1.42	0.156
Risk factor 3-DM duration (per year increase)	12	1.09 (1.06-1.12)	5.93	<0.001
Risk factor 4-Insulin treatment	5	1.99 (1.34-2.95)	3.4	0.001
Risk factor 5-FBG (per mmol/l increase)	9	1.33 (1.12-1.59)	3.23	0.001
Risk factor 6-2h PBG (per mmol/l increase)	3	1.94 (0.81-4.65)	1.48	0.138
Risk factor 7-HbA1c (per % increase)	7	1.15 (1.09-1.20)	5.80	<0.001
Risk factor 8-TC (per mmol/l increase)	3	0.97 (0.78-1.20)	0.32	0.749
Risk factor 9-TG (per mmol/l increase)	3	1.66 (0.74-3.73)	1.24	0.216
Risk factor 10-BMI (per kg/m^2 increase)	6	1.07 (0.94-1.21)	1.06	0.289
Risk factor 11-SBP (per mmHg increase)	5	1.03 (1.00-1.07)	1.96	0.05

Note: OR, odds ratio; CI, confidence interval; DM, diabetes mellitus; FBG, fasting blood glucose; PBG, postprandial blood glucose; HbA1c, glycated haemoglobin A1c; TC, total cholesterol; TG, triglyceride; BMI, body mass index; SBP, systolic blood pressure.

6.4.5 National and subnational number of people with DR in 2010

According to the CHARLS 2011, the weighted prevalence of DM was 17.22% (95% CI: 15.57-19.00) in middle-aged and older Chinese in 2010 (**Table 6.4**). By applying the age-specific prevalence of any DR in people with DM and the corresponding age-specific DM cases, the number of middle-aged and older Chinese with any DR was estimated to be 13.16 million (95% CI: 8.95-18.00) in 2010, translating to an overall prevalence of 3.06% (95% CI: 2.08-4.19) in general middle-aged and older Chinese and of 18.24% (95% CI: 12.41-24.95) in middle-aged and older Chinese with DM (**Table 6.5**). Based on the variations of population age structure, setting, mean FBG and mean HbA1c levels, the national DR cases were distributed into six geographic regions. As illustrated in **Table 6.5** (see **Appendix table 35** for more details) and **Figure 6.17**, South Central China harboured the most DR cases (3.71 million [95% CI: 2.52-5.09]), while Northwest China had the least (0.87 million [95% CI: 0.60-1.18]). Regarding the prevalence of any DR at regional level, it was estimated that the prevalence of any DR in general middle-aged and older Chinese was the highest in North China (3.76% [95% CI: 2.56-5.12]) and the lowest in Southwest China (2.55% [95% CI: 1.74-3.48]); For the

prevalence of any DR in middle-aged and older Chinese with DM, it was the highest in Northwest China, while the lowest in East China (17.67% [95% CI: 11.97-24.24]). In 2010, most DR cases were concentrated in people aged 50-59 years across the six geographic regions.

Table 6.4. Mean fasting blood glucose, mean haemoglobin A1c and prevalence of diabetes mellitus in middle-aged and older Chinese, CHARLS 2011

Characteristic	Study population (11308)	Mean FBG, mmol/l (95% CI)	Mean HbA1c, % (95% CI)	Prevalence of DM, % (95% CI)	Proportion within DM, % (95% CI)	
					KDM	NDM
Age group						
45-49 years	2109 (18.65)	5.85±1.62	5.18±0.77	10.76 (8.59-13.40)	30.63 (23.96-38.21)	69.37 (61.79-76.04)
50-59 years	4007 (35.44)	6.09±1.93	5.26±0.84	16.06 (14.14-18.19)	40.22 (33.53-47.28)	59.78 (52.72-66.47)
60-69 years	3285 (29.05)	6.15±2.11	5.33±0.90	19.99 (17.29-22.99)	50.35 (40.94-59.74)	49.65 (40.26-59.06)
70-79 years	1548 (13.69)	6.16±1.95	5.29±0.82	21.78 (17.91-26.23)	45.48 (31.82-59.86)	54.52 (40.14-68.18)
≥80 years	359 (3.17)	6.25±1.05	5.24±0.59	25.25 (13.64-41.94)	10.17 (3.83-24.35)	89.83 (75.65-96.17)
Sex						
Male	5349 (47.30)	6.08±1.84	5.23±0.73	16.78 (14.54-19.28)	37.32 (32.55-42.35)	62.68 (57.65-67.45)
Female	5959 (52.70)	6.07±1.93	5.30±0.92	17.64 (15.98-19.43)	44.20 (36.57-52.10)	55.80 (47.90-63.43)
Setting						
Urban	4210 (37.23)	6.14±1.65	5.29±0.75	20.51 (18.02-23.26)	47.28 (40.26-54.41)	52.72 (45.59-59.74)
Rural	7098 (62.77)	6.01±2.07	5.24±0.88	14.09 (12.76-15.54)	32.14 (27.30-37.39)	67.86 (62.61-72.70)
Region						
North China	1656 (14.64)	6.16±2.23	5.22±0.97	20.83 (16.25-26.30)	42.55 (30.92-55.08)	57.45 (44.92-69.08)
Northeast China	804 (7.11)	6.21±1.77	5.35±0.80	17.50 (13.27-22.72)	44.75 (35.06-54.86)	55.25 (45.14-64.94)
East China	3420 (30.24)	6.04±1.77	5.20±0.81	15.97 (13.93-18.25)	46.61 (39.41-53.94)	53.39 (46.06-60.59)

Characteristic	Study population (11308)	Mean FBG, mmol/l (95% CI)	Mean HbA1c, % (95% CI)	Prevalence of DM, % (95% CI)	Proportion within DM, % (95% CI)	
					KDM	NDM
South Central China	2570 (22.73)	6.01±1.44	5.29±0.75	18.95 (15.09-23.53)	39.28 (25.76-54.67)	60.72 (45.33-74.24)
Southwest China	1930 (17.07)	6.05±2.50	5.33±0.96	13.99 (10.92-17.76)	30.64 (22.16-40.68)	69.36 (59.32-77.84)
Northwest China	928 (8.21)	6.19±2.26	5.29±0.75	16.39 (12.91-20.58)	35.69 (20.29-54.75)	64.31 (45.25-79.71)
Overall	11308 (100.00)	6.07±1.88	5.26±0.83	17.22 (15.57-19.00)	40.92 (35.51-46.56)	59.08 (53.44-64.49)

Note: Calculations were weighted by taking into account the complex survey design and adopted the blood weight with household and individual response adjustment; data were presented as n (%), proportion (95% CI), means ± SD; KDM, known (diagnosed) diabetes mellitus; NDM, newly detected diabetes mellitus.

Table 6.5. Estimated prevalence and number of middle-aged and older Chinese with any DR in China in 2010, by geographic region

Region	Prevalence of any DR in general people (%, 95% CI)	Prevalence of any DR in people with DM (%, 95% CI)	Number of people with DR (million, 95% CI)
North China	3.76 (2.56-5.12)	18.54 (12.66-25.28)	2.03 (1.39-2.77)
Northeast China	3.22 (2.20-4.39)	18.93 (12.94-25.81)	1.35 (0.92-1.84)
East China	2.74 (1.86-3.76)	17.67 (11.97-24.24)	3.63 (2.46-4.98)
South Central China	3.31 (2.25-4.54)	17.97 (12.19-24.63)	3.71 (2.52-5.09)
Southwest China	2.55 (1.74-3.48)	18.73 (12.76-25.59)	1.56 (1.07-2.14)
Northwest China	3.09 (2.12-4.20)	19.39 (13.30-26.35)	0.87 (0.60-1.18)
China	3.06 (2.08-4.19)	18.24 (12.41-24.95)	13.16 (8.95-18.00)

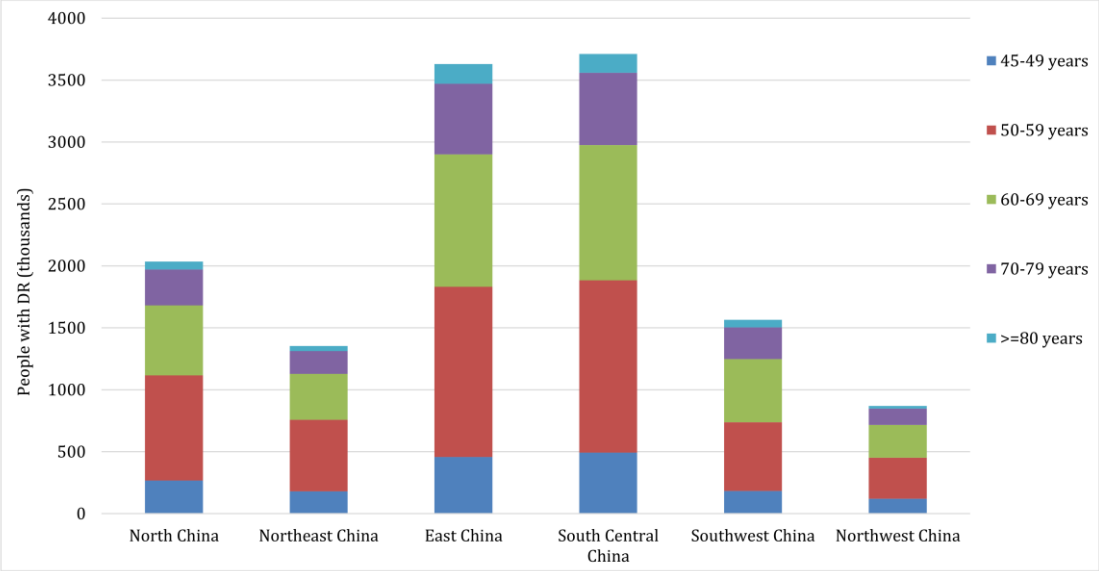


Figure 6.17. Estimated regional number of middle-aged and older Chinese with any DR and contributing age groups in 2010

6.5 Discussion

6.5.1 Statement of principal findings

By combining all available epidemiological data on the prevalence of DR in China from 1990 onwards, I estimated that in general population, the pooled prevalence of any DR, NPDR and

PDR was 1.14% (95% CI: 0.80-1.52), 0.90% (95% CI: 0.56-1.31) and 0.07% (95% CI: 0.02-0.14); In people with DM, the pooled prevalence rates were 18.45% (95% CI: 14.77-22.43), 15.06% (95% CI: 11.59-18.88) and 0.99% (95% CI: 0.40-1.80) for any DR, NPDR and PDR, respectively. The prevalence of any DR in DM patients peaked between 60 and 69 years of age, and increased steeply with the duration of DM. DM patients residing in rural China were at a higher risk to have any DR than those in urban areas. In addition, insulin treatment, elevated FBG level and higher HbA1c concentration were confirmed to be associated with a higher prevalence of any DR in people with DM. In 2010, a total of 13.16 million (95% CI: 8.95-18.00) Chinese aged 45 years and above were living with any DR, among whom the most were in South Central China and the least were in Northwest China. Collectively, these data suggest a considerable burden of DR in China.

6.5.2 Strengths and limitations

To the best of my knowledge, this systematic review and meta-analysis provides a comprehensive estimation of the prevalence, risk factors and burden of DR in China. Although this study is subsequent to the first synthesised analysis by Liu and colleagues, many new merits are highlighted (Liu et al., 2012). The principal strengths of this study include a comprehensive search strategy in both Chinese and English databases and a dual review process, which increased my ability to capture all studies on DR epidemiology in China. Ultimately, my estimation of DR prevalence was based on a total of 31 studies, which was more than 1.5 times the number of studies included in the first systematic review on DR in China. Another important feature that distinguished this study with the previous systematic review by Liu and colleagues was that only community-based studies incorporating both newly detected and already diagnosed DM cases were included for the estimation of DR prevalence, therefore the representativeness of my estimates can be greatly guaranteed. Regarding risk factors for DR, only studies that provided estimates of OR using multivariate study designs were included, therefore community-based, PHCM-based and registry-based studies could all contribute, ensuring sufficient power for conducting reliable synthesised assessments. Furthermore, the definitions of risk factors in included studies were similar, as well as in the CHARLS 2011 (Zhao et al., 2013, Zhao et al., 2012). Before pooling, an arcsine transformation was conducted to stabilise the variance of prevalence rates, which reduced the bias associated with small and large prevalence values on the pooled estimates to a large extent (Barendregt et al., 2013, Nyaga et al., 2014). Although differences existed in the prevalence rates of DR across different subgroups, my detailed assessment of any DR prevalence by age

and DM duration group, and identification of risk factors for any DR could serve as a source of primary information and guide policy making and rational planning of health services, especially in areas where local investigations on the epidemiology of DR are absent.

Before interpreting the findings, potential limitations of this systematic review and meta-analysis should be carefully considered. First, the pooled prevalence of NPDR and PDR in general population might have been affected by publication bias. Generally, publication bias arises because statistically significant results are more likely to be published than non-significant results, combining these studies for analysis could, therefore, introduce bias (Peters et al., 2006, Sterne et al., 2000, Stroup et al., 2000). Unfortunately, I could not completely rule out publication bias because of the observational nature of this study. Second, there are inherent disadvantages in pooling prevalence form disparate studies. Due to the absence of stratified prevalence data for NPDR and PDR, I was not able to further explore sources of heterogeneity by subgroup meta-analysis and meta-regression for these two subtypes of DR. For any DR, sufficient data were available to pool the prevalence estimates and no publication was detected. However, my subgroup analysis on the prevalence of any DR by age group and DM duration group was only based on a limited number of studies that provided correspondingly stratified prevalence estimates. Third, only 11 risk factors with similar definitions across the included studies were systematically assessed, among which advanced age, longer DM duration, insulin treatment, elevated FBG level and higher HbA1c concentration were identified to be associated with a higher prevalence of any DR. However, because of the paucity of reported ORs, the effects of TC, TG and SBP should be further confirmed with new data coming in from future studies. In addition, previous studies have suggested that socioeconomic factors, including the availability and costs of DM management, were also likely to contribute to the disparities in DM severity and DR prevalence rates in different subgroups, but could not to be assessed in the current study (Yau et al., 2012, Sivaprasad et al., 2012, Cheung et al., 2010). Fourth, the number of DM cases in China for generating the national and subnational burden of any DR was derived from the CHARLS 2011, which was nationally representative but only conducted in middle-aged and older population (Zhao et al., 2012, Zhao et al., 2013). Therefore, the estimated number of people with any DR in this study was only for people aged 45 years and above. When distributing the national DR cases into the six geographic regions, I only took the effects of four objective indicators into account, namely, advanced age, rural setting, elevated FBG level and higher HbA1c concentration. Other subjective risk factors (e.g. insulin treatment and DM duration) and potential factors that might be associated with the prevalence of DR were not included in my analysis of regional burden of DR in China, which might reduce the reliability of my

estimation at the subnational level. Bearing those limitations in mind, the results presented in this study should be interpreted judiciously.

6.5.3 Interpretation of findings

In this study, significant heterogeneity was noted in pooling the prevalence rates of DR. The main sources of heterogeneity in the included studies pertained to the different characteristics of study population. After omitting each study at a time, the pooled prevalence of any DR was robust and consistent. The pooled prevalence of any DR in Chinese people with DM was lower in my study than that in the global DR study (18.45% vs. 25.08%) (Yau et al., 2012). Given that the estimated prevalence of any DR in Chinese people with DM presented in the global DR study was based on studies that were conducted both within and outside China, any differences in exposure levels of risk factors might explain this discrepancy. Compared with the pooled prevalence of any DR in Chinese people with DM reported by Liu and colleagues, my study revealed a relatively lower prevalence rate (23.0% vs. 18.45%) (Liu et al., 2012). There are a number of possible reasons for this difference. First, the improvement of primary health care management in China might have resulted in a lower incidence of DR in recent years. Second, more recent investigations might include more newly detected DM patients. The incidence of DM is higher than that of DR, resulting in a relatively larger denominator for calculating the prevalence of DR. Most importantly, individual studies included in the systematic review and meta-analysis by Liu and colleagues were not solely focused on generally Chinese population, where both newly detected and diagnosed DM (self-reported physician diagnosed DM in some studies) cases should exist simultaneously. Two individual studies that were conducted in people with diagnosed DM were included in their final synthesis, the erroneous omission of people with newly detected or early-stage DM from the sample denominator would, therefore, lead to an overestimation of DR prevalence (Liu et al., 2012). Furthermore, a study included in their synthesised analysis was specifically conducted in a group of people with higher risk for pre-diabetes (e.g. people with familial DM history, hypertension, overweight/obesity, dyslipidemia, cardiovascular disease /stroke or a gestational history of large babies [for women]) rather than in general population, which will also add further possibility of an overestimation (Liu et al., 2012, Pang et al., 2012).

In my analysis, the prevalence of any DR was found to peak between 60 and 69 years of age, which is in line with the age-specific prevalence estimates of DR among Americans (Kempen et al., 2004, Cheng et al., 2013b). In elderly with DM, the incidence of DR is relatively lower than that in younger people (Varma et al., 2010, Sivaprasad et al., 2012). Given that DR is a

marker for severe DM and other life-threatening complications, a reduced survival rate has been observed in older people living with DR (Bragg et al., 2017, Targher et al., 2008, Hecke et al., 2005, Kramer et al., 2011, Varma et al., 2004). Therefore, this pattern of declining DR prevalence in the elderly seems to be driven by the combination of reduced incidence and improved mortality. Unsurprisingly, the prevalence of DR is strongly associated with the duration of DM, which has been validated by both sub-group meta-analysis and my meta-analysis on major risk factors for DR in this present study. This finding is consistent with other previous investigations and synthesised analyses (Zhang et al., 2010b, Yau et al., 2012, Varma et al., 2004). As revealed by my analysis, more than half of all patients with DM for 10 years and longer will develop some degree of DR, underscoring the importance of optimal management of DM and early detection of DM complications in those living with DM. In this study, I noticed a higher prevalence of DR in DM patients living in rural China than that in those living in urban areas. This urban-rural disparity of DR prevalence in people with DM is in line with the study by Liu and colleagues (Liu et al., 2012). In the Chinese context, awareness (a history of physician-diagnosed), treatment (proportion of individuals taking diabetes medications), and control (the proportion of individuals with an HbA1c concentration of less than 7.0%) of DM among rural dwellers are all lower than that in urban dwellers, partly due to lower economic development level and restricted primary health resources in rural China (Xu et al., 2013, Bragg et al., 2017, Xu et al., 2016). The delayed diagnosis and non-optimal management of DM might be the primary causes of a higher prevalence of DR in rural China, but still need further confirmation in future studies.

Good glycemic control has long been recognised as one important factor for reducing vascular complications of DM, and it is also important in the prevention of DR (Mohamed et al., 2007, Corcóstegui et al., 2017). In this study, higher levels of FBG and HbA1c have both been suggested as risk factors for DR in people with DM, which is in line with many previous investigations and synthesised results (Zhang et al., 2010b, Ding and Wong, 2012). In addition, insulin treatment was identified to be with a higher odds of DR in DM patients according to my meta-analysis. Herein insulin treatment should not be simply concluded as a "bad treatment" which directly causes DR. In previous studies, it was suggested that a larger proportion of participants using insulin therapy were those with T1DM or with longer-duration of DM, and people with DR may have already been preferentially treated with insulin therapy (Rema et al., 2005, Zhao et al., 2014, Zhang et al., 2010b). In previous studies, higher SBP has been suggested as a risk factor for DR (Corcóstegui et al., 2017, Yau et al., 2012). However, my meta-analysis of risk factors for DR only showed a slightly significant association between elevated SBP and DR. Given the effect of SBP on DR was only assessed based on five

individual studies in my synthesised analysis, the lack of sufficient evidence logically calls for an updated analysis to better understand the role of SBP in the development of DR with new data coming in.

6.5.4 Implications for policy, practice and future research

The increasing burden of DR might bring a higher pressure on available infrastructure and resources. Ideally, periodic eye examinations should be conducted by all patients with DM. Regular follow-up to detect significant retinopathy, together with prompt interventions when necessary, is believed to be the most effective method to reduce potential DR-related visual disabilities (Frank, 2004, Cheung et al., 2010, Ferris III, 1993). In China, screening of DR has not been well established into the primary health care system, and the need for adequate DR eye care remains largely unaddressed (Vela et al., 2012, Wang et al., 2010a). Generally, DR screening could be evaluated in office or through telemedicine, and the latter has been suggested to be accurate and more cost-effective (Ting et al., 2016, Jones and Edwards, 2010, Mansberger et al., 2015). Furthermore, with the development of technology, a wholly automated approach with the assistance of artificial intelligence might be especially beneficial in under-developed areas. Even in established screening centres, those techniques also have the potential to substantially reduce the grading workload (Usher et al., 2004, Wong and Bressler, 2016).

With new epidemiological investigations emerging, the results of this study should be updated in a timely and regular manner. In addition, there remains a genuine need for prompting international standardised DR classification systems in Chinese scientific society, to facilitate communication and comparison across the world.

6.6 Conclusions

To conclude, this contemporary systematic review and meta-analysis estimated the prevalence, risk factors and burden of DR in China. The results from this study revealed a substantial burden of DR in China. Optimal screening of and interventions on DR should be implemented in the Chinese health system. Improved epidemiological studies on DR are still required to guide eye care programmes in China.

Chapter 7 Overall discussion

The discussions about study findings, strengths and limitations, and implications for policy, practice and future research have been respectively presented in each project chapter (Chapters 3-6). In this overall discussion chapter, I will first summarise the overall findings from this thesis, based on which the possible implications on the eye health care and disease management in China will be discussed. The strengths and limitations of methodological approaches adopted in this thesis have been previously considered but more general issues will be emphasised in this chapter. Suggestions for future research will also be provided.

7.1 Key findings

As presented in the introduction chapter (Chapter 1), this thesis has four main objectives, which are 1) estimating the prevalence and burden of AREDs from 1990 to 2015; 2) projecting the prevalence and burden of AREDs from 2020 to 2050; 3) identifying cluster- or individual-level factors that are associated with the prevalence of AREDs; 4) generating the regional burden of AREDs in 2000 and 2010. Those objectives were exactly achieved in the projects of AMD, glaucoma and cataract. Given that DR could only be assessed in people with DM, the estimation of DR prevalence and burden, however, was only performed for the year 2010 by using the DM prevalence from a national representative investigation (CHARLS 2011). Taken together, this project has demonstrated that AREDs, including AMD, glaucoma, cataract and DR, represent a huge disease burden on the Chinese public health system. Based on the estimation in 2010, cataract was the most prevalent disease among the four major AREDs, followed by AMD, DR and glaucoma. As stated in the overall methods in Chapter 2, the estimation of AREDs prevalence was based on the number of affected individuals, rather than the number of affected eyes. When interpreting the findings in this thesis as a whole, one should note that the overall burden of AREDs in a specific year cannot be the total cases of AMD, glaucoma, cataract and DR, given the possible coexistence of two or more AREDs in the same individual (Vizzeri and Weinreb, 2010).

7.2 Implications on disease management

As estimated in this thesis, the increasing burden of AREDs will place a larger demand in the current health system. The latest national five-year plan for eye health in China ("The 13th 5-Year National Eye Health Plan 2016-2020") also emphasises the provision of universal eye health as integrated into health care system (National Health and Family Planning Commission of the People's Republic of China, 2016). The current health insurance systems in China include three programs: New Rural Cooperative Medical Scheme (NRCMS) for rural residents, Urban Employee Basic Medical Insurance (UEBMI) for urban residents with formal employment and Urban Resident Basic Medical Insurance (URBMI) for urban residents without formal employment. Despite the success of universal health insurance coverage, where 95% of China's total population were covered by the current health insurance system, the financial burden remains large for the insured. In 2011, the reimbursement rate of inpatient care was only around 50% in these three insurance systems (68% in UEBMI, 48% in URBMI and 44% in NRCMS in 2011). UEBMI could cover both inpatient and outpatient care, whereas NRCMS and URBMI mainly target on inpatient and critical outpatient care. In 2011, outpatient care could be universally covered though UEBMI in all Chinese counties or cities, but only partly available though NRCMS and URBMI in only 58% and 79% of Chinese counties or cities (Yu, 2015, Wang et al., 2014c).

The large burden of AMD has placed a huge burden on the Chinese public health and medical systems. For patients with advanced AMD in one eye, there is a substantial chance that the other eye would be affected within five years (Jager et al., 2008, Age-Related Eye Disease Study Research Group, 2001a). Since AMD cannot be fully cured and possible treatments are not universally available, especially for GA, it is rather important to accept periodic eye exams and identify preventive strategies that can lead to better visual outcomes (Gehrs et al., 2006, Wong et al., 2008a).

Prevention of AMD is mainly focused on diminishing risk factor effects, with specific interventions including lifestyle modification and antioxidant therapy (Wong et al., 2011). The smoking cessation has been highlighted as an effective strategy, because of its adverse association with AMD is unequivocal (Khan et al., 2006b, Thornton et al., 2005). Although the association between sunlight exposure and AMD is still controversial, in the ten-year follow-up of the Beaver Dam Eye Study, in individuals who reported the highest summer sun exposure levels in their teens and 30s, those who wore hats or sunglasses at least half the time were less likely to develop soft indistinct drusen (RR: 0.55 [95% CI: 0.33-0.90]) and retinal

pigment epithelial depigmentation (RR: 0.51 [95% CI: 0.29-0.91]). This suggests that the use of hats and sunglasses might be regarded as a protective measure in slowing the development of AMD (Tomany et al., 2004). Some studies on nutrient supplementation, such as the Age-Related Eye Disease Study formula, provide other clues for investigation of well-known supplements, including lutein and zeaxanthin, omega-3 fatty acid, and berry extracts (Wong et al., 2011, Chong et al., 2007, Evans and Lawrenson, 2012).

Currently, there is no satisfying treatment that would have a significant influence on blindness caused by AMD. Thermal laser photocoagulation is a traditional treatment for wet AMD in the last decades, using intense laser beams to coagulate the abnormal choroidal neovascular membrane (Bressler, 2002, Wong et al., 2008a). This treatment is very effective in reducing the risk of vision loss in patients with wet AMD. However, recurrence is very common after treatment, and the procedure itself may cause permanent retina scars and scotomas that permanently impair vision, especially when the targeted vessels are close to the fovea (Bressler, 2002, Cook et al., 2008). Photodynamic therapy involves intravenous injection of verteporfin and then a photoactive laser, verteporfin, can accumulate in the abnormal vessels and the following photoactive laser that results in thrombosis of the abnormal blood vessels (Blumenkranz et al., 2002). This therapy has been proven to reduce the risk of vision loss safely, although recurrences are also common (Potter and Szabo, 2007). Since the mid-2000s, antiangiogenic therapy, involving delivery of anti-vascular endothelial growth factor (VEGF) agents directly into the eye, has become the mainstay for the treatment of wet AMD (Cook et al., 2008). Currently, there are four anti-VEGF agents in use: Pegaptanib, Ranibizumab, Bevacizumab and Aflibercept (Agrawal et al., 2013). While Pegaptanib was the first approved anti-VEGF agent for the treatment of wet AMD, its effectiveness has been shown to be inferior to that of Ranibizumab, thereby the use of Pegaptanib is relatively limited (Takeda et al., 2007). Ranibizumab is a recombinant humanised monoclonal antibody fragment that inhibits VEGF, Bevacizumab is the parent molecule from which Ranibizumab is derived, and both are the effective known therapies (Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group et al., 2012). However, Bevacizumab has been widely used off-label in the US because its costs are considerably smaller than Ranibizumab costs when administered intravitreally ($50 vs. $1,950 per dose) (Brechner et al., 2011). Aflibercept is a novel recombinant fusion protein consisting of all isoforms of VEGF-A, VEGF-B, and placental growth factor (Ohr and Kaiser, 2012). Verteporfin and Ranibizumab have been licensed for AMD treatment in China. However, these agents are not covered by medical insurance. The high cost of these two agents has posed a considerable financial burden on patients and limited their widespread use in Chinese clinical practice. At present, Bevacizumab

has also been approved to treat cancers. However, its similar efficacy and much lower cost than Ranibizumab have stimulated the off-label use of Bevacizumab for wet AMD (Li et al., 2012, Wu et al., 2016). Currently, unlike exudative AMD, there are no effective medical treatments to cure or slow the progress of GA, but increasing evidence suggests that there are some protective effects of some micronutrients and vitamins. Furthermore, advances in gene therapy and stem cell therapy are promising in their potential to alleviate vision loss and slow its development (Damico et al., 2012).

For glaucoma, the major characteristic of this disease is that the progress of glaucoma is painless and asymptomatic until at advanced stages, by which point considerable damage to vision has already occurred. Even in developed countries, only fewer than 50% of those with glaucoma are aware of the existence of glaucoma, and this proportion is probably even lower in developing countries (Quigley, 1996). However, most of the risk factors for glaucoma are impossible to remedy, such as age, ethnicity, and genetics, thereby early detection of glaucoma is crucial in reducing morbidity and improving quality of life (Nduaguba and Lee, 2006). However, unlike diabetic retinopathy, which largely benefits from screening programs, early detection or prediction of glaucoma remains challenging. Furthermore, universal screening for glaucoma has been found not to be cost-effective, thereby the targeted screening of high-risk groups may be more practical and cost-effective (Nduaguba and Lee, 2006, Burr et al., 2007). In China, misunderstanding about the asymptomatic nature of glaucoma among patients and physicians, especially those in rural areas, makes identifying patients with glaucoma a special challenge (Yan et al., 2012). Public health initiatives for raising disease awareness might be useful in encouraging routinely comprehensive eye examinations among the elderly. However, it is also suggested that in rural China, the acceptance of comprehensive eye examinations could only be improved when making comprehensive eye examinations free (Dan et al., 2015). In China's primary health system, free comprehensive eye examinations are still not universally provided, restricting the surveillance for and early treatment of glaucoma to a large extent.

Despite the fact that visual loss caused by glaucoma is irreversible and no preventive scheme is under recommendation, it remains possible to slow further progression when adequate therapies are available. The only proven treatment strategy for primary glaucoma is lowering IOP by, either, reducing the amount of aqueous fluid or increasing the size of the drainage channels. Lowering IOP can be achieved by several modalities, including medication (e.g. eye drop), laser treatment (e.g. the older Argon Laser Trabeculoplasty [ALT] or the newer Selective Laser Trabeculectomy [SLT]), and surgery (e.g. trabeculectomy with augmentation)

(The Royal College of Ophthalmologists, 2016, Rulli et al., 2013). Topical administration of ocular medication is usually the initial therapy in mitigating the progression of hypertension associated disease. Commonly used topical medications include beta-blockers and carbonic anhydrase inhibitors for suppressing aqueous inflow, and prostaglandin analogues for increase aqueous inflow (Crowston and Weinreb, 2005, Barton and Hitchings, 2013, Congdon and Friedman, 2003). Although being applied topically to the eye, these agents may have unusual side-effects, such as gradual irreversible darkening of the iris. In addition, daily application of ocular medication is expensive and subject to poor compliance (Weinreb and Khaw, 2004, Weinreb et al., 2014). The most widely adopted laser treatment for POAG as an adjunct to medications is laser trabeculoplasty, which directs laser light at the trabecular meshwork to decrease the resistance to aqueous humour outflow. However, the 5-year success rate is only about 50 % with the majority of patients responding in the first few months, before the effects decrease gradually over time with a failure rate of around 10% per annual (Weinreb and Khaw, 2004, Shingleton et al., 1993, Shingleton et al., 1987). Trabeculectomy is the most widely adopted incisional surgery to enhance aqueous humour drainage, where a fistula is created to allow aqueous humour flowing out from the anterior chamber into the sub-Tenon's space. To inhibit a fibroproliferative response and improve the success rates, adjunctive antiscarring agents are usually applied, but may increase the rate of complications (Weinreb et al., 2014). Moreover, although trabeculectomy is regarded as highly effective in reducing the pressure, the associated high risk of complications cannot be overlooked (Rulli et al., 2013).

As a degenerative disease, cataract is not fully preventable, but lowering the risk of cataract by decreasing exposure to well-established risk factors is still beneficial. Wearing a hat and UV-B protecting sunglasses to avoid direct sunlight have been suggested as effective preventative measures for cortical cataract (McCarty and Taylor, 2002, McCarty et al., 2000). Smoking cessation has also been indicated as an effective measure for reducing the risk of age-related cataract, particular nuclear cataract (Kelly et al., 2005, Ye et al., 2012). Despite the fact that cataract is the most prevalent ARED, as revealed in this thesis. The bright side of cataract is that restoring sight is possible by surgery (Solomon and Donnenfeld, 2003). The most widely adopted surgery is cataract extraction with implantation of an artificial intraocular lens for the restoration of vision. Three main surgical techniques are available for the treatment of cataract, namely, intra-capsular cataract extraction, extra-capsular cataract extraction and phaco-emulsification (Tabin et al., 2008, Asbell et al., 2005). In intra-capsular cataract extraction, a large incision is opened for removal of the entire lens and capsule, and then an artificial intraocular lens is inserted in front of the iris. In extracapsular cataract extraction, a small incision is opened to remove the nucleus, cortex and anterior capsule, but the posterior

capsule is retained, and then an artificial intraocular lens is inserted behind the iris. Phaco-emulsification is an advanced technique of extra-capsular cataract extraction with no damage to the anterior chamber. In this procedure, an ultrasonic hand piece, together with aspiration, was used to emulsify opaque lens into small pieces (Linebarger et al., 1999). Phaco-emulsification is superior to the other two options due to rapid visual recovery and a shorter hospital stay, and has become the standard surgical procedure in most developed countries. However, this advanced technique relied heavily on high-technology equipment, well-trained surgeons and support staff and regular maintenance. Therefore, it is still prohibitive to implement in high volume in developing countries, especially in poor and rural areas (Tabin et al., 2008).

Despite its success on visual outcomes, cataract surgery is still hampered by high costs, the need for professional surgeons and post-surgical complications in developing countries. In China, it appears that cost has no longer been a major barrier to cataract surgical uptake due to the implementation of universal health insurance (Yu, 2015, Huang et al., 2012, Chen et al., 2011). However, the availability of such treatment and its accessibility are still limited, even in developed countries, with longer waiting times hampering its implementation (Brian and Taylor, 2001, Access Economics, 2010). In China, the cataract surgery rate was still the lowest in Asia (446 per million per year), which might be caused by the insufficiency of well-developed ophthalmic infrastructures. Under those circumstances, alternative preventions and treatments are still worthy of investigation. At present, no pharmacological treatments have been developed to stop the formation of cataract or elimination of existing cataract. Some potential anti-cataract therapeutic agents are still under investigations, such as aspirin and aspirin-like drugs, which have shown effects in delaying cataract in animal models. However, the systematic side effects (e.g. gastric ulcer and renal impairment) and ocular side effects (e.g. stinging and corneal disorders), alongside with the drug usage, outweigh the potential benefits, thus limiting its wide adoption (Abdelkader et al., 2015). However, most of the agents were tested on animal lenses, mostly rodent (Tauseef et al., 2008, Yan et al., 2008), and ocular devilry, long-term ocular safety and tolerability have yet to be evaluated in human lenses.

For DR, intensive control of diabetic abnormalities and hypertension remains a primary measure for delaying the progression of diabetic microvascular complications (Mohamed et al., 2007). At initial stages, DR is normally asymptomatic, even for PDR at its most treatable stages. Thus the majority of the diabetic patients are not aware of the existence of this condition, and yet without proper management, DR will affect vision and lead to blindness in end-stages, when it is too late for effective treatment (Stefánsson et al., 2000). Therefore, timely and active

screening and early intervention are critical. Among most widely practised interventions for diabetes, only diabetic retinopathy screening, treatment and pre-conception care were proven to have a "clearly cost-saving" effect (Klonoff and Schwartz, 2000, Jones and Edwards, 2010). Regular eye care services for diabetic patients has also been recommended as essential in the management of DR, this followed by appropriate laser treatment if required (World Health Organization, 2006). Many developed countries have initiated retinal screening to detect the onset of progression of DR. In the UK, DR is the only ocular disease that is actively screened for. Both type 1 and type 2 diabetic patients aged 12 years old are offered annual retinal examination through the National Health Service (NHS) diabetic retinopathy screening program (The Royal College of Ophthalmologists, 2012). In many developing countries, however, DR has been largely neglected in health-care research and planning, and the proportion of recommended eye care among diabetic patients is not optimal (Zheng et al., 2012, Burgess et al., 2013). In China, annual screening of DR in diabetic patients has been recommended by the national diagnosis and treatment guidelines for DR (Chinese Ophthalmological Society, 2014). Some economically developed areas have made annual DR screening free in the primary health care system. However, this is not a common case across the whole country, especially in poor and rural areas, where the need for adequate DR eye care still remains largely unmet (Vela et al., 2012, Wang et al., 2010a). With this said, the proportion of diabetic patients undergoing annual eye examinations has not been estimated in China, it may be speculated as lower than that in the United States, where this proportion was only 40%-50% (Peng et al., 2011). Increasing the proportion of diabetic patients receiving regular eye examination is one of the vision goals set out in the latest national eye health plan for 2016-2020 (National Health and Family Planning Commission of the People's Republic of China, 2016). Although DR screening is generally performed in office, telemedicine or a wholly automated approach with the assistance of artificial intelligence could largely reduce cost and grading workload, especially in settings where availability of regular screening for DR may be inadequate, and access to trained ophthalmic professionals may be limited (Ting et al., 2016, Jones and Edwards, 2010, Mansberger et al., 2015).

For individuals with DR, it is still possible to prevent further visual impairment and blindness, this outcome mainly depending on the timing of treatment (Stefánsson et al., 2000, Mohamed et al., 2007). Present guidelines for optimum eye care of patients with diabetes are tight glycemic and blood pressure control in conjunction with timely laser therapy as needed. Laser treatment for PDR has been available more than five decades ago (Neubauer and Ulbig, 2007, Stefánsson et al., 2000), and its effectiveness at reducing the risk of visual impairment and blindness in patients with PDR or DMO has been well established in previous studies (Group,

1981, Early Treatment Diabetic Retinopathy Study Research Group, 1991a, Ferris III, 1993). Although laser treatment is a remarkable success, it is, however, frequently associated with visual field reduction and other ocular side-effects and, thus any new effective therapies for treatment may of potentials to be important advances (Aiello, 2003).

In recent years, several new treatment approaches have emerged, including vitreoretinal surgery and intravitreal administration of anti-vascular endothelial growth factor (VEGF) for patients with PDR (Elman et al., 2010). Vitreoretinal surgery has an important role in managing advanced PDR, including extensive haemorrhage in or behind the vitreous cavity or a fibrous mass, tractional retinal detachment and severe fibrovascular proliferation, and most patients will benefit from good visual outcomes after the surgery (Newman, 2010, Yorston et al., 2008). However, some significant post-operative complications may occur, including cataract formation, recurrent vitreous haemorrhages and rhegmatogenous retinal detachment, etc. (Newman, 2010). The use of intravitreal anti-VEGF as a preoperative adjunct before vitrectomy surgery has shown some benefit (Yang et al., 2008, Rizzo et al., 2008, Da R Lucena et al., 2009). Moreover, anti-VEGF agents are also beneficial in the treatment of PDR and DMO, especially in cases with neovascular glaucoma and persistent vitreous haemorrhage (Osaadon et al., 2014, Simó and Hernandez, 2008). However, the high cost may limit its applications, especially in low-income settings.

7.3 Methodological strengths and limitations

One of the most important issues in reliable estimation of the prevalence and burden of AREDs is the source of information. Several nationally representative or large-scale investigations in China have reported the epidemiology of cataract and glaucoma, however, the assessments of cataract and glaucoma were based on self-reporting, as is the case for the great majority of investigated diseases in those studies (Popkin et al., 2009, Zhao et al., 2012). Although self-reported data provide valuable information in epidemiological studies, the self-reported physician diagnosed-based prevalence estimates might represent a considerable underestimation, or suffer from retrospective biases. To avoid the shortcomings of self-reported data, only studies that specifically assessed the presence of AREDs by using professional equipment were eligible for inclusion in the systematic reviews. From the methodological perspective, this project provides an example and a strong incentive to utilise the large volume of Chinese literature in understanding the epidemiology of diseases in China. By performing comprehensive literature search in a wide array of databases (including grey

literature), additional reference search, dual systematic review and data extraction, I made extensive efforts to minimise the potential bias in the study identification stage. Therefore, the reviews of those projects are likely to represent the most complete data to address the prevalence of AREDs in China from 1990 onwards. During the study selection process, bias that might arise from inconsistent disease definitions and sampling methods was intensively minimised by using stringent inclusion and exclusion criteria. The quality of the included studies was also assessed, and all the included studies had at least moderate quality scores, as assessed by the STROBE guideline.

Meta-analysis represents a manner of combining results from different studies. In the most basic (or simplest) form, meta-analysis could identify a common effect of interest in all studies (Impellizzeri and Bizzini, 2012). Given the descriptive nature of this study, only observational studies are included. In observational studies, stratum-specific prevalence is commonly reported. For example, age subgroup analysis is commonly presented to illustrate how the epidemiological parameters differ by age (Flaxman et al., 2015). In this thesis, I aimed to make full use of information that could be extracted from the eligible studies. Wherever available, stratum-specific prevalence data were extracted in the data extraction stage, which can be seen as a methodological innovation compared with previous systematic reviews on the prevalence of AREDs in China (glaucoma and DR) (Cheng et al., 2013a, Liu et al., 2012). However, a typical concern with this hierarchical data structure is the considerable amount of heterogeneity between and within studies, especially when the reported age groups are not homogeneous. Although heterogeneity appears to be the norm rather than exception in meta-analyses of observational studies, high amounts of heterogeneity across the included studies could be reasonably reduced by sub-group meta-analysis or meta-regression (Thompson and Higgins, 2002, Borenstein et al., 2009). In this study, the individual associations of AREDs prevalence and multiple factors (age, sex, geographic factors, etc.) were extensively explored using the extracted stratum-specific prevalence data points, based on which a substantial amount of heterogeneity could be explained and the stratum-specific prevalence could be modelled. The exploration of sources of heterogeneity in different strata can be seen as an important function of these meta-analyses and one strength of this work. However, it should be noted that no causal interpretations of the observed associations between AREDs and other factors (age, sex, geographic factors, etc.) could be made due to the cross-sectional nature of this study. Other limitations adherent to each project have been previously stated within the respective chapters (Chapters 3-6).

Despite the increased amount of published meta-analyses of disease prevalence and the existence of reporting guidelines (e.g., PRISMA, GATHER), the absence of a consensus on the ways of conducting a meta-analysis of prevalence is apparent in the literature and represents a large barrier to standardising the research pathway in this research field (Barendregt et al., 2013, Kawasaki et al., 2010, Yau et al., 2012, Tham et al., 2014, Wong et al., 2014, Stroup et al., 2000, Murad and Wang, 2017). The study approach, as adopted throughout this thesis, has been previously promoted by the Global Health Epidemiology Research Group (GHERG) (Chan et al., 2017, Chan et al., 2013). By systematically demonstrating the process of estimating prevalence and burden of diseases, this thesis set out with the intention of being an example of synthesising epidemiological evidence within the same country. The development of a guideline for conducting the meta-analysis of prevalence is recommended as a priority for the future research direction.

Important sources of bias in this study could have arisen in two ways: inadequate amount of information from the included studies and poor ability to control confounding factors. Although only individual studies that were conducted in samples with general characteristics (general population for the AMD, glaucoma and cataract projects, and DM patients for the DR project) were included, the included studies were not evenly distributed across the whole country. If the prevalence of AREDs in a specific group of people is particularly high or low, the inclusion of individual studies that were conducted in such groups could have resulted in a selection bias, especially when the characteristics of those groups were not able to be evaluated (e.g., ethnicity). When assessing the potentially associated factors of AREDs, the number of available variables was limited, largely restricting the analyses that could be conducted for different risk strata. In the projects of AMD, glaucoma and cataract, the available variables were all stratum- or study-level characteristics, including age, sex, setting, geographic features (location, latitude, longitude, etc.), individual-level characteristics were not able to be evaluated. Even when individual-level factors were available for synthesis, as in the DR project, the selection of risk factors for meta-analysis was still largely restricted by the limited information extracted from the included studies. Therefore, when distributing the national burden into different geographic regions, not all confounding factors of AREDs were controlled, which could influence the accuracy of regional estimation to some extent.

7.4 Suggestions for future work

Generally, meta-analyses were conducted using aggregated results from individual studies. On the other hand, meta-analyses could be performed based on individual participant data, where the full dataset of each individual study should be requested from researchers (Stewart and Tierney, 2002). Apparently, this kind of meta-analysis with data coming from the individual level could largely overcome the above-mentioned methodological limitations and is recognised as with higher quality compared with the aggregate-level meta-analysis. However, the process of collecting individual-level data from researchers could be extremely time consuming and heavily rely on the researchers' willingness for cooperation. In some cases, the final database might only include a minority of all the eligible studies, which was the reason why this approach was not considered in this thesis. With more epidemiological investigations being performed, the updated meta-analysis of AREDs prevalence in China could definitely benefit from a larger amount of eligible studies. If time and funding allow, an individual participant data-based meta-analysis of all eligible studies or a nationally representative investigation are probably more accurate and more appropriate approaches to addressing the epidemiology of AREDs in China.

As stated in each project chapter, there is a need to improve the application of international classifications or grading systems in Chinese research society, such as the WARMGS (Wisconsin age-related maculopathy grading system) for AMD and the comprehensive LOCS (Lens Opacities Classification System) for cataract (Klein et al., 1991, Chylack et al., 1988, Chylack et al., 1989, Chylack et al., 1993). This could make the comparison of ARESs in China and other countries a possibility and reduce the bias introduced by methodological disparity to a large extent. Due to the existence of several subtypes of AREDs, it is also important that future epidemiological studies on AREDs focus on all of these, whenever possible. Moreover, standardised reporting should be advocated in future research, with adherence to relevant guidelines or checklists (Von Elm et al., 2007). This should not be only restricted to studies on the topic of AREDs or Chinese epidemiological investigations, but also applicable to all kinds of observational studies across the international research society.

During the dramatic ageing process in China, the epidemiology of many other degenerative diseases is also worthy of further assessment, such as osteoporosis, Parkinson's disease and rheumatoid arthritis. By using the study approaches demonstrated in this thesis, the prevalence and disease burden of major NCDs in China will be evaluated one by one, based on which a

complete picture of disease burden on NCDs for China will be portrayed in the foreseeable future.

7.5 Conclusions

In conclusion, this thesis demonstrates a comprehensive estimation of the prevalence and burden of AREDs in China. By systematically incorporating data from published population-based studies on AREDs in China, the prevalence and burden of AMD, glaucoma and cataract were successfully estimated for the period between 1990 and 2015 and projected to 2050. The prevalence and burden of DR were estimated for the year 2010. In addition, the variations of AREDs prevalence by demographics, geographic features and other associated factors were assessed, based on which the subnational/regional prevalence and burden of AREDs were generated.

According to the results in this thesis, the most common feature of the four AREDs is that they are all highly age-related. Given the ageing trend in China in the next decades, as presented in Chapter 1, the prevalence and burden of AREDs will continue to increase. More elaborate epidemiological studies are needed to optimise public health strategies for mitigating this important health problem. Primary and secondary prevention, treatment and effective government response are urgently needed to optimise public health strategies for mitigating this important health problem.

References

ABDELKADER, H., ALANY, R. G. & PIERSCIONEK, B. 2015. Age-related cataract and drug therapy: opportunities and challenges for topical antioxidant delivery to the lens. *Journal of Pharmacy and Pharmacology,* 67**,** 537-550.

ABRAHAM, A. G., CONDON, N. G. & GOWER, E. W. 2006. The new epidemiology of cataract. *Ophthalmology Clinics of North America,* 19**,** 415-425.

ACCESS ECONOMICS 2010. Clear focus: the economic impact of vision loss in Australia in 2009. Vision 2020.

ADELOYE, D., CHUA, S., LEE, C., BASQUILL, C., PAPANA, A., THEODORATOU, E., NAIR, H., GASEVIC, D., SRIDHAR, D., CAMPBELL, H., CHAN, K. Y., SHEIKH, A., RUDAN, I. & GLOBAL HEALTH EPIDEMIOLOGY REFERENCE GROUP (GHERG) 2015. Global and regional estimates of COPD prevalence: Systematic review and meta–analysis. *Journal of Global Health,* 5**,** 020415.

AGARWAL, S., AGARWAL, A. & APPLE, D. J. 2002. *Textbook of ophthalmology,* New Delhi, Jaypee Brothers Publishers.

AGE-RELATED EYE DISEASE STUDY RESEARCH GROUP 2001a. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. *Archives of Ophthalmology,* 119**,** 1417-1436.

AGE-RELATED EYE DISEASE STUDY RESEARCH GROUP 2001b. Risk factors associated with age-related nuclear and cortical cataract: a case-control study in the age-related eye disease study, AREDS report No. 5. *Ophthalmology,* 108**,** 1400-1408.

AGRAWAL, S., JOSHI, M. & CHRISTOFORIDIS, J. B. 2013. Vitreous inflammation associated with intravitreal anti-VEGF pharmacotherapy. *Mediators of Inflammation,* 2013.

AIELLO, L. M. 2003. Perspectives on diabetic retinopathy. *American Journal of Ophthalmology,* 136**,** 122-135.

ALWAN, A. 2011. *Global status report on noncommunicable diseases 2010,* Geneva, World Health Organization.

ASBELL, P. A., DUALAN, I., MINDEL, J., BROCKS, D., AHMAD, M. & EPSTEIN, S. 2005. Age-related cataract. *The Lancet,* 365**,** 599-609.

ATAL, I., ZEITOUN, J.-D., NÉVÉOL, A., RAVAUD, P., PORCHER, R. & TRINQUART, L. 2016. Automatic classification of registered clinical trials towards the Global Burden of Diseases taxonomy of diseases and injuries. *BMC Bioinformatics,* 17**,** 392.

ATTANÉ, I. 2016. Second Child Decisions in China. *Population and Development Review,* 42**,** 519-536.

AUGOOD, C. A., VINGERLING, J. R., DE JONG, P. T., CHAKRAVARTHY, U., SELAND, J., SOUBRANE, G., TOMAZZOLI, L., TOPOUZIS, F., BENTHAM, G., RAHU, M., VIOQUE, J., YOUNG, I. S. & FLETCHER, A. E. 2006. Prevalence of age-related maculopathy in older Europeans: the European Eye Study (EUREYE). *Archives of Ophthalmology,* 124**,** 529-535.

BAKER, H. 2008. *Glaucoma Awareness.* Doctor of Philosophy, University College London.

BANISTER, J., BLOOM, D. E. & ROSENBERG, L. 2012. Population aging and economic growth in China. *The Chinese Economy.* Springer.

BAO, Y., CAO, X., LI, X., CHEN, J., HU, J. & ZHU, T. 2008. Prevalence of age-related cataract among adults aged 50 and above in four rural areas in western China. *Chinese Medical Journal (中华医学杂志),* 88**,** 1697-1702.

BARENDREGT, J. J., DOI, S. A., LEE, Y. Y., NORMAN, R. E. & VOS, T. 2013. Meta-analysis of prevalence. *Journal of Epidemiology and Community Health,* 67**,** 974-978.

BARTON, K. & HITCHINGS, R. A. 2013. Medical management of glaucoma. *Medical Management of Glaucoma.* New York: Springer.

BATEMAN, D., CLARK, R., AZUARA-BLANCO, A., BAIN, M. & FORREST, J. 2002. The effects of new topical treatments on management of glaucoma in Scotland: an examination of ophthalmological health care. *British Journal of Ophthalmology,* 86**,** 551-554.

BEARD, J. R., OFFICER, A., DE CARVALHO, I. A., SADANA, R., POT, A. M., MICHEL, J.-P., LLOYD-SHERLOCK, P., EPPING-JORDAN, J. E., PEETERS, G. G., MAHANANI, W. R., THIYAGARAJAN, J. A. & CHATTERJI, S. 2016. The World report on ageing and health: a policy framework for healthy ageing. *The Lancet,* 387**,** 2145-2154.

BEGG, C. B. & MAZUMDAR, M. 1994. Operating characteristics of a rank correlation test for publication bias. *Biometrics,* 50**,** 1088-1101.

BIRD, A., BRESSLER, N., BRESSLER, S., CHISHOLM, I., COSCAS, G., DAVIS, M., DE JONG, P., KLAVER, C., KLEIN, B., KLEIN, R., MITCHELL, P., SARKS, J., SARKS, S., SOUBRANE, G., TAYLOR, H., VINGERLING, J. & INTERNATIONAL ARM EPIDEMIOLOGICAL STUDY GROUP 1995. An international classification and grading system for age-related maculopathy and age-related macular degeneration. *Survey of Ophthalmology,* 39**,** 367-374.

BLUMENKRANZ, M. S., BRESSLER, N. M., BRESSLER, S. B., DONATI, G., FISH, G. E., HAYNES, L. A., LEWIS, H., MILLER, J. W., MONÉS, J. M. & POTTER, M. J. 2002. Verteporfin therapy for subfoveal choroidal neovascularization in age-related macular degeneration: three-year results of an open-label extension of 2 randomized clinical trials--TAP Report no. 5. *Archives of Ophthalmology,* 120**,** 1307-1314.

BOLAND, M. V. & QUIGLEY, H. A. 2007. Risk factors and open-angle glaucoma: classification and application. *Journal of Glaucoma,* 16**,** 406-418.

BONASTRE, J., LE PEN, C., ANDERSON, P., GANZ, A., BERTO, P. & BERDEAUX, G. 2002. The epidemiology, economics and quality of life burden of age-related macular

degeneration in France, Germany, Italy and the United Kingdom. *The European Journal of Health Economics,* 3**,** 94-102.

BONGAARTS, J. 2009. Human population growth and the demographic transition. *Philosophical Transactions of the Royal Society of London B: Biological Sciences,* 364**,** 2985-2990.

BONNEL, S., MOHAND-SAID, S. & SAHEL, J.-A. 2003. The aging of the retina. *Experimental Gerontology,* 38**,** 825-831.

BONOVAS, S., PEPONIS, V. & FILIOUSSI, K. 2004. Diabetes mellitus as a risk factor for primary open‐angle glaucoma: a meta‐analysis. *Diabetic Medicine,* 21**,** 609-614.

BORENSTEIN, M., HEDGES, L. V., HIGGINS, J. & ROTHSTEIN, H. R. 2009. *Introduction to Meta-Analysis,* Chichester, UK, Wiley Online Library.

BOURNE, R. R., FLAXMAN, S. R., BRAITHWAITE, T., CICINELLI, M. V., DAS, A., JONAS, J. B., KEEFFE, J., KEMPEN, J. H., LEASHER, J., LIMBURG, H., NAIDOO, K., PESUDOVS, K., RESNIKOFF, S., SILVESTER, A., STEVENS, G. A., TAHHAN, N., WONG, T. Y., TAYLOR, H. R. & VISION LOSS EXPERT GROUP 2017. Magnitude, temporal trends, and projections of the global prevalence of blindness and distance and near vision impairment: a systematic review and meta-analysis. *The Lancet Global Health,* 5**,** e888-e897.

BOURNE, R. R., STEVENS, G. A., WHITE, R. A., SMITH, J. L., FLAXMAN, S. R., PRICE, H., JONAS, J. B., KEEFFE, J., LEASHER, J., NAIDOO, K., PESUDOVS, K., RESNIKOFF, S., TAYLOR, H. R. & VISION LOSS EXPERT GROUP 2013. Causes of vision loss worldwide, 1990–2010: a systematic analysis. *The Lancet Global Health,* 1**,** e339-e349.

BRAGG, F., HOLMES, M. V., IONA, A., GUO, Y., DU, H., CHEN, Y., BIAN, Z., YANG, L., HERRINGTON, W., BENNETT, D., TURNBULL, I., LIU, Y., FENG, S., CHEN, J., CLARKE, R., COLLINS, R., PETO, R., LI, L., CHEN, Z. & CHINA KADOORIE BIOBANK COLLABORATIVE GROUP 2017. Association between diabetes and cause-specific mortality in rural and urban areas of China. *JAMA,* 317**,** 280-289.

BRECHNER, R. J., ROSENFELD, P. J., BABISH, J. D. & CAPLAN, S. 2011. Pharmacotherapy for neovascular age-related macular degeneration: an analysis of the 100% 2008 medicare fee-for-service part B claims file. *American Journal of Ophthalmology,* 151**,** 887-895. e1.

BRESSLER, N. M. 2002. Early detection and treatment of neovascular age-related macular degeneration. *The Journal of the American Board of Family Practice,* 15**,** 142-152.

BRIAN, G. & TAYLOR, H. 2001. Cataract blindness: challenges for the 21st century. *Bulletin of the World Health Organization,* 79**,** 249-256.

BRODY, B. L., GAMST, A. C., WILLIAMS, R. A., SMITH, A. R., LAU, P. W., DOLNAK, D., RAPAPORT, M. H., KAPLAN, R. M. & BROWN, S. I. 2001. Depression, visual acuity, comorbidity, and disability associated with age-related macular degeneration. *Ophthalmology,* 108**,** 1893-1900.

BROMAN, A. T., MUNOZ, B., RODRIGUEZ, J., SANCHEZ, R., QUIGLEY, H. A., KLEIN, R., SNYDER, R. & WEST, S. K. 2002. The impact of visual impairment and eye disease on vision-related quality of life in a Mexican-American population: Proyecto VER. *Investigative Ophthalmology & Visual Science,* 43**,** 3393-3398.

BRON, A., VRENSEN, G., KORETZ, J., MARAINI, G. & HARDING, J. 2000. The ageing lens. *Ophthalmologica,* 214**,** 86-104.

BROOKS, S. 1998. Markov chain Monte Carlo method and its application. *Journal of the Royal Statistical Society: Series D (the Statistician),* 47**,** 69-100.

BROWN, M. M., BROWN, G. C., STEIN, J. D., ROTH, Z., CAMPANELLA, J. & BEAUCHAMP, G. R. 2005. Age-related macular degeneration: economic burden and value-based medicine analysis. *Canadian Journal of Ophthalmology/Journal Canadien d'Ophtalmologie,* 40**,** 277-287.

BURGESS, P. I., MSUKWA, G. & BEARE, N. A. 2013. Diabetic retinopathy in sub-Saharan Africa: meeting the challenges of an emerging epidemic. *BMC Medicine,* 11**,** 157.

BURGOYNE, C. F. & MORRISON, J. C. 2001. The anatomy and pathophysiology of the optic nerve head in glaucoma. *Journal of Glaucoma,* 10**,** S16-S18.

BURR, J. M., MOWATT, G., HERNÁNDEZ, R., SIDDIQUI, M., COOK, J., LOURENCO, T., RAMSAY, C., VALE, L., FRASER, C., AZUARA-BLANCO, A., DEEKS, J., CAIRNS, J., WORMALD, R., MCPHERSON, S., RABINDRANATH, K. & GRANT, A. 2007. The clinical effectiveness and cost-effectiveness of screening for open angle glaucoma: a systematic review and economic evaluation. *Health Technology Assessment (Winchester, England),* 11**,** 1-190.

BUSBEE, B. G., BROWN, M. M., BROWN, G. C. & SHARMA, S. 2002. Incremental cost-effectiveness of initial cataract surgery. *Ophthalmology,* 109**,** 606-612.

BUSBEE, B. G., BROWN, M. M., BROWN, G. C. & SHARMA, S. 2003. Cost-utility analysis of cataract surgery in the second eye. *Ophthalmology,* 110**,** 2310-2317.

CACCIATORE, F., ABETE, P., MAGGI, S., LUCHETTI, G., CALABRESE, C., VIATI, L., LEOSCO, D., FERRARA, N., VITALE, D. F. & RENGO, F. 2004. Disability and 6-year mortality in elderly population. Role of visual impairment. *Aging Clinical and Experimental Research,* 16**,** 382-388.

CAI, F., GILES, J., O'KEEFE, P. & WANG, D. 2012. The elderly and old age support in rural China. Washington: The World Bank.

CANO, M., THIMMALAPPULA, R., FUJIHARA, M., NAGAI, N., SPORN, M., WANG, A. L., NEUFELD, A. H., BISWAL, S. & HANDA, J. T. 2010. Cigarette smoking, oxidative stress, the anti-oxidant response through Nrf2 signaling, and Age-related Macular Degeneration. *Vision Research,* 50**,** 652-664.

CASSON, R., NEWLAND, H., MUECKE, J., MCGOVERN, S., ABRAHAM, L., SHEIN, W., SELVA, D. & AUNG, T. 2007. Gonioscopy findings and prevalence of occludable angles in a Burmese population: the Meiktila Eye Study. *British Journal of Ophthalmology,* 91**,** 856-859.

CASTEN, R. J., ROVNER, B. W. & TASMAN, W. 2004. Age-related macular degeneration and depression: a review of recent research. *Current Opinion in Ophthalmology,* 15**,** 181-183.

CERULLI, L. & MISSIROLI, F. 2008. Aging of the Cornea. *Age-Related Changes of the Human Eye.* Springer.

CHADER, G. J. & TAYLOR, A. 2013. Preface: The Aging Eye: Normal Changes, Age-Related Diseases, and Sight-Saving ApproachesPreface: The Aging Eye. *Investigative Ophthalmology & Visual Science,* 54**,** ORSF1-ORSF4.

CHAKRAVARTHY, U., WONG, T. Y., FLETCHER, A., PIAULT, E., EVANS, C., ZLATEVA, G., BUGGAGE, R., PLEIL, A. & MITCHELL, P. 2010. Clinical risk factors for age-related macular degeneration: a systematic review and meta-analysis. *BMC Ophthalmology,* 10**,** 31.

CHAN, E. W. E., LI, X., THAM, Y.-C., LIAO, J., WONG, T. Y., AUNG, T. & CHENG, C.-Y. 2016. Glaucoma in Asia: regional prevalence variations and future projections. *British Journal of Ophthalmology,* 100**,** 78-85.

CHAN, K. Y., LI, X., CHEN, W., SONG, P., WONG, N. W. K., POON, A. N., JIAN, W., SOYIRI, I. N., COUSENS, S., ADELOYE, D., SHEIKH, A., CAMPBELL, H., RUDAN, I. & GLOBAL HEALTH EPIDEMIOLOGY RESEARCH GROUP 2017. Prevalence of chronic obstructive pulmonary disease (COPD) in China in 1990 and 2010. *Journal of Global Health,* 7**,** 020704.

CHAN, K. Y., WANG, W., WU, J. J., LIU, L., THEODORATOU, E., CAR, J., MIDDLETON, L., RUSS, T. C., DEARY, I. J., CAMPBELL, H., WANG, W., RUDAN, I. & GLOBAL HEALTH EPIDEMIOLOGY REFERENCE GROUP (GHERG) 2013. Epidemiology of Alzheimer's disease and other forms of dementia in China, 1990–2010: a systematic review and analysis. *The Lancet,* 381**,** 2016-2023.

CHEN, X., CHEN, C., ZHANG, Y., YUAN, R. & JIAN, Y. 2011. The effect of health insurance reform on the number of cataract surgeries in Chongqing, China. *BMC health services research,* 11**,** 67.

CHEN, Y., BEDELL, M. & ZHANG, K. 2010. Age-related macular degeneration: genetic and environmental factors of disease. *Molecular Interventions,* 10**,** 271–281.

CHENG, J.-W., CHENG, S.-W., MA, X.-Y., CAI, J.-P., LI, Y. & WEI, R.-L. 2013a. The prevalence of primary glaucoma in mainland China: a systematic review and meta-analysis. *Journal of Glaucoma,* 22**,** 301-306.

CHENG, J.-W., ZONG, Y., ZENG, Y.-Y. & WEI, R.-L. 2014. The prevalence of primary angle closure glaucoma in adult Asians: a systematic review and meta-analysis. *PLOS ONE,* 9**,** e103222.

CHENG, Y. J., IMPERATORE, G., GEISS, L. S., WANG, J., SAYDAH, S. H., COWIE, C. C. & GREGG, E. W. 2013b. Secular changes in the age-specific prevalence of diabetes among US adults: 1988–2010. *Diabetes Care,* 36**,** 2690-2696.

CHEUNG, C. M. G., LI, X., CHENG, C.-Y., ZHENG, Y., MITCHELL, P., WANG, J. J., JONAS, J. B., NANGIA, V. & WONG, T. Y. 2013. Prevalence and risk factors for

age-related macular degeneration in Indians: a comparative study in Singapore and India. *American Journal of Ophthalmology,* 155**,** 764-773. e3.

CHEUNG, N., MITCHELL, P. & WONG, T. Y. 2010. Diabetic retinopathy. *The Lancet,* 376**,** 124-136.

CHINA DISABLED PERSON'S FEDERATION (CDPF) 2005. Statistics Yearbook on the Undertakings of People with Disabilities in China. Beijing: CDPF Information Cente.

CHINA MEDICAL ASSOCIATION 1987. Age-related Macular Degeneration Clinical Diagnosis Standard (老年性黄斑变性临床诊断标准). *Chinese Journal of Ophthalmology (中华眼科杂志),* 23**,** F02.

CHINESE OPHTHALMOLOGICAL SOCIETY 2014. Retinopathy Working Group: diagnosis and treatment guideline of diabetic retinopathy. *Chinese Journal of Ophthalmology,* 50**,** 851-865.

CHO, H. & SOBRIN, L. 2014. Genetics of diabetic retinopathy. *Current Diabetes Reports,* 14**,** 515.

CHONG, E. W., WONG, T. Y., KREIS, A. J., SIMPSON, J. A. & GUYMER, R. H. 2007. Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis. *BMJ: British Medical Journal,* 335**,** 755.

CHOUKHMANE, T., COEURDACIER, N. & JIN, K. 2013. *The one-child policy and household savings. CEPR Discussion Paper No. DP9688.* [Online]. Available: https://ssrn.com/abstract=2341051 [Accessed 01/08/2018.

CHU, L.-W. & CHI, I. 2008. Nursing homes in China. *Journal of the American Medical Directors Association,* 9**,** 237-243.

CHYLACK, L. T., LESKE, M. C., MCCARTHY, D., KHU, P., KASHIWAGI, T. & SPERDUTO, R. 1989. Lens opacities classification system II (LOCS II). *Archives of Ophthalmology,* 107**,** 991-997.

CHYLACK, L. T., LESKE, M. C., SPERDUTO, R., KHU, P. & MCCARTHY, D. 1988. Lens opacities classification system. *Archives of Ophthalmology,* 106**,** 330-334.

CHYLACK, L. T., WOLFE, J. K., SINGER, D. M., LESKE, M. C., BULLIMORE, M. A., BAILEY, I. L., FRIEND, J., MCCARTHY, D. & WU, S.-Y. 1993. The lens opacities classification system III. *Archives of Ophthalmology,* 111**,** 831-836.

COHEN, J. F., KOREVAAR, D. A., WANG, J., SPIJKER, R. & BOSSUYT, P. M. 2015. Should we search Chinese biomedical databases when performing systematic reviews? *Systematic reviews,* 4**,** 23.

COLEMAN, H. R., CHAN, C.-C., FERRIS, F. L. & CHEW, E. Y. 2008. Age-related macular degeneration. *The Lancet,* 372**,** 1835-1845.

COMPARISON OF AGE-RELATED MACULAR DEGENERATION TREATMENTS TRIALS (CATT) RESEARCH GROUP, MARTIN, D. F., MAGUIRE, M. G., FINE, S. L., YING, G.-S., JAFFE, G. J., GRUNWALD, J. E., TOTH, C., REDFORD, M. &

FERRIS, F. L. 2012. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. *Ophthalmology,* 119**,** 1388-1398.

CONGDON, N., FOSTER, P., WAMSLEY, S., GUTMARK, J., NOLAN, W., SEAH, S., JOHNSON, G. & BROMAN, A. 2002. Biometric gonioscopy and the effects of age, race, and sex on the anterior chamber angle. *British Journal of Ophthalmology,* 86**,** 18-22.

CONGDON, N., VINGERLING, J., KLEIN, B., WEST, S., FRIEDMAN, D., KEMPEN, J., O'COLMAIN, B., WU, S., TAYLOR, H. & EYE DISEASES PREVALENCE RESEARCH GROUP 2004. Prevalence of cataract and pseudophakia/aphakia among adults in the United States. *Archives of Ophthalmology,* 122**,** 487-494.

CONGDON, N. G. & FRIEDMAN, D. S. 2003. Angle-closure glaucoma: impact, etiology, diagnosis, and treatment. *Current Opinion in Ophthalmology,* 14**,** 70-73.

COOK, D. J., MULROW, C. D. & HAYNES, R. B. 1997. Systematic reviews: synthesis of best evidence for clinical decisions. *Annals of Internal Medicine,* 126**,** 376-380.

COOK, H., PATEL, P. & TUFAIL, A. 2008. Age-related macular degeneration: diagnosis and management. *British Medical Bulletin,* 85**,** 127-149.

COOPER, H. M. 2016. *Research synthesis and meta-analysis: A step-by-step approach*, SAGE Publications.

COPETTI, M., FONTANA, A., GRAZIANO, G., VENEZIANI, F., SIENA, F., SCARDAPANE, M., LUCISANO, G. & PELLEGRINI, F. 2013. Advances in meta-analysis: Examples from internal medicine to neurology. *Neuroepidemiology,* 42**,** 59-67.

CORCÓSTEGUI, B., DURÁN, S., GONZÁLEZ-ALBARRÁN, M. O., HERNÁNDEZ, C., RUIZ-MORENO, J. M., SALVADOR, J., UDAONDO, P. & SIMÓ, R. 2017. Update on diagnosis and treatment of diabetic retinopathy: a consensus guideline of the working group of ocular health (Spanish Society of Diabetes and Spanish Vitreous and Retina Society). *Journal of Ophthalmology,* 2017.

CORREIA, C., LOPEZ, K. J., WROBLEWSKI, K. E., HUISINGH‐SCHEETZ, M., KERN, D. W., CHEN, R. C., SCHUMM, L. P., DALE, W., MCCLINTOCK, M. K. & PINTO, J. M. 2016. Global Sensory Impairment in Older Adults in the United States. *Journal of the American Geriatrics Society,* 64**,** 306-313.

CROWSTON, J. G. & WEINREB, R. N. 2005. Glaucoma medication and aqueous humor dynamics. *Current Opinion in Ophthalmology,* 16**,** 94-100.

CRUESS, A., ZLATEVA, G., XU, X. & ROCHON, S. 2007. Burden of illness of neovascular age-related macular degeneration in Canada. *Canadian Journal of Ophthalmology/Journal Canadien d'Ophtalmologie,* 42**,** 836-843.

CRUESS, A. F., ZLATEVA, G., XU, X., SOUBRANE, G., PAULEIKHOFF, D., LOTERY, A., MONES, J., BUGGAGE, R., SCHAEFER, C., KNIGHT, T. & GOSS, T. F. 2008. Economic Burden of Bilateral Neovascular Age-Related Macular Degeneration. *PharmacoEconomics,* 26**,** 57-73.

CRUICKSHANKS, K. J., KLEIN, R., KLEIN, B. E. & NONDAHL, D. M. 2001. Sunlight and the 5-year incidence of early age-related maculopathy: the beaver dam eye study. *Archives of Ophthalmology,* 119**,** 246-250.

DA R LUCENA, D., RIBEIRO, J. A., COSTA, R. A., BARBOSA, J. C., SCOTT, I. U., DE FIGUEIREDO-PONTES, L. L. & JORGE, R. 2009. Intraoperative bleeding during vitrectomy for diabetic tractional retinal detachment with versus without preoperative intravitreal bevacizumab (IBeTra study). *British Journal of Ophthalmology,* 93**,** 688-691.

DAMICO, F. M., GASPARIN, F., SCOLARI, M. R., PEDRAL, L. S. & TAKAHASHI, B. S. 2012. New approaches and potential treatments for dry age-related macular degeneration. *Arquivos Brasileiros De Oftalmologia,* 75**,** 71-75.

DAN, A., RAUBVOGEL, G., CHEN, T., YE, T., JIN, L., XIAO, B., SANCHEZ, A. & CONGDON, N. 2015. The impact of multimedia education on uptake of comprehensive eye examinations in rural China: a randomized, controlled trial. *Ophthalmic epidemiology,* 22**,** 283-290.

DANDONA, L. & DANDONA, R. 2006. What is the global burden of visual impairment? *BMC Medicine,* 4**,** 6.

DAS, B., THOMPSON, J., PATEL, R. & ROSENTHAL, A. 1994. The prevalence of eye disease in Leicester: a comparison of adults of Asian and European descent. *Journal of the Royal Society of Medicine,* 87**,** 219-222.

DE JONG, P. T. 2006. Age-related macular degeneration. *New England Journal of Medicine,* 355**,** 1474-1485.

DEFO, B. K. 2014. Demographic, epidemiological, and health transitions: are they relevant to population health patterns in Africa? *Global Health Action,* 7**,** 22443.

DELCOURT, C., MICHEL, F., COLVEZ, A., LACROUX, A., DELAGE, M. & VERNET, M.-H. 2001. Associations of cardiovascular disease and its risk factors with age-related macular degeneration: the POLA study. *Ophthalmic Epidemiology,* 8**,** 237-249.

DEPARTMENT OF AGEING AND LIFE COURSE, WORLD HEALTH ORGANIZATION 2015. China country assessment report on ageing and health. Geneva: World Health Organization.

DIABETES CONTROL AND COMPLICATIONS TRIAL RESEARCH GROUP 1997. Clustering of long-term complications in families with diabetes in the diabetes control and complications trial. *Diabetes,* 46**,** 1829-1839.

DING, J. & WONG, T. Y. 2012. Current epidemiology of diabetic retinopathy and diabetic macular edema. *Current Diabetes Reports,* 12**,** 346-354.

DIXON-WOODS, M., AGARWAL, S., JONES, D., YOUNG, B. & SUTTON, A. 2005. Synthesising qualitative and quantitative evidence: a review of possible methods. *Journal of Health Services Research & Policy,* 10**,** 45-53.

EARLY TREATMENT DIABETIC RETINOPATHY STUDY RESEARCH GROUP 1991a. Early photocoagulation for diabetic retinopathy: ETDRS report number 9. *Ophthalmology,* 98**,** 766-785.

EARLY TREATMENT DIABETIC RETINOPATHY STUDY RESEARCH GROUP 1991b. Grading diabetic retinopathy from stereoscopic color fundus photographs-an extension of the modified Airlie House classification: ETDRS report number 10. *Ophthalmology,* 98**,** 786-806.

EGGER, M., DAVEY-SMITH, G. & ALTMAN, D. 2008. *Systematic reviews in health care: meta-analysis in context*, London, BMJ Publishing Group.

EGGER, M., SCHNEIDER, M. & SMITH, G. D. 1998. Spurious precision? meta-analysis of observational studies. *BMJ: British Medical Journal,* 316**,** 140-144.

EGGER, M., SMITH, G. D., SCHNEIDER, M. & MINDER, C. 1997. Bias in meta-analysis detected by a simple, graphical test. *BMJ: British Medical Journal,* 315**,** 629-634.

ELMAN, M. J., AIELLO, L. P., BECK, R. W., BRESSLER, N. M., BRESSLER, S. B., EDWARDS, A. R., FERRIS, F. L., FRIEDMAN, S. M., GLASSMAN, A. R. & MILLER, K. M. 2010. Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema. *Ophthalmology,* 117**,** 1064-1077. e35.

ERKE, M. G., BERTELSEN, G., PETO, T., SJØLIE, A. K., LINDEKLEIV, H. & NJØLSTAD, I. 2014. Cardiovascular risk factors associated with age-related macular degeneration: the Tromsø Study. *Acta Ophthalmologica,* 92**,** 662-669.

EVANS, J. B. & SYED, B. A. 2013. New hope for dry AMD? *Nature Reviews Drug Discovery,* 12**,** 501-502.

EVANS, J. R. & LAWRENSON, J. G. 2012. Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration. *Cochrane Database of Systematic Reviews*.

EYE DISEASES PREVALENCE RESEARCH GROUP 2004a. Prevalence of age-related macular degeneration in the United States. *Archives of Ophthalmology,* 122**,** 564-572.

EYE DISEASES PREVALENCE RESEARCH GROUP 2004b. Prevalence of open-angle glaucoma among adults in the United States. *Archives of Ophthalmology,* 122**,** 532-538.

FAIRCHILD, M. D. 2013. *Color appearance models*, Chichester, John Wiley & Sons.

FANG, J., WANG, X., LIN, Z., YAN, J., YANG, Y. & LI, J. 2010. Variation of cataract surgery costs in four different graded providers of China. *BMC Public Health,* 10**,** 543.

FARIA, B. M., DUMAN, F., ZHENG, C. X., WAISBOURD, M., GUPTA, L., ALI, M., ZANGALLI, C., LU, L., WIZOV, S. S., SPAETH, E., RICHMAN, J. & SPAETH, G. L. 2015. Evaluating contrast sensitivity in age-related macular degeneration using a novel computer-based test, the spaeth/richman contrast sensitivity test. *Retina,* 35**,** 1465-1473.

FERRIS III, F. L. 1993. How effective are treatments for diabetic retinopathy? *JAMA,* 269**,** 1290-1291.

FERRIS III, F. L., WILKINSON, C., BIRD, A., CHAKRAVARTHY, U., CHEW, E., CSAKY, K., SADDA, S. R. & BECKMAN INITIATIVE FOR MACULAR RESEARCH CLASSIFICATION COMMITTEE 2013. Clinical classification of age-related macular degeneration. *Ophthalmology,* 120**,** 844-851.

FLAXMAN, A. D., VOS, D. T. & MURRAY, C. J. 2015. *An integrative metaregression framework for descriptive epidemiology,* Seattle, University of Washington Press.

FLETCHER, A. E., BENTHAM, G. C., AGNEW, M., YOUNG, I. S., AUGOOD, C., CHAKRAVARTHY, U., DE JONG, P. T., RAHU, M., SELAND, J. & SOUBRANE, G. 2008. Sunlight exposure, antioxidants, and age-related macular degeneration. *Archives of Ophthalmology,* 126**,** 1396-1403.

FOSTER, P. J., BUHRMANN, R., QUIGLEY, H. A. & JOHNSON, G. J. 2002. The definition and classification of glaucoma in prevalence surveys. *British Journal of Ophthalmology,* 86**,** 238-242.

FOSTER, P. J. & JOHNSON, G. J. 2001. Glaucoma in China: how big is the problem? *British Journal of Ophthalmology,* 85**,** 1277-1282.

FOSTER, P. J., OEN, F. T., MACHIN, D., NG, T.-P., DEVEREUX, J. G., JOHNSON, G. J., KHAW, P. T. & SEAH, S. K. 2000. The prevalence of glaucoma in Chinese residents of Singapore: a cross-sectional population survey of the Tanjong Pagar district. *Archives of Ophthalmology,* 118**,** 1105-1111.

FOWKES, F. G. R., RUDAN, D., RUDAN, I., ABOYANS, V., DENENBERG, J. O., MCDERMOTT, M. M., NORMAN, P. E., SAMPSON, U. K., WILLIAMS, L. J., MENSAH, G. A. & CRIQUI, M. H. 2013. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *The Lancet,* 382**,** 1329-1340.

FRANK, R. N. 2004. Diabetic retinopathy. *New England Journal of Medicine,* 350**,** 48-58.

FREEMAN, M. F. & TUKEY, J. W. 1950. Transformations related to the angular and the square root. *The Annals of Mathematical Statistics***,** 607-611.

FRIEDMAN, D. S., GAZZARD, G., MIN, C. B., BROMAN, A. T., QUIGLEY, H., TIELSCH, J., SEAH, S. & FOSTER, P. J. 2008. Age and sex variation in angle findings among normal Chinese subjects: a comparison of UBM, Scheimpflug, and gonioscopic assessment of the anterior chamber angle. *Journal of Glaucoma,* 17**,** 5-10.

FRIEDMAN, D. S., KATZ, J., BRESSLER, N. M., RAHMANI, B. & TIELSCH, J. M. 1999. Racial differences in the prevalence of age-related macular degeneration: The Baltimore eye survey11The authors have no proprietary interest in any of the instruments used in this study. *Ophthalmology,* 106**,** 1049-1055.

FUNG, I. C. 2008. Chinese journals: a guide for epidemiologists. *Emerging Themes in Epidemiology,* 5**,** 20.

GABELT, B. A. T. & KAUFMAN, P. L. 2005. Changes in aqueous humor dynamics with age and glaucoma. *Progress in Retinal and Eye Research,* 24**,** 612-637.

GAO, H. & HOLLYFIELD, J. 1992. Aging of the human retina. Differential loss of neurons and retinal pigment epithelial cells. *Investigative Ophthalmology & Visual Science,* 33**,** 1-17.

GBD 2015 DALYS AND HALE COLLABORATORS 2016. Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990-2015. *The Lancet,* 388**,** 1603-1658.

GBD 2015 DISEASE AND INJURY INCIDENCE AND PREVALENCE COLLABORATORS 2016. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet,* 388**,** 1545-1602.

GEHRS, K. M., ANDERSON, D. H., JOHNSON, L. V. & HAGEMAN, G. S. 2006. Age-related macular degeneration—emerging pathogenetic and therapeutic concepts. *Annals of Medicine,* 38**,** 450-471.

GOHDES, D. M., BALAMURUGAN, A., LARSEN, B. A. & MAYLAHN, C. 2005. Age-related eye diseases: an emerging challenge for public health professionals. *Preventing Chronic Disease,* 2.

GONG, P., LIANG, S., CARLTON, E. J., JIANG, Q., WU, J., WANG, L. & REMAIS, J. V. 2012. Urbanisation and health in China. *The Lancet,* 379**,** 843-852.

GOTTLIEB, J. L. 2002. Age-related macular degeneration. *JAMA,* 288**,** 2233-2236.

GROUP, A.-R. E. D. S. R. 2001. The Age-Related Eye Disease Study (AREDS) system for classifying cataracts from photographs: AREDS report no. 4. *American Journal of Ophthalmology,* 131**,** 167-175.

GROUP, A.-R. E. D. S. R. 2005. The Age-Related Eye Disease Study severity scale for age-related macular degeneration: AREDS report no. 17. *Archives of Ophthalmology,* 123**,** 1484–1498.

GROUP, D. R. S. R. 1981. Photocoagulation treatment of proliferative diabetic retinopathy: clinical application of Diabetic Retinopathy Study (DRS) findings, DRS Report Number 8. *Ophthalmology,* 88**,** 583-600.

GUAN, H. J., LU, H., DAI, Z., LI, M., WANG, Y., HU, J. Y., SHI, J., ZHAO, J. L., LEON, E., WANG, Y. & GAO, X. C. 2012. Prevalence and surgery status of cataract among adults aged 50 years or above in Qidong City of Jiangsu Province: the China Nine-Province Survey (我国九省眼病调查中江苏省启东市 50 岁及以上人群白内障患病率和手术状况的调查). *Chinese Journal of Ophthalmology (中华眼科杂志)***,** 219-225.

GUARIGUATA, L., WHITING, D. R., HAMBLETON, I., BEAGLEY, J., LINNENKAMP, U. & SHAW, J. E. 2014. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Research and Clinical Practice,* 103**,** 137-149.

GUILMOTO, C. Z. & JONES, G. W. 2015. *Contemporary Demographic Transformations in China, India and Indonesia,* Basel, Springer.

GUPTA, V. B., RAJAGOPALA, M. & RAVISHANKAR, B. 2014. Etiopathogenesis of cataract: an appraisal. *Indian Journal of Ophthalmology,* 62**,** 103-110.

HAIDICH, A. 2011. Meta-analysis in medical research. *Hippokratia,* 14**,** 29-37.

HAPPICH, M., REITBERGER, U., BREITSCHEIDEL, L., ULBIG, M. & WATKINS, J. 2008. The economic burden of diabetic retinopathy in Germany in 2002. *Graefe's Archive for Clinical and Experimental Ophthalmology,* 246**,** 151-159.

HASSAN, S. E., LOVIE-KITCHIN, J. E. & WOODS, R. L. 2002. Vision and mobility performance of subjects with age-related macular degeneration. *Optometry & Vision Science,* 79**,** 697-707.

HE, M., CHAN, V., BARUWA, E., GILBERT, D., FRICK, K. D. & CONGDON, N. 2007. Willingness to pay for cataract surgery in rural Southern China. *Ophthalmology,* 114**,** 411-416.

HE, M., FOSTER, P., JOHNSON, G. & KHAW, P. 2006. Angle-closure glaucoma in East Asian and European people. Different diseases? *Eye,* 20**,** 3-12.

HE, W., GOODKIND, D. & KOWAL, P. 2016. An aging world: 2015. Washington, DC: U.S. Government Publishing Office.

HECKE, M. V. V., DEKKER, J. M., STEHOUWER, C. D., POLAK, B. C., FULLER, J. H., SJOLIE, A. K., KOFINIS, A., ROTTIERS, R., PORTA, M. & CHATURVEDI, N. 2005. Diabetic retinopathy is associated with mortality and cardiovascular disease incidence. *Diabetes Care,* 28**,** 1383-1389.

HEIBA, I. M., ELSTON, R. C., KLEIN, B. E. & KLEIN, R. 1994. Sibling correlations and segregation analysis of age-related maculopathy: The beaver dam eye study. *Genetic Epidemiology,* 11**,** 51-67.

HERNÁNDEZ, R., RABINDRANATH, K., FRASER, C., VALE, L., BLANCO, A. A., BURR, J. M. & OAG SCREENING PROJECT GROUP 2008a. Screening for open angle glaucoma: systematic review of cost-effectiveness studies. *Journal of Glaucoma,* 17**,** 159-168.

HERNÁNDEZ, R. A., BURR, J. M. & VALE, L. D. 2008b. Economic evaluation of screening for open-angle glaucoma. *International Journal of Technology Assessment in Health Care,* 24**,** 203-211.

HESKETH, T., LU, L. & XING, Z. W. 2005. The effect of China's one-child family policy after 25 years. *New England Journal of Medicine,* 353**,** 1171-1176.

HIETALA, K., FORSBLOM, C., SUMMANEN, P., GROOP, P.-H. & FINNDIANE STUDY GROUP 2008. Heritability of proliferative diabetic retinopathy. *Diabetes,* 57**,** 2176-2180.

HIGGINS, J. & THOMPSON, S. G. 2002. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine,* 21**,** 1539-1558.

HIGGINS, J. P. & GREEN, S. 2008. *Cochrane handbook for systematic reviews of interventions*, Chichester, John Wiley & Sons.

HIGGINS, J. P., THOMPSON, S. G., DEEKS, J. J. & ALTMAN, D. G. 2003. Measuring inconsistency in meta-analyses. *BMJ: British Medical Journal*, 327**,** 557-560.

HOLZ, F. G., BELLMAN, C., STAUDT, S., SCHÜTT, F. & VÖLCKER, H. E. 2001. Fundus autofluorescence and development of geographic atrophy in age-related macular degeneration. *Investigative Ophthalmology & Visual Science*, 42**,** 1051-1056.

HOLZ, F. G., BINDEWALD-WITTICH, A., FLECKENSTEIN, M., DREYHAUPT, J., SCHOLL, H. P., SCHMITZ-VALCKENBERG, S. & FAM-STUDY GROUP 2007. Progression of geographic atrophy and impact of fundus autofluorescence patterns in age-related macular degeneration. *American Journal of Ophthalmology*, 143**,** 463-472. e2.

HOX, J. J., MOERBEEK, M. & VAN DE SCHOOT, R. 2010. *Multilevel analysis: Techniques and applications*, New York, Routledge.

HU, F. B., HANKINSON, S. E., STAMPFER, M. J., MANSON, J. E., COLDITZ, G. A., SPEIZER, F. E., HENNEKENS, C. H. & WILLETT, W. C. 2001. Prospective study of cataract extraction and risk of coronary heart disease in women. *American Journal of Epidemiology*, 153**,** 875-881.

HUANG, S., ZHENG, Y., FOSTER, P. J., HUANG, W. & HE, M. 2009. Prevalence and causes of visual impairment in Chinese adults in urban southern China: the Liwan Eye Study. *Archives of Ophthalmology*, 127**,** 1362-1367.

HUANG, W., ZHENG, Y., WANG, L., HUANG, S., LIU, B., JIN, L., CONGDON, N. G. & HE, M. 2012. Five-year incidence and postoperative visual outcome of cataract surgery in urban southern China: the Liwan Eye Study. *Investigative ophthalmology & visual science*, 53**,** 7936-7942.

HUEDO-MEDINA, T. B., SÁNCHEZ-MECA, J., MARÍN-MARTÍNEZ, F. & BOTELLA, J. 2006. Assessing heterogeneity in meta-analysis: Q statistic or I² index? *Psychological Methods*, 11**,** 193-206.

HUNTER, A. A., CHIN, E. K., ALMEIDA, D. R. & TELANDER, D. G. 2014. Drusen Imaging: A Review. *Journal of Clinical and Experimental Ophthalmology*, 5**,** 327.

IANCHULEV, T., LITOFF, D., ELLINGER, D., STIVERSON, K. & PACKER, M. 2016. Office-based cataract surgery: population health outcomes study of more than 21 000 cases in the United States. *Ophthalmology*, 123**,** 723-728.

IMPELLIZZERI, F. M. & BIZZINI, M. 2012. Systematic review and meta-analysis: A primer. *International Journal of Sports Physical Therapy*, 7**,** 493-503.

INSTITUTE FOR HEALTH METRICS AND EVALUATION, UNIVERSITY OF WASHINGTON. 2015. *Global Health Data Exchange* [Online]. Available: http://ghdx.healthdata.org/ [Accessed 12/01/2017.

INTERNATIONAL FEDERATION ON AGEING 2012. The high cost of low vision: the evidence on ageing and the loss of sight.

JAGER, R. D., MIELER, W. F. & MILLER, J. W. 2008. Age-related macular degeneration. *New England Journal of Medicine,* 358**,** 2606-2617.

JAMPEL, H. D., SCHWARTZ, G. F., ROBIN, A. L., ABRAMS, D. A., JOHNSON, E. & MILLER, R. B. 2003. Patient preferences for eye drop characteristics: a willingness-to-pay analysis. *Archives of Ophthalmology,* 121**,** 540-546.

JOHN, W. & DAVID, R. 2013. Cost of vision problems: The economic burden of vision loss and eye disorders in the United States. Chicago: NORC at the University of Chicago.

JONES, S. & EDWARDS, R. 2010. Diabetic retinopathy screening: a systematic review of the economic evidence. *Diabetic Medicine,* 27**,** 249-256.

JUNI, M. H. 2015. Ageing Population: A Public Health Implications. *International Journal of Public Health and Clinical Sciences,* 2.

KANSKI, J. J. & BOWLING, B. 2011. *Clinical ophthalmology: a systematic approach,* Edinburgh, London, New York, Oxford, Philadelphia, St Louis, Toronto, Elsevier Health Sciences.

KAPETANAKIS, V. V., CHAN, M. P., FOSTER, P. J., COOK, D. G., OWEN, C. G. & RUDNICKA, A. R. 2016. Global variations and time trends in the prevalence of primary open angle glaucoma (POAG): a systematic review and meta-analysis. *British Journal of Ophthalmology,* 100**,** 86-93.

KAWASAKI, R., YASUDA, M., SONG, S. J., CHEN, S.-J., JONAS, J. B., WANG, J. J., MITCHELL, P. & WONG, T. Y. 2010. The prevalence of age-related macular degeneration in Asians: a systematic review and meta-analysis. *Ophthalmology,* 117**,** 921-927.

KELLY, S. P., THORNTON, J., EDWARDS, R., SAHU, A. & HARRISON, R. 2005. Smoking and cataract: review of causal association. *Journal of Cataract & Refractive Surgery,* 31**,** 2395-2404.

KEMPEN, J. H., O'COLMAIN, B., LESKE, M. C., HAFFNER, S. M., KLEIN, R., MOSS, S. E., TAYLOR, H. R., HAMMAN, R. F. & EYE DISEASES PREVALENCE RESEARCH GROUP 2004. The prevalence of diabetic retinopathy among adults in the United States. *Archives of Ophthalmology,* 122**,** 552-563.

KHAN, J., SHAHID, H., THURLBY, D., BRADLEY, M., CLAYTON, D., MOORE, A., BIRD, A., YATES, J. & GENETIC FACTORS IN AMD STUDY 2006a. Age related macular degeneration and sun exposure, iris colour, and skin sensitivity to sunlight. *British journal of ophthalmology,* 90**,** 29-32.

KHAN, J., THURLBY, D., SHAHID, H., CLAYTON, D., YATES, J., BRADLEY, M., MOORE, A., BIRD, A. & GENETIC FACTORS IN AMD STUDY 2006b. Smoking and age related macular degeneration: the number of pack years of cigarette smoking is a major determinant of risk for both geographic atrophy and choroidal neovascularisation. *British Journal of Ophthalmology,* 90**,** 75-80.

KHANNA, R., PUJARI, S. & SANGWAN, V. 2011. Cataract surgery in developing countries. *Current Opinion in Ophthalmology,* 22**,** 10-14.

KINSELLA, K. G. & PHILLIPS, D. R. 2005. Global aging: The challenge of success. *Population Bulletin,* 60**,** 1-44.

KITCHENHAM, B. 2004. Procedures for performing systematic reviews. UK: Keele University.

KLEIN, B. E., KLEIN, R., LEE, K. E., MOORE, E. L. & DANFORTH, L. 2001. Risk of Incident Age-related Eye Diseases in People with an Affected Sibling The Beaver Dam Eye Study. *American Journal of Epidemiology,* 154**,** 207-211.

KLEIN, B. E. K. 2007. Overview of epidemiologic studies of diabetic retinopathy. *Ophthalmic Epidemiology,* 14**,** 179-183.

KLEIN, R., DAVIS, M. D., MAGLI, Y. L., SEGAL, P., KLEIN, B. E. & HUBBARD, L. 1991. The Wisconsin age-related maculopathy grading system. *Ophthalmology,* 98**,** 1128-1134.

KLEIN, R. & KLEIN, B. E. 2013. The Prevalence of Age-Related Eye Diseases and Visual Impairment in Aging: Current EstimatesPrevalences of Age-Related Eye Diseases. *Investigative Ophthalmology & Visual Science,* 54**,** ORSF5-ORSF13.

KLEIN, R., KLEIN, B. E. & FRANKE, T. 1993. The relationship of cardiovascular disease and its risk factors to age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology,* 100**,** 406-414.

KLEIN, R., KLEIN, B. E. & JENSEN, S. C. 1997a. The relation of cardiovascular disease and its risk factors to the 5-year incidence of age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology,* 104**,** 1804-1812.

KLEIN, R., KLEIN, B. E., JENSEN, S. C., MARES-PERLMAN, J. A., CRUICKSHANKS, K. J. & PALTA, M. 1999. Age-related maculopathy in a multiracial United States population: the National Health and Nutrition Examination Survey III. *Ophthalmology,* 106**,** 1056-1065.

KLEIN, R., KLEIN, B. E., JENSEN, S. C. & MEUER, S. M. 1997b. The five-year incidence and progression of age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology,* 104**,** 7-21.

KLEIN, R., KLEIN, B. E., KNUDTSON, M. D., MEUER, S. M., SWIFT, M. & GANGNON, R. E. 2007. Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study. *Ophthalmology,* 114**,** 253-262.

KLEIN, R., KLEIN, B. E. & LINTON, K. L. 1992. Prevalence of age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology,* 99**,** 933-943.

KLEIN, R., KLEIN, B. E., MOSS, S. E., DAVIS, M. D. & DEMETS, D. L. 1984a. The Wisconsin Epidemiologic Study of Diabetic Retinopathy: II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Archives of Ophthalmology,* 102**,** 520-526.

KLEIN, R., KLEIN, B. E., MOSS, S. E., DAVIS, M. D. & DEMETS, D. L. 1984b. The Wisconsin Epidemiologic Study of Diabetic Retinopathy: III. Prevalence and risk of

diabetic retinopathy when age at diagnosis is 30 or more years. *Archives of Ophthalmology,* 102**,** 527-532.

KLEIN, R., KLEIN, B. E., TOMANY, S. C. & CRUICKSHANKS, K. J. 2003. The association of cardiovascular disease with the long-term incidence of age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology,* 110**,** 636-643.

KLEIN, R., MEUER, S. M., MYERS, C. E., BUITENDIJK, G. H., ROCHTCHINA, E., CHOUDHURY, F., DE JONG, P. T., MCKEAN-COWDIN, R., IYENGAR, S. K., GAO, X., LEE, K. E., VINGERLING, J. R., MITCHELL, P., KLAVER, C. C., WANG, J. J. & KLEIN, B. E. 2014. Harmonizing the classification of age-related macular degeneration in the three-continent AMD consortium. *Ophthalmic Epidemiology,* 21**,** 14-23.

KLONOFF, D. C. & SCHWARTZ, D. M. 2000. An economic analysis of interventions for diabetes. *Diabetes Care,* 23**,** 390-404.

KRAMER, C. K., RODRIGUES, T. C., CANANI, L. H., GROSS, J. L. & AZEVEDO, M. J. 2011. Diabetic retinopathy predicts all-cause mortality and cardiovascular events in both type 1 and 2 diabetes: meta-analysis of observational studies. *Diabetes Care,* 34**,** 1238-1244.

KUYK, T. & ELLIOTT, J. L. 1999. Visual factors and mobility in persons with age-related macular degeneration. *Journal of Rehabilitation Research and Development,* 36**,** 303-312.

KWON, Y. H., FINGERT, J. H., KUEHN, M. H. & ALWARD, W. L. 2009. Primary open-angle glaucoma. *New England Journal of Medicine,* 360**,** 1113-1124.

LAI, K., CUI, J., NI, S., ZHANG, Y., HE, J. & YAO, K. 2013. The effects of postmenopausal hormone use on cataract: a meta-analysis. *PLOS ONE,* 8**,** e78647.

LAM, B. L., CHRIST, S. L., LEE, D. J., ZHENG, D. D. & ARHEART, K. L. 2008. Reported visual impairment and risk of suicide: the 1986-1996 national health interview surveys. *Archives of Ophthalmology,* 126**,** 975-980.

LAM, D. S., LI, E. Y., CHANG, D. F., ZHANG, M. Z., ZHAN, H. K. & PANG, C. P. 2009. Project vision: a new and sustainable model for eliminating cataract blindness in China. *Clinical & Experimental Ophthalmology,* 37**,** 427-430.

LAMBERT, P. C., SUTTON, A. J., BURTON, P. R., ABRAMS, K. R. & JONES, D. R. 2005. How vague is vague? A simulation study of the impact of the use of vague prior distributions in MCMC using WinBUGS. *Statistics in Medicine,* 24**,** 2401-2428.

LAMOREUX, E. L., CHONG, E., WANG, J. J., SAW, S. M., AUNG, T., MITCHELL, P. & WONG, T. Y. 2008. Visual impairment, causes of vision loss, and falls: the Singapore Malay Eye Study. *Investigative Ophthalmology & Visual Science,* 49**,** 528-533.

LAMOUREUX, E. L., HASSELL, J. B. & KEEFFE, J. E. 2004. The impact of diabetic retinopathy on participation in daily living. *Archives of Ophthalmology,* 122**,** 84-88.

LAMOUREUX, E. L., MITCHELL, P., REES, G., CHEUNG, G., YEO, I., LEE, S. Y., LIU, E. & WONG, T. Y. 2010. Impact of early and late age-related macular degeneration on vision-specific functioning. *British Journal of Ophthalmology,* 95**,** 666-670.

LANSINGH, V. C., CARTER, M. J. & MARTENS, M. 2007. Global cost-effectiveness of cataract surgery. *Ophthalmology,* 114**,** 1670-1678.

LAU, J., IOANNIDIS, J. P. & SCHMID, C. H. 1997. Quantitative synthesis in systematic reviews. *Annals of Internal Medicine,* 127**,** 820-826.

LEASHER, J. L., BOURNE, R. R., FLAXMAN, S. R., JONAS, J. B., KEEFFE, J., NAIDOO, K., PESUDOVS, K., PRICE, H., WHITE, R. A., WONG, T. Y., RESNIKOFF, S., TAYLOR, H. R. & VISION LOSS EXPERT GROUP OF THE GLOBAL BURDEN OF DISEASE STUDY 2016. Global estimates on the number of people blind or visually impaired by diabetic retinopathy: a meta-analysis from 1990 to 2010. *Diabetes Care,* 39**,** 1643-1649.

LEE, G. K., WONG, A. L., LUK, F. O. & LAI, T. Y. 2009. Visual outcome of retinal angiomatous proliferation in Chinese patients following photodynamic therapy or direct laser photocoagulation. *Hong Kong Journal of Ophthalmology,* 13**,** 5-8.

LEE, R. 2003. The demographic transition: three centuries of fundamental change. *Journal of Economic Perspectives,* 17**,** 167-190.

LEE, R. & ZHOU, Y. 2017. Does fertility or mortality drive contemporary population aging? The revisionist view revisited. *Population and Development Review,* 43**,** 285-301.

LEE, R. D. & REHER, D. S. 2011. *Demographic transition and its consequences,* New York, Population and Development Review.

LEO, D. D., HICKEY, P. A., MENEGHEL, G. & CANTOR, C. H. 1999. Blindness, fear of sight loss, and suicide. *Psychosomatics,* 40**,** 339-344.

LESKE, M. C., CHYLACK, L. T., SPERDUTO, R., KHU, P., WU, S.-Y. & MCCARTHY, D. 1988. Evaluation of a lens opacities classification system. *Archives of Ophthalmology,* 106**,** 327-329.

LESKE, M. C., CONNELL, A., WU, S.-Y., HYMAN, L. G. & SCHACHAT, A. P. 1995. Risk factors for open-angle glaucoma: the Barbados Eye Study. *Archives of Ophthalmology,* 113**,** 918-924.

LESKE, M. C., HEIJL, A., HUSSEIN, M., BENGTSSON, B., HYMAN, L., KOMAROFF, E. & EARLY MANIFEST GLAUCOMA TRIAL GROUP 2003. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. *Archives of Ophthalmology,* 121**,** 48-56.

LESLIE, R. & PYKE, D. 1982. Diabetic retinopathy in identical twins. *Diabetes,* 31**,** 19-21.

LEUNG, C., PALMIERO, P., WEINREB, R., LI, H., SBEITY, Z., DORAIRAJ, S., LEUNG, D., LIU, S., LIEBMANN, J., CONGDON, N., LAM, D. & RITCH, R. 2010. Comparisons of anterior segment biometry between Chinese and Caucasians using anterior segment optical coherence tomography. *British Journal of Ophthalmology,* 94**,** 1184-1189.

LI, J. 2015a. *Regional Differences in Life Expectancy in Mainland China.* Bachelor of Commerce, University of New South Wales.

LI, L. 2016. Summary of National Vision Care Report. China Center for Health Development, National School of Development, Peking University.

LI, Q. 2015b. *Automated Pre-screening of Diabetic Retinopathy*. MPhil, University of Manchester.

LI, S., XU, J., HE, M., WU, K., MUNOZ, S. R. & ELLWEIN, L. B. 1999. A survey of blindness and cataract surgery in Doumen County, China. *Ophthalmology,* 106**,** 1602-1608.

LI, T., HE, T., TAN, X., YANG, S., LI, J., PENG, Z., LI, H., SONG, X., WU, Q., YANG, F. & XING, Y. 2009. Prevalence of age-related cataract in high-selenium areas of China. *Biological Trace Element Research,* 128**,** 1.

LI, X., HU, Y., SUN, X., ZHANG, J., ZHANG, M. & NEOVASCULAR AGE-RELATED MACULAR DEGENERATION TREATMENT TRIAL USING BEVACIZUMAB (NATTB) 2012. Bevacizumab for neovascular age-related macular degeneration in China. *Ophthalmology,* 119**,** 2087-2093.

LI, Y., CREWS, J. E., ELAM-EVANS, L. D., FAN, A. Z., ZHANG, X., ELLIOTT, A. F. & BALLUZ, L. 2011. Visual impairment and health-related quality of life among elderly adults with age-related eye diseases. *Quality of Life Research,* 20**,** 845-852.

LI, Z., CUI, H., LIU, P., ZHANG, L., YANG, H. & ZHANG, L. 2008. Prevalence and causes of blindness and visual impairment among the elderly in rural southern Harbin, China. *Ophthalmic Epidemiology,* 15**,** 334-338.

LIM, L. S., MITCHELL, P., SEDDON, J. M., HOLZ, F. G. & WONG, T. Y. 2012. Age-related macular degeneration. *The Lancet,* 379**,** 1728-1738.

LIN, J. B., TSUBOTA, K. & APTE, R. S. 2016. A glimpse at the aging eye. *NPJ Aging and Mechanisms of Disease,* 2**,** 16003.

LINEBARGER, E. J., HARDTEN, D. R., SHAH, G. K. & LINDSTROM, R. L. 1999. Phacoemulsification and modern cataract surgery. *Survey of Ophthalmology,* 44**,** 123-147.

LIU, L., WU, X., LIU, L., GENG, J., YUAN, Z., SHAN, Z. & CHEN, L. 2012. Prevalence of diabetic retinopathy in mainland China: a meta-analysis. *PLOS ONE,* 7**,** e45264.

LIU, Y.-C., WILKINS, M., KIM, T., MALYUGIN, B. & MEHTA, J. S. 2017. Cataracts. *The Lancet,* 390**,** 600-612.

LIU, Y., WEN, F., HUANG, S., LUO, G., YAN, H., SUN, Z. & WU, D. 2007. Subtype lesions of neovascular age-related macular degeneration in Chinese patients. *Graefe's Archive for Clinical and Experimental Ophthalmology,* 245**,** 1441-1445.

LOO, D. L., NG, D. H., TANG, W. & EONG, K. G. A. 2009. Raising awareness of blindness as another smoking-related condition: a public health role for optometrists? *Clinical and Experimental Optometry,* 92**,** 42-44.

LOPEZ, A. D., MATHERS, C. D., EZZATI, M., JAMISON, D. T. & MURRAY, C. J. 2006. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *The Lancet,* 367**,** 1747-1757.

LUNENFELD, B. & STRATTON, P. 2013. The clinical consequences of an ageing world and preventive strategies. *Best Practice & Research Clinical Obstetrics & Gynaecology,* 27**,** 643-659.

MAI, Y., PENG, X. & CHEN, W. 2013. How fast is the population ageing in China? *Asian Population Studies,* 9**,** 216-239.

MANSBERGER, S. L., SHEPPLER, C., BARKER, G., GARDINER, S. K., DEMIREL, S., WOOTEN, K. & BECKER, T. M. 2015. Long-term comparative effectiveness of telemedicine in providing diabetic retinopathy screening examinations: a randomized clinical trial. *JAMA Ophthalmology,* 133**,** 518-525.

MATHERS, C. D. & LONCAR, D. 2006. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Medicine,* 3**,** e442.

MATHERS, W. D. 2000. Why the eye becomes dry: a cornea and lacrimal gland feedback model. *The CLAO Journal: official publication of the Contact Lens Association of Ophthalmologists, Inc,* 26**,** 159-165.

MAZHAR, K., VARMA, R., CHOUDHURY, F., MCKEAN-COWDIN, R., SHTIR, C. J., AZEN, S. P. & LOS ANGELES LATINO EYE STUDY GROUP 2011. Severity of diabetic retinopathy and health-related quality of life: the Los Angeles Latino Eye Study. *Ophthalmology,* 118**,** 649-655.

MCCARTY, C. & TAYLOR, H. 2002. A review of the epidemiologic evidence linking ultraviolet radiation and cataracts. *Progress in Lens and Cataract Research.* Karger Publishers.

MCCARTY, C. A., MUKESH, B., FU, C. L. & TAYLOR, H. R. 1999. The epidemiology of cataract in Australia. *American Journal of Ophthalmology,* 128**,** 446-465.

MCCARTY, C. A., MUKESH, B. N., FU, C. L., MITCHELL, P., WANG, J. J. & TAYLOR, H. R. 2001a. Risk factors for age-related maculopathy: the Visual Impairment Project. *Archives of Ophthalmology,* 119**,** 1455-1462.

MCCARTY, C. A., NANJAN, M. B. & TAYLOR, H. R. 2000. Attributable risk estimates for cataract to prioritize medical and public health action. *Investigative Ophthalmology & Visual Science,* 41**,** 3720-3725.

MCCARTY, C. A., NANJAN, M. B. & TAYLOR, H. R. 2001b. Vision impairment predicts 5 year mortality. *British Journal of Ophthalmology,* 85**,** 322-326.

MCCRACKEN, K. & PHILLIPS, D. R. 2012. *Global health: an introduction to current and future trends,* New York, Routledge.

MICHAEL, R. & BRON, A. 2011. The ageing lens and cataract: a model of normal and pathological ageing. *Philosophical Transactions of the Royal Society B: Biological Sciences,* 366**,** 1278-1292.

MITCHELL, J. & BRADLEY, C. 2006. Quality of life in age-related macular degeneration: a review of the literature. *Health and Quality of Life Outcomes,* 4**,** 97.

MITCHELL, P., CUMMING, R. G., ATTEBO, K. & PANCHAPAKESAN, J. 1997. Prevalence of cataract in Australia: the Blue Mountains eye study. *Ophthalmology,* 104**,** 581-588.

MITCHELL, P., SMITH, W., ATTEBO, K. & WANG, J. J. 1995. Prevalence of age-related maculopathy in Australia: the Blue Mountains Eye Study. *Ophthalmology,* 102**,** 1450-1460.

MOHAMED, Q., GILLIES, M. C. & WONG, T. Y. 2007. Management of diabetic retinopathy: a systematic review. *JAMA,* 298**,** 902-916.

MOHER, D., LIBERATI, A., TETZLAFF, J., ALTMAN, D. G. & PRISMA GROUP 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine,* 151**,** 264-269.

MOTL, R. W. & MCAULEY, E. 2010. Physical activity, disability, and quality of life in older adults. *Physical Medicine and Rehabilitation Clinics of North America,* 21**,** 299-308.

MURAD, M. H. & WANG, Z. 2017. Guidelines for reporting meta-epidemiological methodology research. *Evidence Based Medicine,* 22**,** 139.

MYERS, R. L. 2003. *Display interfaces: fundamentals and standards,* Chichester, John Wiley & Sons.

MYINT, J. 2013. *A study of case finding for chronic open angle glaucoma by UK community optometrists.* Doctor of Philosophy, City University London.

NATIONAL BUREAU OF STATISTICS 2002. *Tabulation on the 2000 population census of the People's Republic of China,* Beijing, China Statistics Press.

NATIONAL BUREAU OF STATISTICS 2012. *Tabulation on the 2010 population census of the People's Republic of China,* Beijing, China Statistics Press.

NATIONAL HEALTH AND FAMILY PLANNING COMMISSION OF THE PEOPLE'S REPUBLIC OF CHINA 2016. The 13th 5-Year National Eye Health Plan (2016-2020). Beijing: National Health and Family Planning Commission of the People's Republic of China

NDUAGUBA, C. & LEE, R. K. 2006. Glaucoma screening: current trends, economic issues, technology, and challenges. *Current Opinion in Ophthalmology,* 17**,** 142-152.

NEMET, A., VINKER, S., LEVARTOVSKY, S. & KAISERMAN, I. 2010. Is cataract associated with cardiovascular morbidity? *Eye,* 24**,** 1352-1358.

NEUBAUER, A. S. & ULBIG, M. W. 2007. Laser treatment in diabetic retinopathy. *Ophthalmologica,* 221**,** 95-102.

NEWMAN, D. 2010. Surgical management of the late complications of proliferative diabetic retinopathy. *Eye,* 24**,** 441-449.

NG, D. H., SANGTAM, T. & EONG, K.-G. A. 2007. The Emerging Challenge of Age-related Eye Diseases in Singapore. *Annals-Academy of Medicine,* 36**,** S9-S14.

NIRMALAN, P., KATZ, J., ROBIN, A., KRISHNADAS, R., RAMAKRISHNAN, R., THULASIRAJ, R. & TIELSCH, J. 2004. Utilisation of eye care services in rural south India: the Aravind Comprehensive Eye Survey. *British Journal of Ophthalmology,* 88**,** 1237-1241.

NIRMALAN, P. K., THULASIRAJ, R., MANEKSHA, V., RAHMATHULLAH, R., RAMAKRISHNAN, R., PADMAVATHI, A., MUNOZ, S. & ELLWEIN, L. 2002. A population based eye survey of older adults in Tirunelveli district of south India: blindness, cataract surgery, and visual outcomes. *British Journal of Ophthalmology,* 86**,** 505-512.

NOWAK, J. Z. 2006. Age-related macular degeneration (AMD): pathogenesis and therapy. *Pharmacological Reports,* 58**,** 353-363.

NYAGA, V. N., ARBYN, M. & AERTS, M. 2014. Metaprop: a Stata command to perform meta-analysis of binomial data. *Archives of Public Health,* 72**,** 39.

OHR, M. & KAISER, P. K. 2012. Aflibercept in wet age-related macular degeneration: a perspective review. *Therapeutic Advances in Chronic Disease,* 3**,** 153-161.

OLSHANSKY, S. J. & AULT, A. B. 1986. The fourth stage of the epidemiologic transition: the age of delayed degenerative diseases. *The Milbank Quarterly,* 64**,** 355-391.

OMRAN, A. R. 2005. The epidemiologic transition: a theory of the epidemiology of population change. *The Milbank Quarterly,* 83**,** 731-757.

OSAADON, P., FAGAN, X., LIFSHITZ, T. & LEVY, J. 2014. A review of anti-VEGF agents for proliferative diabetic retinopathy. *Eye,* 28**,** 510-520.

OWEN, C., FLETCHER, A., DONOGHUE, M. & RUDNICKA, A. 2003. How big is the burden of visual loss caused by age related macular degeneration in the United Kingdom? *British Journal of Ophthalmology,* 87**,** 312-317.

OWSLEY, C., MCGWIN, G., CLARK, M. E., JACKSON, G. R., CALLAHAN, M. A., KLINE, L. B., WITHERSPOON, C. D. & CURCIO, C. A. 2016. Delayed rod-mediated dark adaptation is a functional biomarker for incident early age-related macular degeneration. *Ophthalmology,* 123**,** 344-351.

PALMBERG, P. 2001. Risk factors for glaucoma progression: Where does intraocular pressure fit in? *Archives of Ophthalmology,* 119**,** 897-898.

PANG, C., JIA, L., JIANG, S., LIU, W., HOU, X., ZUO, Y., GU, H., BAO, Y., WU, Q., XIANG, K., GAO, X. & JIA, W. 2012. Determination of diabetic retinopathy prevalence and associated risk factors in Chinese diabetic and pre-diabetic subjects: Shanghai diabetic complications study. *Diabetes/Metabolism Research and Reviews,* 28**,** 276-283.

PASCOLINI, D. & MARIOTTI, S. P. 2011. Global estimates of visual impairment: 2010. *British Journal of Ophthalmology,* 96**,** 614-618.

PENG, J., ZOU, H., WANG, W., FU, J., SHEN, B., BAI, X., XU, X. & ZHANG, X. 2011. Implementation and first-year screening results of an ocular telehealth system for diabetic retinopathy in China. *BMC Health Services Research,* 11**,** 250.

PENG, X., SONG, S., SULLIVAN, S., QIU, J. & WANG, W. 2010. Ageing, the urban-rural gap and disability trends: 19 years of experience in China-1987 to 2006. *PLOS ONE,* 5**,** e12129.

PETERS, J. L., SUTTON, A. J., JONES, D. R., ABRAMS, K. R. & RUSHTON, L. 2006. Comparison of two methods to detect publication bias in meta-analysis. *JAMA,* 295**,** 676-680.

PIZZARELLO, L., ABIOSE, A., FFYTCHE, T., DUERKSEN, R., THULASIRAJ, R., TAYLOR, H., FAAL, H., RAO, G., KOCUR, I. & RESNIKOFF, S. 2004. VISION 2020: The Right to Sight: a global initiative to eliminate avoidable blindness. *Archives of Ophthalmology,* 122**,** 615-620.

POLACK, S., KUPER, H., MATHENGE, W., FLETCHER, A. & FOSTER, A. 2007. Cataract visual impairment and quality of life in a Kenyan population. *British Journal of Ophthalmology,* 91**,** 927-932.

POPKIN, B. M., DU, S., ZHAI, F. & ZHANG, B. 2009. Cohort Profile: The China Health and Nutrition Survey—monitoring and understanding socio-economic and health change in China, 1989–2011. *International journal of epidemiology,* 39**,** 1435-1440.

PORTA, M. & BANDELLO, F. 2002. Diabetic retinopathy. *Diabetologia,* 45**,** 1617-1634.

POTTER, M. J. & SZABO, S. M. 2007. Recurrence of choroidal neovascularisation after photodynamic therapy in patients with age-related macular degeneration. *British Journal of Ophthalmology,* 91**,** 753-756.

PRINCE, M. J., WU, F., GUO, Y., ROBLEDO, L. M. G., O'DONNELL, M., SULLIVAN, R. & YUSUF, S. 2015. The burden of disease in older people and implications for health policy and practice. *The Lancet,* 385**,** 549-562.

PROSPECTIVE STUDIES COLLABORATION 2002. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *The Lancet,* 360**,** 1903-1913.

QU, W., LI, Y., SONG, W., ZHOU, X., KANG, Y., YAN, L., SUI, H. & YUAN, H. 2011. Prevalence and risk factors for angle‐closure disease in a rural Northeast China population: a population‐based survey in Bin County, Harbin. *Acta Ophthalmologica,* 89**,** e515-e520.

QUIGLEY, H. A. 1996. Number of people with glaucoma worldwide. *British Journal of Ophthalmology,* 80**,** 389-393.

QUIGLEY, H. A. 2011. Glaucoma. *The Lancet,* 377**,** 1367–1377.

QUIGLEY, H. A., ADDICKS, E. M. & GREEN, W. R. 1982. Optic nerve damage in human glaucoma: III. Quantitative correlation of nerve fiber loss and visual field defect in glaucoma, ischemic neuropathy, papilledema, and toxic neuropathy. *Archives of Ophthalmology,* 100**,** 135-146.

QUIGLEY, H. A. & BROMAN, A. T. 2006. The number of people with glaucoma worldwide in 2010 and 2020. *British Journal of Ophthalmology,* 90**,** 262-267.

QUIGLEY, H. A., WEST, S. K., MUNOZ, B., MMBAGA, B. & GLOVINSKY, Y. 1993. Examination methods for glaucoma prevalence surveys. *Archives of Ophthalmology,* 111**,** 1409-1415.

R CORE TEAM 2013. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing.

RABIU, M. M. 2001. Cataract blindness and barriers to uptake of cataract surgery in a rural community of northern Nigeria. *British Journal of Ophthalmology,* 85**,** 776-780.

RAMULU, P. 2009. Glaucoma and disability: which tasks are affected, and at what stage of disease? *Current Opinion in Ophthalmology,* 20**,** 92-98.

RECHEL, B., GRUNDY, E., ROBINE, J.-M., CYLUS, J., MACKENBACH, J. P., KNAI, C. & MCKEE, M. 2013. Ageing in the European union. *The Lancet,* 381**,** 1312-1322.

REES, G., TEE, H. W., MARELLA, M., FENWICK, E., DIRANI, M. & LAMOUREUX, E. L. 2010. Vision-specific distress and depressive symptoms in people with vision impairment. *Investigative Ophthalmology & Visual Science,* 51**,** 2891-2896.

REIBALDI, M., LONGO, A., PULVIRENTI, A., AVITABILE, T., RUSSO, A., CILLINO, S., MARIOTTI, C. & CASUCCIO, A. 2016. Geo-epidemiology of age-related macular degeneration: new clues into the pathogenesis. *American Journal of Ophthalmology,* 161**,** 78-93. e2.

REIN, D. B., ZHANG, P., WIRTH, K. E., LEE, P. P., HOERGER, T. J., MCCALL, N., KLEIN, R., TIELSCH, J. M., VIJAN, S. & SAADDINE, J. 2006. The economic burden of major adult visual disorders in the United States. *Archives of Ophthalmology,* 124**,** 1754-1760.

REMA, M., PREMKUMAR, S., ANITHA, B., DEEPA, R., PRADEEPA, R. & MOHAN, V. 2005. Prevalence of diabetic retinopathy in urban India: the Chennai Urban Rural Epidemiology Study (CURES) eye study, I. *Investigative Ophthalmology & Visual Science,* 46**,** 2328-2333.

RICKMAN, C. B., FARSIU, S., TOTH, C. A. & KLINGEBORN, M. 2013. Dry age-related macular degeneration: mechanisms, therapeutic targets, and imagingdry AMD mechanisms, targets, and imaging. *Investigative Ophthalmology & Visual Science,* 54**,** ORSF68-ORSF80.

RIZZO, S., GENOVESI-EBERT, F., DI BARTOLO, E., VENTO, A., MINIACI, S. & WILLIAMS, G. 2008. Injection of intravitreal bevacizumab (Avastin) as a preoperative adjunct before vitrectomy surgery in the treatment of severe proliferative diabetic retinopathy (PDR). *Graefe's Archive for Clinical and Experimental Ophthalmology,* 246**,** 837-842.

ROBMAN, L. & TAYLOR, H. 2005. External factors in the development of cataract. *Eye,* 19**,** 1074-1082.

ROCHTCHINA, E., MUKESH, B. N., WANG, J. J., MCCARTY, C. A., TAYLOR, H. R. & MITCHELL, P. 2003. Projected prevalence of age - related cataract and cataract surgery in Australia for the years 2001 and 2021: pooled data from two population - based surveys. *Clinical & Experimental Ophthalmology,* 31**,** 233-236.

ROULAND, J.-F., BERDEAUX, G. & LAFUMA, A. 2005. The economic burden of glaucoma and ocular hypertension. *Drugs & Aging,* 22**,** 315-321.

RUDAN, I., TOMASKOVIC, L., BOSCHI-PINTO, C., CAMPBELL, H. & WHO CHILD HEALTH EPIDEMIOLOGY REFERENCE GROUP 2004. Global estimate of the incidence of clinical pneumonia among children under five years of age. *Bulletin of the World Health Organization,* 82**,** 895-903.

RUDNICKA, A. R., JARRAR, Z., WORMALD, R., COOK, D. G., FLETCHER, A. & OWEN, C. G. 2012. Age and gender variations in age-related macular degeneration prevalence in populations of European ancestry: a meta-analysis. *Ophthalmology,* 119**,** 571-580.

RUDNICKA, A. R., MT-ISA, S., OWEN, C. G., COOK, D. G. & ASHBY, D. 2006. Variations in primary open-angle glaucoma prevalence by age, gender, and race: a Bayesian meta-analysis. *Investigative Ophthalmology & Visual Science,* 47**,** 4254-4261.

RULLI, E., BIAGIOLI, E., RIVA, I., GAMBIRASIO, G., DE SIMONE, I., FLORIANI, I. & QUARANTA, L. 2013. Efficacy and safety of trabeculectomy vs nonpenetrating surgical procedures: a systematic review and meta-analysis. *JAMA Ophthalmology,* 131**,** 1573-1582.

SAADDINE, J. B., HONEYCUTT, A. A., NARAYAN, K. V., ZHANG, X., KLEIN, R. & BOYLE, J. P. 2008. Projection of diabetic retinopathy and other major eye diseases among people with diabetes mellitus: United States, 2005-2050. *Archives of Ophthalmology,* 126**,** 1740-1747.

SAADDINE, J. B., NARAYAN, K. V. & VINICOR, F. 2003. Vision loss: a public health problem? *Ophthalmology,* 110**,** 253-254.

SALVI, S., AKHTAR, S. & CURRIE, Z. 2006. Ageing changes in the eye. *Postgraduate Medical Journal,* 82**,** 581-587.

SANTOSA, A., WALL, S., FOTTRELL, E., HÖGBERG, U. & BYASS, P. 2014. The development and experience of epidemiological transition theory over four decades: a systematic review. *Global Health Action,* 7**,** 23574.

SAPKOTA, Y., POKHAREL, G., NIRMALAN, P., DULAL, S., MAHARJAN, I. & PRAKASH, K. 2006. Prevalence of blindness and cataract surgery in Gandaki Zone, Nepal. *British Journal of Ophthalmology,* 90**,** 411-416.

SCHWARTZ, G. F. 2005. Compliance and persistency in glaucoma follow-up treatment. *Current Opinion in Ophthalmology,* 16**,** 114-121.

SEDDON, J. M., AJANI, U. A. & MITCHELL, B. D. 1997. Familial aggregation of age-related maculopathy. *American Journal of Ophthalmology,* 123**,** 199-206.

SEDDON, J. M., SHARMA, S. & ADELMAN, R. A. 2006. Evaluation of the clinical age-related maculopathy staging system. *Ophthalmology,* 113**,** 260-266.

SHARMA, A. & HINDMAN, H. B. 2014. Aging: a predisposition to dry eyes. *Journal of Ophthalmology,* 2014.

SHARMA, S., OLIVER-FERNANDEZ, A., LIU, W., BUCHHOLZ, P. & WALT, J. 2005. The impact of diabetic retinopathy on health-related quality of life. *Current Opinion in Ophthalmology,* 16**,** 155-159.

SHAW, J. E., SICREE, R. A. & ZIMMET, P. Z. 2010. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Research and Clinical Practice,* 87**,** 4-14.

SHEN, W., YANG, Y., YU, M., LI, J., WEI, T., LI, X., LI, J., SU, X., ZHONG, H. & YUAN, Y. 2013. Prevalence and outcomes of cataract surgery in adult rural Chinese populations of the Bai nationality in Dali: the Yunnan minority eye study. *PLOS ONE,* 8**,** e60236.

SHENG, Y., HE, F., LIN, J.-F., SHEN, W. & QIU, Y.-W. 2016. Tea and Risk of Age-Related Cataracts: A Cross-Sectional Study in Zhejiang Province, China. *Journal of Epidemiology,* 26**,** 587-592.

SHETTY, P. 2012. Grey matter: ageing in developing countries. *The Lancet,* 379**,** 1285-1287.

SHI, G.-Y., HAYASAKA, T., OHMURA, A., CHEN, Z.-H., WANG, B., ZHAO, J.-Q., CHE, H.-Z. & XU, L. 2008. Data quality assessment and the long-term trend of ground solar radiation in China. *Journal of Applied Meteorology and Climatology,* 47**,** 1006-1016.

SHIELS, A. & HEJTMANCIK, J. 2013. Genetics of human cataract. *Clinical Genetics,* 84**,** 120-127.

SHIN, Y., ONG, P. G., CHEUNG, G. C. M., WANG, J. J., MITCHELL, P., TAI, E. S., WONG, T. Y. & CHENG, C.-Y. 2014. Associations of cardiovascular risk factors with age-related macular degeneration in Asians: Pooled analysis from 5 population-based studies. *Investigative Ophthalmology & Visual Science,* 55**,** 654.

SHINGLETON, B. J., RICHTER, C. U., BELLOWS, A. R., HUTCHINSON, B. T. & GLYNN, R. J. 1987. Long-term efficacy of argon laser trabeculoplasty. *Ophthalmology,* 94**,** 1513-1518.

SHINGLETON, B. J., RICHTER, C. U., DHARMA, S. K., TONG, L., BELLOWS, A. R., HUTCHINSON, B. T. & GLYNN, R. J. 1993. Long-term efficacy of argon laser trabeculoplasty: a 10-year follow-up study. *Ophthalmology,* 100**,** 1324-1329.

SIMÓ, R. & HERNANDEZ, C. 2008. Intravitreous anti-VEGF for diabetic retinopathy: hopes and fears for a new therapeutic strategy. *Diabetologia,* 51**,** 1574.

SIVAPRASAD, S., GUPTA, B., CROSBY-NWAOBI, R. & EVANS, J. 2012. Prevalence of diabetic retinopathy in various ethnic groups: a worldwide perspective. *Survey of Ophthalmology,* 57**,** 347-370.

SMITH, J. P. & MAJMUNDAR, M. 2012. *Aging in Asia: findings from new and emerging data initiatives,* Washington, D.C., National Academies Press.

SMITH, W., ASSINK, J., KLEIN, R., MITCHELL, P., KLAVER, C. C., KLEIN, B. E., HOFMAN, A., JENSEN, S., WANG, J. J. & DE JONG, P. T. 2001. Risk factors for age-related macular degeneration: pooled findings from three continents. *Ophthalmology,* 108**,** 697-704.

SMITH, W., MITCHELL, P. & WANG, J. 1997. Gender, oestrogen, hormone replacement and age‐related macular degeneration: Results from the Blue Mountains Eye Study. *Australian and New Zealand Journal of Ophthalmology,* 25**,** 13-15.

SOLOMON, R. & DONNENFELD, E. D. 2003. Recent advances and future frontiers in treating age-related cataracts. *JAMA,* 290**,** 248-251.

SONG, E., SUN, H., XU, Y., MA, Y., ZHU, H. & PAN, C.-W. 2014. Age-related cataract, cataract surgery and subsequent mortality: a systematic review and meta-analysis. *PLOS ONE,* 9**,** e112054.

SONG, P., CHANG, X., WANG, M. & AN, L. 2017a. Variations of pterygium prevalence by age, gender and geographic characteristics in China: A systematic review and meta-analysis. *PLOS ONE,* 12**,** e0174587.

SONG, P., DU, Y., CHAN, K. Y., THEODORATOU, E. & RUDAN, I. 2017b. The national and subnational prevalence and burden of age–related macular degeneration in China. *Journal of Global Health,* 7**,** 020703.

SONG, P., THEODORATOU, E., LI, X., LIU, L., CHU, Y., BLACK, R. E., CAMPBELL, H., RUDAN, I. & CHAN, K. Y. 2016. Causes of death in children younger than five years in China in 2015: an updated analysis. *Journal of Global Health,* 6**,** 020802.

SONG, P., WANG, J., BUCAN, K., THEODORATOU, E., RUDAN, I. & CHAN, K. Y. 2017c. National and subnational prevalence and burden of glaucoma in China: A systematic analysis. *Journal of Gobal Health,* 7**,** 020705.

SONG, P., XIA, W., WANG, M., CHANG, X., WANG, J., JIN, S., WANG, J., WEI, W. & RUDAN, I. 2018. Variations of dry eye disease prevalence by age, sex and geographic characteristics in China: a systematic review and meta-analysis. *Journal of Global Health,* 8**,** 020503.

SONG, W., SHAN, L., CHENG, F., FAN, P., ZHANG, L., QU, W., ZHANG, Q. & YUAN, H. 2011. Prevalence of glaucoma in a rural northern China adult population: a population-based survey in Kailu County, Inner Mongolia. *Ophthalmology,* 118**,** 1982-1988.

SOUBRANE, G., CRUESS, A., LOTERY, A., PAULEIKHOFF, D., MONÈS, J., XU, X., ZLATEVA, G., BUGGAGE, R., CONLON, J. & GOSS, T. F. 2007. Burden and health care resource utilization in neovascular age-related macular degeneration: findings of a multicountry study. *Archives of Ophthalmology,* 125**,** 1249-1254.

SOUSA, R. M., FERRI, C. P., ACOSTA, D., ALBANESE, E., GUERRA, M., HUANG, Y., JACOB, K., JOTHEESWARAN, A., RODRIGUEZ, J. J. L., PICHARDO, G. R., RODRIGUEZ, M. C., SALAS, A., SOSA, A. L., WILLIAMS, J., ZUNIGA, T. & PRINCE, M. 2009. Contribution of chronic diseases to disability in elderly people in countries with low and middle incomes: a 10/66 Dementia Research Group population-based survey. *The Lancet,* 374**,** 1821-1830.

SPARROW, J., BRON, A., BROWN, N., AYLIFFE, W. & HILL, A. 1986. The Oxford clinical cataract classification and grading system. *International Ophthalmology,* 9**,** 207-225.

SPIEGELHALTER, D., THOMAS, A., BEST, N. & GILKS, W. 1996. BUGS 0.5: Bayesian inference using Gibbs sampling manual (version ii). Cambridge, UK: MRC Biostatistics Unit, Institute of Public Health.

STEFÁNSSON, E., BEK, T., PORTA, M., LARSEN, N., KRISTINSSON, J. K. & AGARDH, E. 2000. Screening and prevention of diabetic blindness. *Acta Ophthalmologica Scandinavica,* 78**,** 374-385.

STERNE, J. A., GAVAGHAN, D. & EGGER, M. 2000. Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature. *Journal of Clinical Epidemiology,* 53**,** 1119-1129.

STEVENS, G. A., ALKEMA, L., BLACK, R. E., BOERMA, J. T., COLLINS, G. S., EZZATI, M., GROVE, J. T., HOGAN, D. R., HOGAN, M. C., HORTON, R., LAWN, J. E., MARUŠIĆ, A., MATHERS, C. D., MURRAY, C. J., RUDAN, I., SALOMON, J. A., SIMPSON, P. J., VOS, T., WELCH, V. & GATHER WORKING GROUP 2016. Guidelines for accurate and transparent health estimates reporting: the GATHER statement. *PLoS Medicine,* 13**,** e1002116.

STEVENS, G. A., WHITE, R. A., FLAXMAN, S. R., PRICE, H., JONAS, J. B., KEEFFE, J., LEASHER, J., NAIDOO, K., PESUDOVS, K., RESNIKOFF, S., TAYLOR, H., BOURNE, R. R. & VISION LOSS EXPERT GROUP 2013. Global prevalence of vision impairment and blindness: magnitude and temporal trends, 1990–2010. *Ophthalmology,* 120**,** 2377-2384.

STEWART, L. A. & TIERNEY, J. F. 2002. To IPD or not to IPD? Advantages and disadvantages of systematic reviews using individual patient data. *Evaluation & the health professions,* 25**,** 76-97.

STEWART, W. C., KOLKER, A. E., SHARPE, E. D., DAY, D. G., HOLMES, K. T., LEECH, J. N., JOHNSON, M. & CANTRELL, J. B. 2000. Factors associated with long-term progression or stability in primary open-angle glaucoma. *American Journal of Ophthalmology,* 130**,** 274-279.

STROUP, D. F., BERLIN, J. A., MORTON, S. C., OLKIN, I., WILLIAMSON, G. D., RENNIE, D., MOHER, D., BECKER, B. J., SIPE, T. A., THACKER, S. B. & META-ANALYSIS OF OBSERVATIONAL STUDIES IN EPIDEMIOLOGY (MOOSE) GROUP 2000. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA,* 283**,** 2008-2012.

SUN, J., ZHOU, X., KANG, Y., YAN, L., SUN, X., SUI, H., QIN, D. & YUAN, H. 2012. Prevalence and risk factors for primary open-angle glaucoma in a rural northeast China population: a population-based survey in Bin County, Harbin. *Eye,* 26**,** 283-291.

SUTTON, A. J. & ABRAMS, K. R. 2001. Bayesian methods in meta-analysis and evidence synthesis. *Statistical Methods in Medical Research,* 10**,** 277-303.

SWAROOP, A., BRANHAM, K. E., CHEN, W. & ABECASIS, G. 2007. Genetic susceptibility to age-related macular degeneration: a paradigm for dissecting complex disease traits. *Human Molecular Genetics,* 16**,** R174-R182.

TABIN, G., CHEN, M. & ESPANDAR, L. 2008. Cataract surgery for the developing world. *Current Opinion in Ophthalmology,* 19**,** 55-59.

TAKEDA, A. L., COLQUITT, J., CLEGG, A. J. & JONES, J. 2007. Pegaptanib and ranibizumab for neovascular age-related macular degeneration: a systematic review. *British Journal of Ophthalmology,* 91**,** 1177-1182.

TARGHER, G., BERTOLINI, L., ZENARI, L., LIPPI, G., PICHIRI, I., ZOPPINI, G., MUGGEO, M. & ARCARO, G. 2008. Diabetic retinopathy is associated with an increased incidence of cardiovascular events in Type 2 diabetic patients. *Diabetic Medicine,* 25**,** 45-50.

TAUSEEF, M., SHAHID, M., SHARMA, K. K. & FAHIM, M. 2008. Antioxidative action of aspirin on endothelial function in hypercholesterolaemic rats. *Basic & Clinical Pharmacology & Toxicology,* 103**,** 314-321.

TAYLOR, H., PEZZULLO, M. & KEEFFE, J. 2006. The economic impact and cost of visual impairment in Australia. *British Journal of Ophthalmology,* 90**,** 272-275.

TAYLOR, H. R. 1999. Epidemiology of age-related cataract. *Eye,* 13**,** 445.

TEZEL, G., LUO, C. & YANG, X. 2007. Accelerated aging in glaucoma: immunohistochemical assessment of advanced glycation end products in the human retina and optic nerve head. *Investigative Ophthalmology & Visual Science,* 48**,** 1201-1211.

THAM, Y.-C., LI, X., WONG, T. Y., QUIGLEY, H. A., AUNG, T. & CHENG, C.-Y. 2014. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology,* 121**,** 2081-2090.

THE ROYAL COLLEGE OF OPHTHALMOLOGISTS 2012. Diabetic Retinopathy Guidelines. London: The Royal College of Ophthalmologists.

THE ROYAL COLLEGE OF OPHTHALMOLOGISTS 2016. Commissioning Guide: Glaucoma. London: The Royal College of Ophthalmologists.

THOMPSON, S. G. & HIGGINS, J. P. 2002. How should meta‐regression analyses be undertaken and interpreted? *Statistics in Medicine,* 21**,** 1559-1573.

THORNTON, J., EDWARDS, R., MITCHELL, P., HARRISON, R., BUCHAN, I. & KELLY, S. 2005. Smoking and age-related macular degeneration: a review of association. *Eye,* 19**,** 935-944.

THYLEFORS, B., CHYLACK JR, L., KONYAMA, K., SASAKI, K., SPERDUTO, R., TAYLOR, H. & WEST4, S. 2002. A simplified cataract grading system The WHO Cataract Grading Group. *Ophthalmic Epidemiology,* 9**,** 83-95.

TIELSCH, J. M., KATZ, J., SOMMER, A., QUIGLEY, H. A. & JAVITT, J. C. 1994. Family history and risk of primary open angle glaucoma: the Baltimore Eye Survey. *Archives of Ophthalmology,* 112**,** 69-73.

TING, D. S. W., CHEUNG, G. C. M. & WONG, T. Y. 2016. Diabetic retinopathy: global prevalence, major risk factors, screening practices and public health challenges: a review. *Clinical & Experimental Ophthalmology,* 44**,** 260-277.

TOMANY, S. C., CRUICKSHANKS, K. J., KLEIN, R., KLEIN, B. E. & KNUDTSON, M. D. 2004. Sunlight and the 10-year incidence of age-related maculopathy: the Beaver Dam Eye Study. *Archives of Ophthalmology,* 122**,** 750-757.

TOMANY, S. C., KLEIN, R. & KLEIN, B. E. 2003. The relationship between iris color, hair color, and skin sun sensitivity and the 10-year incidence of age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology,* 110**,** 1526-1533.

TOPOUZIS, F., COLEMAN, A. L., HARRIS, A., KOSKOSAS, A., FOUNTI, P., GONG, G., YU, F., ANASTASOPOULOS, E., PAPPAS, T. & WILSON, M. R. 2008. Factors associated with undiagnosed open-angle glaucoma: the Thessaloniki Eye Study. *American Journal of Ophthalmology,* 145**,** 327-335. e1.

TOSATO, M., ZAMBONI, V., FERRINI, A. & CESARI, M. 2007. The aging process and potential interventions to extend life expectancy. *Clinical Interventions in Aging,* 2**,** 401-412.

TRAVERSO, C., WALT, J., KELLY, S., HOMMER, A., BRON, A., DENIS, P., NORDMANN, J., RENARD, J., BAYER, A., GREHN, F., PFEIFFER, N., CEDRONE, C., GANDOLFI, S., ORZALESI, N., NUCCI, C., ROSSETTI, L., AZUARA-BLANCO, A., BAGNIS, A., HITCHINGS, R., SALMON, J., BRICOLA, G., BUCHHOLZ, P., KOTAK, S., KATZ, L., SIEGARTEL, L. & DOYLE, J. 2005. Direct costs of glaucoma and severity of the disease: a multinational long term study of resource utilisation in Europe. *British Journal of Ophthalmology,* 89**,** 1245-1249.

UK PROSPECTIVE DIABETES STUDY (UKPDS) GROUP 1998. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *The Lancet,* 352**,** 837-853.

UK PROSPECTIVE DIABETES STUDY GROUP 1998. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ: British Medical Journal,* 317**,** 703-713.

UNITED NATIONS 2015a. World population ageing 2015. New York: Department of Economic and Social Affairs, United Nations.

UNITED NATIONS, DEPARTMENT OF ECONOMIC AND SOCIAL AFFAIRS, POPULATION DIVISION 2002. World population ageing: 1950-2050. New York: United Nations.

UNITED NATIONS, DEPARTMENT OF ECONOMIC AND SOCIAL AFFAIRS, POPULATION DIVISION 2004. World population to 2300. New York: United Nations.

UNITED NATIONS, DEPARTMENT OF ECONOMIC AND SOCIAL AFFAIRS, POPULATION DIVISION 2005. Living arrangements of older persons around the world. New York: United Nations.

UNITED NATIONS, DEPARTMENT OF ECONOMIC AND SOCIAL AFFAIRS, POPULATION DIVISION 2015b. World Population Prospects, the 2015 Revision. New York: United Nations.

UNITED NATIONS POPULATION FUND 2012. Ageing in the twenty-first century: a celebration and a challenge. New York: United Nations Population Fund.

USHER, D., DUMSKYJ, M., HIMAGA, M., WILLIAMSON, T. H., NUSSEY, S. & BOYCE, J. 2004. Automated detection of diabetic retinopathy in digital retinal images: a tool for diabetic retinopathy screening. *Diabetic Medicine,* 21**,** 84-90.

VAAHTORANTA‐LEHTONEN, H., TUULONEN, A., ARONEN, P., SINTONEN, H., SUORANTA, L., KOVANEN, N., LINNA, M., LÄÄRÄ, E. & MALMIVAARA, A. 2007. Cost effectiveness and cost utility of an organized screening programme for glaucoma. *Acta Ophthalmologica Scandinavica,* 85**,** 508-518.

VAJARANANT, T. S., NAYAK, S., WILENSKY, J. T. & JOSLIN, C. E. 2010. Gender and glaucoma: what we know and what we need to know. *Current Opinion in Ophthalmology,* 21**,** 91-99.

VAN HOUWELINGEN, H. C., ARENDS, L. R. & STIJNEN, T. 2002. Advanced methods in meta‐analysis: multivariate approach and meta‐regression. *Statistics in Medicine,* 21**,** 589-624.

VAN LEIDEN, H. A., DEKKER, J. M., MOLL, A. C., NIJPELS, G., HEINE, R. J., BOUTER, L. M., STEHOUWER, C. D. & POLAK, B. C. 2003. Risk factors for incident retinopathy in a diabetic and nondiabetic population: the Hoorn study. *Archives of Ophthalmology,* 121**,** 245-251.

VANNEWKIRK, M. R., NANJAN, M. B., WANG, J. J., MITCHELL, P., TAYLOR, H. R. & MCCARTY, C. A. 2000. The prevalence of age-related maculopathy: The visual impairment project. *Ophthalmology,* 107**,** 1593-1600.

VARMA, R., CHOUDHURY, F., KLEIN, R., CHUNG, J., TORRES, M., AZEN, S. P. & LOS ANGELES LATINO EYE STUDY GROUP 2010. Four-year incidence and progression of diabetic retinopathy and macular edema: the Los Angeles Latino Eye Study. *American Journal of Ophthalmology,* 149**,** 752-761. e3.

VARMA, R., LEE, P. P., GOLDBERG, I. & KOTAK, S. 2011. An assessment of the health and economic burdens of glaucoma. *American Journal of Ophthalmology,* 152**,** 515-522.

VARMA, R., MACIAS, G. L., TORRES, M., KLEIN, R., PEÑA, F. Y., AZEN, S. P. & LOS ANGELES LATINO EYE STUDY GROUP 2007. Biologic risk factors associated with diabetic retinopathy: the Los Angeles Latino Eye Study. *Ophthalmology,* 114**,** 1332-1340.

VARMA, R., TORRES, M., PEÑA, F., KLEIN, R., AZEN, S. P. & LOS ANGELES LATINO EYE STUDY GROUP 2004. Prevalence of diabetic retinopathy in adult Latinos: the Los Angeles Latino eye study. *Ophthalmology,* 111**,** 1298-1306.

VASHIST, P., TALWAR, B., GOGOI, M., MARAINI, G., CAMPARINI, M., RAVINDRAN, R. D., MURTHY, G. V., FITZPATRICK, K. E., JOHN, N., CHAKRAVARTHY, U., RAVILLA, T. D. & FLETCHER, A. E. 2011. Prevalence of cataract in an older population in India: the India study of age-related eye disease. *Ophthalmology,* 118**,** 272-278. e2.

VELA, C., SAMSON, E., ZUNZUNEGUI, M. V., HADDAD, S., AUBIN, M.-J. & FREEMAN, E. E. 2012. Eye care utilization by older adults in low, middle, and high income countries. *BMC Ophthalmology,* 12**,** 5.

VELEZ-MONTOYA, R., OLIVER, S. C., OLSON, J. L., FINE, S. L., QUIROZ-MERCADO, H. & MANDAVA, N. 2014. Current knowledge and trends in age-related macular degeneration: genetics, epidemiology, and prevention. *Retina,* 34**,** 423-441.

VIECHTBAUER, W. 2010. Conducting meta-analyses in R with the metafor package. *Journal of Statistical Software,* 36**,** 1-48.

VINGERLING, J. R., DIELEMANS, I., HOFMAN, A., GROBBEE, D. E., HIJMERING, M., KRAMER, C. F. & DE JONG, P. T. 1995. The prevalence of age-related maculopathy in the Rotterdam Study. *Ophthalmology,* 102**,** 205-210.

VINSON, J. A. 2006. Oxidative stress in cataracts. *Pathophysiology,* 13**,** 151-162.

VITTINGHOFF, E. & MCCULLOCH, C. E. 2007. Relaxing the rule of ten events per variable in logistic and Cox regression. *American Journal of Epidemiology,* 165**,** 710-718.

VIZZERI, G. & WEINREB, R. N. 2010. Cataract surgery and glaucoma. *Current opinion in ophthalmology,* 21**,** 20-24.

VOLETI, V. B. & HUBSCHMAN, J.-P. 2013. Age-related eye disease. *Maturitas,* 75**,** 29-33.

VON ELM, E., ALTMAN, D. G., EGGER, M., POCOCK, S. J., GØTZSCHE, P. C., VANDENBROUCKE, J. P. & STROBE INITIATIVE 2007. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLoS Medicine,* 4**,** e296.

WALLACE, B. C., SCHMID, C. H., LAU, J. & TRIKALINOS, T. A. 2009. Meta-Analyst: software for meta-analysis of binary, continuous and diagnostic data. *BMC Medical Research Methodology,* 9**,** 80.

WANG, C.-W., CHAN, C. L. & CHI, I. 2014a. Overview of quality of life research in older people with visual impairment. *Advances in Aging Research,* 3**,** 79-94.

WANG, C. H., ZHAO, R., TANG, H. Y., YOU, J. H., ZHANG, S. P., ZHANG, C. D. & HE, X. G. 2014b. Status survey and preventive and control research of eye disease among the elderly in Wuqiao community of Shanghai (上海市邬桥社区老年人眼病现状调查和防治研究). *Occupation and Health (职业与健康).*

WANG, D., DING, X., HE, M., YAN, L., KUANG, J., GENG, Q. & CONGDON, N. 2010a. Use of eye care services among diabetic patients in urban and rural China. *Ophthalmology,* 117**,** 1755-1762.

WANG, W.-Y., ZHANG, L., LI, H.-R., LI, R.-B., YANG, L.-S. & LIAO, Y.-F. 2005. Spatial-temporal changes and trends of ageing in China. *Chinese Geographical Science,* 15**,** 200-205.

WANG, X., ZHENG, A., HE, X. & JIANG, H. 2014c. Integration of rural and urban healthcare insurance schemes in China: an empirical research. *BMC health services research,* 14**,** 142.

WANG, Y. X., XU, L., YANG, H. & JONAS, J. B. 2010b. Prevalence of glaucoma in North China: the Beijing eye study. *American Journal of Ophthalmology,* 150**,** 917-924.

WANG, Z. 2009. *China has 9.4m disabled elderly* [Online]. Available: http://china.org.cn/china/2009-10/10/content_18675068.htm [Accessed 15/01/2017.

WEINREB, R. N., AUNG, T. & MEDEIROS, F. A. 2014. The pathophysiology and treatment of glaucoma: a review. *JAMA,* 311**,** 1901-1911.

WEINREB, R. N. & KHAW, P. T. 2004. Primary open-angle glaucoma. *The Lancet,* 363**,** 1711-1720.

WELCH, V. A., GHOGOMU, E., HOSSAIN, A., AWASTHI, S., BHUTTA, Z. A., CUMBERBATCH, C., FLETCHER, R., MCGOWAN, J., KRISHNARATNE, S., KRISTJANSSON, E., SOHANI, S., SURESH, S., TUGWELL, P., WHITE, H. & WELLS, G. A. 2017. Mass deworming to improve developmental health and wellbeing of children in low-income and middle-income countries: a systematic review and network meta-analysis. *The Lancet Global Health,* 5**,** e40-e50.

WEST, S. K., RUBIN, G. S., BROMAN, A. T., MUNOZ, B., BANDEEN-ROCHE, K., TURANO, K. & SEE PROJECT TEAM 2002. How does visual impairment affect performance on tasks of everyday life?: The SEE Project. *Archives of Ophthalmology,* 120**,** 774-780.

WEST, S. L., GARTLEHNER, G., MANSFIELD, A. J., POOLE, C., TANT, E., LENFESTEY, N., LUX, L. J., AMOOZEGAR, J., MORTON, S. C. & CAREY, T. C. 2010. Comparative effectiveness review methods: clinical heterogeneity. Agency for Healthcare Research and Quality.

WHITMORE, A. V., LIBBY, R. T. & JOHN, S. W. 2005. Glaucoma: thinking in new ways—a role for autonomous axonal self-destruction and other compartmentalised processes? *Progress in Retinal and Eye Research,* 24**,** 639-662.

WIGGS, J. L. 2007. Genetic etiologies of glaucoma. *Archives of Ophthalmology,* 125**,** 30-37.

WILD, M., GILGEN, H., ROESCH, A., OHMURA, A., LONG, C. N., DUTTON, E. G., FORGAN, B., KALLIS, A., RUSSAK, V. & TSVETKOV, A. 2005. From dimming to brightening: Decadal changes in solar radiation at Earth's surface. *Science,* 308**,** 847-850.

WILKINSON, C., FERRIS, F. L., KLEIN, R. E., LEE, P. P., AGARDH, C. D., DAVIS, M., DILLS, D., KAMPIK, A., PARARAJASEGARAM, R., VERDAGUER, J. T. & GLOBAL DIABETIC RETINOPATHY PROJECT GROUP 2003. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. *Ophthalmology,* 110**,** 1677-1682.

WILLIAMS, R., AIREY, M., BAXTER, H., FORRESTER, J., KENNEDY-MARTIN, T. & GIRACH, A. 2004. Epidemiology of diabetic retinopathy and macular oedema: a systematic review. *Eye,* 18**,** 963–983.

WILSON, C. 2004. Fertility below replacement level. *Science,* 304**,** 207-209.

WOLFS, R. C., KLAVER, C. C., RAMRATTAN, R. S., VAN DUIJN, C. M., HOFMAN, A. & DE JONG, P. T. 1998. Genetic risk of primary open-angle glaucoma: population-based familial aggregation study. *Archives of Ophthalmology,* 116**,** 1640-1645.

WONG, I. Y. H., KOO, S. C. Y. & CHAN, C. W. N. 2011. Prevention of age-related macular degeneration. *International Ophthalmology,* 31**,** 73-82.

WONG, T., CHAKRAVARTHY, U., KLEIN, R., MITCHELL, P., ZLATEVA, G., BUGGAGE, R., FAHRBACH, K., PROBST, C. & SLEDGE, I. 2008a. The natural history and prognosis of neovascular age-related macular degeneration: a systematic review of the literature and meta-analysis. *Ophthalmology,* 115**,** 116-126. e1.

WONG, T., LOON, S. & SAW, S. 2006a. The epidemiology of age related eye diseases in Asia. *British Journal of Ophthalmology,* 90**,** 506-511.

WONG, T. Y. & BRESSLER, N. M. 2016. Artificial intelligence with deep learning technology looks into diabetic retinopathy screening. *JAMA,* 316**,** 2366-2367.

WONG, T. Y., CHEUNG, N., TAY, W. T., WANG, J. J., AUNG, T., SAW, S. M., LIM, S. C., TAI, E. S. & MITCHELL, P. 2008b. Prevalence and risk factors for diabetic retinopathy: the Singapore Malay Eye Study. *Ophthalmology,* 115**,** 1869-1875.

WONG, T. Y., KLEIN, R., ISLAM, F. A., COTCH, M. F., FOLSOM, A. R., KLEIN, B. E., SHARRETT, A. R., SHEA, S. & MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS (MESA) 2006b. Diabetic retinopathy in a multi-ethnic cohort in the United States. *American Journal of Ophthalmology,* 141**,** 446-455.e1.

WONG, W. L., SU, X., LI, X., CHEUNG, C. M. G., KLEIN, R., CHENG, C.-Y. & WONG, T. Y. 2014. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. *The Lancet Global Health,* 2**,** e106-e116.

WOO, J., KWOK, T., SZE, F. & YUAN, H. 2002. Ageing in China: health and social consequences and responses. *International Journal of Epidemiology,* 31**,** 772-775.

WORLD BANK. 2015. *Poverty & Equity Data-China* [Online]. Available: http://povertydata.worldbank.org/poverty/country/CHN [Accessed 23/01/2017.

WORLD HEALTH ORGANIZATION 1993. ICD-10: International statistical classification of diseases and health-related problems. Tenth Revision. Geneva: World Health Organization.

WORLD HEALTH ORGANIZATION. 2002. *Proposed Working Definition of an Older Person in Africa for the MDS Project: Definition of an older or elderly person* [Online]. Available: http://www.who.int/healthinfo/survey/ageingdefnolder/en/ [Accessed 07/01/2017.

WORLD HEALTH ORGANIZATION 2006. Prevention of blindness from diabetes mellitus. Geneva: World Health Organization.

WORLD HEALTH ORGANIZATION 2008. The global burden of disease: 2004 update. Geneva: World Health Organization.

WORLD HEALTH ORGANIZATION 2011a. Global health and aging. Geneva: World Health Organization.

WORLD HEALTH ORGANIZATION 2011b. Health Situation Analysis in the African Region: Atlas of Health Statistics, 2011. Brazzaville: World Health Organization Regional Office for Africa.

WORLD HEALTH ORGANIZATION 2011c. World report on disability. Geneva: World Health Organization.

WORLD HEALTH ORGANIZATION 2013. Universal eye health: a global action plan 2014–2019. Geneva: World Health Organization.

WORLD HEALTH ORGANIZATION. 2014a. *Glaucoma is second leading cause of blindness globally* [Online]. Available: http://www.who.int/bulletin/volumes/82/11/feature1104/en/ [Accessed 31/01/2017.

WORLD HEALTH ORGANIZATION. 2014b. *Visual impairment and blindness* [Online]. World Health Organization. Available: http://www.who.int/mediacentre/factsheets/fs282/en/ [Accessed 17/01/2017.

WORLD HEALTH ORGANIZATION. 2015a. *Projections of mortality and burden of disease, 2004-2030* [Online]. Available: http://www.who.int/healthinfo/global_burden_disease/projections2004/en/ [Accessed 14/01/2017.

WORLD HEALTH ORGANIZATION 2015b. World report on ageing and health. Geneva: World Health Organization.

WORLD HEALTH ORGANIZATION. 2017a. *Blindness as a public health problem in China* [Online]. World Health Organization. Available: http://www.who.int/mediacentre/factsheets/fs230/en/ [Accessed 17/01/2017.

WORLD HEALTH ORGANIZATION. 2017b. *Global health observatory (GHO) data* [Online]. Available: http://www.who.int/gho/en/ [Accessed 08/01/2017.

WU, B., LI, J., LIN, H. & WU, H. 2016. Different Strategies for the Treatment of Age-Related Macular Degeneration in China: An Economic Evaluation. *Journal of Ophthalmology*, 2016.

WU, L., FERNANDEZ-LOAIZA, P., SAUMA, J., HERNANDEZ-BOGANTES, E. & MASIS, M. 2013. Classification of diabetic retinopathy and diabetic macular edema. *World Journal of Diabetes,* 4**,** 290–294.

XIA, J., WRIGHT, J. & ADAMS, C. E. 2008. Five large Chinese biomedical bibliographic databases: accessibility and coverage. *Health Information & Libraries Journal,* 25**,** 55-61.

XU, H., LUO, J. & WU, B. 2016. Self–reported diabetes education among Chinese middle–aged and older adults with diabetes. *Journal of Global Health,* 6**,** 020402.

XU, L., CAO, W. F., WANG, Y. X., CHEN, C. X. & JONAS, J. B. 2008. Anterior chamber depth and chamber angle and their associations with ocular and general parameters: the Beijing Eye Study. *American Journal of Ophthalmology,* 145**,** 929-936.e1.

XU, L., WANG, Y., LI, Y., WANG, Y., CUI, T., LI, J. & JONAS, J. B. 2006. Causes of blindness and visual impairment in urban and rural areas in Beijing: the Beijing Eye Study. *Ophthalmology,* 113**,** 1134. e1-1134. e11.

XU, Y., WANG, L., HE, J., BI, Y., LI, M., WANG, T., WANG, L., JIANG, Y., DAI, M., LU, J., XU, M., LI, Y., HU, N., LI, J., MI, S., CHEN, C.-S., LI, G., MU, Y., ZHAO, J., KONG, L., CHEN, J., LAI, S., WANG, W., ZHAO, W., NING, G. & 2010 CHINA NONCOMMUNICABLE DISEASE SURVEILLANCE GROUP 2013. Prevalence and control of diabetes in Chinese adults. *JAMA,* 310**,** 948-959.

YAMAMOTO, T., IWASE, A., ARAIE, M., SUZUKI, Y., ABE, H., SHIRATO, S., KUWAYAMA, Y., MISHIMA, H. K., SHIMIZU, H., TOMITA, G., INOUE, Y., KITAZAWA, Y., TAJIMI STUDY GROUP & JAPAN GLAUCOMA SOCIETY 2005. The Tajimi Study report 2: prevalence of primary angle closure and secondary glaucoma in a Japanese population. *Ophthalmology,* 112**,** 1661-1669.

YAN, H., GUO, Y., ZHANG, J., DING, Z., HA, W. & HARDING, J. 2008. Effect of carnosine, aminoguanidine, and aspirin drops on the prevention of cataracts in diabetic rats. *Molecular vision,* 14**,** 2282–2291.

YAN, X., LIU, T., GRUBER, L., HE, M. & CONGDON, N. 2012. Attitudes of physicians, patients, and village health workers toward glaucoma and diabetic retinopathy in rural China: a focus group study. *Archives of Ophthalmology,* 130**,** 761-770.

YANAGI, M., KAWASAKI, R., WANG, J. J., WONG, T. Y., CROWSTON, J. & KIUCHI, Y. 2011. Vascular risk factors in glaucoma: a review. *Clinical & Experimental Ophthalmology,* 39**,** 252-258.

YANG, C.-M., YEH, P.-T., YANG, C.-H. & CHEN, M.-S. 2008. Bevacizumab pretreatment and long-acting gas infusion on vitreous clear-up after diabetic vitrectomy. *American Journal of Ophthalmology,* 146**,** 211-217. e1.

YAU, J. W., ROGERS, S. L., KAWASAKI, R., LAMOUREUX, E. L., KOWALSKI, J. W., BEK, T., CHEN, S.-J., DEKKER, J. M., FLETCHER, A., GRAUSLUND, J., HAFFNER, S., HAMMAN, R. F., IKRAM, M. K., KAYAMA, T., KLEIN, B. E., KLEIN, R., KRISHNAIAH, S., MAYURASAKORN, K., O'HARE, J. P., ORCHARD, T. J., PORTA, M., REMA, M., ROY, M. S., SHARMA, T., SHAW, J., TAYLOR, H., TIELSCH, J. M., VARMA, R., WANG, J. J., WANG, N., WEST, S.,

XU, L., YASUDA, M., ZHANG, X., MITCHELL, P., WONG, T. Y. & META-ANALYSIS FOR EYE DISEASE (META-EYE) STUDY GROUP 2012. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care,* 35**,** 556-564.

YE, H., ZHANG, Q., LIU, X., CAI, X., YU, W., YU, S., WANG, T., LU, W., LI, X., JIN, H., HU, Y., KANG, X. & ZHAO, P. 2014. Prevalence of Age-Related Macular Degeneration in an Elderly Urban Chinese Population in China: The Jiangning Eye StudyThe Jiangning Eye Study. *Investigative Ophthalmology & Visual Science,* 55**,** 6374-6380.

YE, J., HE, J., WANG, C., WU, H., SHI, X., ZHANG, H., XIE, J. & LEE, S. Y. 2012. Smoking and Risk of Age-Related Cataract: A Meta-Analysis. *Investigative Ophthalmology & Visual Science,* 53**,** 3885-3895.

YIN, Q., HU, A., LIANG, Y., ZHANG, J., HE, M., LAM, D. S., GE, J., WANG, N., FRIEDMAN, D. S., ZHAO, J. & CONGDON, N. 2009. A two-site, population-based study of barriers to cataract surgery in rural China. *Investigative Ophthalmology & Visual Science,* 50**,** 1069-1075.

YORSTON, D., WICKHAM, L., BENSON, S., BUNCE, C., SHEARD, R. & CHARTERIS, D. 2008. Predictive clinical features and outcomes of vitrectomy for proliferative diabetic retinopathy. *British Journal of Ophthalmology,* 92**,** 365-368.

YU, H. 2015. Universal health insurance coverage for 1.3 billion people: what accounts for China's success? *Health policy,* 119**,** 1145-1152.

YU, P., SONG, X., SHI, J., MITNITSKI, A., TANG, Z., FANG, X. & ROCKWOOD, K. 2012. Frailty and survival of older Chinese adults in urban and rural areas: results from the Beijing Longitudinal Study of Aging. *Archives of Gerontology and Geriatrics,* 54**,** 3-8.

ZENG, Y. & HESKETH, T. 2016. The effects of China's universal two-child policy. *The Lancet,* 388**,** 1930-1938.

ZETTERBERG, M. & CELOJEVIC, D. 2015. Gender and cataract–the role of estrogen. *Current Eye Research,* 40**,** 176-190.

ZHANG, K., ZHU, X. & LU, Y. 2016. Effect of Mild Heating on Human Lens Epithelial Cells: A Possible Model of Lens Aging. *Scientific Reports,* 6**,** 33917.

ZHANG, K. H. & SONG, S. 2003. Rural–urban migration and urbanization in China: Evidence from time-series and cross-section analyses. *China Economic Review,* 14**,** 386-400.

ZHANG, L., CHOW, E. P., JING, J., ZHUANG, X., LI, X., HE, M., SUN, H., LI, X., GORGENS, M., WILSON, D., WANG, L., GUO, W., LI, D., CUI, Y., WANG, L., WANG, N., WU, Z. & WILSON, D. P. 2013. HIV prevalence in China: integration of surveillance data and a systematic review. *The Lancet Infectious Diseases,* 13**,** 955-963.

ZHANG, M., WU, J., LI, L., XU, D., LAM, D. S., LEE, J., GRIFFITHS, S. & CONGDON, N. 2010a. Impact of cataract screening outreach in rural China. *Investigative Ophthalmology & Visual Science,* 51**,** 110-114.

ZHANG, N. J., GUO, M. & ZHENG, X. 2012. China: Awakening giant developing solutions to population aging. *The Gerontologist,* 52**,** 589–596.

ZHANG, X., SAADDINE, J. B., CHOU, C.-F., COTCH, M. F., CHENG, Y. J., GEISS, L. S., GREGG, E. W., ALBRIGHT, A. L., KLEIN, B. E. & KLEIN, R. 2010b. Prevalence of diabetic retinopathy in the United States, 2005-2008. *JAMA,* 304**,** 649-656.

ZHANG, Y., HU, S. & CHANG, J. 2015. Burden of Wet Age-related Macular Degeneration in China (湿性老年性黄斑变性的疾病负担研究). *Chinese Health Economics (中国卫生经济)***,** 63-65.

ZHAO, C., WANG, W., XU, D., LI, H., LI, M. & WANG, F. 2014. Insulin and risk of diabetic retinopathy in patients with type 2 diabetes mellitus: data from a meta-analysis of seven cohort studies. *Diagnostic Pathology,* 9**,** 130.

ZHAO, J., ELLWEIN, L. B., CUI, H., GE, J., GUAN, H., LV, J., MA, X., YIN, J., YIN, Z. Q., YUAN, Y. & LIU, H. 2010. Prevalence and outcomes of cataract surgery in rural China: the China nine-province survey. *Ophthalmology,* 117**,** 2120-2128.

ZHAO, J., SUI, R. & JIA, L. 2001. Prevalence of cataract and surgical coverage among adults aged 50 or above in Shunyi District of Beijing, China. *Chinese Journal of Ophthalmology (中华眼科杂志),* 37**,** 3-8.

ZHAO, Y., HU, Y., SMITH, J. P., STRAUSS, J. & YANG, G. 2012. Cohort profile: The China health and retirement longitudinal study (CHARLS). *International Journal of Epidemiology,* 43**,** 61-68.

ZHAO, Y., STRAUSS, J., YANG, G., GILES, J., HU, P., HU, Y., LEI, X., LIU, M., PARK, A., SMITH, J. P. & WANG, Y. 2013. China health and retirement longitudinal study–2011–2012 national baseline users' guide. Beijing: National School of Development, Peking University.

ZHENG, Y., HE, M. & CONGDON, N. 2012. The worldwide epidemic of diabetic retinopathy. *Indian Journal of Ophthalmology,* 60**,** 428–431.

ZHOU, C., QIAN, S., WU, P. & QIU, C. 2013. Anxiety and depression in Chinese patients with glaucoma: sociodemographic, clinical, and self-reported correlates. *Journal of Psychosomatic Research,* 75**,** 75-82.

ZHOU, C., QIAN, S., WU, P. & QIU, C. 2014. Quality of life of glaucoma patients in China: sociodemographic, clinical, and psychological correlates—a cross-sectional study. *Quality of Life Research,* 23**,** 999-1008.

ZHOU, Q., FRIEDMAN, D. S., LU, H., DUAN, X., LIANG, Y., YANG, X., WANG, F. & WANG, N. 2007. The epidemiology of age-related eye diseases in Mainland China. *Ophthalmic Epidemiology,* 14**,** 399-407.

ZHOU, Y. & JIA, X.-P. 2011. An investigation of cataract prevalence in elderly in one community (某社区老年人口白内障患病率调查). *Guide of China Medicine (中国医药指南),* 9**,** 136-137.

ZHU, M., ZHU, J., LU, L., HE, X., ZHAO, R. & ZOU, H. 2014. Four-year analysis of cataract surgery rates in Shanghai, China: a retrospective cross-sectional study. *BMC Ophthalmology,* 14**,** 3.

ZIMMER, Z. & KWONG, J. 2003. Family size and support of older adults in urban and rural China: Current effects and future implications. *Demography,* 40**,** 23-44.

APPENDICES

Appendix table 1. level-one ethical self-assessment

University of Edinburgh,

Usher Institute of Population Health Sciences and Informatics
RESEARCH ETHICS SUBGROUP

Self-Audit Checklist for Level 1 Ethical Review for PGR projects

See **Intra** website for further information: http://www.cphs.mvm.ed.ac.uk/intra/research/ethicalReview.php

NOTE to student: *Completion of this form should be under the **oversight** of your supervisor. A good strategy would be to complete a draft as best you can, then discuss with your supervisor before completing a final copy for your supervisor to sign.*

***Proposed Project** (State research question and topic area, and briefly describe method/ data. Specify also countries in which data will be collected.):*

Project title: The national and subnational disease burden of age-related eye diseases in China

In this project, the prevalence and disease burden of four major age-related eye diseases, including age-related macular degeneration, glaucoma, cataract and diabetic retinopathy will be estimated. The primary research methods will be systematic review and meta-analysis. For the project of diabetic retinopathy, a open-accessed dataset- China Health and Retirement Longitudinal Study will be additionally used. This project will be conducted in the UK.

1. Bringing the University into disrepute

Is there any aspect of the proposed research which might bring the University into disrepute? *YES/ NO ✓*

2. Data protection and consent

Are there any issues of DATA PROTECTION or CONSENT which are NOT adequately dealt with via established procedures? YES/ NO √

These include well-established sets of undertakings. For example, a 'No' answer is justified *only if*:

(a) There is compliance with the University of Edinburgh's Data Protection procedures (see www.recordsmanagement.ed.ac.uk);

(b) Respondents give consent regarding the collection, storage and, if appropriate, archiving and destruction of data;

(c) Identifying information (eg consent forms) is held separately from data;

(d) There is Caldicott Guardian approval for (or approval will be obtained prior to) obtaining/ analysing NHS patient-data.

(e) There are no other special issues arising about confidentiality/consent.

3. Study participants

a) Will a study researcher be in direct contact with participants to collect data, whether face-to-face, or by telephone, electronic means or post, or by observation? (eg interviews, focus groups, questionnaires, assessments) YES/ NO√

***b)* Answer this only if qu. 3 above = 'YES':**

In ethical terms, could any participants in the research be considered to be 'vulnerable'? e.g. children & young people under age of 16, people who are in custody or care (incl. school), a marginalised/stigmatised group ☐

Please tick one: 'vulnerable' ☐ not 'vulnerable'

4. Moral issues and Researcher/Institutional Conflicts of Interest

Are there any SPECIAL MORAL ISSUES/CONFLICTS OF INTEREST? YES/ NO√

(a) An example of conflict of interest for a researcher would be a financial or non-financial benefit for him/herself or for a relative of friend.

(b) Particular moral issues or concerns could arise, for example where the purposes of research are concealed, where respondents are unable to provide informed consent, or where research findings could impinge negatively/ differentially upon the interests of participants.

(c) Where there is a dual relationship between researcher and participant (eg where research is undertaken by practitioners so that the participant might be unclear as to the distinction between 'care' and research)

5. Protection of research subject confidentiality

Are there any issues of CONFIDENTIALITY which are NOT adequately handled by normal tenets of confidentiality for academic research? YES/ NO√

These include well-established sets of undertakings that should be agreed with collaborating and participating individuals/organisations. For example, a 'No' answer is justified *only if*:

(a) There will be no attribution of individual responses;

(b) Individuals (and, where appropriate, organisations) are anonymised in stored data, publications and presentation;

(c) There has been specific agreement with respondents regarding feedback to collaborators and publication.

6. Potential physical or psychological harm, discomfort or stress

(a) Is there a FORSEEABLE POTENTIAL for PSYCHOLOGICAL HARM or STRESS for participants? YES/ NO√

(b) Is there a FORSEEABLE POTENTIAL for PHYSICAL HARM or DISCOMFORT for participants? YES/ NO√

(c) Is there a FORSEEABLE RISK to the researcher? YES/ NO√

Examples of issues/ topics that have the potential to cause psychological harm, discomfort or distress and should lead you to answer 'yes' to this question include, but are not limited to:

relationship breakdown; bullying; bereavement; mental health difficulties; trauma / PTSD; violence or sexual violence; physical, sexual or emotional abuse in either children or adults.

7. Duty to disseminate research findings

Are there issues which will prevent all relevant stakeholders having access to a clear, understandable and accurate summary of the research findings if they wish?* YES/ NO√

** If, and only if, you answered 'yes' to 3 above, 'stakeholders' includes the participants in the research*

Overall assessment

➢ If every answer above is a definite NO, the self-audit has been conducted and confirms the ***ABSENCE OF REASONABLY FORESEEABLE ETHICAL RISKS*** – *please tick box* [√]

*This means that regarding this study, as currently self-audited, no further ethical review actions are required within Usher. However, if in the coming weeks/months there is any change to the research plan envisaged now (and outlined above), the study should be **re-audited** against a Level 1 form, because it may be that the change made negates the absence of ethical risks signed off here.*

Two copies of this form should be taken for inclusion in the final dissertation/thesis and **the original should be returned to Usher Ethics admin –** usher.ethics@ed.ac.uk

The Usher Ethics Subgroup cannot check validity of responses made here (the light touch Level 1 form means we have insufficient detail to do so). ***Receipt of this form will be acknowledged, but no formal letter of approval can be/will be sent.*** *If some formal letter is required e.g.for a funder, please ask in your covering email. We will then send a form of words re the self-audit process.*

➢ If one or more answers are YES, then risks have been identified and prior to commencing any data collection **formal ethical review** is required - either:

~ by NHS REC (NB a copy of ethics application and decision letter, and this level 1 form, must be sent to Usher Ethics usher.ethics@ed.ac.uk); or

~ if not to be formally reviewed by NHS REC, then Usher level 2/3 ethical review required. *[If either 4 is 'yes' or 3b is 'vulnerable' then it is possible level 3 review is required.]*

Peige Song	Kit Yee Chan
Student Name	Supervisor Name
Peige Song	
Student Signature	Supervisor Signature *****

*** NOTE to supervisor:** *By counter-signing this check-list as truly warranting all 'No' answers,* ***you*** *are taking responsibility, on behalf of Usher and UoE, that the research proposed truly poses no potential ethical risks. Therefore, if there is any doubt on any issue, it would be a wise precaution to mark it as 'uncertain' and contact the Ethics Subgroup as to whether a level 2 form might be required as well. (See Intra Ethics website – URL at top of form)* *28 Oct 2018*

Appendix table 2. Search strategy to identify studies reporting the prevalence of age-related macular degeneration in China

CNKI

Access Date: 26 JUN 2016

Subject category: Medicine & Public Health

Sub-database: Journal, Featured journal, Doctoral dissertation, Master dissertation, Domestic conferences, International conferences

检索表达式:

(SU % '年龄相关黄斑变性' + '年龄相关性黄斑变性' + '老年黄斑变性'+ '老年性黄斑变性' + '年龄相关黄斑病变'+ '年龄相关性黄斑病变' + '老年黄斑病变'+ '老年性黄斑病变') AND (SU % '发病率' + '发生率' + '患病率'+ '罹患率' + '现患率'+ '死亡率' + '病死率'+ '流行' + '负担'+ '现况调查'+ '现况研究')

发表时间: 从 1990-01-01 到 2016-06-26

Search Terms: (SU % 'nianlingxiangguanhuangbanbianxing' + 'nianlingxiangguanxinghuangbanbianxing' + 'laonianhuangbanbianxing'+ 'laonianxinghuangbanbianxing' + 'nianlingxianghguanhuangbanbingbian'+ 'nianlingxiangguanxinghuangbanbingbian' + 'laonianhuangbanbingbian'+ 'laonianxinghuangbanbingbian') AND (SU % 'fabinglv' + 'fashenglv' + 'huanbinglv'+ 'lihuanlv' + 'xianhuanlv'+ 'siwanglv' + 'bingsilv'+ 'liuxing' + 'fudan'+ 'xiankuangdiaocha'+ 'xiankuangyanjiu')

Published time: From 01/01/1990 to 26/06/2016

Wanfang

Access Date: 26 Jun 2016

Sub-database: Journal articles, Dissertations, Conference articles, Foreign journals, Foreign conferences

检索表达式：(主题:(年龄相关黄斑变性) + 主题:(年龄相关性黄斑变性) + 主题:(老年黄斑变性) + 主题:(老年性黄斑变性) + 主题:(年龄相关黄斑病变) + 主题:(年龄相关性黄斑病变) + 主题:(老年黄斑病变) + 主题:(老年性黄斑病变)) * (主题:(发病率) + 主题:(发生率) + 主题:(患病率) +主题:(罹患率) + 主题:(现患率) + 主题:(死亡率) +主题:(病死率) + 主题:(流行) + 主题:(负担)+ 主题:(现况调查) + 主题:(现况研究))

时间：1990-2016

Search Terms: (subject: (nianlingxiangguanhuangbanbianxing) + subject: (nianlingxiangguanxinghuangbanbianxing) + subject: (laonianhuangbanbianxing) + subject: (laonianxinghuangbanbianxing) + subject: (nianlingxianghguanhuangbanbingbian)+ subject: (nianlingxiangguanxinghuangbanbingbian) + subject: (laonianhuangbanbingbian) + subject: (laonianxinghuangbanbingbian))* (subject: (fabinglv) + subject: (fashenglv) + subject: (huanbinglv)+ subject: (lihuanlv) + subject: (xianhuanlv) + subject: (siwanglv)+ subject: (bingsilv) + subject: (liuxing) + subject: (fudan)+ subject: (xiankuangdiaocha) + subject: (xiankuangyanjiu))

Date: 1990-2016

CBM-SinoMed

Access Date: 26 Jun 2016

Journal category: All journals

检索表达式：

((年龄相关黄斑变性) OR (年龄相关性黄斑变性) OR (老年黄斑变性) OR (老年性黄斑变性) OR (年龄相关黄斑病变) OR (年龄相关性黄斑病变) OR (老年黄斑病变) OR (老

年性黄斑病变)) AND ((发病率) OR (发生率) OR (患病率) OR (罹患率) OR (现患率) OR (死亡率) OR (病死率) OR (流行) OR (负担) OR (现况调查) OR (现况研究))

时间：1990-2016

Search Terms: ((nianlingxiangguanhuangbanbianxing) OR (nianlingxiangguanxinghuangbanbianxing) OR (laonianhuangbanbianxing) OR (laonianxinghuangbanbianxing) OR (nianlingxianghguanhuangbanbingbian) OR (nianlingxiangguanxinghuangbanbingbian) OR (laonianhuangbanbingbian) OR (laonianxinghuangbanbingbian))* ((fabinglv) OR (fashenglv) OR (huanbinglv) OR (lihuanlv) OR (xianhuanlv) OR (siwanglv) OR (bingsilv) OR (liuxing) OR (fudan) OR (xiankuangdiaocha) OR (xiankuangyanjiu))

Date: 1990-2016

PubMed

Access Date: 16 Sep 2016

Search Terms:

((age-related macular degeneration OR age related macular degeneration OR age-related maculopathy OR age related maculopathy) AND (China OR Chinese OR Hongkong OR Macao OR Taiwan) AND (inciden* OR prevalen* OR morbidity OR mortality OR epidemiology)) AND ("1990/01/01"[Date - Publication] : "2016/09/17"[Date - Publication])

Embase (Ovid)

Access Date: 17 Sep 2016

#	Searches
1	age-related macular degeneration.mp. or exp retina macula age related degeneration/ or exp age related macular degeneration/ or exp retina macula degeneration/
2	exp retina maculopathy/ or age-related maculopathy.mp.

3	China.mp. or exp China/
4	exp Chinese/ or Chinese.mp.
5	Hong Kong.mp. or exp Hong Kong/
6	Macao.mp. or exp Macao/
7	Taiwan.mp. or exp Taiwan/
8	exp incidence/ or inciden*.mp.
9	exp prevalence/ or prevalen*.mp.
10	morbidity.mp. or morbidity/
11	mortality/ or Mortality.mp.
12	exp epidemiology/ or Epidemiology.mp.
13	1 or 2
14	3 or 4 or 5 or 6 or 7
15	8 or 9 or 10 or 11 or 12
16	13 and 14 and 15
17	limit 16 to yr="1990 -Current"

Medline (Ovid)

Access Date: 17 Sep 2016

Search Terms:

#	Searches
1	age-related macular degeneration.mp. or exp Macular Degeneration/
2	age-related maculopathy.mp.
3	China.mp. or exp China/
4	Chinese.mp.
5	Hong Kong.mp. or exp Hong Kong/
6	Macao.mp. or exp Macau/
7	Taiwan.mp. or exp Taiwan/
8	exp Incidence/ or inciden*.mp.

9	exp Prevalence/ or prevalen*.mp.
10	morbidity.mp. or exp Morbidity/
11	mortality.mp. or exp Mortality/
12	epidemiology.mp. or exp Epidemiology/
13	1 or 2
14	3 or 4 or 5 or 6 or 7
15	8 or 9 or 10 or 11 or 12
16	13 and 14 and 15
17	limit 16 to yr="1990 -Current"

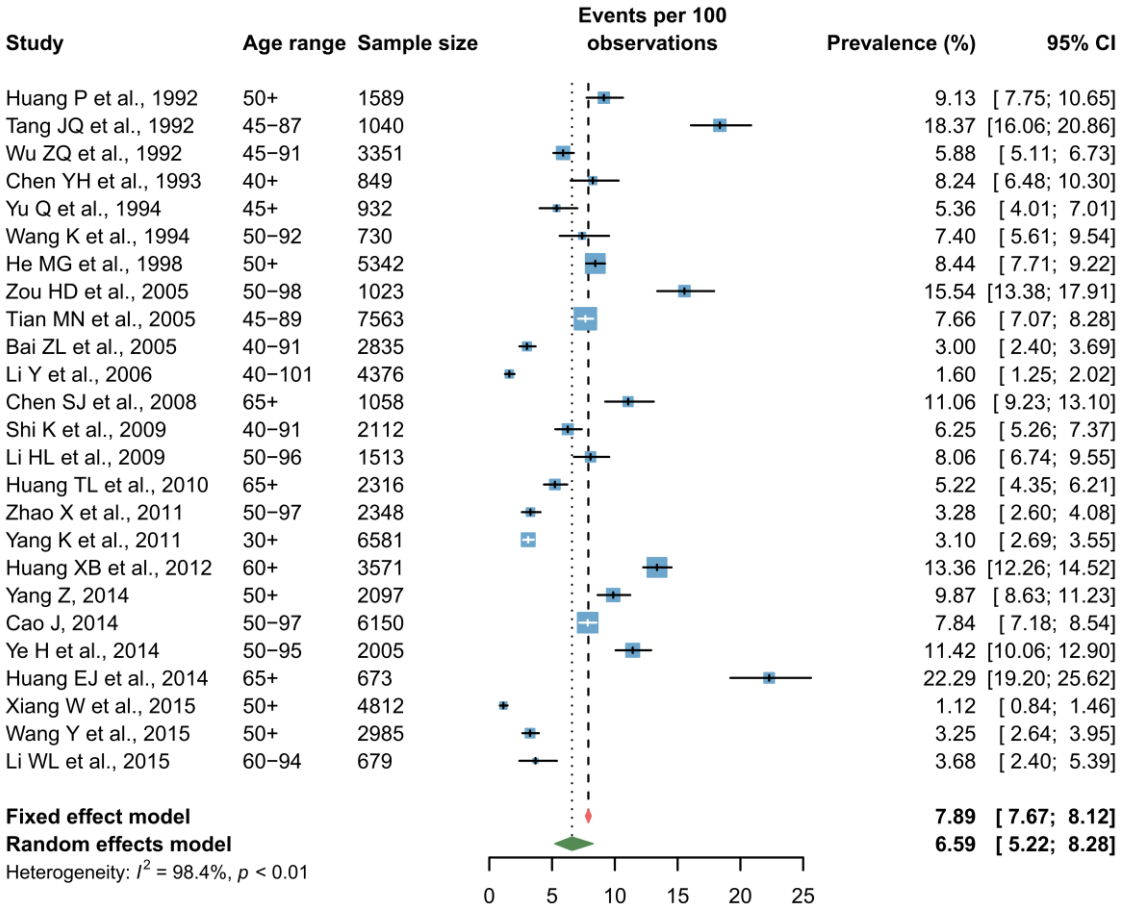
Appendix table 3. The year of publication and investigation and corresponding time-lag in the included studies on AMD prevalence in China (n=25)

Study ID	Study	Year Published	Median investigation year	Time-lag
AMD-01	Huang P et al. (1992)	1992	1987	5
AMD-02	Tang JQ et al. (1992)	1992	-	-
AMD-03	Wu ZQ et al. (1992)	1992	1989	3
AMD-04	Chen YH et al. (1993)	1993	1991	2
AMD-05	Yu Q et al. (1994)	1994	1990	4
AMD-06	Wang K et al. (1994)	1994	1989	5
AMD-07	He MG et al. (1998)	1998	1997	1
AMD-08	Zou HD et al. (2005)	2005	2003	2
AMD-09	Tian MN et al. (2005)	2005	-	-
AMD-10	Bai ZL et al. (2005)	2005	2003	2
AMD-11	Shi K et al. (2009)	2009	2006	3
AMD-12	Li HL et al. (2009)	2009	2009	0
AMD-13	Zhao X et al. (2011)	2011	2006	5
AMD-14	Huang XB et al. (2012)	2012	2008	4
AMD-15	Yang Z (2014)	2014	2013	1
AMD-16	Cao J (2014)	2014	2010	4
AMD-17	Xiang W et al. (2015)	2015	2014	1
AMD-18	Wang Y et al. (2015)	2015	2015	0
AMD-19	Li WL et al. (2015)	2015	2013	2
AMD-20	Li Y et al. (2006)	2006	2001	5
AMD-21	Chen SJ et al. (2008)	2008	1999	9
AMD-22	Huang TL et al. (2010)	2010	-	-
AMD-23	Yang K et al. (2011)	2011	2006	5
AMD-24	Ye H et al. (2014)	2014	2013	1
AMD-25	Huang EJ et al. (2014)	2014	2011	3

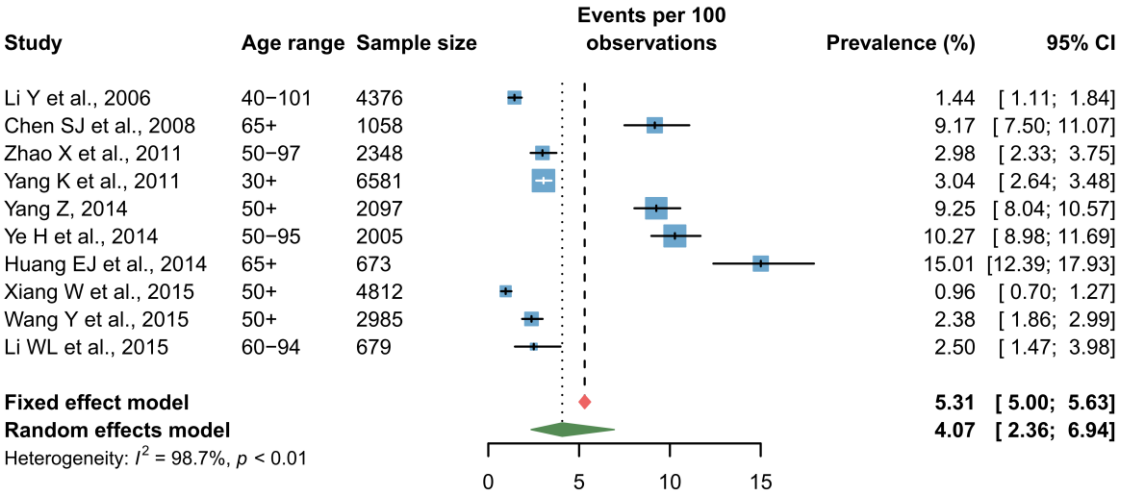
Note: "-" represents unavailable data; Based on the information from 22 studies, the average time-lag between year of publication and year of investigation was 3.05.

Appendix table 4. Meta-analysis of the prevalence of AMD for assessing heterogeneity between studies

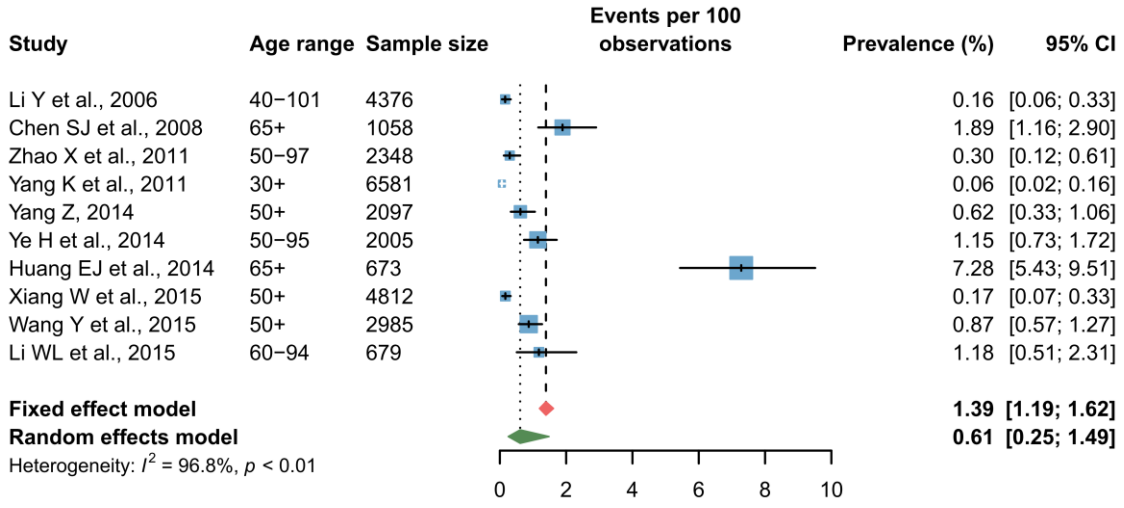
To assess heterogeneity between studies that reported prevalence rates of AMD, standard meta-analyses were performed. First, the variances of the raw prevalence estimates were stabilised by using logit transformation. Then the heterogeneity between studies was assessed by the Cochran's Q and I^2 statistics, a p-value<0.05 indicates heterogeneity between studies in Q statistic, and I^2 represents the proportion of total variation that is due to heterogeneity rather than chance, where a value of 0% indicates no observed heterogeneity and values of <25%, 25–75%, and >75% reflect low, moderate and high heterogeneity, respectively (Higgins and Thompson, 2002, Higgins et al., 2003). As shown in **Appendix figures 1-5**, significant high heterogeneity was indicated between studies that reported prevalence rates of any AMD (I^2=98.4%, p<0.0001), early AMD (I^2=98.7%, p<0.0001), late AMD (I^2=96.8%, p<0.0001), GA (I^2=90.5%, p<0.0001) and NVAMD (I^2=94.0%, p<0.0001).



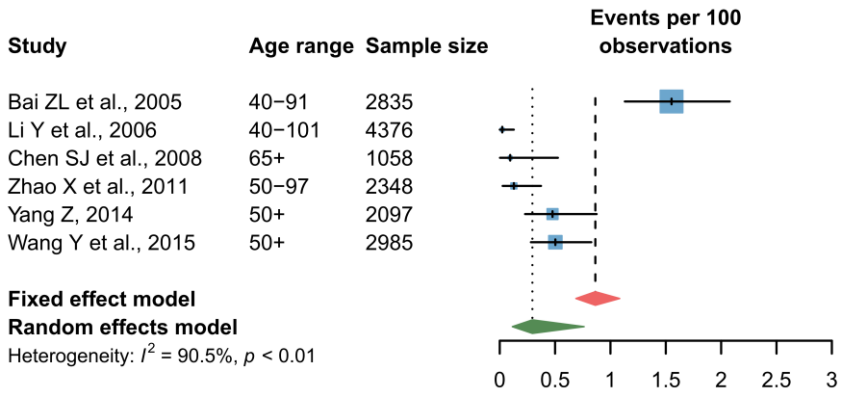
Appendix figure 1. Meta-analysis of the prevalence of any AMD (n=25)



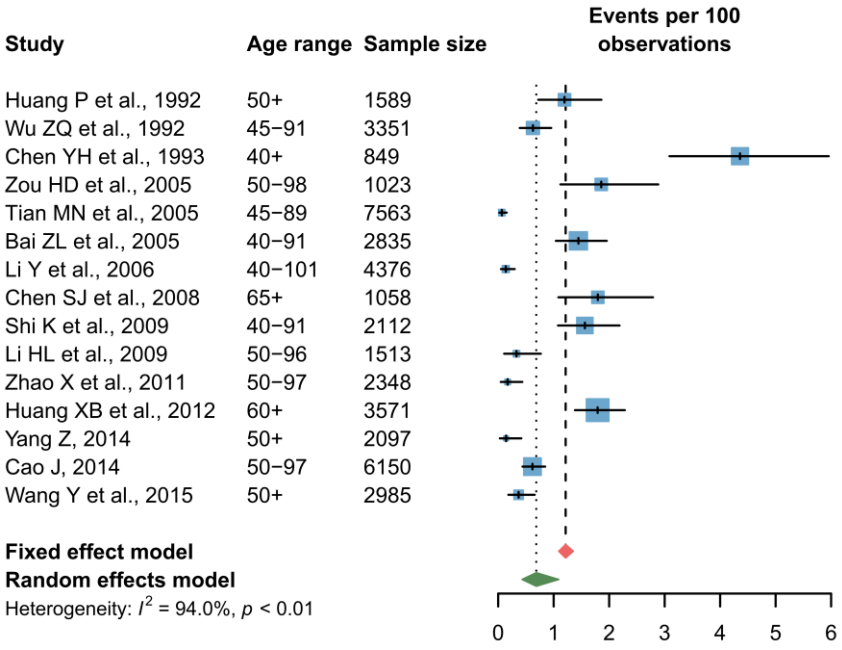
Appendix figure 2. Meta-analysis of the prevalence of early AMD (n=9)



Appendix figure 3. Meta-analysis of the prevalence of late AMD (n=9)



Appendix figure 4. Meta-analysis of the prevalence of GA (n=6)



Appendix figure 5. Meta-analysis of the prevalence of NVAMD (n=15)

Appendix table 5. Full list of the included studies on AMD prevalence in China (n=25)

Study ID	Reference
AMD-01	Ping Huang, Ren-xiu He, Guo-zhen He, et al. 黄平，何仁秀，何国桢，等. The investigation of Age-related Macular Degeneration in Hunan Province* (湖南省老年黄斑变性流行病学调查) [J]. Chinese Ophthal Res (眼科研究). 1992(01): 60-61.
AMD-02	Jia-quan Tan, Ai-guang Nie, De-yong Jiang, et al. 谭家铨，聂爱光，姜德泳，等. The investigation of Age-related Macular Degeneration* (老年性黄斑变性流行病学调查) [J]. Hunan Medical Journal (湖南医学). 1992(05): 274-275.
AMD-03	Zheng-qing Wu, Jin-e Cao, Xiu-heng Yao, et al. 武正清，曹金娥，姚秀衡，等. Epidemiologic survey of senile macular degeneration (老年黄斑变性的流行病学调查) [J]. Chinese Journal of Ophthalmology (中华眼科杂志). 1992, 28(4): 246-247.
AMD-04	Yu-hua Chen, Ji-kui Shen, Yu-hong Zhang, et al. 陈玉华，申济奎，张宇弘，等. Senile macular degeneration in plateau aerea (高原地区老年性黄斑变性) [J]. Journal of High Altitude Medicine (实用眼科杂志). 1993(04): 57-58.
AMD-05	Qiang Yu, Jing-jing Xu, Si-ping Zhu, et al. 于强，许京京，朱斯平，等. Epidemiologic survey of Age-related Macular Degeneration in Doumen County, Guangdong province* (广东省斗门县老年黄斑变性流行病学调查) [J]. Chinese Journal of Ocular Fundus Diseases (中华眼底病杂志). 1994(2).
AMD-06	Kuang Wang, Jin Zhao, Jie-kai Jiang, et al. 王况，赵瑾，姜节凯，等. Epidemiologic survey of Age-related Macular Degeneration* (老年性黄斑变性的流行病学调查) [J]. Journal of Zhejiang Medical University (浙江医科大学学报). 1994(2).
AMD-07	Ming-guang He, Jing-jing Xu, Kai-li Wu, et al. 何明光，许京京，吴开力，等. The prevalence of age-related macular degeneration in Doumen county, Guangdong (广东省斗门县老年性黄斑变性流行病学调查) [J]. Chin J Ocul Fundus Dis (中华眼底病杂志). 1998(02): 61-63.

Study ID	Reference
AMD-08	Hai-dong Zou, Zhe Zhang, Xun Xu, et al. 邹海东，张晢，许迅，等. Prevalence study of age-related macular degeneration in Caojiadu blocks, Shanghai (上海市静安区曹家渡街道年龄相关性黄斑变性的患病率调查) [J]. Chin J Ophthalmol (中华眼科杂志). 2005, 41(1): 15-19.
AMD-09	Man-nan Tian, Yue-mei Zhang, Li Li, et al. 田蔓男，张月梅，李丽，等. Epidemiologic survey of Age-related Macular Degeneration* (老年性黄斑变性的流行病学调查)[J]. Journal of Lanzhou University (Medical Sciences) (兰州大学学报（医学版）). 2005, 31(2): 70-71.
AMD-10	Zhi-lan Bai, Bai-chao Ren, Jian-gang Yang, et al. 白芝兰，任百超，杨建刚，等. Epidemiological investigation on age-related macular degeneration in rural area of Shaanxi Province, China (中国陕西省农村年龄相关性黄斑变性流行病学调查) [J]. International Journal of Ophthalmology (国际眼科杂志). 2005, 5(6): 1114-1121.
AMD-11	Kai Shi, Wen-fang Zhang, Xiao-yan Zhou, et al. 史凯，张文芳，周晓燕，等. Epidemiological investigation of ocular funds disease in Mongol above 40 years in Henan county (青海省河南县 40 岁以上世居蒙古族人群眼底病的流行病学调查) [J]. Chin Ophthal Res (眼科研究). 2009, 27(3): 239-242.
AMD-12	Hui-li Li, Ai-lin You, Di-ling Wan, et al. 李慧丽，犹爱林，万迪玲，等. Prevalence study of age-related macular degeneration in central urban area of Chongqing (重庆市主城区年龄相关性黄斑变性患病率调查) [J]. Chin J Pract Ophthalmol (中国实用眼科杂志). 2009, 27(12): 1425-1429.
AMD-13	Xin Zhao, Bi-qi Tian, Yun-he Hao, et al. 赵欣，田碧琪，郝云赫，等. Prevalence of age-related maculopathy in community of Xi Chang'an street of Beijing (北京西长安街社区 50 岁以上人群年龄相关性黄斑变性患病率调查) [J]. Int J Ophthalmol (国际眼科杂志). 2011, 11(8): 1364-1368.
AMD-14	Xiao-bo Huang, Hai-dong Zou, Ning Wang, et al. 黄晓波，邹海东，王宁，等. Prevalence of age-related macular degeneration in Beixinjing Community of Shanghai (上海市北新泾街道老年人年龄相关性黄斑变性的患病率调查) [J]. Journal of Shanghai Jiaotong University (Medical Science) (上海交通大学学报(医学版)). 2012(02): 155-159.

Study ID	Reference
AMD-15	Zhen Yang 杨桢. Prevalence and Associated Risk Factors of Age-Related Macular Degeneration in 50 years and older Population in ShunQing District, NanChong (南充市顺庆区 50 岁及以上人群年龄相关性黄斑变性患病率及相关因素分析) [D]. North Sichuan Medical University (川北医学院), 2014.
AMD-16	Jia Cao 曹葭. Prevalence study of age-related macular degeneration over the age of 50's in Wuxi (无锡市 50 岁及以上人群年龄相关性黄斑变性流行病学调查)[D]. Nanjing Medical University (南京医科大学), 2014.
AMD-17	Wei Xiang, Hui-ping Li, Yang Liu, et al. 向伟，李慧平，刘洋，等. Prevalence Investigation of Age-related Macular Degeneration among Population Aged 50 Years or Above in Tongxin County of Ningxia (宁夏同心县≥50 岁人群年龄相关性黄斑变性患病率、危险因素及致盲情况分析) [J]. Journal of Ningxia Medical University (宁夏医科大学学报). 2015, 37(8): 927-930.
AMD-18	Ying Wang, Huai-jin Guan, Hong Lu, et al. 汪颖，管怀进，陆宏，等. The Prevalence of age-related macular degeneration in the rural area of Qidong County, Jiangsu Province (江苏省启东市农村地区老年性黄斑变性流行病学调查分析) [J]. Chin J Ocul Fundus Dis (中华眼底病杂志). 2015, 31(5): 459-461.
AMD-19	Wu-liang Li, Hui-ping Li, Na Li, et al. 李武靓，李慧平，李娜，等. Prevalence of age-related macular degeneration in elderly population in the rural area of Ningxia (宁夏农村地区 60 岁以上人群年龄相关性黄斑变性的患病率调查) [J]. Ningxia Medical Journal (宁夏医学杂志). 2015, 37(5): 401-404.
AMD-20	Li Y, Xu L, Jonas JB, et al. Prevalence of age-related maculopathy in the adult population in China: the Beijing eye study. AM J OPHTHALMOL 2006;142:788-793
AMD-21	Chen SJ, Cheng CY, Peng KL, et al. Prevalence and associated risk factors of age-related macular degeneration in an elderly Chinese population in Taiwan: the Shihpai Eye Study. Invest Ophthalmol Vis Sci 2008;49:3126-3133

Study ID	Reference
AMD-22	Huang TL, Hsu SY, Tsai RK, Sheu MM. Etiology of ocular diseases in elderly Amis aborigines in Eastern Taiwan (The Amis Eye Study). JPN J OPHTHALMOL 2010;54:266-271
AMD-23	Yang K, Liang YB, Gao LQ, et al. Prevalence of age-related macular degeneration in a rural Chinese population: the Handan Eye Study. OPHTHALMOLOGY 2011;118:1395-1401
AMD-24	Ye H, Zhang Q, Liu X, et al. Prevalence of age-related macular degeneration in an elderly urban chinese population in China: the Jiangning Eye Study. Invest Ophthalmol Vis Sci 2014;55:6374-6380
AMD-25	Huang EJ, Wu SH, Lai CH, et al. Prevalence and risk factors for age-related macular degeneration in the elderly Chinese population in south-western Taiwan: the Puzih eye study. Eye (Lond) 2014;28:705-714

Note: The Chinese publication list employed the journals' official English names or abbreviations, English titles were obtained from journals or literature databases (CNKI, Wanfang and CBM). Where official English translation of journal names is not available, a pinyin title is adopted; where the English translation of titles is not available, I translated the titles, labelled with "" and marked as green.*

Appendix table 6. Detailed characteristics of the included studies on AMD prevalence in China (n=25)

Study ID	Study	Province	Setting	Sex	Study year	Assessment	Grading system	Sample size	Any AMD	Early AMD	Late AMD	GA	NVAMD
AMD-01	Huang P et al. (1992)	Hunan	Mixed	Both	1987	FI	CMA1986	1589	145	-	-	-	19
AMD-02	Tang JQ et al. (1992)	Hunan	Mixed	Both	1989	FI	CMA1986	1040	191	-	-	-	-
AMD-03	Wu ZQ et al. (1992)	Hunan	Mixed	Both	1989	FI	CMA1986	3351	197	-	-	-	21
AMD-04	Chen YH et al. (1993)	Shaanxi Qinghai	Mixed	Mixed	1991	FI	CMA1986	849	70	-	-	-	37
AMD-05	Yu Q et al. (1994)	Guangdong	Rural	Both	1990	FI	CMA1986	932	50	-	-	-	-
AMD-06	Wang K et al. (1994)	Zhejiang	Mixed	Both	1989	FI	CMA1986	730	54	-	-	-	-
AMD-07	He MG et al. (1998)	Guangdong	Rural	Both	1997	FI	CMA1986	5342	451	-	-	-	-
AMD-08	Zou HD et al. (2005)	Shanghai	Urban	Both	2003	FI	CMA1986	1023	159	-	-	-	19
AMD-09	Tian MN et al. (2005)	Gansu	Mixed	Mixed	2002	FI	CMA1986	7563	579	-	-	-	5
AMD-10	Bai ZL et al. (2005)	Shaanxi	Rural	Both	2003	FI	IC	2835	85	-	-	44	41
AMD-11	Shi K et al. (2009)	Qinghai	Rural	Mixed	2006	FI	CMA1986	2112	132	-	-	-	33
AMD-12	Li HL et al. (2009)	Chongqing	Urban	Both	2009	FI	"Ophthalmology" (7th version)	1513	122	-	-	-	5
AMD-13	Zhao X et al. (2011)	Beijing	Urban	Both	2006	FI	CARMS	2348	77	70	7	3	4
AMD-14	Huang XB et al. (2012)	Shanghai	Urban	Both	2008	FI	CMA1986	3571	477	-	-	-	64
AMD-15	Yang Z (2014)	Sichuan	Urban	Both	2013	FI	CARMS	2097	207	194	13	10	3
AMD-16	Cao J (2014)	Jiangsu	Urban	Both	2010	FI	CMA1986	6150	482	-	-	-	38

Study ID	Study	Province	Setting	Sex	Study year	Assessment	Grading system	Sample size	Any AMD	Early AMD	Late AMD	GA	NVAMD
AMD-17	Xiang W et al. (2015)	Ningxia	Rural	Both	2014	FI	CARMS	4812	54	46	8	-	-
AMD-18	Wang Y et al. (2015)	Jiangsu	Rural	Both	2015	FI	CARMS	2985	97	71	26	15	11
AMD-19	Li WL et al. (2015)	Ningxia	Rural	Both	2013	FI	CARMS	679	25	17	8	-	-
AMD-20	Li Y et al. (2006)	Beijing	Mixed	Mixed	2001	FI	WARM	4376	70	63	7	1	6
AMD-21	Chen SJ et al. (2008)	Taiwan	Mixed	Both	1999	FI	WARM	1058	117	97	20	1	19
AMD-22	Huang TL et al. (2010)	Taiwan	Rural	Both	2007	FI	WARM	2316	121	-	-	-	-
AMD-23	Yang K et al. (2011)	Hebei	Rural	Mixed	2006	FI	WARM	6581	204	200	4	-	-
AMD-24	Ye H et al. (2014)	Shanghai	Urban	Both	2013	FI	WARM	2005	229	206	23	-	-
AMD-25	Huang EJ et al. (2014)	Taiwan	Mixed	Both	2011	FI	WARM	673	150	101	49	-	-

Note: "-" represents unavailable data; FI, Fundus imaging; CAM 1986, the "Age-related Macular Degeneration Clinical Diagnosis Standard" proposed by the China Medical Association in 1986; WARMGS, the Wisconsin age-related maculopathy system; CARMS, the Clinical Age-Related Maculopathy Grading System; IC, the International Classification and Grading system.

Appendix table 7. Risk of bias scores of the included studies on AMD prevalence in China (n=25)

Study ID	Study	Quality score					
		Sample population	Sample size	Participation	Outcome assessment	Analytical methods	Total scores
AMD-01	Huang P et al. (1992)	2	1	2	2	2	9
AMD-02	Tang JQ et al. (1992)	2	0	0	2	2	6
AMD-03	Wu ZQ et al. (1992)	2	1	2	2	2	9
AMD-04	Chen YH et al. (1993)	2	0	0	2	2	6
AMD-05	Yu Q et al. (1994)	2	1	2	2	2	9
AMD-06	Wang K et al. (1994)	2	1	2	2	2	9
AMD-07	He MG et al. (1998)	2	1	2	2	2	9
AMD-08	Zou HD et al. (2005)	2	2	2	2	2	10
AMD-09	Tian MN et al. (2005)	1	1	0	2	2	6
AMD-10	Bai ZL et al. (2005)	2	1	1	2	2	8
AMD-11	Shi K et al. (2009)	2	2	0	2	2	8
AMD-12	Li HL et al. (2009)	1	1	0	2	2	6
AMD-13	Zhao X et al. (2011)	2	2	2	2	2	10
AMD-14	Huang XB et al. (2012)	2	2	2	2	2	10
AMD-15	Yang Z (2014)	2	2	2	2	2	10
AMD-16	Cao J (2014)	2	2	2	2	2	10
AMD-17	Xiang W et al. (2015)	2	2	2	2	2	10
AMD-18	Wang Y et al. (2015)	2	1	1	2	2	8

Study ID	Study	Quality score					
		Sample population	**Sample size**	**Participation**	**Outcome assessment**	**Analytical methods**	**Total scores**
AMD-19	Li WL et al. (2015)	2	0	0	2	2	6
AMD-20	Li Y et al. (2006)	2	2	1	2	2	9
AMD-21	Chen SJ et al. (2008)	2	1	0	2	2	7
AMD-22	Huang TL et al. (2010)	2	1	0	2	2	7
AMD-23	Yang K et al. (2011)	2	1	2	2	2	9
AMD-24	Ye H et al. (2014)	2	2	1	2	2	9
AMD-25	Huang EJ et al. (2014)	1	1	2	2	2	8

Appendix table 8. Estimated and projected number of people with any AMD, early AMD, late AMD, GA and NVAMD in China from 1990 to 2050, by age group (million, 95% CI)

1990					
Age group	**Any AMD**	**Early AMD**	**Late AMD**	**GA**	**NVAMD**
45-49 years	1.19 (0.90-1.56)	1.09 (0.87-1.32)	0.23 (0.13-0.42)	0.09 (0.04-0.20)	0.14 (0.09-0.22)
50-54 years	1.45 (1.11-1.90)	1.27 (1.02-1.52)	0.29 (0.17-0.51)	0.11 (0.05-0.23)	0.18 (0.12-0.27)
55-59 years	1.71 (1.32-2.23)	1.42 (1.16-1.70)	0.35 (0.21-0.59)	0.13 (0.06-0.26)	0.22 (0.15-0.33)
60-64 years	1.78 (1.37-2.29)	1.41 (1.16-1.67)	0.37 (0.23-0.61)	0.13 (0.06-0.26)	0.24 (0.17-0.35)
65-69 years	1.75 (1.35-2.24)	1.33 (1.09-1.56)	0.37 (0.23-0.61)	0.12 (0.06-0.25)	0.25 (0.17-0.35)
70-74 years	1.73 (1.35-2.21)	1.26 (1.05-1.47)	0.38 (0.24-0.62)	0.12 (0.06-0.25)	0.26 (0.18-0.37)
75-79 years	1.32 (1.03-1.67)	0.93 (0.77-1.07)	0.30 (0.19-0.50)	0.09 (0.04-0.19)	0.21 (0.14-0.30)
80-84 years	0.77 (0.60-0.96)	0.52 (0.44-0.60)	0.19 (0.11-0.31)	0.05 (0.02-0.12)	0.13 (0.09-0.19)
85-89 years	0.32 (0.25-0.40)	0.21 (0.18-0.24)	0.08 (0.05-0.14)	0.02 (0.01-0.05)	0.06 (0.04-0.09)
Total (45-89 years)	12.01 (9.29-15.46)	9.44 (7.74-11.15)	2.58 (1.56-4.30)	0.87 (0.40-1.83)	1.71 (1.16-2.47)
2000					
Age group	**Any AMD**	**Early AMD**	**Late AMD**	**GA**	**NVAMD**
45-49 years	2.09 (1.59-2.75)	1.91 (1.53-2.32)	0.41 (0.23-0.75)	0.16 (0.07-0.36)	0.25 (0.16-0.39)
50-54 years	1.94 (1.48-2.54)	1.69 (1.37-2.03)	0.39 (0.23-0.67)	0.14 (0.07-0.31)	0.24 (0.16-0.36)
55-59 years	1.91 (1.47-2.48)	1.59 (1.29-1.89)	0.39 (0.23-0.66)	0.14 (0.06-0.29)	0.25 (0.17-0.36)
60-64 years	2.23 (1.72-2.88)	1.77 (1.45-2.09)	0.47 (0.29-0.77)	0.16 (0.08-0.33)	0.31 (0.21-0.43)

65-69 years	2.42 (1.88-3.11)	1.84 (1.52-2.16)	0.52 (0.32-0.84)	0.17 (0.08-0.35)	0.35 (0.24-0.49)
70-74 years	2.19 (1.71-2.79)	1.59 (1.32-1.85)	0.48 (0.30-0.78)	0.15 (0.07-0.32)	0.33 (0.23-0.47)
75-79 years	1.72 (1.35-2.18)	1.21 (1.00-1.40)	0.40 (0.24-0.65)	0.12 (0.06-0.25)	0.28 (0.19-0.39)
80-84 years	1.23 (0.97-1.55)	0.84 (0.70-0.96)	0.30 (0.18-0.49)	0.09 (0.04-0.19)	0.21 (0.14-0.31)
85-89 years	0.58 (0.46-0.72)	0.38 (0.32-0.44)	0.15 (0.09-0.25)	0.04 (0.02-0.09)	0.11 (0.07-0.16)
Total (45-89 years)	16.31 (12.62-20.99)	12.81 (10.51-15.13)	3.50 (2.11-5.86)	1.18 (0.54-2.50)	2.32 (1.57-3.36)
2010					
Age group	**Any AMD**	**Early AMD**	**Late AMD**	**GA**	**NVAMD**
45-49 years	2.47 (1.87-3.25)	2.26 (1.81-2.75)	0.49 (0.27-0.88)	0.19 (0.08-0.42)	0.30 (0.19-0.46)
50-54 years	2.60 (1.98-3.40)	2.27 (1.83-2.72)	0.52 (0.03-0.90)	0.19 (0.09-0.42)	0.33 (0.21-0.49)
55-59 years	3.42 (2.63-4.44)	2.84 (2.32-3.39)	0.70 (0.42-1.18)	0.25 (0.12-0.53)	0.45 (0.30-0.65)
60-64 years	3.06 (2.36-3.95)	2.43 (1.99-2.87)	0.64 (0.39-1.05)	0.22 (0.10-0.45)	0.42 (0.29-0.60)
65-69 years	2.81 (2.18-3.60)	2.13 (1.76-2.50)	0.60 (0.37-0.98)	0.20 (0.09-0.41)	0.40 (0.28-0.57)
70-74 years	2.90 (2.26-3.70)	2.11 (1.75-2.46)	0.64 (0.40-1.04)	0.20 (0.10-0.42)	0.44 (0.30-0.62)
75-79 years	2.58 (2.02-3.26)	1.81 (1.51-2.09)	0.59 (0.37-0.97)	0.18 (0.08-0.38)	0.41 (0.28-0.59)
80-84 years	1.72 (1.36-2.16)	1.17 (0.98-1.35)	0.42 (0.25-0.69)	0.12 (0.05-0.26)	0.30 (0.20-0.43)
85-89 years	0.88 (0.70-1.09)	0.58 (0.49-0.66)	0.22 (0.13-0.38)	0.06 (0.03-0.14)	0.16 (0.11-0.24)
Total (45-89 years)	22.43 (17.36-28.85)	17.60 (14.45-20.78)	4.83 (2.91-8.07)	1.62 (0.75-3.43)	3.21 (2.16-4.64)
2015					

Age group	Any AMD	Early AMD	Late AMD	GA	NVAMD
45-49 years	3.02 (2.29-3.97)	2.76 (2.22-3.36)	0.59 (0.33-1.08)	0.23 (0.10-0.52)	0.36 (0.23-0.56)
50-54 years	3.19 (2.43-4.16)	2.78 (2.25-3.34)	0.64 (0.37-1.11)	0.24 (0.11-0.51)	0.40 (0.26-0.59)
55-59 years	3.31 (2.54-4.30)	2.75 (2.25-3.28)	0.68 (0.41-1.14)	0.24 (0.11-0.51)	0.43 (0.29-0.63)
60-64 years	4.26 (3.29-5.50)	3.38 (2.78-3.99)	0.89 (0.55-1.46)	0.31 (0.14-0.63)	0.58 (0.40-0.83)
65-69 years	3.64 (2.82-4.67)	2.76 (2.28-3.24)	0.78 (0.48-1.27)	0.26 (0.12-0.53)	0.52 (0.36-0.74)
70-74 years	3.10 (2.42-3.96)	2.26 (1.88-2.63)	0.69 (0.43-1.11)	0.22 (0.10-0.45)	0.47 (0.32-0.66)
75-79 years	2.85 (2.24-3.61)	2.00 (1.67-2.32)	0.66 (0.41-1.07)	0.20 (0.09-0.42)	0.46 (0.31-0.65)
80-84 years	2.15 (1.69-2.70)	1.46 (1.22-1.68)	0.52 (0.31-0.86)	0.15 (0.07-0.33)	0.37 (0.25-0.53)
85-89 years	1.13 (0.89-1.40)	0.75 (0.63-0.85)	0.29 (0.17-0.49)	0.08 (0.04-0.18)	0.21 (0.14-0.31)
Total (45-89 years)	26.65 (20.62-34.27)	20.91 (17.16-24.68)	5.74 (3.46-9.59)	1.93 (0.89-4.08)	3.81 (2.57-5.51)
2020					
Age group	**Any AMD**	**Early AMD**	**Late AMD**	**GA**	**NVAMD**
45-49 years	2.88 (2.19-3.79)	2.65 (2.12-3.22)	0.57 (0.32-1.03)	0.22 (0.10-0.50)	0.35 (0.22-0.54)
50-54 years	3.90 (2.98-5.10)	3.41 (2.76-4.10)	0.78 (0.46-1.36)	0.29 (0.13-0.63)	0.49 (0.32-0.73)
55-59 years	4.07 (3.13-5.28)	3.39 (2.77-4.04)	0.83 (0.50-1.40)	0.30 (0.14-0.63)	0.54 (0.36-0.77)
60-64 years	4.14 (3.20-5.34)	3.29 (2.71-3.89)	0.87 (0.53-1.43)	0.30 (0.14-0.62)	0.57 (0.39-0.81)
65-69 years	5.11 (3.97-6.55)	3.89 (3.22-4.56)	1.10 (0.68-1.79)	0.36 (0.17-0.75)	0.74 (0.51-1.04)
70-74 years	4.08 (3.18-5.21)	2.99 (2.48-3.48)	0.91 (0.56-1.47)	0.29 (0.14-0.59)	0.62 (0.43-0.88)

75-79 years	3.12 (2.45-3.96)	2.20 (1.83-2.55)	0.72 (0.45-1.18)	0.22 (0.10-0.46)	0.50 (0.34-0.72)
80-84 years	2.45 (1.93-3.08)	1.67 (1.40-1.92)	0.60 (0.36-0.98)	0.17 (0.08-0.37)	0.42 (0.28-0.61)
85-89 years	1.46 (1.16-1.83)	0.97 (0.82-1.11)	0.38 (0.22-0.64)	0.11 (0.05-0.23)	0.27 (0.18-0.40)
Total (45-89 years)	31.23 (24.18-40.14)	24.47 (20.1-28.87)	6.76 (4.08-11.28)	2.26 (1.04-4.78)	4.50 (3.04-6.50)
2030					
Age group	**Any AMD**	**Early AMD**	**Late AMD**	**GA**	**NVAMD**
45-49 years	2.38 (1.80-3.13)	2.21 (1.78-2.69)	0.48 (0.27-0.86)	0.18 (0.08-0.41)	0.29 (0.19-0.45)
50-54 years	2.97 (2.26-3.88)	2.63 (2.13-3.16)	0.60 (0.35-1.05)	0.22 (0.10-0.49)	0.38 (0.25-0.56)
55-59 years	4.79 (3.68-6.21)	4.04 (3.30-4.81)	0.99 (0.60-1.67)	0.36 (0.17-0.75)	0.64 (0.43-0.92)
60-64 years	6.29 (4.86-8.12)	5.08 (4.17-5.99)	1.34 (0.82-2.20)	0.46 (0.22-0.95)	0.88 (0.60-1.25)
65-69 years	6.22 (4.83-7.98)	4.80 (3.97-5.62)	1.36 (0.84-2.20)	0.45 (0.21-0.92)	0.91 (0.63-1.28)
70-74 years	5.76 (4.49-7.35)	4.27 (3.54-4.97)	1.30 (0.81-2.10)	0.41 (0.19-0.85)	0.89 (0.61-1.25)
75-79 years	6.10 (4.78-7.73)	4.36 (3.63-5.04)	1.43 (0.88-2.33)	0.44 (0.20-0.91)	1.00 (0.68-1.42)
80-84 years	3.84 (3.03-4.83)	2.66 (2.22-3.05)	0.95 (0.57-1.56)	0.28 (0.12-0.59)	0.67 (0.45-0.97)
85-89 years	2.05 (1.62-2.55)	1.38 (1.15-1.57)	0.53 (0.31-0.90)	0.15 (0.06-0.33)	0.38 (0.25-0.57)
Total (45-89 years)	40.40 (31.36-51.78)	31.42 (25.90-36.90)	8.98 (5.45-14.87)	2.95 (1.36-6.20)	6.03 (4.09-8.67)
2040					
Age group	**Any AMD**	**Early AMD**	**Late AMD**	**GA**	**NVAMD**
45-49 years	2.52 (1.91-3.32)	2.37 (1.91-2.87)	0.51 (0.29-0.92)	0.20 (0.09-0.44)	0.31 (0.20-0.48)
50-54 years	4.00	3.58	0.82	0.31	0.52

	(3.05-5.23)	(2.91-4.29)	(0.48-1.42)	(0.14-0.66)	(0.34-0.76)
55-59 years	3.97 (3.05-5.16)	3.39 (2.77-4.02)	0.83 (0.50-1.40)	0.30 (0.14-0.62)	0.53 (0.36-0.77)
60-64 years	4.83 (3.73-6.24)	3.93 (3.24-4.63)	1.04 (0.64-1.70)	0.36 (0.17-0.73)	0.68 (0.47-0.96)
65-69 years	7.46 (5.79-9.56)	5.81 (4.81-6.79)	1.64 (1.02-2.66)	0.54 (0.26-1.11)	1.10 (0.76-1.55)
70-74 years	9.08 (7.08-11.57)	6.79 (5.65-7.88)	2.07 (1.29-3.33)	0.66 (0.31-1.35)	1.41 (0.98-1.99)
75-79 years	7.88 (6.17-9.98)	5.68 (4.74-6.55)	1.87 (1.15-3.03)	0.57 (0.26-1.18)	1.30 (0.89-1.85)
80-84 years	5.93 (4.67-7.46)	4.14 (3.47-4.74)	1.47 (0.89-2.43)	0.43 (0.19-0.92)	1.04 (0.70-1.51)
85-89 years	4.55 (3.61-5.67)	3.10 (2.60-3.52)	1.20 (0.71-2.01)	0.34 (0.15-0.74)	0.86 (0.56-1.27)
Total (45-89 years)	50.22 (39.07-64.18)	38.78 (32.10-45.28)	11.45 (6.97-18.90)	3.69 (1.71-7.76)	7.76 (5.26-11.13)
2050					
Age group	**Any AMD**	**Early AMD**	**Late AMD**	**GA**	**NVAMD**
45-49 years	1.77 (1.35-2.33)	1.68 (1.36-2.03)	0.36 (0.20-0.65)	0.14 (0.06-0.31)	0.22 (0.14-0.34)
50-54 years	2.42 (1.85-3.17)	2.19 (1.78-2.62)	0.50 (0.29-0.87)	0.19 (0.08-0.40)	0.32 (0.21-0.47)
55-59 years	4.23 (3.25-5.50)	3.65 (2.99-4.32)	0.90 (0.54-1.50)	0.32 (0.15-0.67)	0.58 (0.39-0.83)
60-64 years	6.58 (5.08-8.49)	5.41 (4.47-6.35)	1.42 (0.88-2.33)	0.49 (0.23-1.01)	0.93 (0.65-1.32)
65-69 years	6.29 (4.88-8.07)	4.95 (4.12-5.77)	1.40 (0.87-2.26)	0.46 (0.22-0.94)	0.94 (0.65-1.32)
70-74 years	7.19 (5.60-9.16)	5.43 (4.53-6.29)	1.65 (1.03-2.66)	0.52 (0.25-1.07)	1.13 (0.78-1.58)
75-79 years	9.95 (7.80-12.60)	7.25 (6.07-8.34)	2.38 (1.48-3.86)	0.72 (0.34-1.51)	1.66 (1.14-2.35)
80-84 years	10.15 (7.99-12.76)	7.16 (6.01-8.18)	2.55 (1.55-4.18)	0.74 (0.34-1.59)	1.80 (1.21-2.60)

85-89 years	6.60 (5.23-8.23)	4.54 (3.82-5.15)	1.75 (1.04-2.94)	0.49 (0.22-1.08)	1.26 (0.82-1.86)
Total (45-89 years)	55.19 (43.04-70.30)	42.26 (35.15-49.05)	12.92 (7.89-21.26)	4.09 (1.89-8.59)	8.84 (6.00-12.66)

Appendix table 9. Estimation of age-specific number of people with any AMD in China from 2000 to 2010, by geographical region (million, 95% CI)

2000						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**
45-49 years	0.17 (0.12-0.24)	0.11 (0.07-0.18)	0.67 (0.53-0.85)	0.70 (0.53-0.94)	0.36 (0.28-0.47)	0.09 (0.06-0.12)
50-54 years	0.15 (0.11-0.21)	0.09 (0.06-0.15)	0.62 (0.49-0.78)	0.66 (0.50-0.87)	0.34 (0.27-0.44)	0.08 (0.06-0.11)
55-59 years	0.14 (0.10-0.19)	0.09 (0.05-0.14)	0.59 (0.47-0.74)	0.63 (0.48-0.83)	0.37 (0.29-0.47)	0.09 (0.07-0.13)
60-64 years	0.17 (0.12-0.24)	0.11 (0.07-0.18)	0.68 (0.54-0.85)	0.75 (0.58-0.97)	0.41 (0.32-0.52)	0.11 (0.08-0.15)
65-69 years	0.19 (0.14-0.26)	0.11 (0.07-0.18)	0.79 (0.63-0.97)	0.82 (0.63-1.05)	0.41 (0.33-0.51)	0.10 (0.07-0.13)
70-74 years	0.16 (0.12-0.22)	0.10 (0.06-0.16)	0.73 (0.60-0.89)	0.73 (0.57-0.91)	0.38 (0.30-0.47)	0.07 (0.06-0.10)
75-79 years	0.12 (0.09-0.17)	0.07 (0.04-0.11)	0.60 (0.49-0.72)	0.57 (0.45-0.71)	0.28 (0.22-0.34)	0.06 (0.04-0.08)
80-84 years	0.08 (0.06-0.11)	0.04 (0.03-0.07)	0.44 (0.36-0.52)	0.42 (0.34-0.52)	0.20 (0.16-0.24)	0.04 (0.03-0.05)
85-89 years	0.04 (0.03-0.05)	0.02 (0.01-0.03)	0.21 (0.17-0.24)	0.21 (0.17-0.25)	0.10 (0.08-0.12)	0.02 (0.01-0.02)
Total (45-89 years)	1.23 (0.88-1.70)	0.76 (0.47-1.21)	5.32 (4.29-6.57)	5.50 (4.24-7.05)	2.85 (2.26-3.56)	0.66 (0.49-0.89)
2010						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**
45-49 years	0.21 (0.15-0.30)	0.13 (0.08-0.21)	0.81 (0.64-1.03)	0.90 (0.67-1.21)	0.38 (0.30-0.50)	0.12 (0.09-0.16)
50-54 years	0.25 (0.18-0.35)	0.16 (0.10-0.25)	0.84 (0.67-1.07)	0.88 (0.66-1.17)	0.36 (0.28-0.47)	0.12 (0.09-0.16)
55-59 years	0.29 (0.21-0.41)	0.18 (0.11-0.29)	1.11 (0.88-1.39)	1.13 (0.86-1.48)	0.57 (0.44-0.72)	0.14 (0.10-0.19)
60-64 years	0.24 (0.17-0.34)	0.15 (0.09-0.23)	0.99 (0.79-1.23)	1.02 (0.78-1.32)	0.52 (0.41-0.66)	0.13 (0.10-0.17)

65-69 years	0.21 (0.15-0.29)	0.13 (0.08-0.20)	0.88 (0.71-1.08)	0.91 (0.71-1.17)	0.52 (0.42-0.65)	0.13 (0.10-0.18)
70-74 years	0.23 (0.17-0.31)	0.14 (0.09-0.22)	0.90 (0.73-1.10)	0.96 (0.75-1.21)	0.51 (0.41-0.63)	0.14 (0.10-0.18)
75-79 years	0.20 (0.15-0.27)	0.12 (0.07-0.18)	0.87 (0.71-1.05)	0.86 (0.68-1.06)	0.41 (0.34-0.50)	0.10 (0.08-0.13)
80-84 years	0.13 (0.09-0.17)	0.08 (0.05-0.12)	0.61 (0.50-0.72)	0.56 (0.45-0.68)	0.28 (0.23-0.34)	0.05 (0.04-0.07)
85-89 years	0.06 (0.04-0.08)	0.04 (0.02-0.05)	0.33 (0.27-0.38)	0.29 (0.24-0.35)	0.13 (0.11-0.16)	0.03 (0.02-0.03)
Total (45-89 years)	1.82 (1.31-2.51)	1.11 (0.69-1.76)	7.33 (5.91-9.04)	7.52 (5.80-9.64)	3.70 (2.94-4.62)	0.95 (0.71-1.28)

Appendix table 10. Search strategy to identify studies reporting the prevalence of glaucoma in China

CNKI

Access Date: 18 Aug 2017

Subject category: Medicine & Public Health

Sub-database: Journal, Featured journal, Doctoral dissertation, Master dissertation

检索表达式:

(SU % '青光眼') AND (SU % '发病率' + '发生率' + '患病率'+ '罹患率' + '现患率'+ '死亡率' + '病死率'+ '流行' + '负担'+ '现况调查'+ '现况研究')

发表时间：从 1990-01-01 到 2017-08-18

Search Terms: (SU % 'qingguangyan') AND (SU % 'fabinglv' + 'fashenglv' + 'huanbinglv'+ 'lihuanlv' + 'xianhuanlv'+ 'siwanglv' + 'bingsilv'+ 'liuxing' + 'fudan'+ 'xiankuangdiaocha'+ 'xiankuangyanjiu')

Published time：From 01/01/1990 to 26/06/2016

Wanfang

Access Date: 18 Aug 2017

Sub-database: Journal articles, Dissertations

检索表达式：检索表达式：(主题:(青光眼)) * (主题:(发病率) + 主题:(发生率) + 主题:(患病率) +主题:(罹患率) + 主题:(现患率) + 主题:(死亡率) +主题:(病死率) + 主题:(流行) + 主题:(负担)+ 主题:(现况调查) + 主题:(现况研究))

时间：1990-2017

Search Terms: (subject: (qingguangyan))* (subject: (fabinglv) + subject: (fashenglv) + subject: (huanbinglv)+ subject: (lihuanlv) + subject: (xianhuanlv) + subject: (siwanglv)+ subject: (bingsilv) + subject: (liuxing) + subject: (fudan)+ subject: (xiankuangdiaocha) + subject: (xiankuangyanjiu))

Date: 1990-2017

CBM-SinoMed

Access Date: 18 Aug 2017

Journal category: All journals

检索表达式:

(青光眼) AND (发病率 or 发生率 or 患病率 or 罹患率 or 现患率 or 死亡率 or 病死率 or 流行 or 负担 or 现况调查 or 现况研究)

时间：1990-2017

Search Terms: ((qingguangyan))* ((fabinglv) OR (fashenglv) OR (huanbinglv) OR (lihuanlv) OR (xianhuanlv) OR (siwanglv) OR (bingsilv) OR (liuxing) OR (fudan) OR (xiankuangdiaocha) OR (xiankuangyanjiu))

Date: 1990-2017

PubMed

Access Date: 18 Aug 2017

Search Terms:

((Glaucoma) AND (China OR Chinese OR Hongkong OR Macao OR Taiwan) AND (inciden* OR prevalen* OR morbidity OR mortality OR epidemiology)) AND ("1990/01/01"[Date - Publication] : "2017/08/18"[Date - Publication])

Embase (Ovid)

Access Date: 18 Aug 2017

#	Searches
1	exp glaucoma/ or Glaucoma.mp.
2	China.mp. or exp China/
3	exp Chinese/ or Chinese.mp.
4	Hong Kong.mp. or exp Hong Kong/
5	Macao.mp. or exp Macao/
6	Taiwan.mp. or exp Taiwan/
7	exp incidence/ or inciden*.mp.
8	exp prevalence/ or prevalen*.mp.
9	morbidity.mp. or morbidity/
10	mortality/ or Mortality.mp.
11	exp epidemiology/ or Epidemiology.mp.
12	2 or 3 or 4 or 5 or 6
13	7 or 8 or 9 or 10 or 11
14	1 and 12 and 13
15	limit 14 to yr="1990 -Current"

Medline (Ovid)

Access Date: 18 Aug 2017

Search Terms:

#	Searches
1	Glaucoma.mp. or exp Glaucoma/
2	China.mp. or exp China/

3	Chinese.mp.
4	Hong Kong.mp. or exp Hong Kong/
5	Macao.mp. or exp Macau/
6	Taiwan.mp. or exp Taiwan/
7	exp Incidence/ or inciden*.mp.
8	exp Prevalence/ or prevalen*.mp.
9	morbidity.mp. or exp Morbidity/
10	mortality.mp. or exp Mortality/
11	epidemiology.mp. or exp Epidemiology/
12	2 or 3 or 4 or 5 or 6
13	7 or 8 or 9 or 10 or 11
14	1 and 12 and 13
15	limit 14 to yr="1990 -Current"

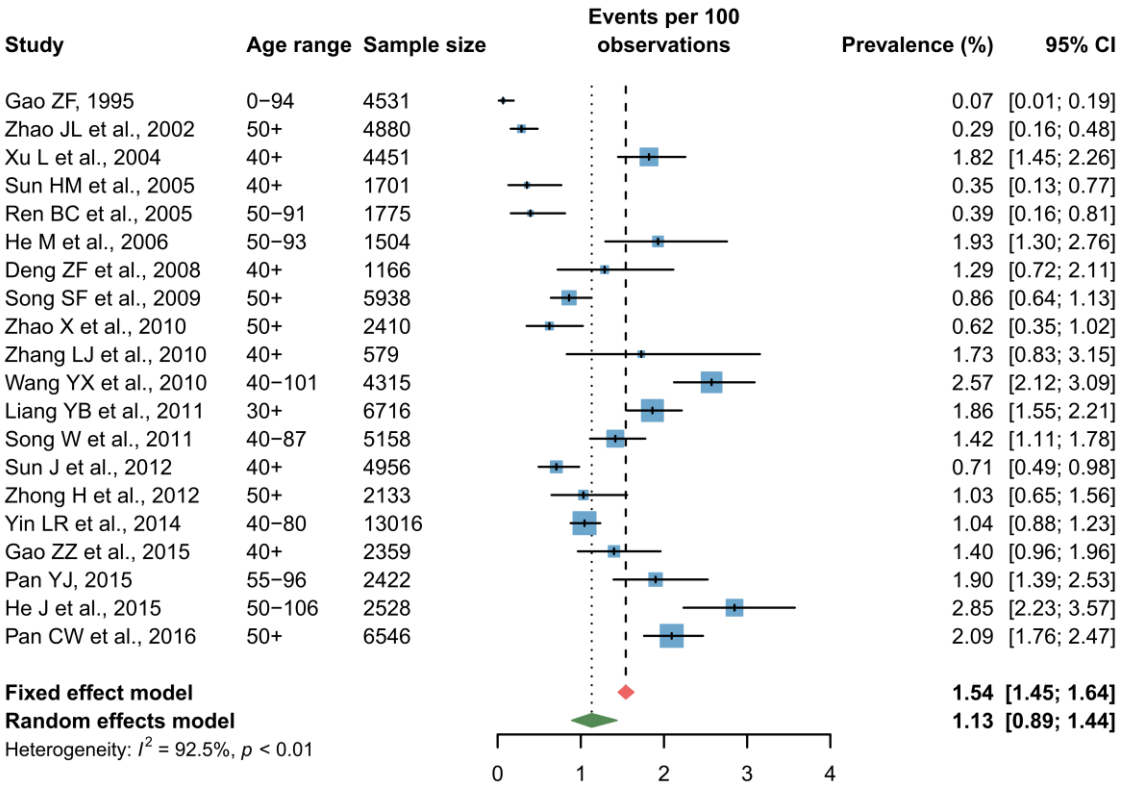
Appendix table 11. The year of publication and investigation and corresponding time-lag in the included studies on glaucoma prevalence in China (n=30)

Study ID	Study	Year Published	Median investigation date	Time-lag
G-01	Gao ZF (1995)	1995	1987	8
G-02	Yu Q et al. (1995)	1995	1990	5
G-03	He MG et al. (2000)	2000	1997	3
G-04	Zhao JL et al. (2002)	2002	1996	6
G-05	Xu L et al. (2004)	2004	2001	3
G-06	Bai ZL et al. (2005)	2005	2003	2
G-07	Xu L et al. (2005)	2005	2001	4
G-08	Sun HM et al. (2005)	2005	2003	2
G-09	Ren BC et al. (2005)	2005	2003	2
G-10	Bai YQ et al. (2007)	2007	2006	1
G-11	Yuan HP et al. (2007)	2007	2004	3
G-12	Deng ZF et al. (2008)	2008	-	-
G-13	Song SF et al. (2009)	2009	2005	4
G-14	Zhao X et al. (2010)	2010	2006	4
G-15	Zhang LJ et al. (2010)	2010	2009	1
G-16	Yu YY et al. (2013)	2013	-	-
G-17	Sheng WD (2014)	2014	2013	1
G-18	Yin LR et al. (2014)	2014	2010	4
G-19	Gao ZZ et al. (2015)	2015	2011	4
G-20	Pan YJ (2015)	2015	2014	1
G-21	He M et al. (2006)	2006	2003	3
G-22	Wang YX et al. (2010)	2010	2001	9
G-23	Liang YB et al. (2011)	2011	2007	4
G-24	Liang Y et al. (2011)	2011	2007	4
G-25	Qu W et al. (2011)	2011	2007	4
G-26	Song W et al. (2011)	2011	2009	2
G-27	Sun J et al. (2012)	2012	2007	5
G-28	Zhong H et al. (2012)	2012	2010	2
G-29	He J et al. (2015)	2015	2011	4
G-30	Pan CW et al. (2016)	2016	2010	6

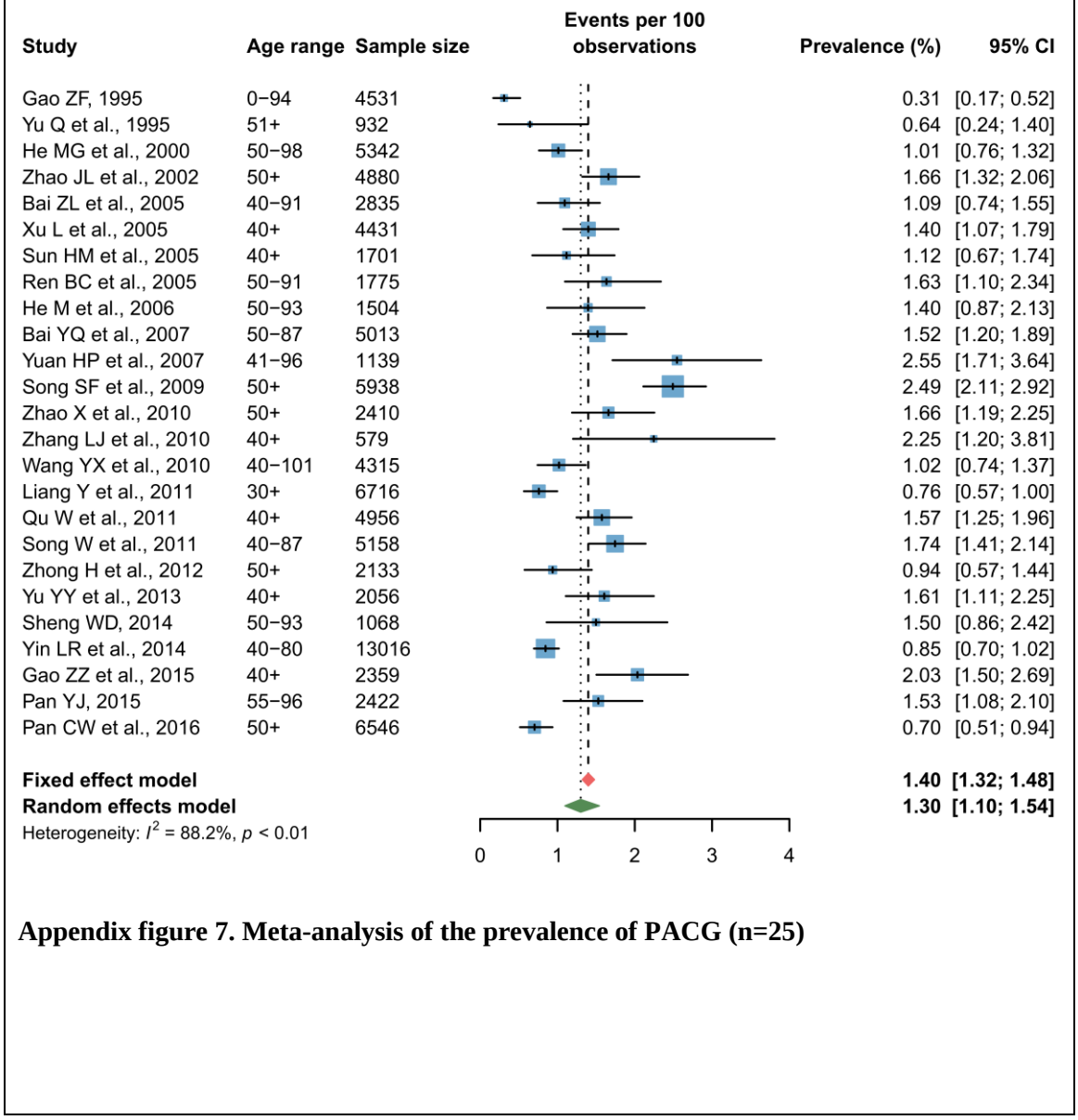
Note: "-" represents unavailable data; Based on the information from 28 studies, the average time-lag between year of publication and year of investigation was 3.61.

Appendix table 12. Meta-analysis of the prevalence of glaucoma for assessing heterogeneity between studies

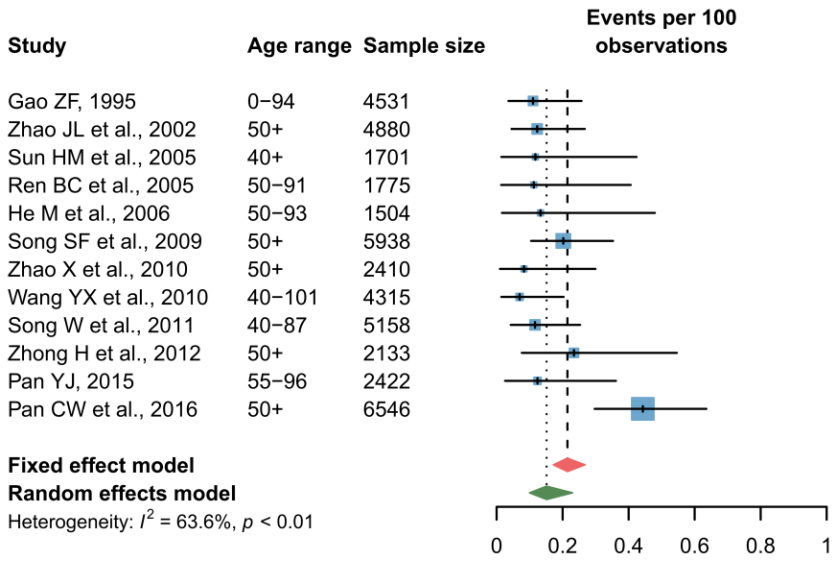
To address the issue of heterogeneity across all eligible studies, the Cochran's Q and I^2 statistics were calculated. A p-value<0.05 indicates heterogeneity between studies in Q statistic, and I^2 represents the proportion of total variation that is due to heterogeneity rather than chance, where values of <25%, 25–75%, and >75% representing low, moderate and high heterogeneity, respectively (Higgins and Thompson, 2002, Higgins et al., 2003). As shown in **Appendix figures 6-8**, significant high heterogeneity was detected between studies that reported prevalence rates of POAG (I^2=92.5%, p<0.0001), PACG (I^2=88.2%, p<0.0001), and moderate heterogeneity existed between studies on secondary glaucoma (I^2=63.6%, p=0.0015).



Appendix figure 6. Meta-analysis of the prevalence of POAG (n=20)



Appendix figure 7. Meta-analysis of the prevalence of PACG (n=25)



Appendix figure 8. Meta-analysis of the prevalence of secondary glaucoma (n=12)

Appendix table 13. Full list of the included studies on glaucoma prevalence in China (n=30)

Study ID	Reference
G-01	Zong-feng Gao. 高宗峰. An epidemiologic study of glaucoma in Tongcheng county, Anhui province (安徽省桐城县青光眼流行病学调查)[J]. Chinese Journal of Ophthalmology (中华眼科杂志). 1995(02):149-51.
G-02	Qiang Yu, Jing-jing Xu, Si-ping Zhu, et al. 于强, 许京京, 朱斯平, 柳青. An epidemiological survey of primary angle-closure glaucoma in Doumen county Guangdong (广东省斗门县原发性闭角型青光眼流行病学调查)[J]. Chinese Journal of Ophthalmology (中华眼科杂志). 1995(02):118-21.
G-03	Ming-guang He, Jing-jing Xu, Kai-li Wu, et al. 何明光, 许京京, 吴开力, 李绍珍. The prevalence of primary angle-closure glaucoma in elderly rural population (斗门县农村中老年人群原发闭角性青光眼流行病学调查)[J]. Acad J SUMS (中山医科大学学报). 2000(03):212-4.
G-04	Jia-liang Zhao, Rui-fang Sui, Li-jun Jia, et al. 赵家良, 睢瑞芳, 贾丽君, et al. Prevalence of glaucoma and normal intraocular pressure among adults aged 50 years or above in Shunyi county of Beijing (北京市顺义县 50 岁及以上人群中青光眼患病率和正常眼眼压的调查)[J]. Chin J Ophthalmol (中华眼科杂志). 2002(06):18-22.
G-05	Liang Xu, Jian-hua Chen, Jian-jun Li, et al. 徐亮, 陈建华, 李建军, et al. The prevalence and its screening methods of primary open angle glaucoma in defined population-based study of rural and urban in Beijing (北京农村及城市特定人群原发性开角型青光眼的患病率调查及其筛查方法评价)[J]. Chin J Ophthalmol (中华眼科杂志). 2004(11):9-15.

Study ID	Reference
G-06	Lan-zhi Bai, Bai-chao Ren, Jian-gang Yang, et al. 白芝兰, 任百超, 杨建刚, 何媛, 陈莉, 孙乃学. Epidemiology of primary angle-closure glaucoma in a rural population in Shaanxi province of China (中国陕西省农村原发性闭角型青光眼流行病学调查)[J]. International journal of ophthalmology (国际眼科杂志). 2005;5(5):872-80.
G-07	Liang Xu, Li Zhang, Cui-ran Xia, et al. 徐亮, 张莉, 夏翠然, et al. The prevalence and its effective factors of primary angle-closure glaucoma in defined population of rural and urban in Beijing (北京农村及城市特定人群原发性闭角型青光眼的患病率及其影响因素)[J]. Chin J Ophthalmol (中华眼科杂志). 2005(01):12-8.
G-08	Hui-min Sun, Xiu-juan Zhang, Zhi-qing Li, et al. 孙慧敏, 张秀娟, 李志清, et al. Prevalence of glaucoma in Sangzi village, Ji county of Tianjin aged 40 years and above (天津市蓟县桑梓村 40 岁及以上人群中青光眼患病率调查)[J]. Chin J Pract Ophthalmol (中国实用眼科杂志). 2005(08):782-4.
G-09	Bai-chao Ren, Yuan He, Li Chen, et al. 任百超, 何媛, 陈莉, 杨建刚, 孙乃学. Epidemiology of glaucoma in a rural population in Shaanxi province (陕西省农村人群青光眼的流行病学调查)[J]. International journal of ophthalmology (国际眼科杂志). 2005(05):214-9.
G-10	Yong-quan Bai, Jing-lin Yi, Hui Xie, et al. 白永泉, 易敬林, 谢晖, et al. Epidemiological survey of primary angle-closure glaucoma in rural population aged 50 and elderly (吉安县农村 50 岁以上人群原发性闭角型青光眼流行病学调查)[J]. Medical Information section of operative surgery (医学信息(手术学分册)). 2007(09):774-7.
G-11	Hui-ping Yuan, Hong Yu, Zheng Xiao, et al. 原慧萍, 于泓, 肖铮, et al. The prevalence of primary angle-closure glaucoma and its causes in rural area of Shuangyang district in Changchun, Jilin province (吉林省长春市双阳区齐家乡原发性闭角青光眼的患病率调查及其影响因素)[J]. Chin J Ophthalmol (中华眼科杂志). 2007;43(9):775-8.

Study ID	Reference
G-12	Zhi-feng Deng, Hong-juan Zhang. 邓志峰, 张洪娟. Epidemiology of primary open angle glaucoma in rural population in Heze (农村原发性开角型青光眼流行病学研究)[J]. Journal of Heze Medical College (菏泽医学专科学校学报). 2008(03):58-9.
G-13	Sheng-fang Song, Yong-ye Zhang, Xiang-ge He, et al. 宋胜仿, 张永烨, 贺翔鸽, et al. Prevalence of glaucoma among adults aged 50 years or above in Yongchuan district of Chongqing (重庆市永川地区 50 岁以上人群中青光眼患病率调查)[J]. Chin J Pract Ophthalmol (中国实用眼科杂志). 2009;27(2):168-72.
G-14	Xin Zhao, Yun-he He, Bi-qi Tian, et al. 赵欣, 郝云鹤, 田碧琪, et al. Glaucoma survey in population of 50 years old or more in the Xi Chang'an street community of Beijing (北京市西长安街社区 50 岁以上人群青光眼调查)[J]. Ophthalmol CHN (眼科). 2010(01):37-42.
G-15	Li-juan Zhang, Li Shan, Pan Fan, et al. 张丽娟, 单丽, 樊攀, 宋武莲, 原慧萍. Prevalence investigation on primary glaucoma in Kailu county, Inner Mongolia* (内蒙古开鲁县蒙古族原发性青光眼的患病率调查)[J]. Inner Mongolia Med J (内蒙古医学杂志). 2010(07):817-9.
G-16	Yang-yang Yu, Su-yun Wang, Shao-wei Wang. 于洋洋, 王素云, 王绍伟. Survey of prevalence of primary angle-closure glaucoma in rural population of Zhaozhou county (肇州县农村房角关闭疾病患病率调查)[J]. Chin J School Doctor (中国校医). 2013(08):599-601.
G-17	Wei-dong Sheng. 绳伟东. Epidemiological investigation on primary angle-closure glaucoma in middle-and-old aged people in Zhalantun city, Inner Mongolia* (内蒙古扎兰屯市中老年人群中原发性闭角型青光眼流行病学调查)[J]. China Prac Med (中国实用医药). 2014(24):261-3.

Study ID	Reference
G-18	Lian-rong Yin, Hua Yang, Xin Li, et al. 尹连荣, 杨华, 李欣, 高健生. Primary discussion for education and screening on glaucoma in the western community in Beijing (京西社区青光眼宣教及筛查的初步探讨)[J]. Chinese Journal of Chinese Ophthalmology (中国中医眼科杂志). 2014(06):437-9.
G-19	Zhi-zhuo Gao, Tong Li, Yi-yuan Sun, et al. 高志卓, 李童, 孙艺源, et al. Epidemiological investigation of primary glaucoma in cold region of northern China (我国北方寒冷地区原发性青光眼流行病学调查分析)[J]. Chin J of Public Health Eng (中国卫生工程学). 2015(06):552-4.
G-20	Yu-jin Pan. 潘裕锦. Prevalence of primary angle-closure glaucoma: a over 55 years population based survey in Sijihuacheng community of Shenzhen (深圳市四季花城社区 55 岁以上人群原发性闭角型青光眼的流行病学调查)[D]. Jinan University (暨南大学), 2015.
G-21	He M, Foster PJ, Ge J, et al. Prevalence and clinical characteristics of glaucoma in adult Chinese: a population-based study in Liwan District, Guangzhou. Invest Ophthalmol Vis Sci 2006;47(7):2782-8.
G-22	Wang YX, Xu L, Yang H, Jonas JB. Prevalence of glaucoma in North China: the Beijing Eye Study. AM J OPHTHALMOL 2010;150(6):917-24.
G-23	Liang YB, Friedman DS, Zhou Q, et al. Prevalence of primary open angle glaucoma in a rural adult Chinese population: the Handan eye study. Invest Ophthalmol Vis Sci 2011;52(11):8250-7.
G-24	Liang Y, Friedman DS, Zhou Q, et al. Prevalence and characteristics of primary angle-closure diseases in a rural adult Chinese population: the Handan Eye Study. Invest Ophthalmol Vis Sci 2011;52(12):8672-9.
G-25	Qu W, Li Y, Song W, et al. Prevalence and risk factors for angle-closure disease in a rural Northeast China population: a population-based survey in Bin County, Harbin. ACTA OPHTHALMOL 2011;89(6):e515-20.

Study ID	Reference
G-26	Song W, Shan L, Cheng F, et al. Prevalence of glaucoma in a rural northern China adult population: a population-based survey in kailu county, inner Mongolia. OPHTHALMOLOGY 2011;118(10):1982-8.
G-27	Sun J, Zhou X, Kang Y, et al. Prevalence and risk factors for primary open-angle glaucoma in a rural northeast China population: a population-based survey in Bin County, Harbin. Eye (Lond) 2012;26(2):283-91.
G-28	Zhong H, Li J, Li C, et al. The prevalence of glaucoma in adult rural Chinese populations of the Bai nationality in Dali: the Yunnan Minority Eye Study. Invest Ophthalmol Vis Sci 2012;53(6):3221-5.
G-29	He J, Zou H, Lee RK, et al. Prevalence and risk factors of primary open-angle glaucoma in a city of Eastern China: a population-based study in Pudong New District, Shanghai. BMC OPHTHALMOL 2015;15:134.
G-30	Pan CW, Zhao CH, Yu MB, et al. Prevalence, types and awareness of glaucoma in a multi-ethnic population in rural China: the Yunnan Minority Eye Study. Ophthalmic Physiol Opt 2016;36(6):664-70.

Note: The Chinese publication list employed the journals' official English names or abbreviations, English titles were obtained from journals or literature databases (CNKI, Wanfang and CBM). Where official English translation of journal names was not available, a pinyin title was adopted; where the English translation of titles was not available, the authors translated the titles, labelled with "" and marked as green.*

Appendix table 14. Detailed characteristics of the included studies on glaucoma prevalence in China (n=30)

Study ID	Study	Province	Region	Setting	Sex	Survey Year	Anterior chamber angle/depth evaluation	IOP measurement	Optic disc evaluation	Visual field testing	Age range	Sample size	POAG	PACG	Secondary glaucoma
G-01	Gao ZF (1995)	Anhui	East China	Rural	Both	1987	Yes, all	Yes, all	Yes, suspects	Yes, suspects	0-94	4531	3	14	5
G-02	Yu Q et al. (1995)	Guangdong	South Central China	Rural	Mixed	1990	Yes, all	Yes, all	Yes, suspects	Yes, suspects	51+	932	-	6	-
G-03	He MG et al. (2000)	Guangdong	South Central China	Rural	Both	1997	Yes, all	Yes, all	Yes, all	Yes, suspects	50-98	5342	-	54	-
G-04	Zhao JL et al. (2002)	Beijing	North China	Mixed	Both	1996	Yes, all	Yes, all	Yes, all	Yes, suspects	50+	4880	14	81	6
G-05	Xu L et al. (2004)	Beijing	North China	Both	Both	2001	Yes, suspects	Yes, all	Yes, all	Yes, all	40+	4451	81	-	-
G-06	Bai ZL et al. (2005)	Shaanxi	Northwest China	Rural	Both	2003	Yes, all	Yes, all	Yes, all	Yes, suspects	40-91	2835	-	31	-
G-07	Xu L et al. (2005)	Beijing	North China	Both	Both	2001	Yes, suspects	Yes, all	Yes, all	Yes, all	40+	4431	-	62	-
G-08	Sun HM et al. (2005)	Tianjin	North China	Rural	Both	2003	Yes, all	Yes, all	Yes, all	Yes, suspects	40+	1701	6	19	2
G-09	Ren BC et al. (2005)	Shaanxi	Northwest China	Rural	Both	2003	Yes, all	Yes, all	Yes, all	Yes, suspects	50-91	1775	7	29	2
G-10	Bai YQ et al. (2007)	Jiangxi	East China	Rural	Both	2006	Yes, all	Yes, suspects	Yes, all	Yes, suspects	50-87	5013	-	76	-

Study ID	Study	Province	Region	Setting	Sex	Survey Year	Anterior chamber angle/depth evaluation	IOP measurement	Optic disc evaluation	Visual field testing	Age range	Sample size	POAG	PACG	Secondary glaucoma
G-11	Yuan HP et al. (2007)	Jilin	Northeast China	Rural	Both	2004	Yes, all	Yes, all	Yes, all	Yes, suspects	41-96	1139	-	29	-
G-12	Deng ZF et al. (2008)	Shandong	East China	Rural	Both	2005*	Yes, all	Yes, all	Yes, all	Yes, suspects	40+	1166	15	-	-
G-13	Song SF et al. (2009)	Chongqing	Southwest China	Mixed	Both	2005	Yes, all	Yes, all	Yes, all	Yes, suspects	50+	5938	51	148	12
G-14	Zhao X et al. (2010)	Beijing	North China	Urban	Both	2006	Yes, all	Yes, all	Yes, all	Yes, suspects	50+	2410	15	40	2
G-15	Zhang LJ et al. (2010)	Inner Mongolia	North China	Rural	Both	2009	Yes, all	Yes, all	Yes, all	Yes, suspects	40+	579	10	13	-
G-16	Yu YY et al. (2013)	Heilongjiang	Northeast China	Rural	Both	2010*	Yes, all	Yes, all	Yes, all	Yes, suspects	40+	2056	-	33	-
G-17	Sheng WD (2014)	Inner Mongolia	North China	Mixed	Both	2013	Yes, all	Yes, all	Yes, all	Yes, suspects	50-93	1068	-	16	-
G-18	Yin LR et al. (2014)	Beijing	North China	Urban	Mixed	2010	Yes, all	Yes, all	Yes, all	Yes, all	40-80	13016	136	110	-
G-19	Gao ZZ et al. (2015)	Jilin	Northeast China	Urban	Both	2011	Yes, all	Yes, all	Yes, all	Yes, suspects	40+	2359	33	48	-
G-20	Pan YJ (2015)	Guangdong	South Central China	Urban	Both	2014	Yes, all	Yes, all	Yes, all	Yes, suspects	55-96	2422	46	37	3
G-21	He M et al. (2006)	Guangdong	South Central China	Urban	Both	2003	Yes, all	Yes, all	Yes, all	Yes, suspects	50-93	1504	29	21	2

Study ID	Study	Province	Region	Setting	Sex	Survey Year	Anterior chamber angle/depth evaluation	IOP measurement	Optic disc evaluation	Visual field testing	Age range	Sample size	POAG	PACG	Secondary glaucoma
G-22	Wang YX et al. (2010)	Beijing	North China	Both	Both	2001	Yes, all	Yes, all	Yes, all	Yes, all	40-101	4315	111	44	3
G-23	Liang YB et al. (2011)	Hebei	North China	Rural	Both	2007	Yes, all	Yes, all	Yes, all	Yes, suspects	30+	6716	125	-	-
G-24	Liang Y et al. (2011)	Hebei	North China	Rural	Both	2007	Yes, all	Yes, all	Yes, all	Yes, suspects	30+	6716	-	51	-
G-25	Qu W et al. (2011)	Heilongjiang	Northeast China	Rural	Both	2007	Yes, all	Yes, all	Yes, all	Yes, suspects	40+	4956	-	78	-
G-26	Song W et al. (2011)	Inner Mongolia	North China	Rural	Both	2009	Yes, all	Yes, all	Yes, all	Yes, suspects	40-87	5158	73	90	6
G-27	Sun J et al. (2012)	Heilongjiang	Northeast China	Rural	Both	2007	Yes, all	Yes, all	Yes, all	Yes, suspects	40+	4956	35	-	-
G-28	Zhong H et al. (2012)	Yunnan	Southwest China	Rural	Both	2010	Yes, all	Yes, all	Yes, all	Yes, suspects	50+	2133	22	20	5
G-29	He J et al. (2015)	Shanghai	East China	Urban	Both	2011	Yes, all	Yes, all	Yes, all	Yes, suspects	50-106	2528	72	-	-
G-30	Pan CW et al. (2016)	Yunnan	Southwest China	Rural	Both	2010	Yes, all	Yes, all	Yes, all	Yes, suspects	50+	6546	137	46	29

Note: "-" represents unavailable data; "" indicates studies whose survey year was imputed.*

Appendix table 15. Risk of bias scores of the included studies on glaucoma prevalence in China (n=30)

Study ID	Study	Quality score					
		Sample population	Sample size	Participation	Outcome assessment	Analytical methods	Total scores
G-01	Gao ZF (1995)	2	2	2	2	2	10
G-02	Yu Q et al. (1995)	2	1	2	2	2	9
G-03	He MG et al. (2000)	2	1	2	2	2	9
G-04	Zhao JL et al. (2002)	2	2	2	2	2	10
G-05	Xu L et al. (2004)	2	1	1	2	2	8
G-06	Bai ZL et al. (2005)	2	1	1	2	2	8
G-07	Xu L et al. (2005)	2	1	1	2	2	8
G-08	Sun HM et al. (2005)	2	1	2	2	2	9
G-09	Ren BC et al. (2005)	2	2	1	2	2	9
G-10	Bai YQ et al. (2007)	2	1	2	2	2	9
G-11	Yuan HP et al. (2007)	2	1	1	2	2	8
G-12	Deng ZF et al. (2008)	2	1	2	2	2	9
G-13	Song SF et al. (2009)	2	2	2	2	2	10
G-14	Zhao X et al. (2010)	2	1	2	2	2	9
G-15	Zhang LJ et al. (2010)	2	1	2	2	2	9
G-16	Yu YY et al. (2013)	2	1	2	2	2	9
G-17	Sheng WD (2014)	2	1	2	2	2	9
G-18	Yin LR et al. (2014)	2	1	0	2	2	7

Study ID	Study	Quality score					
		Sample population	**Sample size**	**Participation**	**Outcome assessment**	**Analytical methods**	**Total scores**
G-19	Gao ZZ et al. (2015)	2	1	0	2	2	7
G-20	Pan YJ (2015)	2	2	2	2	2	10
G-21	He M et al. (2006)	2	1	1	2	2	8
G-22	Wang YX et al. (2010)	2	1	1	2	2	8
G-23	Liang YB et al. (2011)	2	1	0	2	2	7
G-24	Liang Y et al. (2011)	2	1	1	2	2	8
G-25	Qu W et al. (2011)	2	1	2	2	2	9
G-26	Song W et al. (2011)	2	1	2	2	2	9
G-27	Sun J et al. (2012)	2	1	2	2	2	9
G-28	Zhong H et al. (2012)	2	1	1	2	2	8
G-29	He J et al. (2015)	2	2	1	2	2	9
G-30	Pan CW et al. (2016)	2	2	1	2	2	9

Appendix table 16. Estimated and projected number of people with POAG and PACG in China from 1990 to 2050, by sex and age group (million, 95% CI)

1990						
Age group	**POAG**			**PACG**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	0.19 (0.12-0.29)	0.12 (0.08-0.19)	0.31 (0.20-0.48)	0.12 (0.10-0.15)	0.21 (0.17-0.26)	0.33 (0.27-0.41)
50-54 years	0.21 (0.14-0.32)	0.14 (0.09-0.21)	0.35 (0.23-0.53)	0.15 (0.12-0.18)	0.25 (0.21-0.29)	0.40 (0.33-0.47)
55-59 years	0.22 (0.15-0.34)	0.15 (0.10-0.23)	0.38 (0.25-0.57)	0.17 (0.14-0.20)	0.29 (0.25-0.34)	0.46 (0.39-0.54)
60-64 years	0.21 (0.14-0.32)	0.15 (0.10-0.22)	0.36 (0.23-0.54)	0.17 (0.14-0.20)	0.30 (0.26-0.35)	0.47 (0.40-0.55)
65-69 years	0.18 (0.12-0.28)	0.14 (0.09-0.21)	0.32 (0.21-0.48)	0.16 (0.13-0.19)	0.30 (0.26-0.35)	0.46 (0.39-0.53)
70-74 years	0.16 (0.11-0.25)	0.13 (0.08-0.20)	0.29 (0.19-0.44)	0.15 (0.12-0.18)	0.30 (0.26-0.36)	0.45 (0.38-0.54)
75-79 years	0.10 (0.07-0.16)	0.10 (0.06-0.15)	0.20 (0.13-0.31)	0.10 (0.08-0.13)	0.25 (0.21-0.30)	0.35 (0.29-0.42)
80–84 years	0.05 (0.03-0.07)	0.06 (0.04-0.09)	0.11 (0.07-0.17)	0.05 (0.04-0.06)	0.16 (0.13-0.20)	0.21 (0.17-0.26)
85-89 years	0.02 (0.01-0.03)	0.03 (0.02-0.04)	0.04 (0.03-0.07)	0.02 (0.01-0.02)	0.07 (0.06-0.09)	0.09 (0.07-0.12)
Total (45-89 years)	1.35 (0.88-2.05)	1.01 (0.66-1.55)	2.35 (1.54-3.60)	1.09 (0.90-1.32)	2.13 (1.80-2.53)	3.22 (2.70-3.84)
2000						
Age group	**POAG**			**PACG**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	0.32 (0.21-0.50)	0.23 (0.15-0.35)	0.55 (0.36-0.85)	0.21 (0.17-0.26)	0.38 (0.31-0.46)	0.59 (0.48-0.73)
50-54 years	0.27 (0.18-0.42)	0.19 (0.13-0.29)	0.46 (0.30-0.71)	0.19 (0.16-0.23)	0.35 (0.29-0.41)	0.54 (0.45-0.64)
55-59 years	0.25 (0.16-0.38)	0.17 (0.11-0.26)	0.42 (0.27-0.64)	0.19 (0.16-0.22)	0.33 (0.28-0.38)	0.51 (0.44-0.60)

60-64 years	0.27 (0.18-0.40)	0.18 (0.12-0.27)	0.45 (0.29-0.68)	0.22 (0.18-0.25)	0.37 (0.32-0.43)	0.59 (0.50-0.68)
65-69 years	0.26 (0.17-0.39)	0.19 (0.12-0.28)	0.44 (0.29-0.67)	0.22 (0.19-0.27)	0.41 (0.35-0.47)	0.63 (0.54-0.74)
70-74 years	0.21 (0.14-0.31)	0.16 (0.10-0.25)	0.37 (0.24-0.56)	0.19 (0.16-0.23)	0.38 (0.32-0.44)	0.57 (0.48-0.67)
75-79 years	0.14 (0.09-0.21)	0.13 (0.08-0.19)	0.27 (0.17-0.41)	0.14 (0.11-0.17)	0.32 (0.26-0.38)	0.45 (0.38-0.55)
80–84 years	0.09 (0.06-0.13)	0.09 (0.06-0.14)	0.18 (0.11-0.27)	0.09 (0.07-0.12)	0.24 (0.19-0.29)	0.33 (0.27-0.41)
85-89 years	0.03 (0.02-0.05)	0.04 (0.03-0.07)	0.08 (0.05-0.12)	0.04 (0.03-0.05)	0.12 (0.10-0.15)	0.16 (0.13-0.20)
Total (45-89 years)	1.84 (1.20-2.80)	1.37 (0.89-2.11)	3.21 (2.09-4.91)	1.49 (1.23-1.80)	2.88 (2.43-3.43)	4.37 (3.66-5.23)

2010						
Age group	**POAG**			**PACG**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	0.38 (0.25-0.59)	0.27 (0.17-0.41)	0.65 (0.42-1.00)	0.25 (0.20-0.31)	0.45 (0.37-0.55)	0.70 (0.57-0.86)
50-54 years	0.36 (0.24-0.56)	0.26 (0.17-0.39)	0.62 (0.41-0.95)	0.26 (0.21-0.31)	0.46 (0.39-0.55)	0.72 (0.60-0.86)
55-59 years	0.44 (0.29-0.66)	0.31 (0.20-0.47)	0.75 (0.49-1.13)	0.33 (0.28-0.39)	0.60 (0.51-0.70)	0.93 (0.79-1.09)
60-64 years	0.35 (0.23-0.54)	0.26 (0.17-0.39)	0.61 (0.40-0.93)	0.29 (0.24-0.34)	0.53 (0.46-0.61)	0.81 (0.70-0.95)
65-69 years	0.30 (0.20-0.46)	0.21 (0.14-0.33)	0.51 (0.34-0.78)	0.26 (0.22-0.31)	0.47 (0.41-0.54)	0.73 (0.63-0.85)
70-74 years	0.28 (0.18-0.43)	0.21 (0.14-0.32)	0.49 (0.32-0.75)	0.26 (0.22-0.31)	0.49 (0.42-0.57)	0.75 (0.63-0.89)
75-79 years	0.22 (0.14-0.33)	0.18 (0.12-0.28)	0.40 (0.26-0.61)	0.22 (0.18-0.27)	0.46 (0.38-0.55)	0.67 (0.56-0.81)
80–84 years	0.13 (0.08-0.19)	0.12 (0.08-0.19)	0.25 (0.16-0.38)	0.13 (0.11-0.17)	0.32 (0.26-0.40)	0.46 (0.37-0.57)
85-89 years	0.06 (0.03-0.09)	0.06 (0.04-0.10)	0.12 (0.07-0.19)	0.06 (0.05-0.08)	0.18 (0.14-0.22)	0.24 (0.19-0.31)

Total (45-89 years)	2.51 (1.64-3.84)	1.88 (1.22-2.88)	4.39 (2.86-6.72)	2.05 (1.70-2.48)	3.95 (3.33-4.69)	6.01 (5.03-7.18)

2015						
Age group	**POAG**			**PACG**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	0.46 (0.30-0.71)	0.33 (0.21-0.51)	0.79 (0.51-1.22)	0.30 (0.24-0.38)	0.55 (0.45-0.68)	0.86 (0.70-1.05)
50-54 years	0.45 (0.29-0.68)	0.32 (0.21-0.48)	0.76 (0.50-1.16)	0.31 (0.26-0.38)	0.57 (0.48-0.67)	0.88 (0.74-1.05)
55-59 years	0.42 (0.28-0.64)	0.30 (0.20-0.46)	0.72 (0.47-1.10)	0.32 (0.27-0.38)	0.58 (0.50-0.67)	0.90 (0.76-1.05)
60-64 years	0.49 (0.32-0.75)	0.36 (0.23-0.54)	0.85 (0.56-1.29)	0.40 (0.34-0.47)	0.73 (0.64-0.85)	1.13 (0.97-1.32)
65-69 years	0.38 (0.25-0.58)	0.28 (0.19-0.43)	0.66 (0.44-1.01)	0.33 (0.28-0.39)	0.63 (0.54-0.72)	0.96 (0.82-1.11)
70-74 years	0.30 (0.20-0.46)	0.22 (0.15-0.34)	0.52 (0.34-0.80)	0.28 (0.23-0.33)	0.53 (0.45-0.62)	0.80 (0.68-0.95)
75-79 years	0.25 (0.16-0.38)	0.20 (0.13-0.31)	0.44 (0.29-0.68)	0.24 (0.20-0.30)	0.50 (0.41-0.60)	0.74 (0.61-0.90)
80–84 years	0.16 (0.10-0.25)	0.15 (0.10-0.23)	0.31 (0.20-0.48)	0.17 (0.14-0.21)	0.40 (0.32-0.49)	0.57 (0.46-0.70)
85-89 years	0.07 (0.05-0.11)	0.08 (0.05-0.12)	0.15 (0.10-0.24)	0.08 (0.06-0.11)	0.22 (0.17-0.28)	0.31 (0.24-0.39)
Total (45-89 years)	2.98 (1.95-4.55)	2.24 (1.45-3.43)	5.22 (3.40-7.98)	2.44 (2.01-2.95)	4.70 (3.96-5.58)	7.14 (5.97-8.53)

2020						
Age group	**POAG**			**PACG**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	0.44 (0.29-0.68)	0.31 (0.20-0.48)	0.76 (0.49-1.17)	0.29 (0.23-0.36)	0.52 (0.43-0.64)	0.81 (0.66-1.00)
50-54 years	0.54 (0.35-0.83)	0.39 (0.25-0.60)	0.93 (0.61-1.42)	0.38 (0.31-0.46)	0.70 (0.59-0.83)	1.08 (0.90-1.29)
55-59 years	0.52 (0.34-0.79)	0.37 (0.24-0.56)	0.89 (0.58-1.35)	0.39 (0.33-0.46)	0.71 (0.61-0.83)	1.10 (0.94-1.29)
60-64 years	0.48	0.35	0.82	0.39	0.71	1.10

	(0.32-0.73)	(0.23-0.53)	(0.54-1.25)	(0.33-0.46)	(0.62-0.82)	(0.94-1.28)
65-69 years	0.53	0.40	0.93	0.46	0.88	1.34
	(0.35-0.81)	(0.26-0.61)	(0.61-1.42)	(0.39-0.55)	(0.76-1.02)	(1.15-1.57)
70-74 years	0.38	0.30	0.69	0.36	0.71	1.07
	(0.25-0.59)	(0.20-0.46)	(0.45-1.05)	(0.30-0.43)	(0.60-0.83)	(0.90-1.26)
75-79 years	0.27	0.22	0.49	0.27	0.55	0.81
	(0.17-0.41)	(0.14-0.34)	(0.31-0.75)	(0.22-0.33)	(0.45-0.66)	(0.67-0.98)
80–84 years	0.19	0.17	0.35	0.20	0.45	0.65
	(0.12-0.29)	(0.11-0.26)	(0.23-0.55)	(0.16-0.25)	(0.36-0.55)	(0.52-0.80)
85-89 years	0.10	0.10	0.20	0.11	0.28	0.40
	(0.06-0.15)	(0.06-0.16)	(0.13-0.31)	(0.09-0.14)	(0.22-0.36)	(0.31-0.50)
Total	3.45	2.60	6.06	2.84	5.51	8.36
(45-89 years)	(2.26-5.28)	(1.69-3.99)	(3.95-9.27)	(2.35-3.44)	(4.65-6.54)	(7.00-9.98)
2030						
Age group	**POAG**			**PACG**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	0.37	0.26	0.62	0.24	0.43	0.67
	(0.24-0.57)	(0.17-0.40)	(0.40-0.96)	(0.19-0.30)	(0.35-0.53)	(0.55-0.83)
50-54 years	0.42	0.29	0.71	0.29	0.53	0.82
	(0.27-0.64)	(0.19-0.45)	(0.46-1.08)	(0.24-0.35)	(0.44-0.63)	(0.68-0.98)
55-59 years	0.61	0.43	1.04	0.46	0.83	1.29
	(0.40-0.93)	(0.28-0.66)	(0.68-1.59)	(0.39-0.55)	(0.72-0.97)	(1.10-1.52)
60-64 years	0.72	0.53	1.25	0.58	1.09	1.68
	(0.48-1.10)	(0.35-0.81)	(0.82-1.90)	(0.49-0.69)	(0.94-1.26)	(1.44-1.95)
65-69 years	0.65	0.48	1.14	0.57	1.06	1.63
	(0.43-0.99)	(0.32-0.74)	(0.75-1.73)	(0.48-0.67)	(0.92-1.23)	(1.40-1.90)
70-74 years	0.55	0.42	0.97	0.51	0.99	1.50
	(0.36-0.83)	(0.27-0.65)	(0.63-1.48)	(0.42-0.61)	(0.84-1.16)	(1.27-1.77)
75-79 years	0.52	0.43	0.95	0.51	1.08	1.59
	(0.34-0.79)	(0.28-0.66)	(0.61-1.46)	(0.42-0.63)	(0.90-1.30)	(1.32-1.93)
80–84 years	0.29	0.27	0.55	0.31	0.71	1.02
	(0.18-0.45)	(0.17-0.42)	(0.36-0.86)	(0.24-0.38)	(0.58-0.87)	(0.82-1.26)
85-89 years	0.14	0.14	0.28	0.16	0.39	0.55
	(0.09-0.22)	(0.09-0.22)	(0.18-0.44)	(0.12-0.20)	(0.31-0.50)	(0.43-0.70)
Total	4.26	3.25	7.51	3.63	7.12	10.75

(45-89 years)	(2.78-6.51)	(2.12-4.99)	(4.90-11.5)	(3.00-4.39)	(6.00-8.45)	(9.00-12.84)
2040						
Age group	**POAG**			**PACG**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	0.40 (0.26-0.62)	0.27 (0.17-0.41)	0.66 (0.43-1.03)	0.26 (0.21-0.32)	0.45 (0.36-0.54)	0.71 (0.57-0.87)
50-54 years	0.57 (0.37-0.87)	0.39 (0.25-0.60)	0.96 (0.63-1.47)	0.40 (0.33-0.48)	0.70 (0.59-0.83)	1.10 (0.92-1.32)
55-59 years	0.51 (0.33-0.77)	0.36 (0.23-0.55)	0.87 (0.57-1.32)	0.38 (0.32-0.46)	0.69 (0.59-0.80)	1.07 (0.91-1.26)
60-64 years	0.56 (0.37-0.85)	0.40 (0.26-0.61)	0.96 (0.63-1.46)	0.45 (0.38-0.54)	0.83 (0.72-0.95)	1.28 (1.10-1.49)
65-69 years	0.79 (0.52-1.20)	0.58 (0.38-0.88)	1.36 (0.90-2.07)	0.68 (0.58-0.81)	1.27 (1.09-1.47)	1.95 (1.67-2.28)
70-74 years	0.86 (0.57-1.32)	0.66 (0.43-1.01)	1.53 (1.00-2.33)	0.80 (0.67-0.96)	1.56 (1.33-1.83)	2.36 (2.00-2.79)
75-79 years	0.68 (0.44-1.04)	0.55 (0.35-0.84)	1.23 (0.79-1.89)	0.67 (0.55-0.83)	1.37 (1.14-1.65)	2.05 (1.69-2.47)
80–84 years	0.46 (0.29-0.71)	0.40 (0.26-0.63)	0.86 (0.55-1.33)	0.49 (0.39-0.61)	1.07 (0.87-1.32)	1.56 (1.26-1.93)
85-89 years	0.31 (0.20-0.48)	0.31 (0.19-0.49)	0.62 (0.39-0.97)	0.35 (0.27-0.45)	0.87 (0.69-1.10)	1.22 (0.96-1.56)
Total (45-89 years)	5.14 (3.35-7.85)	3.91 (2.54-6.01)	9.04 (5.89-13.86)	4.49 (3.70-5.46)	8.81 (7.38-10.50)	13.3 (11.08-15.97)
2050						
Age group	**POAG**			**PACG**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	0.29 (0.19-0.44)	0.18 (0.12-0.28)	0.47 (0.30-0.72)	0.19 (0.15-0.23)	0.31 (0.25-0.37)	0.49 (0.40-0.61)
50-54 years	0.35 (0.23-0.54)	0.23 (0.15-0.35)	0.58 (0.38-0.89)	0.25 (0.20-0.30)	0.41 (0.35-0.49)	0.66 (0.55-0.79)
55-59 years	0.56 (0.37-0.85)	0.37 (0.24-0.56)	0.93 (0.61-1.41)	0.42 (0.35-0.50)	0.71 (0.61-0.83)	1.13 (0.96-1.33)
60-64 years	0.78 (0.51-1.18)	0.54 (0.35-0.82)	1.32 (0.86-2.00)	0.63 (0.53-0.74)	1.11 (0.96-1.28)	1.74 (1.49-2.02)

65-69 years	0.67 (0.44-1.02)	0.48 (0.31-0.73)	1.15 (0.76-1.75)	0.58 (0.49-0.69)	1.06 (0.91-1.23)	1.64 (1.41-1.92)
70-74 years	0.70 (0.46-1.07)	0.51 (0.33-0.79)	1.21 (0.79-1.85)	0.65 (0.54-0.78)	1.21 (1.03-1.42)	1.86 (1.57-2.20)
75-79 years	0.88 (0.57-1.34)	0.68 (0.44-1.04)	1.55 (1.01-2.39)	0.87 (0.71-1.07)	1.70 (1.41-2.04)	2.57 (2.13-3.10)
80–84 years	0.80 (0.51-1.24)	0.67 (0.43-1.05)	1.47 (0.94-2.29)	0.85 (0.68-1.07)	1.80 (1.46-2.21)	2.65 (2.13-3.28)
85-89 years	0.47 (0.30-0.73)	0.43 (0.27-0.68)	0.90 (0.57-1.41)	0.53 (0.41-0.69)	1.22 (0.96-1.55)	1.76 (1.37-2.24)
Total (45-89 years)	5.49 (3.57-8.41)	4.10 (2.65-6.31)	9.59 (6.23-14.72)	4.97 (4.07-6.07)	9.52 (7.94-11.41)	14.49 (12.01-17.48)

Appendix table 17. Estimation of age-specific number of people with POAG in China from 2000 to 2010, by geographical region (million, 95% CI)

2000						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**
45-49 years	0.072 (0.047-0.109)	0.061 (0.042-0.088)	0.173 (0.114-0.263)	0.142 (0.091-0.220)	0.081 (0.051-0.130)	0.034 (0.021-0.053)
50-54 years	0.056 (0.037-0.086)	0.046 (0.031-0.066)	0.146 (0.096-0.221)	0.121 (0.078-0.187)	0.070 (0.044-0.112)	0.030 (0.019-0.047)
55-59 years	0.047 (0.031-0.071)	0.039 (0.027-0.056)	0.127 (0.084-0.192)	0.107 (0.069-0.165)	0.069 (0.043-0.111)	0.030 (0.019-0.046)
60-64 years	0.054 (0.036-0.080)	0.044 (0.032-0.062)	0.133 (0.088-0.201)	0.116 (0.075-0.178)	0.070 (0.044-0.112)	0.032 (0.021-0.049)
65-69 years	0.054 (0.036-0.081)	0.041 (0.029-0.057)	0.141 (0.093-0.213)	0.116 (0.075-0.179)	0.064 (0.040-0.102)	0.027 (0.017-0.041)
70-74 years	0.042 (0.028-0.064)	0.033 (0.023-0.046)	0.120 (0.079-0.182)	0.094 (0.060-0.147)	0.054 (0.034-0.086)	0.018 (0.012-0.029)
75-79 years	0.029 (0.019-0.044)	0.021 (0.015-0.031)	0.090 (0.059-0.137)	0.069 (0.043-0.108)	0.037 (0.023-0.058)	0.013 (0.008-0.021)
80-84 years	0.017 (0.011-0.027)	0.013 (0.009-0.018)	0.061 (0.039-0.092)	0.047 (0.029-0.074)	0.025 (0.015-0.039)	0.008 (0.005-0.013)
85-89 years	0.007 (0.005-0.011)	0.006 (0.004-0.008)	0.026 (0.017-0.040)	0.021 (0.013-0.033)	0.011 (0.007-0.018)	0.003 (0.002-0.005)
Total (45-89 years)	0.379 (0.250-0.573)	0.304 (0.212-0.433)	1.016 (0.669-1.540)	0.832 (0.534-1.292)	0.482 (0.301-0.768)	0.194 (0.124-0.303)
2010						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**
45-49 years	0.087 (0.058-0.131)	0.070 (0.047-0.103)	0.205 (0.136-0.309)	0.178 (0.116-0.273)	0.085 (0.054-0.134)	0.045 (0.029-0.071)
50-54 years	0.092 (0.061-0.139)	0.076 (0.051-0.112)	0.195 (0.130-0.291)	0.159 (0.104-0.244)	0.073 (0.046-0.115)	0.041 (0.026-0.065)
55-59 years	0.098 (0.065-0.149)	0.079 (0.053-0.117)	0.234 (0.155-0.354)	0.188 (0.121-0.290)	0.104 (0.065-0.166)	0.044 (0.028-0.070)
60-64 years	0.075 (0.049-0.113)	0.058 (0.039-0.086)	0.191 (0.126-0.289)	0.155 (0.100-0.239)	0.088 (0.055-0.141)	0.037 (0.024-0.059)

65-69 years	0.058 (0.039-0.087)	0.046 (0.032-0.068)	0.156 (0.103-0.237)	0.128 (0.082-0.200)	0.081 (0.051-0.131)	0.035 (0.022-0.055)
70-74 years	0.058 (0.039-0.086)	0.046 (0.032-0.066)	0.148 (0.097-0.224)	0.125 (0.080-0.193)	0.073 (0.046-0.117)	0.033 (0.021-0.051)
75-79 years	0.047 (0.031-0.070)	0.035 (0.024-0.050)	0.130 (0.085-0.199)	0.103 (0.065-0.161)	0.055 (0.034-0.087)	0.022 (0.014-0.034)
80-84 years	0.027 (0.018-0.040)	0.021 (0.014-0.030)	0.084 (0.055-0.129)	0.063 (0.040-0.099)	0.035 (0.021-0.056)	0.011 (0.007-0.017)
85-89 years	0.012 (0.008-0.017)	0.009 (0.006-0.013)	0.042 (0.027-0.064)	0.031 (0.019-0.049)	0.015 (0.010-0.025)	0.005 (0.003-0.007)
Total (45-89 years)	0.554 (0.367-0.832)	0.440 (0.299-0.644)	1.385 (0.913-2.097)	1.129 (0.728-1.748)	0.610 (0.382-0.972)	0.274 (0.175-0.429)

Appendix table 18. Estimation of age-specific number of people with PACG in China from 2000 to 2010, by geographical region (million, 95% CI)

2000						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**
45-49 years	0.081 (0.075-0.086)	0.092 (0.081-0.104)	0.157 (0.123-0.200)	0.117 (0.096-0.143)	0.098 (0.077-0.124)	0.044 (0.034-0.056)
50-54 years	0.070 (0.067-0.073)	0.076 (0.068-0.085)	0.144 (0.114-0.182)	0.109 (0.091-0.130)	0.092 (0.073-0.115)	0.043 (0.034-0.054)
55-59 years	0.062 (0.061-0.064)	0.069 (0.063-0.076)	0.135 (0.107-0.170)	0.104 (0.088-0.122)	0.098 (0.079-0.121)	0.046 (0.036-0.057)
60-64 years	0.075 (0.074-0.076)	0.083 (0.075-0.090)	0.154 (0.121-0.194)	0.122 (0.104-0.142)	0.107 (0.087-0.131)	0.051 (0.041-0.065)
65-69 years	0.083 (0.082-0.084)	0.082 (0.074-0.090)	0.179 (0.140-0.227)	0.135 (0.116-0.156)	0.107 (0.087-0.131)	0.047 (0.037-0.059)
70-74 years	0.072 (0.071-0.074)	0.072 (0.064-0.079)	0.170 (0.132-0.218)	0.123 (0.106-0.142)	0.099 (0.080-0.121)	0.035 (0.027-0.045)
75-79 years	0.055 (0.053-0.057)	0.051 (0.046-0.058)	0.143 (0.110-0.186)	0.101 (0.087-0.118)	0.074 (0.060-0.092)	0.028 (0.022-0.036)
80-84 years	0.036 (0.034-0.038)	0.033 (0.029-0.037)	0.107 (0.081-0.141)	0.077 (0.066-0.090)	0.055 (0.044-0.068)	0.020 (0.015-0.025)
85-89 years	0.017 (0.015-0.018)	0.016 (0.014-0.019)	0.052 (0.038-0.069)	0.039 (0.033-0.046)	0.028 (0.022-0.035)	0.008 (0.006-0.010)
Total (45-89 years)	0.552 (0.532-0.570)	0.574 (0.514-0.637)	1.242 (0.967-1.587)	0.927 (0.786-1.089)	0.758 (0.610-0.938)	0.321 (0.252-0.407)
2010						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**
45-49 years	0.095 (0.089-0.102)	0.107 (0.094-0.121)	0.184 (0.144-0.234)	0.145 (0.118-0.177)	0.100 (0.078-0.126)	0.058 (0.045-0.074)
50-54 years	0.111 (0.106-0.115)	0.127 (0.114-0.142)	0.189 (0.149-0.239)	0.141 (0.118-0.170)	0.094 (0.075-0.117)	0.058 (0.046-0.073)
55-59 years	0.129 (0.126-0.133)	0.145 (0.131-0.160)	0.251 (0.198-0.316)	0.183 (0.155-0.216)	0.149 (0.120-0.184)	0.069 (0.054-0.086)
60-64 years	0.108 (0.106-0.110)	0.117 (0.106-0.128)	0.223 (0.175-0.282)	0.164 (0.140-0.192)	0.137 (0.111-0.168)	0.064 (0.050-0.080)
65-69 years	0.090 (0.088-0.091)	0.099 (0.089-0.109)	0.197 (0.154-0.251)	0.149 (0.128-0.172)	0.136 (0.111-0.167)	0.064 (0.050-0.081)

70-74 years	0.096 (0.093-0.098)	0.104 (0.093-0.115)	0.204 (0.158-0.261)	0.157 (0.135-0.182)	0.132 (0.107-0.163)	0.063 (0.049-0.080)
75-79 years	0.086 (0.082-0.089)	0.084 (0.075-0.094)	0.201 (0.154-0.261)	0.146 (0.125-0.170)	0.109 (0.088-0.135)	0.046 (0.036-0.059)
80-84 years	0.054 (0.051-0.058)	0.055 (0.048-0.063)	0.147 (0.110-0.193)	0.101 (0.085-0.118)	0.077 (0.061-0.096)	0.024 (0.018-0.031)
85-89 years	0.026 (0.024-0.028)	0.026 (0.022-0.030)	0.081 (0.060-0.108)	0.056 (0.047-0.066)	0.038 (0.030-0.047)	0.012 (0.009-0.016)
Total (45-89 years)	0.795 (0.765-0.823)	0.864 (0.772-0.962)	1.676 (1.301-2.146)	1.242 (1.050-1.463)	0.972 (0.780-1.204)	0.457 (0.358-0.580)

Appendix table 19. Search strategy to identify studies reporting the prevalence of cataract and cataract blindness in China

CNKI

Access Date: 21 Nov 2017

Subject category: Medicine & Public Health

Sub-database: Journal, Featured journal, Doctoral dissertation, Master dissertation

检索表达式：

(SU % '白内障') AND (SU % '发病率' + '发生率' + '患病率'+ '罹患率' + '现患率'+ '死亡率' + '病死率'+ '流行' + '负担'+ '现况调查'+ '现况研究')

发表时间：从 1990-01-01 到 2017-11-21

Search Terms: (SU % 'baineizhang') AND (SU % 'fabinglv' + 'fashenglv' + 'huanbinglv'+ 'lihuanlv' + 'xianhuanlv'+ 'siwanglv' + 'bingsilv'+ 'liuxing' + 'fudan'+ 'xiankuangdiaocha'+ 'xiankuangyanjiu')

Published time：From 01/01/1990 to 21/11/2017

Wanfang

Access Date: 21 Nov 2017

Sub-database: Journal articles, Dissertations

检索表达式：(主题:(白内障)) * (主题:(发病率) + 主题:(发生率) + 主题:(患病率) +主题:(罹患率) + 主题:(现患率) + 主题:(死亡率) +主题:(病死率) + 主题:(流行) + 主题:(负担)+ 主题:(现况调查) + 主题:(现况研究))

时间：1990-2017

Search Terms: (subject: (baineizhang))* (subject: (fabinglv) + subject: (fashenglv) + subject: (huanbinglv)+ subject: (lihuanlv) + subject: (xianhuanlv) + subject: (siwanglv)+ subject: (bingsilv) + subject: (liuxing) + subject: (fudan)+ subject: (xiankuangdiaocha) + subject: (xiankuangyanjiu))

Date: 1990-2017

CBM-SinoMed

Access Date: 21 Nov 2017

Journal category: All journals

检索表达式:

(白内障) AND (发病率 or 发生率 or 患病率 or 罹患率 or 现患率 or 死亡率 or 病死率 or 流行 or 负担 or 现况调查 or 现况研究)

时间：1990-2017

Search Terms: ((baineizhang))* ((fabinglv) OR (fashenglv) OR (huanbinglv) OR (lihuanlv) OR (xianhuanlv) OR (siwanglv) OR (bingsilv) OR (liuxing) OR (fudan) OR (xiankuangdiaocha) OR (xiankuangyanjiu))

Date: 1990-2017

PubMed

Access Date: 22 Nov 2017

Search Terms:

((cataract*) AND (China OR Chinese OR Hongkong OR Macau OR Taiwan) AND (inciden* OR prevalen* OR morbidity OR mortality OR epidemiology)) AND ("1990/01/01"[Date - Publication] : "2017/11/22"[Date - Publication])

Embase (Ovid)

Access Date: 22 Nov 2017

#	Searches
1	cataract*.mp. or exp cataract/
2	China.mp. or exp China/
3	exp Chinese/ or Chinese.mp.
4	Hong Kong.mp. or exp Hong Kong/
5	Macau.mp. or exp Macau/
6	Taiwan.mp. or exp Taiwan/
7	exp incidence/ or inciden*.mp.
8	exp prevalence/ or prevalen*.mp.
9	morbidity.mp. or exp morbidity/
10	exp mortality/ or Mortality.mp.
11	exp epidemiology/ or Epidemiology.mp.
12	2 or 3 or 4 or 5 or 6
13	7 or 8 or 9 or 10 or 11
14	1 and 12 and 13
15	limit 14 to yr="1990 -Current"

Medline (Ovid)

Access Date: 22 Nov 2017

Search Terms:

#	Searches
1	exp Cataract/ or cataract*.mp.
2	China.mp. or exp China/

3	Chinese.mp.
4	Hong Kong.mp. or exp Hong Kong/
5	Macau.mp. or exp Macau/
6	Taiwan.mp. or exp Taiwan/
7	exp Incidence/ or inciden*.mp.
8	exp Prevalence/ or prevalen*.mp.
9	Morbidity.mp. or exp Morbidity/
10	Mortality.mp. or exp Mortality/
11	Epidemiology.mp. or exp Epidemiology/
12	2 or 3 or 4 or 5 or 6
13	7 or 8 or 9 or 10 or 11
14	1 and 12 and 13
15	limit 14 to yr="1990 -Current"

Appendix table 20. A "data microarray" illustrating the definitions of cataract and cataract blindness adopted in population-based studies in China

Study ID	Study	Cataract type		Blindness				Cataract definition						
		Any cataract	ARC	PVA< 0.10	PVA< 0.05	BCVA< 0.10	BCVA< 0.05	Lens opacities	PVA< 0.70	BCVA≤ 0.70	BCVA< 0.63	BCVA< 0.60	Including operated cases	LOCS grading
CA-01	Li SZ et al. (1999)													
CA-02	Zhao JL et al. (2001)													
CA-03	Tang X (2008)													
CA-04	Tang XY (2002)													
CA-05	Wang YX et al. (2003)													
CA-06	Li ZQ et al. (2004)													
CA-07	Chen L et al. (2004)													
CA-08	Ding L et al. (2005)													
CA-10	Li L et al. (2006)													
CA-12	Li ZJ et al. (2007)													
CA-14	Huang XB et al. (2009)													
CA-15	Zhou Y et al. (2011)													
CA-16	Tang B et al. (2011)													
CA-17	Xie TY et al. (2011)													
CA-18	Zhao MG et al. (2011)													
CA-19	Zhang HF (2013)													
CA-20	Li FR et al. (2012)													
CA-21A	Bi JX (2012)													
CA-21B	Guan HJ et al. (2012)													

Study ID	Study	Cataract type		Blindness				Cataract definition						
		Any cataract	ARC	PVA< 0.10	PVA< 0.05	BCVA< 0.10	BCVA< 0.05	Lens opacities	PVA< 0.70	BCVA≤ 0.70	BCVA< 0.63	BCVA< 0.60	Including operated cases	LOCS grading
CA-22	Luo R et al. (2012)													
CA-23A	Guan HJ et al. (2013)													
CA-23B	J M et al. (2015)													
CA-23C	Cai N et al. (2013)													
CA-24	Jiao WZ (2014)													
CA-25A	Wang GM (2013)													
CA-25B	Tang HY (2012)													
CA-26	Tian F et al. (2014)													
CA-27	Shen W (2015)													
CA-28	Shen W et al. (2013)													
CA-29	Wang TY (2015)													
CA-32	Jiang HF et al. (2015)													
CA-33	Long XX (2015)													
CA-34	Hu Y et al. (2016)													
CA-35	Cai HB (2016)													
CA-36	Zhou J et al. (2017)													
CA-37	Yao HY et al. (2012)													
CA-38	Gao RF et al. (2012)													
CA-39	Geng JQ (2017)													
CA-30	Luan L et al. (2014)													
CA-09	Zhao JL et al. (2010)													
CA-11	Fu YZ et al. (2005)													

Study ID	Study	Cataract type		Blindness				Cataract definition						
		Any cataract	ARC	PVA< 0.10	PVA< 0.05	BCVA< 0.10	BCVA< 0.05	Lens opacities	PVA< 0.70	BCVA≤ 0.70	BCVA< 0.63	BCVA< 0.60	Including operated cases	LOCS grading
CA-13	Xu P (2003)													
CA-31	Wu SF et al. (2015)													
ARC-9	Peng YS et al. (2007)													
ARC-6	Quan YL et al. (2006)													
ARC-1A	Feng J et al. (2008)													
ARC-1B	Bai JS et al. (2012)													
ARC-2	Xiang W et al. (2015)													
ARC-3	Zheng H et al. (2001)													
ARC-4	Cui W et al. (2012)													
ARC-5	Zeng H et al. (2011)													
ARC-7	Sheng Y et al. (2016)													
ARC-8	Liu WJ (2009)													
ARC-10	Chang L et al. (2009)													
ARC-11	Yue Y (2001)													

Note: The full reference list can be found in Appendix table 23.

Appendix table 21. The year of publication and investigation and corresponding time-lag in the included studies on cataract or cataract blindness prevalence in China (n=55)

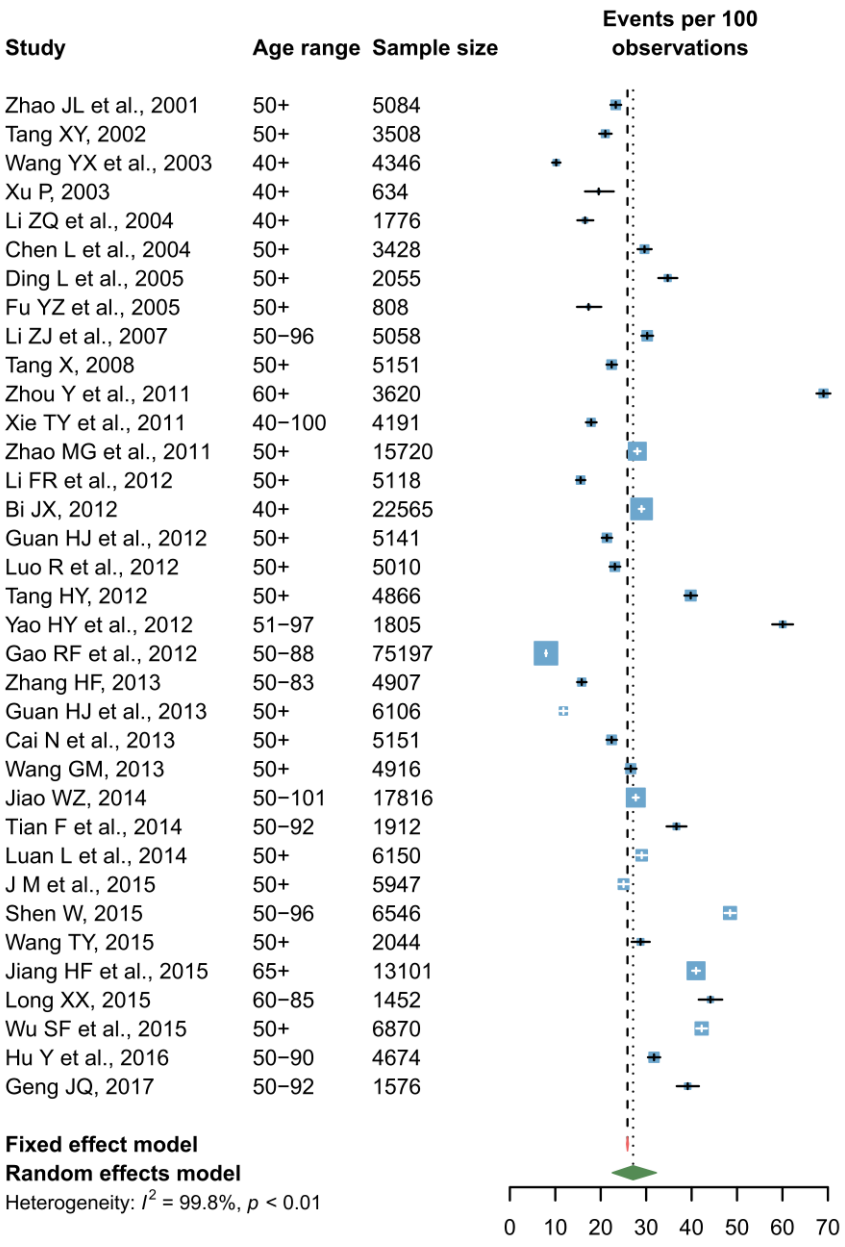
Study ID	Study	Year Published	Median investigation date	Time-lag
CA-01	Li SZ et al. (1999)	1999	1997	2
CA-02	Zhao JL et al. (2001)	2001	1996	5
CA-03	Tang X (2008)	2008	2007	1
CA-04	Tang XY (2002)	2002	-	-
CA-05	Wang YX et al. (2003)	2003	2002	1
CA-06	Li ZQ et al. (2004)	2004	2003	1
CA-07	Chen L et al. (2004)	2004	2002	2
CA-08	Ding L et al. (2005)	2005	2002	3
CA-09	Li L et al. (2006)	2006	2003	3
CA-10	Li ZJ et al. (2007)	2007	2007	0
CA-11	Huang XB et al. (2009)	2009	2008	1
CA-12	Zhou Y et al. (2011)	2011	2007	4
CA-13	Tang B et al. (2011)	2011	2007	4
CA-14	Xie TY et al. (2011)	2011	2009	2
CA-15	Zhao MG et al. (2011)	2011	2007	4
CA-16	Zhang HF (2013)	2013	2012	1
CA-17	Li FR et al. (2012)	2012	2006	6
CA-18	Bi JX (2012)	2012	2010	2
CA-19	Guan HJ et al. (2012)	2012	2006	6
CA-20	Luo R et al. (2012)	2012	2006	6
CA-21A	Guan HJ et al. (2013)	2013	2010	3
CA-21B	J M et al. (2015)	2015	2010	5
CA-22	Cai N et al. (2013)	2013	2012	1
CA-23A	Jiao WZ (2014)	2014	2008	6
CA-23B	Wang GM (2013)	2013	2008	5
CA-23C	Tang HY (2012)	2012	2008	4
CA-24	Tian F et al. (2014)	2014	2011	3
CA-25A	Shen W (2015)	2015	2010	5
CA-25B	Shen W et al. (2013)	2013	2010	3
CA-26	Wang TY (2015)	2015	2013	2
CA-27	Jiang HF et al. (2015)	2015	2014	1

Study ID	Study	Year Published	Median investigation date	Time-lag
CA-28	Long XX (2015)	2015	2011	4
CA-29	Hu Y et al. (2016)	2016	2015	1
CA-30	Cai HB (2016)	2016	2014	2
CA-31	Zhou J et al. (2017)	2017	2008	9
CA-32	Yao HY et al. (2012)	2012	2011	1
CA-33	Gao RF et al. (2012)	2012	2007	5
CA-34	Geng JQ (2017)	2017	-	-
CA-35	Luan L et al. (2014)	2014	2010	4
CA-36	Zhao JL et al. (2010)	2010	2006	4
CA-37	Fu YZ et al. (2005)	2005	2004	1
CA-38	Xu P (2003)	2003	2002	1
CA-39	Wu SF et al. (2015)	2015	2014	1
ARC-1A	Peng YS et al. (2007)	2007	2003	4
ARC-1B	Quan YL et al. (2006)	2006	2003	3
ARC-2	Feng J et al. (2008)	2008	-	-
ARC-3	Bai JS et al. (2012)	2012	2008	4
ARC-4	Xiang W et al. (2015)	2015	2014	1
ARC-5	Zheng H et al. (2001)	2001	1997	4
ARC-6	Cui W et al. (2012)	2012	2010	2
ARC-7	Zeng H et al. (2011)	2011	2009	2
ARC-8	Sheng Y et al. (2016)	2016	2014	2
ARC-9	Liu WJ (2009)	2009	2008	1
ARC-10	Chang L et al. (2009)	2009	2005	4
ARC-11	Yue Y (2001)	2001	-	-

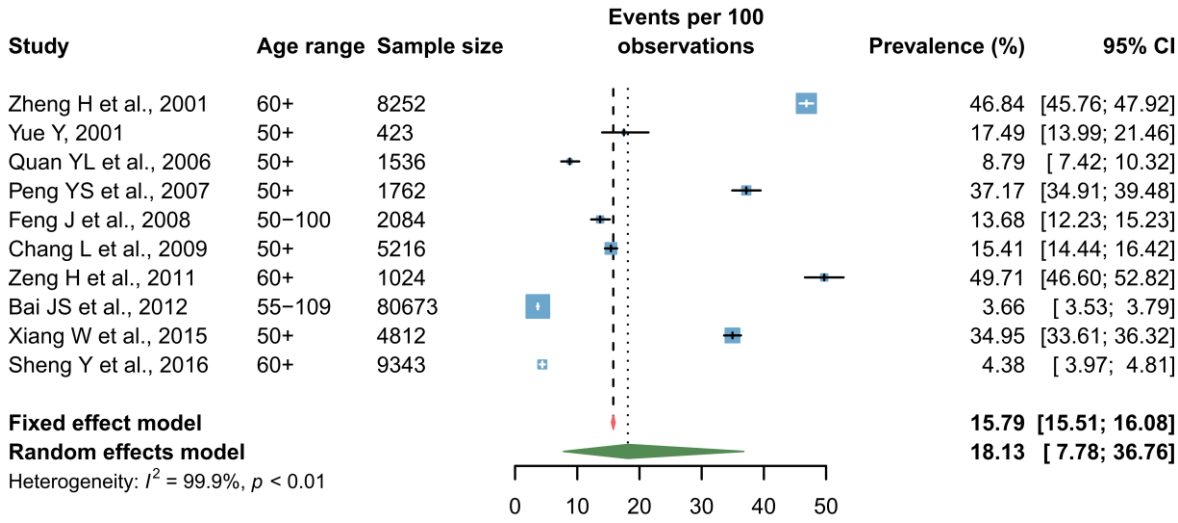
Note: "-" represents unavailable data; Based on the information from 51 studies, the average time-lag between year of publication and year of investigation was 2.98.

Appendix table 22. Meta-analysis of the prevalence of cataract and cataract blindness for assessing heterogeneity between studies

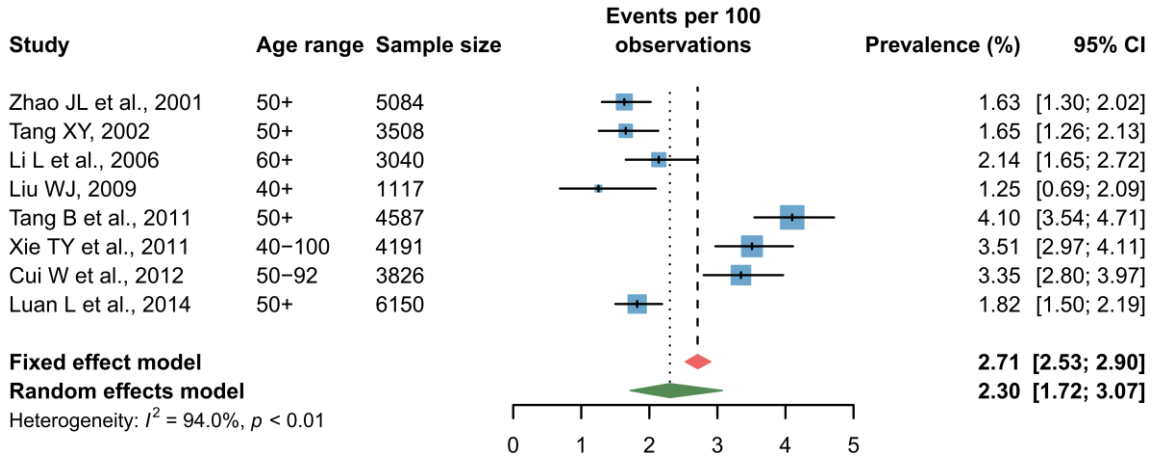
Heterogeneity across included studies was assessed using the $\chi 2$ test on Cochran's Q statistic, and quantified using the I^2 statistics, with a two-sided p value of less than 0.05 being indicative of heterogeneity between studies in Q statistic and I^2 represents the proportion of total variation that is due to heterogeneity rather than chance (with values of <25%, 25–75%, and >75% indicating low, moderate and high heterogeneity, respectively) (Higgins and Thompson, 2002, Higgins et al., 2003). As shown in **Appendix figures 9-13**, significant high heterogeneity was detected between studies that reported prevalence rates of any cataract (I^2=99.8% [95% CI: 99.8-99.9], p<0.0001), ARC (I^2=99.9% [95% CI: 99.9-99.9], p<0.0001), cataract blindness by BCVA<0.05 (I^2=94.0% [95% CI: 90.3-96.2], p<0.0001), cataract blindness by BCVA<0.10 (I^2=97.4% [95% CI: 96.4-98.2], p<0.0001) and cataract blindness by PVA<0.10 (I^2=97.6% [95% CI: 96.8-98.2], p<0.0001).



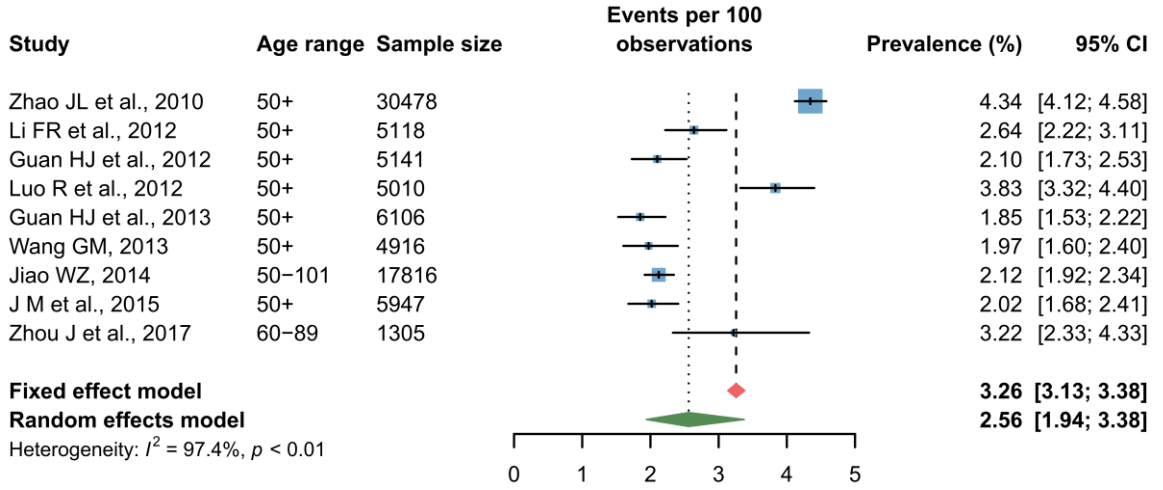
Appendix figure 9. Meta-analysis of the prevalence of any cataract (n=35)



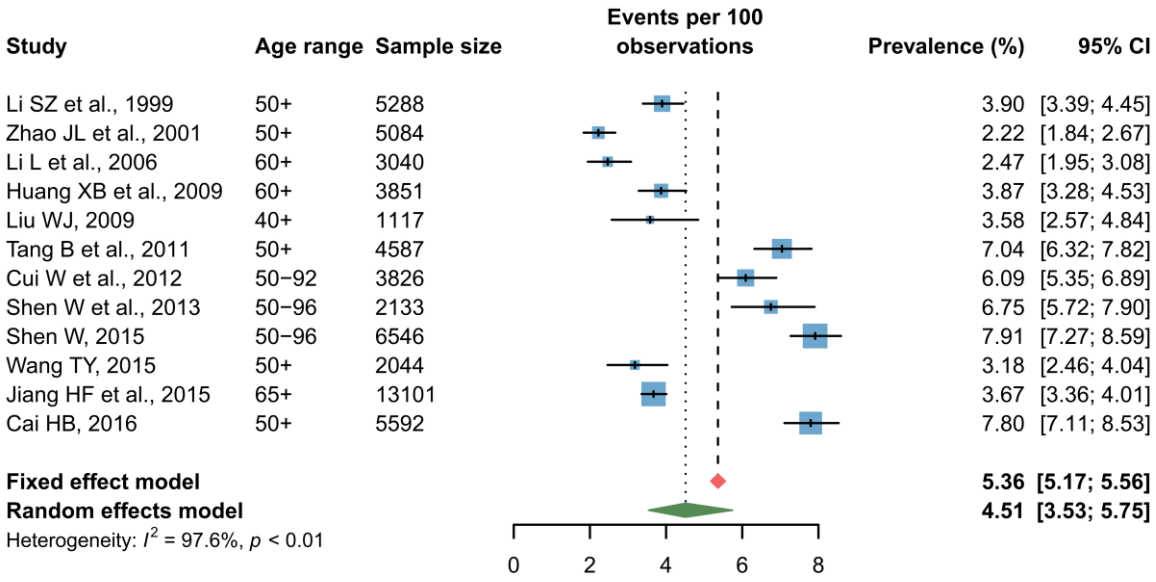
Appendix figure 10. Meta-analysis of the prevalence of ARC (n=10)



Appendix figure 11. Meta-analysis of the prevalence of cataract blindness by BCVA<0.05 (n=8)



Appendix figure 12. Meta-analysis of the prevalence of cataract blindness by BCVA<0.10 (n=9)



Appendix figure 13. Meta-analysis of the prevalence of cataract blindness by PVA<0.10 (n=12)

Appendix table 23. Full list of the included studies on cataract and cataract blindness prevalence in China (n=55)

Study ID	Reference
CA-01	Li S, Xu J, He M, Wu K, Munoz SR, Ellwein LB. A survey of blindness and cataract surgery in Doumen County, China. OPHTHALMOLOGY 1999;106(8):1602-8.
CA-02	Jia-liang Zhao, Rui-fang Sui, Li-jun Jia, et al. 赵家良, 睢瑞芳, 贾丽君, et al. Prevalence of cataract and surgical coverage among adults aged 50 or above in Shunyi district of Beijing, China (北京市顺义区白内障患病和手术状况的调查)[J]. Chin J Ophthalmol (中华眼科杂志). 2001(01):6-11.
CA-03	Xiang Tang. 唐香. Prevalence of cataract and surgical coverage among adults aged 50 or above in Luxi county of Yunnan province (云南省泸西县 50 岁及以上人群白内障患病情况及手术状况调查)[D]. Kunming Medical University (昆明医科大学), 2008.
CA-04	Xiao-yun Tang. 唐晓云. Investigation of the cataract epidemiology and surgery in Jiagedaqi District* (加格达奇区患白内障情况和手术状况的调查)[J]. Heilongjiang Medical Journal (黑龙江医学). 2002(02):148.
CA-05	Yun-xun Wang, Yan Zhao, Yong-mei Sun, et al. 王云旭, 赵艳, 孙永梅, et al. Establishment and implementation of cataract blindness prevention and treatment in Mongolian* (蒙古族白内障防盲治盲三级网站建立与实施)[J]. Ophthalmol CHN (眼科). 2003(03):160-1.
CA-06	Zhi-qing Li, Xiu-juan Zhang, Hui-min Sun, et al. 李志清, 张秀娟, 孙慧敏, et al. Investigation of cataract prevalence in people aged 40 years and above in Sangzi village, Ji County, Tianjin* (天津蓟县桑梓村 40 岁及以上人群白内障患病率调查)[J]. Chin J Pract Ophthalmol (中国实用眼科杂志). 2004(09):749-50.
CA-07	Lu Chen, Li-na Huang, Xiao-xia Li, et al. 陈璐, 黄丽娜, 李晓霞, 赖小兰, 曾平. Prevalence of cataract and surgical coverage among adults aged 50 or above in Baoan district of Shenzhen, China (深圳宝安区 50 岁及以上人群白内障患病情况及手术状况调查)[J]. International Journal of Ophthalmology (国际眼科杂志). 2004(05):919-21.

Study ID	Reference
CA-08	Lin Ding, Xiu-rong Zhao, Xin Yang, et al. 丁琳, 赵秀蓉, 杨昕, 史韶华. Epidemiological investigation of cataract in Urumqi, Xinjiang* (新疆乌鲁木齐市白内障的流行病学调查)[J]. Xinjiang Medical Journal (新疆医学). 2005(01):40-2.
CA-09	Lin Li, Huai-jin Guan, Ji-bo Zhou, et al. 李琳, 管怀进, 周激波, et al. An epidemiological survey of cataract among adults aged 60 years and above in Xinchengqiao Blocks, Nantong (南通市新城桥街道 60 岁及以上人群白内障流行病学调查)[J]. Chin J Pract Ophthalmol (中国实用眼科杂志). 2006(07):752-7.
CA-10	Zhi-jian Li, Hao Cui, Ping Liu, et al. 李志坚, 崔浩, 刘平, 张丽琼, 李彬. Survey of cataract among the people aged 50 years and older in a rural area of Harbin (哈尔滨南部 50 岁及以上农村人口白内障的调查)[J]. International Journal of Ophthalmology (国际眼科杂志). 2007(05):1460-3.
CA-11	Xiao-bo Huang, Hai-dong Zou, Ning Wang, et al. 黄晓波, 邹海东, 王宁, et al. Epidemiological survey of cataract among the elder in Beixinjing Blocks, Shanghai (上海北新泾老人白内障流行病学调查)[J]. Int J Ophthalmol (国际眼科杂志). 2009(07):1321-4.
CA-12	Yan Zhou, Xue-ping Jia. 周燕, 贾雪平. An investigation of cataract prevalence in elderly in one community* (某社区老年人口白内障患病率调查)[J]. Guide of China Medicine (中国医药指南). 2011(16):136-7.
CA-13	Bin Tang, Zhi Li, Yi Luo, et al. 唐斌, 李治, 罗羿, et al. The survey comparisons on the epidemiology of cataracts among the old aged 50 and above in the urban and rural areas in Jiangbei district of Chongqing (重庆市江北区城乡 50 岁及以上人群白内障的流行病学调查)[J]. Chongqing Medicine (重庆医学). 2011(06):561-4.
CA-14	Ting-yu Xie, Yan Wang, Liang Gao, et al. 谢婷玉, 王燕, 高亮, et al. Prevalence of cataract and surgical coverage among Urger adults aged 40 or above in Kuche rural area of Xinjiang, China (新疆库车县维吾尔族农民白内障患病状况调查)[J]. Chin J Epidemiol (中华流行病学杂志). 2011;32(1):95-6.

Study ID	Reference
CA-15	Ming-gui Zhao, Shi-hong Zhang, Le-xin Wang. 赵明贵, 张士红, 王乐新. An investigation report of cataract epidemiology in adults aged 50 years and above in rural Lanshan, Rizhao* (日照市岚山区农村 50 岁以上人群白内障流行病学调查报告)[J]. Chinese Community Doctors (中国社区医师（医学专业）). 2011(14):311-2.
CA-16	Hai-fang Zhang. 张海芳. An investigation on the prevalence of cataract and its surgical situation in Binhu district, Wuxi city * (无锡市滨湖区白内障患病和手术状况的调查) [J]. China Health Care and Nutrition (中国保健营养（下旬刊)). 2013;23(12):7654-5.
CA-17	Feng-rong Li, Jia-liang Zhao, Hong Lu, et al. 李凤荣, 赵家良, 陆宏, et al. Prevalence and surgery status of cataract among adults aged 50 years or above in the Shunyi district of Beijing: the China Nine-Province Survey (我国九省眼病调查中北京市顺义区 50 岁及以上人群白内障患病率和手术状况的调查)[J]. Chin J Ophthalmol (中华眼科杂志). 2012;48(3):211-8.
CA-18	Jing-xiang Bi. 毕经香. An epidemiological survey on cataract in different professions* (不同职业人群白内障患病情况的流行病学调查)[J]. Hebei Medicine (河北医学). 2012(09):1328-30.
CA-19	Huai-jin Guan, Hong Lu, Zhui Dai, et al. 管怀进, 陆宏, 戴追, et al. Prevalence and surgery status of cataract among adults aged 50 years or above in Qidong city of Jiangsu Province: the China Nine-Province Survey (我国九省眼病调查中江苏省启东市 50 岁及以上人群白内障患病率和手术状况的调查)[J]. Chin J Ophthalmol (中华眼科杂志). 2012;48(3):219-25.
CA-20	Rong Luo, Jia-liang Zhao, Jing-lin Yi, et al. 罗荣, 赵家良, 易敬林, et al. Province of blindness and low vision among adults aged 50 years or above in Ji'an county of Jiangxi province: the China Nine-Province Survey (我国九省眼病调查中江西省吉安县 50 岁及以上人群白内障患病率和手术状况的调查)[J]. Chin J Ophthalmol (中华眼科杂志). 2012;48(6):530-6.

Study ID	Reference
CA-21A	Huai-jin Guan, Yong Yao, Cong-kai Liang, et al. 管怀进, 姚勇, 梁从凯, et al. Prevalence and surgical status of cataract among adults aged 50 years or above in rural Jiangsu Province (江苏省农村 50 岁及以上人群白内障患病率和手术状况调查)[J]. Natl Med J China (中华医学杂志). 2013;93(5):330-5.
CA-21B	Min Ji, Mei Yang, Rong-rong Zhu, et al. 季敏, 杨梅, 朱蓉嵘, et al. An investigation on reasons of bad prognosis after cataract surgery in people aged 50 years and above in rural Funing, Jiangsu* (江苏省阜宁县农村 50 岁及以上人群白内障术后视力恢复不良原因调查)[J].Med J of Communications (交通医学). 2015;29(5):457-9.
CA-22	Ning Cai, Miao-miao Chen, Yuan-sheng Yuan, et al. 蔡宁, 陈苗苗, 袁援生, 蔡山. Prevalence rate and surgery status of cataract in Luxi county of Yunnan Province (云南省泸西县白内障患病率及手术覆盖率调查)[J]. Journal of Kunming Medical University (昆明医科大学学报) 2013;34(5):74-8.
CA-23A	Wan-zhen Jiao. 焦万珍. Prevalence of visual impairment and blindness, prevalence and surgery status of cataract in rural older adults in Shandong province (山东省农村 50 岁及以上人群盲与视力损伤、白内障患病率及白内障手术状况的调查研究)[D]. Shandong University (山东大学), 2014.
CA-23B	Gui-min Wang. 王桂敏. Prevalence and surgery status of cataract among adults aged 50 years and above in Tengzhou city of Shandong province (山东省滕州市 50 岁及以上居民白内障患病率及手术服务利用研究)[D].Shandong University (山东大学), 2013.
CA-23C	Hong-ying Tang. 唐红迎. A prevalence study on blindness and vision impairment with moderate and severe degree due to cataract among rural residents aged 50 years and above in Juancheng county (鄄城县 50 岁及以上农村居民白内障致盲与中重度视力损伤现况研究)[D]. Shandong University (山东大学), 2012.

Study ID	Reference
CA-24	Fang Tian, Bai-chao Chen, Yuan He, et al. 田芳, 任百超, 何媛, 贾俊, 刘慧峰, 裴金枝. An epidemiological survey of cataract among adults aged 50 years and above in rural, Shaanxi Province (陕西省农村 50 岁及以上人群白内障流行病学调查)[J]. Int Eye Sci (国际眼科杂志). 2014;14(4):629-32.
CA-25A	Wei Shen. 沈蔚. Prevalence and surgery status of cataract in adult rural Bai, Yi and Han nationality in Yunnan province (云南省白族、彝族和汉族农村人群白内障流行病学调查)[D]. Kunming Medical University (昆明医科大学), 2015.
CA-25B	Shen W, Yang Y, Yu M, et al. Prevalence and outcomes of cataract surgery in adult rural Chinese populations of the Bai nationality in Dali: the Yunnan minority eye study. PLOS ONE 2013;8(4):e60236.
CA-26	Tian-yu Wang. 王天宇. An epidemiological survey of cataract among adults aged 50 or above in Jing'an district in Shanghai (上海市静安区江宁街道 50 岁及以上人群白内障流行病学调查)[D].Shanghai Jiao Tong University School of Medicine (上海交通大学), 2015.
CA-27	Hui-fang Jiang, Yun Peng, Wen-quan Zhang, et al. 蒋惠芳, 彭云, 张文权, 孙伟, 俞正娟. Investigation of the prevalence of cataract and operation status in the elderly of Sanlin community (三林社区老年人白内障患病和手术状况调查)[J]. Chinese community doctors (中国社区医师). 2015(23):78-9.
CA-28	Xiao-xiang Long. 龙小香. An investigation of prevalence situation among cataract patients in Taizhou* (台州市白内障患者的患病情况调查)[J]. Journal of Traditional Chinese Medicine Management (中医药管理杂志). 2015(04):18-20.
CA-29	Yi Hu, Jian-ping Chen, Shu-xiang He, et al. 胡煜, 陈建萍, 贺书香, 林燕梅. Survey on status of cataract in Xiangdong district of Pingxiang Jiangxi in 2015 (2015 年江西萍乡湘东区各乡镇白内障情况的调查)[J]. China Modern Medicine (中国当代医药). 2016;23(7):164-6, 169.
CA-30	Hong-bing Cai. 蔡红兵. An epidemiological survey of cataract among people aged 50 and over in Luxi County of Yunnan Province (云南省泸西县 50 岁及以上人群白内障流行病学调查)[D]. Kunming Medical University (昆明医科大学), 2016.

Study ID	Reference
CA-31	Jing Zhou, Yuan Yuan, Xu Zhang, et al. 周婧, 袁媛, 张徐, 杨梅, 管怀进. Prevalence and surgery status of cataract among adults aged 60 years or above in two villages of Nantong (2008 年江苏省南通市两个自然村 60 岁及以上人群白内障患病率和手术状况调查)[J]. Chin J Ophthalmol (中华眼科杂志). 2017;53(7):514-21.
CA-32	Hong-yan Yao, Hong-jian Zhou, Shan-jun Wu, et al. 姚红艳, 周宏健, 吴善君, 李黎. An epidemiological investigation of eye diseases in people aged 50 years and above in Beilun district, Ningbo city * (宁波市北仑区 50 岁以上人群眼病流行病学调查)[J]. Modern Practical Medicine (现代实用医学). 2012(5):544-5.
CA-33	Rui-fang Gao, Peng Li, Ai-min Sang, et al. 高瑞芳, 李鹏, 桑爱民, 谌绍林. Analysis on the prevalence of cataract of Hui and Han people in Xiji county (西吉县回汉族 50 岁以上人群白内障患病率分析)[J]. Modern Prevention Medicine (现代预防医学). 2012(02):342-4.
CA-34	Jian-qiong Geng. 耿剑琼. Analysis of prevalence and related factors of cataract among residents aged 50 years and above in Wushan county (武山县 50 岁及以上人群白内障患病率及相关因素分析)[D].Lanzhou University (兰州大学). 2017.
CA-35	Lan Luan, Yong Yao, Dong-hong Fu, et al. 栾兰, 姚勇, 傅东红, et al. Survey of the cataract prevalence and surgical coverage rate among 50 or above in Wuxi city (无锡市 50 岁及以上人群白内障患病率和手术情况调查)[J]. Chin J Exp Ophthalmol (中华实验眼科杂志). 2014;32(6):551-5.
CA-36	Zhao J, Ellwein LB, Cui H, et al. Prevalence and outcomes of cataract surgery in rural China the China nine-province survey. OPHTHALMOLOGY 2010;117(11):2120-8.
CA-37	Yi-zhou Fu, Huan-ran Chen, Zhong-ming Wang, et al. 伏奕舟, 陈焕然, 王仲明, 洪仲思. A survey of 5248 cases for eye diseases screening in Zhuhai (珠海市 5248 例体检者眼病患病率调查分析)[J]. Journal of Chinese Modern Ophthalmology (中华现代眼科学杂志). 2005(4).

Study ID	Reference
CA-38	Ping Xu.徐萍. The situation and related factors of cataract and glaucoma in 729 university staffs * (高校教职工 729 名白内障、青光眼患病情况及相关因素分析)[J]. Chin J School Health (中国学校卫生) 2003(4).
CA-39	Su-feng Wu, Jing-xin Guo, You Lai. 吴素锋, 郭景新, 赖友. An investigation and analysis of the prevalence of cataract and surgeries in people aged 50 years and above in Yangdong area* (阳东地区 50 岁白内障患病及手术状况的调查与分析)[J]. China Medical Engineering (中国医学工程). 2015 (11):52, 55.
ARC-1A	Yang-sheng Peng, Ai-yi Zhou, Li Chen, et al. 彭秧生, 周爱意, 陈莉, 何媛, 任百超. Prevalence of age related cataract and blindness in rural areas of Shaanxi province (陕西省农村 50 岁以上人群白内障和盲的患病率调查)[J]. International Journal of Ophthalmology (国际眼科杂志). 2007;7(1):220-3.
ARC-1B	Yan-long Quan, Jian-gang Yang, Bai-chao Ren. 权彦龙, 杨建刚, 任百超. Epidemic survey for cataract in Yang county, Shaanxi Province (陕西省洋县白内障的流行病学调查)[D]. International Journal of Ophthalmology (国际眼科杂志). 2006;6(6):1464-7.
ARC-2	Jie Feng, Yu-jing Wan, Guo-hui Yang, et al. 冯洁, 万玉景, 杨国慧, et al. Contrast observation of cataract and surgical coverage in rural and urban defined population in Jining (社区与农村白内障患病及手术状况的对比观察)[J]. China Clin Prac Med (中国临床实用医学). 2008;2(5):36-7.
ARC-3	Jin-song Bai, Pei-lin An, Yu-ling Liu, et al. 柏劲松, 安培林, 刘玉玲, 付瑜. An investigation of cataract prevalence among adults aged 55 years and above in one rural area of Beijing* (北京市某区农村≥55 岁人群白内障患病情况调查)[J]. Guide of China Medicine (中国医药指南). 2012(17):113-4.

Study ID	Reference
ARC-4	Wei Xiang, Feng Gao, Xun-lun Sheng, et al. 向伟, 高峰, 盛迅伦, et al. Prevalence investigation of age related cataract among population aged 50 years or elder in Tongxin of Ningxia (宁夏同心县 50 岁及以上人群年龄相关性白内障患病率调查)[J]. Ningxia Med J (宁夏医学杂志). 2015;37(5):405-7.
ARC-5	Hong Zheng, Pu-lin Yu, Yi-shu Hong, et al. 郑宏, 于普林, 洪依舒, 段春波, 杨泽, 高芳坤. A survey of the current status and distribution of cataract in the elderly (我国城乡老年人白内障的患病情况调查)[J]. Chin J Epidemiol (中华流行病学杂志). 2001(06):52-4.
ARC-6	Wei Cui, Zhi-ying Liu, Gui-bin Yu. 崔巍, 刘志英, 于桂斌. Survey of cataract rate and surgical coverage in agricultural and pastoral area of Keshenketeng in Inner Mongolia (内蒙古赤峰市克什克腾旗农牧区白内障患病率及手术覆盖率调查)[J]. Chin J Exp Ophthalmol (中华实验眼科杂志). 2012;30(5):462-6.
ARC-7	Hua Zeng, Yu-juan Zhan. 曾华, 詹玉娟. An investigation on age-related cataract in Haikougang, Haikou city * (海口市海口港区年龄相关性白内障发病状况调查)[J]. Hainan Medical Journal (海南医学). 2011(16):131-3.
ARC-8	Sheng Y, He F, Lin JF, Shen W, Qiu YW. Tea and Risk of Age-Related Cataracts: A Cross-Sectional Study in Zhejiang Province, China. J EPIDEMIOL 2016;26(11):587-92.
ARC-9	Wen-jie Liu. 刘文洁. Epidemiological survey of cataract among adults aged 40 or above in Gongshan County of Yunnan province (云南省怒江州贡山县 40 岁及以上人群白内障的流行病学调查)[D]. Tianjin Medical University (天津医科大学), 2009.
ARC-10	Li Chang, Li-juan Zhang, Jian Zhao, et al. 常莉, 张丽娟, 赵健, 赵媚鲜, 饶华祥. A survey of age-related cataract epidemiology in Taiyuan city (太原市年龄相关性白内障的流行病学调查)[J]. Proceeding of Clinical Medicine (临床医药实践). 2009(16):420-2.

Study ID	Reference
ARC-11	Yong Yue. 岳镛. Investigation analysis of cataract among retired personnel of southwest university for nationalities (西南民族学院退离休职工白内障的调查)[J]. Journal of Southwest University for Nationalities. Natural Science Edition (西南民族学院学报(自然科学版)). 2001(03):378-80.

Note: The Chinese publication list employed the journals' official English names or abbreviations, English titles were obtained from journals or literature databases (CNKI, Wanfang and CBM). Where official English translation of journal names is not available, a pinyin title is adopted; where the English translation of titles is not available, I translated the titles, labelled with "" and marked as green.*

Appendix table 24. Detailed characteristics of the included studies on cataract and cataract blindness prevalence in China (n=55)

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
CA-01	Li SZ et al. (1999)	Guangdong	South Central China	Both	Rural	50+	Random cluster sampling	1997	Unclear	5288	-	-	-	206
CA-02	Zhao JL et al. (2001)	Beijing	North China	Both	Mixed	50+	Random cluster sampling	1996	Unclear	5084	1185	83	-	113
CA-03	Tang X (2008)	Yunnan	Southwest China	Both	Mixed	50+	Random cluster sampling	2007	Unclear	5151	1154	-	-	-
CA-04	Tang XY (2002)	Heilongjiang	Northeast China	Both	Urban	50+	Random cluster sampling	1999*	Unclear	3508	737	58	-	-

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
CA-05	Wang YX et al. (2003)	Inner Mongolia	North China	Both	Rural	40+	Stratified random cluster sampling	2002	Unclear	4346	443	-	-	-
CA-06	Li ZQ et al. (2004)	Tianjin	North China	Both	Rural	40+	Cluster sampling	2003	Unclear	1776	294	-	-	-
CA-07	Chen L et al. (2004)	Guangdong	South Central China	Both	Urban	50+	Random cluster sampling	2002	Unclear	3428	1016	-	-	-
CA-08	Ding L et al. (2005)	Xinjiang	Northwest China	Mixed	Urban	50+	Random cluster sampling	2002	Unclear	2055	714	-	-	-

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
CA-09	Li L et al. (2006)	Jiangsu	East China	Both	Urban	60+	Random cluster sampling	2003	Unclear	3040	-	65	-	75
CA-10	Li ZJ et al. (2007)	Heilongjiang	Northeast China	Both	Rural	50-96	Random cluster sampling	2007	Unclear	5058	1529	-	-	-
CA-11	Huang XB et al. (2009)	Shanghai	East China	Both	Urban	60+	Random cluster sampling	2008	Unclear	3851	-	-	-	149
CA-12	Zhou Y et al. (2011)	Henan	South Central China	Both	Urban	60+	Cluster sampling	2007	Unclear	3620	2499	-	-	-
CA-13	Tang B et al. (2011)	Chongqing	Southwest China	Both	Both	50+	Cluster sampling	2007	Unclear	4587	-	188	-	323

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
CA-14	Xie TY et al. (2011)	Xinjiang	Northwest China	Both	Rural	40-100	Random cluster sampling	2009	Unclear	4191	750	147	-	-
CA-15	Zhao MG et al. (2011)	Shandong	East China	Both	Rural	50+	Cluster sampling	2007	Unclear	15720	4410	-	-	-
CA-16	Zhang HF (2013)	Jiangsu	East China	Both	Urban	50-83	Random cluster sampling	2012	Unclear	4907	776	-	-	-
CA-17	Li FR et al. (2012)	Beijing	North China	Both	Mixed	50+	Random cluster sampling	2006	Unclear	5118	797	-	135	-
CA-18	Bi JX (2012)	Hebei	North China	Mixed	Mixed	40+	Cluster sampling	2010	Unclear	22565	6542	-	-	-

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
CA-19	Guan HJ et al. (2012)	Jiangsu	East China	Both	Mixed	50+	Random cluster sampling	2006	Unclear	5141	1098	-	108	-
CA-20	Luo R et al. (2012)	Jiangxi	East China	Both	Mixed	50+	Random cluster sampling	2006	Unclear	5010	1158	-	192	-
CA-21A	Guan HJ et al. (2013)	Jiangsu	East China	Both	Rural	50+	Random cluster sampling	2010	Unclear	6106	720	-	113	-
CA-21B	J M et al. (2015)	Jiangsu	East China	Both	Rural	50+	Random cluster sampling	2010	Unclear	5947	1488	-	120	-

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
CA-22	Cai N et al. (2013)	Yunnan	Southwest China	Both	Mixed	50+	Random cluster sampling	2012	Unclear	5151	1154	-	-	-
CA-23A	Jiao WZ (2014)	Shandong	East China	Both	Rural	50-101	Random cluster sampling	2008	Unclear	17816	4938	-	378	-
CA-23B	Wang GM (2013)	Shandong	East China	Both	Rural	50+	Random cluster sampling	2008	Unclear	4916	1308	-	97	-
CA-23C	Tang HY (2012)	Shandong	East China	Both	Rural	50+	Random cluster sampling	2008	Unclear	4866	1937	-	-	-
CA-24	Tian F et al. (2014)	Shaanxi	Northwest China	Both	Rural	50-92	Stratified random	2011	Unclear	1912	701	-	-	-

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
							cluster sampling							
CA-25A	Shen W (2015)	Yunnan	Southwest China	Both	Rural	50-96	Random cluster sampling	2010	Unclear	6546	3172	-	-	518
CA-25B	Shen W et al. (2013)	Yunnan	Southwest China	Both	Rural	50-96	Random cluster sampling	2010	Unclear	2133	-	-	-	144
CA-26	Wang TY (2015)	Shanghai	East China	Both	Urban	50+	Random sampling	2013	Unclear	2044	588	-	-	65
CA-27	Jiang HF et al. (2015)	Shanghai	East China	Both	Urban	65+	Cluster sampling	2014	Unclear	13101	5369	-	-	481

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
CA-28	Long XX (2015)	Zhejiang	East China	Both	Both	60-85	Stratified cluster sampling	2011	Unclear	1452	641	-	-	-
CA-29	Hu Y et al. (2016)	Jiangxi	East China	Mixed	Mixed	50-90	Cluster sampling	2015	Unclear	4674	1483	-	-	-
CA-30	Cai HB (2016)	Yunnan	Southwest China	Both	Mixed	50+	Random cluster sampling	2014	Unclear	5592	-	-	-	436
CA-31	Zhou J et al. (2017)	Jiangsu	East China	Both	Rural	60-89	Cluster sampling	2008	Unclear	1305	-	-	42	-
CA-32	Yao HY et al. (2012)	Zhejiang	East China	Both	Mixed	51-97	Random cluster sampling	2011	Unclear	1805	1084	-	-	-
CA-33	Gao RF et al. (2012)	Ningxia	Northwest China	Both	Mixed	50-88	Cluster sampling	2007	Unclear	75197	5983	-	-	-

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
CA-34	Geng JQ (2017)	Gansu	Northwest China	Both	Both	50-92	Stratified random cluster sampling	2014*	Unclear	1576	617	-	-	-
CA-35	Luan L et al. (2014)	Jiangsu	East China	Both	Urban	50+	Random cluster sampling	2010	Unclear	6150	1785	112	-	-
CA-36	Zhao JL et al. (2010)	Guangdong/Heilongjiang/Hebei/Xinjiang/Chongqing/Yunnan	North China, Northeast China, South Central China,	Both	Mixed	50+	Random cluster sampling	2006	Unclear	30478	-	-	1324	-

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
CA-37	Fu YZ et al. (2005)	Guangdong	Southwest China and Northwest China South Central China	Both	Urban	50+	General health screening	2004	Unclear	808	140	-	-	-
CA-38	Xu P (2003)	Beijing	North China	Mixed	Urban	40+	General health screening	2002	Unclear	634	124	-	-	-
CA-39	Wu SF et al. (2015)	Guangdong	South Central China	Both	Urban	50+	General health screening	2014	Unclear	6870	2900	-	-	-

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
ARC-1A	Peng YS et al. (2007)	Shaanxi	Northwest China	Both	Rural	50+	Stratified random cluster sampling	2003	Yes	1762	655	-	-	-
ARC-1B	Quan YL et al. (2006)	Shaanxi	Northwest China	Both	Rural	50+	Stratified random cluster sampling	2003	Yes	1536	135	-	-	-
ARC-2	Feng J et al. (2008)	Shandong	East China	Both	Both	50-100	Cluster sampling	2005*	Yes	2084	285	-	-	-
ARC-3	Bai JS et al. (2012)	Beijing	North China	Both	Rural	55-109	Cluster sampling	2008	Yes	80673	2953	-	-	-

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
ARC-4	Xiang W et al. (2015)	Ningxia	Northwest China	Both	Rural	50+	Random cluster sampling	2014	Yes	4812	1682	-	-	-
ARC-5	Zheng H et al. (2001)	Beijing, Shanghai,Guangdong, Sichuan, Shaanxi, Liaoning	North China, Northeast China, East China, South Central China, Southwest China and	Both	Mixed	60+	Stratified cluster sampling	1997	Yes	8252	3865	-	-	-

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
			Northwest China											
ARC-6	Cui W et al. (2012)	Inner Mongolia	North China	Both	Rural	50-92	Random cluster sampling	2010	Yes	3826	-	128	-	233
ARC-7	Zeng H et al. (2011)	Hainan	South Central China	Both	Urban	60+	Cluster sampling	2009	Yes	1024	509	-	-	-
ARC-8	Sheng Y et al. (2016)	Zhejiang	East China	Both	Mixed	60+	Random cluster sampling	2014	Yes	9343	409	-	-	-
ARC-9	Liu WJ (2009)	Yunnan	Southwest China	Both	Rural	40+	Random cluster sampling	2008	Yes	1117	-	14	-	40

Study ID	Study	Province	Region	Sex	Setting	Age range	Sampling	Study Year	Is ARC?	Sample size	Cataract	Cataract blindness (BCVA<0.05)	Cataract blindness (BCVA<0.1)	Cataract blindness (PVA<0.1)
ARC-10	Chang L et al. (2009)	Shanxi	North China	Both	Urban	50+	Random health screening	2005	Yes	5216	804	-	-	-
ARC-11	Yue Y (2001)	Sichuan	Southwest China	Both	Urban	50+	Health screening	1998*	Yes	423	74	-	-	-

Note: "-" represents unavailable data; "" indicates studies whose survey year was imputed.*

Appendix table 25. Risk of bias scores of the included studies on cataract and cataract blindness prevalence in China (n=55)

Study ID	Study	Quality score					
		Sample population	Sample size	Participation	Outcome assessment	Analytical methods	Total scores
CA-01	Li SZ et al. (1999)	2	2	2	2	2	10
CA-02	Zhao JL et al. (2001)	2	2	2	2	2	10
CA-03	Tang X (2008)	2	2	0	2	2	8
CA-04	Tang XY (2002)	2	0	0	2	2	6
CA-05	Wang YX et al. (2003)	2	1	2	2	2	9
CA-06	Li ZQ et al. (2004)	2	1	2	2	2	9
CA-07	Chen L et al. (2004)	2	1	0	2	2	7
CA-08	Ding L et al. (2005)	2	2	2	2	2	10
CA-09	Li L et al. (2006)	2	2	0	2	2	8
CA-10	Li ZJ et al. (2007)	2	1	2	2	2	9
CA-11	Huang XB et al. (2009)	2	2	2	2	2	10
CA-12	Zhou Y et al. (2011)	2	0	0	2	2	6
CA-13	Tang B et al. (2011)	2	1	0	2	2	7
CA-14	Xie TY et al. (2011)	2	1	2	2	2	9
CA-15	Zhao MG et al. (2011)	2	1	2	2	2	9
CA-16	Zhang HF (2013)	2	1	0	2	2	7
CA-17	Li FR et al. (2012)	2	2	2	2	2	10
CA-18	Bi JX (2012)	2	0	0	2	2	6

Study ID	Study	Quality score					
		Sample population	**Sample size**	**Participation**	**Outcome assessment**	**Analytical methods**	**Total scores**
CA-19	Guan HJ et al. (2012)	2	2	2	2	2	10
CA-20	Luo R et al. (2012)	2	2	2	2	2	10
CA-21A	Guan HJ et al. (2013)	2	2	2	2	2	10
CA-21B	J M et al. (2015)	2	1	0	2	2	7
CA-22	Cai N et al. (2013)	2	1	0	2	2	7
CA-23A	Jiao WZ (2014)	2	2	2	2	2	10
CA-23B	Wang GM (2013)	2	2	2	2	2	10
CA-23C	Tang HY (2012)	2	2	2	2	2	10
CA-24	Tian F et al. (2014)	2	1	2	2	2	9
CA-25A	Shen W (2015)	2	2	1	2	2	9
CA-25B	Shen W et al. (2013)	2	2	1	2	2	9
CA-26	Wang TY (2015)	2	1	1	2	2	8
CA-27	Jiang HF et al. (2015)	2	1	2	2	2	9
CA-28	Long XX (2015)	2	1	2	2	2	9
CA-29	Hu Y et al. (2016)	2	1	0	2	2	7
CA-30	Cai HB (2016)	2	2	2	2	2	10
CA-31	Zhou J et al. (2017)	2	2	2	2	2	10
CA-32	Yao HY et al. (2012)	2	1	0	2	2	7
CA-33	Gao RF et al. (2012)	2	1	0	2	2	7

Study ID	Study	Quality score					
		Sample population	**Sample size**	**Participation**	**Outcome assessment**	**Analytical methods**	**Total scores**
CA-34	Geng JQ (2017)	2	2	0	2	2	8
CA-35	Luan L et al. (2014)	2	2	2	2	2	10
CA-36	Zhao JL et al. (2010)	2	1	2	2	2	9
CA-37	Fu YZ et al. (2005)	2	1	0	2	2	7
CA-38	Xu P (2003)	2	1	0	2	2	7
CA-39	Wu SF et al. (2015)	2	1	0	2	2	7
ARC-1A	Peng YS et al. (2007)	2	1	1	2	2	8
ARC-1B	Quan YL et al. (2006)	2	2	0	2	2	8
ARC-2	Feng J et al. (2008)	2	1	2	2	2	9
ARC-3	Bai JS et al. (2012)	2	1	2	2	2	9
ARC-4	Xiang W et al. (2015)	2	2	2	2	2	10
ARC-5	Zheng H et al. (2001)	2	1	2	2	2	9
ARC-6	Cui W et al. (2012)	2	1	2	2	2	9
ARC-7	Zeng H et al. (2011)	2	1	0	2	2	7
ARC-8	Sheng Y et al. (2016)	1	1	0	2	2	6
ARC-9	Liu WJ (2009)	2	2	2	2	2	10
ARC-10	Chang L et al. (2009)	2	1	0	2	2	7
ARC-11	Yue Y (2001)	2	1	0	2	2	7

Appendix table 26. Estimated and projected number of people with any cataract and ARC in China from 1990 to 2050, by sex and age group (million, 95% CI)

1990						
Age group	**Any cataract**			**ARC**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	1.71 (1.29-2.26)	1.93 (1.46-2.52)	3.64 (2.76-4.78)	0.83 (0.38-1.74)	1.08 (0.51-2.24)	1.91 (0.89-3.98)
50-54 years	2.45 (1.90-3.12)	2.68 (2.10-3.39)	5.12 (4.00-6.51)	1.26 (0.6-2.59)	1.61 (0.77-3.23)	2.88 (1.37-5.82)
55-59 years	3.24 (2.58-4.02)	3.59 (2.89-4.42)	6.83 (5.48-8.44)	1.80 (0.87-3.56)	2.33 (1.15-4.44)	4.14 (2.02-8.01)
60-64 years	3.67 (3.00-4.45)	4.13 (3.41-4.95)	7.80 (6.40-9.40)	2.22 (1.10-4.17)	2.90 (1.48-5.17)	5.12 (2.59-9.34)
65-69 years	3.72 (3.09-4.41)	4.45 (3.75-5.20)	8.17 (6.84-9.61)	2.46 (1.27-4.31)	3.38 (1.83-5.55)	5.84 (3.10-9.86)
70-74 years	3.70 (3.13-4.29)	4.61 (3.96-5.26)	8.31 (7.10-9.56)	2.67 (1.47-4.31)	3.77 (2.19-5.65)	6.45 (3.66-9.95)
75-79 years	2.52 (2.18-2.86)	3.67 (3.23-4.10)	6.20 (5.41-6.96)	1.99 (1.17-2.91)	3.21 (2.04-4.37)	5.20 (3.21-7.29)
80–84 years	1.20 (1.06-1.33)	2.20 (1.97-2.40)	3.40 (3.03-3.73)	1.02 (0.66-1.36)	2.02 (1.41-2.53)	3.04 (2.07-3.89)
85-89 years	0.39 (0.35-0.43)	0.89 (0.81-0.95)	1.28 (1.17-1.37)	0.35 (0.25-0.43)	0.85 (0.65-0.99)	1.20 (0.90-1.42)
Total (45-89 years)	22.60 (18.59-27.17)	28.15 (23.58-33.19)	50.75 (42.17-60.37)	14.61 (7.78-25.39)	21.17 (12.03-34.16)	35.77 (19.81-59.55)
2000						
Age group	**Any cataract**			**ARC**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	2.93 (2.21-3.86)	3.51 (2.66-4.59)	6.44 (4.88-8.45)	1.41 (0.66-2.97)	1.97 (0.93-4.08)	3.39 (1.59-7.05)
50-54 years	3.14 (2.44-4.01)	3.73 (2.92-4.73)	6.87 (5.37-8.74)	1.62 (0.77-3.33)	2.25 (1.08-4.50)	3.87 (1.85-7.82)
55-59 years	3.58 (2.86-4.45)	4.04 (3.25-4.97)	7.62 (6.11-9.42)	2.00 (0.96-3.95)	2.62 (1.29-4.99)	4.62 (2.26-8.94)

60-64 years	4.65 (3.80-5.64)	5.13 (4.23-6.15)	9.78 (8.03-11.79)	2.82 (1.40-5.29)	3.60 (1.85-6.42)	6.42 (3.24-11.71)
65-69 years	5.29 (4.40-6.27)	6.04 (5.09-7.06)	11.33 (9.49-13.33)	3.49 (1.81-6.13)	4.58 (2.48-7.53)	8.08 (4.29-13.66)
70-74 years	4.74 (4.01-5.50)	5.73 (4.93-6.55)	10.47 (8.94-12.05)	3.42 (1.88-5.52)	4.69 (2.73-7.02)	8.12 (4.61-12.54)
75-79 years	3.41 (2.94-3.87)	4.67 (4.11-5.22)	8.08 (7.05-9.08)	2.68 (1.59-3.93)	4.09 (2.59-5.56)	6.77 (4.18-9.49)
80–84 years	2.16 (1.90-2.39)	3.27 (2.93-3.57)	5.43 (4.83-5.96)	1.83 (1.18-2.44)	3.01 (2.10-3.76)	4.84 (3.28-6.20)
85-89 years	0.83 (0.75-0.90)	1.48 (1.36-1.58)	2.31 (2.10-2.48)	0.75 (0.53-0.92)	1.41 (1.08-1.65)	2.16 (1.61-2.56)
Total (45-89 years)	30.73 (25.31-36.89)	37.60 (31.48-44.41)	68.33 (56.79-81.29)	20.03 (10.77-34.47)	28.24 (16.12-45.52)	48.26 (26.89-79.99)
2010						
Age group	**Any cataract**			**ARC**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	3.46 (2.61-4.55)	4.15 (3.15-5.43)	7.61 (5.76-9.98)	1.67 (0.78-3.51)	2.33 (1.10-4.82)	4.00 (1.87-8.33)
50-54 years	4.21 (3.27-5.37)	5.00 (3.91-6.33)	9.20 (7.19-11.70)	2.17 (1.03-4.45)	3.01 (1.44-6.02)	5.19 (2.47-10.47)
55-59 years	6.26 (5.00-7.78)	7.42 (5.97-9.13)	13.69 (10.97-16.91)	3.49 (1.68-6.90)	4.82 (2.37-9.17)	8.31 (4.06-16.07)
60-64 years	6.17 (5.03-7.48)	7.28 (6.00-8.72)	13.45 (11.04-16.20)	3.73 (1.85-7.01)	5.11 (2.62-9.11)	8.84 (4.47-16.12)
65-69 years	6.15 (5.12-7.29)	6.96 (5.86-8.14)	13.11 (10.98-15.43)	4.06 (2.10-7.13)	5.29 (2.86-8.69)	9.35 (4.96-15.81)
70-74 years	6.47 (5.48-7.51)	7.39 (6.36-8.44)	13.86 (11.83-15.95)	4.68 (2.56-7.53)	6.05 (3.52-9.05)	10.72 (6.08-16.59)
75-79 years	5.34 (4.61-6.06)	6.73 (5.91-7.51)	12.07 (10.52-13.57)	4.21 (2.49-6.17)	5.88 (3.73-8.01)	10.09 (6.22-14.18)
80–84 years	3.13 (2.76-3.47)	4.45 (4.00-4.86)	7.58 (6.76-8.33)	2.66 (1.72-3.55)	4.10 (2.86-5.12)	6.76 (4.58-8.67)
85-89 years	1.33 (1.20-1.44)	2.17 (1.99-2.32)	3.50 (3.19-3.77)	1.20 (0.85-1.47)	2.07 (1.58-2.42)	3.27 (2.44-3.89)

Total (45-89 years)	42.52 (35.08-50.96)	51.56 (43.16-60.88)	94.07 (78.24-111.84)	27.86 (15.07-47.72)	38.67 (22.08-62.42)	66.54 (37.15-110.14)
2015						
Age group	**Any cataract**			**ARC**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	4.20 (3.17-5.53)	5.11 (3.87-6.68)	9.31 (7.05-12.21)	2.02 (0.94-4.26)	2.87 (1.35-5.94)	4.90 (2.29-10.20)
50-54 years	5.15 (4.00-6.57)	6.14 (4.81-7.78)	11.29 (8.81-14.35)	2.66 (1.26-5.45)	3.70 (1.77-7.40)	6.36 (3.03-12.85)
55-59 years	6.06 (4.84-7.53)	7.18 (5.78-8.82)	13.24 (10.61-16.35)	3.38 (1.63-6.68)	4.66 (2.30-8.87)	8.04 (3.93-15.54)
60-64 years	8.58 (7.00-10.40)	10.15 (8.37-12.16)	18.73 (15.37-22.56)	5.19 (2.58-9.75)	7.13 (3.65-12.71)	12.32 (6.23-22.46)
65-69 years	7.78 (6.47-9.23)	9.26 (7.80-10.82)	17.04 (14.27-20.05)	5.14 (2.66-9.01)	7.03 (3.80-11.55)	12.17 (6.46-20.56)
70-74 years	6.87 (5.81-7.97)	7.97 (6.86-9.11)	14.84 (12.67-17.07)	4.96 (2.72-8.00)	6.53 (3.79-9.77)	11.49 (6.51-17.77)
75-79 years	6.04 (5.21-6.85)	7.33 (6.44-8.18)	13.36 (11.65-15.03)	4.75 (2.81-6.97)	6.41 (4.06-8.72)	11.16 (6.87-15.69)
80–84 years	3.99 (3.52-4.43)	5.45 (4.89-5.95)	9.45 (8.41-10.38)	3.39 (2.19-4.53)	5.02 (3.50-6.27)	8.41 (5.69-10.80)
85-89 years	1.77 (1.60-1.92)	2.72 (2.49-2.91)	4.49 (4.09-4.83)	1.60 (1.13-1.96)	2.60 (1.98-3.03)	4.20 (3.12-4.99)
Total (45-89 years)	50.44 (41.63-60.43)	61.30 (51.31-72.41)	111.74 (92.94-132.84)	33.10 (17.93-56.61)	45.94 (26.21-74.25)	79.04 (44.14-130.85)
2020						
Age group	**Any cataract**			**ARC**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	4.04 (3.05-5.32)	4.84 (3.67-6.33)	8.88 (6.72-11.65)	2.87 (1.35-5.94)	2.72 (1.28-5.63)	4.67 (2.19-9.73)
50-54 years	6.26 (4.87-7.99)	7.57 (5.93-9.59)	13.83 (10.80-17.58)	3.70 (1.77-7.40)	4.57 (2.19-9.12)	7.80 (3.72-15.75)
55-59 years	7.44 (5.94-9.24)	8.83 (7.11-10.86)	16.27 (13.05-20.1)	4.66 (2.30-8.87)	5.74 (2.83-10.92)	9.88 (4.83-19.11)
60-64 years	8.35	9.85	18.20	7.13	6.91	11.97

	(6.81-10.12)	(8.12-11.80)	(14.93-21.92)	(3.65-12.71)	(3.54-12.33)	(6.05-21.81)
65-69 years	10.93 (9.09-12.96)	12.99 (10.95-15.19)	23.92 (20.04-28.15)	7.03 (3.80-11.55)	9.87 (5.34-16.21)	17.09 (9.08-28.87)
70-74 years	8.83 (7.48-10.25)	10.73 (9.23-12.25)	19.55 (16.70-22.50)	6.53 (3.79-9.77)	8.78 (5.10-13.15)	15.16 (8.60-23.43)
75-79 years	6.57 (5.67-7.46)	8.06 (7.08-9.00)	14.63 (12.75-16.45)	6.41 (4.06-8.72)	7.05 (4.47-9.59)	12.22 (7.53-17.18)
80–84 years	4.67 (4.12-5.18)	6.12 (5.49-6.68)	10.79 (9.61-11.86)	5.02 (3.50-6.27)	5.63 (3.93-7.03)	9.60 (6.49-12.33)
85-89 years	2.36 (2.12-2.56)	3.48 (3.19-3.72)	5.84 (5.31-6.28)	2.60 (1.98-3.03)	3.32 (2.54-3.87)	5.45 (4.05-6.48)
Total (45-89 years)	59.45 (49.15-71.08)	72.47 (60.76-85.42)	131.92 (109.91-156.49)	45.94 (26.21-74.25)	54.59 (31.21-87.85)	93.83 (52.52-154.69)
2030						
Age group	**Any cataract**			**ARC**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	3.35 (2.53-4.40)	3.98 (3.02-5.21)	7.32 (5.55-9.61)	1.61 (0.75-3.39)	2.24 (1.05-4.63)	3.85 (1.80-8.02)
50-54 years	4.81 (3.74-6.14)	5.70 (4.46-7.22)	10.51 (8.20-13.35)	2.48 (1.17-5.09)	3.44 (1.65-6.86)	5.92 (2.82-11.95)
55-59 years	8.77 (7.00-10.89)	10.36 (8.34-12.74)	19.13 (15.34-23.63)	4.89 (2.36-9.66)	6.73 (3.31-12.80)	11.62 (5.67-22.46)
60-64 years	12.62 (10.30-15.30)	15.07 (12.43-18.05)	27.69 (22.73-33.35)	7.64 (3.79-14.34)	10.58 (5.42-18.86)	18.22 (9.21-33.20)
65-69 years	13.35 (11.11-15.84)	15.75 (13.27-18.41)	29.11 (24.38-34.25)	8.82 (4.57-15.47)	11.96 (6.47-19.66)	20.78 (11.04-35.13)
70-74 years	12.56 (10.63-14.57)	15.02 (12.92-17.15)	27.57 (23.55-31.72)	9.07 (4.98-14.62)	12.29 (7.15-18.40)	21.36 (12.12-33.02)
75-79 years	12.66 (10.93-14.37)	15.95 (14.01-17.81)	28.62 (24.95-32.18)	9.97 (5.89-14.62)	13.95 (8.84-18.98)	23.92 (14.74-33.61)
80–84 years	7.17 (6.32-7.95)	9.75 (8.75-10.64)	16.92 (15.07-18.59)	6.08 (3.93-8.12)	8.98 (6.26-11.21)	15.06 (10.19-19.33)
85-89 years	3.36 (3.03-3.64)	4.79 (4.39-5.12)	8.15 (7.41-8.76)	3.03 (2.15-3.72)	4.57 (3.49-5.32)	7.60 (5.64-9.04)
Total	78.65	96.36	175.01	53.60	74.73	128.33

(45-89 years)	(65.58-93.11)	(81.58-112.35)	(147.16-205.46)	(29.60-89.04)	(43.64-116.73)	(73.24-205.78)
2040						
Age group	**Any cataract**			**ARC**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	3.64 (2.75-4.79)	4.10 (3.11-5.37)	7.74 (5.86-10.16)	1.75 (0.82-3.69)	2.31 (1.09-4.78)	4.06 (1.90-8.46)
50-54 years	6.57 (5.11-8.38)	7.58 (5.93-9.60)	14.15 (11.04-17.98)	3.39 (1.60-6.95)	4.57 (2.19-9.13)	7.96 (3.80-16.08)
55-59 years	7.31 (5.84-9.08)	8.55 (6.89-10.52)	15.87 (12.72-19.60)	4.08 (1.97-8.05)	5.55 (2.74-10.57)	9.63 (4.70-18.62)
60-64 years	9.82 (8.01-11.90)	11.42 (9.42-13.68)	21.24 (17.43-25.58)	5.94 (2.95-11.16)	8.02 (4.11-14.29)	13.96 (7.06-25.45)
65-69 years	16.13 (13.41-19.13)	18.74 (15.79-21.91)	34.87 (29.21-41.04)	10.66 (5.52-18.69)	14.23 (7.70-23.39)	24.89 (13.22-42.08)
70-74 years	19.82 (16.79-23.01)	23.60 (20.30-26.96)	43.42 (37.09-49.96)	14.32 (7.85-23.08)	19.32 (11.23-28.92)	33.64 (19.09-52.01)
75-79 years	16.63 (14.36-18.88)	20.27 (17.80-22.62)	36.90 (32.16-41.50)	13.10 (7.74-19.21)	17.72 (11.24-24.12)	30.82 (18.98-43.33)
80–84 years	11.35 (10.01-12.59)	14.74 (13.23-16.09)	26.09 (23.23-28.68)	9.64 (6.23-12.86)	13.57 (9.46-16.95)	23.21 (15.69-29.82)
85-89 years	7.45 (6.71-8.08)	10.67 (9.78-11.41)	18.12 (16.49-19.49)	6.71 (4.77-8.24)	10.19 (7.78-11.87)	16.90 (12.55-20.11)
Total (45-89 years)	98.72 (82.98-115.84)	119.69 (102.26-138.17)	218.41 (185.24-254.01)	69.59 (39.44-111.94)	95.49 (57.53-144.03)	165.08 (96.98-255.97)
2050						
Age group	**Any cataract**			**ARC**		
	Male	**Female**	**Overall**	**Male**	**Female**	**Overall**
45-49 years	2.61 (1.97-3.44)	2.83 (2.14-3.70)	5.44 (4.12-7.13)	1.26 (0.59-2.65)	1.59 (0.75-3.29)	2.85 (1.33-5.93)
50-54 years	4.08 (3.18-5.21)	4.47 (3.50-5.66)	8.55 (6.67-10.87)	2.11 (1.00-4.32)	2.69 (1.29-5.38)	4.80 (2.29-9.70)
55-59 years	8.01 (6.39-9.94)	8.86 (7.13-10.89)	16.86 (13.52-20.83)	4.46 (2.15-8.82)	5.75 (2.83-10.94)	10.21 (4.99-19.76)
60-64 years	13.57 (11.07-16.45)	15.29 (12.61-18.32)	28.86 (23.68-34.77)	8.21 (4.08-15.42)	10.73 (5.50-19.14)	18.94 (9.58-34.56)

65-69 years	13.74 (11.43-16.30)	15.66 (13.20-18.31)	29.41 (24.63-34.61)	9.08 (4.70-15.92)	11.89 (6.43-19.54)	20.97 (11.14-35.47)
70-74 years	16.04 (13.58-18.62)	18.28 (15.73-20.88)	34.32 (29.31-39.50)	11.59 (6.36-18.68)	14.97 (8.70-22.40)	26.56 (15.06-41.09)
75-79 years	21.50 (18.56-24.40)	25.05 (22.01-27.96)	46.55 (40.56-52.36)	16.93 (10.00-24.82)	21.90 (13.89-29.82)	38.83 (23.89-54.64)
80–84 years	19.90 (17.54-22.08)	24.67 (22.14-26.93)	44.58 (39.68-49.01)	16.90 (10.92-22.56)	22.72 (15.83-28.37)	39.61 (26.75-50.93)
85-89 years	11.32 (10.19-12.27)	14.95 (13.70-15.99)	26.27 (23.89-28.27)	10.20 (7.24-12.53)	14.28 (10.91-16.63)	24.48 (18.15-29.16)
Total (45-89 years)	110.76 (93.92-128.70)	130.07 (112.15-148.65)	240.83 (206.07-277.35)	80.73 (47.04-125.71)	106.53 (66.13-155.52)	187.26 (113.17-281.23)

Appendix table 27. Estimation of age-specific number of people with any cataract in China from 2000 to 2010, by geographical region (million, 95% CI)

2000						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**
45-49 years	0.54 (0.35-0.83)	0.85 (0.45-1.56)	1.66 (1.43-2.00)	2.48 (1.69-3.61)	0.94 (0.56-1.55)	0.31 (0.21-0.48)
50-54 years	0.55 (0.37-0.82)	0.81 (0.44-1.38)	1.79 (1.59-2.08)	2.63 (1.87-3.61)	1.03 (0.64-1.63)	0.36 (0.24-0.53)
55-59 years	0.57 (0.40-0.82)	0.83 (0.48-1.29)	1.94 (1.77-2.18)	2.79 (2.08-3.58)	1.27 (0.82-1.88)	0.45 (0.31-0.63)
60-64 years	0.80 (0.57-1.08)	1.07 (0.66-1.50)	2.48 (2.33-2.69)	3.47 (2.74-4.14)	1.53 (1.04-2.11)	0.57 (0.41-0.76)
65-69 years	0.97 (0.72-1.25)	1.10 (0.73-1.39)	3.10 (3.01-3.24)	3.89 (3.29-4.29)	1.64 (1.18-2.07)	0.57 (0.43-0.71)
70-74 years	0.89 (0.70-1.07)	0.95 (0.70-1.09)	3.02 (3.03-3.03)	3.38 (3.07-3.47)	1.54 (1.20-1.79)	0.45 (0.36-0.52)
75-79 years	0.68 (0.57-0.76)	0.64 (0.52-0.67)	2.47 (2.57-2.37)	2.51 (2.46-2.42)	1.11 (0.94-1.19)	0.35 (0.31-0.38)
80-84 years	0.43 (0.39-0.45)	0.37 (0.33-0.36)	1.71 (1.85-1.58)	1.65 (1.73-1.52)	0.75 (0.69-0.75)	0.23 (0.22-0.23)
85-89 years	0.18 (0.18-0.18)	0.16 (0.15-0.14)	0.72 (0.81-0.65)	0.70 (0.77-0.62)	0.33 (0.33-0.31)	0.08 (0.08-0.08)
Total (45-89 years)	5.62 (4.26-7.26)	6.80 (4.47-9.37)	18.89 (18.39-19.83)	23.50 (19.70-27.26)	10.14 (7.39-13.26)	3.37 (2.58-4.31)
2010						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**
45-49 years	0.64 (0.42-0.99)	1.01 (0.53-1.83)	1.95 (1.68-2.35)	3.08 (2.10-4.48)	0.96 (0.58-1.59)	0.42 (0.28-0.65)
50-54 years	0.88 (0.60-1.31)	1.37 (0.75-2.32)	2.36 (2.09-2.74)	3.44 (2.44-4.72)	1.06 (0.66-1.67)	0.49 (0.34-0.73)
55-59 years	1.20 (0.83-1.72)	1.75 (1.01-2.71)	3.61 (3.29-4.06)	4.93 (3.68-6.32)	1.92 (1.24-2.84)	0.68 (0.47-0.95)
60-64 years	1.14 (0.82-1.55)	1.52 (0.93-2.12)	3.59 (3.38-3.90)	4.70 (3.72-5.60)	1.96 (1.33-2.70)	0.70 (0.51-0.93)

65-69 years	1.05 (0.78-1.34)	1.33 (0.89-1.68)	3.45 (3.35-3.60)	4.33 (3.67-4.78)	2.10 (1.52-2.66)	0.77 (0.59-0.96)
70-74 years	1.20 (0.94-1.43)	1.39 (1.02-1.57)	3.69 (3.71-3.69)	4.40 (4.01-4.52)	2.08 (1.62-2.42)	0.80 (0.65-0.92)
75-79 years	1.08 (0.90-1.20)	1.05 (0.86-1.09)	3.54 (3.70-3.40)	3.69 (3.62-3.56)	1.66 (1.40-1.77)	0.58 (0.50-0.62)
80-84 years	0.66 (0.59-0.68)	0.62 (0.56-0.60)	2.37 (2.57-2.19)	2.20 (2.31-2.01)	1.07 (0.98-1.06)	0.29 (0.27-0.29)
85-89 years	0.28 (0.27-0.28)	0.26 (0.25-0.23)	1.16 (1.31-1.04)	1.01 (1.12-0.89)	0.46 (0.46-0.43)	0.13 (0.13-0.12)
Total (45-89 years)	8.13 (6.16-10.50)	10.30 (6.79-14.16)	25.72 (25.09-26.98)	31.79 (26.67-36.88)	13.28 (9.79-17.13)	4.87 (3.75-6.18)

Appendix table 28. Search strategy to identify studies reporting the prevalence of and risk factors for DR in China

CNKI

Access Date: 05 Dec 2017

Subject category: Medicine & Public Health

Sub-database: Journal, Featured journal, Doctoral dissertation, Master dissertation

检索表达式：

(SU % '糖尿病') AND (SU % '视网膜') AND (SU % '发病率' + '发生率' + '患病率'+ '罹患率' + '现患率'+ '死亡率' + '病死率'+ '流行' + '负担'+ '现况调查'+ '现况研究')

发表时间：从 1990-01-01 到 2017-12-05

Search Terms: (SU % 'tangniaobing') AND (SU % 'shiwangmo') AND (SU % 'fabinglv' + 'fashenglv' + 'huanbinglv'+ 'lihuanlv' + 'xianhuanlv'+ 'siwanglv' + 'bingsilv'+ 'liuxing' + 'fudan'+ 'xiankuangdiaocha'+ 'xiankuangyanjiu')

Published time：From 01/01/1990 to 05/12/2017

Wanfang

Access Date: 04 Dec 2017

Sub-database: Journal articles, Dissertations

检索表达式：(主题:(糖尿病)) * (主题:(视网膜)) * (主题:(发病率) + 主题:(发生率) + 主题:(患病率) +主题:(罹患率) + 主题:(现患率) + 主题:(死亡率) +主题:(病死率) + 主题:(流行) + 主题:(负担)+ 主题:(现况调查) + 主题:(现况研究))

时间：1990-2017

Search Terms: (subject: (tangniaobing))* (subject: (shiwangmo))* (subject: (fabinglv) + subject: (fashenglv) + subject: (huanbinglv)+ subject: (lihuanlv) + subject: (xianhuanlv) + subject: (siwanglv)+ subject: (bingsilv) + subject: (liuxing) + subject: (fudan)+ subject: (xiankuangdiaocha) + subject: (xiankuangyanjiu))

Date: 1990-2017

CBM-SinoMed

Access Date: 04 Dec 2017

Journal category: All journals

检索表达式:

(糖尿病) AND (视网膜) AND (发病率 or 发生率 or 患病率 or 罹患率 or 现患率 or 死亡率 or 病死率 or 流行 or 负担 or 现况调查 or 现况研究)

时间：1990-2017

Search Terms: ((tangniaobing))* ((shiwangmo))* ((fabinglv) OR (fashenglv) OR (huanbinglv) OR (lihuanlv) OR (xianhuanlv) OR (siwanglv) OR (bingsilv) OR (liuxing) OR (fudan) OR (xiankuangdiaocha) OR (xiankuangyanjiu))

Date: 1990-2017

PubMed

Access Date: 04 Dec 2017

Search Terms:

((diabetic retinopathy) AND (China OR Chinese OR Hongkong OR Macau OR Taiwan) AND (inciden* OR prevalen* OR morbidity OR mortality OR epidemiology)) AND ("1990/01/01"[Date - Publication] : "2017/12/04"[Date - Publication])

Embase (Ovid)

Access Date: 04 Dec 2017

#	Searches
1	diabetic retinopathy.mp. or exp diabetic retinopathy/
2	China.mp. or exp China/
3	exp Chinese/ or Chinese.mp.
4	Hong Kong.mp. or exp Hong Kong/
5	Macau.mp. or exp Macao/
6	Taiwan.mp. or exp Taiwan/
7	exp incidence/ or inciden*.mp.
8	exp prevalence/ or prevalen*.mp.
9	morbidity.mp. or exp morbidity/
10	exp mortality/ or Mortality.mp.
11	exp epidemiology/ or Epidemiology.mp.
12	2 or 3 or 4 or 5 or 6
13	7 or 8 or 9 or 10 or 11
14	1 and 12 and 13
15	limit 14 to yr="1990 -Current"

Medline (Ovid)

Access Date: 04 Dec 2017

Search Terms:

#	Searches
1	diabetic retinopathy.mp. or exp Diabetic Retinopathy/
2	China.mp. or exp China/

3	Chinese.mp.
4	Hong Kong.mp. or exp Hong Kong/
5	Macau.mp. or exp Macau/
6	Taiwan.mp. or exp Taiwan/
7	exp Incidence/ or inciden*.mp.
8	exp Prevalence/ or prevalen*.mp.
9	Morbidity.mp. or exp Morbidity/
10	Mortality.mp. or exp Mortality/
11	Epidemiology.mp. or exp Epidemiology/
12	2 or 3 or 4 or 5 or 6
13	7 or 8 or 9 or 10 or 11
14	1 and 12 and 13
15	limit 14 to yr="1990 -Current"

Appendix table 29. The year of publication and investigation and corresponding time-lag in the included studies on DR prevalence in China (n=41)

Study ID	Study	Year Published	Median investigation date	Time-lag
DR_C1	Zhang XM et al. (1996)	1996	1994	2
DR_C2	He SZ et al. (1997)	1997	-	-
DR_C3	Li SL et al. (1998)	1998	1994	4
DR_C4	Li N et al. (1999)	1999	1995	4
DR_C5	Wang GL et al. (2001)	2001	1994	7
DR_C6	Yang X et al. (2004)	2004	2000	4
DR_C7	Liu JP (2006)	2006	2005	1
DR_C8	Hu HY et al. (2007)	2007	2006	1
DR_C9	Dong B et al. (2008)	2008	-	-
DR_C10	Liu L (2009)	2009	2007	2
DR_C11	Zhang HX et al. (2009)	2009	2005	4
DR_C12	Xin Z et al. (2010)	2010	2008	2
DR_C13	Wang HB et al. (2010)	2010	2008	2
DR_C14	Shu XW et al. (2010)	2010	2007	3
DR_C15	Gao LT (2011)	2011	2009	2
DR_C16	Li BZ et al. (2011)	2011	2007	4
DR_C17	Hu YD (2011)	2011	2007	4
DR_C18	Liu QX et al. (2012)	2012	-	-
DR_C19	Zhang J (2012)	2012	2011	1
DR_C20	Yuan MX et al. (2012)	2012	2010	2
DR_C21	Cui Y (2013)	2013	2012	1
DR_C22	Li N et al. (2013)	2013	2010	3
DR_C23	Xie TH et al. (2013)	2013	2010	3
DR_C24	Wu PC et al. (2014)	2014	2012	2
DR_C25	Mou XY et al. (2014)	2014	-	-
DR_C26	Shao L et al. (2014)	2014	2011	3
DR_C27	Jiang XF et al. (2015)	2015	2012	3
DR_C28	Wang WC et al. (2015)	2015	2011	4
DR_C29	Ye BL et al. (2016)	2016	2011	5
DR_C30	Hu BJ et al. (2016)	2016	2014	2

Study ID	Study	Year Published	Median investigation date	Time-lag
DR_C31	Zhang GS et al. (2017)	2017	2014	3
DR_C32	Xie XW et al. (2008)	2008	2006	2
DR_C33	Xie XW et al. (2009)	2009	2001	8
DR_C34	Wang FH et al. (2011)	2011	2007	4
DR_C35	Wang B et al. (2016)	2016	2011	5
DR_P1	Liu LP et al. (2015)	2015	2013	2
DR_P2	Liang C et al. (2016)	2016	2014	2
DR_P3	Zhang XH et al. (2016)	2016	-	-
DR_P4	Xu J et al. (2012)	2012	2009	3
DR_P5	Pan CW et al. (2017)	2017	2015	2
DR_R1	Wang WJ et al. (2015)	2015	-	-

Note: "-" represents unavailable data; Based on the information from 35 studies, the average time-lag between year of publication and year of investigation was 3.03.

Appendix table 30. Full list of the included studies on the prevalence of and risk factors for DR in China (n=41)

Study ID	Reference
Community-based studies	
DR_C1	Xiao-mei Zhang, Shi-hong Hu. 张晓湄, 胡世红. Diabetes retinopathy detected in a population in Liuzhou municipal during epidemiologic survey of diabetes mellitus (柳州市人群糖尿病调查中视网膜病变检出情况)[J]. Journal of Clinical Ophthalmology (临床眼科杂志). 1996(04):244-5.
DR_C2	Shou-zhi He, Yu-luan Guo, Zhao-hui Li, et al. 何守志, 郭玉銮, 李朝辉, et al. Epidemiologic study of diabetic retinopathy in Capital Steel Company (首钢职工糖尿病视网膜病变流行病学调查)[J]. Chin J Ophthalmol (中华眼科杂志). 1997(05):62-4.
DR_C3	Shou-ling Li, Yan-feng Zhou, Ti Chen, et al. 李寿玲, 周艳枫, 陈逖, 杨明功, 朱美玲. Epidemiologic study about the related factors of diabetic retinopathy (糖尿病视网膜病变相关因素的流行病学调查)[J]. Chin J Ocul Fundus Dis (中华眼底病杂志). 1998(02):58-60.
DR_C4	Nong Li, Li-jun Ao, Shou-jun Meng, et al. 李农, 敖丽君, 孟寿军, 王华权, 杨媛魁, 许道盛. An analysis of risk factors of diabetic retinopathy in type 2 diabetic patients* (2 型糖尿病患者并发视网膜病变危险因素的分析)[J]. West China Medical Journal (华西医学). 1999(03):304-5.
DR_C5	Guang-lu Wang, Feng Zhang, Shen-yuan Yuan, et al. 王光璐, 张风, 袁申元, et al. A screening survey of diabetic retinopathy and other chronic complications in Beijing district (北京地区糖尿病视网膜病变及其他慢性并发症的调查)[J]. Ophthalmol CHN (眼科). 2001(03):180-2.

Study ID	Reference
DR_C6	Xin Yang, Li-li Zhou, Ying-chun Zhao, et al. 阳新, 周黎黎, 赵迎春, 刘光英, 陈红. The relation of obesity, diabetes and vascular complications* (肥胖与糖尿病、血管并发症的关系)[J]. Liaoning Journal of Practical Diabetology (辽宁实用糖尿病杂志). 2004(03):38-9.
DR_C7	Ju-ping Liu. 刘巨平. Epidemiologic study of diabetic retinopathy in type 2 diabetes mellitus in Tianjin (天津市 2 型糖尿病患者糖尿病视网膜病变流行病学调查)[D]. Tianjin Medical University (天津医科大学). 2006.
DR_C8	Hai-ying Hu, Bin Lu, Zhao-yun Zhang, et al. 胡海英, 鹿斌, 张朝云, et al. An epidemiological study on diabetic retinopathy among type 2 diabetic patients in Shanghai (上海市中心城区 2 型糖尿病患者视网膜病变现况调查)[J]. Chin J Epidemiol (中华流行病学杂志). 2007(09):838-40.
DR_C9	Bin Dong, Xiang-wen Yang, Hong-juan Li, et al. 董斌, 阳湘文, 黎红娟, 周恩林. An analysis of the epidemiology and risk factors of diabetic retinopathy in communities* (社区糖尿病性视网膜病变流行病学调查及相关因素分析)[J]. Chinese Community doctors (中国社区医师(医学专业半月刊)). 2008(14):202.
DR_C10	Lei Liu. 刘磊. Prevalence rate and risk factors of diabetic retinopathy in Shenyang Dadong district (沈阳大东区糖尿病视网膜病变患病率及相关危险因素)[D].China Medical University (中国医科大学). 2009.
DR_C11	Hong-xia Zhang, Li-li Jia, Xu-hong Hou, et al. 张红霞, 贾丽丽, 侯旭宏, et al. Prevalence of and risk factors associated with diabetic retinopathy in pre-diabetic and diabetic population in Shanghai community (上海社区糖尿病前期及糖尿病人群视网膜病变患病率及相关危险因素分析)[J]. Natl Med J China (中华医学杂志). 2009;89(25):1749-52.

Study ID	Reference
DR_C12	Zhong Xin, Ya-hong Ma, Lei Zhao, et al. 信中, 马亚红, 赵蕾, 卢毅, 石敬, 杨金奎. Prevalence and risk factors of diabetic retinopathy in rural population of Beijing (北京农村地区高血糖人群糖尿病视网膜病变患病率及危险因素分析)[J]. Clinical Focus (临床荟萃). 2010(08):672-5.
DR_C13	Hong-bo Wang, Feng-xian Sun, Qin Zhang, et al. 王红波, 孙凤仙, 张勤, 翟敏, 王素芳, 卢海. Epidemiologic study on the prevalence rate and risk factors of diabetic retinopathy in eastern countryside of Changzhi (山西省长治东部农村地区糖尿病视网膜病变的流行病研究)[J]. Chin J Ocul Fundus Dis (中华眼底病杂志). 2010;26(2):109-12.
DR_C14	Xiang-wen Shu, Yu Wang, Chuan-feng Fan, et al. 舒相汶, 王玉, 范传峰, 盛艳娟, 张华, 吴昌龙. Epidemiology study on the prevalence rate and risk factors of diabetic retinopathy in rural residents in Shandong province (山东省农村人群糖尿病视网膜病变的流行病学调查)[J]. Chin J Ocul Fundus Dis (中华眼底病杂志). 2010;26(2):113-5.
DR_C15	Li-tao Gao. 高丽涛. Analysising the prevalence and risk factors of diabetic retinopathy in Shenyang Heping district (沈阳和平区糖尿病视网膜病变的患病率及相关危险因素分析)[D]. China Medical University (中国医科大学). 2010.
DR_C16	Bing-zhen Li, Yu-ling Liu, Liang Han, et al. 李炳震, 刘瑜玲, 韩亮, et al. Epidemiological survey of diabetic retinopathy in Shunyi district of Beijing (北京市顺义 40 岁及以上人群糖尿病视网膜病变的流行病学调查)[J]. Chin J Exp Ophthalmol (中华实验眼科杂志). 2011;29(8):747-52.
DR_C17	Yue-dong Hu. 胡悦东. Prevalence of diabetic retinopathy in Liaoning province China and the expression and mechanism of MicroRNA in patients with proliferative diabetic retinopathy (辽宁省自然人群糖尿病视网膜病变现况研究及增殖性糖尿病视网膜病变患者 miRNA 表达及其机制的研究)[D]. China Medical University (中国医科大学). 2011.

Study ID	Reference
DR_C18	Qing-xia Liu, Pei-feng Liang, Lai-jun Xu, et al. 刘青霞, 梁沛枫, 胥来军, et al. Epidemiology research of diabetic retinopathy in Ningxia region (宁夏地区糖尿病视网膜病变的流行病学研究)[J]. Int Eye Sci (国际眼科杂志). 2012(08):1566-9.
DR_C19	Jun Zhang. 张俊. Epidemiological study on diabetic retinopathy and the analysis of correlative factors in Luzhou city, Sichuan Province (四川省泸州市糖尿病视网膜病变的流行病学调查及相关因素分析)[D]. Southwest Medical University (泸州医学院 西南医科大学). 2012.
DR_C20	Ming-xia Yuan, Zhong Xin, Jian-ping Feng, et al. 袁明霞, 信中, 冯建萍, et al. A population-based prevalence survey and risk factor analysis of diabetic retinopathy in Beijing Changping District (北京市昌平区自然人群糖尿病视网膜病变患病率调查及危险因素分析)[J]. Journal of Capital Medical University (首都医科大学学报). 2012(05):669-75.
DR_C21	Ying Cui. 崔颖. Epidemiological study of diabetic retinopathy in Dongguan city, Guangdong province (广东省东莞市糖尿病视网膜病变流行病学研究)[D].Southern Medical University (南方医科大学). 2013.
DR_C22	Na Li, Xiu-fen Yang, Yu Deng, et al. 李娜, 杨秀芬, 邓禹, et al. Diabetes self-management and its association with diabetic retinopathy in patients with type 2 diabetes (2 型糖尿病患者自我管理水平与糖尿病视网膜病变的相关性研究)[J]. Chin J Ophthalmol (中华眼科杂志). 2013;49(6):500-6.
DR_C23	Tian-hua Xie, Jing, Zhu, Dong-hong Fu, et al. 谢田华, 朱靖, 傅东红, et al. Prevalence of diabetic retinopathy in residents aged 50 and above in Binhu community of Wuxi city (无锡市滨湖区 50 岁及以上人群糖尿病视网膜病变患病情况调查)[J]. Chin J Ocul Fundus Dis (中华眼底病杂志). 2013;29(5):495-8.

Study ID	Reference
DR_C24	Peng-cheng Wu, Wen-fang Zhang, Peng Lv, et al. 吴鹏程, 张文芳, 律鹏, 陈盛举, 陶明. Epidemical survey of relative factors of retinal vessels disease of the native Tibetan among the people aged 40 and above in Maqin county, Qinghai province (青海省玛沁县 40 岁以上世居藏族人群视网膜血管性疾病相关因素的流行病学调查)[J]. Int Eye Sci (国际眼科杂志). 2014(07):1288-91.
DR_C25	Xiao-yan Mou, Ying Wang, Lin Fu, et al. 牟晓燕, 王颖, 付琳, 王楠, 杨晶, 马莉. Prevalence and risk factors of diabetic retinopathy in type 2 diabetic patients in an island population in Dalian (海岛人群糖尿病患者视网膜病变流行现状及影响因素分析)[J]. Modern Preventive Medicine (现代预防医学). 2014(20):3655-8.
DR_C26	Lei Shao, Ya-xing Wang, Jie Chen, et al. 邵蕾, 王亚星, 徐捷, et al. Subfoveal choroidal thickness of Chinese aged over 50 years and patients with diabetes mellitus and glaucoma (北京地区 50 岁以上人群及糖尿病和青光眼患者的脉络膜厚度及其影响因素)[J]. Chin J Ophthalmol (中华眼科杂志). 2014(6):414-20.
DR_C27	Xue-feng Jiang, Zheng-yu Zhu, Yong-wu He, et al. 江雪丰, 褚征宇, 何勇武, 程玲, 张宏娣. Prevalence and risk factors of Nanchang community diabetic retinopathy (南昌市社区糖尿病视网膜病变患病率及危险因素分析)[J]. Rec Adv Ophthalmol (眼科新进展). 2015(11):1047-50.
DR_C28	Wei-chao Wang, Jie Zhang, Hong Wang, et al. 王伟超, 张洁, 王虹, et al. Relationship between the levels of tear fluid TNF-α, serum TNF-α and serum HbA1c and diabetic retinopathy in middle-aged and elderly diabetes patients (社区中老年糖尿病患者泪液和血清肿瘤坏死因子 α 及血清糖化血红蛋白与糖尿病视网膜病变的关系)[J]. Chinese General Practice (中国全科医学). 2015(35):4288-92.

Study ID	Reference
DR_C29	Bing-lin Ye, Min Lu, Hao-ying Tang, et al. 叶炳林, 卢敏, 唐浩英, et al. An epidemiological investigation on diabetic retinopathy in people aged 60 years and above in Sanshui district, Foshan city* (佛山市三水区 60 岁及以上人群糖尿病视网膜病变的流行病学调查)[J]. Heilongjiang Medical Journal (黑龙江医学). 2016(04):336-8.
DR_C30	Bo-jie Hu, Qiu-hai Lu, Jian-qun Zhan. 胡博杰, 路秋海, 谌建群. Epidemiological survey on diabetic retinopathy in Uyghur patients aged 40 or older with type 2 diabetes mellitus in Hotan region of Xinjiang (新疆和田地区 40 岁及以上维吾尔族 2 型糖尿病患者糖尿病视网膜病变流行病学调查)[J]. Journal of Logistics University of PAP (Medical Sciences) (武警后勤学院学报(医学版)). 2016(08):664-6.
DR_C31	Gui-sen Zhang, Jilitu Morige, Feng-mei Ren, et al. 张贵森, 莫日格吉力吐, 任凤梅, 惠延年. Epidemiological investigation of diabetic retinopathy in Hohhot (呼和浩特地区糖尿病视网膜病变流行病学调查)[J]. Chin J Pract Ophthalmol (中国实用眼科杂志). 2017;35(4):428-33.
DR_C32	Xie XW, Xu L, Wang YX, Jonas JB. Prevalence and associated factors of diabetic retinopathy. The Beijing Eye Study 2006. Graefes Arch Clin Exp Ophthalmol 2008;246(11):1519-26.
DR_C33	Xie XW, Xu L, Jonas JB, Wang YX. Prevalence of diabetic retinopathy among subjects with known diabetes in China: the Beijing Eye Study. EUR J OPHTHALMOL 2009;19(1):91-9.
DR_C34	Wang FH, Liang YB, Peng XY, et al. Risk factors for diabetic retinopathy in a rural Chinese population with type 2 diabetes: the Handan Eye Study. ACTA OPHTHALMOL 2011;89(4):e336-43.
DR_C35	Wang B, Liu M, Li X, et al. Cutoff Point of HbA1c for Diagnosis of Diabetes Mellitus in Chinese Individuals. PLOS ONE 2016;11(11):e166597.
PHCM-based studies	

Study ID	Reference
DR_P1	Li-ping Liu, Ji-wei Zhu, Yi Xiong, et al. 刘丽萍, 朱吉伟, 熊毅, 陈雁, 黄红儿. The prevalence and related factors of diabetic retinopathy in Shanghai Songnan community (上海市淞南社区糖尿病居民中糖尿病视网膜病变患病率及其影响因素调查分析)[J]. Chin J Ocul Dundus Dis (中华眼底病杂志). 2015;31(2):126-9.
DR_P2	Chen Liang, Rong Shi, Jing-fen Zhu, et al. 梁辰, 施榕, 朱静芬, et al. Prevalence of diabetic retinopathy of type 2 diabetes mellitus patients in Shanghai Pudong New Area and influencing factors (上海市浦东新区社区 2 型糖尿病患者糖尿病性视网膜病变的患病情况及影响因素调查)[J]. Chinese General Practice (中国全科医学). 2016(04):474-8.
DR_P3	Xiao-hua Zhang, Cheng-jun Liu, Wei Zhou, et al. 章小花, 刘成军, 周伟, et al. Survey and analysis on diabetic retinopathy and its factors among type 2 diabetic patients in the Southern Suburb of Pudong New Area (浦东新区南郊 2 型糖尿病患者视网膜病变及相关因素调查分析)[J]. Chinese Primary Health Care (中国初级卫生保健). 2016(04):52-4.
DR_P4	Xu J, Wei WB, Yuan MX, et al. Prevalence and risk factors for diabetic retinopathy: the Beijing Communities Diabetes Study 6. Retina 2012;32(2):322-9.
DR_P5	Pan CW, Wang S, Qian DJ, Xu C, Song E. Prevalence, Awareness, and Risk Factors of Diabetic Retinopathy among Adults with Known Type 2 Diabetes Mellitus in an Urban Community in China. Ophthalmic Epidemiol 2017;24(3):188-94.
Registry-based study	
DR_R1	Wei-jie Wang, Yi-nan Liu, Yu-jie Yan, et al. 王伟杰, 刘奕男, 严玉洁, 姚保栋, 周凡, 郦伦强. The investigation of risk factors of diabetic retinopathy in type 2 diabetes mellitus in Minhang, Shanghai (上海市闵行区 2 型糖尿病患者糖尿病视网膜病变患病率及相关危险因素分析)[J]. Chinese Primary Health Care (中国初级卫生保健). 2015(08):66-8.

Note: The Chinese publication list employed the journals' official English names or abbreviations, English titles were obtained from journals or literature databases (CNKI, Wanfang and CBM); Where official English translation of journal names is not available, a pinyin title is adopted; where the English translation of titles is not available, I translated the titles, labelled with "" and marked as green; PHCM, Primary Health Care Management.*

Appendix table 31. Detailed characteristics of the included studies on the prevalence of and risk factors for DR in China (n=41)

Study ID	Study	Province	Region	Study Year	Sex	Urban/ Rural	Grading system of DR	For Prevalence analysis	For risk factor analysis	General sample size	Diabetic sample size	Any DR	NPDR	PDR
Community-based studies														
DR_C1	Zhang XM et al. (1996)	Guangxi	South Central China	1994	Both	Mixed	NCOFD	Yes	No	11866	275	27	26	1
DR_C2	He SZ et al. (1997)	Beijing	North China	1994*	Both	Urban	NOFDG	Yes	Yes	29938	534	90	88	2
DR_C3	Li SL et al. (1998)	Anhui	East China	1994	Mixed	Mixed	NCOFD	Yes	No	11618	216	67	-	-
DR_C4	Li N et al. (1999)	Xinjiang	Northwest China	1995	Mixed	Urban	CMB	Yes	No	-	276	54	52	2
DR_C5	Wang GL et al. (2001)	Beijing	North China	1994	Mixed	Mixed	NCOFD	Yes	No	20682	293	33	28	5
DR_C6	Yang X et al. (2004)	Xinjiang	Northwest China	2000	Mixed	Urban	NCOFD	Yes	No	6542	224	26	-	-
DR_C7	Liu JP (2006)	Tianjin	North China	2005	Both	Mixed	ICDRDSS	Yes	No	23212	650	106	102	4
DR_C8	Hu HY et al. (2007)	Shanghai	East China	2006	Both	Urban	ICDRDSS	No	Yes	-	672	154	145	9
DR_C9	Dong B et al. (2008)	Guangdong	South Central China	2005*	Mixed	Urban	NCOFD	Yes	No	5731	196	22	-	-
DR_C10	Liu L (2009)	Liaoning	Northeast China	2007	Both	Urban	NCOFD	Yes	Yes	1534	137	17	17	0

Study ID	Study	Province	Region	Study Year	Sex	Urban/ Rural	Grading system of DR	For Prevalence analysis	For risk factor analysis	General sample size	Diabetic sample size	Any DR	NPDR	PDR
DR_C11	Zhang HX et al. (2009)	Shanghai	East China	2005	Both	Urban	ICDRDSS	Yes	Yes	-	642	78	76	2
DR_C12	Xin Z et al. (2010)	Beijing	North China	2008	Mixed	Rural	ICDRDSS	Yes	Yes	1293	114	27	25	2
DR_C13	Wang HB et al. (2010)	Shanxi	North China	2008	Mixed	Rural	NOFDG	Yes	No	57500	2632	986	-	-
DR_C14	Shu XW et al. (2010)	Shandong	East China	2007	Both	Rural	ICDRDSS	Yes	No	16330	689	181	136	45
DR_C15	Gao LT (2011)	Liaoning	Northeast China	2009	Both	Urban	NCOFD	Yes	No	740	66	6	-	-
DR_C16	Li BZ et al. (2011)	Beijing	North China	2007	Both	Mixed	ICDRDSS	Yes	No	4167	445	130	124	6
DR_C17	Hu YD (2011)	Liaoning	Northeast China	2007	Both	Mixed	ETDRS	Yes	Yes	3201	339	57	-	-
DR_C18	Liu QX et al. (2012)	Ningxia	Northwest China	2009*	Mixed	Mixed	ICDRDSS	Yes	No	3001	76	13	-	-
DR_C19	Zhang J (2012)	Sichuan	Southwest China	2011	Both	Urban	NCOFD	Yes	Yes	7478	1374	214	194	20
DR_C20	Yuan MX et al. (2012)	Beijing	North China	2010	Mixed	Mixed	ICDRDSS	Yes	No	8155	614	61	59	2
DR_C21	Cui Y (2013)	Guangdong	South Central China	2012	Both	Rural	ICDRDSS	Yes	Yes	8592	1310	235	-	-
DR_C22	Li N et al. (2013)	Beijing	North China	2010	Both	Urban	ETDRS	No	Yes	-	1100	353	300	53
DR_C23	Xie TH et al. (2013)	Jiangsu	East China	2010	Both	Urban	ICDRDSS	Yes	No	6150	663	36	34	2

Study ID	Study	Province	Region	Study Year	Sex	Urban/ Rural	Grading system of DR	For Prevalence analysis	For risk factor analysis	General sample size	Diabetic sample size	Any DR	NPDR	PDR
DR_C24	Wu PC et al. (2014)	Qinghai	Northwest China	2012	Mixed	Rural	NCOFD	Yes	No	2511	12	5	-	-
DR_C25	Mou XY et al. (2014)	Liaoning	Northeast China	2011*	Both	Rural	ICDRDSS	Yes	Yes	-	603	219	217	2
DR_C26	Shao L et al. (2014)	Beijing	North China	2011	Mixed	Mixed	ETDRS	Yes	No	3468	246	23	-	-
DR_C27	Jiang XF et al. (2015)	Jiangxi	East China	2012	Both	Urban	ICDRDSS	Yes	Yes	9776	730	223	-	-
DR_C28	Wang WC et al. (2015)	Hebei	North China	2011	Mixed	Urban	ICDRDSS	No	Yes	1447	396	212	149	63
DR_C29	Ye BL et al. (2016)	Guangdong	South Central China	2011	Both	Urban	ETDRS	Yes	Yes	3751	286	82	57	25
DR_C30	Hu BJ et al. (2016)	Xinjiang	Northwest China	2014	Mixed	Mixed	ETDRS	Yes	No	7462	618	77	76	1
DR_C31	Zhang GS et al. (2017)	Inner Mongolia	North China	2014	Both	Mixed	NOFDG	Yes	No	3967	352	26	25	1
DR_C32	Xie XW et al. (2008)	Beijing	North China	2006	Both	Mixed	ETDRS	Yes	Yes	3251	362	101	-	-
DR_C33	Xie XW et al. (2009)	Beijing	North China	2001	Mixed	Mixed	ETDRS	No	Yes	4127	232	86	-	-
DR_C34	Wang FH et al. (2011)	Hebei	North China	2007	Both	Rural	ETDRS	Yes	No	5597	368	165	-	-
DR_C35	Wang B et al. (2016)	Liaoning	Northeast China	2011	Mixed	Urban	ICDRDSS	Yes	No	8391	1809	233	-	-
PHCM-based studies														

Study ID	Study	Province	Region	Study Year	Sex	Urban/ Rural	Grading system of DR	For Prevalence analysis	For risk factor analysis	General sample size	Diabetic sample size	Any DR	NPDR	PDR
DR_P1	Liu LP et al. (2015)	Shanghai	East China	2013	Both	Urban	ICDRDSS	No	Yes	-	1120	264	261	3
DR_P2	Liang C et al. (2016)	Shanghai	East China	2014	Both	Urban	ICDRDSS	No	Yes	-	2083	445	-	-
DR_P3	Zhang XH et al. (2016)	Shanghai	East China	2013*	Both	Urban	ICDRDSS	No	Yes	-	1437	151	147	4
DR_P4	Xu J et al. (2012)	Beijing	North China	2009	Both	Urban	ETDRS	No	Yes	-	2007	496	429	67
DR_P5	Pan CW et al. (2017)	Jiangsu	East China	2015	Both	Urban	ETDRS	No	Yes	-	880	158	-	-
Registry-based study														
DR_R1	Wang WJ et al. (2015)	Shanghai	East China	2012*	Both	Urban	ICDRDSS	No	Yes	-	2152	736	687	49

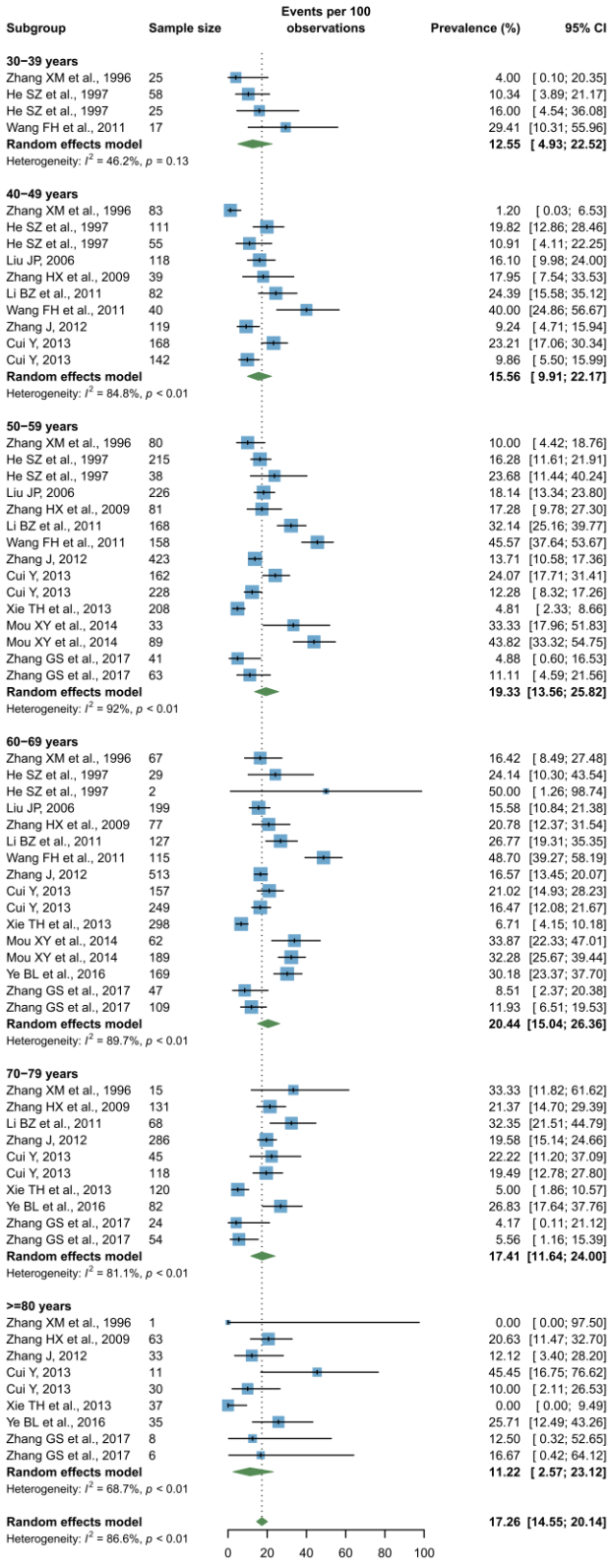
Note: "-" represents unavailable data; "" indicates studies whose survey year was imputed. PHCM, Primary Health Care Management; NCOFD, National Conference on Ocular Fundus Diseases; NOFDG, National Ocular Fundus Diseases Group; CBM, China Medical Board; ICDRDSS, International Clinical Diabetic Retinopathy Disease Severity Scale; ETDRS, Early Treatment of Diabetic Retinopathy Study.*

Appendix table 32. Risk of bias scores of the included studies on the prevalence of and risk factors for DR in China (n=41)

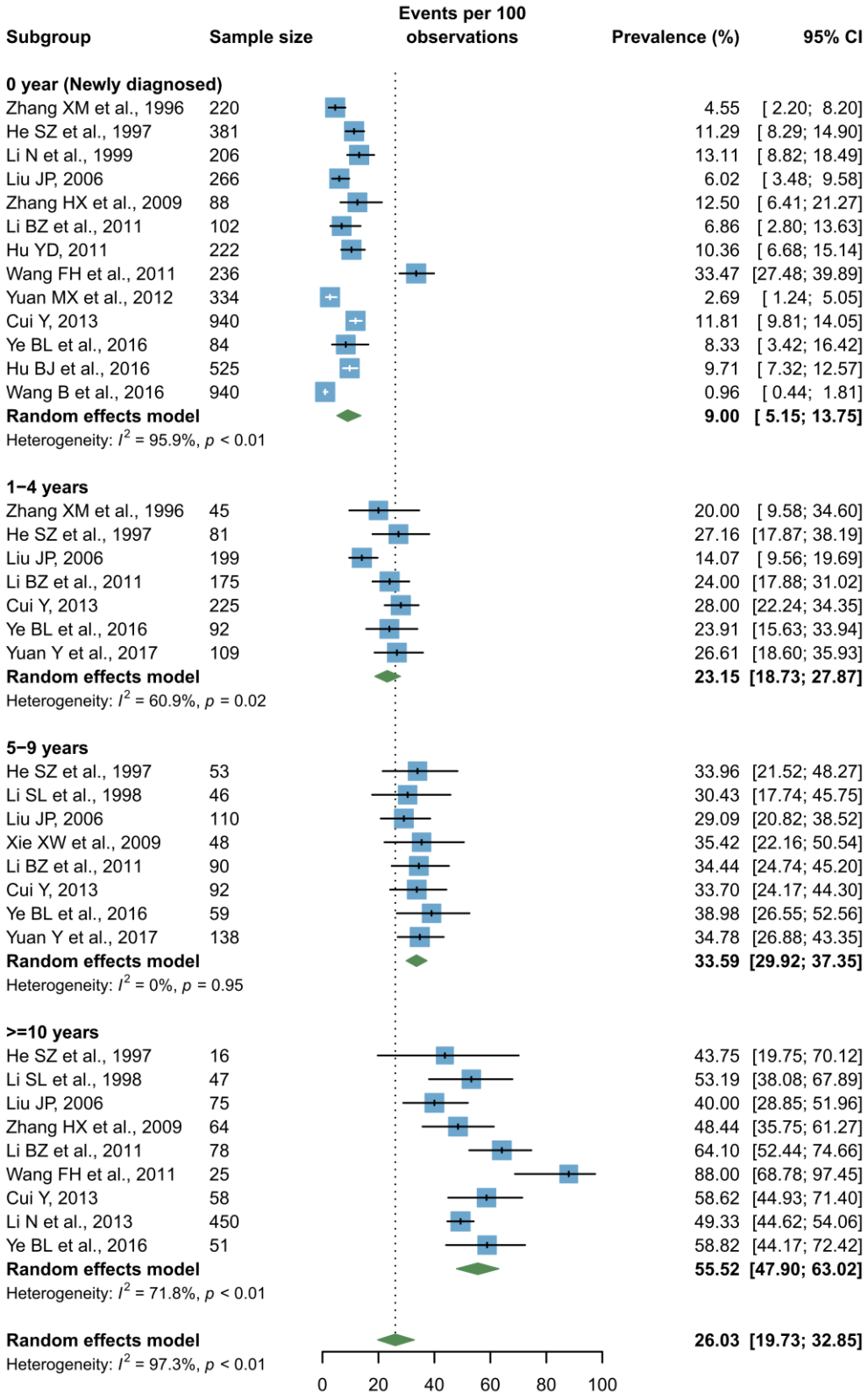
Study ID	Study	Quality score					
		Sample population	Sample size	Participation	Outcome assessment	Analytical methods	Total scores
DR_C1	Zhang XM et al. (1996)	2	1	0	2	2	7
DR_C2	He SZ et al. (1997)	1	1	2	2	2	8
DR_C3	Li SL et al. (1998)	2	1	2	2	2	9
DR_C4	Li N et al. (1999)	1	1	0	2	2	6
DR_C5	Wang GL et al. (2001)	2	1	2	2	2	9
DR_C6	Yang X et al. (2004)	2	1	0	2	2	7
DR_C7	Liu JP (2006)	2	2	0	1	1	6
DR_C8	Hu HY et al. (2007)	2	1	0	2	2	7
DR_C9	Dong B et al. (2008)	1	1	0	2	2	6
DR_C10	Liu L (2009)	2	1	0	2	2	7
DR_C11	Zhang HX et al. (2009)	2	1	0	2	2	7
DR_C12	Xin Z et al. (2010)	2	1	0	2	2	7
DR_C13	Wang HB et al. (2010)	1	1	2	2	2	8
DR_C14	Shu XW et al. (2010)	2	1	0	2	2	7
DR_C15	Gao LT (2011)	1	1	0	2	2	6
DR_C16	Li BZ et al. (2011)	2	2	2	2	2	10
DR_C17	Hu YD (2011)	2	1	2	2	2	9
DR_C18	Liu QX et al. (2012)	2	2	0	2	2	8

Study ID	Study	Quality score					
		Sample population	**Sample size**	**Participation**	**Outcome assessment**	**Analytical methods**	**Total scores**
DR_C19	Zhang J (2012)	2	1	2	2	2	9
DR_C20	Yuan MX et al. (2012)	2	1	0	2	2	7
DR_C21	Cui Y (2013)	2	1	1	2	2	8
DR_C22	Li N et al. (2013)	1	1	0	2	2	6
DR_C23	Xie TH et al. (2013)	2	1	2	2	2	9
DR_C24	Wu PC et al. (2014)	2	2	0	2	2	8
DR_C25	Mou XY et al. (2014)	2	1	0	2	2	7
DR_C26	Shao L et al. (2014)	2	1	1	2	2	8
DR_C27	Jiang XF et al. (2015)	2	1	2	2	2	9
DR_C28	Wang WC et al. (2015)	2	1	2	2	2	9
DR_C29	Ye BL et al. (2016)	2	2	2	2	2	10
DR_C30	Hu BJ et al. (2016)	2	2	0	2	2	8
DR_C31	Zhang GS et al. (2017)	2	2	2	2	2	10
DR_C32	Xie XW et al. (2008)	2	1	2	2	2	9
DR_C33	Xie XW et al. (2009)	2	1	2	2	2	9
DR_C34	Wang FH et al. (2011)	2	1	1	2	2	8
DR_C35	Wang B et al. (2016)	1	1	0	2	2	6
DR_P1	Liu LP et al. (2015)	1	1	2	2	2	8
DR_P2	Liang C et al. (2016)	1	1	0	2	2	6

Study ID	Study	Quality score					
		Sample population	**Sample size**	**Participation**	**Outcome assessment**	**Analytical methods**	**Total scores**
DR_P3	Zhang XH et al. (2016)	1	1	2	2	2	8
DR_P4	Xu J et al. (2012)	1	1	0	2	2	6
DR_P5	Pan CW et al. (2017)	2	1	0	2	2	7
DR_R1	Wang WJ et al. (2015)	1	2	2	2	2	9



Appendix figure 14. The prevalence of any DR in people with DM in different age groups, by random-effects meta-analysis



Appendix figure 15. The prevalence of any DR in people with DM in different DM duration groups, by random-effects meta-analysis

Appendix table 33. Full list of studies reporting risk factors for DR in China (n=21)

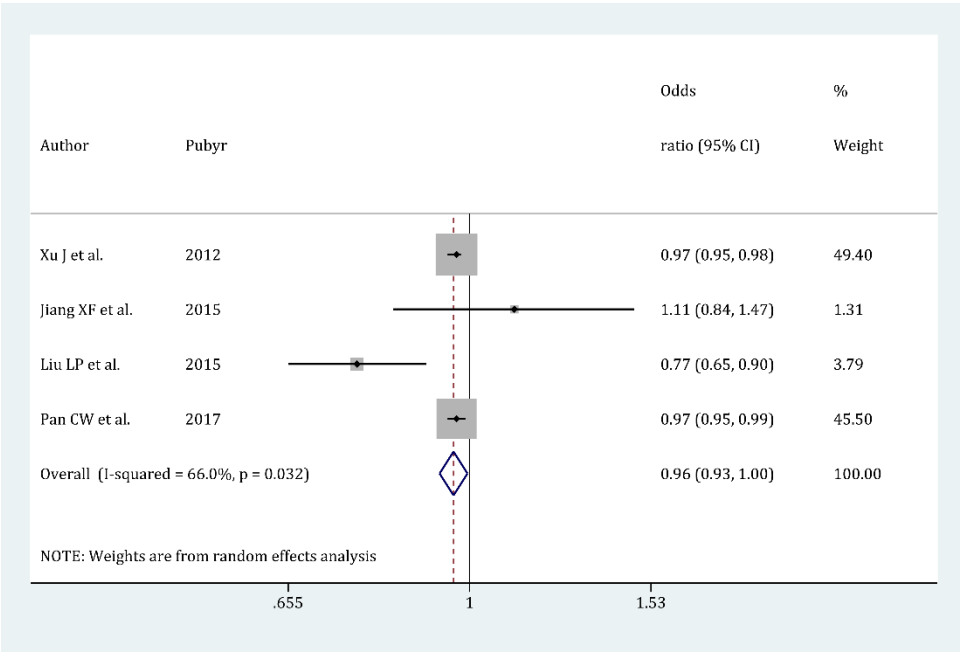
Study ID	Study	Reported risk factor
DR_P2	He SZ et al. (1997)	DM_Duration (per year), Dietary control, FBG (mmol/l), HbA1c (%), Scr, Ucr, TC (mmol/l), TG (mmol/l)
DR_P8	Hu HY et al. (2007)	DM_Duration (per year), FBG (mmol/l)
DR_P10	Liu L (2009)	DM_Duration group comparison (>10 vs. <5), FBG (mmol/l), BMI (kg/m^2), Drinking
DR_P12	Xin Z et al. (2010)	DM_Duration (per year), FBG (mmol/l), SBP (mmHg)
DR_P19	Li BZ et al. (2011)	DM_Duration (per year), FBG (mmol/l), BMI (kg/m^2), Education (literacy vs. illiteracy), Insulin treatment
DR_P21	Hu YD (2011)	DM history, Income
DR_P23	Zhang J (2012)	DM_Duration (per year), HbA1c (%), HDL (mmol/l), Hypertension
DR_P28	Cui Y (2013)	DM_Duration group comparison (>=10 vs. 0), FBG level group comparison (>=7.0 vs. <5.6), HbA1c level group comparison (>=6.5 vs. <6.5), SBP level group comparison (>=140 vs. <120), Male sex
DR_P29	Li N et al. (2013)	DM_Duration group comparison (>=10 vs. <10), HbA1c level group comparison (>=7.0 vs. <7.0), Low-education, Insulin treatment, Low income, Male sex
DR_P34	Mou XY et al. (2014)	DM_Duration (per year), FBG (mmol/l), BMI (kg/m^2), Insulin treatment, Weight (kg), Hyperlipidemia
DR_P36	Jiang XF et al. (2015)	Age (per year), DM_Duration group comparison (>10 vs. <=5), 2h-PBG, TC (mmol/l), TG (mmol/l), BMI (kg/m^2), SBP (mmHg), DBP (mmHg), Male sex, 24h UP (mg.d)
DR_P37	Wang WC et al. (2015)	Age group comparison (>65 vs. 45-65), FBG (mmol/l), 2h-PBG, HbA1c (%), TG (mmol/l), BMI (kg/m^2), WHR, DM family history, Male sex, Tear TFN-α (ng/l), Blood TFN-α (ng/l)
DR_P38	Ye BL et al. (2016)	DM_Duration group comparison (per year increase vs. 0), FBG (mmol/l), Education (literacy vs. illiteracy), Insulin treatment
DR_P43	Xie XW et al. (2008)	DM_Duration (per year), FBG (mmol/l), TC (mmol/l), SBP (mmHg), Insulin treatment vs. diet only, HDL (mmol/l), Rural, Hyperopic refractive error (per diopter)
DR_P44	Xie XW et al. (2009)	DM_Duration group comparison (>=20 vs. 5), Insulin treatment vs. diet only, Rural
DR_M7	Liu LP et al. (2015)	Age (per year), DM_Duration (per year), SBP (mmHg), Insulin treatment
DR_M9	Liang C et al. (2016)	Age of DM onset, DM_Duration (per year), 2h-PBG, HbA1c (%)
DR_M10	Zhang XH et al. (2016)	DM_Duration group comparison (>15 vs. <5), FBG level group comparison (>6.8 vs. <6.8)

Study ID	Study	Reported risk factor
DR_M13	Xu J et al. (2012)	Age (per year), DM_Duration (per year), HbA1c (%), BMI (kg/m^2), SBP (mmHg), BUN (mmol/l)
DR_M15	Pan CW et al. (2017)	Age (per year), DM_Duration (per year), HbA1c (%), Smoking, DM family history, Hypertension, Male sex
DR_R1	Wang WJ et al. (2015)	DM_Duration (per year), HbA1c (%)

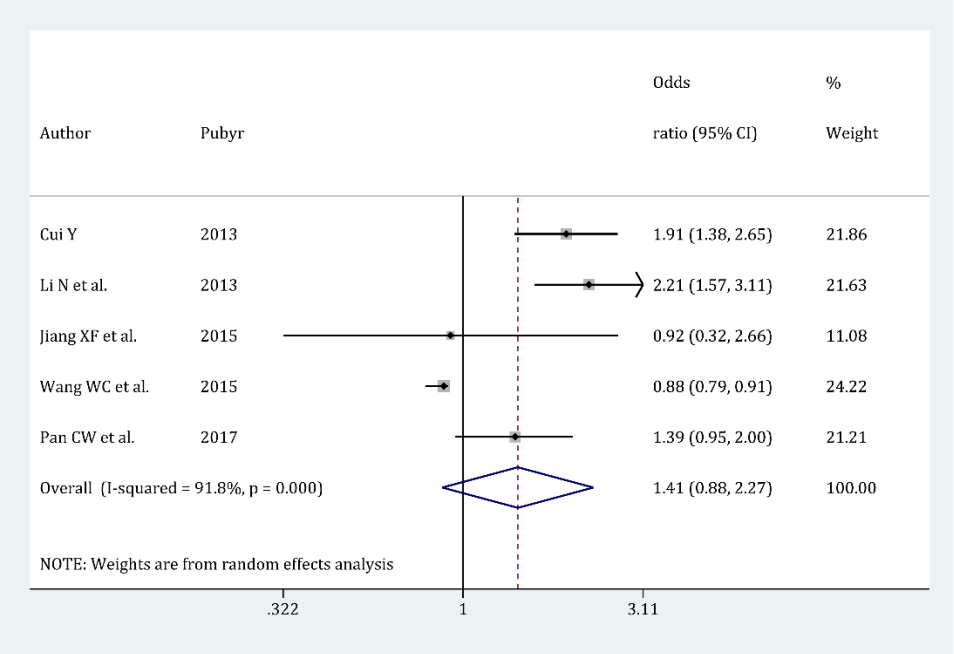
Note: DM, diabetes mellitus; FBG, fasting blood glucose; PBG, postprandial blood glucose; HbA1c, glycated haemoglobin A1c; Scr, serum creatinine; Ucr, urine creatinine; TC, total cholesterol; TG, triglyceride; BMI, body mass index; SBP, systolic blood pressure; HDL, high-density lipoprotein; DBP, diastolic blood pressure; UP, urine protein; WHR, waist-to-hip ratio; TFN-α, Tumour necrosis factor alpha; BUN, blood urea nitrogen. Some studies didn't specify the units for some specific risk factors, in circumstances where assumptions could not be made, risk factors without units were not included for subsequent meta-analyses.

Appendix table 34. Meta-analyses of 11 risk factors for any DR in people with DM

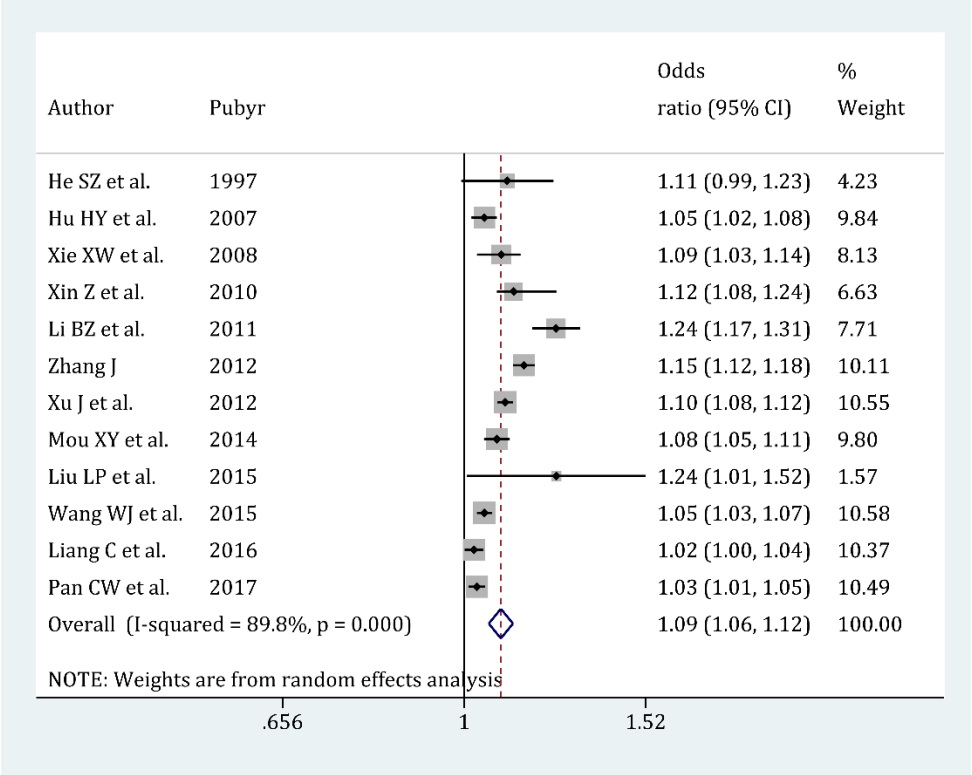
Risk factor 1-Advanced age (per year increase)



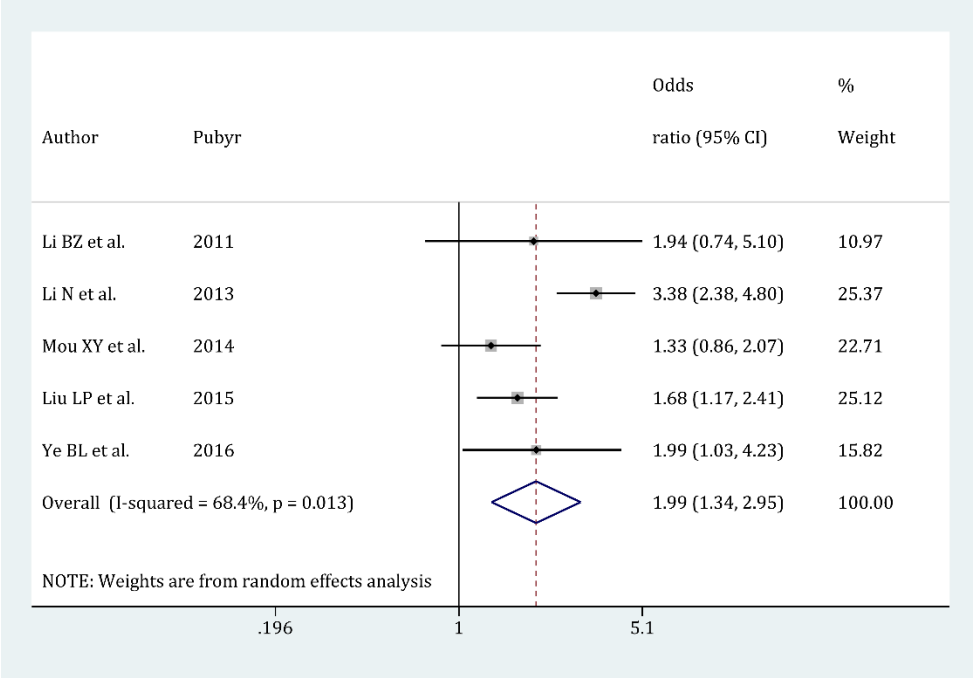
Risk factor 2-Male



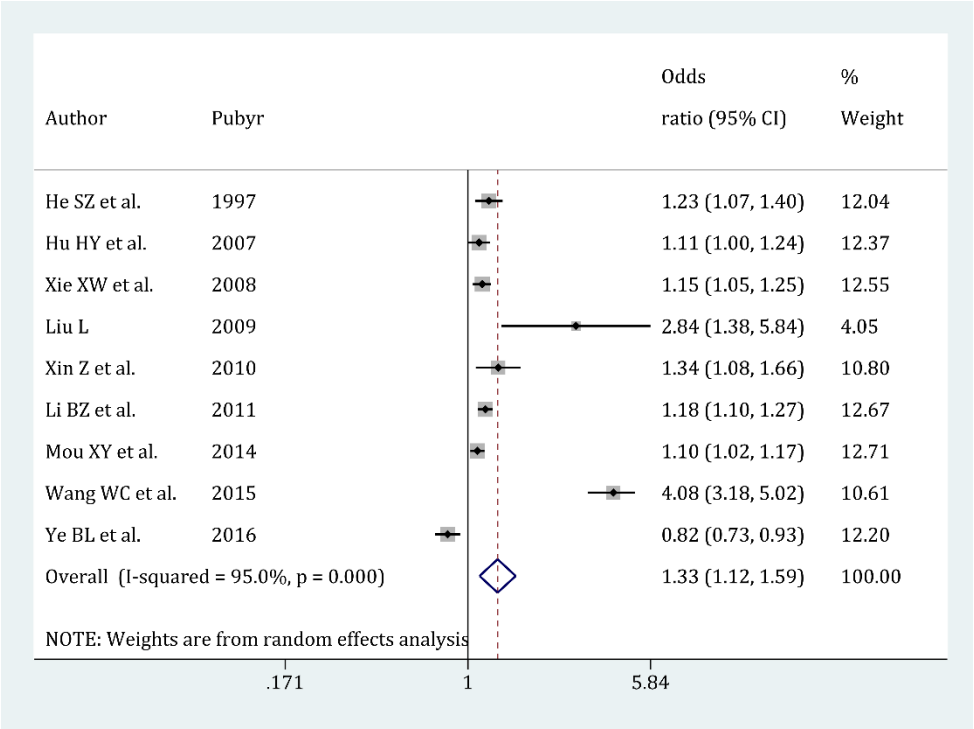
Risk factor 3-DM duration (per year increase)



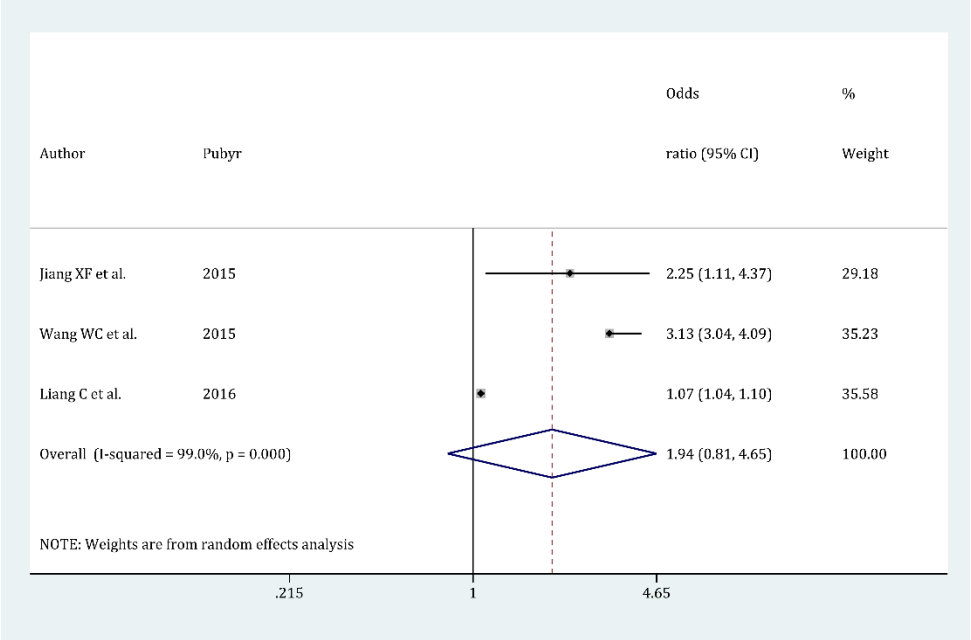
Risk factor 4-Insulin treatment



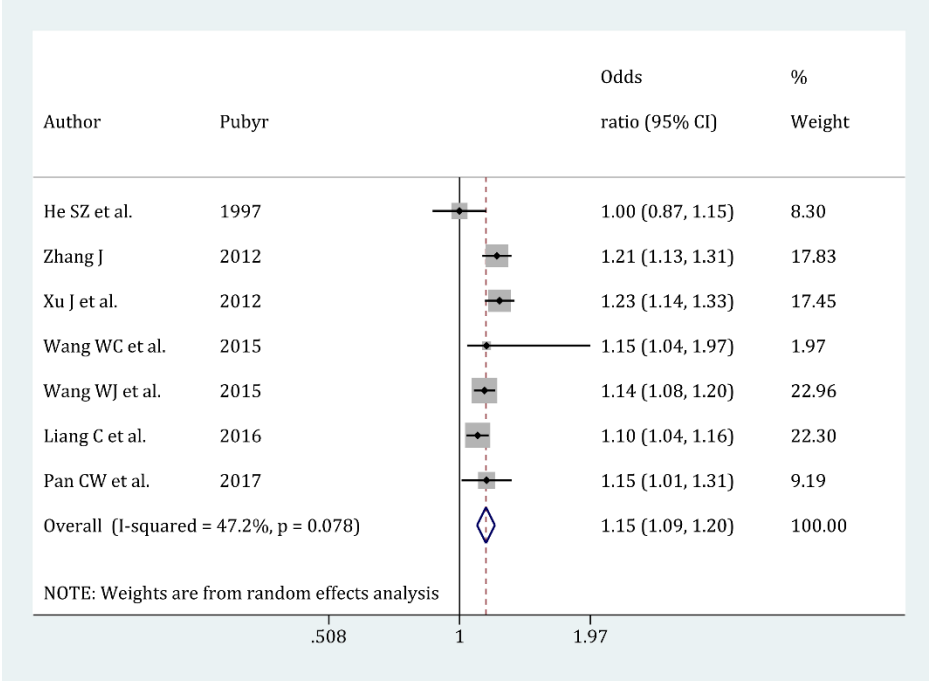
Risk factor 5-FBG (per mmol/l increase)



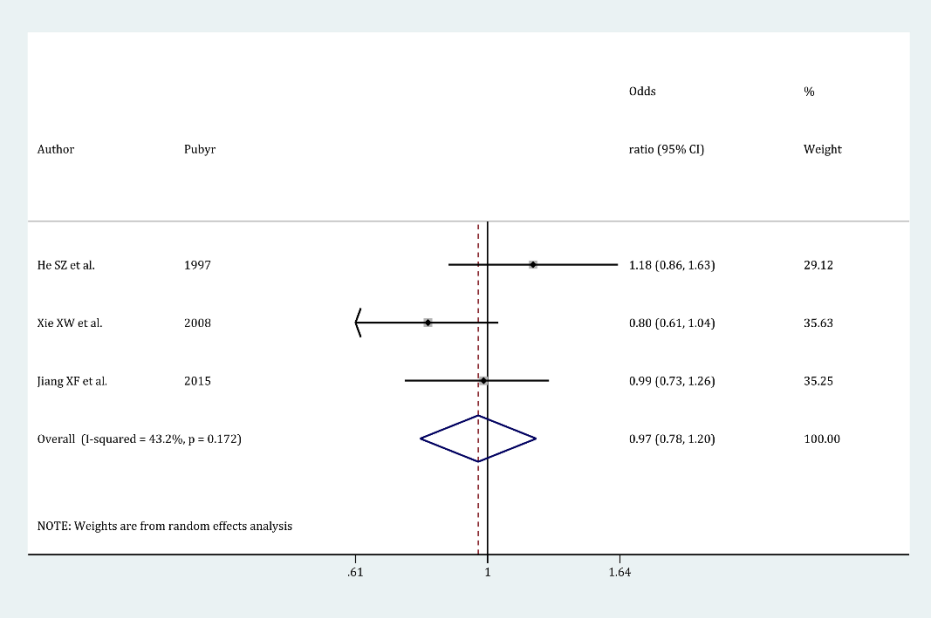
Risk factor 6-2h PBG (per mmol/l increase)



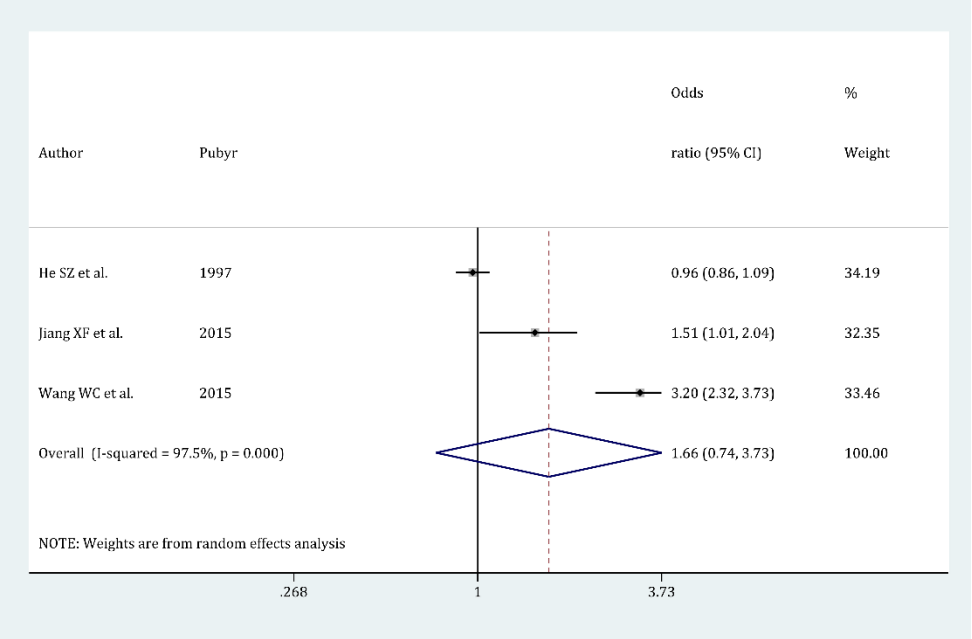
Risk factor 7-HbA1c (per % increase)



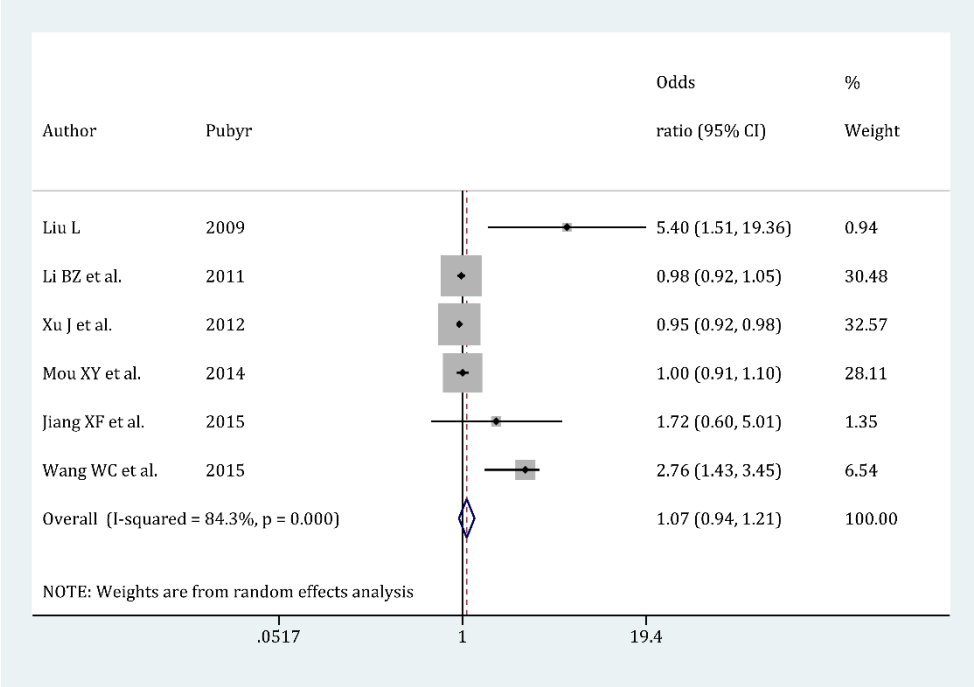
Risk factor 8-TC (per mmol/l increase)



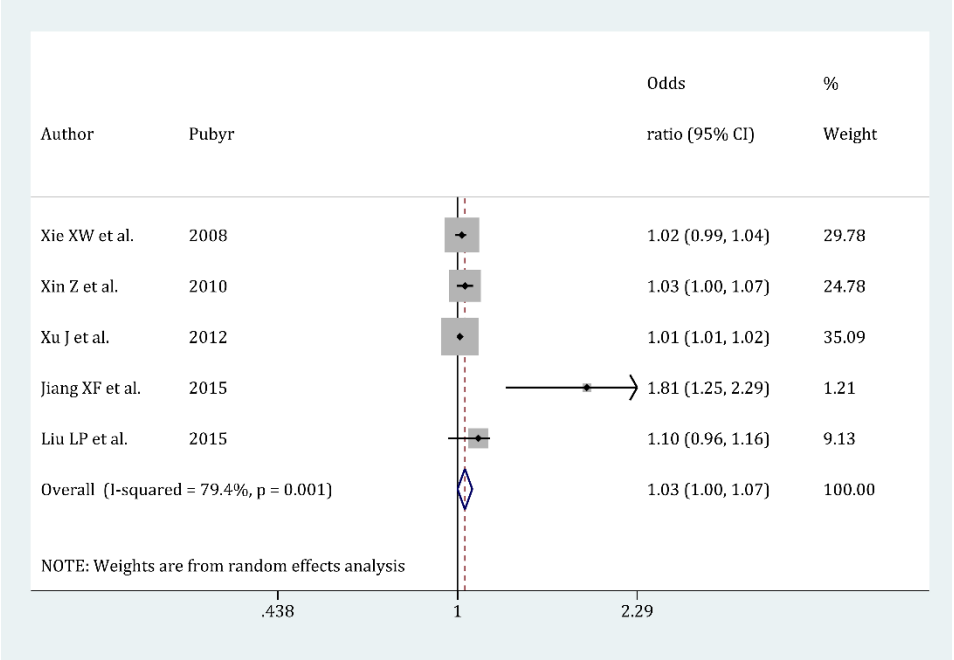
Risk factor 9-TG (per mmol/l increase)



Risk factor 10-BMI (per kg/m2 increase)



Risk factor 11-SBP (per mmHg increase)



Appendix table 35. Estimation of age-specific prevalence and number of middle-aged and older Chinese with any DR in China in 2010, by geographic region

Prevalence of any DR in general people (%, 95% CI)						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**
45-49 years	2.07 (1.32-2.95)	1.78 (1.14-2.54)	1.50 (0.95-2.13)	1.82 (1.16-2.59)	1.37 (0.87-1.95)	1.70 (1.08-2.42)
50-59 years	3.84 (2.69-5.13)	3.31 (2.32-4.42)	2.78 (1.95-3.71)	3.37 (2.36-4.50)	2.54 (1.78-3.39)	3.15 (2.21-4.21)
60-69 years	5.05 (3.72-6.52)	4.35 (3.20-5.61)	3.66 (2.69-4.71)	4.44 (3.26-5.72)	3.34 (2.46-4.31)	4.15 (3.05-5.35)
70-79 years	4.69 (3.13-6.47)	4.04 (2.70-5.57)	3.39 (2.27-4.68)	4.12 (2.75-5.68)	3.10 (2.07-4.27)	3.85 (2.57-5.31)
>=80 years	3.50 (0.80-7.22)	3.02 (0.69-6.22)	2.53 (0.58-5.22)	3.08 (0.70-6.34)	2.31 (0.53-4.77)	2.88 (0.66-5.93)
Total (>=45 years)	3.76 (2.56-5.12)	3.22 (2.20-4.39)	2.74 (1.86-3.76)	3.31 (2.25-4.54)	2.55 (1.74-3.48)	3.09 (2.12-4.20)
Prevalence of any DR in people with DM (%, 95% CI)						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**
45-49 years	15.75 (10.03-22.44)	16.07 (10.23-22.90)	15.12 (9.63-21.55)	15.38 (9.79-21.91)	15.93 (10.14-22.70)	16.42 (10.45-23.39)
50-59 years	19.56 (13.72-26.13)	19.96 (14.00-26.66)	18.79 (13.18-25.10)	19.10 (13.40-25.52)	19.79 (13.88-26.44)	20.39 (14.30-27.24)
60-69 years	20.68 (15.22-26.68)	21.11 (15.53-27.22)	19.87 (14.62-25.63)	20.20 (14.86-26.05)	20.93 (15.39-26.99)	21.56 (15.86-27.81)
70-79 years	17.62 (11.77-24.29)	17.98 (12.01-24.79)	16.92 (11.30-23.33)	17.20 (11.49-23.72)	17.82 (11.90-24.57)	18.37 (12.27-25.32)
>=80 years	11.35 (2.60-23.40)	11.59 (2.65-23.88)	10.91 (2.50-22.48)	11.09 (2.54-22.85)	11.49 (2.63-23.67)	11.84 (2.71-24.39)
Total (>=45 years)	18.54 (12.66-25.28)	18.93 (12.94-25.81)	17.67 (11.97-24.24)	17.97 (12.19-24.63)	18.73 (12.76-25.59)	19.39 (13.30-26.35)
Number of people with DR (million, 95% CI)						
Age group	**North China**	**Northeast China**	**East China**	**South Central China**	**Southwest China**	**Northwest China**

45-49 years	0.27 (0.17-0.38)	0.18 (0.11-0.26)	0.46 (0.29-0.65)	0.49 (0.31-0.70)	0.18 (0.12-0.26)	0.12 (0.08-0.17)
50-59 years	0.85 (0.60-1.13)	0.58 (0.41-0.77)	1.37 (0.96-1.84)	1.39 (0.98-1.86)	0.55 (0.39-0.74)	0.33 (0.23-0.44)
60-69 years	0.57 (0.42-0.73)	0.37 (0.27-0.48)	1.07 (0.79-1.38)	1.09 (0.80-1.41)	0.51 (0.38-0.66)	0.27 (0.20-0.34)
70-79 years	0.29 (0.19-0.40)	0.18 (0.12-0.25)	0.57 (0.38-0.79)	0.58 (0.39-0.81)	0.26 (0.17-0.35)	0.13 (0.09-0.18)
>=80 years	0.06 (0.01-0.13)	0.04 (0.01-0.08)	0.16 (0.04-0.33)	0.15 (0.03-0.31)	0.06 (0.01-0.13)	0.02 (0.01-0.05)
Total (>=45 years)	2.03 (1.39-2.77)	1.35 (0.92-1.84)	3.63 (2.46-4.98)	3.71 (2.52-5.09)	1.56 (1.07-2.14)	0.87 (0.60-1.18)