# Prevalence of Diabetic Retinopathy in Mainland China: A Meta-Analysis

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### Abstract

**Background:** Although diabetic retinopathy (DR) is considered to be a major cause of blindness, this is the first metaanalysis to investigate the pooled prevalence of DR in mainland China.

*Methodology/Principal Findings:* We conducted a search of all English reports on population-based studies for the prevalence of DR using Medline, EMbase, Web of Science, Google (scholar), and all Chinese reports were identified manually and on-line using CBMDisc, Chongqing VIP database, and CNKI database. A meta-analysis was carried out. The fixed effects model or random effects model was used as a statistical test for homogeneity. Nineteen studies were included. The prevalence of DR, non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) in the pooled general population was 1.3% (95%CI: 0.5%–3.2%), 1.1% (95%CI: 0.6%–2.1%), and 0.1% (95%CI: 0.1%–0.3%), respectively, but was 23% (95%CI: 17.8%–29.2%), 19.1% (95%CI: 13.6%–26.3%), and 2.8% (95%CI: 1.9%–4.2%) in the diabetic group. The prevalence rate of DR in the pooled rural population was higher than that in the urban population, 1.6% (95%CI: 1.3%–2%), and the diabetic population, 29.1% (95%CI: 20.9%–38.9%). The prevalence of DR was higher in the Northern region compared with the Southern region.

*Conclusions/Significance:* The prevalence of DR in mainland China appeared a little high, and varied according to area. NPDR was more common. This study highlights the necessity for DR screening in the rural areas of China.

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#### Introduction

Diabetic retinopathy (DR) is one of the foremost causes of blindness in the working age population [1]. As the prevalence of diabetes mellitus (DM) increases globally and patients live longer, the development of DR as a microvascular complication of DM also rises. DR is a priority disease in the "VISION 2020" initiative for the global elimination of avoidable blindness. The World Health Organization (WHO) has recommended its member countries integrate a program approach for DR within their prevention of blindness programs. In contrast to studies in Western countries, age-related macular degeneration (AMD) and DR appear to play a minor role as a cause of visual impairment in elderly Chinese [2].

In mainland China, many previous reports have shown the prevalence of DR in population-based studies, however, the prevalence of DR varies in different samples, and the data remain limited and localized. To date, there is no national, population-based study of the prevalence of DR in mainland China, and it would seem that a national, pooled estimate based on the

mainland population is necessary. Satisfactory and reasonable prevalence estimates will be useful for China to manage this problem. In this meta-analysis, we carried out a systematic review of previous population-based studies on DR prevalence in mainland China, and investigated any differences among areas. The results are presented here.

#### Methods

#### Search Strategy

We searched all English reports on population-based studies for the prevalence of DR using Medline, EMbase, Web of Science, Google (scholar), and all Chinese reports were searched manually and on-line using CBMDisc (Chinese Biochemical Literature on Disc), Chongqing VIP database, and CNKI (China National Knowledge Infrastructure) database. The search keywords were: diabetic retinopathy, prevalence, and Chinese population. A total of 196 reports published in the period from 1991 to 2012 were identified.

#### Inclusion and Exclusion Criteria

Reports potentially eligible for inclusion in this meta-analysis had to meet the following criteria: they had to be population-based studies, subjects had to be in mainland China, and the studies needed to provide sufficient information to estimate the pooled prevalence of DR. If more than one study was based on the same population sample, the study of the highest quality was included. Reports were excluded for the following reasons: the study was on a duplicate population group but of lower quality, and the study did not satisfy one or more inclusion criteria. A total of 196 potentially relevant studies were identified and screened. After systematic review, only 19 of these were included in the metaanalysis. The progress for study inclusion is shown in Figure 1.

#### Data Extraction

The literature was searched independently by two researchers (Lei Liu and Jin Geng). Data were extracted from each article

using a standardized form, designed in advance. The characteristics of the population-based studies included in this meta-analysis on the pooled prevalence of DR in mainland China are shown in Table 1.

#### Data Analysis

Meta-analyst statistical software offered by http://tuftscaes.org/ meta\_analyst/was used to analyze the data. The pooled prevalence was used to estimate the prevalence of DR in China mainland. All meta-analyses were evaluated for heterogeneity using the Chi-square based Q test and  $I^2$  test [3].  $I^2$  estimated the percentage of the total variance in all of the data under consideration that was related to heterogeneity. The authors suggested using 25%, 50%, and 75% to indicate low, moderate, or high level heterogeneity. If there was moderate or high level heterogeneity, a random-effects meta-analysis was performed by the DerSimonian and Laird method, unless using fixed-effects

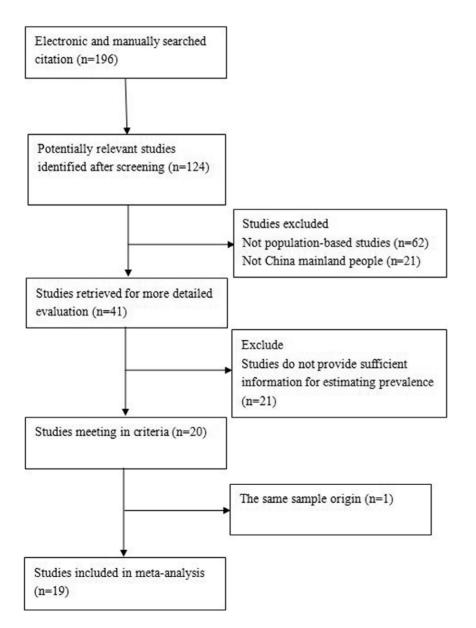


Figure 1. Flow chart demonstrating those studies that were processed for inclusion in the meta-analysis. doi:10.1371/journal.pone.0045264.g001

Table 1. Characteristics of population-based studies on the prevalence of diabetic retinopathy (DR) in mainland China.

First Author	Publication year	Area	Region	Rural/Urban	Examination methodolo gies for DR	Diagnosis standard for DR	Diagnosis standard for DM	Age (year)	Survey day	Sample (n)	M C L	i	DR (n)
											to	total NPDR	DR PDR
Yinghua HU [17]	1991	Daqing	Northern	Urban	MDOC+fundus photography	NA	ОНМ	25-74	1986	110660	423 129	9 119	10
Shouzhi He [18]	1997	Beijing	Northern	Urban	MDOC+FFA	Staging of DR for Chinese*	ОНМ	>30	NA	29938	534 90	88	3
Shouling Li [19]	1998	Anhui	Southern	Rural+Urban	MDOC	Staging of DR for Chinese*	ОНМ	~15	1994–1995	11618	216 67	NA	NA
Guanglu Wang [20]	2001	Beijing	Northern	Rural+Urban	MDOC	NA	МНО	≥25	1994–1995	1483	326 37	30	7
Haidong Zhou [21]	2006	Shanghai	Southern	Urban	NMFP for 45 digree field	Staging of DR for Chinese*	NA	44-87	Jul 2003–Apr 2004	43762	535 146	6 123	23
Xianjun Liang [22]	2006	Foshan	Southern	Urban	MDOC	NA	ОНМ	>18	2003-2005	10723	356 38	NA	NA
Xiwei Xie [23]	2009	Beijing	Northern	Rural+Urban	MFP for 50 digree field	ETDRS	Self-reported history	>40	2001	4391	434 285	5 273	12
Lei Liu [24]	2009	Shenyang	Northern	Urban	NMFP for 45 digree field	ETDRS	ОНМ	14-82	Oct-Dec 2007	1534	137 17	17	NA
Xiangwen Shu [25]	2010	Shandong	Northern	Rural	MDOC	ETDRS	МНО	>25	2007-2008	16330	689 181	1 107	74
Zhong Xin [26]	2010	Beijing	Northern	Rural	MFP for seven field	Proposed international severity scales**	ОНМ	>35	May-Jul 2008	1293	114 27	25	2
Yan Teng [27]	2010	Shuangcheng	Northern	Rural	MFP for 45 digree field	Staging of DR for Chinese*	ОНМ	>50	Nov 2006–Feb 2007	5053	NA 56	49	7
Hailian Dong [28]	2010	Shunyi	Northern	Rural	NMFP for three field		NA	>18	Jan-Dec 2009	5734	554 94	. 76	18
Mingzhu Ynag [29]	2010	Shijiazhuang	Northern	Urban	MDOC	Staging of DR for Chinese*	ОНМ	35-80	Sep 2006-Sep 2008	3318	381 87	69	18
Hongbo Wang [30]	2010	Changzhi	Northern	Rural	NMFP for 45 digree field	Staging of DR for Chinese*	ОНМ	>15	Oct 2007-Dec 2008	57500	2632 986	6 NA	NA
Xiuqun Ye [31]	2010	Huizhou	Southern	Urban	MDOC+fundus photography+FFA	ETDRS	ОНМ	>20	2003-2005	11723	1046 101	1 71	30
Fenghua Wang [32]	2011	Handan	Northern	Rural	MFP for two field	ETDRS	self-reported history and FPG	>30	2006–2007	6830	368 165	5 145	20
Bingzhen Li [33]	2011	Beijing Shunyi Northern	Northern	Urban	NMFP for one field	ETDRS	ОНМ	≥40	May-Oct 2005	4167	445 130	0 124	9
Can Pang [34]	2011	Shanghai	Southern	Urban	NMFP for 45 digree field	Diabetic Retinopathy Disease Severity Scale	ОGIT	~ 15	1996–2007	3259	799 75	74	-
Jie Xu [35]	2012	Beijing	Northern	Urban	NMFP for 45 digree field	ETDRS	ОНМ	20-80	August 2008- July 2009	NA	2007 496	6 329	67

models. Publication bias was assessed by visually inspecting a funnel plot. A p value less than 0.05 was considered statistically significant [4,5]. The results were analyzed statistically using the  $\chi^2$  (Chi-square) test with the SPSS 13.0 program (SPSS Software, Chicago, USA) to compare the difference between two groups with different prevalence rates.

#### Results

The prevalence of DR, NPDR and PDR in the pooled general population was 1.3% (95%CI: 0.5%-3.2%), 1.1% (95%CI: 0.6%-2.1%), and 0.1% (95%CI: 0.1%-0.3%), respectively, but was 23% (95%CI: 17.8%-29.2%), 19.1% (95%CI: 13.6%-26.3%), and 2.8% (95%CI: 1.9%-4.2%) in the diabetic group. The pooled prevalence rates of DR were higher in the rural population, 1.6% (95%CI: 1.3%-2%), compared with the urban population, 0.8% (95%CI: 0.3%-1.7%), ( $\chi^2 = 771.35$ , p < 0.001), and higher in the rural diabetic group, 29.1% (95%CI: 20.9%-38.9%) compared with the urban diabetic group, 18.1% (95%CI: 13.6%-23.7%)

 $(\chi^2 = 263.37, p < 0.001)$ . In the general population, the pooled prevalence of DR was higher in the Northern region of China, 1.4% (95%CI: 0.8%–2.5%), compared with the Southern region, 0.7% (95%CI: 0.3%–1.4%), ( $\chi^2 = 115.91, p < 0.001$ ). In the diabetic group, the pooled prevalence of DR in the Northern region of China, 26.5% (95%CI: 20.6%–33.3%), was also higher compared with the Southern region, 15.7% (95%CI: 8.9%–26.3%) ( $\chi^2 = 281.61, p < 0.001$ ). The data are shown in Figure 2, 3, and 4, and Table 2.

All comparisons passed the test of heterogeneity, as previously defined Random-effects models were used for meta-analyses. There was no significant publication bias in this meta-analysis. The funnel plot of prevalence of DR in diabetes is shown in Figure 5.

#### Discussion

To our knowledge, this is the first meta-analysis of DR prevalence in mainland China. In this meta-analysis, a total of

Study Name	Ν	4	Confidence Interval
Yinghua HU (1991)	110660		0.001 (0.001, 0.001)
Shouzhi He (1997)	29938		0.003 (0.002, 0.004)
Shouling Li (1998)	11618		0.006 (0.005, 0.007)
Guanglu Wang (2001)	1483		0.025 (0.018, 0.034)
Haidong Zhou (2006)	43762		0.003 (0.003, 0.004)
Xianjun Liang (2006)	10723		0.004 (0.003, 0.005)
Xiwei Xie (2009)	4391	=	0.065 (0.058, 0.073)
Lei Liu (2009)	1534		0.011 (0.007, 0.018)
Xiangwen Shu (2010)	16330		0.011 (0.010, 0.013)
Juan Wang (2010)	1293	=	0.083 (0.069, 0.099)
Zhong Xin (2010)	5053		0.005 (0.004, 0.008)
Yan Teng (2010)	5734		0.010 (0.008, 0.013)
Hailian Dong (2010)	3318		0.028 (0.023, 0.035)
Mingzhu Ynag (2010)	11723		0.007 (0.006, 0.009)
Xiuqun Ye (2010)	57500		0.002 (0.001, 0.002)
Hongbo Wang (2010)	3259	=	0.303 (0.287, 0.319)
Can Pang (2011)	6830		0.011 (0.009, 0.014)
Fenghua Wang (2011)	4167		0.040 (0.034, 0.046)
Bingzhen Li (2011)	2007	=	0.065 (0.055, 0.076)
Overall		<b>♦</b>	0.013 (0.005, 0.032)
			ı
		0.0 0.2 0.4 0.6 0.8 1.0	

Figure 2. A forest plot displaying the pooled prevalence of diabetic retinopathy (DR) in the population of mainland China. doi:10.1371/journal.pone.0045264.g002

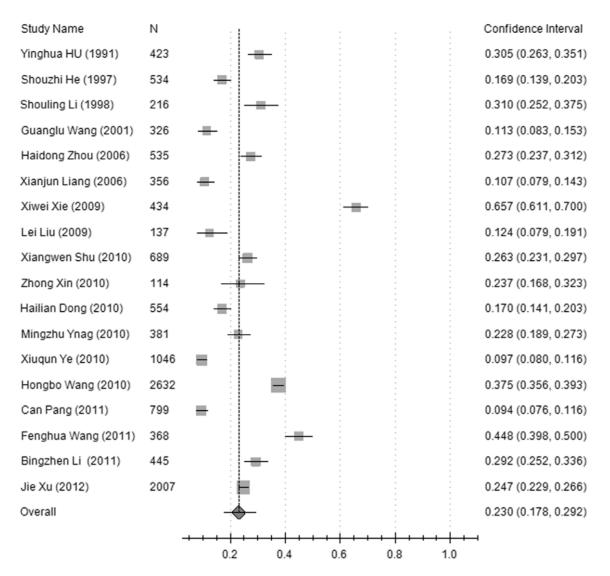


Figure 3. A forest plot displaying the pooled prevalence of diabetic retinopathy (DR) in the diabetic population of mainland China. doi:10.1371/journal.pone.0045264.g003

19 studies with 329,316 samples were included. We showed that the pooled prevalence rate of DR was 1.3% in the general population, and 23% (95%CI: 17.8%–29.2%) in the diabetic group. In mainland China there are 31 provinces (including 22 provinces, four municipalities, five autonomous regions) totally. The eligible studies covered 12/31 Chinese provinces. China mainland's population has increased to 1.3 billion, including 92.4 million diabetics [6], inferring (from our results) 16.9 million with DR, and 21.2 million diabetics with DR, respectively. This indicates a strong requirement for prevention and treatment strategies to control DR.

A previous study suggested that the overall, age-standardized prevalence of DR was 20.1% in Chinese diabetics living in Singapore [7]. The prevalence was lower than that of this metaanalysis (23%). However, in a US population of Chinese people with diabetes, the prevalence of DR was even higher (25.7%) [8]. In Taiwan, the prevalence of DR in diabetes was shown to be 35% [9], but 18.2% in Hong Kong [10]. Thus, the prevalence of DR in Chinese diabetics living abroad appeared to be a little lower than in mainland China, except for those living in the U.S. and Taiwan. The pooled prevalence rate of DR in the rural population was higher than that in the urban population. This was similar to a study conducted in India [11]. The reasons for this discrepancy in a developing country may be: a lower socioeconomic life, a poorer health care system, and fewer social activities for Chinese rural residents [12].

The pooled prevalence of DR was higher in the Northern region compared with the Southern region, both for the general population (1.4% compared with 0.7%), and the diabetic population (26.5% compared with 15.7%). A different life style and socioeconomic status may play an important role in the discrepancy of the pooled prevalence of DR between the Northern and Southern regions. The per capita Gross Domestic Product (GDP) is a little higher in Northern than that in Southern regions (http://tieba.baidu.com/f?kz = 1064355963). In addition, urbanization is associated with changes in a number of lifestyle factors, such as physical inactivity, unhealthy diet, and obesity, which are implicated in the aetiology of diabetes especially in Northern of China. As the apparent epidemic of diabetes complications, such as DR are also prevalent in developed societies. Previous studies



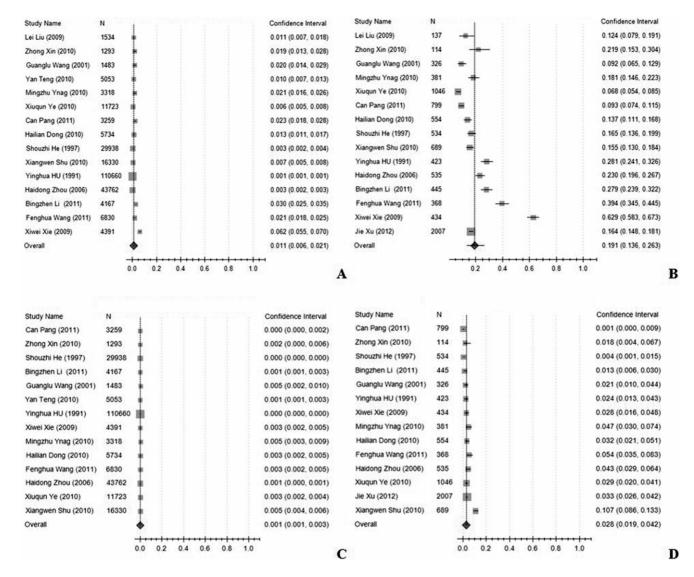


Figure 4. A forest plot displaying the pooled prevalence rates of NPDR and PDR (A, NPDR in general mainland China population; B, NPDR in diabetic population; C, PDR in general mainland China population; D, PDR in diabetic population). doi:10.1371/journal.pone.0045264.g004

**Table 2.** The pooled prevalence of diabetic retinopathy (DR) in mainland China with comparisons between different regions (North vs. South and rural vs. urban).

	Region	No. of articles	Case/Total	Pooled Estimate (%)	95%Cl(%)	Heterogeneity I <sup>2</sup> (%)	Q value	e <i>p</i> value
General population	Urban	9	1309/219084	0.8	0.3–1.7	49.80	0.99	< 0.001
	Rural	6	1509/92740	1.6	1.3–2	48.00	0.98	< 0.001
Diabetics	Urban	10	1309/6663	18.1	13.6–23.7	49.00	0.99	< 0.001
	Rural	5	1453/4357	29.1	20.9-38.9	49.20	0.99	< 0.001
General population	Northern	13	2284/248231	1.4	0.8–2.5	49.80	0.99	< 0.001
	Southern	5	427/81085	0.7	0.3–1.4	49.50	0.99	< 0.001
Diabetics	Northern	13	2724/9044	26.5	20.6-33.3	49.40	0.99	< 0.001
	Southern	5	427/2952	15.7	8.9-26.3	49.30	0.99	< 0.001

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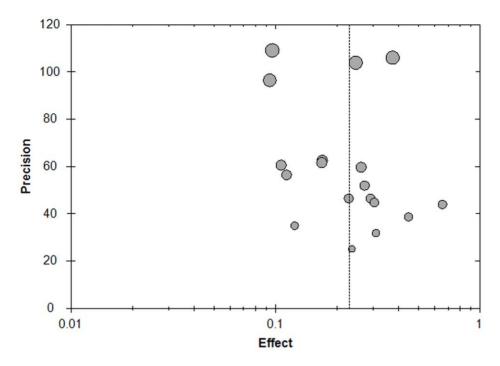


Figure 5. A funnel plot of studies conducted on the prevalence of diabetic retinopathy (DR) in mainland China. doi:10.1371/journal.pone.0045264.g005

also showed us that the prevalence of diabetes was higher in residents of Northern compared to Southern in China. As the prevalence of DM rising, we can conclude the prevalence of DR is a little higher in population or diabetic population of Northern compared to Southern in mainland China [13–16]. In addition, a difference in the number of studies conducted in the two regions may also explain this discrepancy. Thirteen of the studies on DR prevalence were conducted in the Northern region, but only five were from the Southern region.

As shown in the results (Table 2), there were moderate heterogeneity among included studies. In this meta-analysis, the different prevalence rates of DR might have also impacted by the heterogeneity of studies with different examination methodologies and ophthalmologic definitions. For example, between populations of different regions, the prevalence rates of DR were reported 26.27% in Shandong rural diabetes but 16.97% in Beijing Shunyi county rural diabetes. Similarly, between different diabetes of the same region the prevalence rates of DR were varied from 24.71% in Beijing Shunyi to 16.85% in other Beijing samples. According to the different time points, the prevalence rates of DR might also be varied. However, the pooled prevalence rates of DR were also estimated by Random-effects meta-analysis model.

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Although we have estimated the pooled prevalence of DR in mainland China, which is very important for preventative public health, there were some limitations in this meta analysis. First, we used pooled prevalence data using meta-analysis, rather than the prevalence in a single national population-based study. Second, as we cannot have access to unpublished results, a publication bias cannot be excluded. Third, there were limited studies in the Southern areas in China.

In view of the results of this meta-analysis, and given that the prevalence rates of DR appeared to vary in different regions and population groups, it would seem that we need to prioritize the treatment of DR in the rural population.

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#### **Author Contributions**

Conceived and designed the experiments: LL LC LML. Performed the experiments: LL LC ZY. Analyzed the data: XMW LL JG. Wrote the paper: LL LML LC ZYS.

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