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# Prevalence of carotid atherosclerosis and carotid plaque in Chinese adults: A systematic review and meta-regression analysis

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ABSTRACT

*Background and aims:* The national representative prevalence of carotid atherosclerosis (CAS) or carotid plaque (CP) in the general Chinese population has never been estimated. We aim to generate the prevalence and number of people with CAS and CP in the general Chinese population.
*Methods:* We searched China National Knowledge Infrastructure, Wanfang Data, VIP Database for Chinese Technical Periodical, PubMed, Embase and Medline. Articles reporting the prevalence of CAS or CP in the general Chinese population were included. A multilevel mixed-effects logistic regression was used to estimate the age- and gender-specific prevalence of CAS and CP. The effects of risk factors for CAS were assessed by a random-effects meta-analysis.
*Results:* The prevalence of CAS and CP increased with advanced age. Males had a higher prevalence of CAS and CP than females consistently across all age groups. Overall, 27.22% and 20.15% of Chinese people aged 30–79 years were with CAS and CP, respectively, in 2010, equivalent to 207.73 million and 153.82 million affected individuals. With demographic ageing, the number of people affected by CAS and CP will increase to 267.25 million and 199.83 million, respectively, by 2020. In addition, current smoking, hypertension and diabetes were found to be risk factors for CAS. More than 70% of the national CAS cases were in rural China in 2010.
*Conclusions:* CAS and CP are highly prevalent in China. The huge disease burden of CAS and CP calls for efforts on effective preventive health strategies and early-detection of CVDs in people with CAS or CP, especially in rural areas.



## 1. Introduction

Cardiovascular diseases (CVDs), including cerebrovascular disease (stroke), coronary heart disease (CHD) and ischemic brain attack, are the most prevalent cause of mortality and morbidity worldwide [1,2]. In 2015, CVDs affected 422.7 million people and accounted for 17.9 million deaths globally [2]. Disproportionally, more than 80% of CVD deaths occur in low and middle-income countries (LMICs) [3,4]. In China, the largest LMIC in the world, CVDs are also a leading cause of death and represent a severe public health problem. With rapid urbanization and population ageing, it is expected that CVD morbidity and mortality will keep rising in the next decade in China [5,6].

Atherosclerosis, a generalized disease characterized by the accumulation of lipids and fibrous elements in the large arteries, is worldwide an important cause of CVDs [1,7,8]. Atherosclerosis mainly occurs at the carotid bifurcation and the proximal internal carotid artery [9]. Carotid intima-media thickness (cIMT), the distance from the lumen-intima interface to the media-adventitia interface of the artery wall, has been suggested to be independently associated with CVD [8,10–13]. By using non-invasive imaging, cIMT could be simply measured and a value of ≥1.0 mm is generally suggested as abnormal [14–16]. Carotid plaque (CP) refers to a focal cIMT≥1.5 mm protruding into the lumen or the presence

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of focal wall thickening that is ≥ 0.5 mm or 50% than the surrounding vessel wall [14,17,18]. In population-based studies, as well as in clinical practice, cIMT has been widely adopted as a surrogate marker for the presence of carotid atherosclerosis (CAS) or CP [10,11,14,15,19].

In 2013, the 66th World Health Assembly adopted the Global action plan for the prevention and control of noncommunicable diseases 2013–2020, in which a target of reduction of premature mortality from CVDs worldwide by 25% by 2025 was set [3,20,21]. Despite the fact that there have already been abundant research and data on CVDs, CAS and CP are still relatively neglected in terms of research priority [22,23]. In addition, due to the lack of a standardized definition and measurement of cIMT, as well as the large disparity of study design and study population between studies, the reported prevalence of CAS and CP varied considerably [10,23,24]. Furthermore, those individual epidemiological investigations are generally small in sample size or limited to a specific geographic area. Therefore, the generality of those results is largely restricted.

In China, where an upward trend of CVD morbidity and mortality is very likely in the foreseen future, a detailed understanding of the epidemiology of CAS, the major cause of CVDs, has become imperative. Data from the China National Stroke Prevention Project (CSPP) showed that the standardized prevalence of CAS among asymptomatic Chinese aged ≥40 years was 36.2% in 2010. However, this prevalence estimate might be relatively lower than that in the general population where asymptomatic and symptomatic people should simultaneously exist [25]. Furthermore, the temporal trend of CAS prevalence has never been revealed in previous investigations. To fill this gap of knowledge, in this study, we set out to determine the prevalence of ultrasonography-based CAS and CP in general Chinese population by using a systematic review and meta-analysis, and to estimate and project the number of people with CAS or CP in China from 2000 to 2020. The major risk factors for CAS and subnational-level number of CAS cases were also investigated.

## 2. Materials and methods

### 2.1. Search strategy and selection criteria

This systematic review and meta-analysis is in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines [26]. The PRISMA checklist for this study is available in Supplementary Data. Two authors (S. Jin and J. Wang) independently performed a comprehensive systematic review of literature that was published from 1st January 1990 to 15th April 2017, and reported the prevalence of CAS or CP in China. The period from 1990 onwards was chosen to capture literature in the last three decades, as well as to mask a rather recent prevalence of CAS or CP in China. The literature search was limited to three Chinese and three English bibliographic databases, namely, China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP Database for Chinese Technical Periodical (VIP), PubMed, Embase and Medline. No language restrictions were placed. The search terms included “prevalence” or “rate” or “epidemiology”, in combination with “carotid atherosclerosis or carotid plaque” and “China or Chinese”, in the forms of controlled vocabulary (i.e., medical subject headings) or free words. The detailed search strategies customized for each database are listed in Supplementary Table 1. Reference lists in potentially relevant articles were hand-searched to locate any additional studies.

All records were independently screened by two authors (S. Jin and J. Wang) for relevance. To be included in this systematic review and meta-analysis, studies had to be population-based that reported the numerical estimates of CAS or CP prevalence in general Chinese population. Studies that were hospital- or health care facility-based were excluded because an overestimation was likely. Similarly, studies that were in a sample with potentially higher risks of CVDs were also excluded. In the included studies, the assessment of CAS or CP should be based on ultrasound imaging. Furthermore, to ensure our ability of synthesizing prevalence data from different studies, the definitions of CAS and CP should be consistent and accord with the 2016 European Guidelines on cardiovascular disease prevention in clinical practice and the Mannheim Carotid Intima-Media Thickness and Plaque Consensus respectively, where CAS was defined as a cIMT ≥1.0 mm and CP as 1) a focal structure that encroaches into the arterial lumen of ≥0.5 mm or 50% than the surrounding wall; or 2) a cIMT ≥1.5 mm [14,18]. For multiple publications that were based on the same single study, the most recent one or the one with the most comprehensive results or the largest sample size was included.

### 2.2. Data extraction

From the included studies, two authors (M. Wang and X. Chang) independently extracted relevant information, which included study characteristics (authors, publication year, investigation year, study setting, sampling method, case assessment and definition), characteristics of the investigated sample (sample size, gender and age) and prevalence estimates (CAS/CP cases). Where possible, the prevalence estimates should be extracted by age group, gender and setting. Any discrepancies over the systematic review or extracted data were resolved by consensus through group discussion. For studies where censoring age groups were reported (e.g., younger than 40 years or older than 60 years), we imputed the missing age band by taking the same width as other complete age groups in the same study. The midpoint of the age range reported or the reported mean or median age was adopted for analysis. For studies where the year of investigation was not reported, we imputed the investigation year by subtracting three years from the publication year. This was done for six studies based on the average time lag between investigation and publication in the other 31 studies with available information (Supplementary Table 2).

### 2.3. Statistical analysis

In this study, the prevalence rates of CAS and CP were estimated separately. In the data extraction process, age-, gender- or setting-stratified prevalence estimates were generally available in a single study, to take this hierarchical data structure into account, a multilevel mixed-effects meta-regression was adopted [27,28]. The variance of prevalence rates was stabilized by the logit transformation [29]. Given that:

$$\text{prevalence} = \text{p} = (CAS/CP\ cases)/(number\ of\ participants)$$

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

$$\text{logit(p)} = \ln(p/[1-p]) = \ln(odds) = \alpha + \beta_1{*}x_1 + \beta_2{*}x_2 + \ldots$$

To assess the associations of cluster-level variables (age, gender, setting and investigation year) and the prevalence of CAS/CP, a univariable meta-regression was conducted, followed by a multivariable meta-regression (Supplementary Table 3). Age and investigation year were treated as continuous variables, whereas gender and setting were as categorical variables. The study identification number was used as a random effect ($u_i$). Ultimately, age and gender were found to be significantly associated with the prevalence of CAS/CP. Therefore,