

REVIEW

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Unique and Varied Contributions of Traditional CVD Risk Factors: A Systematic Literature Review of CAD Risk Factors in China

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Abstract: This study is the first systematic review of risk factors for stroke in China and supports the importance of current public health initiatives to manage the risk factors appropriately to reduce risk of stroke in high risk patients. Additionally, this study has been co-authored by prominent Chinese and US physicians and researchers with expertise in cardiovascular disease, neurologic disorders, epidemiology, and real world data. While there have been several systematic reviews of real world associations of risk factors for coronary artery disease, none focus specifically on the population of China, where there is growing evidence that such risk factors are poorly treated or uncontrolled, especially in rural areas.

Background: To better understand the impact of traditional cardiovascular risk factors on risk of coronary artery disease (CAD) in China, a systematic review of all Chinese observational studies published in either English or Chinese in MEDLINE and EMBASE over the last 5 years was performed and the association between any of 5 traditional risk factors (ie, hypertension, diabetes, elevated lipid levels, obesity, and smoking) and the risk of CAD was studied.

Methods and results: The study found a consistent relationship between lipid levels and CAD. Higher low-density lipoprotein cholesterol values were associated with greater risk of CAD, with an odds ratio as high as 3.31. Other factors found to be significant contributors to the risk of CAD included hypertension (crude odds ratio range of 1.40–5.11), diabetes (1.50–5.97), and smoking (1.37–5.19). An association between obesity and CAD in China was observed, but the evidence supporting this was considered weak due to the paucity of studies found as part of this review.

Conclusions: This review provides a systematic summary of CAD risk factors in China and demonstrates the important differences that exist in CAD risk factors between countries and regions. Approaches to reduce CAD globally must take into account the unique risk factors that drive CAD in each country and region as is demonstrated by these findings.

Keywords: coronary disease, risk factors, smoking, diabetes, hypertension, dyslipidemia

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Introduction

Worldwide, over 7 million people each year die from coronary artery disease (CAD),¹ a condition where plaque builds up in the blood vessels supplying the heart. Evidence supports an association between CAD trends with major cardiovascular risk factors.² Major modifiable risk factors include high blood pressure, diabetes, obesity, metabolic syndrome, abnormal lipids, tobacco use, and physical inactivity.¹ The prevention and control of major risk factors of CAD among the developed nations has contributed to a significant reduction in CAD mortality rates.³

Contrary to trends in developed nations, China has experienced a considerable increase in the prevalence of CAD over the past several decades.⁴ CAD has climbed from the fifth most common heart disease in 1948–1957 to the most common in 1980–1989, where it has remained to this day.⁴ CAD is reported as one of the leading causes of death in China, where it contributes to 51.4% of the mortality attributed to cardiovascular disease (CVD) in urban areas and 32.8% in rural areas. It is projected that from 1990 to 2020, CAD is likely to have reached 72.7 million men and 72.1 million women⁵ in the general Chinese population, with CVD mortality likely to increase by 108% in men and 79% in women.⁵

China is also not experiencing a decrease in these risk factors, especially in diabetes and smoking. Hypertension,^{6–11} diabetes,^{7,9,11,12} obesity,^{6,7,9–11,13} dyslipidemia,¹¹ and hypercholesterolemia¹⁰ are rising rapidly in the Chinese population and an estimated 28.1% of adults and 52.9% of males were current smokers in 2010, contributing to China as the world’s largest consumer and producer of tobacco products. Hypertension, diabetes, abnormal lipid conditions, obesity, and smoking are all major risk factors of CAD.

Given the potential economic, social, and public health burden of CAD on China’s large population, effective primary and secondary prevention strategies for risk factors can greatly reduce the risk of CAD. However, the impact of each of these risk factors in the Chinese population is unknown, and most models linking these traditional risk factors to CAD have been derived from studies on largely Caucasian populations including whether there might be geographic variation of the impact of these traditional risk factors. Regarded as a leading developing economy with an

estimated population of 1.3 billion people,¹⁴ a careful examination of this epidemic increase in China will benefit the future prevention of the disease worldwide and contribute to a stronger understanding of the relationship between cardiovascular risk factors and CAD within the Chinese population. We performed a systematic review of the literature to assess the impact of hypertension, diabetes, abnormal lipid conditions, obesity, and smoking on the risk of CAD in China.

Methods

The literature search was performed in MEDLINE (via PubMed) and EMBASE for all observational studies published in either English or Chinese in the last 5 years (2006–2011) on the association between any of the 5 risk factors (ie, hypertension, diabetes, abnormal lipid conditions, obesity, and smoking) and the risk of CAD in the general population of China. Chinese literature databases Wanfang Data and Chinese National Knowledge Infrastructure (CNKI) were also searched but with no significant yield. The main search terms used were as follows: “coronary artery disease” [Mesh], “China,” “incidence” [MeSH Terms], “prevalence” [MeSH Terms], “epidemiology” [MeSH Terms], “observational,” “community-based,” and “cross-section.”

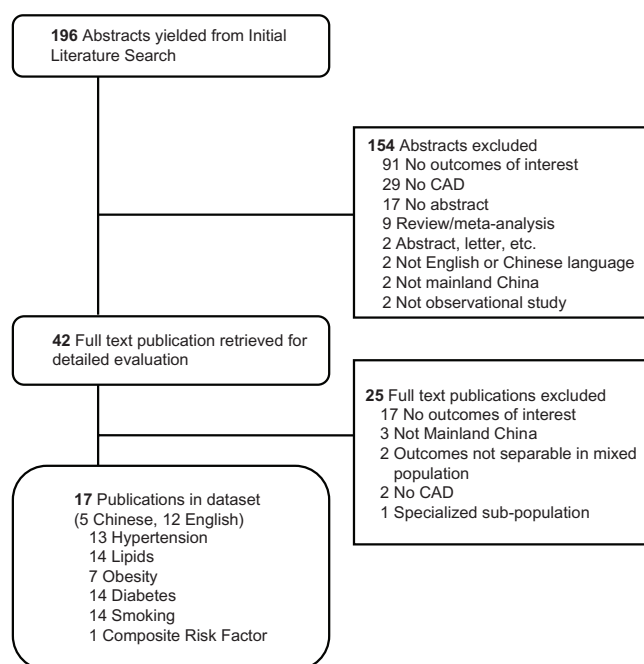


Figure 1. Attrition diagram. **Notes:** Rounded corners = Accepted articles at each stage. Squared corners = Rejected articles.



Procedures for the review followed established methods used in the science of systematic review research.^{15,16}

The initial search yielded 196 abstracts. We manually reviewed the abstracts of the articles to exclude study types such as abstracts, case reports, letters, commentaries, editorials, reviews, meta-analyses and clinical trials, studies not on population from mainland China, and studies with no apparent outcomes of interest. If an article did not have an abstract, the article was still retrieved if the title suggested the full text would include the outcomes of interest. Forty-two articles were selected for detailed evaluation. The full text was reviewed to identify only observational studies reporting the association of any of the 5 risk factors and risk of CAD. Seventeen publications met these criteria and were selected for review (Table 1). The article attrition diagram lists the number of articles excluded at each step and the reason for exclusion.

Both study-level and patient-level information from each article were reviewed. Study-level information included publication language, patient population characteristics, geographic region of China, study design (prospective/retrospective cohort, survey or case control), and characteristics such as study period and length of follow-up. Information on distinctive sample characteristics, sample size, baseline demographics, and comorbidities was reviewed for each cohort patient population if reported, such as CAD patients versus non-CAD patients. Main outcomes of interest included any reported association between the 5 risk factors (hypertension, abnormal lipid conditions, obesity, diabetes, and smoking) and CAD, such as odds ratios (OR) or relative risks (RR). Only half of the articles reported adjusted hazard ratios or relative risks. For those that did not, we calculated crude odds ratios from the counts available.

Review was performed by 1 investigator and checked by another who reviewed the extracted data for consistency and accuracy. Data discrepancies were resolved by consensus of the 2 investigators. Articles published in Chinese were translated into English by a native Chinese speaker with fluency in English. Translation was validated by a second native speaker. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the *International Journal of Cardiology*.¹⁷

Results

Of the 17 articles identified and reviewed for reported association between any of the 5 risk factors and risk of CAD, 12 were published in English and 5 in Chinese. Most studies (70.6%) reported on multiple risk factors. The review included 8 cohort studies (7 prospective, 1 retrospective), most of which examined consecutive patients referred for coronary angiography with suspected or confirmed CAD. Sample sizes ranged from 237 to 3,513 patients (mean: 843). There were 6 case-control studies with sample sizes ranging from 384 to 1,127 (mean: 664). Three of the larger studies were survey studies. One specifically targeted retired military men over age 55 and had a sample size of 1,268. Another, Liu et al,¹⁸ included 3,223 inpatients diagnosed with acute coronary syndrome (ACS) from 64 hospitals representative of China. The third, Wang et al,¹⁹ surveyed 30,378 individuals among the general Chinese population across 11 provinces. With regard to geographic coverage, only 1 study¹⁸ was found to be representative of both urban and rural China. The other 16 focused on major cities (Beijing, Shanghai, Nanjing, Shenyang, and Xi'an) or provincial areas (Shandong, Jiangsu, and Zhejiang provinces).

Association between hypertension and CAD was reported in 13 studies (Table 2A). Association between abnormal lipid conditions and CAD was reported in 12 studies (Table 2B). Seven studies reported the association between obesity and CAD (Table 2C). Associations between CAD and diabetes, and between CAD and smoking were reported each in 14 studies (Tables 2D–E). One study reported association with a composite risk factor (Table 2F).

Hypertension and risk of CAD

Thirteen studies were selected for review on the association between hypertension and CAD. The association ranged between 1.40 and 5.11 for crude ORs and between 1.68 and 2.47 for adjusted relative ratios. Seven studies had crude ORs derived from the available prevalence of hypertension in the CAD group versus non-CAD group. Four studies reported crude ORs between 1.40 and 1.94, while 3 others^{20–22} reported much higher crude ratios of 5.11, 4.69, and 3.46. Adjusted RR ratios ranged between 1.28 and 2.47. Cui et al²³ did not report the magnitude of the association, but found the risk association among women to be significant while that among men to

**Table 1.** Systematic literature review of risk factors of coronary artery disease (CAD) in China.

Author, year	Citation	Publication language	Region	Patient population
Su G, 2011	Su G, Mi S, Tao H, et al. Association of glycemic variability and the presence and severity of coronary artery disease in patients with type 2 diabetes. <i>Cardiovascular Diabetology</i> . 2011;10:19.	English	Beijing	Consecutive T2DM patients with chest pain referred to coronary angiography
Sai XY, 2007	Sai XY, He Y, Men K, et al. All-cause mortality and risk factors in a cohort of retired military male veterans, Xi'an, China: an 18-year follow up study. <i>BMC Public Health</i> . 2007;7:290.	English	Xi'an	Retired military men aged 55 or older from 22 military retirement centers in Xi'an
Hu DY, 2006	Hu DY, Pan CY, Yu JM. The relationship between coronary artery disease and abnormal glucose regulation in China: The China Heart Survey. <i>European Heart Journal</i> . 2006;27(21):2573–9.	English	Seven cities	Patients admitted to hospital cardiovascular wards, T1DM excluded
Chen ZW, 2011	Chen ZW, Qian JY, Jian Y, et al. Prevalence and severity of coronary artery disease in diabetic patients with aortic valve calcification. <i>Acta Cardiol</i> . 2011;66(1):15–20.	English	Shanghai	Consecutive patients with chest pain or chest distress referred for coronary angiography
Zhang K, 2010	Zhang K, Wang YY, Liu QJ, et al. Two single nucleotide polymorphisms in ALOX15 are associated with risk of coronary artery disease in a Chinese Han population. <i>Heart Vessels</i> . 2010;25(5):368–3.	English	Shandong province	Subjects consecutively recruited from hospital inpatients who underwent coronary angiography. History of other diseases were excluded
Han Y, 2010	Han Y, Xu W, Zhang W, Liu N, Ji Y. T-786C polymorphism in the endothelial nitric oxide synthase gene is associated with increased risk of coronary artery disease in a Chinese population. <i>Pharmacology</i> . 2010;85(4):211–6.	English	Jianshu province	Chinese Han subjects, CAD confirmed by angiography and healthy controls
Xu H, 2008	Xu H, Hou X, Wang N, et al. Gender-specific effect of estrogen receptor-1 gene polymorphisms in coronary artery disease and its angiographic severity in Chinese population. <i>Clin Chim Acta</i> . 2008;395(1–2):130–3.	English	Nanjing	Angiographically defined CAD patients and controls in hospital
Tang NP, 2008	Tang NP, Wang LS, Yang L, et al. Genetic variant in glutathione peroxidase 1 gene is associated with an increased risk of coronary artery disease in a Chinese population. <i>Clin Chim Acta</i> . 2008;395(1–2):89–93.	English	Jiangsu province	Consecutive CAD inpatients admitted for angina pectoris or other symptoms/signs of cardiovascular diseases and controls
Cui, 2007	Cui HB, Wang SH, Wang DQ, et al. Modified classic risk factors for coronary artery disease in Chinese Han population. <i>Chin Med Sci J</i> . 2007;22(4):216–23.	English	Xi'an, Shanxi, Lanzhou, Ningbo, Shiyuan	Angiographic assessed consecutive subjects from Chinese coronary collaborative group presenting at five hospitals with coronary angiography
Ni M, 2007	Ni M, Zhang XH, Jiang SL, Zhang Y. Homocysteinemia as an independent risk factor in the Chinese population at a high risk of coronary artery disease. <i>Am J Cardiol</i> . 2007;100(3):455–8.	English	Shandong province	Consecutive patients undergoing coronary angiography



Sample size	Risk factors	Study design	Study length	Risk of CAD
344 (CAD: 252; non CAD: 92)	Hypertension, lipids, obesity, diabetes, smoking	Prospective cohort	NR	
1268	Smoking	Survey	1987–2005/ 18 years	CHD adjusted mortality rates: 421 per 100,000 person years
3513	Smoking, obesity, hypertension, hyperlipidemia, diabetes	Prospective cohort	Jun–Aug 2005	
325 (CAD: 222; non-CAD: 103)	Diabetes, Hypertension	Prospective cohort	Jun–Dec 2007	
1127 (CAD: 519; control 608)	Hypertension, lipids, obesity, diabetes, smoking	Case control	2006–2008	
622 (CAD 312; control 310)	Hypertension, lipids, smoking	Case-control	NR	
384 (CAD 210; control 174)	Hypertension, lipids, BMI, diabetes, smoking	Case control	NR	
530 (CAD 265; control 265)	Hypertension, lipids, obesity, diabetes, smoking	Case control	NR	
762 (CAD 423; control 339)	Hypertension, lipids, diabetes, smoking	Prospective cohort	NR	
237 (CAD:138; control 99)	Hypertension, lipids, obesity, smoking, diabetes	Prospective cohort	NR	

(Continued)



Table 1. (Continued)

Author, year	Citation	Publication language	Region	Patient population
Han Y, 2007	Han Y, Yang Y, Zhang X, Yan C, Xi S, Kang J. Relationship of the CAG repeat polymorphism of the MEF2A gene and coronary artery disease in a Chinese population. <i>Clin Chem Lab Med</i> . 2007;45(8):987–92.	English	Shenyang	Coronary angiography patients and healthy controls, Han Chinese
Jin Z, 2006	Jin Z, Zhang Y, Chen J, et al. Study of the correlation between blood lipid levels and the severity of coronary atherosclerosis in a Chinese population sample. <i>Acta Cardiol</i> . 2006;61(6):603–6.	English	Zhejiang	Patients with coronary artery atherosclerosis verified by coronary angiography
Liu, 2008	Liu J, Zhao D, Liu Q, et al. Study on the prevalence of diabetes mellitus among acute coronary syndrome inpatients in a multiprovincial study in China. <i>Zhonghua Liu Xing Bing Xue Za Zhi = Zhonghua Liuxingbingxue Zazhi</i> . 2008;29(6):526–9.	Chinese	64 hospitals representative of China	Inpatients diagnosed with acute coronary syndrome (ACS)
Wang, 2007	Wang Y, Huang JY, Cao YF, et al. Risk factors for type 2 diabetes mellitus in middle-aged and elderly populations of Shanghai rural areas: A nested case-control study. <i>Journal of Clinical Rehabilitative Tissue Engineering Research</i> . 2007;11(52):10433–6.	Chinese	Shanghai	Diabetes patients and control
Li, 2007	Li BL, Li L, Hou XL, et al. Prevalence of coronary artery disease in patients with rheumatic heart disease in China. <i>National Medical Journal of China</i> . 2007;87(47):3313–6.	Chinese	Shanghai	Patients with rheumatic heart disease aged > 40 who were scheduled for valve surgery
Wang, 2006	Wang W, Zhao D, Sun JY, et al. Risk factors comparison in Chinese patients developing acute coronary syndrome, ischemic or hemorrhagic stroke: a multi-provincial cohort study. <i>Zhonghua Xin Xue Guan Bing Za Zhi [Chinese Journal of Cardiovascular Diseases]</i> . 2006;34(12):1133–7.	Chinese	11 provinces	Chinese population aged 35–64
Li, 2006	Li X, Gao X, Zhang B, Gu Q, Ren LM, Gao J. Glucose metabolism status and angiographic features of coronary artery in patients undergoing their first coronary angiography: study of 553 cases. <i>Zhonghua Yi Xue Za Zhi</i> . 2006;86(24):1689–92.	Chinese	NR	Inpatients with suspected or confirmed CAD

be insignificant. Chen et al²⁴ reported differential ratios among diabetic and non-diabetic populations. The adjusted ORs among diabetics were found to be higher than that among non-diabetics (1.85 vs. 1.28).

There were 6 case-control studies, 6 cohort studies, and 1 survey. The case-control studies generally

reported higher ORs compared to the cohort studies (mean 3.8 vs. 1.55).

The largest crude ORs and adjusted RR ratios were both found in Han et al.²⁵ The study was a case-control study that recruited 378 CAD patients and 348 healthy controls from Northern Hospital in Shenyang.



Sample size	Risk factors	Study design	Study length	Risk of CAD
726 (CAD 378; control 348)	Hypertension, diabetes, hyperlipidemia, smoking	Case control	2003–2006	
363	Lipids	Prospective cohort	Jan–Dec 2004	
3223	Diabetes	Survey	March 2006–May 2006	
597 (type 2 diabetes: 199 non diabetes 398)	Diabetes	Case control	2003 and 2005	
651: CAD 71 non CAD 580	Diabetes mellitus, hypertension, smoking, dyslipidemia	Retrospective cohort	Sep 2001–Apr 2006	71 (10.91%) Male: 17.94%, Female 4.86% ($P < 0.01$) Age: 40–59, 6.39% 60–69 21.47% ($P < 0.01$) ≥ 70 22.22% ($P < 0.01$)
30,378 (ACS 227 stroke 582 non CVD 29,569)	Hypertension, smoking, diabetes, high TC, low HDL-C, obesity	Survey	1992–2003/ 6.6 years	Overall: 114 per 100,000 person-year 35–44: 53 per 100,000 person-year 45–54: 106 per 100,000 person-year 55–64: 249 per 100,000 person-year (3.7 folds compared to 35–44)
553: CAD 388 non CAD 165	Hypertension, smoking, TC, TG, HDL-C, LDL-C, diabetes	Prospective cohort	Aug 2004–Oct 2005	

Lipid profile and risk of CAD

Twelve studies were selected for review on the association between lipid conditions and risk of CAD. Three studies reported the association between hyperlipidemia and risk of CAD, 2 between dyslipidemia and risk of CAD, and 10 between values on total cholesterol (TC), triglyceride (TG), LDL cholesterol

(LDL-C) and HDL cholesterol levels (HDL-C), and risk of CAD.

For the association between hyperlipidemia and the risk of CAD, significant crude and adjusted odds ratios were reported in only 1 case-control study conducted in Shenyang,²¹ where the crude OR was reported as 2.77 and adjusted OR as 2.63 (95% confidence interval



Table 2A. Association between hypertension and risk of CAD.

Author, year	Study design	Number of patients	Age	Gender (M:F)	Treatment history
Han Y, 2007	Case-control	726 (CAD 378; control 348)	Mean: 57.2 (10.5) Range: 29–89 CAD: mean: 57.7 (10.7) Control: 55.6 (10.4)	492:234 CAD: 284:94 Control: 210:138	
Cui, 2007	Prospective cohort	762 (CAD 423; control 339)	Mean: 60 (10) Range 17–81	481:281 CAD: 261:162 Control: 220:119	100%: lipid-lowering agents
Han Y, 2010	Case-control	622 (CAD 312; control 310)	Mean: 61.96 (10.71) CAD: 61.96 (10.71) Control: 60.54 (10.18) <i>P</i> = 0.09	209:103 CAD: 209:103 Control: 184:126 <i>P</i> = 0.056	
Ni M, 2007	Case-control	237 (CAD:138; control 99)	Mean: 54.18 (9.25) Range 35–70 CAD: 55.28 (9.03) Control: 52.65 (9.39) <i>P</i> = 0.031	163:74 CAD: 108:30 Control: 55:44 <i>P</i> < 0.01	
Su G, 2011	Prospective cohort	344 (CAD: 252; non CAD: 92)	CAD: mean: 65 (9) Non CAD: 61 (9)	CAD: 165:87 Non CAD: 48:44	Oral anti-hyperglycemic CAD: 45.7% Non-CAD: 44.0% Not significant Insulin CAD: 35.9% Non-CAD: 40.9% Not significant Statins CAD: 61.9% Non CAD: 69.4% Not significant
Tang NP, 2008	Case-control	530 (CAD 265; control 265)	CAD: 64 (56–71) Control: 64 (55–71) NS	CAD: 194:71 Non CAD: 194:71 NS	
Xu H, 2008	Case-control	384 (CAD 210; control 174)	CAD: 56 (7.3) Non CAD: 55 (8.6)	201:183 CAD: 116:94 Control: 85:89	
Zhang K, 2010	Case-control	1127 (CAD: 519; control 608)	CAD: 61.285 (10.755) Control: 60.3777 (10.730) <i>P</i> = 0.16	CAD: 362:157 Control: 401:207	
Chen ZW, 2011	Prospective cohort	325 (CAD: 222; non-CAD: 103)	63.4 (9.7) Diabetic: 66.2 (8.1) Non diabetic: 62.2 (10.2) <i>P</i> < 0.01	218:107 Diabetic 61:43 Non diabetic: 157:64 <i>P</i> = 0.027	



Definition of risk factor	Crude OR	Adjusted association	Adjusted model configuration
Being treated for hypertension According to Joint National Committee (JNC) VI guideline NR	5.11 ($P = 0.002$) 1.94 ($P < 0.01$)	OR (95% CI): 2.47 (2.20–2.78) ($P = 0.00$) Women: 95% significant association with hypertension Men: No significant association with hypertension	Logistic: age, gender, hypertension, diabetes mellitus, hyperlipidemia, smoking
Systolic and diastolic BP \geq 140/90 mmHg or use of antihypertensive treatment	4.69 ($P < 0.01$)		
Systolic blood pressure \geq 140 mmHg and/ or diastolic blood pressure \geq 90 mmHg or treatment with oral anti-hypertension drugs	1.52 (NS)	OR: 1.857 (95% CI: 0.969, 3.557, $P = 0.062$)	Logistic: smoking, male, older age, MAGE (mean amplitude of glycemic excursions), hs-CRP, hyperlipidemia, hypertension, renal insufficiency
Resting systolic blood pressure \geq 140 mmHg and/or diastolic blood pressure \geq 90 mmHg or in the presence of active treatment with antihypertensive agents NR	3.46 ($P < 0.001$)	OR: 1.676 (95% CI: 1.165–2.788); $P = 0.014$	Logistic: diabetes, hypertension, high LDL levels and genotype
NR	Health control cohort had zero patients with hypertension. (OR can't be calculated.) % of patients with hypertension: 63% in the CAD vs. 0% in the non CAD		
Systolic pressure $>$ 140 mmHg or diastolic pressure $>$ 90 mmHg or being treated with antihypertensive medication		Diabetic: OR: 1.846 ($P = 0.389$) Non diabetic: OR: 1.280 ($P = 0.638$)	Logistic regression: aortic valve calcification (AVC), sex, age, hypertension, smoking, serum level of fibrinogen, total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, apoprotein

(Continued)

**Table 2A.** (Continued)

Author, year	Study design	Number of patients	Age	Gender (M:F)	Treatment history
Hu DY, 2006	Prospective cohort	3513 (CAD: 3513)	69 (65–77)	2341:1172	
Li, 2007	Retrospective cohort	651: CAD 71 non CAD 580	Mean: 56 (8) Range: 42–75 CAD: 63 (9) Non-CAD: 54 (9)	301:350 CAD: 54:17 Non-CAD: 247:333	
Li, 2006	Prospective cohort	553: CAD 388: non-CAD 165	Mean: 60.1 (9.7) CAD: 61.4 (9.7) Non CAD: 57.2 (8.8) <i>P</i> = 0.00	CAD: 82.6% Non-CAD: 63.9% <i>P</i> = 0.00	
Wang, 2006	Survey	30,378 (ACS 227 stroke 582 non CVD 29,569)	Mean: 46.89 ASC: 52.4 (7.9) Non-CVD: 46.7 (8.0)	ASC: male 70.5% Non CVD: male 53.2%	

[CI]: 2.32–2.99). The criteria for defining hyperlipidemia were not provided in this study. For the association between dyslipidemia and the risk of CAD, significance was found in 2 of 3 studies reviewed. Ni et al²⁰ reported the crude ORs to be 3.71 for a case-control study conducted in Shandong province. The study population consisted of 138 CAD patients and 99 controls, where the CAD patient cohort was significantly older (55.3 vs. 52.7, *P* = 0.03) and had a higher percentage of male patients (78.3% vs. 55.6%, *P* < 0.01) than the control cohort. Dyslipidemia was defined as total cholesterol \geq 5.2 mmol/L, LDL \geq 3.4 mmol/L, triglycerides \geq 1.7 mmol/L or HDL \geq 1.03 mmol/L. Tang et al²² reported the crude OR to be 2.76. This study had a similar study design as Ni et al,²⁰ where 265 patients were selected each for a CAD cohort and healthy control cohort. However, Tang et al²² found no significant difference in baseline patient characteristics. Dyslipidemia in this study was defined as total cholesterol \geq 6.2 mmol/L or on drugs.

For the association between total cholesterol (TC), triglycerides (TG), HDL-C, LDL-C, and risk of CAD, 7 studies compared values of lipoprotein profile between CAD patients and the healthy controls. Su et al²⁶ found the difference in the lipid conditions reported between the 2 cohorts to be generally insignificant. Two studies^{25,27} found CAD patients

had slightly lower TC values than healthy controls (*P* < 0.01); 2 studies^{22,28} found CAD patients had significant higher values; and 1 study²⁹ found the difference to be insignificant. For reported TG values, 2 studies^{22,27} found CAD patients to have significant higher values than their comparative healthy controls, although 3 studies^{25,28,29} found the difference to be insignificant. Comparison on HDL-C and LDL-C values is more consistent between studies. All 5 studies^{22,25,27–29} reported significantly lower HDL-C values than non-CAD patients. Wang et al¹⁹ reported a crude OR of 1.75 and adjusted RR of 1.39 for low HDL-C among CAD patients, and Cui et al²³ reported the adjusted risk among men to be higher at 2.80 (95% CI: 1.50–4.20). For LDL-C values, 4 studies^{22,27–29} found significantly higher levels among CAD patients, but 1 study²⁵ found the opposite. This is consistent with the adjusted RR reported in Xu et al,²⁹ where LDL-C is associated with an OR of 3.31 for risk of CAD.

Jin et al³⁰ reported the association between the severity of CAD and lipoprotein profiles. Severity was positively correlated with the number of coronary arteries diseased. Among the lipid conditions examined, which include TG, TC, HDL-C, LDL-C, and non-HDL-C, only LDL-C was found to be consistently related to the progression of the disease. Patients in more severe disease conditions were found to have significantly higher LDL-C values. Chen et al²⁴ reported differential

**Table 2B.** Association between lipids and risk of CAD.

Author, year	Study design	Number of patients	Age	Gender (M:F)	Treatment history
Han Y, 2007	Case-control	726 (CAD 378; control 348)	Mean: 57.2 (10.5) Range: 29–89 CAD: mean: 57.7 (10.7) Control: 55.6 (10.4)	492:234 CAD: 284:94 Control: 210:138	
Cui, 2007	Prospective cohort	762 (CAD 423; control 339)	Mean: 60 (10) Range: 17–81	481:281 CAD: 261:162 Control: 220:119	100%: lipid-lowering agents
Han Y, 2010	Case-control	622 (CAD 312; control 310)	Mean: 61.96 (10.71) CAD: 61.96 (10.71) Control: 60.54 (10.18) <i>P</i> = 0.09	209:103 CAD: 209:103 Control: 184:126 <i>P</i> = 0.056	
Jin Z, 2006	Prospective cohort	363	NR	NR	
Ni M, 2007	Case-control	237 (CAD:138; control 99)	Mean: 54.18 (9.25) Range: 35–70 CAD: 55.28 (9.03) Control: 52.65 (9.39) <i>P</i> = 0.031	163:74 CAD: 108:30 Control: 55:44 <i>P</i> < 0.01	



Definition of risk factor	Crude OR	Adjusted association	Adjusted model configuration
Hyperlipidemia	2.77 ($P < 0.01$)	OR (95% CI): 2.63 (2.32–2.99) ($P = 0.00$)	Logistic: age, gender, hypertension, diabetes mellitus, hyperlipidemia, smoking
Low HDL-C, LDL, TC, TG, LDL/HDL		Low HDL-C (men): RR = 2.8 (95% CI: 1.5–4.2) LDL, TC, TG (men): 95% significant association LDL/HDL: 95% significant association	
TC, TG, HDL, LDL values	TC (mmol/l): CAD 4.38 (1.19) vs. non CAD 4.84 (1.09) $P < 0.01$ TG (mmol/l): CAD 1.76 (1.23) vs. non CAD 1.72 (0.95) $P = 0.657$ HDL (mmol/l): CAD 1.05 (0.27) vs. non CAD 1.25 (0.31) $P < 0.01$ LDL (mmol/l): CAD 2.50 (0.94) vs. non CAD 2.82 (0.85) $P < 0.01$		
TC, TG, HDL-C, LDL-C, non-HDL-C values	TG (mmol/l): Group I 1.91 (1.20) vs. group II 1.73 (0.88) vs. group III 1.86 (1.40) vs. group IV 1.48 (0.60) TC (mmol/l): Group I 4.38 (0.93) vs. group II 4.73 (0.99) ($P < 0.05$) vs. group III 4.87 (1.50) ($P < 0.01$) vs. group IV 4.78 (0.82) HDL-C (mmol/l): Group I 1.21 (0.39) vs. group II 1.30 (0.34) vs. group III 1.28 (0.38) vs. group IV 1.20 (0.27) LDL-C (mmol/l): Group I 2.30 (0.77) vs. group II 2.64 (0.84) ($P < 0.01$) vs. group III 2.74 (1.23) ($P < 0.01$) vs. group IV 2.91 (0.68) ($P < 0.01$) Non-HDL-C (mmol/l): Group I 3.17 (0.91) vs. group II 3.43 (0.94) ($P < 0.05$) vs. group III 3.59 (1.41) ($P < 0.05$) vs. group IV 3.58 (0.75) ($P < 0.05$) *Group according to the number of coronary arteries diseased		
Dyslipidemia: Total cholesterol level 5.2 mmol/L (200 mg/dL), LDL cholesterol level 3.4 mmol/L (130 mg/dL), triglyceride level 1.7 mmol/L (150 mg/dL), or HDL cholesterol level 1.03 mmol/L (40 mg/dL)	3.71 ($P < 0.001$)		

(Continued)



Table 2B. (Continued)

Author, year	Study design	Number of patients	Age	Gender (M:F)	Treatment history
Su G, 2011	Prospective cohort	344 (CAD: 252; non CAD: 92)	CAD: mean: 65 (9) Non CAD: 61 (9)	CAD: 165:87 Non CAD: 48:44	Oral anti-hyperglycemic CAD: 45.7% Non CAD: 44.0% Not significant Insulin CAD: 35.9% Non CAD: 40.9% Not significant Statins CAD: 61.9% Non CAD: 69.4% Not significant
Tang NP, 2008	Case-control	530 (CAD 265; control 265)	CAD: 64 (56–71) Control: 64 (55–71)	CAD: 194:71 Non CAD: 194:71 NS	
Xu H, 2008	Case-control	384 (CAD 210; control 174)	CAD: 56 (7.3) Non CAD: 55 (8.6)	201:183 CAD: 116:94 Control: 85:89	
Zhang K, 2010	Case-control	1127 (CAD: 519; control 608)	CAD: 61.285 (10.755) Control: 60.3777 (10.730) <i>P</i> = 0.16	CAD: 362:157 Control: 401:207	
Chen ZW, 2011	Prospective cohort	325 (CAD: 222; non-CAD: 103)	63.4 (9.7) Diabetic: 66.2 (8.1) Non diabetic: 62.2 (10.2) <i>P</i> < 0.01	218:107 Diabetic: 61:43 Non diabetic: 157:64 <i>P</i> = 0.027	



Definition of risk factor	Crude OR	Adjusted association	Adjusted model configuration
Hyperlipidemia: diagnosed according to guideline of the National Cholesterol Education Program (ATP III). TC, LDL-C, HDL-C, TG values	Hyperlipidemia: 1.44 (NS) TC (mmol/l): CAD 4.8 (1.2) vs. non CAD 4.6 (1.1) (NS) LDL-C (mmol/l): CAD 2.9 (1.0) vs. non CAD 2.7 (0.8) (NS) HDL-C (mmol/l): CAD 1.1 (0.3) vs. Non CAD 1.0 (0.2) (NS) TG (mmol/l): CAD 2.2 (1.6) vs. non CAD 2.1 (1.2) (NS)	Hyperlipidemia: OR: 1.425 (95% CI: 0.817, 2.486, $P = 0.212$)	Logistic: smoking, male, older age, MAGE (mean amplitude of glycemic excursions), hs-CRP, hyperlipidemia, hypertension, renal insufficiency
Dyslipidemia: total cholesterol level of 6.2 mmol/l or on drugs TC, TG, HDL-C, LDL-C values	Dyslipidemia: 2.76 ($P < 0.01$) TC (mmol/l): CAD 4.11 (3.48–4.71) vs. non CAD 3.95 (3.31–4.54) ($P = 0.036$) TG (mmol/l): CAD 1.46 (1.05–2.14) vs. non CAD 1.14 (0.79–1.62) ($P < 0.001$) HDL-C (mmol/l): CAD 0.98 (0.84–1.14) non CAD 1.08 (0.90–1.29) ($P < 0.001$) LDL-C (mmol/l): 2.36 (1.83–2.82) vs. Non CAD 2.14 (1.66–2.63) ($P = 0.005$)	LDL: OR: 3.314 (95% CI: 1.565–7.174); $P = 0.002$	Logistic: diabetes, hypertension, high LDL levels and genotype
TC, TG, HDL-C, LDL values	TC (mg/dL): CAD 194 (8.6) vs. non CAD 186 (10.2) (NS) TG (mg/dL): CAD 4.7 (1.4) vs. non CAD 4.5 (1.9) (NS) HDL-C (mg/dL): CAD 39.2 (11.4) vs. non CAD 44.6 (10.3) ($P = 0.057$) LDL (mg/dL): CAD 119 (17.7) vs. non CAD 99.2 (16.4) ($P = 0.003$)		
TC, TG, HDL-C, LDL values	TC (mmol/l): CAD 4.71 (1.06) vs. non CAD 4.78 (0.67) ($P = 0.066$) TG (mmol/l): CAD 2.02 (1.37) vs. non CAD 1.04 (0.33) ($P < 0.001$) HDL-C (mmol/l): CAD 1.12 (0.34) vs. non CAD 1.43 (0.30) ($P < 0.001$) LDL (mmol/l): CAD 2.98 (0.91) vs. non CAD 2.67 (0.49) ($P = 0.001$)		
TC, TG, HDL-C, LDL-C		TC (mmol/l) Diabetic: OR: 2.543 ($P = 0.504$) Non diabetic: OR: 0.172 ($P = 0.043$) TG (mmol/l) Diabetic: OR: 0.780 ($P = 0.651$)	Logistic regression: aortic valve calcification (AVC), sex, age, hypertension, smoking, serum level of fibrinogen, total cholesterol, triglyceride, high-density lipoprotein

(Continued)



Table 2B. (Continued)

Author, year	Study design	Number of patients	Age	Gender (M:F)	Treatment history
Li, 2006	Prospective cohort	553: CAD 388 non CAD 165	Mean: 60.1 (9.7) CAD: 61.4 (9.7) Non CAD: 57.2 (8.8) <i>P</i> = 0.00	CAD: 82.6% Non CAD: 63.9% <i>P</i> = 0.00	
Wang, 2006	Survey	30,378 (ACS 227 stroke 582 non CVD 29,569)	Mean: 46.89 ASC: 52.4 (7.9) Non CVD: 46.7 (8.0)	ASC: male 70.5% Non CVD: male 53.2%	

and risk of CAD. Two studies^{19,20} defined obesity as ≥ 28 kg/m² and ≥ 30 kg/m² and reported statistically significant crude ORs to be 2.05 and 1.68, respectively. Only 1 study¹⁹ reported adjusted RR of 1.29. Four studies^{22,26,27,29} used BMI as a surrogate for obesity and reported the difference in BMI between CAD patients and non-CAD patients. Three of these studies^{22,27,29} found CAD patients had significantly higher levels of BMI, while 1 study²⁶ found the difference in BMI between CAD and non-CAD groups to be statistically insignificant.

Smoking and risk of CAD

Fourteen studies were reviewed for the association between smoking and risk of CAD. The definition of smoking applied varied between studies, which included former smokers, current smokers, or ever smokers. Ever smokers included former smokers and current smokers. Thus reported crude ORs ranged widely, between 1.37 and 5.19. For the studies that provided the categories of smokers included, current smokers had crude ORs reported of 3.06,²⁰ 2.02,²² and 1.69¹⁹; while ever smokers had crude ORs

reported of 1.42²¹ and 1.37.²¹ Seven studies did not refine the definition of smoking status used in the study. However, except for 1 study,²⁹ the rest found smoking to be a significant factor to the risk of CAD. The highest crude association was reported in Zhang et al²⁷ at 5.19, which had 519 CAD patients and 608 controls comparable in demographic characteristics at baseline.

Adjusted risk ratios ranged between 1.23 and 3.83. Current smokers had adjusted OR of 3.83 (95% CI: 1.08–13.68)²⁰ and 1.75,¹⁹ while men had a RR of 2.40 (95% CI: 1.60–3.30).²³ Ever smokers had adjusted OR of 1.23 (95% CI: 1.09–1.39). One study²¹ reported the risk ratio for CAD mortality. Former smokers had a risk ratio of 0.68 for CAD when compared to never smokers, while current smokers had a risk ratio of 1.81. When stratified by diabetic and non-diabetic populations, the adjusted RR ratios were not significant.²⁴

Composite risk factor and CAD

One study, in addition to reporting on the association of the risk factors of interest, also reported an



Definition of risk factor	Crude OR	Adjusted association	Adjusted model configuration
TC, TG, HDL-C, LDL values	TC (mmol/l): CAD 4.5 (1.1) vs. non CAD 4.4 (0.9) ($P = 0.09$) TG (mmol/l): CAD 1.9 (1.7) vs. non CAD 2.0 (1.6) ($P = 0.64$) HDL-C (mmol/l): CAD 1.0 (0.3) vs. non CAD 1.1 (0.3) ($P = 0.00$) LDL (mmol/l): CAD 2.6 (0.9) vs. non CAD 2.4 (0.8) ($P = 0.01$)	Non diabetic: OR: 1.345 ($P = 0.334$) HDL-C (mmol/l) Diabetic: OR: 0.008 ($P = 0.053$) Non diabetic: OR: 0.866 ($P = 0.891$) LDL-C (mmol/L) Diabetic: OR: 1.131 ($P = 0.941$) Non diabetic: OR: 3.588 ($P = 0.082$)	Cholesterol, low-density lipoprotein cholesterol, apoprotein
High TC: TC \geq 240 mg/dL Low HDL-C: HDL-C < 40 mg/dL	High TC 1.48 ($P = 0.116$) Low HDL-C 1.75 ($P < 0.001$)	High TC RR: 1.732 Low HDL-C RR: 1.387	Cox regression: age, gender, Blood pressure, TC, smoking, low HDL-C, diabetes, obesity

association between composite risk factors and risk of CAD.¹⁹ The composite risk factor was defined as having any 1, 2, or 3 of the conditions, which include hypertension, smoking, high TC, low HDL-C, diabetes, and obesity. Among CAD patients, 83.7% had at least 1 risk factor, 47.6% had at least 2, and 18.5% had at least 3 risk factors. Among patients with no CAD, only 64.7%, 25.3%, and 6.6% had at least 1, 2, or 3 risk factors, respectively, and these were each statistically different from the results for CAD patients. Of all patients with at least 1 risk factor, CAD patients had more additional risk factors than non CAD patients by a factor of more than 2 to 1. Additionally, each of the individual risk factors were significant contributors to the risk of CAD ($P < 0.001$).

Discussion

This study provides the first large systematic review of the available evidence on the association between the traditional risk factors—hypertension, abnormal lipid levels (hyperlipidemia, dyslipidemia, TC, TG, HDL-C, LDL-C), diabetes, obesity, and smoking—

and risk of CAD within the last 5 years in China. Of the 5 risk factors examined, lipid conditions, especially high LDL-C values, were found consistently to be associated with high risk of CAD. The adjusted RR rate was as high as 3.31 and consistent with findings in Western populations, which report adjusted RR rates of 1.74 in men and 0.68 in women.³² As in other countries, such as the United States,³³ diabetes was also a significant contributor to the risk of CAD, with an adjusted RR rate as high as 1.191 and adjusted ORs of 3.28 and 4.381 ($P < 0.001$). Hypertension and smoking were found to be significant contributors to the risk of CAD, with adjusted RR rates as high as 1.91 and 1.75 and crude ORs as high as 5.11 and 5.19, respectively. While data on the association between obesity and CAD was suggestive of a positive association (adjusted RR rate of 1.91), we consider the evidence to be weak due to the small number of studies examining that particular risk factor.

Northeast China had the highest CAD mortality rate (28.0%), while Southern China had the lowest rate (17.1%).²¹ A study conducted in the North²¹ reported

**Table 2C.** Association between obesity and risk of CAD.

Author, year	Study design	Number of patients	Age	Gender (M:F)
Ni M, 2007	Case-control	237 (CAD:138; control 99)	Mean: 54.18 (9.25) Range: 35–70 CAD: 55.28(9.03) Control: 52.65 (9.39) <i>P</i> = 0.031	163:74 CAD: 108:30 Control: 55:44 <i>P</i> < 0.01
Su G, 2011	Prospective cohort	344 (CAD: 252; non CAD: 92)	CAD: mean: 65 (9) Non CAD: 61(9)	CAD: 165:87 Non CAD: 48:44
Tang NP, 2008	Case-control	530 (CAD 265; control 265)	CAD: 64 (56–71) Control: 64 (55–71)	CAD: 194:71 non CAD: 194:71 NS
Xu H, 2008	Case-control	384 (CAD 210; control 174)	CAD: 56 (7.3) Non CAD: 55 (8.6)	201:183 CAD: 116:94 Control: 85:89
Zhang K, 2010	Case-control	1127 (CAD: 519; control 608)	CAD: 61.285 (10.755) Control: 60.3777 (10.730) <i>P</i> = 0.16	CAD: 362:157 Control: 401:207
Hu DY, 2006	Prospective cohort	3513 (CAD: 3513)	69 (65–77)	2341:1172
Wang, 2006	Survey	30,378 (ACS 227 stroke 582 non CVD 29,569)	Mean: 46.89 ASC: 52.4 (7.9) Non CVD: 46.7 (8.0)	ASC: male 70.5% Non CVD: male 53.2%

the highest crude ORs and adjusted RR ratios for hypertension, diabetes, smoking, and hyperlipidemia in CAD patients, suggesting that the population of Northern China may be at greater risk for stroke than the Chinese population as a whole. Such geographic variation was also found in the United States, and this was largely suspected to be because areas with higher CAD prevalence were frequently characterized as rural and poor.³⁴ However, while differences in measurement were in part based on geography, studies were mostly regional in scope and lacked comparison across different areas of the country. Well-designed epidemiological studies are needed to better estimate the impact of individual and overall risk factors on reduction and prevention of CAD in China.

Gender and age differences in CAD mortality and prevalence were widely reported in the articles included in this review, and gender played a significant role in the differentiation of prevention and reduction of CAD. CAD mortality rates increased by 50% in men and 21% in women when adjusted for age. This systematic review also confirmed previous findings⁹ that in China, hypertension among women was found to be significant, while hypertension among men was found not to be significant.⁹ Prevalence also seemed to differ by age group with the likelihood of having diabetes among CAD patients increasing with age. This observation is supported by a meta-analysis of 41 cohort studies conducted from Asia, Australia, and New Zealand that



Treatment history	Definition of risk factor	Crude OR	Adjusted association	Adjusted model configuration
	BMI ≥ 30 kg/m ²	2.05 ($P = 0.032$)		
Oral anti-hyperglycemic CAD: 45.7% Non CAD: 44.0% Not significant			BMI not statistically difference between CAD and non-CAD groups	
Insulin CAD: 35.9% Non CAD: 40.9% Not significant				
Statins CAD: 61.9% Non CAD: 69.4% Not significant				
	BMI	BMI: CAD 25.1 (3.3) Non CAD 23.8 (3.6) ($P < 0.001$) BMI: CAD 24.6 (4.2) Non CAD 23.6 (6.1) ($P = 0.056$)		
	BMI (kg/m ²)	BMI: CAD 26.0 (13.6) vs. non CAD 24.3 (13.3) ($P < 0.001$)		
	BMI (kg/m ²)	BMI: CAD Median: 24.2 (quartiles: 22.1–26.4)		
	BMI ≥ 28 kg/m ²	1.68 ($P < 0.001$)	RR: 1.290	Cox regression: age, gender, Blood pressure, TC, smoking, low HDL-C, diabetes, obesity

found higher CAD risk among stratified age groups, particularly amongst women.³³

When looking at other countries such as the United States^{35,36} and France,³⁷ CAD has declined significantly due to treatments and changes in diet,³⁸ the addition of health and nutrition programs, and promoting healthy eating and physical activity via marketing.¹⁹ A study conducted in Singapore³⁸ suggested changes in diet to address incidence of CAD. Additionally, Wang et al¹¹ advised that preparations be made in the health care infrastructure to accommodate the growing need for treatment of CAD and related chronic disease. Additionally, antihypertensives and statins have proved an effective treatment for preventing coronary events and death from coronary heart disease, especially for

preventing secondary coronary events. Three large trials in the United States^{39,40} and Scandinavia⁴¹ demonstrated that statin treatment reduced coronary events by 23%–34% and reduced CAD mortality by 20%–42%. Antihypertensive medication use in China is only 28.2% even among those aware of their hypertensive condition. Increasing antihypertensive medication use, therefore, has the potential to greatly impact hypertension-related CAD mortality.

Meta-analyses were considered, but differences represented in these studies in terms of study design (eg, case-control vs. cohort, blinding vs. non-blinding) patient population, and outcome measurement can have large effects on results.⁴² These problems were exacerbated in the current dataset by heterogeneity in



Table 2D. Association between diabetes and risk of CAD.

Author, year	Study design	Number of patients	Age	Gender (M:F)	Treatment history
Han Y, 2007	Case-control	726 (CAD 378; control 348)	Mean: 57.2 (10.5) Range: 29–89 CAD: mean: 57.7 (10.7) Control: 55.6 (10.4)	492:234 CAD: 284:94 Control: 210:138	
Cui, 2007	Prospective cohort	762 (CAD 423; control 339)	Mean: 60 (10); Range: 17–81	481:281 CAD: 261:162 Control: 220:119	100%: lipid-lowering agents
Ni M, 2007	Case-control	237 (CAD:138; control 99)	Mean: 54.18 (9.25) Range: 35–70 CAD: 55.28 (9.03) Control: 52.65 (9.39) <i>P</i> = 0.031	163:74 CAD: 108:30 Control: 55:44 <i>P</i> < 0.01	
Su G, 2011	Prospective cohort	344 (CAD: 252; non CAD: 92)	CAD: mean: 65 (9) Non CAD: 61 (9)	CAD: 165:87 Non CAD: 48:44	Oral anti-hyperglycemic CAD: 45.7% Non CAD: 44.0% Not significant Insulin CAD: 35.9% Non-CAD: 40.9% Not significant Statins CAD: 61.9% Non CAD: 69.4% Not significant
Tang NP, 2008	Case-control	530 (CAD 265; control 265)	CAD: 64 (56–71) Control: 64 (55–71)	CAD: 194:71 non CAD: 194:71 NS	
Xu H, 2008	Case-control	384 (CAD 210; control 174)	CAD: 56 (7.3) Non CAD: 55 (8.6)	201:183 CAD: 116:94 Control: 85:89	
Zhang K, 2010	Case-control	1127 (CAD: 519; control 608)	CAD: 61.285 (10.755) Control: 60.3777 (10.730) <i>P</i> = 0.16	CAD: 362:157 Control: 401:207	
Chen ZW, 2011	Prospective cohort	325 (CAD: 222; non-CAD: 103)	63.4 (9.7) Diabetic: 66.2 (8.1) Non diabetic: 62.2 (10.2) <i>P</i> < 0.01	218:107 Diabetic: 61:43 Non diabetic: 157:64 <i>P</i> = 0.027	
Hu DY, 2006	Prospective cohort	3513 (CAD: 3513)	69 (65–77)	2341:1172	
Li, 2007	Retrospective cohort	651: CAD 71 non CAD 580	Mean: 56 (8) Range: 42–75 CAD: 63 (9) Non CAD: 54 (9)	301:350 CAD: 54:17 Non CAD: 247:333	
Li, 2006	Prospective cohort	553: CAD 388 Non CAD 165	Mean: 60.1 (9.7) CAD: 61.4 (9.7) Non CAD: 57.2 (8.8) <i>P</i> = 0.00	CAD: 82.6% Non CAD: 63.9% <i>P</i> = 0.00	
Wang, 2007	Survey	597 (Type 2 Diabetes: 199 non diabetes 398)	Range: 40–85	Diabetes: 76:123 Non diabetes: 152:246	
Wang, 2006	Survey	30,378 (ACS 227 stroke 582 non CVD 29,569)	Mean: 46.89 ASC: 52.4 (7.9) Non CVD: 46.7 (8.0)	ASC: male 70.5% Non CVD: male 53.2%	



Definition of risk factor	Crude OR	Adjusted association	Adjusted model configuration
Type 1 and type 2	3.83 ($P < 0.01$)	OR (95% CI): 3.28 (2.60–4.14) ($P = 0.00$)	Logistic: age, gender, hypertension, diabetes mellitus, hyperlipidemia, smoking
Self-reported or oral glucose tolerance and insulin level assayed NR	3.02 ($P = 0.005$)	95% significant association with diabetes	
Diagnosed according to the American Diabetes Association criteria	Duration of diabetes (months): CAD: 78 (77) No CAD: 58 (68) $P = 0.022$		
Fasting blood glucose ≥ 7.8 mmol/l or a diagnosis of diabetes needing diet or antidiabetic drug therapy NR	1.47 (NS) 1.50 ($P = 0.02$)	OR: 4.381 (95% CI: 2.536–7.764); $P < 0.001$	Logistic: diabetes, hypertension, high LDL levels and genotype
1999 WHO diagnostic criteria	22% of CAD patients had diabetes, 0% in non CAD patients. ($P = 1.00$) 1.50 ($P = 0.31$)		
Type 2 diabetes only: ≥ 7.0 or ≥ 11.1 mmol/L on FPG test	52.9% CAD patients had diabetes 5.97 ($P < 0.01$)		
History of DM and Newly diagnosed	2.97 ($P < 0.05$)		
1999 WHO and International Diabetes Association criteria	2.08 (1.16–3.74) ($P < 0.01$)		
Fasting blood glucose ≥ 7 mmol/L or previous diagnosis by physicians	1.53 ($P < 0.001$)	RR: 1.191	Cox regression: age, gender, blood pressure, TC, smoking, low HDL-C, diabetes, obesity

(Continued)



Table 2D. (Continued)

Author, year	Study design	Number of patients	Age	Gender (M:F)	Treatment history
Liu, 2008	Survey	3223 (ACS history 27.1%)	65 (11)	2183:1040	

Table 2E. Association between smoking and risk of CAD.

Author, year	Study design	Number of patients	Age	Gender (M:F)	Treatment history
Han Y, 2007	Case-control	726 (CAD 378; control 348)	Mean: 57.2 (10.5) Range: 29–89 CAD: mean: 57.7 (10.7) Control: 55.6 (10.4)	492:234 CAD: 284:94 Control: 210:138	
Cui, 2007	Prospective cohort	762 (CAD 423; control 339)	Mean: 60 (10); range 17–81	481:281 CAD: 261:162 Control: 220:119	100%: lipid-lowering agents
Han Y, 2010	Case-control	622 (CAD 312; control 310)	Mean: 61.96 (10.71) CAD: 61.96 (10.71) Control: 60.54 (10.18) <i>P</i> = 0.09	209:103 CAD: 209:103 Control: 184:126 <i>P</i> = 0.056	
Ni M, 2007	Case-control	237 (CAD:138; control 99)	Mean: 54.18 (9.25) Range: 35–70 CAD: 55.28 (9.03) Control: 52.65 (9.39) <i>P</i> = 0.031	163:74 CAD: 108:30 Control: 55:44 <i>P</i> < 0.01	
Sai XY, 2007	Cross-sectional survey	1268	Mean: 62.95 (5.18) Never smoker: 62.52 (5.20) Ever smoker: 63.13 (5.16)	1268:0	
Su G, 2011	Prospective cohort	344 (CAD: 252; non CAD: 92)	CAD: mean: 65 (9) Non CAD: 61 (9)	CAD: 165:87 Non CAD: 48:44	Oral anti-hyperglycemic CAD: 45.7% Non CAD: 44.0% Not significant Insulin CAD: 35.9% Non CAD: 40.9% Not significant Statins CAD: 61.9% Non CAD: 69.4% Not significant



Definition of risk factor	Crude OR	Adjusted association	Adjusted model configuration
History of DM or newly diagnosed	22.6% By gender Female: 26.3% Male: 20.8% $P < 0.01$ By age <45 10.4% 45 ~ 20.2% 55 ~ 23.2% 65 ~ 23.8% ≥75 25.2%		
Past and present (former smoker + current smoker)	1.42 ($P < 0.01$)	OR (95% CI): 1.23 (1.09–1.39) ($P = 0.00$)	Logistic: age, gender, hypertension, diabetes mellitus, hyperlipidemia, smoking
Smoked at least one cigarette per day in at least one year		Men: RR = 2.4 (95% CI: 1.6–3.3)	
NR	0.41 ($P < 0.01$)		
Current smoker	3.06 ($P < 0.001$)	OR (95% CI): 3.83 (1.08–13.68) $P = 0.038$	Logistic: age, male, gender, CAD family history, smoking, obesity, dyslipidemia, diabetes mellitus, hypertension, systolic BP, diastolic BP, fasting glucose, total cholesterol, triglycerides, LDL-C, HDL-C, hs-CRP, homocysteine
Ever vs. never (ever-smoker: one who had smoked at least one cigarette daily for one year or more) Former smoker: those who had stopped for at least 2 years. Current smoker: ever-smokers who were smoking at baseline	Ever smoker: 1.37	CHD mortality: former smoker HR 0.681 (95% CI: 0.376–1.233) Current smoker HR 1.805 (95% CI: 1.022–3.188)	
	2.17 ($P = 0.007$)	OR: 2.492 (95% CI: 1.315, 4.720, $P = 0.005$)	Logistic: smoking, male, older age, MAGE (mean amplitude of glycemic excursions), hs-CRP, hyperlipidemia, hypertension, renal insufficiency

(Continued)



Table 2E. (Continued)

Author, year	Study design	Number of patients	Age	Gender (M:F)	Treatment history
Tang NP, 2008	Case-control	530 (CAD 265; control 265)	CAD: 64 (56–71) Control: 64 (55–71)	CAD: 194:71 Non CAD: 194:71 NS	
Xu H, 2008	Case-control	384 (CAD 210; control 174)	CAD: 56 (7.3) Non CAD: 55 (8.6)	201:183 CAD: 116:94 Control: 85:89	
Zhang K, 2010	Case-control	1127 (CAD: 519; control 608)	CAD: 61.285 (10.755) Control: 60.3777 (10.730) $P = 0.16$	CAD: 362:157 Control: 401:207	
Chen ZW, 2011	Prospective cohort	325 (CAD: 222; non-CAD: 103)	63.4 (9.7) Diabetic: 66.2 (8.1) Non diabetic 62.2 (10.2) $P < 0.01$	218:107 Diabetic: 61:43 Non diabetic: 157:64 $P = 0.027$	
Hu DY, 2006	Prospective cohort	3513 (CAD: 3513)	69 (65–77)	2341:1172	
Li, 2007	Retrospective cohort	651: CAD 71 non CAD 580	Mean: 56 (8) Range: 42–75 CAD: 63 (9) Non CAD: 54 (9)	301:350 CAD: 54:17 Non CAD: 247:333	
Li, 2006	Prospective cohort	553: CAD 388 non CAD 165	Mean: 60.1 (9.7) CAD: 61.4 (9.7) Non CAD: 57.2 (8.8) $P = 0.00$	CAD: 82.6% Non CAD: 63.9% $P = 0.00$	
Wang, 2006	Survey	30,378 (ACS 227 stroke 582 non CVD 29,569)	Mean: 46.89 ASC: 52.4 (7.9) Non CVD: 46.7 (8.0)	ASC: male 70.5% Non CVD: male 53.2%	

the statistical methods employed when examining relationships between comorbidities and outcomes. For instance, in the 23 hypertension studies, there were:

1. Differences in definition of hypertension (eg, $\geq 140/90$ vs. $\geq 160/95$)
2. Differences in the type of stroke (ischemic vs. total vs. hemorrhagic vs. stroke mortality, with several different types of ischemic stroke)
3. Differences in patient population (eg, some studies are on the general population, some on only diabetics, some only on patients with atrial fibrillation (AF), some only on elderly patients)
4. Differences in how relationships are measured (some analyses given a crude OR/RR, others adjust for multiple factors)
5. Differences in factors controlled for in multivariate analyses (some control for age and duration of diabetes, while some control for 10 or more variables such as familial stroke history, ie, variables which may be endogenous to risk, thus resulting in a lower than expected hazard ratio between the variables of interest)
6. Differences in study design (prospective cohort vs. retrospective cohort vs. survey vs. case-control)

Given this host of differences, we concluded that while meta-analysis was statistically viable, the results would not be interpretable without digging down into very small subsets of studies.

Another weakness of the data extracted is that fewer than half of the articles reported adjusted hazard ratios



Definition of risk factor	Crude OR	Adjusted association	Adjusted model configuration
≥10 cigarettes/d	2.02 ($P < 0.001$)		
NR	1.53 (NS)		
	5.19 ($P < 0.001$)		
NR		Diabetic: OR: 2.941 ($P = 0.199$) Non diabetic: OR: 1.603 ($P = 0.256$)	Logistic regression: aortic valve calcification (AVC), sex, age, hypertension, smoking, serum level of fibrinogen, total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, apoprotein
	50% of CAD were never smokers, 30% former smokers, 20% current smokers 3.89 ($P < 0.01$)		
	3.30 ($P = 0.00$)		
Currently smoking and ≥1 cigarette per day	1.69 ($P < 0.001$)	RR: 1.750	Cox regression: age, gender, blood pressure, TC, smoking, low HDL-C, diabetes, obesity

or RRs. Much of the discussion relies on crude ORs extracted from the reported frequencies. This dependence on crude ORs ignores the role of other important risk factors for CAD such as age and gender. Though a strong association was found in this review between lipid levels and risk of CAD, evidence relating these 5 risk factors to CAD has largely gone unexamined in the Chinese population. As noted earlier, the lack of quality data makes difficult comparisons between the different regions of China, both geographic and economic. More large epidemiologic studies relating CAD to its risk factors, especially nationwide studies, would go a long way towards clarifying the effects these 5 conditions have on incidence of CAD in China. The need for large, regional studies is made more important by the fact that China has experienced

a considerable increase in the prevalence of CAD in recent decades, and understanding the contribution of the leading 5 risk factors to CAD in China is a critical first step toward future prevention of this disease.

Regardless of the quantity or quality of research in this area, this review found that all 5 of the risk factors examined—hypertension, smoking, diabetes, obesity, and, in particular, low LDL-C levels—were associated with CAD in China. Hypertension, diabetes, and smoking were associated with CAD, with crude ORs ranging from 1.37 to 5.97. While few ORs or RR ratios were calculated, high LDL-C levels were consistently associated with CAD, and to a somewhat lesser extent, so were low HDL-C levels. While the connection between obesity and CAD deserves additional study due to a paucity of existing research within the subject



Table 2F. Association between composite risk factor and risk of CAD.

Author, year	Study design	Number of patients	Age	Gender (M:F)	Treatment history	Definition of risk factor	Crude OR	Adjusted association	Adjusted model configuration
Wang, 2006	Survey	30,378 (ACS 227 stroke 582 non CVD 29,569)	Mean: 46.89 ASC: 52.4 (7.9) Non CVD: 46.7 (8.0)	ASC: male 70.5% Non CVD: male 53.2%		<p>Composite 1 Any one of the list: hypertension, smoking, high TC, low HDL-C, diabetes, obesity</p> <p>Composite 2 Any two of the list: hypertension, smoking, high TC, low HDL-C, diabetes, obesity</p> <p>Composite 3 Any three of the list: hypertension, smoking, high TC, low HDL-C, diabetes, obesity</p>	<p>Composite 1: 2.80 ($P < 0.001$)</p> <p>Composite 2: 2.68 ($P < 0.001$)</p> <p>Composite 3: 3.21 ($P < 0.001$)</p>		

population, studies in this review did find that obesity was positively associated with CAD in China, and this matches results of similar studies conducted in Western populations. Addressing these 5 risk factors through drug treatment as well as diet and lifestyle changes has led to reduced risk of CAD in countries such as the United States. Given that the prevalence of these risk factors in China, especially smoking, is comparatively greater than these other populations, we suspect that treating the risk factors discussed in this review will lead to dramatic and positive effects in the risk of CAD in China. Therefore, we recommend that the Chinese health care system accommodate the increased need for treatment of CAD and its related chronic diseases, in particular the risk factors hypertension, smoking, diabetes, obesity, and elevated lipid levels.

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Author Contributions

Conceived and designed the experiments: JF, HJM, SS. Analyzed the data: DB, SS. Wrote the first draft of the manuscript: DB, SS. Contributed to the writing of the manuscript: SS. Jointly developed the structure and arguments for the paper: Made critical revisions and approved final version: JF, YH, LJ, DZ, DH. All authors reviewed and approved of the final manuscript.

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Competing Interests

Prof. Yong Huo, Prof. Linong Ji, Prof. Dong Zhao, and Prof. Dayi Hu have no conflicts of interest. Dr. JoAnne Foody is a Pfizer Inc, consultant. Dylan Boyd is an employee of United BioSource Corporation. Dr. Hai Jin Meng is an employee of Pfizer, Ltd, Dr. Susan Shiff is a Pfizer Inc, medical employee and is also an owner of Pfizer stock.



Disclosures and Ethics

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests.

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