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Meta-analytic evaluation for the spatio-temporal patterns of the associations between common risk factors and type 2 diabetes in mainland China

Ting Zhou, MB[a], Xiang Liu, MD, PhD[b], Yuanyuan Liu, MD, PhD[a,*], Xiaosong Li, MD, PhD[a,*]

Abstract

There is a dearth of accurate information about the associations between risk factors and type 2 diabetes in mainland China. We conducted a systematic review and meta-analysis to explore the spatio-temporal patterns of the associations between common risk factors and type 2 diabetes in adults at least 18 years old in mainland China.

We searched English and Chinese databases from January 1st, 1997 to December 31st, 2017 for relevant observational studies. Overall and stratification analyses including secular trends and temporal distributions were conducted, odds ratio (OR) and 95% confidence interval (CI) were calculated by applying random-effects model.

Thirty-five studies were included. Type 2 diabetes was positively associated with a family history of type 2 diabetes (*OR* 2.89, 95% *CI* 2.38–3.49), hypertension (*OR* 2.73, 95%*CI* 2.25–3.36), central obesity (*OR* 2.28, 95%*CI* 1.94–2.68), dyslipidemia (*OR* 2.23, 95% *CI* 1.70–2.91), hypertriglyceridemia (*OR* 2.18, 95%*CI* 1.64–2.92), general obesity (*OR* 1.90, 95%*CI* 1.66–2.18), hypercholesterolemia (*OR* 1.65, 95%*CI* 1.32–2.06), smoking (*OR* 1.26, 95%*CI* 1.13–1.40), and drinking (*OR* 1.20, 95%*CI* 1.05–1.36), whereas a negative association with female gender (*OR* 0.87, 95%*CI* 0.78–0.97) existed. Except for female gender and drinking, the pooled effects of temporal and spatial stratification for the other five risk factors were consistent with the above results. For temporal stratification, the *OR*s of general obesity increased gradually during the periods of 1992 to 2005, 2006 to 2010, and 2011 to 2017, while the *OR*s of a family history declined. For regional stratification, the magnitudes of *OR*s for hypertension, dyslipidemia, and hypercholesterolemia in northern areas were larger than that in southern areas, while opposite situation occurred for a family history. Except for the factor a family history, provincial results for the other nine risk factors differed from the overall results and among provinces.

Effect differences existed for modifiable and non-modifiable risk factors in secular trends and regional distribution, which is of potential public health importance for type 2 diabetes prevention.

Abbreviations: ADA = American Diabetes Association, BMI = body mass index, CI = confidence interval, FPG = fasting plasma glucose, HDL-C = high-density lipoprotein cholesterol, ID = international dollar, IDF = international diabetes federation, OGTT = oral glucose tolerance test, OR = odds ratio, TC/HDL-C = ratio of cholesterol to high density lipoprotein cholesterol, TG/HDL-C = ratio of triglyceride to high-density lipoprotein cholesterol, WC = waist circumference, WHO = World Health Organization, WHR = high waist-hip ratio.

Keywords: meta-analysis, risk factors, spatio-temporal patterns, type 2 diabetes

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Ting Zhou and Xiang Liu contributed equally to this work.

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[a] Department of Epidemiology and Biostatistics, [b] Department of Health and Social Behavior, West China School of Public Health and West China Fourth Hospital, Sichuan University, Chengdu, China.

[*] Correspondence: Yuanyuan Liu, and Xiaosong Li, Department of Epidemiology and Biostatistics, West China School of Public Health and West China Fourth Hospital, Sichuan University, 610041 Chengdu, China (e-mails: y_multi@126.com, lixiaosong1101@126.com).

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1. Introduction

Type 2 diabetes has been a salient global public health issue. According to the latest 8th edition of IDF (International Diabetes Federation) diabetes atlas[1] published in 2017, 425 million people (20–79 years) were estimated to have diabetes in the world, there into, the diabetes population in mainland China alone amounts to 114 million, ranking the first place among the 222 countries or territories included in the atlas. And the corresponding total healthcare expenditure is estimated to reach ID (International Dollar) 110 billion, only following the United of States.[1] Although it is a developing country, China has exhibited a constantly increasing prevalence of diabetes over recent decades, from 2.5%[2] and 2.6%[3] in 1994 and 2002, to 9.7%[4] and 11.6%[5] in 2007 and 2010, respectively. The most recent national survey reported a relatively high overall prevalence of 10.9% in 2013.[6] In China, more than 95% of people with diabetes have type 2 diabetes.[7] As type 2 diabetes is a complex chronic disease that could be contributed to by both hereditary and environmental factors, it is necessary to conduct a systematic study on the possible associations of common risk factors for type 2 diabetes, especially regarding modifiable risk factors and their spatio-temporal patterns.

Since many epidemiological surveys of different scales and regions in China have been conducted and no meta-analysis has been conducted focusing on the potential associations of common risk factors with type 2 diabetes and their temporal and spatial distributions for adults in the general population of mainland China, the objectives of this comprehensive systematic review and meta-analysis were the following:

I. to examine the potential associations between common risk factors and type 2 diabetes reported in 1997 to 2017 in mainland China;
II. to investigate the temporal distribution of the associations and determine their secular trends;
III. to assess the spatial distribution of the associations and make comparisons among different regions.

As there have been no pooled studies of the associations and their concrete spatio-temporal patterns, this study is the first to explore the above points extensively. The findings could contribute to more appropriate type 2 diabetes prevention strategies and provide references for other territories and countries.

2. Methods

2.1. Search methods

Systematic literature searches were conducted to identify studies concerning type 2 diabetes among those in the general population more than 18 years old in mainland China in both English (PubMed, Medline, Embase, EBSCO, and Science Direct) and Chinese (China National Knowledge Infrastructure [CNKI], VIP, CBM, and Wanfang) electronic databases and the search was supplemented with manual retrieval. The search terms were "type 2 *diabetes* AND (*influencing factors* OR *risk factors*) AND *China*", related references of the retrieved studies were inspected for more information. Considering that there have been great changes in the diagnostic criteria for type 2 diabetes since 1997, the search ranged from January 1997 to December 2017.

2.2. Study selection and eligibility criteria

Two authors (TZ and XL) screened titles and abstracts independently and disagreements were resolved by a third author (YYL). Studies were eligible for inclusion if they met the following criteria:

I. observational (cross-sectional, case-control or cohort) study whose objects could be categorized into type 2 diabetes and non-type 2 diabetes groups;
II. the type 2 diabetes group included adults from the general population with type 2 diabetes, and non-type 2 diabetes group comprised adults from the general population without type 2 diabetes, all of whom were more than 18 years old;
III. diagnostic criteria for type 2 diabetes were fasting plasma glucose (FPG) $\geq$7.0 mmol/l or 2-h plasma glucose of oral glucose tolerance test (OGTT) $\geq$11.1 mmol/l, according to 1997 American Diabetes Association (ADA) criteria/1999 World Health Organization (WHO) criteria or later versions;
IV. data of both groups for all studied factors were reported.

The exclusion criteria included the following:

I. non-original studies;
II. repeated reports;
III. type 1 diabetes as an outcome;
IV. studies with unqualified quality;
V. studies without available information (e.g., abstracts);
VI. studies published not in English or Chinese.

2.3. Data extraction and quality assessment

Two authors (TZ and XL) conducted data extraction and quality assessment independently; disagreements were resolved by a third author (YYL). The following information was extracted for better interpretation: first author, publication year, study location, study design, diagnosis criteria, sample size, number of subjects in the type 2 diabetes and non-type 2 diabetes groups, risk factors, effect index, and other available data (e.g., years of the material derived, provinces and regions, quality scores). Authors were contacted by email if the information of a study included was unresolved to the utmost extent.

For the quality assessment, criteria from the Joanna Briggs Institute Reviewer's Manual[8] were utilized for cross-sectional, case-control, and cohort studies, and a 0–2 score was awarded for each of the 8, 10, and 11 items of the corresponding study designs. Studies with a score greater than half the full mark were categorized as having qualified quality.

2.4. Data analysis

Heterogeneity among the studies was quantified by the I^2 statistic, and 50% was set as the cut-off point. If the I^2 statistic $\leq$50% and $P>.10$, the results of the fixed-effects model were adopted; otherwise, a random-effects model was used to attain the estimated effects.[9] Odds ratio (*OR*) and the corresponding 95% confidence interval (*CI*) was calculated. Sensitivity analysis was conducted through comparison of the pooled results estimated by the fixed- and random-effects models. Publication bias was detected by asymmetry of the forest plot for the overall analysis.

For comprehensive and in-depth analysis, temporal, and spatial stratification groups were devised. For the former, we divided studies into several groups in line with the time periods set based on the ease of interpretation according to the year of the material. For the latter, we subgrouped the studies based on whether they were conducted in southern and northern regions to attain the regional pooled estimations considering different geographical environments and customs between northern and southern China. We further explored the provincial pooled effects by classifying provincial subgroups. Then, statistical maps were plotted to demonstrate the spatial distribution for the pooled results.

All statistical procedures for the meta-analysis were performed in Review Manager 4.4.2, and statistical maps (Figure 2) were plotted in R version 3.3.3 (https://www.R-project.org/).

The MOOSE checklist is appropriate for this manuscript and all the checklist items can be found.

3. Results

3.1. Literature search results and study characteristics

In all, 9685 publications were retrieved from electronic databases, and 35 studies[10–44] with qualified quality were finally included after checking their eligibility. There were 16 case-control studies, 8 cohort studies and 11 cross-sectional studies. These studies covered 20 provinces in mainland China, and the years of the materials for these studies ranged from 1992* to 2017. Participants reached 242,481, including 21,932 type 2 diabetes cases and 220,549 non-type 2 diabetes cases. In all, 10 factors were analyzed in this study: a family history of type 2 diabetes (abbr. family history), hypertension, drinking status (abbr. drinking), smoking status (abbr. smoking), the female gender (abbr. gender), central obesity (including high waist-hip ratio [WHR] and waist circumference [WC]), general obesity (high body mass index [BMI]),[45] dyslipidemia, hypercholesterolemia, and hypertriglyceridemia.

A flow chart demonstrating the detailed selection process is presented in Figure 1, and more information about the included studies is shown in Table 1. The quality assessment scores showed that the included studies were qualified.

3.2. Overall characteristics of common risk factors for type 2 diabetes

The results of the random-effects model for all 10 factors were adopted for their $I^2 \geq 50\%$. As shown in Table 2, all 10 factors were statistically associated with type 2 diabetes. Among them, there was a positive correlation between type 2 diabetes and family history ($OR=2.89$, $95\%CI=2.38$–3.49), hypertension ($OR=2.73$, $95\%CI=2.25$–3.36), drinking ($OR=1.20$, $95\%CI=1.05$–1.36), smoking ($OR=1.26$, $95\%CI=1.13$–1.40), central obesity ($OR=2.28$, $95\%CI=1.94$–2.68), general obesity ($OR=1.90$, $95\%CI=1.66$–2.18), dyslipidemia ($OR=2.23$, $95\%CI=1.70$–2.91), hypercholesterolemia ($OR=1.65$, $95\%CI=1.32$–2.06), and hypertriglyceridemia ($OR=2.18$, $95\%CI=1.64$–2.92) and a negative correlation with gender ($OR=0.87$, $95\%CI=0.78$–0.97). Though both were indices of obesity, the overall estimation of central obesity was higher than that of general obesity. As the index indicated lipid metabolism dysfunction, the overall estimation of hypertriglyceridemia was higher than that of hypercholesterolemia, and dyslipidemia, which consisted of but was not constrained to the first 2 patterns of hypertriglyceridemia and hypercholesterolemia, ranked top among these 3 indicators. The *OR*s of family history ranked top among all these common risk factors, and those of hypertension, central obesity, hyperlipidemia, and hypertriglyceridemia followed closely, all surpassing 2.00. More information for each factor in the meta-analysis is listed in Table 2.

The sensitivity analysis results showed consistent outcomes for the fixed- and random-effects models for all 10 factors, this suggested that the results were quite stable and highly reliable, which in a degree justified our exclusion criteria. The forest plots were almost symmetrical, except for family history, general obesity and hypercholesterolemia, which suggested little likelihood of publication bias overall.

3.3. Temporal characteristics of common risk factors for type 2 diabetes

See Table 3. Because the time frame of the included studies ranged from 1992 to 2017, we divided it into 3 periods with cut-offs of 2005 and 2010, which roughly corresponded to the years of the national type 2 diabetes prevalence reported. The subgroup analysis results showed that family history, hypertension, smoking, central obesity, general obesity, dyslipidemia, hypercholesterolemia, and hypertriglyceridemia were consistent with the overall pooled effects and were statistically associated with type 2 diabetes, excluding gender and drinking. There were 4 main traits of the temporal distribution regarding the above factors:

I. Change pattern. Four change patterns existed among the former 8 factors with significant effects along the periods. The estimated effects of hypercholesterolemia, hypertension, and smoking increased after dropping; the first 2 exhibited a rising tendency, while smoking remained almost steady. In contrast, the estimated effects of hypertriglyceridemia, dyslipidemia and central obesity decreased after rising, and all 3 factors showed nearly stable trends. The estimation of family history decreased, while that of general obesity increased.

II. Transfer of the dominant factor. The top 3 dominant factors in this study transferred from family history ($OR=3.15$, $95\%CI=2.39$–4.15), dyslipidemia ($OR=2.45$, $95\%CI=1.43$–4.21), and hypertension ($OR=2.37$, $95\%CI=1.81$–3.12) in 1992 to 2005 to hypertension ($OR=3.16$, $95\%CI=2.11$–4.75), family history ($OR=2.97$, $95\%CI=2.14$–3.80), and hypercholesterolemia ($OR=2.60$, $95\%CI=1.89$–3.58) in 2006 to 2010 and hypertension ($OR=2.75$, $95\%CI=2.25$–3.36), dyslipidemia ($OR=2.46$, $95\%CI=1.75$–3.87), and central obesity ($OR=2.39$, $95\%CI=1.82$–3.12) in 2011 to 2017.

III. Indices of a similar category. The estimated effects of central obesity were larger than those of general obesity for each time period, but that of general obesity approached that of central obesity. The rank of estimations for dyslipidemia, hypertriglyceridemia, and hypercholesterolemia were almost the same as for the overall study, with only an abnormally widened magnitude for hypercholesterolemia in 2006 to 2010 compared with the other 2 periods.

* For studies containing consecutive years' data, the following criteria for identification of the year of the material and classification of time periods were set based on the provision of the most information: studies with the highest coverage in year span for a specific time period were classified into this time period, and the year of the material was identified by the start year of the study's time frame or the start year of this specific time period. For example, the study of He et al[10]. Included data ranging from 1992 to 2007; it had the most coverage for the time period of 1992 to 2005, so it was classified into 1992 to 2005, and the year of the material was 1992.

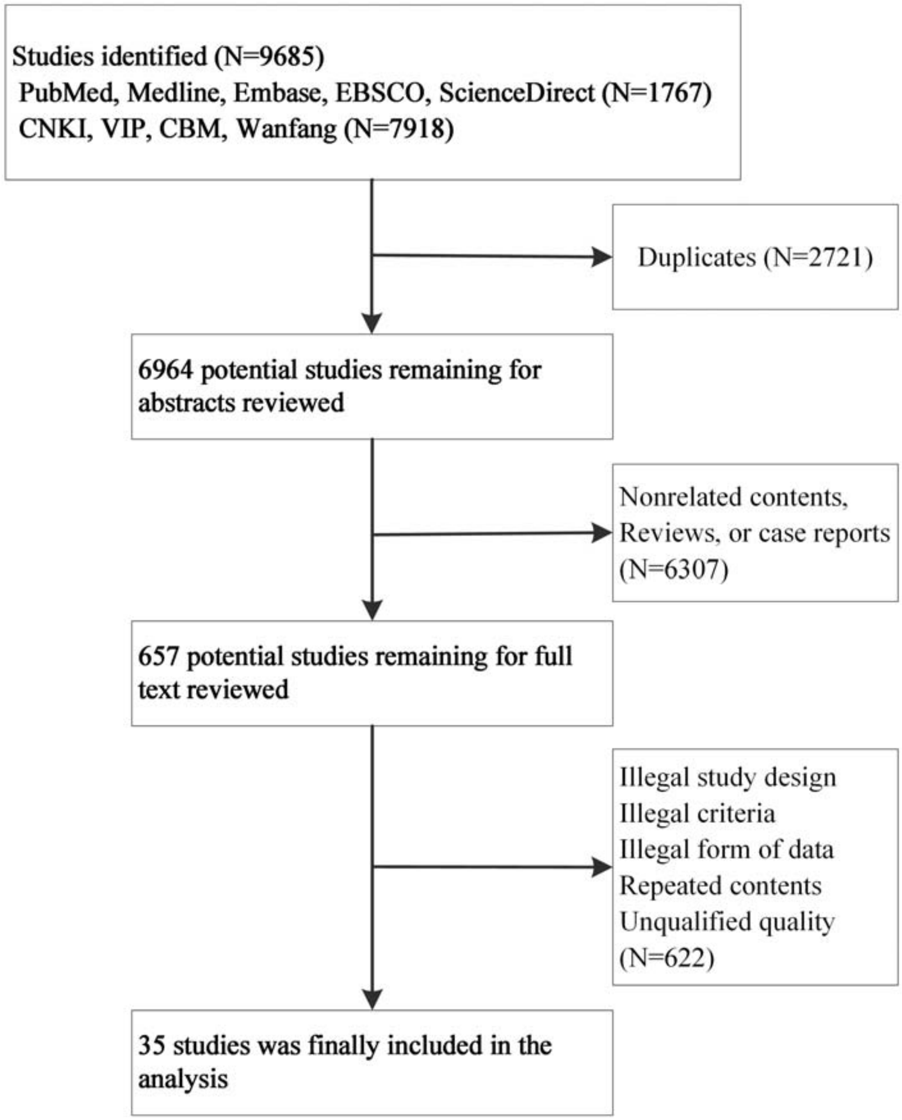

Figure 1. Literature search profile and selection process.

IV. Inconsistent factors. Though the overall effect of drinking and gender suggested their positive correlation with type 2 diabetes, their exact estimations in the three specified time periods differed from each other.

3.4. Spatial distribution of common risk factors for type 2 diabetes

The 35 studies comprised 15 studies conducted in northern provinces, 19 studies conducted in southern provinces, and 1 study[26] conducted in multiple provinces; this last study could appropriately be classified into either the northern or southern region. Thus, we pooled the 34 provincial studies by dividing them into northern and southern categories. As shown in Table 4, there were differences between the northern and southern regions, given that the relationship of all common risk factors with type 2 diabetes was almost consistent with the overall results, with only one exception for gender. The female gender was statistically less likely to be associated with type 2 diabetes in the northern region ($OR=0.77$, $95\%CI=0.67–0.88$), while no association existed in the southern region ($OR=0.94$, $95\%CI=0.77–1.16$). Among the other 9 factors, the estimated effects of dyslipidemia ($OR=2.88$, $95\%CI=1.74–4.75$) and hypercholesterolemia ($OR=2.03$, $95\%CI=1.44–2.87$) were more remarkable in northern China, and yet there was a higher estimated effect of family history ($OR=3.15$, $95\%CI=2.42–4.10$) in southern China. Little differences were observed for hypertension, drinking, smoking, hypertriglyceridemia, central obesity, and general obesity between the 2 regions.

See Figure 2. To explore the spatial distribution of common risk factors for type 2 diabetes in greater detail, an analysis based on provinces was performed. The above total of 34 provincial studies covered 20 provinces. The estimated effect of family history was in accordance with the overall results in every province, with the highest effect being observed in Beijing ($OR=6.02$, $95\%CI=3.90–9.29$), whereas significantly different outcomes appeared for the other 9 factors among different provinces. For hypertension, drinking, smoking, central obesity,

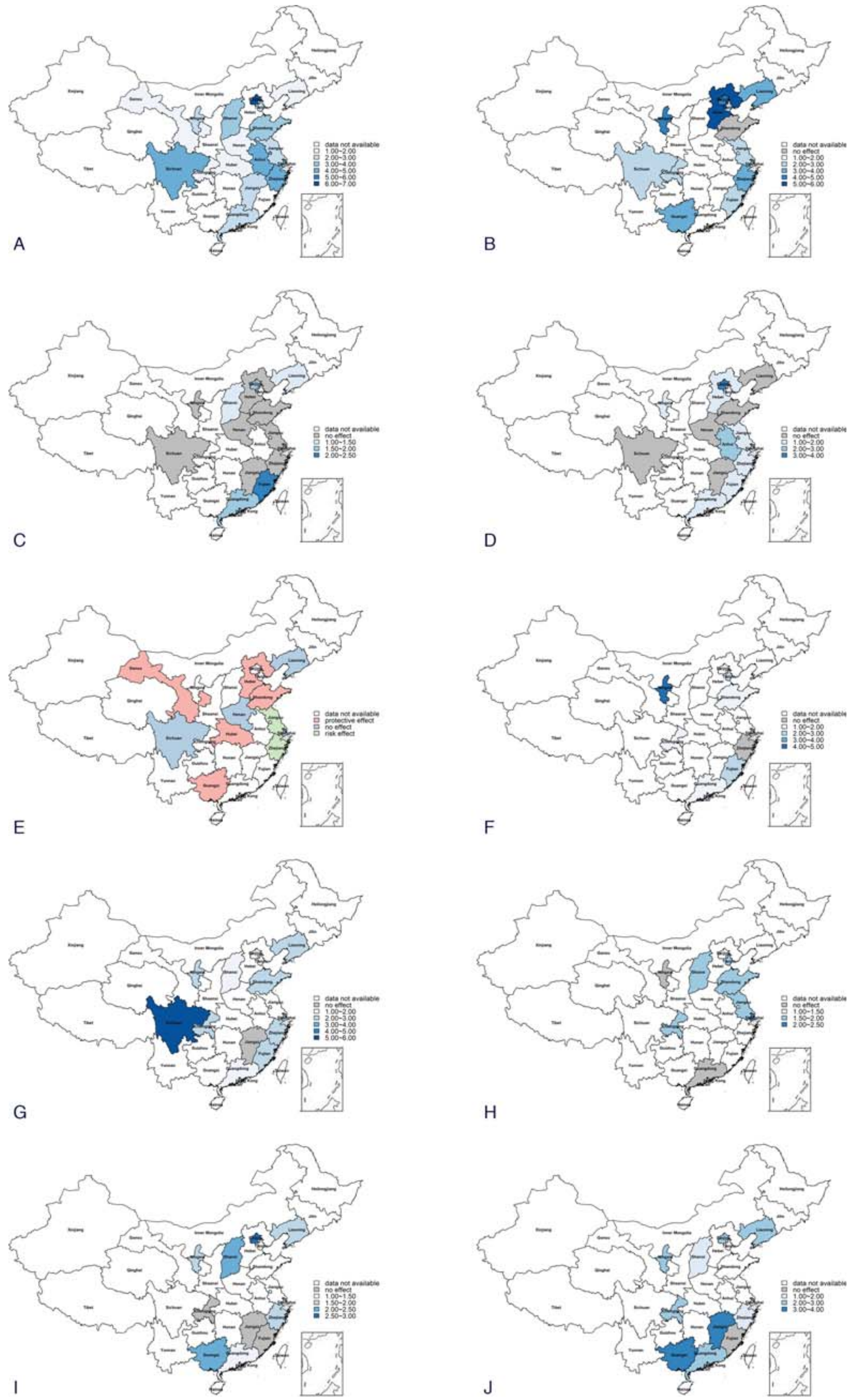

Figure 2. Spatial distribution of associations between common risk factors and type 2 diabetes in mainland China. (A) family history, (B) hypertension, (c) drinking, (d) smoking, (E) gender, (F) dyslipidemia, (G) central obesity, (H) general obesity, (I) hypercholesterolemia, (J) hypertriglyceridemia.

Table 1

Characteristics of the studies included in the meta-analysis for common risk factors of type 2 diabetes in the general population in mainland China.

Source	Year of material	Province	Region	Design type*	Diagnosis criteria	Non-case/case	Score	Factors †
He et al[10], 2012	1992	Sichuan	southern	A	FPG≥7.0 mmol/L	613/74	18	1, 2, 3, 4, 5
Wu et al[11], 2000	1998	Sichuan	southern	B	ADA 1997	200/200	14	1, 2, 6
Tang et al[12], 2004	2002	Chongqing	southern	B	WHO 1999	315/315	14	1, 2, 3, 4, 6, 7, 8, 9, 10
Zhu et al[13], 2004	2002	Shanghai	southern	B	WHO 1999	150/150	15	1, 2, 3, 4, 6, 7, 8
Liu et al[14], 2008	2004	Guangdong	southern	B	WHO 1999	214/295	13	1, 3, 4, 7, 9, 10
Xu et al[15], 2015	2004	Jiangsu	southern	A	WHO 1999	4318/232	16	1, 2, 3, 4
Chen et al[16], 2006	2005	Ningxia	northern	C	FPG≥7.0 mmol/L	1169/144	10	1, 2, 6, 8
Cheng[17], 2007	2005	Shanghai	southern	B	WHO 1999	205/202	15	1, 2, 3, 4, 6, 7, 8, 9, 10
Zhang et al[18], 2006	2005	Ningxia	northern	B	ADA 1997	205/202	11	1, 2, 8
Sun[19], 2012	2006	Shandong	northern	B	WHO 1999	212/106	16	1, 2, 3, 4, 8
Wang et al[20], 2009	2006	Guangdong	southern	C	WHO 1999	4990/639	12	1, 8
Chen et al[21], 2017	2006	Shandong	northern	A	FPG≥7.0 mmol/L	28138/1068	16	1, 2, 3, 4, 5
Ding et al[22], 2008	2007	Shandong	northern	B	WHO 1999	120/152	13	1, 3, 4, 6, 7
Jiang[23], 2009	2007	Shanghai	southern	B	WHO 1999	80/80	15	1, 2, 6, 8
Peng[24], 2009	2007	Jiangxi	southern	C	WHO 1999	66/66	10	1, 3, 4, 6, 7, 9, 10
Xue et al[25], 2016	2007	National	national	A	ADA 2003	14583/1101	17	5
Guo[26], 2009	2008	Shanxi	northern	B	WHO 1999	226/226	14	1, 3, 6, 7, 9, 10
Song et al[27], 2016	2008	Hubei	southern	A	ADA 2014	51689/4899	16	1, 5
Liu et al[28], 2011	2009	Zhejiang	southern	A	WHO 1999	501/501	13	1, 2, 3
Xiao et al[29], 2010	2009	Tianjin	northern	B	WHO 1999	620/585	14	1, 2, 7, 8
Weng et al[30], 2012	2010	Beijing	northern	B	ADA 1997	243/233	12	1, 2, 3, 4, 6, 9, 10
Jin et al[31], 2012	2011	Anhui	southern	B	ADA 1997	125/124	12	1, 4
Li et al[32], 2016	2011	Liaoning	northern	B	FPG≥7.0 mmol/L or OGTT≥11.1 mmol/L	1219/1177	14	1, 2, 3, 4, 5, 6, 7, 9, 10
Wang et al[33]. 2016	2011	Shandong	northern	C	FPG≥7.0 mmol/L or OGTT≥11.1 mmol/L	1430/284	11	2, 3, 4, 5
Hu et al[34], 2015	2012	Jiangsu	southern	C	FPG≥7.0 mmol/L	36605/1820	12	1, 2, 3, 4, 5, 7
Zou et al[35], 2017	2012	Guangxi	southern	C	WHO 1999	6322/338	10	2, 5, 9, 10
Hua et al[36], 2015	2013	Zhejiang	southern	C	FPG≥7.0 mmol/L or OGTT≥11.1 mmol/L	2848/258	11	1, 2, 3, 4, 5, 6, 9, 10
Ju et al[37]. 2015	2013	Gansu	northern	C	WHO 1999	872/150	11	1, 5
Li et al[38], 2014	2013	Henan	northern	C	ADA 2005	7777/1842	10	3, 4, 5
Wang et al[39], 2015	2013	Hebei	northern	C	ADA 2013	6110/525	12	2, 3, 4, 5
Zhang[40], 2015	2013	Fujian	southern	B	WHO 1999	298/298	15	2, 3, 4, 6, 7, 8, 9, 10
Zhang et al[41], 2015	2013	Jiangsu	southern	B	FPG≥7.0 mmol/L	771/771	13	2, 3, 4
Lin et al[42], 2017	2014	Zhejiang	southern	C	WHO1999	3997/476	11	1, 2, 5
Zhang et al[43], 2016	2014	Henan	northern	A	FPG≥7.0 mmol/L	11497/775	16	1, 3, 4, 5
Su et al[44], 2017	2017	Shandong	northern	A	FPG≥7.0 mmol/L or OGTT≥11.1 mmol/L	31821/1624	18	2, 3, 4, 5

* Design type: A = cohort study, B = case-control study, C = cross-sectional study.

† Factors: 1 = family history, 2 = hypertension, 3 = drinking, 4 = smoking, 5 = gender, 6 = central obesity (male: WHR≥0.90, or WC≥85 cm; female: WHR≥0.85, or WC≥80 cm), 7 = general obesity (BMI≥24 kg/m^2, or BMI≥25 kg/m^2), 8 = dyslipidemia, 9 = hypercholesterolemia (TC ≥5.18 mmol/L), 10= hypertriglyceridemia (TG≥1.70 mmol/L).

Table 2

Overall results for the meta-analysis of common risk factors of type 2 diabetes in the general population in mainland China.

Factors	*N* (studies)	*N* (cases)	*N* (non-cases)	Estimated effects* (95%*CI*)	
				Fixed effect model	Random effect model
Family history	27	17,978	200,073	2.04 (1.93, 2.16)	2.89 (2.38, 3.49)
Hypertension	24	11,751	128,550	2.68 (2.66, 2.99)	2.73 (2.25, 3.36)
Drinking	23	12,994	135,697	1.20 (1.14, 1.26)	1.20 (1.05, 1.36)
Smoking	22	12,487	137,134	1.20 (1.14, 1.25)	1.26 (1.13, 1.40)
Gender	15	19,688	265,000	0.87 (0.84, 0.90)	0.87 (0.78, 0.97)
Central obesity	13	3581	7299	2.30 (2.09, 2.52)	2.28 (1.94, 2.68)
General obesity	11	5286	40,038	2.00 (1.57, 2.12)	1.90 (1.66, 2.18)
Dyslipidemia	10	2721	8244	1.95 (1.75, 2.18)	2.23 (1.70, 2.91)
Hypercholesterolemia	10	3408	11,956	1.34 (1.26, 1.43)	1.65 (1.32, 2.06)
Hypertriglyceridemia	10	3408	11,956	2.20 (2.01, 2.40)	2.18 (1.64, 2.92)

* Estimated effects: the estimated effect index for all factors is *OR* (95%*CI*).

Table 3

Subgroup analysis of common risk factors for type 2 diabetes in the general population in mainland China based on temporal stratification.

	1992–2005		2006–2010		2011–2017	
Factors	*N* (study)	*OR* (95%*CI*)	*N* (study)	*OR* (95%*CI*)	*N* (study)	*OR* (95%*CI*)
Family history	9	3.15 (2.39, 4.15)	11	2.97 (2.14, 3.80)	7	2.18 (1.59, 2.99)
Hypertension	8	2.37 (1.81, 3.12)	6	3.16 (2.11, 4.75)	10	2.75 (2.25, 3.36)
Drinking	6	1.11 (0.91, 1.35)	7	1.55 (1.41, 1.69)	10	1.07 (0.92, 1.25)
Smoking	6	1.27 (1.11, 1.45)	5	1.64 (1.08, 2.49)	11	1.13 (1.01, 1.26)
Gender	1	0.73 (0.44, 1.20)	3	0.98 (0.80, 1.21)	11	0.83 (0.71, 0.97)
Central obesity	5	2.35 (1.95, 2.84)	5	1.98 (1.44, 2.73)	3	2.39 (1.82, 3.12)
General Obesity	4	1.56 (1.29, 1.89)	4	1.83 (1.57, 2.12)	3	2.23 (1.87, 2.67)
Dyslipidemia	5	2.45 (1.43, 4.21)	4	2.02 (1.39, 2.93)	1	2.46 (1.75, 3.87)
Hypercholesterolemia	3	1.18 (1.09, 1.29)	3	2.60 (1.89, 3.58)	4	1.59 (1.11, 2.29)
Hypertriglyceridemia	3	2.29 (1.90, 2.77)	3	1.95 (1.54, 2.45)	4	2.01 (1.16, 3.45)

general obesity, hyperlipidemia, hypercholesterolemia, and hypertriglyceridemia, the highest value was observed in Hebei ($OR=5.87$, $95\%CI=4.84$–7.13), Fujian ($OR=2.07$, $95\%CI=$ 1.15–2.61), Beijing ($OR=3.63$, $95\%CI=2.31$–5.69), Sichuan ($OR=5.85$, $95\%CI=2.32$–14.78), Shanghai ($OR=2.50$, $95\%CI=1.52$–4.10), Ningxia ($OR=4.29$, $95\%CI=2.67$–6.88), Beijing ($OR=2.82$, $95\%CI=1.68$–4.74), and Guangxi ($OR=3.85$, $95\%CI=3.08$–4.82), respectively. For gender, being female was positively associated with type 2 diabetes in Jiangsu ($OR=1.15$, $95\%CI=1.05$–1.27) and Zhejiang ($OR=1.15$, $95\%CI=1.02$–1.29), whereas a negative association with type 2 diabetes was observed in Gansu ($OR=0.55$, $95\%CI=0.38$–0.79), Hebei ($OR=0.67$, $95\%CI=0.56$–0.81), Shandong ($OR=0.72$, $95\%CI=0.65$–0.79), Guangxi ($OR=0.60$, $95\%CI=0.47$–0.75) and Hubei ($OR=0.78$, $95\%CI=0.73$–0.84). The remaining provinces showed no significant effects.

4. Discussion

4.1. Main findings

Being the first meta-analysis focusing on the potential associations of common risk factors, both modifiable and non-modifiable risk factors simultaneously, with type 2 diabetes and their temporal and spatial distributions for adults in the general population of mainland China, this study fills some of the gaps in this field. By conducting overall and stratified analyses, we found that the estimations were not exactly the same either in the comparison of overall study and stratified studies or within stratified studies themselves. Both overall study and stratified studies showed that family history and hypertension were positively associated with the incidence of type 2 diabetes among adults in mainland China. Drinking, smoking, gender, dyslipidemia, hypertriglyceridemia and hypercholesterolemia were positively associated with type 2 diabetes, with some variations in consideration of the temporal trends and spatial distributions, among which drinking and gender showed significant difference in terms of temporal and spatial distribution. One of the modifiable risk factors, general obesity, demonstrated an increasing trend of estimated effects, and hypertension, dyslipidemia, and hypercholesterolemia seemed to play a more important role in northern areas than in southern areas, whereas a family history of type 2 diabetes faced an opposite situation.

4.2. Family history of type 2 diabetes

A family history of type 2 diabetes, as a genetic predisposition, has been reported as a risk factor for type 2 diabetes.[46,47] Our results support this idea by showing that those with a family history are 2.89 times ($OR=2.89$, $95\%CI$: 2.38–3.49) more likely to develop type 2 diabetes than those without. The role of family history might vary according to other elements, such as socioeconomic position[47] and type of kinship with the family member who had type 2 diabetes.[48] By and large, a declining trend was observed for family history in our study. The estimated effect in the period of 1992 to 2005 was $OR=3.15$ ($95\%CI$: 2.39–4.15) and became $OR=2.18$ ($95\%CI$: 1.59–2.99) in 2011 to 2017, which might be a consequence of the prevailing modifiable risk factors along with rapid urbanization in China.[49] Furthermore, there was an obvious disparity in the estimated effect of family history among the region stratifications, yet the possible causes remain to be determined.

4.3. Hypertension

The overall effect of hypertension was $OR=2.73$ ($95\%CI$: 2.25–3.36), suggesting a close link between hypertension and type 2 diabetes; this finding is in agreement with previous reports[46,50] indicating a close predictive association between hypertension and type 2 diabetes. The comorbidity of hypertension with type 2 diabetes could be ascribed to adiposity and insulin resistance via the shared pathophysiological mechanisms, for example, inappropriate activation of the renin-angiotensin-aldosterone system,[51] which is consistent with our results regarding obesity. At the macro level, some risk factors for hypertension and type 2 diabetes, such as tobacco consumption and improper alcohol use, could overlap;[52] however, the prevalence of hypertension has increased from 17.6%[3] for people more than 15 years old in 2002 to 25.2%[53] for adults more than 18 years old in 2012. This rising trend is in line with that of diabetes, which is consistent with the upward trend of the estimated effect of hypertension.

4.4. Dyslipidemia

Dyslipidemia has long been reported as a follower of type 2 diabetes, and they together promote the progression of cardiovascular disease and other complications.[54] Those with dyslipidemia have a higher risk for developing type 2 diabetes than those without.[55] Our study confirmed this relationship and showed a comparatively strong link of $OR=2.23$ ($95\%CI$: 1.70–2.91), which is in accordance with the result of $OR=2.93$ ($95\%CI$: 2.37–3.63) from a recent cross-sectional survey in Shanghai, China.[56] Hypercholesterolemia and hypertriglyceridemia, 2

Table 4

Spatial distribution for common risk factors of type 2 diabetes in the general population in mainland China.

Province	Family history	Hypertension	Drinking	Smoking	Gender	Central obesity	General obesity	Dyslipidemia	Hypercholesterolemia	Hypertriglyceridemia
Northern	**2.46 (1.78, 3.40)**	**3.00 (2.19, 4.12)**	**1.18 (1.01, 1.38)**	**1.26 (1.03, 1.53)**	**0.77 (0.67, 0.88)**	**2.05 (1.50, 2.79)**	**1.97 (1.36, 2.87)**	**2.88 (1.74, 4.75)**	**2.03 (1.44, 2.87)**	**2.27 (1.73, 2.97)**
Beijing	6.02 (3.90, 9.29)	4.58 (3.06, 6.87)	1.68 (1.11, 2.54)	3.63 (2.31, 5.69)	–	1.84 (1.28, 2.65)	–	–	2.82 (1.68, 4.74)	2.04 (1.40, 2.65)
Gansu	1.77 (1.17, 2.68)	–	–	–	0.55 (0.38, 0.79)	–	–	–	–	–
Hebei	–	5.87 (4.84, 7.13)	1.20 (0.98, 1.49)	1.47 (1.22, 1.77)	0.67 (0.56, 0.81)	–	–	–	–	–
Henan	1.76 (1.35, 2.29)	–	1.08 (0.95, 1.22)	1.03 (0.87, 1.22)	0.83 (0.59, 1.17)	–	–	–	–	–
Liaoning	1.26 (1.03, 1.54)	3.07 (2.59, 3.63)	1.45 (1.21, 1.73)	1.10 (0.90, 1.34)	0.99 (0.85, 1.17)	2.88 (2.42, 3.41)	–	–	1.51 (1.28, 1.78)	2.77 (2.32, 3.32)
Ningxia	2.49 (1.78, 3.48)	4.43 (3.05, 6.42)	1.60 (0.93, 2.73)	1.80 (1.16, 2.81)	–	2.25 (1.50, 3.37)	1.42 (0.96, 2.11)	4.29 (2.67, 6.88)	1.96 (1.06,3.61)	2.82 (1.82, 4.38)
Shandong	3.37 (0.97,11.74)	1.75 (0.99, 3.10)	1.09 (0.67, 1.79)	1.13 (0.68, 1.89)	0.72 (0.65, 0.79)	2.07 (1.25, 3.44)	1.79 (1.10, 2.90)	1.52 (1.06, 2.17)	–	–
Shanxi	3.02 (1.48, 5.29)	–	1.47 (1.13, 1.95)	–	–	1.37 (1.05, 2.04)	1.64 (1.16, 2.65)	–	2.48 (1.47, 3.57)	1.56 (1.13, 2.41)
Tianjin	2.39 (1.75, 3.26)	2.83 (2.21, 3.62)	–	–	–	–	1.82 (1.53, 2.17)	2.99 (2.17, 4.13)	–	–
Southern	**3.15 (2.42, 4.10)**	**2.60 (2.11, 3.05)**	**1.21 (0.98, 1.49)**	**1.25 (1.17, 1.33)**	**0.94 (0.77, 1.16)**	**2.26 (1.98, 2.59)**	**1.89 (1.55, 2.31)**	**1.93 (1.44, 2.59)**	**1.42 (1.05, 1.93)**	**2.16 (1.36, 3.45)**
Anhui	4.45 (1.15,17.18)	–	–	2.82 (1.02, 7.81)	–	–	–	–	–	–
Chongqing	1.98 (1.08, 3.63)	2.10 (1.50, 2.96)	–	–	–	2.08 (1.52, 2.86)	1.67 (1.21, 2.29)	1.44 (1.02, 2.04)	1.15 (0.83, 1.61)	2.38 (1.71, 3.30)
Fujian	–	2.10 (1.41, 3.12)	2.07 (1.15, 2.61)	1.63 (1.04, 2.56)	–	2.38 (1.68, 3.38)	–	2.46 (1.04, 2.56)	0.86 (0.69, 1.09)	0.93 (0.73, 1.17)
Guangdong	2.90 (2.39, 3.52)	–	1.79 (1.18, 3.56)	1.47 (1.01, 2.26)	–	1.45 (1.20, 1.76)	1.19 (0.69, 1.44)	1.45 (1.20, 1.76)	1.18 (1.08,1.28)	2.07 (1.59, 2.71)
Guangxi	–	3.18 (2.55, 3.97)	–	–	0.60 (0.47, 0.75)	–	–	–	2.27 (1.82, 2.82)	3.85 (3.08, 4.82)
Hubei	1.45 (1.29, 1.64)	–	–	–	0.78 (0.73, 0.84)	–	–	–	–	–
Jiangsu	2.09 (1.90, 2.29)	2.31 (1.56, 3.41)	0.93 (0.84, 1.04)	1.13 (1.03, 1.25)	1.15 (1.05, 1.27)	–	1.75 (1.16, 2.63)	–	–	–
Jiangxi	2.94 (1.06, 8.14)	–	1.14 (0.69, 1.89)	1.15 (0.68, 1.95)	–	1.85 (0.92, 3.69)	–	–	2.45 (0.87,6.91)	3.53 (1.68, 7.41)
Shanghai	3.81 (2.66, 5.44)	2.49 (1.87, 3.30)	0.84 (0.43, 1.64)	1.20 (0.98, 1.47)	1.33 (0.69, 2.55)	2.86 (1.92, 4.25)	2.50 (1.52, 4.10)	2.28 (1.35, 3.85)	–	–
Sichuan	4.82 (1.69, 3.78)	2.31 (1.28, 4.18)	1.39 (0.72, 2.70)	1.40 (0.86, 2.28)	0.72 (0.44, 1.20)	5.85 (2.32,14.78)	–	–	–	–
Zhejiang	4.04 (3.45, 4.73)	3.06 (1.96, 4.77)	1.31 (0.92, 1.86)	1.28 (0.90, 1.82)	1.15 (1.02, 1.29)	2.11 (1.35, 3.31)	–	0.38 (0.14, 1.11)	1.85 (1.41,2.41)	1.90 (1.46,2.47)

– denotes no data.

common patterns of dyslipidemia, showed estimated effects consistent with those of previous studies,[50,57] with only some differences in magnitude. Although the estimated values of hypercholesterolemia and hyperglyceridemia tended to approach each other, type 2 diabetes seemed to prevail more frequently in those with hyperglyceridemia those with hypercholesterolemia, except in 2006 to 2010. This difference could also be observed in the regional stratification results; the southern region appeared to have smaller magnitudes for dyslipidemia, hypercholesterolemia and hypertriglyceridemia. Other patterns concerning dyslipidemia have also been reported, such as for high-density lipoprotein cholesterol (HDL-C),[50] the ratio of triglyceride to high-density lipoprotein cholesterol (TG/HDL-C),[58] and the ratio of cholesterol to high-density lipoprotein cholesterol (TC/HDL-C),[57] yet the index that can better indicate the relationship between dyslipidemia and type 2 diabetes has yet to be determined.

4.5. Obesity

Obesity is commonly acknowledged as a crucial modifiable risk factor for type 2 diabetes worldwide.[1] A recent publication indicated that the population-attributable fraction of overweight was 46.8%, and it could contribute to nearly 44 million diabetes cases in 2011 in China.[49] Our study supports this role of obesity by suggesting a statistically positive relationship, with an effect of $OR=2.28$ (95%*CI*: 1.94–2.68) for central obesity and $OR=1.90$ (95%*CI*: 1.66–2.18) for general obesity. Regarding the magnitude of estimated effects of central obesity and general obesity, we found that central obesity constantly had a higher risk than general obesity, as in previous studies.[45] However, there have also been publications reporting that the estimations for both types of obesity were comparable[59] or that the estimated effect of general obesity overrode that of central obesity.[60] There was an increasing trend of overweight rates among adults in China, from 22.8% in 2002, 26.6% in 2007, to 30.1% in 2012,[61,62] which corresponded to the prevalence of diabetes mentioned in the introduction, as well as the rising tendency of the estimated effects of general obesity in this study.

4.6. Smoking

In line with previous studies,[63] our results showed that cigarette consumption was significantly related to an increased likelihood of type 2 diabetes, and this positive effect was consistent with the results of the temporal and spatial stratifications, although a recent study suggested a decreased risk.[64] Because type 2 diabetes is a multifactorial disease, the fluctuating overall tobacco use rate (26.0% in 2003,[65] 28.1% in 2010[66] and 27.7% in 2015[67]) in China might not correspond to the rising trend of diabetes prevalence, yet the biological mechanisms[68] have helped to explain their causal relationship. Regarding the pooled effect size, our study showed that the overall risk of type 2 diabetes was 26% ($OR=1.26$, 95%*CI*: 1.13–1.40) higher for smokers than for non-smokers, slightly lower than the results of previous meta-analyses of other populations. For instance, Pan et al reported a 37% higher risk,[69] Shamima Akter et al 38%,[70] and Carole Willi et al 44%.[71] This difference might be partly due to different diagnostic criteria for type 2 diabetes. Although no significant disparities were detected among time frames and regions, it was suggested that smoking habits generally require attention in the context of type 2 diabetes.

4.7. Drinking

In this study, the overall pooled effect of drinking was $OR=1.20$ (95%*CI*: 1.05–1.36), and it differed from the results of stratification analysis. No significant association was found in the time periods of 1992 to 2005 and 2011 to 2017, while a 55% higher risk was found in 2006 to 2010 for drinkers than non-drinkers. Similar results were observed in the spatial distribution; the significant relationship was consistent in both the southern and northern regions, whereas different provinces exhibited various associations, positive, negative, or non-related. Whether drinking is related to the incident of type 2 diabetes is a complex issue, and previous studies have also seemed to observe the multifaceted nature of this link. First, many studies have reported a protective effect of alcohol drinking,[72] especially on the condition of moderate consumption.[73] This type of protective effect might vary in terms of variations in gender,[74] BMI,[75] alcohol type[76], and race.[74] Second, contrary to the effect of moderate consumption, high alcohol intake might increase the risk of type 2 diabetes with a nonlinear effect,[77] whereas there could be circumstances in which high alcohol consumption exerts little or no effect.[78] Third, no association between alcohol intake and type 2 diabetes was found in the overall analysis, even though there might still be a relationship concerning heavy alcohol consumption.[79] Fourth, there are risk effects for drinking behavior on type 2 diabetes,[80] and this relationship might be specific to gender.[81] Therefore, it could be concluded that the effects of alcohol consumption and the mechanisms require further research.

4.8. Gender

Our estimation results for gender were not straightforward. The overall outcome suggested that the female gender had a higher possibility for type 2 diabetes, yet different effects were observed when analyzed separately in the temporal and regional stratification analyses. There was a shift from no preponderance to a gender preponderance over time and from the southern to the northern region, but there was no obvious effect regarding provinces. This dilemma corresponds with the results of previous studies.[4,82] For other Asian countries, Nguyen et al[83] noted that the effect of gender was variable, showing no difference in national studies and a female preponderance in regional studies in Vietnam. Rahmanian et al[84] concluded that gender exerted no effect in the urban population in Iran, which was similar to a population-based study by Azimi-Nezhad et al,[85] but with male preponderance in all age groups except 20 to 29 years. However, it is noteworthy that male preponderance was common in Europe.[47] A brief report indicated that a shift in preponderance from female to male among middle-aged groups in both ratio and secular trends in Sweden.[86] Notably, gender preponderance might be associated with age, as hinted by the references above. Naveed Sattar et al[87] summarized that the reason why middle-age men had a higher risk for type 2 diabetes than age-matched females was basically their susceptibility to insulin resistance, such that insulin resistance contributed to the female gender dominance among pre-pubertal children. As for the Chinese, much more researches are needed to explore comprehensively whether there is gender preponderance regarding temporal and spatial distributions, age groups or ethnicities, and the potential mechanisms.

4.9. Limitations

Several limitations of this study must be acknowledged. First, causal relationship could not be established by observational studies between exposures and outcome, however, by which we could explore and depict the potential associations between common risk factors and type 2 diabetes and their spatio-temporal patterns through stratification analysis and it would help with the control of type 2 diabetes. Second, we aimed to detect the associations of common risk factors in the general population more than 18 years old, but some studies focused on middle-aged or elderly citizens, which might magnify or diminish the estimated effects of certain factors. Considering the different characteristics of subjects in different age groups, subgroup analysis by age group should be considered, yet it was limited in our study due to the lack of available data. Third, investigating the temporal and spatial distributions of the effects of different factors was one of our objectives; however, the number of studies meeting the inclusion criteria was unevenly distributed temporally and regionally, which might cause variations in the results of the different subgroups. And owing to the disparities among the numbers of provinces concerned in the included studies and the 31 provinces, autonomous regions, and municipalities in mainland China, the spatial distribution did not fully cover all these regions; thus, more studies need to be incorporated to attain a more complete description.

4.10. Conclusions and implications

In conclusion, our study suggests that there are important associations between a family history of type 2 diabetes, hypertension, central obesity, dyslipidemia, hypertriglyceridemia, general obesity, hypercholesterolemia, smoking, drinking, the female gender and type 2 diabetes, and that these associations might differ for different time periods and locations. Further studies could be into analysis with more detailed categories, as discussed in the discussion part, and multivariate analyses, such as meta-regression analysis since there are still limitations as referred above. Possible explanations for the difference of the observed relationships compared with previous studies and among different time periods and locations might be attributed to the great changes of socioeconomic environment and personal lifestyle.

According to the IDF,[1] 1 in 11 adults has diabetes, and 3 quarters of people with diabetes live in low- and middle-income countries, adding that the majority of these diabetes cases are type 2 diabetes[88] and type 2 diabetes is largely preventable,[89] it is necessary for us to figure out the magnitude of the effect for potential risk factors and estimate their trend and spatial distribution to curb the growing prevalence of diabetes as one of the developing countries which severely suffer from diabetes. And in line with the mission of the WHO Diabetes Program[90] to prevent diabetes whenever possible, this study provides a new perspective for diabetes epidemiology research on risk factors and helps with highlighting the major risk factors and key people at higher risk, and thus provides references for targeted strategies and measures against diabetes prevention.

Author contributions

Conceptualization: Ting Zhou, Yuanyuan Liu
Data Duration: Ting Zhou, Xiang Liu
Formal analysis: Ting Zhou
Methodology: Ting Zhou, Xiang Liu
Supervision: Yuanyuan Liu, Xiaosong Li
Validation: Yuanyuan Liu, Xiaosong Li
Writing – original draft: Ting Zhou
Writing – review and editing: Xiang Liu, Yuanyuan Liu, Xiaosong Li.

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