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Risk factors for progression to type 2 diabetes in prediabetes: a systematic review and meta-analysis

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Abstract

Background Prediabetes is the earliest identifiable stage of glycemic dysregulation, and its progression can be delayed by effective control of risk factors. Currently, various risk factors for the progression from prediabetes to type 2 diabetes mellitus (T2DM) need to be further summarized.

Objective This systematic evaluation of the risk factors for the progression of prediabetes to type 2 diabetes mellitus provides a theoretical basis for early recognition and intervention. The meta-analysis identifies the Fatty Liver Index as a significant risk factor [OR = 6.14, 95% CI (5.22, 7.22)] for the progression from prediabetes to type 2 diabetes, highlighting its predictive value.

Methods PubMed, Web of Science, Embase, The Cochrane Library, CNKI, WANFANG, and VIP databases were searched to collect cohort studies on risk factors for progressing to type 2 diabetes in prediabetes from inception to February 15, 2024. STATA 17.0 was used for Meta-analysis.

Results A total of 59 studies were included, all of which were of medium to high quality. The factors were categorized into four major groups: sociodemographic factors, lifestyle factors, psychosocial factors, and comorbidities and clinical indicators. Meta-analysis results showed that sociodemographic factors [age [OR = 1.03, 95% CI (1.01, 1.04)], family history [OR = 1.48, 95% CI (1.36, 1.61)], male sex [OR = 1.13, 95% CI (1.08, 1.19)], high BMI [OR = 1.21, 95% CI (1.15, 1.27)], high waist circumference [OR = 1.49, 95% CI (1.23, 1.79)], and high waist-to-hip ratio [OR = 2.44, 95% CI (2.17, 2.74)]]. Lifestyle factors included a lack of physical exercise [OR = 1.86, 95% CI (1.19, 2.88)], smoking [OR = 1.31, 95% CI (1.22, 1.41)], and moderate physical activity [OR = 0.24, 95% CI (0.09, 0.67)]. Psychosocial factors included anxiety [OR = 2.61, 95% CI (1.36, 5.00)], depression [OR = 1.88, 95% CI (1.35, 2.61)], and social deprivation level 4 [OR = 1.15, 95% CI (1.13, 1.18)]. Comorbidities and clinical indicators included hypertension [OR = 1.41, 95% CI (1.33, 1.50)], high triglycerides [OR = 1.25, 95% CI (1.10, 1.43)], high cholesterol [OR = 1.09, 95% CI (1.06, 1.12)], fatty liver index [OR = 6.14, 95% CI (5.22, 7.22)], low HDL-C [OR = 1.13, 95% CI (1.09, 1.36)], and high blood glucose levels [OR = 1.01, 95% CI (1.01, 1.02)].

Conclusions This study found that age, male sex, positive family history of type 2 diabetes, high BMI, unhealthy lifestyle, anxiety, depression, high blood pressure, high triglycerides, and a high fatty liver index are risk factors

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for the progression from prediabetes to type 2 diabetes and should be given sufficient attention. Moderate physical activity and Low HDL-C are protective factors. Future studies should also increase follow-up, explore the best diagnostic criteria for prediabetes, and fully consider the definitions of various factors. The study was registered in PROSPERO (CRD42024513931).

Keywords Prediabetes, Type 2 diabetes mellitus, Risk factors, Meta-analysis, Systematic Review

Introduction

Prediabetes is a state of abnormal glucose metabolism where glucose levels are higher than normal but not high enough for a diabetes diagnosis. It serves as a warning sign for the future risk of diabetes, cardiovascular disease, microvascular complications, tumors, dementia, and other conditions [1]. Patients in this stage may exhibit impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT), or HbA1c levels between 5.7% and 6.4% [2]. Although not yet diagnosable as diabetes, these characteristics indicate a high-risk state that requires significant attention from both patients and healthcare providers. Up to 70% of patients with prediabetes eventually develop diabetes [3], and by 2030, over 470 million people globally are expected to have prediabetes [4]. In China, the prevalence of prediabetes is between 35.2% and 38.1% [5].

Diabetes is a group of clinical syndromes characterized by hyperglycemia due to absolute or relative insulin deficiency and/or insulin dysfunction. It can be categorized into four types [6] based on etiology: Type 1 diabetes mellitus (T1DM), Type 2 diabetes mellitus (T2DM), specific types of diabetes, and gestational diabetes mellitus (GDM). Among these, T2DM is the most prevalent, primarily caused by insulin resistance and insufficient insulin secretion [7]. It is a significant global public health issue, with the diabetes prevalence in the 20–79 age group estimated at 10.5% in 2021, projected to rise to 12.2% by 2045, with 96.0% of cases being T2DM [8]. At the same time, the proportion of undiagnosed diabetes patients has been high, accounting for about 45% [9]. In China, the diabetes prevalence is particularly severe, at approximately 12.4% [5, 10], with over 90% being T2DM cases. However, the current rate of achieving treatment targets for T2DM is low, with less than 50% of patients having HbA1c levels below 7%. The awareness and control rates of diabetes are also low, exacerbating the disease burden [11], Diabetes significantly impacts the quality of life [12], and untreated or improperly treated T2DM is associated with numerous complications [13].

Growing evidence suggests that prediabetes is an independent predictor [14, 15] for T2DM conversion and is associated with higher risks of subclinical myocardial injury, atherosclerotic cardiovascular disease, and all-cause mortality. Without timely intervention, the risk of prediabetes patients progressing to diabetes increases significantly. Effective intervention at this stage can greatly reduce the risk of progression. Therefore, timely identification and the effective recognition of risk factors for progression from prediabetes to T2DM are crucial for preventing the onset of T2DM, improving quality of life, and reducing medical resource consumption.

Materials and methods

Data collection

This meta-analysis was conducted following the PRISMA guidelines. The protocol was registered in the PROSPERO database (CRD42024513931).

Data collection

The inclusion criteria were as follows: (1) cohort study; (2) meeting the diagnostic criteria for prediabetes including IFG and/or IGT and/or HbA1c (5.7–6.4). (3) Exposure factors: influential factors associated with the progression of prediabetes, including but not limited to sociodemographic characteristics, lifestyle, and anthropometric indicators; (4) Conclusion Indicator: T2DM event or DM, that is, meeting the diagnostic criteria for T2DM /DM of international organizations such as ICD-10/ICD-9/ADA/WHO for each year, or receiving anti-T2DM treatment during the follow-up period (including, but not limited to, the use of anti-T2DM medications, insulin, receiving dietary treatment for T2DM, outpatient visits for T2DM, etc.) or self-reporting of T2DM, or a confirmed diagnosis of T2DM; (5) The literature should report original data concerning odds ratio (OR) or relative risk (RR) and the 95% confidence interval (CI). The exclusion criteria were as follows: (1) exclusion of study subjects with clinically confirmed pregnancy or other serious comorbidities such as malignancy, AIDS, and tuberculosis; (2) exclusion of study participants receiving anti-T2DM therapy; (3) duplicate publications; (4) publications with data that could not be extracted, transformed, or calculated; (5) unavailability of full text; (6) non-Chinese/English literature; and (7) exclusion of studies with a score of ≤ 3 on the Newcastle–Ottawa Scale (NOS).

Search strategy

We performed a systematic search of PubMed, Web of Science, Embase, The Cochrane Library, China Knowledge Network (CNKI), Wanfang Database (WANFANG), and VIP from the inception of each database to January 17, 2024. The references of the included literature were also screened for supplementation. The following terms were used in automatic search: "prediabet*/pre-diabet*/overall diabetes/borderline diabetes" "impaired glucose/ impaired fasting glucose/ glucose intolerance/ IGT / IFG" "intermediate hyperglycemi*/ non-diabetic hyperglycemi*/ dysglycemia" "risk/risk factors/predictive factor/age/sex/education status/dyslipidemia/hypertension/obesity/lifestyle/sleep/diet/smoke/alcohol/exercise/environmental pollution/mental health" "type 2 diabetes mellitus/type 2 diabetes / T2DM / T2D" "cohort/ Prospective study/prevalence study". The search strategy is detailed for the English databases in Appendix A.

Study selection and data extraction

Endnote 20 was used to remove duplicates. Two trained researchers independently read the titles and abstracts for initial screening, then read the full texts for re-screening, and in case of disagreement, they discussed or consulted a third-party expert for a decision. Data were independently extracted by two trained researchers using a standardized form, and missing information was supplemented by contacting the original authors. The form included the following: first author, year of publication, type of study, country or region of the study population, type of diagnosis, diagnostic criteria, sample size, duration of follow-up, method of assessing the exposure factors, method of assessing the controls, assessment tools for the endpoint indicators, and adjustment for confounders.

Study quality assessment

Quality assessment of all the literature was conducted independently by two trained researchers, who cross-checked the results at each step. In case of disagreement, the decision was made through discussion or consultation with a third-party expert. The Newcastle–Ottawa Scale (NOS) was used for assessment, with a maximum score of 9, which included study population selection (4 points), comparability of cohort design or analyses (2 points), and outcome evaluation and follow-up (3 points). Scores of 0–3, 4–6, and 7–9 were assigned to low, moderate, and high-quality studies, respectively, based on this scale.

Statistical methods

STATA 17.0 software and RStudio were used to process the data. In this study, the OR was used as the combined effect size, and the 95% CI was calculated for effect analysis. The analysis was performed according to different exposure factor subgroups. For factors that were not amenable to meta-analysis, qualitative summary descriptions were used. If the original article only reported the results of analyses grouped by Pre-DM phenotype, the subgroups were combined and then described. Heterogeneity in systematic reviews was generally described as clinical, methodological, and statistical heterogeneity (the result of clinical and/or methodological diversity among individual studies) and was assessed by the I^2 statistic and Q-test (P-value); if $P > 0.10$ and $I^2 < 50\%$, a fixed effects model was chosen; otherwise, a random effects model was adopted. we performed a leave-one-out method by iteratively removing the included study of sensitivity analysis. Then, sensitivity analysis was also used to detect the stability of the results. Meanwhile, Egger's test was used to detect publication bias. In addition, we assigned three grades of evidence in support of the conclusion according to two elements including the pooled sample size and heterogeneity: 'grade I evidence'.

Results

Literature screening process and results

The PRISMA flowchart (Fig. 1) summarizes the literature search and inclusion process. Initially, 18,441 articles were retrieved, and 3,636 duplicates were removed. After screening the titles and abstracts, 14,571 articles were excluded. A further review of the full texts resulted in the exclusion of 174 articles, leaving 59 articles for inclusion.

Characteristics and quality evaluation of included studies

A total of 59 studies were included, 54 in English and 5 in Chinese. There were 52 prospective cohort studies and 7 retrospective cohort studies, covering three continents and 19 countries. The studies included 32 from Asia (13 from China, 5 from South Korea, 4 from Japan, 2 from India, 2 from Iran, 1 from Thailand, and 1 from Singapore), 22 from Europe (2 from Germany, 1 from Denmark, 1 from France, 3 from Sweden, 2 from the Netherlands, 1 from Poland, 4 from the United Kingdom, 8 from Spain), and 6 from North America (4 from the United States and 2 from Canada). The detailed content is presented in Table 1.

Table 1 Basic characteristics and quality evaluation of the included literatures.

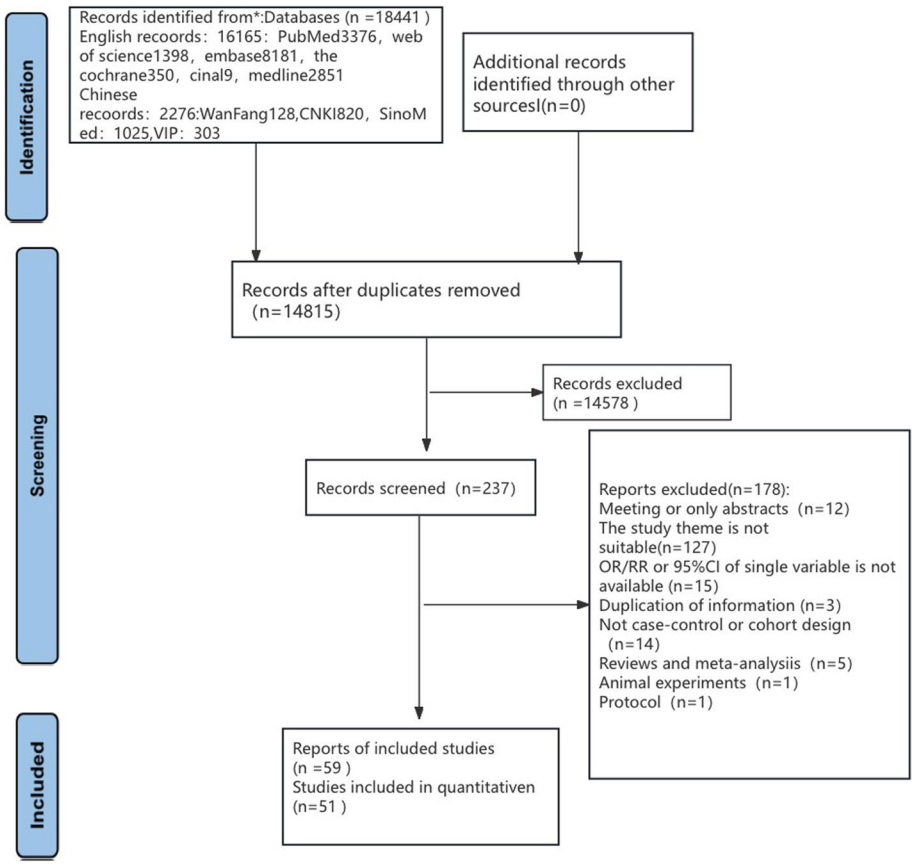

Fig. 1 Flow chart of literature screening

Meta-analysis results of factors influencing the transition from prediabetes to type 2 diabetes

The meta-analysis summarized factors related to the progression from prediabetes to type 2 diabetes (T2DM). The evidence was classified into three levels based on sample size and heterogeneity: 'Level I evidence' with a combined population > 5000 and low heterogeneity ($I^2 < 50\%$); 'Level II-A evidence' with a combined population > 5000 but high heterogeneity ($I.^2 \geq 50\%$); 'Level II-B evidence' with low heterogeneity but a combined population < 5000; and 'Level III evidence' with a combined population < 5000 and high heterogeneity. Of the 27 influencing factors analyzed, 20 factors (10 Level I evidence, 6 Level II-A evidence, 3 Level II-B evidence, 1 Level III evidence) showed significant positive or negative correlations with the disease, while 7 factors showed no statistical correlation. These factors were categorized into four major categories: sociodemographic factors, lifestyle factors, psychosocial factors, and comorbidities and clinical indicators. Significant influencing factors are described as follows: Significant influencing factors are described in Table 1

Sociodemographic factors

Age [OR=1.03, 95%CI (1.01, 1.04)], Family history [OR=1.48, 95%CI (1.36, 1.61)], Male sex [OR=1.13, 95%CI (1.08, 1.19)], High BMI [OR=1.21, 95%CI (1.15, 1.27)], High waist circumference [OR=1.49, 95%CI (1.23, 1.79)], High waist-to-hip ratio [OR=2.44, 95%CI (2.17, 2.74)].

Lifestyle factors

Lack of physical exercise [OR=1.86, 95%CI (1.19, 2.88)], Smoking [OR=1.31, 95%CI (1.22, 1.41)], Moderate physical activity [OR=0.24, 95%CI (0.09, 0.67)], protective factor.

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Table 1 Basic characteristics and quality evaluation of the included literatures

Inclusion of studies	States	Population (Prediabetes/ Diabetes)	Duration of follow-up (years)	Exposure factors	Research target	Pre-DM Diagnostic Criteria	Outcome Indicators	DM Diagnostic Criteria	Type of STUDY	Nos score
Sun YL 2012 [16]	China	337	3	①⑧⑯	IFG/IGT	1997ADA	DM	OGTT	Prospective study	8
Liu SB 2020 [17]	China	809/200	5.9	③⑯㉚	IFG/IGT	1999WHO	DM	Self-reported/FBG/OGTT	Prospective study	7
Che XL 2015 [18]	China	1125	3	⑲	IFG/IGT	1999WHO	DM	1999WHO	Prospective study	5
Wang JY 2020 [19]	China	192/90	1	①③⑧⑮⑰	IFG/IGT	2013 Chinese Medical Association	T2DM	Blood glucose	Prospective study	5
W. M. Admiraal2014 [20]	Nether-lands	456	10	④	IFG	FPG:5.7 *mmol/L* -6.9 *mmol/L*。	T2DM	FPG ≥ 7.0 *mmol/L*、HbA1c ≥ 48 *mmol/mol* (6.5%)，Self-reported 2DM。	Prospective study	7
K. Kohansal2022 [21]	Germany	1329/252	10	①②③⑧⑱㉖㉙㉛	IFG/IGT	IFG: 5.55 *mmol/L*≤FPG<7 *mmol/L*，7.77 *mmol/L*≤ 2h-PG<11.1 *mmol/L*	DM	FPG ≥7 or 2h-PG ≥11.1 *mmol/L* or taking anti diabe-tes drugs	Prospective study	8
R. M.2015 [22]	India	299	10	①②③⑰㉖㉜㉝	IFG/IGT	FPG 100–125 *mg/dL* (5.6–6.9 *mmol/L*) or 2 h PG 140–199 *mg/dL* (7.8–11.0 *mmol/L*)	DM	OGTT/self-report/physician diagnosis/medication taken	Prospective study	9
Belsky2023 [23]	America	552/36	7	①②㉜	IFG/IGT	FPG 100–125 *mg/dl* or 2 h PG 140–199 *mg/dL*	T2DM	2022ADA:FPG ≥126 *mg/ dL*、2 h Plasma glucose≥200 *mg /dL* or HbA1C ≥ 6.5%	Retrospective study	8
L. Cea-Soriano2022 [24]	Spain	1184/211	4.2	⑬	IFG/ HbA1c	FPG 100–125 *mg/dL* (5.6–6.9 *mmol/L*) and/ or HbA1c 5.7% to 6.4% (39–47 mmol/mol) （HbA1c）	T2DM	FPG ≥7 *mmol/L* (126 *mg/ dL*) or HbA1c ≥48 *mmol/ mol* (6.5%)	Prospective study	7
L. Chaker2016 [25]	Denmark	1338	7.9	㉝	IFG/IGT	FPG(6*mmol/l*-7*mmol/L*) or Nonfasting blood glu-cose> 7.7 *mmol/L* and< 11.1 *mmol/L*（	T2DM	FBG≥7.0mmol/L，Nonfasting blood glucose≥11.1*mmol/ L*，Or use of hypoglycemic medications.	Prospective study	8
G. Chatzi2020 [26]	Britain	562/349	12	①②④⑥㉟	HbA1c	HbA1c 5.7-6.4%	T2DM	Self-reported、HbA1c	Prospective study	7
S. S. Deschênes2016 [27]	Canada	1428	5	㉒㉓	HbA1c	HbA1c 5.7-6.4%	T2DM	Self-reported	Prospective stud	6
S. S. Deschênes2023 [28]	Nether-lands	27,976	9	㉒㉓	HbA1c	HbA1c 5.7-6.4%	T2DM	Self-reported or HbA1c> 47 *mmol/mol* (6.5%)	Prospective stud	8
T. D. Filippatos2016 [29]	Athens, Greece	343	10	⑬	IFG	IFG 100-125 *mg/dl*	T2DM	ADA	Prospective stud	9
J.Franch-Nadal2018 [30]	Spain	1,142	3	③⑨⑯㉑㉖㉙	IFG/ HbA1c	FPG 100 -125 *mg/dl* and/ or HbA1c 5.7% -6.4%（39 to 46 *mmol/mol*）	T2DM	Two basic plasma glucose level ≥126 *mg/dl*，or twice HbA1c≥6.5%（≥48 *mmol/ mol*），or both at the same time	Prospective stud	6

Table 1 (continued)

Inclusion of studies	States	Population (Prediabetes/ Diabetes)	Duration of follow-up (years)	Exposure factors	Research target	Pre-DM Diagnostic Criteria	Outcome Indicators	DM Diagnostic Criteria	Type of STUDY	Nos score
M. P. Gardner2023 [31]	Britain	397,853	5.2	①④⑦⑧	HbA1c/IFG/ Prediabetes reads the code	HbA1c 6.0%-6.5%, FPG 6-7*mmol/L*	T2DM	ICD	Prospective stud	8
C.Giráldez-García2018 [32]	Spain	1184	2.84	⑧⑨	HbA1c/IFG	FPG 100 to 125 *mg/dL* or HbA1c5.7%-6.4%	T2DM	Fasting blood sugar twice in a row≥126*mg/dL*，Or twice HbA1c in a row≥6.5% or both。	Prospective stud	7
U. P. Gujral2020 [33]	America	481/152	5	⑫㉛	IFG/IGT	FPG 5.6 - 6.9 *mmol/L*，or 2h-PG7.8 -11.0 *mmol/L*	T2DM	Doctor diagnosis, use of hypoglycemic drugs or ≥7.0 *mmol/L* or 2 hours after a meal blood glucose ≥11.1 *mmol/*	Prospective study	8
R. Gupta2023 [34]	India	97/54	10.27	①③⑧⑨⑰	IFG/IGT	WHO2006	T2DM	WHO2006	Prospective study	8
A. Hruby2014 [35]	America	928/154	6.9	⑮	IFG/IGT	IFG 5.6-7.0 *mmol/L*，IGT 2 h OGTT7.8 -<11.1 *mmol/L*)	T2DM	Doctors diagnose and use hypoglycemic drugs or IFG ≥7.0 *mmol/L* or OGTT2h-glu≥11.1 *mmol/L*	Prospective study	8
L. Jiang2020 [36]	Augsburg	24777	6.5	㉒	IFG	IFG 5.6-7.0 *mmol/L*	T2DM	WHO/ Doctor diagnosis/ medication/FBG/OGTT	Prospective study	7
K. Kuwahara2019 [37]	Japan	18,174 /1613	3.2	⑳㉔	IFG/HbA1C	ADA2018 IFG 100 to <126 mg/dL and/or HbA1c5.7-6.5%	T2DM	FPG≥126 *mg/dL*，Random blood glucose level≥200 *mg/dL*，HbA1c≥6.5%，or ADA2018	Prospective study	7
N. Li2022 [38]	China	1685 /212	2	②⑧⑨⑩㉛㉞	IFG/IGT	IFG：6.1≤FPG＜7.0*mmol/L*且2hPG＜7.8*mmol/L*； IGT： FPG＜6.1*mmol/L* and 7.8≤2hPG＜*11.1mmol/L*；	T2DM	FPG7.0*mmol/L*and/or 2hPG≥11.1*mmol/L* or have a history of diabetes.	Retrospective study	8
S. Nabila2023 [39]	Korea	10,358	4	①③⑤⑧⑨⑱㉖㉛	IFG/HbA1C	ADA2018 IFG 100 to <126 mg/dL and/ or HbA1c 5.7-6.5%	T2DM	FPG7.0*mmol/L* and/ or 2hPG≥11.1*mmol/L*or have a history of diabetes。	Prospective study	8
M. Sadeghi2015 [40]	Iran	373/131	7	①②⑤⑧⑨⑱⑳㉑㉖㉛	IFG/IGT	OGTT2hPG≥140 mg/dL (7.8 *mmol/L*) and <200 mg/dL (11.1 mmol/L) （IGT） and/or FPG ≥100 mg/dL (5.5 mmol/L) and<126 mg/dL (7.0 mmol/L) （IFG）	T2DM	FPG ≥126 *mg/dL* (7.0 *mmol/L*) or OGTT2hPG 200 *mg/dL*≥ (11.1 *mmol/L*) or are taking anti-diabetic medications	Prospective study	8
A. Święcicka-Klama2022 [41]	Poland	283/59	9	①⑧⑨⑩⑪	IFG	IFG：5.6 -6.9 *mmol/L*	T2DM	Self-report, blood glucose testing	Prospective study	9
M. Toshihiro2008 [42]	Japan	128/36	3.2	⑥㉕㉜	IFG/IGT	ADA1997	T2DM	FPG≥7.0*mmol/ l*，OGTT2hPG≥11.1*mmol/l* or Non-fasting blood glucose levels>11.1*mmol/l*	Prospective study	7

Table 1 (continued)

Inclusion of studies	States	Population (Prediabetes/ Diabetes)	Duration of follow-up (years)	Exposure factors	Research target	Pre-DM Diagnostic Criteria	Outcome Indicators	DM Diagnostic Criteria	Type of STUDY	Nos score
H. Wang2010 [43]	America	1677	7.8	①②⑧⑨㉜㉝	IFG/IGT	ADA2003	T2DM	FPG≥ 126 *mg/dL*，2 h PG ≥ 200 *mg/dL*，being treated with insulin and/or hypoglycemic agents, or had a history of diabetes on a questionnaire	Prospective study	7
F. He2018 [44]	China	640/127	5	⑮	IFG/IGT/HbA1c	ADA2016	T2DM	ADA2016	Prospective study	8
M. Wargny2019 [45]	France	389/138	3.9	①②㉗㉛㉜	IFG	FPG 5.6 - 6.9 *mmol/*	T2DM	OGTT	Prospective study	6
J. Zhou2014 [46]	China	384/60	10	①②⑱⑲㉖㉘㉚㉛	IFG	FPG 5.6 - 6.9 *mmol/*	T2DM	FPG≥7．0*mmo/L*	Prospective study	7
M. Bennasar-Veny2020 [47]	Spain	23293	5	①⑧⑭⑯⑱㉚	IFG	FPG :100- 125 *mg/dL*	T2DM	FPG≥126 *mg/dL* or use hypoglycemic drugs	Prospective study	8
I.Roncero-Ramos2020 [48]	Spain	213	5	⑬⑮	FG/IGT/Hba1c	FPG 5.6 - 6.9 *mmol/*; 2-hPG 7.8-11.0 and/ or HbA1C 5.7% -6.4%	T2DM	FPG≥126 *mg/dL*，OGT-T2hPG≥200 *mg/dL* and/ or HbA1c≥6.5%。	Prospective study	8
D. B. Z. Chia2017 [49]	Singapore	2295/492	5	①②⑧㉛㉜	IFG	Newly diagnosed IFG FPG 6.1–6.9 *mmol/L* and 2HOGTT <7.8 *mmol/L*， ICD-9-CM	T2DM	FPG≥126 *mg/ dL*，OGTT2hPG≥200 *mg/dL* and/or HbA1c≥6.5%。	Retrospective	7
A. Deleskog2012 [50]	Stockholm	1189/145	8-10	㉞	IFG/IGT	FPG 100–125 *mg/dL* or 2 h PG 140–199 *mg/d*L (7.8–11.0 *mmol/L*)	T2DM	FPG≥126 *mg/dL*，OGTT 2hPG200 *mg/dL* and/or HbA1c≥6.5%	Prospective study	8
M. Sharafi2023 [51]	Iran	157/94	5	⑩㉑	IFG	FPG 100–125 *mg/dL*	T2DM	FPG≥126 *mg/ dL*，OGTT2hPG≥200 *mg/dL* and/or HbA1c≥6.5%	Prospective study	7
C. Busquets-Cortes2021 [52]	Spain	16 648	5	①⑦⑧⑭⑯㉛㉜	IFG	FPG 100–125 *mg/dL*	T2DM	FPG≥126 mg/dL, taking hypoglycemic drugs	Prospective study	6
V. Y. W. Guo2018 [53]	China	1101	0.5	⑨㉖	IFG	FPG 100–125 *mg/dL*	DM	FPG ≥ 7.0 *mmol/L* and/ or 2h-OGTT ≥ 11.1 *mmol/l* and/or HbA1C≥ 47.5 *mmol/ mol* (≥ 6.5%)	Prospective study	8
T. Wirstrom2013 [54]	Stockholm	5477/145	8-10	⑮	IFG/IGT	FPG 100–125 *mg/dL* or 2 hPG 140–199 *mg/d*L (7.8–11.0 *mmol/L*)	DM	OGTT	Prospective study	7
X. Cao2022 [55]	Britain	38,950	15	㉕	HbA1C	HbA1c 5.7% - 6.4%	T2DM	Self-reported or medical history or medication information or hospitalization records and ADA standards	Prospective study	9
J. P. Chaput2009 [56]	Canada	276	6	⑳	IGT	2 hPG 140–199 *mg/d*L (7.8–11.0 *mmol/L*)	T2DM	Use insulin or hypoglycemic drug、FPG⩾126 *mg/dL* (⩾7.0 *mmol/L*)，or OGT-T2hPG⩾200 mg/dL（⩾11.1 *mmol/L*）	Prospective study	7

Table 1 (continued)

Inclusion of studies	States	Population (Prediabetes/ Diabetes)	Duration of follow-up (years)	Exposure factors	Research target	Pre-DM Diagnostic Criteria	Outcome Indicators	DM Diagnostic Criteria	Type of STUDY	Nos score
C. Eades2014 [57]	Britain	4548	2.8	①②⑦	IFG/IGT	FPG 100–125 *mg/dL* or 2h PG 140–199 *mg/d*L (7.8–11.0 *mmol/L*)	T2DM	OGTT	Prospective study	7
S. N. Fu2014 [58]	China	9161/1998	5	①②㉛㉜	IFG	FPG 100–125 *mg/d*（6.0-6.9*mmol/l*）	T2DM	WHO1999 or use hypoglycemic medications	retrospective	8
H. Harati2009 [59]	internation	1368/506	3.3	㉑㉚㉛㉜㉞	IFG/IGT	FPG 100–125 *mg/dL* or 2 h PG 140–199 *mg/d*L (7.8–11.0 *mmol/L*)	T2DM	WHO1999 OGTTPG-2h>11.1 *mmol/L*或 FPG ≥ 7.0 *mmol/l*	Prospective study	8
J A Marshall 1994 [60]	Spain	134/20	1.9	①②④⑧⑩㉞	IGT	WHO985	T2DM	WHO1985	Prospective study	6
Y. Osaki2021 [61]	Japan	1686/217	8	㉔㉕	IFG/HbA1C	FPG 100–125 *mg/d* or HbA1c 5.7–6.4%	T2DM	FPG≥ 126 *mg/dL*）、random blood sugar≥ 200 *mg/dL*）、HbA1c（≥ 6.5%）or self-report	Prospective study	6
E. Seo2022 [62]	Korea	14258	3.0	㉔	HbA1c	HbA1c 5.7%–6.4%	T2DM	HbA1c≥ 6.5%	Prospective study	6
S. Wu2017 [63]	Spain	285/96	2.25	①②⑧㉑	IFG/HbA1C	FPG 100–125 *mg/d* or HbA1c 5.7–6.4%	T2DM	FBG ≥126 *mg/dL* or HbA1c >6.5%，doctors diagnose, hypoglycemic drugs	Prospective study	8
A.Wutthisathaporn-chai 2021 [64]	Thailand	325/65	3	③⑤⑧⑯㉜	IFG/IGT	FPG 6.1-6.9 *mmol/l*，IGT：7.8-11.0 *mmol/l*	T2DM	OGTT	Prospective study	8
Takumi Nishi2014 [65]	Japan	9667/89	3	㉗	HbA1c	HbA1c 5.7-6.4%	T2DM	self-report	Prospective study	5
H.-S.kim 2013 [66]	Korea	5085	4.4	①②⑧⑨㉜㉞	IFG	FPG (100–125 *mg/dL*)	T2DM	Fasting blood glucose levels, diabetes treatment outpatient visits, hospitalization for diabetes, and use of diabetes management or treatment prescriptions	Prospective study	8
Xiaoqing Wang2023 [67]	China	685277/1273	3	①②③⑧⑱⑲㉖㉙㉚㉞	IFG	2022ADA	DM	FPG>7.00 *mmol/L* and/ or Self-reported diabetes	retrospective	7
Siyu Chen2023 [68]	China	3632/893	2.5	②⑧⑫㉜	IFG/IGT	WHO1999	DM	WHO1999	Prospective study	8
A. Neumann2013 [69]	Sweden	1879	10	①②③⑧㉖㉛	IFG/IGT	WHO1999	T2DM	WHO1999	Prospective study	8
J. Huang2020 [70]	China	5035/754	3	㉞	IFG	ADA2003	T2DM	ADA2003 or taking hypoglycemic medication	Prospective study	8
J.Y. Jung2018 [71]	Korea	2830/881	10	㉛㉜	IFG/HbA1C/IGT	HbA1c 5.7-6.4% ,IFG :FPG 100 - 125 *mg/dL*，IGT :OGTT2hPG140 to 199 *mg/dL*	DM	FPG≥126*mg/dL*、HbA1c≥6.5%、OGTT（2h-PG）≥200*mg/dL*，Medical history	Prospective study	9
Y. Sun2022 [72]	China	15017/1731	3.0	①②③⑧⑱⑲㉖㉙㉛	IFG	FPG5.6-6.9*mmol/L*	DM	self-report or FPG≥7.0 *mmol/l*	retrospective	7

Table 1 (continued)

Inclusion of studies	States	Population (Prediabetes/ Diabetes)	Duration of follow-up (years)	Exposure factors	Research target	Pre-DM Diagnostic Criteria	Outcome Indicators	DM Diagnostic Criteria	Type of STUDY	Nos score
Gan, Ting 2021 [73]	China	5457/854	3	⑤⑧㉖㉘㉛㉟	IFG	FPG5.6-6.9*mmol/L*	T2DM	FPG≥7.0*mmol/L*，doctor diagnosis/using hypoglycemic drugs	Prospective study	7
D. K. Nagi1995 [74]	Pima Indian	124/75	5	①⑧㉞	IGT	2 hPG 140–199 *mg/d*L (7.8–11.0 *mmol/L*)	T2DM	OGTT	Prospective study	9

Sociodemographic data：① Age: including baseline age increase and old age② Sex: Male, female③ Family history④ Race: including black, Asian, and Hispanic⑤ Education level: College or above, college, continuing self-education⑥ Occupation: including executive business⑦ Social class: Social deprivation level 1, 2, 3, 4, poverty level⑧ High BMI ⑨ High waist circumference: including abdominal obesity, central obesity, ⑩ high waist-to-hip ratio Height obesity index⑫ visceral fat area

Lifestyle factors: ⑬ Mediterranean Diet ⑭ Daily intake of fruits and vegetables ⑮ Other diets: High GL diet, high intake of magnesium in foods, low fat diet, intake of whole grains⑯ Moderate physical activity⑰ Lack of physical activity: no moderate physical activity, lack of physical activity⑱ Smoking: Past smoking, present smoking⑲ Drinking ⑳ Sleep time

Psychosocial factors:㉒ Anxiety ㉓ depression ㉔ Working hours ㉕ Others: stress, shift work, night work, frailty Clinical factors：㉑ Metabolic syndrome㉖ High triglycerides㉗ Fatty liver index㉘ LDL-C㉙ HDL-C㉚ High cholesterol level ㉛ Blood pressure level: hypertension, high systolic blood pressure, high diastolic blood pressure, prehypertension ㉜ Blood glucose level: Fasting blood glucose level, 2h blood glucose level, glycated blood glucose hemoglobin㉝ HOMA-IR ㉞ Other clinical indicators: Adiponectin level, TSH level, FT4, HOMA- β , leukocyte inflammatory factors, insulin level, AST, ALT, AST/ALT, cholelithiasis, gallstones, cholecystectomy, early insulin response, proteinuria, 25(OH)D㉟ Other influencing factors: heavy metal exposure, disability

1.79)], High waist-to-hip ratio [OR = 2.44, 95%CI (2.17, 2.74)].

Lifestyle factors

Lack of physical exercise [OR=1.86, 95%CI (1.19, 2.88)], Smoking [OR=1.31, 95%CI (1.22, 1.41)], Moderate physical activity [OR=0.24, 95%CI (0.09, 0.67)], protective factor.

Psychosocial factors

Anxiety [OR=2.61, 95%CI (1.36, 5.00)], Depression [OR=1.88, 95%CI (1.35, 2.61)], Social deprivation level 4 [OR=1.15, 95%CI (1.13, 1.18)].

Comorbidities and clinical indicators

Hypertension [OR=1.41, 95%CI (1.33, 1.50)], High triglycerides [OR=1.25, 95%CI (1.10, 1.43)], High cholesterol [OR=1.09, 95%CI (1.06, 1.12)], Fatty liver index [OR=6.14, 95%CI (5.22, 7.22)],Low HDL-C [OR=1.13, 95%CI (1.09, 1.36)], High blood glucose levels [OR=1.01, 95%CI (1.01, 1.02)].

Meta-analysis of risk factors for type 2 diabetes in prediabetes are shown in Table 2 in detail.

Table 2 meta-analysis of risk factors.

Subgroup analysis

We conducted subgroup analyses based on high body mass index (BMI), high triglycerides, blood pressure levels, and blood glucose levels. The results are shown in Table 3.

For high BMI, the analyses were conducted with BMI as a continuous variable and as a categorical variable (BMI ≥ 24 kg/m^2 and BMI ≥ 30 kg/m^2). Subgroup analyses showed a decrease in heterogeneity across groups. For BMI ≥ 24 kg/m^2, the evidence was rated as Grade I, indicating an increased risk of diabetes (OR from 1.21 to 1.76) with low heterogeneity (I^2 = 27.0%). This suggests that individuals with prediabetes have an increased risk of developing type 2 diabetes (OR from 1.21 to 1.76). For BMI ≥ 30 kg/m^2, the evidence was rated as Grade II-A, also indicating an increased risk of diabetes (OR from 1.21 to 1.58) with low heterogeneity (I^2 = 24.7%). However, the OR value was lower compared to the BMI ≥ 24 kg/m^2 group, which contradicts previous studies that showed a dose–response relationship between high BMI and diabetes risk. This discrepancy might be due to the smaller population size in the BMI ≥ 30 kg/m^2 group.

For blood pressure levels, subgroup analyses were conducted based on reported blood pressure as hypertension, high systolic blood pressure, and high diastolic blood pressure. Hypertension was rated as Grade I evidence, showing an increased risk of diabetes (OR from 1.01 to 1.41) with low heterogeneity (I^2 = 12.1%).

For blood glucose levels, subgroup analyses were conducted based on fasting blood glucose, postprandial 2-h blood glucose, and glycated hemoglobin. Fasting blood glucose was rated as Grade II-A evidence, showing the most significant increase in diabetes risk (OR from 1.01 to 1.54) with high heterogeneity (I^2 = 96.5%).Subgroup analysis of risk factors for type 2 diabetes in prediabetes is shown in Table 3.

Table 3 Subgroup analysis of risk factors for type 2 diabetes in prediabetes.

Sensitivity analysis

For anxiety, excluding Deschênes 2023 due to differences in control groups (comparing anxiety state versus progressive anxiety), heterogeneity decreased from 54.8% to 0.0%, and the combined effect slightly increased (OR from 1.77 to 2.61).For high cholesterol levels, excluding Gan Ting 2021 due to different definitions and lack of representative study populations, heterogeneity decreased from 65.6% to 31.9%, and the combined effect slightly decreased (OR from 1.15 to 1.09).For metabolic syndrome, excluding J. Franch-Nadal 2018 due to differences in single-factor analysis results and diagnostic standards, heterogeneity decreased from 80.3% to 15.7%, and the combined effect decreased (OR from 1.76 to 1.32).

For high waist circumference, excluding four articles with unclear definitions (K. Kohansal 2022, N. Li 2022, A. Święcicka-Klama 2022, H.-S. Kim 2013), heterogeneity decreased from 89.9% to 31.9%, and the combined effect slightly increased (OR from 1.31 to 1.49).

Sensitivity analysis was conducted for 27 factors, with robust meta-analysis results for 26 factors. However, the result for moderate physical activity was not robust (see Fig. 2).

Publication bias

As shown in Figs. 3, 4, 5, 6, and 7, the funnel plots exhibit a symmetrical distribution, indicating minimal publication bias. Egger's test results were non-significant (P > 0.05), confirming low publication bias.

Discussion

To comprehensively and systematically explore the factors influencing the transition from prediabetes to type 2 diabetes, 59 articles were included, covering three continents and 19 countries, and examining 38 factors affecting the transition. Qualitative results indicated that a high glycemic load diet, a high-fat diet, increased stress, shift work, and conditions such as gallstones and frailty are risk factors, while elevated 25(OH)D and FT4

Table 2 Meta-analysis of risk factors for type 2 diabetes in prediabetes

		Number of Published studies	Combined population	Level of evidence	Heterogeneity test			Effect model	Combined effect size
					I^2	Q	p		OR(95%CI)
Sociodemographic factors	Age	20 [16, 19, 22, 23, 34, 39–41, 43, 45–47, 52, 60, 63, 66, 67, 69, 72, 74]	768891	II-A	96.85%	566.86	0.000	Random effects model	1.03 (1.01 , 1.04)
	Family history	11 [17, 19, 21, 22, 30, 34, 39, 64, 67, 69, 72]	705597	I	9.4%	12.14	0.353	Fixed effect model	1.48 (1.36 , 1.61)
	Male	6 [23, 38, 40, 47, 57, 68]	34083	I	39.1%	8.20	0.145	Fixed effect model	1.13 (1.08 , 1.19)
	High BMI	20 [16, 19, 21, 30–32, 34, 38, 39, 41, 43, 47, 49, 60, 63, 64, 66–69, 72–74]	749587	II-A	84.6%	123.39	0.000	Random effects model	1.21(1.15 , 1.27)
	* High waist circumference	8 [17, 30, 32, 34, 39, 40, 43, 53]	6383	I	31.9%	10.27	0.174	Fixed effect model	1.49 (1.23 , 1.79)
	High waist-to-hip ratio	4 [38, 41, 51, 60]	2259	II-B	0.0%	1.30	0.730	Fixed effect model	2.44 (2.17 , 2.74)
Lifestyle factors	Moderate physical activity	5 [16, 30, 47, 52, 64]	25097	II-A	97.4%	114.95	0.00	Random effects model	0.24 (0.09 , 0.67)
	Lack of physical activity	3 [19, 22, 34]	588	III	55.6%	4.50	0.105	Random effects model	1.86 (1.19 , 2.88)
	Smoking	8 [21, 22, 39, 40, 46, 47, 67, 72]	725972	I	8.9%	7.68	0.361	Fixed effect model	1.31 (1.22 , 1.41)
	Drinking	4 [18, 22, 46, 72]	16825	I	0.0%	2.32	0.509	Fixed effect model	1.07 (0.91 ; 1.27)
	Mediterranean Diet	2 [24, 29]	1527	III	69.1%	3.23	0.072	Random effects model	0.33 (0.08 , 1.30)
	Daily intake of fruits and vegetables	3 [30, 47, 52]	41083	II-A	71.2%	6.94	0.031	Random effects model	0.81 (0.64 , 1.03)
Psychosocial factors	* Anxiety	2 [27, 36]	26205	I	0.00%	0.14	0.704	Fixed effect model	2.61 (1.36 , 5.00)
	depression	2 [27, 28]	29404	I	28.3%	1.39	0.238	Fixed effect model	1.88 (1.35 , 2.61)
	Long working hours	3 [37, 61, 62]	34118	II-A	88.3%	17.03	0.122	Random effects model	1.36 (0.93 , 1.97)
	Sleep time	2 [37, 56]	18450	II-A	94.9%	19.77	0.000	Random effects model	1.36 (0.93 , 11.97)
	Social deprivation level3	2 [31, 57]	402401	II-A	73.4%	3.76	0.052	Random effects model	1.11 (0.97 , 1.27)
	Social deprivation level4	2 [31, 57]	402401	I	0.0%	0.24	0.626	Fixed effect model	1.15 (1.13 , 1.18)

Table 2 (continued)

		Number of Published studies	Combined population	Level of evidence	Heterogeneity test			Effect model	Combined effect size
					I^2	Q	p		OR(95%CI)
Associated diseases and test indicators	High triglycerides	12 [17, 21, 22, 30, 39, 40, 46, 53, 67, 69, 72, 73]	723425	II-A	82.3%	62.02	0.00	Random effects model	1.25 (1.10.1.43)
	Fatty liver index	3 [30, 52, 65]	27457	I	29.4%	2.83	0.242	Fixed effect model	6.14 (5.22，7.22)
	Low HDL-C	4 [22, 40, 72, 73]	21146	I	32.9%	4.47	0.215	Fixed effect model	1.128(1.0921.359)
	High HDL-C	2 [21, 30]	2471	II-B	0%	0.81	0.368	Fixed effect model	0.65 (0.50，0.83)
	*High TG	5 [19, 46, 47, 59, 67]	710514	I	31.9%	5.88	0.208	Fixed effect model	1.091 (1.063，1.120)
	Blood pressure level	17[6, 14, 17, 22–24, 29, 30, 33, 36, 42, 48, 51, 53, 55–57]	755030	II-A	90.5%	200.93	0.000	Random effects model	1.01 (1.01，1.02)
	Blood sugar level	9 [22, 23, 43, 45, 58, 59, 64, 66, 68]	22488	II-A	96.9%	388.50	0.00	Random effects model	1.01(1.01，1.02)
	Insulin resistance	2 [20, 36]	1984	II-B	0.00%	0.36	0.551	Fixed effect model	1.05 (0.96，1.15)
	* Metabolic syndrome	4 [38, 49, 57, 61]	2183	II-B	15.7%	3.56	0.313	Fixed effect model	1.32 (1.08，1.61)

levels are protective factors. The meta-analysis results identified 19 factors influencing the transition from prediabetes to type 2 diabetes, including sex, family history, high BMI, low physical activity, smoking, and high blood pressure.

This study employed a comprehensive search strategy to investigate factors related to the transition from prediabetes to type 2 diabetes, including sociodemographic, lifestyle, psychosocial, comorbidities, and laboratory indicators, with a particular focus on disease and psychosocial factors, which have been less reported in previous studies. The results provide a reference for developing prediction models for type 2 diabetes in prediabetes populations, aiding in the early detection, diagnosis, and treatment of diabetes.

Sociodemographic factors

Age

This study found that increasing age is a risk factor for the progression from prediabetes to type 2 diabetes, consistent with previous research [75] indicating that the age of onset of prediabetes may affect the rate of progression to diabetes. However, due to the limited number of original studies and significant heterogeneity in age cut-off values, we did not find a lower rate of progression from prediabetes to diabetes in older adults compared to middle-aged individuals with prediabetes. Ravindrarajah et al. [76] found that compared to individuals aged 18–44, those over 75 had a reduced risk of progression from prediabetes to type 2 diabetes ($P < 0.01$), possibly due to survival effects in older adults and faster loss of β-cell function in younger individuals. Rooney et al. [77] found that prediabetes in the elderly may not be a strong diagnostic entity for predicting the progression of diabetes, and the prevalence of prediabetes and diabetes increases substantially with age, despite the high prevalence of diabetes and prediabetes in the elderly. However, the progression of hyperglycemia over time (that is, from normal blood sugar to pre-diabetes or diabetes, or from pre-diabetes to diabetes) in this population is characterized by few. Further research is needed to explore differences in the progression of prediabetes to type 2 diabetes at different ages to provide more targeted intervention programs.

Race

Due to the limited number of original studies, we could not conduct a meta-analysis on the impact of race on

Table 3 Subgroup analysis of risk factors for type 2 diabetes in prediabetes

Grouping basis	Factors	Combined population	Level of evidence	Heterogeneity test			Effect model	Combined effect size
				I^2	Q	p		OR (95%CI)
	High BMI	749,587	II-A	84.6%	123.39	0.000	Random effects model	1.21 (1.15,1.27)
BMI continuous variable	High BMI (continuous variable)	734,176	II-A	52.6%	14.76	0.039	Random effects model	1.09 (1.07,1.11)
BMI≧24	High BMI≧24	9728	I	27.0%	8.22	0.222	Fixed effect model	1.76 (1.58,1.95)
BMI≧30	High BMI≧30	3144	II-B	24.7%	5.31	0.257	Fixed effect model	1.58 (1.33,1.88)
	High triglycerides	723,425	II-A	82.3%	62.02	0.00	Random effects model	1.25 (1.10,1.43)
Single factor analysis	High triglycerides (Single factor analysis)	II-A	95.2%	41.93	0.000	1.24	Random effects model	1.51 (1.02,2.12)
Multifactor analysis	High triglycerides (Multifactor analysis)	21,989	II-A	57.5%	18.85	0.016	Random effects model	1.26 (1.10,1.37)
	Blood pressure level	22,488	II-A	90.5%	200.93	0.000	Random effects model	1.01 (1.01,1.02)
hypertension	hypertension	36,375	I	12.1%	12.51	0.326	Fixed effect model	1.41 (1.33,1.50)
High systolic blood pressure	High systolic blood pressure	702,305	I	0.0%	0.35	0.840	Fixed effect model	1.00 (1.00,1.00)
High diastolic blood pressure	High diastolic blood pressure	702,007	I	48.7%	5.85	0.119	Fixed effect model	1.01 (1.01,1.02)
	Blood sugar level	22,488	II-A	96.9%	388.50	0.00	Random effects model	1.01(1.01,1.02)
FPG	FPG	11,407	II-A	96.5%	142.67	0.000	Random effects model	1.54 (1.17,2.01)
2 h-PG	2 h-PG	10,529	I	0.00%	0.00	1.000	Fixed effect model	1.01(1.01,1.01)
HbA1C	HbA1C	12,104	II-A	60.1%	10.03	0.040	Random effects model	1.49(1.28,1.73)

the progression of prediabetes. The main results of the American Diabetes Prevention Program (DPP) indicated that the rate of progression from impaired glucose tolerance to type 2 diabetes was similar across major racial and ethnic groups in the United States, with no significant racial differences in the rate of diabetes progression.

Sex

This study found that compared to females, males are at higher risk for the progression from prediabetes to type 2 diabetes (OR = 1.13, 95% CI 1.08–1.19). Existing studies have demonstrated differences in prediabetes prevalence between males and females, with males more likely to have impaired fasting glucose (IFG) and increased hepatic glucose output and early insulin secretion impairment, while females are more prone to impaired glucose tolerance (IGT) and peripheral insulin resistance [78]. Additionally, there are differences between males and females in biological factors such as genetic susceptibility, sex hormones, and neuroendocrine pathways, as well as in lifestyle, psychosocial, and environmental factors [79].

Lifestyle factors

The study found that lack of physical activity and smoking are lifestyle-related risk factors. Based on these findings and current expert recommendations, lifestyle modifications [80] should be the first-line approach in treating prediabetes. Lifestyle interventions, as a cornerstone in diabetes prevention, should be continuously implemented in prediabetic individuals. These interventions include a balanced diet, exercise, weight reduction, calorie control, smoking cessation, and limiting alcohol consumption.

In this study, no correlation was found between alcohol consumption and the progression of prediabetes, likely due to the limited number of original studies. Future research should explore this correlation further. Nonetheless, considering the impact of prediabetes on cardiovascular outcomes, limiting alcohol consumption remains an essential part of lifestyle interventions in individuals with prediabetes.

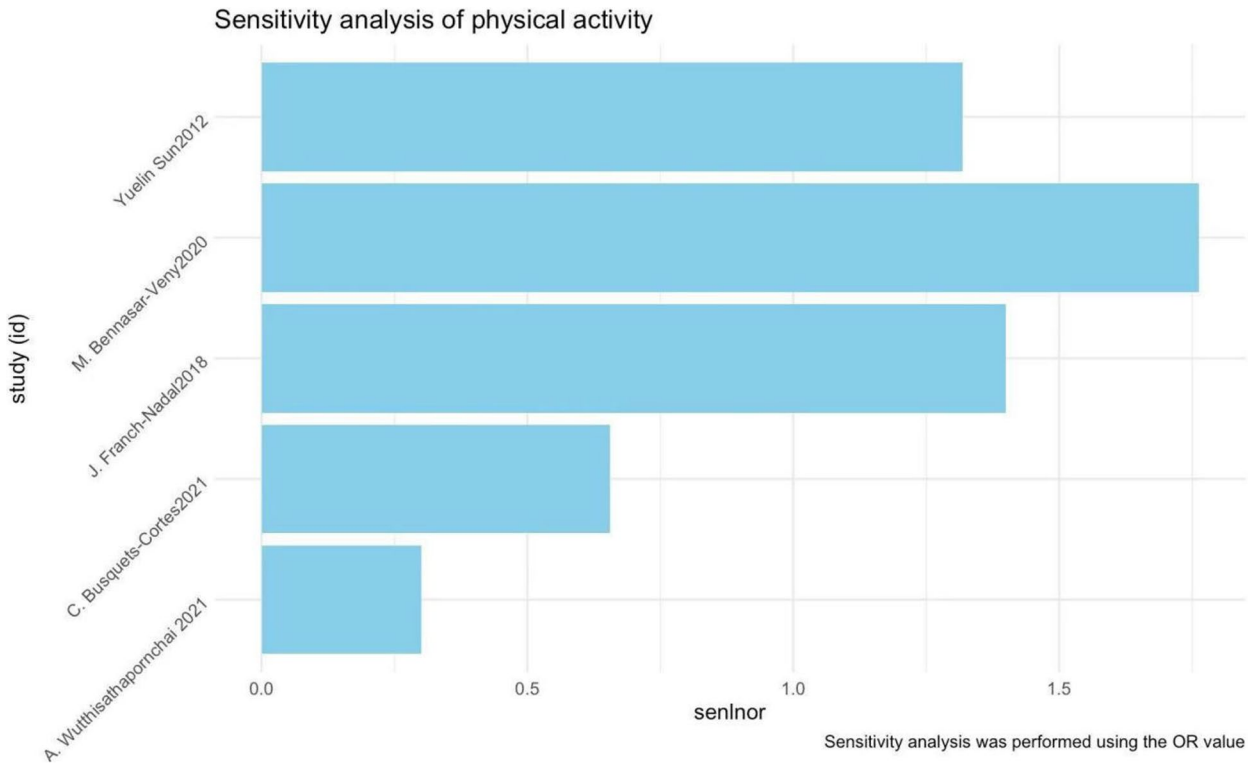

Fig. 2 Sensitivity analysis of moderate-intensity physical activity

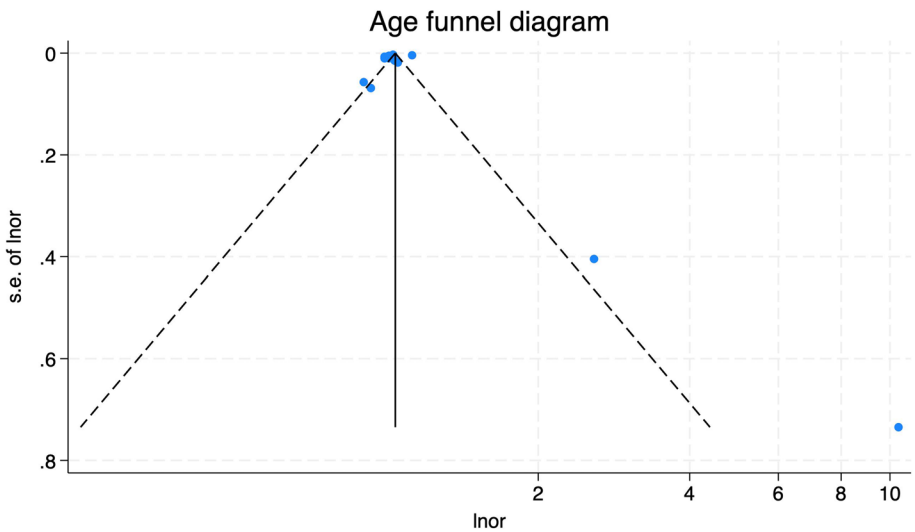

Fig. 3 Age funnel diagram

Psychological health

The study found a strong association between anxiety and the progression from prediabetes to type 2 diabetes, individuals with poorer psychological health were more likely to develop type 2 diabetes during follow-up. This finding suggests that psychological issues may not only affect quality of life but also directly impact disease progression and health outcomes. Anxiety can exacerbate insulin resistance, inflammation, and stress-related hormonal imbalances, all of which contribute to glucose dysregulation. Recent experiment [75] in this area suggested that individuals with higher anxiety levels are at an increased

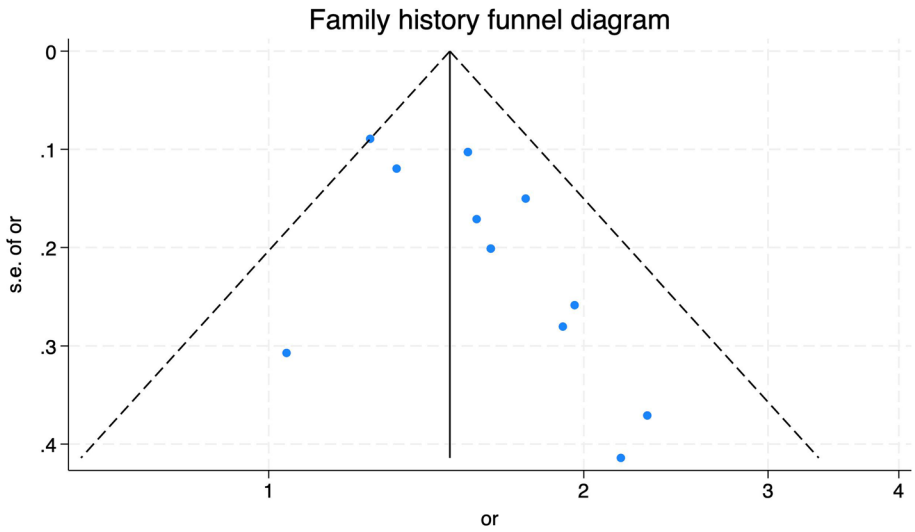

Fig. 4 Family history funnel diagram

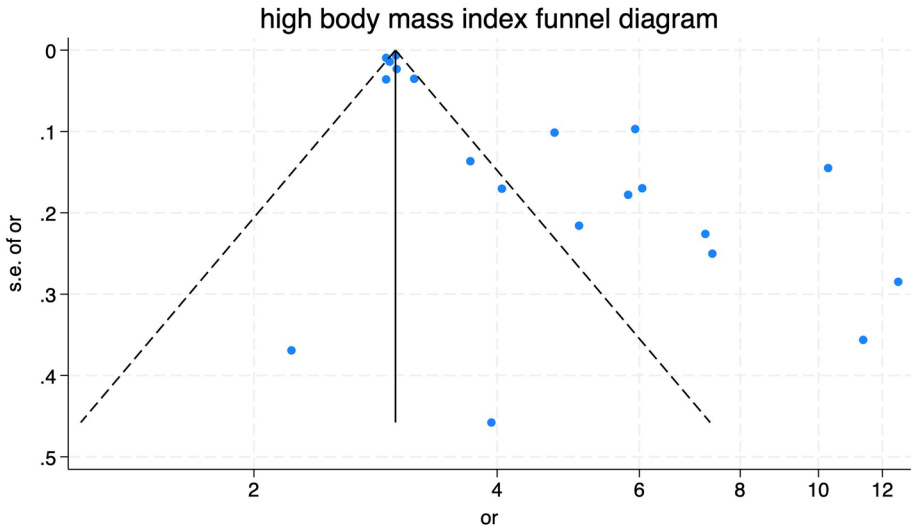

Fig. 5 High body mass index funnel diagram

risk of developing type 2 diabetes due to the physiological and behavioral consequences of chronic stress, such as elevated cortisol levels and unhealthy coping mechanisms (e.g., poor diet, reduced physical activity).

This association could be because of psychological stress on the neuroendocrine and autonomic nervous systems. Prolonged stress may activate the hypothalamic–pituitary–adrenal axis, releasing stress hormones such as cortisol and adrenaline, which affect insulin sensitivity and secretion. Additionally, emotional issues may lead to unhealthy lifestyle choices, such as emotional overeating and lack of exercise, increasing the risk of diabetes development.

Future research should adopt more rigorous designs to explore the biological mechanisms underlying the relationship between psychological health and diabetes progression and develop effective interventions. Additionally, research should investigate the impact of different types of psychological issues on disease progression and the differences between various populations.

Disease risk factors

Cardiovascular risk factors

This study indicates that hypertension, hyperlipidemia, and high cholesterol levels are risk factors for the progression from prediabetes to type 2 diabetes (T2D).

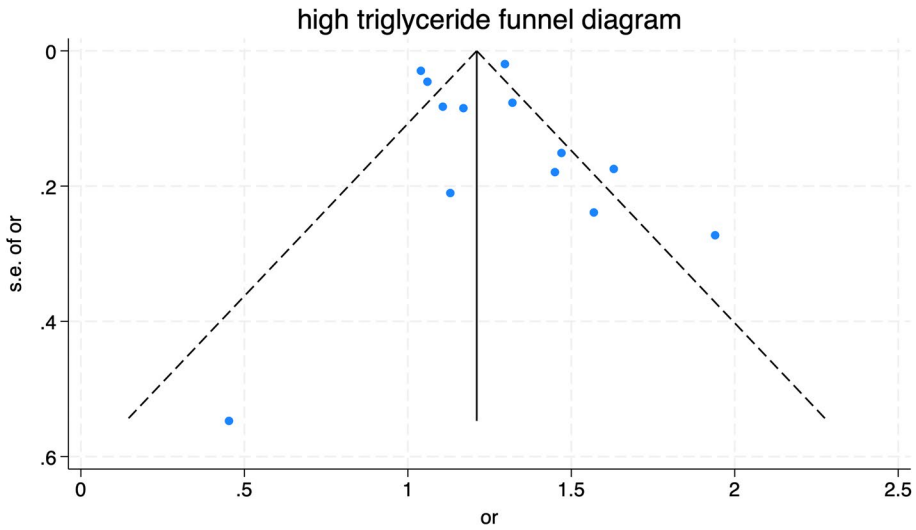

Fig. 6 High triglyceride funnel diagram

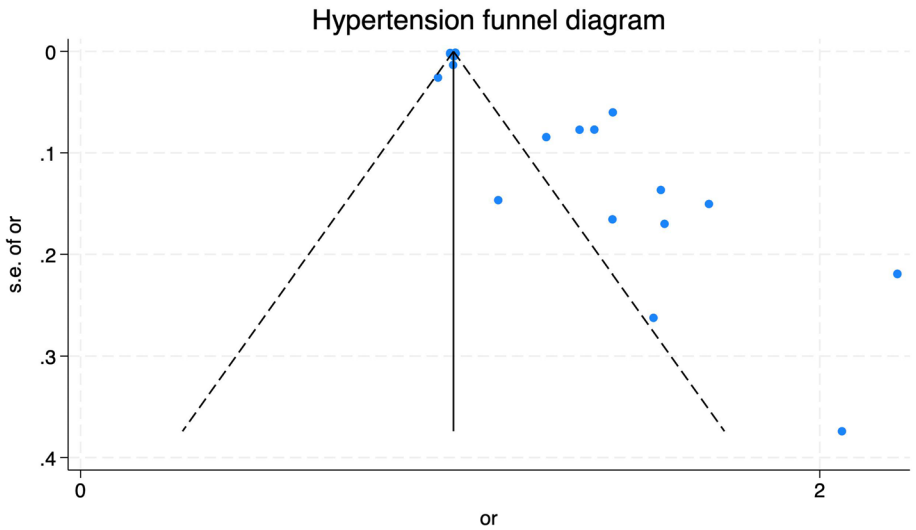

Fig. 7 Hypertension funnel

These cardiovascular risk factors might increase the likelihood of developing T2D among individuals with prediabetes, highlighting their significance in diabetes progression. Several physiological mechanisms may link hypertension, hyperlipidemia, and high cholesterol to diabetes development. For instance, hypertension might lead to vascular damage and insulin resistance, thereby promoting diabetes development. Hyperlipidemia and high cholesterol may influence insulin sensitivity by exacerbating insulin resistance, affecting lipid metabolism, and activating inflammatory responses, thus increasing the risk of diabetes. These findings have crucial implications for clinical practice. Clinicians should prioritize the cardiovascular health of prediabetic patients and manage their hypertension, hyperlipidemia, and high cholesterol levels actively. Effective interventions, such as medication and lifestyle changes, could delay or prevent the onset of diabetes, reduce related complications, and enhance the quality of life for these patients.

Baseline blood glucose levels

The study finds that elevated baseline blood glucose levels are a risk factor for the progression from prediabetes to T2D. The higher the blood glucose levels within the prediabetic diagnostic criteria, the higher the risk of developing T2D. Additionally, different diagnostic

criteria for prediabetes present varying risks for progression to T2D. According to the Chinese Expert Consensus on Prediabetes, it is recommended to assess patients and analyze their risk levels before intervening in the prediabetic population.

Fatty liver index, high waist-to-hip ratio

The findings of this meta-analysis highlight several risk factors with significant clinical relevance, particularly the Fatty Liver Index (FLI) and high waist-to-hip ratio (WHR), both of which are strongly associated with the progression from prediabetes to type 2 diabetes. Elevated FLI reflects the presence of nonalcoholic fatty liver disease (NAFLD), which is closely linked to insulin resistance and increased diabetes risk. NAFLD is a frequent complication in individuals with metabolic syndrome, exacerbating glucose dysregulation. Clinical interventions targeting liver fat reduction, such as lifestyle changes and pharmacotherapy, may help reduce diabetes incidence [81]. Similarly, a high WHR indicates central adiposity, a key contributor to insulin resistance and chronic inflammation, which accelerates the transition from prediabetes to diabetes. Since WHR is an easy-to-measure indicator of visceral fat, incorporating it into routine risk assessment could improve early identification of at-risk individuals. Targeted interventions like dietary changes, physical activity, and potentially medications aimed at reducing abdominal obesity can help delay or prevent diabetes onset. Both FLI and WHR provide valuable insights for personalized, targeted interventions in clinical practice.

Limitations

This study has several limitations:

1. Some studies lacked usable data and could not be included, which might have affected the reliability of the results to some extent.
2. Differences in diagnostic criteria, tools, sample sizes, and study regions among the subjects led to significant heterogeneity in some influencing factors.
3. The language restriction applied during the literature search, as we included only studies published in English and Chinese. This may have led to the exclusion of relevant studies published in other languages, particularly from regions where research might be conducted in local languages. Consequently, this restriction could introduce a bias, limiting the generalizability of our findings to populations that are underrepresented in English and Chinese language publications. While we aimed to ensure the inclusion of a comprehensive set of studies by using major international and regional databases, we acknowledge that the exclusion of non-English and non-Chinese studies may affect the overall representation of the global evidence base on risk factors for the progression from prediabetes to type 2 diabetes. Future research efforts could focus on broadening language inclusion to mitigate this potential bias.

Future outlook

Future research should prioritize large-scale prospective cohort studies with standardized definitions and assessment methods for risk factors, as these are crucial for addressing the gaps identified in the current evidence base. Such studies would provide clearer insights into the progression from prediabetes to type 2 diabetes by enabling more reliable cross-study comparisons. Additionally, further exploration of specific subgroups, including variations by age, sex, ethnicity, and socio-economic status, is essential to tailor prevention strategies for high-risk populations. More research is also needed on the mechanistic pathways through which psychological factors, such as anxiety, and comorbid conditions influence diabetes progression. Finally, interventional studies targeting modifiable risk factors could offer valuable insights into effective prevention strategies and improve overall management of diabetes risk.

Although lifestyle changes have proven significantly beneficial in preventing the progression to T2D, many currently defined impaired glucose homeostasis (IH) patients will continue to progress. Additionally, most individuals at risk of T2D are not identified promptly, and those at risk often do not receive adequate referrals for lifestyle interventions. Therefore, it is crucial to adopt more sensitive and practical methods to identify high-risk individuals for prediabetes and T2D at an earlier stage, allowing for timely intervention. The International Diabetes Federation's (IDF) position statement on the 1-h post-load plasma glucose for diagnosing intermediate hyperglycemia and T2D highlights those existing diagnostic standards like fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), and 2-h oral glucose tolerance test (2-h PG) might not identify individuals in the early stages of diabetes development promptly. This can lead to missing diagnoses of individuals with elevated blood glucose levels who have not yet reached diagnostic thresholds. Traditional diagnostic methods may also fail to accurately predict the risk of progressing to T2D or its complications. The position statement suggests that a 1-h post-load plasma glucose (1-h PG) level of $\geq$ 8.6 mmol/L (155 mg/dL) in normoglycemic individuals is highly accurate for predicting T2D progression. Although our study demonstrates the risk of progression from prediabetes to T2D, our results are influenced by diagnostic criteria.

Future research should consider comparing various diagnostic standards to comprehensively assess the risk of progression from prediabetes to T2D. Larger, multicenter studies are needed to further validate these findings. Healthcare professionals should focus on risk screening in prediabetic populations, provide precise stratified management, slow the progression from prediabetes to diabetes, and strive for self-remission in individuals with prediabetes, thereby improving patient quality of life.

Conclusion

In summary, sociodemographic factors such as age, male sex, high body mass index (BMI), high waist circumference, and high waist-hip ratio; lifestyle factors such as smoking and lack of physical activity; psychosocial factors such as anxiety, depression, and social deprivation level 4; and disease factors such as hypertension, hyperlipidemia, high cholesterol, metabolic syndrome, elevated fatty liver index, and increased baseline blood glucose levels are risk factors for the progression from prediabetes to T2DM. Diabetes is a chronic, lifelong disease that severely impacts patients' quality of life. Therefore, early intervention targeting these risk factors is crucial in reducing the incidence of T2DM.

Supplementary Information

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Supplementary Material 1.

Authors' contributions

Study design: Shengying Hu. Search strategy, study selection, data extraction, Assessment of methodological quality, data analysis: Shengying Hu, Wenting Ji, Yizhu Zhang. Grading the quality of evidence: Shengying Hu, Wenting Ji, Yizhu Zhang, Hongyu Sun Supervision: Hongyu Sun, Yumei Sun. Writing—original draft preparation: Shengying Hu, Wendi Zhu. Writing—review and editing: Wenting, Ji, Yumei Sun, Hongyu Sun. Funding acquisition: Hongyu Sun

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Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

It is not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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