INPLASY

Association of different lipid metabolism indexes (LAP, VAI, AIP) with type 2 diabetes : a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 September 2025 and was last updated on 19 September 2025.

INTRODUCTION

Review question / Objective Research Question (PICOS Framework) Population: Adults aged ≥18 years without underlying diseases, generally healthy individuals.
Exposure: Levels of composite lipid indices (LAP, VAI, AIP) as the exposure factor.
Comparator: Low-risk group or reference interval based on lipid index stratification.
Outcomes:
Primary outcome: Risk of incident type 2 diabetes mellitus (T2DM) expressed as OR/RR/HR.
Secondary outcomes: Differences across study designs, dose–response relationships, subgroup variations (sex, ethnicity, etc.).
Study design: Cohort, case–control, and cross-sectional studies will be included.

Condition being studied T2DM constitutes a major global public-health burden, already affecting >400 million adults. Conventional lipid metrics fail to fully capture underlying metabolic dysregulation. Recently developed composite lipid indices—LAP (waist × TG), VAI (BMI, waist, TG, HDL-C) and AIP (log[TG/HDL-C])—provide a more integrated reflection of visceral adiposity and atherogenic risk. Observational studies linking these indices to incident T2DM have yielded inconsistent findings, and no meta-analysis has simultaneously evaluated all three while exploring sources of heterogeneity. We will therefore conduct a systematic review and meta-analysis to quantify the associations of LAP, VAI and AIP with T2DM onset, assess key confounders through stratified analyses, and furnish evidence for their potential use in risk prediction and early intervention.

METHODS

Participant or population Community-dwelling adults aged ≥18 years who were free of diabetes at baseline and had no selected chronic diseases (e.g., obesity, hypertension, coronary heart

disease), ensuring a representative and homogeneous study population.

Intervention Not applicable.

Comparator The lowest quantile (Q1) or reference category of each composite lipid index—LAP, VAI, or AIP—served as the comparator; participants in the highest quantile (or extreme category) were contrasted against this referent group to estimate incident type 2 diabetes risk.

Study designs to be included Cohort, case–control, and cross-sectional studies.

Eligibility criteria 1) Population: Community-dwelling adults aged ≥ 18 years who were free of diabetes at baseline; studies focusing on specific patient groups (e.g., obesity, hypertension, coronary heart disease) were excluded to ensure homogeneity.
2) Study design: Observational studies—cohort, case–control, or cross-sectional.
3) Outcomes: Had to report the association between at least one composite lipid index (LAP, VAI, or AIP) and incident type 2 diabetes mellitus (T2DM), providing multivariable-adjusted effect estimates (OR/RR/HR with 95 % CI) derived from logistic or Cox regression models.

Information sources A systematic search was conducted across four databases, namely PubMed, Web of Science, Embase, and the Cochrane Library, with the search period spanning from the inception of each database to April 20, 2025. The search strategy combined MeSH/Emtree controlled vocabulary terms with free-text keywords, including "type 2 diabetes mellitus", "T2DM", "lipid accumulation product (LAP)", "visceral adiposity index (VAI)", and "atherogenic index of plasma (AIP)". For study type, observational studies (cohort studies, cross-sectional studies, and case-control studies) were included, with the requirement that these studies reported multivariable-adjusted effect estimates (odds ratio [OR], relative risk [RR], hazard ratio [HR]) along with their corresponding 95% confidence intervals (CIs).

Main outcome(s) The primary outcome measures included two aspects: first, the association between composite lipid metabolism indices (Lipid Accumulation Product [LAP], Visceral Adiposity Index [VAI], and Atherogenic Index of Plasma [AIP]) and the risk of incident type 2 diabetes mellitus (T2DM); second, the predictive ability (diagnostic efficacy) of each index for T2DM, which was evaluated by the pooled area under the receiver operating characteristic curve (AUC). For the effect measure, the odds ratio (OR) was used as the primary effect size.

Quality assessment / Risk of bias analysis For cohort studies, the Newcastle-Ottawa Scale (NOS) was used for quality assessment, covering evaluation dimensions including the representativeness of the exposed cohort, the selection of the unexposed cohort, the method of exposure confirmation, outcome assessment, and completeness of follow-up.

For cross-sectional studies, the Joanna Briggs Institute (JBI) 9-item checklist was applied, which includes aspects such as sampling frame and method, sample size, description of participants, data completeness, disease identification method, and statistical method.

Regarding the assessment method, two reviewers independently conducted quality scoring, and any discrepancies were resolved through discussion. The quality scores were used for descriptive analysis and not employed as inclusion or exclusion criteria.

Strategy of data synthesis STATA 18.0 software was used for statistical analysis. For the pooling of effect sizes, either a random-effects model or a fixed-effects model was adopted based on the results of heterogeneity tests: the random-effects model was used when $I^2 > 50\%$ and $P \leq 0.1$, otherwise the fixed-effects model was applied.

Heterogeneity across studies was assessed using the I^2 statistic and Cochran's Q test. Sensitivity analysis was conducted by sequentially excluding each individual study to observe whether the pooled effect remained stable.

Subgroup analyses were performed by stratifying according to study design (cohort vs. cross-sectional), country (China vs. non-China), age, BMI, gender ratio, follow-up duration, and whether confounding factors were adjusted for, among other variables.

Publication bias was evaluated using funnel plots and Egger's test to determine if publication bias existed.

Subgroup analysis We conducted extensive subgroup analyses to explore potential sources of heterogeneity and to assess the consistency of the associations across different study-level characteristics. Stratification was performed according to study design (cohort vs. cross-

sectional), geographic region (China vs. non-China), mean age (≤45 vs. >45 years), median body-mass index (non-obese vs. obese), proportion of females (≤50 % vs. >50 %), follow-up duration (≤5 vs. >5 years), and adjustment status for key confounders such as alcohol consumption, family history of diabetes, BMI and other lipid indices. Random-effects meta-analysis was applied within each stratum, and between-subgroup differences were evaluated with meta-regression or Q-tests. These analyses allowed us to quantify the extent to which clinical and methodological characteristics explained inter-study variability and to identify the main drivers of heterogeneity.

Sensitivity analysis Sensitivity analyses were carried out to examine the robustness of the pooled effect estimates. We employed a "leave-one-out" approach in which each study was sequentially excluded and the meta-analysis recalculated to determine whether any single investigation disproportionately influenced the overall results. Additionally, influence diagnostics (standardised residuals, Cook's distance and tau-squared contribution) were computed for every study. Publication bias was assessed visually with funnel plots and statistically with Egger's regression test; when asymmetry was detected, the trim-and-fill method was used to estimate the number of potentially missing studies and their impact on the pooled odds ratio. All sensitivity computations were performed in Stata 18.0 using the metan, metainf and metabias routines.

Country(ies) involved China.

Keywords Composite Lipid Indices; Lipid Accumulation Product (LAP); Visceral Adiposity Index (VAI); Atherogenic Index of Plasma (AIP); Type 2 Diabetes Mellitus.

Contributions of each author

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