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INPLASY

Small for Gestational Age as a Risk Factor for Adult Metabolic Syndrome: A Systematic Review and Meta-Analysis for Prevention

INPLASY202670080

doi: 10.37766/inplasy2026.7.0080

Received: 20 July 2026

Published: 20 July 2026

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ADMINISTRATIVE INFORMATION

Support - No support.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202670080

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 July 2026 and was last updated on 20 July 2026.

INTRODUCTION

Review question / Objective The aim of this systematic review and meta-analysis is to quantify the association between small for gestational age (SGA) and the risk of adult metabolic syndrome (MetS), and to determine whether between-study heterogeneity arises from methodological differences or from biologically meaningful moderators to inform precision prevention strategies.The review question was constructed around the PICOS framework:
(P) Population: Infants born small for gestational age (SGA), defined as birth weight below the 10th percentile for gestational age, regardless of sex, ethnicity, or geographic region. Preterm or term infants are eligible provided SGA status is clearly defined.
(I) Exposure: Being born small for gestational age (SGA).
(C) Comparator: Individuals born appropriate for gestational age (AGA), defined as birth weight between the 10th and 90th percentiles for gestational age, matched or adjusted for key confounders including gestational age, sex, and maternal factors.
(O) Outcomes: at least one of the following metabolic outcomes was reported in childhood, adolescence, or adulthood: impaired glucose tolerance or type 2 diabetes, insulin resistance, dyslipidemia (e.g., elevated triglycerides, low HDL cholesterol), central obesity (e.g., waist circumference ≥90th percentile), hypertension, metabolic syndrome, or a composite thereof, with studies required to report odds ratios, risk ratios, hazard ratios, or sufficient data for their calculation
(S) Study design: the study design was a prospective or retrospective cohort, nested case-control, or cross-sectional study with a clearly defined comparison group and a minimum follow-up of one year for outcomes assessed in childhood or adolescence.

Condition being studied Metabolic syndrome (MetS) is a cluster of cardiometabolic risk factors—central obesity, insulin resistance, dyslipidemia, and hypertension—that predisposes individuals to type 2 diabetes and cardiovascular disease,

affecting approximately 20–25% of the global adult population. Individuals born small for gestational age (SGA) are at increased risk of developing MetS in adulthood, yet the strength and consistency of this association remain uncertain, and the modifying role of early-life growth patterns has not been systematically examined. This review synthesizes evidence on the SGA–MetS association to inform risk stratification and preventive strategies.

METHODS

Participant or population Infants born small for gestational age (SGA), defined as birth weight below the 10th percentile for gestational age, irrespective of sex, ethnicity, or geographic region. Both preterm and term infants are eligible if SGA status is clearly defined. Studies on extremely preterm infants or genetic syndromes are excluded.

Intervention No intervention will be evaluated. This review assesses the exposure of being born small for gestational age (SGA, birth weight <10th percentile) compared with appropriate for gestational age (AGA, birth weight 10th–90th percentile) in observational studies.

Comparator The comparator is individuals born appropriate for gestational age (AGA), defined as birth weight between the 10th and 90th percentiles for gestational age, matched or adjusted for key confounders such as gestational age, sex, and maternal factors.

Study designs to be included The study design was a prospective or retrospective cohort, nested case-control, or cross-sectional study with a clearly defined comparison group and a minimum follow-up of one year for outcomes assessed in childhood or adolescence.

Eligibility criteria Inclusion:
Population: SGA infants (birth weight <10th percentile); preterm or term eligible.
Exposure: SGA birth.
Comparator: AGA (birth weight 10th–90th percentile).
Outcomes: Metabolic syndrome or its components (insulin resistance, dyslipidemia, central obesity, hypertension, impaired glucose tolerance), with effect estimates (OR, RR, HR) reported or calculable.
Design: Cohort, case-control, or cross-sectional with comparison group;
Language: English.
Exclusion:
Animal/in vitro studies, reviews, case reports/series, editorials, conference abstracts.
No clearly defined AGA comparator.
Insufficient data for effect estimation.
Duplicate/overlapping populations; inaccessible full texts.

Information sources PubMed, Web of Science, EMBASE, Cochrane Library (inception to June 30, 2026).

Main outcome(s) At least one of the following metabolic outcomes was reported in childhood, adolescence, or adulthood: impaired glucose tolerance or type 2 diabetes, insulin resistance, dyslipidemia (e.g., elevated triglycerides, low HDL cholesterol), central obesity (e.g., waist circumference ≥90th percentile), hypertension, metabolic syndrome, or a composite thereof, with studies required to report odds ratios, risk ratios, hazard ratios, or sufficient data for their calculation.

Quality assessment / Risk of bias analysis Two reviewers independently assessed the methodological quality of included studies using the Newcastle-Ottawa Scale (NOS), which evaluates three domains: selection (e.g., cohort representativeness, exposure ascertainment), comparability (e.g., control for gestational age, sex, and maternal factors), and outcome (e.g., assessment validity, follow-up adequacy), with a maximum total of 9 stars. Studies were classified as high (≥7 stars), moderate (4–6 stars), or low (≤3 stars) quality. Disagreements were resolved by consensus or adjudication by a third reviewer.

Strategy of data synthesis Quantitative meta-analysis will be performed using random-effects models (DerSimonian–Laird) when $I^2 \geq 50\%$; otherwise, fixed-effects models will be used. Pooled relative risks (RRs) with 95% CIs will be calculated for dichotomous outcomes. Heterogeneity will be assessed via I^2. Leave-one-out sensitivity analyses will examine the influence of individual studies. Publication bias will be assessed using funnel plots and Egger's test. Subgroup analyses and meta-regression are planned but contingent on sufficient study numbers. All analyses will be conducted in R (version 4.3.2) using the meta and metafor packages. If meta-analysis is not feasible, a narrative synthesis will be provided.

Subgroup analysis Subgroup analyses are planned, contingent on sufficient study numbers, to explore heterogeneity sources. Potential subgroup variables include: (1) catch-up growth

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definition/velocity (rapid vs. non-rapid); (2) SGA threshold (<3rd vs. <10th percentile); (3) MetS diagnostic criteria (ATP III, IDF, WHO); (4) study design (cohort, case-control, cross-sectional); and (5) geographic region. Interaction tests will be used to assess subgroup differences. If study numbers are insufficient, subgroup findings will be interpreted descriptively.

Sensitivity analysis Leave-one-out sensitivity analyses will be performed to assess the influence of individual studies on the pooled estimates. If studies at high risk of bias are identified, they will be excluded in a separate sensitivity analysis. Changes in effect estimates and heterogeneity (I^2) will be compared to evaluate robustness. Results of sensitivity analyses will be reported alongside the primary findings.

Country(ies) involved China.

Keywords Small for Gestational Age; Metabolic Syndrome; Catch-up Growth; Early Life Growth Trajectory; Risk Stratification; Primary Prevention.

Contributions of each author
Author 1 - Weina Zhang.
Author 2 - Yingxue Ding.

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