INPLASY

# AI-Enabled Opportunistic Coronary Artery Calcium Assessment on Routine Non–ECG-Gated Chest CT: a Systematic Review and Meta-analysis

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## ADMINISTRATIVE INFORMATION

**Support -** No specific financial support has been received for this review.

**Review Stage at time of this submission -** Preliminary searches.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY202660006

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 June 2026 and was last updated on 2 June 2026.

## INTRODUCTION

**Review question / Objective** This systematic review and meta-analysis aims to determine whether artificial intelligence-enabled opportunistic coronary artery calcium assessment on routine non–ECG-gated chest CT can accurately identify clinically actionable CAC categories and thresholds, improve ASCVD risk stratification or reclassification, and support preventive-care implementation. The population will include adults undergoing routine non–ECG-gated chest CT. The index test will be AI, machine learning, deep learning, or fully automated CAC detection, scoring, quantification, or categorization. Reference standards will include expert manual or semi-manual CAC scoring on the same non-gated CT, paired ECG-gated CAC CT, or expert visual CAC categories. Outcomes will include diagnostic threshold performance, CAC category agreement, risk reclassification, prognostic associations, statin initiation, lipid management, referrals, reporting, notification, and downstream testing.

**Condition being studied** The condition being studied is coronary artery calcium detected on routine non–ECG-gated chest computed tomography. CAC represents calcified coronary atherosclerotic plaque and is associated with future ASCVD risk. This review focuses on CAC burden sufficient to alter cardiovascular prevention risk stratification, especially CAC >0, CAC ≥100, and high-burden CAC thresholds such as CAC ≥300 or CAC ≥400. The clinical context is opportunistic detection from routine chest CT performed for non-cardiac indications rather than dedicated cardiac CAC scanning.

## METHODS

**Participant or population** Adults aged 18 years or older undergoing routine non–ECG-gated chest CT will be eligible. This may include low-dose chest CT for lung cancer screening, routine diagnostic chest CT, oncology surveillance CT, noncardiac thoracic CT, and PET/CT CT components if the CT images are sufficient for CAC assessment. Studies

limited to dedicated ECG-gated CAC CT without routine non-gated chest CT will be excluded.

**Intervention** The intervention or index test is AI-enabled opportunistic CAC assessment from routine non–ECG-gated chest CT, including machine learning, deep learning, fully automated algorithms, commercial AI software, or automated image-processing methods that detect, segment, quantify, score, or categorize coronary artery calcium. Outputs may include Agatston score, volume score, CAC category, CAC-DRS category, ordinal CAC severity, or binary CAC detection.

**Comparator** Comparators or reference standards will include expert manual or semi-manual CAC scoring on the same non-gated chest CT, paired ECG-gated CAC CT, expert visual CAC categorization, usual radiology reporting, standard care without AI notification, or traditional clinical risk assessment alone, depending on the study design and outcome. Reference standards will be analyzed separately where possible.

**Study designs to be included** Diagnostic accuracy studies, agreement studies, cohort studies, prognostic studies, risk reclassification studies, randomized or cluster-randomized trials, nonrandomized intervention studies, before-after studies, and quality improvement studies evaluating AI-enabled CAC assessment on routine non–ECG-gated chest CT will be included.

**Eligibility criteria** Inclusion criteria: adult participants; routine non–ECG-gated chest CT; AI, machine learning, deep learning, automated, or commercial software-based CAC assessment; and at least one extractable diagnostic, agreement, prognostic, reclassification, or implementation outcome. Eligible CT types include noncontrast or contrast-enhanced non–ECG-gated chest CT, LDCT, diagnostic chest CT, oncology surveillance CT, noncardiac thoracic CT, and PET/CT CT components.

Exclusion criteria: dedicated ECG-gated CAC CT only; coronary CT angiography only unless routine non-gated CT-based CAC is separately evaluated; manual-only or visual-only incidental CAC reporting without AI or automation; phantom-only, simulation-only, animal-only studies; case reports; case series with fewer than 10 patients; reviews, editorials, and commentaries; studies evaluating only non-coronary calcification; and studies without extractable CAC-related outcomes. Uncorrected AI outputs will be prioritized for primary analyses, while human-corrected AI outputs will be considered secondary.

**Information sources** Information sources will include MEDLINE/PubMed, Embase, Web of Science Core Collection, Scopus, Cochrane CENTRAL, IEEE Xplore, ClinicalTrials.gov, WHO ICTRP, FDA AI-enabled medical device resources, FDA 510(k) database, Google Scholar, conference abstracts when available, reference lists of included studies, reference lists of relevant reviews, and forward citation tracking. Study authors may be contacted for missing 2×2 tables, confusion matrices, or implementation outcome data.

**Main outcome(s)** The main outcomes will be diagnostic performance and actionable classification of AI-derived CAC on routine non–ECG-gated chest CT. Co-primary diagnostic outcomes will be sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratios, diagnostic odds ratio, and area under the curve for clinically actionable CAC thresholds, especially CAC ≥100 and CAC >0. Co-primary agreement outcomes will include CAC category agreement, weighted or unweighted kappa, exact category agreement, one-category misclassification, severe misclassification, and actionable misclassification, particularly false-negative classification of reference CAC ≥100 as AI-CAC <100. Outcomes will be assessed at the patient level whenever possible.

**Additional outcome(s)** Additional outcomes will include performance for CAC ≥300 and CAC ≥400; ICC, Pearson or Spearman correlation, mean absolute error, root mean squared error, Bland-Altman bias, and limits of agreement; ASCVD risk reclassification, C-statistic change, net reclassification improvement, integrated discrimination improvement, and statin eligibility reclassification; adjusted hazard ratios for MACE, myocardial infarction, stroke, revascularization, cardiovascular mortality, and all-cause mortality; and preventive-care implementation outcomes including statin prescription, statin initiation, lipid-lowering therapy intensification, lipid testing, clinician or patient notification, radiology report inclusion, primary care or cardiology referral, downstream testing, and potential overtreatment.

**Quality assessment / Risk of bias analysis** Diagnostic and agreement studies will be assessed using QUADAS-3 with AI-adapted signaling questions covering patient selection, index test, reference standard, flow, timing, algorithm locking, data leakage, blinding, failure rate, algorithm version, and human correction. Randomized trials will be assessed using RoB 2. Nonrandomized intervention or implementation studies will be

assessed using ROBINS-I. Prognostic studies will be assessed using QUIPS or an adapted ROBINS-E framework. Prediction or reclassification models combining AI-CAC with clinical variables will be assessed using PROBAST+AI where applicable. An additional AI transparency table will summarize model type, training data, validation strategy, external validation, regulatory status, scanner context, and vendor involvement.

**Strategy of data synthesis** Diagnostic threshold data will be synthesized separately for CAC >0, CAC ≥100, CAC ≥300, and CAC ≥400. When sufficient studies are available, pooled sensitivity and specificity will be estimated using a bivariate random-effects generalized linear mixed model; HSROC models will be considered when threshold definitions vary. Positive and negative likelihood ratios, diagnostic odds ratios, 95% confidence intervals, prediction intervals, forest plots, and SROC plots will be reported where possible. Categorical agreement outcomes, including kappa, exact agreement, and actionable misclassification, will be pooled using random-effects meta-analysis when appropriate. Correlations will be transformed using Fisher z before pooling and back-transformed. Adjusted hazard ratios will be pooled on the log scale if at least three comparable studies are available. Implementation outcomes will be summarized as risk ratios, odds ratios, or narrative synthesis, with randomized and nonrandomized studies analyzed separately. If meta-analysis is inappropriate because of heterogeneity or sparse data, structured narrative synthesis will be performed.

**Subgroup analysis** Planned subgroup analyses include reference standard type: same-scan expert manual non-gated CT, paired ECG-gated CAC CT, or expert visual category; noncontrast versus contrast-enhanced CT; LDCT lung screening versus routine diagnostic chest CT; slice thickness; reconstruction kernel; scanner vendor; commercial or regulator-approved AI versus academic prototype; external validation versus internal validation only; prospective versus retrospective design; fully automated AI versus human-corrected AI; low versus high risk of bias; and studies with versus without vendor involvement. CAC ≥300 and CAC ≥400 will be analyzed separately where possible.

**Sensitivity analysis** Sensitivity analyses will exclude studies at high risk of bias, studies with case-control or enriched designs, studies with unclear AI independence or potential data leakage, studies using human-corrected AI outputs, studies with nonstandard CT protocols, and studies with incomplete or partial heart coverage. For paired ECG-gated CAC CT reference standards, analyses will be repeated using scan-interval restrictions of ≤30 days, ≤90 days, ≤180 days, and ≤365 days where data allow. Noncontrast CT will be analyzed as the primary imaging context, with contrast-enhanced CT assessed separately. Influence analyses will be performed by omitting one study at a time when sufficient studies are available.

**Country(ies) involved** Taiwan.

**Keywords** coronary artery calcium; artificial intelligence; chest CT; meta-analysis; prevention.

**Contributions of each author**

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