INPLASY

# Contrast Media-Induced Nephropathy and Renal Imaging Biomarkers: An Independent Systematic Review and Updated Meta-Analysis of CIN Incidence by Population Setting, Early-Rise Biomarker Performance, Prophylaxis Evidence Verdicts, and GBCA Renal Safety from January 2000 Through May 2026

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Alanazi, AS; Alanazi, BA.

**Corresponding author:**
Abdulrahman S. Alanazi
aas2@hotmail.com

**Author Affiliation:**
Department of Clinical Pharmacy, College of Pharmacy, University of Hail, Hail 81411, Saudi Arabia.

## ADMINISTRATIVE INFORMATION

**Support -** Self-funded. University of Hail College of Pharmacy academic resources. No pharmaceutical industry or commercial funding received.

**Review Stage at time of this submission -** The review has not yet started.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY202660026

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 June 2026 and was last updated on 5 June 2026.

## INTRODUCTION

**Review question / Objective** What are the population-stratified CIN incidence rates, the NGAL and cystatin C AUCs versus creatinine, and the definitive prophylaxis evidence verdicts — including the NAC deimplementation case — from January 2000 through May 2026?

**Rationale** This systematic review addresses a critical evidence gap in radiological pharmacovigilance. No comprehensive synthesis with pre-specified pattern analyses exists for this topic. Prospective registration ensures transparency and minimises reporting bias.

**Condition being studied** Contrast-induced nephropathy (CIN) and contrast-induced acute kidney injury (CI-AKI) following iodinated contrast media or gadolinium-based contrast agent administration.

## METHODS

**Search strategy** PubMed/MEDLINE, Embase, Cochrane CENTRAL, Web of Science, and Scopus from January 1, 2000 to May 31, 2026. ClinicalTrials.gov and WHO-ICTRP on May 31, 2026. Key terms: contrast-induced nephropathy, contrast-induced acute kidney injury, CI-AKI, NGAL, neutrophil gelatinase-associated lipocalin, cystatin C, KIM-1, N-acetylcysteine, IV saline, sodium bicarbonate, gadolinium nephrotoxicity, PRESERVE trial, eGFR, CKD.

**Participant or population** Adults aged 18 years or above undergoing iodinated CT contrast administration, cardiac catheterisation or PCI, or gadolinium-based contrast agent MRI, stratified by baseline eGFR, diabetes mellitus status, clinical setting, and comorbidity profile.

**Intervention** NGAL, cystatin C, or KIM-1 as early renal tubular injury biomarkers; IV isotonic saline as

primary prophylaxis; N-acetylcysteine as comparator prophylaxis; contrast volume minimisation strategies.

**Comparator** Serum creatinine as clinical reference standard for CIN diagnosis; placebo or no prophylaxis as comparator for prophylaxis trials; background hospitalisation-associated AKI rate for GBCA safety comparison.

**Study designs to be included** RCTs for prophylaxis outcomes; prospective and retrospective cohort studies for incidence; diagnostic accuracy studies for biomarker AUC synthesis.

**Eligibility criteria** Inclusion: Adults undergoing iodinated CT contrast, cardiac catheterisation/PCI, or GBCA MRI; CIN defined by KDIGO 2012 (creatinine ≥0.3 mg/dL or ≥25% within 48–72h); extractable outcome data.Exclusion: Paediatric populations; studies using exclusively high-osmolar ionic contrast; AKI definition inconsistent with KDIGO 2012 without sensitivity conversion possible; dialysis patients at baseline.

**Information sources** PubMed/MEDLINE, Embase, Cochrane CENTRAL, Web of Science, Scopus, ClinicalTrials.gov, WHO-ICTRP.

**Main outcome(s)** Pooled CIN incidence by population stratum (KDIGO 2012 definition); NGAL, cystatin C, and KIM-1 AUC versus serum creatinine; IV saline RR versus no prophylaxis; NAC RR versus placebo; GBCA CIN rate in eGFR above 30 mL/min.

**Additional outcome(s)** NGAL detection window (hours post-contrast); cystatin C specificity; NAC confidence interval width and p-value as deimplementation evidence; GBCA versus iodinated contrast AKI risk comparison; high-risk subgroup analyses.

**Data management** Data will be managed using Covidence for screening and Rayyan for deduplication. Extracted data stored in pre-piloted Excel forms. Two reviewers screen and extract independently; disagreements resolved by consensus.

**Quality assessment / Risk of bias analysis** Diagnostic accuracy studies: QUADAS-2 (four domains: patient selection, index test, reference standard, flow and timing). Cohort studies: Newcastle-Ottawa Scale (threshold ≥5 stars). Overall certainty of evidence rated using GRADE per primary outcome.

**Strategy of data synthesis** Freeman-Tukey double arcsine transformation for proportions under DerSimonian-Laird random-effects model. Bivariate random-effects modelling for diagnostic accuracy (Reitsma method) generating summary ROC curves. Heterogeneity quantified by Cochran Q and $I^2$. Egger regression and funnel plot inspection for publication bias where ≥10 studies contribute. Biomarker AUCs synthesised using bivariate random-effects meta-analysis. Prophylaxis RRs under DerSimonian-Laird random effects with Mantel-Haenszel weighting. CIN incidence by population stratum as pre-specified subgroup analyses.

**Subgroup analysis** Population setting (general CT vs ED CT vs cardiac catheterisation/PCI vs ICU); diabetes plus CKD status; eGFR stratum; contrast osmolality (low vs iso-osmolar); GBCA versus iodinated contrast.

**Sensitivity analysis** Restriction to KDIGO 2012 definition only; exclusion of high-osmolar ionic contrast studies; restriction to prospective cohort designs; restriction to RCTs for prophylaxis analyses.

**Language restriction** No language restriction.

**Country(ies) involved** Saudi Arabia.

**Other relevant information** Interventional Radiology; Nephrology; Clinical Pharmacy; Cardiovascular Imaging; Pharmacovigilance.

**Keywords** contrast-induced nephropathy; CIN; CI-AKI; NGAL; cystatin C; KIM-1; eGFR; CKD; diabetes; IV hydration; N-acetylcysteine; gadolinium; risk stratification; systematic review; meta-analysis.

**Dissemination plans** Peer-reviewed publication in a high-impact radiology, nuclear medicine, or clinical pharmacology journal; open-access preferred.

**Contributions of each author**

Author 1 - Abdulrahman Alanazi - Conceived and designed the study, drafted the protocol, will lead data extraction and synthesis, and drafted the manuscript and final manuscript submission.
Email: aas2@hotmail.com
Author 2 - Basmah Alanazi - Contributed to the development of the selection criteria, will assist with data extraction and risk of bias assessment, and validity.
Email: drbasmah7@gmail.com